Updates in RSV

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No Disclosures

Objectives

- **Describe the natural history of Respiratory Syncytial Virus (RSV) infection and opportunities for prevention in children, pregnant patients, and adults.**
- **Demonstrate the impact of preventative strategies on hospitalization**
- **Differentiate the different treatment modalities in children and adults currently under active research**

Prevention

The next patient on your clinic schedule is a 32-year-old woman currently 31 weeks pregnant presenting for URI symptoms. You diagnose her with a viral URI and send her home with supportive care. She asks whether she has RSV and how she can protect herself and her baby on the way…

Photo credit: Wikimedia

RSV Basics

200,000

Hospitalizations per RSV season for Adults

15 per 1000

Children hospitalized during the worst RSV seasons

1st & 3rd

Most commonly identified respiratory virus in hospitalized kids and adults

Havers et al., Burden of Respiratory Syncytial Virus-Associated Hospitalizations in US Adults, October 2016-September 2023
McMorrow et al., Respiratory Syncytial Virus-Associated Hospitalizations in Children < 5 years: 2016-2022

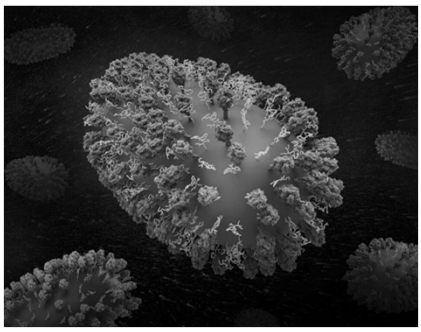
RSV Basics

	Influenza	RSV
Risk of CV event and readmission	⇧	⇧⇧
Homecare at Discharge	⇧	⇧⇧
Long-Term Mortality	81%	74%

Wildenbeest J, et al. Respiratory syncytial virus infections in adults: a narrative review (2024).

RSV Basics

- Transmission
  - Direct contact and fomites
  - Respiratory aerosols
  - Precautions



- Incubation and Disease Course
  - 4-6 days
  - Peaks between 3-5 days
- Pathogenesis
  - Highly restricted to respiratory epithelium
  - Cytokine and chemokine release
  - F fusion protein

United States Center for Disease Control and Prevention. 2007 Guideline for Isolation Precautions: Preventing Transmission in Healthcare Settings (2007) - Photo Credit: Wikimedia

Prevention: RSV Vaccines

"Vaccines" for Kids

- Nirsevimab-alip (Beyfortus)
  - Monoclonal Antibody
- Palivizumab (Synagis)
  - Monoclonal Antibody

Vaccines for Adults

- RSV Vaccine preF A and B (Abrysvo)
  - Bivalent
  - Pregnancy
- RSV Vaccine mRNA (mResvia)
  - mRNA
- RSV Vaccine Adjuvanted (Arexvy)
  - Enhanced immune response

Graham BS. The Journey to RSV Vaccines – Heralding an Era of Structure-Based Design (2023)

RSV Vaccine Efficacy

Population	RSV-associated lower respiratory tract illness	Hospitalization due to RSV disease	All cause mortality	Significant Adverse Events (SAEs)
Infants (Maternal)	13 fewer per 1000	10 fewer per 1000	2 fewer per 1000	0 fewer per 1000
Women of Childbearing Age	107 fewer per 1000	Not estimatable	Not estimatable	Not estimatable
Older Adults	4 fewer per 1000	Not estimatable	No events	0 fewer per 1000

Saif-Ur-Rahman K., et al. Efficacy and safety of respiratory syncytial virus vaccines (Review) (2025)

Nirsevimab-alip Efficacy

- 31900 healthy, term infants
- 75% received Nirsevimab in November and December
- 2.5 months of age
- 85% received Nirsevimab outpatient

Treated Infants	Untreated Infants
35 first episodes of RSV Lower Respiratory Tract Infection	462 first episodes of RSV Lower Respiratory Tract Infection

87% effectiveness

Hsiao PhD, MPH, et al. Effectiveness of Nirsevimab Against RSV and RSV-Related Events in Infants (2025)

Cost Incentives

- Study using maternal vaccination alone
  - Year round maternal vaccination would prevent:
    - ~46000 outpatient visits
    - ~16000 ED visits
    - Societal incremental cost of ~$400000-$800000 per quality adjusted life year

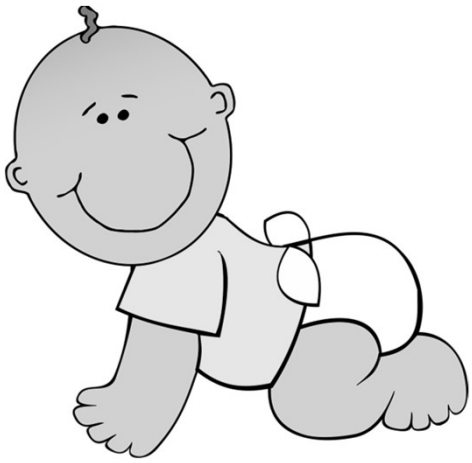
Hutton PhD, et al. Cost-Effectiveness of Maternal Vaccination to Prevent Respiratory Syncytial Virus Illness (2025) - Photo credig: Pixabay

Barriers to Vaccine Uptake

- Maternal and Infant Vaccination Data (2023-2024)
  - 60% decrease in vaccination for non-Hispanic Black and non-Hispanic Middle Eastern or North African mothers.
- Older Adults Vaccination Data (2023-2024)
  - Worst uptake was found in >85 years of age, those with 3 or more comorbidities, and Southern states
  - Decreased uptake in those of Hispanic, Black, and low-income subsidy patients

Irving et al. Infant Respiratory Syncytial Virus Immunization Coverage in the Vaccine Safety Datalink: 2023-2024 (2025).
Murphy A, et al. Disparities in Respiratory Syncytial Virus Vaccine Uptake in the Medicare Fee-for-service Population During 2023-2024 Season (2025)

Nursery Vaccination



- Universal immunization campaign in all eligible infants
  - Able to offer 99% eligible infants, with an uptake of 71%
  - Deferral
    - Deferral of Hep B
    - Discharge from Newborn Nursery vs NICU
    - Public Insurance

Puckett L, et al. Successful Implementation of Nirsevimab and Factors Influencing Uptake in Neonatal Care (2024).

Addressing RSV Vaccine Hesitancy

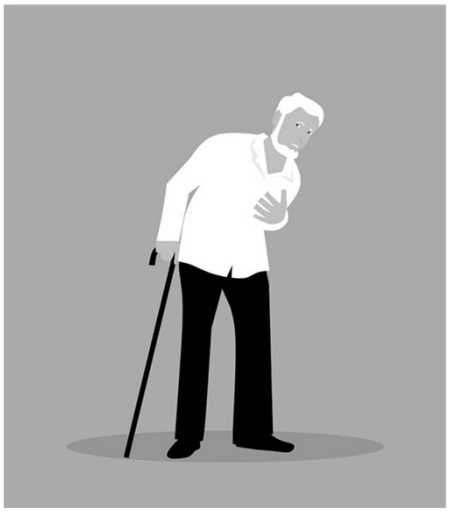
- 28 Semi-structured interviews of parents with newborns
  - Themes
    - Knowledge Gaps
    - Trust
    - Side effect concerns
- What was useful?
  - Awareness
  - Early conversations
  - PCPs/prenatal clinicians

Hinderstein S, et al. Parent Perspective on Nirsevimab for Their Newborn (2024)

Treatment

Armed with that knowledge, your patient receives the RSV vaccine prior to delivery and brings home a healthy baby boy.

During the fourth month of life, however, the infant develops a cold and passes it on to his grandfather…



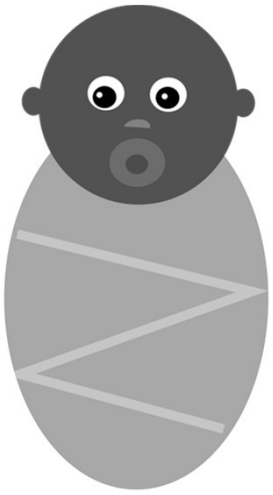


Photo Credit: Pixabay

RSV Treatment, Outpatient

Testing for RSV

Point of Care Antigen Testing

RT-PCR

Treatment

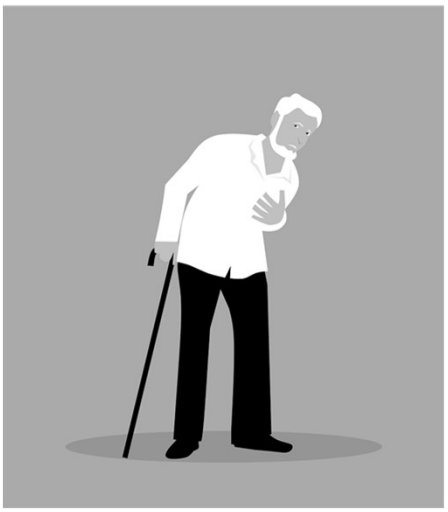
Supportive care

- No Albuterol*
- No Steroids
- No Antibiotics
- No Pulse Oximetry*

Ison MG, et al. Community Acquired Respiratory Viruses in Transplant Patients: Diversity, Impact, Unmet Clinical Needs (2019) Nam H, et al. Respiratory Syncytial Virus Infection in Adults (2019)

Hospitalization

Unfortunately, both baby and grandpa worsen, and require hospitalization…



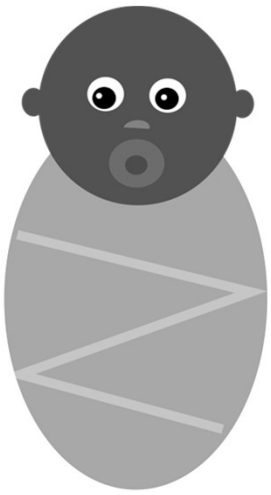


Photo Credit: Pixabay

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Inpatient RSV - Pediatric Bronchiolitis

- Bronchiolitis refers to viral inflammation of the small airways
  - Results in airway edema, increased mucous production, air trapping, and atelectasis
  - Affects children 2 years and younger
  - The most common indication for pediatric hospitalization
- Risk factors for hospitalization due to RSV bronchiolitis:
  - Age < 5 months
  - Prematurity (especially <32 weeks)
  - Chronic lung disease
  - Hemodynamically significant congenital heart disease

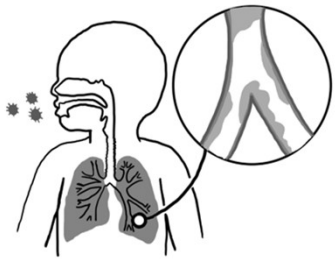
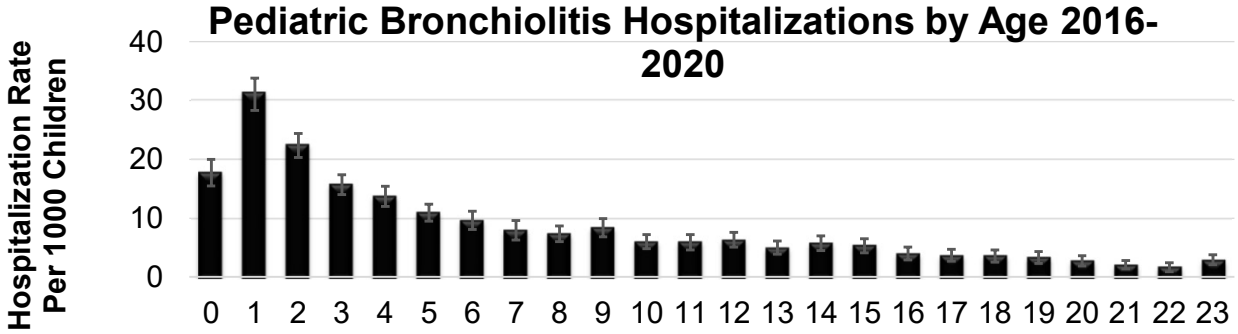


Image: Wikimedia Commons

Demographics – Pediatric RSV

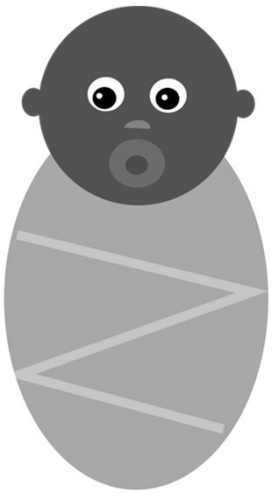
- Worldwide estimates in 2019: **33 million** episodes of LRTI with **3.6 million** hospitalizations and **118,200 overall deaths** (~0.02% of children < 5 years old)
- In the US the average annual RSV hospitalization rate was **4.0 [3.8-4.1] per 1000 children < 5 years**



Curns AT, Rha B, Lively JY, et al. Respiratory Syncytial Virus-Associated Hospitalizations Among Children <5 Years Old: 2016 to 2020. *Pediatrics*. 2024;153(3):e2023062574.

Pediatric Inpatient Care

The 4-month-old presents to the local emergency department where he is found to have increased work of breathing and an oxygen saturation of 88% on room air.



Pediatric RSV – Indications for Hospitalization

- Hypoxia
- Severe or worsening respiratory distress
- Inadequate oral intake
- Secretion burden

- Indications for ICU care:
  - Apnea
  - Respiratory failure

Testing not indicated for non-critical patients:

Expanded viral testing

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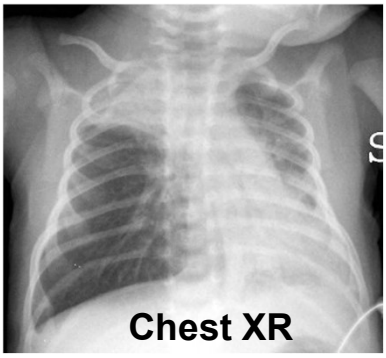


Chest XR

Pediatric RSV – Inpatient Treatment

- **<u>Supportive Care</u>**
  - Suctioning
  - Hydration
  - Nutrition
  - Antipyretics
  - Respiratory support

Pediatric RSV – Inpatient Treatment

- Nebulized Hypertonic Saline
  - May decrease length of inpatient stay by a few hours for those admitted longer than 3 days
- Topical alpha-adrenergic decongestants
  - Widespread use without much evidence
  - Cannot be used for >72 hours due to risk of rebound congestion
- Bronchodilators
  - Not recommended for widespread use

Ralston et. al. Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis. *Pediatrics* November 2014; 134 (5): e1474–e1502.

25

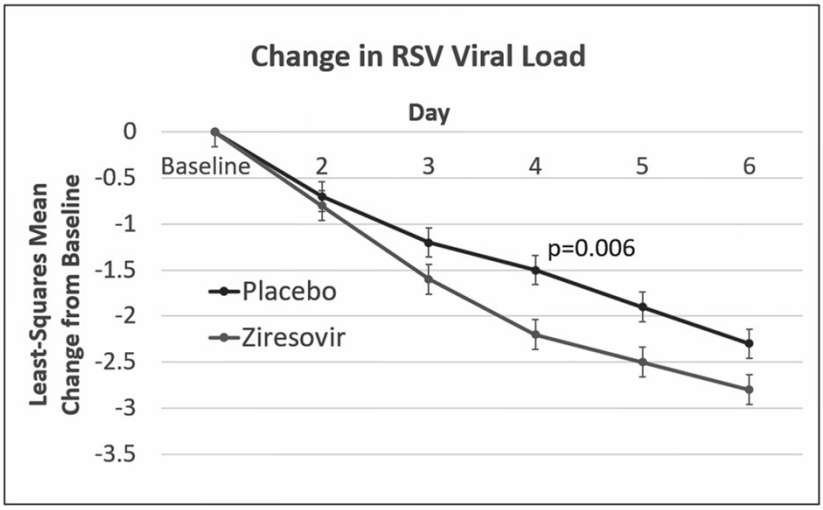
Pediatric RSV – Inpatient Treatment

- Heated High Flow Nasal Cannula
  - A support modality, not a “treatment”
  - Use weight-based protocols to determine flow rate
    - Optimal support achieved at ~ 1.5 to 2 L/min/kg

Weiler T, Kamerkar A, Hotz J, Ross PA, Newth CJL, Khemani RG. The Relationship between High Flow Nasal Cannula Flow Rate and Effort of Breathing in Children. *J Pediatr*. 2017;189:66-71.e3.

Pediatric RSV – Emerging Treatments

- Phase 3 double-blind RCT of the antiviral Ziresovir published in NEJM
- Performed at 30 sites in China
- Infants 1-24 months of age with RSV infection <7 days from symptom onset
- Significant differences in:
  - Bronchiolitis score at day 3
  - Decrease in viral load



Zhao S, Shang Y, Yin Y, et al. Ziresovir in Hospitalized Infants with Respiratory Syncytial Virus Infection. *N Engl J Med*. 2024;391(12):1096-1107.

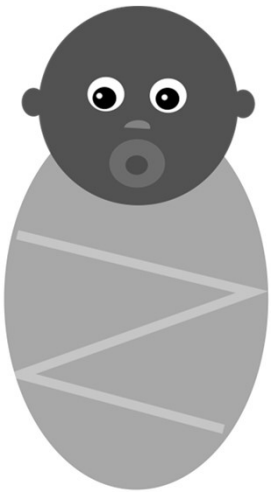
Pediatric RSV – Outcomes

- Median LOS for RSV is around 5 days (IQR 4-7 days)
  - Longer than for viral bronchiolitis in general
- Mortality in the US is <0.1% of hospitalized infants
- RSV bronchiolitis is associated with a threefold risk of childhood asthma
  - Relative risk = 3.1 (95% CI 2.9 to 3.3)

Hartmann K, Liese JG, Kemmling D, et al. Clinical Burden of Respiratory Syncytial Virus in Hospitalized Children Aged ≤5 Years (INSPIRE Study). *J Infect Dis*. 2022;226(3):386-395.
Coutts J, Fullarton J, Morris C, et al. Association between respiratory syncytial virus hospitalization in infancy and childhood asthma. *Pediatr Pulmonol.* 2020;55(5):1104-1110.

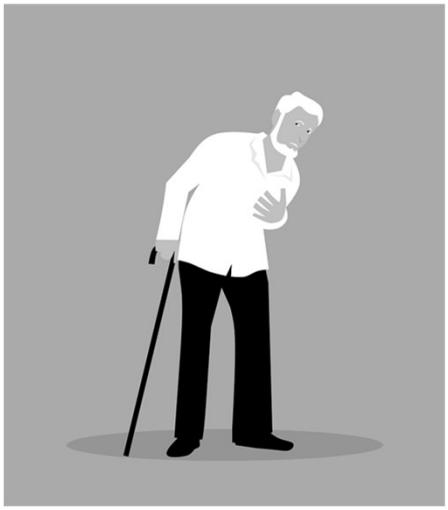
Discharge

On the second night of his hospitalization the patient is weaned to room air. He is taking 1-2 oz per feed and feeding more frequently than usual. Secretions are cleared with standard nasal suctioning every 4 hours and before feeds.



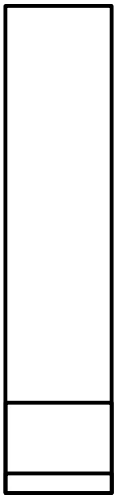
Adult Inpatient Care

Grandfather is 78 years old and has moderate COPD. He presents to the ED with cough and shortness of breath, found to be hypoxic on room air. He receives IV steroids and nebulized albuterol-ipratropium treatments. He is admitted to the hospital and tests positive for RSV.



Adult RSV – Hospitalization

- Estimated RSV-associated hospitalization rates are 48.9 to 76.2 per 100,000 US adults per season
  - 123,000 to 193,000 hospitalizations
  - 24,400 to 34,900 ICU admissions (~20%)
  - 4,680 to 8,620 in-hospital deaths (~4%)
- Risk factors:
  - Age >65 years
  - Chronic conditions (COPD, CHF, diabetes, CKD, immunocompromised)
  - Lower socioeconomic status



Havers FP, Whitaker M, Melgar M, et al. *JAMA Netw Open.* 2024;7(11):e2444756.
Evans SE, Jennerich AL, Azar MM, et al. *Am J Respir Crit Care Med.* 2021;203(9):1070-1087.

RSV vs Influenza

- Influenza generally has a higher seasonal rate of hospitalization
- Patients hospitalized with RSV tend to be older and have more comorbidities
- RSV hospitalizations similar in severity to non-vaccinated influenza or COVID patients
  - Higher rates of mechanical ventilation and in-hospital death with RSV than for vaccinated patients with COVID or influenza
  - Overall survival and hospitalization duration were not significantly different after adjustment for confounders
- The American Thoracic Society recommends expanded viral testing (including RSV) in adult patients with severe CAP or those who are immunocompromised
  - The IDSA recommends NAAT testing for RSV over rapid antigen testing or culture

Clausen CL, Egeskov-Cavling AM, Hayder N, et al. *Open Forum Infect Dis*. 2024;11(10):ofae513.
Surie D, Yuengling KA, DeCuir J, et al. *MMWR Morb Mortal Wkly Rep* 2023;72:1083–1088.

Adult RSV – Inpatient Care

- Supportive care and management of complications is the cornerstone of inpatient care
- Ribavirin is the only FDA-approved antiviral treatment
  - Inhaled (or IV/oral)
  - Used primarily in immunocompromised patients with LRTI
  - Recommended for all lung transplant patients with URTI
- Other adjunctive therapies:
  - Corticosteroids
  - IVIG
  - Monoclonal antibodies

Wildenbeest JG, Lowe DM, Standing JF, Butler CC. *Lancet Respir Med*. 2024;12(10):822-836.
Manuel O, Estabrook M; *Clin Transplant*. 2019;33(9):e13511.

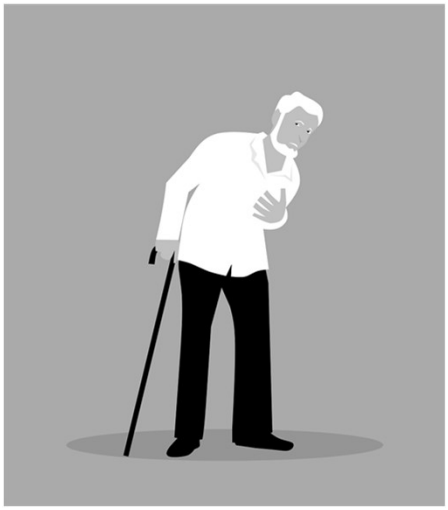
Adult RSV – In-Hospital Complications

- Respiratory failure occurs in ~20% of hospitalized RSV patients
- Bacteremia/sepsis occurred in 28.5%
- Acute renal failure occurred in 17.3%
- Acute cardiovascular complications in 30.1%
  - Acute myocardial infarction in 2.4%
- RSV frequently triggers exacerbations of chronic conditions in hospitalized patients
  - CHF – 38.2%
  - COPD – 80.4%
  - Asthma – 49.5%

Tseng HF, Sy LS, Ackerson B, et al. Severe Morbidity and Short- and Mid- to Long-term Mortality in Older Adults Hospitalized with Respiratory Syncytial Virus Infection. *J Infect Dis*. 2020;222(8):1298-1310.

Discharge

After several days on intermittent BiPap, he is slowly weaned to 3 L/min O2 via nasal cannula. It is determined that he is deconditioned enough to require a stay in a skilled nursing facility before returning home.



Adult RSV – Outcomes

- In-hospital mortality ~5-10% in various studies
- Disposition: 2.6% to hospice, 10.4% to SNF, 48.7% home with new home care services
- One third of patients experience a sustained loss of general function in the year following hospital admission
- Rate of 30-day readmission 16.7%
- Late deaths commonly due to secondary infections, cardiovascular events, and decompensation of comorbid conditions

Survival Post-Discharge	3 months	6 months	12 months
Age 60-74	93.7%	90.3%	84.2%
Age 75+	84.3%	78.6%	68.4%

Tseng HF, Sy LS, Ackerson B, et al. Severe Morbidity and Short- and Mid- to Long-term Mortality in Older Adults Hospitalized with Respiratory Syncytial Virus Infection. *J Infect Dis*. 2020;222(8):1298-1310.

RSV – Key Take-Aways

- PREVENTION >> TREATMENT
- Highly effective vaccines (and prophylactic monoclonal Ab) are now widely available
- Highest risk populations include infants <6 months, adults >75 years, and patients with specific comorbidities
- Supportive care is the cornerstone of treatment in most cases
- Disease burden is high for both pediatric and adult populations