RSV – Evolution of Treatment

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Goals

- The evolution of treatment from harmful vaccine to present day
- The evolution of medical intervention

Objectives

- Review – Basic virology and epidemiology of RSV
- Recognize – Health disparities of RSV
- Discuss – The history of RSV immunization
- Explain – The current ACIP recommendations for RSV immunization

My Infectious Disease History - 1950s

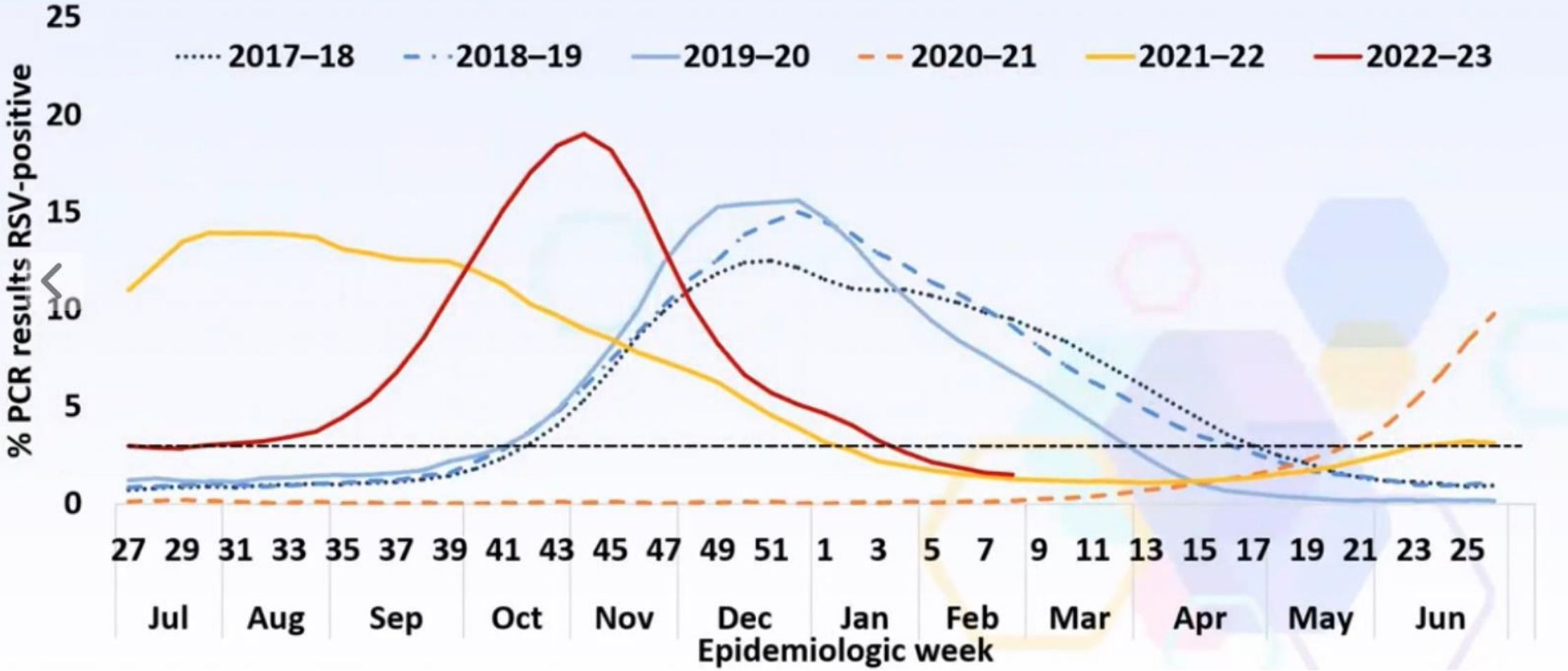
- Rheumatic Fever
- Measles
- German Measles
- Mumps
- Oral Polio vaccine

RSV and Infants

- Leading cause of hospitalization among infants – up to 80,000 per year
- Up to 300 children die in the U.S. annually
- Most infants infected in the first year of life
- Up to 79% of children hospitalized with RSV less than 2 years of age have no underlying medical problems
- Previous monoclonal antibody (palivizumab) indicated only for children with certain medical problems (less than 2% of the annual birth cohort), high cost, and requires monthly injections


COVID
SEASON
RSV
SEASON
INFLUENZA
SEASON
imgflip.com

Changes in seasonality of RSV transmission following SARS-CoV2 introduction— NREVSS[1], 2017–2023



Reset Filters

Season | Age Group | Race/Ethnicity | Sex | Site

View

Monthly Rates

Weekly Rates

Weekly Rates (All Seasons)

Cumulative Rates

Filters

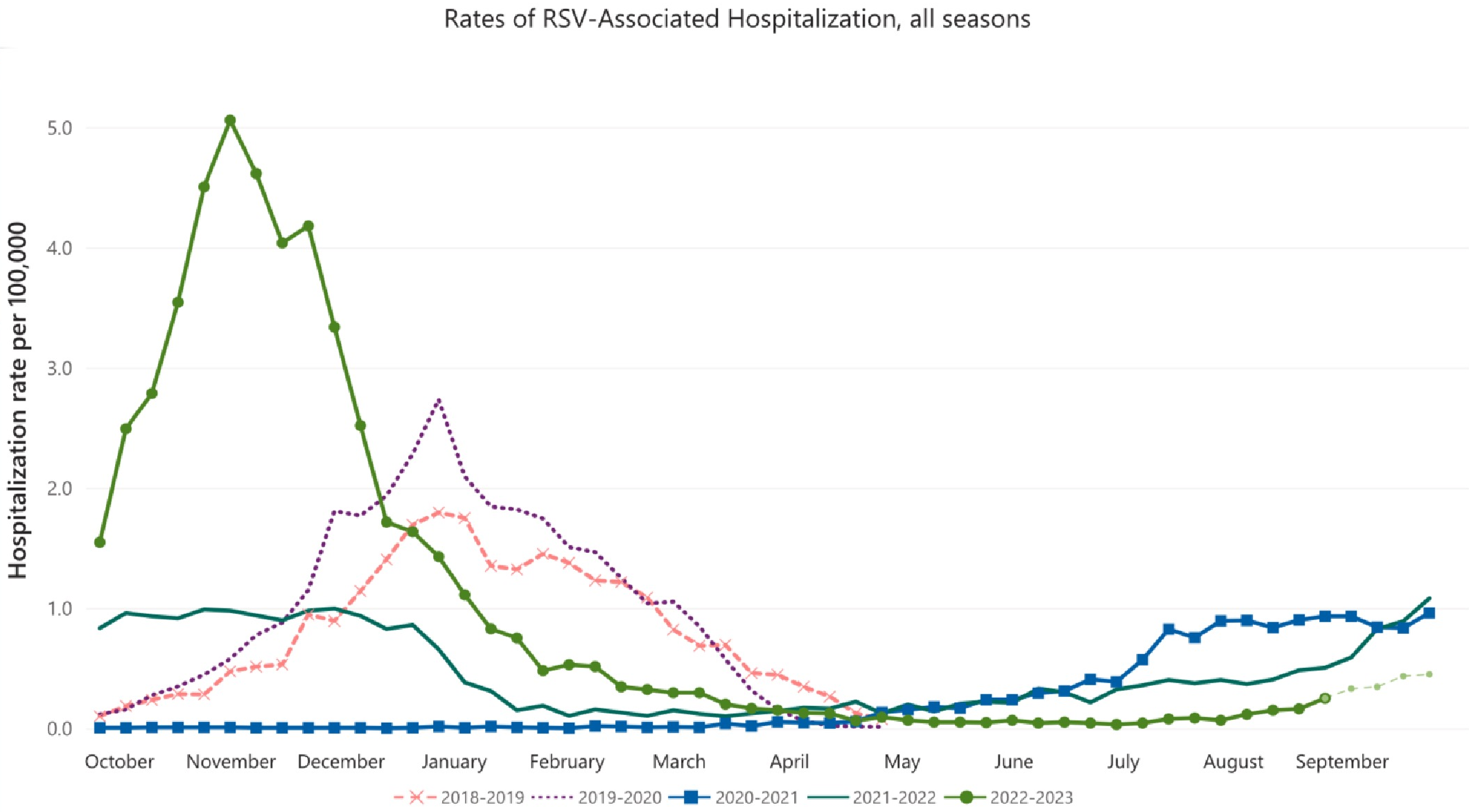
Season: All

Site: RSV-NET

Age Group: All

Race/Ethnicity: All

Sex: All



Data last updated: 10/05/2023 | **Accessibility:** Hover over graph area to display options such as show data as table and copy visual.

Note: AI/AN, American Indian or Alaska Native; A/PI, Asian and Pacific Islander.

CDC

Download Data

In the 2022-2023 season, the overall rate of RSV-associated hospitalizations was 52.7 per 100,000 people.

Reset Filters

Season | Age Group | Race/Ethnicity | Sex | Site

View

Monthly Rates

Weekly Rates

Weekly Rates (All Seasons)

Cumulative Rates

Filters

Season

2022-2023 (All Ages)

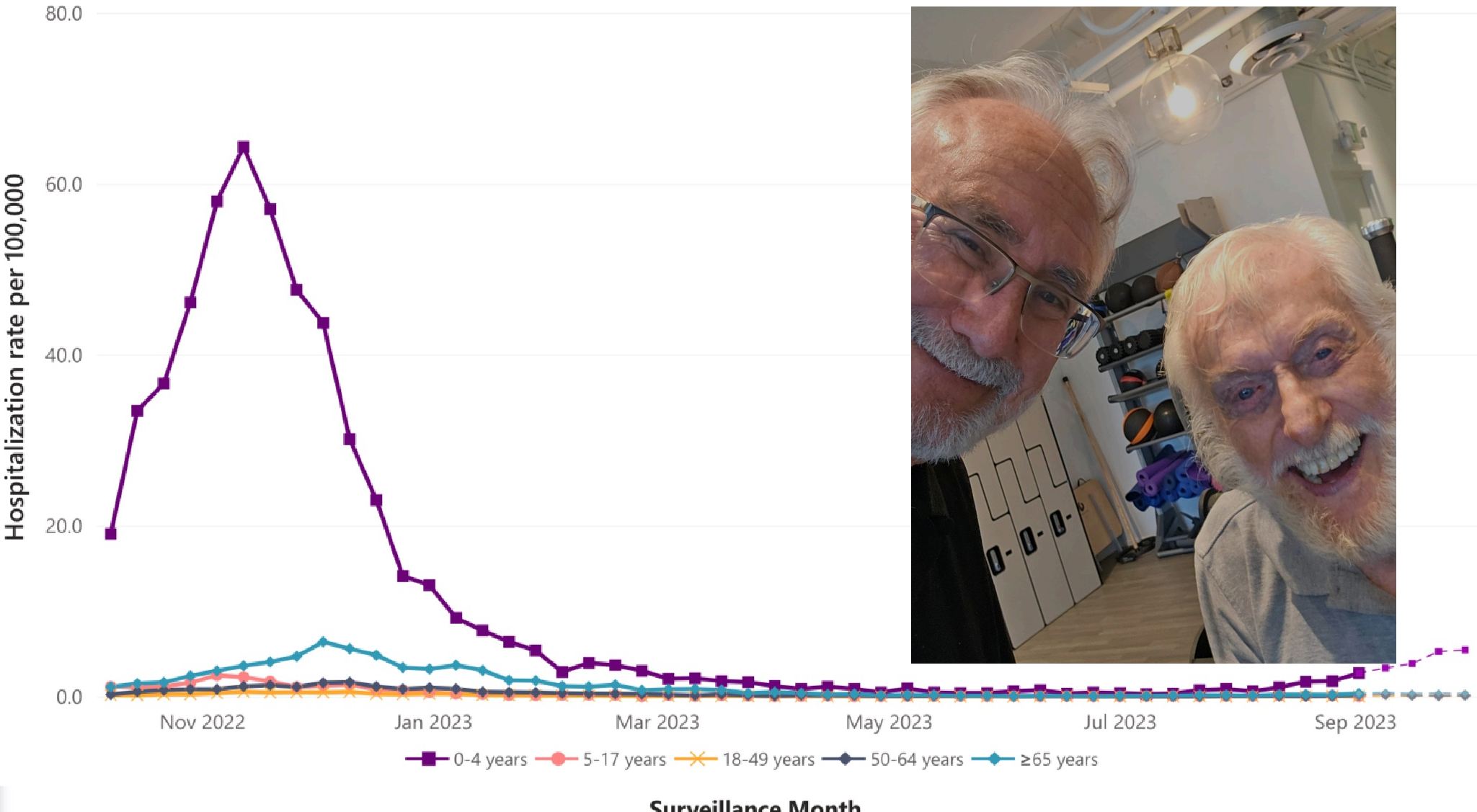
Site

RSV-NET

Age Group

Multiple selections

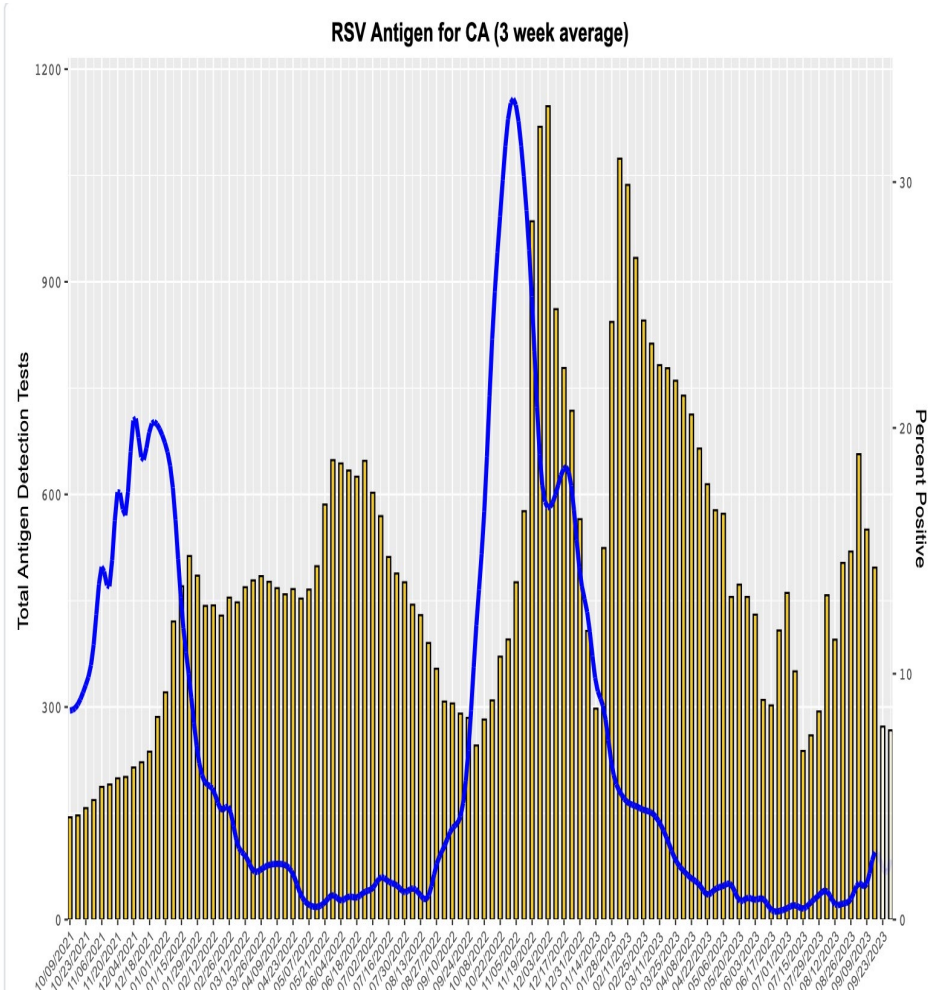
Rates of RSV-Associated Hospitalization, 2022-2023 (All ages)

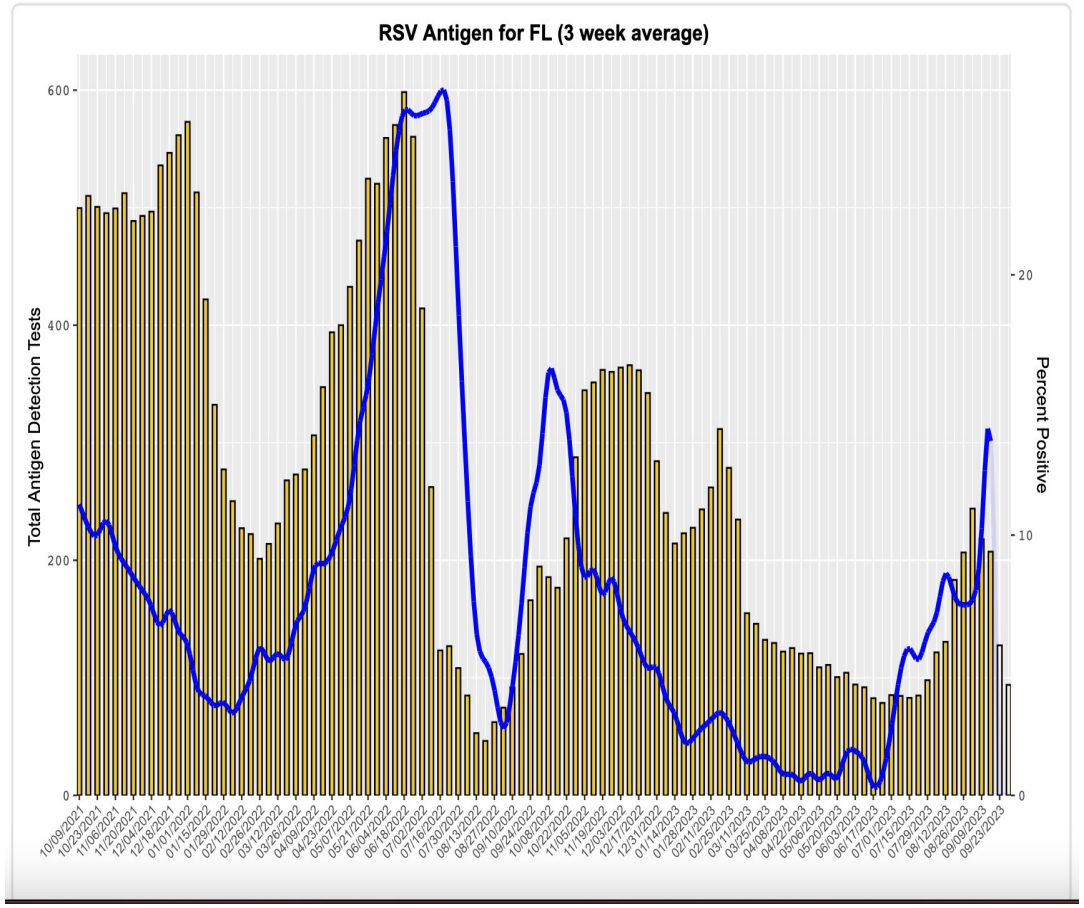


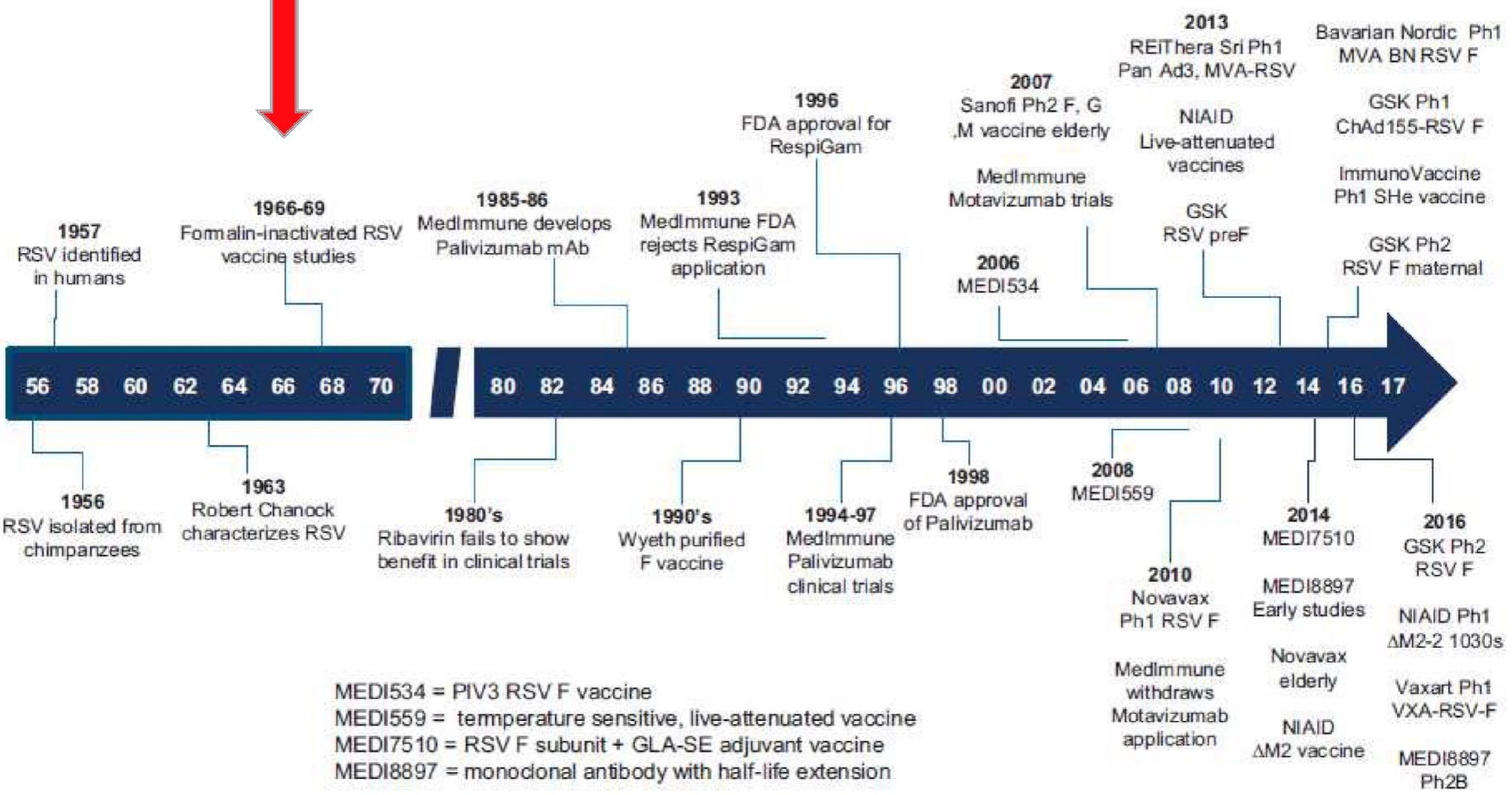
HEALTH DISPARITIES

- RATES OF RSV-ASSOCIATED ICU ADMISSIONS AMONG U.S. INFANTS LESS THAN 6 MONTHS OLD FOR NON-HISPANIC BLACK INFANTS IN RSV-NET WERE 1.2 TO 1.6 TIMES HIGHER THAN FOR NON-HISPANIC WHITE INFANTS ACROSS THE FOUR SEASONS
- THE INCIDENCE OF RSV-ASSOCIATED HOSPITALIZATION AMONG SOME AMERICAN INDIAN (AI) AND ALASKA NATIVE (AN) CHILDREN AGED 12–23 MONTHS WAS 4 TO 10 TIMES THAT OF SIMILAR-AGED CHILDREN ACROSS SEVEN SITES IN THE UNITED STATES
- SOME AI/AN COMMUNITIES LIVE IN REMOTE REGIONS, MAKING ACCESS TO MEDICAL CARE OF CHILDREN WITH SEVERE RSV MORE CHALLENGING

RSV Seasonality







onya Villafana, Judith Falloon, M. Pamela Griffin, Qing Zhu & Mark T. Esser
:017): Passive and active immunization against respiratory syncytial virus for the young and old. Expert Review of Vaccines

National Institute Allergy and Infectious Diseas

The First RSV Vaccine

- 1966 TRIAL OF FORMALIN INACTIVATED AGAINST RSV (FIRSV) CONDUCTED IN THE US
- 80% OF CHILDREN IN THE VACCINE ARM HAD TO BE HOSPITALIZED AFTER RSV INFECTION
- COMPARED TO ONLY 5% IN THE CONTROL ARM
- 2 IMMUNIZED INFANTS DIED AS A CONSEQUENCE OF SUBSEQUENT RSV INFECTION
- THIS PHENOMENON LATER WAS KNOWN AS ENHANCED RSV DISEASE (ERD)

- ON AUGUST 3RD, 2023 THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES RECOMMENDED NIRSEVIMAB FOR INFANTS < 8 MONTHS BORN DURING OR ENTERING THEIR FIRST RSV SEASON AND FOR INFANTS AND CHILDREN AGED 9-19 MONTHS WHO ARE AT INCREASED RISK OF SEVERE RSV DISEASE ENTERING THEIR SECOND RSV SEASON (OCTOBER THROUGH END OF MARCH).

ACIP RECOMMENDATIONS

- **ADMINISTER NIRSEVIMAB WITHIN 1 WEEK OF BIRTH DURING OR RIGHT BEFORE RSV SEASON**
- **INFANTS WITH PROLONGED BIRTH HOSPITALIZATIONS RELATED TO PREMATURITY OR OTHER CAUSES SHOULD RECEIVE NIRSEVIMAB SHORTLY BEFORE OR PROMPTLY AFTER HOSPITAL DISCHARGE**

ACIP RECOMMENDATIONS

- **INCREASED RISK FOR SEVERE RSV**
  - **CHRONIC LUNG DISEASE OF PREMATURITY WHO REQUIRED MEDICAL SUPPORT (CHRONIC CORTICOSTEROID THERAPY, DIURETIC THERAPY, OR SUPPLEMENTAL OXYGEN) ANY TIME DURING THE 6-MONTH PERIOD BEFORE THE START OF THE SECOND RSV SEASON**
  - **SEVERE IMMUNOCOMPROMISE**
  - **CYSTIC FIBROSIS WHO HAVE EITHER 1) MANIFESTATIONS OF SEVERE LUNG DISEASE (PREVIOUS HOSPITALIZATION FOR PULMONARY EXACERBATION IN THE FIRST YEAR OF LIFE OR ABNORMALITIES ON CHEST IMAGING THAT PERSIST WHEN STABLE), OR 2) WEIGHT-FOR-LENGTH <10TH PERCENTILE**
  - **AMERICAN INDIAN OR ALASKA NATIVE CHILDREN**

For infants born during or entering the RSV season[5]

Beyfortus Administration at the Hospital Based on the Infant Birth Month and RSV Season

Administration of a single dose of Beyfortus

Born	Setting	Timing	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar
During or entering the season	Hospital	From birth							For infants born during or entering the RSV season, Beyfortus should be administered starting from birth.					

Duration of protection of Beyfortus (extending through 5 months)

Baby birth month

Immunization with Beyfortus

If the Infant Is Born Between October and March

Example: Administer Beyfortus in the hospital as follows		**Example:** If Beyfortus is not given at the hospital, administer Beyfortus in the pediatric clinic as follows	
Birth Month	**Timing**	**Birth Month**	**Timing**
October	At birth, prior to discharge	November	3- to 5-day well-baby visit

For infants born outside the RSV season[5]

Beyfortus Administration at the Hospital Based on the Infant Birth Month and RSV Season

Administration of a single dose of Beyfortus

Born	Setting	Timing	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar
Outside the season	Clinic	Prior to the start of their first RSV season	← For infants born outside of the RSV season, Beyfortus should be administered once prior to the start of the RSV season. →											

Duration of protection of Beyfortus (extending through 5 months)

Baby birth month

Immunization with Beyfortus

If the Infant Is Born Between April and September

Example: Administer Beyfortus in the pediatric clinic (at the 2-, 4-, or 6-month well-baby visit)

Birth Month	Timing	Setting
April	October (6-month well-baby visit)	At the pediatric clinic
May	November (6-month well-baby visit)	
June	October (4-month well-baby visit)	
July	November (4-month well-baby visit)	
August	October (2-month well-baby visit)	
September	November (2-month well-baby visit)	

17. Table S3: Primary Case Definition of Medically Attended RSV LRTI.

RSV confirmed	**LRT involvement** (must have ≥1)	**Clinical sign of severity** (must have ≥1)
Positive by central laboratory RT-PCR	Rhonchi Rales Crackles Wheeze	Increased respiratory rate* Hypoxemia† Acute hypoxic or ventilatory failure New-onset apnea Nasal flaring Retractions Grunting Dehydration owing to respiratory distress

Select pregnancy-related serious adverse events at any time following vaccination[1,2]: Pfizer phase 3 trial, trial dosing interval (24–36 weeks gestation)

	RSVpreF Vaccine N= 3,682		Placebo N= 3,675	
Serious Adverse Reaction	**n (%)**	**95% CI**	**n (%)**	**95% CI**
All Maternal Serious Adverse Events (SAEs)	**598 (16.2)**	**(15.1, 17.5)**	**558 (15.2)**	**(14.0, 16.4)**
Pre-eclampsia	68 (1.8)	(1.4, 2.3)	53 (1.4)	(1.1, 1.9)
Gestational hypertension	41 (1.1)	(0.8, 1.5)	38 (1.0)	(0.7, 1.4)
Premature rupture of membranes	15 (0.4)	(0.2, 0.7)	16 (0.4)	(0.2, 0.7)
Preterm premature rupture of membranes	15 (0.4)	(0.2, 0.7)	10 (0.3)	(0.1, 0.5)
Hypertension	13 (0.4)	(0.2, 0.6)	6 (0.2)	(0.1, 0.4)
Maternal death[3]	1 (<0.1)	(0.0, 0.2)	0	(0.0, 0.1)
Fetal death[4]	10 (0.3)	(0.1, 0.5)	8 (0.2)	(0.1, 0.4)

1 Table 3 ABRYSVO package insert Package Insert - ABRYSVO (STN 125768) (fda.gov)

2 Includes all SAEs from vaccination to 6 months post-delivery (up to approximately 10 months, depending on the gestational age at the time of vaccination). In the phase 3 RCT, eclampsia occurred in 5 participants (3 in the RSVpreF group and 2 in the placebo group) and HELLP syndrome occurred in 5 participants (2 in the RSVpreF group and 3 in the placebo group).

3 There was one maternal death in the vaccine group due to postpartum hemorrhage that was not likely to be associated with vaccination.

4 A total of 18 intrauterine deaths were reported for the index pregnancy: 10 intrauterine deaths in the vaccine group (0.3%) and 8 intrauterine deaths in the placebo group (0.2%). The intrauterine deaths represented various clinical conditions and presentations resulting in fetal demise without clear evidence of a common pathophysiology

GSK maternal RSV vaccine clinical trial and preterm birth

- Trial of a similar GSK maternal RSV vaccine (stabilized prefusion F protein vaccine without an adjuvant) was halted due to an imbalance of preterm births with higher numbers in the vaccine vs placebo group

Outcome	Vaccine group, n (%) N=3,496	Placebo group, n (%) N=1,739	Relative Risk (95% CI)
Preterm birth (<37 weeks gestation)	238 (6.81%)	86 (4.95%)	1.38 (1.08, 1.75)
Neonatal death	13 (0.37%)	3 (0.17%)	2.16 (0.62, 7.55)

- Imbalance of neonatal deaths was a consequence of preterm birth imbalance
- Imbalance in preterm births was seen in low and middle-income countries (RR: 1.57, 95% CI: 1.17, 2.10) but not high-income countries (RR: 1.04, 95% CI: 0.68, 1.58)
- Imbalance was observed from April–December 2021, but not consistently after December 2021
- Reason for the imbalance remains unclear

Study vaccine given at 24 0/7 to 34 0/7 weeks gestation

Vaccines and Related Biological Products Advisory Committee February 28 - March 1, 2023 Meeting Briefing Document- Sponsor GSK (fda.gov)

Simultaneous administration of RSV vaccine with other vaccines in pregnant people

- Pregnant people may potentially be eligible to receive RSV, Tdap, COVID-19, and influenza vaccines at same visit
- Pfizer Phase 2b study in healthy non-pregnant women ages 18–49 years on simultaneous administration of Tdap and Pfizer RSVpreF found decreased immune response to pertussis components (i.e., non-inferiority criteria were not met)[1]
- Given lack of correlates of protection for pertussis, it is unclear how this might impact protection against pertussis from maternal Tdap when simultaneously administered with RSVpreF vaccine

1 Peterson et al. Safety and Immunogenicity of a Respiratory Syncytial Virus Prefusion F Vaccine When Coadministered With a Tetanus, Diphtheria, and Acellular Pertussis Vaccine. The Journal of Infectious Diseases. 2022 June 15; 225(12): 2077–2086. doi: 10.1093/infdis/jiab505

RSV vaccine and Tdap dosing timing

- Tdap recommended every pregnancy, preferably during the early part of gestational weeks 27 through 36[1]
- Tdap would be preferably given before 32 weeks (based on recommendation) and RSV vaccine would be given at or after 32 weeks
- In MarketScan data from 2018–2021, about half of captured Tdap doses were given before 32 weeks gestation[2]

1 CDC, https://www.cdc.gov/vaccines/vpd/dtap-tdap-td/hcp/recommendations.html
2 MarketScan data, 2018-2021

Relative risks and benefits of maternal vaccination and nirsevimab

Both products are safe and effective in preventing RSV lower respiratory infection in infants

Maternal RSV vaccine	Nirsevimab
Benefits • Provides protection immediately after birth • May be more resistant to virus mutation • Avoids injection of infant **Risks** • Protection reduced if fewer antibodies produced or are transferred from mother to baby (e.g., mother immunocompromised or infant born soon after vaccination) • Potential risk of preterm birth	**Benefits** • Studies of antibody levels suggest that protection might wane more slowly • Can provide antibodies directly if infant receives less antibodies from mother • No risk of adverse pregnancy outcomes **Risks** • Potentially limited availability during 2023-2024 RSV season

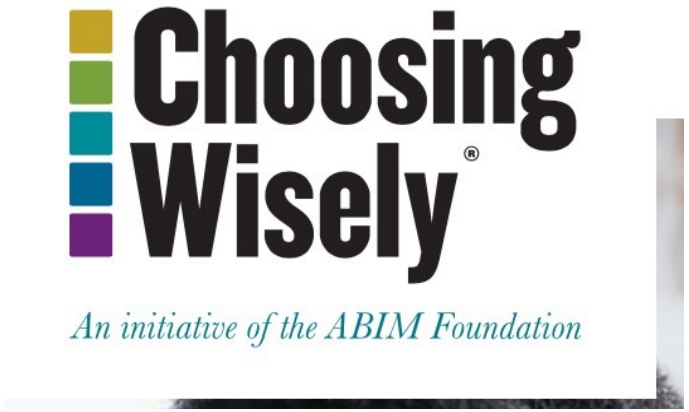
Proposed recommendations for use of nirsevimab in setting of an available maternal RSV vaccine

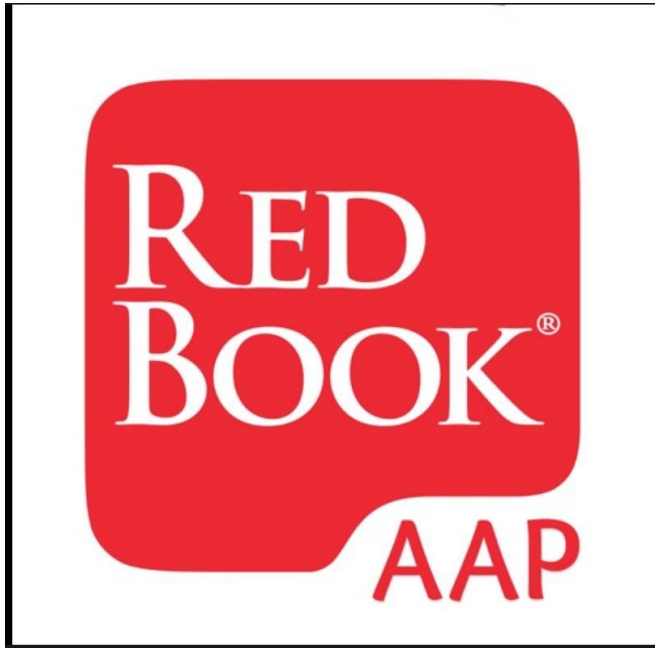
- Nirsevimab is recommended for infants aged <8 months born during or entering their first RSV season if
  - Mother did not receive RSV vaccine or unknown if mother received RSV vaccine
  - Mother vaccinated but infant born <14 days after vaccination
- Nirsevimab is not needed for most infants born ≥14 days after maternal vaccination

Circumstances for which nirsevimab can be considered when mother has received RSV vaccine ≥14 days prior to birth

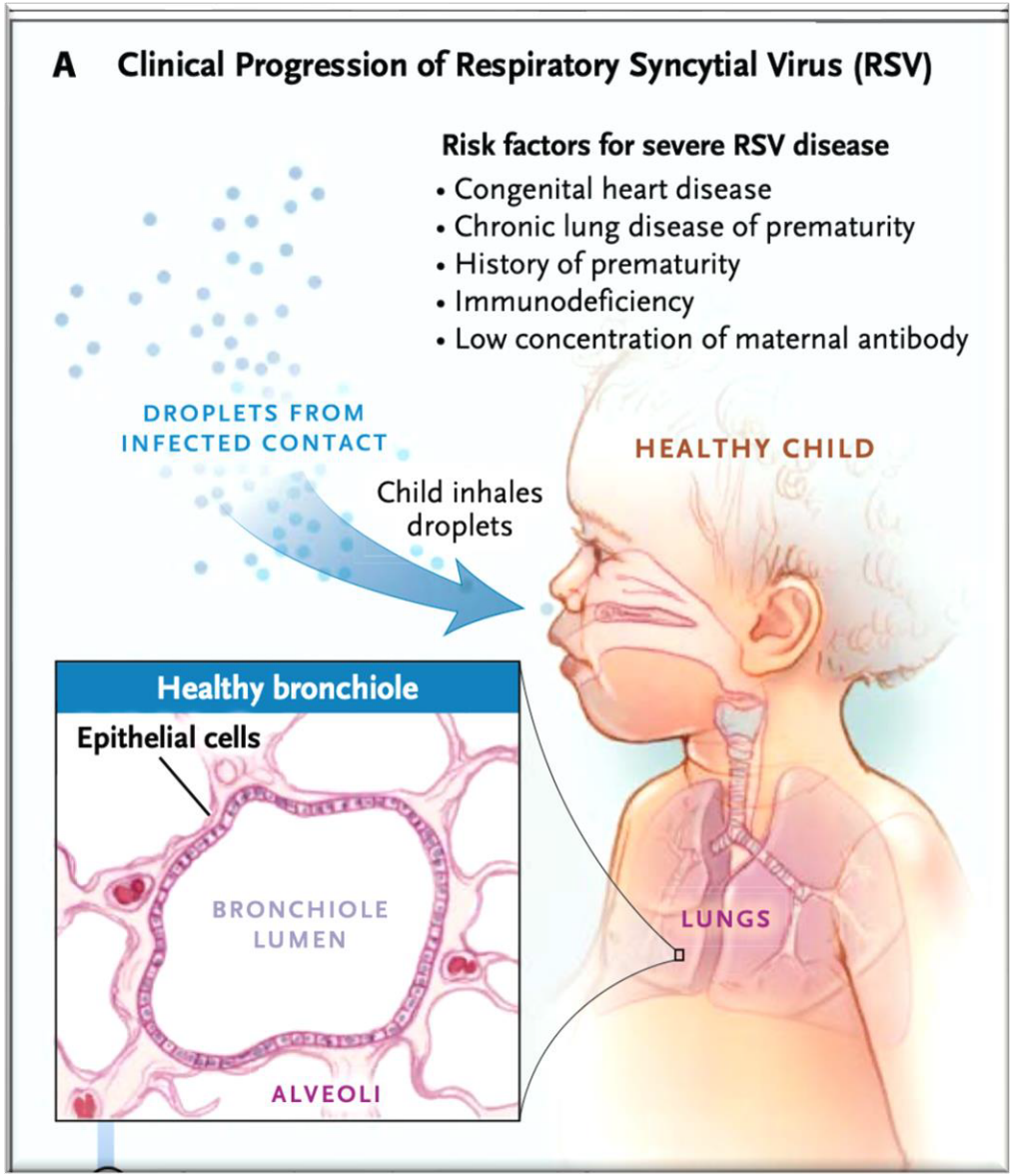
- Nirsevimab can be considered in rare circumstances when, per the clinical judgment of the healthcare provider, the potential incremental benefit of administration is warranted
  - Infants born to pregnant people who may not mount an adequate immune response to vaccination (e.g., people with immunocompromising conditions) or have conditions associated with reduced transplacental antibody transfer (e.g., people living with HIV infection)[1]
  - Infants who have undergone cardiopulmonary bypass, leading to loss of maternal antibodies[2]
  - Infants with substantial increased risk for severe RSV disease (e.g., hemodynamically significant congenital heart disease, intensive care admission and requiring oxygen at discharge)

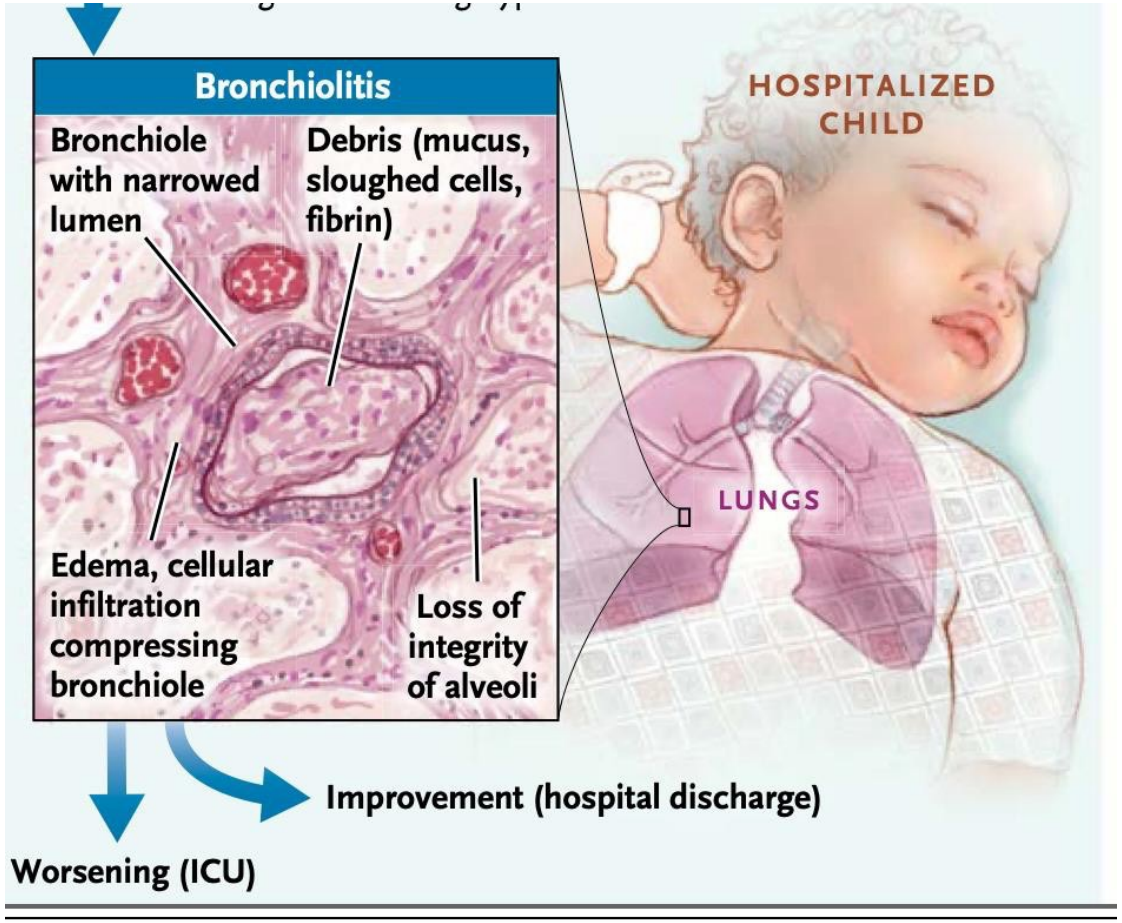
[1] Palmerira Clin Dev Immunol 2012. [2] Feltes J Pediatr 2003.





- NO AVAILABLE TREATMENT SHORTENS THE COURSE OF BRONCHIOLITIS OR HASTENS THE RESOLUTION OF SYMPTOMS
- SUPPORTIVE CARE WHICH INCLUDES HYDRATION, CAREFUL ASSESSMENT OF RESPIRATORY STATUS, SUCTION OF UPPER AIRWAYS
- SUPPLEMENTAL OXYGEN FOR O2 SAT LESS THAN 90%
- DON'T ROUTINELY USE BRONCHODILATORS IN CHILDREN WITH BRONCHIOLITIS
- ANTIBIOTICS SHOULD NOT BE USED FOR VIRAL RESPIRATORY ILLNESSES (SINUSITIS, PHARYNGITIS, BRONCHITIS AND BRONCHIOLITIS)





Miessner. Viral Bronchiolitis in Children. N Engl J Med 2016;374:62-72.

Differential Diagnosis

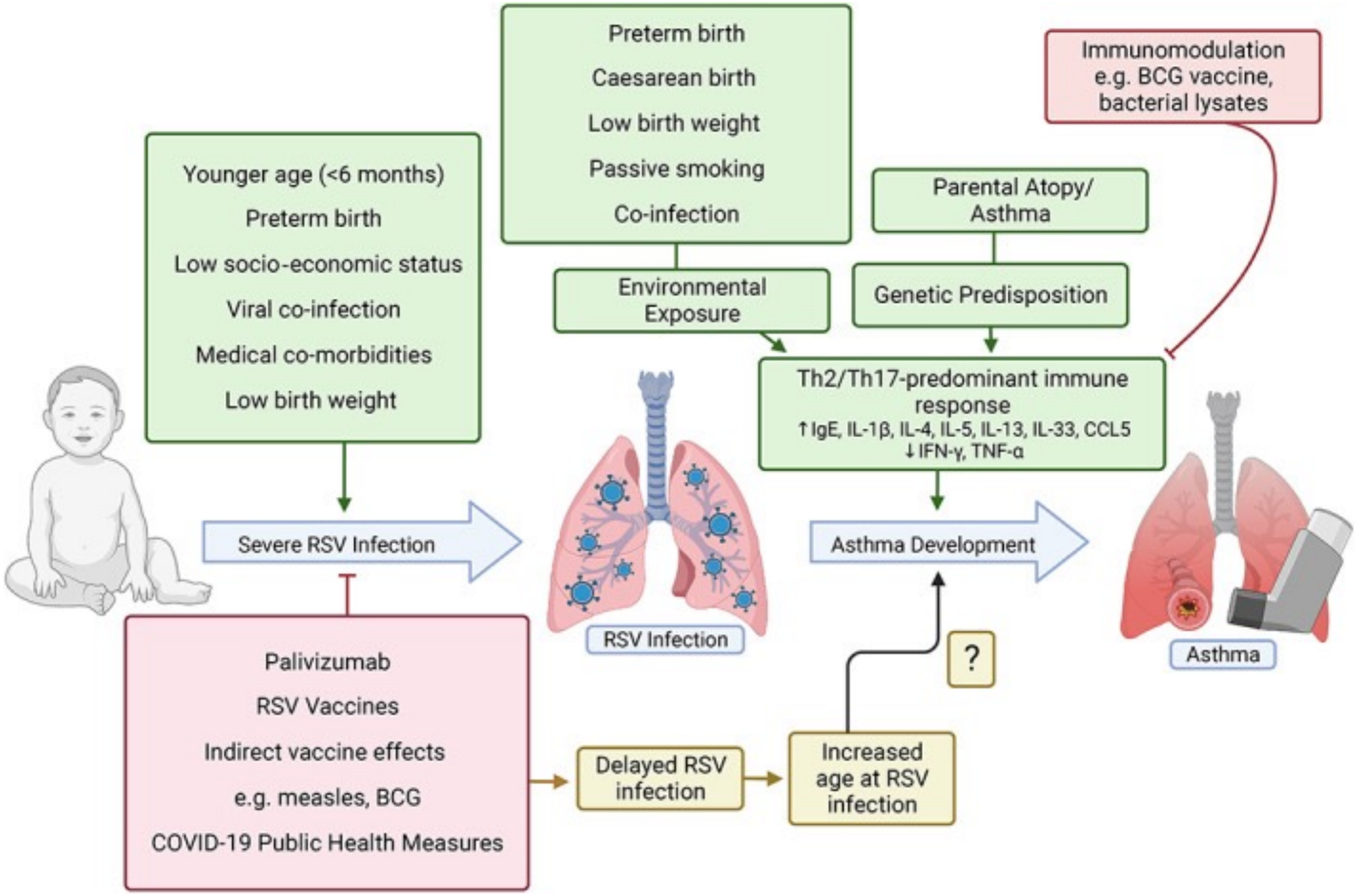
Bronchiolitis

LIFE-THREATENING CAUSES
Infection: pneumonia, Chlamydia, Pertussis (apnea) Foreign body: aspirated or esophageal Cardiac anomaly: congestive heart failure, vascular ring Allergic reaction Bronchopulmonary disorder exacerbation (CLD)
NON-LIFE THREATENING CAUSES
Congenital anomaly: tracheoesophageal fistula, bronchogenic cyst, laryngotracheomalacia Gastroesophageal reflux disease Mediastinal mass Cystic fibrosis

SPAG2

- The anti-viral drug ribavirin primarily used for the treatment of respiratory syncytial virus (RSV) infection in infants is delivered by continuous nebulization with the Small Particle Aerosol Generator (SPAG). Clinical data suggest that the SPAG is an efficient nebulizer for ribavirin; it is also being used for the delivery of other pulmonary agents.
- The aerosol of either solution had a mass median aerodynamic diamter (MMAD) of approximately 1.2 microns, and this seemed insensitive to solution strength and nebulization period. Of the solutions of ribavirin and cromolyn sodium 92.3% and 95.0%, respectively, by weight of delivered particles, had aerodynamic diameters less than 5 microns and about 70-75% of the aerosol particles had an aerodynamic diameter in the 1-5 microns range. This implies that the aerosol cloud is adequate for delivery through a ventilator circuit.
- Performance was maintained over long (16 hours), continuous periods of delivery. The SPAG could be useful for delivery of other respiratory drugs by continuous nebulization.

As The Acorn Is Planted



Binns E, Tuckerman J, Licciardi PV, Wurzel D. Respiratory syncytial virus, recurrent wheeze and asthma: A narrative review of pathophysiology, prevention and future directions. J Paediatr Child Health. 2022 Oct;58(10):1741-1746. doi: 10.1111/jpc.16197. Epub 2022 Sep 8. PMID: 36073299; PMCID: PMC9826513.

Bronchiolitis Quality Improvement 466.19

patients positive for RSV

hospitalized with bronchiolitis

sent home with nebulizers without documentation of reversibility

chest xrays ordered associated with the diagnosis code of bronchiolitis

cbc ordered with the associated code of bronchiolitis

blood culture ordered

antibiotics ordered or prescribed

steroids ordered or prescribed

discontinuation of continuous cardiac monitoring

discontinuation of nasal cannula oxygen.

RSV nasal swab prior to admission versus standard isolation and droplet precaution for all patients

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Bronchiolitis OPPE – Pre-Test

- Nasal suction via bulb or neosucker is recommended to clear the upper airway.
- I or my staff demonstrate suctioning to parents
- I feel comfortable demonstrating suctioning to my parents
- I know where to send my parents to purchase a nasal suction bulb
- I review with my parents not to discard the neonatal suction bulb they received at newborn discharge
- Deep suction (beyond the nasopharynx) is not recommended and requires a special order.
- Oxygen is recommended for hypoxia, defined as a persistent oxygen saturation (SpO2),90%.
- I do not agree with this guideline and maintain oxygen saturation >94% on room air before discharge and discontinuation of oximetry.

- I would consider sending a baby home on oxygen if it could be easily ordered, delivered to the home, the parents had access to transportation to bring the patient to the ER or primary care physician for follow-up, and the parents were able to demonstrate back knowledge regarding the symptoms of worsening status.
- SpO2 spot checks are recommended to monitor for hypoxia in patients not on oxygen
- I order continuous oximetry on all patients on oxygen
- Continuous SpO2 monitoring is suggested for monitoring patients on oxygen.
- Continuous cardiopulmonary monitoring (CAM) is recommended for patients at high risk of apnea. It is recommended that CAM be discontinued if there are no apneas for 24 h.

Bronchiolitis OPPE – Pre-Test

- Bronchodilators should not be used routinely in the management of bronchiolitis. A single trial of inhaled epinephrine or albuterol for respiratory distress may be considered, but only if h/o asthma, atopy, or allergy. It is recommended to discontinue inhalation therapy if there is no clinical response.
- Steroids, antibiotics, nasal decongestants, and chest physiotherapy are not recommended.
- Diagnostic studies (CXRs, complete blood count, C-reactive protein, and blood cultures) are not routinely indicated.
- Standard isolation (contact or droplet) precautions are recommended for all patients

Risk Factors For Severe Illness In Hospitalized Patients

- PICNIC network (Pediatric Investigators Collaborative Network on Infections in Canada 1995):
  - 689 hospitalized children < 2 years:
    - 6 out of 689 patients died (0.9%)
    - 4 out of 6 had underlying disease (congenital heart disease, chronic lung disease, immunocompromised)
    - 2 were either premature or < 6 weeks old
  - None of 372 pts died if older than 6 weeks and without other risk factors for severe disease (95% CI 0-0.8%)

Risk Factors for Severe Bronchiolitis History

- Age < 6 - 12 weeks
- Prematurity < 34 - 37 weeks gestation
- Underlying chronic respiratory illness such as CF, CLD or BPD
- Significant congenital heart disease
- Immune deficiency including human immunodeficiency virus, organ or bone marrow transplants, or congenital immune deficiencies
- Prior intubation
- First 48 hours of illness

Recovery Bronchiolitis

- Degree of obstruction may vary as some of the airways clear resulting in rapidly changing clinical severity
- Epithelial cells recover after 3 – 4 days
- Cilia regenerate after 2 weeks
- Median duration of illness ~ 12 days
- Symptoms may persist for 3 (18%) to 4 (9%) weeks

Bronchiolitis Respiratory Score (Liu, 2004)

	0	1	2	3
Respiratory Rate	0-6 mo < 50 6mo – 1yr < 40 1 yr+ < 30	0-6 mo < 60 6mo – 1yr < 50 1 yr+ < 45	0-6 mo < 70 6mo – 1yr < 60 1 yr+ < 60	0-6 mo > 70 6mo – 1yr > 60 1 yr+ > 60
SaO_2	≥ 90 %	≥ 88 %	≥ 86 %	≤ 85 %
General Appearance	Calm No distress	Mildly irritable; easy to console	Moderately irritable; difficult to console	Extremely irritable; cannot be comforted
Retractions and nasal flaring (NF, SS, IC, SC)	None	1 of 4	2 of 4	3 or more
Auscultation	Clear	Scattered wheezes	Diffuse expiratory wheezing	Biphasic wheezing or very poor air movement

Criteria for Discharge

Bronchiolitis

- Oxygen sats consistently ≥ 92%
- No respiratory distress (RS < 5)
- No apnea or significant risk factors
- Respiratory rate < 60 breaths per minute
- Adequate oral intake
- Family education complete
- Adequate bulb suctioning
- Physician discretion
- Caretaker comfortable and reliable

Risk Factors for ED Return Visit

Bronchiolitis

- 17 - 20% ED return rate:
  - 65% within 2 days
- Norwood A, Mansbach JM, Clark S, et al. Prospective multi-center study of bronchiolitis: predictors of an unscheduled visit after discharge from the emergency department. *Acad. Emerg Med.* 2010 Apr;17(4):376-82. [722 patients younger than 2 years of age]:

	OR	p-value
• < 2 months of age:	2.1	0.03
• Sex: male:	1.7	0.02
• History of hospitalizations:	1.7	0.02
• Prematurity (< 35 weeks):	1.6	0.16

Risk Factors for Apnea

- Full-term birth and < 1 month of age
- Preterm birth (< 37 weeks gestation) and age < 2 months post conception
- History of Apnea of prematurity
- Emergency Department presentation with apnea
- Apnea witnessed by a caregiver

Conclusion: RSV in Febrile Infants Bronchiolitis

- Young febrile infants with RSV or clinical Bronchiolitis are at lower risk of SBI than febrile infants without these findings
    - Routine RSV testing not necessary

- Risk of UTI, however, remains significant

State of California—Health and Human Services Agency
California Department of Public Health

TOMÁS J. ARAGÓN, MD, DrPH
Director and State Public Health Officer

GAVIN NEWSOM
Governor

June 14, 2023

Dear Laboratory Partners,

To better align laboratory reporting for SARS-CoV-2, influenza virus, and respiratory syncytial virus (RSV), the California Department of Public Health (CDPH) is issuing updated reporting requirements for the types of results to report for these three pathogens. Please note, SARS-CoV-2 and influenza virus results are currently required to be reported to public health per CCR Title 17 section 2505. CDPH is in the process of adding RSV to section 2505 and asks laboratories to voluntarily report these results until CCR Title 17 section 2505 is officially updated.

Factors influencing eradication of polio

- Eradication of polio has been defined in various ways:
- As elimination of the occurrence of poliomyelitis even in the absence of human intervention.[8]
- As extinction of poliovirus, such that the infectious agent no longer exists in nature or in the laboratory.[9]
- As control of an infection to the point at which transmission of the disease ceased within a specified area.[8]
- As reduction of the worldwide incidence of poliomyelitis to zero as a result of deliberate efforts, and requiring no further control measures.[10]
- In theory, if the right tools were available, it would be possible to eradicate all infectious diseases that reside only in a human host. In reality, there are distinct biological features of the organisms and technical factors of dealing with them that make their potential eradicability more or less likely. Three indicators, however, are considered of primary importance in determining the likelihood of successful eradication: that effective interventional tools are available to interrupt transmission of the agent, such as a vaccine; that diagnostic tools, with sufficient sensitivity and specificity, be available to detect infections that can lead to transmission of the disease; and that humans are required for the life-cycle of the agent, which has no other vertebrate reservoir and cannot amplify in the environment.[11]

- The most important step in eradication of polio is interruption of endemic transmission of poliovirus. Stopping polio transmission has been pursued through a combination of routine immunization, supplementary immunization campaigns, and surveillance of possible outbreaks. Several key strategies have been outlined for stopping polio transmission:[12]
- High infant immunization coverage with four doses of oral polio vaccine (OPV) in the first year of life in developing and endemic countries, and routine immunization with OPV or IPV elsewhere.
- Organization of "national immunization days" to provide supplementary doses of oral polio vaccine to all children less than five years old.
- Active surveillance for poliovirus through reporting and laboratory testing of all cases of acute flaccid paralysis. Acute flaccid paralysis (AFP) is a clinical manifestation of poliomyelitis characterized by weakness or paralysis and reduced muscle tone without other obvious cause (e.g., trauma) among children less than fifteen years old. Other pathogenic agents can also cause AFP, such as enteroviruses, echoviruses, and adenoviruses.[13]
- Expanded environmental surveillance to detect the presence of poliovirus in communities.[14] Sewage samples are collected at regular and random sites and tested in laboratories for the presence of WPV or cVDPV. Since most polio infections are asymptomatic, transmission can occur in spite of the absence of polio-related AFP cases, and such monitoring helps to evaluate the degree to which virus continues to circulate in an area.
- Targeted "mop-up" campaigns once poliovirus transmission is limited to specific geographical foci.

Assessing the Real-World Effectiveness of Immunizations for Respiratory Syncytial Virus

- The early introduction phase of newly licensed RSV immunizations in the US poses multiple challenges to the assessment of real-world effectiveness and impact. Low immunization uptake among the recommended groups during the 2023-2024 season may hinder assessments of immunization effectiveness using traditional observational study designs.
- As of February 2024, uptake of the maternal RSV vaccine among eligible pregnant persons was estimated to be 18%, uptake of nirsevimab among infants younger than 8 months of age was 41%, and uptake of RSV vaccines among adults aged 60 years or older was 22%.[6]

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- RSV season and for some children aged 8 to 19 months with certain high-risk conditions entering their second RSV season. For adults aged 60 years or older, 2 RSV vaccines (Arexvy [GSK] and Abrysvo [Pfizer]) are recommended to prevent RSV lower respiratory tract infection.
- All 3 newly licensed RSV immunization products were efficacious in preventing severe RSV illness in prelicensure trials.[1,3-5] Postlicensure studies are needed to corroborate findings from these trials in real-world settings and in populations underrepresented in the prelicensure trials (eg, adults with immunocompromising conditions or frailty and older age groups among adults aged ≥60 years).
- Observational studies of real-world immunization effectiveness typically compare the frequency of the illness outcome among persons who were immunized vs those who were not (cohort design) or the frequency of immunization among persons with the illness outcome vs those without the outcome (case-control or test-negative design). In both approaches, uptake of the immunization in the population must be sufficiently high to allow for an effectiveness evaluation. Immunization and outcome status also must be accurately identified. In addition, differences in the characteristics of immunized and unimmunized persons that might be associated with risk of the illness outcome must be addressed in analyses to optimize validity.

Assessing the Real-World Effectiveness of Immunizations for Respiratory Syncytial Virus

- Effectiveness estimates for RSV immunization may only be generalizable to groups that had sufficient uptake to study the effectiveness. For example, if nirsevimab was largely given to infants younger than 6 months of age because of updated prioritization guidance during supply shortages, the estimates may not be generalizable to older children.
- In addition, protection from immunization is expected to wane, especially in the case of passive immunization of infants through maternal vaccination and immunization in infants and young children with long-acting monoclonal antibodies. Immunization effectiveness is likely to appear higher when estimated early in the season with a shorter interval from vaccination or immunization than when estimated for the full season or over multiple seasons. Two early reports[7,8] on nirsevimab from Spain and the US suggest high levels of effectiveness against RSV-associated hospitalization early after receipt (with a median interval of 6 weeks from receipt in the US analysis), but emphasize the need for additional estimates of effectiveness for a complete RSV season.
- Despite these anticipated challenges, the advent of immunizations for RSV to protect infants and young children and older adults presents unique opportunities to monitor and measure their public health effectiveness and potential shifts in RSV epidemiology. Real-world studies may answer key questions about immunizations for RSV that could not be fully addressed in prelicensure trials, including (1) the durability of protection from RSV immunization; (2) whether effectiveness varies by vaccine product in older adults, strategy (maternal vaccination or infant immunization) in young infants, and risk groups (eg, those with immunocompromising conditions); and (3) whether RSV immunization protects against a broader range of outcomes than studied in the prelicensure trials.
- Newly licensed immunizations for RSV have the potential to prevent substantial numbers of hospitalizations and deaths, and real-world evidence of immunization effectiveness may support eventual introduction in low- and middle-income countries where the public health benefit may be greatest. There are rare moments in public health when decades of effort toward prevention of a specific disease culminate in the introduction of new immunization products with the potential to dramatically reduce morbidity and mortality—for RSV, the real-world evidence will determine if that time is now.

Assessing the Real-World Effectiveness of Immunizations for Respiratory Syncytial Virus

- In addition, there may be differential uptake within groups recommended for immunization, with some subgroups more likely to be immunized than others. For example, among infants and young children, differential uptake of nirsevimab during the 2023-2024 season may have occurred because of early nirsevimab shortages.
- Similarly, among adults aged 60 years or older, current recommendations use a shared clinical decision-making framework informed by both the patients' characteristics, values, and preferences and the health care professionals' clinical discretion.[2]
- For both older adults aged 60 years or older and pregnant people, vaccination may also occur more frequently in retail pharmacy settings than for other routine vaccines (eg, because of the cost of stocking vaccines and insurance reimbursement mechanisms). Collectively, factors influencing differential uptake within groups recommended for immunization could lead to increased uptake either among those with poorer health and at greater risk of severe RSV illness (some of whom may be at greater risk of suboptimal immune responses to vaccination) or conversely, among healthier individuals who can more easily seek out vaccination. Both phenomena have been observed in studies of influenza vaccine effectiveness and can lead to bias in effectiveness estimates unless patient differences by immunization status and risk of infection are identified, appropriately measured, and addressed in the analyses.

Assessing the Real-World Effectiveness of Immunizations for Respiratory Syncytial Virus

- Accurate identification of RSV immunization status may be hampered by patients' or caregivers' recall now that up to 3 respiratory virus immunizations (COVID-19 vaccines, influenza vaccines, and RSV immunizations) are available, and timely verification is likely to be challenging because of varying reporting requirements, jurisdictional immunization information systems, and settings for the administration of vaccines and immunizations.
- To assess effectiveness in young infants, accurate identification of both maternal RSV vaccination and infant immunization (including receipt of both nirsevimab and palivizumab) is important because all 3 immunizations prevent severe RSV illness.
- Direct comparison of the effectiveness of maternal RSV vaccination vs infant administration of nirsevimab to prevent severe RSV will require adequate use of both strategies in the same source population, standardized outcomes, and rigorous analytic methods to address differences between infants with maternal RSV vaccination exposure vs infant receipt of nirsevimab.

Real-world studies may answer key questions about immunizations for RSV that could not be fully addressed in prelicensure trials

- the durability of protection from RSV immunization
- whether effectiveness varies by vaccine product in older adults, strategy (maternal vaccination or infant immunization) in young infants, and risk groups (eg, those with immunocompromising conditions)
- whether RSV immunization protects against a broader range of outcomes than studied in the prelicensure trials.

Assessing the Real-World Effectiveness of Immunizations for Respiratory Syncytial Virus

- Newly licensed immunizations for RSV have the potential to prevent substantial numbers of hospitalizations and deaths, and real-world evidence of immunization effectiveness may support eventual introduction in low- and middle-income countries where the public health benefit may be greatest.
- There are rare moments in public health when decades of effort toward prevention of a specific disease culminate in the introduction of new immunization products with the potential to dramatically reduce morbidity and mortality—for RSV, the real-world evidence will determine if that time is now.

Thank You