



## **Emerging Infections Newsletter for Clinicians**

*Jan. 18, 2024*

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### **Topics**

1. Measles Again
  - a. WHO and unvaccinated and under-vaccinated children
  - b. Europe
  - c. Philadelphia
2. Syphilis
  - a. Congenital syphilis
  - b. Emergency resolution of benzathine penicillin shortage
  - c. Linezolid does not work
3. Post-Exposure Prophylaxis (PEP) Against Invasive Meningococcal Infections
4. The Tripledemic
5. COVID-19
  - a. United States hospitalization data
  - b. Wastewater activity levels
  - c. Sutter data
  - d. Take-home COVID
6. RSV
  - a. CDPH data
  - b. Sutter data
  - c. Nirsevimab supply improved
  - d. Take-home RSV
7. Influenza
  - a. WHO
  - b. National data
  - c. Influenza-like-illness (ILI) in the United States
  - d. CDPH data
  - e. Sutter data
  - f. Take-home influenza
8. Other Respiratory Viruses
9. Share the Newsletter

## **Measles (Rubeola)**

- Measles remains the most contagious, airborne-transmitted virus known to infect people. Measles vaccine is extremely effective and safe, but vaccination coverage has been declining in multiple areas of the world.
- The WHO estimates that 33 million children in the world did not receive two doses of the measles vaccine in 2022, with most of those never even receiving their first dose. [From 2021 to 2022](#), estimated cases of measles increased by 18% and deaths by 43%.
- [Europe](#) has had a 30-fold increase in measles cases in 2023, rising from 941 cases in 2022 to over 30,000 cases in 2023. Over 21,000 people required hospitalization.
- In the United States, 48 cases were reported in 2023. This compares to 121 cases in 2022.
- Most cases in the United States do not lead to large outbreaks because of the rapid implementation of control measures by local and state health departments.
- Nine confirmed cases of measles were recently identified in Philadelphia. The scenario is fairly typical. An unvaccinated person contracts measles outside of the United States, returns home, becomes sick and spreads the infection to other unvaccinated persons, mostly children.
  - In this case, an infant was the index case. The infant was hospitalized with fevers and respiratory symptoms and was subsequently recognized as having measles after the rash developed.
  - Three additional patients were identified including an [infant](#) too young to get vaccinated, an unvaccinated older child and the older child's unvaccinated parent.
  - One of the children violated quarantine and exposed and infected five other children in a daycare environment. At least six patients were hospitalized with measles. Because of increased contact tracing, testing, and quarantining, no additional cases have been identified so far.
  - Philadelphia reports a 93% vaccination rate against measles by age 6 years old. Experts say that 95% coverage with two doses of the measles containing vaccine (MCV) is necessary to protect against community outbreaks.
- The [WHO](#) estimates that 83% of the world's children population had received at least one dose of a MCV in 2022 by their first birthday and only 74% had the necessary two doses for nearly complete protection. That was the lowest percentage since 2008.

## **Measles Take-Home**

Measles is a highly contagious, vaccine-preventable disease. Most cases in the United States begin with unvaccinated travelers from the United States returning home after being exposed to measles.

- Transmission then proceeds to additional unvaccinated or under-vaccinated persons, especially children. The best way to prevent outbreaks is for over 95% of the population to have received two doses of a measles-containing vaccine (measles, mumps and rubella). Outbreaks are usually limited in the U.S. because most people in the U.S. are vaccinated, plus the rapid response from local health departments. Unfortunately, as more communities have two-dose measles vaccination rates below 95%, the risk of outbreaks will simultaneously increase.
- The recent outbreak in Pennsylvania demonstrates how easily the disease can be transmitted to unvaccinated or under-vaccinated persons. More than 30,000 cases of measles were reported in Europe in the first 10 months of 2023. This huge resurgence is largely due to decreased vaccination coverage from 2020-2022.
- Measles vaccine as part of the MMR vaccine is extremely effective. It is important to provide accurate, honest information as misinformation results in under-vaccinated, vulnerable communities and disease transmission.

## **Syphilis**

- [Congenital syphilis](#) is a preventable disease. The [CDC](#) released a report in November 2023 on missed opportunities to prevent congenital syphilis.
- Syphilis during pregnancy can lead to miscarriage, stillbirth, neonatal or infant death, and maternal mortality. In 2012, there were 334 cases reported, but in 2022, that number was up to 3,761 cases. That is over a 1,000% increase in cases in 11 years.
- Just from 2021 to 2022, cases increased 32%. Concurrently there was a 17% increase in rates of primary and secondary syphilis cases among 15 to 44-year-old persons who could become pregnant. Lack of timely testing and adequate treatment during pregnancy contributed to 88% of the cases.
- Benzathine penicillin (Bicillin -LA) has been on shortage since April 2023. On Jan.10, the [FDA](#) announced approval to import the French drug Extencilline (benzathine benzylpenicillin). Although the dosages are identical between Extencilline and Bicillin-LA, there are [multiple differences](#).
  - French product barcode may not register on U.S. scanning systems.
  - Extencilline contains soy phospholipids and may cause hypersensitivity reactions in patients with a history of allergies to soybeans.
  - Extencilline is delivered as a powder for reconstitution compared to prefilled disposable syringes for Bicillin-LA.
  - Reconstituted Extencilline doses are a significantly larger volume of 5mL for 1.2 million units (2 mL for Bicillin-LA) and 7 mL for 2.4 million units (4mL for Bicillin-LA).
  - Package insert does not have detailed instructions for deep IM administration.
- Supply shortage is anticipated to recover in Q2 2024 with the next batch of Bicillin-LA being released by Pfizer in April.
- [Lancet](#) Infectious Diseases Jan. 8 published a randomized, 1:1, prospective, multicenter, open-label, non-inferiority trial comparing five days of oral linezolid with benzathine penicillin for early syphilis.
- After only 59 patients were enrolled, the prespecified interim analysis revealed that linezolid was not non-inferior to benzathine penicillin (i.e., was inferior). The cure rate with linezolid was only 70% compared to 100% for benzathine penicillin and the trial was stopped for futility.

## **Syphilis Take-Home**

- Rates of congenital syphilis remain very high. Treatment has been complicated by a national shortage of Bicillin-LA.
- The FDA has approved temporary importation of the French drug Extencilline. Although Extencilline has the same dosages available as Bicillin-LA, the preparation and administration volumes of the medicines are very different. Careful attention to the difference is critical to ensure proper and safe administration.
- Pfizer is anticipated to release significant supplies of Bicillin-LA in April.
- Linezolid is not approved for and should not be used as a treatment for syphilis.

## **PEP Against Invasive Meningococcal Infections**

- Post-exposure prophylaxis (PEP) after close contact with a patient with meningococcal disease has been a standard of care for many years.
- Antibiotic resistance has been increasing and the [CDC](#) published guidance in May 2023 for when to discontinue recommending ciprofloxacin and use alternative agents—specifically rifampin, ceftriaxone, or azithromycin—for PEP. Health departments were encouraged to use flexibility in recommending a change in PEP.

- Both the San Francisco Bay Area and Sacramento regions have each identified one patient in the last 12 months with ciprofloxacin-resistant invasive meningococcal disease (IMD).
- Local health jurisdictions in the Bay Area and Sacramento regions are recommending discontinuation of ciprofloxacin for IMD PEP. This notification encompasses 18 counties.
- Recommended alternatives are rifampin, ceftriaxone or azithromycin.
- CDPH published an associated [Meningococcal Quicksheet](#).

### ***N. meningitidis* Take-Home**

Ciprofloxacin-resistant *N. meningitidis* has been identified as a high risk in the San Francisco Bay Area and Sacramento Regions. Alternative agents should be used for IMD PEP.

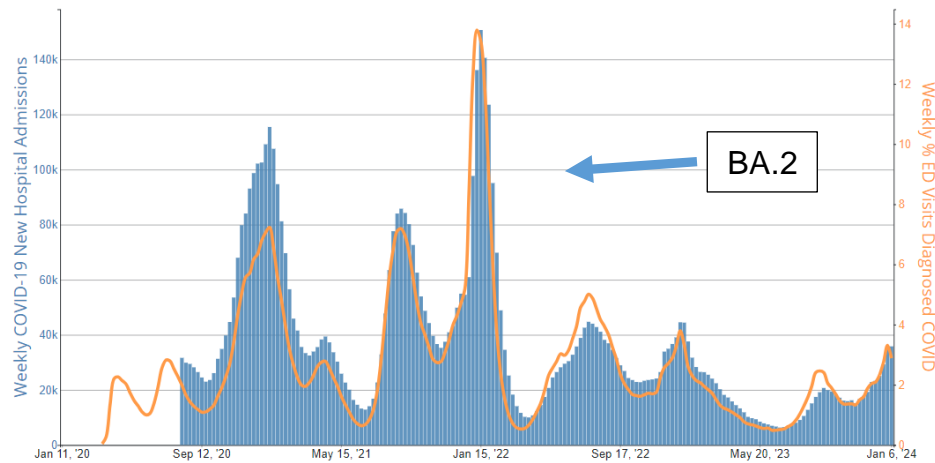
### **The Tripledemic**

- SARS-CoV-2 is widely circulating mostly due to JN.1. Positivity rates remain above 10% in the United States and Europe and they appear to be slowly increasing. The trend could spike up soon because SARS-CoV-2 levels in wastewater are very high in many parts of the country.
- The RSV season appears to be on the decline. Positivity rates, although still elevated, are dropping in California and throughout Sutter. Children under 6 years old still comprise most patients, but RSV pneumonia in adults is occurring.
- Influenza activity has also declined but looking at previous trends, this may be a temporary finding and a rebound might occur, possibly with influenza B. Although less likely, the 2022-23 season ended very early and that scenario could repeat itself this year.
- It is critical to note that regardless of the trends, all three infections are circulating at increased levels and a lot of people will continue to get sick.
- Nirsevimab for newborns and children entering their first RSV season should be more readily available very soon. Nirsevimab is an antibody and not a vaccine. It provides protection immediately after infusion.
- RSV vaccine appears to be well tolerated and data on effectiveness should be very positive.
- Influenza vaccine matches circulating strains in the world.

### **COVID-19**

- The [WHO](#) reports surveillance positivity rates in Europe of 16%.
- [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 being 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

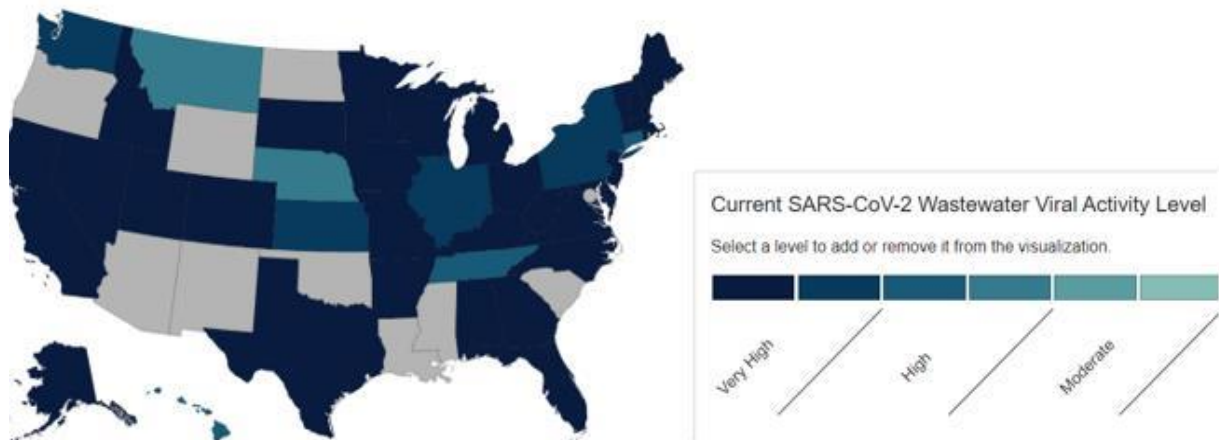


- The CDC tracks hospital admissions per 100,000 county population. Less than 10/100,000 is considered a low number of new hospital admissions. National rates have been progressively increasing. They remain moderate at 10.78/100,000. Hospitalizations during the last week only increased by over 3.2%. That is a very small increase compared to the 20% increase in the prior week.

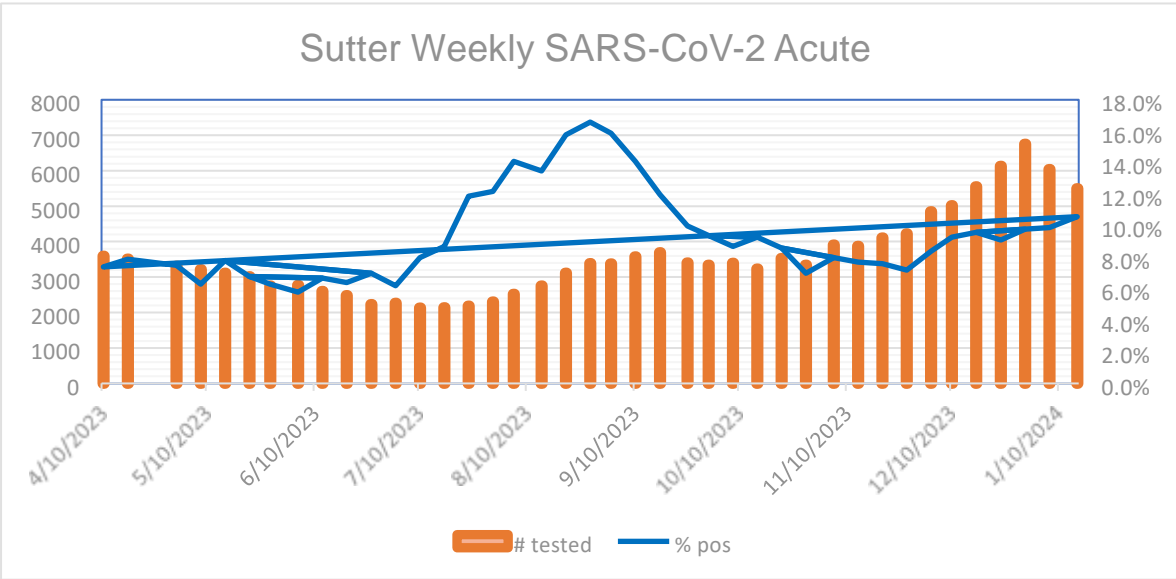
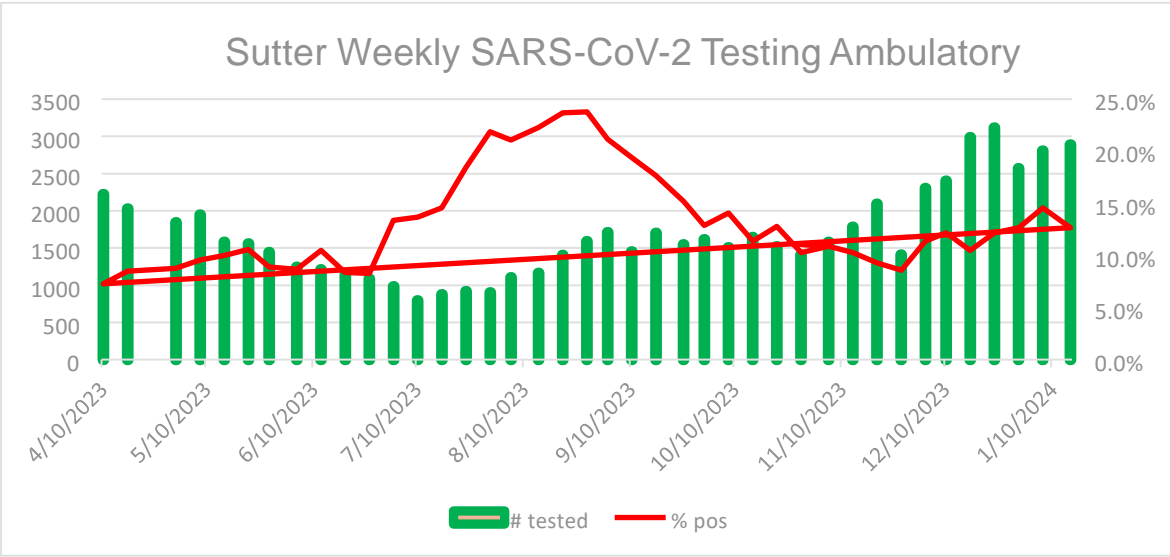
<p>COVID-19 HOSPITAL ADMISSIONS (PAST WEEK)</p> <p><b>35,801</b></p>	<p>% CHANGE IN COVID-19 HOSPITAL ADMISSIONS</p> <p><b>3.2%</b></p>	<p>COVID-19 HOSPITAL ADMISSIONS PER 100,000 (PAST WEEK)</p> <p><b>10.78</b></p>
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CDC | Data through: January 6, 2024. Posted: January 12, 2024

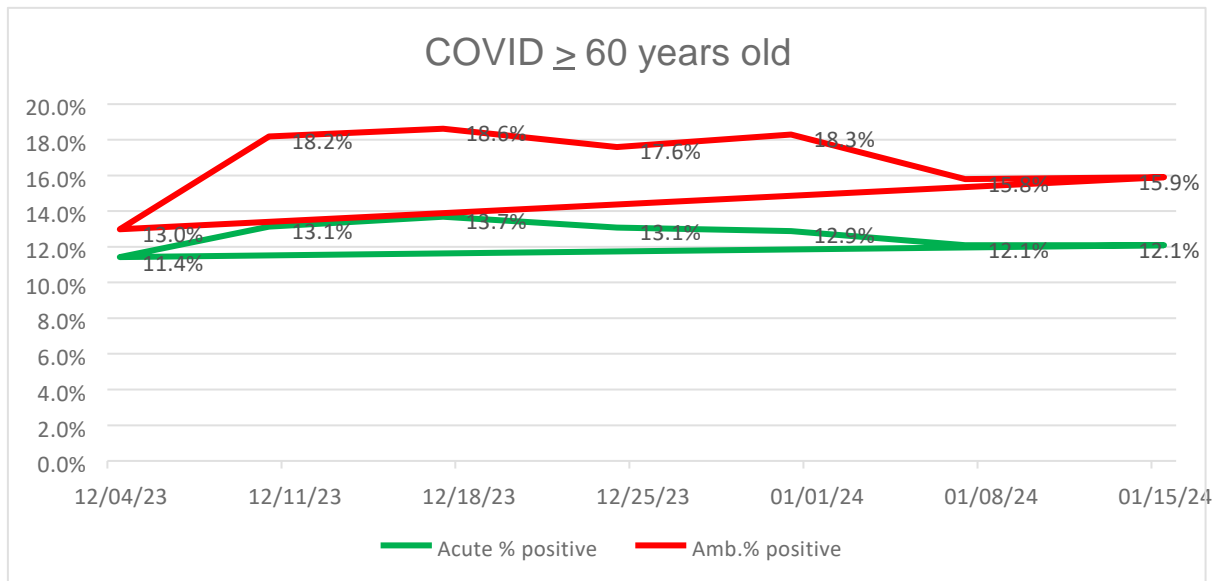
- [National genomic sequencing](#) is updated by the CDC every 2 weeks. A new report will be released next week.
- SARS-Co-V-2 wastewater levels are high to very high almost everywhere that it is measured. The map below is from the [CDC](#) site, Grey represents insufficient data.



- Updated Sutter testing data below show elevated positivity rates in combination with high levels of testing. Positivity rates continue to slowly increase in both environments.



- COVID test positivity rates in persons greater than 60 years old are being pulled out to analyze. Rates in this age group are higher than the total cohort of all ages.



#### COVID-19 Take-Home:

Wastewater rates are very high. Although positivity rates are relatively stable, a significant increase may occur within the next month.

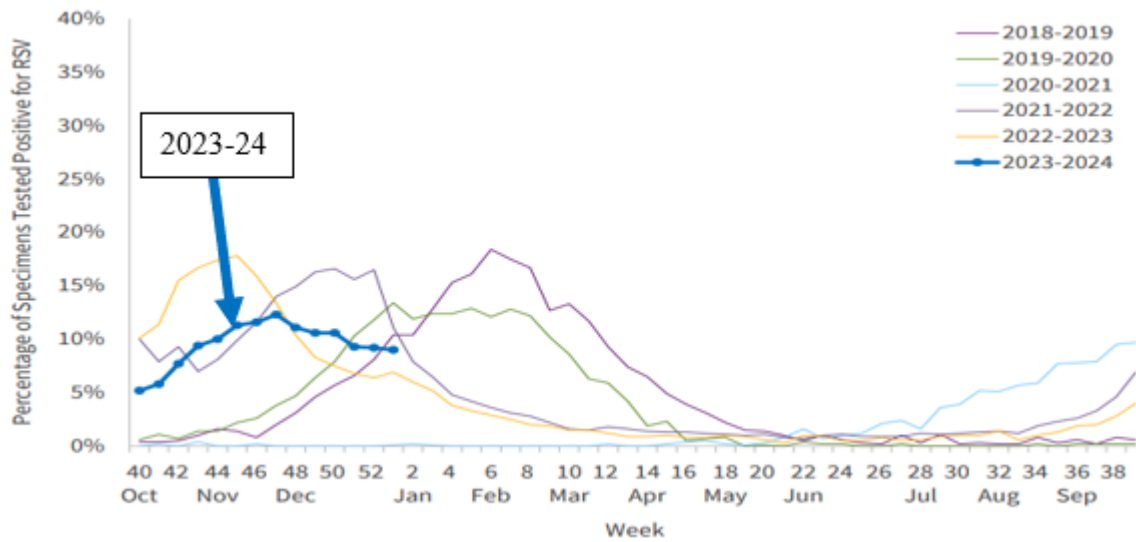
- SARS-CoV-2 positivity rates remain elevated in Europe, nationally and within Sutter.
- Persons 60 years and older, which comprise a very high-risk group, have a higher positivity rate than the composite of all ages

#### • Related Links

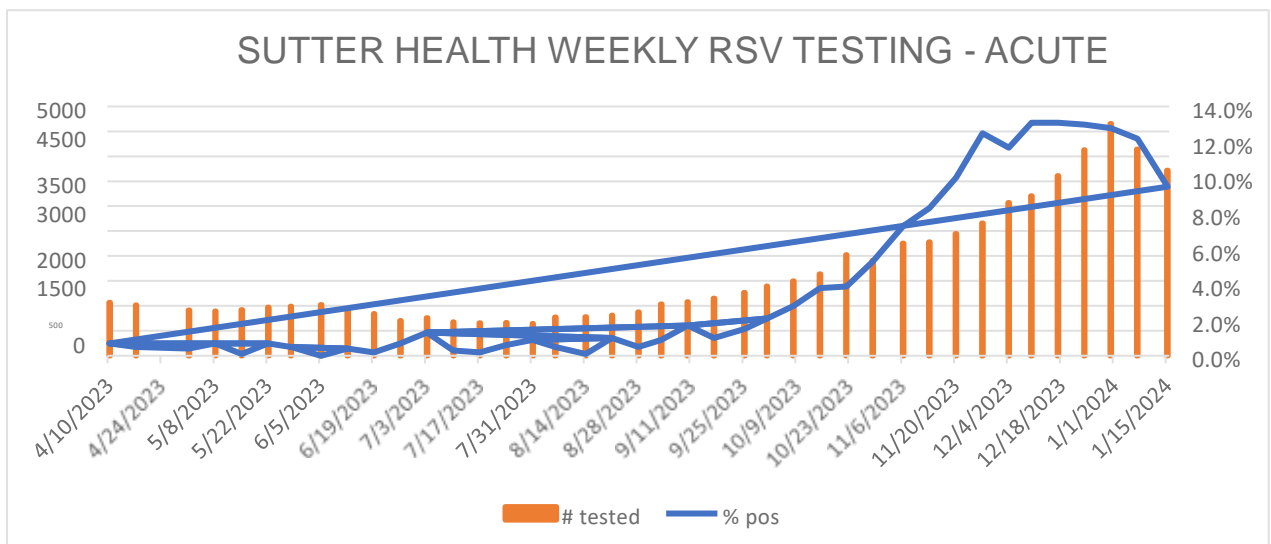
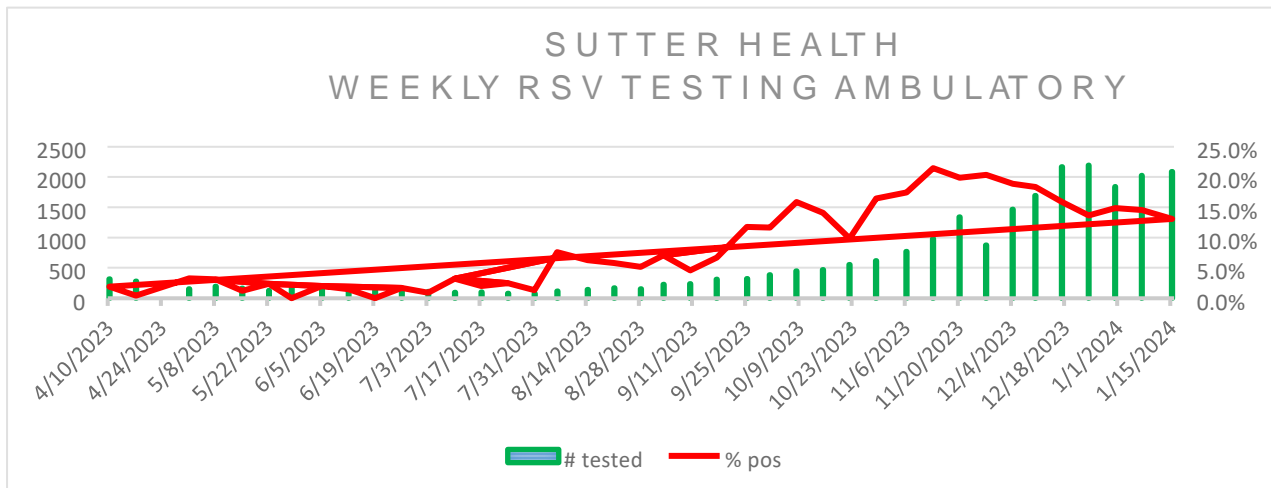
- [CDC Caring for Patients](#)
- [CDC Data Tracker](#)
- [CDC Latest Updates](#)
- [CDC Vaccine Information](#)
- [CDPH Tracking and Vaccination Updates](#)
- [Sutter Health for Clinicians](#)
- [Sutter Health for Patients](#)
- [WHO Table of Contents](#)

#### **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 are still elevated but they are slowly continuing to decrease.



- RSV identification rates remain elevated in both the ambulatory (13.1%) and emergency departments (9.5%) in Sutter but are clearly decreasing. 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 Jan. 15. Children less than 6 years old still dominate but positivity rates are continuing to decrease.
- Our Sutter data show that most diagnosed infections this season continue to be in children less than 6 years old.
- Positivity rates in children 6 to <12 years old are also elevated.
- The number of people > 60 years being diagnosed with RSV, although elevated, are reasonably stable.

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>Acute (ED)</b>	634	27.6% (175)	128	10.2% (13)	1,938	5.7% (110)
<b>Ambulatory</b>	449	26.1% (117)	183	10.4% (19)	442	11.5% (51)

### Nirsevimab Supplies Resume

Sanofi released a [statement](#) on the supply issues since approval and launch of nirsevimab. In summary:

- Sanofi miscalculated how rapidly the uptake of nirsevimab would be at launch and this product has a long lead time from request to production.
- The wide ACIP (Advisory Committee on Immunization Practices) recommendations included most newborns born during ‘RSV season’ plus all infants entering their first RSV season.
- Vaccines for Children and several other payors announced covering nirsevimab to avoid delay in administration.
- Approximately 230,000 additional doses of both 50mg and 100mg doses will be released for the U.S. in January.
- The CDC released an updated [guidance](#) in December as nirsevimab production and supplies improve.

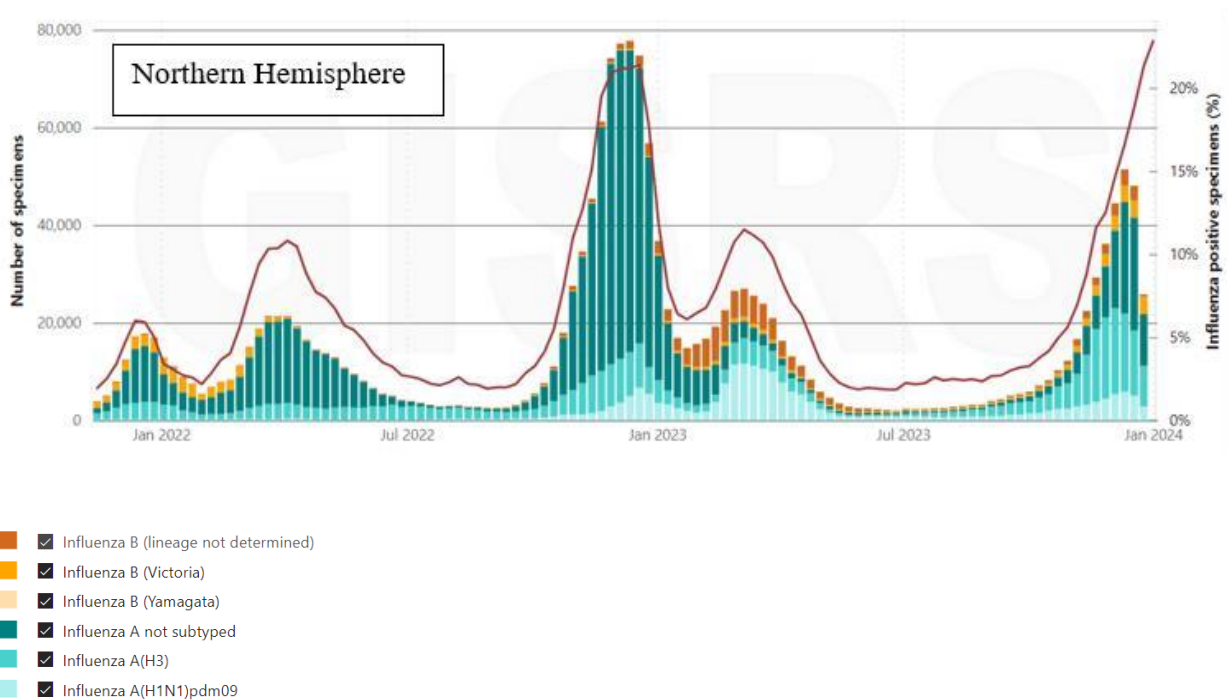
### RSV Take-Home:

- The RSV season appears to be on the decline in California but rates still remain elevated.
- Within Sutter, high positivity rates continue at all ages with children < 6 years old still dominating.
- Check nirsevimab inventory as supplies may still vary. Immunize eligible newborns and infants.
- If supply is limited, prioritize immunizing the youngest infants first.

### Influenza

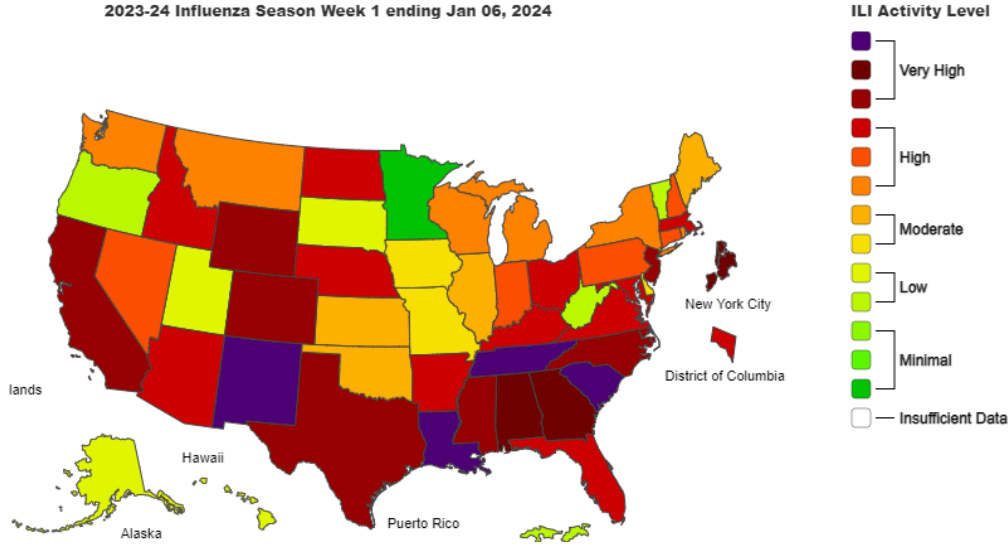
- The [WHO](#) released its biweekly global influenza update on Jan. 9. This includes the most recent two weeks of data, but it is only up to Dec. 24.

- Influenza detections are increasing in Europe, North America, and Central Asia. Europe, similar to the United States, is seeing predominantly A H1N1 in primary care surveillance. Europe crossed the 10% epidemic threshold during the week ending Dec. 17.
- The Southern Hemisphere continues with inter-seasonal, low levels of detection.
- From Dec. 11 to Dec. 24, 585,784 specimens were tested with 100,109 positives. Compared to the prior 2-week report, this represents a 40% increase in the number of positive specimens and the positivity rate increased from 14% to 17%.
- 87% were influenza A. Contrary to the United States, A H3N2 remains three times as common as H1N1 worldwide.
- The [WHO graph](#) below shows influenza activity in the Northern Hemisphere. Positivity rates and number of specimens should be ignored for the last reported week on the graph as it is likely incomplete data.



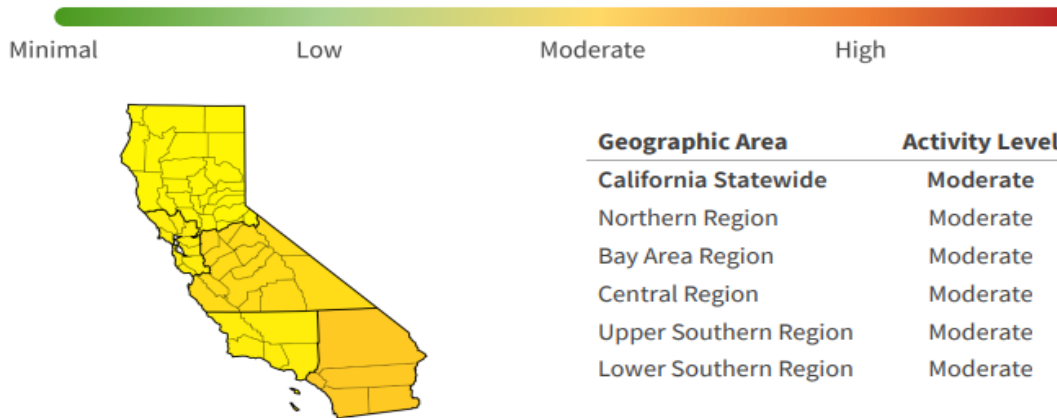
- Influenza rates were higher in [Europe](#) than RSV or SARS-CoV-2 during the first week of January. It is predominantly A H1N1, similar to the United States.
- The weekly [CDC](#) Influenza Surveillance Report was released on Jan. 12.
- For the first time in several weeks, seasonal activity has decreased slightly in terms of hospitalizations and outpatient respiratory illness.
- The first week of 2024, 18,526 patients were admitted to hospitals with influenza (down from 20,066 the prior week).
- Positivity rates decreased to 14.0% from 17.5%.
- Although influenza A continues to dominate throughout the United States, influenza B identifications are increasing. Rates vary by state and region.
- Influenza-like illness (ILI), the surrogate for influenza used by the [CDC](#), is on the map below showing data in the week ending Jan. 6. Large swaths of the country have high to very high levels of ILI.

2023-24 Influenza Season Week 1 ending Jan 06, 2024



- CDC testing for hemagglutination or neutralization titers continue to show a good vaccine match to circulating strains.
- The [CDPH](#) map below of influenza (last updated through Jan. 6), shows that influenza rates are still elevated but are decreasing throughout California. The state influenza positivity rate in the report released Jan.12 was down to 13.0% from 16.8% the week before.

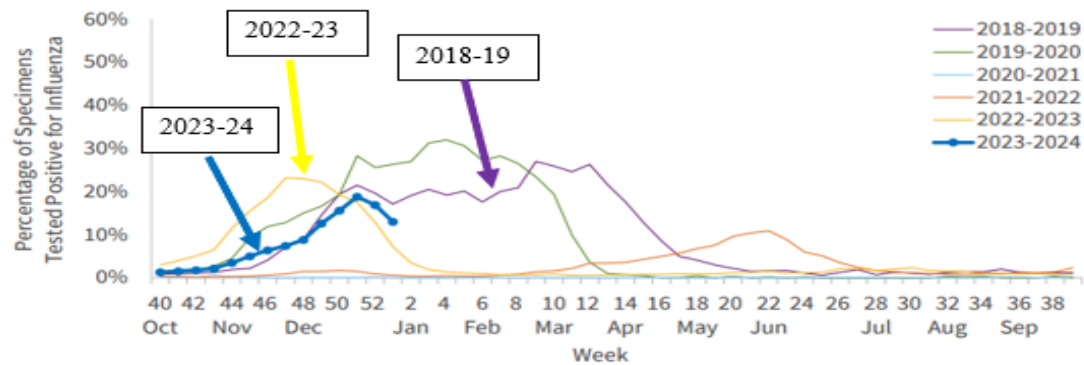
### Influenza Activity Levels\*



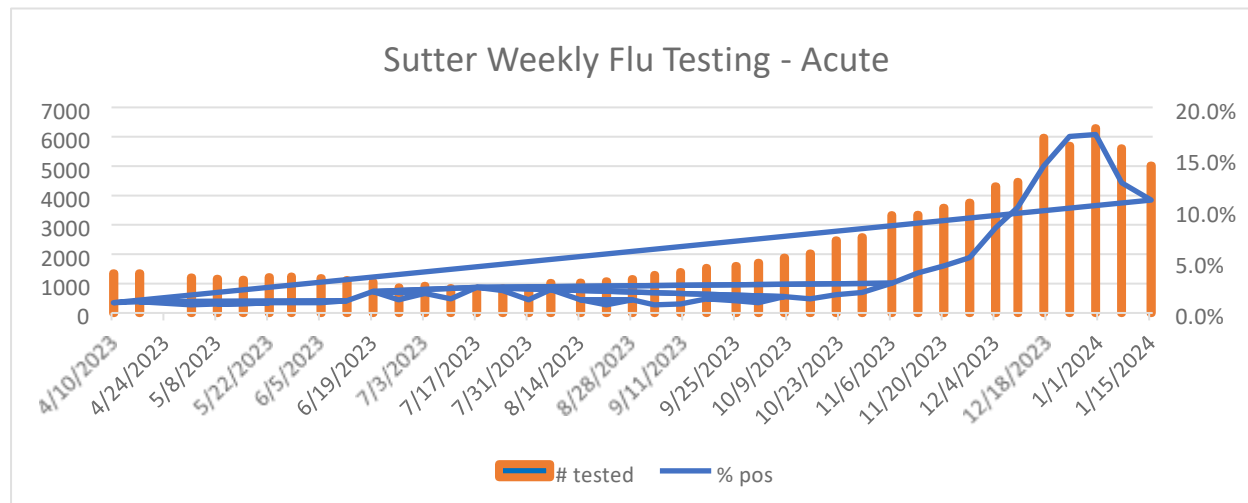
### CDPH Influenza Activity Levels\*

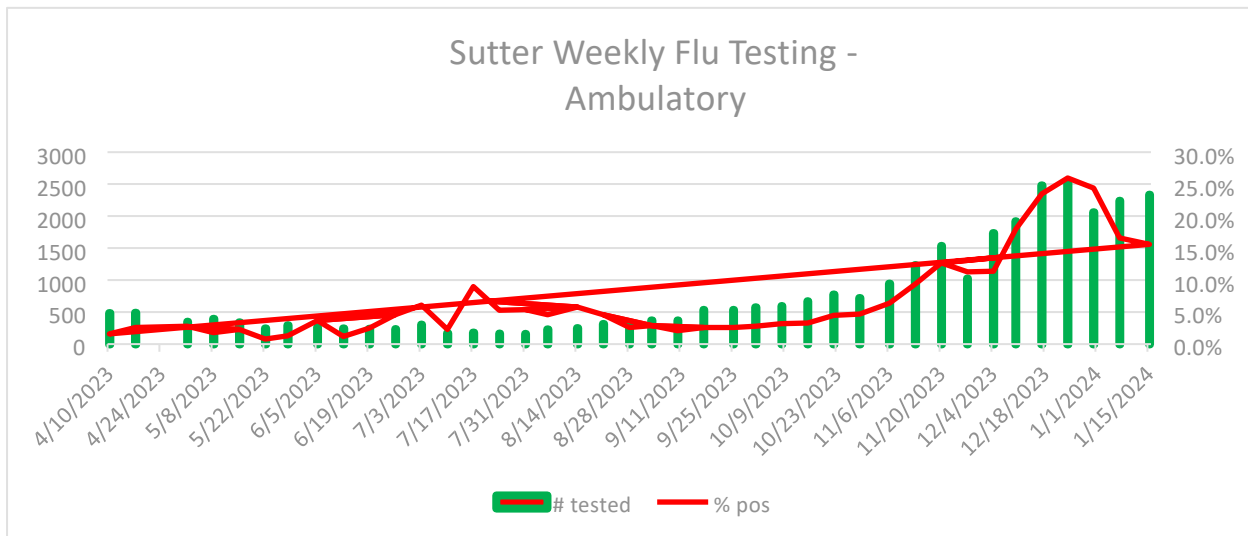
- **Minimal:** The percentage of specimens positive for influenza is <2%.
  - **Low:** The percentage of specimens positive for influenza is between 2% and <10%.
  - **Moderate:** The percentage of specimens positive for influenza is between 10% and <20%.
  - **High:** The percentage of specimens positive for influenza is between 20% and <40%.
  - **Very High:** The percentage of specimens positive for influenza is ≥40%.
- The [CDPH graph](#) below demonstrates that our present influenza season (blue arrow) continues to be similar to the pre-COVID 2018-19 season (purple arrow).
  - Based on our last season (yellow arrow), we could be seeing an early end to the flu season. However, the WHO report above showed that the number of positive tests increased by 40% in the most recent 2 weeks and rates are rising in Europe.

- In addition, influenza B is starting to be identified more frequently in the Southern part of the United States as a second wave. Adding this information to the graph below (showing similarities between our present season and the 2018-19 season) suggests that rates will continue to be elevated for at least another month.

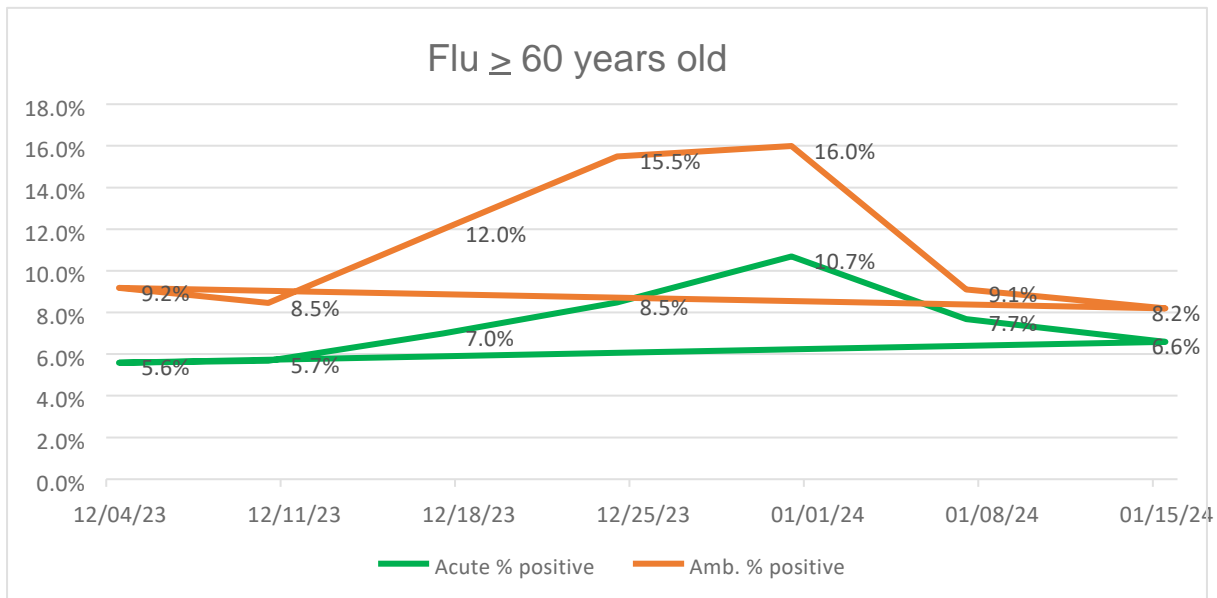


- The graph below shows Sutter emergency department and ambulatory influenza positivity rates. In the acute setting (emergency departments), positivity rates decreased to 12.7% in the last week. In the ambulatory setting, the rate is 16.6%. These are similar to state rates.





- The positivity rate in persons  $\geq 60$  years old is shown on the following graph.



**Take-Home Influenza:**

- Influenza remains well above the 10% epidemic threshold in North America and Europe.
- Influenza is widespread in the United States. Most cases are due to influenza A. Influenza B varies by region and state.
- Although the current influenza season in California appears to be a mirror of the 2018-19 season, patterns could be diverging and the season could end early.
- ILI levels are very high in multiple states.
- During the week ending Jan. 14, Sutter emergency department positivity rates were down to 11% and ambulatory rates 15.6%.
- Influenza rates in persons  $\geq 60$  years old have also been declining. Rates among this high-risk group are lower than the all-ages cohort, possibly because of higher vaccine uptake in the older population.
- The flu vaccine appears to be a good match against circulating strains.

**Other Respiratory Viruses**

- [CDPH](#) tracks respiratory viruses beyond SARS-CoV-2, flu and RSV. They started reporting again in October. SARS-CoV-2 (yellow arrow), included in the graph below, is the only virus that is increasing.
- Enterovirus/Rhinovirus (green arrow) remains the one most commonly identified as a percentage of positive tests but positivity rates between SARS-CoV-2 and rhinoviruses are converging. SARS-CoV-2 is anticipated to be the dominant virus on this graph.

