

Emerging Infections Newsletter for Clinicians

Dec. 7, 2023

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The Tripledemic

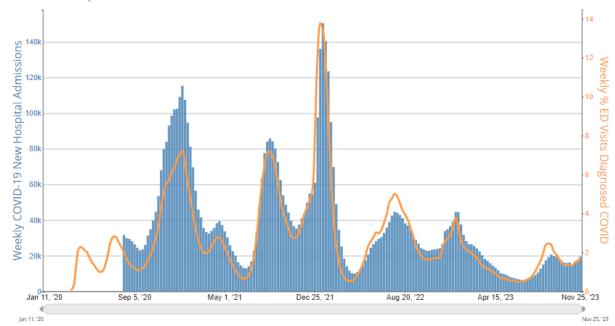
 The tripledemic is here. As a reminder, the tripledemic is a term that refers to the simultaneous circulation of three respiratory viruses, specifically SARS-CoV-2, RSV and influenza. It does not refer to multiple simultaneous infections in an individual, although they do occasionally occur.

- The term tripledemic does not reflect the severity of the outbreaks. For those who wonder about the impact, the data below should answer questions.
- It is not too late to get vaccinated. Mask, perform frequent hand hygiene and stay home if you are sick.

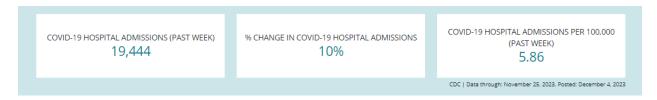
COVID-19

- Hospitalizations in the United States are a surrogate for the virulence of the circulating strain. The graph below and the subsequent table show:
 - Hospitalization rates (blue vertical bars) and percentage of patients being diagnosed with COVID in emergency departments (orange run line) are significantly increasing. Both of these measurements are now approaching four-fold higher than the trough during the first week of July.

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



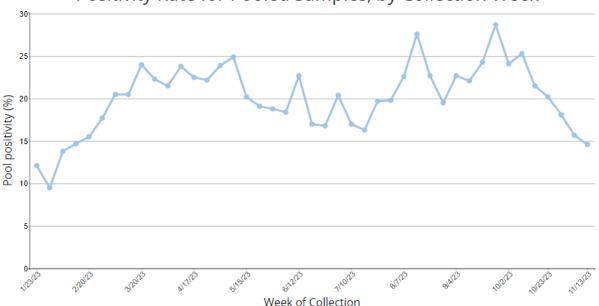
• The CDC tracks hospital admissions per 100,000 county population. Less than 10/100,000 is considered a low number of new hospital admissions. In the last week, national rates increased from 4.89/100,000 to 5.89/100,000. The week of Nov. 16, there were 14,728 hospitalizations. This week the number was 19,444. That is a 32% increase in only 3 weeks.



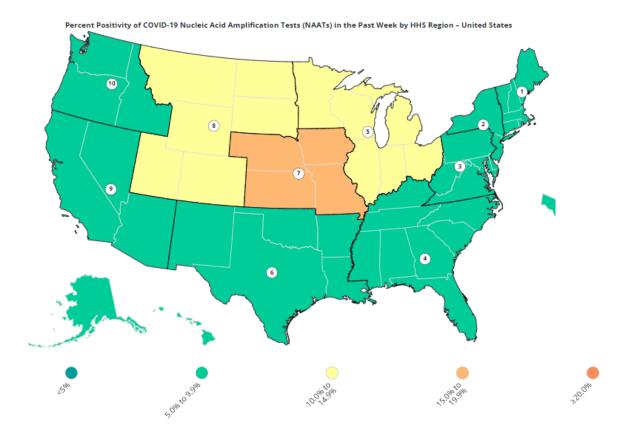
 National genomic sequencing is updated every 2 weeks by the CDC. A new report will be published next week.

- Voluntary surveillance of international air travelers is conducted at six major U.S. airports as an early warning system and to fill gaps in worldwide genomic surveillance. It covers flights from more than 135 countries.
- Participating returning international travelers self-collect a nasal swab and answer a short survey. A weakness of the survey is that it only determines where the final flight originated and not where participants actually spent their last 10 days.
- The graph below shows a downward trend with the latest positivity rate down to 14.6%.
- <u>Twelve</u> different strains (up one from 11) were identified the week of Nov.16 (data not shown). BA.2.86 remains the most frequently sequenced international isolate increasing from 21.2% to 25%.

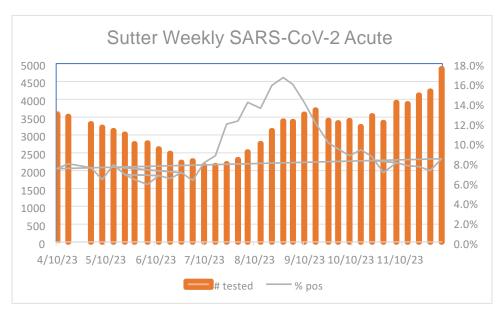


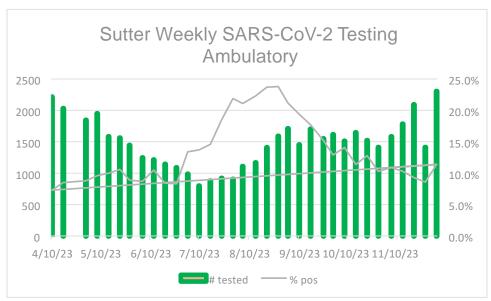


• The map below shows <u>national</u> molecular test positivity rates by region, updated through Nov. 25. Two regions are yellow (10-14.9% positivity) and region 7 in the Midwest is now orange (15-19.9%). This map is most useful following weekly over time. For comparison, the week of Nov. 16, only region 8 was yellow. Regions 5 and 7 were both green. This map is consistent with the increased hospitalizations and ED positivity rates shown in the graph and table above.



- Updated testing data below show stable positivity rates in combination with significantly increased testing being performed in emergency departments and ambulatory environments.
- Actual number of positive results increased by 34% in the last week in the acute (ED) settings. Ambulatory increased by over 50% but the comparison in ambulatory is amplified by the short holiday week in the prior week. The actual number of positives in the last week in each of the two settings was the highest since September.





 COVID test positivity rates in persons greater than 60 years old are now being pulled out from Sutter data. Positivity rates are higher in this age group than the composite of all ages. They comprise a higher risk group for severe COVID and vaccination should be strongly encouraged.

COVID	≥ 60 years old		
Location			
	Number Tested	% Positive (number)	
Ambulatory	431	13.0% (56)	
Acute (ED)	1,827	11.4% (209)	

COVID-19 Take-Home:

- Hospitalizations and emergency department visits, nationally and in Sutter, are increasing. The weekly absolute number of positive tests in Sutter is increasing at a substantial rate. Persons 60 years and older have a higher positivity rate than the composite of all ages.
- BA.2.86 is continuing to be identified more frequently in international travelers, now up to 25% of sequenced isolates. It is believed to have the potential to become the overwhelming predominant variant in the next few months.
- Combined with the influenza and RSV trends discussed below, the risk from the tripledemic appears to be quite significant.
- Sutter ambulatory and emergency department positivity rates are increased to 11.4% and 8.4% respectively.
- The vaccine should provide coverage against BA.2.86. Encourage vaccinations, especially in those with co-morbidities and 60 years or older in age.

Related Links

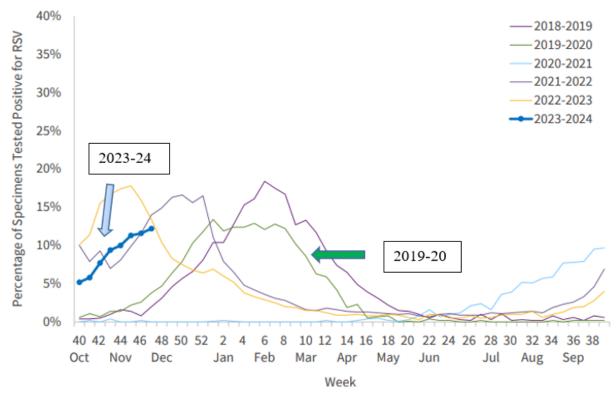
- CDC Caring for Patients
- o CDC Data Tracker
- CDC Latest Updates

- CDC Vaccine Information
- o CDPH Tracking and Vaccination Updates
- Sutter Health for Clinicians
- Sutter Health for Patients
- WHO Table of Contents

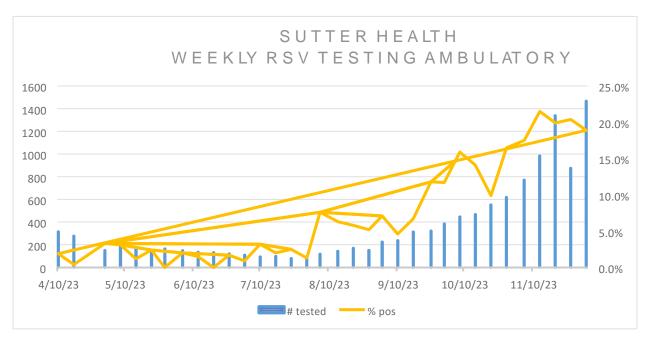
RSV

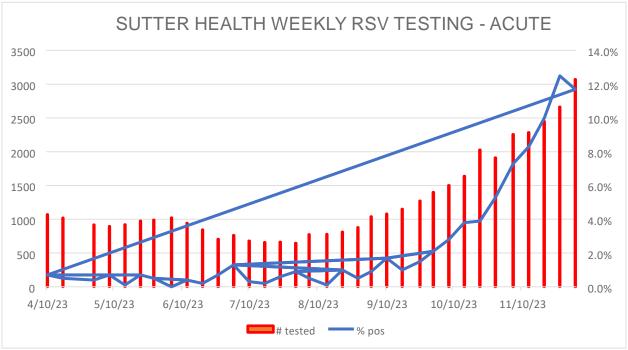
• <u>CDPH</u> reports RSV data weekly during the season. The CDPH graph below demonstrates that our RSV season (blue arrow) started early again this year, compared to the pre-COVID 2019-20 season (green arrow), but otherwise it appears pretty typical in shape.

Figure 12. Percentage of RSV Detections at Clinical Sentinel Laboratories, 2018-2024 Season to Date



- RSV identification rates are elevated in both the ambulatory and emergency departments in Sutter. The amount of testing is simultaneously increasing. Positivity rates in ambulatory are over 20% for 4 weeks now. Emergency departments' positivity rates for RSV are 12%. The RSV season in Northern California seems widespread.
- See two graphs below.





- RSV results by age are in the following table for the week ending Dec. 3. Children less than 6 years old dominate, with positivity rates of 40.5% in ambulatory and 34.7% in acute care settings.
 - Our Sutter data shows that the vast majority of diagnosed infections this season are in children less than 6 years old.
- Smaller numbers of persons 6 to <12 years old are tested in general, but positivity rates are much lower than children less than 6 years old.
- More people 60 years and older are being diagnosed with RSV. In the emergency department the positivity rate was 3.9%. That is a slight increase from the prior week of 3.4%. Ambulatory positivity increased from 8.8% to10.7%.

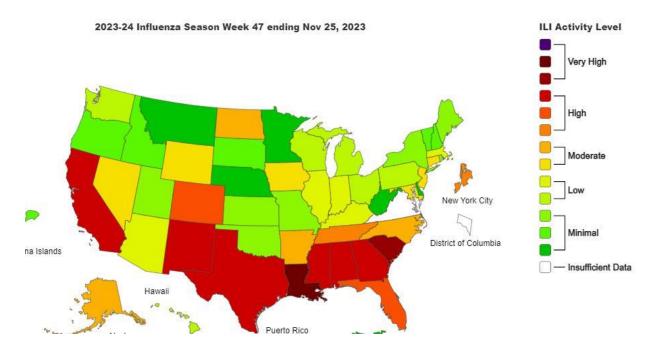
Location	<6 years old		6 to < 12 years old		≥ 60 years old	
	Number Tested	% Positive (number)	Number Tested	% Positive (number)	Number Tested	% Positive (number)
Ambulatory	449	40.5% (182)	136	12.5% (17)	291	10.7% (31)
Acute (ED)	718	34.7% (249)	154	9.1% (14)	1,556	3.9% (60)

RSV Take-Home:

- The RSV season in California started earlier than the pre-COVID "normal," but not as early as last season. Within Sutter, high positivity rates continue, especially amongst children <6 years old.
- Higher numbers of cases are also being seen in persons 60 years and older. The risk of hospitalization and/or death related to RSV increases in older persons, especially if the person also has a history of heart failure or chronic obstructive lung disease.
- o In Northern California, over 40% of children <6 years old tested for RSV in the outpatient environment are positive and 35% are now positive in the ED.
- o Nirsevimab supply remains limited.
- Vaccinate all eligible pregnant persons between 32-36 weeks of gestation against RSV.
- Persons 60 years and older, especially with co-morbidities, should be vaccinated against RSV.

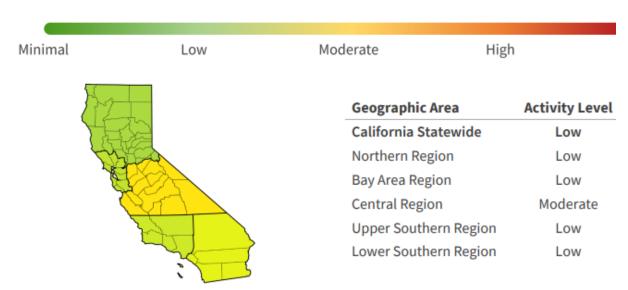
<u>Influenza</u>

- The <u>CDC</u> reports that out of 69,884 specimens tested by clinical labs during week 47 (ending Nov. 25), 4,336 were positive (up to 6.2% from 4.9% in the prior week). Influenza A H1N1 continues to dominate, representing almost 80% of the influenza A isolates. Influenza-associated hospitalizations are increasing.
- There are four different subclades of A H3N2 that have been identified by the CDC since May 2023. Over 90% are from one subclade.
- Influenza-like illness (ILI), the surrogate for influenza used by the <u>CDC</u>, is on the map below showing data in the week ending Nov. 25. Disease in the United States is increasing.
- California has now moved up two more notches on the color scale and is now at the top end
 of high.
- As identifications continue to increase, the thought is that this map should be a reasonable surrogate for true influenza. ILI is a surveillance measurement defined by any illness with fever (≥100° F or 37.8° C) plus cough and/or sore throat.



- The <u>CDPH</u> map below of influenza (last updated on Dec. 1), however shows true influenza activity in California to be low to moderate. The state influenza positivity rate is 7.4%.
- These very different representations of influenza activity can be reconciled by CDPH
 measuring true influenza and the CDC using a surrogate for influenza. The CDC uses a
 complicated formula to determine ILI.
- Previously they only included illnesses that did not have a known alternative diagnosis, but that was eliminated as a criterion. Advanced epidemiologists and statisticians developed their methodology.
- On the surface, CDPH information appears more accurate, but data are incomplete because influenza reporting is not required except for hospitalizations and influenza- associated deaths. Influenza activity levels are derived from the percentage of specimens from clinical sentinel laboratories that tested positive for influenza.

Influenza Activity Levels⁺

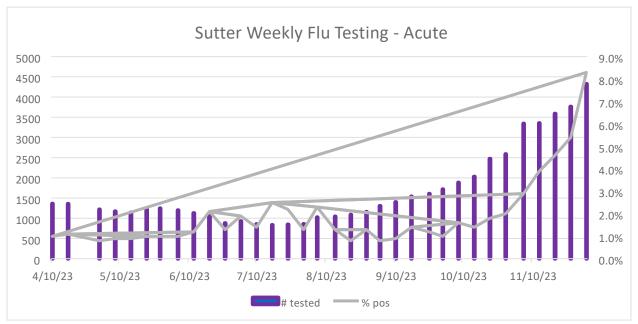


CDPH Influenza Activity Levels*

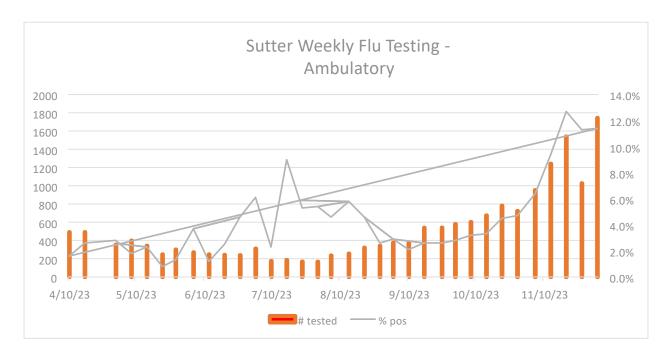
- Minimal: The percentage of specimens positive for influenza is <2%.
- Low: The percentage of specimens positive for influenza is between 2% and <10%.
- Moderate: The percentage of specimens positive for influenza is between 10% and <20%.
- **High:** The percentage of specimens positive for influenza is between 20% and <40%.
- Very High: The percentage of specimens positive for influenza is ≥40%.
- Below is the CDPH map from same time interval 1 year ago (Nov. 27 to Dec. 3, 2022).
 Influenza activity was much higher.



• The graph below shows Sutter emergency department and ambulatory influenza positivity rates. In the acute setting (emergency departments) positivity rates increased from 5.4% to 8.3% in the last week, consistent with increasing circulation of influenza.



• In the ambulatory, setting positivity rates are between 11-12%. Interpretation of this graph (below) needs to be tempered by the fact that many clinics use a rapid, non-molecular, influenza test that has been noted to result in increased false positive influenza B results.



 Influenza test positivity rates in persons greater than 60 years old are now being pulled out from Sutter data. Table below. Influenza rates in this population seen in the acute settings are lower than our total population rates. That by itself can be interpreted as good news since the older patients are at higher risk of complications, but there are many co-morbidities associated with severe influenza that are not accounted for. Serial graphing of data for trends will follow in future editions.

Influenza Location	≥ 60 years old		
	Number Tested	% Positive (number)	
Ambulatory	316	9.2% (29)	
Acute (ED)	1,625	5.6% (91)	

- Antiviral treatment of influenza is <u>recommended</u> as soon as possible, for outpatients as well
 as hospitalized patients, who have severe complicated or progressive illness or are at
 increased risk for complications from influenza <u>even if it is started >48 hours after illness
 onset.</u>
- High risk for complications from influenza include:
 - o Children < 2 yo
 - <19 yo and on long-term treatment with aspirin or salicylates</p>
 - Adults \geq 65 yo
 - BMI \geq 40 Kg/M²
 - Pregnant or ≤ 2 weeks post-partum
 - Residents of chronic care facilities
 - Immunosuppressed
 - Chronic medical conditions (kidneys, heart, lungs, liver, neurological, diabetes)

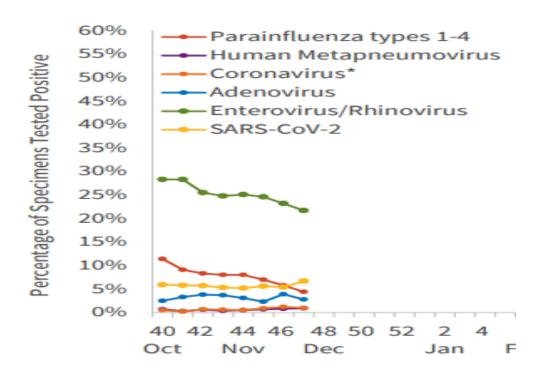
 Anticipated vaccine match is determined by measuring the activity of ferret-derived vaccine antibodies against samples from circulating strains. Since May 2023, all the circulating strains were recognized by the vaccine antibodies.

Take-Home Influenza:

- Influenza activity and influenza-associated hospitalizations are increasing in the United States
- The CDC and CDPH have different methodologies for estimating influenza activity. Each approach has strengths and weaknesses. The CDPH reported positivity rate increased to 7.4%.
- Sutter emergency department positivity rates of 8.3% during the week ending Dec. 3 are comparable to what is reported by CDPH. By CDPH definition, that equates to low activity (2-9.9%).
- Comparing the similar week, year to year, CDPH influenza activity maps, it is notable that influenza activity, while elevated, is significantly lower than 2022.
- Influenza A continues to dominate in the United States with A H1N1 still representing 80% of the influenza A isolates.
- Treat patients with influenza who are at increased risk of complications, even if treatment is started more than 48 hours after illness onset.
- Influenza vaccination is a critical strategy to help protect high-risk and older adults against influenza-related hospitalizations and continues to be recommended throughout the influenza season.

Other Respiratory Viruses

- CDPH tracks respiratory viruses beyond SARS-CoV-2, flu, and RSV. They started reporting
 again in October. The graph below shows that other viruses are all declining with
 Enterovirus/Rhinovirus remaining the most common one identified.
- These are usually identified on multiplex respiratory panels other than the Cepheid panel (COVID, RSV, Flu A/B). No denominators are provided. Testing with these expensive, large respiratory panels should remain very limited as treatments will not likely be changed based on their results.



Final Take-Home Message

- The tripledemic is here. RSV remains predominantly a disease of children < 6 years old but is starting to cause more disease in persons > 60 years old.
- Influenza is increasing. Although not as widespread right now compared to last season, it is still early. There is a definite possibility that A H3N2 will ultimately replace A H1N1, and we might have a biphasic season or even triphasic (if influenza B shows up late). The vaccine looks like a very good match at this time.
- COVID is increasing. It never went away, but BA.2.86 appears to be escalating and the number of persons with disease will increase.
- Looking at all three components of the tripledemic, it appears likely that hospitalization rates will continue to increase.
- Use appropriate PPE, encourage broader use of masks, vaccinate appropriate candidates, stay home if sick, and treat influenza following CDC guidelines.