



Emerging Infections Newsletter for Clinicians

March 20, 2024

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Measles

- Measles is the most contagious virus known to infect humans. Perhaps some SARS-CoV-2 strains matched that for a short period of time but the basic reproduction number (R_0) for measles is often cited to be [12-18](#).
- Many current healthcare workers have limited experience caring for patients with measles. Multiple [classic movies](#) have been made about widespread potentially devastating infectious diseases including bubonic plague, yellow fever, tuberculosis, Spanish flu, HIV and smallpox. Measles has been presented differently. A 1969 episode of [The Brady Bunch](#) featured the whole family contracting measles and laughing and joking about it. This unfortunate mischaracterization of the disease in a widely viewed, G-rated family TV comedy is quite unfortunate. Some people opposed to vaccinations and with limited experience with measles refer to this episode.
- Measles in the United States is a disease mostly affecting unvaccinated or under-vaccinated groups/communities including families, day-cares, religious groups and schools. Most cases are initially introduced when an unvaccinated international traveler returns home with the disease. In just the first 10 weeks of 2024, the number of cases identified in the U.S. already matches the total reported in all of 2023. Over 90% have been linked to international travel.
- Overall childhood vaccination rates decreased during the COVID-19 pandemic as people were instructed to restrict routine healthcare visits for a period of time.
- This gap in vaccination has been complicated by both the politicization and misinformation being spread about vaccines. Everywhere that measles vaccinations decrease below the critical 95% rate needed for herd immunity, the disease could become much more widespread.
- In the [WHO European region](#), 40 of the 53 countries reported cases and outbreaks in 2023 with over 30,000 cases and 21,000 hospitalizations. Measles is endemic in most of the world outside of North and South America; 46 countries in the world are identified in the [CDC measles travel health notice](#).
- As summer is approaching and international travel is anticipated to increase, the [CDC](#) updated their pre-travel health safety guidance for measles. The recommendation now states that Americans planning to fly to other countries should consult their doctors at least 6 weeks before departure if they are unsure about their measles vaccination status.
- A measles [CDC health advisory](#) was released on March 18. All travelers, regardless of their international destination, should be current on their MMR vaccinations.
 - Infants 6 through 11 months should receive one dose of MMR prior to departure. This special dose does not count towards the two doses that are usually started at 12 through 15 months.
 - Children \geq 12 months should receive two doses of MMR, separated by at least 28 days.
 - Teenagers and adults without evidence of measles immunity should receive two doses of MMR separated by at least 28 days.
- The risks of complications from measles need to be clearly discussed when addressing concerns about the MMR vaccine.
 - One out of five unvaccinated persons in the U.S. who contract measles will be hospitalized. The worst disease is in children younger than 5 years old. Children will usually require hospitalization for dehydration and/or pneumonia.
 - One out of 20 children develop primary viral or secondary bacterial pneumonia.
 - One out of 1000 children develop severe encephalitis. Even those with encephalitis who survive frequently have life-changing debilities including seizures, hearing loss, blindness or intellectual disabilities.
 - As many as one out of every 350 children die from respiratory or neurologic complications.

- Measles during pregnancy can lead to onset of labor, miscarriage, fetal demise, stillbirth low birth weight, and/or severe disease in the pregnant person.
- [Open Forum Infectious Diseases](#) in 2016 published California data showing that subacute sclerosing panencephalitis (SSPE) developed in one out of every 600 children who developed measles when under 15 months of age. Routine vaccination of children does not start until 12-15 months of age.
- The best way to prevent the development of that tragic complication is to ensure that everyone has completed their two doses of MMR and vaccinate children as soon as they are eligible. The latency period of [SSPE](#) averages 7 years and the disease is usually fatal.
- There are no specific antiviral medications to treat measles. Vitamin A, with age-adjusted dosing, is recommended for all children with severe measles, such as persons requiring hospitalization.
 - Measles infection induces a decrease in vitamin A. Levels are low in children with severe measles. Vitamin A deficiency is associated with delayed recovery, worsened disease severity, increased risk of death or blindness.
 - Vitamin A supplementation is associated with decreased morbidity and mortality. The American Academy of Pediatrics, WHO and [National Foundation for Infectious Diseases](#) all recommend administering vitamin A to all children with severe measles. The WHO actually recommends giving vitamin A to all children with measles, regardless of severity or country.
 - Dosage guidelines are very specific, age adjusted and must be followed for efficacy and safety.
 - Vitamin A does not protect against developing the disease.
- Post exposure measles prophylaxis with the MMR vaccine within 72 hours of exposure or human immune globulin within 6 days of exposure may mitigate the disease.
- Testing for measles needs to separate immunity from acute disease. Sutter has an order panel. Screen shot is below. For immunity, only order a rubeola IgG antibody. Rubeola IgM titers can be false positives and should never be ordered as a single test.

▼ Orders

▼ Measles Diagnosis Testing

Measles Diagnosis Testing Panel

Panel orders are pre-checked and meant to be ordered together for the diagnosis of acute measles.

Establishing an acute measles diagnosis requires the following four steps.

1. Call the local public health department to notify of a potential measles case and request testing

After approval, do the following:

2. Collect urine and order urine rubeola (measles) PCR.

3. Collect a nasopharyngeal swab and order NP rubeola (measles) PCR.

4. Order rubeola (measles) serology (IgG and IgM). False positive rubeola (measles) IgM titers are common and **should not** be used alone for diagnosis.

If evaluating for previous measles immunity, order **only** the rubeola (measles) IgG test.

Do not order measles IgM for previous measles immunity.

Rubeola (Measles) PCR Throat Swab CDPH Routine Once

Routine, ONCE, today at 1005, For 1 occurrence

And

Rubeola (Measles) PCR Urine CDPH Routine Once

Routine, ONCE, today at 1005, For 1 occurrence

And

Rubeola (Measles) Antibody IgG Routine Next Draw

Routine, NEXT DRAW, today at 1005, For 1 occurrence

And

Rubeola (Measles) Antibody IgM Routine Next Draw

Routine, NEXT DRAW, today at 1005, For 1 occurrence

- Any patient with possible measles should be isolated in an airborne infection isolation room (also called negative pressure or AIIR), when available.

- In the ambulatory setting without an AIIR, the patient should immediately be placed in a private room with the door closed.
- People entering the room should wear a [fit-tested N95](#) plus standard precautions.
- Room closure policies for an airborne transmissible disease should be followed after the patient leaves.
- Video visits are a valid option for some patients understanding that dehydration and pneumonia are common complications that require additional evaluation and/or treatment.
- [CDPH](#) published excellent guidelines on healthcare facility infection control recommendations for patients suspected of having measles.

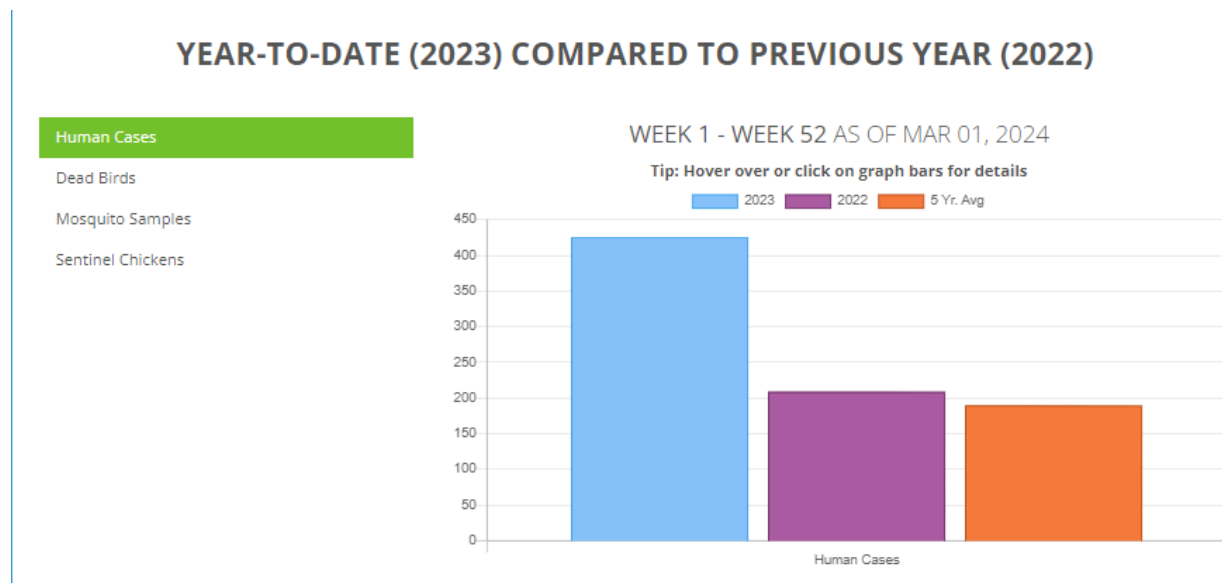
Measles Take-Home:

Measles is a vaccine-preventable re-emerging infectious disease. Large numbers of people do not understand the risk of life-altering complications or death.

- Most disease in the United States is being introduced by unvaccinated or under-vaccinated persons returning infected after international travel.
- All patients discussing international travel plans should be queried about measles vaccination status.
- All children as young as 6 months should be vaccinated against measles before international travel.
- Vitamin A (dosage and age adjusted) should be administered to all children with severe measles.
- Isolate and test all patients suspected of having measles.

West Nile Virus

- West Nile Virus (WNV) is the most common and serious vector-borne (mosquito) disease in California. In 2023, a total of 425 human infections were reported in California and identified in almost every county. The [graph](#) below demonstrates that the reported number of cases in 2023 was more than twice the number reported in 2022 or in the prior 5-year average.



- Alameda County identified two positive birds in January and the first positive mosquito in 2024 on March 13. For comparison, the first positive mosquito in Alameda County last year was in January. WNV is usually a disease of the summer with most cases between July and October.

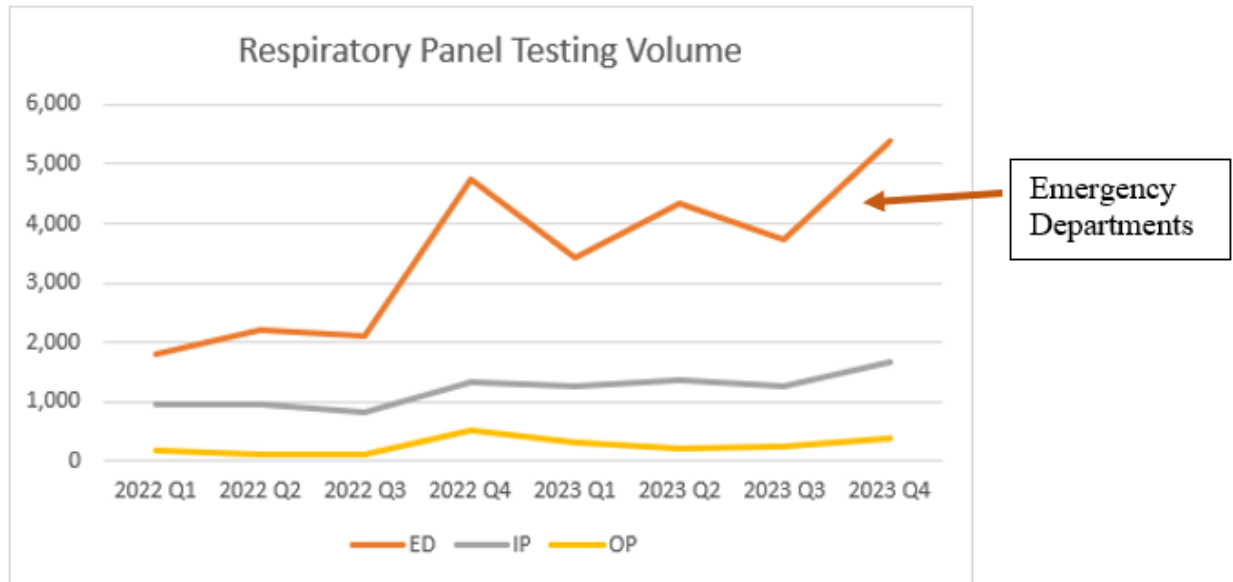
Lab Stewardship

- Everyone in healthcare is responsible for protecting our valuable resources. Multiplex molecular panels are revolutionizing the diagnosis and treatment of many infectious diseases, but appropriate ordering is critical. Results from the upper respiratory infection panels performed in Sutter during February 2024 are below.
- The positivity rate was 45% (1,121 patients), which by itself looks excellent. When broken down, however, 24% could have been tested with the COVID/Flu/RSV combo test at a much lower cost to the patient.
- Over 50% of the positive tests reported a common cold virus (*rhinovirus* or non-COVID *coronavirus*) for which there is no specific treatment and is usually easily diagnosed clinically. In one month, that amounts to 560 positive tests that didn't need to be performed and 269 tests where a more cost-effective test should have been ordered.

Respiratory Multiplex Panel	Positive Patients
February 2024 (n=2,508)	44.7%

Respiratory Pathogen	% of Positive Results	Other Alternative Tests
Rhinovirus/Enterovirus	39.5%	
Human Metapneumovirus	12.1%	
Coronavirus (Non-COVID)	11.3%	
SARS-CoV-2, NAA	9.1%	COVID PCR; Combo COVID/Flu/RSV
RSV	8.2%	RSV PCR; RSV Antigen; Combo COVID/Flu/RSV
Adenovirus	6.1%	
Parainfluenza (1-4) Virus	5.3%	
Influenza A	4.4%	Flu PCR; Combo COVID/Flu/RSV
Influenza B	2.4%	Flu PCR; Combo COVID/Flu/RSV
Mycoplasma pneumoniae	1.1%	
Bordetella parapertussis	0.4%	Pertussis PCR
Chlamydia pneumoniae	0.2%	
Bordetella pertussis	0.1%	Pertussis PCR

- The following graph shows run charts of Sutter emergency departments, inpatient and outpatient testing. Data for all of 2022 and 2023 are included. Previous data before that was severely affected by testing shortages. The orange run line shows that most of the tests are being performed in emergency departments (ED).



- Recognizing that emergency departments are the main source of testing orders, the question has to be asked about what is being done with the results.
 - [JAMA](#) March 4 published a review and meta-analysis specifically addressing that question.
 - Twelve studies including more than 6,000 patients revealed that there was no association with ED return visits or rates of hospitalizations.
 - Studies that only tested for influenza did reveal lower use of antibiotics and increased anti-influenza treatment in test positive patients.
 - The multiplex panels compared to no viral testing did not affect the ordering of antibiotics. This did not vary by subgroups including age, test method, publication date, number of viral targets, risk of bias, or industry funding.

Lab Stewardship Take-Home:

- Multiplex testing panels are a wonderful improvement in our diagnostic abilities with excellent sensitivity and the ability to detect a large number of organisms.
- They are expensive, but the cost is easily justified if the results will lead to measurable outcomes such as decreased antibiotic use. Studies do not support that desired outcome.
- The Cepheid cartridge that tests for COVID, flu and RSV is a better choice when those three diseases are being considered. When out of the respiratory season, testing only for SARS-CoV-2 will be the best option.
- Testing a patient with symptoms of a common cold is usually an unnecessary use of resources.
- The multiplex respiratory panel is probably most useful in immunocompromised patients or patients hospitalized for a viral respiratory infection who are negative for COVID/Flu/RSV.

Ebola Virus Disease (EVD) and Post-Exposure Prophylaxis (PEP)

- Filoviruses include Ebola Virus Disease and Marburg virus disease. The orthoebolavirus genus includes four different species that are associated with disease in humans. The Western Africa outbreak in 2013-2016 was due to the *O. zairense* species whereas the 2018-2020 outbreak in the Democratic Republic of Congo (DRC) and Uganda was caused by the *O. sudanense* species, more frequently referred to as Sudan ebolavirus.

- The relevance is that the two approved EVD vaccines and monoclonal antibody treatments are against *O. zairensis*. Studies are underway but there are no approved vaccines or treatment for the other three ebolavirus species or the Marburg virus. An oral medication for PEP is needed.
- [Science](#), March 15 published the study of obeldesivir (an oral prodrug of remdesivir) utilized as PEP in non-human primates (NHP) exposed to Sudan ebolavirus. Once daily for 10 days within 24 hours of exposure provided 100% protection against lethal infection. Although this is not the first medication being tested for PEP in NHP, this is the first oral formulation.

Ebolavirus Take-Home:

A 10-day course of once daily oral prodrug of remdesivir has been shown to prevent the development of Sudan ebolavirus in NHP. Whether this same efficacy will be seen when started after a longer incubation period still needs to be studied.

- Another option besides monoclonal antibodies or other IV medications is needed.

Benzathine Penicillin Shortage

- The FDA and Pfizer announced that the long-acting benzathine penicillin G shortage is now anticipated to continue until at least the fourth quarter of 2024. Extencillin has been approved by the FDA until the Bicillin-LA shortage resolves.
 - 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](#).
 - Benzathine penicillin should be reserved predominantly for pregnant people with syphilis and certain infants exposed to syphilis in utero.
 - Alternative regimens include doxycycline for 14 or 28 days depending on the stage of the syphilis.
 - [CDPH](#) released another health advisory on March 18.
 - Some counties also recommend benzathine penicillin for patients who are unable to comply with the full course of oral doxycycline.

The Tripledemic

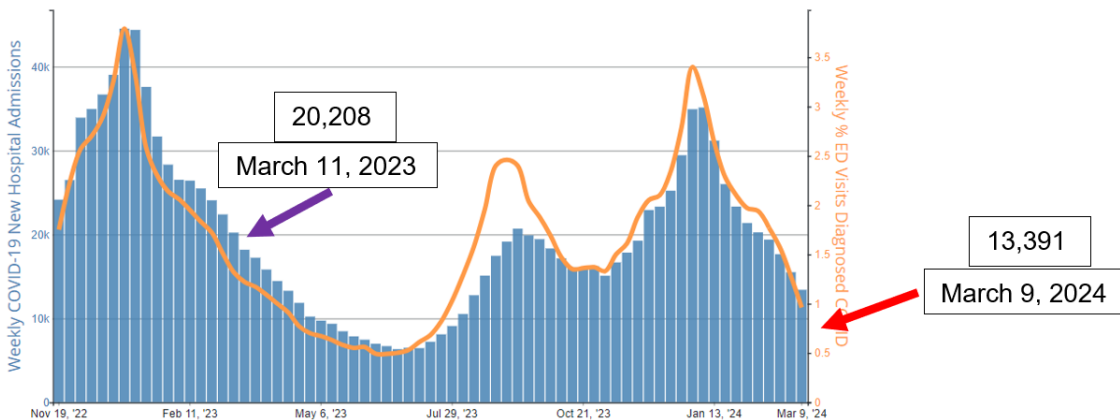
- JN.1 remains dominant, although JN.1.13 is increasing.
- Test positivity for SARS-CoV-2 within Sutter is at the lowest level since we started weekly reporting April 2023.
- Circulating influenza has transitioned from predominantly A H1N1 to all three strains (A H1N1, A H3N2 and B). The flu season is waning but will continue a little longer because of this.
- The 2023-24 RSV is over in California

COVID-19

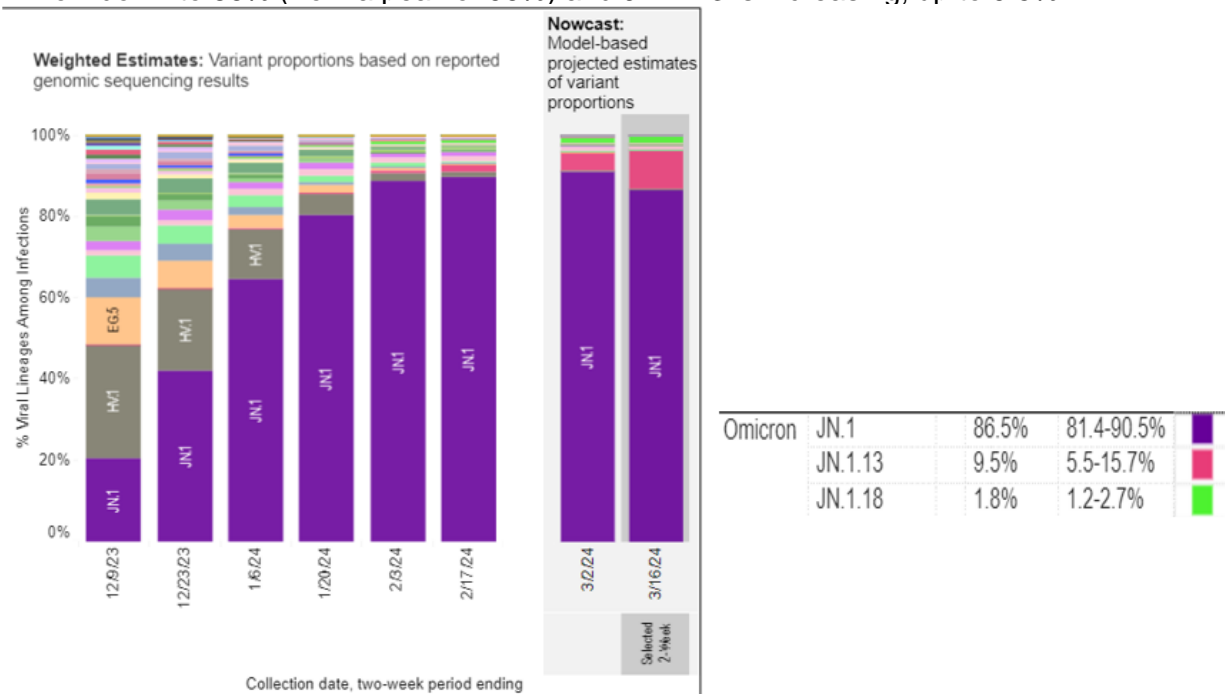
- JN.1 remains the most dominant strain in the world, but continues to be replaced by subvariants, especially JN.1.13 in the United States.
- [Hospitalizations](#) in the United States are a surrogate for the virulence of the circulating strain. The graph below has been modified to make it easier to see trends from the last 18 months. As before, the blue vertical bars represent the number of hospitalizations per week and the orange run line demonstrates the percentage of patients being diagnosed with COVID in emergency departments.

- Looking at the trend of the blue bars, the recent drop in hospitalization rates remains similar to one year ago. However, there remains a very important difference in the number of patients hospitalized due to circulating variants this year versus last year.
- The week of March 9, 2024 resulted in 13,391 hospitalizations (red arrow) compared to 20,208 during the week ending March 11, 2023 (purple arrow). Hospitalizations are 34% less year over year. Over 6,800 less people were in the hospital during this week in 2024 compared to 2023. Emergency department positivity rates were about the same during that 1-year comparison.

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

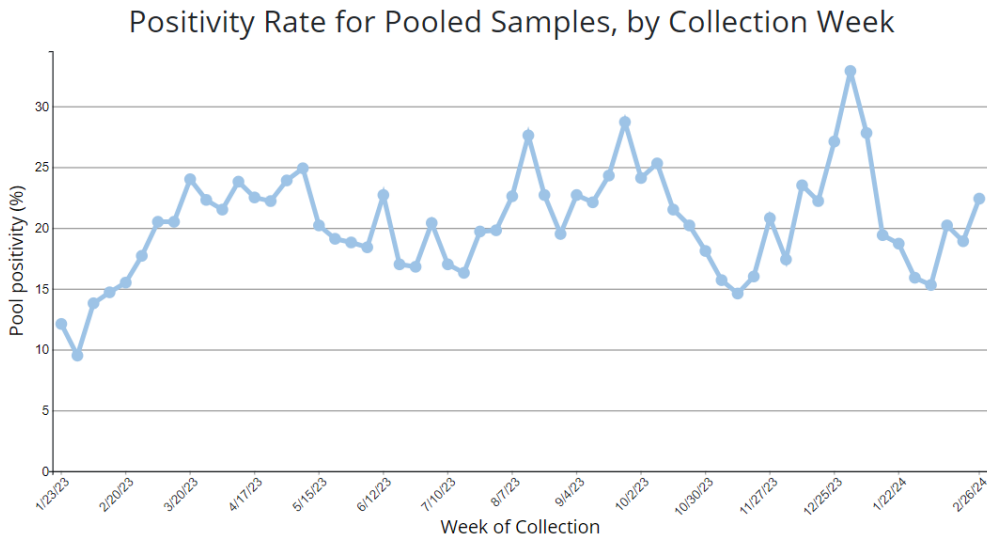


- [National genomic sequencing](#) was updated on March 15. JN.1 continues to slowly decrease, now down to 86% (from a peak of 96%) and JN.1.13 is increasing, up to 9.5%.

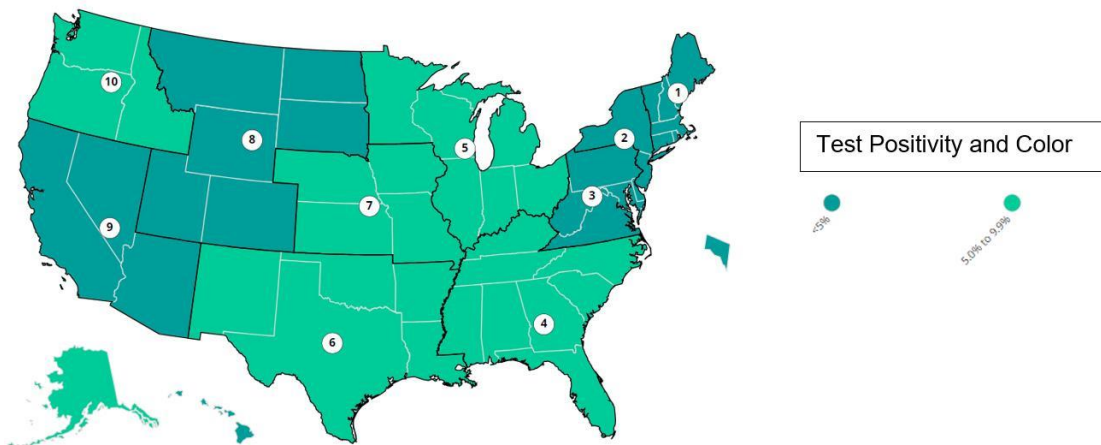


- Surveillance of international air travelers is conducted at several major U.S. airports as an early warning system and to fill gaps in worldwide genomic surveillance. It covers flights from more than 135 countries.

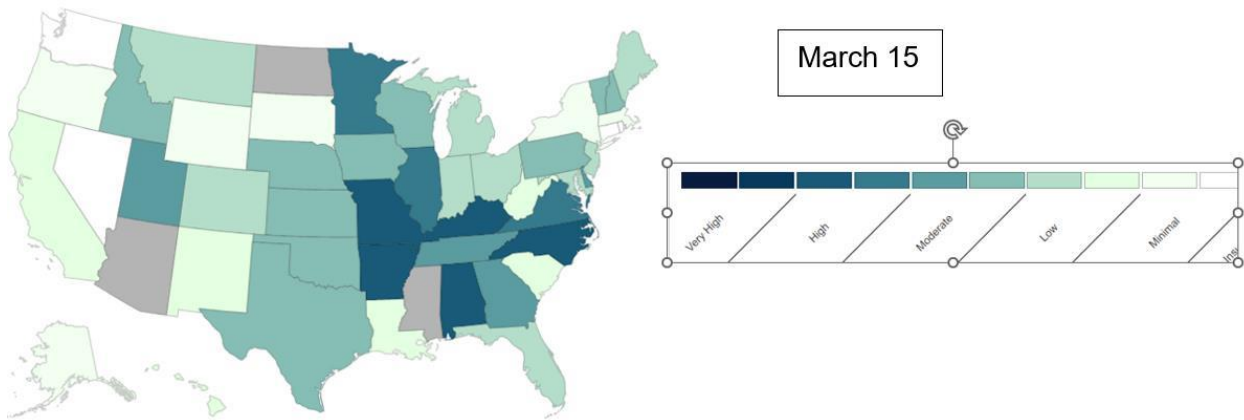
- Traveler-based genomic surveillance positivity rates are on the graph below. Positivity rates for the latest week reported (ending Feb. 26) increased to 22.4%. This is closer to the positivity rates seen over the last year. Remember that international testing data is at least 2 weeks from collection until reported on the graph.
- Notably, JN.1 identification increased back up to 95% from 88% (data not shown). None of the JN.1 subvariants are listed. Either they are still being included in the JN.1 data or the number of cases with those subvariants remains insignificant.



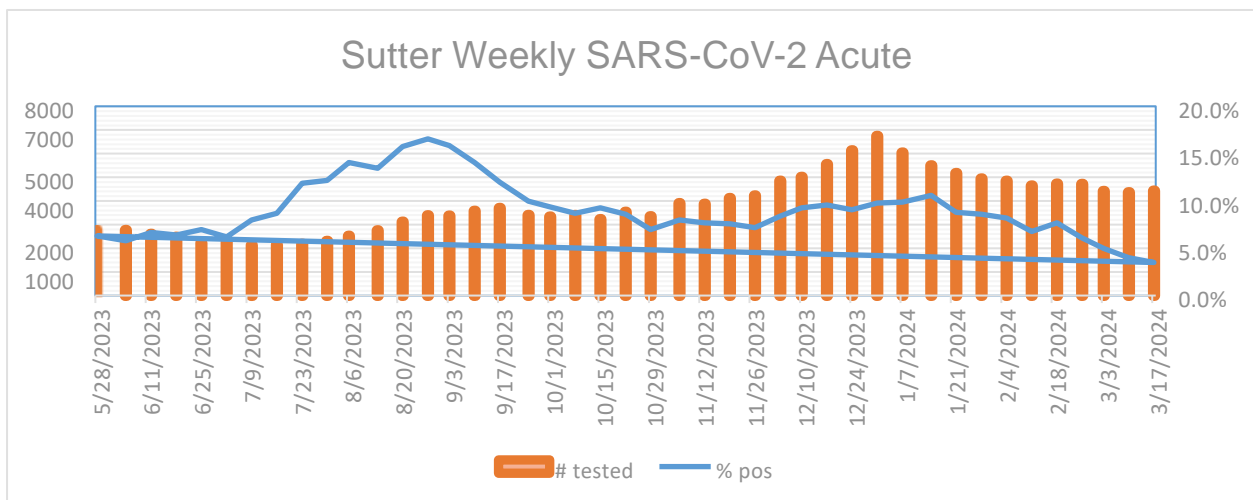
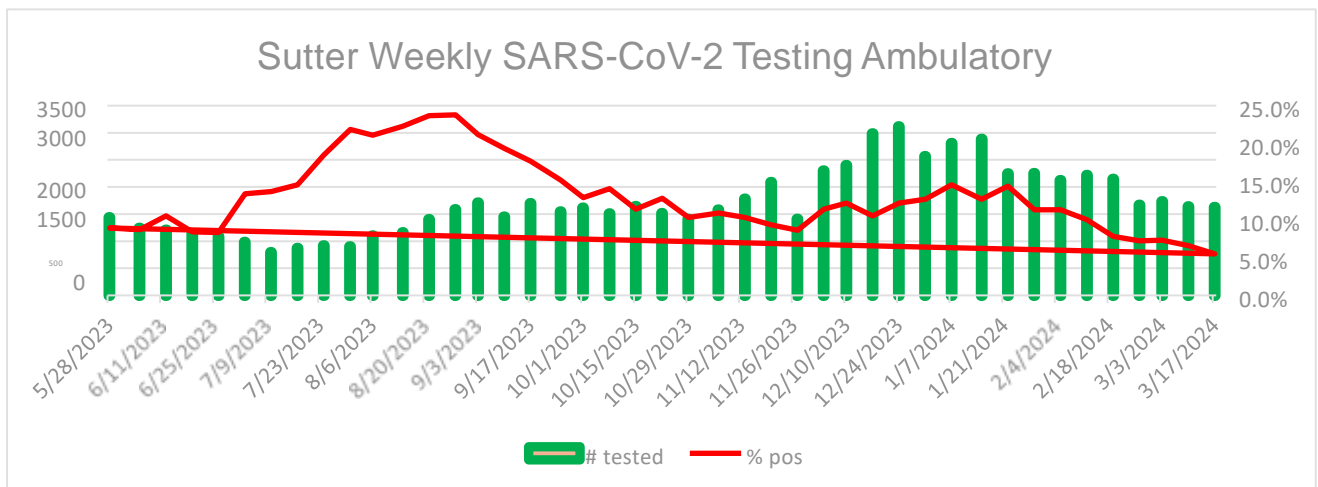
- The map below shows [national](#) molecular test positivity rates by region (updated March 15). Every region is now green with four regions being the dark green, representing the lowest positivity rate of <5%.



- SARS-Co-V-2 wastewater levels are shown on the map below from March 14. Similar to hospitalizations and testing positivity, wastewater levels have progressively decreased since JN.1 became the dominant strain. Most are moderate to low.



- Updated Sutter testing data below show a continued decline in positivity rates in both the ambulatory and acute ED settings. Acute is down to 3.5% and ambulatory is 5.5%. These are the lowest numbers since tracking started in April 2023.



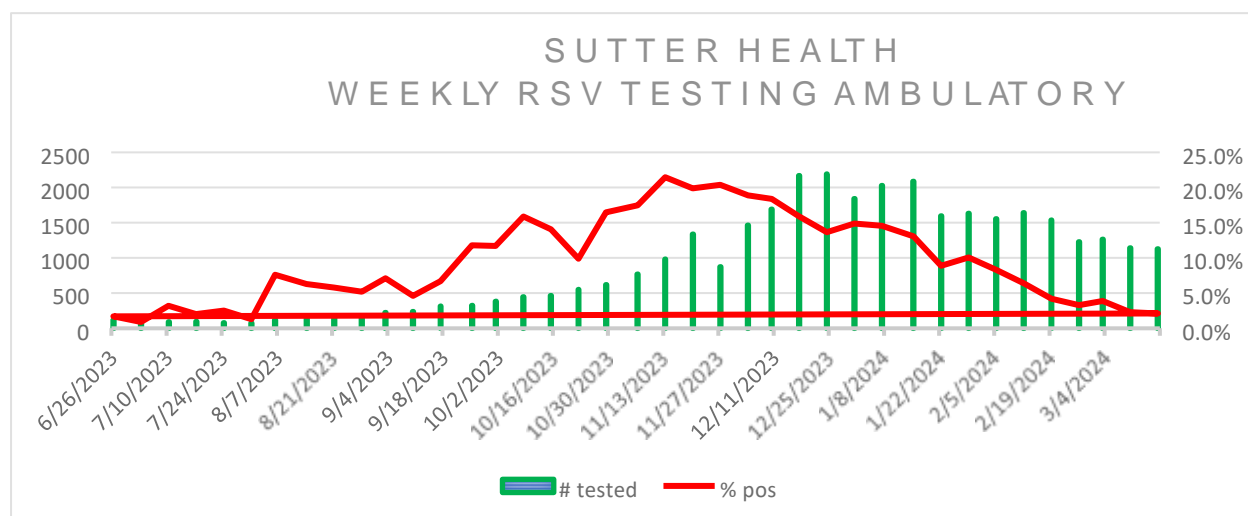
COVID-19 Take-Home:

JN.1 dominance has probably peaked. Vigilance remains necessary as the new strains start to appear.

- Hospitalizations and emergency department visits are much lower now compared to the identical week 1 year ago. This has to do with immunity, vaccines, available treatments and some changes in social behavior.

RSV

- The 2023-24 RSV season in California is over. CDPH reported rates are down to 1.8%, well below the 3% outbreak threshold.
- Sutter data, which is more real time, demonstrate that rates are down to 1%.



Nirsevimab Update

In early March, [CDC MMWR published](#) their latest effectiveness data for nirsevimab in preventing RSV-associated hospitalizations among infants entering their first RSV season. Nirsevimab effectiveness was estimated using a test-negative, case-control design among infants aged <8 months who were hospitalized with acute respiratory illness between Oct. 1, 2023 through Feb. 29, 2024. In summary:

- Infants who received nirsevimab <7 days before symptom onset were excluded.
- Nirsevimab effectiveness was 90% (95% CI = 75–96) against RSV-associated hospitalization in infants in their first RSV season.

	RSV Test Result		Receipt of Nirsevimab	
	Positive no. (%)	Negative no. (%)	Yes no. (%)	No no. (%)
Overall (all infants)				
699	407 (58)	292 (42)	59 (8)	640 (92)

- Of the 59 infants who received nirsevimab, only six patients tested positive for RSV and 53 patients tested negative following receipt.
- Median time from receipt of nirsevimab to symptom onset was 45 days.
- Receipt of nirsevimab was more frequent among infants with high-risk medical conditions than those without (46% versus 6%, $p < 0.001$).

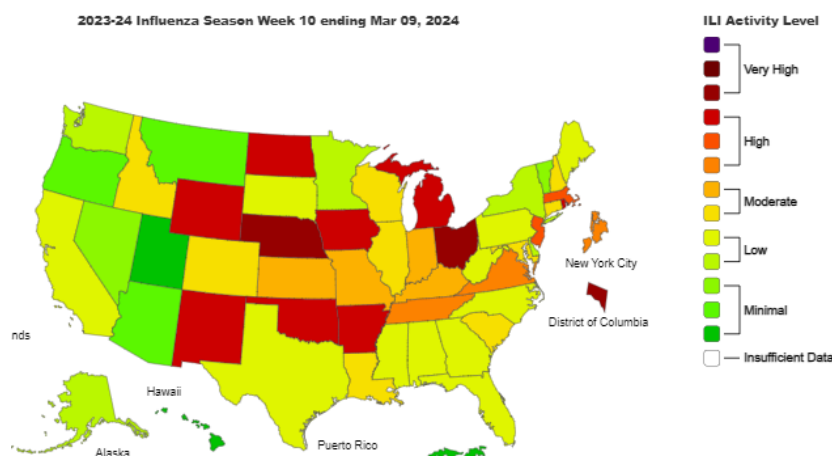
RSV Take-Home:

- The 2023-24 RSV season is done in California.
- A single dose of nirsevimab was highly effective against RSV-associated hospitalization in infants during the first RSV season it was available.

- The [CDC](#) writes that the best time to vaccinate adults > 60 years old against RSV is late summer or early fall. However, the vaccine can be administered anytime because the vaccine may provide protection for at least two winter seasons.

Influenza

- The weekly [CDC](#) Influenza Surveillance Report was released on March 15. It contains information ending March 9.
- Nationally influenza A H1N1, A H3N2 and B are circulating at approximately equal percentages. Rates do vary by region.
- Influenza-like illness (ILI), the surrogate for influenza used by the [CDC](#), is represented by the maps below. There are still substantial parts of the country where ILI is still quite high. Remember that this does not measure influenza but measures fever plus either sore throat or cough.



- The [CDPH](#) map below of influenza (last updated through March 9) shows that influenza rates remain low everywhere. The state influenza positivity rate decreased from 5.7% to 5.3% over the last 2 weeks.

Influenza Activity Levels*

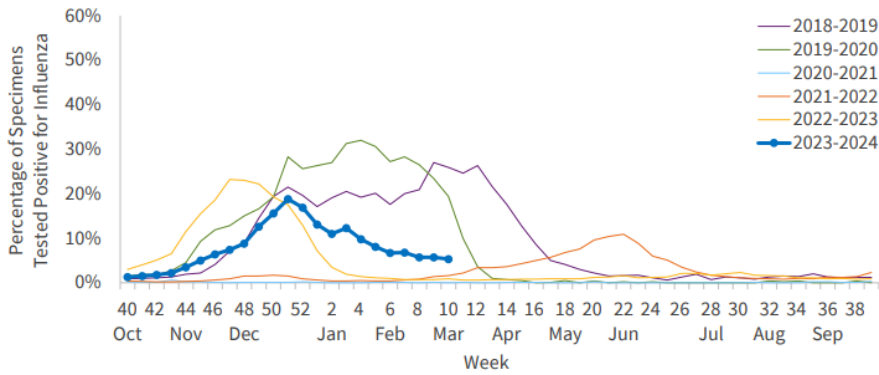


CDPH Influenza Activity Levels:

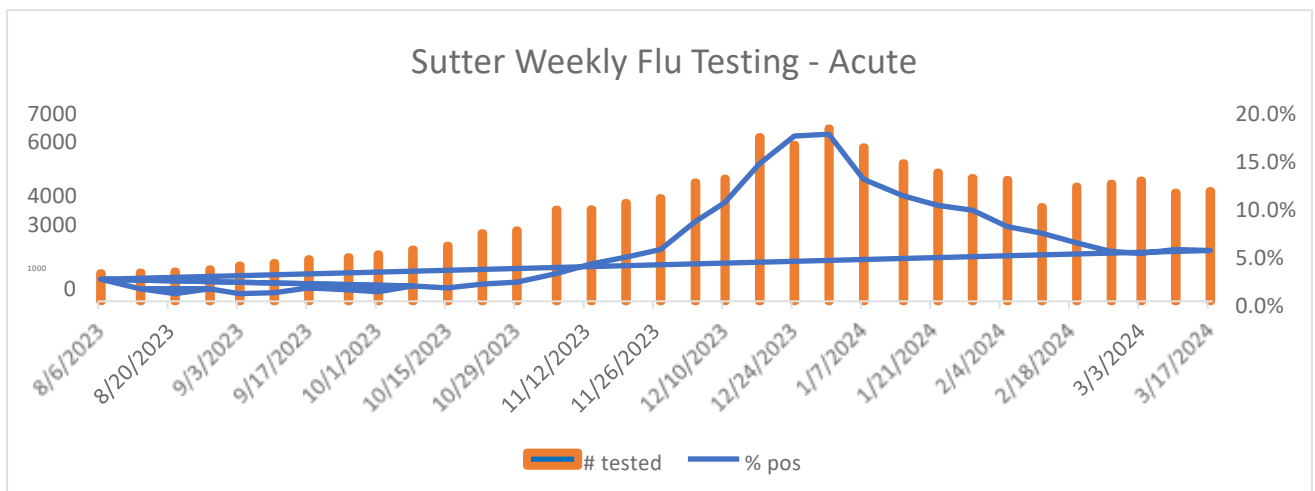
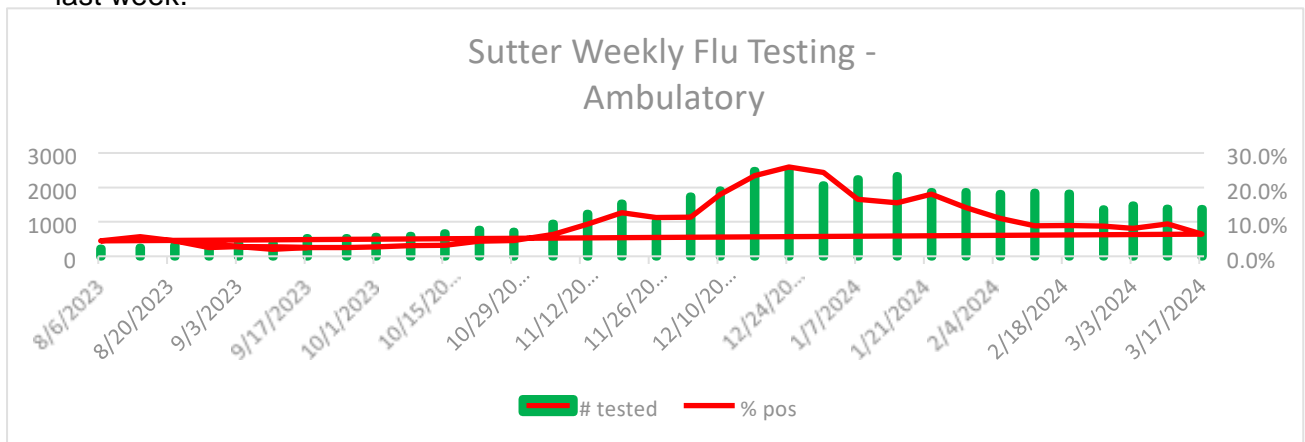
- Minimal:** The percentage of positive specimens is <2%
- Low:** The percentage of positive specimens is 2 - <10%
- Moderate:** The percentage of positive specimens is 10 - <20%

- The [CDPH graph](#) below demonstrates that present influenza activity continues to slowly drop (blue run line). The decreased slope is likely due to the increased circulation of influenza B and AH3N2, as well as the continued circulation of Influenza A H1N1.

Figure 1. Percentage of Influenza Detections at Clinical Sentinel Laboratories, 2018–2024 Season to Date



- The graphs below show Sutter emergency department and ambulatory influenza positivity rates. Although the ambulatory setting rates are improving, they are still 6.5%. In the acute setting (emergency departments), positivity rates are essentially unchanged at 5.3% in the last week.



Take-Home Influenza:

- All three strains of influenza are circulating at approximately similar levels, although there is significant variation by region.
- Because of the transition from predominantly A H1N1 to all three types of influenza circulating, the season is anticipated to continue at low elevated levels through part of April