Sent on behalf of William Isenberg, M.D., Ph.D, Chief Medical & Quality Officer, Sutter Health, and Jeffrey Silvers, M.D., Medical Director of Pharmacy and Infection Control, Sutter Health

Emerging Infections Newsletter for Clinicians

Oct. 25, 2023

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

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Birth Person Vaccine Antibodies and Newborn Protection

- Immunizing a pregnant person to protect a baby until the baby is old enough to be immunized is a common approach. It's common to ask questions about vaccine efficacy and duration of efficacy in the very young baby for the first 6 months of life.
- If the birth-person was immunized against RSV for the current season, at least 2 weeks before delivery, the risk of the newborn developing RSV is decreased by about 70% for up to 6 months. Nirsevimab (Beyfortus), given to newborns within 7 days after delivery during the RSV season, protects the infant for up to 6 months.
- If the birth person received an influenza vaccine anytime during the pregnancy, at least 2 weeks prior to delivery, and breastfeeds, the risk of influenza in the newborn is decreased by at least 50% for up to 6 months. Breastfeeding by itself does not provide statistically significant protection if the birth person was not immunized. Vaccine match can influence these results.
- COVID vaccination during pregnancy also protects the newborn against severe disease for up to 6 months, with the highest efficacy during the first 3 months of life. This can be significantly impacted by major variant changes and vaccine match.

First Pentavalent (serogroups—A, B, C, W-135 and Y) Meningococcal Vaccine Approved

- Meningococcal vaccines have been complicated because the serogroup B vaccine has been administered separately from the quadrivalent vaccine that includes serogroups A, C, W and Y.
- On Oct. 20, the FDA approved Penbraya™, the first pentavalent meningococcal vaccine, for use in persons 10 to 25 years of age. Penbraya™ combines the components from two meningococcal vaccines, Trumenba™ (meningococcal group B vaccine) and Nimenrix™ (meningococcal groups A, C, W and Y conjugate vaccine).
- Approval was based on data from Phase 2 and Phase 3 trials demonstrating non-inferiority to Trumenba™ (MenB) plus Menveo™ (MenACWY) for all covered meningococcal serogroups.
    - This includes serologic response, tolerance, safety and duration of efficacy measured for up to 4 years.
- The CDC must provide recommendations for use of Penbraya™ before local implementation can occur. The Advisory Committee of Immunization Practices (ACIP) will discuss at the Oct. 25-26 meeting.

MPOX

- The Oct. 20 WHO MPOX situation report noted that cases of MPOX increased in September in parts of Europe, notably Portugal, Spain and the United Kingdom. There was a 660% increase between August and September.
    - This needs to be interpreted with caution as the WHO went from weekly reporting to monthly reporting in October and there could be some surveillance artifact in the data.
- CDPH reported on Oct.18 that cases of MPOX in California have been increasing. From February to May 2023, approximately one case per week was reported. This increased to approximately seven cases per week from June to August 2023 and most recently

has been about 14 cases per week (Sept.12 through Oct. 3, 2023). More than 10 counties have been reporting new cases.
    - The rise in cases, although very notable, needs to be tempered by looking at the September 2022 rate of 210 cases per week.
- Second cases of MPOX and breakthrough infections after vaccination continue to be reported.
- Neutralization titers are used as a surrogate of protection against disease. Orthopox viruses, which includes MPOX, produce two different types of infectious virions during the replication cycle—the IMV (intracellular mature virus) and the EEV (extracellular enveloped virus).
- The EEV is believed to facilitate the spread of the virus within an infected host, whereas the IMV is believed to facilitate transmission between hosts. Plaque reduction assays generally measure the neutralization of IMV rather than EEV.
- Theoretically the plaque reduction assay may reflect risk of contagion more than severity of disease, however the MMWR from Sept. 8 reported vaccine effectiveness data. Vaccinated persons are less likely to require hospitalization compared to those who were unvaccinated.
    - From May 2022 to May 2023, 83% of patients with MPOX infections and 93% of hospitalized patients were unvaccinated.
    - The odds of hospitalization among persons with MPOX who had received one or two JYNNEOS doses were 0.27 (95% CI = 0.08–0.65) and 0.20 (95% CI = 0.01–0.90), respectively, compared with unvaccinated MPOX patients.
- The duration of vaccine efficacy and effectiveness are uncertain. Properly planned vaccine trials are underway, but design is complicated by the ethics of a control group. In the interim, some small studies are being published.
- Lancet, Oct. 11, published a study from Italy looking at neutralizing antibody titers 6 months after natural infection versus two doses of vaccine. 180 participants were included, 95 with infection while unvaccinated, and 85 who had received both doses of the MPOX vaccine.
    - All male and 99% were reported as MSM.
    - Titers were categorized as undetectable, low, medium or high.
    - After 6 months, all patients with natural infection had detectable titers whereas almost 50% had low to undetectable titers in the vaccinated population. As anticipated, vaccinated persons living with HIV had the lowest titers.
    - The major weakness of this trial is that numbers in each sub-group were too small for any statistical analysis.
- A study in Nature Medicine January 2023 from the Netherlands, measured neutralizing antibody response after one dose of the Jynneos MPOX vaccine, after two doses (the standard recommended protocol), after an additional dose in both groups 1 year later, and in a group of participants who had receive the smallpox vaccine before 1974.
    - Individuals with a history of smallpox vaccination had the most robust immune response.
    - In this study, a single vaccine dose and the standard two-dose vaccine series led to relatively low neutralizing antibody titers.
    - A third dose of the MPOX vaccine 1 year after the initial series significantly boosted the neutralizing antibody titers. This suggests that a booster might be a useful recommendation for high-risk individuals who remain disease free.

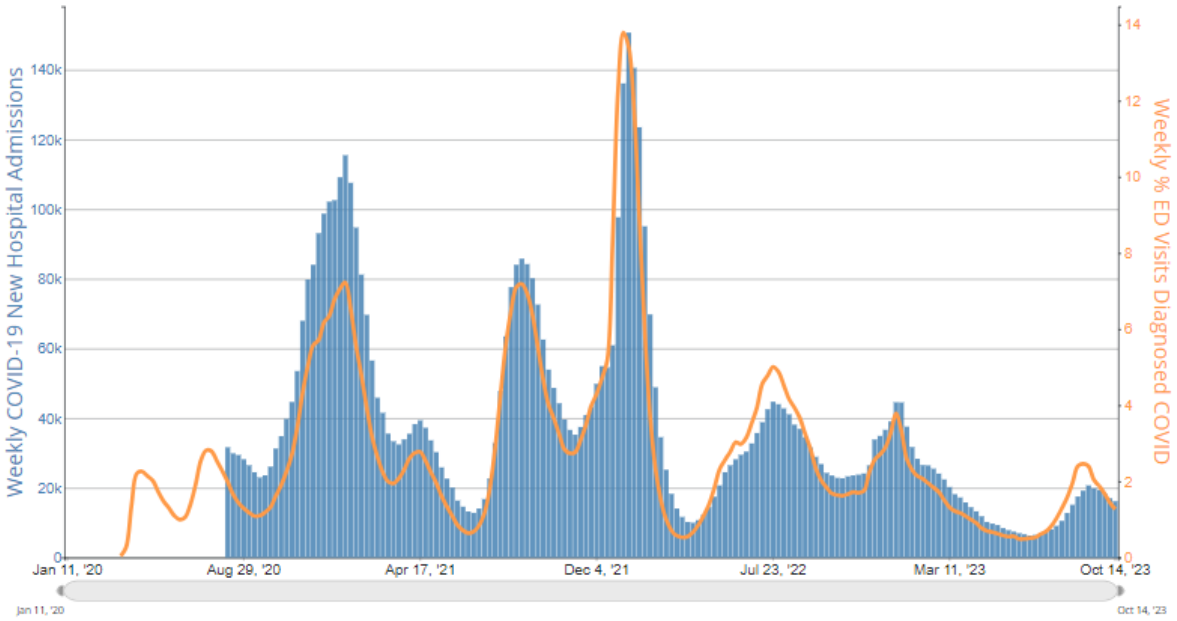
- **MPOX Take-Home:**
    - Reported cases of MPOX in September increased in parts of Europe and California in September.

        - Although rates are still very low compared to September 2022, increased vigilance to diagnose disease and offering/encouraging vaccination of appropriate high-risk individuals should continue.
    - Post-vaccine breakthrough infections are likely due to declining neutralization antibodies.
    - MPOX neutralization titers developed after the two-dose vaccine series may be lower than after natural infection.
    - A booster 1 year after the initial series in an infection-naïve population led to a significant boost in neutralization titers and may be a useful recommendation. Further data are needed.

COVID-19

- The U.S. government has distributed five-day courses of nirmatrelvir plus ritonavir (Paxlovid™) at no cost to patients since December 2021 under the FDA's emergency use authorization (EUA) labeling. Following FDA approval on May 25, 2023, the pre-purchased EUA supply has continued to be available.
- Paxlovid™ supply will transition to the commercial market Jan.1, 2024. The retail price will be $1,390 for the 5-day course.
    - That is more than a 160% increase from what the U.S. government paid.
- Financial assistance programs will be available for commercially insured patients through 2028. Further details are pending.
- Medicare and Medicaid beneficiaries through 2024, and uninsured and underinsured patients through 2028 will be eligible for Paxlovid™ free of charge via a patient assistance program.
- Molnupiravir, recommended for the treatment of COVID-19 when Paxlovid™ or remdesivir is not available, feasible or appropriate, is expected to be commercially available in the 4th quarter 2023. Pricing has not yet been announced.
- Hospitalizations in the United States are a surrogate for the virulence of the circulating strain. The graph below and the subsequent table show:
    - Continued decreasing hospitalizations (blue vertical bars).
    - Concomitant continued decrease in 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

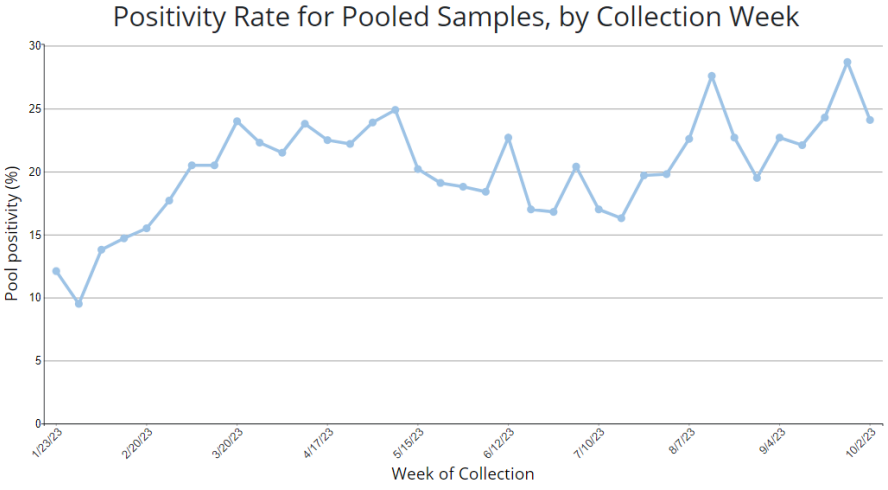


- The CDC tracks hospital admissions per 100,000 county population. Less than 10/100,000 is consider a low number of new hospital admissions. Nationally, rates are now below 5/100,000. Hospitalization rates continue to decrease. The admissions percent change in the last week is -5%.

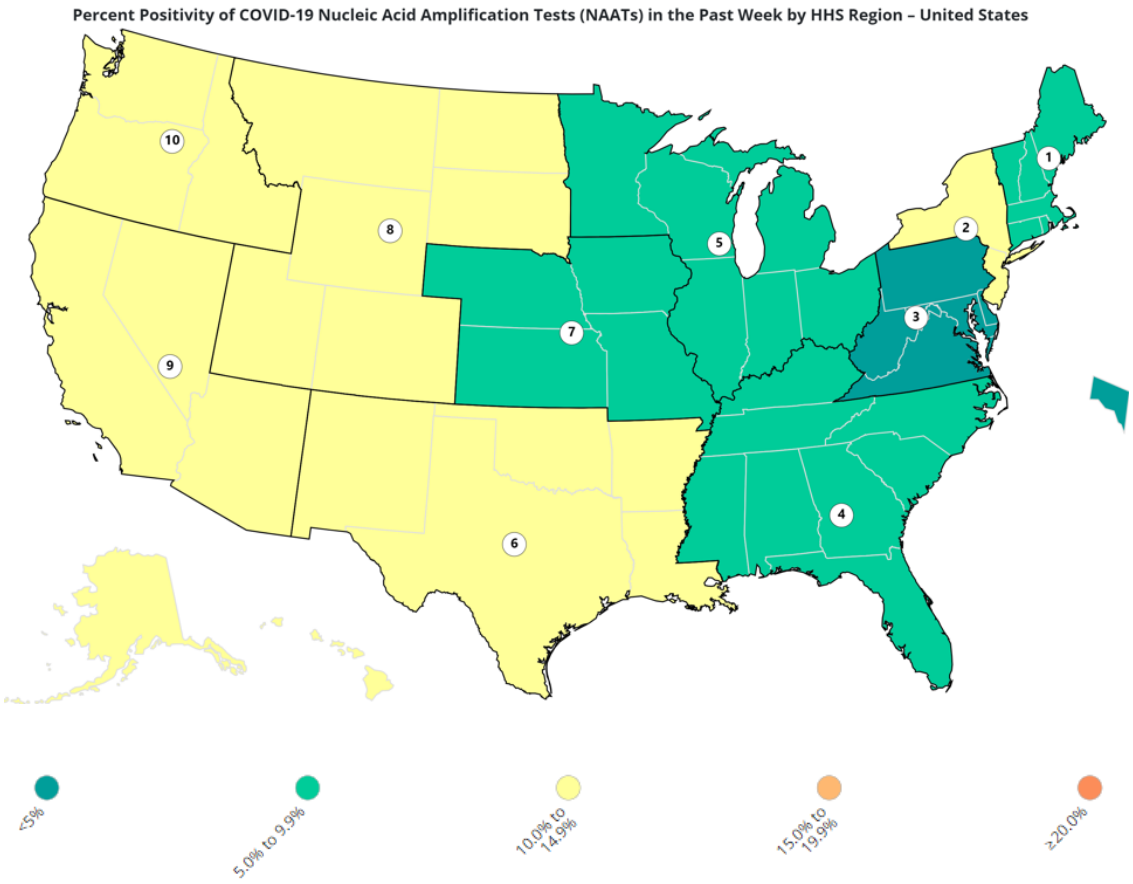
COVID-19 HOSPITAL ADMISSIONS (PAST WEEK)	% CHANGE IN COVID-19 HOSPITAL ADMISSIONS	COVID-19 HOSPITAL ADMISSIONS PER 100,000 (PAST WEEK)
16,158	-5%	4.87

CDC | Data through: October 14, 2023. Posted: October 20, 2023

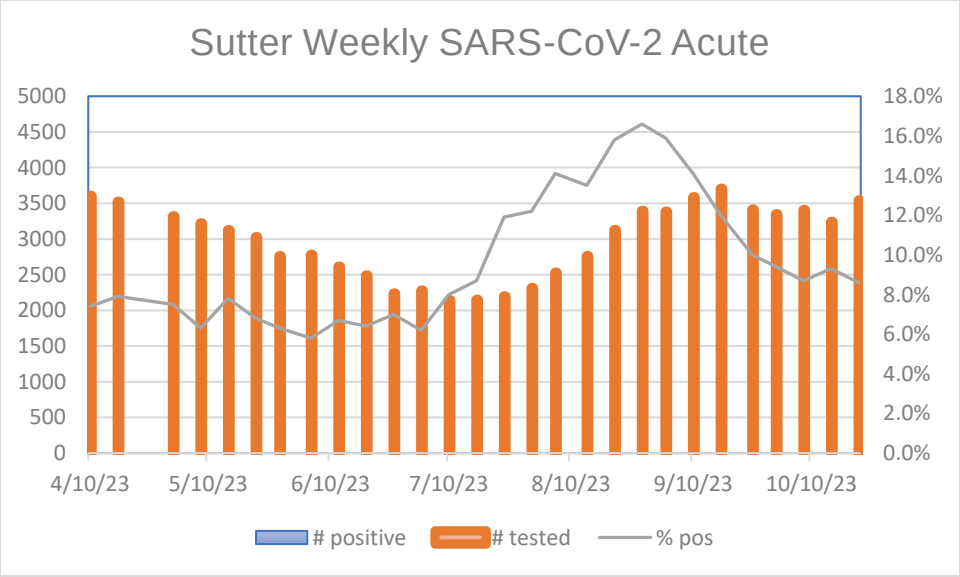
- Surveillance of international air travelers is conducted at several major U.S. airports as an early warning system and to fill gaps in worldwide genomic surveillance. The graph below shows a continued high positivity rate. The updated CDC web site now shows that HV.1 has been identified this year.

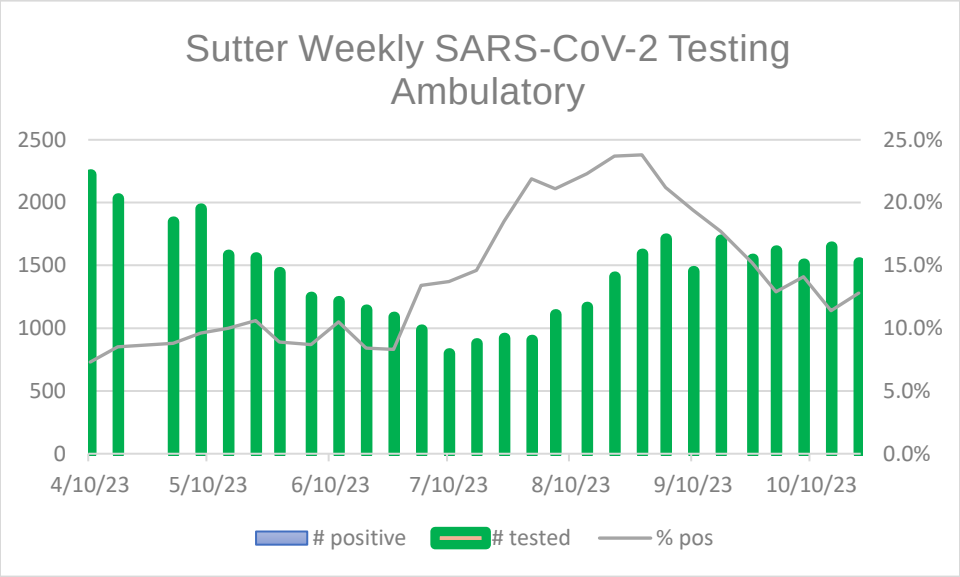


- National molecular test positivity rates by region are demonstrated on the map below. Although there are minor changes compared to the last week, rates remain moderate (yellow) to low (green) in the country. Yellow represents a 10-14.9% test positivity rate.



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





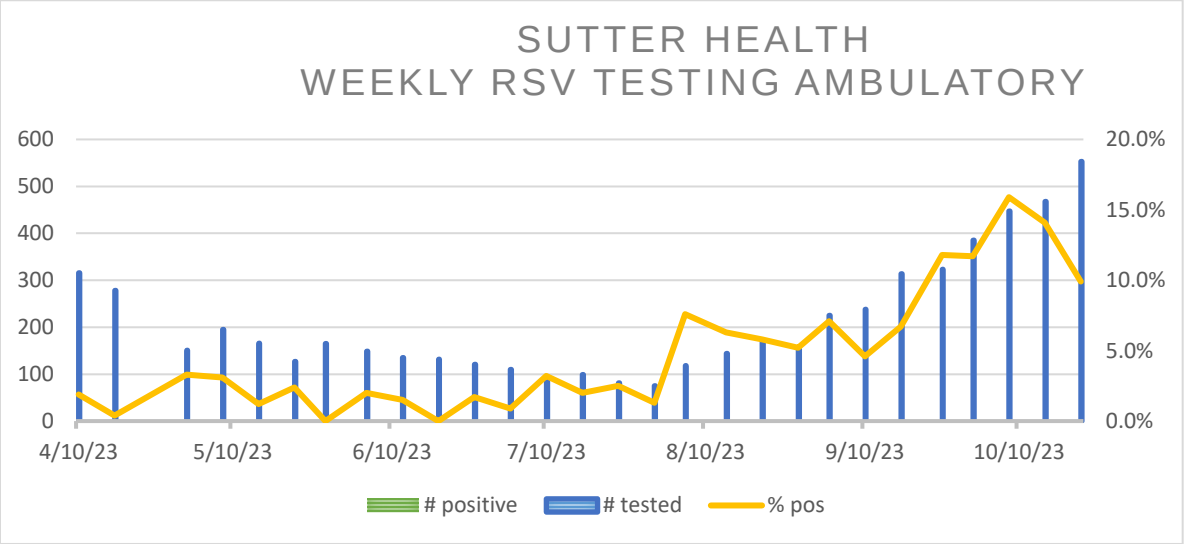
- **COVID-19 Take-Home:**
  - Paxlovid is going to be very expensive once the government supply is depleted.
  - HV.1 is now being reported by the CDC in international travelers being tested at U.S. airports.
  - Hospitalizations, emergency department visits and Sutter Health testing positivity rates are all trending down. COVID appears to have peaked for now.
  - Although still not low, Sutter ambulatory and emergency department positivity rates are 12.8% and 8.6% respectively.
  - The XBB vaccine has significant potential to mitigate a winter outbreak. Don't miss an opportunity to provide this important protection.

- **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

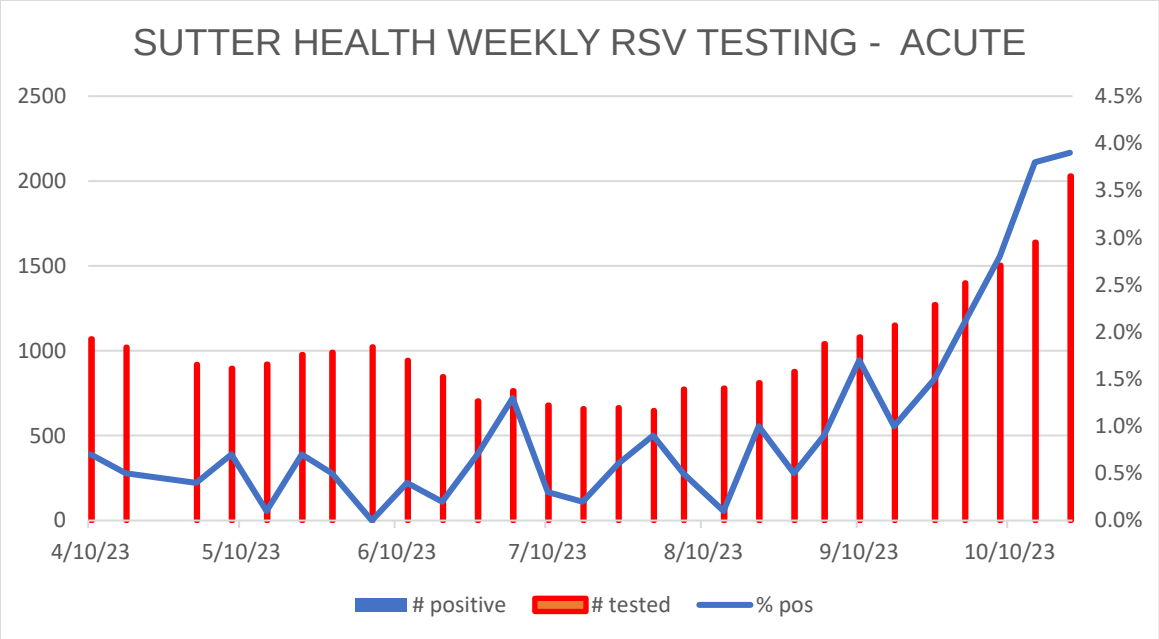
RSV

- Nirsevimab remains in limited supply. The CDC published guidance Oct. 23 on how to prioritize patients.
- The Abrysvo™ RSV vaccination administered between 32 through 36 weeks of gestation is an available option that should be discussed with patients during prenatal care.
- RSV is still being identified in the ambulatory setting. The amount of testing in ambulatory has increased by 18% in the last week. Positivity rates are well above the 3% threshold for 12 weeks now. Ambulatory positivity rates appear to be declining for the last 2 weeks.

- See graph below.



- The following graph demonstrates that ED positivity rates are now over 3% for 2 consecutive weeks at 3.9%. The number of tests being performed has also continued to increase.



- RSV results by age are in the following table for the week ending Oct.15. Positivity rates in children less than 6 years old have decreased a little but remain over 22% in the ambulatory environment and are up to 12.2% in the emergency departments.
- Most of the increased RSV activity continues to be identified in children less than 6 years old, both in the ambulatory environment and the emergency departments. There are some children between 6 years up to 12 years old being identified
- More disease is starting to be identified in persons 60 years and older. Because of their increased risk, more older persons may start to be hospitalized secondary to RSV. In

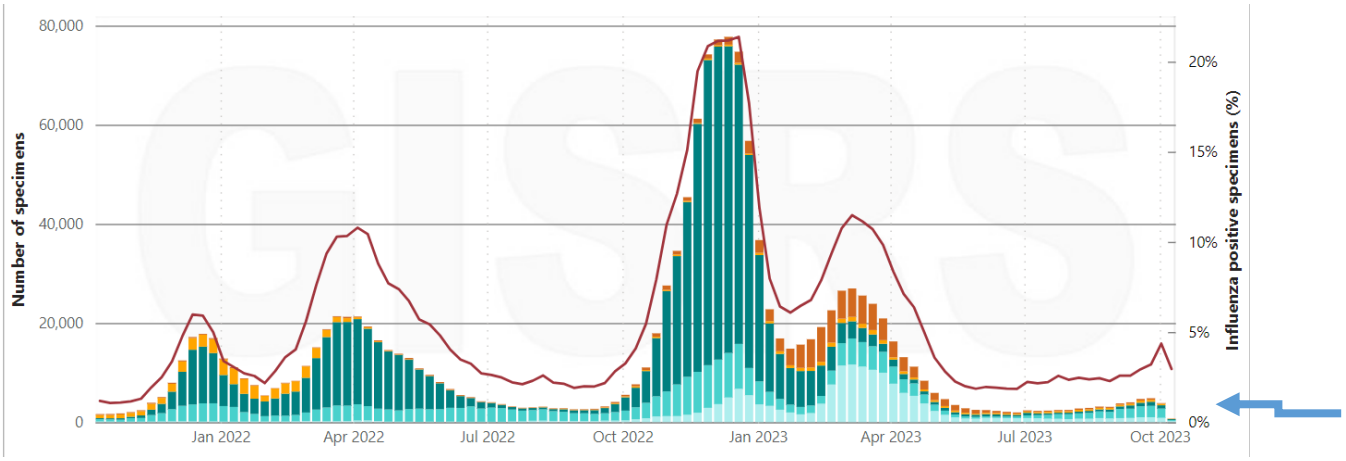
addition to older age, hospitalizations with RSV are more common in persons with CHF or COPD. Vaccination of high-risk persons can mitigate this risk. See table below.

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	190	22.6% (43)	57	3.5% (6)	93	6.5%
Acute (ED)	441	12.2% (54)	144	5.6% (12)	629	1.9%

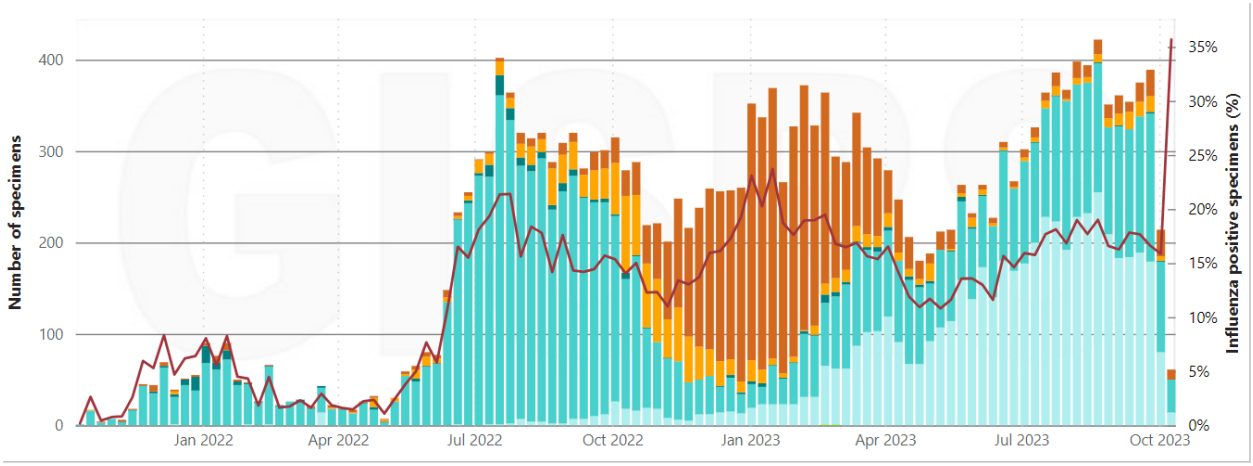
- **RSV Take-Home:**
  - Nirsevimab supply remains limited. The CDC has published guidance on prioritization.
  - The Abrysvo™ RSV vaccine should be discussed with patients between 32 through 36 weeks of gestation and administered if birth person consents.
  - RSV continues to be identified in Northern California in increasing numbers. About one out of every four children < 6 years old tested for RSV in the outpatient environment is positive and 12% are positive in the ED in that age group. More disease is being diagnosed in persons 60 years and older.
  - In appropriate symptomatic patients, testing should still be performed.
  - High-risk patients 60 years and older should be offered the RSV vaccine.

Influenza

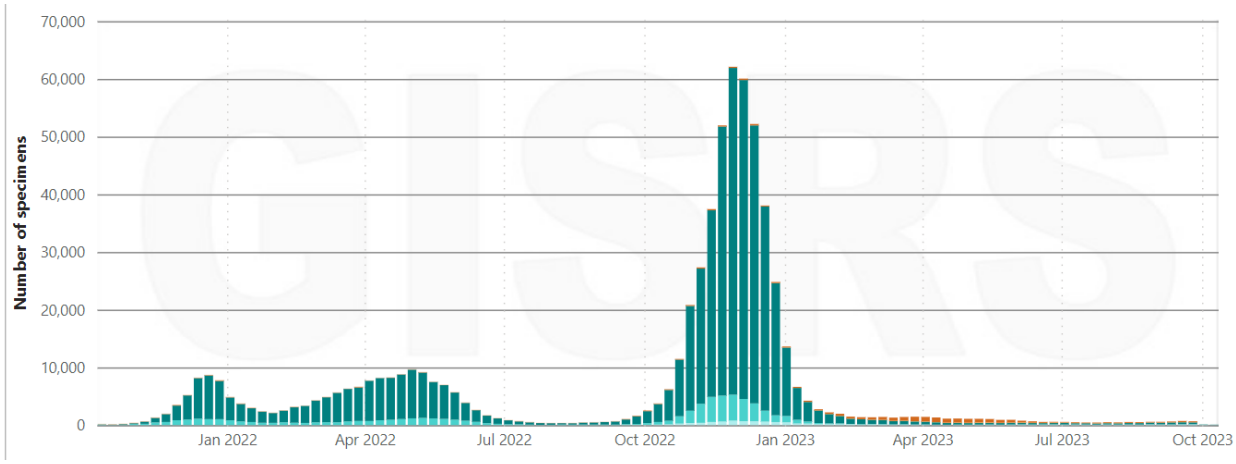
- The WHO released their biweekly global influenza update on Oct. 16. This includes the most recent two weeks of data up to Oct.1.
  - Increased activity in the Northern Hemisphere is now in South-East, Western and Eastern Asia.
  - Influenza A predominates with both A H3N2 and A H1N1 being detected.
  - The southern hemisphere has inter-seasonal, low levels of detection.
  - From Sept.18 to Oct.1, 336,169 specimens were tested.
  - 10,167 were positive (0.76%).
    - 80% 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 following graph shows influenza activity in South-East Asia. Positivity rates (the right Y axis) remain elevated, but the number of specimens tested (left Y axis) remain exceptionally low.



- The final graph in this series shows influenza activity in North America. Positivity rates remain stable and very low. No evidence of any increase at this time.



- Influenza activity in the United States remains low. The CDC reports that out of 49,296 specimens tested by clinical labs during week 41 (Oct. 9-15), only 661 were positive (1.3%). Influenza A H1N1 dominated.
- Anticipated vaccine match is determined by measuring the activity of ferret-derived vaccine antibodies against samples from circulating strains. Since May 2023, 68 strains of A H1N1, 14 strains of A H3N2 and 45 strains of B Victoria have been tested. All of the circulating strains were recognized by the vaccine antibodies.

- **Influenza Take-Home:**
  - Influenza activity remains very low in the United States
  - It seems we will not have an early influenza season. Very small increases are being noted in some locations in the world.
  - 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.

Guidance for Masking and Vaccinations During Respiratory Illness Season

Masking Guidelines During Respiratory Illness Season

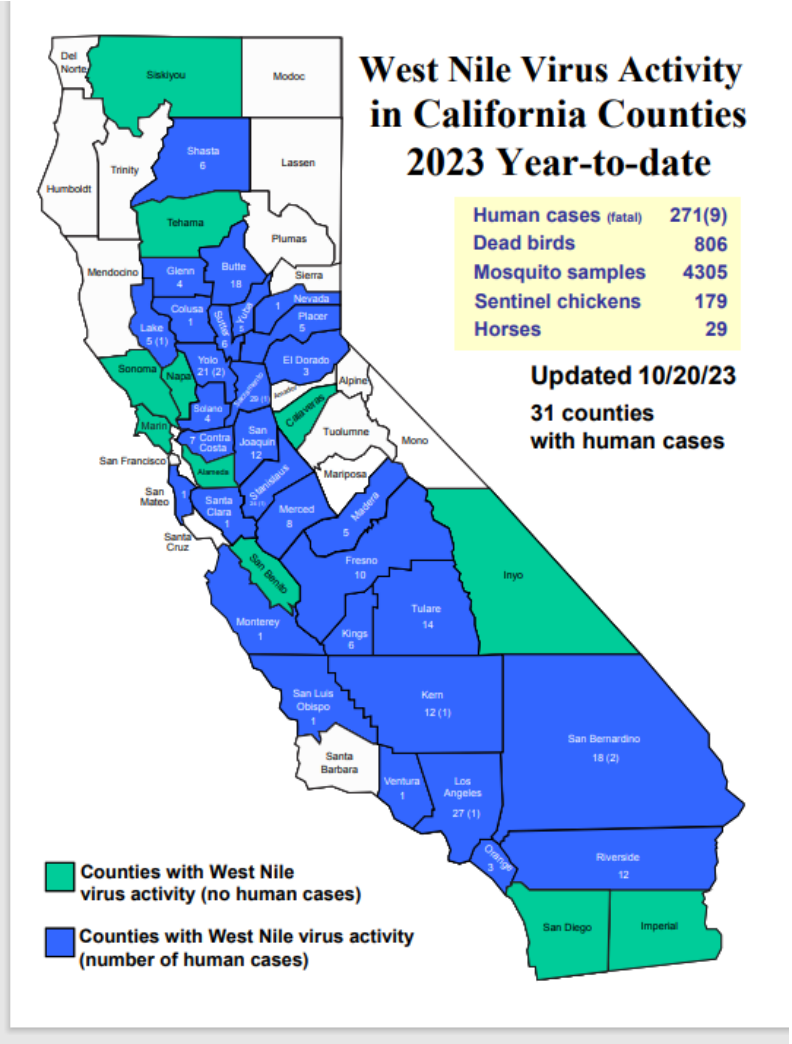
- Sutter's approach to masking will somewhat differ this season due to varying recommendations from local jurisdictions, including city and county public health departments. **In patient care areas, our care teams members will follow the local (city/county) requirements in the location where their facility is situated**.
  - **Given the considerable variation among the counties where our facilities are located, and the evolving nature of local requirements, please refer to this link for specific local requirements and the most up-to-date information.**
  - We will continue to update this site as any new requirements are released. Most of these masking requirements are expected to be in effect from Nov. 1 through April 30, although this may change depending on the length of the season.
  - For facilities in counties not specifically identified, we continue to strongly recommend that all HCWs, patients and visitors mask during patient care interactions or when entering care facilities.

Stay Up to Date with COVID-19 and Flu Vaccines

- As we've recently communicated, all our employees and physicians, irrespective of where they work, have been offered access to free influenza and the newest monovalent XBB COVID-19 vaccines. While vaccination participation remains voluntary, we strongly encourage you to take advantage of this offering—both vaccines offer added protection against these highly contagious viruses and help prevent severe illness and hospitalization.

West Nile Virus (WNV)

- Cases of WNV in California are continuing to be identified and are widespread throughout the state. The state map below shows counties with reported WNV cases in humans, colored blue. Cases have now been identified in 31 counties.
    - The counties reporting cases in the last week include Contra Costa, El Dorado, Fresno, Kern, Lake, Los Angeles, Orange, San Luis Obispo, San Mateo, Stanislaus, Sutter and Yolo. These are the first WNV positive human case from San Luis Obispo and San Mateo counties this year.



- Year-to-date total for reported cases in humans in California increased by 27 in the last week. (pictograph below) with nine deaths in humans now reported. That is down from 39 new cases in the prior week.

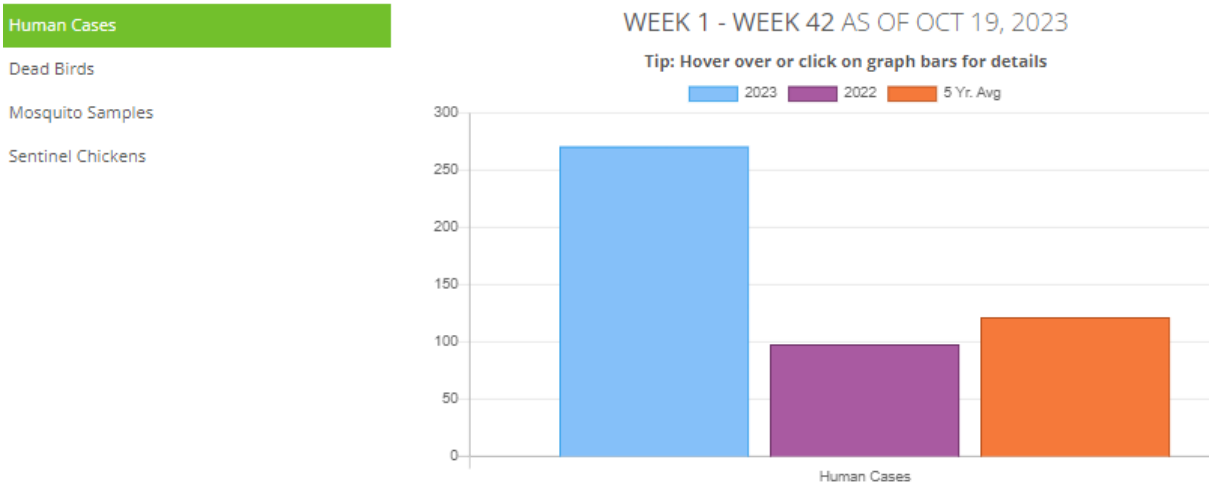
2023 **WEST NILE VIRUS ACTIVITY** IN CALIFORNIA

LAST UPDATED: OCT 19, 2023 2:14PM PST

271	806	4,305	179	27
HUMAN CASES	DEAD BIRDS	MOSQUITO SAMPLES	SENTINEL CHICKENS	HORSES

- The graph below shows that reported cases of WNV in California this year are more than twice the five-year average and are approaching triple the amount reported in 2022.

YEAR-TO-DATE (2023) COMPARED TO PREVIOUS YEAR (2022)



- **West Nile Virus in California Take-Home Message**
  - WNV transmission and reported cases in humans remain widespread throughout California.
  - This latest report shows a decrease in weekly reported cases, but reported numbers remain high.
  - Continue to keep WNV in the differential for meningitis, encephalitis, or a poliomyelitis-like syndrome.

Share the Newsletter

Anyone who would like to be added to the Emerging Infections newsletter should send a request to bryan.gardner@sutterhealth.org

This communication is intended for clinicians caring for Sutter patients. If you have questions, please reach out to us at clinicians@sutterhealth.org.

Sutter Health