



***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**

Oct. 12, 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. Future Vaccines
  - a. Combination influenza and COVID-19
  - b. Take-home future vaccines
2. Testing for Respiratory Viruses in Sutter Health – Go Live today
3. COVID-19 – Encouraging Data
  - a. United States hospitalization data
  - b. United States genomic surveillance
  - c. Testing results
    - i. National data
    - ii. Sutter data
  - d. Treatment update
    - i. Nirmatrelvir/ritonavir (Paxlovid™) versus Omicron
    - ii. Molnupiravir mutations – a controversial topic
  - e. Vaccine
    - i. Updated\_Novavax gets approval
  - f. Take-home COVID
4. RSV
  - a. RSV is circulating in young children
    - i. Sutter Health positivity rates and by age
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  - c. Take-home RSV
5. Influenza
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  - c. Take-home influenza
6. West Nile Virus
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### **Future Vaccines**

- Combination vaccines offer the advantage of fewer injections, simplification of scheduling, increased patient satisfaction and increased compliance with public health recommendations. Studies have been ongoing to develop a combination influenza and COVID-19 vaccine. With the simplification of the COVID-19 vaccine to a single dose that synchronizes up with administration of the influenza vaccine, the value of a combination flu/COVID vaccine becomes apparent.
- [Moderna](#) announced the initial results of an observer-blinded, randomized, phase I/II trial comparing an mRNA flu/COVID combination vaccine versus separate site co-administration of the COVID-19 and influenza vaccines. Adults 50-64 years of age received a standard dose flu vaccine and the enhanced vaccine was given to persons 65 years and older.
  - Phase I/II trials measure safety and immunogenicity.
  - Titers measured were hemagglutination inhibition against influenza and neutralizing antibodies against SARS-CoV-2.
  - The table below shows reported findings. Measured results were geometric mean titer ratios of the new vaccine over the approved individual vaccines.
  - No significant difference in titers between the new combined vaccine or separate vaccines.

Participants Group	GMT Ratio (standard flu dose)	GMT Ratio (enhanced flu dose)	GMT Ratio (spike protein vaccine)
50-64 years old	≥ 1.0	N/A	≥ 0.9
≥ 65 years old	N/A	≥ 1.0	≥ 1.0

- Local and systemic reactions to the vaccine were solicited. The combination vaccine rates were found to be similar to the bivalent COVID vaccine alone.
- The phase 3 trial proving equivalent efficacy will start this year, but regulatory approval (presuming successful results) is not anticipated until 2025.

### **Testing for Respiratory Viruses**

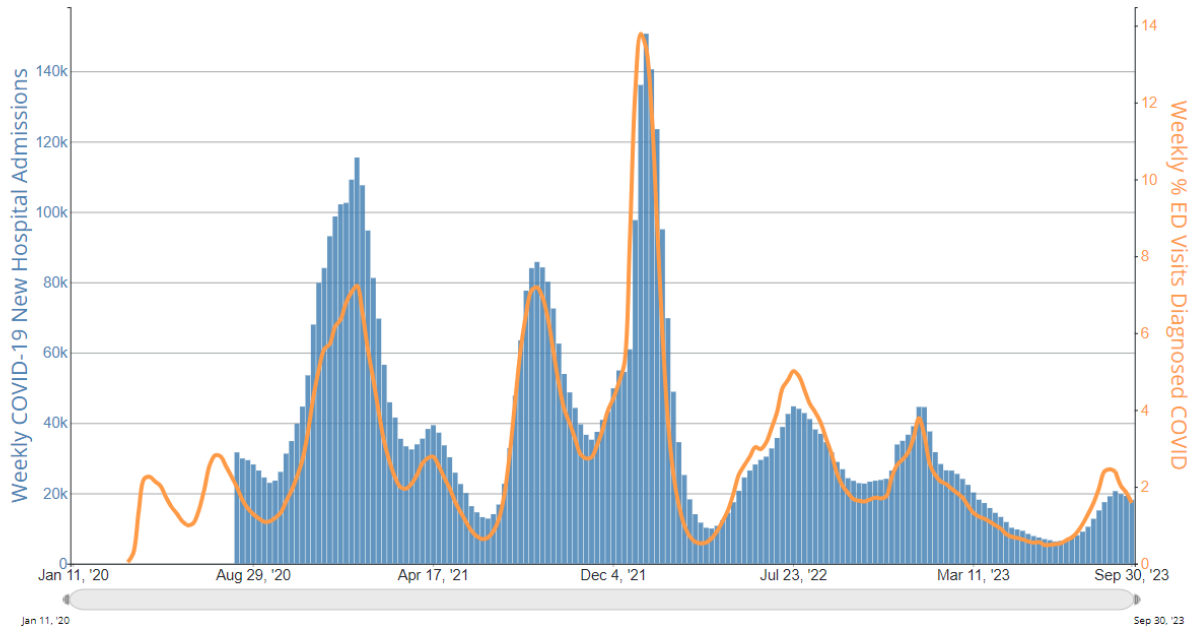
- Today, Sutter Health EPIC [COVID-19 order sets](#) will be updated to default the appropriate COVID/Flu/RSV orders in the acute hospital setting and support the expansion of Cepheid and COVID-19 antigen testing in the ambulatory foundation. [Bay](#) and [Valley](#) urgent care locations with Cepheid testing will transition at the same time.
  - When testing is indicated, co-testing for COVID-19 and influenza A/B is recommended.
  - For patients < 6 or >59 years old, RSV should also be considered.
  - COVID/flu/RSV testing is recommended as initial testing before ordering any other multiplex panel (such as BioFire).
  - Full respiratory panel testing should only be used if COVID/flu/RSV is negative and additional testing is necessary for clinical decision making.

### **COVID-19**

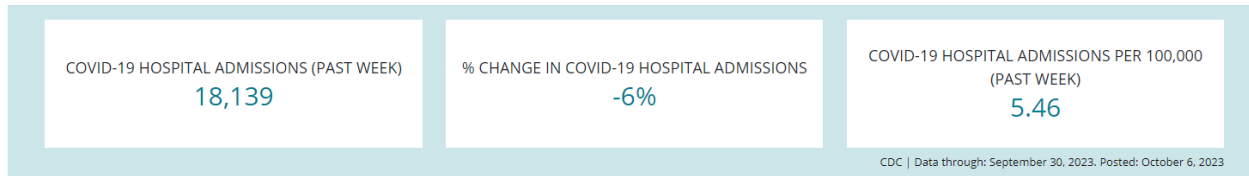
- Hospitalizations in the United States are a surrogate for the virulence of the circulating strain. The graph below and the subsequent table now show:
  - Decreasing hospitalizations (blue vertical bars).

- Concomitant continued decrease in the percentage of patients being diagnosed with COVID in emergency departments (orange run line).

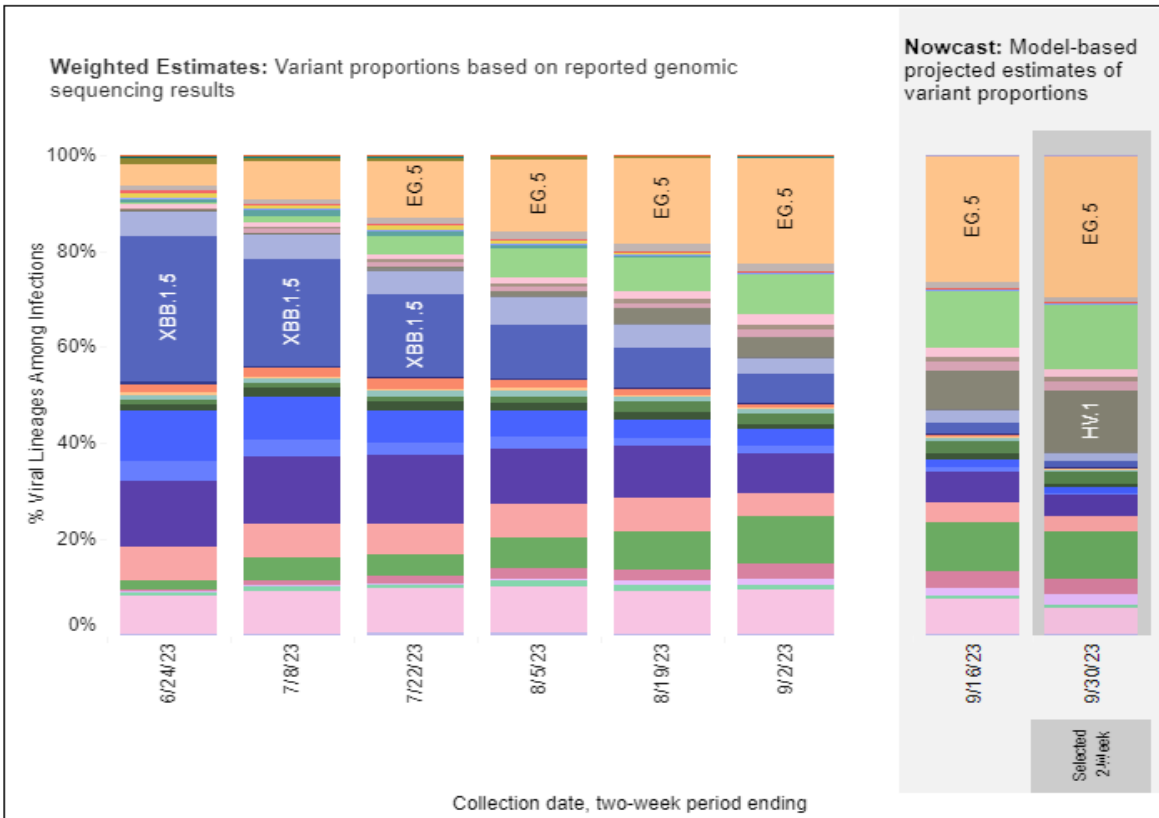
COVID-19 New Hospital Admissions and Percentage of Emergency Department (ED) Visits Diagnosed as COVID-19, by Week, in The United States, Reported to CDC



- The CDC tracks hospital admissions per 100,000 county population. Less than 10/100,000 is considered a low number of new hospital admissions. Hospitalization rates continue to decrease. The admissions percent change in the last week is -6%.

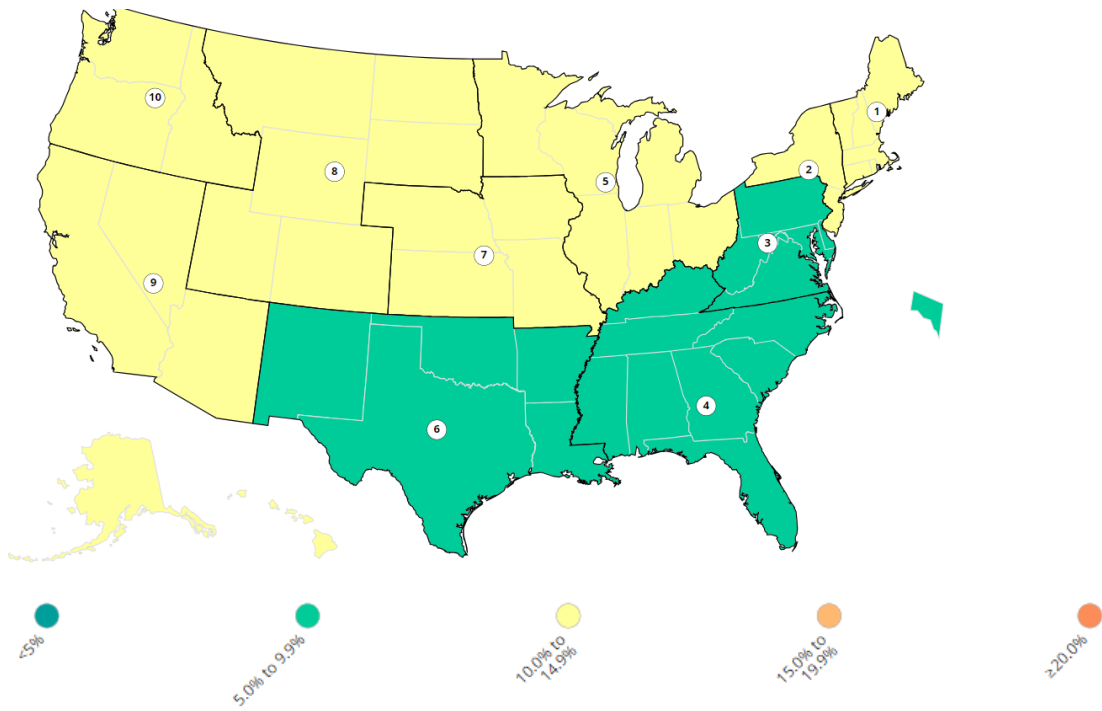


- [National genomic sequencing](#) was updated on Oct. 1 (graph below). EG.5 rates are slowly increasing. FL.1.5.1 and now HV.1 are second and third respectively. They are all derived from XBB. Combined they constitute 56% of isolates.

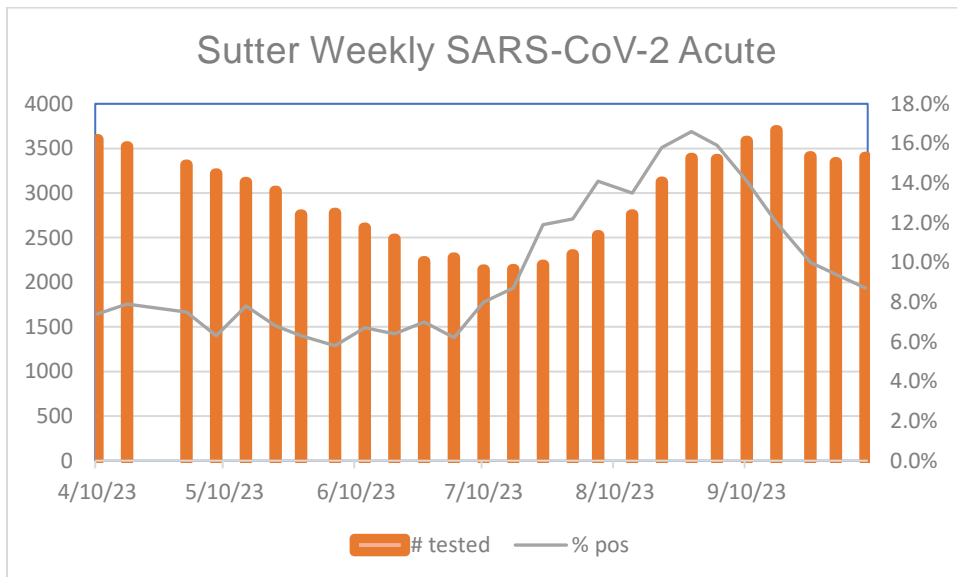


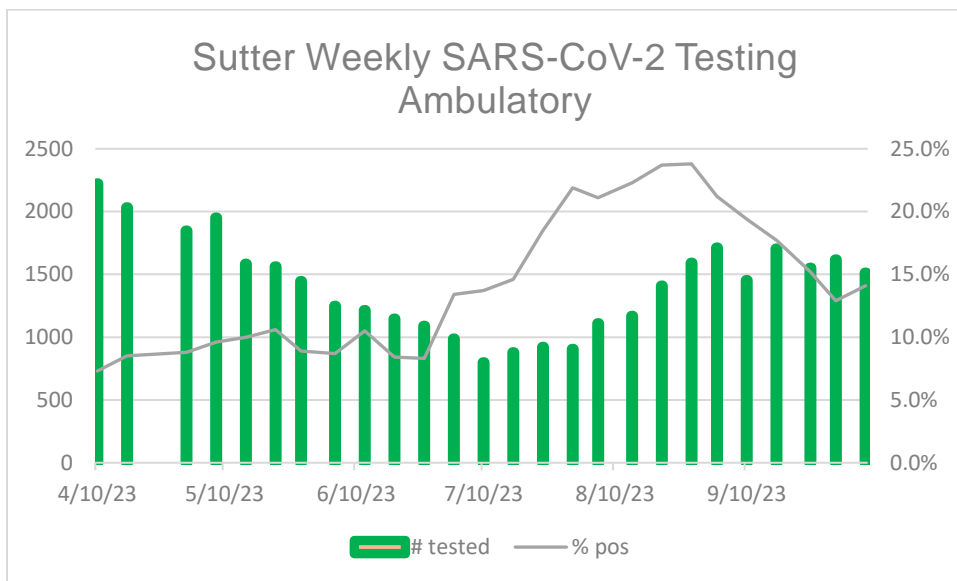
WHO label	Lineage #	% Total	95%PI
Omicron	EG.5	29.4%	26.4-32.6%
	FL.1.5.1	13.7%	10.8-17.1%
	HV.1	12.9%	10.5-15.6%
	XBB.1.16.6	10.1%	8.6-11.7%
	XBB.2.3	5.6%	4.7-6.5%
	XBB.1.16	4.3%	3.8-4.9%
	XBB.1.16.11	3.2%	2.6-3.9%
	XBB.1.16.1	3.0%	2.4-3.8%
	XBB.1.5.70	2.5%	1.9-3.4%
	XBB.1.16.15	2.0%	1.4-3.0%

- [National](#) molecular test positivity rates by region continue a definite downward trend. See the map below. Many regions are now green, and some yellow regions are on the cusp of turning green.



- Updated Sutter testing data below shows continued decreasing positivity rates with significant levels of testing both in emergency departments and ambulatory environments.





- **Paxlovid effectiveness against newer variants.**

- A recent [report](#) of almost 7,000 persons with COVID suggests nirmatrelvir-ritonavir (Paxlovid™) treatment may only have selected benefit in preventing hospitalization or death.
  - This observational study evaluated the prevention of mortality or hospital admission in four different high-risk cohorts (6,866 patients) within 28 days of infection.
  - The study was from February 2022 to February 2023, and most of this population had either vaccine and/or prior disease.
  - Two groups included “clinically extremely vulnerable” (CEV) people who were severely (CEV1) or moderately immunocompromised (CEV2).
  - CEV3 individuals were not immunocompromised, but had medical conditions associated with a high risk for complications from COVID-19.
  - A fourth expanded eligibility (EXEL) group was added to allow wider access to nirmatrelvir and ritonavir for certain other higher-risk individuals who were not in the other groups.
  - Omicron variant, which was circulating at the time of the study, was noted to be associated with less severe disease than previous variants.
  - Nirmatrelvir-ritonavir was only associated with lower risk of death or hospitalization in the immunocompromised individuals (CEV1 and CEV2).
  - There were only nonsignificant trends to benefiting other groups in the study, including persons 70 years and older without other serious co-morbidities.

- **Molnupiravir Mutations**

- <https://www.nature.com/articles/s41586-023-06649-6>
  - Molnupiravir acts by inducing mutations in the virus genome during replication, resulting in reduced viral replication. Even with treatment, severely immunocompromised persons may not fully clear their SARS-CoV-2 infection, resulting in molnupiravir-mutated viruses. Theoretically, these mutated viruses may be transmissible and could even lead to a future outbreak.
  - The authors associate particular SARS-CoV-2 sequence mutations since the release of molnupiravir in 2022 in countries with widespread use of this treatment. Virus obtained in patients treated with molnupiravir shows that its sequencing matches that seen in the genomic data banks. In some cases, onward transmission of molnupiravir-derived lineages is suggested.



- Severe or moderately Immunocompromised patients continue to have a significant benefit with nirmatrelvir/ritonavir in preventing COVID-related hospitalization and death.
  - Molnupiravir mechanism of action leads to usually detrimental mutations in the virus. In the severely immunocompromised patient, viral clearance may not be complete after treatment and residual mutated virus could potentially spread and cause disease with a new strain. A recent study reported suggestive evidence of this risk. The FDA released a response, recognizing this concern, but anticipating this to be a low risk in terms of impact.
  - The Novavax COVID vaccine has now been updated and offers an alternative technology to the mRNA vaccines. The significance of this difference is not clear.
  - The XBB vaccine has significant potential to mitigate a winter outbreak. Don't miss an opportunity to provide this important protection.
- **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](#)

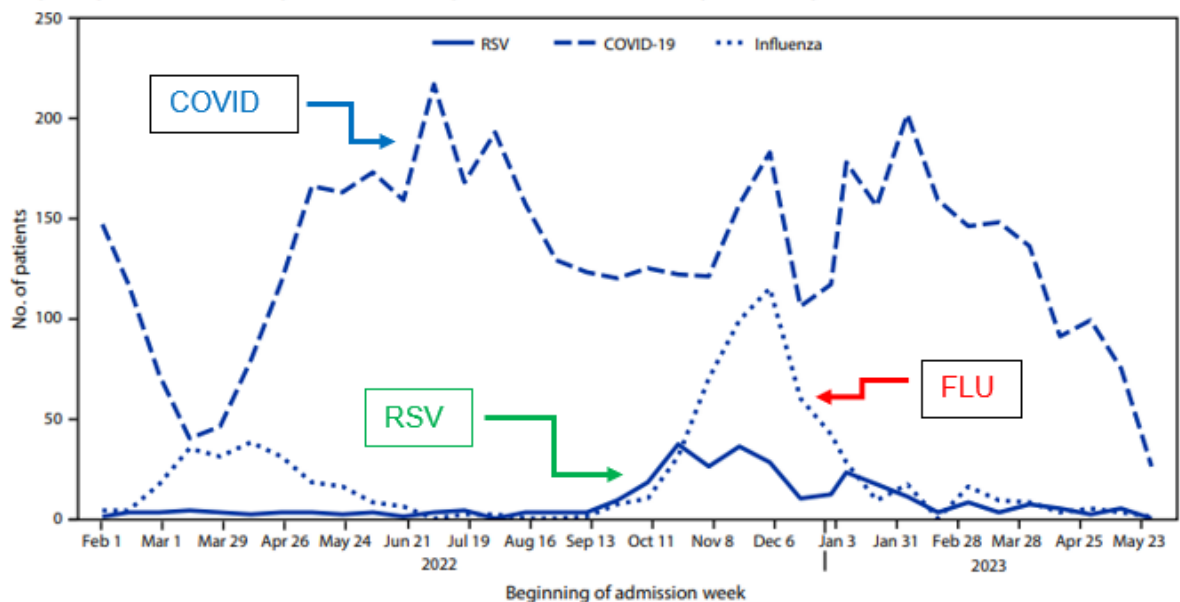
## **RSV**

- The potential severity of RSV in older adults has been underappreciated for many years. With the availability of a new vaccine to mitigate or prevent disease in adults 60 years and older, increasing attention is being given to this respiratory virus.
- [Clinical Infectious Diseases](#), June 2023, published a prospective, 4-year, multicenter comparison of the outcomes in adults hospitalized with either RSV or influenza.
  - Between 2016 and 2019, 10,311 adults hospitalized for an acute respiratory infection (ARI) were tested for RSV and influenza. The study was conducted in four different states with the CDC and included academic and community hospitals.
  - This was a prospective study and daily review of the chart was performed. In addition to an admitting diagnosis of an ARI, exacerbations of cystic fibrosis, asthma, CHF or COPD were included (if accompanied by at least one systemic sign or symptom of infection).
  - 25% of the patients had either RSV or influenza. Influenza was three times more common, comprising 18.8% versus only 6% for RSV.
  - About 50% of patients hospitalized with RSV or influenza were 65 years or older, but cardiopulmonary co-morbidities were more common in patients with RSV.
  - Fifty percent of the patients hospitalized with influenza had been vaccinated
  - Compared to influenza, patients with RSV were more likely to have CHF, COPD, remain hospitalized for more than 1 week or require mechanical ventilation.
  - Mortality was similar in patients with influenza, RSV or admitted with an ARI not due to influenza or RSV.
  - Strength of the study was the prospective design over multiple respiratory seasons at multiple institutions.
  - Weaknesses of the study include the inability to identify all potential patients, predominantly white population of participants, and the inability to accurately track mortality post-discharge.

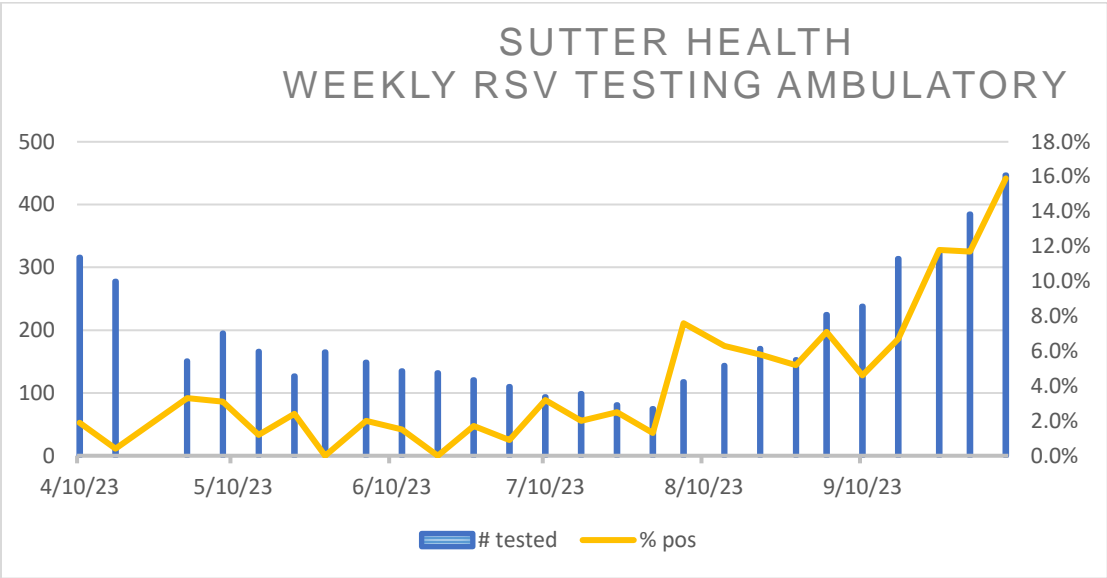


- The [MMWR](#) dated Oct. 6 published a similar study but limited it to persons 60 years and older, expanded from four to 25 states, and included COVID-19. A newer time interval was studied (February 2022 through May 2023).
  - 5,784 persons hospitalized with ARI and laboratory-confirmed RSV, flu or COVID-19
  - Multivariable, logistic, regression analysis looked at four different categories:
    - Standard oxygen flow
    - High-flow or noninvasive ventilation
    - ICU admission
    - Invasive mechanical ventilation or death
  - 5,574 test positive patients were enrolled.
    - 82% COVID
    - 13% influenza
    - 5% RSV
  - Patients hospitalized with RSV were more likely to receive oxygen at all levels or to be admitted to the ICU. The odds of the composite of invasive mechanical ventilation or death was higher with RSV compared to influenza, but similar to COVID-19.
  - Similar to the study above, about 50% of the patients hospitalized with influenza had been vaccinated. Patients with COVID-19 had a similar 50% COVID immunization rate but that was not further specified.
  - The graph below shows the number of patients hospitalized by month over a 16-month time frame. Notably, COVID-19 did not appear to be seasonal.

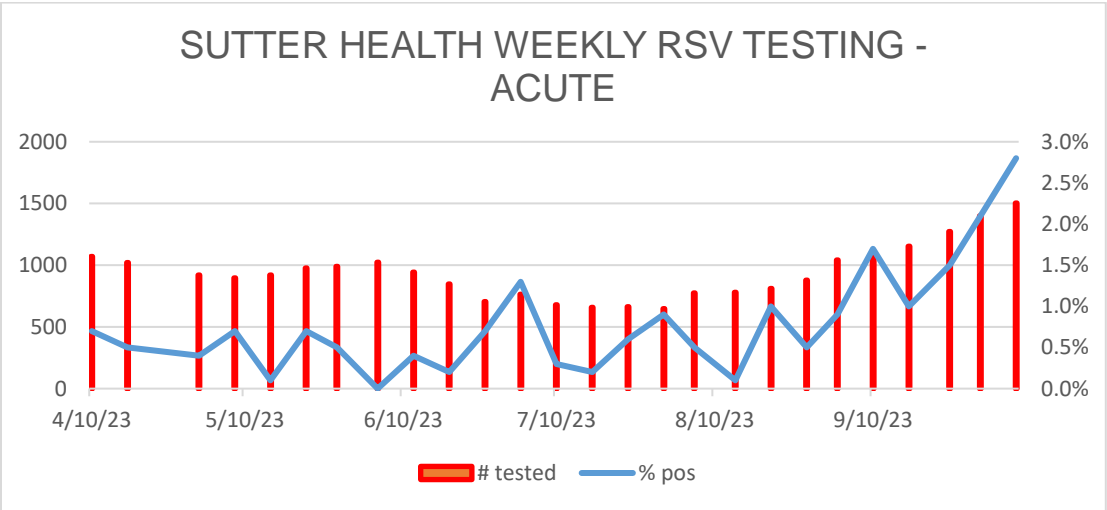
FIGURE. Date of admission for adults aged ≥60 years hospitalized with respiratory syncytial virus, COVID-19, or influenza — Investigating Respiratory Viruses in the Acutely Ill Network, 25 hospitals, 20 U.S. states,\* February 1, 2022–May 31, 2023



- Weakness of the study includes too few patients to look at trends based on co-morbidity.
- Both of these studies show that hospitalization for RSV is much less common than influenza but the morbidity of patients with RSV is higher.
- RSV is still being identified in the ambulatory setting. The amount of testing in ambulatory is gradually increasing and positivity rates are well above the 3% threshold for 10 weeks now. The week ending Oct. 8 had 447 tests ordered. This reflects a 38% increase in testing compared to the prior 2 weeks with a continued increased positivity rate. See graph below.



- Although ED positivity rates remain below 3%, they are now up to 2.8%. The number of tests being performed has also continued to increase.



- RSV results by age are in the following table for the week ending Oct. 1. Positivity rates in children less than 6 years old are now almost 27% in the ambulatory environment and up to 7% in the emergency departments.

Location	<6 years old		Less than 18 years old		60 years old and older	
	Number Tested	% Positive	Number Tested	% Positive	Number Tested	% Positive
<b>Ambulatory</b>	219	26.9%	279	23.7%	60	0.0%
<b>Acute (ED)</b>	427	7.0%	594	5.7%	500	1.0%

- Most of the increased RSV activity continues to be identified in children less than 6 years old in the ambulatory environment. Emergency department positivity rates continue to climb. There is increasing disease in the 6-18 years old population, but very little identified infection in persons 60 years and older.
- **RSV Take-Home:**
  - Both studies demonstrated that adults with RSV are less likely to require hospitalization compared to influenza. However, patients hospitalized secondary to RSV are more likely to require supplemental oxygen, mechanical ventilation or admission to an ICU.
  - RSV continues to be identified in Northern California in increasing numbers. More than one out of every four children ≤ 6 years old tested for RSV in the outpatient environment are positive. There is increasing disease in patients 6-18 years old, but very little in the high risk 60 years and older population.
  - In appropriate symptomatic patients, testing should still be performed.
  - High-risk patients 60 years and older should be offered the RSV vaccine.

## **Influenza**

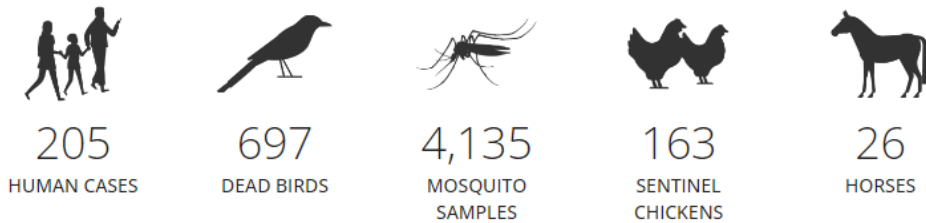
- The [WHO](#) released their latest biweekly worldwide influenza report on Oct. 9.
- Overall worldwide levels remain below or at inter-seasonal rates. All three viruses (influenza A H1N1, A H3N2, and B) are circulating.
- From Sept. 4 to Sept.17, 298,993 specimens were tested with only 7,793 positive results (2.6%).
- **Influenza Take-Home:**
  - Influenza activity remains very low in the United States and much of the world (except for parts of SE Asia).
  - At this time, it appears that we will not have an early influenza season. We may be lucky and have a below-average influenza season or perhaps a late season.
  - Vaccination can still decrease the morbidity and mortality of those who do get infected with Influenza.

## **West Nile Virus (WNV)**

- California still has the second-highest number of reported cases this year.
- Year-to-date total for reported cases in humans in [California](#) is up to 205 cases (pictograph below). This remains twice the 5-year state average looking at calendar week 1 to week 40.
- This is an increase of 23 new cases in the last week, including the first positive human case from Marin County this year. San Diego County reported its first positive mosquito sample this year.
- Six deaths have been reported. The counties reporting include Lake (1), Los Angeles (1), Sacramento (1), San Bernardino (2) and Yolo (1).

## 2023 WEST NILE VIRUS ACTIVITY IN CALIFORNIA

LAST UPDATED: OCT 05, 2023 2:06PM PST



- **West Nile Virus in California Take-Home:**
  - Reported cases of WNV in humans, mosquitoes, dead birds, sentinel chickens and horses have continued to increase.
  - California has the second-highest number of reported cases in people, now up to 205.
  - Cases typically decrease dramatically in October, but climate change may affect what is seen. Continue to keep WNV in the differential for meningitis, encephalitis or poliomyelitis-like syndrome.

### **Share the Newsletter**

Anyone who would like to be added to the Emerging Infections newsletter should send a request to [bryan.gardner@sutterhealth.org](mailto: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](mailto:clinicians@sutterhealth.org).*

