Fred Hutch
Cancer Center

RSV Updates

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Learning objectives

1. Understand risk factors for RSV and key target populations for vaccination and prophylaxis

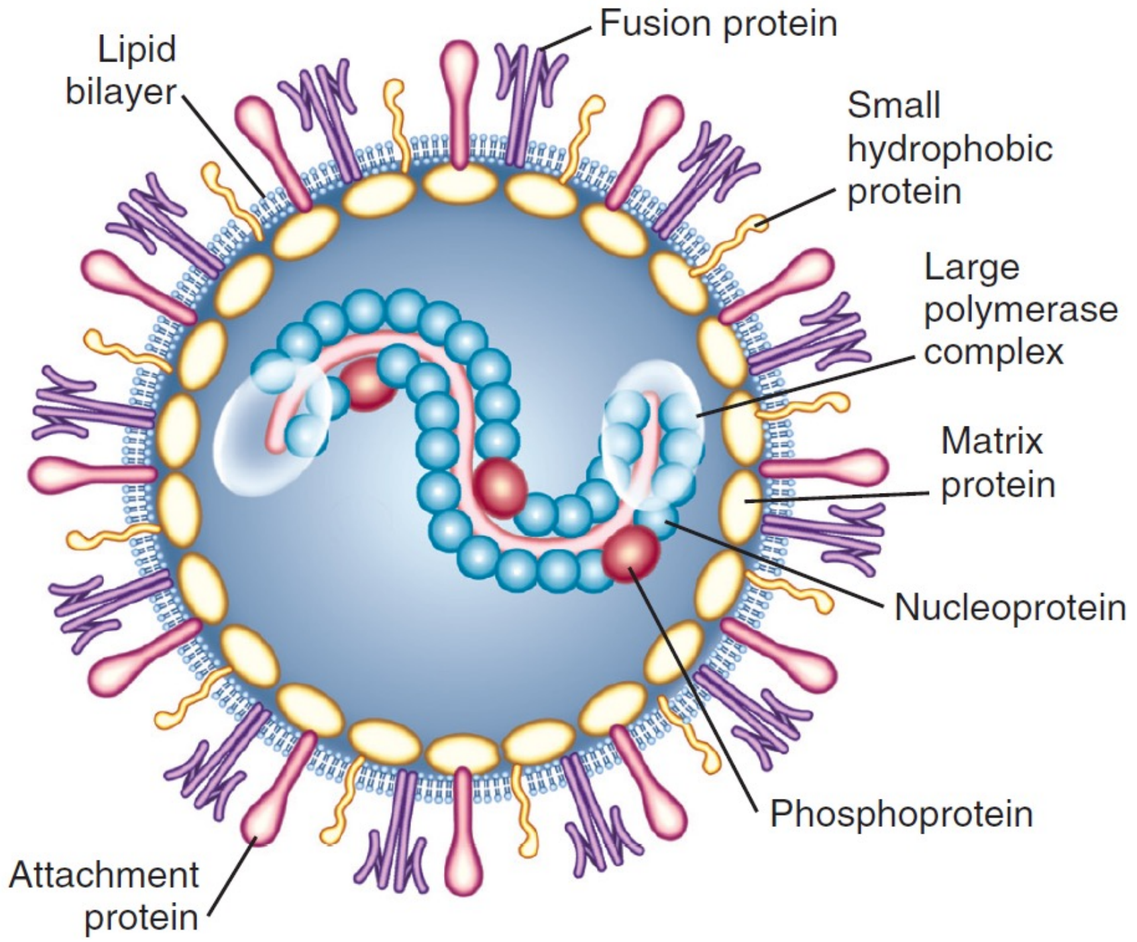
2. Compare the 2 newly approved RSV vaccines for older adults

3. Describe the roles of maternal immunization and nirsevimab in pediatric RSV prevention

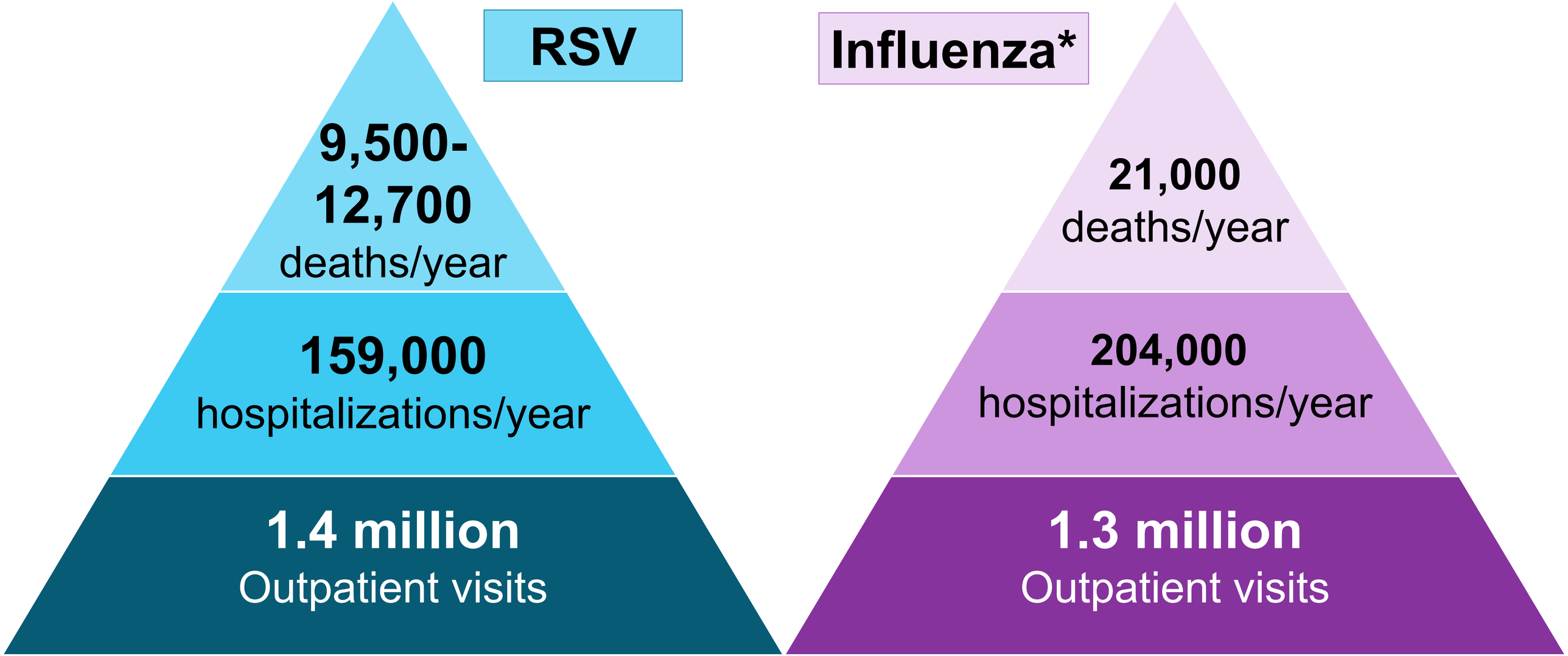
Background

Background: What is RSV?

- Enveloped RNA virus
- Seasonal outbreaks
- Infects all kids
- Reinfects throughout life



RSV is associated with substantial morbidity and mortality in adults > 65 in the US, comparable to influenza



McLaughlin, OFID 2022; https://www.cdc.gov/flu/about/burden/2018-2019.html; *utilizing 2018-2019 data

Slide courtesy of Helen Chu, MD

RSV: clinical picture

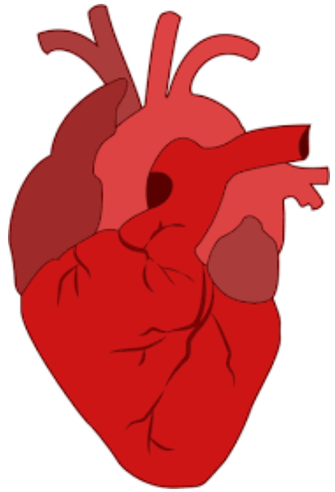
- Infants often present with lower respiratory tract infection
  - Bronchiolitis or pneumonia
- Older children & adults – upper respiratory symptoms
  - Higher risk groups may develop lower respiratory infection, severe disease
- Treatment: supportive care

Risk factors for severe RSV disease

Infants

Elderly

Asthma &
COPD



Heart failure
& coronary heart disease

Immunocompromised

Prasad, 2020

RSV vaccines for older adults

2 newly FDA-approved RSV vaccines

	GSK - Arexvy	Pfizer - ABRYSVO
Age	Adults ≥ 60	Adults ≥ 60
Doses	Single dose	Single dose
Vaccine type	**Adjuvanted** RSV prefusion F protein–based vaccine	**Unadjuvanted** bivalent RSV prefusion F protein−based vax
Vaccine efficacy *vs. symptomatic, lab-confirmed lower respiratory disease*	**82.6%** (RSV LRTI) (≥ 2 or ≥ 3 signs/symptoms)	**66.7%** (RSV LRTI w. ≥ 2 s/sx) **85.7%** (RSVI LRTI w. ≥ 3 s/sx)

Papi A, et al. N Engl J Med. 2023;388:595-608.

Safety profile

	GSK - Arexvy	Pfizer - ABRYSVO
Serious adverse events (SAE)		
Unsolicited adverse events		
Inflammatory neurologic events	3 **inflammatory neurologic events** among 17,992 participants • 1 Guillain-Barré syndrome (GBS) • 2 cases acute disseminated encephalomyelitis (ADEM) • Both received RSV + Flu vax	3 **inflammatory neurologic events** among 20,255 participants • 2 Guillain-Barré syndrome • 1 undifferentiated motor-sensory axonal polyneuropathy (GBS variant)

GBS: body's immune system attacks nerves – weakness in arms, legs +/- face; can progress to respiratory muscle weakness requiring ventilation

ADEM: autoimmune disorder with fever, brain dysfunction (encephalopathy), nerve dysfunction, vision problems, abnormal brain MRI

Papi A, et al. N Engl J Med. 2023;388:595-608; MMWR July 2023

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ACIP recommendation

Adults ≥ 60 may receive a single dose of RSV vaccine, using shared clinical decision making

- Rationale:
  - Moderate-high efficacy vs. symptomatic RSV lower respiratory tract disease
  - Both vaccines generally well tolerated, but 6 cases of inflammatory neurologic events
    - Unclear whether due to vaccine vs chance; post-marketing surveillance planned
  - Until more evidence, targeted adults at highest risk for severe RSV

MMWR, July 21, 2023

Co-administration of RSV vaccine + other vaccines

- ACIP: “Coadministration of RSV vaccines with other adult vaccines is acceptable”[1]
- Immunogenicity: RSV + Flu combo noninferior
  - Except FluA/Darwin strain – did not meet noninferiority criteria[1]
  - Additional evidence of a trend toward lower influenza immune responses, particularly in younger groups[2]
- Safety & reactogenicity of simultaneous vaccination is unknown
  - 2/3 of the inflammatory neuro events in GSK vaccine occurred in participants who received flu vaccine at the same time
- Consider patient factors
  - Ability to return for a subsequent vaccine, risk of severe illness

1. MMWR, July 21, 2023
2. Falsey, JID, 2022

RSV vaccines in older adults – key points

- Both vaccines have moderate to high efficacy in preventing RSV lower respiratory tract disease
- Both overall safe and well tolerated
  - Neuro events are severe but occurred in 0.014% of participants – very rare
- Still many unknowns:
  - Vaccine efficacy against hospitalization & death
  - Vaccine efficacy in the highest-risk patients: immunocompromised, very elderly, many comorbidities
  - Durability of protection
  - Better characterization of rare neurologic events and degree to which these may or may not be vaccine associated
  - Safety and efficacy of co-administration with influenza and SARS-CoV-2 vaccines

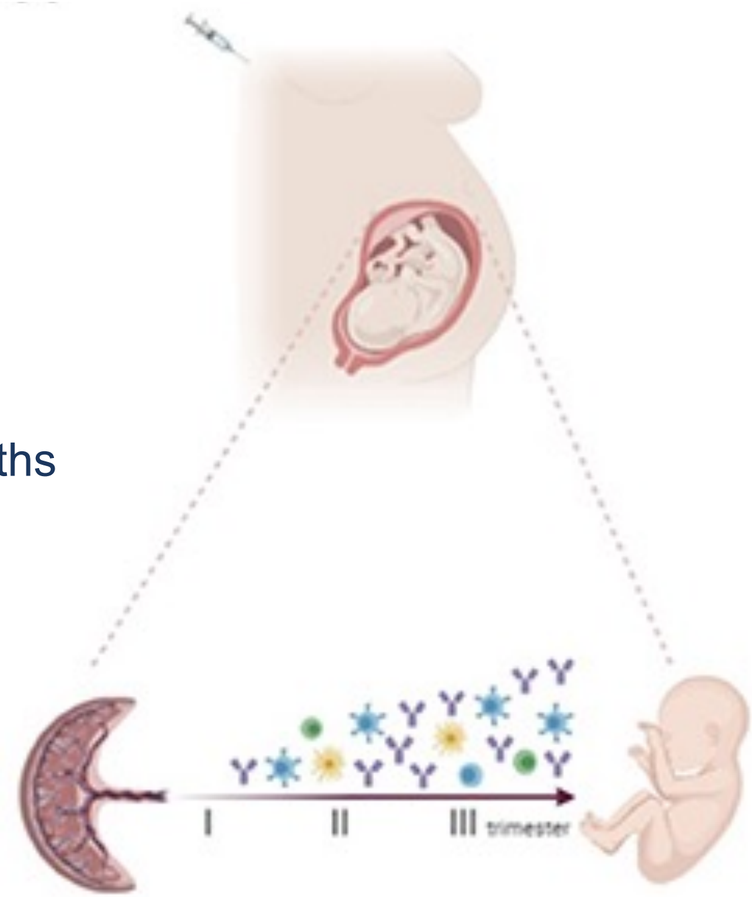
Pediatrics

Maternal immunization

- Transplacental antibody transfer
- Protects infants in first few months of life
- Same strategy used for tetanus, pertussis (Tdap)
- Bivalent vaccine – RSV A and B – Abrysvo (Pfizer)

- Approved for use at **32 - 36 weeks** of pregnancy
- **Vaccine efficacy** among pregnant individuals 32 - 36 weeks
  - ↓ risk of severe lower respiratory disease by 91.1% within first 3 months
  - ↓ risk of severe lower respiratory disease by 76.5% within 6 months
  - ↓ risk of lower respiratory disease by 57.3% within 6 months

- **Safety**:
  - Most common: injection-site pain, headache, muscle aches, nausea
  - **Pre-eclampsia**: **1.8%** of vaccine recipients vs. **1.4%** placebo
  - **Preterm birth**: **5.7%** of vaccine recipients, **4.7%** placebo
  - FDA requiring post-marketing studies of preterm birth and preeclampsia



Kampmann, NEJM 2023 and FDA press release

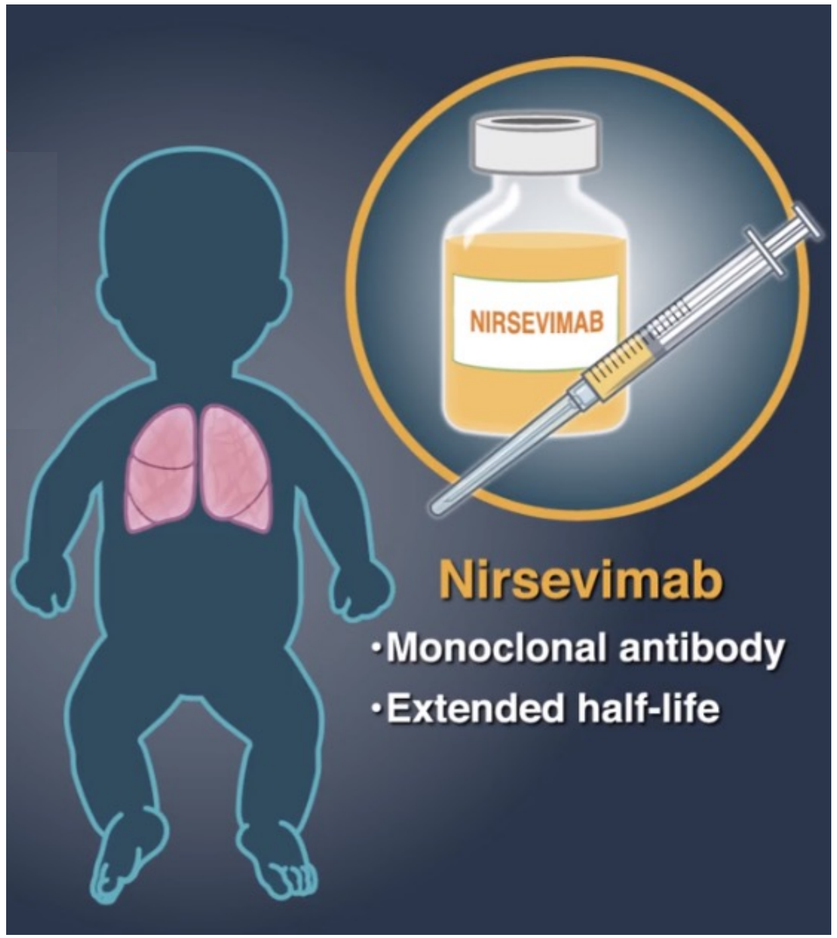
Image: Cinicola, Front. Pediatr., 28 April 2021

Nirsevimab (Beyfortus)

- Long-acting monoclonal antibody
- Intramuscular injection
- Single dose (unlike palivizumab) → cheaper
- 79% efficacy in preventing medically attended RSV LRTI

- **Infants <8 months** born during or entering their 1st RSV season
  - Within 1 week of birth
  - During birth hospitalization or outpatient

- **Infants & children 8–19 months** at increased risk for severe RSV disease, entering their 2nd RSV season
  - Chronic lung disease of prematurity requiring medical support
  - Severe immunocompromise
  - Cystic fibrosis with severe lung disease or <10th %ile wt/length
  - American Indian or Alaska Native children



MMWR, August 25, 2023; Hammitt, NEJM, 2022

Pediatric RSV prevention

- **Vaccine advantages**
  - Cheaper
    - More accessible in low-resource settings
    - Area of greatest need: >97% of RSV-attributable deaths are in low-income and middle-income countries
  - Immune response to multiple epitopes
    - Reduce risk of immune escape
    - Anti-drug antibodies in 6% of nirsevimab group vs 1% of placebo group
- **Monoclonal advantages**
  - No concerning safety signals
  - Ideal for preterm infants (mother not yet vaccinated) and infants with impaired transplacental antibody transfer

What’s next

What's next for RSV prevention and treatment

Products in development:

Moderna: mRNA RSV vaccine[1]

- Phase 3 trials
- Vaccine efficacy of 83%

EDP-938[2]

- Phase 2a (human challenge) trials
- **Adults**
- Replication inhibitor

↓ Viral load

↓ Symptom scores

↓ Mucus

Ark Biopharma: Ziresovir[3]

- Phase 3 trials
- Hospitalized **infants**
- Small molecule fusion protein inhibitor
- ↓ symptoms
- ↓ length of ICU stay
- ↓ viral load

1. Wilson E, et al. Presented at: the 7th ReSViNET Conference. https://s29.q4cdn.com/435878511/files/doc_presentations/2023/02/rsvvw-p301-ia-oral-presentation_final-update.pdf.
2. Ahmad NEJM 2022
3. Oral abstracts, RSV 2022

Slide adapted from slides by Helen Chu, MD

Thank you

Teaching Peer Evaluation
for Dr. Denise McCulloch