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Preventing RSV:

Providing **OLDER PATIENTS** With the Information They Need



Provided by the
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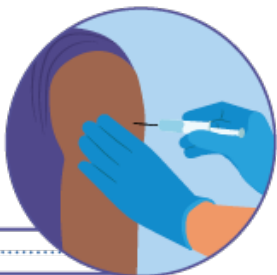


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Learning Objectives

- Describe the mechanism of RSV illness in adults, as well as its overall incidence in this population
- Summarize the disease burden of RSV illness in US adults, with a focus on hospitalizations, comorbidities, and health disparities
- Evaluate the data on performance of RSV vaccines to assess their potential role in prevention strategies for older adults



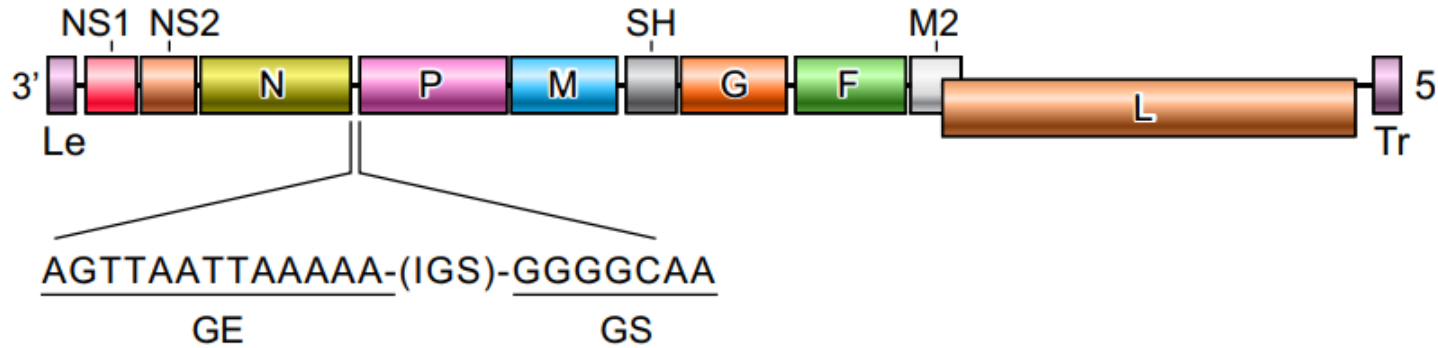
Mechanisms and Occurrence of RSV Illness in Adults







RSV Components

Viruses classified in A and B subgroups based on reactivity to monoclonal antibodies against surface proteins

RSV Genomic RNA



Nucleocapsid Proteins




-  Nucleoprotein N
-  Phosphoprotein P
-  Large polymerase subunit L
-  Transcription anti-termination factor M2-1

SS RNA

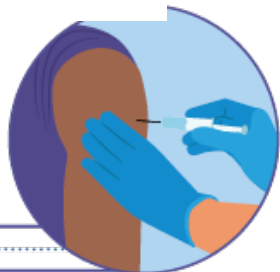
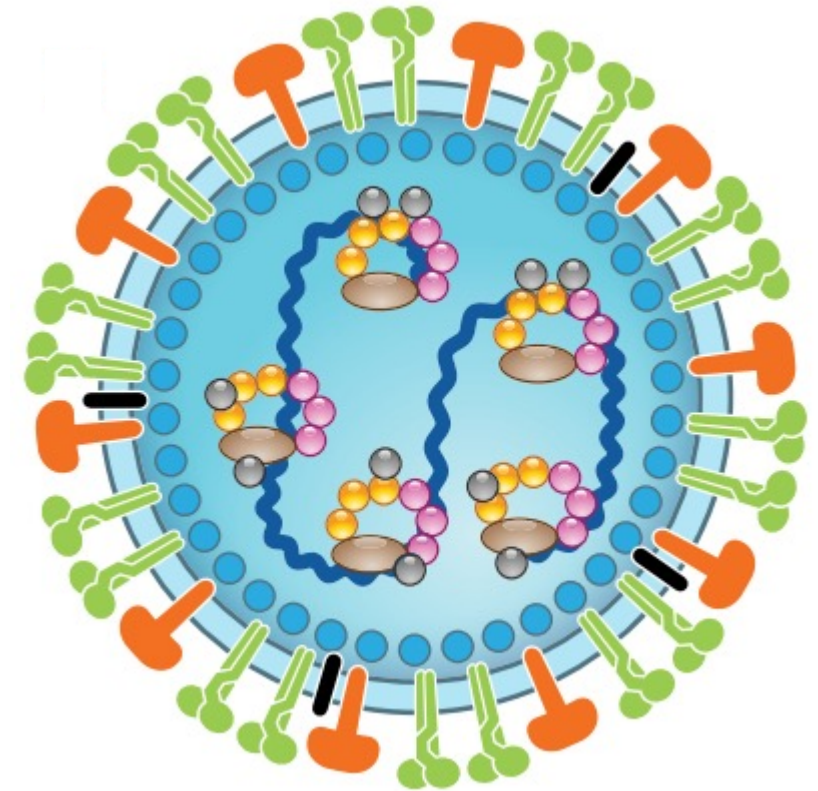
Viral Assembly Factor

-  Matrix protein M

Membrane Envelope Glycoproteins

-  Attachment G
-  Fusion F
-  Small hydrophobic SH

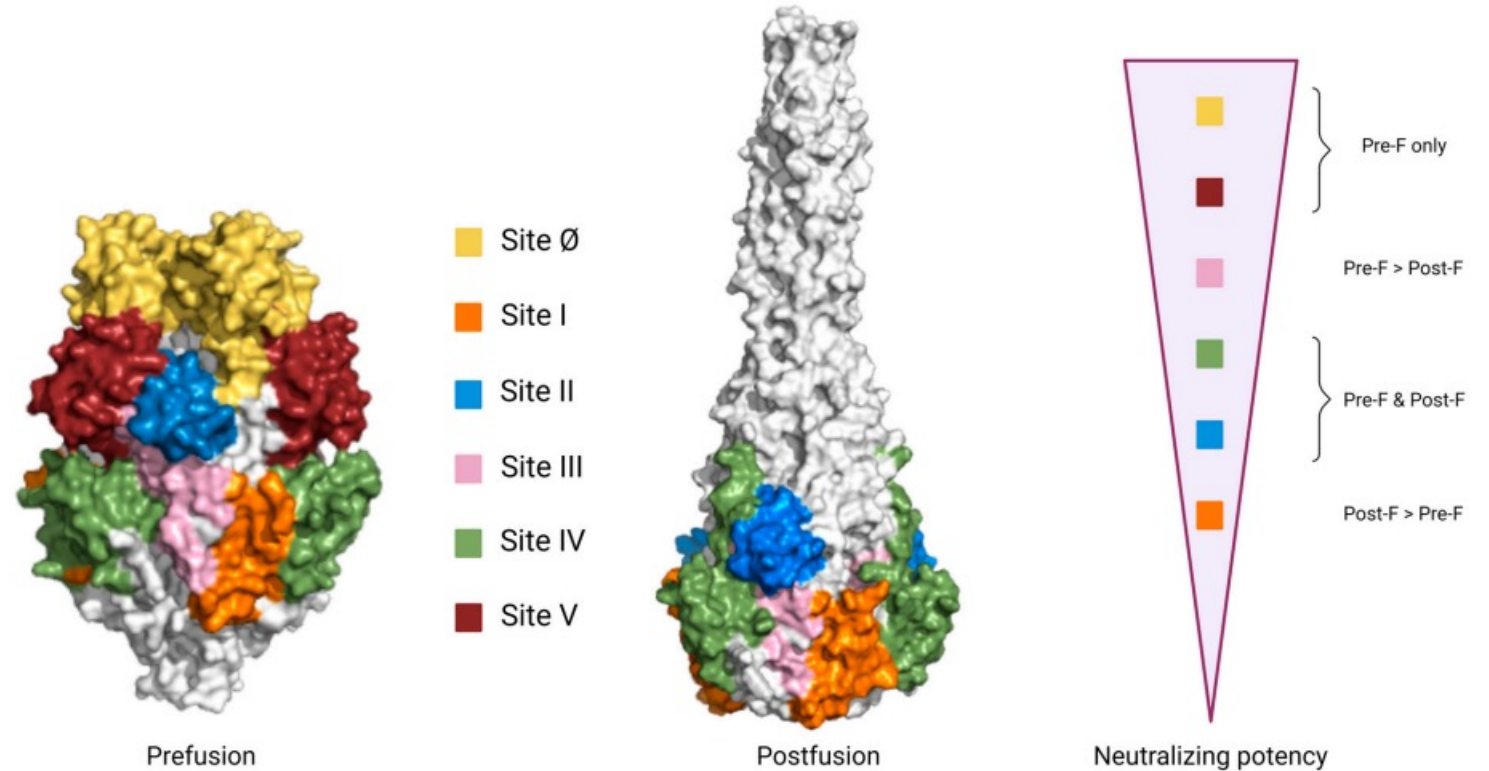
RSV Virus Particle



The RSV F Protein: Membrane Fusion and Vaccine Target

F Protein Conformations and Antigenic Sites⁴

- Conformational changes in the F protein facilitate membrane fusion¹
 - Viral and cell membranes (infection)
 - Membranes of neighboring cells (syncytia formation)
 - Fusion enables viral cell entry
- The F protein (pre-fusion conformation) is the target of FDA-approved adult vaccines^{2,3}



1. Hu M, et al. *Physiol Rev.* 2020;100:1527-1594; 2. GSK. https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Arexvy/pdf/AREXVY.PDF; 3. Pfizer. <https://labeling.pfizer.com/ShowLabeling.aspx?id=19589>; 4. Schaerlaekens S, et al. *Vaccines.* 2024;12:97.



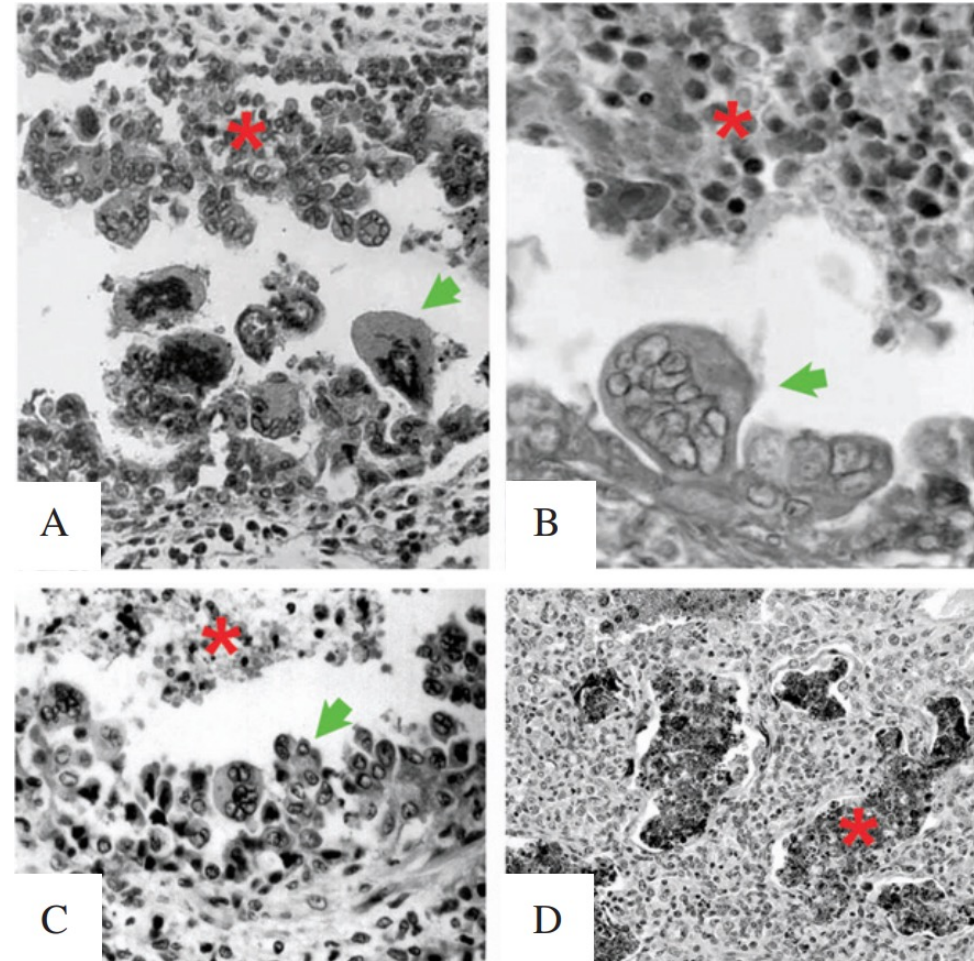
RSV

Infection Cycle

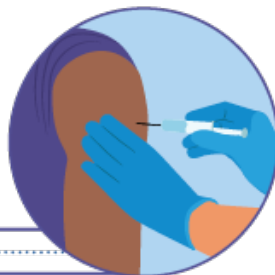
- Viral attachment and entry¹
 - Upper respiratory tract first (nasal epithelium), with potential to move to the lower respiratory tract
 - Main targets: ciliated epithelial cells, alveolar type II cells
- Viral transcription and replication¹
- Viral assembly and budding¹
- Pathological changes with lower respiratory tract infection may include^{1,2}
 - Syncytia formation
 - Epithelial cell sloughing
 - Debris accumulation in lumen

Histopathology of RSV-Infected Small Airways²

- Epithelial cells retained in lumen (arrows)
- Giant cell/polyploid formation (asterisks)

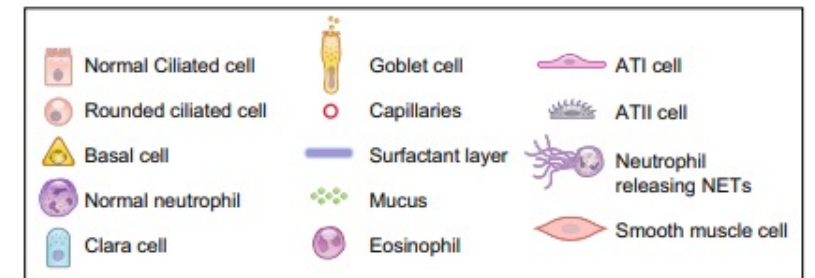
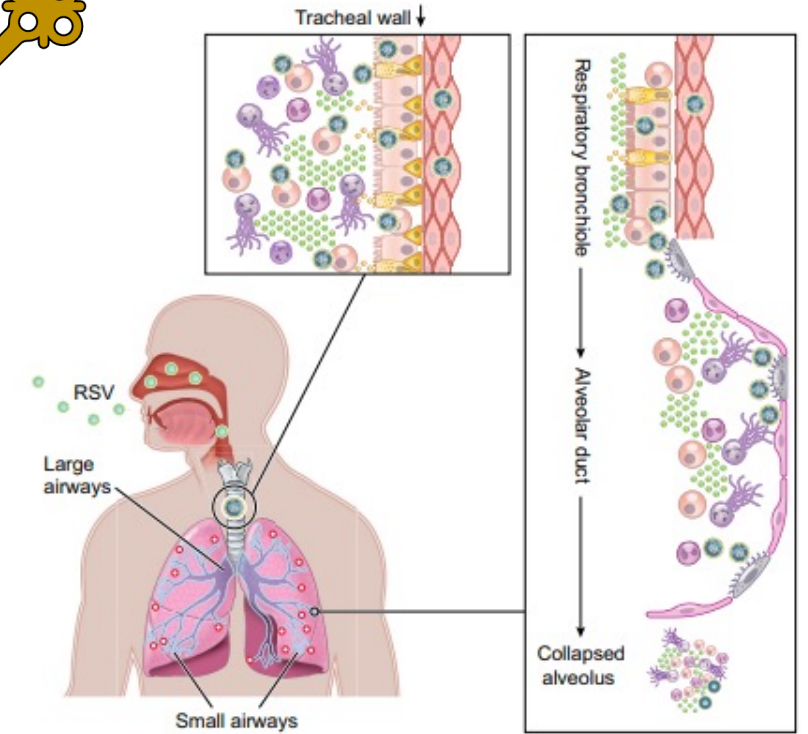


1. Hu M, et al. *Physiol Rev.* 2020;100:1527-1594; 2. Pickles RJ, DeVincenzo JP. *J Pathol.* 2015;235:266-276.



RSV Pathology in Adults

- Illness is usually limited to the upper respiratory tract in healthy adults¹
- Adults with certain underlying medical conditions (e.g., cardiopulmonary disease) have higher risk of severe illness^{1,2}
 - Exacerbation of underlying condition
 - Lower respiratory tract illness
- Pathological changes with RSV lower respiratory tract infection may include¹
 - Epithelial cell sloughing, syncytia formation, luminal debris accumulation
 - Lower airway obstruction and plugging
 - Inflammation (cell recruitment, cytokine production)
 - Increased mucus production
 - Airway hyperreactivity
 - Surfactant deficiency
 - Impaired mucociliary transport
 - Extracellular matrix remodeling

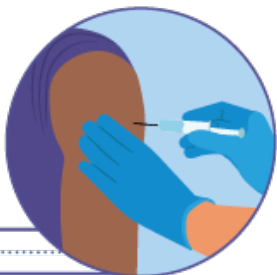


1. Hu M, et al. *Physiol Rev.* 2020;100:1527-1594; 2. Villanueva D, et al. *Ther Adv Infect Dis.* 2022;9:1-13.

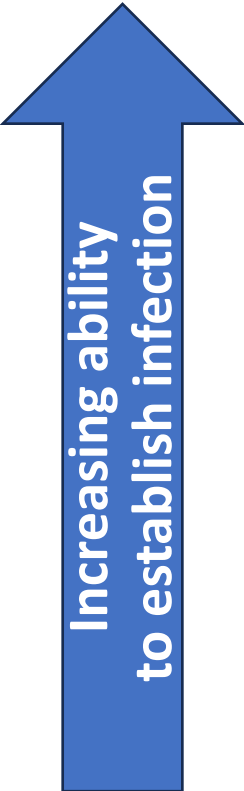


RSV Transmission

- Can spread via^{1,2}
 - **Respiratory transmission:** via droplets (e.g., cough)
 - **Contact transmission:** direct contact with infected individual or virus on a surface
 - **Airborne transmission:** increasing evidence indicates RSV and other respiratory viruses spread this way
- Virus can survive³
 - Up to 6 hours on nonporous surfaces
 - Up to 2 hours on porous surfaces
 - Up to 30 min on skin



RSV: Ability to Establish Infection



| Virus | Secondary Attack Rate (proportion infected among susceptible individuals in contact with the primary case), % ^a |
|------------------------------------|--|
| Measles virus | 52.0 – 84.6 |
| Varicella zoster virus | 61.0 – 78.1 |
| Parainfluenza virus | 36.0 – 67.0 |
| Rhinovirus | 28.0 – 58.0 |
| Respiratory syncytial virus | 11.6 – 39.3 |
| Influenza virus | 1.4 – 38.0 |
| Human coronavirus | 0 – 38.2 |

^a Values are range of reported estimates of mean or median.
Leung NHL. Nat Rev Microbiol. 2021;19(8):528-545.



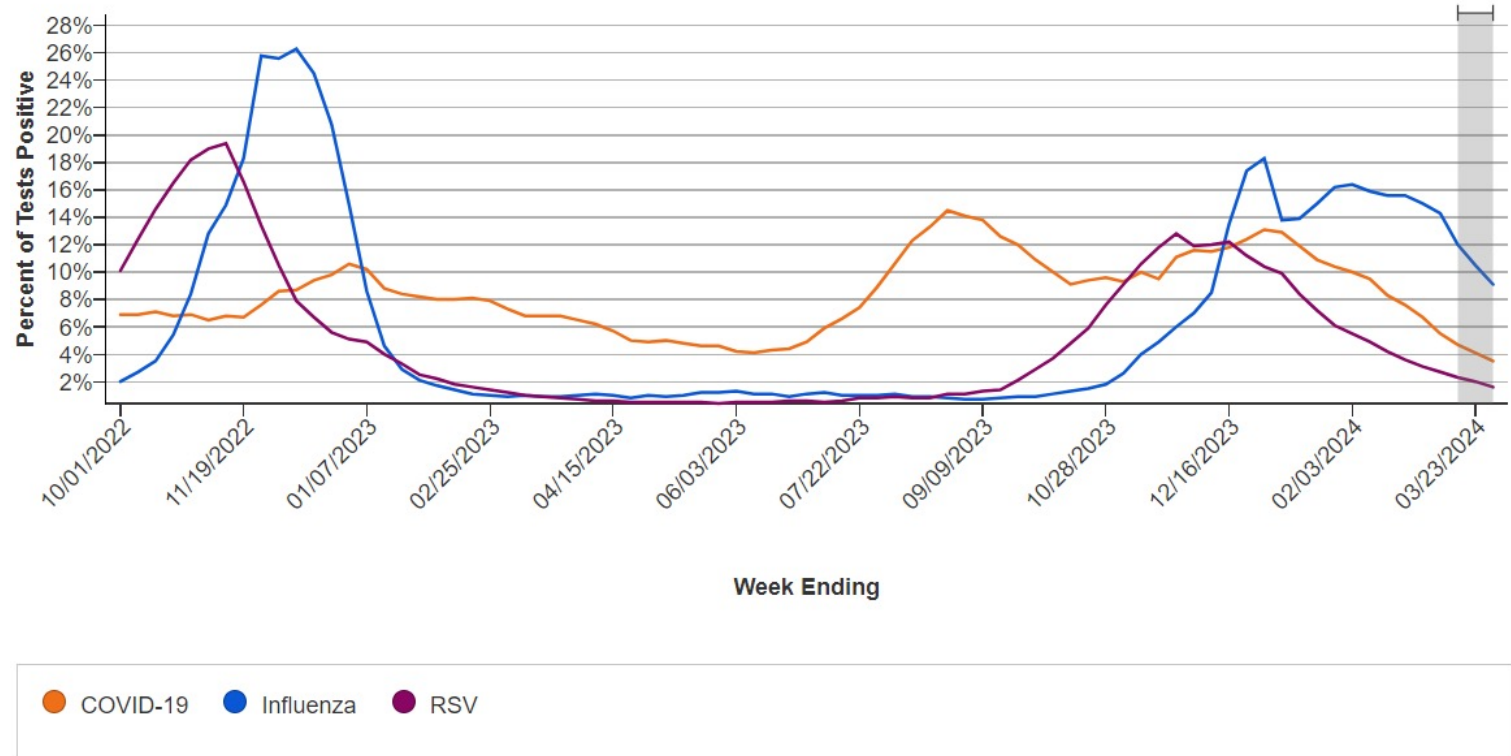
Seasonality of RSV Cases

- Data from sentinel network of laboratories throughout the US, reported weekly to Centers for Disease Control and Prevention¹
- Impact of COVID-19 pandemic²
 - RSV seasonality was disrupted by COVID-19 pandemic (2020-2022)
 - 2022-2023 data suggest return to pre-pandemic seasonality

1. CDC. Respiratory virus activity levels. <https://www.cdc.gov/respiratory-viruses/data-research/dashboard/activity-levels.html>; 2. Hamid S, et al. *MMWR Morb Mortal Wkly Rep.* 2023;72(14):335-361.

Percent of Tests Positive for Respiratory Viruses, October 2022 to March 2024¹

Weekly percent of tests positive for the viruses that cause COVID-19, influenza, and RSV at the national level. Preliminary data are shaded in gray.



Data Sources

- COVID-19, RSV: National Respiratory and Enteric Virus Surveillance System (NREVSS)
- Influenza: NREVSS and U.S. World Health Organization collaborating laboratories



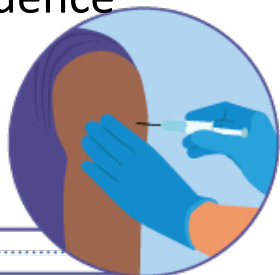
RSV Symptoms and Disease Course in Older Adults

Most Common RSV Symptoms in Older Adults, Present in >50% of Patients¹

| Symptoms: Upper respiratory tract infection | Symptoms: Lower respiratory tract infection | Other symptoms |
|---|---|-------------------|
| Runny nose | Cough | Fatigue/ weakness |
| Nasal congestion | Sputum production | Lethargy |
| Sore throat | Dyspnea | Headache |
| | Wheezing | |
| | Tachypnea | |

- Symptoms of respiratory disease caused by different viruses are similar^{1,2}
- Time to care/diagnosis is longer than for infants – symptoms often attributed to another cause (e.g., influenza)²
- Factors associated with increased risk of severe illness³⁻⁵
 - Older age (>60-65 years)
 - Chronic heart or lung disease
 - Weakened immune system (e.g., patients taking immunosuppressive medications for cancer, transplant)
 - Nursing home/long-term care facility residence

1. Kenmoe S, Nair H. *Curr Opin Infect Dis.* 2024;37:129-136; 2. Kaler J, et al. *Cureus.* 2023;15(3):e36342; 3. Hu M, et al. *Physiol Rev.* 2020;100:1527-1594; 4. CDC. <https://www.cdc.gov/rsv/high-risk/older-adults.html>; 5. Melgar M, et al. *MMWR Morb Mortal Wkly Rep.* 2023;72(29):793-801.



RSV Diagnosis and Treatment in Adults

Identifying RSV as the Cause of Respiratory Illness

- Often unrecognized¹
 - Indistinguishable from other viral respiratory infections – testing needed to confirm
 - People often admitted to the hospital for exacerbations of complications, even when RSV may be precipitating cause
 - No motivation to test because no treatments are available
- Respiratory pathogen panels available^{2,3}
 - RSV, influenza, and SARS-CoV-2
 - Also available in at-home versions

Treatment

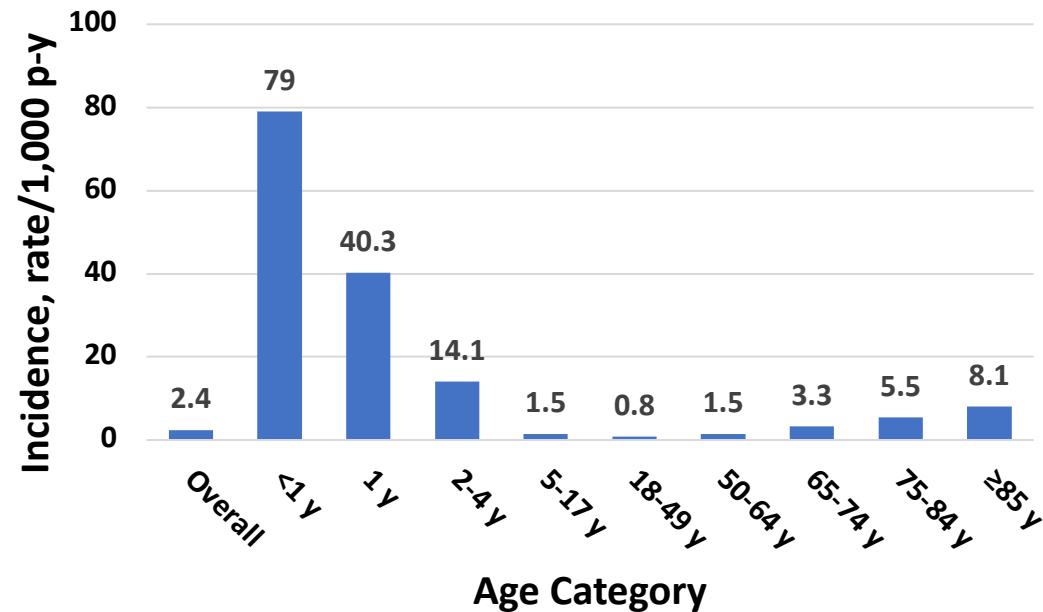
- No specific treatments^{4,5}
- Supportive care⁴⁻⁶
 - Fever/pain management
 - Hydration
 - Management of exacerbated illness (e.g., change in medication dose for asthma, COPD)
 - Oxygen
 - Supportive therapy (e.g., mucus clearance)
- Ribavirin (aerosolized)
 - Approved only for hospitalized infants/young children⁷
 - Not recommended for routine use⁸

1. Hurley L. <https://clinicaloptions.com/CE-CME-program/rsv-in-older-adults/100002577>; 2. NLM. Medline Plus. <https://medlineplus.gov/lab-tests/respiratory-syncytial-virus-rsv-tests/>; 3. Boukli N, et al. *Front Med (Lausanne)*. 2023;10:1161268; 4. American Lung Association. <https://www.lung.org/lung-health-diseases/lung-disease-lookup/rsv/rsv-in-adults>; 5. Hu M, et al. *Physiol Rev*. 2020;100:1527-1594; 6. Cleveland Clinic. <https://my.clevelandclinic.org/health/diseases/rsv-in-adults>; 7. Ribavirin for inhalation. Prescribing information. <https://pi.bauschhealth.com/globalassets/BHC/PI/Virazole-PI.pdf>.; 8. American Academy of Pediatrics. <https://publications.aap.org/redbook/book/347/chapter-abstract/5755493/Respiratory-Syncytial-Virus?redirectedFrom=fulltext>.



Relative RSV Incidence by Age

Average Incidence of RSV-Associated Disease by Age, 2008-2014



- Seven-year study (U.S. claims database analysis)
- Relatively stable year-to-year incidence by age
- Each year, 43%-48% of cases were infants <1 year old
- Over the study
 - 85% of cases were in children ≤17 years old
 - 12% of cases were in adults 18-64 years old
 - 3% of cases were in adults ≥65 years old



RSV Infection in Children and Older Adults

Incidence in Infants and Children

- 69% with illness by 1 year and 97% with illness by 2 years¹
- In children under 5 y, associated with²
 - 15% of office visits for ARI
 - 20% of hospitalizations for ARI

Incidence in Older Adults

- Annual rates of illness 3%-7% in healthy older adults³
- In adults ≥60-65 y, associated with
 - 11% of outpatient visits for ARI⁴
 - 6% of hospitalizations for ARI⁵

- Studies demonstrate increasing incidence of RSV illness with age in people ≥65 years old^{6,7}
- Infection can recur throughout life^{7,8}

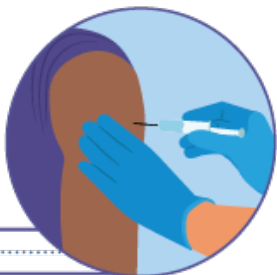
ARI = acute respiratory infection; LRTI = lower respiratory tract infection.

1. Glezen WP, et al. *Am J Dis Child*. 1986;140(6):543-546; 2. Hall CB, et al. *N Engl J Med*. 2009;360(6):588-598; 3. Falsey AR, et al. *N Engl J Med*. 2005;352:1749-1759; 4. Belongia EA, et al. *Open Forum Infect Dis*. 2018;5(12):ofy316; 5. Nowalk MP, et al. *Vaccine*. 2022;40(31):4121-4127; 6. Tong S, et al. *J Glob Health*. 2020;10(2):020422. doi: 10.7189/jogh.10.020422; 7. Kenmoe S, Nair H. *Curr Opin Infect Dis*. 2024;37:129-136; 8. Hu M, et al. *Physiol Rev*. 2020;100:1527-1594.



Rates of RSV Illness in Older Adults Are Likely Underestimated

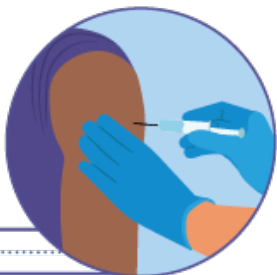
- Low testing rates may contribute – in older patients hospitalized for LRTI in the US from 2016-2019¹:
 - Only 4.3% with LRTI were tested for RSV
 - Most hospitals performed testing in <25% of LRTI patients
- Cases may not be appropriately attributed to RSV²
- Increased RSV rates have been reported in older adults as use of RT-PCR tests has become more common^{2,3}



Section Summary

You have a patient in a long-term rehabilitation facility, and his wife would like more information on RSV because several other residents have been diagnosed with RSV disease. Here are some key points:

- RSV is highly transmissible.
- Symptoms don't distinguish RSV illness from other respiratory infections – they are similar.
- Symptoms of RSV-associated lower respiratory tract disease include cough, sputum production, dyspnea, wheezing, and tachypnea.
- Incidence of RSV illness increases with age.
- Risk factors for severe RSV illness include age ≥ 65 y, cardiopulmonary disease, and weakened immune system.



Clinical and Public Health Impact of RSV in the Adult Population



Older Adults Are More Susceptible to Severe RSV Disease



- Age-related changes can increase risk of complications with viral infections
 - Decreases in protective mucus, lung compliance, elastin¹
 - Declining immune system function/immunosenescence^{1,2}
 - Increased presence of certain chronic conditions³
 - Greater potential for exacerbation of chronic conditions, such as cardiopulmonary diseases¹
- Medical conditions and characteristics associated with increased risk for RSV-associated hospitalization in adults⁴
 - COPD
 - Asthma
 - CHF/CAD
 - Cerebrovascular disease
 - Diabetes mellitus
 - Chronic kidney disease
 - Residence in a long-term care facility
 - Frailty
 - Advanced age (≥75 years)

CAD = coronary artery disease; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; RSV = respiratory syncytial virus.

1. Kaler J, et al. *Cureus*. 2023;15(3):e36342; 2. Hu M, et al. *Physiol Rev*. 2020;100:1527-1594; 3. Tong S, et al. *J Glob Health*. 2020;10(2):020422; 4. Melgar M, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72(29):793-801.



RSV-Associated Hospitalization and Death: Older Adults and Young Children in the U.S.¹



| Outcome | Older Adults, ≥65 years of age | Young Children, <5 years of age |
|-----------------------|-----------------------------------|------------------------------------|
| Hospitalizations/year | ≈177,000 ^{1,2} | 58,000 – 80,000 ^{1,3,4} |
| Deaths/year | ≈14,000 ^{1,2} | 100 – 300 ^{1,5,6} |

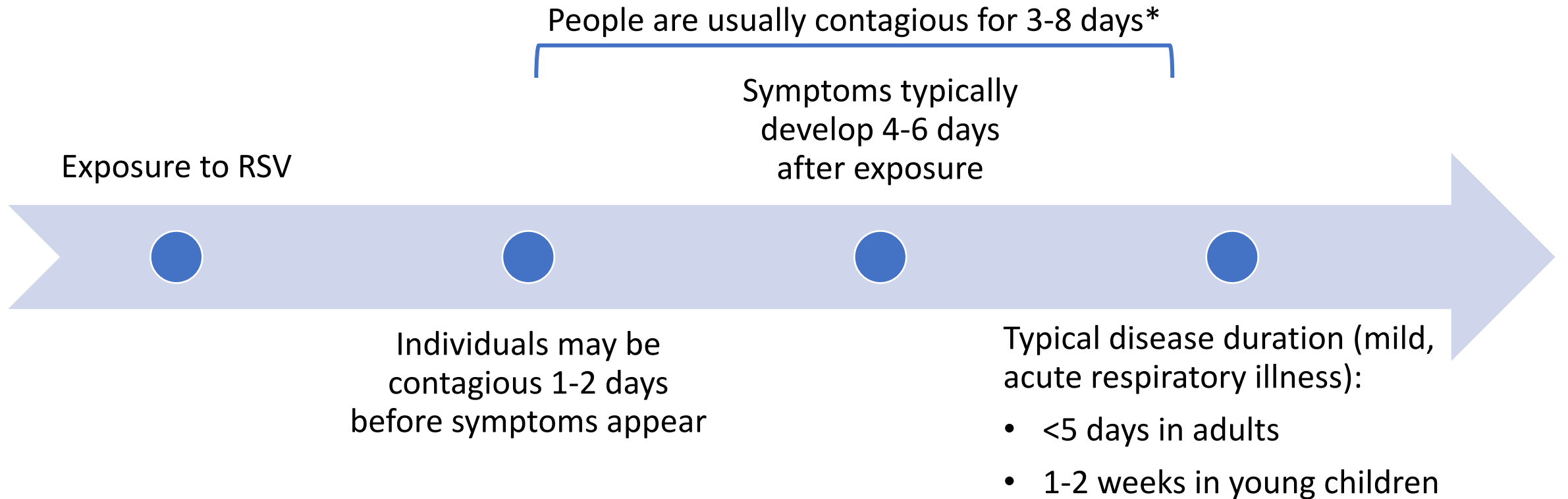
In the U.S.⁷

- Highest infection rates are in infants and young children
- Highest mortality is among older adults

1. Havers F. Presented at the Advisory Committee on Immunization Practices meeting on June 23, 2022. <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-06-22-23/04-RSV-Havers-508.pdf>; 2. Falsey AR, et al. *N Engl J Med.* 2005;352(17):1749-1759; 3. Hall CB, et al. *N Engl J Med.* 2009;360(6):588-598; 4. McLaughlin JM, et al. *J Infect Dis.* 2022;225(6):1100-1111; 5. Thompson WW, et al. *JAMA,* 2003;289(2):179-186; 6. Hansen CL, et al. *JAMA Netw Open.* 2022;5(2):e220527; 7. Tong S, et al. *J Glob Health.* 2020;10(2):020422.



Timing of RSV Infection¹



*Some people, including infants and people with weakened immune systems (e.g., individuals on immunosuppressant medications) can spread the virus for up to 4 weeks, even if they no longer have symptoms^{1,2}

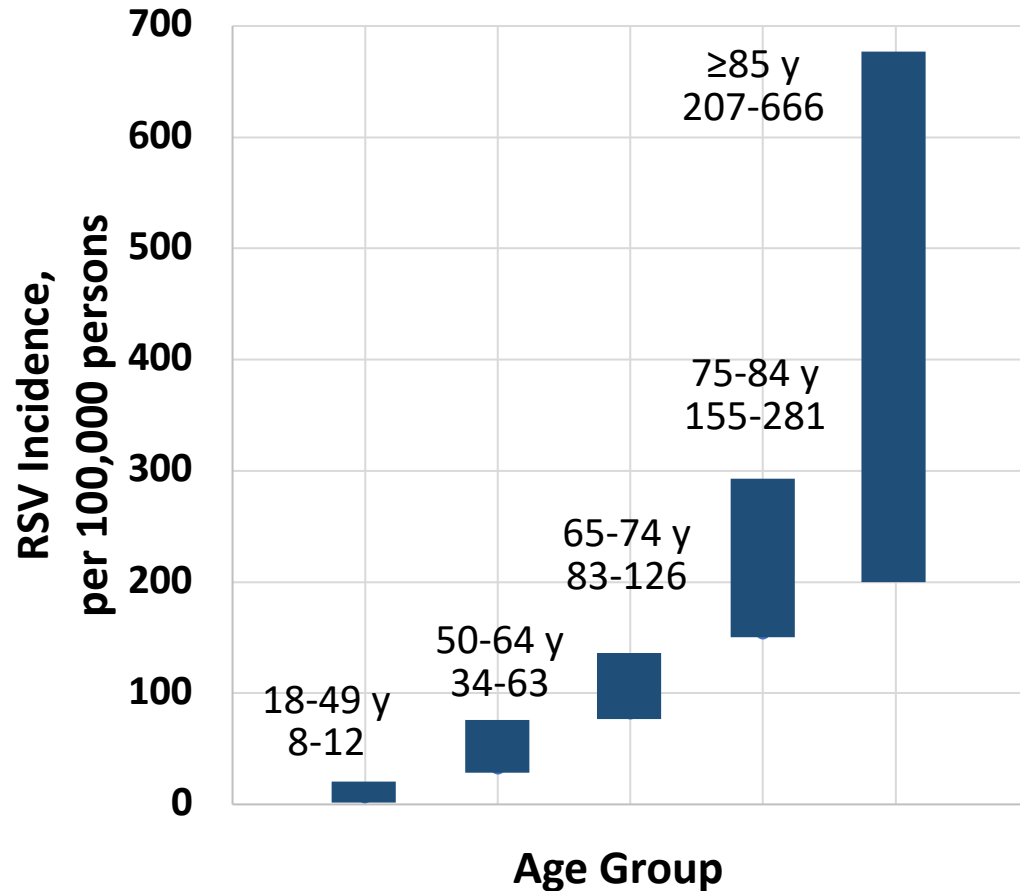
1. CDC. Respiratory syncytial virus infection (RSV): Symptoms & Care, Transmission, Healthcare Professionals. <https://www.cdc.gov/rsv/index.html>;
2. Melgar M, et al. *MMWR Morb Mortal Wkly Rep.* 2023;72(29):793-801.





RSV and Hospitalizations Among U.S. Adults

Results of RSV Surveillance in Hospitalized Patients (NY, USA, 2017-2020)¹



Characteristics and Outcomes Among Adults ≥60 Years Old Hospitalized with RSV (RSV-NET, July 2022-June 2023)²

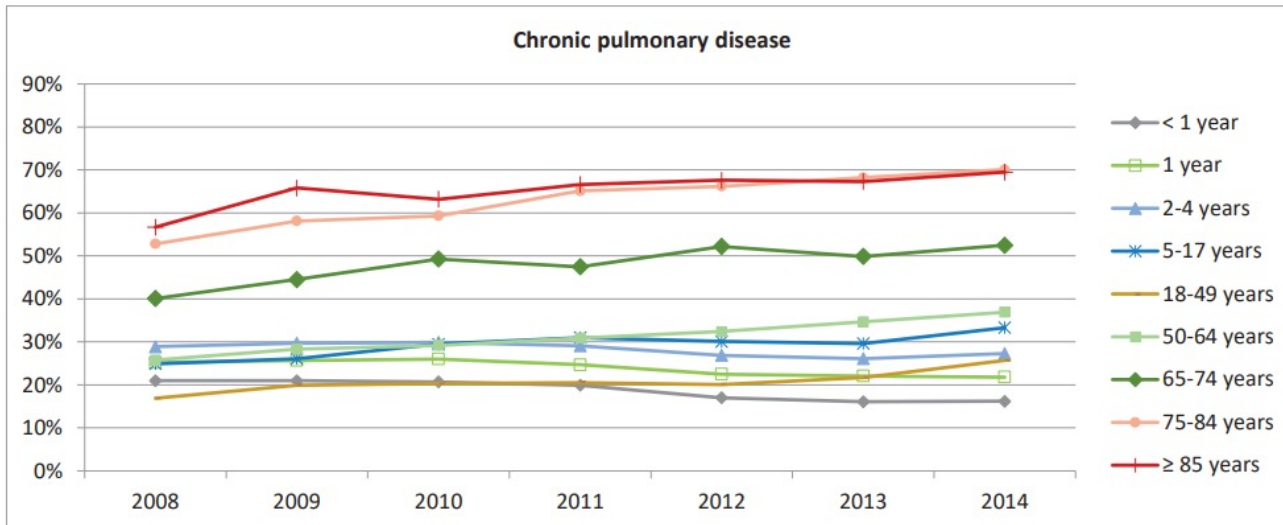
- Over 75 years of age: 54.1%
- Underlying medical condition: 95.5%
- Intensive care admission: 17.0%
- Mechanical ventilation: 4.8%
- Death: 4.7%

RSV-NET, Respiratory Syncytial Virus-Associated Hospitalization Surveillance Network.

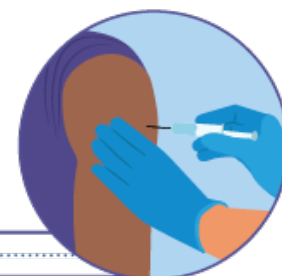
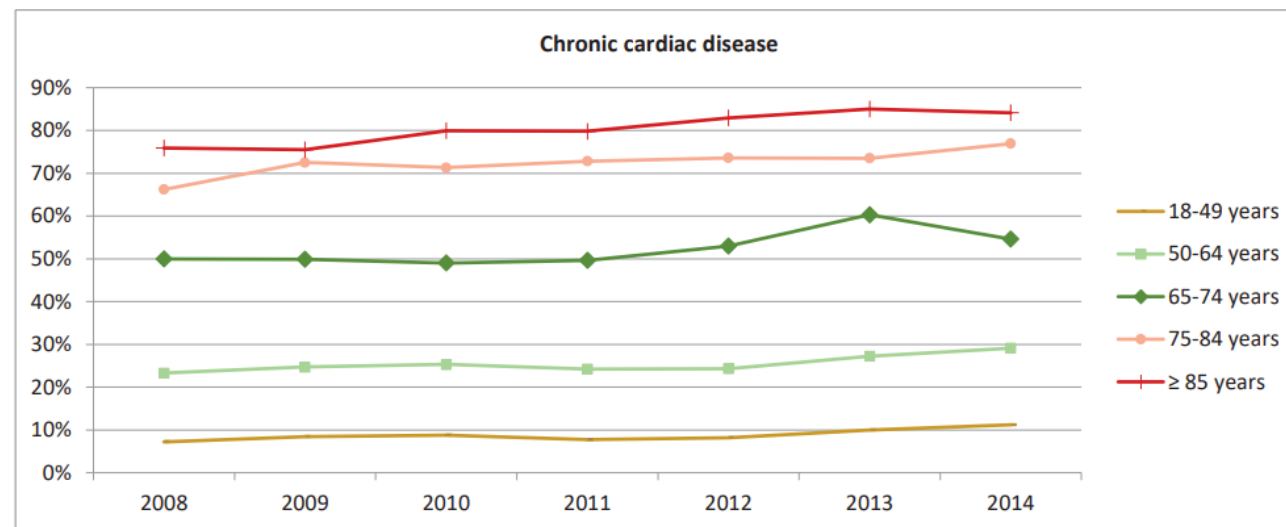
1. Branche A, et al. *Clin Infect Dis*. 2022;74(6):1004-1011; 2. Havers FP, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72(40):1075-1082.



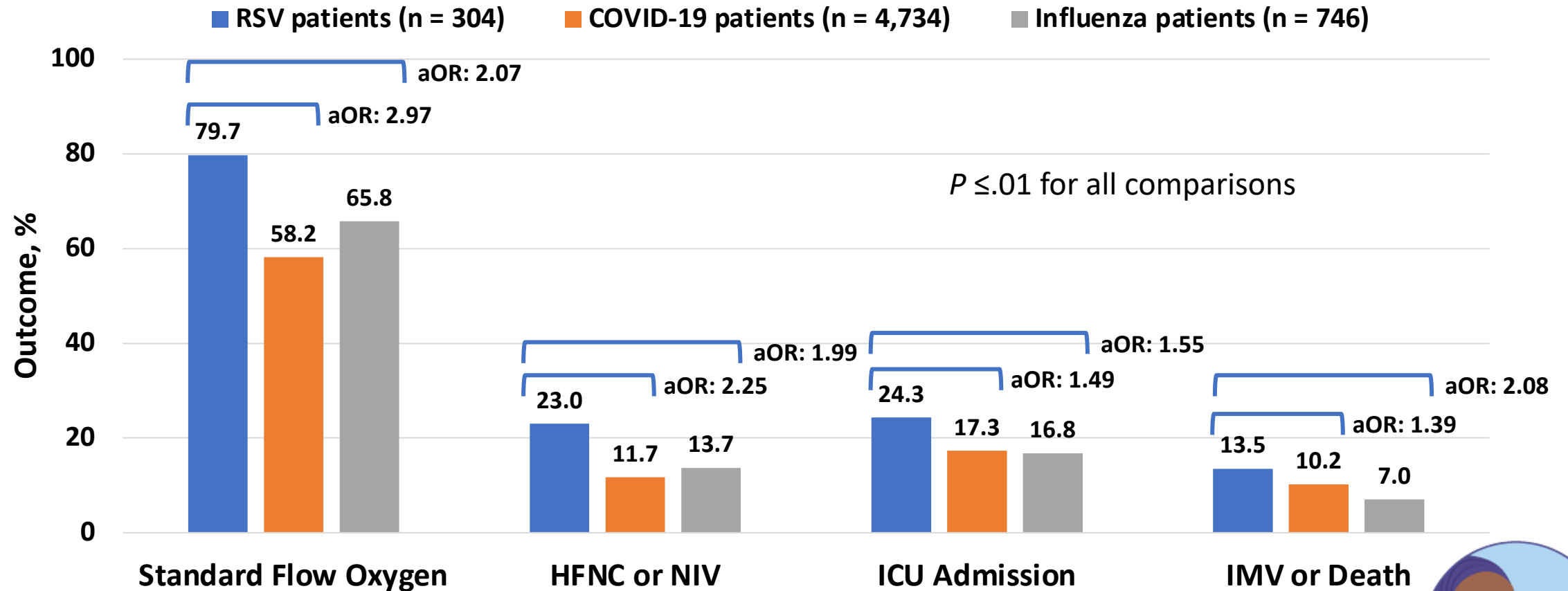
Relationship Between High-Risk Conditions and Age in RSV Patients



- Results of a U.S. claims database analysis (2008-2014) of RSV episodes
- RSV episode:
 - Inpatient admission with principal diagnosis
 - Outpatient visit with diagnosis (first or secondary)

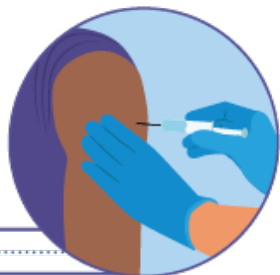


Outcomes in Hospitalized Older Adults With RSV, COVID-19, or Influenza (February 2022 – May 2023)



aOR = adjusted odds ratio; COVID = corona virus disease; HFNC – high-flow nasal cannula; ICU = intensive care unit; IMV = invasive mechanical ventilation; NIV – noninvasive ventilation; RSV = respiratory syncytial virus.

Surie D, et al. *MMWR Morb Mortal Wkly Rep.* 2023;72:1083-1088.



Medical Resource Utilization During Hospitalization and 3-Month Follow-up: RSV vs Influenza

| Resource Utilization During Hospitalization | RSV Patients With Core Risk Factors ^a (n = 99) | Influenza Patients With Core Risk Factors ^a (n = 153) | Resource Utilization During 3-Month Follow-up | RSV Patients With Core Risk Factors ^a (n = 99) | Influenza Patients With Core Risk Factors ^a (n = 153) |
|---|---|--|---|---|--|
| Mean stay, days | 5.7 | 4.7 | Readmission, % | 13.4 | 11.9 |
| Stay >3 days, % | 69.7 | 56.2 | Antibiotic use ^b , % | 17.1 | 9.5 |
| O ₂ supplementation, % | 79.8 | 59.5 | Antitussive use ^b , % | 9.8 | 3.2 |
| ICU stay, % | 8.1 | 5.2 | Bronchodilator use ^b , % | 42.7 | 38.1 |
| | | | Inhaled steroid use ^b , % | 39.0 | 25.4 |
| | | | Systemic steroid use ^b , % | 19.5 | 14.3 |

^aCore risk factors for severe disease: age ≥65 years of age, chronic heart or renal disease, chronic obstructive pulmonary disease, asthma; ^bPost-discharge. Hartnett J, et al. *Influenza Other Respir Viruses*. 2022;16:906-915.



RSV Illness in Long-Term Care Facilities

Adults ≥ 60 years old residing in a long-term care facility have been found to be high risk for RSV complications.¹

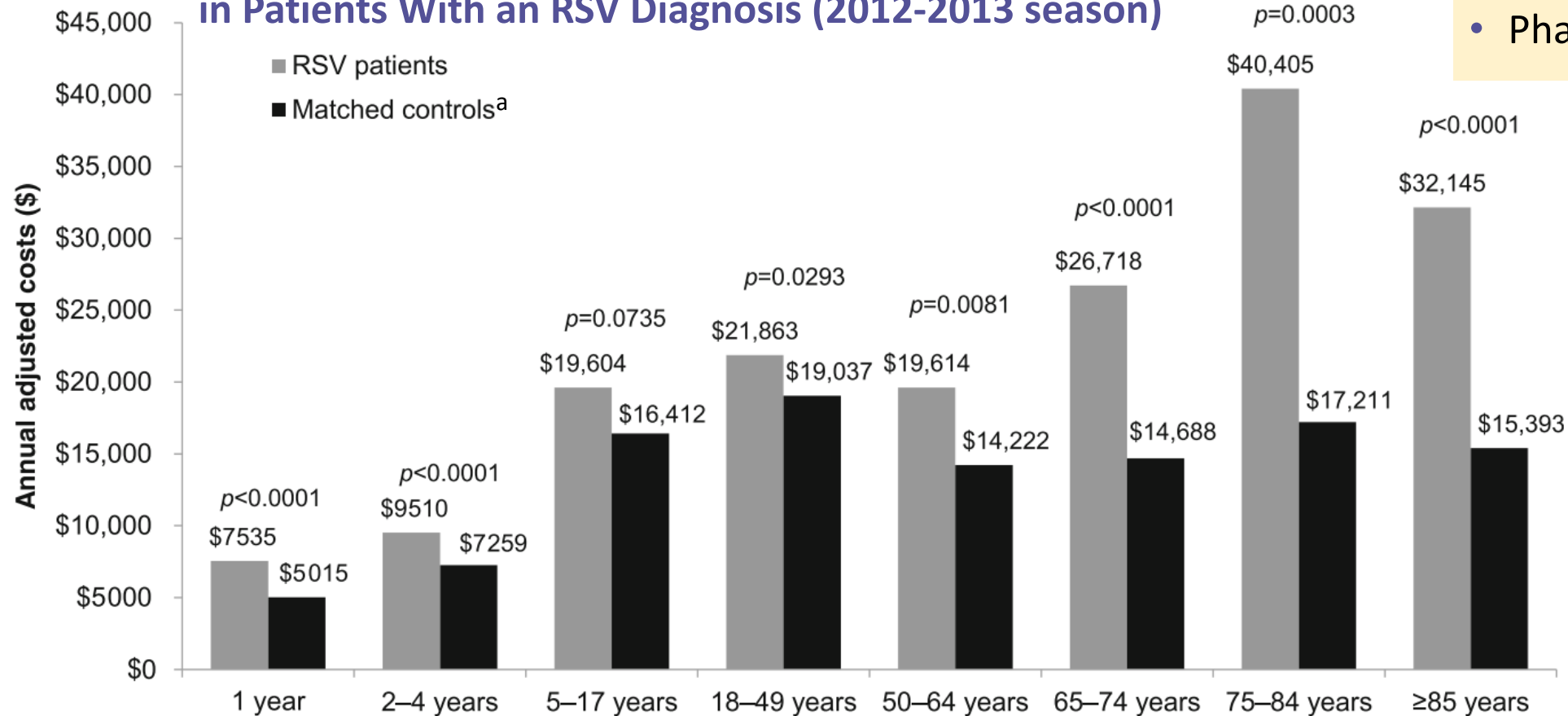
17.2% of RSV hospitalizations in adults ≥ 60 years old occurred in long-term care facility residents.¹

In December 2023, vaccine coverage among reporting nursing homes was 9.8% for RSV and 72.0% for influenza.²



US RSV Economic Burden

Adjusted Annual Healthcare Costs for Index Event and 12-Month Follow-up (2014 US Dollars) in Patients With an RSV Diagnosis (2012-2013 season)



Costs include

- Inpatient visits
- ED and urgent care visits
- Ambulatory visits
- Outpatient visits
- Pharmacy prescriptions

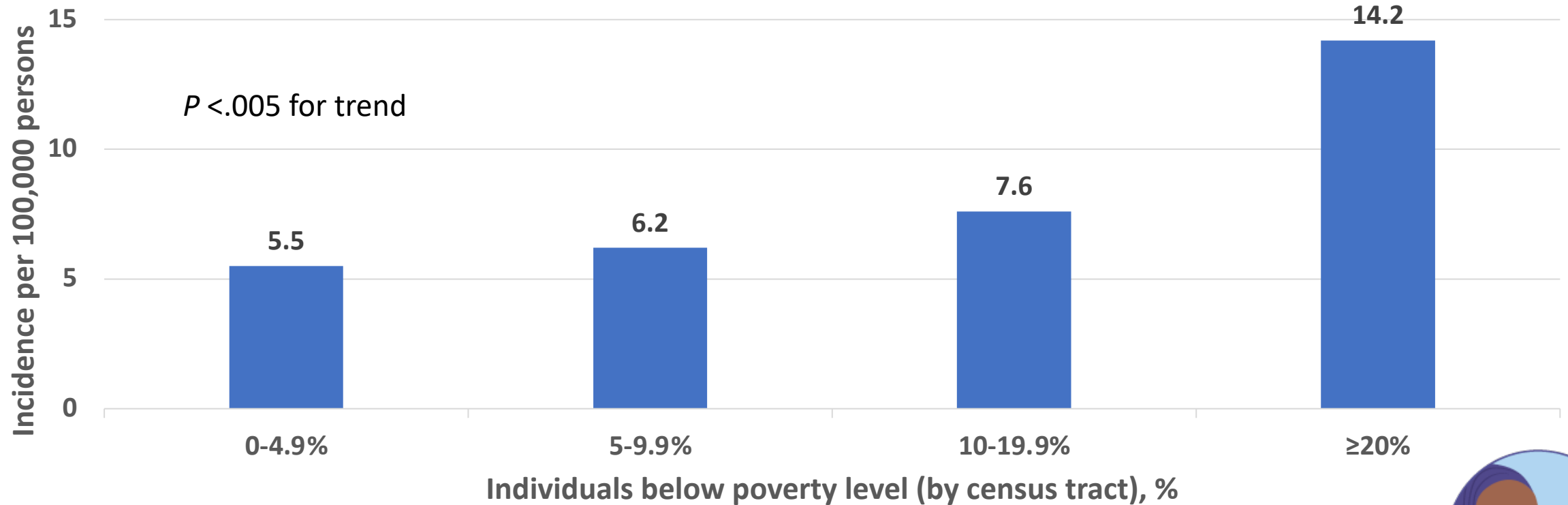
^aPatients without RSV matched based on age, sex, region, health plan, and index date.



Relationship Between RSV-Associated Hospitalizations and Poverty Level in Adults



Age-adjusted Incidence of RSV-Associated Hospitalization in Adults by Census-tract Poverty Level



Case Consideration/Section Summary

One of your patients, a 74-year-old grandfather of 2 kindergarteners, says he doesn't understand why you've recommended an RSV vaccine for him because RSV is a kid's disease. You might ask him to consider the following points:

- While RSV illness rates are highest in children <4 years old, risk for RSV illness is higher for people over 60 years of age than for older children and younger adults
- More hospitalizations and deaths attributable to RSV occur in adults over 60 years of age than in children under 5 years of age
- Adults with high-risk medical conditions are more likely to develop RSV complications
- RSV illness can be expensive in older adults



Preventing RSV in Older Adults: Focus on the Role of Vaccination



Older Adults and RSV Prevention

With no specific treatments, prevention is important.^{1,2}

- RSV infections usually go away on their own, but they can cause severe illness¹
- No treatments for RSV are licensed for use in adults¹⁻³
- Treatment is supportive¹⁻⁴


Approaches for RSV Prevention: Points for Patients

- Everyday measures you already know (e.g., stay home when sick, cover coughs/sneezes, wash hands often with soap)⁵
- Other steps (e.g., actions for cleaner air, masking, physical distancing)⁶
- Immunization⁵⁻⁸
 - Active: vaccines now available for older adults – but NOT approved for pediatric use
 - Passive:
 - » Immunoprophylaxis (monoclonal antibodies) for infants and young children
 - » Maternal prenatal vaccination

1. CDC. <https://www.cdc.gov/rsv/about/symptoms.html>; 2. Hu M, et al. *Physiol Rev.* 2020;100:1527-1594; 3. CDC. <https://www.cdc.gov/rsv/about/prevention.html>; 3. American Lung Association. <https://www.lung.org/lung-health-diseases/lung-disease-lookup/rsv/rsv-in-adults>; 4. Cleveland Clinic. <https://my.clevelandclinic.org/health/diseases/rsv-in-adults>; 5. CDC. <https://www.cdc.gov/rsv/about/prevention.html>; 6. CDC. <https://www.cdc.gov/respiratory-viruses/prevention/index.html>; 7. GSK. https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Arexvy/pdf/AREXVY.PDF; 8. Pfizer. <https://labeling.pfizer.com/ShowLabeling.aspx?id=19589>



RSV Vaccines (Active Immunization) for Adults

| FDA-Approved Vaccines ¹ | Population | Indication(s) |
|---|------------------------------------|---|
| GSK ² (RSV vaccine, Adjuvanted) | Older adults ^{1,2} | Active immunization for prevention of LRTD caused by RSV in individuals ≥60 years of age ² |
| Pfizer ³ (RSV vaccine) | Older adults ^{1,3} | Active immunization for prevention of LRTD caused by RSV in individuals ≥60 years of age ³ |
|  | Maternal ^{1,3} | Active immunization of pregnant individuals at 32-36 weeks gestational age for prevention of LRTD caused by RSV in infants from birth through 6 months of age ³ |

Pending Decisions

- Moderna mRNA-1345 (FDA and others globally): RSV-associated LRTD and ARD in adults ≥60 years old (Priority Review; FDA decision anticipated April 2024)⁴
- GSK RSVPreF3 (FDA): adults aged 50-59 at increased risk with underlying medical conditions (Priority Review; FDA decision anticipated 06/07/2024)⁵

ARD = acute respiratory disease; LRTD = lower respiratory tract disease.

1. PATH. <https://www.path.org/our-impact/resources/rsv-vaccine-and-mab-snapshot/>;

2. GSK. https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Arexvy/pdf/AREXVY.PDF; 3. Pfizer.

<https://labeling.pfizer.com/ShowLabeling.aspx?id=19589>; 4. Moderna. <https://finance.yahoo.com/news/moderna-expands-field-mrna-medicine-103000511.html>;

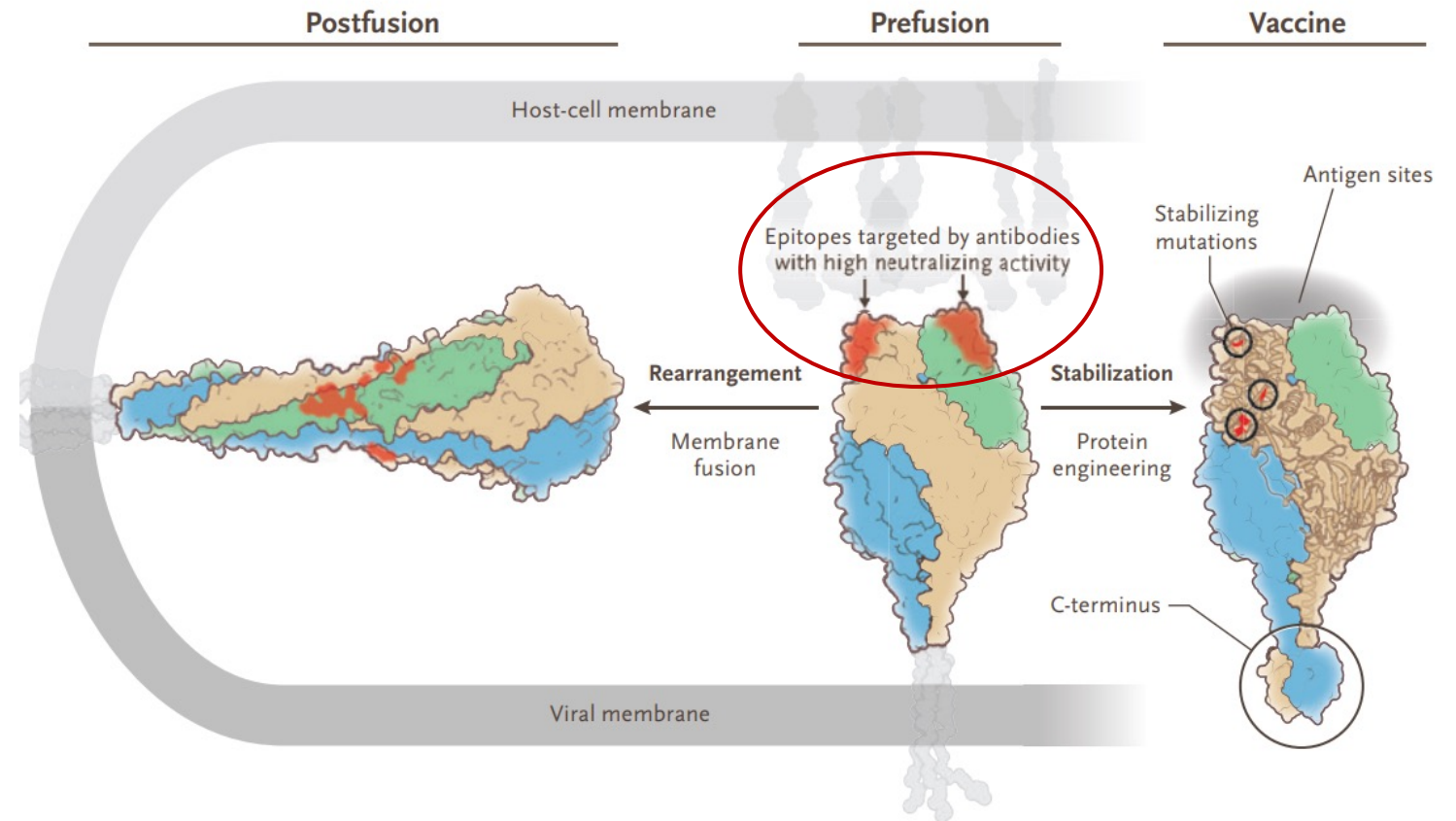
5. GSK. <https://www.gsk.com/media/10948/press-release-arexvy-file-acceptance-us-50-59.pdf>.



How Do the Vaccines Work?

RSV Fusion Glycoprotein F⁴

- Vaccines approved or submitted for approval contain recombinant protein antigen components OR mRNA encoding antigen
 - GSK: RSV preF3 protein¹
 - Pfizer: RSV preF A and RSV preF B proteins²
 - Moderna: mRNA encoding RSV preF A^{3,a}
- In facilitating fusion of virus and cell membranes, RSV prefusion F (preF) protein changes to the postfusion F (postF) conformation⁴
- “PreF” is more immunogenic for production of neutralizing antibodies than “postF”⁵



^a Not FDA-approved.

1. GSK. https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Arexvy/pdf/AREXVY.PDF;
2. Pfizer. <https://labeling.pfizer.com/ShowLabeling.aspx?id=19589>; 3. Wilson E, et al. *N Engl J Med.* 2023;389 (24):33-44;
4. Hu M, et al. *Physiol Rev.* 2020;100:1527-1594; 5. Graham BS. *N Engl J Med.* 2023;388(7):579-581.

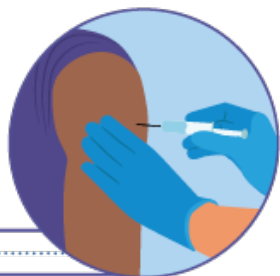


Features of Published Phase 3 Efficacy Trials for RSV Vaccines for Older Adults

| Feature | RSVPreF3 OA (GSK) ¹ AReSVi-006 (NCT04886596) | RSVpreF (Pfizer) ² RENOIR (NCT05035212) | mRNA-1345 (Moderna) ^{3,a} ConquerRSV (NCT05127434) |
|------------------------------------|--|--|--|
| Control | Placebo | Placebo | Placebo |
| Participants, N | 24,966 | 34,284 | 35,541 |
| Randomization ratio | 1:1 (single vaccine dose:placebo) | 1:1 (single vaccine dose:placebo) | 1:1 (single vaccine dose:placebo) |
| Mean age, y | 69.5 | 68.3 | 68.1 |
| High risk, % | Vaccine: 33.9 ^b Placebo: 33.1 ^b | Vaccine: 51.5 ^c Placebo: 51.7 ^c | Vaccine: 6.9 ^d Placebo: 7.0 ^d |
| Mean follow-up | 6.7 months | 7 months | 112 days |
| Primary endpoint(s)/ outcome(s) | Efficacy preventing RSV-related LRT disease, confirmed by RT-PCR | Efficacy preventing RSV-associated LRT illness (confirmed by RT-PCR) with ≥ 2 or ≥ 3 signs or symptoms | Efficacy preventing RSV-associated LRT disease (confirmed by RT-PCR) with ≥ 2 or ≥ 3 signs or symptoms |

^a Phase 2/3, not FDA-approved; ^bBased on Charlson comorbidity index; ^cBased on presence of ≥ 1 prespecified, high-risk condition; ^d Risk factors for LRT disease (CHF, COPD, or both). CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; LRT = lower respiratory tract; RSV = respiratory syncytial virus.

1. Papi A, et al. *N Engl J Med.* 2023;388(7):595-560; 2. Walsh EE, et al. *N Engl J Med.* 2023;388(16):1465-1477; 3. Wilson E, et al. *N Engl J Med.* 2023;389(24): 2233-2244.



GSK RSVPreF3 OA Efficacy: Incidence of RSV-Related Lower Respiratory Tract Disease (LRTD)¹

Efficacy against LRTD¹
82.6% (96.95% CI, 57.9 to 94.1)

Episodes

- Vaccine group: 7/12,466
- Placebo group: 40/12,494

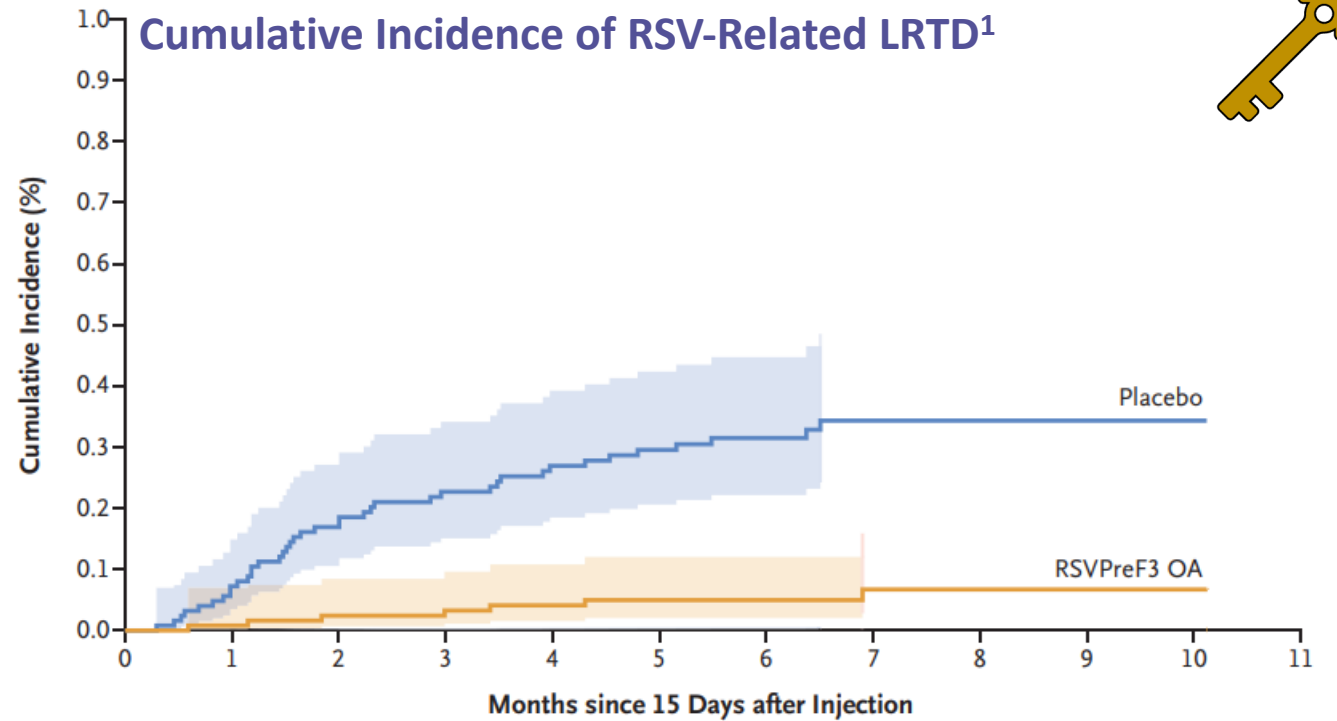
(Primary objective met)

Efficacy against severe LRTD¹
94.1% (95% CI, 62.4 to 99.9)

Episodes

- Vaccine group: 1/12,466
- Placebo group: 17/12,494

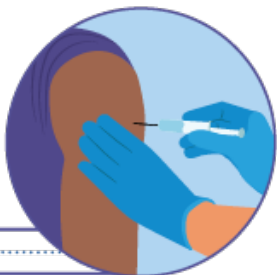
1. Papi A, et al. *N Engl J Med.* 2023;388(7):595-560; 2. Melgar M. Presented at the Advisory Committee on Immunization Practices meeting on February 23, 2023. <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-02/slides-02-23/rsv-adults-04-melgar-508.pdf>



| No. at Risk | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
|-------------------------|--------|--------|--------|--------|--------|--------|------|------|------|-----|----|----|
| Placebo | 12,494 | 12,403 | 12,290 | 11,887 | 11,640 | 11,022 | 8291 | 5464 | 2709 | 559 | 2 | 0 |
| RSVPreF3 OA | 12,466 | 12,392 | 12,286 | 11,892 | 11,655 | 11,046 | 8320 | 5495 | 2727 | 571 | 2 | 0 |
| Cumulative No. of Cases | | | | | | | | | | | | |
| Placebo | 0 | 9 | 21 | 28 | 33 | 36 | 38 | 40 | 40 | 40 | 40 | 40 |
| RSVPreF3 OA | 0 | 1 | 3 | 4 | 5 | 6 | 6 | 7 | 7 | 7 | 7 | 7 |

In adults ≥60 years old, number needed to vaccinate to prevent²:

- 1 outpatient visit = 90
- 1 RSV hospitalization = 1,348
- 1 RSV death = 27,284



GSK RSVPreF3 OA: Safety and Tolerability

- No reported RSV- or treatment-related deaths in the clinical trial¹
- In the exposed group¹
 - More reported adverse events related to treatment for vaccine vs placebo (24.9% vs 5.8%)
 - » Most were due to reactogenicity, such as injection site reaction (pain, erythema swelling) or systemic reactions (fever, headache, fatigue, myalgia, arthralgia)
 - » Most reactogenicity events were mild-to-moderate
 - Serious adverse events were balanced between groups
- Most common ($\geq 10\%$) adverse reactions^{1,2}
 - Local: **injection site pain** (60.9%)
 - Systemic: **fatigue** (33.6%), **myalgia** (28.9%), **headache** (27.2%), **arthralgia** (18.1%)

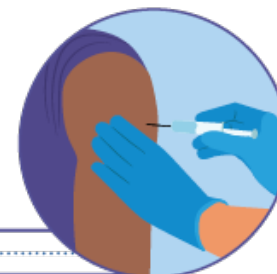
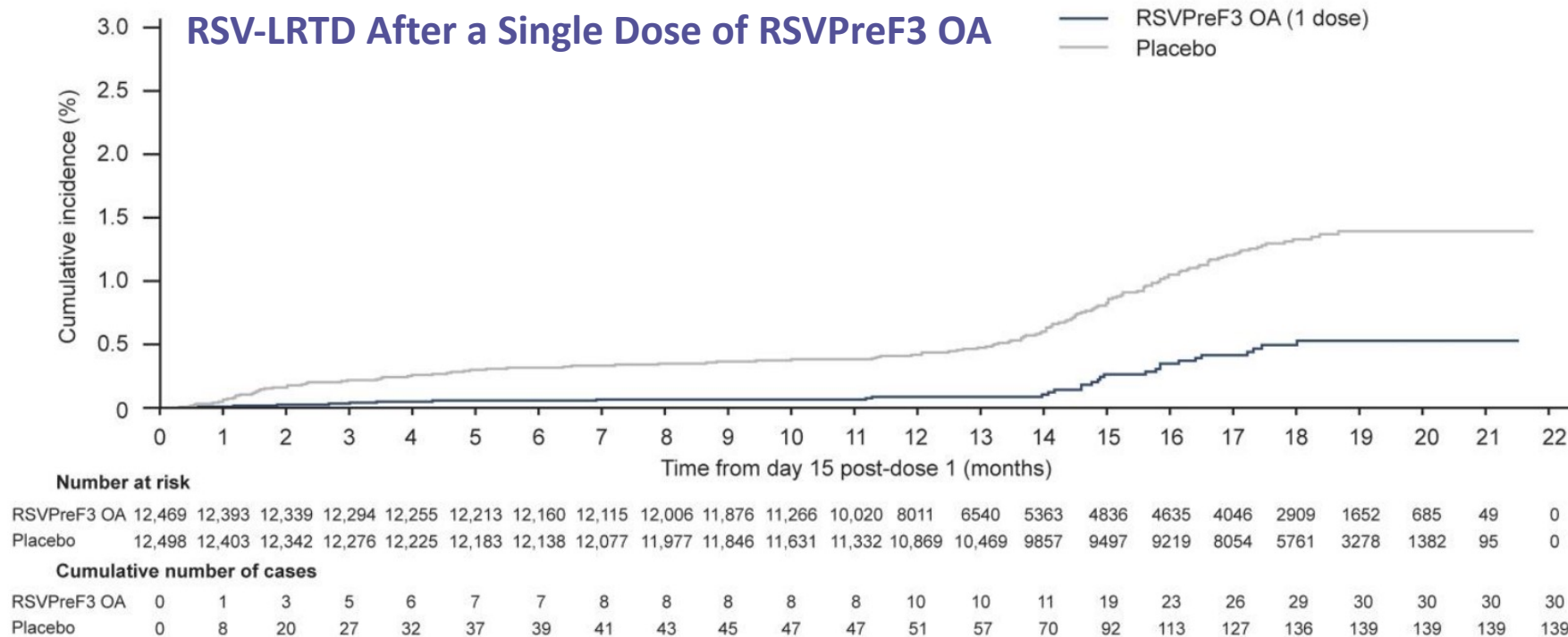
1. Papi A, et al. *N Engl J Med*. 2023;388(7):595-560;

2. GSK. https://gskpro.com/content/dam/global/hcportal/en_US/Prescribing_Information/Arexvy/pdf/AREXVY.PDF.

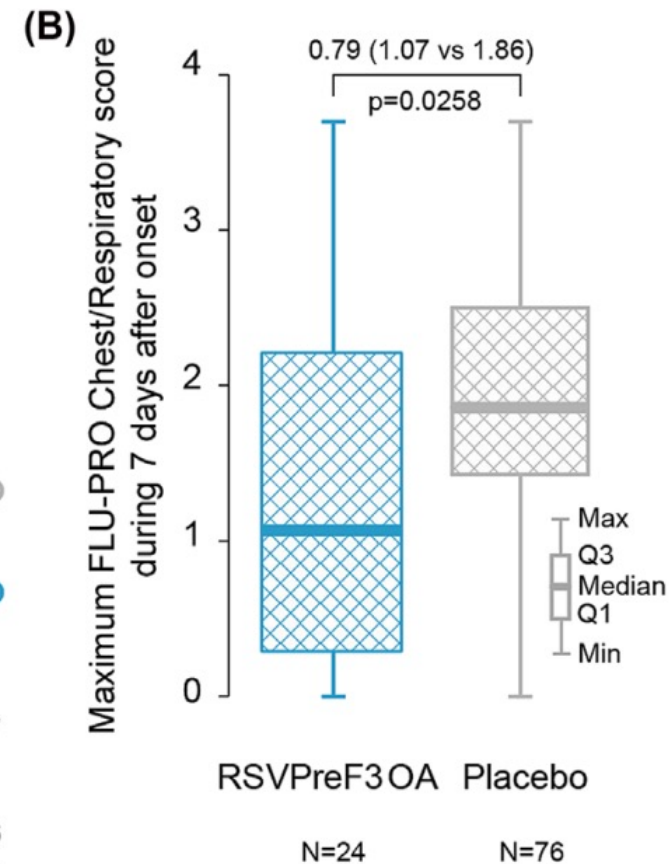
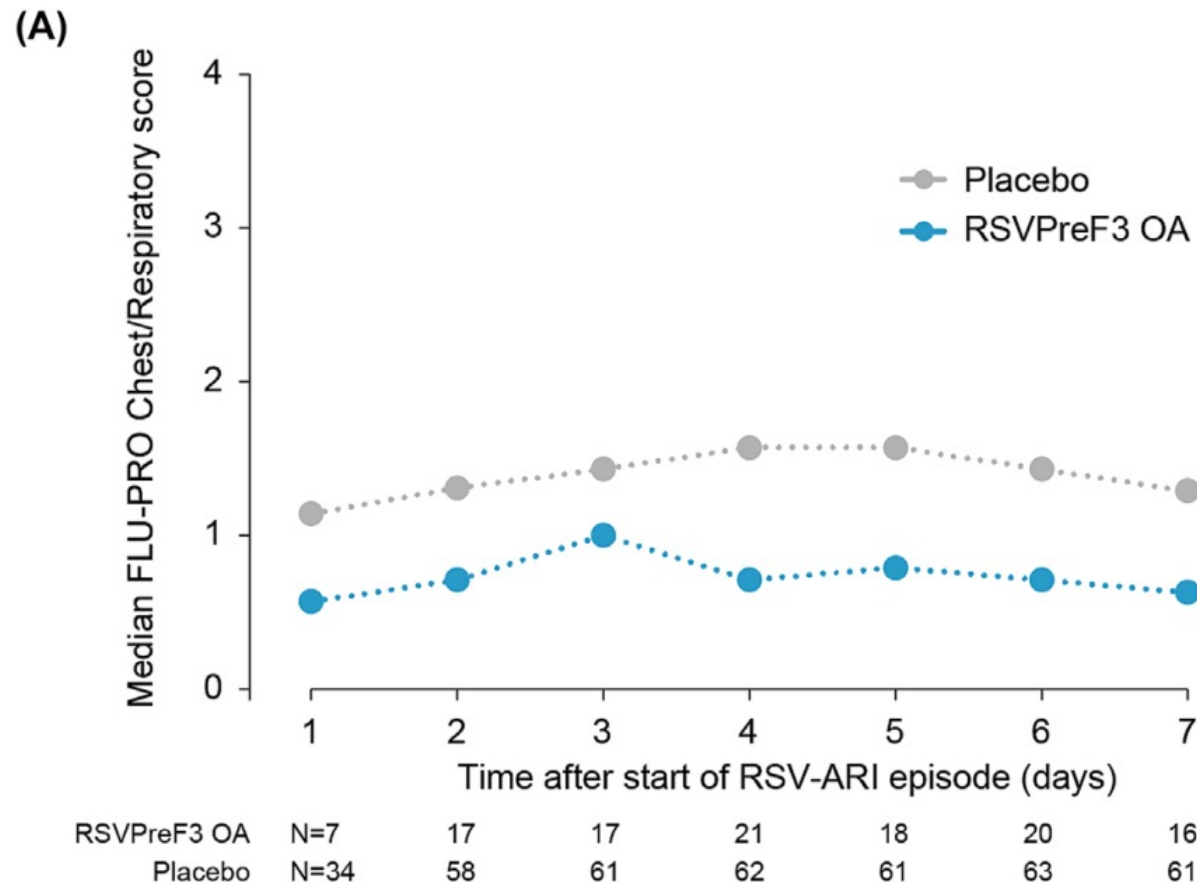


GSK RSVPreF3 OA: Cumulative RSV Lower Respiratory Tract Disease (LRTD) Incidence with One Dose vs Revaccination Over 2 Seasons

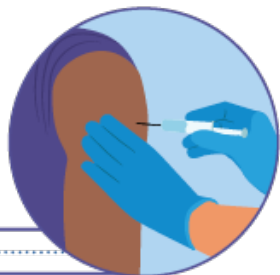
- Efficacy in season 2 was similar with one dose in season 1 and second dose (revaccination) in season 2
- Revaccination within one year does not seem to provide additional efficacy benefit



GSK RSVPreF3 OA: Patient-Reported Improvement in RSV-ARI Symptoms (FLU-PRO Chest/Respiratory Score)



FLU-PRO = InFLUenza Patient-Reported Outcome; RSV-ARI = respiratory syncytial virus-related acute respiratory illness.
Curran D, et al. *Influenza Other Respir Viruses*. 2024;18(2):e13236.



Pfizer RSVpreF Efficacy: Prevention of RSV-Associated Lower Respiratory Tract Infection (LRTI)¹

Efficacy against LRTI with ≥ 2 signs or symptoms¹
66.7% (96.66% CI, 28.8 to 85.8)

Episodes

- **Vaccine group: 11/17,215**
- **Placebo group: 33/17,069**
(Primary end point met)

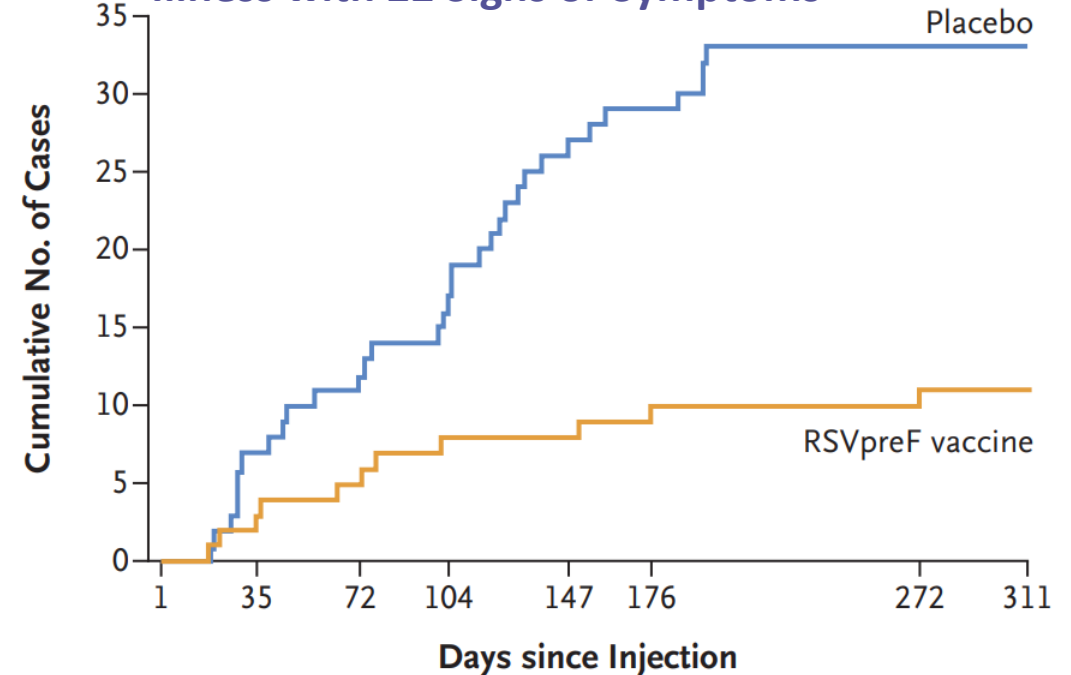
Efficacy against severe LRTI ≥ 3 signs or symptoms¹
85.7% (96.6% CI, 32.0 to 98.7)

Episodes

- **Vaccine group: 2/17,215**
- **Placebo group: 14/17,069**

1. Walsh EE, et al. *N Engl J Med.* 2023;388(16):1465-1477; 2. Melgar M. Presented at the Advisory Committee on Immunization Practices meeting on February 23, 2023. <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-02/slides-02-23/rsv-adults-04-melgar-508.pdf>

**RSV-Associated Lower Respiratory Tract
Illness with ≥ 2 Signs or Symptoms¹**

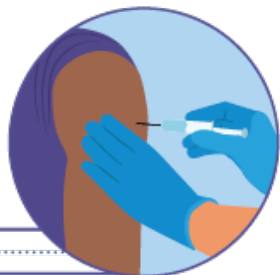


Cumulative No. of Cases

| | | | | | | | | |
|-----------------|---|---|----|----|----|----|----|----|
| Placebo | 0 | 7 | 12 | 17 | 27 | 29 | 33 | 33 |
| RSVpreF vaccine | 0 | 3 | 5 | 8 | 8 | 10 | 11 | 11 |

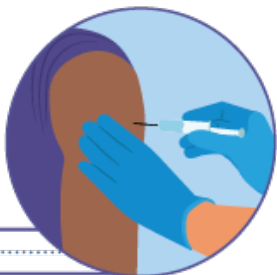
In adults ≥ 60 years old, number needed to vaccinate to prevent²:

- 1 outpatient visit = 103
- 1 RSV hospitalization = 1,567
- 1 RSV death = 31,717



Pfizer RSVpreF: Safety and Tolerability

- No trial intervention-related deaths were reported¹
- In the exposed population
 - More reported local reactions with vaccine vs placebo (12% vs 7%)
 - Similar systemic event for vaccine vs placebo (27% vs 26%)
 - Balance in serious adverse events between groups (2.3% in each group)
- Most common ($\geq 10\%$) adverse reactions^{1,2}
 - Older individuals: fatigue (15.5%), headache (12.8%), injection site pain (10.5%), muscle pain (10.1%)
 - Pregnant individuals: injection site pain (40.6%), headache (31%), muscle pain (26.5%), nausea (20%)



Moderna mRNA-1345^a: Prevention of RSV-Associated Lower Respiratory Tract Disease (LRTD)

Efficacy against LRTD with ≥ 2 signs or symptoms

83.7% (95.88% CI, 66.0 to 92.2)

Episodes

- Vaccine group: 9/17,572
- Placebo group: 55/17,516

Efficacy against severe LRTD ≥ 3 signs or symptoms

82.4% (96.36% CI, 34.8 to 95.3)

Episodes

- Vaccine group: 3/17,572
- Placebo group: 17/17,516

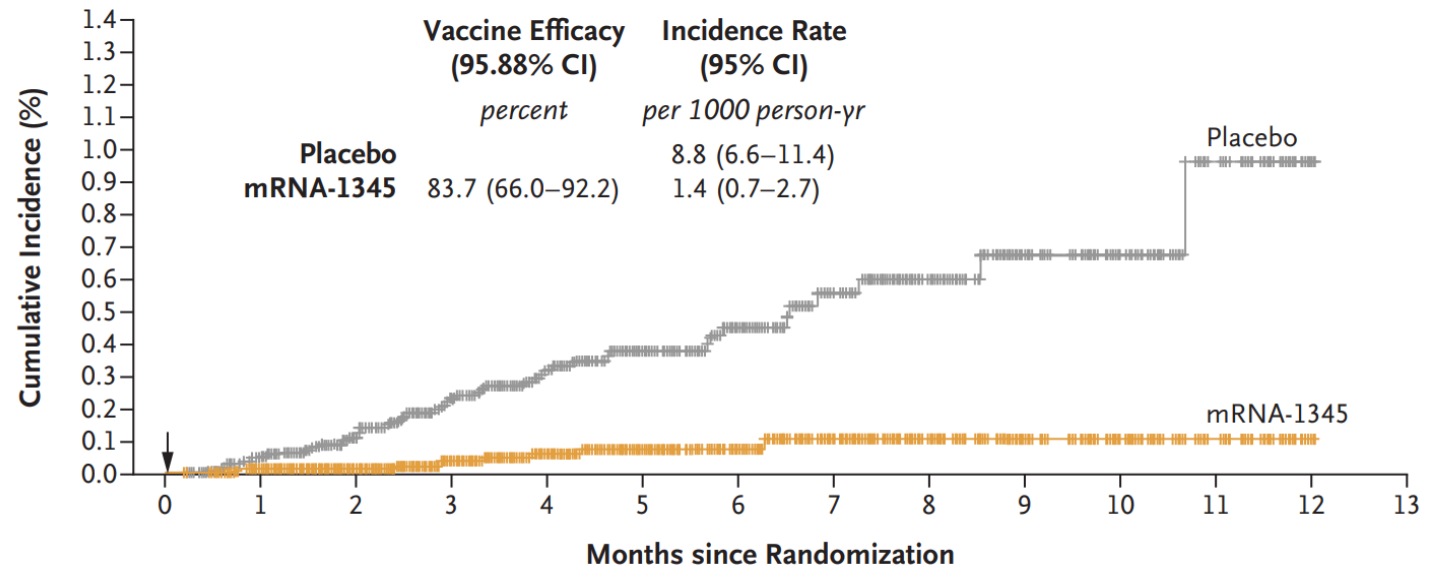
(Primary end points met)

^aNot FDA-approved.

LRTD = lower respiratory tract disease.

Wilson E, et al. *N Engl J Med.* 2023;389(24): 2233-2244.

RSV-Associated Lower Respiratory Tract Disease with ≥ 2 Signs or Symptoms



No. at Risk
Placebo
mRNA-1345

| | | | | | | | | | | | | | |
|--------|--------|--------|--------|------|------|------|------|------|------|-----|-----|----|---|
| 17,516 | 17,433 | 14,735 | 11,275 | 7866 | 5314 | 3657 | 2384 | 1682 | 1058 | 629 | 267 | 43 | 0 |
| 17,572 | 17,514 | 14,783 | 11,293 | 7892 | 5333 | 3648 | 2389 | 1694 | 1062 | 645 | 273 | 47 | 0 |

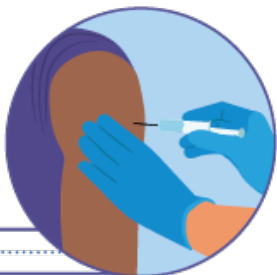


Moderna mRNA-1345^a: Safety and Tolerability

- No trial intervention-related deaths were reported
- In the safety population
 - More reported local reactions with vaccine vs placebo (58.7% vs 16.2%)
 - Systemic adverse reactions were reported in 47.7% of participants in the vaccine group vs 32.9% of participants in the placebo group
 - Balance in all unsolicited adverse events (20.4% in the vaccine group and 18.8% in the placebo group within 28 days after injection)
- Most common adverse reactions
 - Local: injection site pain (56.3% of vaccine participants, 13.7% of placebo participants)
 - Systemic: fatigue, headache, myalgia, arthralgia

^aNot FDA-approved.

Wilson E, et al. *N Engl J Med*. 2023;389(24): 2233-2244.



Estimated Benefits of US RSV Vaccination in Older Adults (≥ 60 Years Old)

A hypothetical vaccine with

- **Efficacy 50%¹ to 70%²**
 - **Coverage to 60%² to 65%¹**
- could prevent:

8,000-14,900

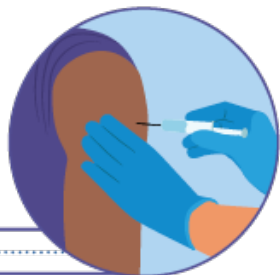
RSV deaths per season

**43,700-81,500 RSV hospitalizations
per season**

Costs of \$557 million to \$1 billion per year

Up to 2.0 million symptomatic RSV-ARI cases per year

1. Herring WL, et al. *Vaccine*. 2022;40:483-493; 2. Van Effelterre T, et al. *Clin Infect Dis*. 2023;77(3):480-489.



ACIP: Adults over 60 years of age may receive a single dose of RSV vaccine following discussion of benefits/risks and shared decision-making with a healthcare professional



Shared Decision-making¹

- **Consider patient risk for severe RSV-associated disease**
 - ✓ Chronic medical conditions
 - ✓ Residence in nursing homes/long-term care facilities
- **Consider patient's values/preferences (e.g., tolerance of illness vs adverse events)**

Vaccination Timing^{1,2}

- Insufficient evidence regarding revaccination
- Seasonality – vaccination late summer to early fall, before RSV starts to spread

Coadministration With Other Vaccines²

- **Acceptable**
- Post-licensure monitoring will provide more guidance

ACIP = Advisory Committee on Immunization Practices.

1. Melgar M, et al. *MMWR Morb Mortal Wkly Rep.* 2023;72(29):793-801; 2. CDC. <https://www.cdc.gov/rsv/about/prevention.html>.



Standards for Adult Immunization Practice for All Healthcare Professionals^{1,2}

- ASSESS patients' immunization status at every clinical encounter
 - Stay informed of the latest CDC recommendations
 - Ensure patients' vaccine needs are reviewed
 - Remind patients of the vaccines they need
- Strongly RECOMMEND needed vaccines – be prepared to discuss:
 - Why vaccination is right for the patient
 - Patient concerns
 - Potential costs/consequences of getting sick
- ADMINISTER or REFER patients to a vaccination provider
- DOCUMENT (e.g., stat immunization registry) and FOLLOW UP

1. National Vaccine Advisory Committee. *Public Health Report*. 2014;129(2):115-123.

2. CDC. Adult Vaccination Resources. <https://www.cdc.gov/vaccines/hcp/adults/for-practice/standards/index.html>.



Case Consideration/Section Summary

You have recommended RSV vaccination for your patient, a 74-year-old woman with diabetes, overweight, hypertension, and young grandchildren. Points to consider as part of shared decision-making include:

- Current treatment recommendations
- Strong evidence of efficacy – prevention of as many as 83% of cases of lower respiratory tract disease
- Evidence of safety
- Increased risk posed by RSV infection, given her age and health status
- Likelihood of exposure with young grandchildren and high transmissibility
- Her values and preferences (e.g., risk aversion, health practices)



Thank You!

