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

Sept. 7, 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

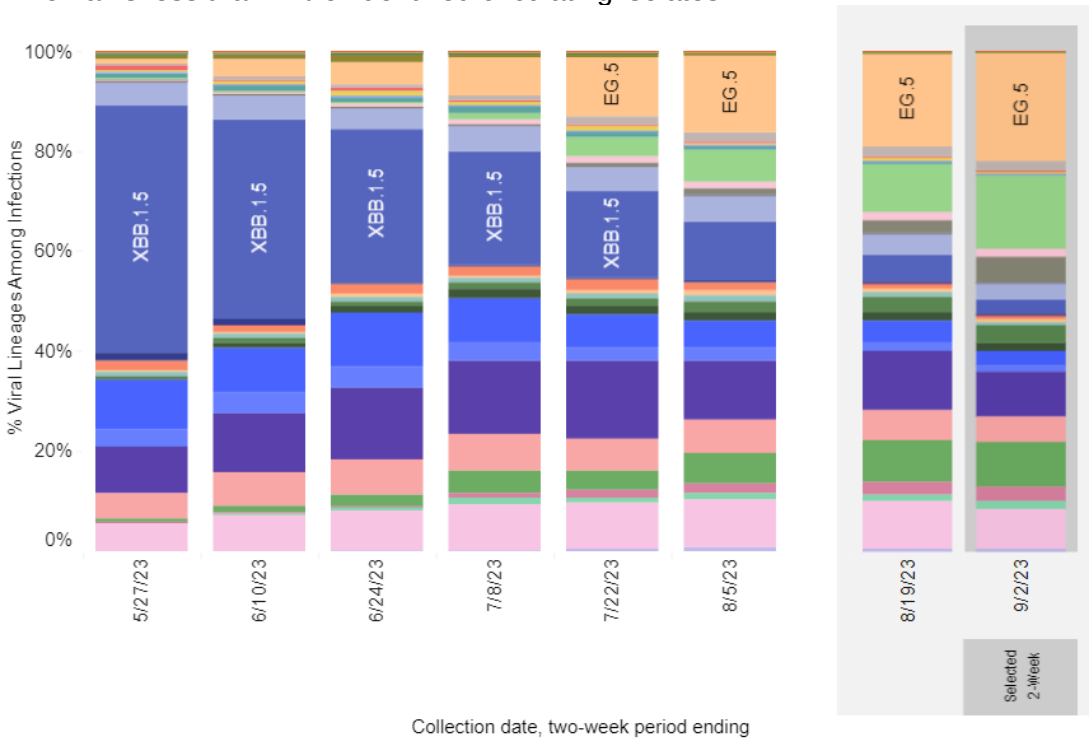
1. The tripledemic may have started in the southeast.
    a. Now is the time to get prepared.
2. COVID-19
    a. Genomic sequencing
        i. Multiple strains co-circulating
        ii. Nothing is dominant
    b. BA.2.86 may not be the threat that was feared
    c. Testing results
        i. Sutter data
    d. Vaccine
    e. Take-home COVID
3. RSV
    a. Predicting our RSV season
        i. What was seen in Australia earlier in 2023
        ii. What has been seen in the U.S. in the last 5 years
    b. RSV is starting to circulate
        i. Southeastern United States
        ii. Sutter Health ambulatory
    c. Vaccine and antibody products
    d. Take-home RSV
4. Influenza
    a. Activity increasing in multiple states, most notable in the southeast
    b. Time to vaccinate
    c. Take-home influenza
5. Share the newsletter

Tripledemic

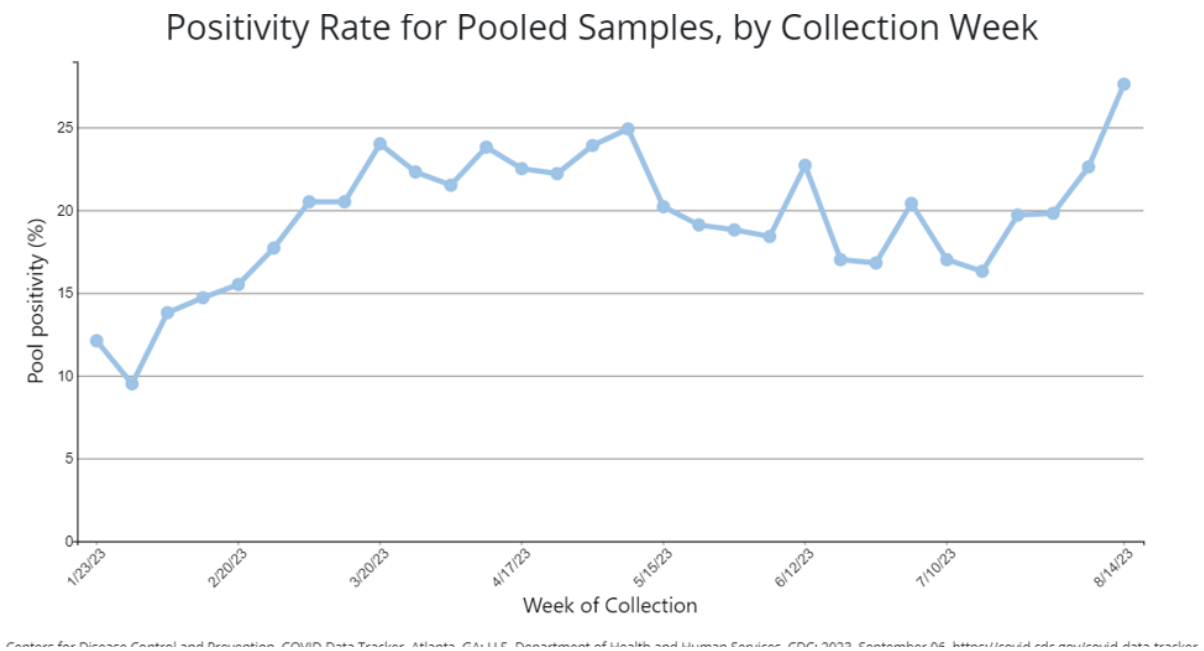
- A tripledemic is an informal term that refers to a simultaneous increase in cases of SARS-Cov-2, Influenza and RSV.
- Although the term is not based on the severity of the outbreaks, simultaneous or sequential infections can lead to increased morbidity and mortality compared to any one infection alone.
- Portions of the southeastern United States are already experiencing upticks in cases of influenza-like illnesses and RSV, joining the national increase in cases of COVID. This newsletter will discuss what is being seen with these three viruses internationally, nationally, statewide and within Sutter Health.
- Healthcare workers need to understand all three of these respiratory viruses and know what they can do to protect themselves, their family members, friends and patients.
- Additional guidance will be provided on the new RSV products.

COVID-19

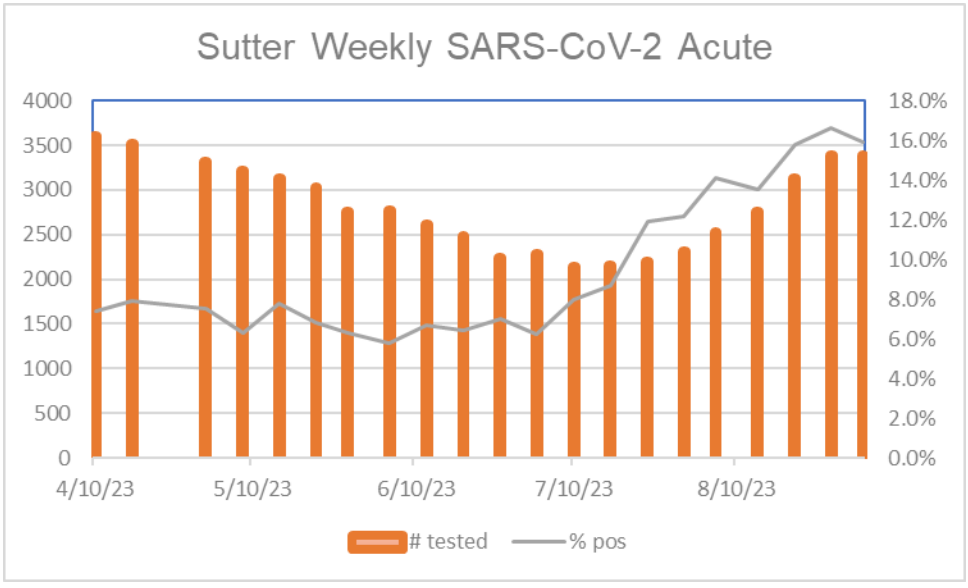
- Genomic sequencing was updated on Sept. 1. Twelve different strains are co-circulating ranging from 2.8-21.5% of isolates. Although EG.5 is the most common, it does not appear that it will dominate over all of the others. BA.2.86 is not on this graph because it remains less than 1% of identified circulating isolates.



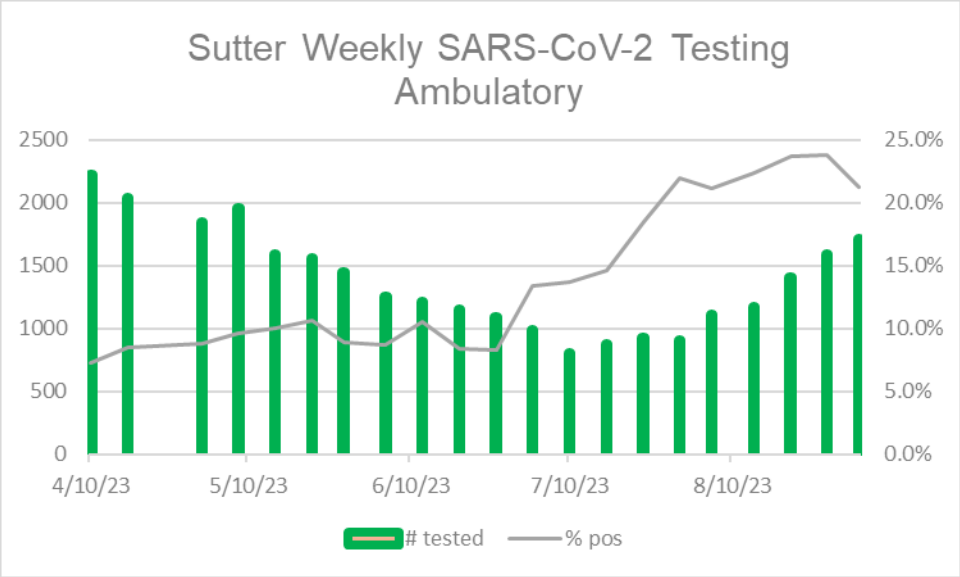
- International traveler-based testing is performed at several major airports. The CDC run chart below demonstrates the high-pooled positivity rates, now up to 27.6% over the last week. Multiple strains are co-circulating in the world



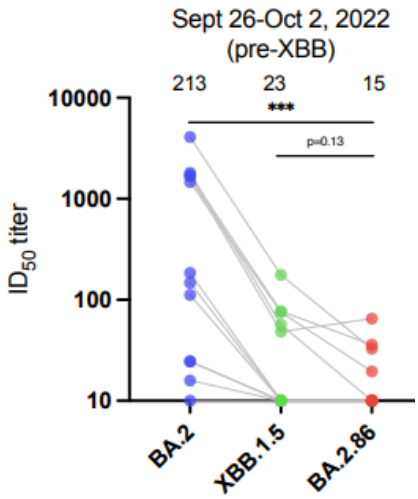
- Updated Sutter data below shows unchanged positivity rates with significant levels of testing. COVID is actively circulating, patients are becoming more symptomatic with newer strains and are seeking medical care.



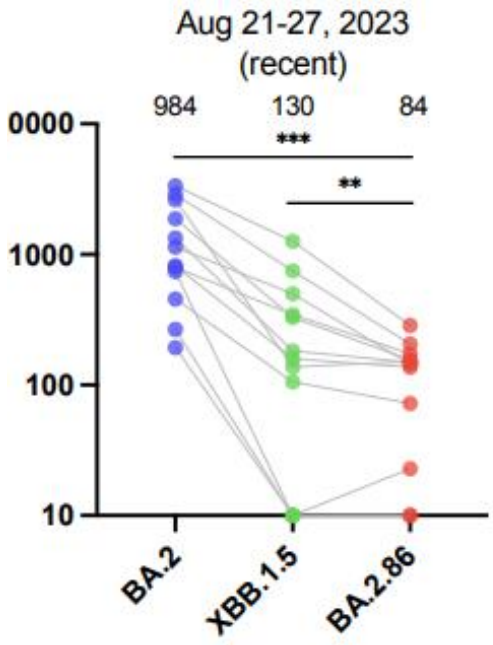
- The Sutter Health graph below shows that ambulatory positivity rates remain over 20% along with increasing ambulatory testing.



- The potential effect of BA.2.86 is unknown but early data suggests that it may not have increased virulence or transmissibility.
- BA.2.86 was recently highlighted by the WHO and CDC because of the dramatic increase in mutations found on the spike protein, many of which are at key antigenic sites. It was rapidly labelled a variant-under-monitoring, recognizing that very limited information was known on viral fitness, virulence, or transmissibility. Several leading scientists expressed concern that the large number of mutations could allow antibody evasion from prior disease or vaccines.
- Information is starting to accumulate with some encouraging results.
- A study from Sweden found the following:
  - Similar to all other circulating strains, BA.2.86 was resistant to previously utilized monoclonal antibodies including Evusheld™, bebtelovimab and sotrovimab.
  - Neutralizing antibodies from 12 persons who had disease prior to XBB were tested. All 12 samples had inadequate neutralization titers against BA.2.86 An ID50 (infective dose in 50% of normal adults) below 100 is not anticipated to be protective. Results in graph below.
  - Note that pre-XBB antibody was not protective against XBB in 11 of the 12 serum samples. This supports why we need a new vaccine.



- Out of 12 patient samples from persons with infections secondary to XBB, eight of the 12 had adequate neutralization titers against BA.2.86. This is demonstrated in the following graph.
- Interesting that only nine of the 12 persons had adequate neutralization titers against XBB.



- The take-home message from this study is that persons with infection prior to XBB (that includes Omicron and all preceding strains) are unlikely to have any protection against BA.2.86.
- On the other hand, persons who have been infected since XBB (starting Oct.1, 2022) are likely to have protection against BA.2.86 and it is likely that the new upcoming monovalent vaccine will provide protection against BA.2.86.

- United Kingdom released a situation update on Sept. 1. A total of 25 BA.2.86 isolates from eight different countries underwent genomic sequencing and clinical case review.
  - There is no clear evidence of significant spread within any of the eight countries.
  - No conclusions about viral fitness can be made yet.
  - Although there is uncertainty, this variant does not meet the definition of a variant of concern.
- Moderna released data on Sept. 6 reporting an 8.7-fold increase in neutralizing titers against BA.2.86 after administration of the new monovalent vaccine.
  - Moderna's vaccine was also tested against both the EG.5, and FL.1.5.1 variants, which demonstrated between an eight to 11-fold increase in neutralizing antibody response in a prior analysis.
  - These results support excellent neutralization titer from the vaccine against BA.2.86 and other circulating variants.

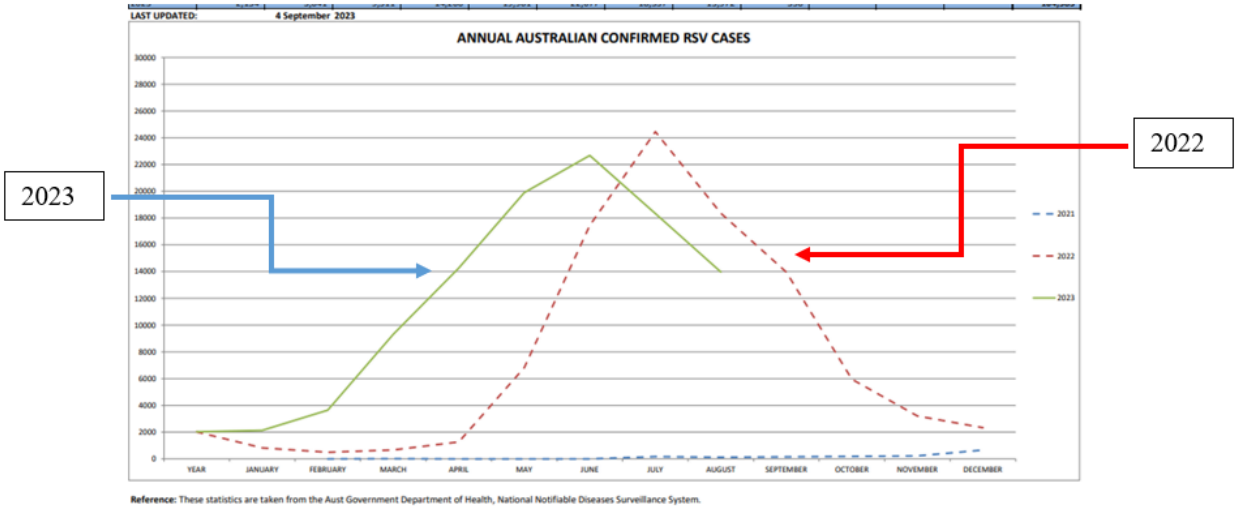
- **COVID Take-Home:**
  - Multiple strains of SARS-CoV-2 are widely co-circulating.
  - Testing positivity rates continue at high levels.

        - International travelers-based testing at United States airports shows a positivity rate of 27.6% with a wide variety of circulating variants.
        - Sutter ambulatory and emergency departments continue to increase testing and positivity rates remain elevated.
            - ✓ Ambulatory and emergency department positivity rates are 21% and 16% respectively.
    - The clinical impact of BA.2.86 remains unknown but data are accumulating that the new monovalent vaccine and recent disease are likely protective. Nothing suggests that BA.2.86 will create a surge in cases.
    - Updated information on the Moderna mRNA vaccine suggests that the updated XBB.1.5 formulation of COVID-19 vaccines continues to be effective against emerging variants, particularly in reducing hospitalization and severe disease.

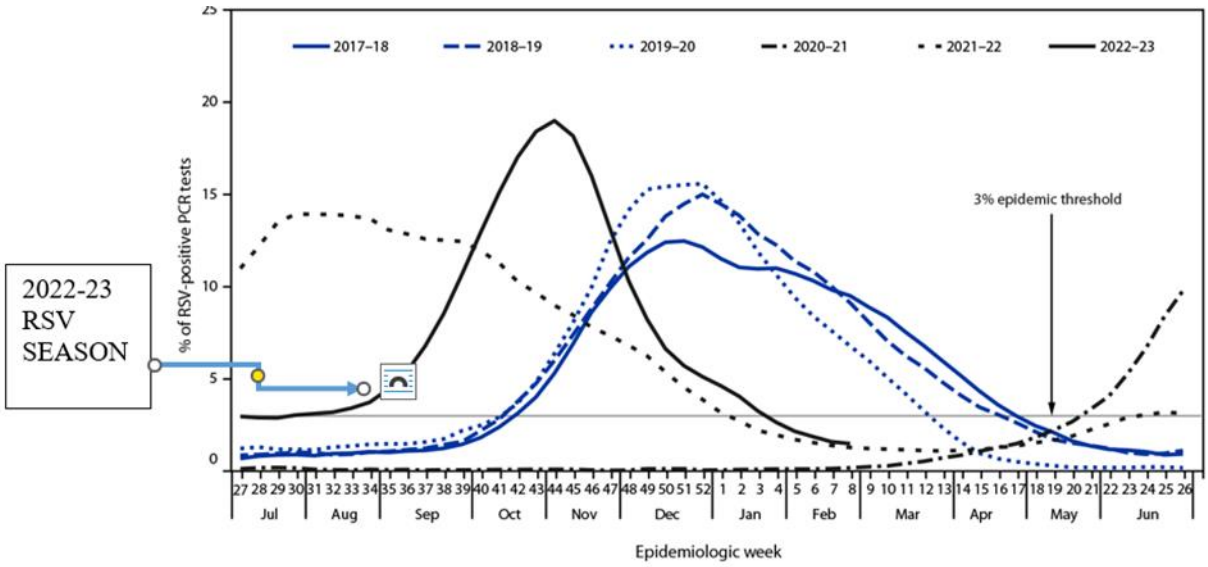
- **Related Links**
    - CDC Caring for Patients
    - CDC Data Tracker
    - CDC Latest Updates
    - CDC Vaccine Information
    - CDPH Tracking and Vaccination Updates
    - Sutter Health for Clinicians
    - Sutter Health for Patients
    - WHO Table of Contents

RSV

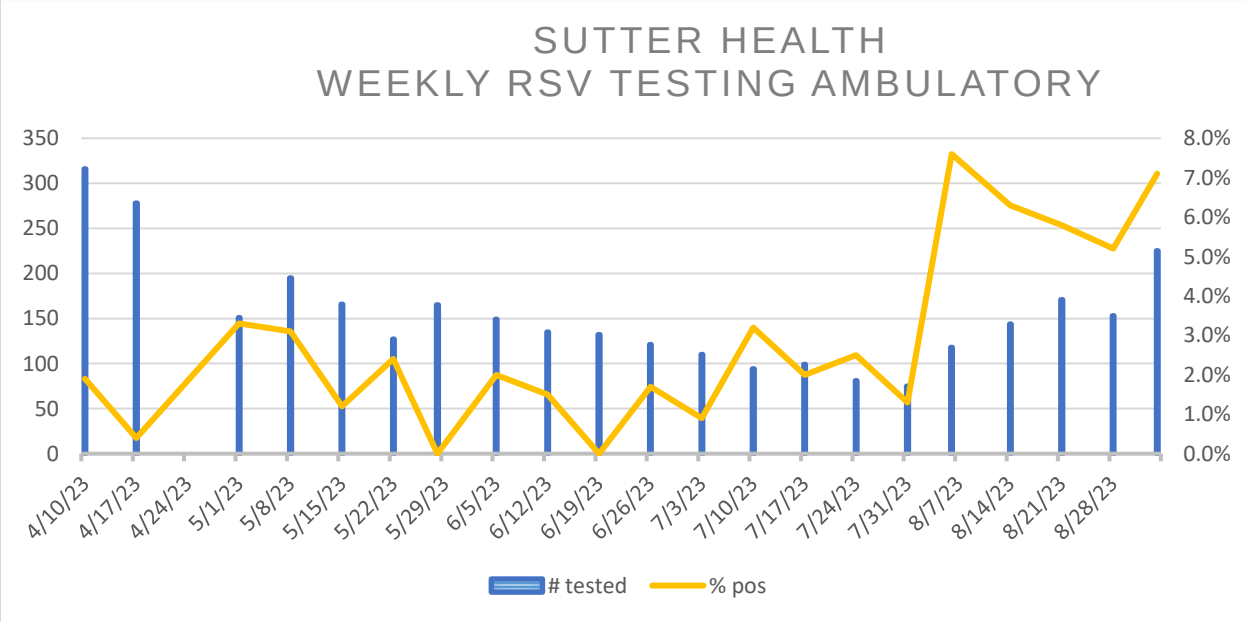
- As with influenza, we can use the last winter season in Australia to help prognosticate what we might expect from RSV.
- The Australian Immunization Coalition graph below demonstrates that RSV never caused an outbreak in 2021 during the COVID pandemic.
- Australia had a large, early onset and prolonged RSV season in 2022.
- The 2023 RSV season in Australia actually started even earlier than in 2022. It began in February (equivalent to August for us), and otherwise has a similar shape to the 2022 season. Parts of Australia experienced different times of onset of the outbreak.



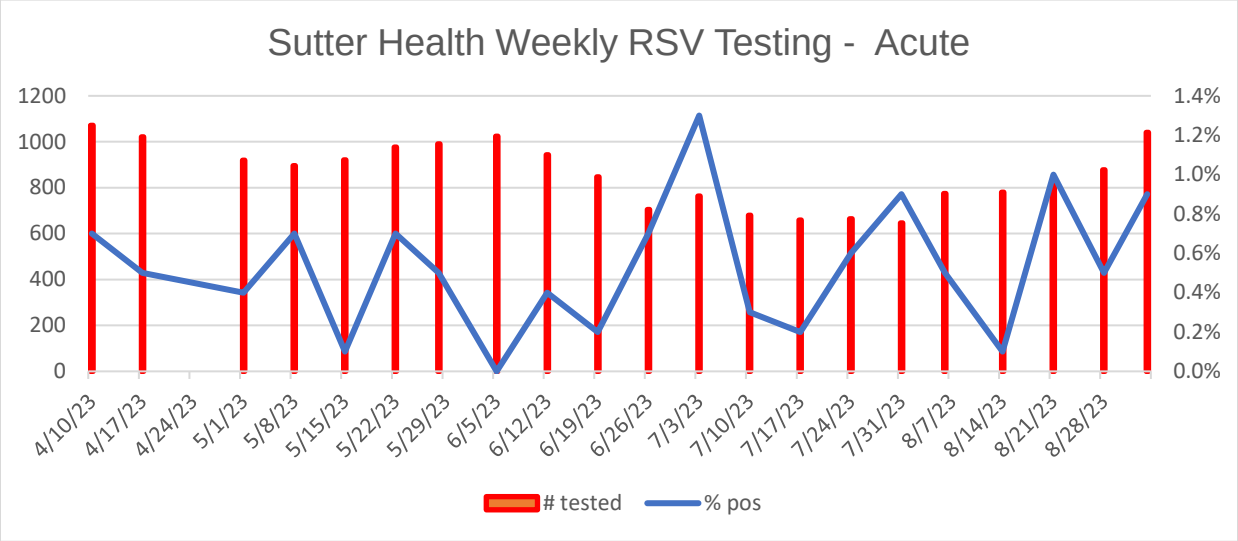
- The United States had a similar early onset, very large RSV outbreak starting in August of 2022 and continuing until the middle of January 2023. CDC graph is below.



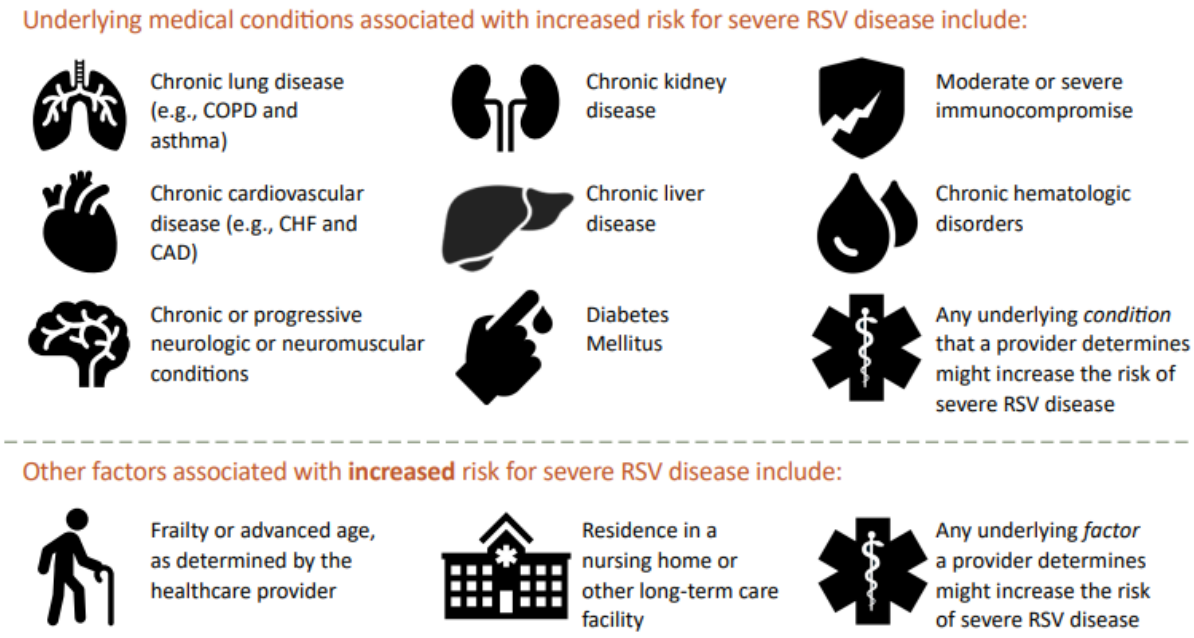
- The CDC released a [health advisory] on Sept. 5, reporting increased RSV activity in parts of the southeastern United States. Historically, regional increases in the eastern part of the United States presage the gradual spread of RSV (or influenza) north and west across the country. They predict that it will reach the west in the next few months.
- However, RSV is already starting to be identified in the ambulatory setting. The amount of testing in ambulatory is gradually increasing and positivity rates are well above the 3% threshold for 5 weeks now. See graph below.



- On the other hand, the following graph demonstrates that ED positivity rates remain low at <1%.



- Looking at Sutter combined ambulatory and emergency department testing, positivity rates are 2%, well below the state 3% outbreak threshold.
- Sutter data is probably an early clue that the virus is starting to circulate in Northern California. The number of persons infected, and disease severity are both probably low at this time, so positivity rates in emergency departments remain less than 1%.
- To date, the FDA has recently approved two unique products to help prevent RSV lower respiratory tract disease ahead of the 2023-2024 RSV season:
  - Nirsevimab (Beyfortus™), a long-acting monoclonal antibody, is approved and recommended for RSV prevention in neonates and infants less than 8 months of age, born during or entering their first RSV season, and in children 8 to 19 months of age who remain vulnerable to severe RSV disease through their second RSV season.
    - While nirsevimab supply and ability to order is not yet available at this time, Sutter has begun preparations to offer it in the acute and ambulatory care setting.
    - Coordination among the manufacturer, supply chain, formulary evaluation and provider education will be established prior to release. More information on availability will be provided in the upcoming weeks.
  - Two vaccines (Arexvy™ and Abrysvo™) may be administered using shared decision making for protection in adults 60 years of age and older.
  - Sutter is preparing to offer Abrysvo in the ambulatory care setting to adults 60 years and older as early as next week, with communications forthcoming. Patients can also receive RSV vaccines through their outpatient pharmacy if offered.
- Guidance for usage is “shared decision making.” The CDC has a very useful, one-page pictograph with information to assist with those discussions. The picture below is taken from that education piece.



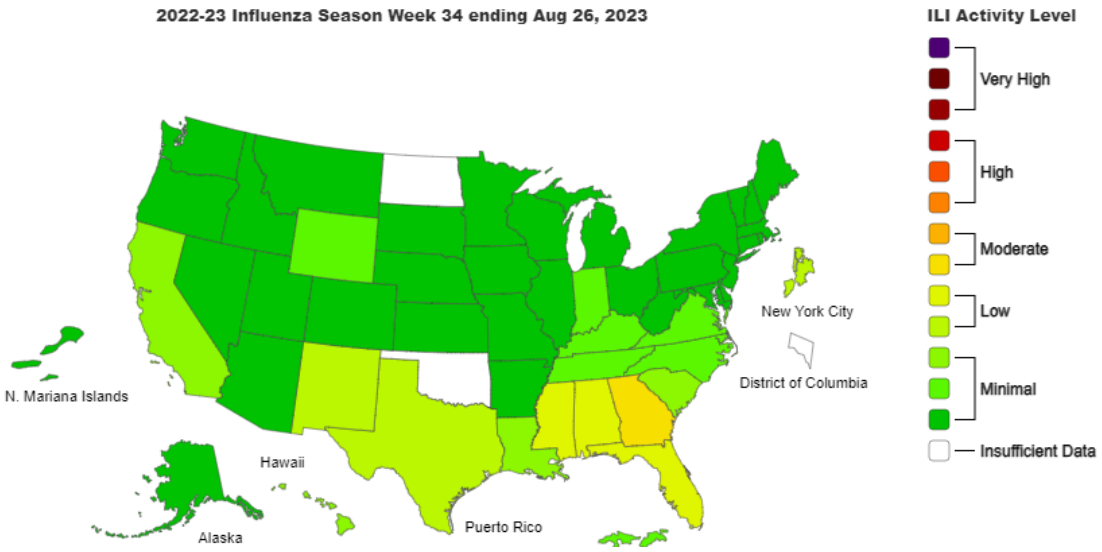
- Abrysvo™ is FDA approved for use in pregnant individuals 32-36 weeks gestational age to protect infants from birth to 6 months of age. However, the CDC has not met yet to discuss its recommendations for use in this population.
    - Sutter will prepare to offer Abrysvo™ to this population once recommendations are developed and official.

RSV Take-Home:

- Based on data from Australia, we may see a normal to relatively large RSV season, perhaps smaller than what we experienced last year.
- Increased RSV activity is already being identified by the CDC in parts of the southeastern United States.
- Although the CDC may be correct that the full impact of RSV will gradually move across the country towards California over the new 2-3 months, we are already seeing indications of some increased activity in ambulatory settings.
- RSV vaccines for persons 60 years and older is approved and should be available in some Sutter ambulatory settings next week.
- RSV vaccine for pregnant individuals is not available until CDC guidance is approved and released.
- Nirsevimab is not available yet but preparations are being made to offer in acute and ambulatory settings once the product is released.

Influenza

- Influenza may be starting to circulate more in the United States.
- This is difficult to track as many states only require reporting of influenza when associated with hospitalization or death.
- The CDC generated map below shows influenza-like activity (ILI) in different states. This is typically considered a surrogate for actual influenza activity.
- The southeastern part of the United States is also starting to see increased cases of ILI, similar to their RSV numbers.



- Vaccine is anticipated to be a good match this season.
- September and October are the best times to get vaccinated.
- Co-administration with the COVID vaccine is acceptable
  - As mentioned in last week's newsletter, the CDC suggests considering using separate arms for co-administration of the enhanced flu and the COVID vaccines.
  - The same arm can be used for the standard flu and COVID vaccines.

Influenza Take-Home:

- Data suggests that influenza activity may be increasing in some parts of the United States, especially in the southeast.
  - If true, then the tripledemic has probably started in the southeast.
- September and October are the ideal months to vaccinate persons against influenza.
- Co-administration of the flu and COVID vaccines may increase likelihood of completing both of these vaccines.

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.

Sutter Health