



Emerging Infections Newsletter for Clinicians

Jan.10, 2024

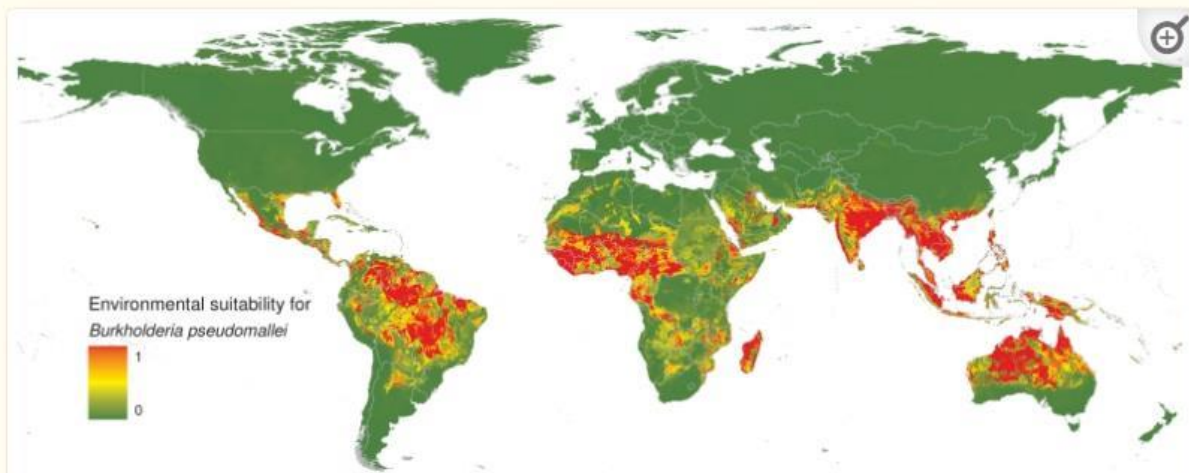
Written by Dr. Silvers with contributions from Dr. Joan Etzell , Lisa Rieg and Gordon Sproul .Please use Google Chrome for the best experience.

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Melioidosis

- Melioidosis is considered an important emerging infectious disease with newly demonstrated endemicity in the United States.
- It is an opportunistic infection caused by an environmental pathogen, *Burkholderia pseudomallei*. Commonly found in soil in tropical and semi-tropical environments, the highest number of reported cases are from Southeast Asia and Northern Australia.
- Because of the diverse variety of presentations, diagnosis can be difficult. *B. pseudomallei* is frequently resistant to multiple antimicrobials. Mortality in poorly resourced locations is estimated to be up to 70%, but still is 10-20% in well-developed, healthcare environments.
- Transmission is predominantly from skin inoculation, but inhalation and ingestion of contaminated water are additional important routes of infection. Introduction into the environment from infected, imported animals is considered an ongoing risk.
- Incubation period is typically about 1 week, ranging from 1 to 21 days. Presentation varies, but acutely presents as sepsis with fever, bacteremia, pneumonia and/or localized organ abscesses.
- A rash often presents as a nodule that progresses to an ulcer or abscess. About 10% of patients present with signs and symptoms of chronic disease that suggest tuberculosis, including weight loss, fever, cough, hemoptysis, and cavitary lung infiltrates.
- Most patients have underlying health issues, notably diabetes or alcohol abuse.
- [Nature Microbiology](#) in 2016 published an article on the predicted global distribution of *B. pseudomallei* and the global burden of melioidosis.
- They estimated 165,000 global cases annually. Below is a map, based on a worldwide database and statistical modeling, showing where the environment is predicted to be suitable for persistent colonization by *B. pseudomallei*.
- Many of those places already have regular transmission of disease. Note that in the United States it is predominantly Southeastern states.



[Figure 2](#)

Predicted environmental suitability for *B. pseudomallei* persistence at 5 km × 5 km spatial resolution

Areas of high environmental suitability are shown in red and areas of low suitability in green.

- In 2021, the [CDC](#) released a health advisory of non-travel associated *B. pseudomallei* infections in Kansas, Texas, and Minnesota. The organisms all appeared to be from the same strain, suggesting a common unidentified exposure.

- In 2021, the [CDC](#) reported an aromatherapy spray, contaminated with *B. pseudomallei*, linked to four patients with Melioidosis in different states. Two persons died.
- [NEJM](#), Dec. 31, 2023, reported three cases of locally acquired melioidosis in Mississippi between 2020-2023. These three patients presented over a 30-month interval.
- The organisms from the three patients plus three positive environmental samples all matched on multilocus sequencing but did not match any other previously identified strains. This all supports endemicity with a new strain in this part of Mississippi.
- A prospective [study](#) looked at the risk of disease acquisition after a muddy endurance challenge during the wet season in an endemic area of Australia. Only one person out of the 113 study participants developed cutaneous melioidosis.
- This was much lower than the infection rate from *Aeromonas* exposure at the Tough Mudder race in [Sonoma County](#) in August 2023 where approximately [300 people](#) were believed to have developed infection.

Melioidosis Take-home:

Melioidosis is caused by *B. pseudomallei*, an opportunistic, environmental pathogen. It is associated with significant morbidity and mortality. Intermittent cases have been identified in different states in the last few years, without an identifiable source. The recent [NEJM](#) article demonstrates that it is now endemic in Mississippi.

- As an opportunistic organism, disease is uncommon in healthy people. This was shown by the <1% incidence in a muddy endurance challenge in an endemic area in Australia. Participants in a similar type of muddy water challenge in Sonoma in 2023, demonstrated that *Aeromonas* is much more contagious than *B. pseudomallei*.
- The risk of acquiring disease in the United States remains exceptionally low but should be considered in select patients with sepsis and organ abscesses, gram-negative pneumonia with bacteremia or a clinical picture of tuberculosis with negative PCR and smears.

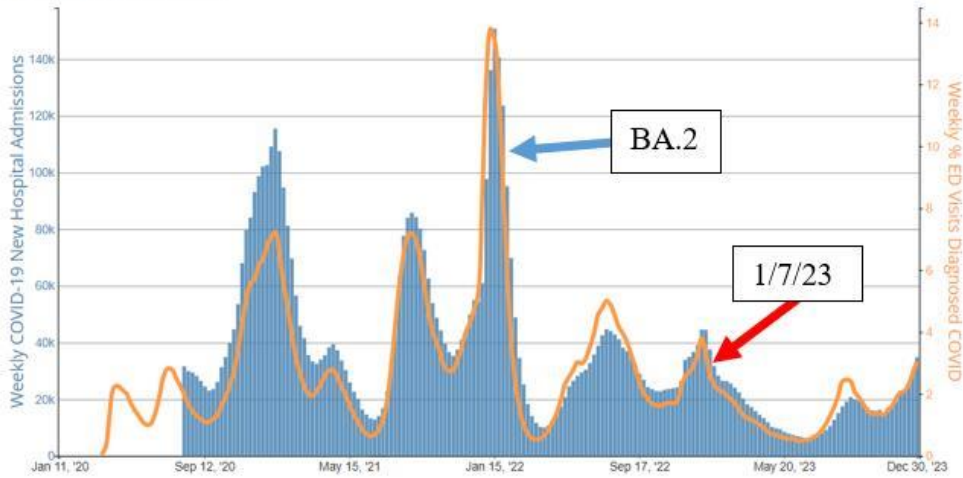
The Tripledemic

- The last week of 2023, 20,066 patients were admitted to hospitals with influenza. That same week, the CDC reported that 34,800 patients were admitted with COVID. This amounts to almost 55,000 patients admitted to hospitals in one week with one of these two infections.
- JN.1 continues its surge to totally dominate.
- RSV is slowly declining but still widely circulates.

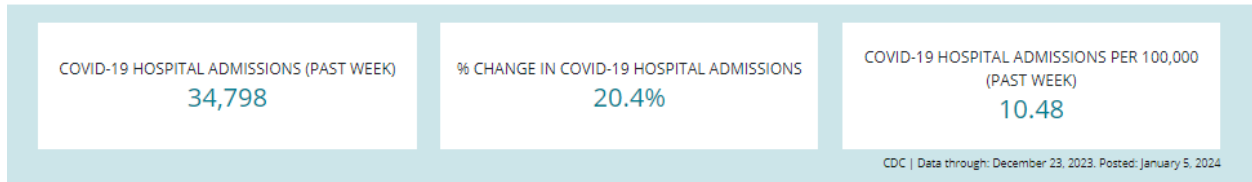
COVID-19

- [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 being diagnosed with COVID in emergency departments (orange run line).
- They are now at the highest level since Jan. 7, 2023 (red arrow). At that time, rates were on a decline, whereas they are increasing now.
- 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

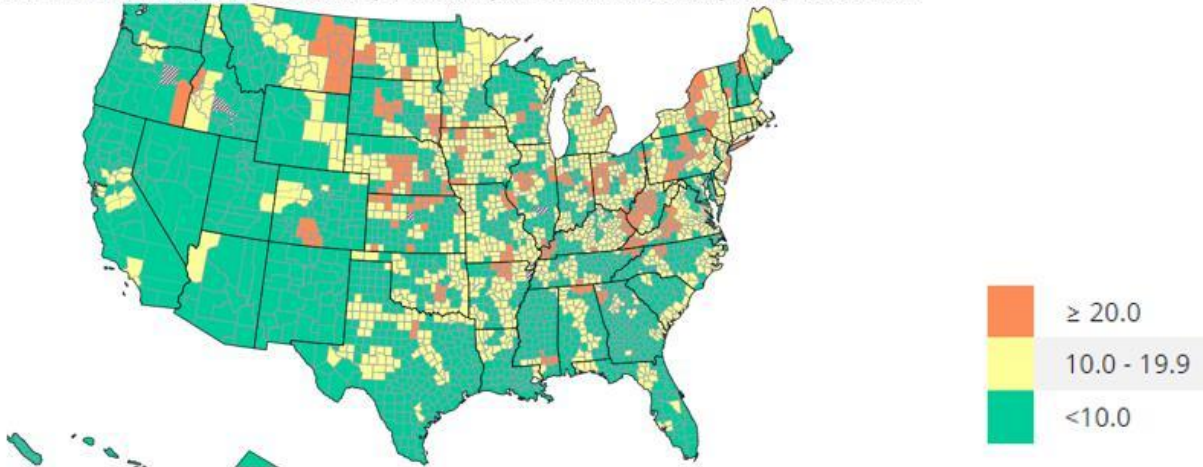


- The CDC tracks hospital admissions per 100,000 county population. Less than 10/100,000 is considered a low number of new hospital admissions. National rates have been progressively increasing. They are now moderate at 10.48/100,000. Hospitalizations during the last week increased by over 20%.



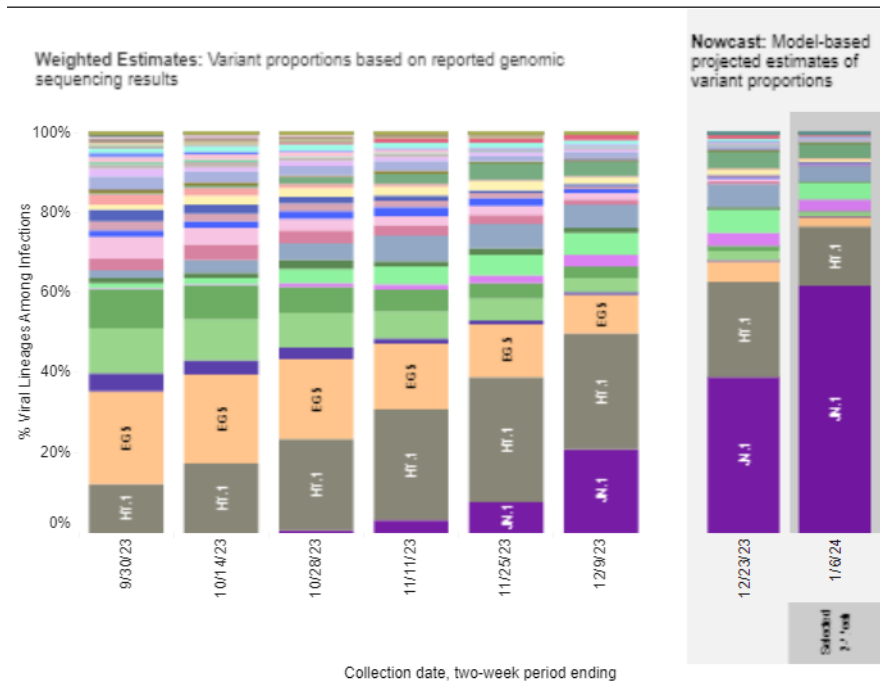
- The map below shows how the hospitalization rates vary by county. Much of the eastern half of the country is yellow or red and most of the western half is still green with some yellow.

Reported COVID-19 New Hospital Admissions Rate per 100,000 Population in the Past Week, by County - United States

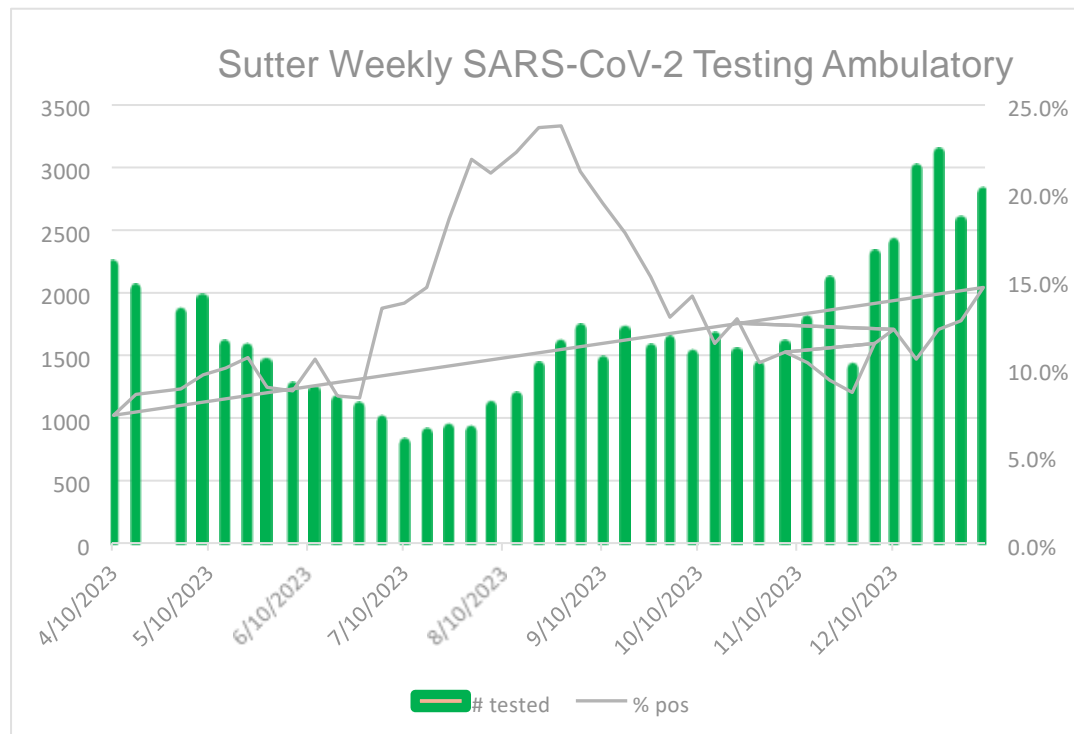


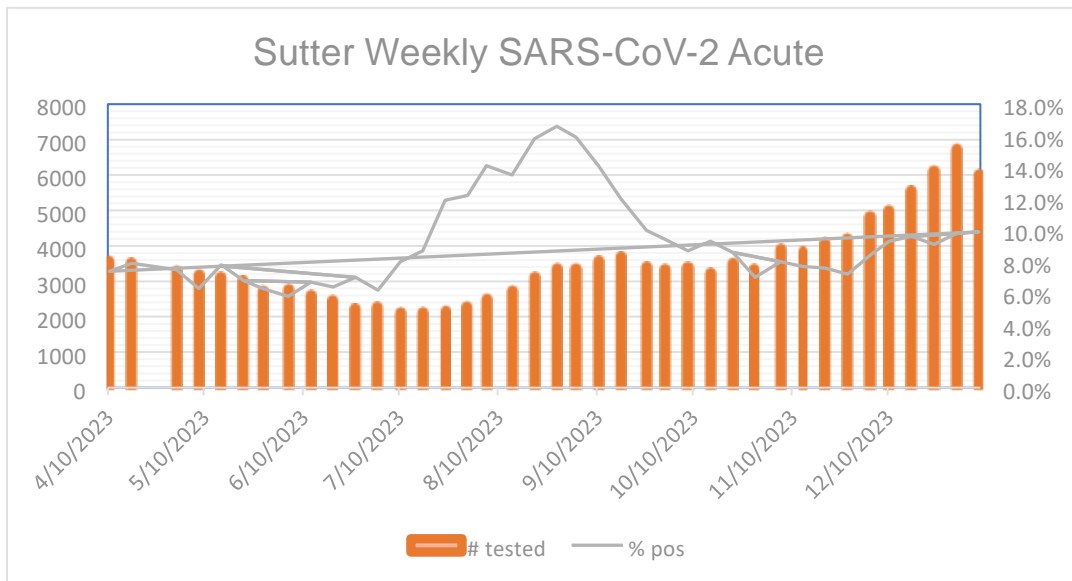
- [National genomic sequencing](#) is updated by the CDC every 2 weeks (graph below). The most recent report includes estimates from Dec. 24, 2023 to Jan. 6, 2024. JN.1 has clearly established itself as the dominant variant at 61.6% of sequenced isolates (purple bar) in the United States. JN.1 has only 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 14.8% of isolates.



- Updated Sutter testing data below show elevated positivity rates in combination with high levels of testing. Positivity rates continue to increase in the ambulatory environment but are stable in the emergency departments (acute).





- COVID test positivity rates in persons greater than 60 years old are being 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.

COVID Location	≥ 60 years old		Composite Positivity Rates for All Ages
	Number Tested	% Positive (number)	
Ambulatory	660	18.3% (104)	14.6%
Acute (ED)	2,325	12.1% (281)	9.9%

Treatment Pipeline

Monoclonal antibodies for early treatment, and pre-exposure prophylaxis of immunocompromised persons against COVID remain a challenge.

- Several products had been introduced and ultimately removed because SARS-CoV-2 mutations rendered them inactive. Immunocompromised persons remain a very high-risk population since immune responses to the disease and vaccines are usually dampened.
- Adintrevimab was being investigated for treatment, but the agent had reduced efficacy against Omicron and studies were terminated early. [Open Forum Infectious Diseases](#), May 2023, published the results obtained prior to study closure. Adintrevimab was efficacious against susceptible variants, well tolerated and did not demonstrate any safety concerns.
- VYD222 was [engineered](#) from Adintrevimab into a long-acting monoclonal antibody. It has demonstrated potency against multiple, currently circulating variants including the rapidly spreading JN.1 as well as XBB.1.5, BA.2.86, EG.5, and HV.1.
- A phase 3, multi-site, United States, clinical trial ([CANOPY](#)) enrolled approximately 750 participants, including 300 immunocompromised adults and adolescents. Sustained in-vitro neutralization activity against circulating strains at day 28 (the measured endpoint) is anticipated to translate into prevention or at least lessening of the severity of disease.

- Early clinical data supports that belief, but more time is needed before making any conclusions.
- A request for an EUA was submitted to the [FDA](#) on Jan. 3, 2024. If approved, this would be the second product ever approved for pre-exposure prophylaxis against COVID in immunocompromised adults and adolescents. The first product, Evusheld, was EUA approved December 2021, but was removed from the market January 2023 due to loss of efficacy against circulating variants.
- VYD222, like previous anti-SARS-CoV-2 monoclonal antibodies, acts on the receptor binding domain of the spike protein. Eventually, resistance should be expected to develop.

COVID-19 Take-Home:

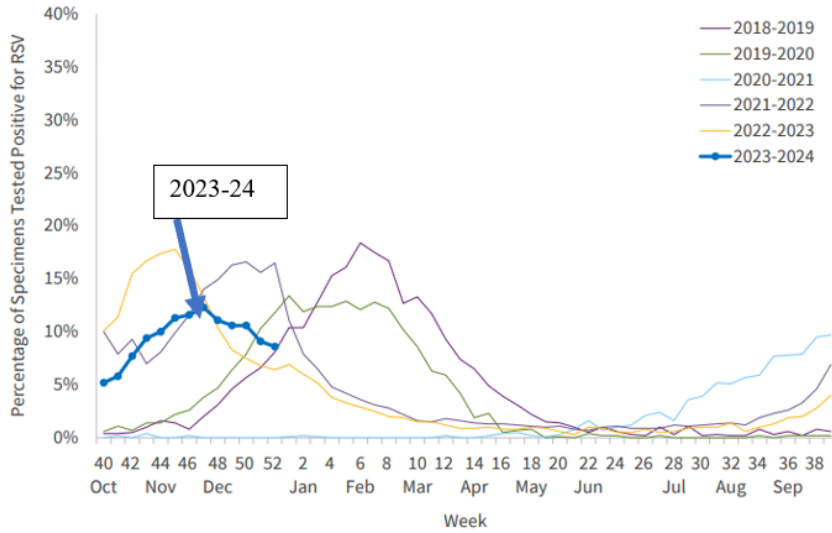
JN.1 is now being found in over 60% of sequenced isolates in the United States. Looking at historical data, this trend of progressive dominance may be expected to continue for at least another 4-6 weeks.

- National hospitalizations and emergency department visits are now at the highest levels since Jan. 7, 2023. The map shown above displays the rate variance in different parts of the country.
- SARS-CoV-2 positivity rates remain elevated 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.
- A new extended-duration, monoclonal antibody for prevention of COVID in immunocompromised persons may soon receive emergency use authorization. A new product to fill this category is critically needed.
- **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](#)

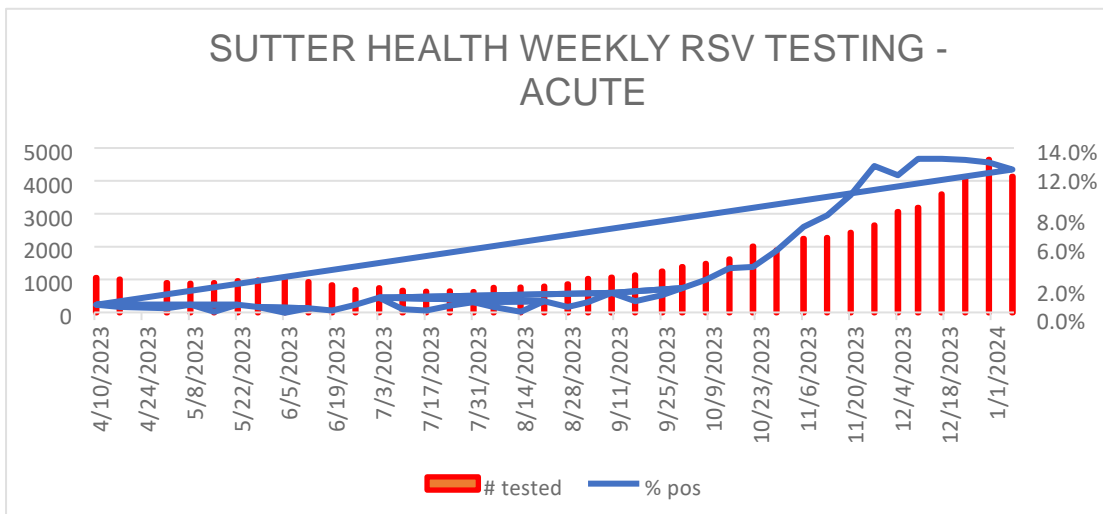
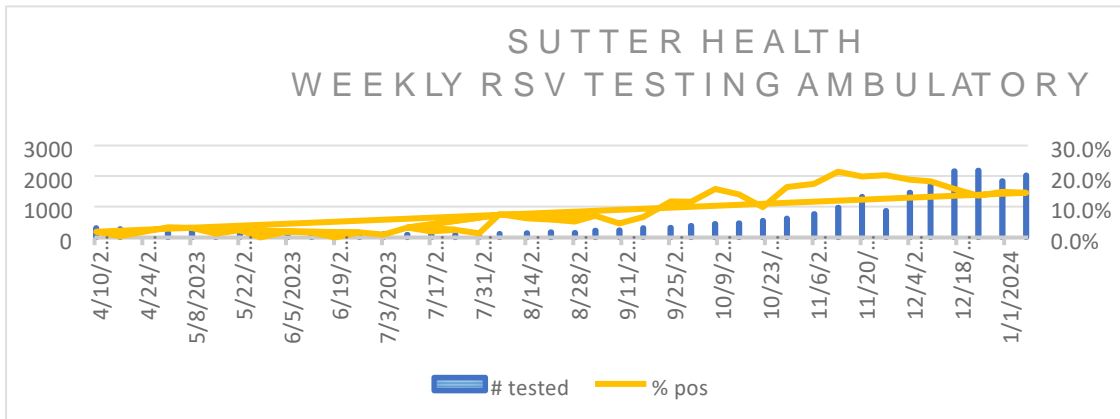
RSV

- [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 continuing to decrease.

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



- RSV identification rates remain elevated in both the ambulatory (14.6%) and emergency departments (12.2%) 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 Jan. 7. 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. Testing numbers have decreased, which is appropriate since they are typically a low-risk group.
- The number of people ≥ 60 years being diagnosed with RSV is in the table below. Positivity rates, 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)
Acute (ED)	790	33.2% (262)	134	14.2% (19)	2123	6.6% (140)
Ambulatory	422	29.1% (123)	128	11.7% (15)	516	12.8% (66)

RSV Vaccine

In mid-December, the [NEJM](#) published positive, ongoing, Phase 2-3 clinical trial results for the first mRNA-based RSV vaccine (mRNA-1345) currently seeking FDA approval in adults 60 years of age and older.

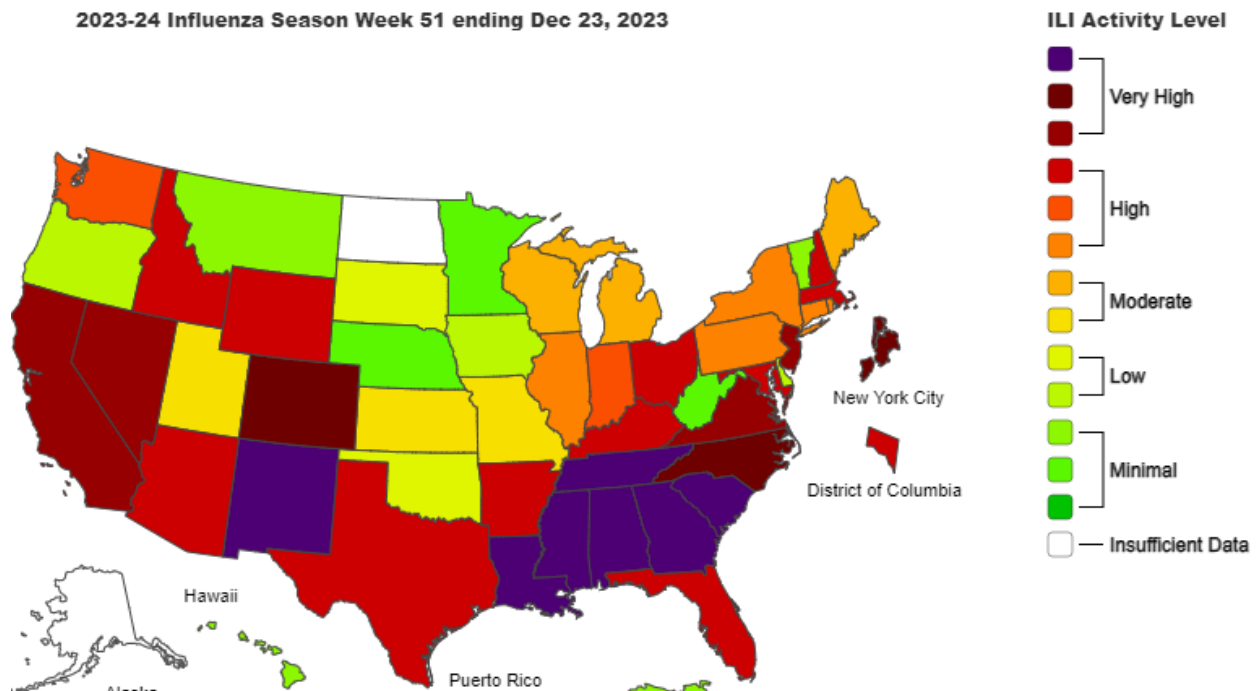
- Among 35,541 adult participants randomized 1:1 to receive mRNA-1345 versus placebo:
 - Vaccine efficacy (VE) against diagnosis confirmed, RSV-associated lower respiratory tract disease (LRTD) was 83.7% (95.9% CI, 66.0 to 92.2) with ≥ 2 signs or symptoms and 82.4% (96.36% CI, 34.8 to 95.3) with ≥ 3 signs or symptoms after 112 days. Signs and symptoms included tachypnea, shortness of breath, sputum production, pleuritic chest pain, wheezing, fever, and cough.
 - VE was lower but still encouraging against mild RSV-associated acute respiratory disease 68.4% (95% CI, 50.9 to 79.7).
 - mRNA-1345 showed higher solicited local (58.7% vs. 16.2%) and systemic (47.7% vs. 32.9%) adverse events (AE) than placebo, with most reactions mild to moderate in severity.
- mRNA-1345 encodes for the stabilized RSV prefusion F glycoprotein that is highly conserved across RSV A and B subtypes, making it a strong target for neutralizing antibody response.
- The F glycoprotein target for the vaccine is equivalent to the already approved protein-based RSV vaccines on market.
- Availability of the mRNA RSV vaccine in the U.S. is anticipated by the summer of 2024, pending FDA approval and CDC recommendations for use.

RSV Take-Home:

- The RSV season appears to be on the decline in California. Rates still remain elevated.
- Within Sutter, high positivity rates continue at all ages with children < 6 years old still dominating.
- A new mRNA-based RSV vaccine candidate for older adults, mRNA-1345, reduced incidence of RSV associated lower respiratory tract disease compared to placebo and is currently pending FDA approval. Increased solicited AE from the mRNA vaccine are anticipated.

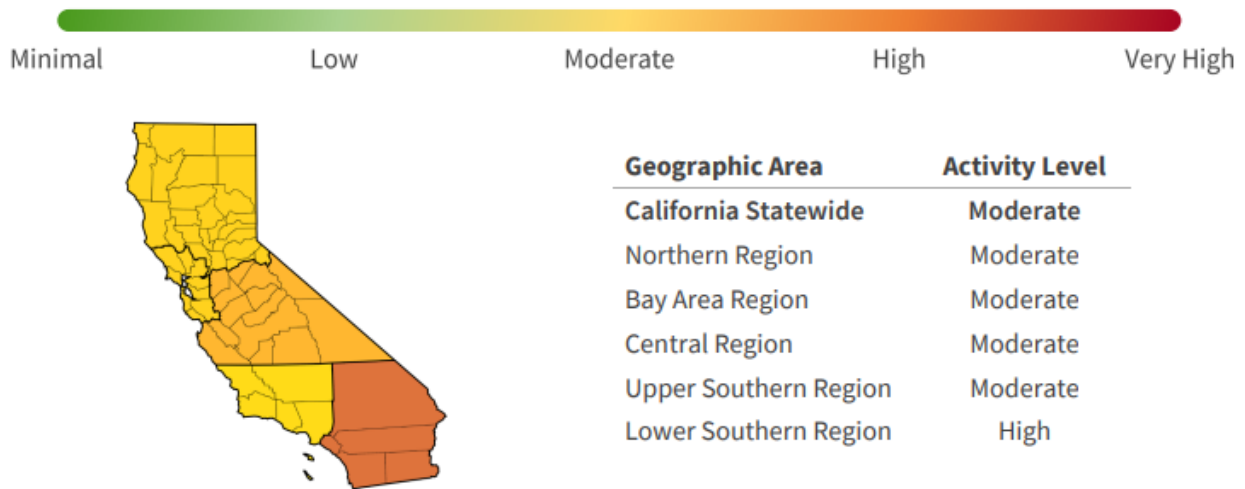
Influenza

- The weekly [CDC](#) Influenza Surveillance Report was released on Jan. 5.
- Influenza-associated hospitalizations continue to increase. The last week of 2023, 20,066 patients were admitted to hospitals with influenza.
- Out of 102,294 specimens tested by clinical labs during week 52, 17,925 were positive (up to 17.5% from 16.1%).
- Influenza A continues to dominate throughout the United States. Influenza B varies 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 Dec. 23. Large swaths of the country have high to very high levels of ILI.



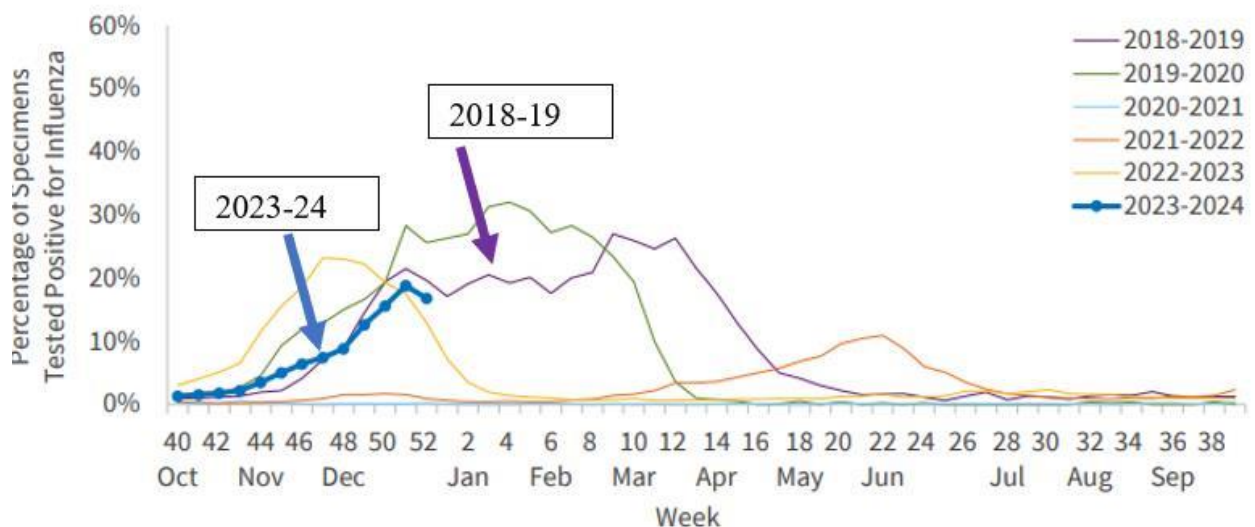
- The [CDPH](#) map below of influenza (last updated through Dec. 30), shows that influenza is increasing throughout California, with the southern part of the state having high levels (20-40% positivity rates). The state influenza positivity rate in the report released Jan. 5 was 16.8%.

Influenza Activity Levels[†]

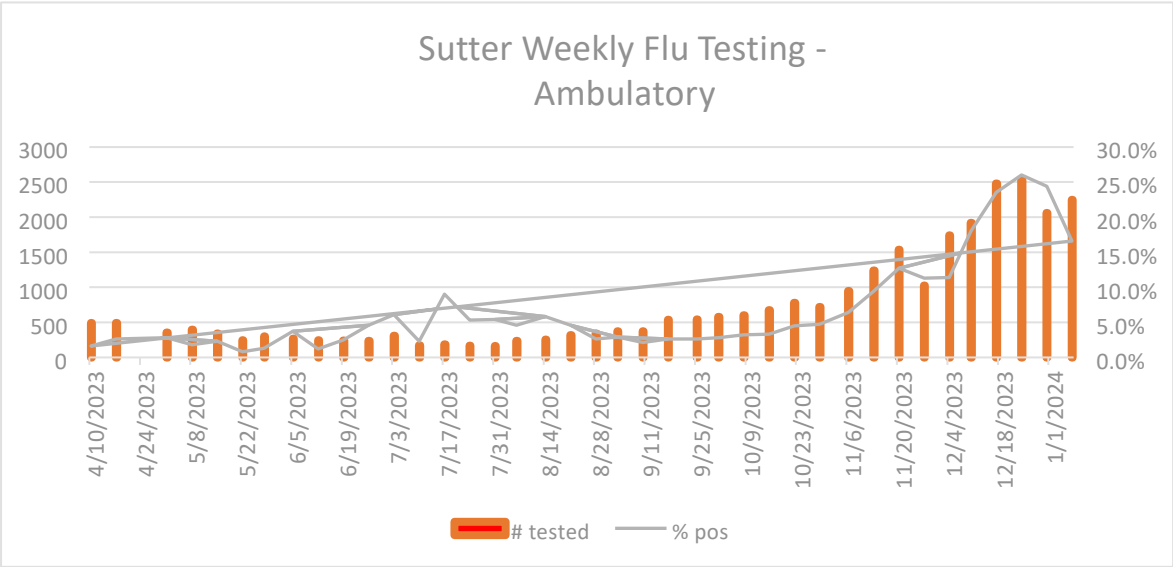
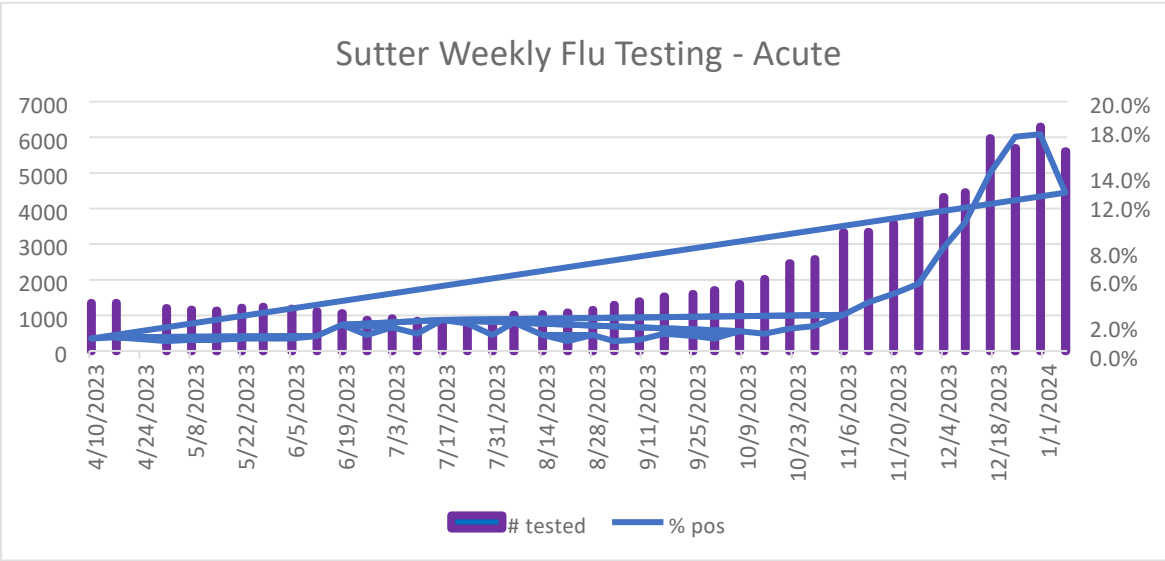


CDPH Influenza Activity Levels[†]

- **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 $\geq 40\%$.
- 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). Although the 2018-19 season extended until April, nothing suggests that pattern will be repeated.



- 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.



- Influenza positivity rates, similar to CDPH findings, have decreased in the last week. 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.

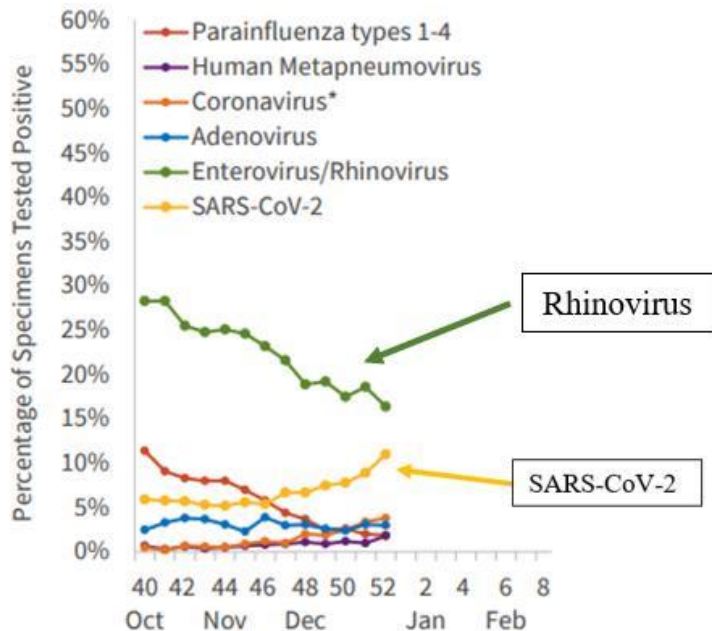
Influenza Location	≥ 60 years old		Composite Positivity Rates for All Ages
	Number Tested	% Positive (number)	
Ambulatory	525	9.1% (48)	16.6%
Acute (ED)	2169	7.7% (168)	12.7%

Take-Home Influenza:

- 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 may diverge as the season progresses.
- ILI levels are very high in multiple states.
- During the week ending Jan. 7, Sutter emergency department positivity rates were down to 12.7% and ambulatory rates have fallen to 16.6%.
- Although less flu is being 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. 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 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.
- 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 elevated.
- 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.