



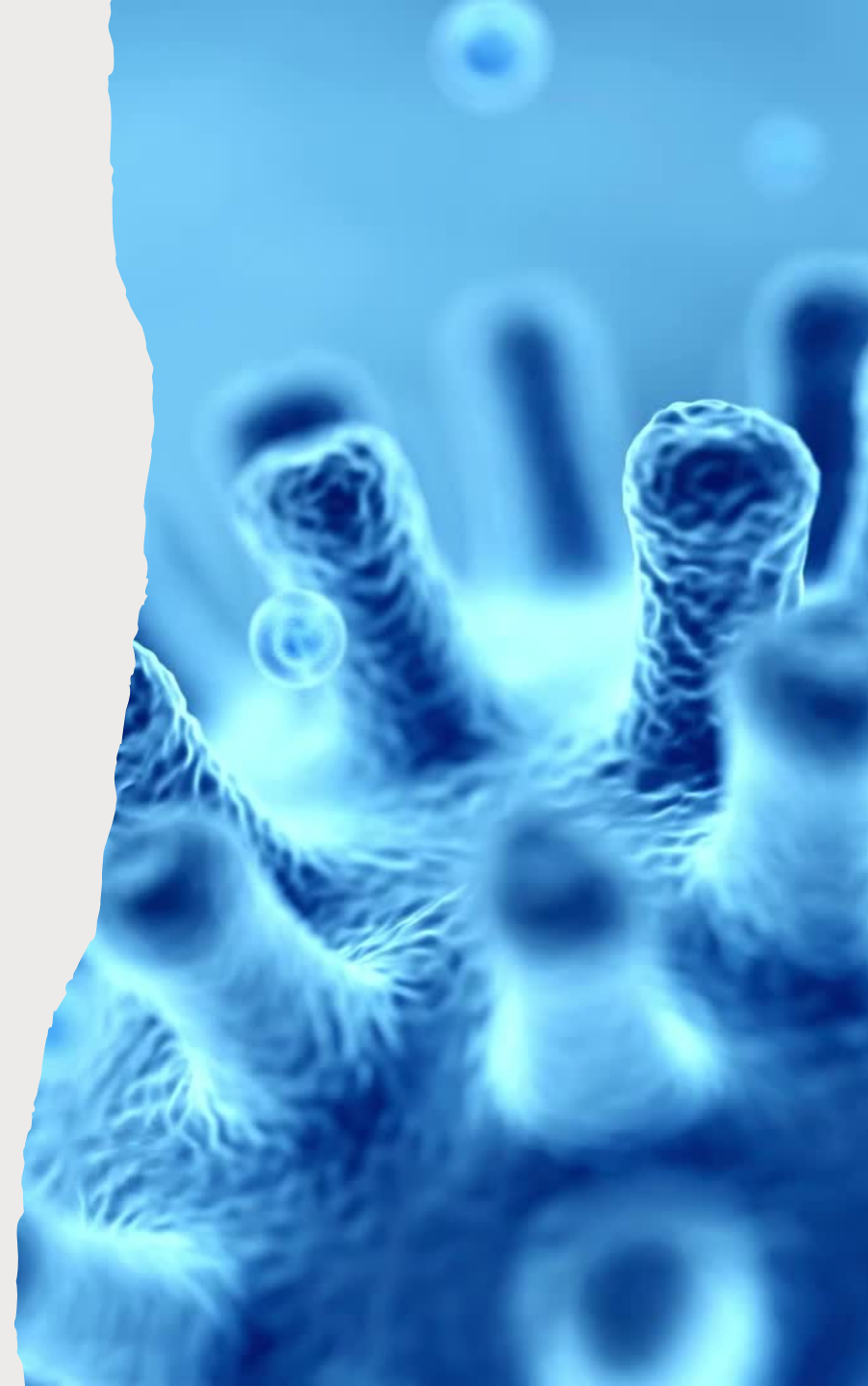
The Month in Virology

Jorge Mera, MD, FAACP
Infectious Diseases

March 2024

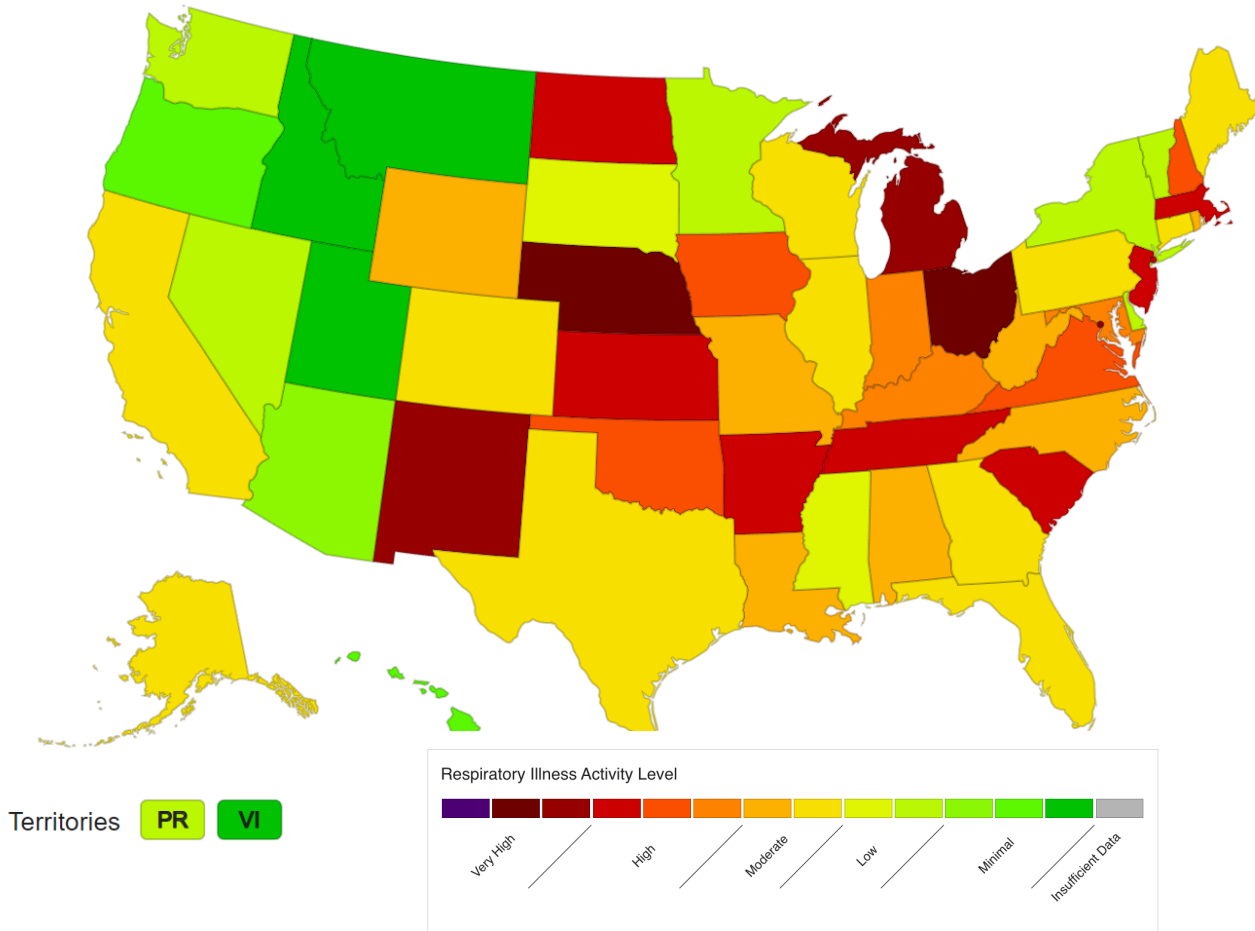
Outline

- Respiratory viruses
- Measles
- CDC respiratory guidelines updated
- HCV



US Level of Respiratory Illness Activity

- Activity levels determined weekly based on the percentage of visits to enrolled outpatient healthcare providers or emergency departments for fever and cough or sore throat reported to ILNet.
- Visits can be attributed to a variety of respiratory pathogens that cause these symptoms.

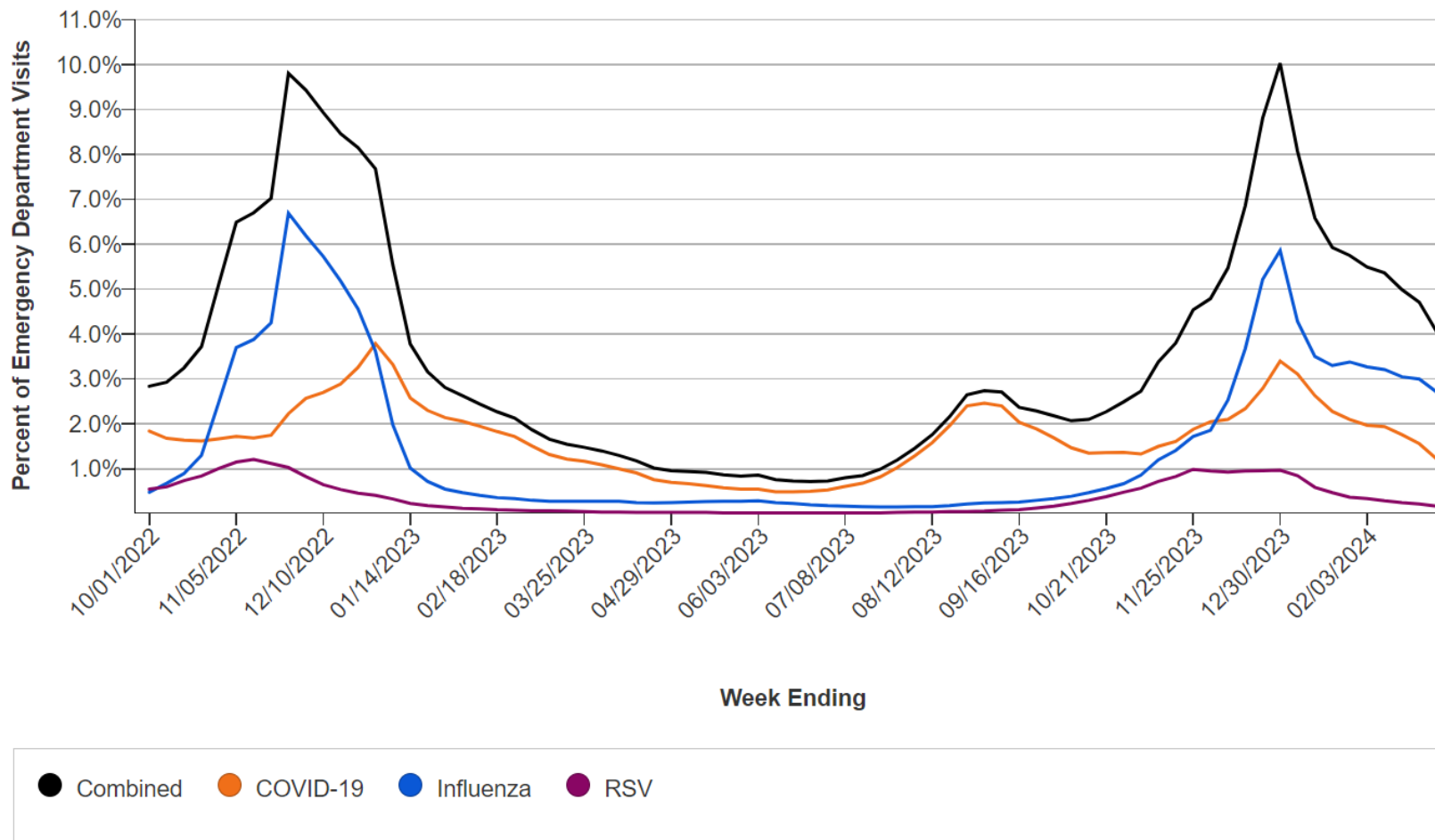


Data presented through: 03/09/2024; Data as of: 03/14/2024

Data presented through: 03/02/2024;
Data as of: 03/07/2024

Emergency Department Visits for Viral Respiratory Illness

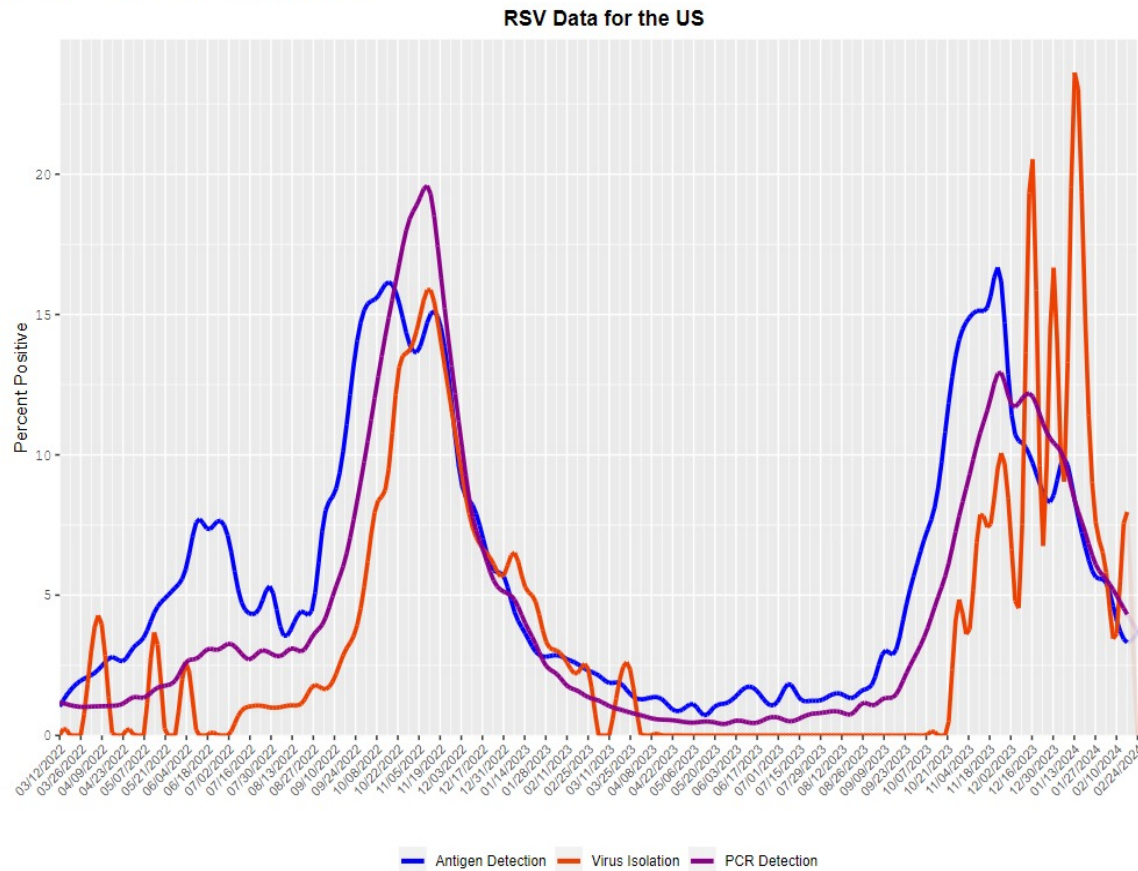
United States, Weekly percent of total emergency department visits associated with COVID-19, influenza, and RSV.



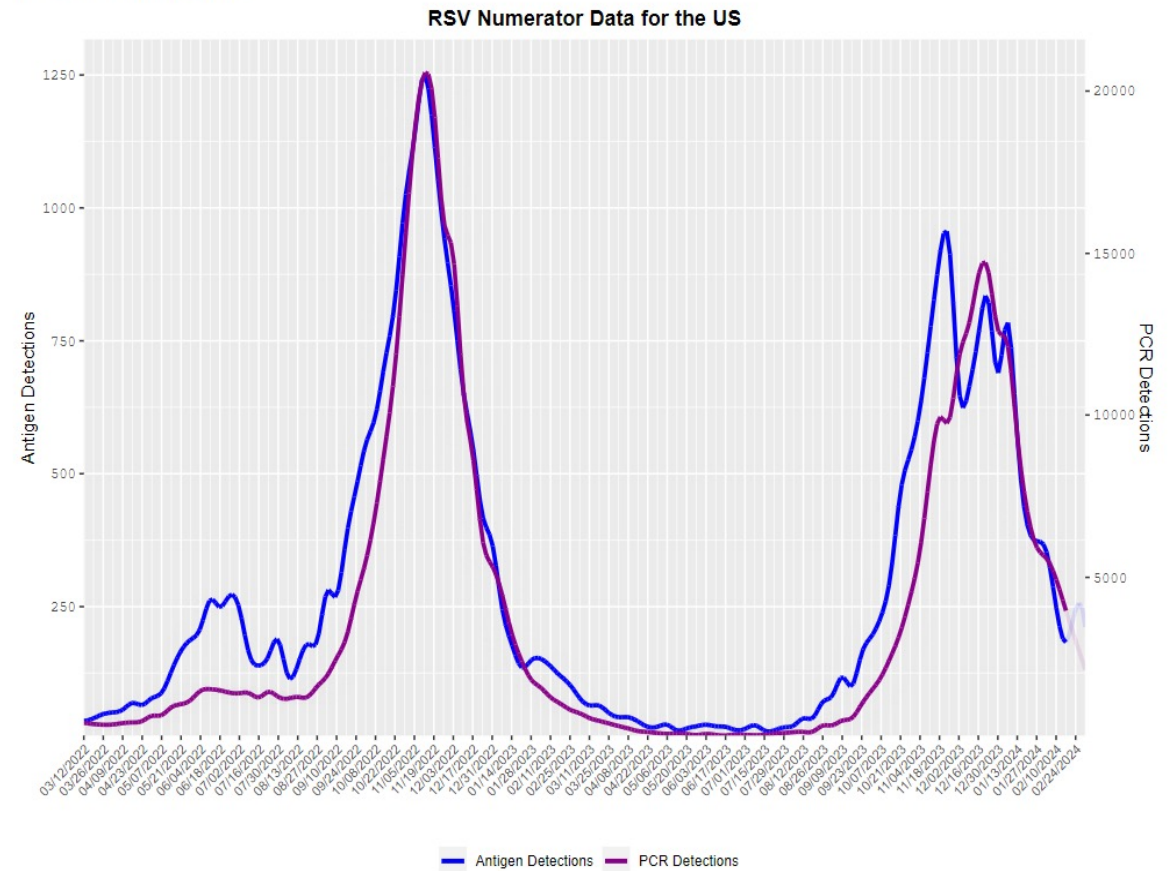
Data presented through: 03/02/2024; Data as of: 03/06/2024

RSV Trends

Percent Positive



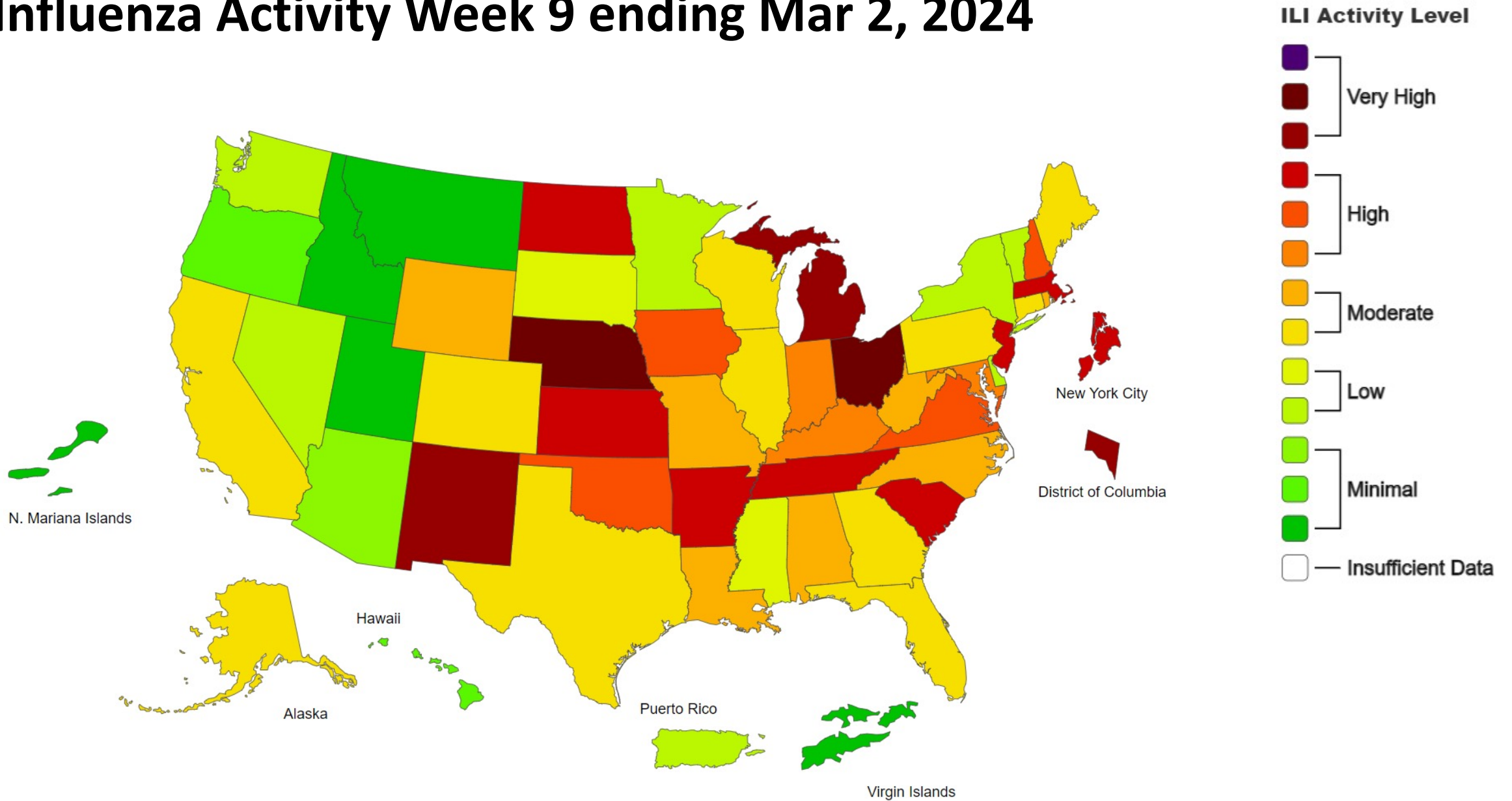
Detections



Last Reviewed: March 7, 2024

Source: [National Center for Immunization and Respiratory Diseases \(NCIRD\), Coronavirus and Other Respiratory Viruses Division](#)

Influenza Activity Week 9 ending Mar 2, 2024



COVID-19 Snapshot

Early Indicators

Test Positivity >

% Test Positivity

6.5%

(February 25 to March 2, 2024)

Trend in % Test Positivity

-1% in most recent week



Jan 13, 2024 Mar 2, 2024

Emergency Department Visits >

% Diagnosed as COVID-19

1.2%

(February 25 to March 2, 2024)

Trend in % Emergency Department Visits

-21.2% in most recent week



Jan 13, 2024 Mar 2, 2024

These early indicators represent a portion of national COVID-19 tests and emergency department visits. [Wastewater](#) information also provides early indicators of spread.

CDC | Test Positivity data through: March 2, 2024; Emergency Department Visit data through: March 2, 2024; Hospitalization data through: February 3, 2024; Death data through: February 3, 2024. Posted: March 11, 2024

COVID-19 Hospitalizations and Deaths

Severity Indicators

Hospitalizations >

Hospital Admissions

15,141

(February 25 to March 2, 2024)

Trend in Hospital Admissions

-13.6% in most recent week



Jan 13, 2024

Mar 2, 2024

Deaths >

% of All Deaths in U.S. Due to COVID-19

2.2%

(February 25 to March 2, 2024)

Trend in % COVID-19 Deaths

No change in most recent week



Jan 13, 2024

Mar 2, 2024

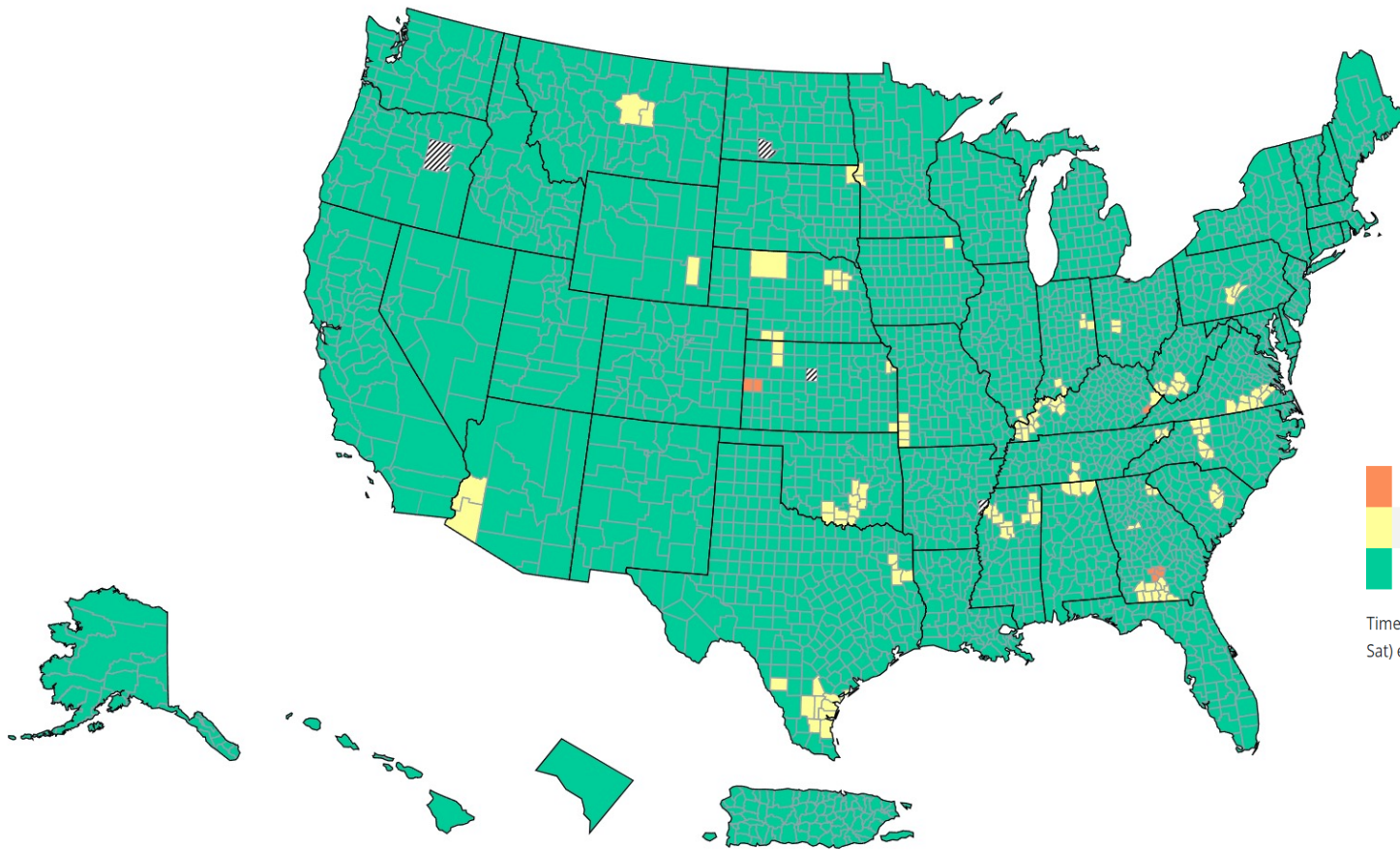
Total Hospitalizations

6,866,673

Total Deaths

1,183,143

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



COVID-19 hospital admissions levels in U.S. by county
Based on new COVID-19 hospital admissions per 100,000 population

	Total	Percent	% Change
≥ 20.0	7	0.22%	-0.31%
10.0 - 19.9	141	4.38%	-2.55%
<10.0	3071	95.4%	2.8%

Time Period: New COVID-19 hospital admissions per 100,000 population (7-day total) are calculated using data from the MMWR week (Sun-Sat) ending March 2, 2024.

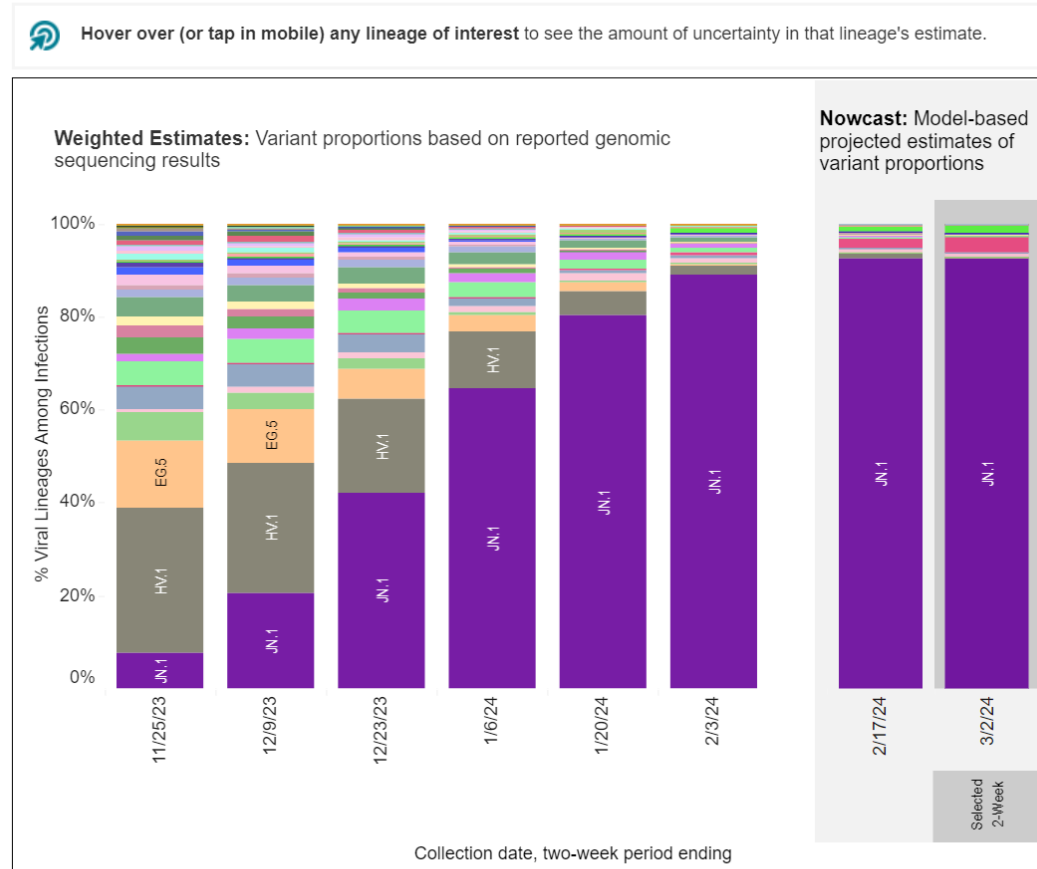
Territories



TheVirus

- The JN.1 variant took over globally with several subvariants
- BA.2.87.1, seems to be a variant of interest
 - Many mutations
 - Less evasive of our immune response
 - The current booster works
 - Earlier monoclonal antibodies may work again

Weighted and Nowcast Estimates in United States for 2-Week Periods in 11/12/2023 – 3/2/2024



Nowcast Estimates in United States for 2/18/2024 – 3/2/2024

USA			
WHO label	Lineage #	%Total	95%PI
Omicron	JN.1	92.3%	90.5-93.8%
	JN.1.13	3.3%	1.8-5.7%
	JN.1.18	1.8%	1.1-2.9%
	HV.1	0.4%	0.3-0.5%
	BA.2.86	0.3%	0.2-0.5%
	JG.3	0.2%	0.1-0.2%
	BA.2	0.2%	0.0-0.7%
	JD.1.1	0.1%	0.1-0.2%
	HK.3	0.1%	0.0-0.1%
	EG.5	0.0%	0.0-0.0%
	XBB	0.0%	0.0-0.0%
	GE.1	0.0%	0.0-0.1%
	EG.5.1.8	0.0%	0.0-0.0%
	JF.1	0.0%	0.0-0.0%
	XBB.1.9.1	0.0%	0.0-0.0%
	FL.1.5.1	0.0%	0.0-0.0%
	XBB.1.16.15	0.0%	0.0-0.0%
	XBB.1.5.70	0.0%	0.0-0.0%
	XBB.2.3	0.0%	0.0-0.0%
	XBB.1.16.6	0.0%	0.0-0.0%
XBB.1.16.11	0.0%	0.0-0.0%	
HF.1	0.0%	0.0-0.0%	
GK.1.1	0.0%	0.0-0.0%	
XBB.1.16	0.0%	0.0-0.0%	
GK.2	0.0%	0.0-0.0%	
XBB.1.9.2	0.0%	0.0-0.0%	
XBB.1.5	0.0%	0.0-0.0%	
XBB.1.42.2	0.0%	0.0-0.0%	
XBB.1.16.1	0.0%	0.0-0.0%	
EG.6.1	0.0%	0.0-0.0%	
Other	Other*	1.1%	0.6-2.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one 2-week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all 2-week periods displayed.
 # While all lineages are tracked by CDC, those named lineages not enumerated in this graphic are aggregated with their parent lineages, based on Pango lineage definitions, described in more detail here.
<https://www.pango.network/the-pango-nomenclature-system/statement-of-nomenclature-rules/>

March 11, 2020

4-year anniversary of COVID Pandemic Declared

Global Impact

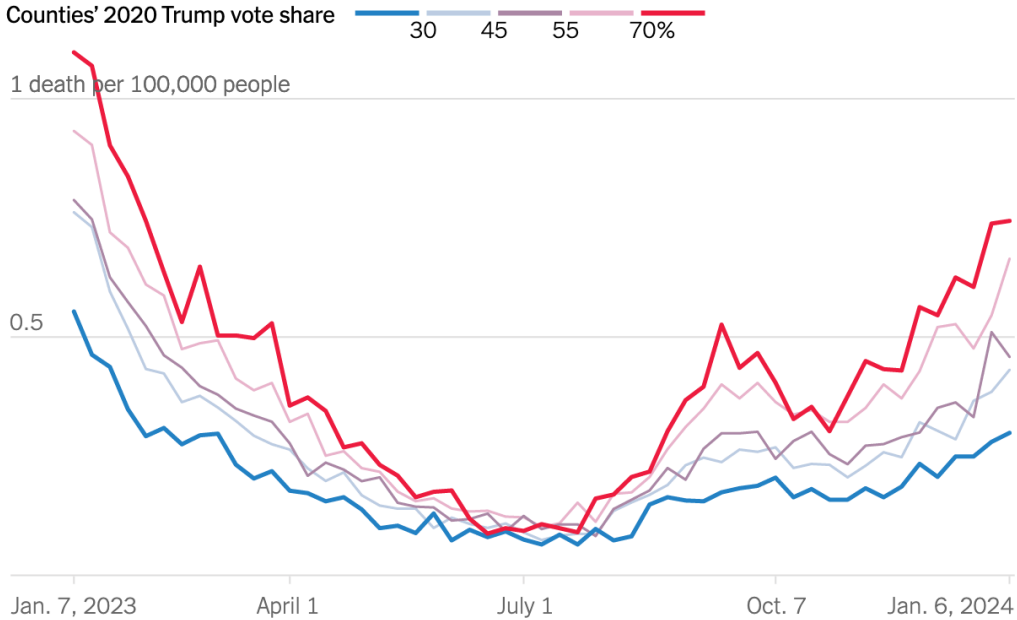
- Excess mortality ~ 30 million deaths
- Global reduction in life expectancy:
- “Most severe drops in life expectancy in 50+ years”
- Impact of long covid not addressed

In the United States

- Significant partisan gap death rates since vaccines were introduced.
- Death rates continue to worsen in counties with 70%+ Republican voters compared with <30%.

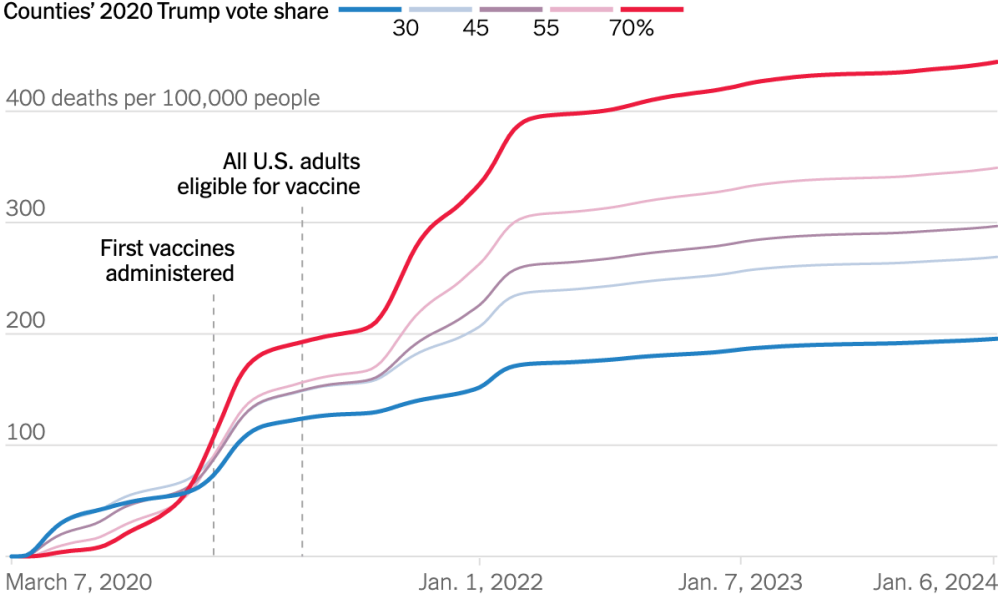
The Partisan GAP in COVID-19 Toll Death

Weekly U.S. Covid death rates in 2023



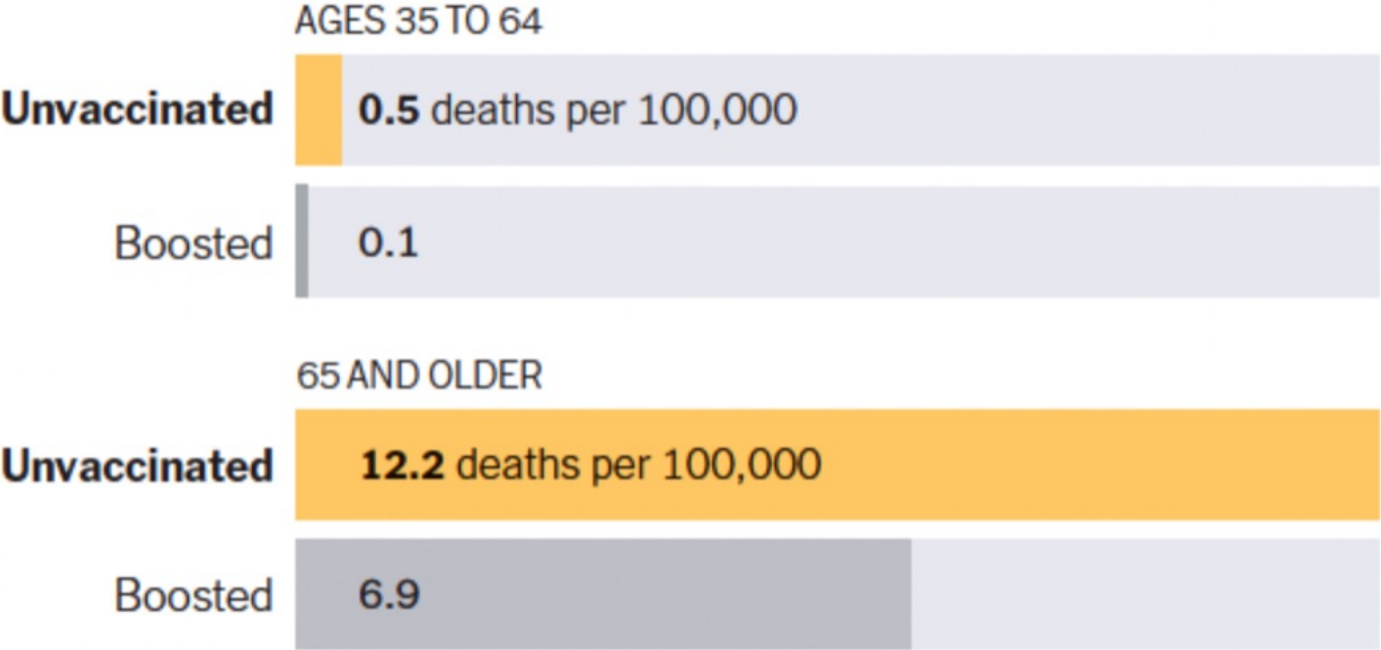
Note: Data excludes Alaska. • Sources: C.D.C. Wonder; Edison Research • By The New York Times

Cumulative U.S. Covid death rates



Note: Data excludes Alaska. • Sources: C.D.C. Wonder; Edison Research • By The New York Times

COVID DEATH RATES IN WASHINGTON STATE FROM OCT. 11 TO NOV. 7, 2023



Sources: Washington State Department of Health (death rates); COVID-19 School Data Hub | Note: Data for California is from 2019, 2022 and 2023.

Poll Question # 1

COVID-19 vaccination reduces the risk of post-COVID-19 cardiac and thromboembolic outcomes only during:

- A. First 30 days post COVID infection
- B. First 90 days post COVID infection
- C. First 180 days post COVID infection
- D. First 30 days post COVID infection and from day 90-180

The role of COVID-19 vaccines in preventing post-COVID-19 thromboembolic and cardiovascular complications

- **Objective**

- To study the association between COVID-19 vaccination and the risk of post-COVID-19 cardiac and thromboembolic complications.

- **Methods**

- Cohort study based on national vaccination campaigns from the UK, Spain and Estonia.
- Outcomes included HF, VTE and ATE
- Outcomes recorded in four-time windows after SARS-CoV-2 infection: 0–30, 31–90, 91–180 and 181–365 days.

Heart failure (HF), Venous Thromboembolism (VTE)
arterial Thrombosis/thromboembolism (ATE)

Mercadé-Besora N, Li X, Kolde R, *et al* The role of COVID-19 vaccines in preventing post-COVID-19 thromboembolic and cardiovascular complications *Heart* Published Online First: 12 March 2024. doi: 10.1136/heartjnl-2023-323483

The role of COVID-19 vaccines in preventing post-COVID-19 thromboembolic and cardiovascular complications:

- **Results**

- Infection were **0.53 for VTE**, 0.72 for **ATE** and **0.61 for HF**
- Included 10.17 million vaccinated and 10.39 million unvaccinated people.
- Vaccinated people had reduced risks of acute (30-day) and post-acute COVID-19 VTE, ATE and HF
 - sHR at 0–30 days after SARS-CoV-2 infection were of **0.22 for VTE**, **0.53 for ATE** and **0.45 for HF**
 - sHR at 91–180 days after SARS-CoV-2 **0.53 for VTE**, 0.72 for **ATE** and and 0.61 for **HF**

- **Conclusions**

- COVID-19 vaccination reduced the risk of post-COVID-19 cardiac and thromboembolic outcomes.
- These effects were more pronounced for acute COVID-19 outcomes

Mercadé-Besora N, Li X, Kolde R, *et al* The role of COVID-19 vaccines in preventing post-COVID-19 thromboembolic and cardiovascular complications *Heart* Published Online First: 12 March 2024. doi: 10.1136/heartjnl-2023-323483

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Notes from the Field: Measles Outbreak — Cook County, Illinois, October–November 2023

Report

On October 10, 2023

- Cook County DPH in Illinois was notified by hospital A, a large pediatric facility, of a suspected measles case in a child aged 2 years
- The child had immigrated from Yemen on September 29
- Had no history of receipt of measles, mumps, and rubella (MMR) vaccine.

October 5 the child visited hospital A's ED

- With fever, cough, and coryza and, after and negative COVID-19, influenza, and RSV test results

October 8, the child visited hospital B's ED with worsening respiratory symptoms

- Received a positive rhinovirus/enterovirus test
- Was transferred to hospital A and admitted for respiratory distress related to bronchiolitis

Poll Question # 2

- Which of the following statements are true about measles?
 - A. Measles outbreaks are increasing in the United States
 - B. Measles is highly contagious, and transmission only occur between children who have social contacts.
 - C. The median cost per measles patient costs ~ \$30,000
 - D. A and C are true
 - E. All the above are true

Notes from the Field: Measles Outbreak — Cook County, Illinois, October–November 2023

Report

October 9 while hospitalized

- The child developed a maculopapular rash

October 10, the child's family reported:

- Contact with a person with clinically diagnosed measles before U.S. arrival.

October 11 measles was confirmed by RT-PCR testing

- The child was discharged the same day.

Notes from the Field: Measles Outbreak — Cook County, Illinois, October–November 2023

Investigation and Outcomes

During the child's October 5–11 health care encounters, 247 health care workers[†] and 177 patients and patient companions were exposed

- Including 13 children aged <1 year, five immunosuppressed children, and one child aged >1 year with no history of MMR vaccination.

Among these 19 children

- Two received a dose of MMR vaccine within 72 hours of the exposure
- Thirteen received immune globulin.

In this community outbreak, five children developed measles

All patients were eligible to have received MMR vaccine before their exposures

- None had been vaccinated because of cultural barriers, limited access to care, and vaccine refusal.

Neither of the affected families was part of a similar close-knit social community,

- Vaccination coverage data for the patients' sociocultural groups were not available.

Public health responses are costly:

- Median cost per measles patient of approximately \$33,000 during during 2004-2017

Measles is highly contagious transmission can occur between children who are not social contacts.

- Outbreaks might become more common as global measles cases continue to rise
- And the number of children with exemptions to childhood vaccines increases.

Consider measles in susceptible patients with febrile rash and compatible symptoms.

- Vaccination is critical to prevent measles and measles outbreaks

Notes from the Field: Measles Outbreak — Cook County, Illinois, October–November 2023

What is already known about this topic?

- Measles is a highly contagious vaccine-preventable disease. In the United States, 2 doses of measles, mumps, and rubella (MMR) vaccine are recommended for all children aged 12–15 months and 4–6 years.

What is added by this report?

- During October 5–November 1, 2023, five measles cases occurred in unvaccinated, vaccine-eligible children aged 1–9 years who lived in the **same apartment building but did not socialize with one another**. **During the outbreak, approximately 400 persons were exposed to measles, including 13 children aged <1 year.**

What are the implications for public health practice?

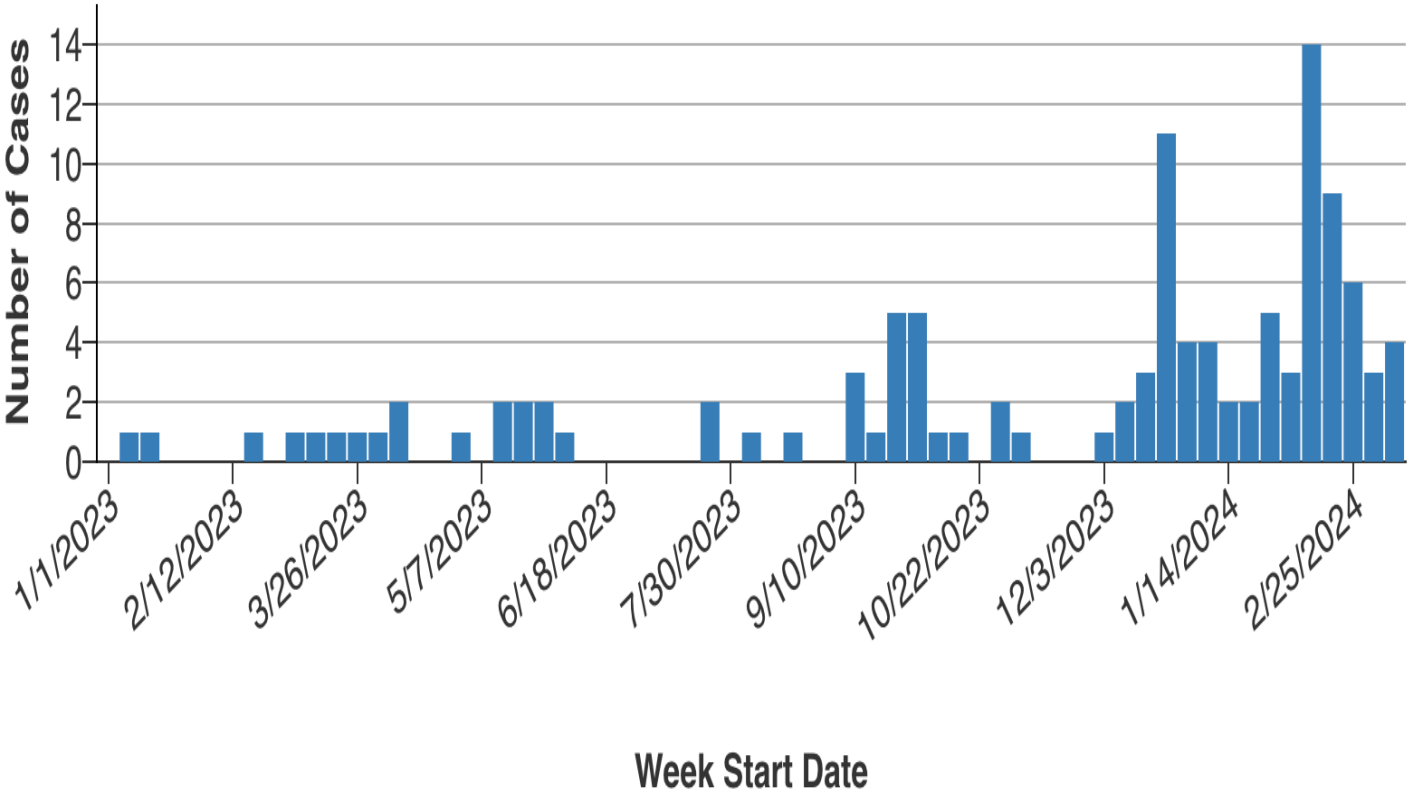
- Two doses of appropriately spaced MMR vaccine are recommended for all children and other susceptible persons to prevent measles cases and outbreaks.

Poll Question # 2

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Number of measles cases reported by week

2023-2024* (as of March 14, 2024)



Measles cases can occur due to:



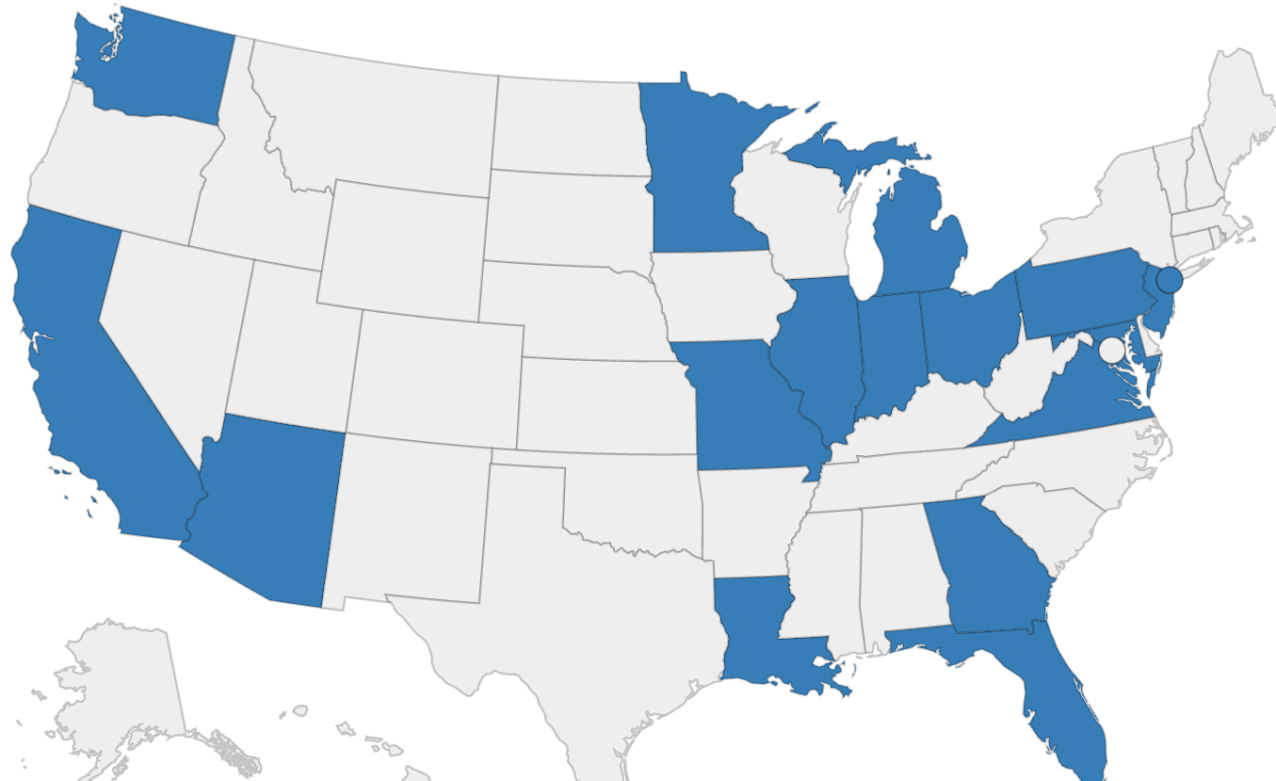
An increase in the number of travelers who get measles abroad and bring it into the U.S., and/or



Further spread in U.S. communities with pockets of unvaccinated people.

<https://www.cdc.gov/measles/cases-outbreaks.html>

Jurisdictions Reporting Cases in 2024



<https://www.cdc.gov/measles/cases-outbreaks.html>

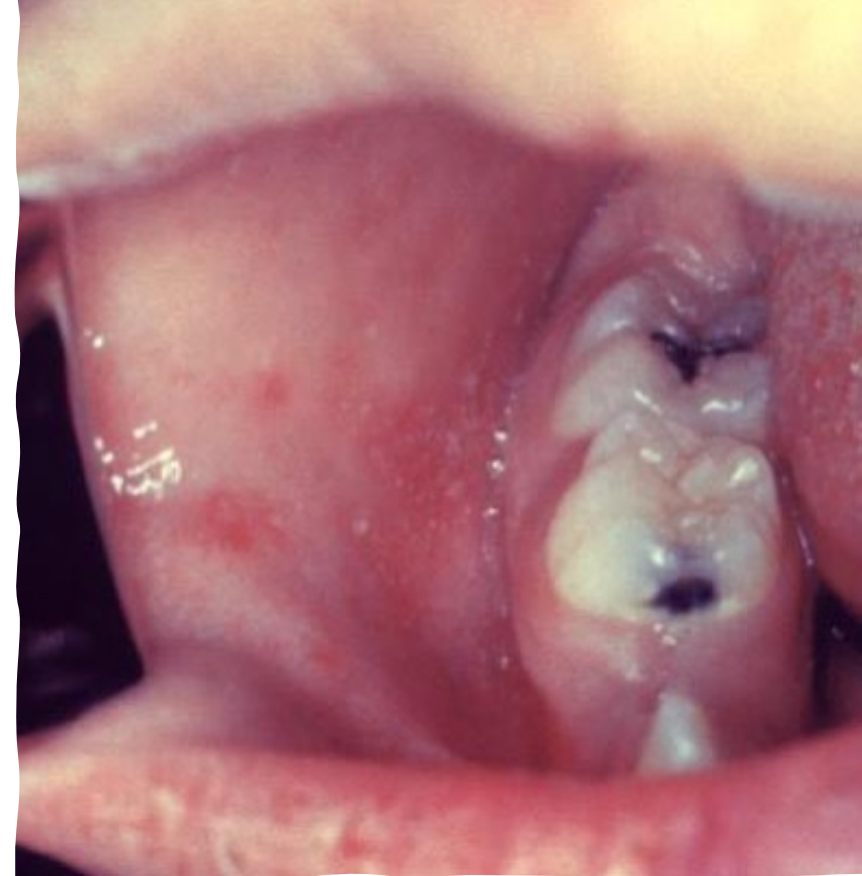
Poll Question # 2

- Which of the following statements are true about measles?
 - A. Koplik spots are pathognomonic of measles
 - B. Incubation period is 10-14 days
 - C. It is one of the most contagious infectious diseases
 - D. Vitamin A should be used for severe cases in children
 - E. A, B and C are true
 - F. A and C are true
 - G. All are true

Measles is an Acute Viral Respiratory Illness Characterized By:

- A prodrome of fever (as high as 105°F) and malaise
- The tree “C”s: Cough, Coryza and Conjunctivitis
- Pathognomonic enanthema (Koplik spots) followed by a rash
 - Described by Henry Koplik of New York in 1896
 - Bluish-white spots with red background present in 70% of patients
 - Destruction of glandular epithelia surrounded by phlebotasia around the submucosal gland duct

<https://www.cdc.gov/measles/hcp/index.html>



Measles is an Acute Viral Respiratory Illness Characterized By:

- Maculopapular rash
 - The rash usually appears about 14 days after a person is exposed.
 - The rash spreads from the head to the trunk to the lower extremities.
 - Patients are contagious from 4 days before to 4 days after the rash appears
 - Immunocompromised patients may not develop the rash.

<https://www.cdc.gov/measles/hcp/index.html>



Complications

- **Common complications from measles include:**
 - Otitis media, bronchopneumonia, laryngotracheobronchitis, and diarrhea.
 - Previously healthy children can have serious illness requiring hospitalization.
- **1/1,000 measles cases will develop acute encephalitis**
 - Which often results in permanent brain damage.
- **1-3/ 1,000 children will die from respiratory and neurologic complications.**
 - SSPE rare, but fatal degenerative disease of the central nervous system
 - Generally, develop 7 to 10 years after measles infection.

People at high risk for complications

- **Infants and children aged <5 years**
- **Adults aged >20 years**
- **Pregnant women**
- **People with compromised immune systems, such as from leukemia and HIV infection**

<https://www.cdc.gov/measles/hcp/index.html>

Transmission

Measles is one of the most contagious of all infectious diseases

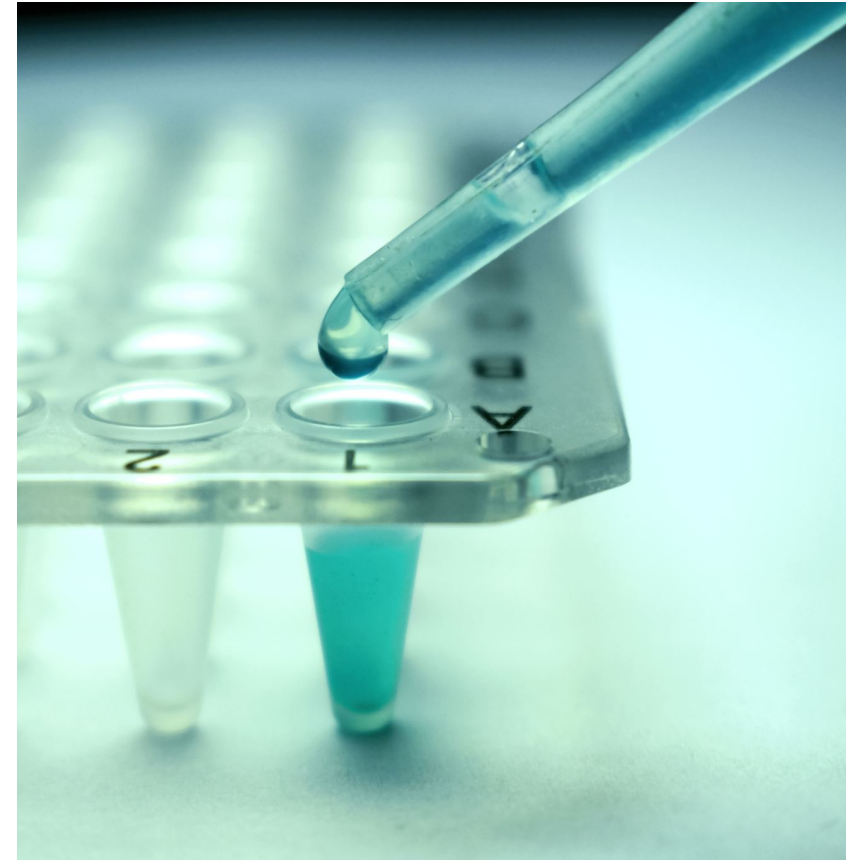
9 out of 10 susceptible persons with close contact to a measles patient will develop measles.

The virus is transmitted by direct contact with infectious droplets or by airborne spread when an infected person breathes, coughs, or sneezes.

Measles virus can remain infectious in the air for up to two hours after an infected person leaves an area.

Diagnosis and laboratory testing

- Detection of measles-specific IgM antibody in serum and measles RT-PCR) in a respiratory specimen
- Obtain both a serum sample and a throat swab (or nasopharyngeal swab) from patients suspected to have measles at first contact with them.
- Collecting both respiratory and urine samples can increase the likelihood of detecting it



Acceptable presumptive evidence of immunity against measles includes at least **one** of the following

- **Written documentation of adequate vaccination:**
 - One or more doses of a measles-containing vaccine administered on or after the first birthday for preschool-age children and adults not at high risk
 - Two doses of measles-containing vaccine for school-age children and adults at high risk, including college students, healthcare personnel, and international travelers
- **Laboratory evidence of immunity**
- **Birth before 1957**

Do not accept verbal reports of vaccination without written documentation as presumptive evidence of immunity

Measles Vaccination

Measles can be prevented with measles-mumps-rubella (MMR) or MMRV vaccine.

- One dose of MMR vaccine is approximately 93% effective at preventing measles;
- two doses are approximately 97% effective.

Vaccine recommendations for children

- MMR vaccine starting with the first dose at 12 through 15 months of age, and the second dose at 4 through 6 years of age or at least 28 days following the first dose
- MMRV vaccine for children 12 months through 12 years of age; the minimum interval between doses is three months.

Vaccine recommendations for adults

- People who are born during or after 1957 who do not have evidence of immunity against measles should get at least one dose of MMR vaccine.

Measles Isolation

- Infected people should be isolated for 4 days after they develop a rash
- Airborne precautions should be followed in healthcare settings regardless of vaccination status
- The preferred placement for patients who require airborne precautions is a single-patient airborne infection isolation room
- Regardless of presumptive immunity status
 - All healthcare staff entering the room should use respiratory protection consistent with airborne infection control

Post-exposure Prophylaxis and Treatment

Post-exposure prophylaxis (PEP)

- People exposed to measles who cannot readily show that they have evidence of immunity against measles should be offered PEP.
 - Administer MMR vaccine within 72 hours of initial measles exposure, **or**
 - Immunoglobulin (IG) within six days of exposure. Do **not** administer MMR vaccine and IG simultaneously, as this practice invalidates the vaccine.

Treatment

- There is no specific antiviral therapy for measles.
- Severe measles cases among children, should be immediately treated with vitamin A.
 - 50,000 IU for infants younger than 6 months of age
 - 100,000 IU for infants 6–11 months of age
 - 200,000 IU for children 12 months of age and older

CDC Eases Isolation Guidance for Respiratory Viruses

Basis of the Recommendations

- States and countries that relaxed their recommended isolation times for infection with SARS-CoV-2 “have not seen increased hospitalizations or deaths related to COVID-19.”
- The recommendations include provisions for those who are at a higher risk of developing severe illness from infection
 - Such as older adults, young children, people who are immunocompromised, people with disabilities, and people who are pregnant.

CDC Eases Isolation Guidance for Respiratory Viruses

Updated measures to combat respiratory viruses such as SARS-CoV-2, influenza, and RSV

Respiratory Virus Guidance Snapshot

Core prevention strategies

- Immunizations**
- Hygiene**
- Steps for Cleaner Air**
- Treatment**
- Stay Home and Prevent Spread***

Additional prevention strategies

- Masks**
- Distancing**
- Tests**

***Stay home and away from others until, for 24 hours BOTH:**

- Your symptoms are getting better
- You are fever-free (without meds)

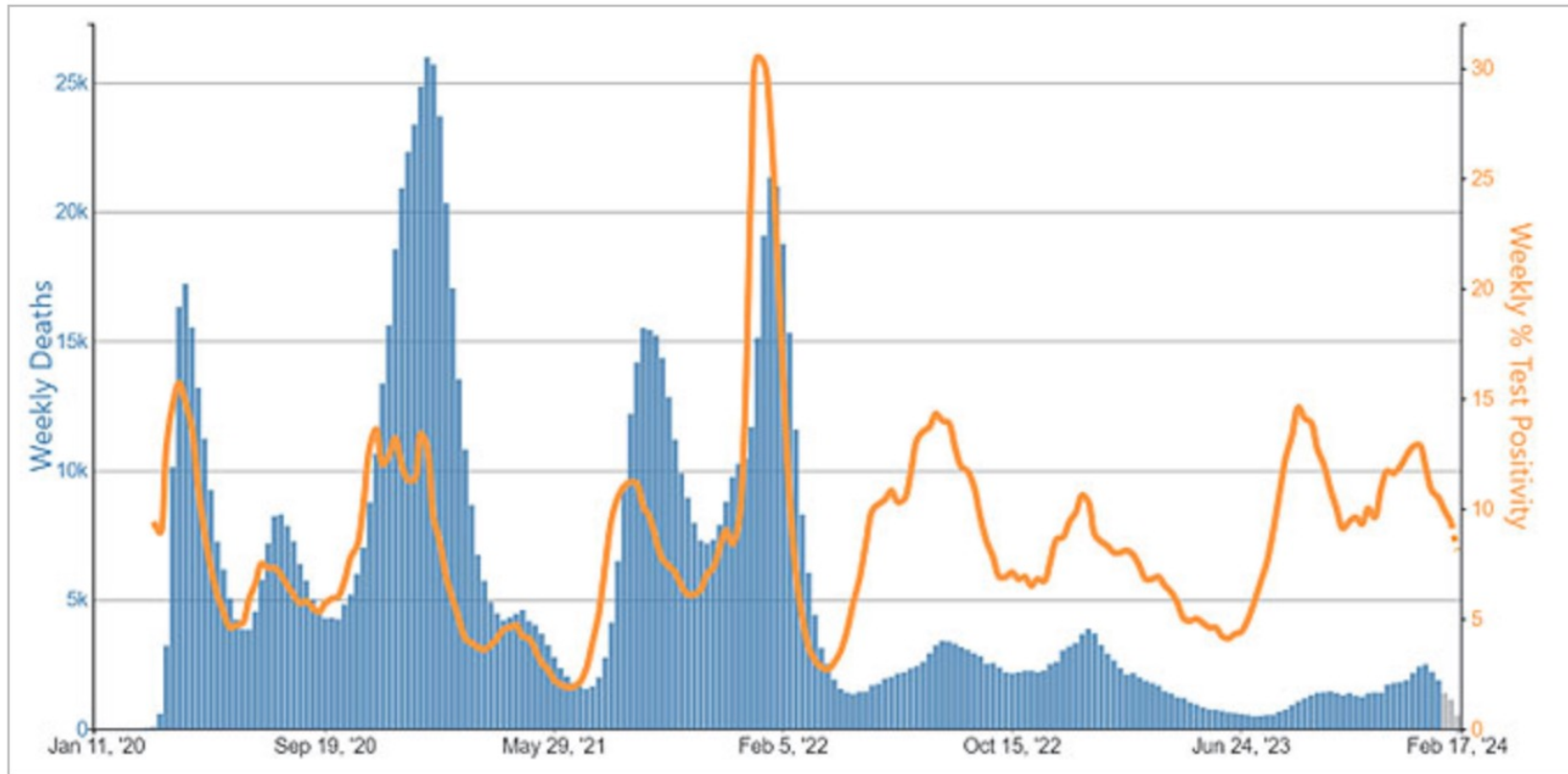
Then take added precaution for the next 5 days

Layering prevention strategies can be especially helpful when:

- ✓ Respiratory viruses are causing a lot of illness in your community
- ✓ You or those around you have risk factors for severe illness
- ✓ You or those around you were recently exposed, are sick, or are recovering

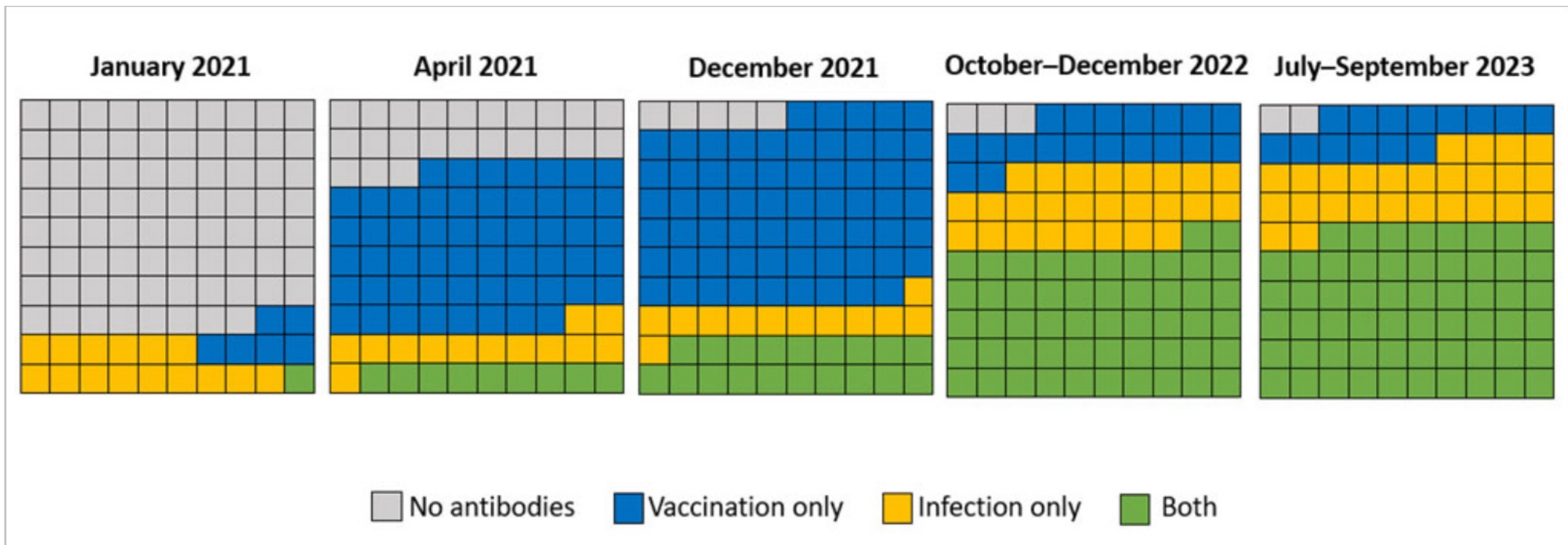
<https://www.cdc.gov/respiratory-viruses/guidance/respiratory-virus-guidance.html>

SARS-CoV-2 test positivity (orange line) has remained elevated, a marker of ongoing COVID-19 spread, but deaths (blue bars) have declined substantially

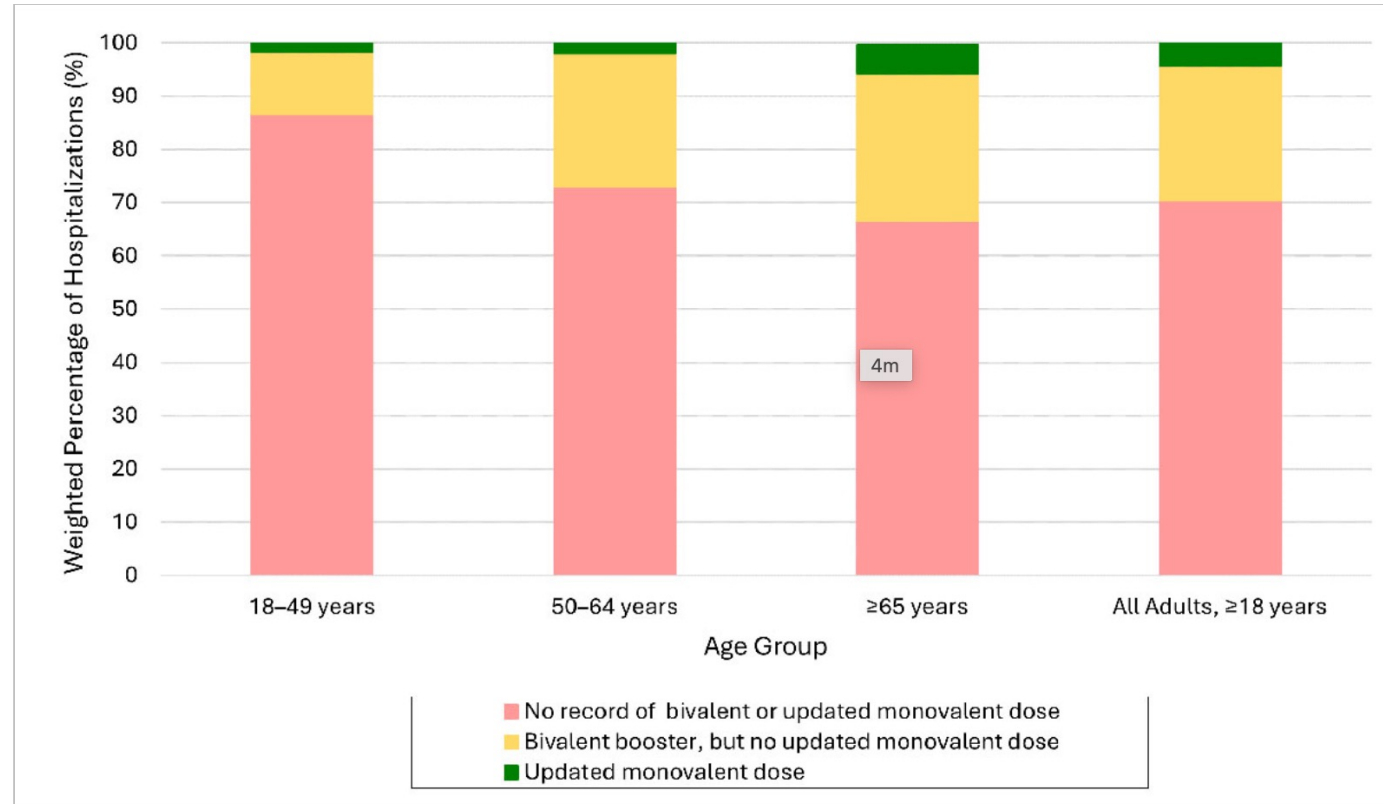


Provisional COVID-19 Deaths and COVID-19 Nucleic Acid Amplification Test (NAAT) Percent Positivity, by Week, in The United States, Reported to CDC. Sources: Provisional Deaths from the CDC's National Center for Health Statistics (NCHS) National Vital Statistics System (NVSS) National Respiratory and Enteric Virus Surveillance System (NREVSS) Figure from CDC's [COVID Data Tracker](#).

Prevalence of vaccine-induced and infection-induced antibodies against SARS-CoV-2 among a cohort of U.S. blood donors ≥ 16 years



Over 95% of adults hospitalized with COVID-19 during October–November 2023 had not received an updated (2023–2024) COVID-19 vaccine (Preliminary)



Data from COVID-NET. Data are preliminary as they only include two months of hospitalization data for which the updated monovalent vaccine dose was recommended. Continued examinations of vaccine registry data are ongoing. **No record of bivalent or updated monovalent dose:** No recorded doses of COVID-19 bivalent or updated 2023-2024 monovalent dose. **Bivalent booster, but no updated monovalent doses:** Received COVID-19 bivalent booster vaccination but no record of receiving updated 2023-2024 monovalent booster dose. **Updated monovalent dose:** Received updated 2023-2024 monovalent dose. Persons with unknown vaccination status are excluded.

Vaccine Effectiveness of 2023-2024 vaccine against hospitalization among immunocompetent adults aged ≥ 18 years

COVID-19 vaccination dosage pattern	No. (col %)		Median interval since last dose for vaccinated, days (IQR)	VE %* (95% CI)	Vaccine Effectiveness (%)
	COVID-19 case-patients	COVID-19 control patients			
No updated dose (Ref)	15,932 (92)	98,218 (88)	669 (403–792)	Ref	
Received updated dose	1,297 (8)	13,378 (12)	44 (26–64)	47 (44–50)	
7–59 days earlier	825 (5)	9,372 (8)	33 (20–46)	51 (47–54)	
60–119 days earlier	472 (3)	4,006 (4)	74 (66–83)	39 (33–45)	

0 20 40 60 80 100

VE estimates adjusted for age, sex, race and ethnicity, geographic region, and calendar time. MMWR February 29, 2024

<https://www.cdc.gov/respiratory-viruses/guidance/respiratory-virus-guidance.html>

COVID-19-associated deaths based on reports on death certificates declined over 5-fold since their peak in 2020-2021 and are now at the same order of magnitude as estimated influenza deaths

Year corresponding with start of influenza season (Oct. 1- Sept. 30)	Reported COVID-19 deaths*	Reported influenza deaths	Estimated influenza deaths**	Reported RSV deaths
2018-2019	0	7,181	19,000–96,000	243
2019-2020	208,601	9,432	17,000–85,000	345
2020-2021	517,783	876	Not estimated	85
2021-2022	331,885	2,856	4,000–24,000	396
2022-2023	89,573	9,559	18,000–97,000	736
2023-2024 (through Feb. 17)	32,949 to date	5,854 to date	17,000–50,000 to date	587 to date

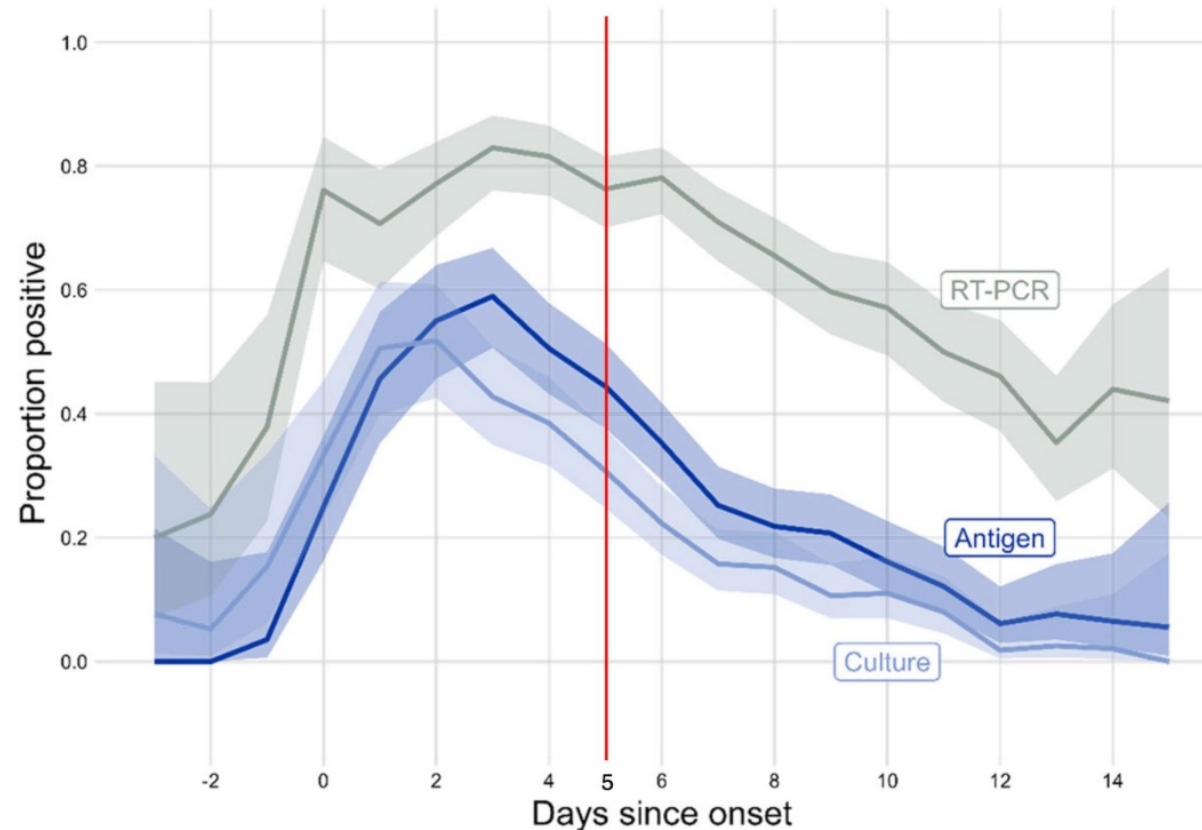
*Reported death data from CDC's National Vital Statistics System based on death certificates, available at [CDC WONDER](https://wonder.cdc.gov/). Data from 2022-2024 are provisional and subject to change.

ERIC TOPOL: GroundTruths

“I remain very disappointed and surprised by the recent change (1 March) of CDC policy towards isolation, without regard to using rapid antigen tests. Their own data shows that at least 1 in 3 people will still be infectious at 5 days after symptom onset! That’s by culturable virus, the gold standard, which tracks very closely with the rapid tests. To reduce infecting others, especially high-risk vulnerable individuals, no less adding to the toll of Long Covid, rapid tests should be used before people circulate.”

<https://erictopol.substack>

Highest levels of culture-positive SARS-CoV-2, an indicator of infectiousness, occur in the days around and after symptom onset, with a small proportion of people continuing to have culturable virus beyond one week



Unpublished data from the [Respiratory Virus Transmission Network](#), involving five U.S. sites that enrolled people who tested positive for SARS-CoV-2 and their household contacts during November 2022–May 2023. Onset was defined as first day of symptoms or, if asymptomatic, first positive test. Note that people can have positive PCR tests, which detect viral genetic material, after they are no longer shedding infectious virus, and culture is the best indicator of infectious virus. This figure is similar to one [previously published](#) based on data from early 2021, underscoring the overall stability of viral shedding across variants.

HCV DAAs Injectables?

- Usman Arshad, Joanne Sharp, Megan Neary, et al. University of Liverpool, Liverpool, United Kingdom. Presented at CROI March 3-6, 2024

- A novel GLE/PIB LAI formulation is presented which demonstrates **sustained therapeutic concentrations in rats** above the human oral C_{trough} and beyond the 56 day treatment duration.
- **Hepatic drug penetration** was similar to that previously reported for oral dosing in humans.
- Pharmacometric assessments of rat data indicate an **optimal drug ratio of 3:1**, which is consistent with oral dosing in humans.
- **No adverse effects** were observed but GLP-toxicology studies are planned to support clinical translation.
- **Manufacturing translation** is underway