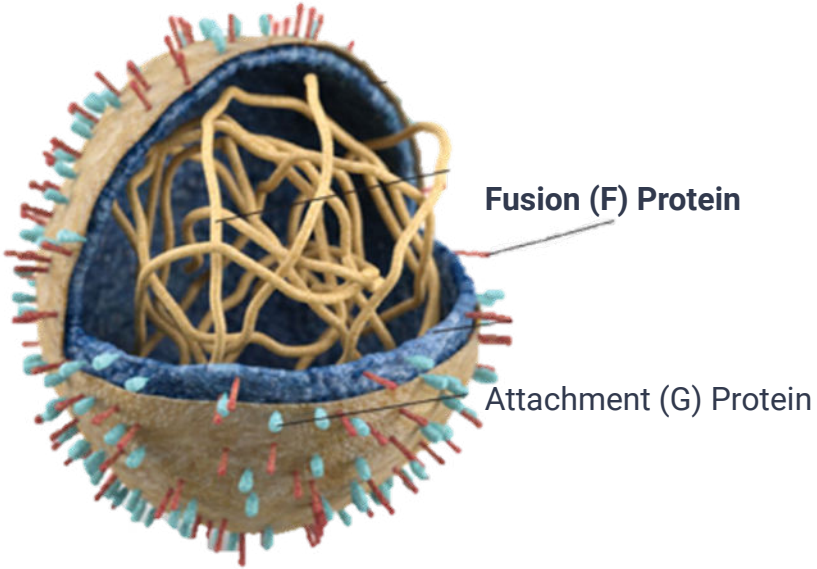
# Updates in Pediatric RSV Prevention for Midwifery Practice

February 9, 2024

# Objectives

- Explain the clinical presentation, treatments and potential complications of RSV in infants
- Recognize public health impacts and need for RSV prevention
- What’s new in RSV prophylaxis? Review clinical evidence around vaccines and monoclonal antibodies recently approved in Canada

# What is Respiratory Syncytial Virus? (RSV)




Member of the paramyxovirus family[1]

Two major strains: A & B[1-3]

Two surface glycoproteins:

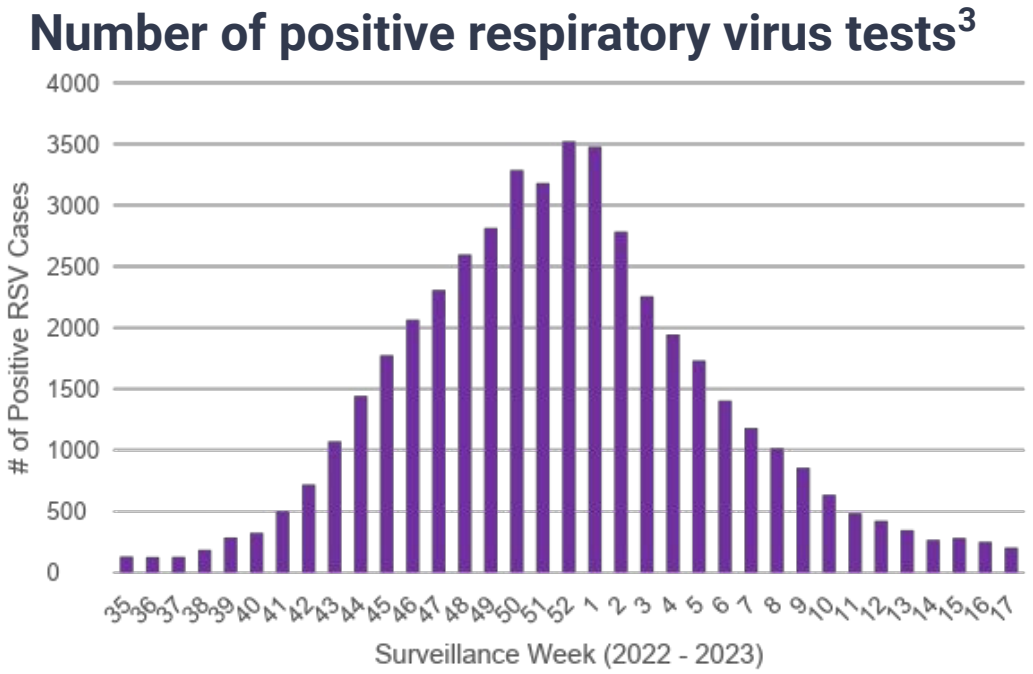
- G (attachment protein) — determines A or B strain
- **F (fusion protein) — target for vaccines/mAbs**

RSV invades the respiratory epithelial cells causing inflammation, edema, **syncytial formation**, and sloughing[1,4]

1. Collins PL, Crowe JE, Jr. Fields Virology. 5th ed (vol. 1). Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins;2007:1601–1646; 2. Walsh EE, *et al. J Infect Dis*. 1997;175(4):814–820; 3. Mufson MA, *et al. J Gen Virol*. 1985;66 (10):2111–2124; 4. Welliver TP, *et al. J Infect Dis*. 2007;195(8):1126–1136.

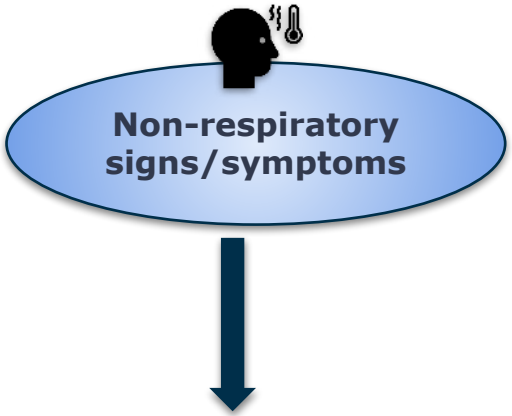
# RSV is Seasonal: Peak Incidence Varies by Region[1]

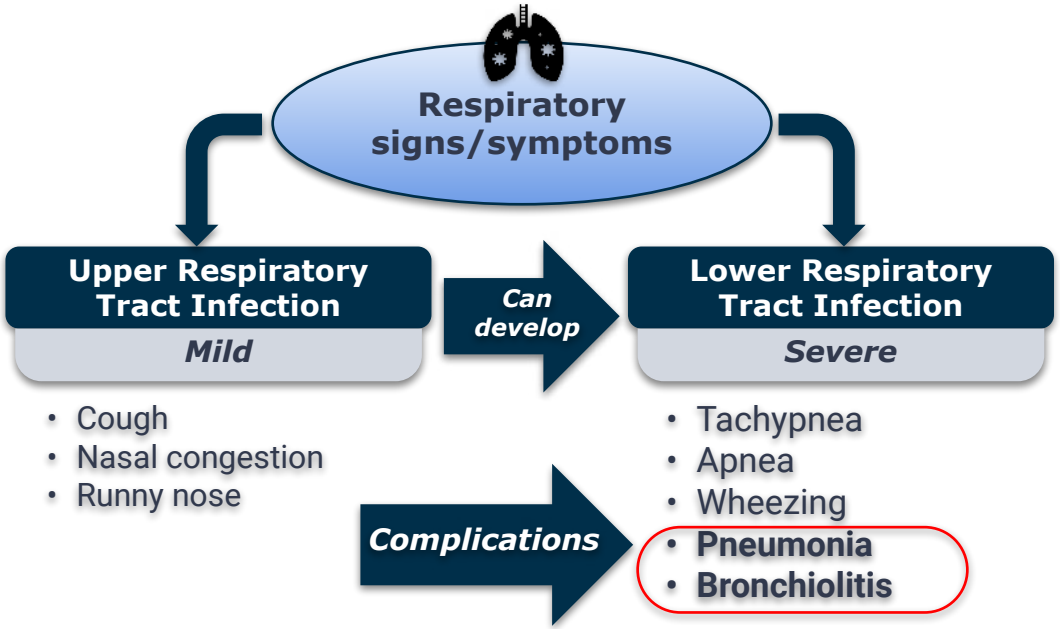
- Typical season in Canada: November - March
- Northern areas shifted to December - April/May




**1**. Hawkes MT, et al. (2021). JAMA Netw Open: 4(9):e2124650 **2**. Rose EB, et al. *MMWR*. 2018;67(2):71-76. **3**. Health Canada. Respiratory Virus Detections in Canada. Respiratory Virus Report, Week 17 - ending April 29, 2023 - Canada.ca [Accessed May 3, 2023].

# RSV Clinical Presentation[1–3]



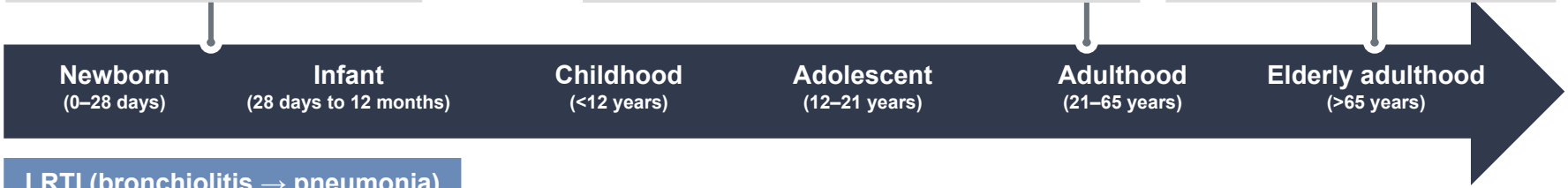

References:
1. Wu P, Hartert TV. Expert Rev Anti Infect Ther. 2011;9(9):731-45.
2. Falsey AR et al. Am J Respir Crit Care Med. 2006;173(6):639-43.
3. Glezen, WP, et al. *Am J Dis Child* 1986;140(6):543-546.

# Age is an Important Determinant of Severity[1]

The greatest risk of **severe LRTI** is during an **infants' first RSV season**

RSV typically causes common colds in healthy adults but may exacerbate pre-existing respiratory conditions (e.g., COPD or asthma)

RSV associated with deaths in older adults due to declining immunity




LRTI (bronchiolitis → pneumonia)

Associated with recurrent wheezing/asthma

May cause exacerbation of COPD/asthma

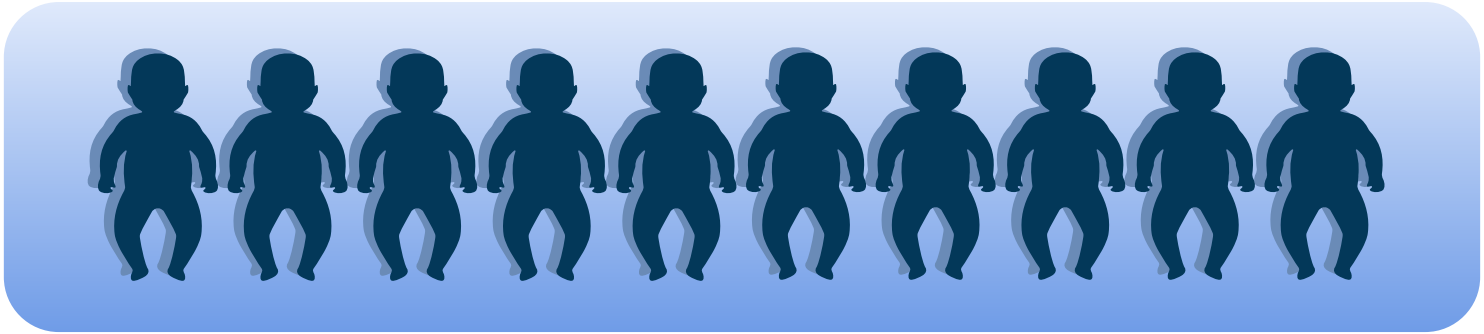
Pneumonia

Upper respiratory tract infection due to primary or repeat infection

COPD, chronic obstructive pulmonary disease; LRTI, lower respiratory tract infection; RSV, respiratory syncytial virus;

**1.** Openshaw PJM, et al. *Annu Rev Immunol*. 2017;35:501–532.

# RSV is Common



**90%**

of children will be infected by RSV by 2 years of age[1]

**1.** Glezen, WP, et al. *Am J Dis Child* 1986;140(6):543-546.

# While most RSV cases are mild, it can't be predicted which infants could get seriously ill and end up in hospital[1,2]

**90% of infants will be infected with RSV by the age of 2.**[3]

?

The course of the **disease is unpredictable. Any infant could be hospitalized in their first RSV season.**

*Width of the arrow is not proportional to the probability of occurrence*

**Most cases – Mild disease**
Upper respiratory tract infection[4]

**Unpredictable cases – Severe disease**
Lower respiratory tract infection that can require hospitalization or ER visits[2]

**Deaths** from RSV are **infrequent** in high income and industrialized countries* but can still occur in healthy infants[5,6]

* Estimated annual deaths among infants aged 0–11 months in industrialized vs. developing countries estimated at <100 and 43,600 respectively (from a systematic review of studies published between Jan 1, 1995, and Dec 31, 2016, and unpublished data from 76 high quality population-based studies, stratified by World Bank income regions).[5]

**1.** Hall CB et al. *Pediatrics* 2013; 132(2): e341–348. **2.** Bianchini S et al. *Microorganisms* 2020; 8(12): 2048. **3.** Simoes EAF. *Lancet* 1999; 354: 847–852. **4.** Karron RA. Plotkin's Vaccines. Seventh edition. Chapter 51, Respiratory Syncytial Virus Vaccines. Elsevier Inc. 2018. **5.** Shi T et al. *Lancet* 2017;390: 946–958. **6.** Arriola C et al. *J Pediatric Infect Dis Soc* 2020; 9(5): 587–595 and SuppInfo.

# Majority of RSV hospitalizations occur in infants without Risk Factors

## Severe RSV disease is unpredictable[2]

**Any infant can be hospitalized** in their first season whether born[2]…

At term

Premature

With underlying health conditions

**In fact, among infants hospitalized for RSV*…**


**were previously healthy and born at term[3]**

- Based on a Canadian study validating an algorithm for hospital admissions at the Children's Hospital of Eastern Ontario (Ottawa) between January 2010 and December 2011 to apply to the provincial health administrative data across Ontario.
- Extrapolated data identified that among 19,815 hospitalized infants between April 2005 – March 2013, 15, 482 (80.0%) of infants <3 years did not have any of the following risk factors: CHD, prematurity, BPD, Trisomy 21

**1.** Hall CB et al. Pediatrics 2013; 132: e34–e348. **2.** Bianchini S et al. *Microorganisms* 2020; 8(12): 2048. 3. Pisesky et al. PloS one 11.3 (2016): e0150416.

Government of Canada | Gouvernement du Canada

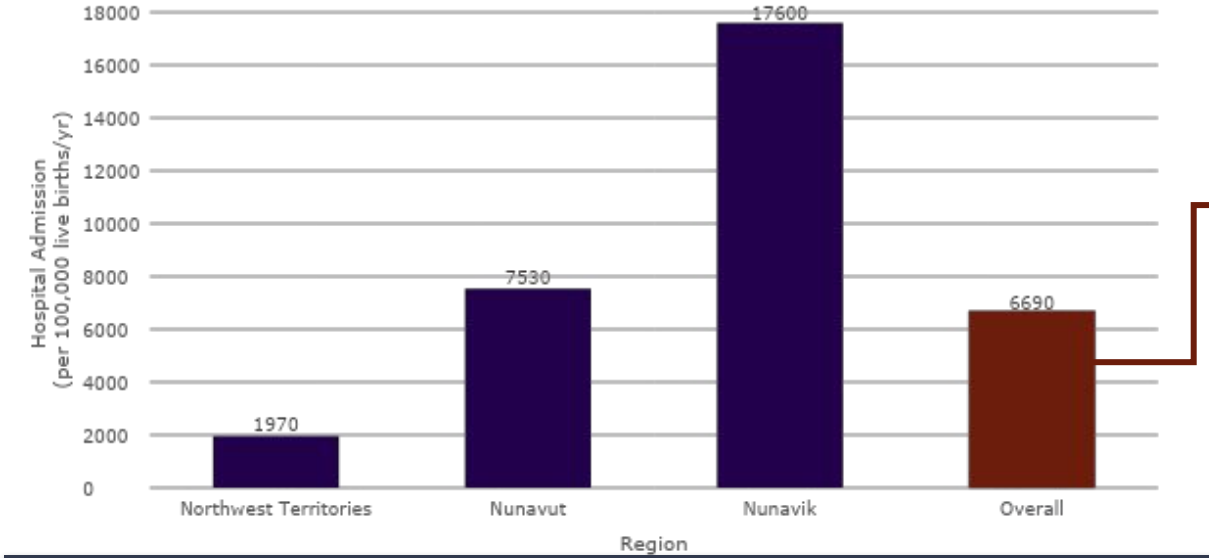
# Respiratory syncytial virus: Canadian Immunization Guide

**Disease distribution**

RSV occurs worldwide, with virtually all children infected by age two. Globally, RSV is an important cause of acute lower respiratory tract infection and a major cause of hospital admissions in young children, for whom it has been estimated that RSV is associated with about 28% of all episodes of acute lower respiratory tract infections. In Canada, approximately 1% of all infants are hospitalized with RSV in their first year of life. In some remote communities, RSV hospitalization rates have been as high as 20 to 50% of all live births.

1. Health Canada. Respiratory syncytial virus: Canadian Immunization Guide. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/respiratory-syncytial-virus.html

# Hospital Admissions due to LRTI Elevated among All Infants <1 yr in the Canadian Arctic

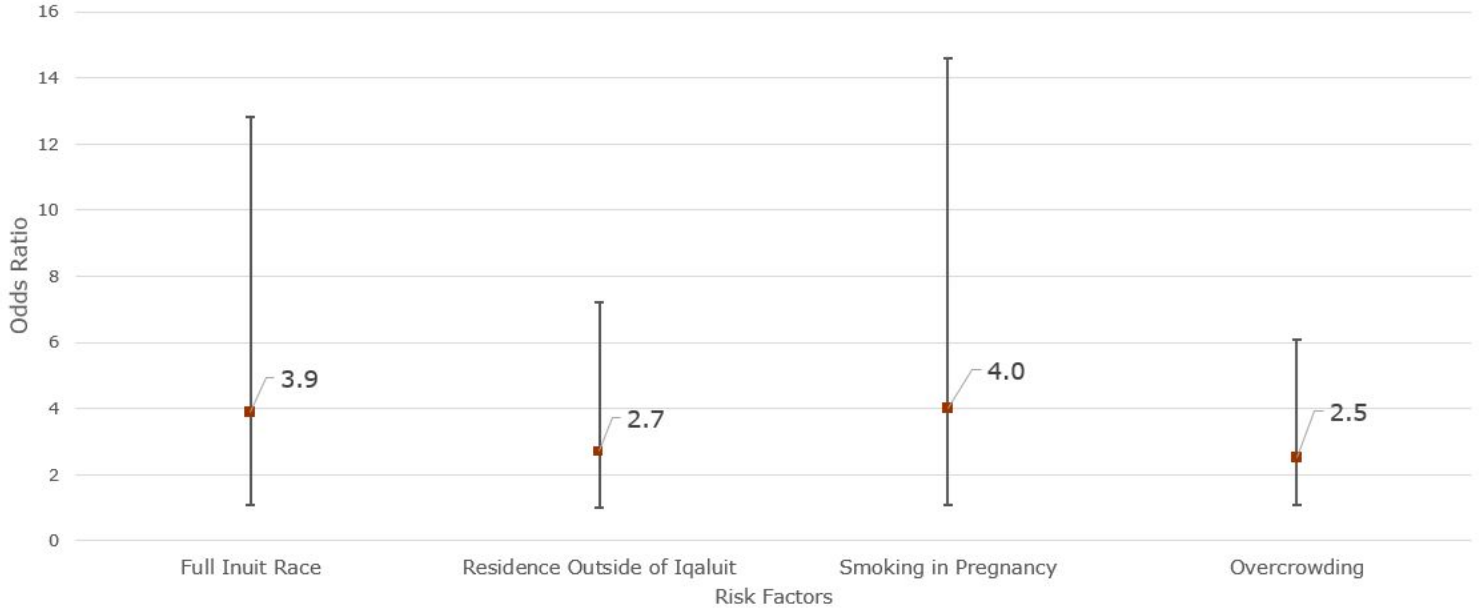



Admission rate in Northern remote infants <1 yr is **6.4 times higher** than infants <2 yrs across Canada[1,3]

RSV related-hospitalization rates in northern and Arctic communities in Canada are amongst the highest rates globally[2]

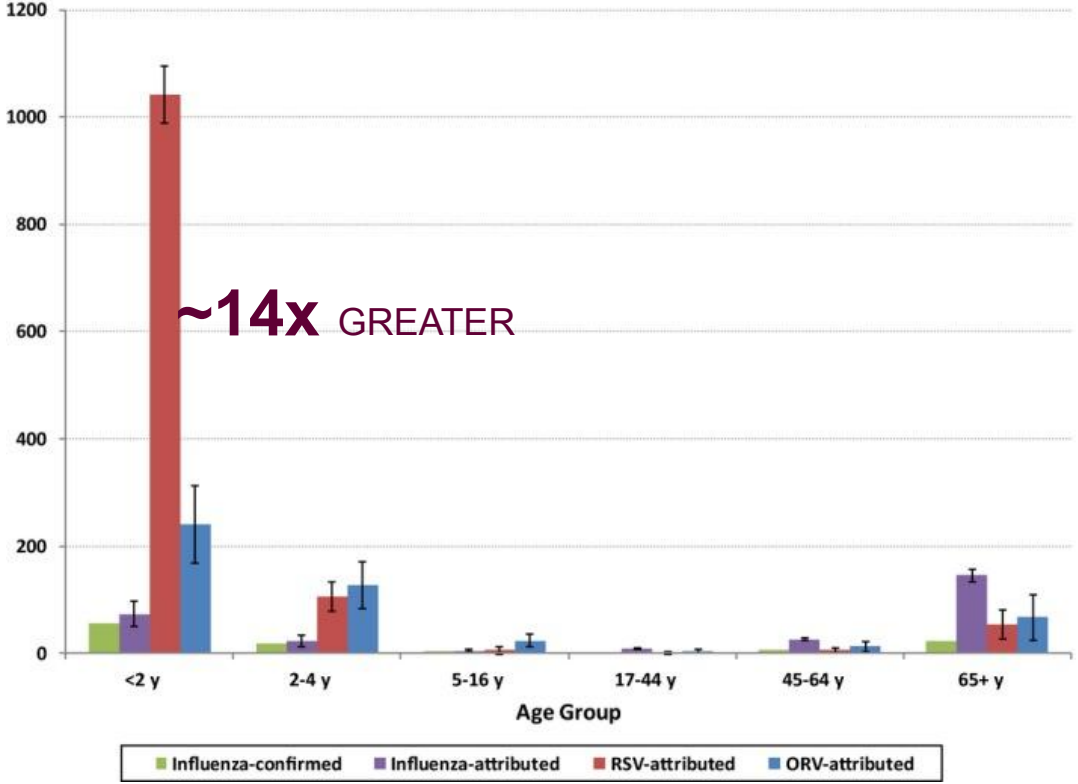

1. Banerji A, Panzov V, Young M, et al. Hospital admissions for lower respiratory tract infections among infants in the Canadian Arctic: a cohort study. CMAJ Open. 2016;4(4):E615-E622. Published 2016 Oct 17. doi:10.9778/cmajo.20150051
2. la Fleur P, Argáez C. Palivizumab for Infection Prevention in Inuit Infants: A Review of the Clinical Effectiveness and Cost-Effectiveness. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; December 17, 2019.
3. Schanzer DL, et al. Burden of influenza, respiratory syncytial virus, and other respiratory viruses and the completeness of respiratory viral identification among respiratory inpatients, Canada, 2003-2014. Influenza and other respiratory viruses. 2018 Jan;12(1):113-21.

# Risk Factors for LRTI Hospitalizations in the Canadian Arctic




Banerji, A., Greenberg, D., White, L. F., Macdonald, W. A., Saxton, A., Thomas, E., Sage, D., Mamdani, M., Lanctôt, K. L., Mahony, J. B., Dingle, M., & Roberts, A. (2009). Risk factors and viruses associated with hospitalization due to lower respiratory tract infections in Canadian Inuit children : a case-control study. *The Pediatric infectious disease journal*, *28*(8), 697–701. https://doi-org.myaccess.library.utoronto.ca/10.1097/INF.0b013e31819f1f89

# RSV burden remains high compared to Influenza in infants under 2 in Canada




1.Schanzer DL, et al. Burden of influenza, respiratory syncytial virus, and other respiratory viruses and the completeness of respiratory viral identification among respiratory inpatients, Canada, 2003-2014. Influenza and other respiratory viruses. 2018 Jan;12(1):113-21.

# Treatments for RSV

**In infants, treatment is limited to supportive care:**

- supplemental oxygen
- hydration[1-5]

**Not recommended per CPS:**

Salbutamol (Ventolin)
Corticosteroids
Antibiotics
Antivirals
3% hypertonic saline nebulization
Chest physiotherapy
Cool mist therapies or therapy with saline aerosol

1. American Academy of Pediatrics. Respiratory syncytial virus. In: Kimberlin DW, Brady MT, Jackson MA, editors. Red Book: 2018–2021 Report of the Committee on Infectious Diseases. Elk Grove Village: American Academy of Pediatrics; 2018;682–92 2. Piedimonte G, Perez MK. Respiratory syncytial virus infection and bronchiolitis [published correction appears in Pediatr Rev. 2015 Feb;36(2):85]. Pediatr Rev. 2014;35(12):519-530. 3. Ralston SL, Lieberthal AS, Meissner HC, et al; American Academy of Pediatrics. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. Pediatrics. 2014;134(5):e1474-e1502. 4. Centers for Disease Control and Prevention. Respiratory Syncytial Virus (RSV): Symptoms and Care. https://www.cdc.gov/rsv/about/symptoms.html 5. Canadian Pediatric Society. Bronchiolitis: Recommendations for diagnosis, monitoring and management of children one to 24 months of age. https://cps.ca/en/documents/position/bronchiolitis

# By their Biology, All Infants are at Increased Risk for RSV [1–4]

**Small Anatomy**

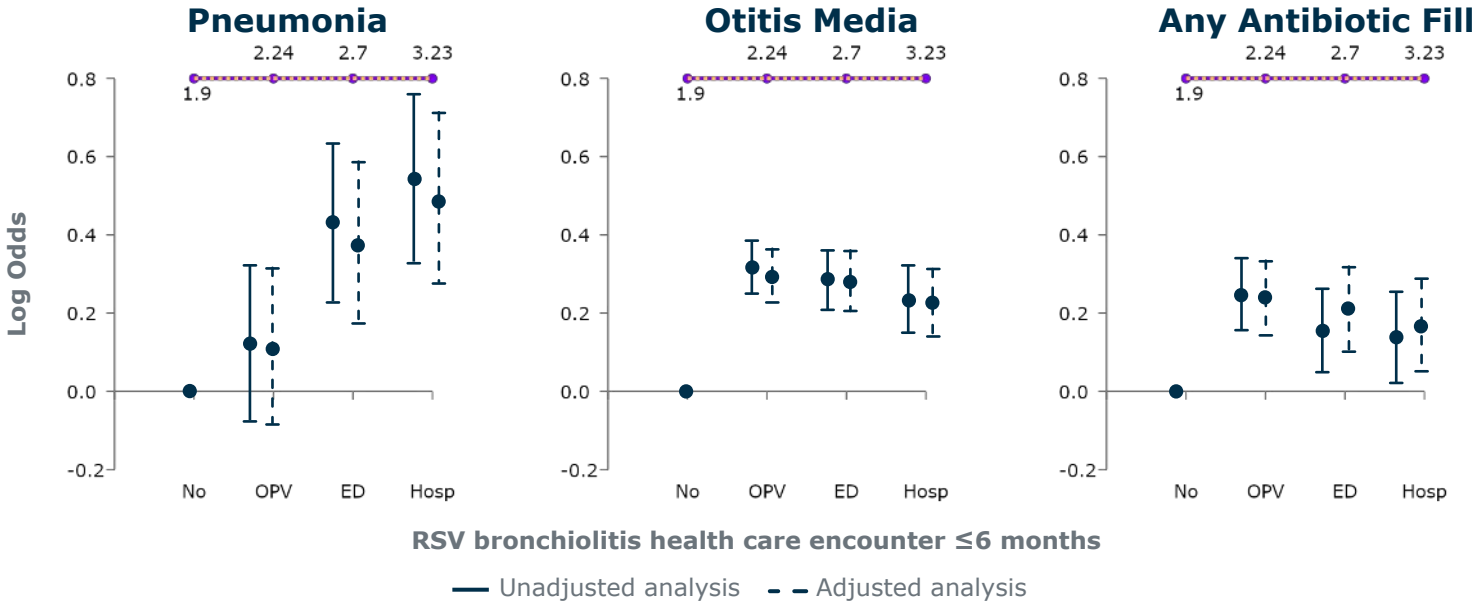
**Naive Immune System**

**Underdeveloped Respiratory System**

- Increased risk from small airway size
- Reduced immune response to infections
- Poor regulation to tissue inflammation
- Reduced lung function (e.g., limitations to airflow, weak respiratory muscles)
- Limited energy reserves

**1.** Wu P, Hartert TV. Expert Rev Anti Infect Ther. 2011;9(9):731-45. **2.** Tregoning W., Schwarze J. American Society for Microbiology. 2010; 23(1):74-98; **3.** Falsey AR et al. Am J Respir Crit Care Med. 2006;173(6):639-43., **4**: Glezen, WP, et al. *Am J Dis Child* 1986;140(6):543-546.

# RSV Bronchiolitis Before 6 Months of Age Is Associated With Subsequent Complications[1]




**Increased severity of RSV bronchiolitis is associated with increased risk for pneumonia***

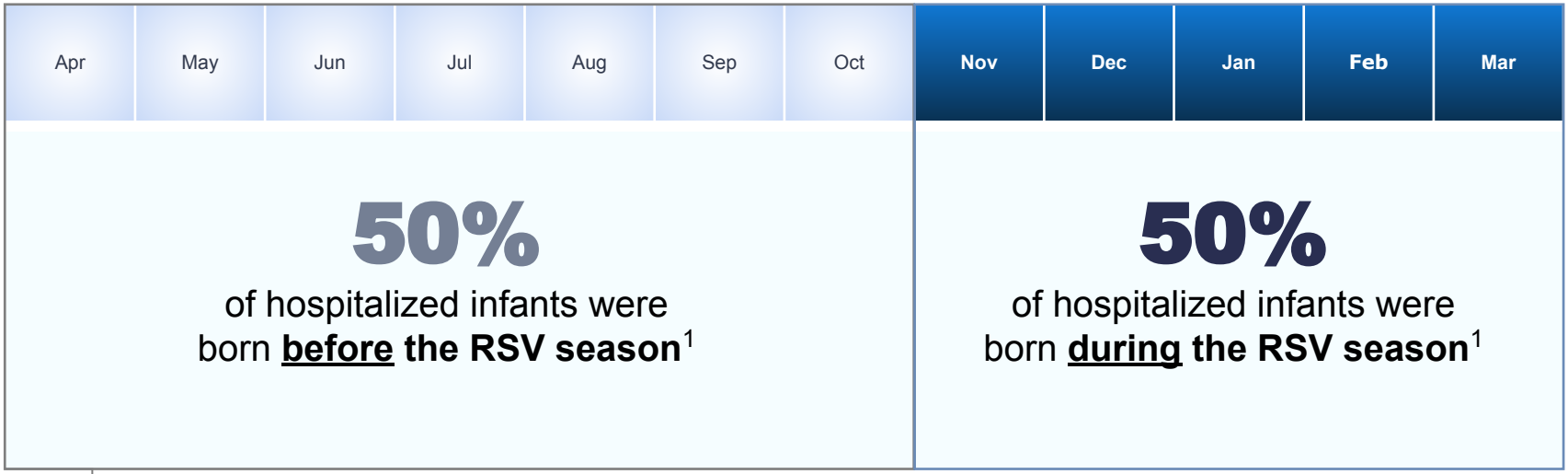
*Severity as measured by health care encounters. Population-based cohort study of 123,301 infants born between 1995 and 2007 enrolled in the Tennessee Medicaid Program. Main predictor variable was bronchiolitis from birth to ≤6 months of age during the first RSV season of life.

ED=emergency department; Hosp=hospitalisation; OPV=outpatient visit; RSV=respiratory syncytial virus.

Permission line placeholder (Sanofi has journal permission rights).

**1.** Abreo A, et al. *Clin Infect Dis*. 2020;71(1):211-214.

# All Infants are at Risk of RSV Regardless of Birth Month and Require Protection[1–3]




Babies born before the RSV season need also need to be protect before entering their first RSV season

**1**. Reeves RM et al. *J Infect*. 2019;78(6):468-475. **2**. Tregoning JS, Schwarze J. *Clin Microbiol Rev*. 2010;23(1):74-98. **3**. Drajac C, et al. *J Immunol Res*. 2017;2017:8734504.

# Prevention of RSV in Infants

What can we do?

# Preventing Transmission

- Educate caregivers regarding RSV transmission control[1]
- Cover coughs and sneezes with a tissue or upper shirtsleeve rather than hands[1-4]
- Wash hands often[1-4]
- Avoid close contact with others (eg, kissing, shaking hands, and sharing cups and eating utensils), especially individuals who are sick[1-4]
- Disinfect and clean toys and surfaces regularly[2-4]
- Refrain from touching one's face with unwashed hands[1-3]
- Stay home when sick[2]
- Limit time spent in child-care centers or other potentially contagious settings[1,2,4]
- Avoid exposure to smoke from tobacco or other substances[1,4]
- Feed babies breast milk[4]

**Despite all this nearly all children experience RSV infection in the first 2 years of life[1,5,6]**

**1.** Domachowske JB, et al. *Infect Dis Ther.* 2021;10(suppl 1):47-60. **2.** Centers for Disease Control and Prevention. Accessed 3 August 2022. https://www.cdc.gov/rsv/about/prevention.html **3.** Centers for Disease Control and Prevention. Accessed 3 August 2022. https://www.cdc.gov/rsv/infographic.html/index.html
**4.** HealthyChildren.org. Accessed 3 August 2022. https://www.healthychildren.org/English/health-issues/conditions/chest-lungs/Pages/RSV-When-Its-More-Than-Just-a-Cold.aspx **5.** Karron R. Respiratory syncytial virus vaccines. In: Plotkin SA, Orenstein WA, Offitt PA, Edwards KM, eds. *Plotkin's Vaccines.* 7th ed. Philadelphia, PA: Elsevier; 2018:943-949. **6.** Glezen WP, et al. *Am J Dis Child.* 1986;140(6):543-546.

# Strategies to Protect Very Young Infants..

## Indirect Protection[1,2]

Herd immunity

Cocooning strategies

## Direct Protection[3]

Vaccination of the newborn

Monoclonal antibodies

Vaccination during pregnancy

**1.** Treskova M, et al. *Pharmacoeconomics*. 2021;39(3):287-315. **2.** Kinyanjui TM, et al. *PLoS One*. 2015;10(9):e0138018. **3.** Eichinger KM, et al. *Ther Adv Vaccines Immunother*. 2021;9:2515135520981516.

# Vs Preventing Illness in Young Infants

## Indirect Protection[1,2]

Herd immunity

Cocooning strategies

## Direct Protection[3]

Vaccination of the newborn

Monoclonal antibodies

Vaccination during pregnancy

**1.** Treskova M, et al. *Pharmacoeconomics*. 2021;39(3):287-315. **2.** Kinyanjui TM, et al. *PLoS One*. 2015;10(9):e0138018. **3.** Eichinger KM, et al. *Ther Adv Vaccines Immunother*. 2021;9:2515135520981516.

# Preventing Illness

**Monoclonal antibodies**

**Vaccination during pregnancy**

# Preparations authorized for use in Canada

## Monoclonal antibodies

- Palivizumab
  SYNAGIS™
- Nirsevimab
  BEYFORTUS™

## Vaccination during pregnancy

- RSV PreF Vaccine
  ABRYSVO™

# Palivizumab SYNAGIS™

Monoclonal antibody

**WHAT:**

The only existing option for RSV prophylaxis in Canada ***until recently***

Approved by Health Canada in 2002

**WHO:**

Limited indications:

- Premature infants born at less than 32 weeks GA
- Infants 33-35 weeks gestation and ages less than 6 months during the RSV season who have a risk assessment tool score of 49-100
- Infants 33-35 weeks gestation and ages less than 6 months during the RSV season who live in remote communities with lack of access to medical care
- Children under 24 months of age with comorbidities

**HOW:**

Risk Scoring tool

Monthly dosing schedule with up to 5 doses required in a given season

# Despite Existing Options for Prophylaxis of RSV Infection, Unmet Medical Needs Remain[1]

## Palivizumab

**Eligible population(s)**

Preterm and newborns with certain comorbidities
(i.e. congenital heart disease, bronchopulmonary dysplasia)

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**Population(s) for which unmet medical need still exists**

Term infants <1 year of age

Children 1–5 years of age

High-risk individuals (eg, transplant, COPD)

Elderly (>60 years of age)

COPD=chronic obstructive pulmonary disease; RSV=respiratory syncytial virus.

**1.** Villafana T, et al. *Expert Rev Vaccines.* 2017;16(7):1-13.

# Preparations authorized for use in Canada

## Monoclonal antibodies

- Palivizumab
  SYNAGIS™
- Nirsevimab
  BEYFORTUS™

## Vaccination during pregnancy

- RSV PreF Vaccine
  ABRYSVO™

# Two New Key Players in the Prevention of RSV

## Monoclonal Antibody

- Palivizumab (AstraZeneca)
  SYNAGIS™
  - Limited indications
  - Monthly Dosing

- Nirsevimab (Sanofi/AstraZeneca)
  BEYFORTUS™
  - Health Canada Approved April 2023
  - Indicated for **all** infants

## Vaccination During Pregnancy

- RSVpreF (Pfizer)
  ABRYSVO™
  - Vaccine for pregnant individuals to transfer of antibodies to the infant
  - Health Canada Approved Dec 2023
  - Also approved for older adults

Vaccination during pregnancy

# RSV Stabilized Prefusion F Subunit Vaccine Overview

ABRYSVO™

# Overview of RSV PreF Vaccine: Indication

Vaccination during pregnancy

INDICATION

- Active immunization of pregnant individuals from **32 through 36 weeks** gestational age for the prevention of lower respiratory tract disease (LRTD) and severe LRTD caused by RSV

TO PROTECT

- Infants from birth through to 6 months of age

Abrysvo Product Monograph Canada

# Overview of RSV PreF Vaccine: Indication

Vaccination during pregnancy

## INDICATION

- Active immunization of pregnant individuals from **32 through 36 weeks** gestational age for the prevention of lower respiratory tract disease (LRTD) and severe LRTD caused by RSV

## TO PROTECT

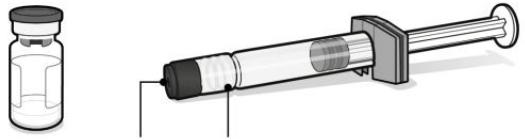
- Infants from birth through to 6 months of age

## DOSE

- 120 mcg per 0.5 mL
- Contains 60 mcg of each pre-fusion protein A and B
- Intramuscular injection

## STORAGE

- Refrigerate at 2° C to 8° C



Abrysvo Product Monograph Canada

# MATISSE Trial (NEJM April 2023)

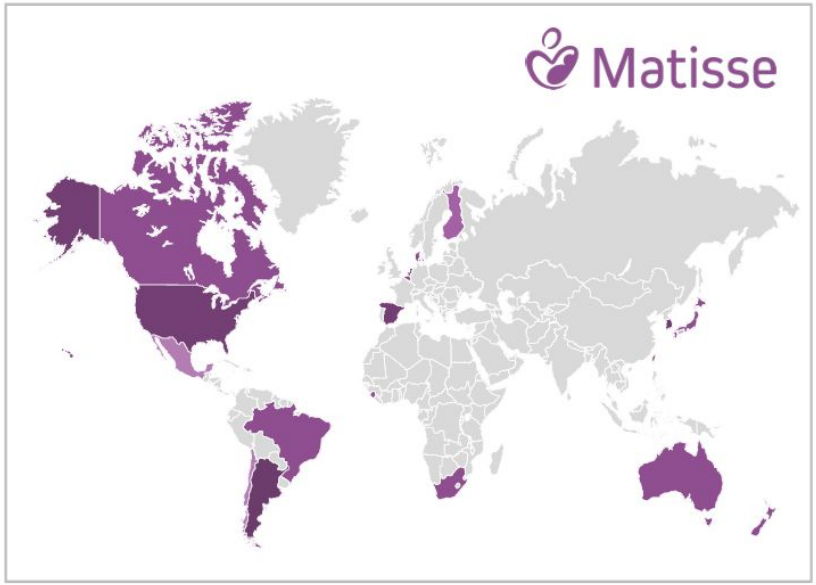
Vaccination during pregnancy

## MATISSE: A Phase 3 Trial to Evaluate the Efficacy and Safety of RSVpreF in Infants Born to Women Vaccinated During Pregnancy

**7,392 Maternal Participants in 18 Countries**
**Randomized 1:1 RSVpreF 120µg or Placebo**

Pregnant persons ≤49 years between ≥24 and ≤36 weeks gestation

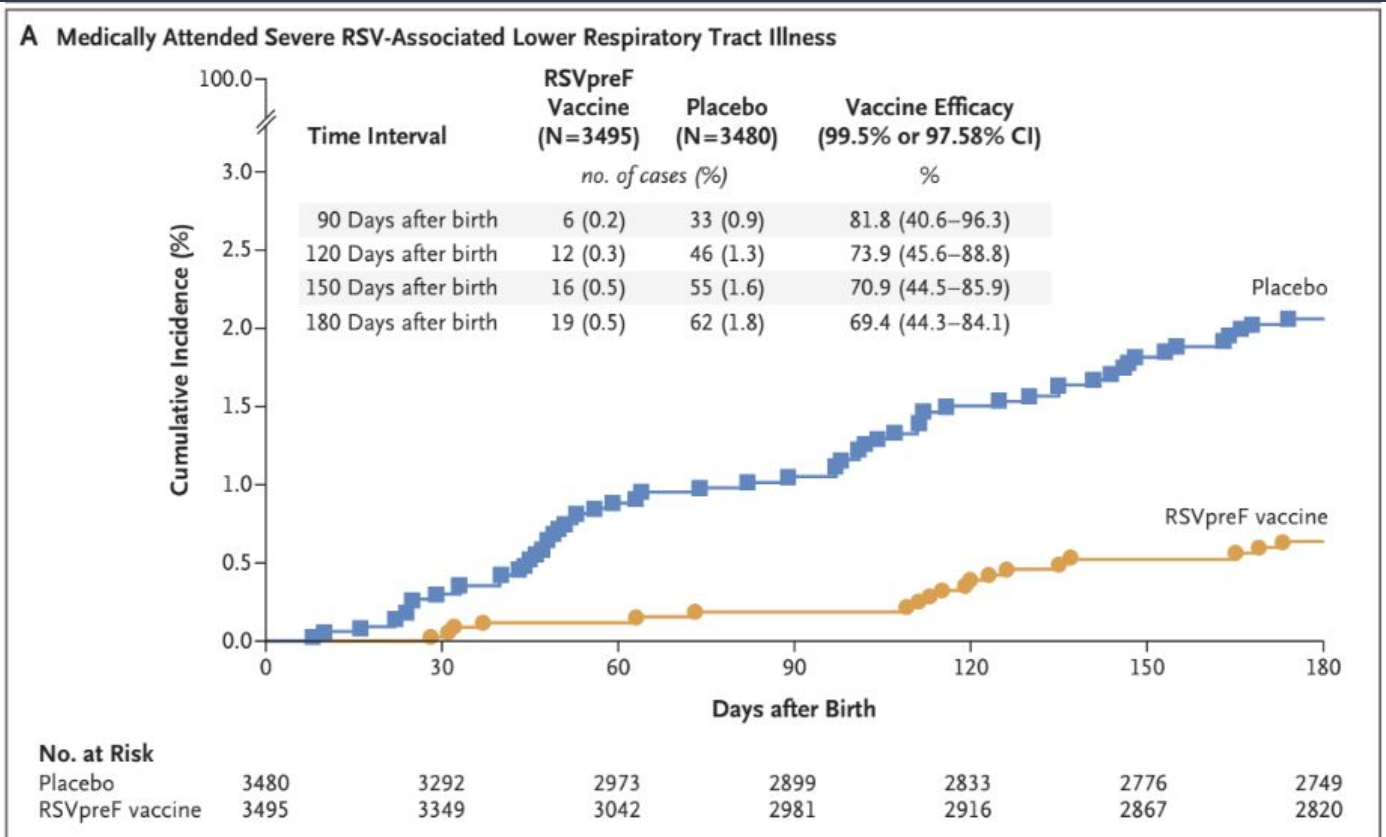
7,128 Infants enrolled




Presented at CDC ACIP meeting February 20, 2023. Slides available from:
https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-02/slides-02-23/RSV-Pediatric-06-Munjal-508.pdf

# MATISSE Trial: RSV PreF Vaccine Efficacy

Vaccination during pregnancy




Kampmann, B., Madhi, S. A., Munjal, I., Simões, E. A. F., Pahud, B. A., Llapur, C., Baker, J., Pérez Marc, G., Radley, D., Shittu, E., Glanternik, J., Snaggs, H., Baber, J., Zachariah, P., Barnabas, S. L., Fausett, M., Adam, T., Perreras, N., Van Houten, M. A., … Gurtman, A. (2023). Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants. *New England Journal of Medicine*, *388*(16), 1451–1464. https://doi.org/10.1056/nejmoa2216480

# RSV PreF Vaccine Product Characteristics: Efficacy

Vaccination during pregnancy

**Table 11 - Vaccine efficacy of Abrysvo against severe medically attended lower respiratory tract illness caused by RSV - infants from birth through 6 months of age by active immunization of pregnant individuals – Study C3671008**

| Time period | Abrysvo Number of cases N=3,495[b] | Placebo Number of cases N=3,480 | VE % (CI)[a] |
|---|---|---|---|
| 90 days | 6 | 33 | 81.8 (40.6, 96.3) |
| 120 days | 12 | 46 | 73.9 (45.6, 88.8) |
| 150 days | 16 | 55 | 70.9 (44.5, 85.9) |
| 180 days | 19 | 62 | 69.4 (44.3, 84.1) |

CI = confidence interval; VE = vaccine efficacy

[a] 99.5% CI at 90 days; 97.58% CI at later intervals

[b] Evaluable efficacy population

Kampmann, B., Madhi, S. A., Munjal, I., Simões, E. A. F., Pahud, B. A., Llapur, C., Baker, J., Pérez Marc, G., Radley, D., Shittu, E., Glanternik, J., Snaggs, H., Baber, J., Zachariah, P., Barnabas, S. L., Fausett, M., Adam, T., Perreras, N., Van Houten, M. A., … Gurtman, A. (2023). Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants. *New England Journal of Medicine*, *388*(16), 1451–1464. https://doi.org/10.1056/nejmoa2216480

# RSV PreF Vaccine Characteristics: Adverse Reactions

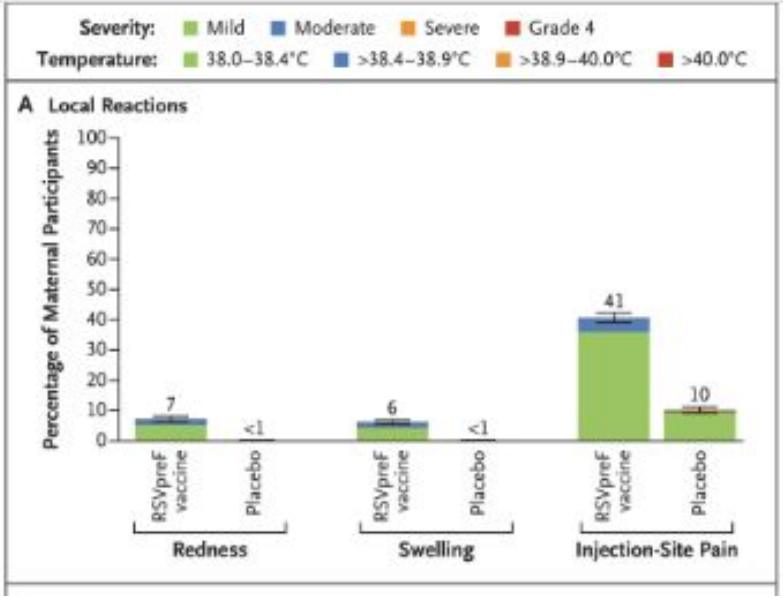
Vaccination during pregnancy

Local reactions:

- Injection Site pain (41% vs 10%)
- Redness (7% vs 0.2%)
- Swelling (6.2% vs 0.2%)

Systemic Reactions:

- Headache 31% vs 28%
- Muscle pain 17% vs 7%




Kampmann, B., Madhi, S. A., Munjal, I., Simões, E. A. F., Pahud, B. A., Llapur, C., Baker, J., Pérez Marc, G., Radley, D., Shittu, E., Glanternik, J., Snaggs, H., Baber, J., Zachariah, P., Barnabas, S. L., Fausett, M., Adam, T., Perreras, N., Van Houten, M. A., … Gurtman, A. (2023). Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants. *New England Journal of Medicine*, *388*(16), 1451–1464. https://doi.org/10.1056/nejmoa2216480

# RSV PreF Vaccine Characteristics: Considerations for Timing of Administration

Vaccination during pregnancy

- Seasonal administration
  - Variability of seasons must be taken into account

VS

- Year Round Dosing
  - Will simply implementation
  - Potentially increase vaccine uptake
  - Less cost effective

# RSV PreF Vaccine Characteristics: Co-administration with other immunizations

Vaccination during pregnancy

- No available data on simulation co-administration of RSV PreF Vaccine in pregnant people with TDAP and Influenza vaccines[1]
- There is limited data in non-pregnant people, which found decreased immunogenicity of the TDAP vaccine component when co-administered with RSV PreF Vaccine, but it is unclear how clinically significant this will be
- CDC guidelines and ACOG guidelines permit coadministration, but this is not reflected in the product monograph[2,3]


1. Abrysvo Product Monograph, Canada
2. Centers for Disease Control and Prevention. (2023, September 29). *Healthcare Providers: RSV vaccination for pregnant people*. Centers for Disease Control and Prevention. https://www.cdc.gov/vaccines/vpd/rsv/hcp/pregnant-people.html
3. *Maternal respiratory syncytial virus vaccination*. ACOG. (2023, December 11). https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2023/09/maternal-respiratory-syncytial-virus-vaccination

# RSV PreF Vaccine: Contraindications to Administration

Vaccination during pregnancy

- RSVpreF Vaccine should not be administered to a person with a history of severe allergic reaction, such as anaphylaxis, to any component of this vaccine.

- Moderate or severe acute illness, with or without fever, is a precaution to vaccination; vaccination should be deferred until patient improves

Health Canada, Abrysvo Product Monograph

# Preparations authorized for use in Canada

## Monoclonal antibodies

- Palivizumab
  SYNAGIS™
- Nirsevimab
  BEYFORTUS™

## Vaccination during pregnancy

- RSV PreF Vaccine
  ABRYSVO™

# Nirsevimab Overview

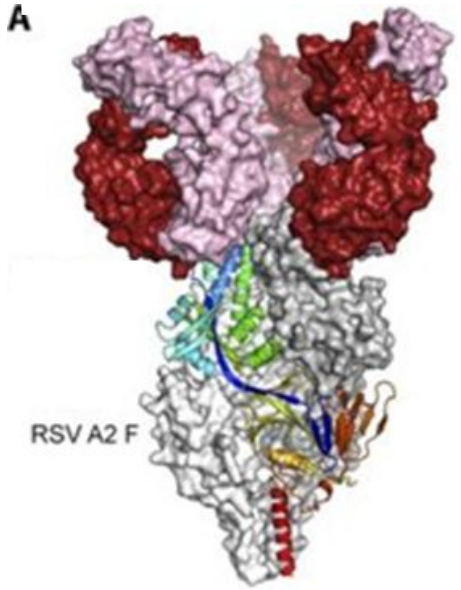
Monoclonal antibody

BEYFORTUS™

# Nirsevimab Product Characteristics

Monoclonal antibody

- Fully human IgG1 monoclonal antibody
- Offers rapid and direct protection against RSV
- Extended half-life allows for protection all season with a single dose
- Fixed, weight-based intramuscular dose



# Nirsevimab Product Characteristics

Monoclonal antibody

## Long-Acting Monoclonal Antibody

1 injection for the RSV season

Expected duration shown in clinical trials: 5 months
Half life: 63-73 days

## Broad infant population

Neonates and infants during their 1st RSV Season
and
Children up to 24 months of age who remain vulnerable to severe RSV disease through their 2nd RSV season

## Weight Banded Dosing

<5kg : 50mg
≥5kg :100mg
Eligible second season infants: 200mg

Intramuscular Injection

## Requires Refrigeration

Stored at 2°C - 8°C

**1**. Health Canada. Beyfortus Monograph. **2.** Ruckwardt TJ, et al. *Immunity* 2019; 51(3): 429-442. **3.** Zhu Q, et al. *Sci Transl Med* 2017; 9(388): eaaj1928. **4.** Domachowske JB, et al.. *Pediatr Infect Dis J* 2018; 37(9): 886-892.

# Nirsevimab Product Characteristics: Indications

Monoclonal antibody

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1 injection for the RSV season

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# Nirsevimab Product Characteristics: Dosing

Monoclonal antibody

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1 injection for the RSV season

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## Weight Banded Dosing

<5kg : 50mg
≥5kg :100mg
Eligible second season infants: 200mg

Intramuscular Injection

## Requires Refrigeration

Stored at 2°C - 8°C

May be kept at room temperature (20°C - 25°C) for a maximum of 8 hours

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# Nirsevimab Product Characteristics: Storage

Monoclonal antibody

## Long-Acting Monoclonal Antibody

1 injection for the RSV season

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## Broad infant population

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# Nirsevimab Product Characteristics: Adverse Reactions + Co-administration

Monoclonal antibody

- Rash
  - 0.7% receiving Nirsevimab vs 0.3% in placebo
- Pyrexia
  - rate of 0.5% vs 0.6% in placebo within 7 days post dose
- Injection site reactions
  - 0.3% (0% in placebo) within 7 days post dose
- **Co-administration with vaccines**[1]

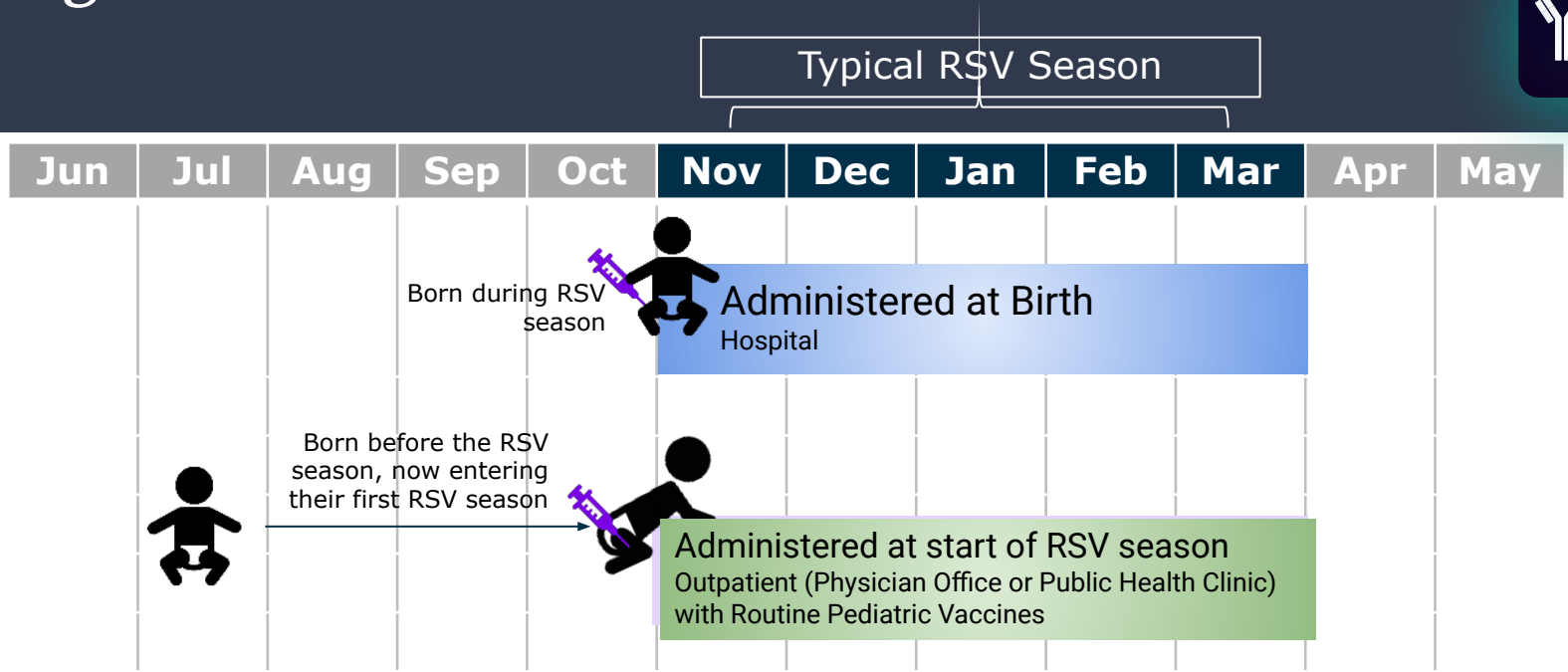
  In clinical trials, when nirsevimab was given with routine childhood vaccines, the safety and reactogenicity was similar to the childhood vaccines given alone

**Nirsevimab can be given with childhood vaccines**

**1**. Health Canada. Beyfortus Monograph. **2.** Ruckwardt TJ, et al. *Immunity* 2019; 51(3): 429-442. **3.** Zhu Q, et al. *Sci Transl Med* 2017; 9(388): eaaj1928. **4.** Domachowske JB, et al.. *Pediatr Infect Dis J* 2018; 37(9): 886-892.

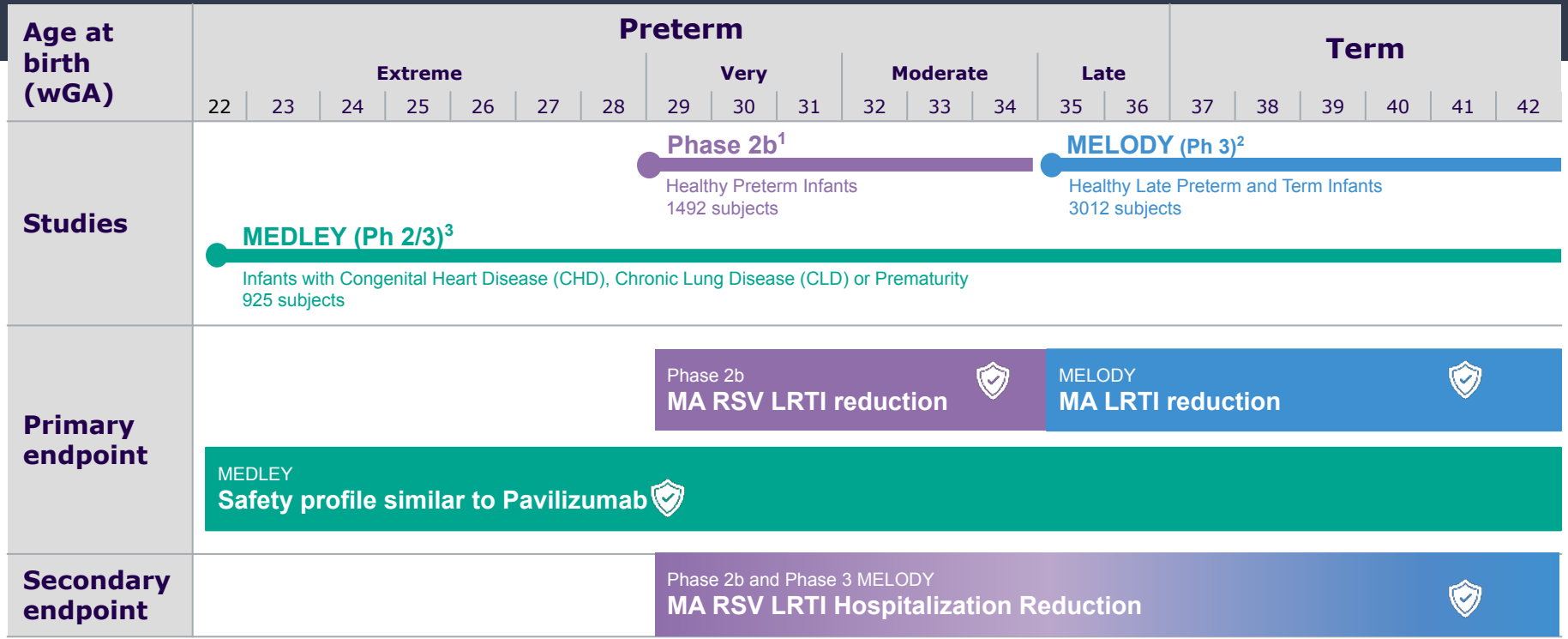
# Timing of administration of Nirsevimab

Monoclonal antibody




| | |
|---|---|
| **Route** | Single Dose: Intramuscular Injection with a Pre-Filled Syringe |
| **Dosing** | Weight Banded (≤5 kg = 50mg; >5kg = 100mg) |

# Nirsevimab Clinical Trials



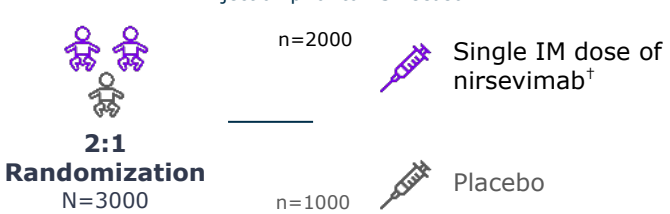

**1.** Griffin MP, et al. N Engl J Med. 2020 Jul 30;383(5):415-425 **2.** Hammitt LL,et al N Engl J Med. 2022 Mar 3;386(9):837-846. **3.** Domachowske Joseph et al. N Engl J Med 2022 Mar 386:9, 892-894. **4.** Simões, E, et al. ESPID 2022 Congress; 2022 May 9-13. Hybrid Congress.

# Phase 3 "MELODY" Study Pivotal Trial

Monoclonal antibody

## Study Population and Intervention

- 3000 healthy infants ≥35 wGA
- Not eligible to receive palivizumab




## Locations and Season (Primary cohort)

- 150 sites in Northern hemisphere across 20 countries; 2019-2020 RSV season
- 10 sites in Southern hemisphere across South Africa; 2020 RSV season (Jan–Mar 2020)

## Primary Endpoint

- Incidence of medically attended LRTI caused by RT-PCR confirmed RSV through 150 days after dosing

## Secondary and Exploratory Endpoints

- Incidence of hospitalizations due to RSV through 150 days after dosing
- Safety

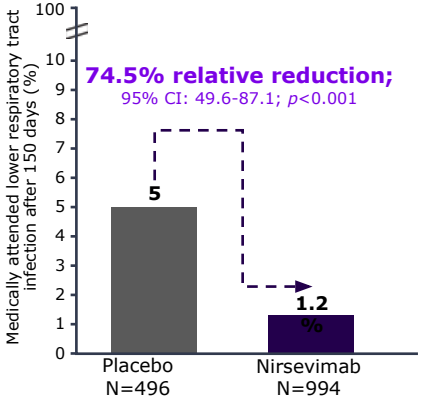
†Nirsevimab dose: Participants received 50 or 100 mg if they weighed <5 kg or ≥5 kg resp.
IM: intramuscular; MA-LRTI: medically attended-lower respiratory tract infection; RSV: Respiratory syncitial virus; wGA: weeks gestational age.

**1.** Hammitt LL, et al. *N Engl J Med*. 2022;386(9):837-846. **2.** NCT03979313 - ClinicalTrials.gov

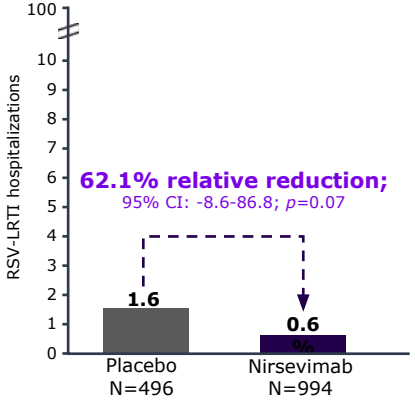
# Efficacy of Nirsevimab against RSV Healthy Term Infants (35 + weeks) MELODY

## Primary Cohort (n=1490)

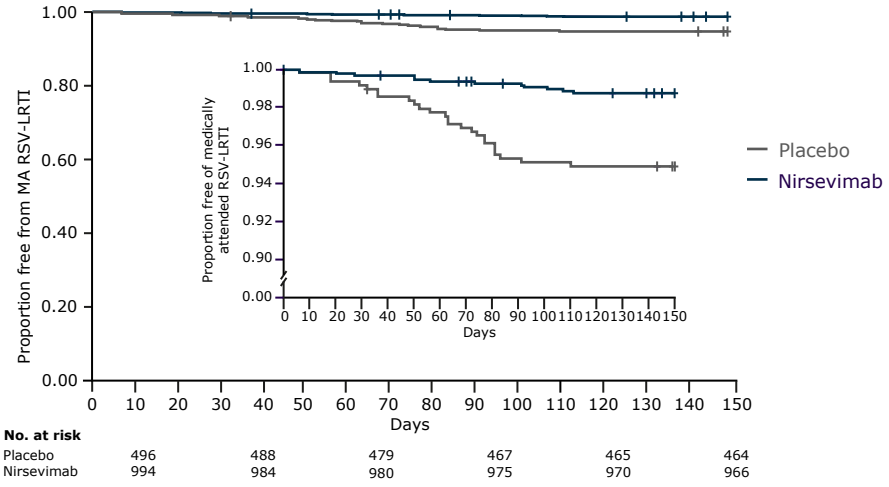
**Incidence of RSV confirmed MA-LRTI**
Primary endpoint




**Incidence of RSV-LRTI hospitalizations**
Secondary endpoint




**Kaplan-Meier plot for time to first RSV confirmed MA-LRTI**




Hazard ratio 0.23 (95% CI, 0.12-0.47) $p<0.001$

CI: confidence interval; MA-LRTI: medically attended-lower respiratory tract infection; RSV: respiratory syncitial virus.

**1.** Hammitt LL, et al. *N Engl J Med*. 2022;386(9):837-846.

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# Communicating with individuals about how to protect their infant

Discuss what you know about upcoming RSV immunization options
“There are two options that are coming to market one is a vaccine for the pregnant person. The other is an immunization for the baby after birth”

Discuss why immunization is important
Significant burden and unpredictability of RSV disease course

Discuss how immunization works
Cross placental transfer of antibodies or administration of monoclonal antibody

Discuss benefits of immunization
“Getting a flu, COVID-19 or RSV immunization is a safer, more reliable way to build protection than taking the risk of getting very sick with a respiratory virus. Your child could still get sick after getting immunized. But their symptoms will usually be less severe than if they did not receive the vaccine.” *Communicating with families about how to protect against fall and winter respiratory viruses.* Home. (2023, August 12). https://www.aap.org/en/patient-care/immunizations/communicating-with-families-about-how-to-protect-against-fall-and-winter-respiratory-viruses/

# Additional Resources

- Resources for Providers
  - Product monograph for Beyfortus, Abrysvo and Synagis
  - “Summary Basis of decision for Beyfortus” on Health Canada Website
  - CADTH Rapid Implementation Advice for Beyfortus
  - CDC, ACIP
  - NACI recommendations pending
  - CPS, AAP

- Resources for Patients
  - Patient Medication Information at the end of the product monograph
  - Speaking to your healthcare professional
  - Respiratory Syncytial Virus (RSV) Fact Sheet (https://www.ontario.ca/page/respiratory-syncytial-virus)

# Key Takeaways

- RSV is a significant healthcare burden and public health concern
- We have RSV prophylactics available for a broad infant population and pregnant individuals for the first time
- Health Canada has approved RSV preF Vaccine AND Nirsevimab for the prevention of RSV in all infants
- We are essential in helping our clients navigate the changing landscape in RSV prevention