



## **Emerging Infections Newsletter for Clinicians**

Dec. 14, 2023

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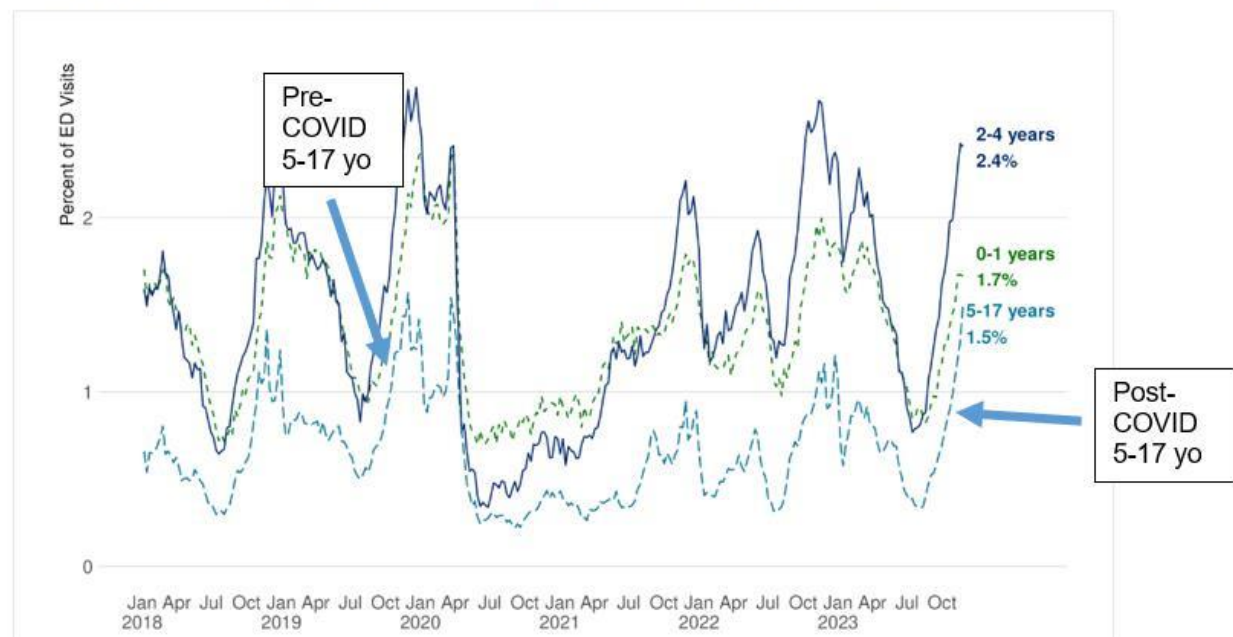
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## **Pediatric Pneumonia**

- China has been challenged with a wave in pediatric pneumonia. The WHO has been working with Chinese health authorities.
- The surge has been attributed to *Mycoplasma pneumoniae*. [Nature](#) published a short informational update Nov. 23. Typically, macrolides (examples: azithromycin or erythromycin) are the treatment of first choice. However, the prevalence of [macrolide-resistant](#) *M. pneumoniae* is estimated to be over 80% in China, compared to 8.3% in the United States.
- [Resistance](#) is usually due to a single macrolide binding site mutation in the 23S ribosomal RNA gene.
- Increased cases of pneumonia in children are also being reported in parts of the United States. The [CDC](#) published a graph below of the national weekly percentage of pediatric emergency department visits for pneumonia up through 17 years of age.
- Note that children 5-17 years old have higher rates this year but they are similar to pre-pandemic levels (blue arrows).
- Children 0 to 5 years old have similar rates to what was seen in the last 2 years. These data support that a new pathogen is not circulating and that this represents a seasonal pattern with pathogens that we usually see at this time of year.

National Weekly Percent of Emergency Department Visits for Pneumonia Among Patients Aged 0-17 Years



- CDPH took an informal survey to look at whether *Mycoplasma* might be causing more infections as reported in China. Although no denominators on the number of tests performed, very few cases have been identified in California.
- A major organization in Southern California has identified 11 cases in November. A children's hospital in Southern California has reported only three positive cases between October and November. Multiple public health laboratories in Northern California check for *Mycoplasma pneumoniae* and no cases have been identified yet this season.

- Sutter also includes *M. pneumoniae* in the expanded multiplex respiratory panel. In November, out of 2,285 panels performed, only five cases of *M. pneumoniae* were identified. This calculates out to 0.2% of tests.
- As will be shown in the discussion of RSV below, RSV is the likely cause of increased pediatric admissions due to pneumonia in the United States.
- **Pediatric pneumonia take-home**
  - The surge in cases in China is likely due to *Mycoplasma pneumoniae*. The severity of the outbreak is not unexpected considering the known, widespread, *M. pneumoniae* macrolide resistance.
  - Increased pediatric pneumonia in the United States is anticipated with the present RSV outbreak.

### **Lab Stewardship During the Respiratory Season**

- All members of the healthcare team are critical to ensure that we provide safe, cost-effective care, while preserving future options.
- The concept of antimicrobial stewardship is well known as the approach to mitigating antimicrobial resistance and preserving the activity of our antibiotics. Opioid stewardship, with multimodal pain management, is being recognized to effectively manage pain while minimizing the risk of causing opioid-use problems.
- The importance of [lab stewardship](#) is not as well known. The fundamental principle of lab stewardship is providing the right test, for the right patient, at the right time. Lab tests should be ordered if the results will possibly lead to a change in care. Overlapping testing should be minimized as that frequently is a waste of resources.
- Currently, the three most important circulating respiratory viruses are SARS-CoV-2, RSV, and influenza. The Cepheid Quadriplex panel measures those three viruses, in addition to separating influenza A from B. If any of those tests are positive, it is unlikely that the larger multiplex respiratory panel will provide results that will lead to additional changes in care.
- Sutter data from November is below. Of the 2,285 expanded multiplex panels that were ordered, 48.4% were positive, consistent with a large number of symptomatic persons seeking care.
- One-third of the positive results would have been picked up by the Cepheid panel (red font color in table below), which is widely available within Sutter, less expensive, and has a faster turn-around time.
- Also notable is that *Rhinovirus* (blue font color), the main cause of the common cold, was identified in 40% of the positive results. Molecular test confirmation of a common cold virus is typically not cost-effective.
- Parainfluenza (14.2%) and Adenovirus (7.9%) were also positive in significant amounts. Results of the multiplex panel, after a negative Cepheid Quadriplex result, and clinical elimination of a common cold as the diagnosis will most likely show *Parainfluenza* or *Adenovirus* at this time.
- Although there are no treatments for these two viruses, identification can help reassure some patients by explaining their prolonged infections or might lead to the discontinuation of unnecessary antibiotics. Trends in respiratory viruses reported by CDPH are in the “other respiratory viruses” later in the newsletter.

Respiratory Multiplex Panel	Positive Patients
November 2023 (n=2285)	48.4%

Respiratory Pathogen	% of Positive Results	Other alternative tests
Rhinovirus/Enterovirus	39.8%	
SARS-CoV-2, NAA	8.8%	COVID PCR; Combo COVID/Flu/RSV
Parainfluenza (1-4) Virus	14.2%	
Adenovirus	7.9%	
Coronavirus (Non-COVID)	1.4%	
RSV	16.6%	RSV PCR; RSV Antigen; Combo COVID/Flu/RSV
Influenza A	6.8%	Flu PCR; Combo COVID/Flu/RSV
Bordetella parapertussis	1.4%	Pertussis PCR
Mycoplasma pneumoniae	0.2%	
Human Metapneumovirus	1.4%	
Influenza B	1.4%	Flu PCR; Combo COVID/Flu/RSV
Bordetella pertussis	0.2%	Pertussis PCR
Chlamydia pneumoniae	0.0%	

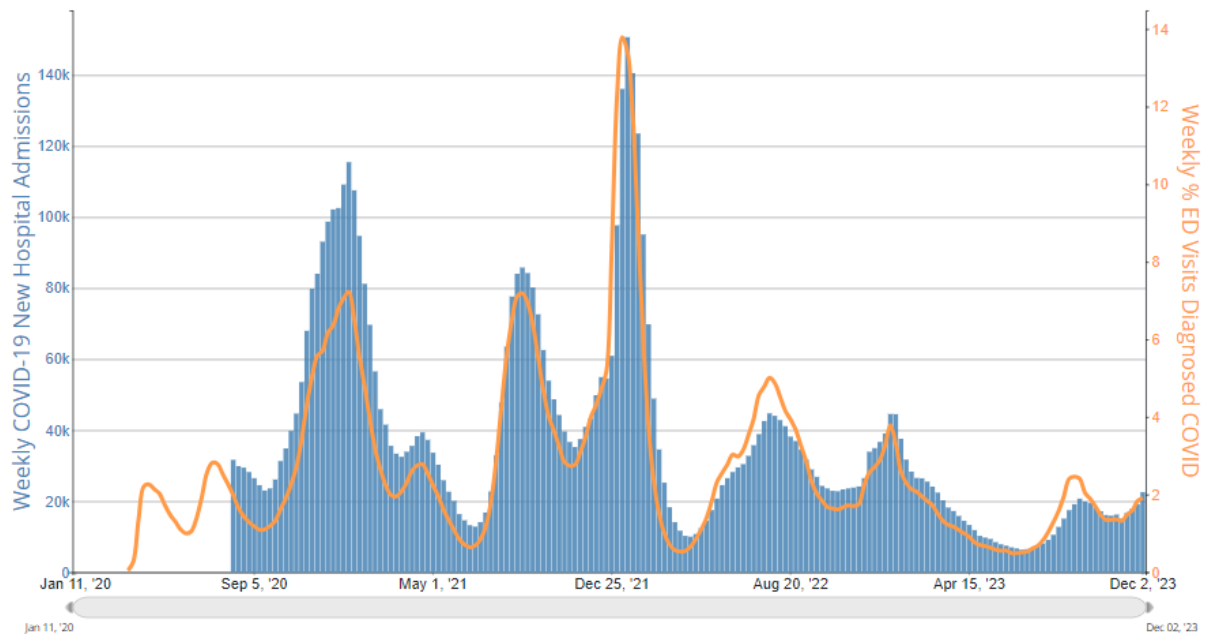
### ***The Tripledemic***

- 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 is not too late to get vaccinated. Mask, perform frequent hand hygiene and stay home if you are sick.

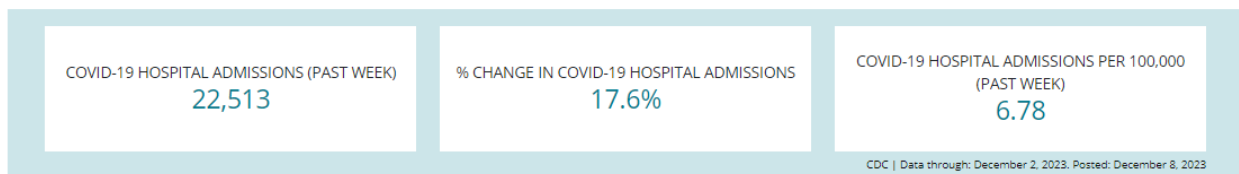
### **COVID-19**

- [Hospitalizations](#) in the United States are a surrogate for the virulence of the circulating strain. The graph below and the subsequent table show very significant increases in hospitalization rates (blue vertical bars) and the percentage of patients being diagnosed with COVID in emergency departments (orange run line).

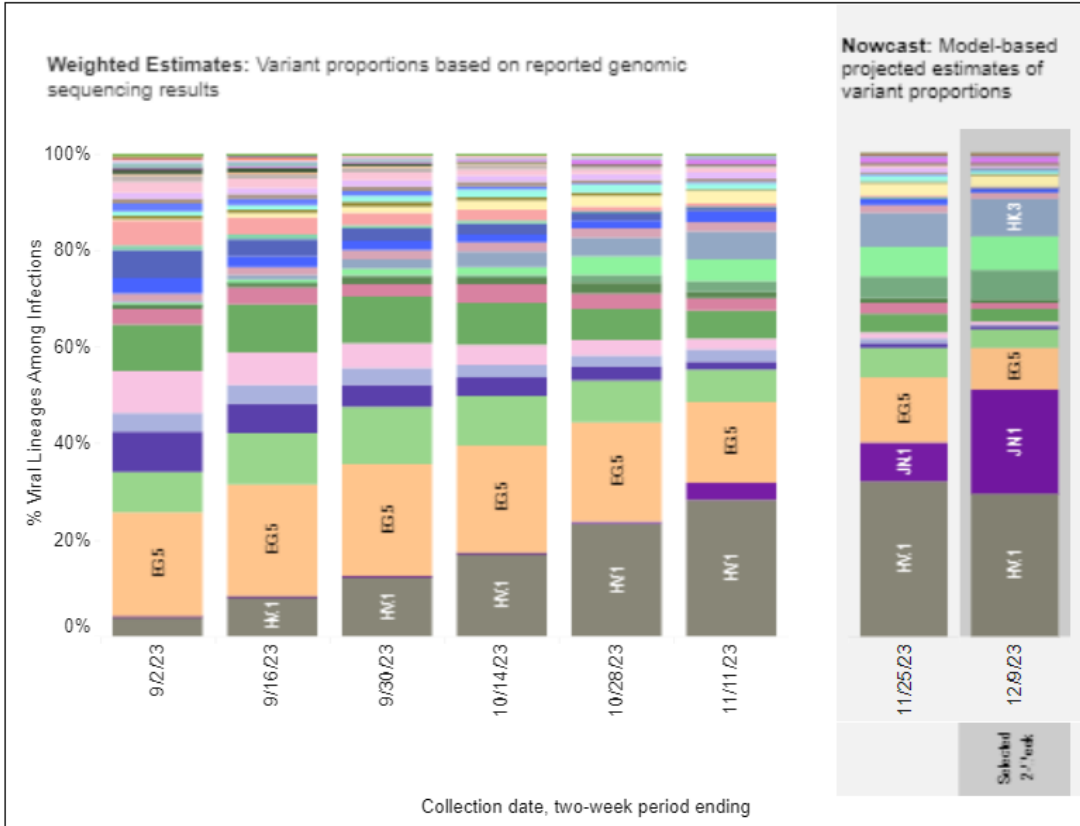
COVID-19 New Hospital Admissions and Percentage of Emergency Department (ED) Visits Diagnosed as COVID-19, by Week, in The United States, Reported to CDC



- The CDC tracks hospital admissions per 100,000 county population. Less than 10/100,000 is considered a low number of new hospital admissions. In the last week, national rates increased from 5.86/100,000 to 6.78/100,000. That is a 17.6% increase in only 1 week. This is on top of the 32% increase over the prior 3 weeks.



- [National genomic sequencing](#) was updated on Dec. 8. BA.2.86 was displaced by JN.1. HV.1 remains the most frequently sequenced isolate at 29.6%. JN.1 has only one amino acid change from BA.2.86. It is not surprising that another subvariant would spin off.



WHO label	Lineage #	%Total	95%PI
Omicron	HV.1	29.6%	26.6-32.7%
	JN.1	21.4%	15.1-29.4%
	EG.5	8.8%	7.6-10.1%
	HK.3	7.7%	6.3-9.2%
	JD.1.1	7.2%	5.8-8.8%
	JG.3	6.2%	4.6-8.2%
	FL.1.5.1	3.8%	3.4-4.4%
	XBB.1.16.6	2.3%	1.8-3.0%
	JF.1	2.3%	1.7-3.1%
BA.2.86	1.6%	1.0-2.5%	

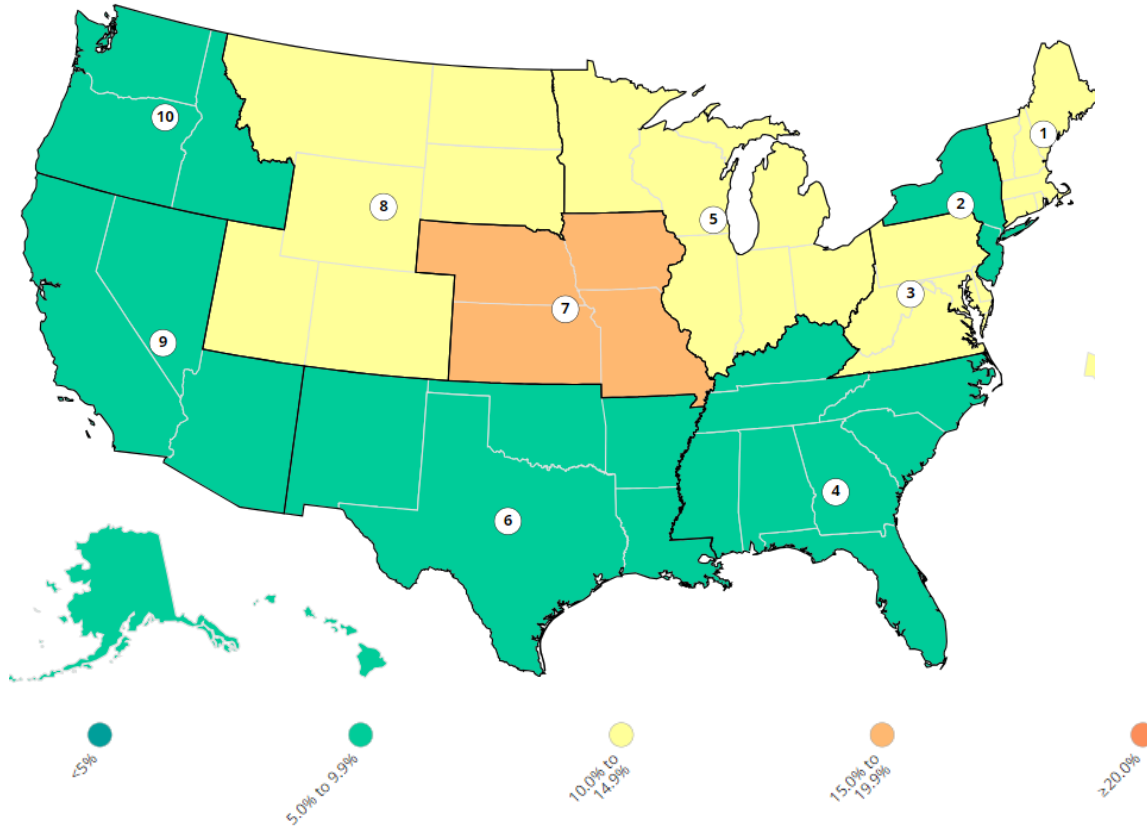
- The Pango Lineage below shows that JN.1 (green arrow) is a direct descendent of BA.2.86 (pink arrow).



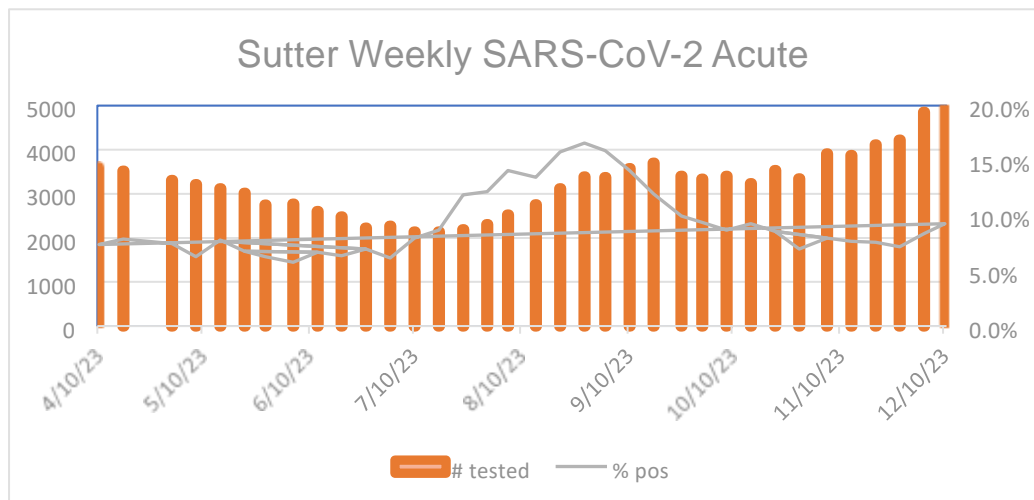


orange (15-19.9%). This map is most useful if you follow it weekly over time. For comparison, the week of Nov. 16 (2 weeks earlier), only region 8 was yellow. This map is consistent with the increased hospitalizations and ED positivity rates shown in the graph and table above.

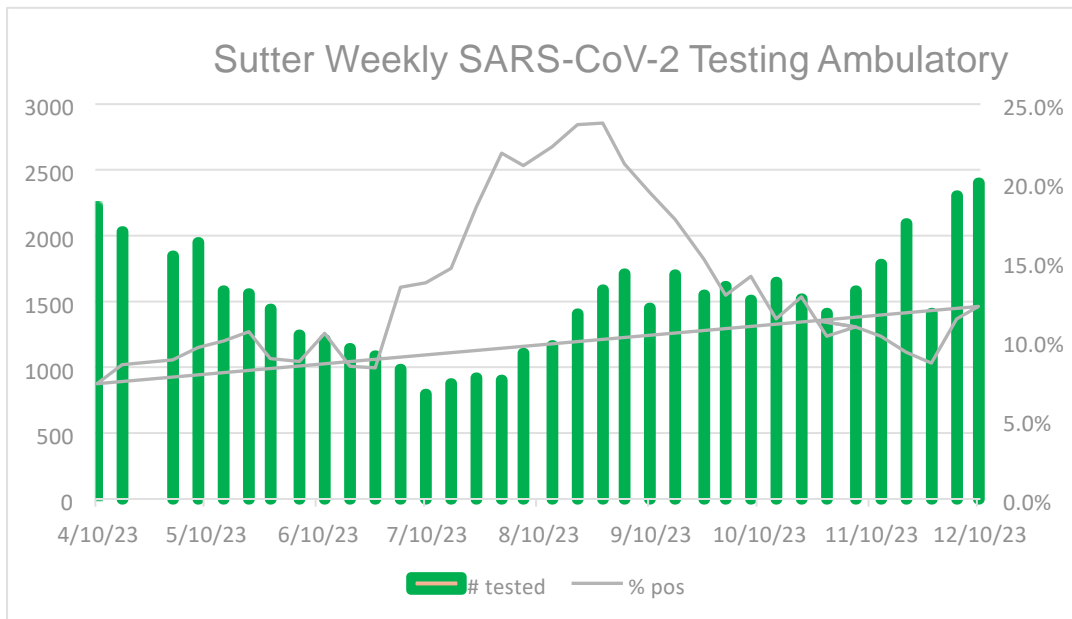
Percent Positivity of COVID-19 Nucleic Acid Amplification Tests (NAATs) in the Past Week by HHS Region – United States



- Updated Sutter testing data below show increasing 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 September.







- 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 than the composite of all ages. They comprise a higher risk group for severe COVID, and vaccination should be strongly encouraged.

COVID Location	≥ 60 years old	
	Number Tested	% Positive (number)
Ambulatory	431	11.4% (209)
Acute (ED)	1,796	13.1% (235)

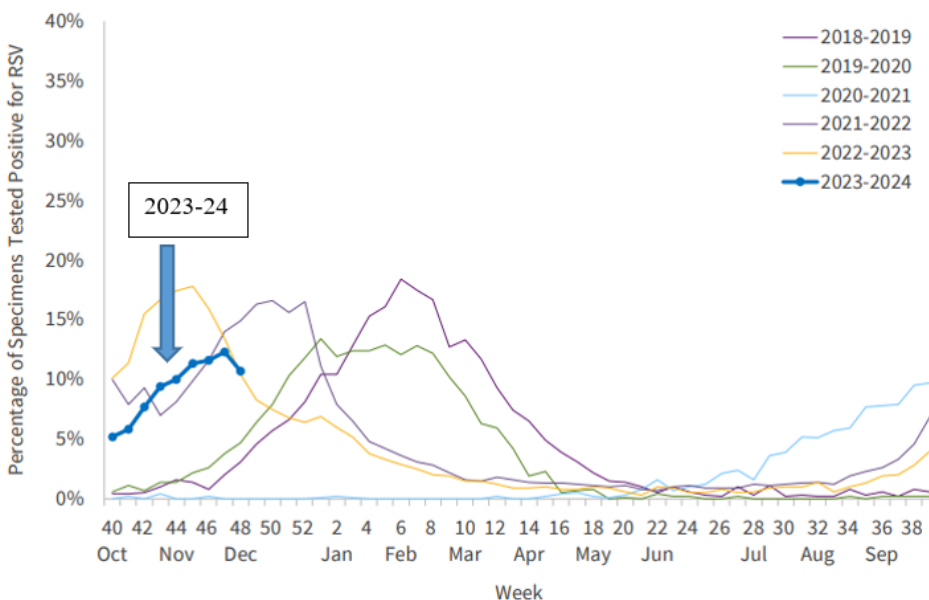
- **COVID-19 Take-Home:**
  - Hospitalizations and emergency department visits, nationally and at Sutter, are increasing. The weekly absolute number of positive tests in Sutter is increasing at a substantial rate. Persons 60 years and older have a higher positivity rate than the composite of all ages.
  - The new subvariant JN.1 is from BA.2.86. BA.2.86 had over 30 new mutations whereas the JN.1 only has one important change. It still appears that BA.2.86, or one of its new derivatives, is likely to dominate the circulating strains.
  - The Pango lineage naming is confusing and very similar strains can have extremely different names.
  - Combined with the influenza and RSV trends discussed below, the risk from the tripledemic remains quite significant.
  - Sutter ambulatory and emergency department positivity rates are increased to 12.2% and 9.3%, respectively.
  - The vaccine should provide coverage against BA.2.86 and derivatives. Encourage vaccinations, especially in those with co-morbidities and 60 years or older in age.

- **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](#)

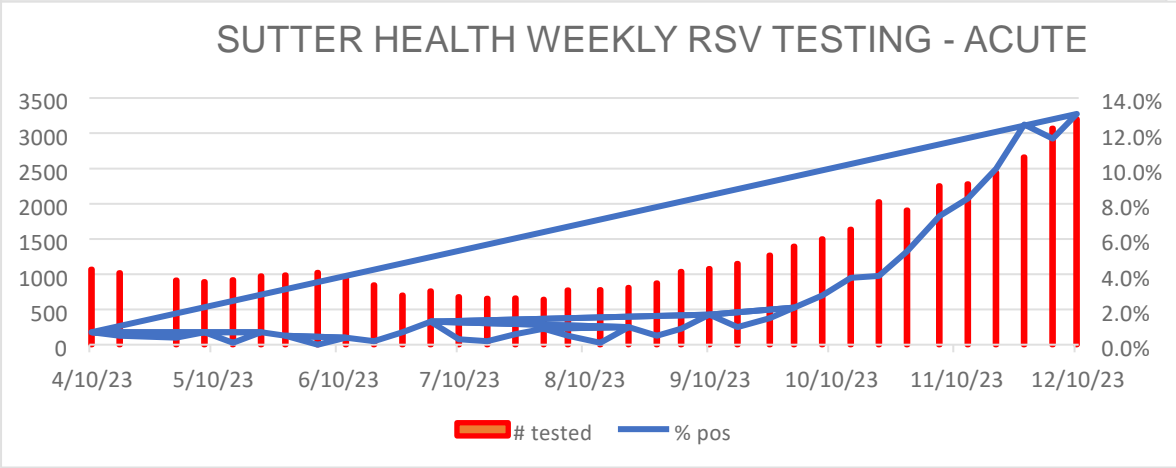
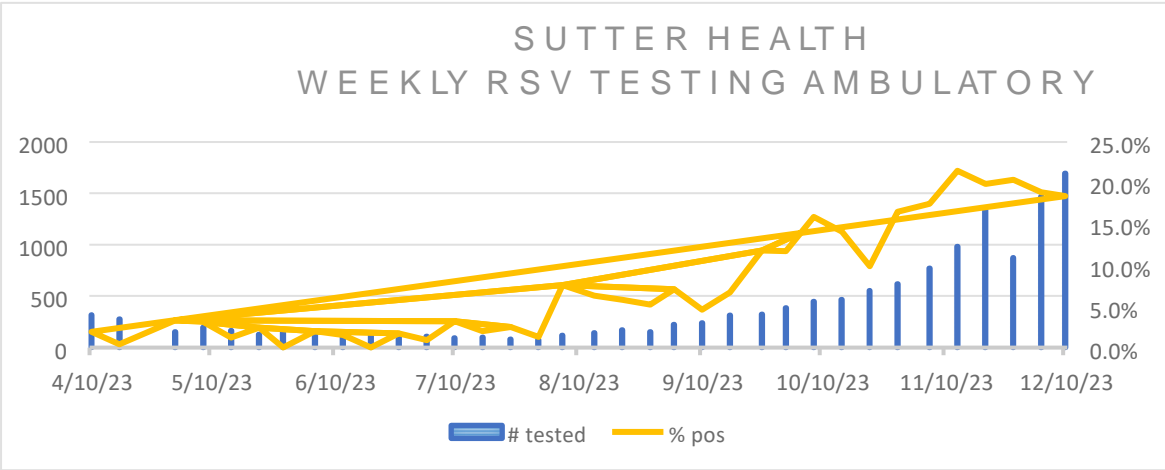
## **RSV**

- [CDPH](#) reports RSV data weekly during the season. The CDPH graph below demonstrates our RSV season (blue arrow) compared to other seasons since 2018. No conclusions can be drawn from one week in a lower percentage of positive tests.

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



- RSV identification rates remain elevated in both the ambulatory and emergency departments in Sutter. The amount of testing continues to increase. Positivity rates in ambulatory are now 18.4%. Emergency departments' positivity rates for RSV are up to 13%. 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. 3. Children less than 6 years old still dominate, with positivity rates of 36.8% in ambulatory and 35.6% in acute care settings.
  - Our Sutter data show that the vast majority of diagnosed infections this season continue to be in children less than 6 years old.
- Smaller numbers of persons 6 to <12 years old are tested in general, and positivity rates remain 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 5.7% (up from 3.9% last week). Ambulatory positivity increased from 10.7% to 12.1%.

Location	<6 years old		6 to < 12 years old		≥ 60 years old	
	Number Tested	% Positive (number)	Number Tested	% Positive (number)	Number Tested	% Positive (number)
<b>Ambulatory</b>	484	<b>36.8%</b> (178)	211	<b>11.4%</b> (24)	306	<b>12.1%</b> (37)
<b>Acute (ED)</b>	745	<b>35.6%</b> (265)	196	<b>12.8%</b> (25)	1,535	<b>5.7%</b> (87)

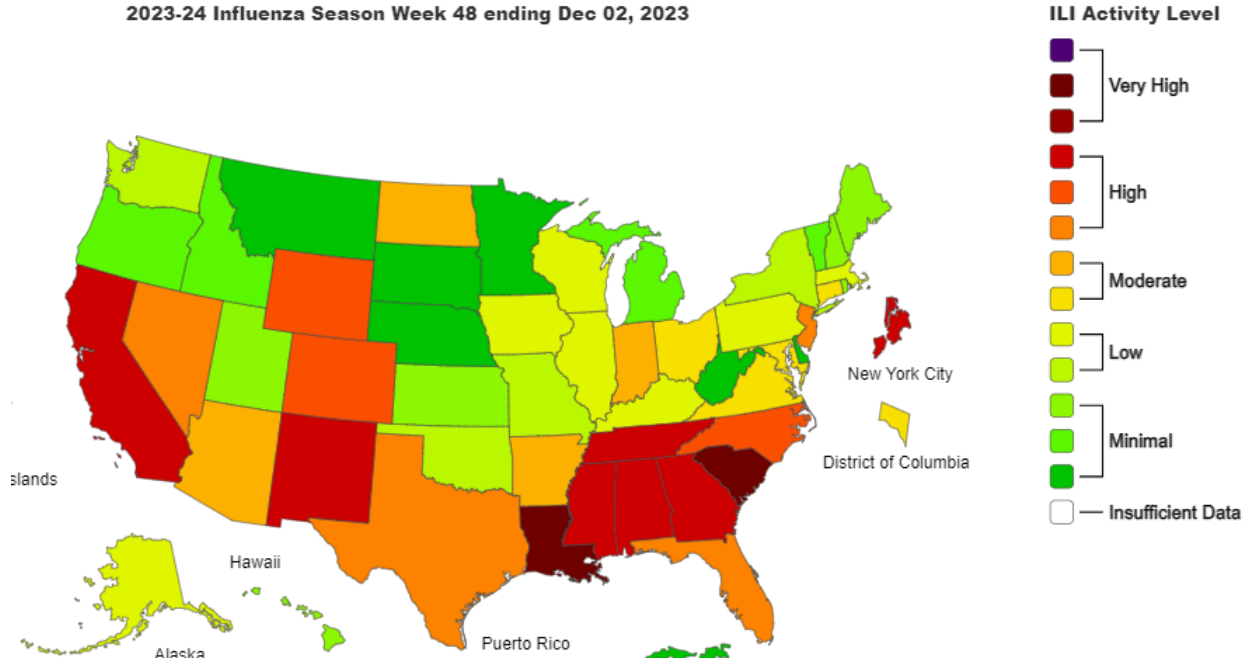
• **RSV Take-Home:**

- 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.
- In Northern California, over 35% of children <6 years old tested for RSV in the outpatient or emergency department environment are positive. This also supports that the increased pneumonia in children is secondary to RSV and not an unusual pathogen.
- Unfortunately, nirsevimab remains extremely limited in supply. Many RSV infections and hospitalizations could have been avoided if nirsevimab was available.
- 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**

- Influenza-associated hospitalizations continue to increase. The [CDC](#) reports that out of 93,944 specimens tested by clinical labs during week 48 (ending Dec. 2), 6,415 were positive (up to 6.8% from 6.2% in the prior week). This also represents a 34% week-to-week increase in testing.
- Influenza A H1N1 continues to dominate, but A H3N2 is starting to be identified more frequently. Influenza A H1N1 only comprises 74% of influenza A isolates, down from a recent peak of 90%. A H3N2 is now 26%.
- Influenza-like illness (ILI), the surrogate for influenza used by the [CDC](#), is on the map below showing data in the week ending Dec. 2. Only minor changes are noted compared to the prior week.
- As identifications continue to increase, the thought is that this map should be a reasonable, but imperfect surrogate for true influenza. ILI is a surveillance measurement defined by any illness with fever ( $\geq 100^{\circ}$  F or  $37.8^{\circ}$  C) plus cough and/or sore throat.

2023-24 Influenza Season Week 48 ending Dec 02, 2023



- The [CDPH](#) map below of influenza (last updated on Dec. 11), however, shows true influenza activity in California to be low to moderate. The state influenza positivity rate has increased in the last week from 7.4% to 8.8%.
- CDPH measure true influenza and the CDC uses a surrogate for influenza.
- 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\*

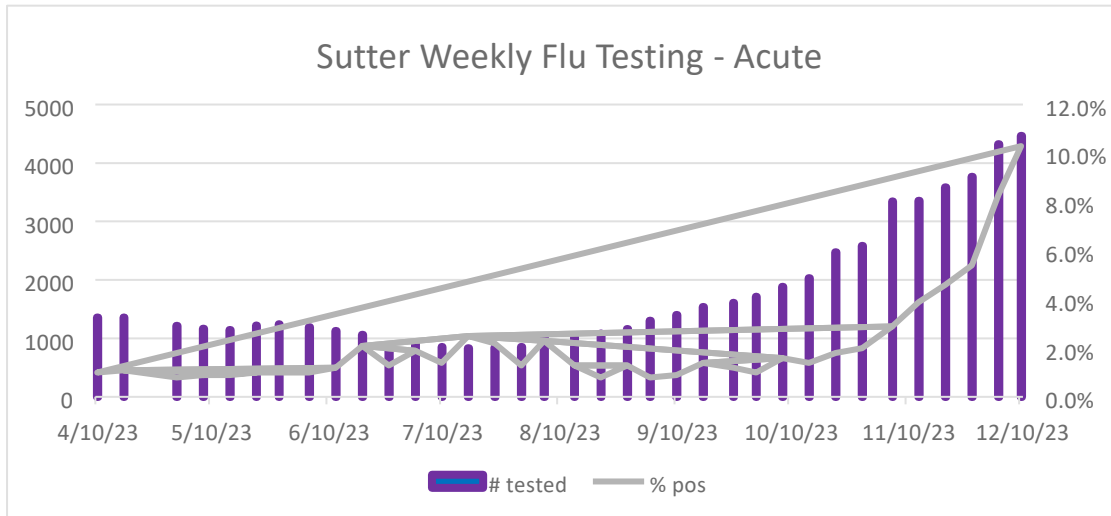


Geographic Area	Activity Level
California Statewide	Low
Northern Region	Low
Bay Area Region	Low
Central Region	Moderate
Upper Southern Region	Low
Lower Southern Region	Low

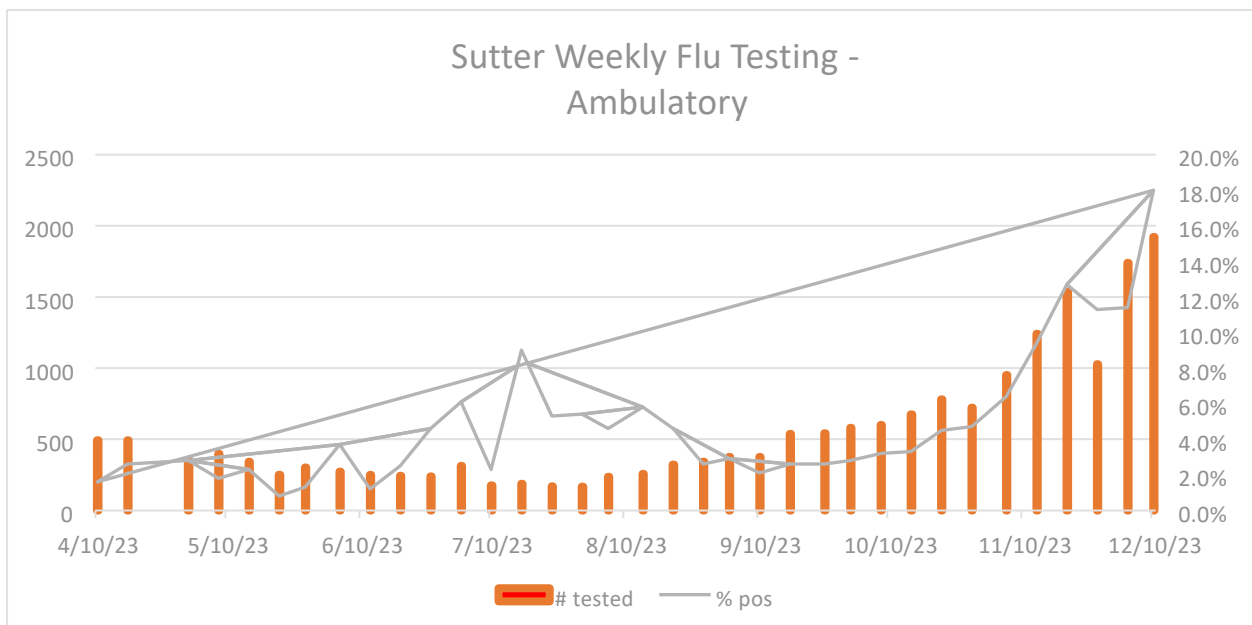
### CDPH Influenza Activity Levels\*

- **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  $\geq 40\%$ .
- The graph below shows Sutter emergency department and ambulatory influenza positivity rates. In the acute setting (emergency departments) positivity rates increased from 8.3% to 10.3% in the last week, consistent with increasing circulation of influenza. That equals a moderate level according to CDPH criteria.



- In the ambulatory setting, positivity rates shot up to 18%. 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 for closer evaluation. Table below. Influenza rates in this population evaluated in the acute settings are lower than our total population rates.
- This is not an unusual pattern and mimics what we saw with the initial RSV outbreak this season. Influenza typically causes outbreaks in children before older adults.

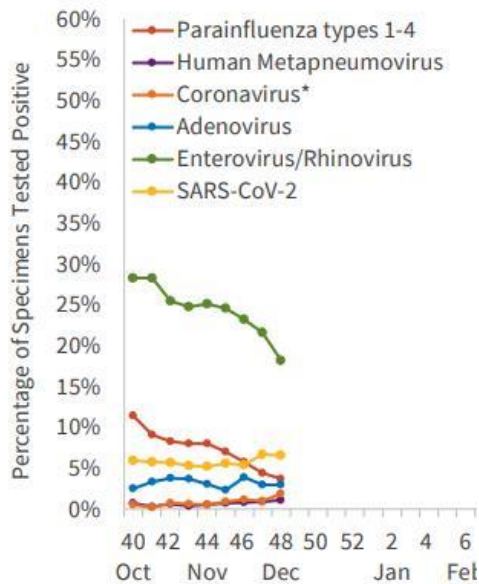
Influenza Location	≥ 60 years old	
	Number Tested	% Positive (number)
Ambulatory	319	8.5% (27)
Acute (ED)	1,597	5.7% (91)

- **Take-Home Influenza:**
  - Influenza activity and influenza-associated hospitalizations are continuing to increase 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 8.8%.
  - Sutter emergency department positivity rates of 10.3% were noted during the week ending Dec. 10. This equates to CDPH-defined moderate influenza activity (10-19.9%). Patterns in the state and within Sutter are the same.
  - Influenza A continues to dominate in the United States with A H1N1 down to 74% 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 one most commonly identified. These are usually identified on multiplex respiratory panels other than the Cepheid panel (COVID, RSV, Flu A/B). No denominators are provided.





- **Final Take-Home Message**

- The tripledemic is here. The impact is being seen and the peak has not been reached.
- COVID is associated with an 18% increase in hospitalizations nationally, just in the last week alone.
- BA.2.86 is approaching 50% of international isolates whereas JN.1 is the fastest increasing sequenced isolate in the United States. As the Pango map above shows, JN.1 is directly derived from BA.2.86. It is not clear whether the international sequencing separates out BA.2.86 from JN.1 but it is likely because of the delay in reporting the international travelers' results.
- RSV remains predominantly a disease of children <6 years old. Disease in persons  $\geq$  60 years old is increasing.
- Influenza activity is climbing. There is a definite possibility that A H3N2 will ultimately replace A H1N1, but more data are needed. The vaccine appears to be a very good match at this time.
- 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.