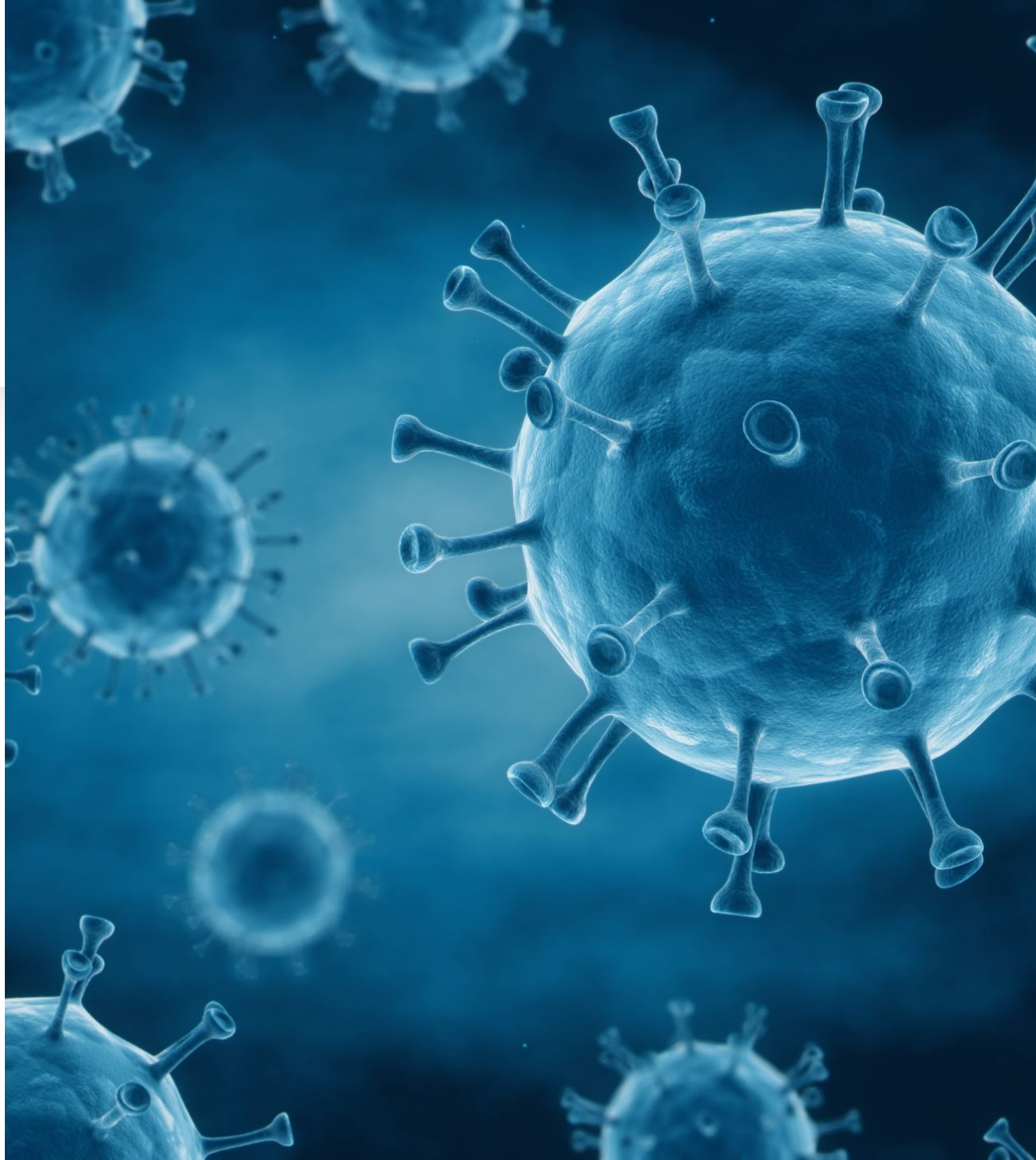
The Month In Virology

Jorge Mera, MD

Outline

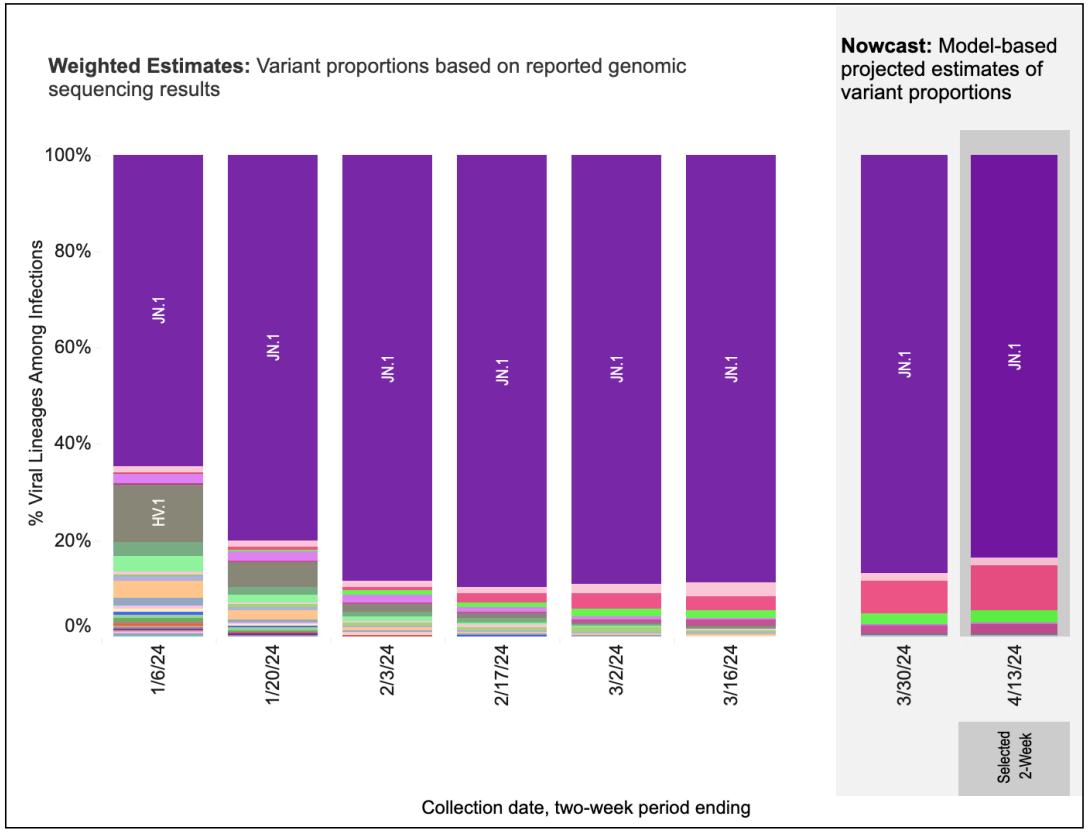
- **Update on respiratory viruses activity**
  - COVID 19
  - Influenza
  - RSV
  - Measles
- **Hepatitis Delta Virus**
- **West Nile**



COVID-19 Variant Proportions

Weighted and Nowcast Estimates in United States for 2-Week Periods in 12/24/2023 – 4/13/2024

Hover over (or tap in mobile) any lineage of interest to see the amount of uncertainty in that lineage's estimate.



Nowcast Estimates in United States for 3/31/2024 – 4/13/2024

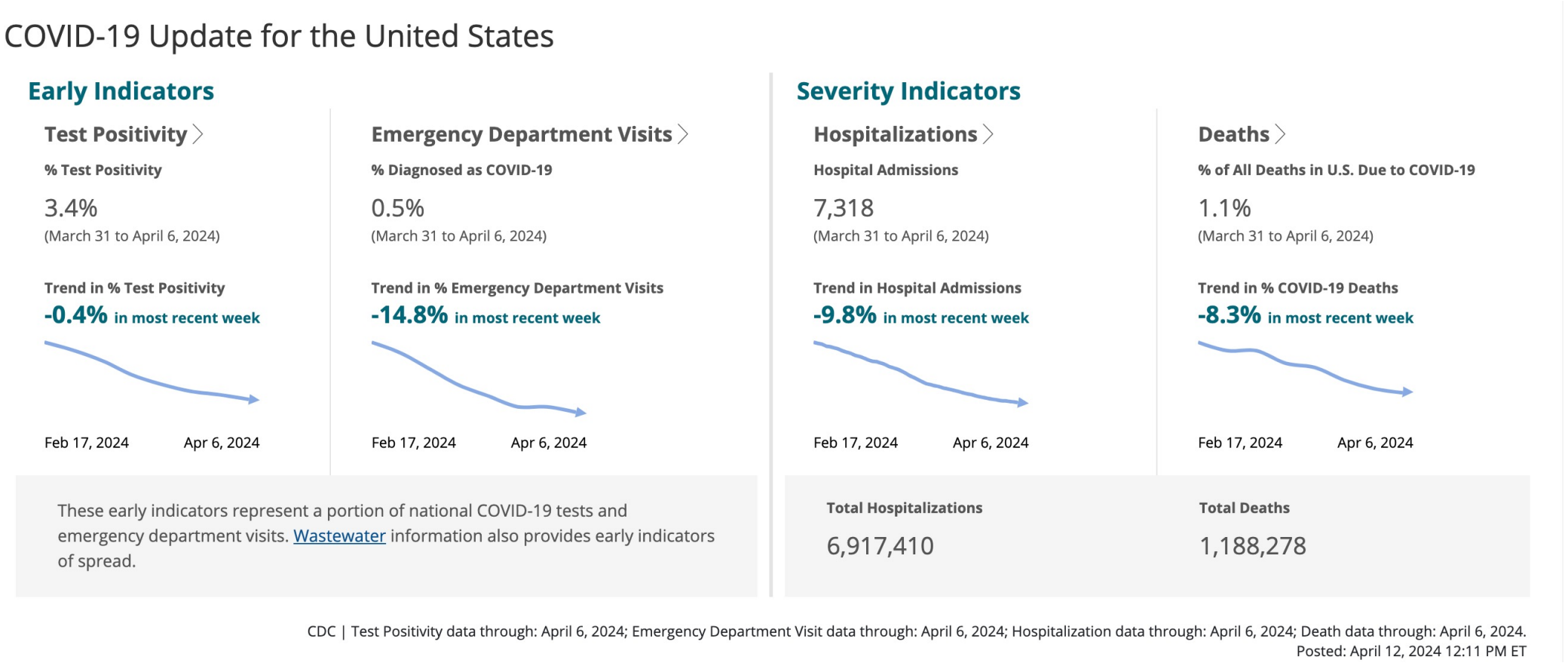
USA

WHO label	Lineage #	%Total	95%PI
Omicron	JN.1	83.7%	80.3-86.7%
	JN.1.13	9.1%	6.2-13.1%
	JN.1.18	2.5%	1.6-3.8%
	JN.1.16	2.4%	1.2-4.6%
	BA.2	0.3%	0.0-1.4%
	B.1.1.529	0.1%	0.0-1.4%
	BA.2.86	0.1%	0.0-0.1%
	GE.1	0.1%	0.0-0.2%
	BA.1.1	0.1%	0.0-0.7%
	HV.1	0.0%	0.0-0.0%
	JG.3	0.0%	0.0-0.0%
	XBB	0.0%	0.0-0.0%
	JD.1.1	0.0%	0.0-0.0%
	XBB.1.16.17	0.0%	0.0-0.0%
	EG.5	0.0%	0.0-0.0%
	HK.3	0.0%	0.0-0.0%
	XBB.1.9.1	0.0%	0.0-0.0%
	XBB.2.3	0.0%	0.0-0.0%
	JF.1	0.0%	0.0-0.0%
	XBB.1.16.6	0.0%	0.0-0.0%
	FL.1.5.1	0.0%	0.0-0.0%
	EG.5.1.8	0.0%	0.0-0.0%
	XBB.1.16	0.0%	0.0-0.0%

* 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.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# 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/.

https://covid.cdc.gov/covid-data-tracker/#variant-proportions

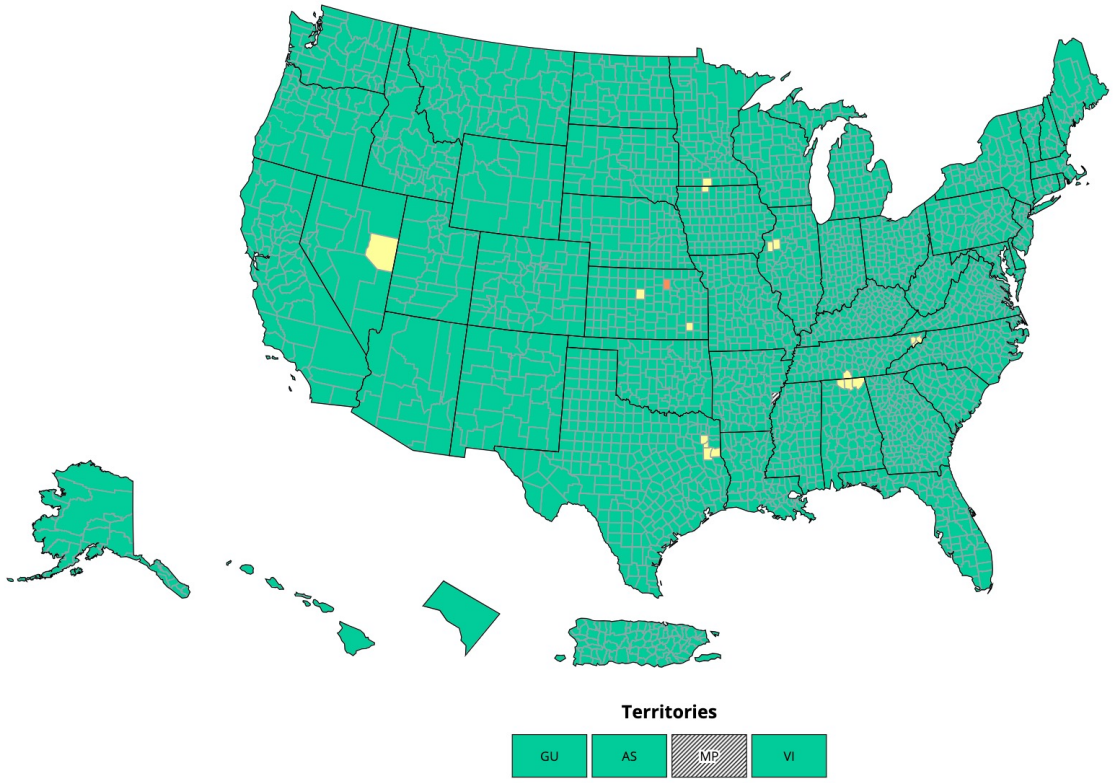
United States COVID-19 Hospitalizations, Deaths, Emergency Department (ED) Visits, and Test Positivity by Geographic Area



https://covid.cdc.gov/covid-data-tracker/#maps_new-admissions-rate-county

Total number of new COVID-19 hospital admissions For every 100,000 people in the past week (not adjusted for age distribution)

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

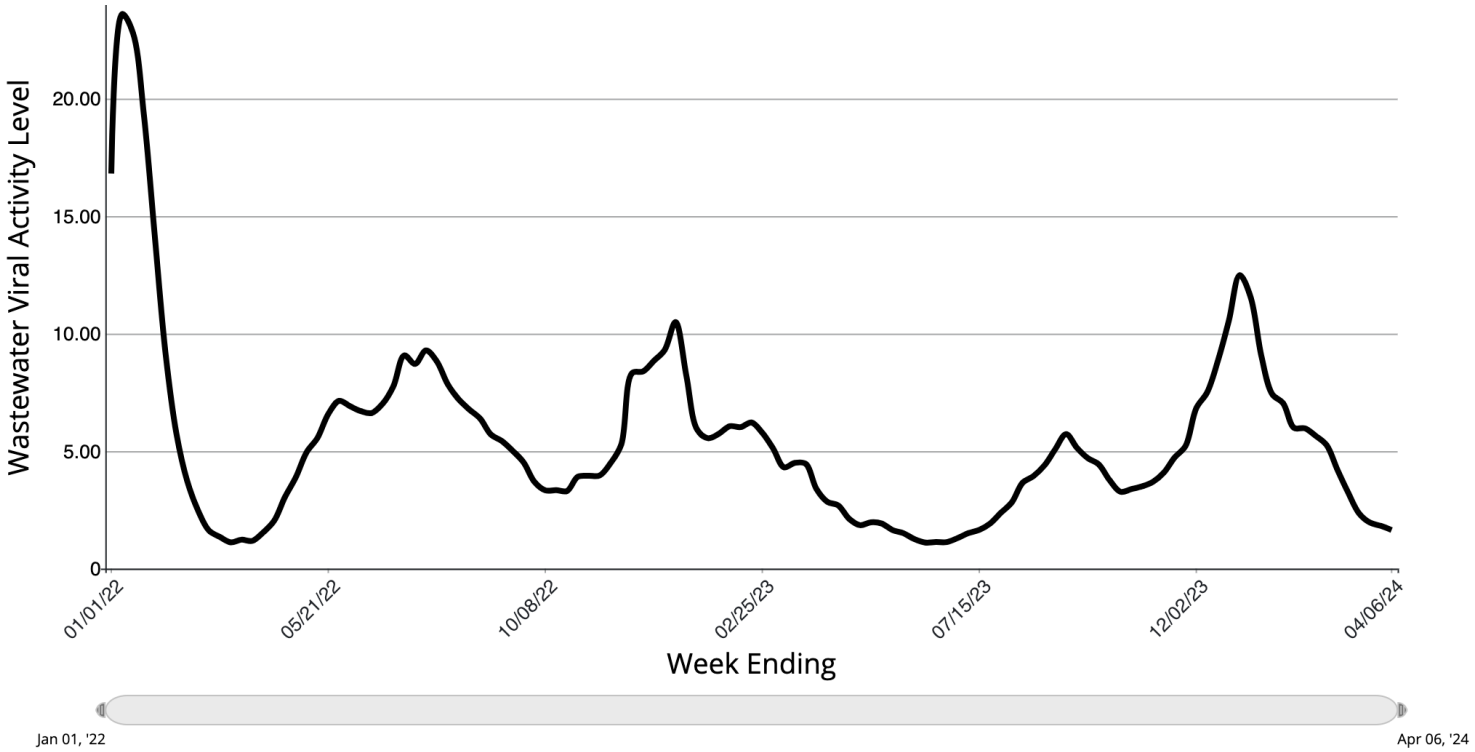
Based on new COVID-19 hospital admissions per 100,000 population

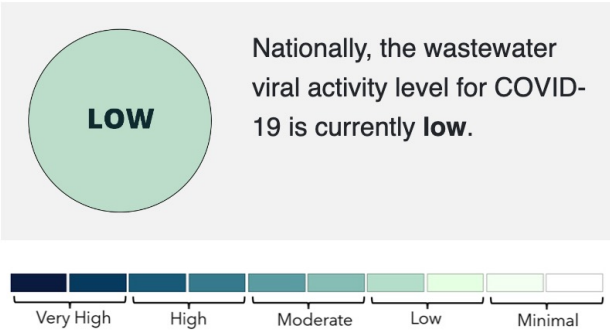
	Total	Percent	% Change
≥ 20.0	1	0.03%	-0.06%
10.0 - 19.9	18	0.56%	-0.06%
<10.0	3203	99.41%	0.28%

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 April 6, 2024.

https://covid.cdc.gov/covid-data-tracker/#maps_new-admissions-rate-county

COVID-19 Wastewater Viral Activity Level United States





https://covid.cdc.gov/covid-data-tracker/#wastewater-surveillance

The FDA has approved a new antibody treatment to help prevent COVID-19 in those who are most at risk from the virus. March 26, 2024

VYD222 (Pemgarda)

- Is a neutralizing, half-life extended monoclonal antibody (mAb)
- Has broad activity and *in vitro* neutralizing activity against various pre-Omicron and Omicron variants, including JN.1.

Preventive treatment

- Indicated for immunocompromised people ages 12 and older
- Who are not currently infected with SARS-COV-2
- Who have not recently been exposed to SARS-COV-2.
- It cannot be given within 2 weeks of a person receiving a COVID vaccine

In a clinical phase III trial

- Only 1% of people had COVID with symptoms within 90 days of getting Pemgarda
- Vs 5% of people from a control group with healthier immune systems

The FDA has approved a new antibody treatment to help prevent COVID-19 in those who are most at risk from the virus.
March 26, 2024

Cohort A (Open-label cohort with moderate-to-severe immune compromise) – Proportion of participants with RT-PCR-confirmed symptomatic COVID-19 (exploratory data):

	As of December 1, 2023 (median 35 days follow-up)	Through Day 90
VYD222	0% (0/306)	1% (3/298)

Cohort B (Randomized, placebo-controlled cohort without moderate-to-severe immune compromise at risk of acquiring SARS-CoV-2 due to regular unmasked face-to-face interactions) – Proportion of participants with RT-PCR-confirmed symptomatic COVID-19 (exploratory data):

	As of December 1, 2023 (median 67 days follow-up)	Through Day 90
VYD222	0% (0/322)	0.3% (1/314)
Placebo	3% (5/162)	5% (8/159)

References

1.Schmidt, Pete et al. "Antibody-mediated protection against symptomatic COVID-19 can be achieved at low serum neutralizing titers." Sci. Transl. Med.15, eadg2783 (2023); Follmann, Dean et al. "Examining protective effects of SARS-CoV-2 neutralizing antibodies after vaccination or monoclonal antibody administration." Nature communications vol. 14,1 3605. 17 Jun. 2023.

2.Ison, Michael, et al. "Prevention of COVID-19 Following a Single Intramuscular Administration of Adintrevimab: Results From a Phase 2/3 Randomized, Double-Blind, Placebo-Controlled Trial (EVADE)." Open Forum Infectious Diseases, Volume 10, Issue 7, July 2023; Levin, Myron J et al. "Intramuscular AZD7442 (Tixagevimab-Cilgavimab) for Prevention of Covid-19." The New England Journal of Medicine vol. 386,23 (2022): 2188-2200.

The Rise and Fall of Paxlovid

1. **December 2021, the FDA issued an Emergency Use Authorization for Paxlovid:**
   Action is based on the efficacy shown in the EPIC-HR study of high-risk outpatients with COVID-19.
   Compared to those receiving placebo, Paxlovid-treated participants had an **89% reduction in risk of hospitalization or death.**

2. **Early 2022, that annoying rebound thing.**
   No, it's never been quite clear whether Paxlovid *caused* rebounds, or just didn't prevent them, or whether it just happened in those people for whom COVID-19 illness lasted longer than the treatment's 5 days (a large group!), but regardless — it was a major disincentive to clinicians and providers alike.

3. **December 2022, the protocol for the EPIC-SR in "standard risk" outpatients was amended to increase the sample size.**
   Though an interim analysis suggested such patients would benefit from treatment, the change in sample size signaled that such a benefit observed in this analysis might be small — or nonexistent.

4. **August 2023, the negative results of EPIC-SR were posted on clinicaltrials.gov.**
   Yes, these results have been in the public domain since last summer.

5. **Last week, the disappointing EPIC-SR results appeared in the *New England Journal of Medicine*.**
   This is the primary endpoint : **Time to sustained alleviation of symptoms**

Paul E. Sax, MD NEJM JOURNAL WATCH INFECTIOUS DISEASES

Treatment Updates

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Nirmatrelvir for Vaccinated or Unvaccinated Adult Outpatients with Covid-19

Hammond J et al. DOI: 10.1056/NEJMoa2309003

CLINICAL PROBLEM

Effective oral treatments for Covid-19 are needed that can shorten the time to symptom resolution and reduce the risk of progression to severe illness. The oral antiviral nirmatrelvir, in combination with ritonavir, has been shown to reduce the risk of Covid-19–related hospitalization or death from any cause in unvaccinated adults at high risk for severe Covid-19, but whether it can reduce the duration of symptoms in a broader group is unknown.

CLINICAL TRIAL

Design: A phase 2–3, double-blind, randomized, controlled trial assessed the efficacy and safety of nirmatrelvir–ritonavir in adult outpatients (either unvaccinated or not vaccinated within the previous year) without risk factors for severe Covid-19 and fully vaccinated adults with at least one risk factor for severe disease.

Intervention: 1296 adults with confirmed Covid-19 and symptom onset within the previous 5 days were assigned to receive either 300 mg of nirmatrelvir plus 100 mg of ritonavir or placebo every 12 hours for 5 days. The primary end point was the time to sustained alleviation of all targeted signs and symptoms of Covid-19.

RESULTS

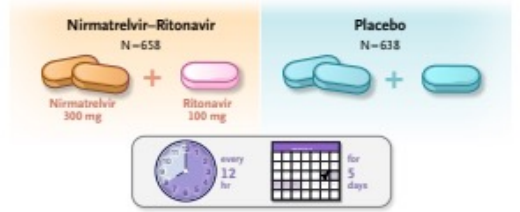
Efficacy: The time to sustained alleviation of symptoms did not differ significantly between the two groups.

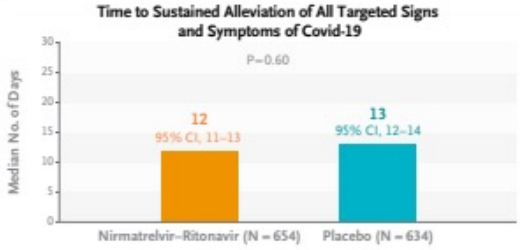
Safety: The percentages of participants with adverse events through day 34 were similar in the two groups; the most common adverse events in the nirmatrelvir–ritonavir group were dysgeusia, diarrhea, and nausea.

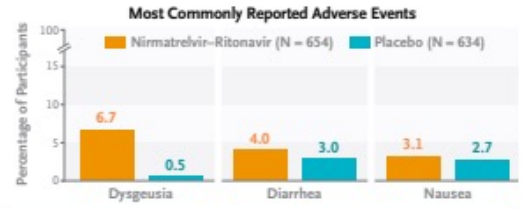
LIMITATIONS AND REMAINING QUESTIONS

- The participants in the vaccinated high-risk subgroup were enrolled regardless of the time since their last administered vaccine dose.
- Nirmatrelvir–ritonavir has a distinctive taste, so participants may have suspected that they were taking that medication.
- The trial was started during the period of delta-variant predominance, and therefore the efficacy of the treatment against other variants is unknown.

Links: Full Article | NEJM Quick Take | Editorial







CONCLUSIONS

Among outpatients with Covid-19 who were at standard risk or high risk for progression to severe Covid-19, nirmatrelvir and ritonavir did not significantly shorten the time to symptom alleviation.

What did I find in the fine print?

Covid-19–related medical visits

- 6 among 6 high-risk participants in the nirmatrelvir–ritonavir group vs
- 26 visits among 17 high-risk participants in the placebo group 0.18; (95% CI, 0.06 to 0.56).

Among 15 hospitalized, mean number of days in the hospital per 100 participants

- 5 in the nirmatrelvir–ritonavir group and 18 in the placebo group.
- The longest hospital stay was 9 days in the treatment group and 32 days in the placebo group.

Viral load (VL) rebound occurred:

- In 4.3% of the participants in the nirmatrelvir–ritonavir group and 4.1% of those in the placebo group
- Three patients who had VL rebound were hospitalized (1 the treatment and 2 in placebo group respectively)
- There was no consistent temporal relationship between viral load rebound and hospitalization.

Symptom rebound occurred

- In 11.4% of the treatment group and 16.1% in the placebo group

Symptom and VL rebound together occurred

- In 1.2% of the treatment group and and 0.5% of the placebo group

Reports of COVID-19 Vaccine Adverse Events in Predominantly Republican vs Democratic States

Importance

- Antivaccine sentiment is increasingly associated with conservative political positions.

Objective

- To assess whether there is an association between state political inclination and the reporting rates of COVID-19 vaccine AEs.

Design, Setting, and Participants

- This cross-sectional study used the AE reports after COVID-19 vaccination from the VAERS database from 2020 to 2022
- Reports after influenza vaccines from 2019 to 2022 used as a reference.
- These reports were examined against state-level percentage of Republican votes in the 2020 US presidential election.

Exposure

- State-level percentage of Republican votes in the 2020 US presidential election.

Main Outcomes and Measures

- Rates of any AE, any severe AE, and the proportion of AEs reported as severe among COVID-19 vaccine recipients

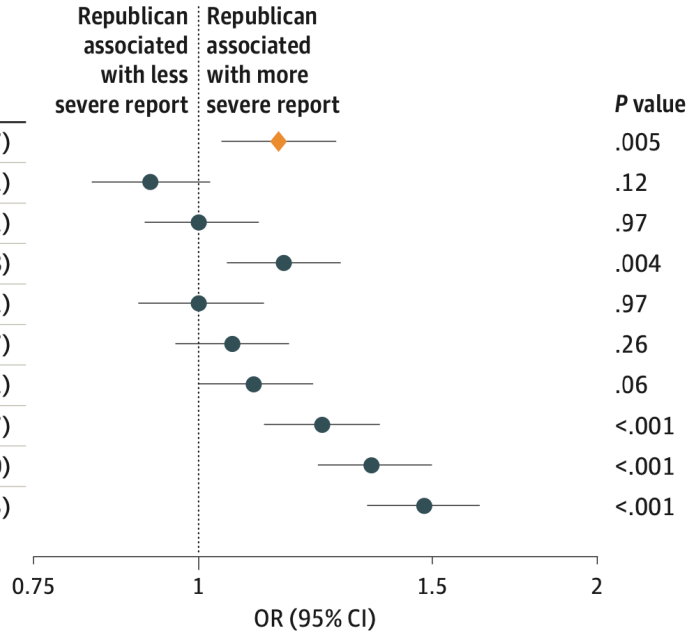
Asch DA, Luo C, Chen Y. R. *JAMA Netw Open.* 2024;7(3):e244177.

VAERS: Vaccine Adverse Event Reporting System

Second Sensitivity Analysis for the Association of Political Inclination With Severe Vaccine Adverse Event Reports

Figure 3. Second Sensitivity Analysis for the Association of Political Inclination With Severe Vaccine Adverse Event Reports

Vaccine	Age, y	Sex	History of medication or allergy	OR (95% CI)	*P* value
COVID-19	50	F	No	1.15 (1.04-1.27)	.005
Other	50	F	No	0.92 (0.83-1.02)	.12
COVID-19	50	F	Yes	1.00 (0.91-1.11)	.97
COVID-19	50	M	No	1.16 (1.05-1.28)	.004
COVID-19	20	F	No	1.00 (0.90-1.12)	.97
COVID-19	30	F	No	1.06 (0.96-1.17)	.26
COVID-19	40	F	No	1.10 (1.00-1.22)	.06
COVID-19	60	F	No	1.24 (1.12-1.37)	<.001
COVID-19	70	F	No	1.35 (1.23-1.50)	<.001
COVID-19	80	F	No	1.48 (1.34-1.63)	<.001



- Individual-level analysis of 620 456 reports associated with COVID-19 vaccines and 62 581 reports associated with any other vaccines
- Each row represents a subgroup of recipients
- The other rows show that at baseline, a change in other factors may change the association of political inclination.
- “Other” indicates vaccines other than the COVID-19 vaccine.

Asch DA, Luo C, Chen Y. R. *JAMA Netw Open.* 2024;7(3):e244177.

Reports of COVID-19 Vaccine Adverse Events in Predominantly Republican vs Democratic States

Results

- A total of 620 456 AE reports, mean age, 51.8 years, women 70.2%
- Significant associations between state political inclination and state AE reporting were observed for all 3 outcomes
- Associations were seen across all age strata and more pronounced among older groups

Conclusions and Relevance

- This study found that the more states were inclined to vote Republican, the more likely their vaccine recipients or their clinicians reported COVID-19 vaccine AEs.
- These results suggest that either the perception of vaccine AEs or the motivation to report them was associated with political inclination.

Asch DA, Luo C, Chen Y. R. *JAMA Netw Open.* 2024;7(3):e244177.

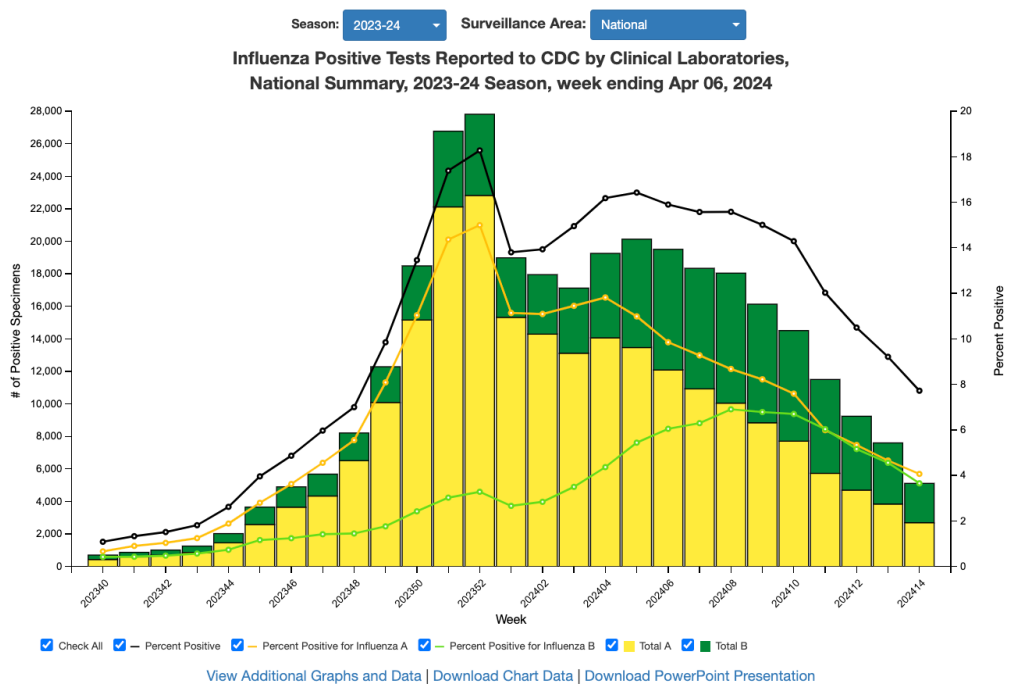
Cognition and Memory after Covid-19 in a Large Community Sample

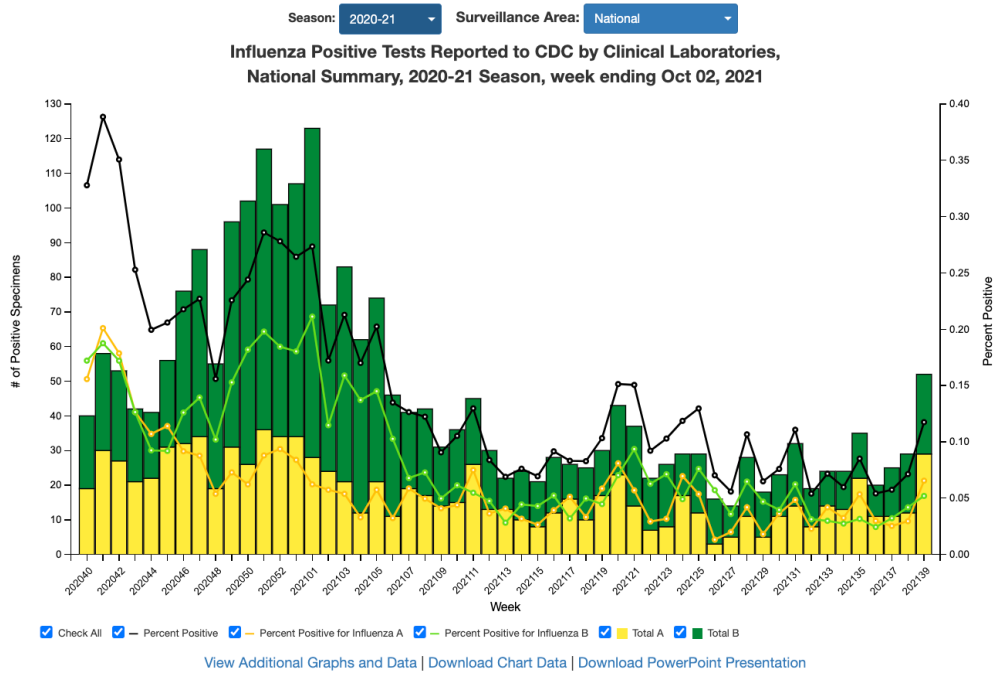
Participants with resolved persistent symptoms after Covid-19 had objectively measured cognitive function similar to that in participants with shorter-duration symptoms, although short-duration Covid-19 was still associated with small cognitive deficits after recovery.

Longer-term persistence of cognitive deficits and any clinical implications remain uncertain.

N Engl J Med, Volume 390(9):806-818, February 29, 2024

Influenza Update





https://www.cdc.gov/flu/weekly/index.htm

Influenza Activity by State

A Weekly Influenza Surveillance Report Prepared by the Influenza Division

Outpatient Respiratory Illness Activity Map Determined by Data Reported to ILINet

This system monitors visits for respiratory illness that includes fever plus a cough or sore throat, also referred to as ILI, not laboratory confirmed influenza and may capture patient visits due to other respiratory pathogens that cause similar symptoms.

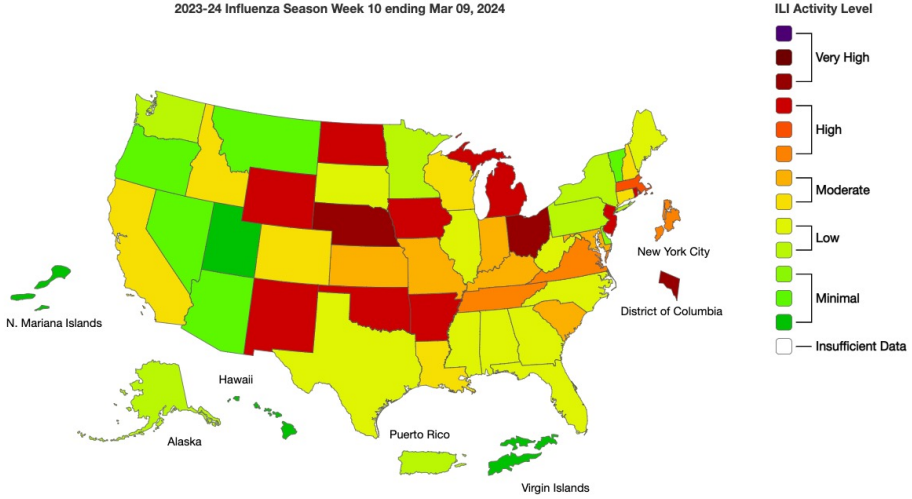
prev Play Pause next

40 50 1 10 14

weeks

State CBSA

2023-24 Influenza Season Week 10 ending Mar 09, 2024



Season: 2023-24

Download Image Download Data

*Data collected in ILINet may disproportionally represent certain populations within a jurisdiction or CBSA, and therefore, may not accurately depict the full picture of influenza activity for the entire jurisdiction or CBSA. Differences in the data presented here by CDC and independently by some health departments likely represent differing levels of data completeness with data presented by the health department likely being the more complete.

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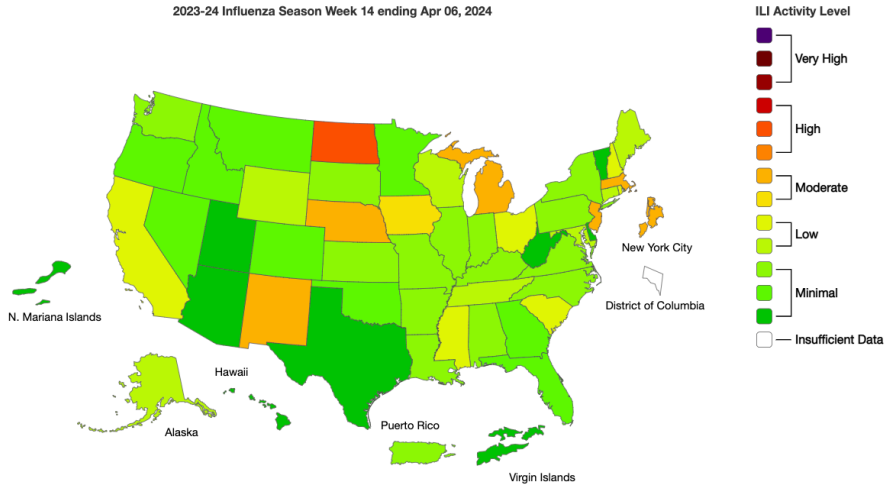
prev Play Pause next

40 50 1 10 14

weeks

State CBSA

2023-24 Influenza Season Week 14 ending Apr 06, 2024



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Avian Influenza

On April 1, 2024—A person in the United States tested positive for avian influenza (HPAI) A(H5N1) virus

- This person had exposure to dairy cattle in Texas presumed to be infected with HPAI A(H5N1) viruses.
- The patient reported eye redness (consistent with conjunctivitis), as their only symptom, and is recovering.
- This infection does not change the H5N1 bird flu human health risk assessment for the U.S. general public, which CDC considers to be low.
- People with close, prolonged, or unprotected exposures to infected birds/animals, or to contaminated environments by them are at greater risk of infection.

https://www.cdc.gov/flu/avianflu/index.htm

Avian Influenza

This is the second person reported to have tested positive for influenza A(H5N1) viruses in the United States.

- A previous human case occurred in 2022 in Colorado.
- Human infections with avian influenza A viruses, including A(H5N1) viruses, are uncommon but have occurred sporadically worldwide.
- Outbreaks were first detected in U.S. wild birds and poultry in late 2021.
- Human illnesses with H5N1 bird flu have ranged from mild to severe illness (e.g., pneumonia) that have resulted in death in other countries.

https://www.cdc.gov/flu/avianflu/index.htm

Avian Influenza

- **CDC's interim ecommendations**
  - **People should avoid unprotected exposures to sick or dead animals** (wild or domesticated), or materials contaminated by them with confirmed or suspected HPAI A(H5N1)-virus infection.
  - **People should not prepare or eat uncooked or undercooked food** or related uncooked food products, from animals with confirmed or suspected HPAI A(H5N1)
  - **People exposed to birds or other animals with confirmed or suspected HPAI A(H5N1) 10 days after the last known exposure**, including people wearing recommended PPE).
- **FDA and USDA**
  - **There are not concerns with the safety of the commercial milk supply at this time** because products are pasteurized before entering the market.
  - Dairies are required to send only milk from healthy animals
  - Pasteurization is required for any milk entering interstate commerce for human consumption.
  - FDA's is reminding consumers of the risks associated with raw milk consumption

Poll Question # 1

It is September and a 26 yo female in her 32nd week of pregnancy asks you about protecting her infant for RSV. What options would you recommend:

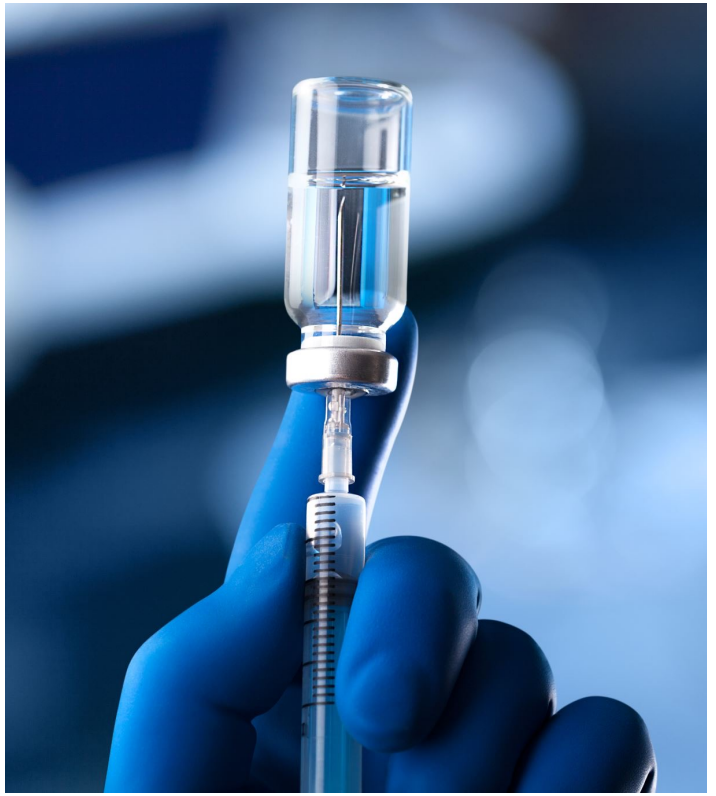
A. Administer one dose of RSV vaccine now

B. It is too late to vaccinate her, she should have asked in August

C. If she declines vaccination nersivambab (monoclonal Ab) for the infant would be an option

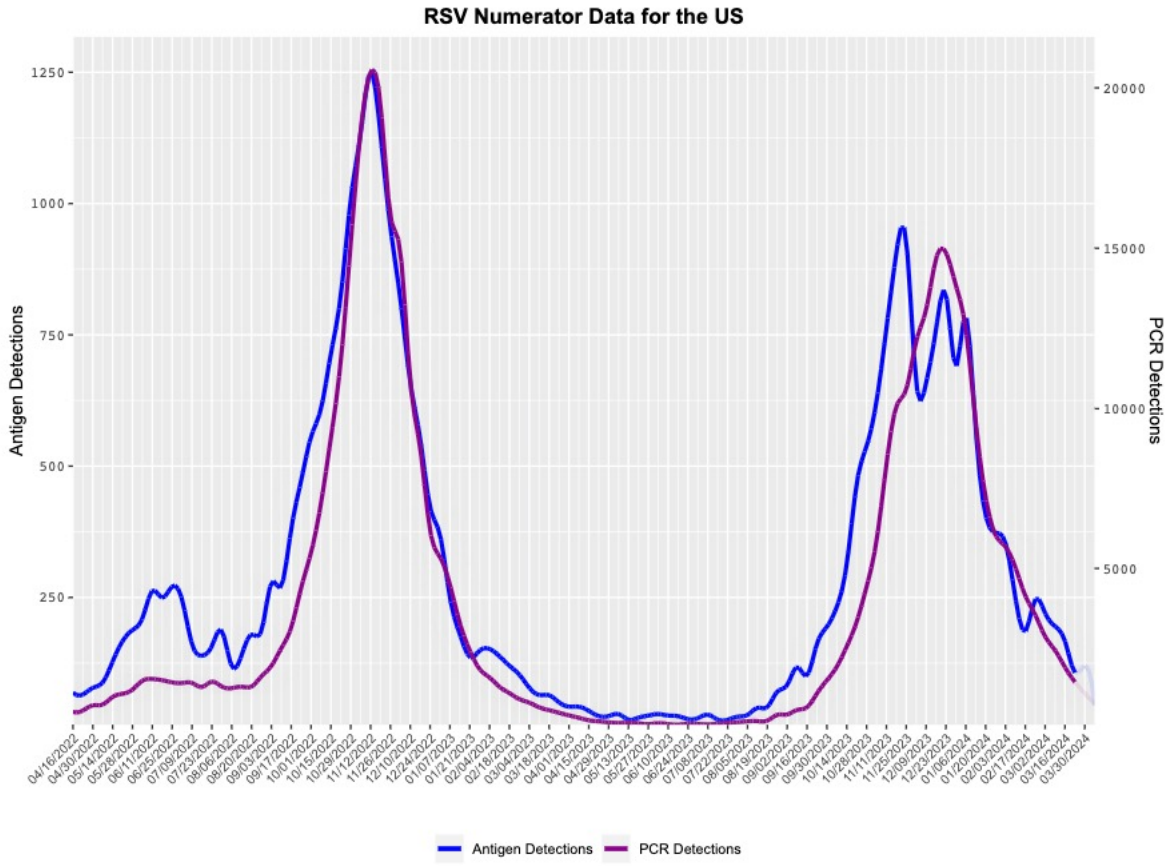
D. Only A and C are correct

E. All are correct



RSV Update

Detections



RSV Prevention

- **General measures:**
  - Hand washing
  - Cough hygiene
  - Avoidance of tobacco
  - Restricting participation in childcare during RSV season for high-risk infants
- **Infection control in the health care setting**
  - Handwashing
  - Proper use of PPE
  - Isolation of
  - Cohorting health care personnel.

RSV Infant Protection

Vaccination for pregnant people

- 1 dose of maternal RSV vaccine during weeks 32 through 36 of pregnancy, administered September through January.
- Pfizer Abrysvo is the only RSV vaccine recommended during pregnancy.
- Severe RSV bronchiolitis during the first 180 days after birth was 0.5% in vaccine group vs 1.8 % in placebo group.

Immunization for infants and young children

- 1 dose of nirsevimab for all infants aged 8 months and younger born during or entering their first RSV season (RSV season October- March)
- 1 dose of nirsevimab for infants and children aged 8–19 months who are at increased risk for severe RSV disease and entering their second RSV season.
- A different monoclonal antibody, palivizumab, is limited to children aged 24 months and younger with certain conditions that place them at high risk for severe RSV disease. It must be given once a month during RSV season.

https://www.cdc.gov/vaccines/vpd/rsv/index.html

RSV Vaccination in Adults

How many vaccines are available

- There are two available vaccines for, an adjuvanted RSV prefusion F vaccine and a non-adjuvanted bivalent RSV prefusion F vaccine

Indications

- For adults ≥60 years of age and with comorbidities that put them at increased risk for severe disease
- Vaccination reduces the incidence of symptomatic infection and can prevent hospitalizations.

Dose and administration

- One-time single dose
- Boosting unknown

Adverse events

- Common: Self-limited discomfort at the injection site, headache, fatigue, and myalgias.
- Rare: GBS have been reported in clinical trials, but the association is not clearly established.

GBS: Guillain-Barré syndrome

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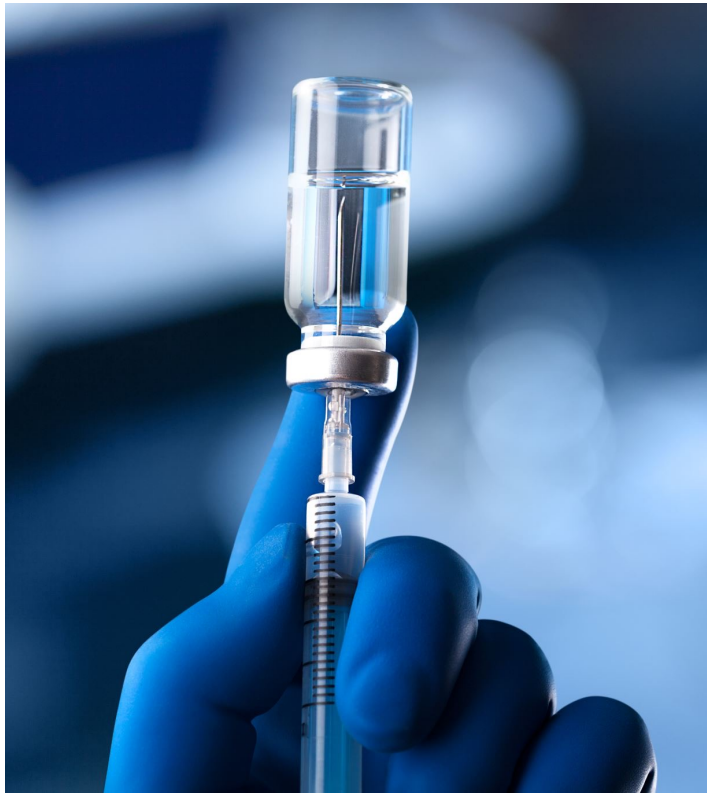
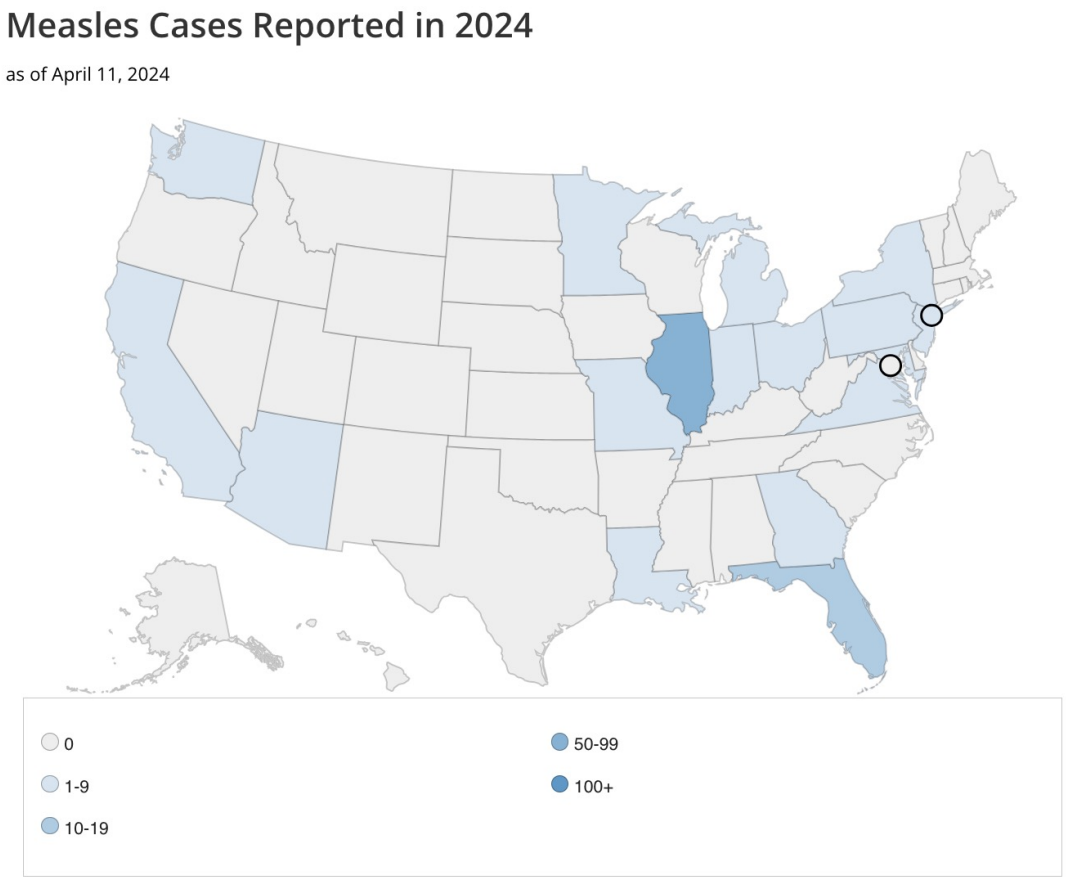
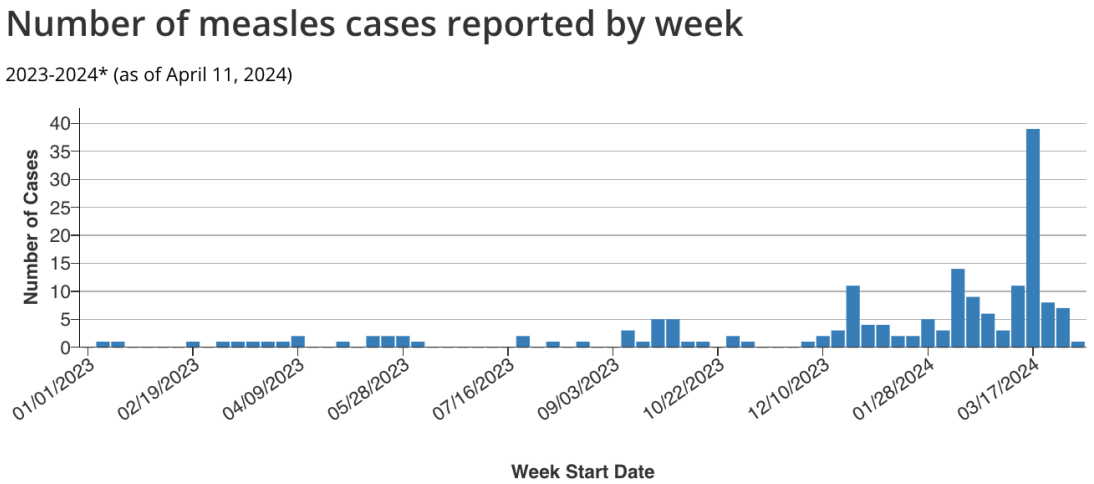


Measles Update

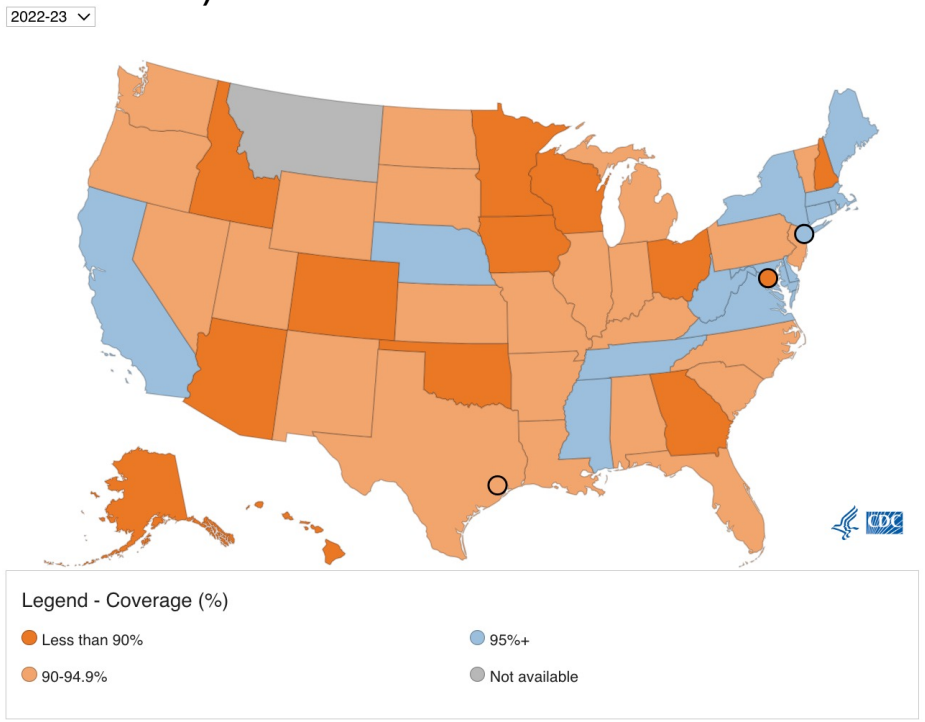


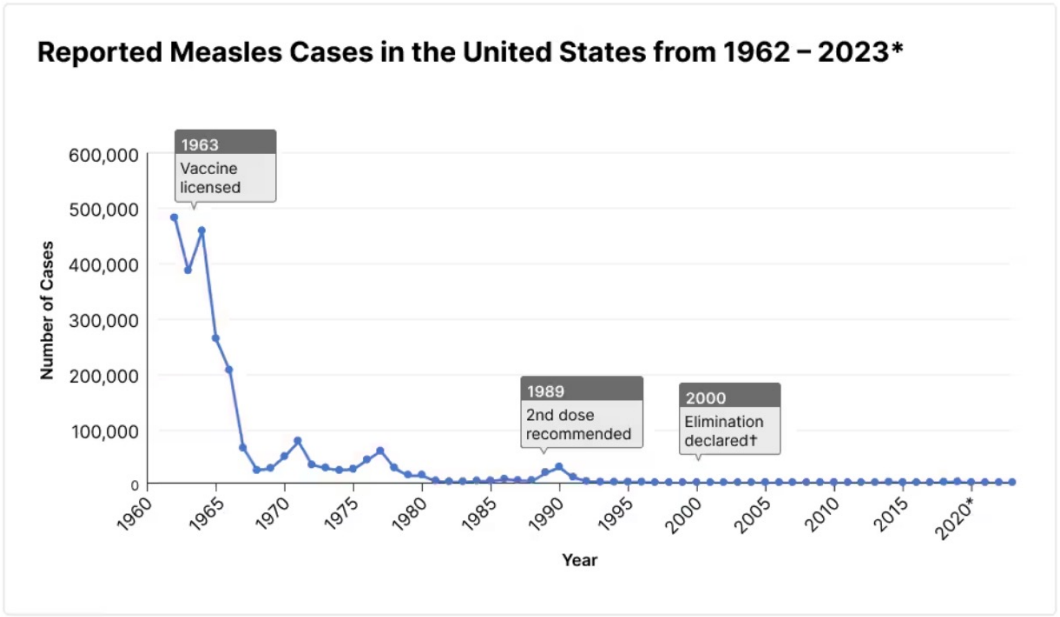


https://www.cdc.gov/measles/cases-outbreaks.html

Measles Update

MMR Vaccine Coverage for Kindergarteners by School Year (2009-2023)





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

Measles Vaccination

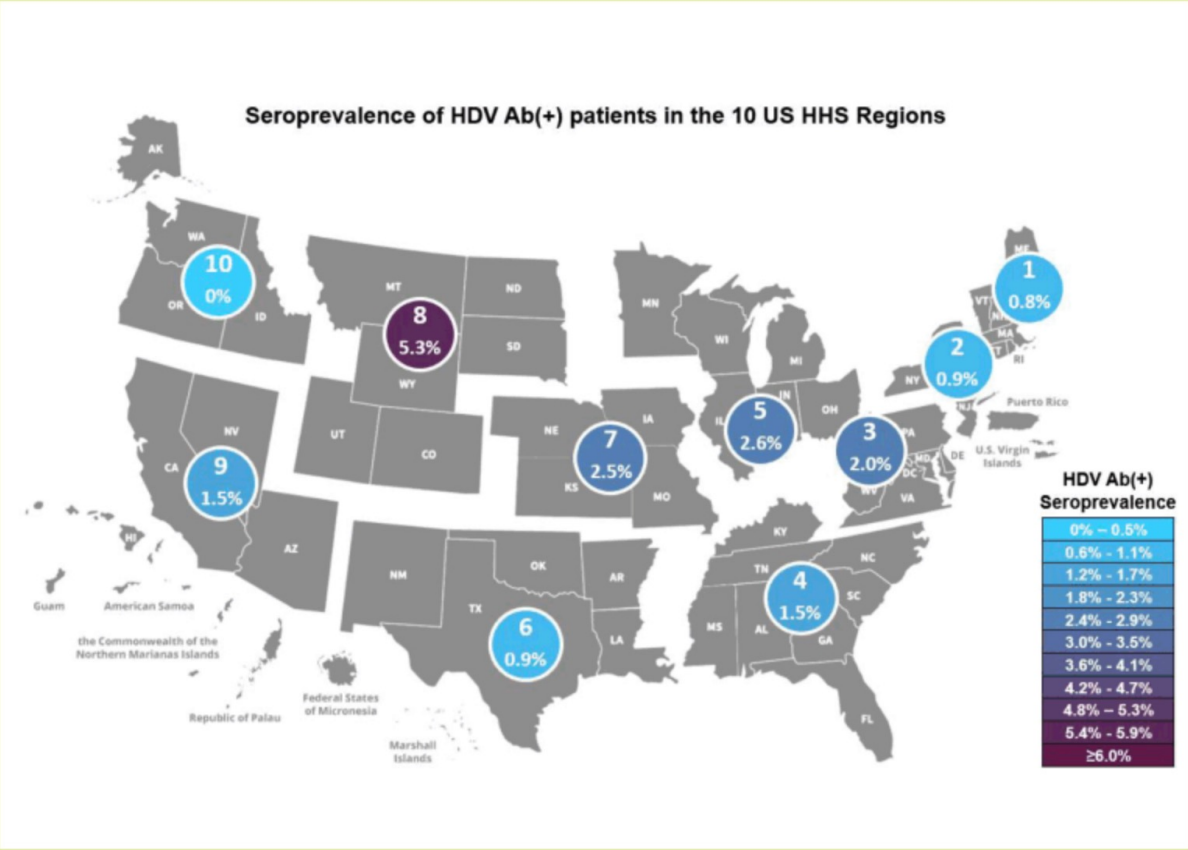
Measles can be prevented with measles-mumps-rubella (MMR) or MMRV vaccine.	Vaccine recommendations for children	Vaccine recommendations for adults
• One dose of MMR vaccine is approximately 93% effective at preventing measles; • two doses are approximately 97% effective.	• MMR vaccine starting with the 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.	• 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.

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

Epidemiologic Burden of Hepatitis D Virus in the United States

Elizabeth M. Marlowe, Brooke E. Swanson, Susan E. Realegeno, Ron M. Kagan, William A. Meye

CROI 2024 March 3-6 Denver



HBsAg-positive specimen remnant sampling from each region was relative to the 2022 US Census population size.
Ab, antibody; HDV, hepatitis D virus; HHS, US Department of Health and Human Services

Results

- First nationwide HDV seroprevalence study.
- The overall HDV seroprevalence in this study was 1.6
- Higher prevalence were noted in HHS regions 8 (5.3%), 5 (2.6%) 7 (2.5%) and 3 (2.0%)
- HD RNA detection in 39.4% of HDV Ab(+) specimens

Conclusions

- Further HDV seroprevalence studies are needed
- Universal testing of HbsAg(+) specimens followed by HDV RNA testing would benefit patients with previouslyunrecognized HV infection.

Neuroinvasive West Nile Virus (NWNV) Infection in Immunosuppressed (IS) and Immunocompetent Adults

Importance

- West Nile virus (WNV) is the leading cause of human arboviral disease in the US, peaking during summer.
- The incidence of WNV, including NWNV, is increasing, due to the expanding distribution of the *Culex* mosquito, and climatic changes (heavy monsoon rains).
- The distinct characteristics and outcomes of NWNV in individuals who are IS and individuals who are not IS remain underexplored.

Objective

- To describe and compare clinical/radiographic/treatment responses, and outcomes of NWNV in individuals who are IS vs those not IS.

Design, Setting, and Participants

- This retrospective cohort study analyzed data from May 12, 2020, to July 20, 2023.
- Adult patients (age ≥18 years) with established diagnosis of NWNV infection.

Exposure

- Immunosuppresion.

Main Outcomes and Measures

- Outcomes of interest were clinical and radiographic features and 90-day mortality among patients with and without IS.

JAMA Netw Open. 2024;7(3):e244294. doi:10.1001/jamanetworkopen.2024.4294

Neuroinvasive West Nile Virus Infection in Immunosuppressed and Immunocompetent Adults

Of 115 participants with NWNV infection

- 72 (63%) were not IS and 43 (37%) were IS

Neurologic manifestations were:

- Meningoencephalitis 85%, encephalitis 9%, and myeloradiculitis 6%.
- Those w/o IS vs those with IS, more frequently reported headache 63% vs 42%and myalgias 44% vs 21%.
- Patients with IS vs those w/o had higher rates of AMS 77% vs 57% and myoclonus 19% vs 4%.

Individuals with IS had more severe disease

- Requiring higher rates of intensive care unit admission, 61% vs 33% and
- Mechanical ventilation 56% vs 31%.

The 90-day all-cause mortality rate was higher in the patients with IS compared with patients without IS

- 28% vs 7% respectively, adjusted for Glasgow Coma Scale score
- Individuals with IS were more likely to receive IVIG than individuals w/o IS (without any survival benefit)

JAMA Netw Open. 2024;7(3):e244294. doi:10.1001/jamanetworkopen.2024.4294

Neuroinvasive West Nile Virus Infection in Immunosuppressed and Immunocompetent Adults

Question

- Do clinical manifestations, radiographic characteristics, and outcomes of neuroinvasive West Nile virus (NWNV) infection differ between adult patients with vs without immunosuppression (IS)?

Findings

- In this cohort study of 115 patients with NWNV infection, there were significant differences in clinical presentations between patients with vs without IS.
- Patients with IS experienced more severe disease, indicated by higher rates of intensive care unit admissions, mechanical ventilation, and 90-day all-cause mortality, compared with patients without IS.

Meaning

- These findings suggest that individuals with IS with NWNV presented with more severe clinical manifestations and had poorer outcomes compared with individuals without IS
- Highlighting the need for targeted disease prevention and treatment strategies for this high-risk group.

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Neuroinvasive West Nile Virus Infection in Immunosuppressed and Immunocompetent Adults

Table 2. Treatment and Outcomes of Individuals With and Without Immunosuppression With Neuroinvasive West Nile Virus Infection

	Patients, No. (%)		
Adjunctive therapy	Not immunosuppressed (n = 72)	Immunosuppressed (n = 43)	Total (N = 115)
None	52 (72)	15 (35)	67 (58)
Any single agent (IVIg, interferon-alfa, ribavirin)	16 (22)	13 (30)	29 (25)
Any combination of agents	4 (6)	15 (35)	19 (16)
Interferon-alfa	5 (7)	16 (37)	21 (18)
IVIg	12 (17)	24 (56)	36 (31)
Other managements			
ICU admission	24 (33)	26 (61)	50 (44)
Mechanical ventilation	22 (31)	24 (56)	46 (41)
Outcome			
Hospital length of stay, median (IQR), d [No. missing]	8 (5-20) [1]	16 (11-26) [0]	12 (6-23) [1]
90-Day mortality,	5 (7)	12 (28)	17 (15)

Conclusions and Relevance

In this cohort study of individuals with NWNV infection, individuals with IS had a higher risk of disease complications and poor outcomes than individuals without IS

Highlighting the need for innovative and effective therapies to improve outcomes in this high-risk population.

JAMA Netw Open. 2024;7(3):e244294. doi:10.1001/jamanetworkopen.2024.4294

From: **Neuroinvasive West Nile Virus Infection in Immunosuppressed and Immunocompetent Adults**

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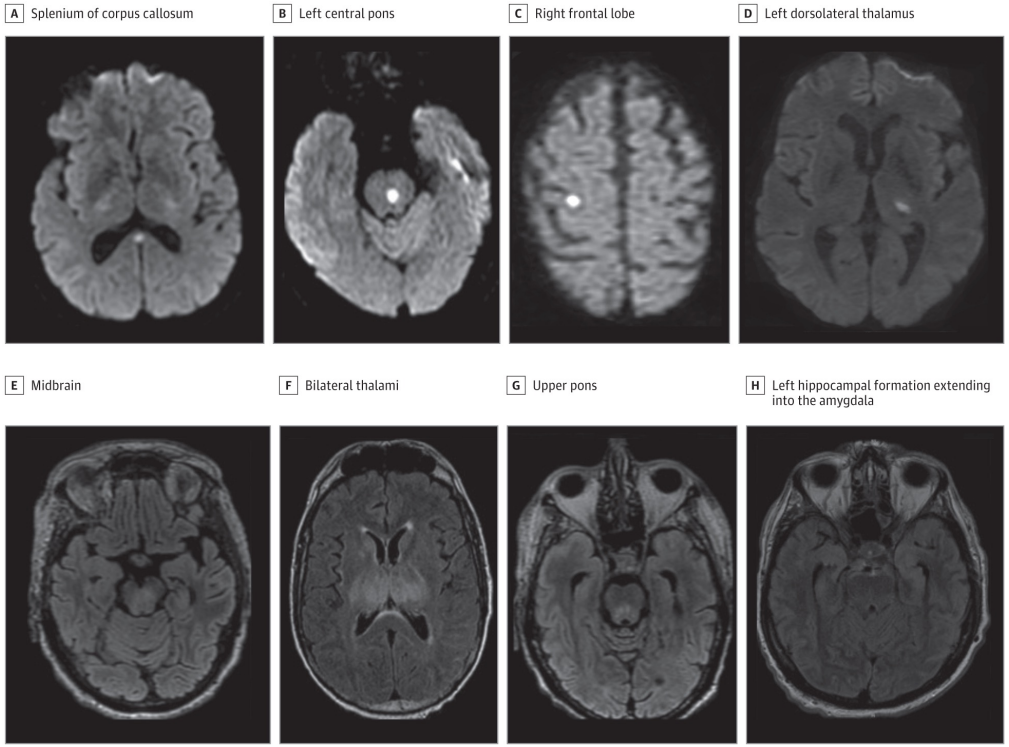

Figure Legend:

Diffusion-Weighted Imaging Brain Magnetic Resonance Imaging Sequences From Different Patients Showing Focal Areas of Diffusion RestrictionA-D, Patients had an apparent diffusion coefficient correlate with decreased signal suggesting acute ischemia. E-G, Fluid-attenuated inversion recovery images of various patients showing areas of subtle increased fluid attenuated inversion recovery signal.

Poll Question # 2

What statements are true about West Nile Virus human infection

A. Most of the infections are asymptomatic
B. Neuroinvasive disease occurs in 20 % of symptomatic patients.
C. Laboratory diagnosis can be achieved by detecting WNV IgM in the serum or CSF
D. All are correct
E. Only A and C are correct

WNV: Clinical Signs and Symptoms

Incubation period is typically 2 to 6 days	• But ranges from 2 to 14 days and can be several weeks in immunocompromised people.
The Majority of WNV infections are asymptomatic.	• 70 -80 %
Most symptomatic persons experience an acute systemic febrile illness	• Headache, weakness, myalgia, or arthralgia; gastrointestinal symptoms and a transient maculopapular rash
Less than 1% of infected persons develop neuroinvasive disease	• Which typically manifests as meningitis, encephalitis, or acute flaccid paralysis.

WNV: Clinical Signs and Symptoms

WNV meningitis is clinically indistinguishable from other viral meningitis

- Typically presents with fever, headache, and nuchal rigidity.

WNV encephalitis is a more severe clinical syndrome

- Presents with fever, altered mental status, seizures, focal neurologic deficits, or movement disorders

WNV acute flaccid paralysis is usually identical to poliomyelitis

- May progress to respiratory paralysis requiring mechanical ventilation
- WNV flaccid paralysis presents as isolated limb paresis or paralysis with or without fever or viral prodrome.
- WNV-associated GBS and radiculopathy has been reported

Rarely WNV presents as:

- Cardiac dysrhythmias, myocarditis, rhabdomyolysis, optic neuritis, uveitis, chorioretinitis, orchitis, pancreatitis, and hepatitis

https://www.cdc.gov/westnile/healthcareproviders/index.html

WNV Diagnostic Testing

- **Laboratory diagnosis:**
  - Testing of serum or CSF to detect WNV-specific IgM antibodies
- **WNV IgM Antibodies**
  - Detectable 3 to 8 days after onset of illness
  - May persist for 30 to 90 days
  - False negatives can occur if serum is collected within 8 days of illness
  - False positives may occur (other flaviviruses or non-specific reactivity)
  - All positive results obtained with these assays should be confirmed by neutralizing antibody testing of acute- and convalescent-phase serum
- **WNV IgG Antibodies**
  - Only evidence of previous infection

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Questions