



ABBOTT RAPID DIAGNOSTICS

# Respiratory Syncytial Virus: It Isn't Just for Kids Anymore

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24 | March | 22

# Objectives

1

**Describe the symptoms, complications, and those at risk for serious disease with RSV infection**

2

**Describe how RSV can affect older adults and why antigen testing may not be an option for adults**

3

**Describe the current prevention and treatment guidelines for those infected with RSV**

# How many people have had RSV in their lives?

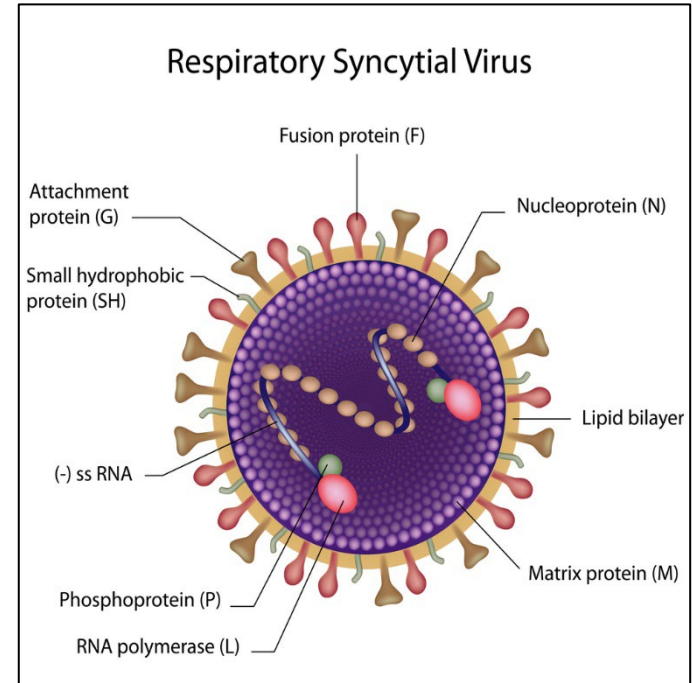
**Almost ALL people  
in this room had RSV  
by the age of 2!**

RESPIRATORY SYNCYTIAL VIRUS

# Introduction

# What is RSV?

- Single-stranded RNA virus of the family *paramyxoviridae*
  - Includes common respiratory viruses such as those causing measles and mumps
- Divided into 2 subtypes: A and B
  - More severe clinical illnesses involve subtype A
    - Tends to predominate in most outbreaks.



# Background on RSV

Incubation period: 4-6 days

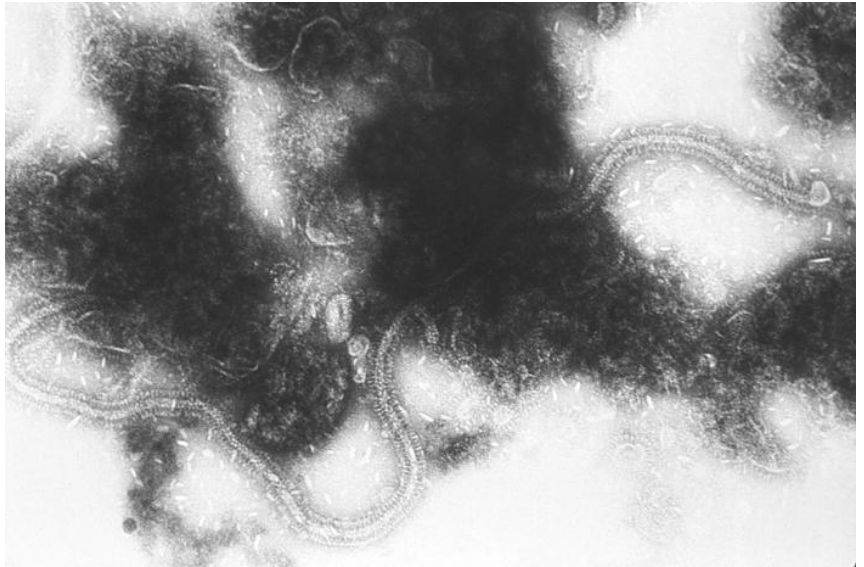
## Symptoms:

- Runny nose
- Decreased appetite
- Coughing
- Sneezing
- Fever
- Wheezing

Reservoir: humans only

# Brief History of RSV<sup>1</sup>

- Discovered in 1956 by Dr. Robert Chanock
  - Determined to be the cause of bronchiolitis in infants
- Recognized primarily in children until 1970s
  - Outbreaks in nursing homes and long-term care facilities were identified



Transmission electron micrograph of RNA genome of RSV. CDC/Dr. Erskine Palmer. 1981.



# How RSV is spread

People infected with RSV are usually contagious for 3 to 8 days. However, in the young and elderly with weakened immune systems, RSV can be contagious for up to 4 weeks.<sup>1</sup>



- Infected person coughs or sneezes into the air, creating virus-containing droplets that can linger briefly in the air.



- Direct and indirect contact with nasal or oral secretions from infected people and then rub their eyes or nose.



- RSV can survive on hard surfaces such as tables and crib rails for many hours. However, RSV typically lives on soft surfaces such as tissues and hands for shorter amounts of time.

# Complications of RSV

RSV disease includes a wide array of symptoms, including<sup>2</sup>:

Rhinitis	Croup	Pneumonia	Bronchiolitis
Inflammation of mucous membranes inside the nose	Inflammation of larynx & trachea causing breathing problems	Inflammation of the lungs	Inflammation of the bronchioles

**However, these symptoms are not specific and can be linked to other respiratory illnesses therefore making rapid and accurate diagnosis of RSV essential for the treatment and management of patients.**

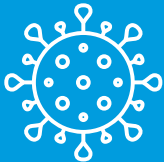
It may also cause other diseases like otitis media (ear aches) that RSV tests aren't currently meant to test for.

# Long-term effects of RSV<sup>1</sup>



RSV infection or hospitalization as a young infant has been linked to persistent wheezing, allergies, and asthma throughout childhood.

- Some studies indicate these conditions persist through adolescence or even into adulthood



Correlation is not well understood, and infection at a young age with other respiratory viruses such as rhinovirus are also linked to childhood wheezing.

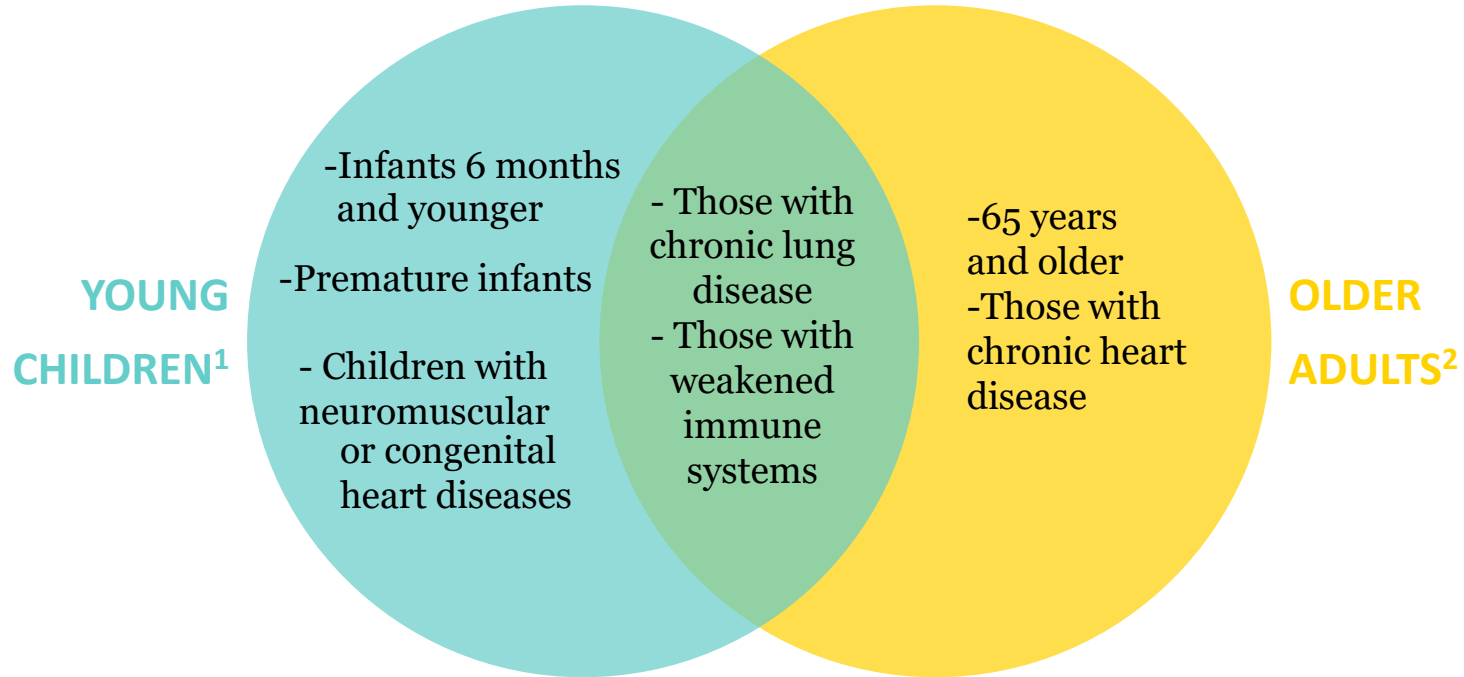
1. Borchers AT, Chang C, Gershwin ME, Gershwin LJ. Respiratory Syncytial Virus – A comprehensive Review. *Clinic Rev Allerg Immunol.* 2013;45:331-379. DOI 10.1007/s12016-013-8368-9

# RSV is Contagious!<sup>1</sup>



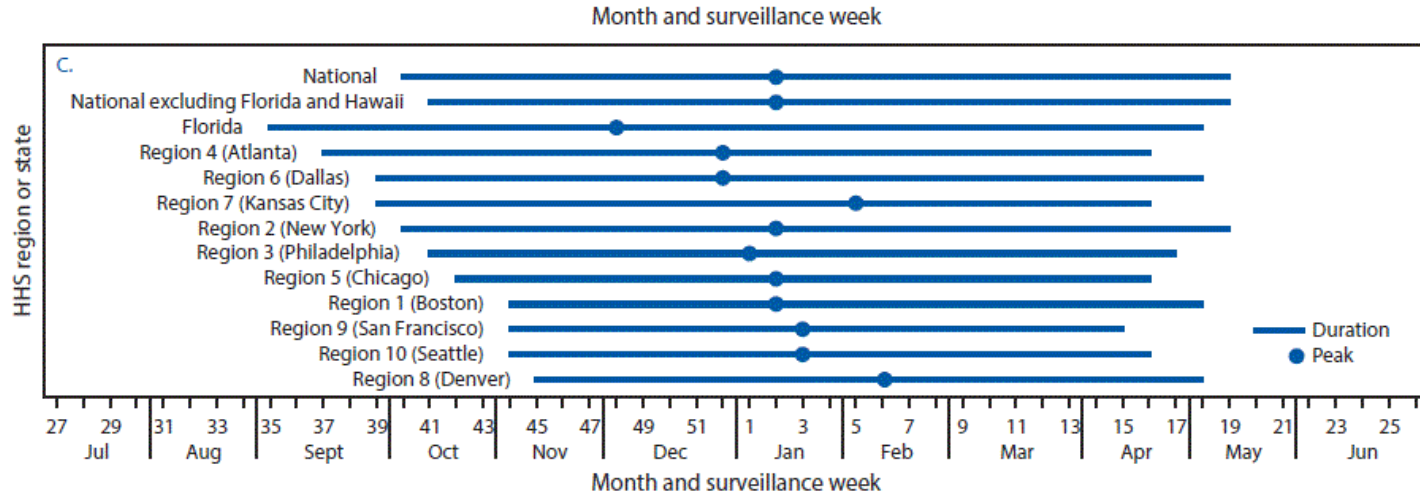
- RSV is one of the most contagious human pathogens
  - Comparable to measles virus.
- In prospective studies, the natural introduction of RSV into a day-care setting resulted in infection of more than 90% of infants and children
- Children pass RSV onto adults and vice versa
- RSV is readily introduced and spreads with ease in hospitals, nursing homes, families, and other close-contact settings

# Who is at high risk for RSV?



# RSV Seasonality in the US

## RESPIRATORY SYNCYTIAL VIRUS SEASON DURATION AND PEAK JULY 2016 - JUNE 2017<sup>1</sup>



1. Rose EB, Wheatley A, Langley G, Gerber S, Haynes A. Respiratory Syncytial Virus Seasonality - United States, 2014–2017. *MMWR* 2018;67:71–76. DOI: <http://dx.doi.org/10.15585/mmwr.mm6702a4external icon>.

# RSV Seasonality<sup>1</sup>



- RSV season varies in Florida and southwest Alaska
  - Longer and less predictable
- Certain areas of the world do not follow the pattern of “RSV seasons”, instead RSV is found in an alternating pattern of epidemic years followed by smaller outbreak years

1. Borchers AT, Chang C, Gershwin ME, Gershwin LJ. Respiratory Syncytial Virus – A comprehensive Review. *Clinic Rev Allerg Immunol*. 2013;45:331-379. DOI 10.1007/s12016-013-8368-9

# RSV during COVID-19

- Many countries reported record lows of RSV during the 2020-2021 season<sup>1-3</sup>
- Presumably due to preventative measures instilled to reduce the transmission of COVID-19
  - Travel restrictions
  - Social distancing
  - Masks
- Followed by an increase in inter-seasonal RSV outbreaks during late spring/early summer 2021 as restrictions began to lift<sup>2-3</sup>



Please wear a mask infographic. CDC. 2020.



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# Burden

# RSV—A significant global pathogen<sup>1</sup>

The **single most important cause of severe respiratory illness** in infants/young children

RSV disease burden is estimated at **64M cases and 160,000 deaths** every year.

RSV is **the most frequent cause of hospitalization** of infants and young children in industrialized countries.

RSV believed to represent a **similar burden to Flu** in >64yrs

RSV-related illness represents a **significant healthcare burden** in the US

# US Burden of RSV

In the US, the **hospitalization rate for RSV is three times** higher than that from influenza in children <5 years old<sup>1</sup>

Over **2 million children 5 years old and younger** receive care for RSV infection in US each year (Extrapolated data<sup>2</sup>):<sup>1</sup>

57,500 require hospitalization<sup>3</sup>; 518,000 receive care in the ED<sup>1</sup>

Over 1.5 million children are treated each year in practices.<sup>1</sup>

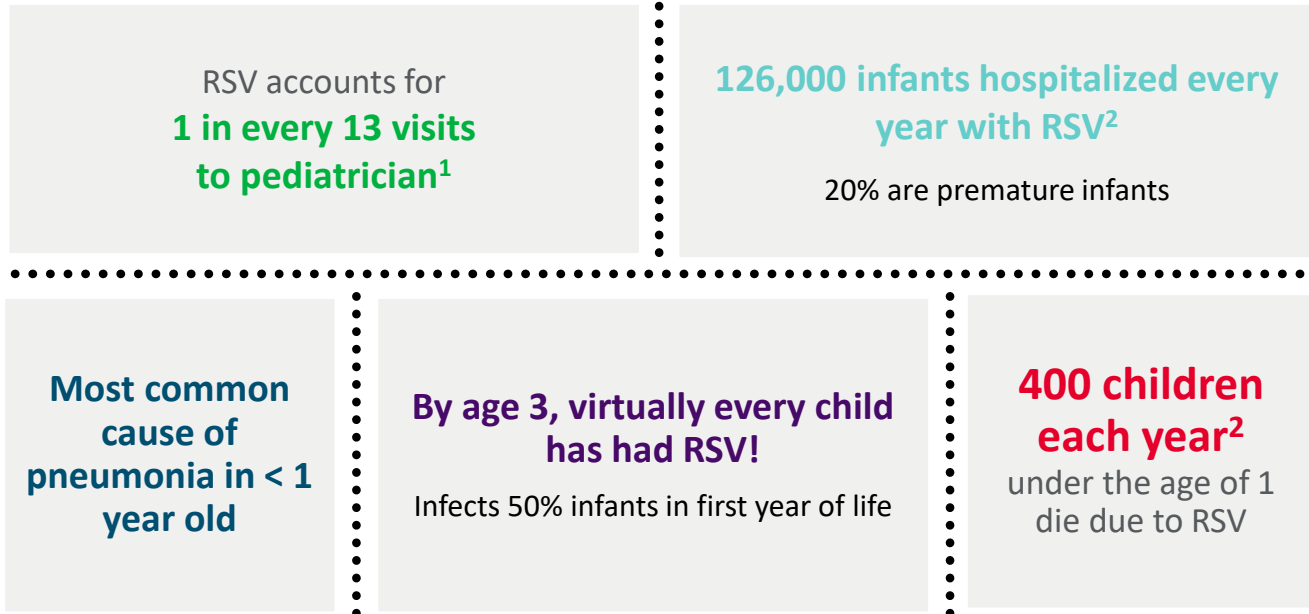
RSV-associated costs based on US Medicaid databases for full-term infants:<sup>1</sup>

**\$11,000 for each RSV hospitalization<sup>1</sup>**

**>\$3,000 for RSV-related outpatient visit<sup>1</sup>**

Total US Healthcare believed to be  
**~\$2.6bN per year** for RSV associated infections<sup>3</sup>

# Prevalence / Incidence in Children

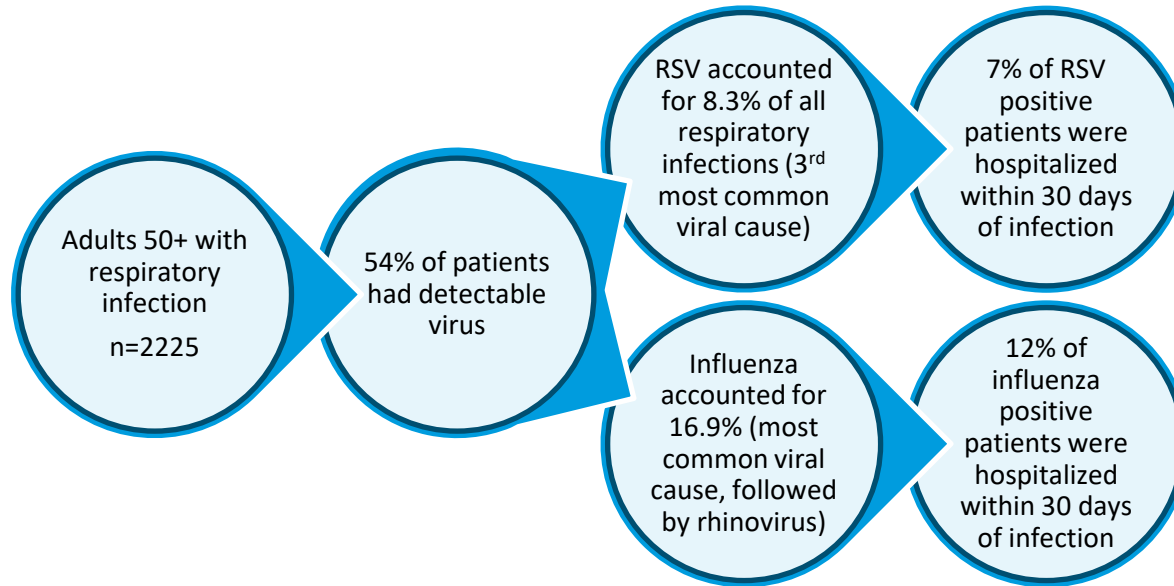


# Prevalence / Incidence in Older Adults



# RSV in Adults<sup>1</sup> : Sundram et al 2014

- 2004-2010 study in Wisconsin of adults with acute respiratory infections



1. Sundram ME, Meece JK, Sifakis F, Gasser RA, Belongia EA. Medically Attended Respiratory Syncytial Virus Infections in Adults Aged  $\geq 50$  years: Clinical Characteristics and Outcomes. *Clin Infect Dis*. 2014;58(3):342-349. doi:10.1093/cid/cit767

# RSV in Adults<sup>1</sup> : Fleming et al 2015

- 1995-2009 analysis of healthcare visits in the UK
  - Estimated that 487,247 general practice visits, 17,799 hospitalizations, and 8,482 deaths among adults over 18 were caused by RSV each year
  - 79% of hospitalizations and 93% of deaths occurred in people over 65
  - RSV estimated to have caused more general practice visits than influenza annually
    - Similar numbers of hospitalizations and deaths most years
    - Year to year variation of cases and mortality was greater for influenza than RSV

1. Fleming DM, Taylor RJ, Lustig RL, et al. Modelling estimates of the burden of Respiratory Syncytial virus infection in adults and the elderly in the United Kingdom. *BMC Infect Dis.* 2015;15:443. DOI 10.1186/s12879-015-1218-z

# RSV in Adults<sup>1</sup> : Anderson et al 2016

- 2012-2013 Mayo Clinic study in Minnesota and Florida of patients seeking care for respiratory illness and testing positive for RSV
  - Stratified data by age group (children:<6, adults: 18 to 65, elderly:>65) and immune status

Immunocompetent adults (n=36)	Immunocompetent children (n=130)	Immunocompetent elderly (n=75):	COPD patients (n=39):
<ul style="list-style-type: none"><li>• 72.2% required admission</li><li>• 0% mortality rate</li></ul>	<ul style="list-style-type: none"><li>• 65.4% required admission</li><li>• 0% mortality rate</li></ul>	<ul style="list-style-type: none"><li>• 88% required admission</li><li>• 4% mortality rate in 30 days</li></ul>	<ul style="list-style-type: none"><li>• 100% required admission</li><li>• 10.3% mortality rate in 30 days</li></ul>

- 43.1% RSV positive patients had been treated with antibiotics or antifungal medications
  - 60% of those prescribed antibiotics/antifungals did not have recoverable bacterial/fungal infection

1. Anderson NW, Binnicker MJ, Harris DM, et al. Morbidity and mortality among patients with respiratory syncytial virus infection: a 2-year retrospective review. *Diagn Microbiol Infect Dis*. 2016;85(3):367-371. DOI: 10.1016/j.diagmicrobio.2016.02.025



# Why isn't RSV in adults discussed more?

Young/immunocompetent adults typically have mild/no symptoms

- Widely circulating - likely infects 3-10% of the population annually<sup>1</sup>
- “Just” the common cold for young/healthy

Lack of testing and diagnosis

- Reduced sensitivity of antigen tests in adults limits testing options
- Not all healthcare providers test for RSV

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# Diagnosis

# Diagnostics

## Common

- Molecular assays
- Antigen testing

## Less common

- Viral culture
- Serology

# Diagnostics

## ANTIGEN TESTING

- Rapid method
- For young children only (under 5 years old)
- Sensitivity: 89%
- Specificity: 100%
  
- For adults suspected of having RSV:
  - Antigen tests are not recommended due to reduced sensitivity in adults
    - Adults have generally been exposed to RSV previously in their lives and thus may have lower viral loads

# Diagnostics

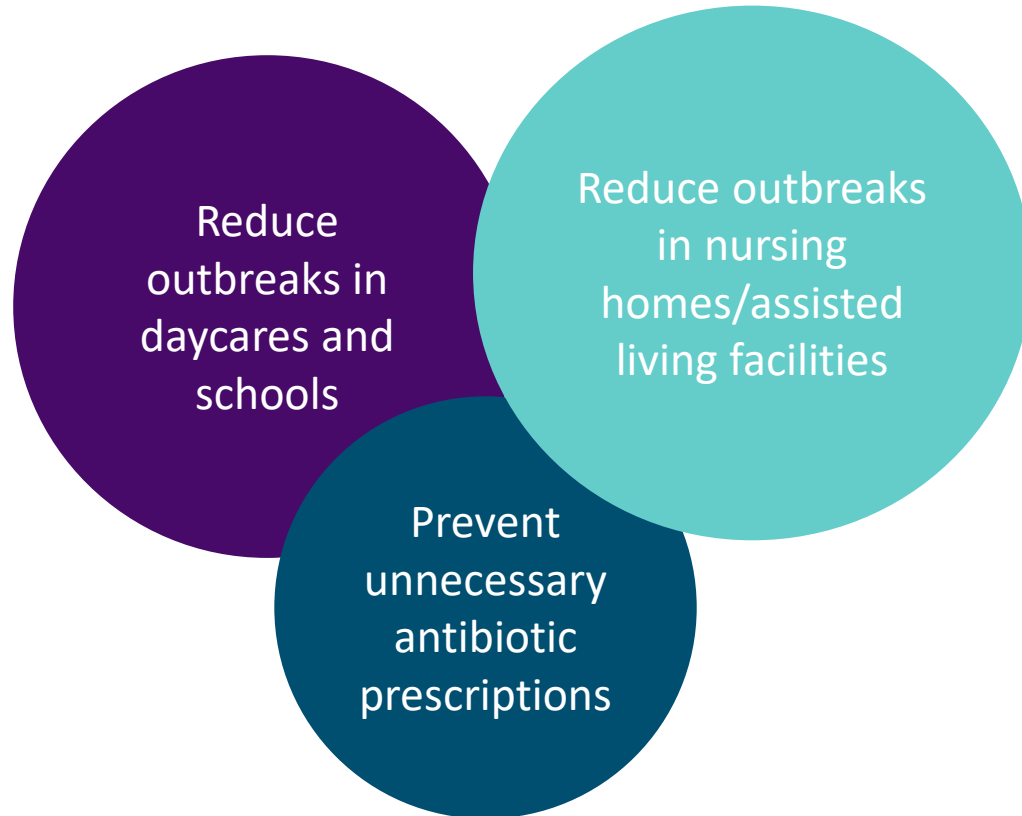
## MOLECULAR TESTING

- rRT-PCR
  - High specificity and sensitivity
  - Results take 4+ hours
  
- iNAAT
  - For children under 18 or adults over 60
  - Results in ~15 minutes
  - Sensitivity: 98.6%
  - Specificity: 97.8-98.0%

# Diagnostics Comparison

	PCR	iNAAT	Rapid Antigen	Viral Culture	Serology
Sensitive in young children	X	X	X	X	X
Sensitive in older children	X	X			
Rapid		X	X		
Ease of use			X		

# Why test for RSV at all?



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# Prevention



# Prevention



**Currently no vaccine for RSV exists**



**Recommendations include handwashing, social distancing, etc.**



**Monoclonal antibody treatment: Palivizumab**



May be used as a preventative for high-risk infants and young children during RSV season

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# Guidelines

# Guidelines for Administration of Palivizumab <sup>1</sup>

## AMERICAN ACADEMY OF PEDIATRICS, 2014

- Administered as monthly intramuscular shot during RSV season (max of 5 doses/year)
- Recommended for:
  - Infants under 1 year who were born before 29 weeks gestation
  - Infants under 1 year who were born before 32 weeks of gestation and have chronic lung disease
- May be used for:
  - Infants under 1 year who have hemodynamically significant congenital heart disease
  - Infants under 1 year who have a pulmonary abnormality or neuromuscular disease that impairs ability to clear secretions from upper airways
  - Infants under 2 years who will be profoundly immunocompromised during RSV season

1. Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. *Pediatrics*. 2014;134(2):415-420. <https://doi.org/10.1542/peds.2014-1665>

# Guidelines for Diagnosis of Bronchiolitis<sup>1</sup>

## AMERICAN ACADEMY OF PEDIATRICS, 2014

- Diagnose based on history and physical exam
- Laboratory testing or radiographic studies are not recommended routinely

### Why?

- Bronchiolitis can be caused by a wide variety of respiratory viruses (RSV, rhinovirus, human metapneumovirus, influenza, adenovirus, coronavirus, parainfluenza virus)
  - One study showed 76% of bronchiolitis cases were caused by RSV<sup>2</sup>
  - No difference in the recommendations for treatment based on etiologic agent
- 
- Testing for RSV is recommended for symptomatic infants receiving Palivizumab
    - If the result is positive, Palivizumab should be discontinued

1. Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis. *Pediatrics*. 2014;134(5):e1474-e1502. <https://doi.org/10.1542/peds.2014-2742>

2. Miller EK, Gebretsadik T, Carroll KN, et al. Viral etiologies of infant bronchiolitis, croup and upper respiratory illness during 4 consecutive years. *Pediatr Infect Dis J*. 2013;32(9):950-955. doi:10.1097/INF.0b013e31829b7e43

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# Treatment

# Treatment of RSV<sup>1</sup>



**No treatments  
for RSV are  
recommended**



**Supportive care  
such as fluids**



**Fever/pain  
management**

# Ribavirin<sup>1</sup>

- Broad spectrum antiviral drug
  - FDA approved for use in infants with RSV
  - Also used for treating hepatitis
- Ribavirin is not recommended routinely by the American Academy of Pediatrics
  - Lack of clarity around its effectiveness
    - More studies needed
  - Potential health risks
  - May be used in extreme cases

1. Borchers AT, Chang C, Gershwin ME, Gershwin LJ. Respiratory Syncytial Virus – A comprehensive Review. Clin Rev Allerg Immunol. 2013;45:331-379. DOI 10.1007/s12016-013-8368-9

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Future



# Future of RSV

## Vaccines

- Many vaccines for RSV are in clinical trials<sup>1</sup>
- For the very young
- For pregnant individuals (so immunity is passed to unborn child)
- For the elderly
- Newer vaccine formats may be promising– mRNA?

## Antiviral medications

- May reduce length of illness like those available for influenza

## Other antibody treatments

- For prophylaxis or aiding in recovery



**Abbott**