Emerging Infections Newsletter for Clinicians

Nov. 9, 2023

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Topics

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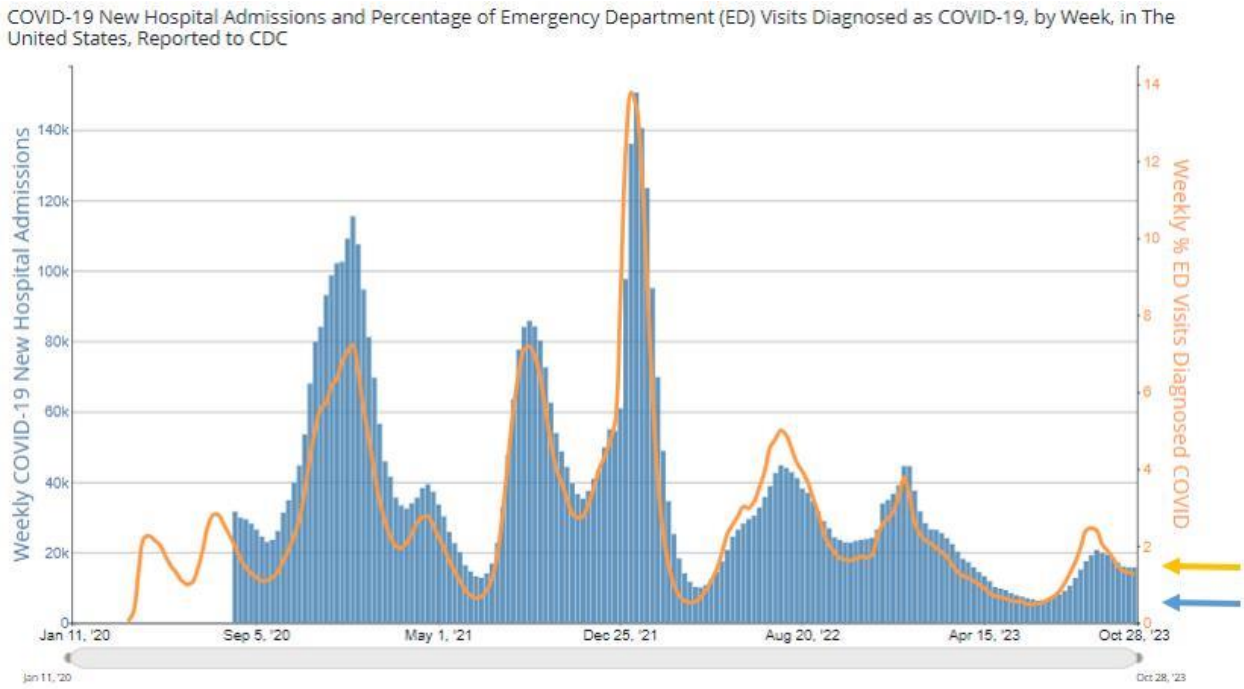
Tripledemic

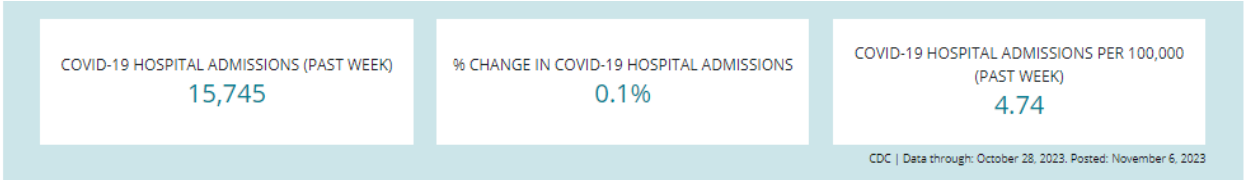
- This week's newsletter has some sobering information. Although COVID positivity rates have been gradually decreasing, they still remain about 10%.
- RSV has been brewing for a number of weeks, and it is now here with positivity rates over 30% in one segment of the population. Influenza continues to lurk in the background with low positivity rates, but data suggests that it may be increasing in the Southeast United States and we will likely follow.
- The twindemic is here and the tripledemic is not far away.
- The good news is that ongoing studies support that vaccine matches look good against circulating strains for all three viruses. Vaccines aren't perfect, but they do reduce severity of disease, and the risk of hospitalization or death.

COVID-19

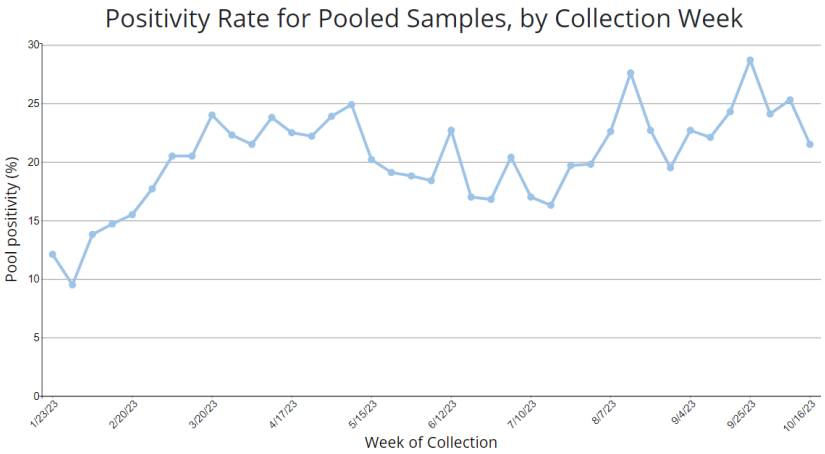
- Hospitalizations in the United States are a surrogate for the virulence of the circulating strain. The graph below and the subsequent table show:
  - Stable rates of hospitalizations (blue arrow and vertical bars) and percentage of patients being diagnosed with COVID in emergency departments (orange arrow and run line).



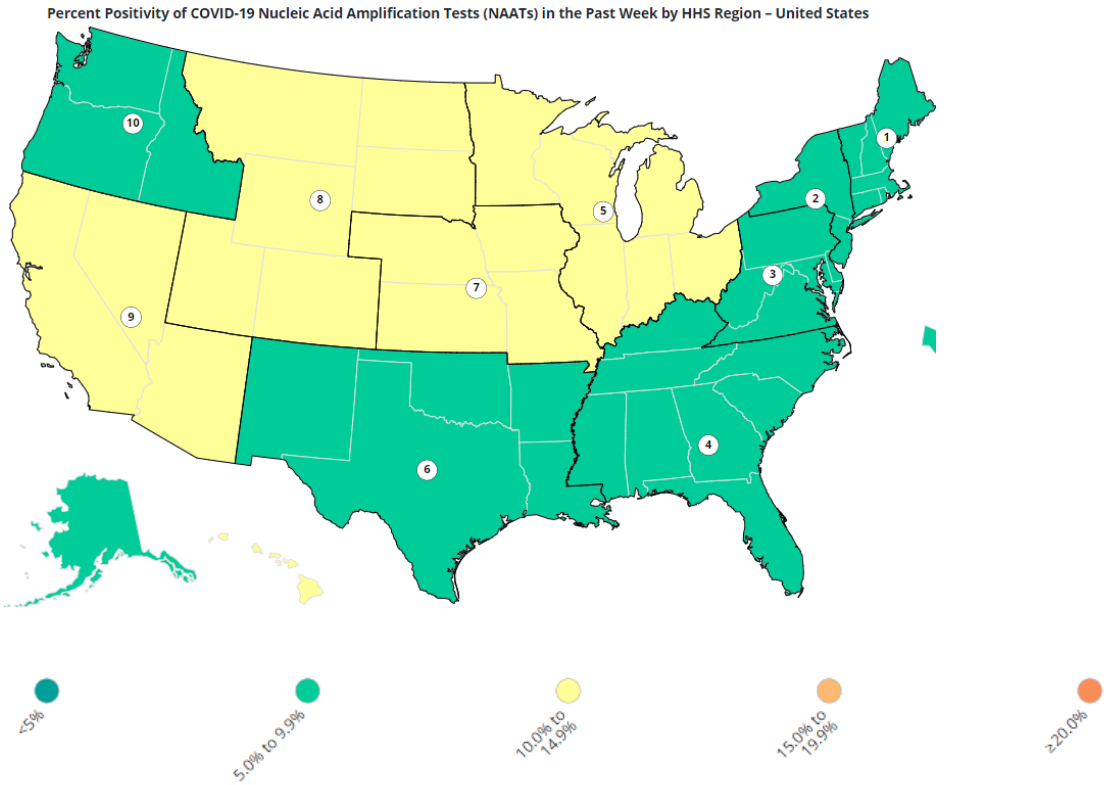
- The CDC tracks hospital admissions per 100,000 county population. Less than 10/100,000 is considered a low number of new hospital admissions. Nationally, rates remain below 5/100,000 and hospitalization rates are stable. The admissions percent change in the last week was only 0.1%.



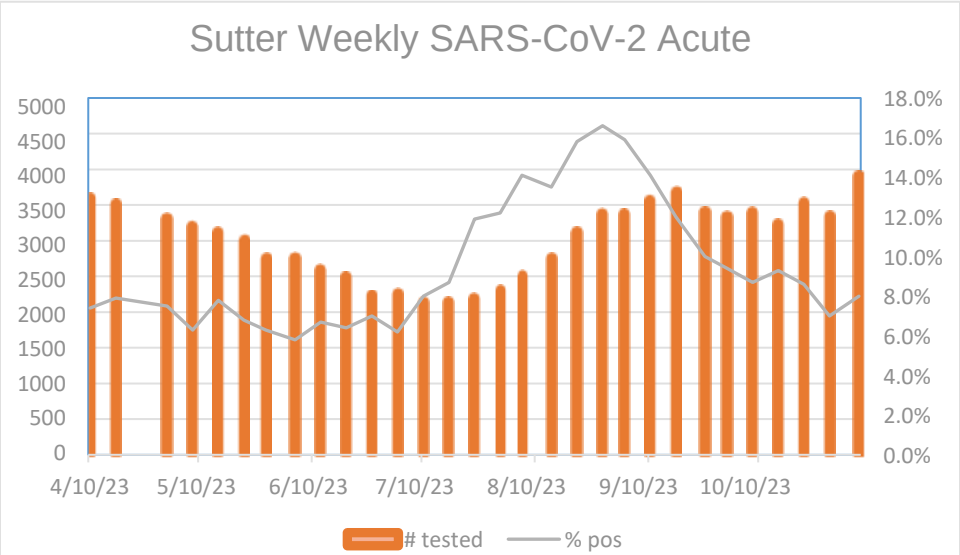
- Surveillance of international air travelers is conducted at several major U.S. airports as an early warning system and to fill gaps in worldwide genomic surveillance. It covers flights from more than 135 countries.
- The graph below shows a continued high positivity rate at over 20%. Data is delayed by 2 weeks for the positivity rates and four weeks for the sequencing of variants. Thirteen different variants were identified the week of Oct. 2. None are dominant
- The CDC announced on Nov. 6, that a several-month pilot is starting. Testing for flu, RSV, and other respiratory viruses will be included when sampling for SARS-CoV-2.

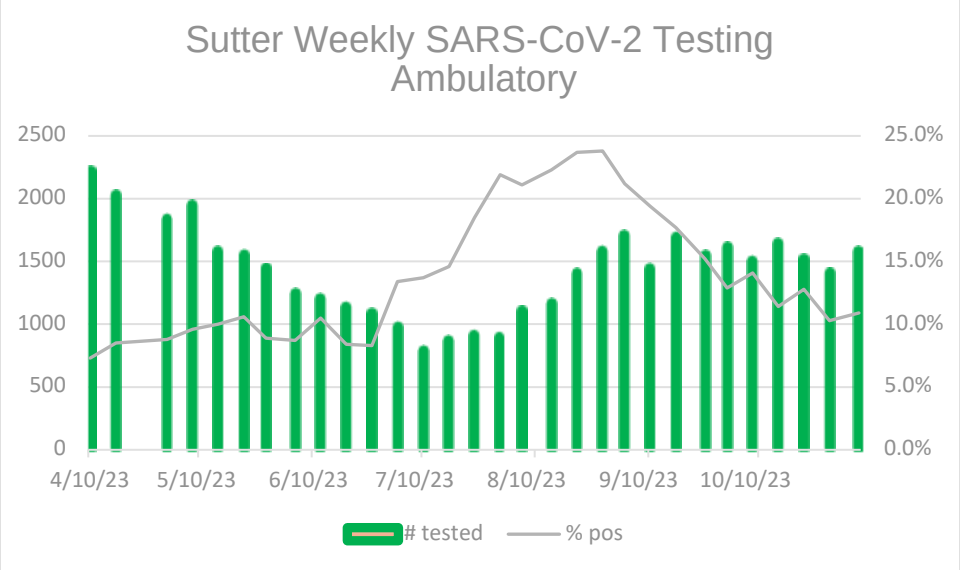


- National molecular test positivity rates by region are demonstrated on the map below. There are minor changes compared to last week. Rates remain moderate (yellow) to low (green) in the country. Yellow represents a 10-14.9% test positivity rate. Region 9, including California has an 11% positivity rate.



- Updated Sutter testing data below shows slowly decreasing positivity rates, well off of the peak reached over 2 months ago. Significant levels of testing are being performed in emergency departments and ambulatory environments.



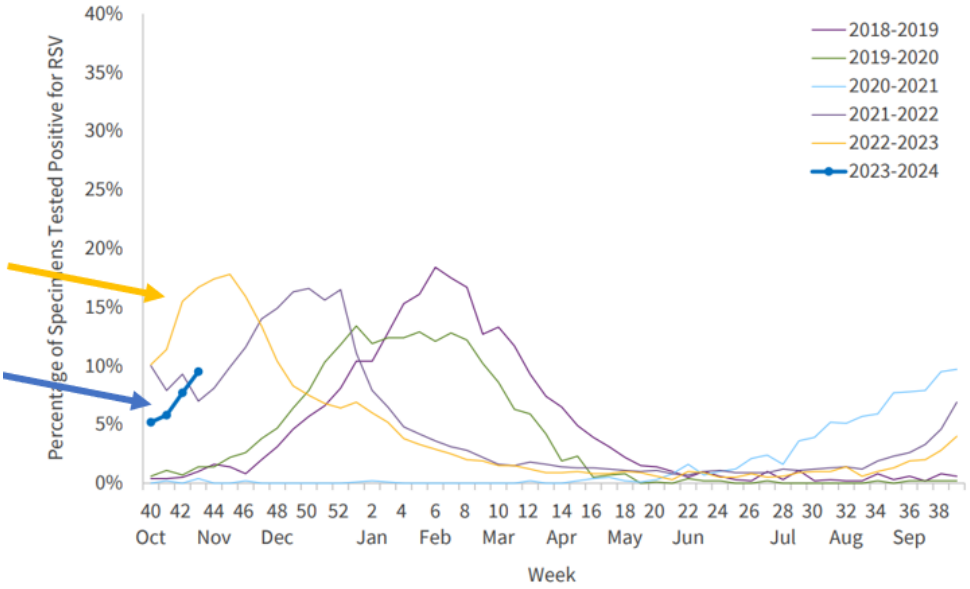


- **COVID-19 Take-Home:**
  - Hospitalizations, emergency department visits and Sutter Health testing positivity rates are all trending down.
  - Random testing of international passengers still shows a SARS-CoV-2 positivity rate of over 20%. Testing will be expanded soon to include influenza, RSV and other respiratory pathogens.
  - Although still not low, Sutter ambulatory and emergency department positivity rates are 10.9% and 8.0% respectively.
- **Related Links**
  - CDC Caring for Patients
  - CDC Data Tracker
  - CDC Latest Updates
  - CDC Vaccine Information

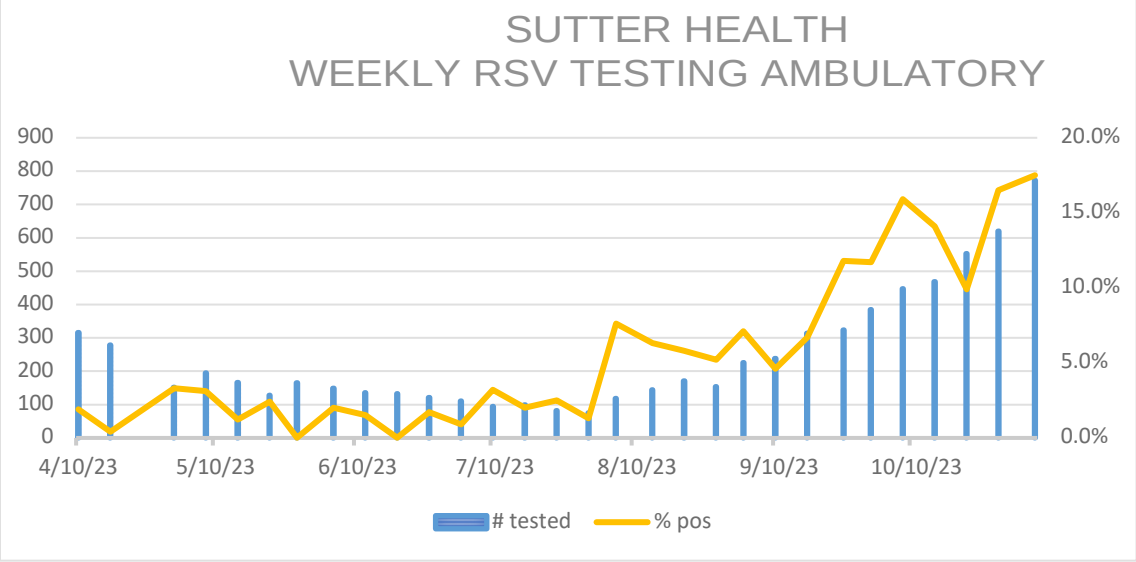
- CDPH Tracking and Vaccination Updates
- Sutter Health for Clinicians
- Sutter Health for Patients
- WHO Table of Contents

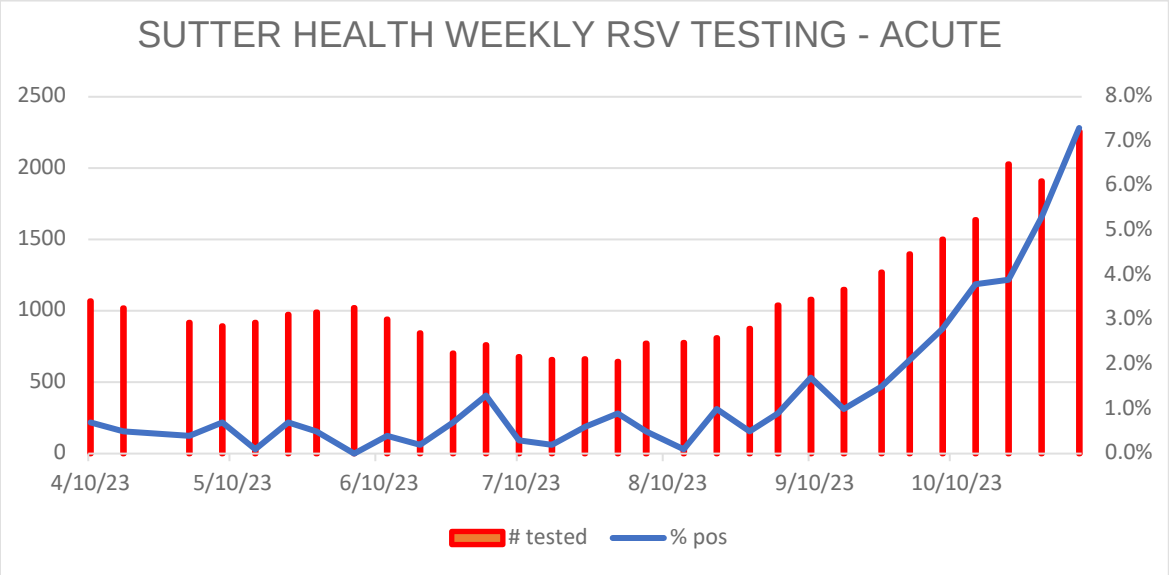
RSV

- RSV is increasing throughout California. The latest CDPH RSV graph shows that rates have increased in the last two weeks (Blue arrow). The rise is about the same time as last year, although positivity rates are still much lower than what we saw last season (orange arrow). Again, this season is early compared to pre-COVID RSV seasons.



- RSV identification rates are increasing significantly in both the ambulatory and emergency departments. The amount of testing is simultaneously increasing and positivity rates in ambulatory are now almost 18% and over 7% in the emergency departments. The RSV season in Northern California appears to be widespread at this time.
- See two graphs below.





- RSV results by age are in the following table for the week ending November 5. Positivity rates have increased significantly, with one-third of children less than 6 years old testing positive in the ambulatory environment and 20% in the emergency departments.
- Small amounts of disease are being identified in persons 60 years and older.
- See table below.

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	310	33.5% (104)	102	6.9% (7)	113	4.4% (5)
Acute (ED)	624	20.2% (126)	125	3.2% (4)	1045	2.6% (27)

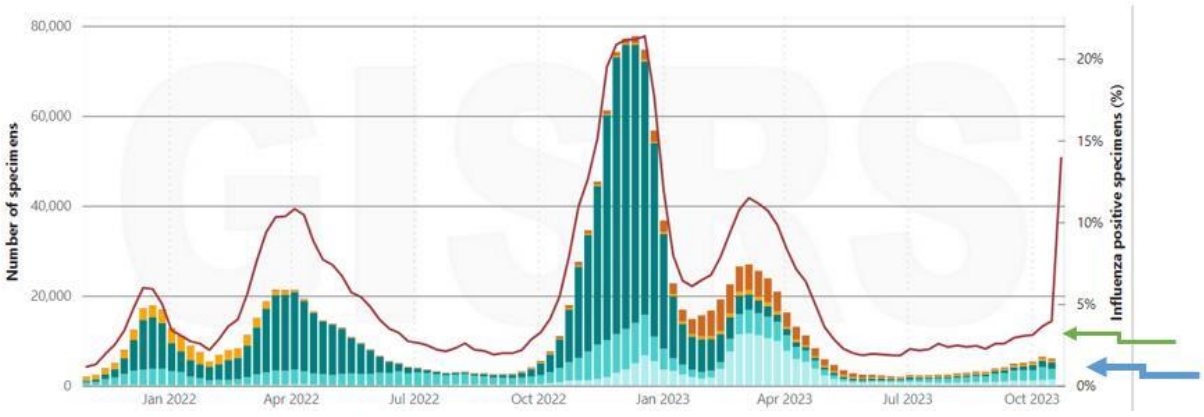
- Nirsevimab (Beyfortus®) continues with limited availability.
  - Unexpected higher than anticipated U.S. demand of Nirsevimab has resulted in a critical shortage of 100 mg doses locally, with declining availability of 50 mg doses in recent weeks.
  - Sutter Health is currently following the latest CDC Health Advisory available to prioritize the remaining supply of Nirsevimab doses during the shortage.
  - Nirsevimab 100 mg doses for infants ≥ 5kg should be prioritized for infants at the highest risk for severe RSV disease: young infants ~~(age <6 months)~~ with underlying conditions.
  - Recommendations for 50 mg doses of Nirsevimab remain unchanged at this time. To preserve supply of 50 mg doses for infants weighing <5 kg (<11 pounds), providers cannot administer two 50 mg injections to give a 100 mg dose to infants ≥5kg.
  - The RSV vaccine (Abrysvo®) for pregnant persons between 32-36 weeks' gestation to prevent RSV lower respiratory tract infection in infants is available.

- Palivizumab (Synagis®) in eligible infants aged <8 months and children aged 8–19 months continue to be recommended as alternative options during the current shortage.

- **RSV Take-Home:**
- RSV season is here in California. In Northern California, about one out of every three children < 6 years old tested for RSV in the outpatient environment is positive and 20% are positive in the ED in that age group.
- High-risk patients 60 years and older should be offered the RSV vaccine, especially with co-morbidities or those living in a congregate living environment.
- Nirsevimab supply remains limited. The CDC has published guidance on prioritization.
- The Abrysvo® RSV vaccine should be discussed with patients between 32 through 36 weeks of gestation and administered if birth person consents.
- Pavilizumab should be used for appropriate high-risk infants when nirsevimab is not available.

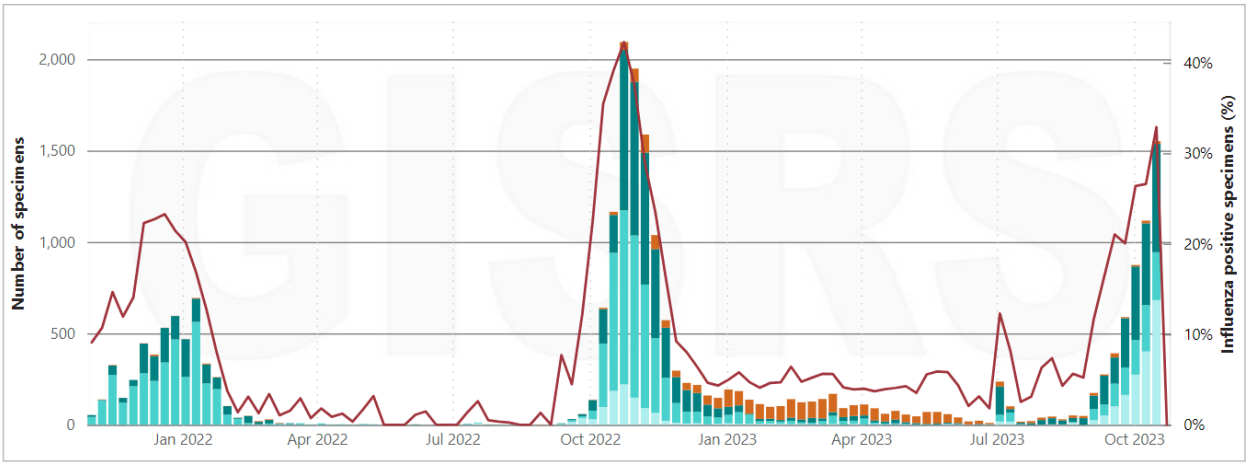
Influenza

- The WHO released their biweekly global influenza update on Oct. 31. This includes the most recent two weeks of data up to Oct.15.
  - Increased activity in the Northern Hemisphere continues in Western and Eastern Asia.
  - Influenza A predominates with both A H3N2 and A H1N1 being detected.
  - The Southern Hemisphere has inter-seasonal, low levels of detection.
  - From Oct. 2-15, 357,752 specimens were tested.
    - 11,470 were positive (3.2%).
    - 83% were influenza A, with H3N2 twice as common as H1N1.
- The graph below shows influenza activity in the Northern Hemisphere for the last 2 years. A slight increase (shown by the blue arrow) is being seen, but no evidence of a spike. Shades of teal represent influenza A and brown represents influenza B.
- The green area points out that the positivity rate has been gradually increasing. The sharp increase at the end is an artifact of incomplete data.

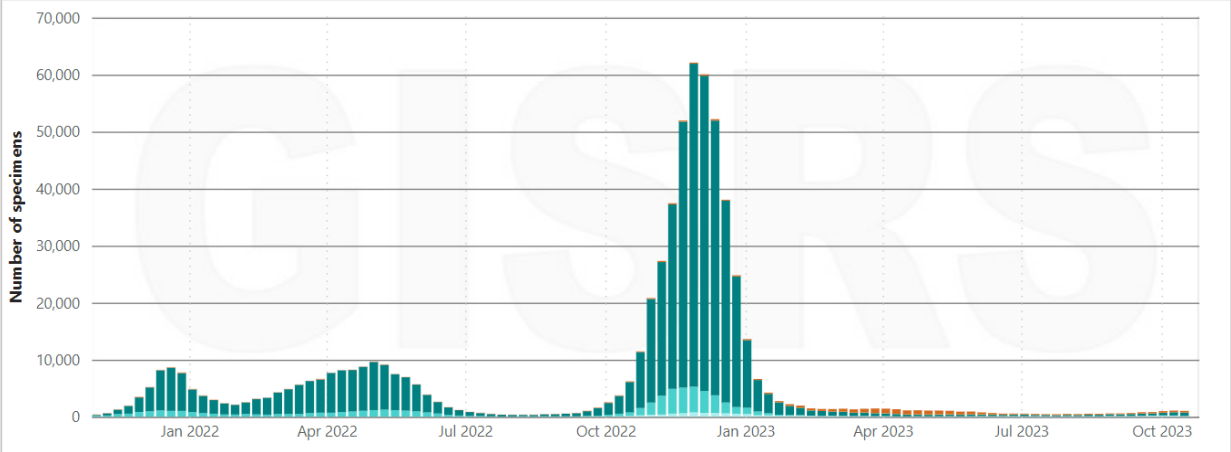


- The following graph shows influenza activity in Iran, where an outbreak is occurring. Positivity rates (the right Y axis) and the number of specimens tested (left Y axis) are

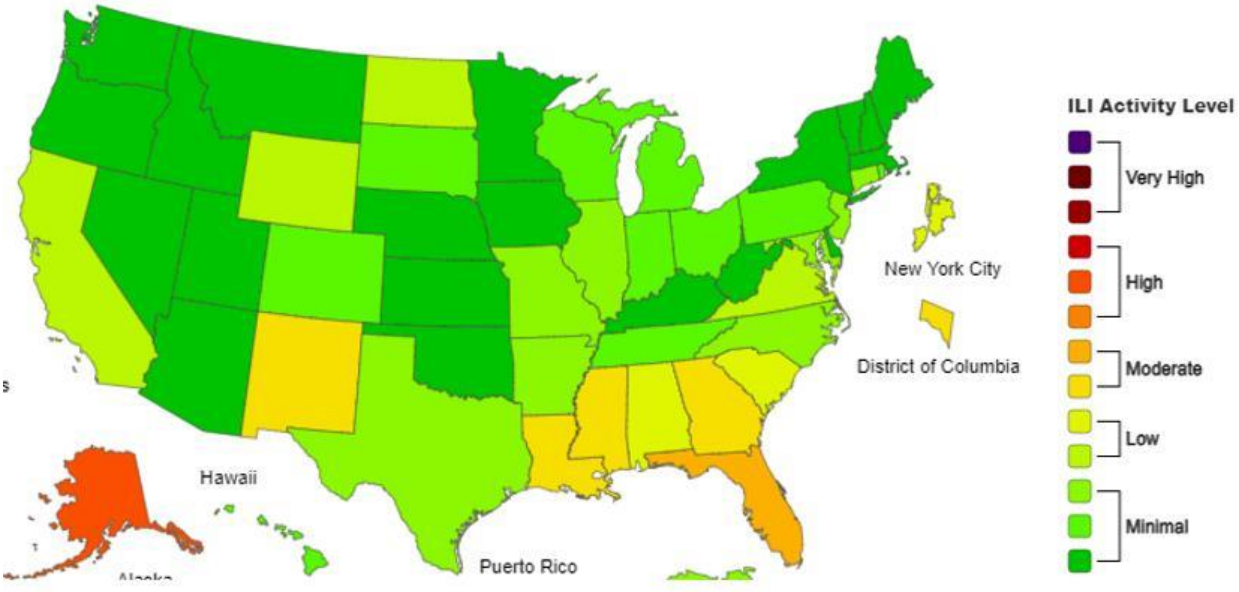
increasing dramatically. Other countries included in Southern Asia by the WHO are not experiencing increased influenza activity.



- The final graph in this series shows influenza activity in North America. Positivity rates remain stable and very low.

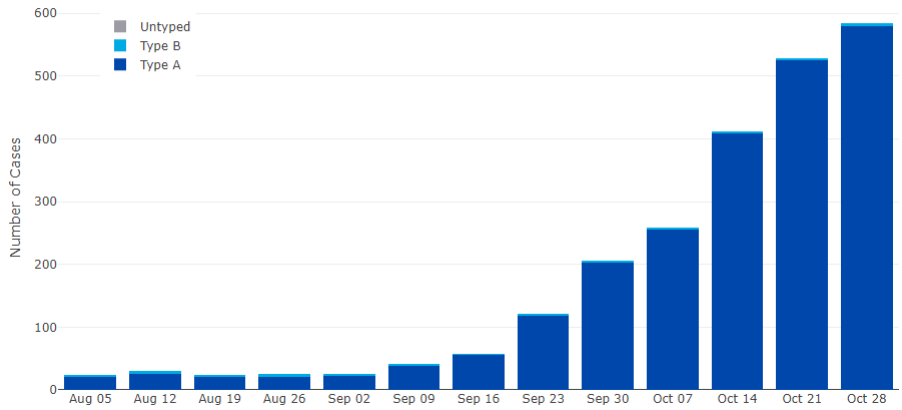


- Influenza-like activity (ILI), the surrogate for influenza used by the CDC, is on the map below. Disease in the United States appears to be increasing, especially in the Southeast. Since influenza is not a reportable disease in many states, except for hospitalizations and deaths, it is difficult to get accurate numbers.



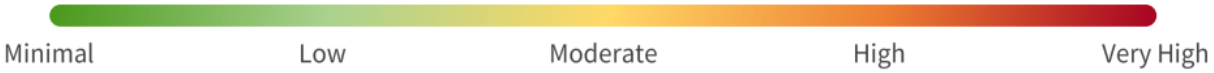
- Alaska does track lab-confirmed cases of influenza. The graph below confirms that an outbreak is occurring in Alaska now.

Lab-Confirmed Flu Types in Alaska



- Influenza activity in the United States remains low but is slowly increasing. The CDC reports that out of 50,459 specimens tested by clinical labs during week 41 (Oct. 21-28), 964 were positive (1.9%). This compares to 1.3%, 2 weeks earlier. Influenza A H1N1 continues to dominate.
- A H1N1 has one circulating clade but two HA subclades. A H3N2 has one circulating clade but three subclades. Ongoing testing for vaccine match is performed by the CDC.
- Anticipated vaccine match is determined by measuring the activity of ferret-derived vaccine antibodies against samples from circulating strains. Since May 2023, 76 strains of A H1N1, 22 strains of A H3N2, and 60 strains of B Victoria have been tested. All of the circulating strains were recognized by the vaccine antibodies.
- CDPH reports influenza activity in California. The map below shows that activity within our state is low. Statewide positivity rates during week 43 were about the same as the national rate at 2.2%.

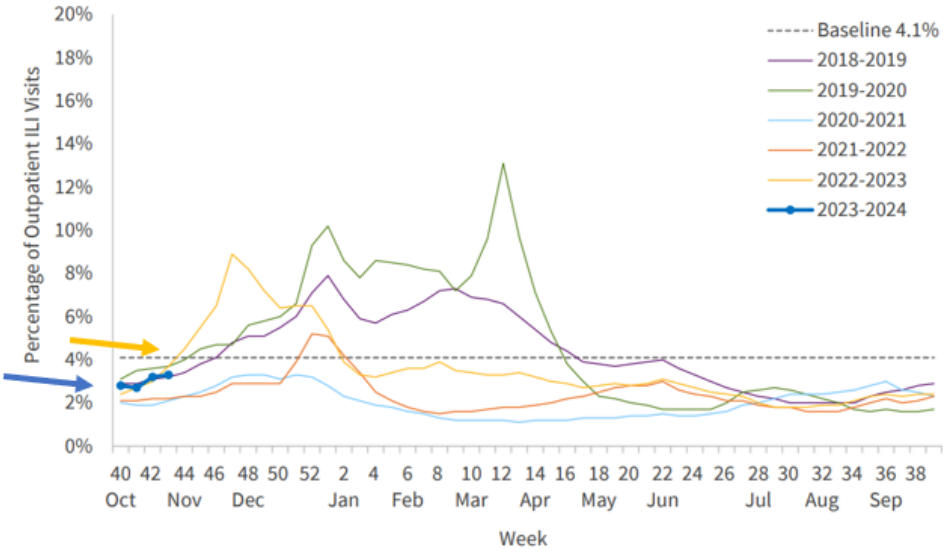
Influenza Activity Levels[+]



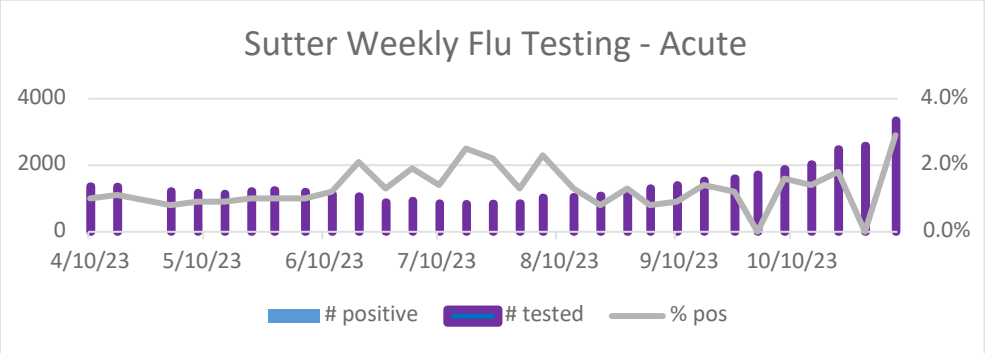
Geographic Area	Activity Level
California Statewide	**Low**
Northern Region	Insufficient data
Bay Area Region	Minimal
Central Region	Low
Upper Southern Region	Minimal
Lower Southern Region	Low

- The graph below shows the percentage of ILI visits in California from 2018 to the present. The blue arrow shows that we are at a fairly typical positivity rate for this time of year. The orange arrows demonstrate that a spike began in the 2022-23 season about this time last year. That however was an early season.

Figure 3. Percentage of Influenza-like Illness Visits Among Patients Seen by California Sentinel Providers, 2018–2024 Season to Date



- The last graph shows Sutter emergency department influenza positivity rates. No particular pattern is being demonstrated yet. Testing rates have increased as all symptomatic persons being seen in emergency departments are being tested for influenza and SARS-CoV-2. RSV tested has age-preferred criteria.



- **Influenza Take-Home:**
  - Overall, worldwide influenza activity remains low, although there remains increased activity in Western and Eastern Asia. Iran is experiencing an outbreak.
  - Worldwide positivity rates reported by the WHO during the first two weeks of October are slowly increasing and are now 3.2%.
  - Influenza activity remains very low in the continental United States although an outbreak of influenza A is in Alaska and ILI activity is increasing in the Southeast.
  - It appears that disease may be increasing in more parts of the United States.
  - Tests by the CDC show that the vaccine match to circulating strains is very good.
  - Vaccination can still decrease the morbidity and mortality of those who do get infected with influenza.

Hepatitis C (HCV) testing among perinatally exposed infants and children

- HCV is a virus that causes acute and chronic liver disease. About 50% of acute infections progress to chronic disease. Untreated, it can lead to cirrhosis or hepatic carcinoma. Most patients can be cured with presently available treatments, although some patients have developed drug resistant viruses.
- Between 2010 and 2021, the rates of acute HCV infections in reproductive-aged persons have more than tripled. See table below.

	Rates in 2010 (per 100,000 population)	Rates in 2021 (per 100,000 population)
20-29 years old	0.8	2.5
30-39 years old	0.6	3.5

- Although in 2020, the CDC released universal guidelines for screening all adults for HCV, including with each pregnancy, no recommendations have previously been provided on screening infants and children exposed to HCV positive pregnant persons.
- On Nov. 3, the CDC released guidance that addresses infants and children that were perinatally exposed to HCV. The table below shows the recommendations. Patients with positive results should be referred to an appropriate specialist for evaluation and timing of treatment.

Age Range	Test of Choice	Comments
2-6 months old	Hepatitis C RNA by Nucleic Acid Amplification Test (NAAT)	If negative no further testing
7-17 months old		Only test if not previously tested
>18 months old and not previously tested	Hepatitis C antibody (Anti-HCV)	Reflex to Hepatitis C RNA by NAAT if antibody positive

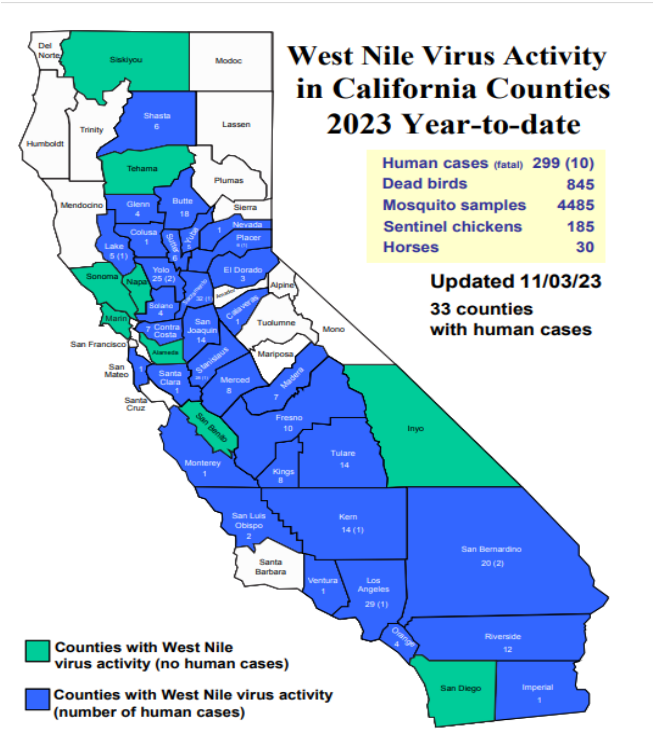
- **Hepatitis C Take-Home:**
  - Guidelines are now available to test at-risk infants and children with perinatal exposure to Hepatitis C.
  - Extremely effective medications are available to treat and cure this infection. Identification with appropriate testing and referral to an appropriate specialist can have major impact on infected infants and children.

Gepotidacin

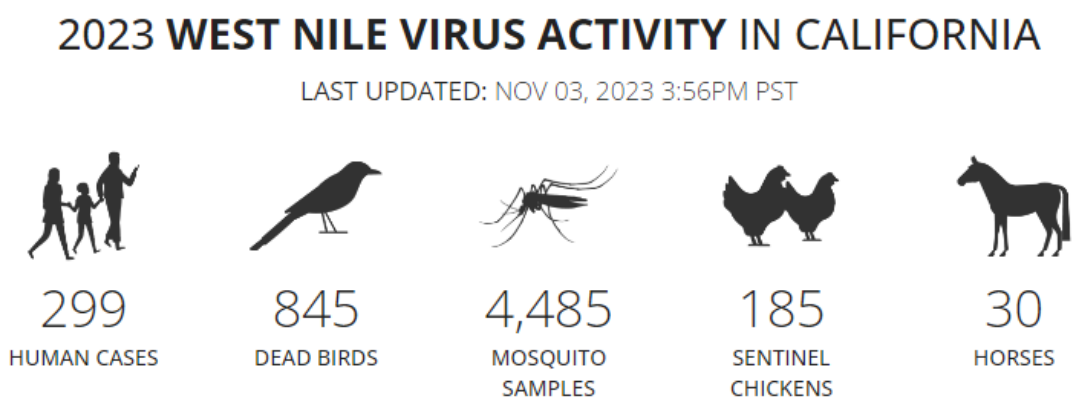
- Another pipeline antibiotic for resistant pathogens has been submitted for review by the FDA for the treatment of uncomplicated UTI (uUTI).
- Gepotidacin is a first-in-class, oral antibiotic targeting different bacterial topoisomerase inhibitors than fluoroquinolones. A nice review was published May 2023 in J. Antimicrobial Chemotherapeutics.
- EAGLE-2 and EAGLE-3 were near-identical global Phase 3, randomized control, non-inferiority studies comparing the efficacy and safety of oral gepotidacin (1500 mg twice daily, 5 days) to nitrofurantoin (100 mg twice daily, 5 days) for uUTI. Nearly 3,000 people were randomized and included between the two studies.
- The studies were stopped early for efficacy due to positive results.
- Gepotidacin is also being studied for urogenital *Neisseria gonorrhea* at a dose of 3000 mg x 1, followed by a second dose approximately 12 hours later. There is no evidence that gepotidacin works on rectal or oral infections.
- GI side effects are extremely common, usually between 50-90% of patients
- If approved, usage would probably be limited to uUTI, with known sensitivity to gepotidacin, and resistance to other oral agents. Future possibilities include urogenital GC (likely excluding all MSM), or urethritis due to drug-resistant *Mycoplasma genitalium.*

West Nile Virus (WNV)

- New cases of WNV in California are continuing to be reported but numbers are decreasing. The state map below shows counties with reported WNV cases in humans, colored blue. Cases have now been identified in 33 counties.
  - The counties reporting cases in the last week include Calaveras, Kings, Madera, Orange, Sacramento, San Bernardino, San Joaquin, Stanislaus and Yolo. This is the first WNV positive human case from Calaveras County this year.



- Year-to-date total for reported cases in humans in California increased by 13 in the last week. (pictograph below) with 10 deaths in humans now reported.



- **West Nile Virus in California Take-Home Message**
  - WNV transmission and reported cases in humans continue throughout California, but numbers are slowly increasing, probably from the delay in reporting. The WNV season is likely near the end.
  - This portion of the newsletter will cease reporting this season, unless something unusual is detected.