

Sent on behalf of William Isenberg, M.D., Ph.D, Chief Medical & Quality Officer, Sutter Health, and Jeffrey Silvers, M.D., Medical Director of Pharmacy and Infection Control, Sutter Health

Emerging Infections Newsletter for Clinicians

July 13, 2023

Written by Dr. Silvers with contributions from Dr. Joan Etzell (Lab), Lisa Rieg (Pharmacy), and Gordon Sproul (Pharmacy). Please use Google Chrome for the best experience.

Topics

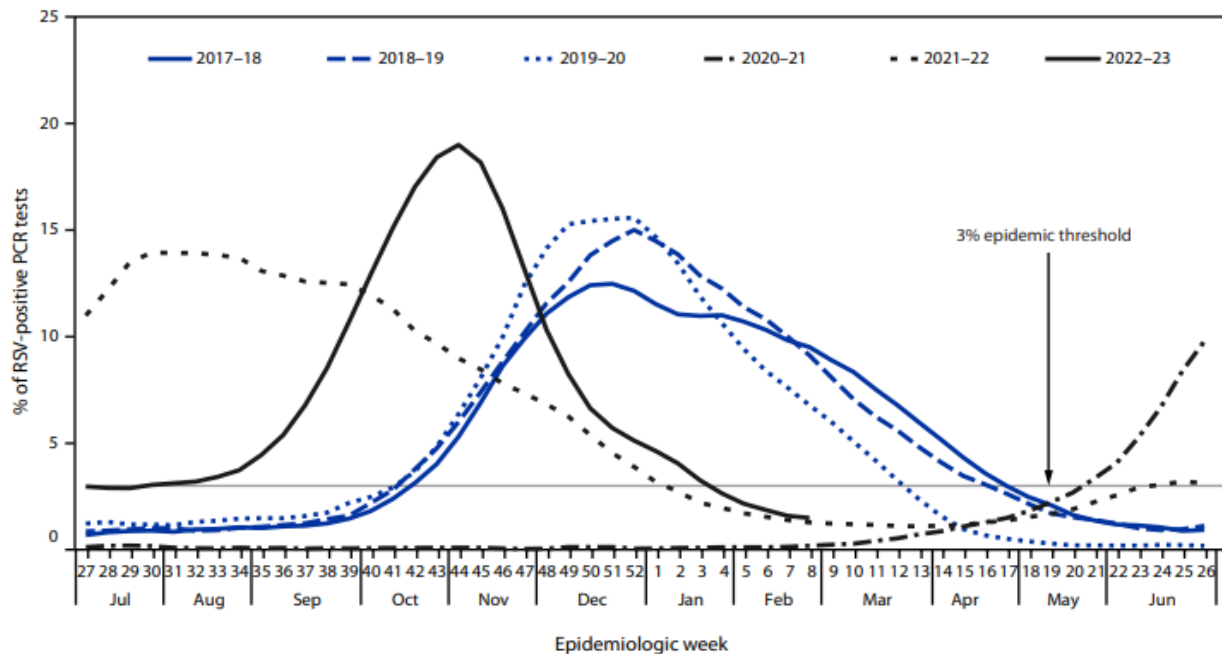
1. RSV
 - a. Vaccine for persons 60 years and older
 - b. What you need to know to provide “shared decision making”
 - i. RSV seasons before, during and after COVID
 - ii. Predicting our next season
 - iii. Recurrent RSV infections
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RSV Vaccine

- [Two RSV vaccines](#) are being approved for persons 60 years and older.
- The Advisory Committee on Immunization Practices (ACIP) has placed them in the “shared decision-making” category.
 - This is a gray zone where the data are not strong enough to support recommending vaccination for everyone in the eligible group, but it is believed to have enough potential benefit that patients should have the opportunity to receive the vaccine.
 - The CDC recommends that the [shared decision](#) to vaccinate an individual may be informed by:
 - Best available evidence of who may benefit.
 - An individual’s characteristics, values and preferences.
 - Healthcare provider’s clinical discretion.
 - Characteristics of the vaccine being considered.
 - Risk vs. benefit of the vaccine discussion by the person ordering the vaccine (if other specifics are lacking).
- Although the RSV antigen test and molecular test (PCR) have about the same sensitivity and specificity, the CDC defines the weeks of a seasonal epidemic by PCR positivity rates $\geq 3\%$.

- RSV epidemics typically follow seasonal patterns with peaks in December and January.
- The COVID-19 pandemic disrupted the [usual pattern](#). The graph below shows 2017-2023 RSV seasons in the United States.
 - 2017-2020 began in October, peaked in December and ended in April.
 - 2020-21, there was not a winter RSV epidemic.
 - 2021-22 season began in May, peaked in July and ended in January.
 - 2022-23 season started in June and peaked in November. It was also notable for the highest percentage positivity rates of any of these seasons.
 - The CDC graph below suggests that RSV seasonality is moving towards the pre-pandemic normal patterns. This, however, is a soft conclusion.

FIGURE 1. Percentage* of polymerase chain reaction test results positive for respiratory syncytial virus, by epidemiologic week — National Respiratory and Enteric Virus Surveillance System, United States, July 2017–February 2023



Abbreviations: PCR = polymerase chain reaction; RSV = respiratory syncytial virus.

- Similar to what we do with influenza, the RSV season in the Southern Hemisphere may be useful to help prognosticate what we will see in our following winter.
- Australia is reporting cases close to [10 times higher](#) in some states compared to the same time last year.
- That would suggest that we might have a very large RSV season again this year. However, drilling down on the information shows that the situation is more complicated.
- According to the Queensland weekly [surveillance report](#), Queensland (the third largest state/territory in Australia) had their RSV season start in March (equivalent to September for us) and it is actually much smaller than the 2022 season (graph below). It is still ongoing with positivity rates staying about 5%.

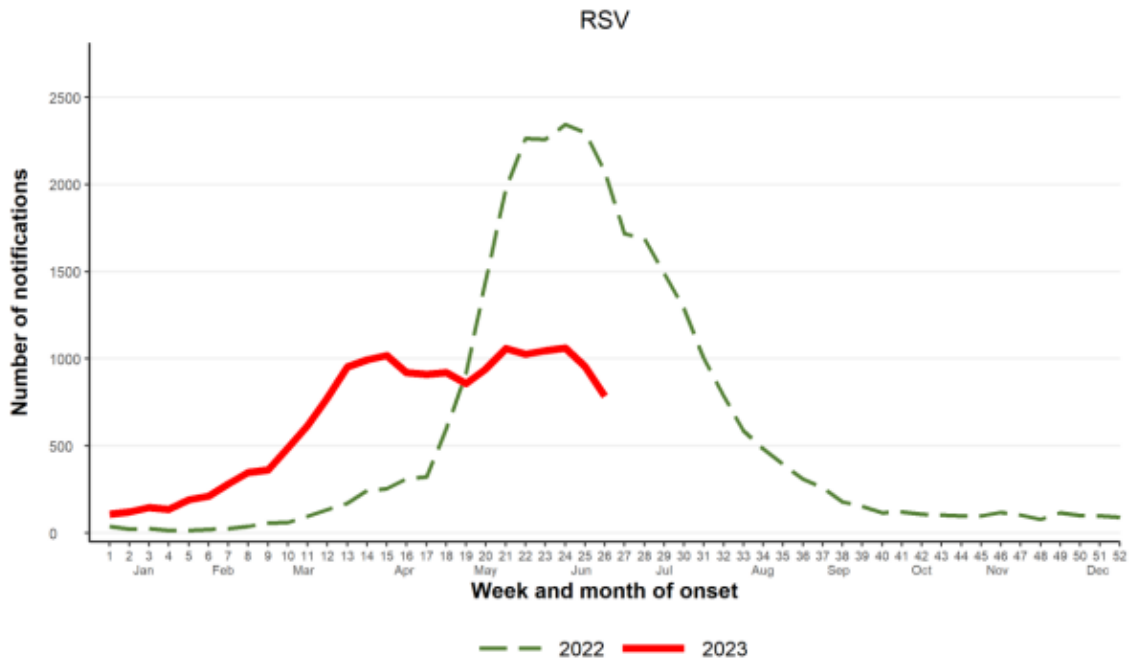
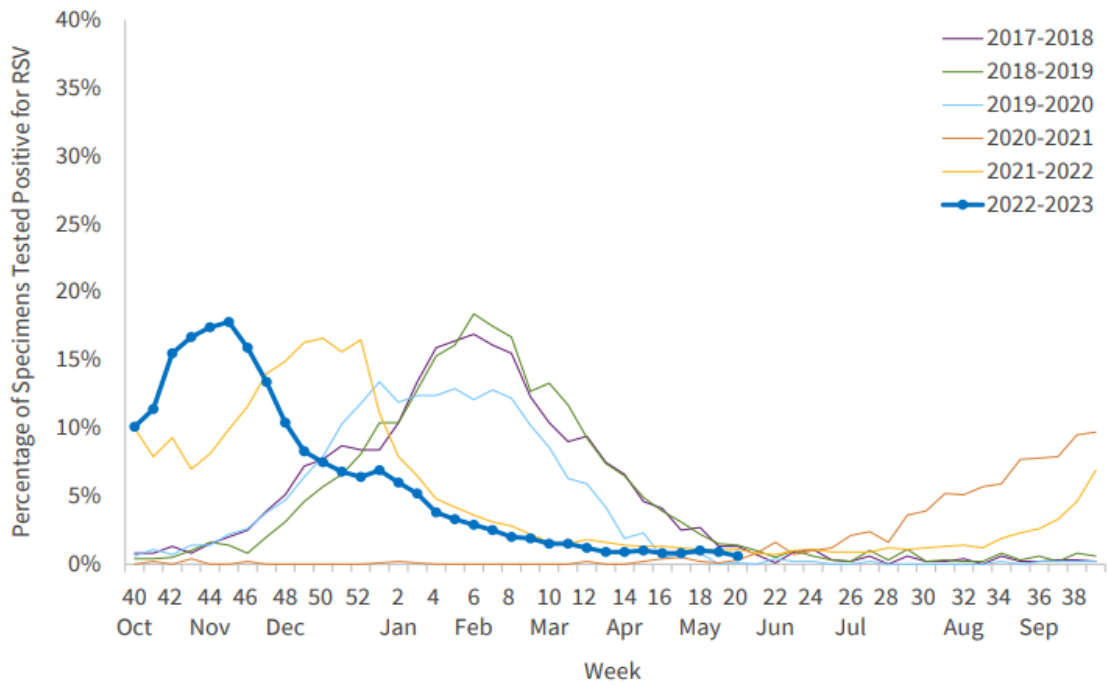


Figure 2: RSV notifications in Queensland, by week and month of onset, 1 Jan 2022 to 2 Jul 2023.

- Other states/territories have very elevated rates now when compared to the same time in 2022, but Australia had a very early, large season in 2022 and it was already past the peak last July. This likely distorts the data.
- Looking at Southern Hemisphere seasonal patterns and case numbers prior to 2022 might be helpful. Unfortunately, Australia did not require reporting of cases of RSV until 2022 so prior historical data is very incomplete.
- [California data](#) from 2017-May 2023 is shown in the graph below. Contrary to what is shown in the CDC graph (first graph labeled Figure 1), the California season in 2022 started earlier than the 2021 season. Otherwise, it appears that the shape of the outbreak, based on test detections, was typical.

Figure 13. Percentage of RSV Detections at Clinical Sentinel Laboratories, 2017–2023 Season to Date



- Testing does not always correspond to severity of the outbreak. Last season was associated with unusually high morbidity and mortality.
- The graphs below illustrate the impact of the 2022-23 season on mortality. The first graph combines all ages. The second graph shows that 2022-23 mortality in persons 65 years and older was more than twice the number reported in 2019-20.

Figure 17. Percentage of RSV-coded Deaths from Death Certificates, 2017–2023 Season to Date

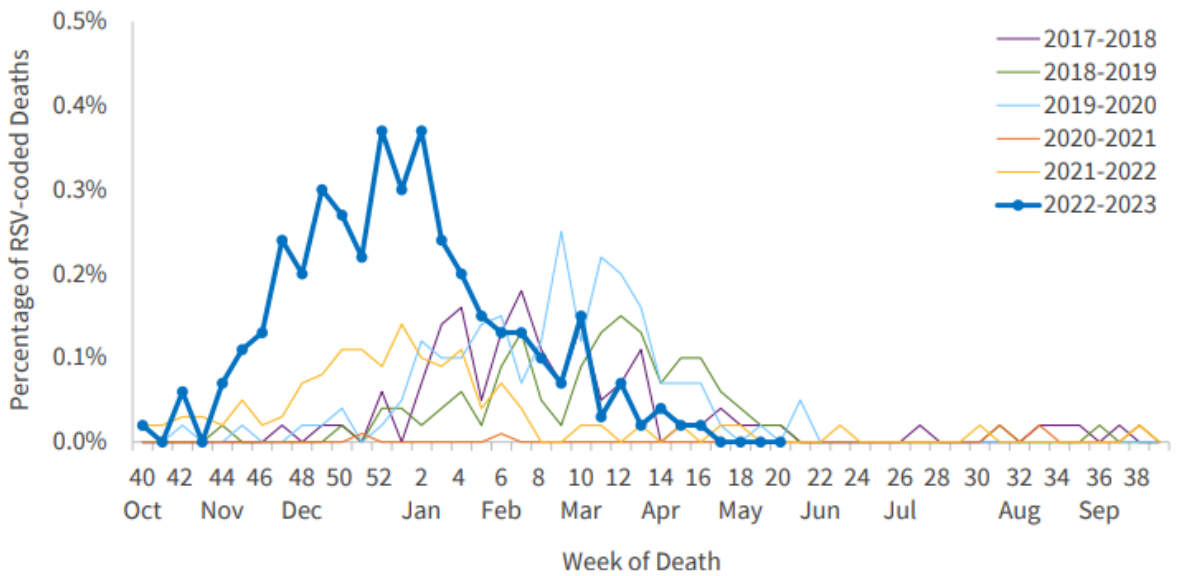
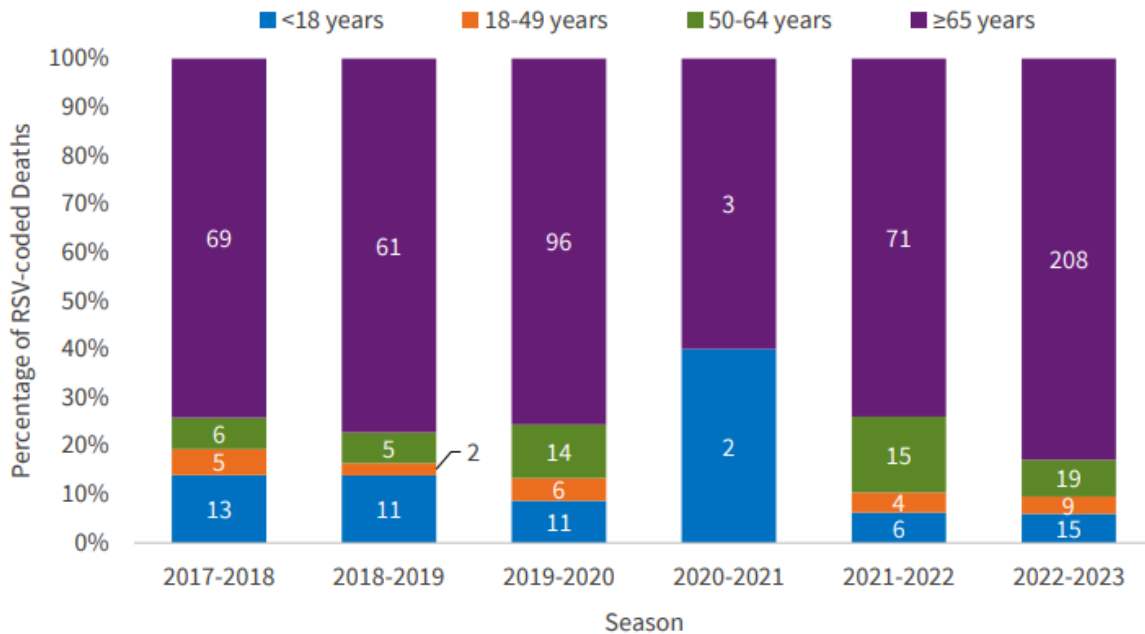
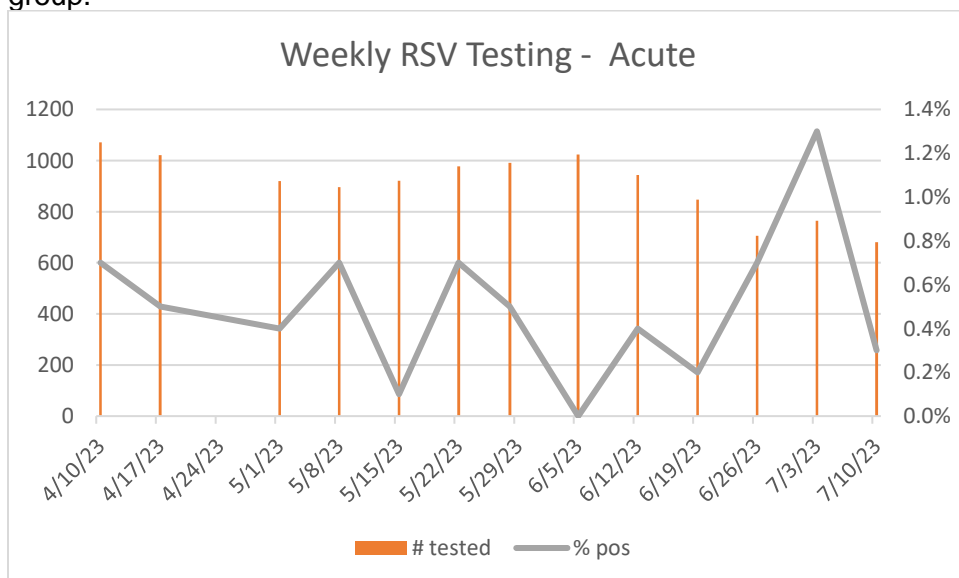
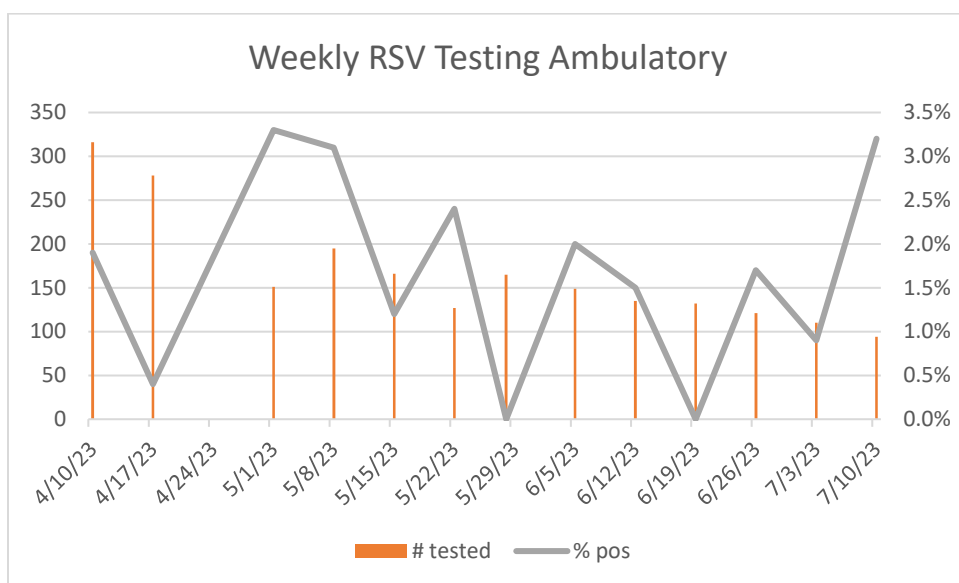


Figure 18. Age Distribution of RSV-coded Deaths from Death Certificates, 2017-2023 Season to Date



- The leading explanation for the unusual 2022-23 RSV season was the gap in herd immunity from decreased infections during the winters of 2020 and 2021 plus social behavior changes secondary to COVID.
 - A November 2022 convenience-sample study from Massachusetts published in the [NEJM](#) (April 6, 2023) demonstrated that at least 10 different lineages were circulating at the same time and they had all been circulating pre-COVID. Nothing supported the presence of a new, more-virulent strain.
- Tracking weekly data in Sutter for number of tests performed and percent-positivity is shown below for both acute (ED and hospitals) and ambulatory. The number of tests performed in acute settings is decreasing and the positivity rates remain low. In ambulatory settings, the rates periodically surpass 3% for a week but less than 100 tests per week are now being performed. This negates the value of the positivity rate in that group.





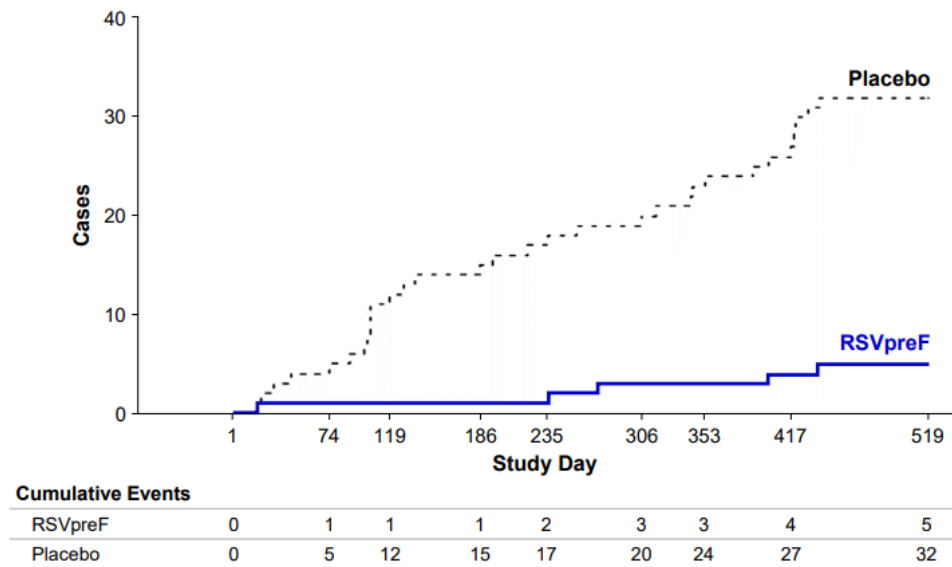
- Looking at the data that led to the ACIP decision explains their recommendation.
- Both Pfizer and GSK conducted studies as a single dose of vaccine versus placebo in persons 60 years or older. An example of the Pfizer data (published in the [NEJM](#) April 20, 2023), is below.
 - Note that there were only 12 cases in persons 75 years and older. There was not any statistically significant efficacy demonstrated in preventing a lower respiratory tract infection (LRTI).

Pfizer: RSV lower respiratory tract illness (LRTI), defined by ≥ 3 lower respiratory signs or symptoms

Population	Case split (vaccine/placebo) ^a	Manufacturer-calculated vaccine efficacy, % (95% CI)
All (age ≥ 60 years)	5/32	84.4 (59.6, 95.2)
Age ≥ 65 years	3/23	87.0 (56.8, 97.5)
Age ≥ 70 years	1/11	90.9 (37.5, 99.8)
Age ≥ 75 years	1/7	85.7 (-11.2, 99.7) ^b
Age ≥ 80 years	0/4	100.0 (-51.5, 100.0) ^b

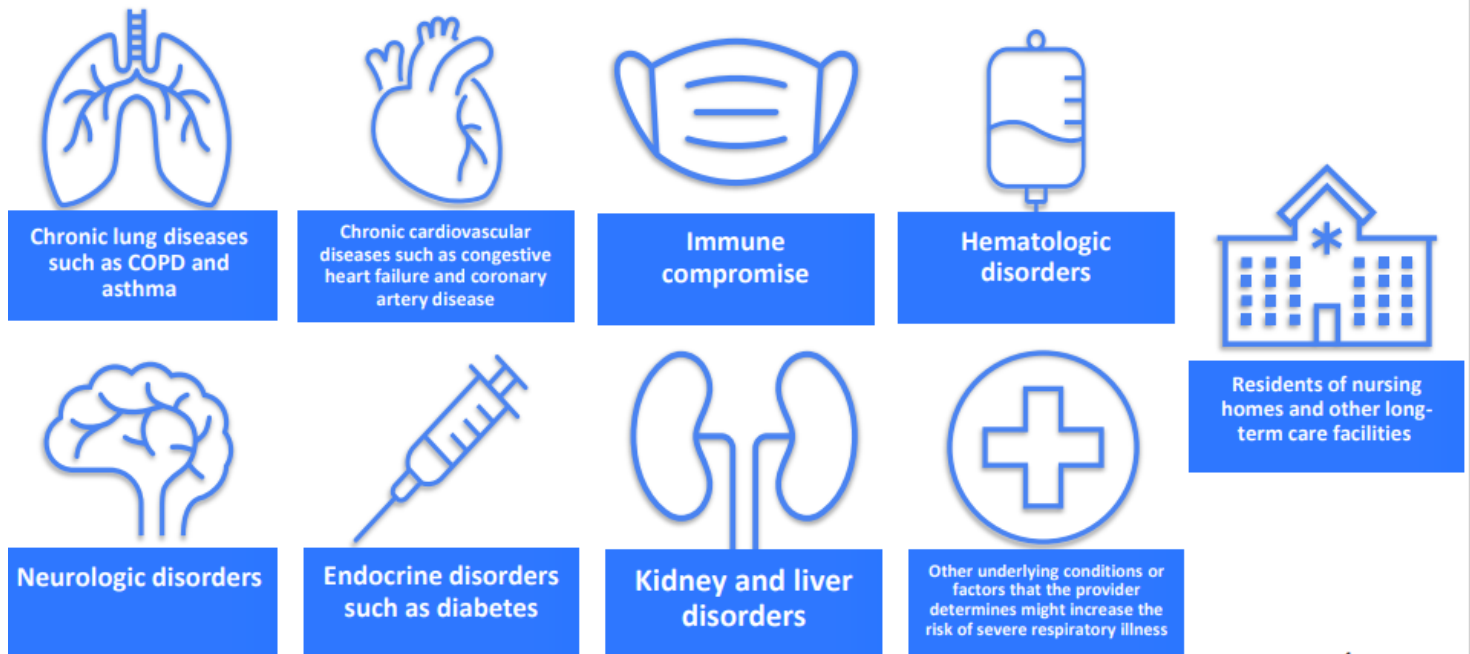
- There was [data](#) supporting vaccine efficacy through mid-season 2 (when the study terminated). Graph below.

Persistent VE against RSV-LRTD with ≥ 3 Symptoms through Mid-Season 2



- Because of the exceptionally small numbers of study persons developing severe RSV illness requiring oxygen support (one in vaccine and one in placebo), and no deaths in almost 16,000 person-years in each group, no conclusions could be drawn about vaccine efficacy to prevent these most serious complications.
- The data does support a vaccine efficacy of about 85% for all persons 60 years and older in the prevention of a lower respiratory tract infection (LRTI) due to RSV.
- More information on possible, vaccine-related, adverse events including inflammatory neurologic events can be found [here](#).
- Data showing the non-inferiority of coadministration with the adjuvanted influenza vaccine can be found [here](#).
- The [CDC slide](#) below shows adults who may be at a higher risk of RSV disease.

If shared clinical decision-making is recommended adults who may be at higher risk of RSV disease include persons with:



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- Recurrent RSV infections occur, and infection in the prior season does not preclude a repeat infection this year.

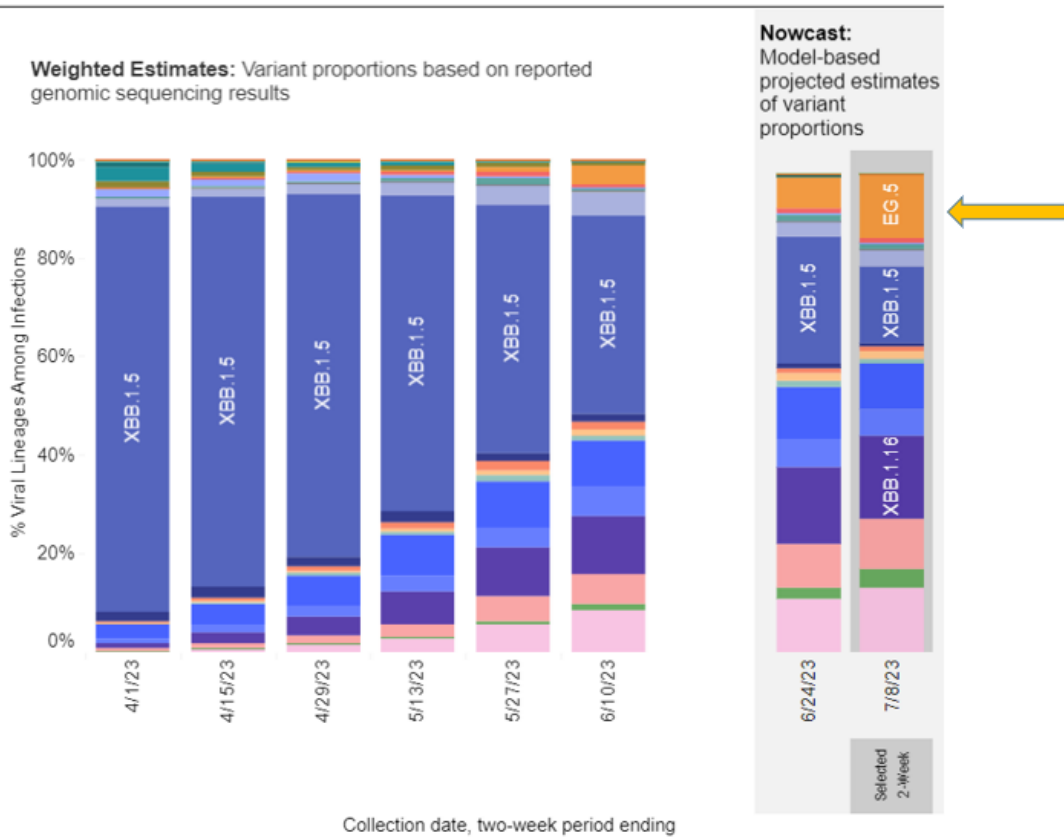
Take Home on RSV and What You Need to Know

- RSV infection last year does not prevent the development of another infection this year.
- COVID-19 changed the typical seasonal timing of respiratory viruses in 2020 through 2022.
- It is uncertain whether typical patterns will return this season.
- Last season, more than twice the number of persons 65 years and older died compared to the 2019-20 season and over three times the number who died in either the 2017-18 or 2018-19 season.
- The explanation for the highly virulent season last year was diminished exposure to disease for several years, social distancing and masking. There were not any unusual circulating strains.
 - Based on that information, the last season could almost be considered a catch-up season.
 - This season might be more similar to pre-COVID in terms of numbers of cases and outcomes.
- The vaccine demonstrated a reduction in the risk of an LRTI in persons 60 years and older that extended until at least the mid-point of the second season. Because of the small number of cases, it was not able to show any effect on severe, oxygen-requiring disease or death.
- Persons who meet the vaccine criteria of 60 years and older should be provided the vaccine, if requested. Sutter Health will provide more information on RSV vaccine availability following system formulary evaluation in August.

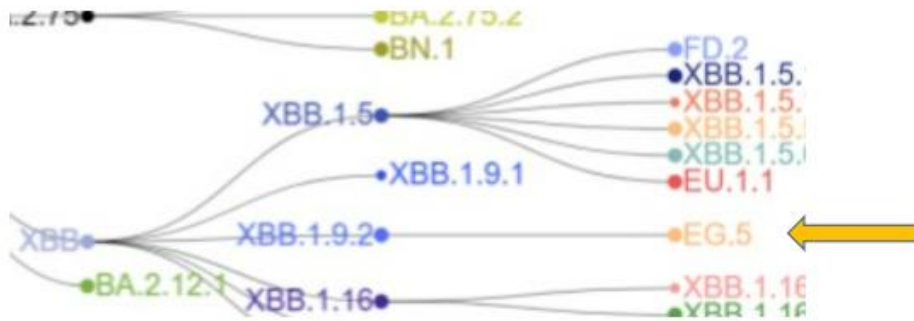
- Residents of congregate, long-term care environments represent a good cohort to vaccinate because they frequently have underlying diseases that increase the risk of severe disease.
- Persons who have frequent contact with [high-risk infants and children](#) are another special cohort to consider vaccinating.
- Other persons with the above CDC risk factors should be considered based on an individual assessment and healthcare provider's conclusions on the risk versus benefit, as well as a thorough risk/benefit discussion with the patient.
- Ideally vaccine should be administered before the onset of increased RSV activity in the community, although this may be difficult to predict.
- The duration of protection from a single RSV vaccine dosage is still unknown.

COVID-19

- Genomic sequencing graph below shows that EG.5 is rapidly becoming a dominant sequenced isolate. This is a derivative of XBB.1.9.2 and should be covered by the upcoming XBB.1.5 monovalent vaccine. No significant increase in transmissibility or virulence identified.



- Pango Lineage below with orange arrow showing EG.5



Share the Newsletter

Anyone who would like to be added to the Emerging Infections newsletter should send a request to bryan.gardner@sutterhealth.org

This communication is intended for clinicians caring for Sutter patients. If you have questions, please reach out to us at clinicians@sutterhealth.org.

