



Emerging Infections Newsletter for Clinicians

Jan. 4, 2024

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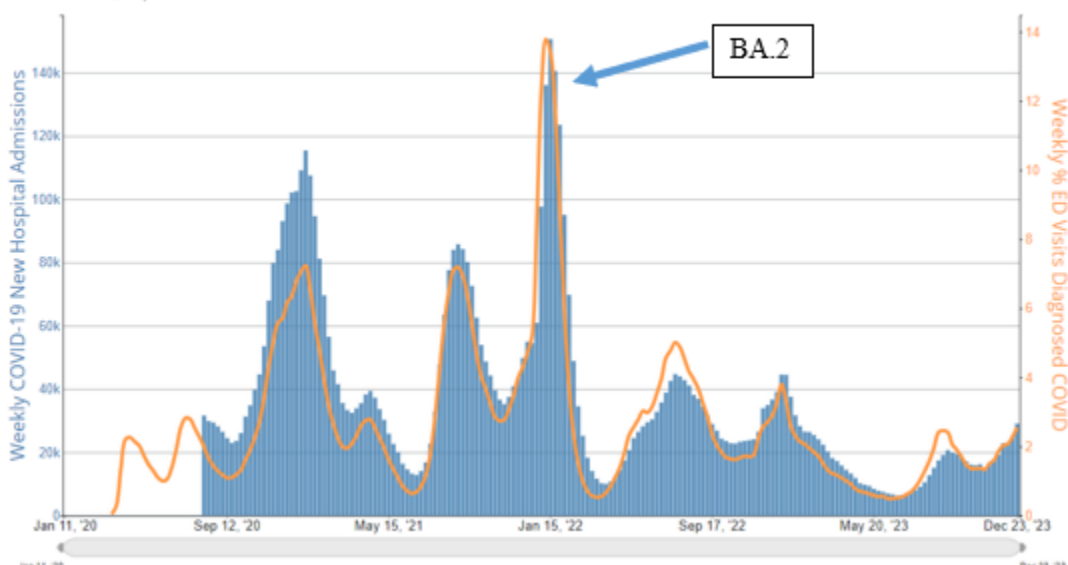
The Tripledemic

- COVID, RSV, and influenza are all circulating at high levels. The following information discusses each of these three viruses.

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 continued increases in hospitalization rates (blue vertical bars) and the percentage of patients diagnosed with COVID in emergency departments (orange run line).
- BA.2 (descendant of omicron) is noted by the blue arrow. That caused the largest outbreak of COVID to date. Notably, the new rapidly increasing JN.1 is based off of BA.2.

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

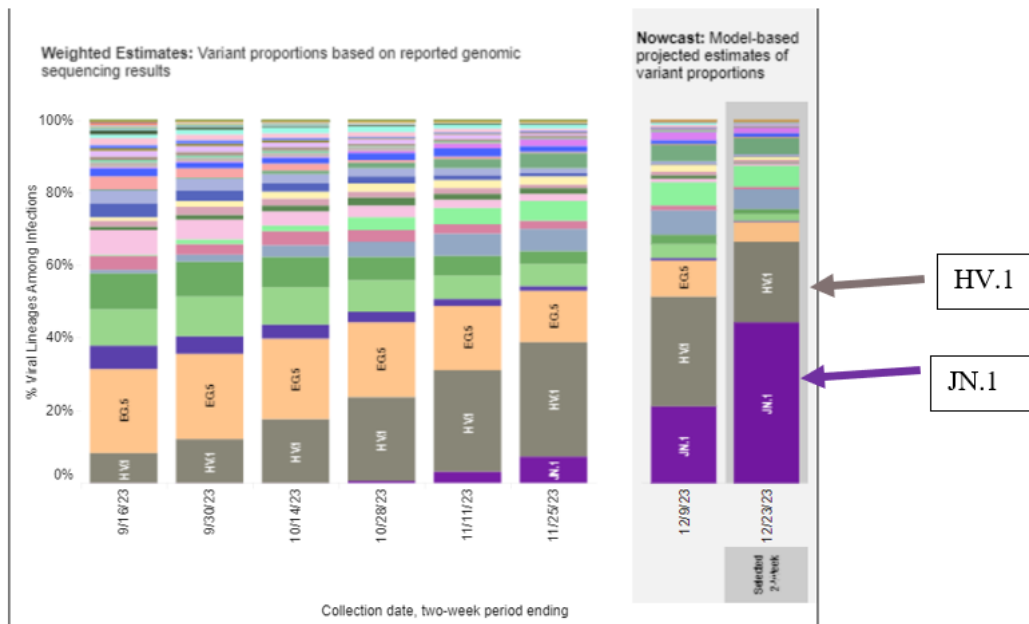


- The CDC tracks hospital admissions per 100,000 county population. Less than 10/100,000 is considered a low number of new hospital admissions. In the last week, national rates are progressively increasing, now up to 8.75/100,000. Hospitalizations during the last week increased by 16.7% again.

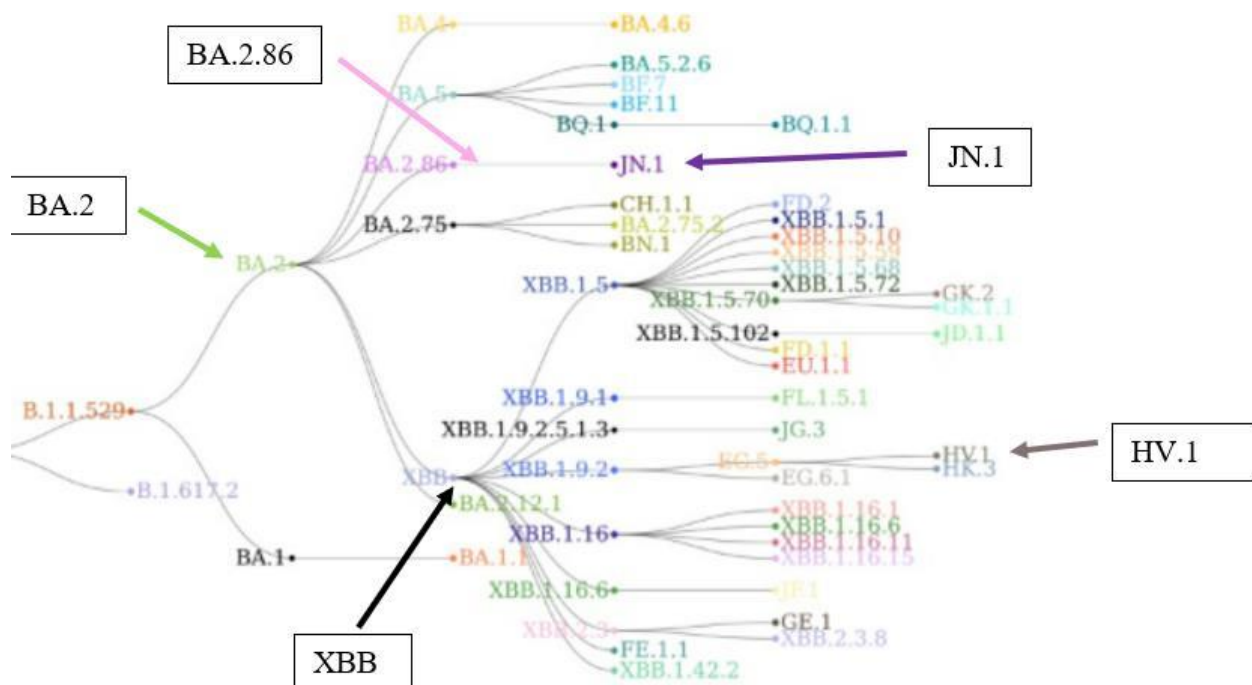
COVID-19 HOSPITAL ADMISSIONS (PAST WEEK)	% CHANGE IN COVID-19 HOSPITAL ADMISSIONS	COVID-19 HOSPITAL ADMISSIONS PER 100,000 (PAST WEEK)
29,059	16.7%	8.75

CDC | Data through: December 23, 2023. Posted: December 29, 2023

- [National genomic sequencing](#) is updated by the CDC every 2 weeks (graph below). The most recent report includes estimates from Dec. 10 to Dec. 23, 2023.
- JN.1 is now the dominant variant at 44.2% of sequenced isolates (purple arrow) in the United States. JN.1 has only one spike protein amino acid change from BA.2.86. That extra mutation has increased the SARS-CoV-2 ability to escape host immune recognition.
- HV.1 (grey-green) is continuing to decrease and represents only 22.1% of isolates.

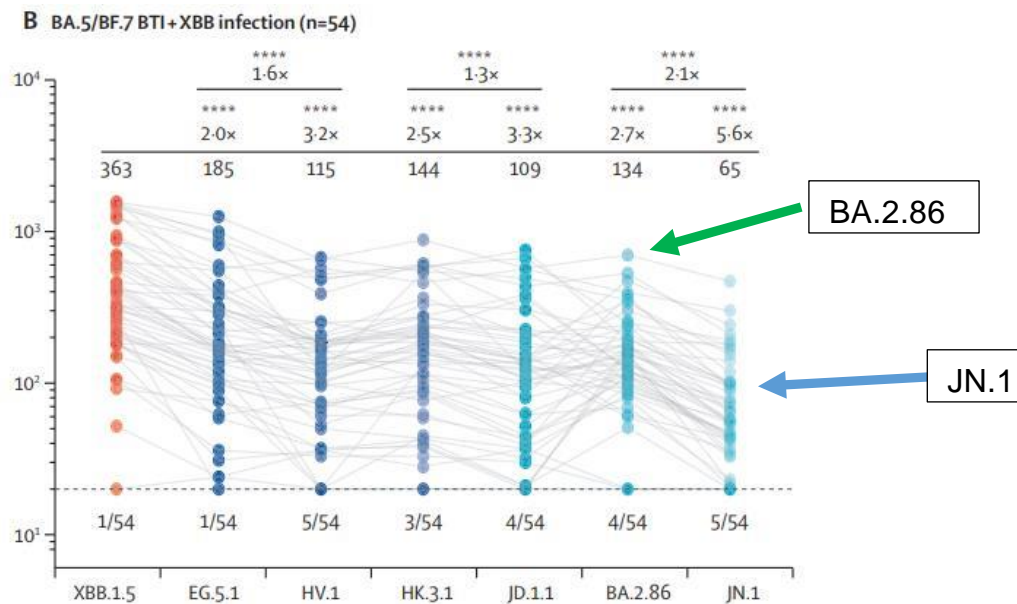


- The Pango Lineage below shows that JN.1 (purple arrow) is a direct descendant of BA.2.86 (pink arrow). BA.2.86 developed from BA.2 (major Omicron subvariant with light green arrow).
- HV.1 is the grey-green arrow. It originated from the recombinant XBB (black arrow), which is closer to the present monovalent COVID vaccine based on XBB.1.5



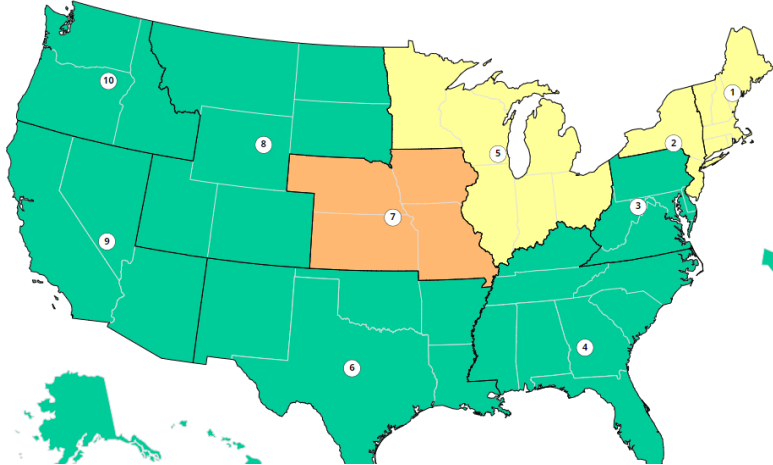
- What is the significance of JN.1?
 - JN.1 is a direct descendant of BA.2.86.
 - BA.2.86 raised concern because of the large number of mutations that it carries, and the concern of increased transmission compared to other circulating variants. That threat never came to fruition as BA.2.86 did not show significant escape from humoral antibodies or a growth advantage.

- Along comes JN.1. With only a single important mutation on the receptor binding domain of the BA.2.86, SARS-CoV-2 developed a substantial increase in humoral immunity escape.
- A [correspondence](#) in Lancet Infectious Diseases Dec. 15, looked at two cohorts. One that developed infection with XBB after three doses of inactivated vaccine and a second group included individuals recovering from infection with XBB breakthrough infection after prior COVID with BA.5 or BF.7.
- Neutralizing titers were measured using in-vitro, pseudovirus-based assays. Lower titers means that the virus is more capable of immune escape. The graph below shows that neutralization titers against JN.1 (blue arrow) were lower and not as strong compared to the other six strains of COVID studied. This includes BA.2.86 (green arrow).

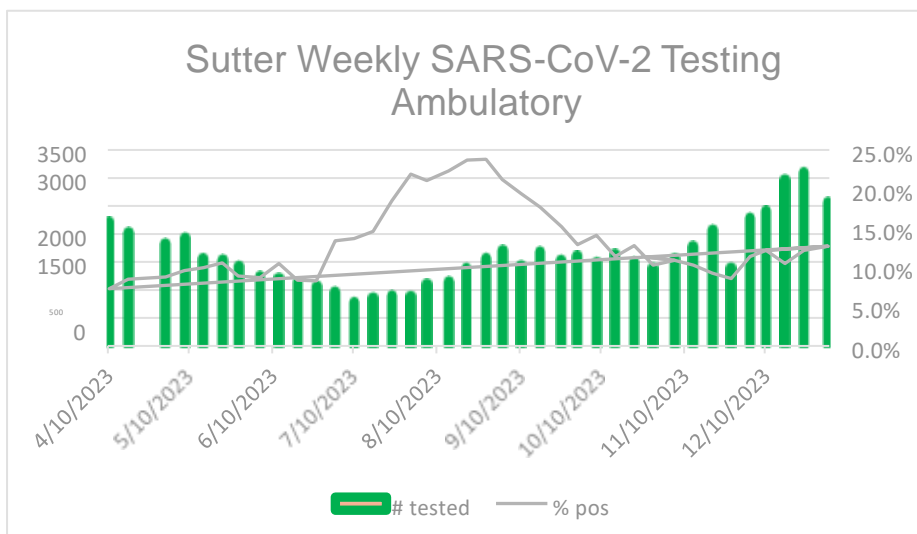
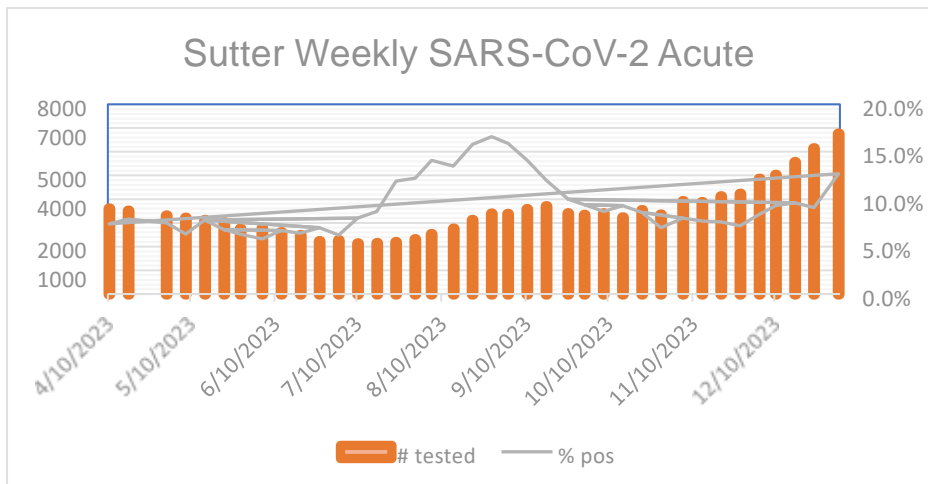


- Fortunately, this additional spike mutation in JN.1 has been shown to reduce the ACE2 binding receptor activity. Binding is the first step in viral invasion.
- Although many are writing that the vaccine should remain effective against the JN.1, data are still pending. Previous data were collected on the BA.2.86, which does not have increased immune escape. It is still very reasonable to anticipate that the current COVID vaccine will decrease the risk of hospitalization or death, although perhaps not prevent as many symptomatic infections.
- The map below shows [national](#) molecular test positivity rates by region, updated through Dec. 23.
- Three regions are yellow (10-14.9% positivity) and region 7 in the Midwest remains orange (15-19.9%). The three yellow regions positivity rates range from 14.4-14.8% and are very close to orange.
- Region 9, which includes California, is green with a positivity rate of only 6.5%.

Percent Positivity of COVID-19 Nucleic Acid Amplification Tests (NAATs) in the Past Week by HHS Region - United States



- Updated Sutter testing data below show elevated positivity rates in combination with significantly increased testing being performed in emergency departments and ambulatory environments. The actual number of positives in the last week in each of the two settings was the highest since April when this data was being collected.



- COVID test positivity rates in persons greater than 60 years old are now being evaluated compared to the entire tested cohort from Sutter data. Positivity rates remain higher in this age group (red) than the composite of all ages (purple). They comprise a higher risk group for severe COVID, and vaccination should be strongly encouraged.

COVID Location	≥ 60 years old		Composite Positivity Rates for All Ages
	Number Tested	% Positive (number)	
Ambulatory	536	18.3% (98)	12.7%
Acute (ED)	2,442	12.9% (314)	9.8%

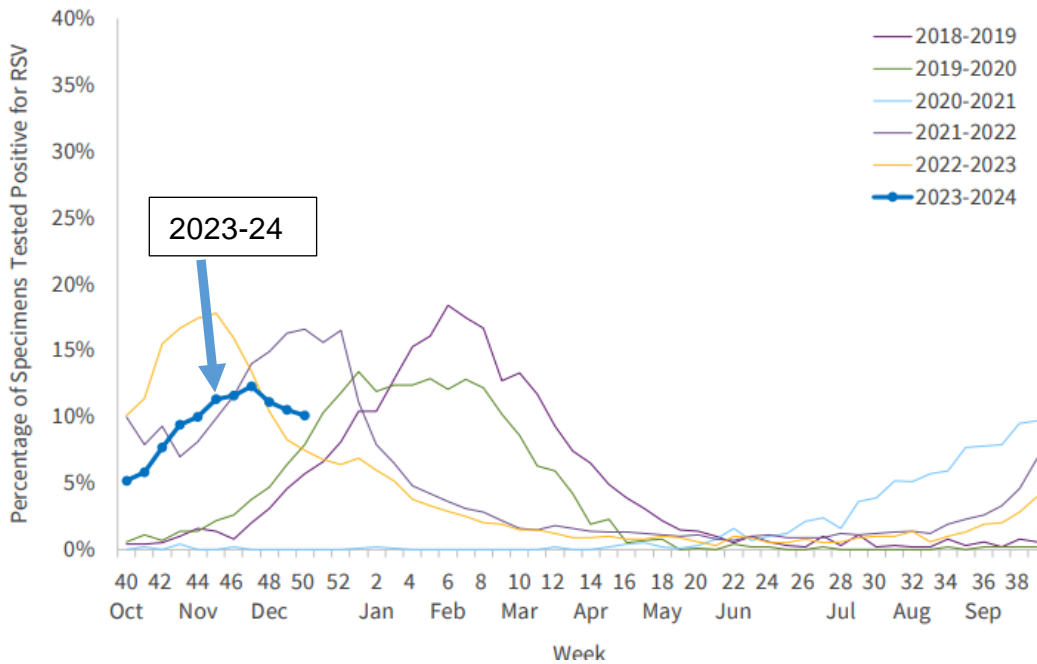
- The NIH panel of experts has provided comprehensive evidence review(s), developed and continuously revised recommendations for the treatment of patients with COVID-19 since the start of the pandemic in Spring of 2020.
 - The last update of the [Guidelines](#) will be published in early 2024 along with a downloadable version of the final.
 - The Sutter Health Emerging Infections Group has referred to the NIH guidance as a key guide. We will, however, continue to evaluate new evidence for therapeutics and repurposing of older therapies as it becomes available.
- COVID-19 Take-Home:**
 - Hospitalizations and emergency department visits, nationally, and at Sutter, are increasing. The weekly absolute number of positive tests in Sutter is now the highest since this data started being collected in April 2023. Persons 60 years and older, which comprise a very high-risk group, have a higher positivity rate than the composite of all ages.
 - The new subvariant JN.1 is originally derived from Omicron. It is quickly becoming dominant in the United States. It should present similarly to omicron with a sore throat, congestion and a dry cough. There are no data that JN.1 is more virulent than other recently circulating strains. It however does have increased ability to escape humoral neutralizing antibodies which could lead to more transmission. The weakened ability to attach to the ACE2 receptor could provide more time for our immune system to attack the virus.
 - The impact of the current vaccine against JN.1 has not been defined.
 - The Pango lineage naming is confusing and similar strains can have extremely different names.
 - Combined with the influenza and RSV trends discussed below, the risk from the triplendemic remains quite significant.
- 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](#)

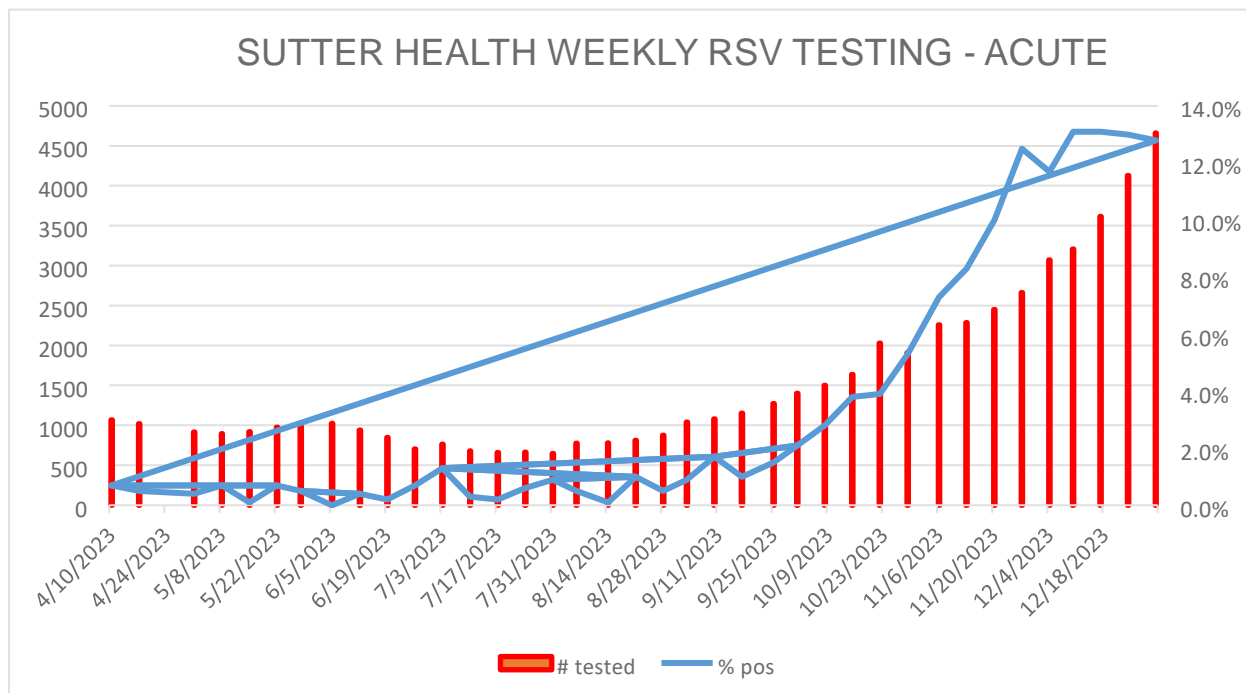
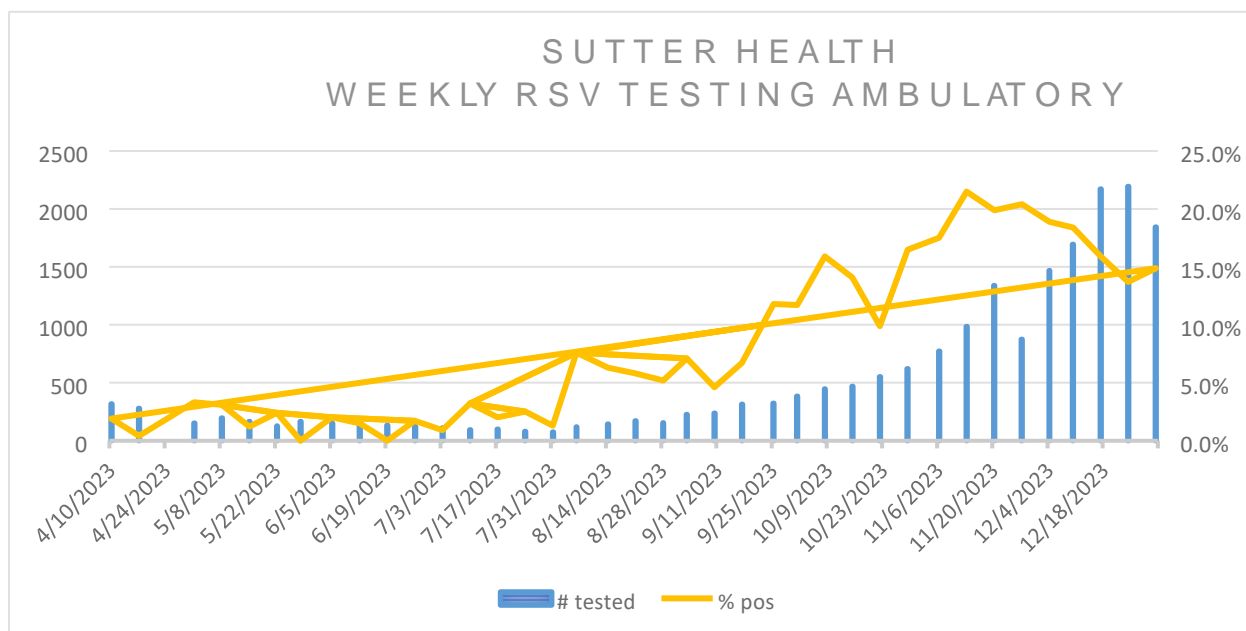
RSV

- [CDPH](#) reports RSV data weekly during the season. The CDPH graph below demonstrates our RSV season (blue arrow) compared to other seasons since 2018. RSV rates remain elevated. Although the peak may have passed, the rate of descent suggests that RSV will continue to circulate for a while still.

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



- RSV identification rates remain elevated in both the ambulatory (13.7%) and emergency departments (13.0%) in Sutter. The RSV season in Northern California remains widespread. See two graphs below.



- RSV results by age are in the following table for the week ending Dec. 31. Children less than 6 years old still dominate.
- Our Sutter data show that the vast majority of diagnosed infections this season continue to be in children less than 6 years old.
- The table below shows that positivity rates in children 6 to <12 years old are also elevated.
- The number of people ≥ 60 years being diagnosed with RSV in the acute settings has been stable for the last few weeks, running between 5-6%. Positivity rates in ambulatory have risen significantly and are now over 15%.

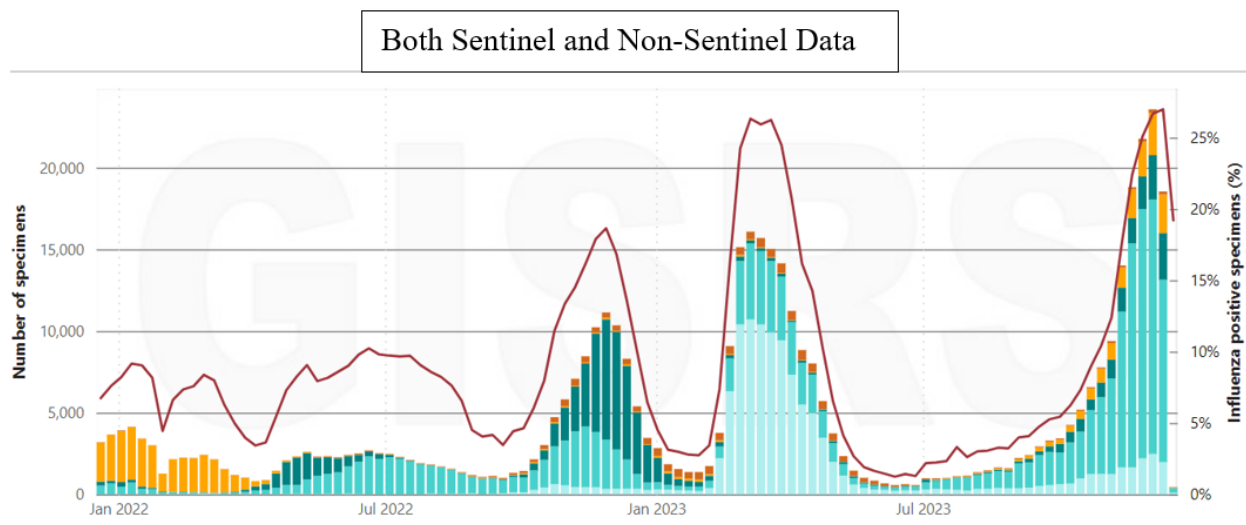
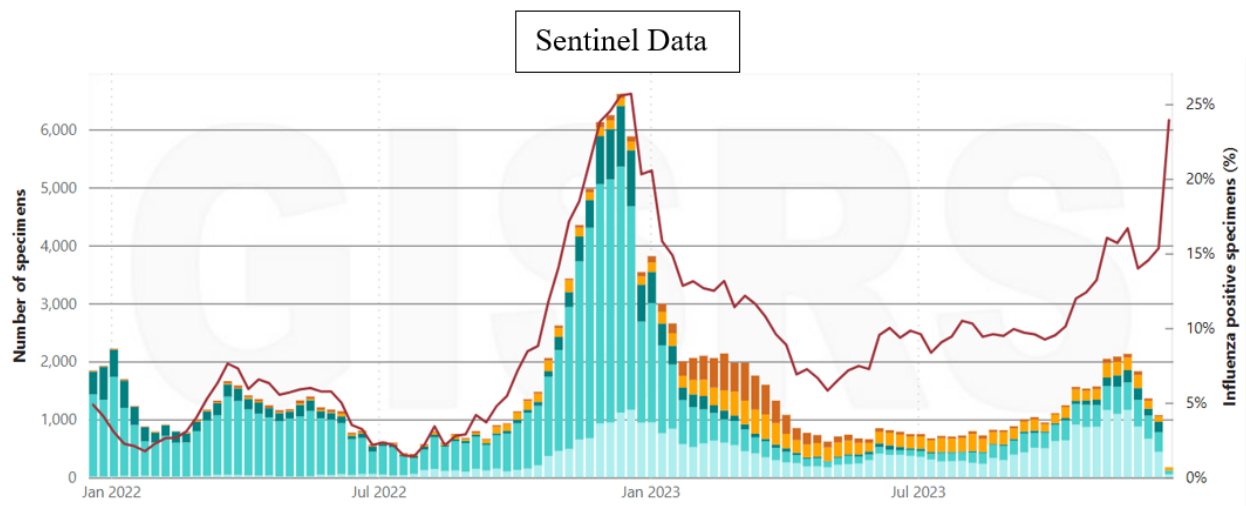
Location	<6 years old		6 to < 12 years old		≥ 60 years old	
	Number Tested	% Positive (number)	Number Tested	% Positive (number)	Number Tested	% Positive (number)
Acute (ED)	1045	35.6% (372)	201	14.9% (30)	2209	5.5% (122)
Ambulatory	518	26.4% (137)	183	9.3% (17)	396	15.4% (61)

- **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 at all ages.
- Higher numbers of cases are also being seen in persons 60 years and older, but this is most apparent in the ambulatory setting where patients tend to be not as sick as those seen in the acute emergency departments. This is encouraging news.
- 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.

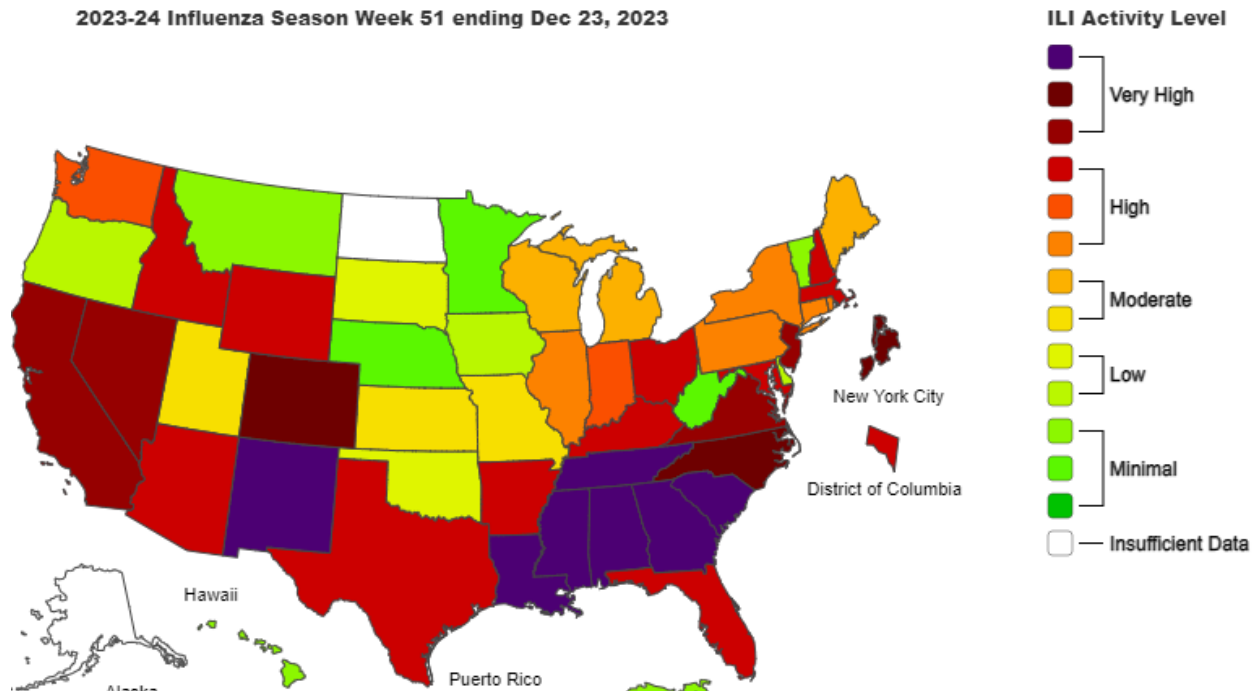
Influenza

- The [WHO](#) released its biweekly global influenza update on Dec. 27. This includes the most recent two weeks of data, but it is only up to Dec. 10.
 - Increased activity is being identified in parts of Europe, North America and Asia (central, eastern and western). Europe and Central Asia activity remains low overall but is predominantly influenza A split pretty evenly between A H1N1 and A H3N2.
 - Influenza A predominates with both A H3N2 and A H1N1 being detected.
 - The Southern Hemisphere continues with inter-seasonal, low levels of detection.
 - From Nov. 27 to Dec. 10, 424,940 specimens were tested with 59,000 positives (14% positivity rate).
 - 89% were influenza A; H3N2 remains four times as common as H1N1.
- Which data is collected and reported can dramatically change the results. Sentinel surveillance sites collect the highest quality data and represent the population under surveillance. However, depending on the number and size of the sentinel coverage, this may introduce significant bias.
- The two [WHO graphs](#) below show influenza activity in the Northern Hemisphere for the last 2 years. The first one shows sentinel site data and the second one reports both sentinel and non-sentinel data.
- The sentinel data suggest that the present outbreak is much smaller than it was the same time last year. The second graph suggests the opposite. That however is a measure of the number of tests performed. Positivity rates (the red run line) are both elevated between 20-25%. The epidemic threshold established by the WHO is a rate above 10%.



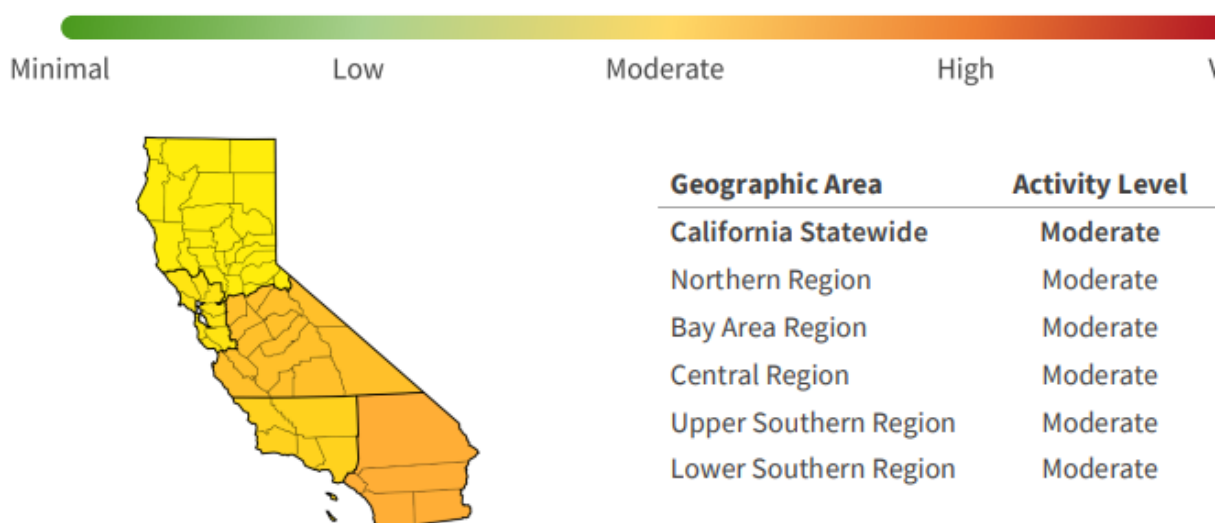
- The weekly [CDC](#) Influenza Surveillance Report was released on Dec. 29.
- Influenza-associated hospitalizations continue to increase. The week ending Dec. 23, 14,732 patients were admitted to hospitals with influenza. Compare that to the 29,000 that the CDC reported (information above) admitted with COVID. The number of patients admitted with a diagnosis of COVID was twice the number admitted with a diagnosis of influenza.
- Out of 79,353 specimens tested by clinical labs during week 51 (ending Dec. 23), 12,775 were positive (up to 16.1% from 12.8%)
- Influenza A H1N1 continues to dominate, but A H3N2 continues to comprise about 20% of influenza A isolates. This is the opposite of what the WHO reports in the world.
- Influenza-like illness (ILI), the surrogate for influenza used by the [CDC](#), is on the map below showing data in the week ending Dec. 23. Large swaths of the country have high to very high levels of ILI.

2023-24 Influenza Season Week 51 ending Dec 23, 2023



- The [CDPH](#) map below of influenza (last updated Dec. 16), shows that influenza is increasing throughout California, with all levels now moderate (10% to <20% positivity rates). The state influenza positivity rate has increased in the last reported week to 15.0%.
- CDPH reports true influenza and the CDC uses a surrogate for influenza. At this time, they appear to be providing similar conclusions.

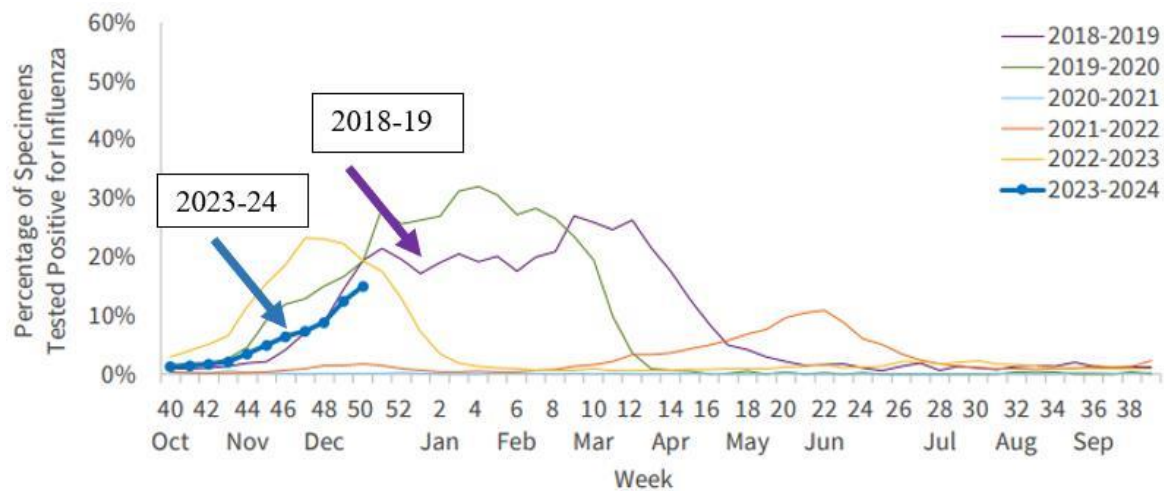
Influenza Activity Levels⁺



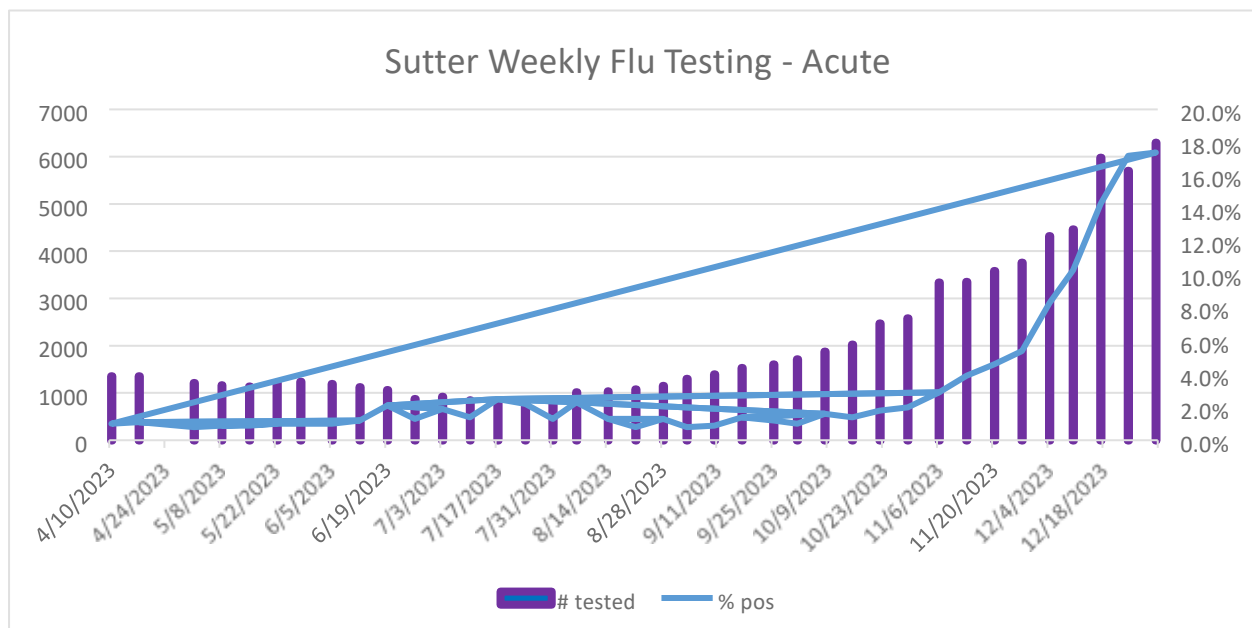
CDPH Influenza Activity Levels⁺

- **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%.

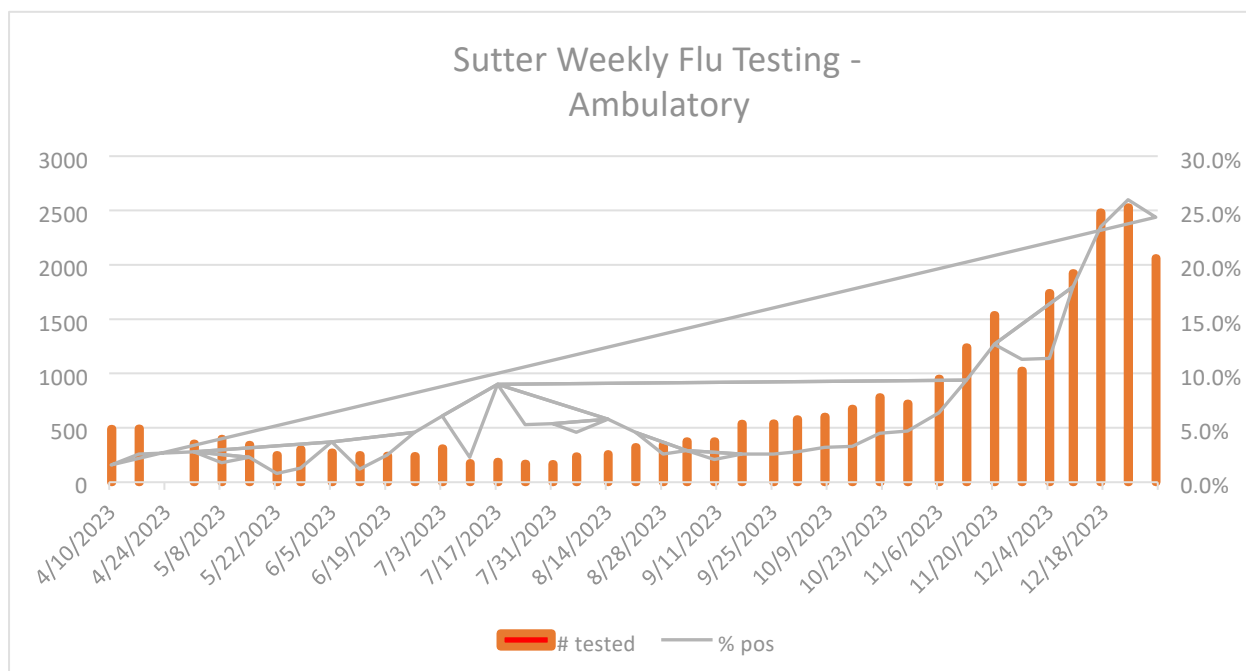
- The [CDPH map](#) below demonstrates that our present influenza season (blue arrow) appears to be similar to the pre-COVID 2018-19 season (purple arrow).



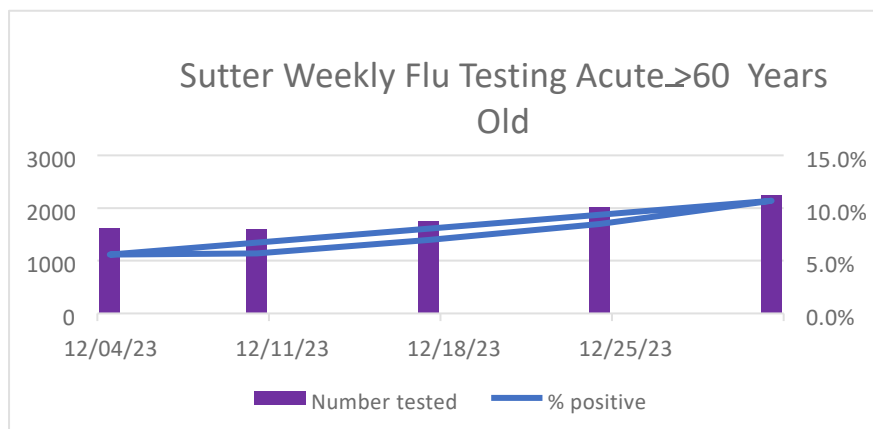
- Influenza A represents 95% of positive isolates reported to CDPH and most hospitalizations are in persons ≥ 65 years old. The CDC reports Influenza B comprises about 15% of isolates.
- The graph below shows Sutter emergency department and ambulatory influenza positivity rates. In the acute setting (emergency departments), positivity rates increased to 17.4% in the last week. In the ambulatory setting, the rate is 24.4%. This is higher than CDPH data, but CDPH information is lagging a few weeks.



- Now that influenza is widely circulating, false positive rapid influenza diagnostic tests should be uncommon.



- Sutter influenza test positivity rates in persons greater than 60 years old are shown below. Influenza rates in this population are increasing. In the acute setting, testing is increasing (vertical purple bars), and positivity rates (blue run line) have increased from 5.6% to 10.7% in 4 weeks. Typically, this reflects patients that are too sick to be seen in the ambulatory setting and are higher risk for requiring admission to the hospital.



- Contrary to what we see with COVID, the positivity rate in persons ≥ 60 years old is lower than the composite rate for all ages. That may reflect higher compliance with the flu vaccine in older persons, a more effective vaccine, or may just be the stage of the current flu outbreak.

Influenza Location	≥ 60 years old		Composite Positivity Rates for All Ages
	Number Tested	% Positive (number)	

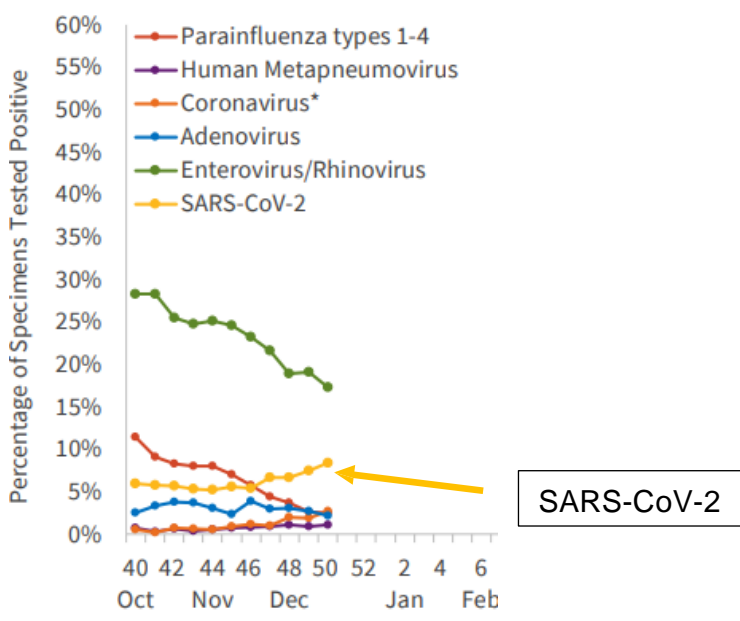
Ambulatory	407	16.0% (65)	24.4%
Acute (ED)	2256	10.7% (241)	17.4%

- **Take-Home Influenza:**

- Influenza is widespread in the United States.
- Data published by the WHO, CDC and CDPH can appear substantially different. Data collection and reporting vary. Interpretation of results should account for the time lag in reporting and the methodology used.
- WHO data from the Northern Hemisphere shows positivity rates of 20-25%.
- Influenza-associated hospitalizations are continuing to increase in the United States. ILI levels are very high in multiple states.
- During the week ending Dec. 31, Sutter emergency department positivity rates were 17.4% and ambulatory rates were 24.4%.
- Although less flu is seen in persons ≥ 60 years old compared to the composite for all ages, the rates are still significantly elevated. This older group is at increased risk of serious complications from influenza.
- 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. SARS-CoV-2, included in the graph below, is the only virus that is increasing. Enterovirus/Rhinovirus remains the one most commonly identified as a percentage of positive tests, but no denominators are provided.



- **Final Take-Home Message**

- The tripledemic is here. The impact is being seen and the peak has not been reached. It appears likely that hospitalization rates will continue to increase.
- Nationally, twice as many people were admitted to hospitals during the week ending Dec. 23 with a diagnosis of COVID compared to influenza.
- JN.1 is the fastest increasing sequenced isolate in the United States. JN.1 is directly derived from BA.2.86, which is a descendant of Omicron.
- RSV remains predominantly a disease of children <6 years old but disease in persons of all ages is increasing.
- Influenza activity is widespread in California. Anticipate increasing cases in older persons and patients with co-morbidities. The good news is that the vaccine appears to be a very good match at this time.
- Encourage proper hand hygiene, use appropriate PPE, encourage broader use of masks, vaccinate appropriate candidates, stay home if sick and treat influenza following CDC guidelines.