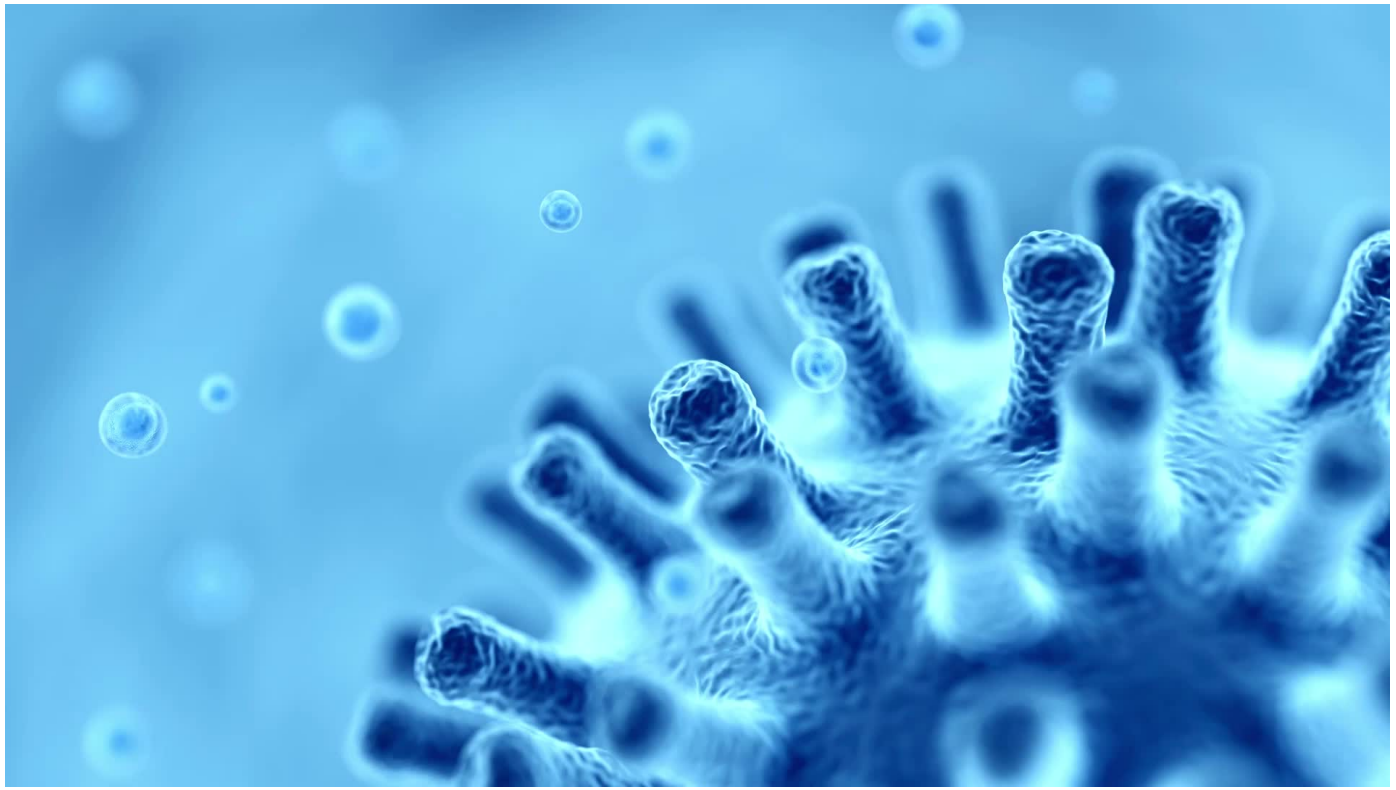


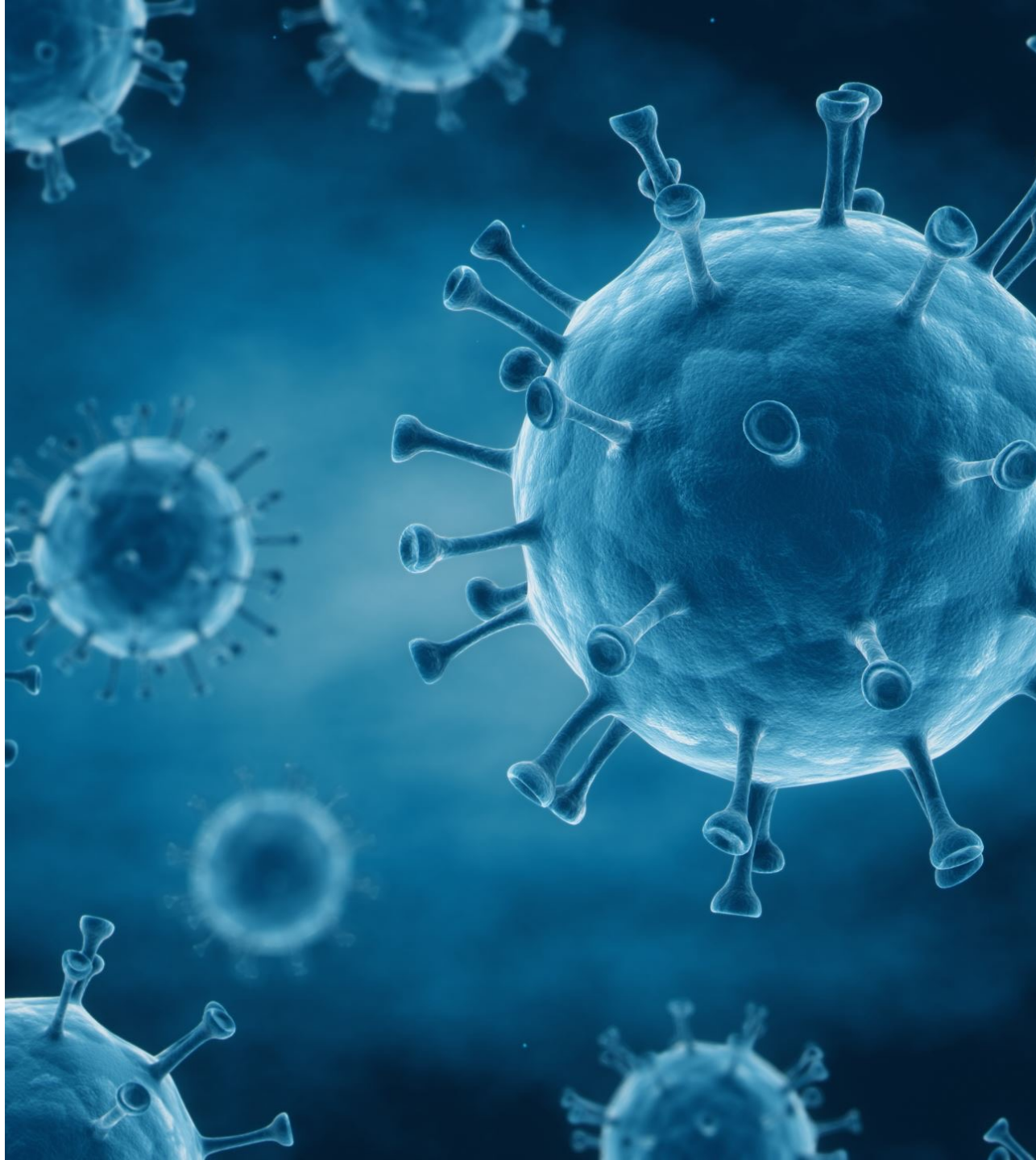
The Month In Virology

October 16, 2024

Jorge Mera, MD

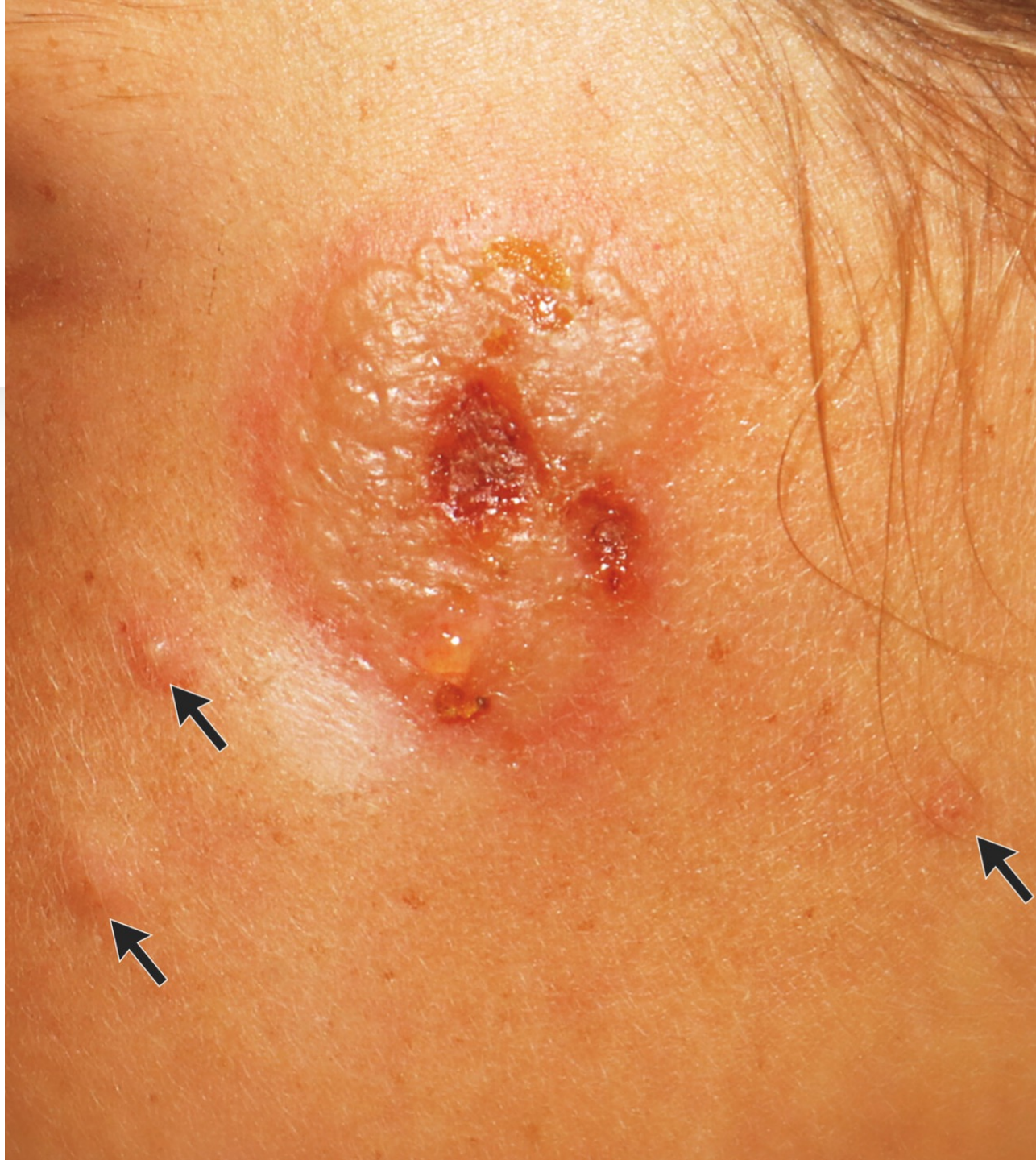
Outline

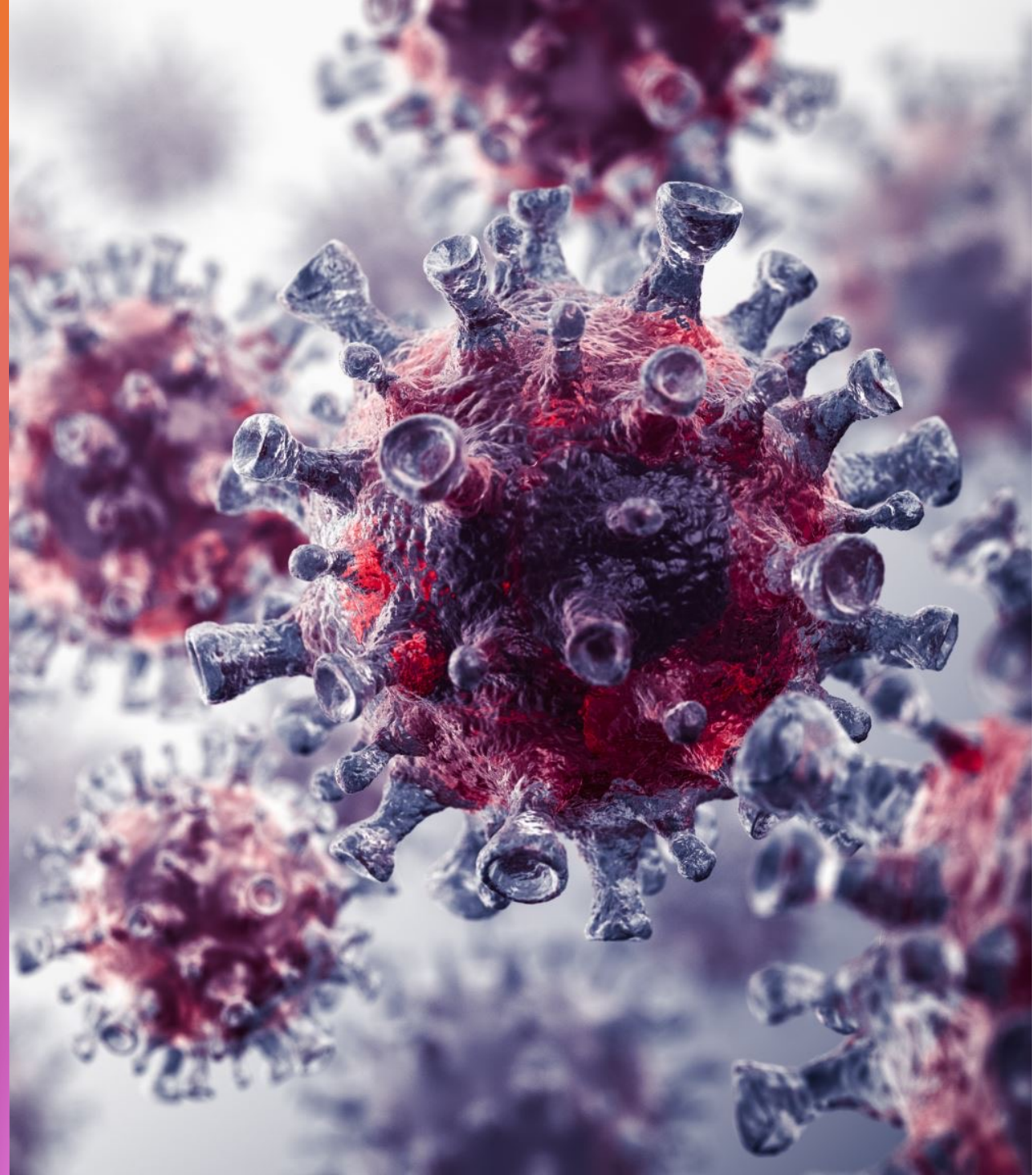
- Images in virology
  - “A cheek infection”
- COVID-19 updates
  - Epidemiology, vaccines and Long COVID
- RSV Updates
  - Vaccines and treatment
- Influenza Updates
  - Avian influenza
- Marburg virus
  - What is going on?



Cutaneous Infection of the Cheek

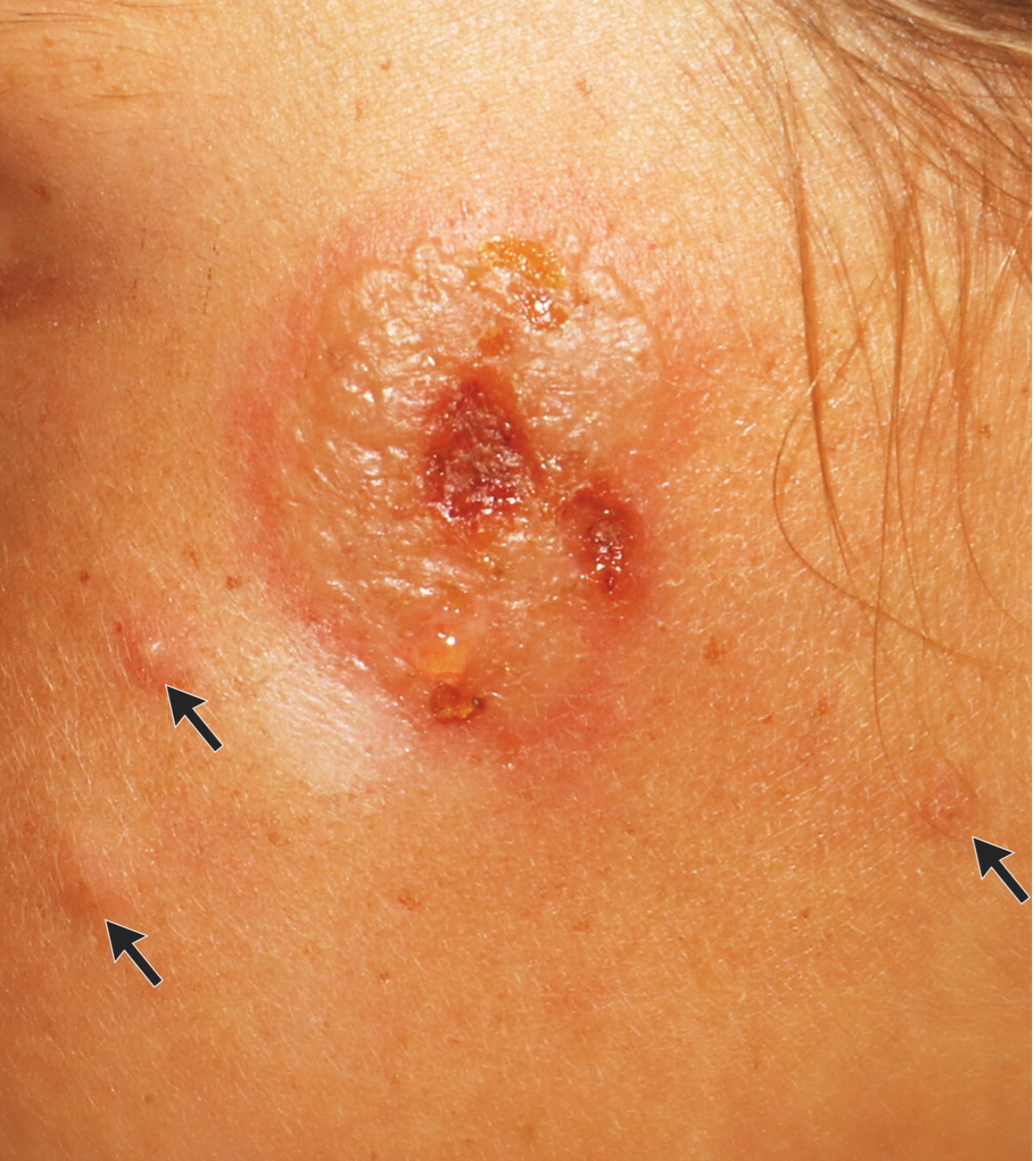
- A 9-year-old girl presented to the dermatology department with a 7-day history of a lesion on the left cheek and a 4-day history of fever.
- Four days before presentation, treatment for possible impetigo had been initiated, but the symptoms had not abated.
- On physical examination, a round plaque 3 cm in diameter on an erythematous base was observed on the patient's left cheek, with overlying crusting and a single intact vesicle.
- Satellite vesicles (arrows) and ipsilateral cervical lymphadenopathy were also present.
- There were no mucosal lesions. The patient's father, who had accompanied her to the appointment, was noted to have crusting of the lower lip that had started 10 days earlier, a symptom consistent with healing herpes labialis.





What is the most likely etiologic diagnosis

A. Group A streptococcus
B. HSV-1
C. M-pox
D. Varicella virus
E. Marburg virus



Primary Cutaneous Herpes Simplex Virus Infection of the Cheek

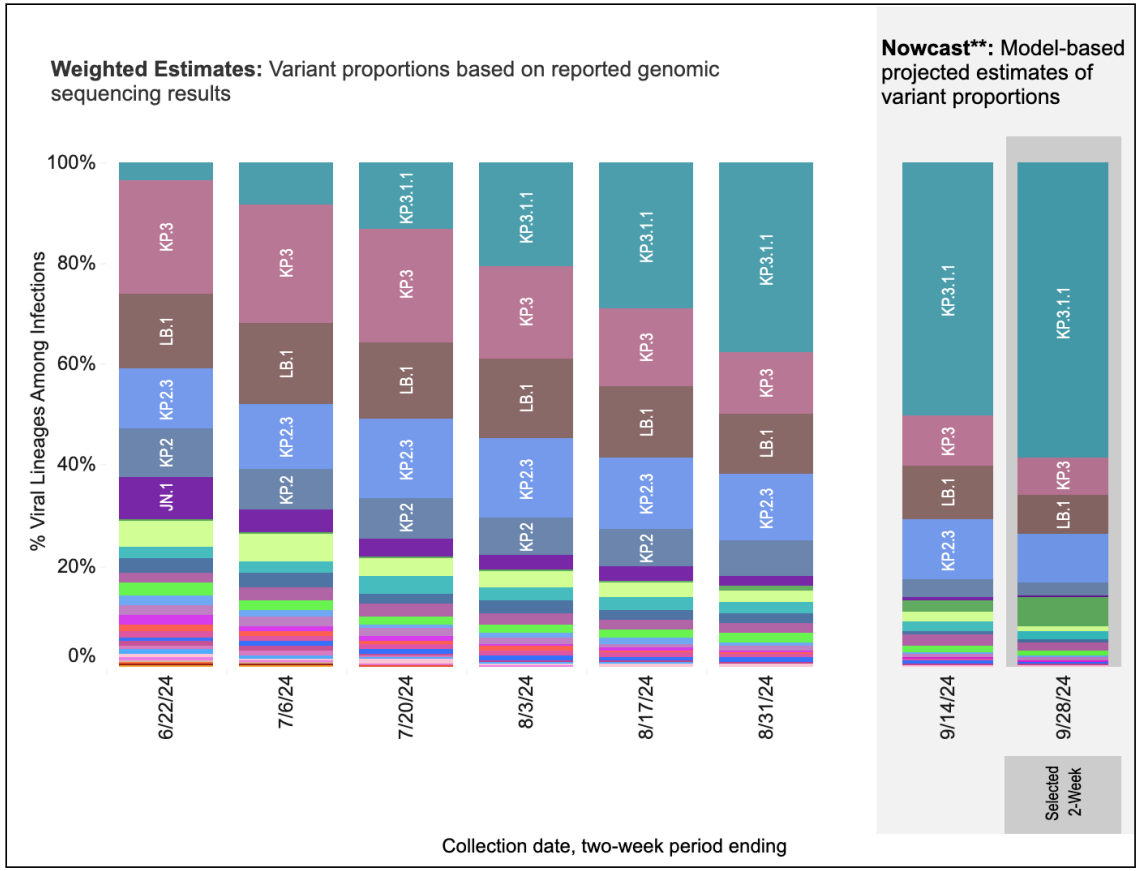
N Engl J Med 2024;391: e20 DOI: 10.1056/NEJMicm2403121 VOL. 391 NO. 9

- A polymerase-chain-reaction assay of an unroofed vesicle on the patient's cheek was positive for herpes simplex virus type 1 (HSV-1).
- A diagnosis of primary cutaneous HSV-1 infection was made.
- HSV-1 spreads through direct contact with herpetic lesions or infected mucosal secretions.
- In this case, there was no concern for sexual abuse.
- When HSV-1 infection manifests in children as cutaneous lesions without mucosal involvement, it may be confused with the honey-crusted appearance of impetigo.
- Treatment with oral acyclovir was given, and the lesion abated without scarring.

Variant Proportions

Weighted and Nowcast Estimates in United States for 2-Week Periods in 6/9/2024 – 9/28/2024

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 9/15/2024 – 9/28/2024

USA

WHO label	Lineage #	%Total	95%PI
Omicron	KP.3.1.1	58.7%	54.4-62.9%
	KP.2.3	9.4%	8.3-10.7%
	LB.1	7.9%	6.6-9.4%
	KP.3	7.1%	6.1-8.4%
	XEC	6.0%	2.4-13.2%
	KP.2	2.5%	1.9-3.5%
	LP.1	1.7%	1.1-2.5%
	KP.1.1.3	1.4%	1.0-2.0%
	KP.1.1	1.1%	0.8-1.5%
	JN.1.18	1.1%	0.5-2.4%
	KS.1	0.6%	0.4-0.9%
	JN.1.16.1	0.6%	0.4-0.8%
	KP.2.15	0.4%	0.2-0.7%
	LF.3.1	0.3%	0.2-0.4%
	JN.1	0.2%	0.1-0.3%
	JN.1.11.1	0.1%	0.1-0.3%
	KP.4.1	0.1%	0.0-0.2%
	XDV.1	0.0%	0.0-0.1%
	KW.1.1	0.0%	0.0-0.0%
	JN.1.7	0.0%	0.0-0.0%
	JN.1.16	0.0%	0.0-0.0%
	KQ.1	0.0%	0.0-0.0%

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

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 tracke 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://web.archive.org/web/20240116214031/https://www.pango.network/the-pango-nomenclature-system/statement-of-nomenclature-rules.

COVID-19 Updates

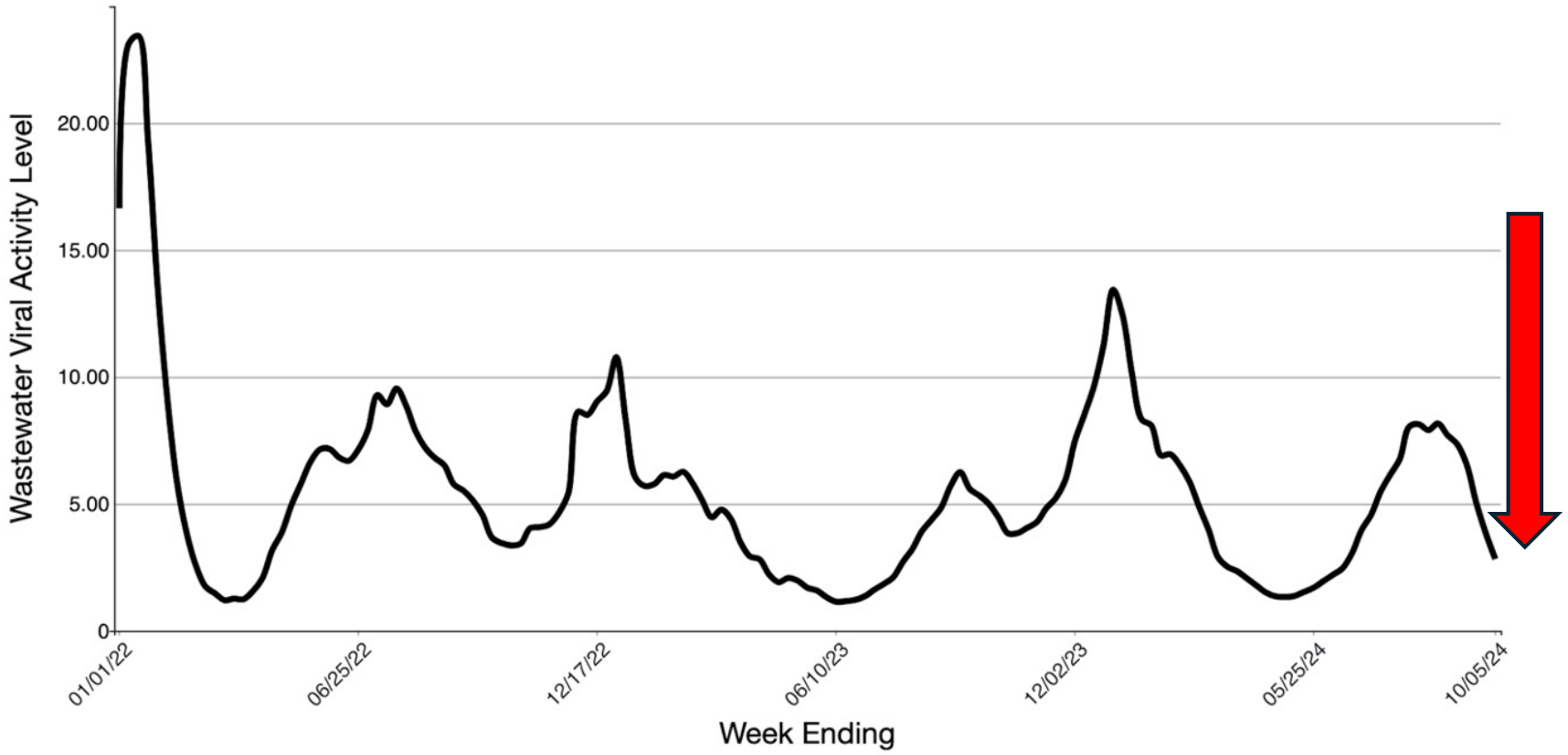
What's going on with the variants?

KP.3.1.1, KP.2.3, and LB.1

- Accounted for most infections in the United States as of the first week of October.

The surge is over, trending back to endemic levels

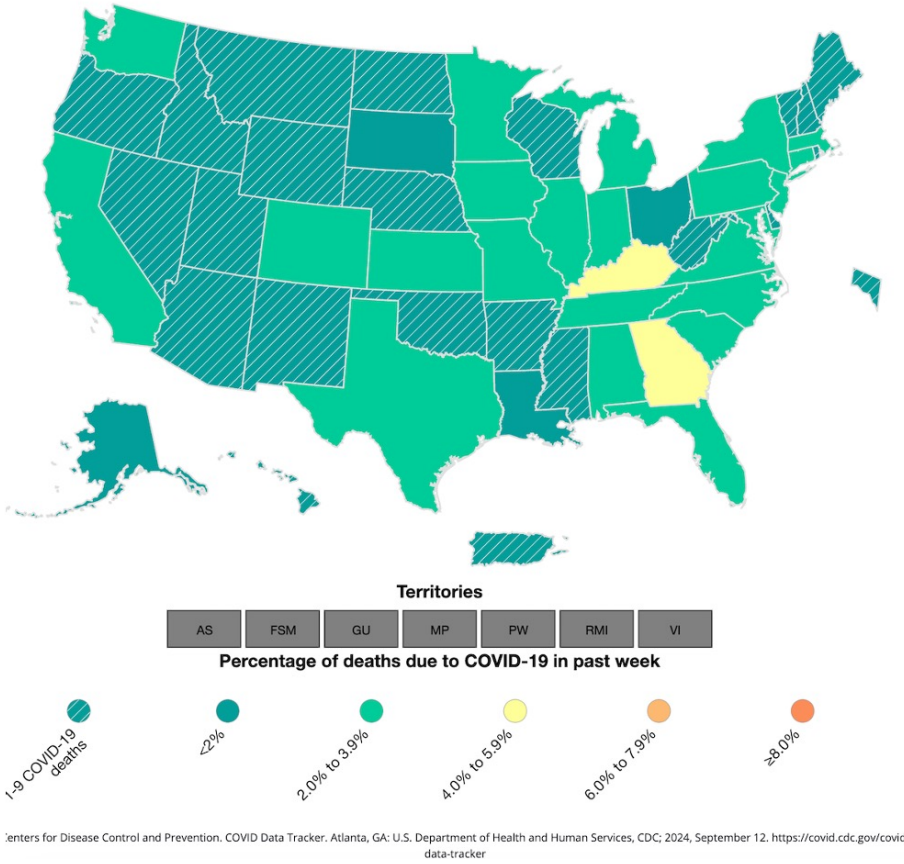
COVID-19 Wastewater Viral Activity Level Over Time, United States



Centers for Disease Control and Prevention. COVID Data Tracker. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2024, October 10. https://covid.cdc.gov/covid-data-tracker

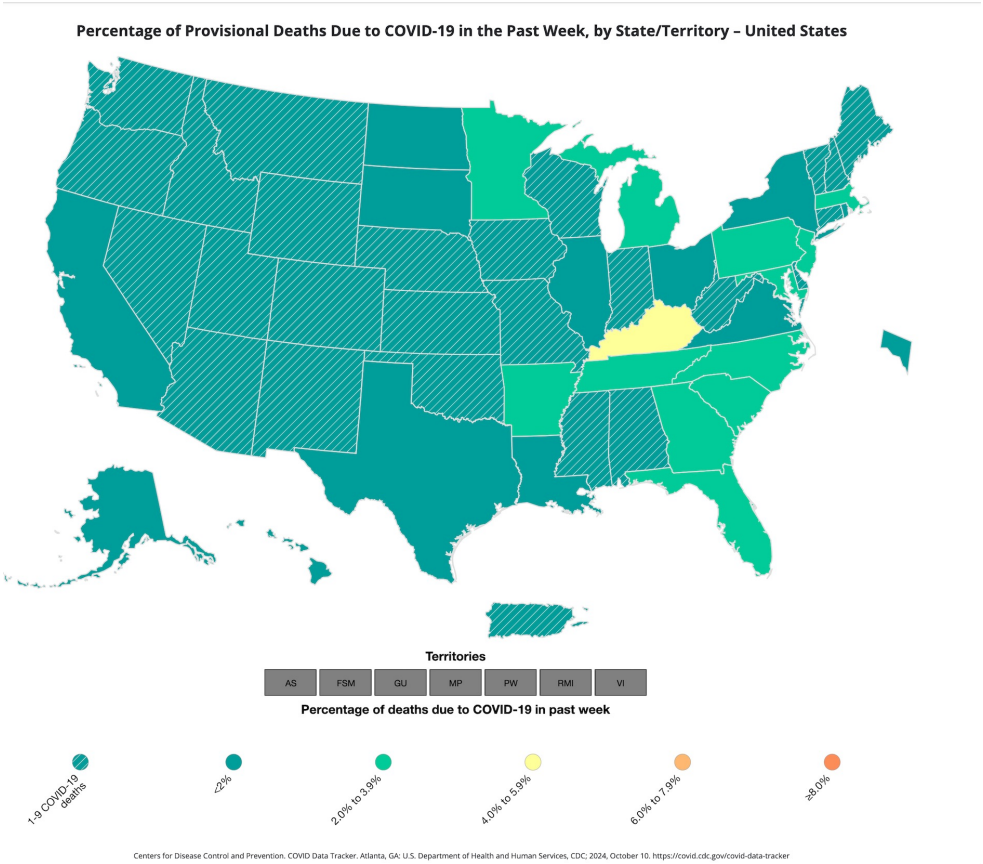
Percentage of Provisional Deaths Due to COVID-19 in the Past week, by State/Territory-United States

Week of September 12



:enters for Disease Control and Prevention. COVID Data Tracker. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2024, September 12. https://covid.cdc.gov/covid-data-tracker

Week of October 8



Centers for Disease Control and Prevention. COVID Data Tracker. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2024, October 10. https://covid.cdc.gov/covid-data-tracker

COVID-19 Update for the United States

COVID-19 Update for the United States

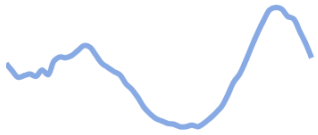
Early Indicators

Test Positivity

% Test Positivity

11.6%

Week ending September 21, 2024
Previous week 13.4%



Sep 30, 2023 Sep 21, 2024

Emergency Department Visits

% Diagnosed as COVID-19

1.1%

Week ending September 28, 2024
Previous week 1.4%

Oct 7, 2023 Sep 28, 2024

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

Severity Indicators

Hospitalizations

Rate per 100,000 population

3.7

Week ending September 14, 2024
Previous week 4.0

Sep 23, 2023 Sep 14, 2024

Deaths

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

1.9%

Week ending September 28, 2024
Previous week 2%

Oct 7, 2023 Sep 28, 2024

CDC | Test Positivity data through: September 21, 2024; Emergency Department Visit data through: September 28, 2024; Hospitalization data through: September 14, 2024; Death data through: September 28, 2024.
Posted: October 8, 2024 12:58 PM ET

COVID-19 Updates

What's going on with the clinical impact?

https://www.cdc.gov/nchs/nvss/vsrr/covid19/index.htm

Deaths involving COVID-19, pneumonia, and influenza reported to NCHS by year and jurisdiction of occurrence.

Data as of: 10/3/2024

State: United States

Year: All

Year in which death occurred	All Deaths involving COVID-19 [1]	Deaths from All Causes	Percent of Expected Deaths [2]	Deaths involving Pneumonia [3]	Deaths involving COVID-19 and Pneumonia [3]	All Deaths involving Influenza [4]	Deaths involving Pneumonia, Influenza, or COVID-19 [5]
2024	37,129	2,195,827	77	132,457	14,562	8,042	162,602
2023	76,024	3,101,011	109	190,752	28,236	6,130	244,200
2022	246,272	3,289,563	116	267,763	110,419	8,764	411,621
2021	463,267	3,471,742	122	412,015	259,617	1,092	616,484
2020	385,676	3,390,079	119	352,022	180,092	8,787	565,242
Total	**1,208,368**	**15,448,222**		**1,355,009**	**592,926**	**32,815**	**2,000,149**

COVID-19 Updates

What's going on with the clinical impact?

https://www.cdc.gov/nchs/nvss/vsrr/covid19/index.htm

Deaths involving COVID-19, pneumonia, and influenza reported to NCHS by month and jurisdiction of occurrence.

Data as of: 10/3/2024

State: United States | Month: All | Year: All

Month in which death occurred	All Deaths involving COVID-19 [1]	Deaths from All Causes	Percent of Expected Deaths [2]	Deaths involving Pneumonia [3]	Deaths involving COVID-19 and Pneumonia [3]	All Deaths involving Influenza [4]	Deaths involving Pneumonia, Influenza, or COVID-19 [5]
September 2024	3,400	161,555	73	9,156	1,367	96	11,278
August 2024	4,975	242,965	108	13,464	1,974	133	16,582
July 2024	2,923	238,045	105	12,960	1,205	127	14,794
June 2024	1,641	239,568	108	13,029	662	178	14,176
May 2024	1,531	249,864	108	13,887	610	303	15,101
April 2024	2,223	249,245	107	14,717	846	689	16,746
March 2024	4,165	263,664	104	16,349	1,606	1,370	20,217
February 2024	6,020	255,663	109	16,792	2,327	1,836	22,201
January 2024	10,251	295,258	109	22,103	3,965	3,310	31,507
December 2023	8,628	284,333	111	19,419	3,194	1,829	26,583
November 2023	6,236	258,271	110	15,894	2,330	408	20,180
October 2023	5,909	258,973	110	15,195	2,201	197	19,077
September 2023	5,967	245,259	111	14,480	2,386	139	18,183
August 2023	4,066	250,843	111	13,494	1,558	99	16,090
Total	**1,208,368**	**15,448,222**		**1,355,009**	**592,926**	**32,815**	**2,000,149**

COVID-19 Updates

What's going on with the clinical impact?

https://www.cdc.gov/nchs/nvss/vsrr/covid19/index.htm

% COVID-19 DEATHS IN PAST WEEK	% CHANGE FROM PRIOR WEEK	ABSOLUTE CHANGE FROM PRIOR WEEK
1.9%	-5%	-0.1%

CDC | Data through: September 28, 2024. Posted: October 8, 2024

Deaths involving COVID-19, pneumonia, and influenza reported to NCHS by week and jurisdiction of occurrence.

Data as of: 10/3/2024

State: United States

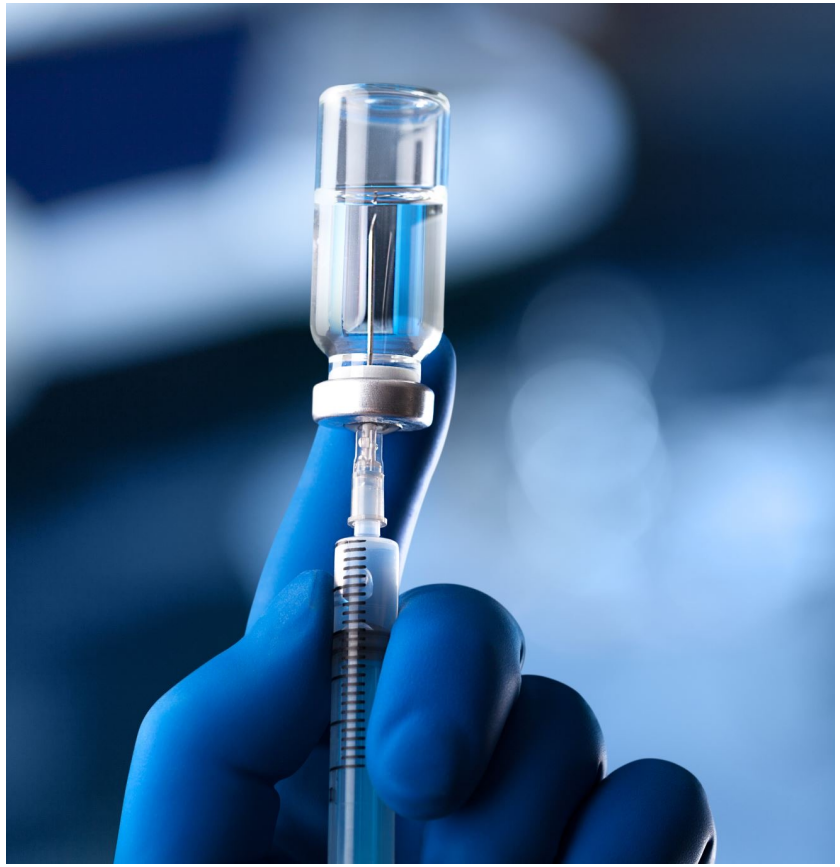
Week ending date in which the death occurred	All Deaths involving COVID-19 [1]	Deaths from All Causes	Percent of Expected Deaths [2]	Deaths involving Pneumonia, Influenza, or COVID-19 [3]
9/28/2024	447	23,248	45	1,587
9/21/2024	767	39,186	76	2,723
9/14/2024	1,063	47,561	92	3,300
9/7/2024	1,123	51,560	101	3,668
8/31/2024	1,288	53,575	105	3,833
8/24/2024	1,196	54,621	108	3,765
8/17/2024	1,045	55,223	109	3,734
8/10/2024	1,032	55,255	108	3,694
8/3/2024	934	55,121	108	3,625
7/27/2024	798	53,675	106	3,467
7/20/2024	654	53,079	104	3,267
7/13/2024	532	53,802	105	3,197
7/6/2024	488	54,218	105	3,266
6/29/2024	433	55,205	107	3,202
6/22/2024	429	55,689	108	3,312
6/15/2024	361	56,239	109	3,313
Total	**1,208,368**	**15,473,380**		**2,001,959**

COVID-19 Updates

What is going on with vaccines?

- **In August 2024 the FDA approved and authorized the Omicron JN.1 lineage (JN.1 and KP.2), 2024–2025 COVID-19 vaccines**
  - By Moderna and Pfizer-BioNTech (KP.2 strain)
  - Novavax (JN.1 strain).

- **The CDC recommends that people in high-risk categories**
  - Get a second dose of vaccine at least four months after their last booster
  - Get the updated 2024-2025 vaccine once it is available.



COVID-19 Disease Incidence and Severity in Previously Infected Unvaccinated Compared with Previously Uninfected Vaccinated Persons

ABSTRACT: Question, Methods and Outcomes Measured

Question:

- What gives you better protection, vaccination or infection

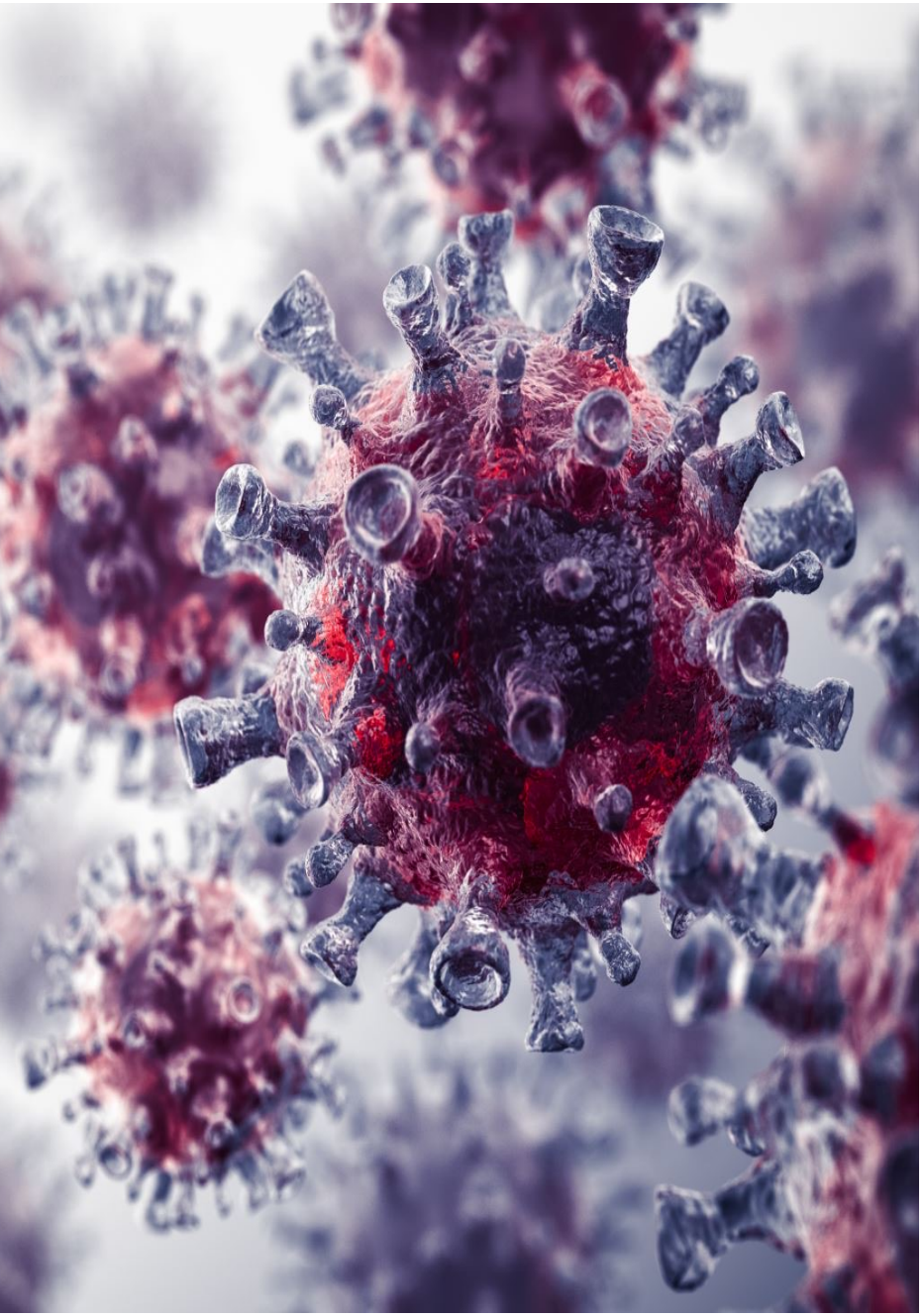
Methods:

- Using the VA COVID-19 National Database, matched pairs of previously uninfected vaccinated (≥2 doses of an mRNA vaccine) and previously infected unvaccinated individuals were created

Outcomes Measured

- The incidence rate (per 1000 person-days) of breakthrough infection
- The incidence rate of hospitalization/death

The Journal of Infectious Diseases, 2024;, jiae484, https://doi.org/10.1093/infdis/jiae484



Which of the following statements is true?

A. The incidence of COVID-19 infection is significantly higher after reinfection among unvaccinated (but previously infected individuals) compared with breakthrough infection after vaccination in individuals without a previous infection

B. The incidence of hospitalization/death is significantly higher after reinfection among unvaccinated (but previously infected individuals) compared with breakthrough infection after vaccination in individuals without a previous infection

C. Incidence of COVID-19 infection and incidence of hospitalization/death is not different among unvaccinated (but previously infected individuals compared with breakthrough infection after vaccination in individuals without a previous infection

COVID-19 Disease Incidence and Severity in Previously Infected Unvaccinated Compared with Previously Uninfected Vaccinated Persons

ABSTRACT: Results

Among vaccinated individuals without previous infection

- The incidence rate (per 1000 person-days) of breakthrough infection was
- 0.30 (95% CI 0.29-0.32)
- The incidence rate of hospitalization/death was 4.69 (95% CI 4.06-5.42)

Among unvaccinated individuals with a previous infection

- The incidence rate of reinfection 0.31 (95% CI 0.30-0.32);
  P=0.5 compared to vaccinated.
- The incidence rate of hospitalization/death was 7.31, 95% CI 6.66-8.03)
  P<0.0001 compared to vaccinated.

The Journal of Infectious Diseases, 2024;, jiae484, https://doi.org/10.1093/infdis/jiae484

COVID-19 Disease Incidence and Severity in Previously Infected Unvaccinated Compared with Previously Uninfected Vaccinated Persons

ABSTRACT: Conclusions

"The incidence of hospitalization/death is significantly higher after reinfection among unvaccinated individuals compared with breakthrough infection after vaccination"

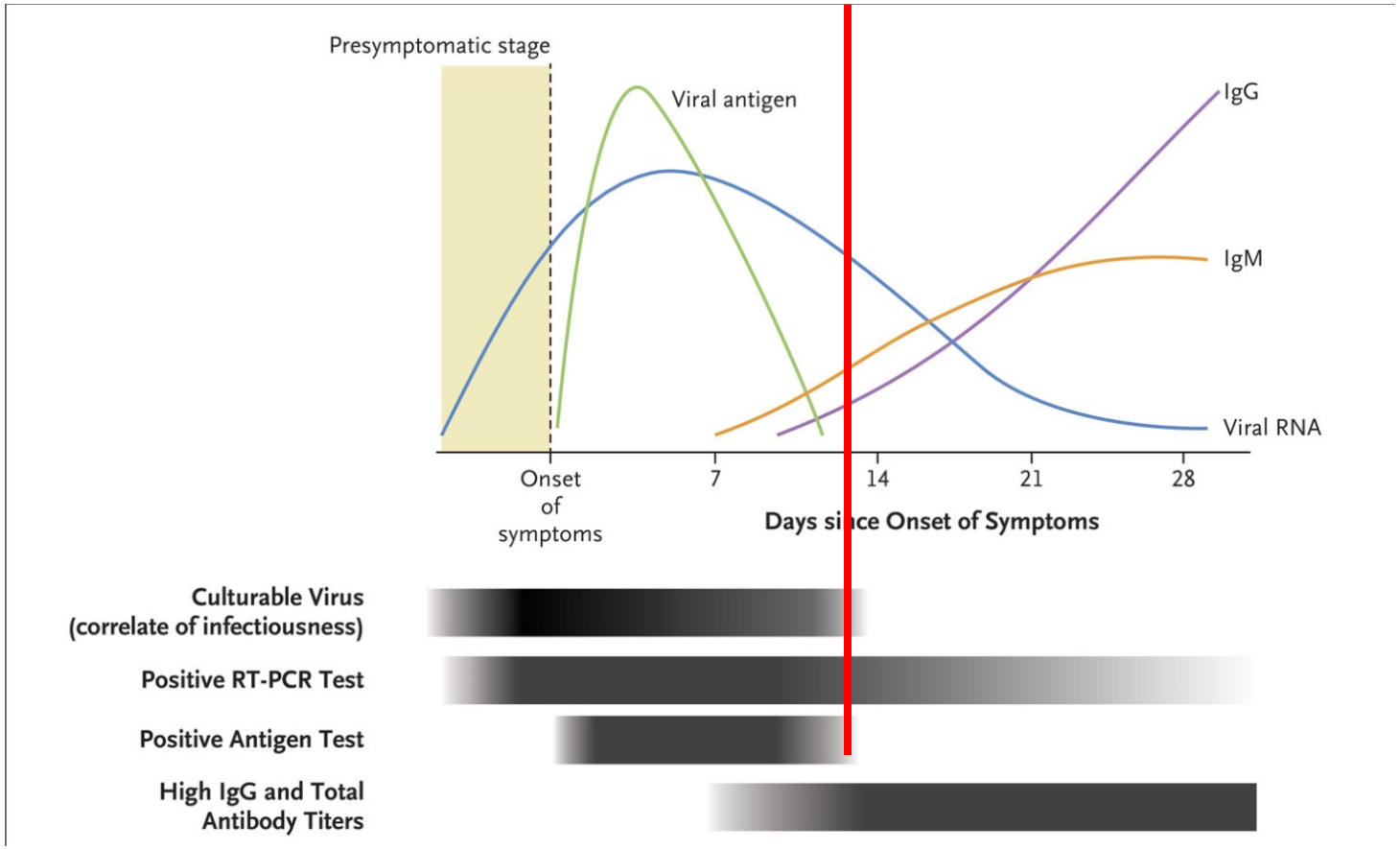
The Journal of Infectious Diseases, 2024;, jiae484, https://doi.org/10.1093/infdis/jiae484

COVID-19 Updates

- ***What is going on with masks?***
  - Especially useful in high-risk environments
  - Specially when the virus is surging
  - Specially indoors and crowded conditions
  - N95 > surgical > cloth

COVID-19 Updates

- ***What is going on with isolation of* Non-Health Care Personnel?**
  - According to CDC guidelines non-health care personnel with acute SARS-CoV-2 infection can resume normal activity if their symptoms have improved for 24 hours and if they haven't had a fever in 24 hours without taking a fever suppressant, but should continue to take extra precautions, like masking, for an additional five days.
- **Guidelines have not changed for health care personnel**



N Engl J Med 2020;383: e120DOI: 10.1056/NEJMp2025631

COVID-19 Updates

- ***What is going on with treatment?***
  - Those in high-risk groups (people 65 and older or anyone over age 12 with a condition that is a risk factor for severe COVID, including diabetes, asthma, heart disease, obesity, or pregnancy) still benefit from an antiviral
  - It must be started within five to seven days of developing symptoms.

COVID-19 Therapeutics for Nonhospitalized Older Adults

Age is a major factor	• In determining risk for severe outcomes
Persons at high risk of severe disease with mild to moderate COVID-19	• Should be offered antivirals. • Treatment should be started within 5 to 7 days of symptom onset among
Regardless of vaccination status or history of prior infection	• All persons 65 years or older should be considered for treatment • Persons with heart disease, obesity, diabetes, or chronic lung disease are likely to benefit from treatment.
Assessing a patient's risk for severe COVID-19 before infection	• Helps predetermining the appropriate regimen that can facilitate timely treatment.

JAMA. Published online October 7, 2024. doi:10.1001/jama.2024.16460

COVID-19 Therapeutics for Nonhospitalized Older Adults

The number of hospitalizations associated with COVID-19:	• Are higher than for influenza during the 2023-2024 season. • Hospitalization rates were highest among adults 65 years or older
Modeling studies showed that increasing treatment uptake by 80%	• Would reduce hospitalizations by 42% and deaths by 51%.
A 2024 survey of 2858 adults at high risk of severe disease found that:	• Only 16.5% had ever received COVID-19 treatment and only 23.3% would choose to take an antiviral if prescribed.

JAMA. Published online October 7, 2024. doi:10.1001/jama.2024.16460

COVID-19 Therapeutics for Nonhospitalized Older Adults

Reasons for this gap in treatment are due to	• Clinicians reluctance to use Paxlovid due to drug-drug interactions and adverse effects. • Inequities in access to health care.
The clinical and public health community needs to	• Strongly consider and promote COVID-19 treatments to improve patient outcomes

JAMA. Published online October 7, 2024. doi:10.1001/jama.2024.16460

COVID-19 Therapeutics for Nonhospitalized Older Adults

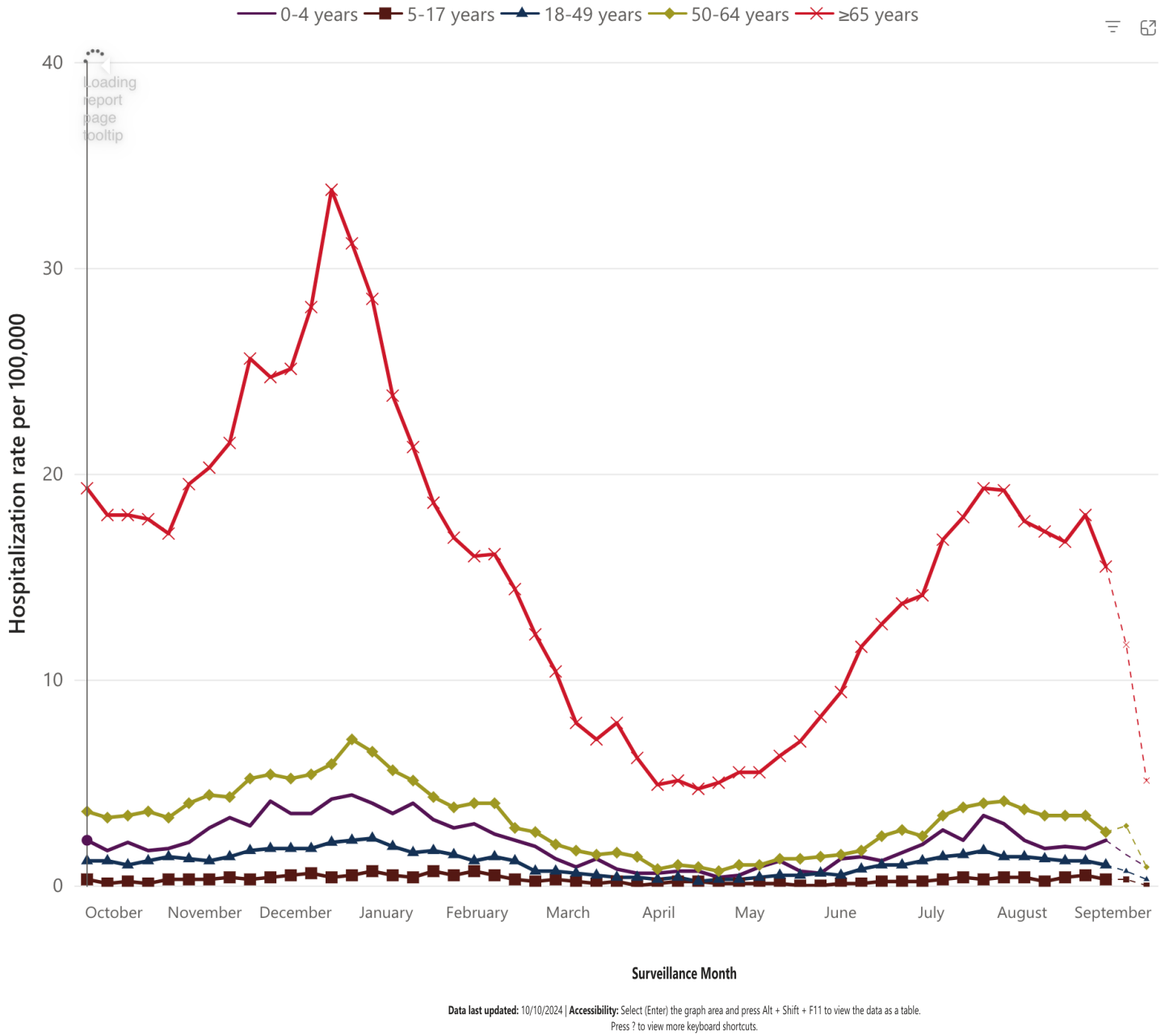
Ending COVID-19 as a public health threat hinges on enhancing the use of primary and secondary disease prevention. Particularly among older adults, who are the most vulnerable to COVID-19 morbidity and mortality.

Public health and medical professionals are best positioned to support patients and their caregivers to make informed choices that prevent COVID-19.

Reducing the burden of COVID-19 is within reach—the opportunity should be seized now.

JAMA. Published online October 7, 2024. doi:10.1001/jama.2024.16460

COVID-NET Laboratory-confirmed COVID-19 hospitalizations



Use of metformin in adults with diabetes linked to lower risk of long COVID

This study was supported by NIH under agreement number OT2HL161847 as part of the RECOVER research program.

- **Background:**
  - An NIH-supported clinical trial in 2023 showed that treatment with metformin, reduced the risk of long COVID by as much as 40% in nearly 1,300 U.S. adults with overweight or obesity, most of whom did not have type 2 diabetes (T2D).
- **Methods:**
  - Electronic health records (EHR) data for nearly 38 million Americans from two large U.S. databases were examined.
  - EHR from 75,996 adults taking metformin for their **T2D** were compared to 13,336 records from patients who were other **T2D** medications but NOT Metformin
- **Outcomes**
  - Death
  - Long COVID diagnosis within six months after infection.

Use of metformin in adults with diabetes linked to lower risk of long COVID

Results	• Patients taking metformin had a 13% to 21% lower incidence of long COVID or death than those in the non-metformin group.
Conclusions	• Patients taking metformin Adults who use the prescription drug metformin to treat their type 2 diabetes have a lower risk of developing long COVID or dying after a COVID-19 infection than people with diabetes who take other anti-diabetes medications
Mechanism of action	• Unknown, but the possibility of several mechanisms that reduce inflammation, decrease viral levels, and suppress the formation of disease-related proteins was entertained

This study was supported by NIH under agreement number OT2HL161847 as part of the RECOVER research program.

From: **Prevalent Metformin Use in Adults With Diabetes and the Incidence of Long COVID: An EHR-Based Cohort Study From the RECOVER Program**

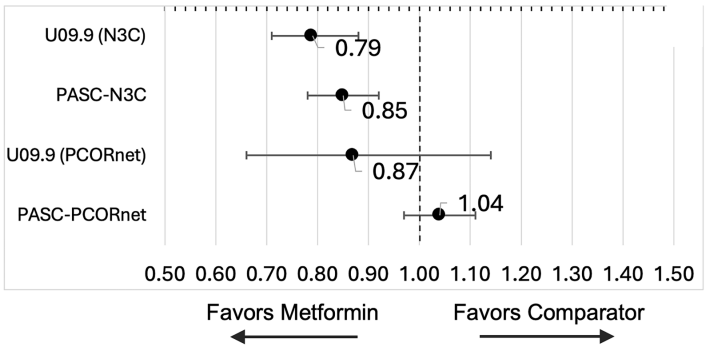
Diabetes Care. Published online September 17, 2024. doi:10.2337/DCa24-0032

Metformin Association with Death or Long COVID (PASC) in Adults with Type 2 Diabetes

Aim: To describe the incidence of PASC and possible association with prevalent metformin use in adults with T2DM.

Methods: Retrospective cohort analysis using **N3C** and **PCORNet** electronic health record databases with an active comparator desing that examined metformin-exosed individuals versus nonmetformin-exposed individuals using other diabetes medications.

Conclusion: Metformin use is associated with a slightly **lower incidence of death or PASC** after SARS-CoV-2 infection.



GSK RSV Vaccine Data Suggest Protection Across 3 Seasons

Arexvy	Is an RSV vaccine approved for adults ages 60 and older in the fall of 2023. FDA expanded the age indication to adults ages 50 to 59 who are at increased risk of RSV complications.
After three RSV seasons	Cumulative protection after a single dose was still meaningful
For individuals 60 years or older:	Efficacy of 62.9% against lower respiratory tract disease (LRTD) caused by RSV Efficacy of 67.9% against severe disease when compared with placebo. **For the third season, efficacy was 48% against RSV-related LRTD.**
Since protection is long:	There is a flexibility to vaccinate patients against RSV all year round. **Revaccination might be needed to maintain protection**

CIDRAP *News brief October 9, 2024*

Endpoint	Season one efficacy*	Season two efficacy	Season three efficacy	Cumulative efficacy over three seasons**
RSV-LRTD	Primary confirmatory endpoint: 6.7 months median follow- up **82.6%** 96.95% CI, 57.9–94.1 7 of 12,466 vs 40 of 12,494	Secondary descriptive endpoint: 6.3 months median follow-up **56.1%** 95% CI, 28.2–74.4 20 of 4,991 vs 91 of 10,031	Secondary descriptive endpoint: 7 months median follow-up **48.0%** 95% CI, 8.7-72.0 16 of 4,988 vs 61 of 10,031	Secondary confirmatory endpoint: 30.6 months median follow-up **62.9% - with season as covariate***** 97.5% CI, 46.7-74.8 48 of 12,468 vs 215 of 12,498 **69.1% - without season as covariate (post-hoc analysis)** 97.5% CI, 55.8-78.9 48 of 12,468 vs 215 of 12,498
Severe LRTD	Secondary descriptive endpoint **94.1%** 95% CI, 62.4–99.9 1 of 12,466 vs 17 of 12,494	Secondary descriptive endpoint **64.2%** 95% CI, 6.19–89.2 5 of 4,991 vs 28 of 10,031	Secondary descriptive endpoint **43.3%** 95% CI, -45.3-81.3 6 of 4,988 vs 21 of 10,031	Secondary descriptive endpoint **67.4% - with season as covariate***** 95% CI, 42.4-82.7 15 of 12,468 vs 75 of 12,498 **72.3 % - without season as covariate (post-hoc analysis)** 95% CI, 51.3 – 85.2 15 of 12,468 vs 75 of 12,498
RSV-LRTD in participants with at least 1 pre-existing comorbidity of interest	Secondary descriptive endpoint **94.6%** 95% CI, 65.9–99.9 1 of 4,937 vs. 18 of 4,861	Secondary descriptive endpoint **51.5%** 95% CI, 7.4 – 76.6 12 of 1,981 vs 48 of 3,895	Secondary descriptive endpoint **57.8 %** 95% CI, 8.0-83.0 8 of 2,000 vs 37 of 3,924	Secondary descriptive endpoint **64.7% - with season as covariate***** 95% CI, 45.1-78.1 25 of 5014 vs 116 of 4951 **71.1% - without season as covariate (post-hoc analysis)** 95% CI, 55.2 – 82.0 25 of 5014 vs 116 of 4951

* The absolute values are being presented vaccinated group vs placebo group.
** The vaccine efficacy is estimated using a Poisson model adjusted by age, region and season.
*** Seasonality covariate means the data have been adjusted to reflect the variability of disease incidence between different seasons.

GSK Announcement, October 8, 2024

Respiratory Syncytial Virus Vaccine, Adjuvanted, contains recombinant RSV glycoprotein F stabilized in the prefusion conformation (RSVPreF3).

The NEW ENGLAND JOURNAL of MEDICINE

Ziresovir in Hospitalized Infants with RSV Infection

A PLAIN LANGUAGE SUMMARY

Based on the NEJM publication: Ziresovir in Hospitalized Infants with Respiratory Syncytial Virus Infection by S. Zhao et al. (published September 26, 2024)

In this trial, researchers assessed the efficacy and safety of ziresovir for treating respiratory syncytial virus (RSV) infection in hospitalized children 1 to 24 months of age.

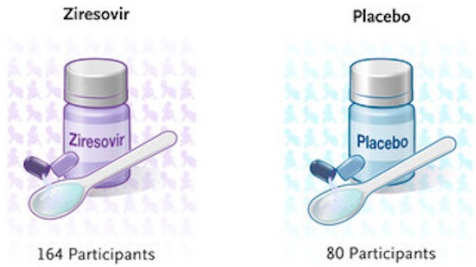
Each year, **RSV infections** cause an estimated 3.6 million hospitalizations and up to 124,900 deaths worldwide among children 5 years of age or younger.

WHY WAS THE TRIAL DONE?

No RSV vaccines are approved for children, and the only currently approved RSV treatment, aerosolized ribavirin, has limited efficacy and an unfavorable safety profile. In a recent phase 2 trial, ziresovir — a selective, orally administered RSV F protein inhibitor — showed promise for treating RSV infection in infants and young children. Additional data are needed.

HOW WAS THE TRIAL CONDUCTED?

Infants and children hospitalized with RSV infection were assigned to receive ziresovir (10 mg, 20 mg, or 40 mg, depending on body weight) or placebo orally every 12 hours for 5 days. The primary efficacy end point was the change from baseline to day 3 in lower respiratory tract infection–related signs and symptoms, as assessed with the Wang bronchiolitis clinical score (range, 0 to 12, with higher scores indicating greater severity of signs and symptoms). The key secondary end point was the change in the RSV viral load from baseline to day 5.



PARTICIPANTS

WHO

311 children, 1 to 24 months of age (244 in intention-to-treat population, 302 in safety population)

Mean age, 6.2 months (safety population) and 6.3 months (intention-to-treat population)

Male: 74%; Female: 26%

CLINICAL STATUS

RSV infection confirmed by virologic methods within 36 hours before the first dose of ziresovir or placebo

Wang bronchiolitis clinical score of at least 5 at the first dose

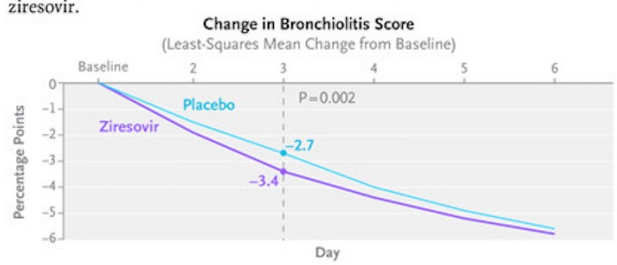
First dose received within 7 days after symptom onset

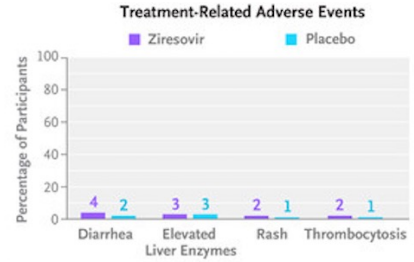
TRIAL DESIGN

- PHASE 3
- DOUBLE-BLIND
- RANDOMIZED
- PLACEBO-CONTROLLED
- LOCATION: 30 CLINICAL SITES IN CHINA

RESULTS

From baseline to day 3, the Wang bronchiolitis clinical score decreased (improved) significantly more in the ziresovir group than in the placebo group. The change in the RSV viral load from baseline to day 5 also favored ziresovir.





The most common treatment-related adverse events with ziresovir were diarrhea, elevated liver-enzyme level, rash, and thrombocytosis.

CLINICAL SCORE COMPONENTS

All components of the Wang bronchiolitis clinical score — respiratory rate, wheezing, respiratory muscle contraction, and general condition — improved with ziresovir as compared with placebo.

LIMITATIONS AND REMAINING QUESTIONS

- The trial used the Wang bronchiolitis clinical score, which is not fully validated in studies of RSV infection.
- The trial was conducted in China; the findings may not be applicable to other regions.
- The researchers did not track the time to the discontinuation of supplemental oxygen or nebulizer use as potential clinical markers of improvement.

CONCLUSIONS

In infants and young children in China who were hospitalized with RSV infection, treatment with ziresovir led to greater reductions in lower respiratory tract infection–related signs and symptoms than placebo.

LINKS: FULL ARTICLE | NEJM QUICK TAKE | EDITORIAL

FURTHER INFORMATION

Trial registration: ClinicalTrials.gov number, NCT04231968

Trial funding: Shanghai Ark Biopharmaceutical

Full citation: Zhao S, Shang Y, Yin Y, et al. Ziresovir in hospitalized infants with respiratory syncytial virus infection. N Engl J Med 2024;391:1096-107. DOI: 10.1056/NEJMoa2313551

Creeping toward Effective Antiviral Agents for RSV Infection

RSV	Is the leading diagnosis in very young infants who are hospitalized.
Reducing hospitalization may be achieved by	RSV vaccine administered during pregnancy Long-acting monoclonal antibody for all newborns proximate to their first RSV season
An effective antiviral agent is needed	To treat infants and older children who are ineligible to vaccines or monoclonals For those who do not benefit from these new interventions.
Aerosolized Ribavirin	Is the only antiviral agent approved for hospitalized patients with RSV With marginal clinical benefit and concerns about toxic effects and cos

Published September 25, 2024 N Engl J Med 2024;391:1155-1156 VOL. 391 NO. 12

Creeping toward Effective Antiviral Agents for RSV Infection

This study had two parts	• An initial part for safety evaluation (54 infants) • Second part for efficacy (an additional 256 infants were randomized)
Infants were randomly assigned in a 2:1 ratio	• To receive ziresovir or placebo every 12 hours for 5 days.
End points	• The primary end point of differential clinical improvement at 48 hours • The secondary end point of the reduction in the nasal viral load at 96 hours.
Adjustments were done for	• Baseline bronchiolitis score, participant age, and illness duration

Published September 25, 2024 N Engl J Med 2024;391:1155-1156 VOL. 391 NO. 12

Creeping toward Effective Antiviral Agents for RSV Infection

The decrease in the bronchiolitis score at 48 hours	• Was 30% greater in the ziresovir group than in the placebo group • Participants ≤ 6 months of age had a significant clinical improvement with ziresovir vs placebo. • > proportion of infants on ziresovir had a reduction 75% in the bronchiolitis score
The nasal viral load	• Decreased more rapidly with ziresovir treatment • Although the difference at 96 hours was modest, at −0.7 $\log_{10}$ copies per milliliter.
Evidence of drug resistance	• emerged in 9% of the treated participants • Importantly, viral rebound was not observed.
Overall	• The results are encouraging, and further studies of ziresovir in more diverse settings and populations are warranted.

Published September 25, 2024 N Engl J Med 2024;391:1155-1156 VOL. 391 NO. 12

Creeping toward Effective Antiviral Agents for RSV Infection Limitation

The Wang bronchiolitis clinical score is not fully validated

- **It is unknown how this treatment will affect:**
  - Earlier hospital discharge
  - Reduction in discharge home with the receipt of supplemental oxygen
  - Limited transfer to the pediatric intensive care unit after admission

The median time from symptom onset to the first dose of ziresovir or placebo

- **Was 4 days** (a time when the viral load is already declining)
- Severity in RSV is driven by the early virus-induced host inflammatory response, not necessarily the viral load

Published September 25, 2024 N Engl J Med 2024;391:1155-1156 VOL. 391 NO. 12

Creeping toward Effective Antiviral Agents for RSV Infection Limitation

Timing of the intervention

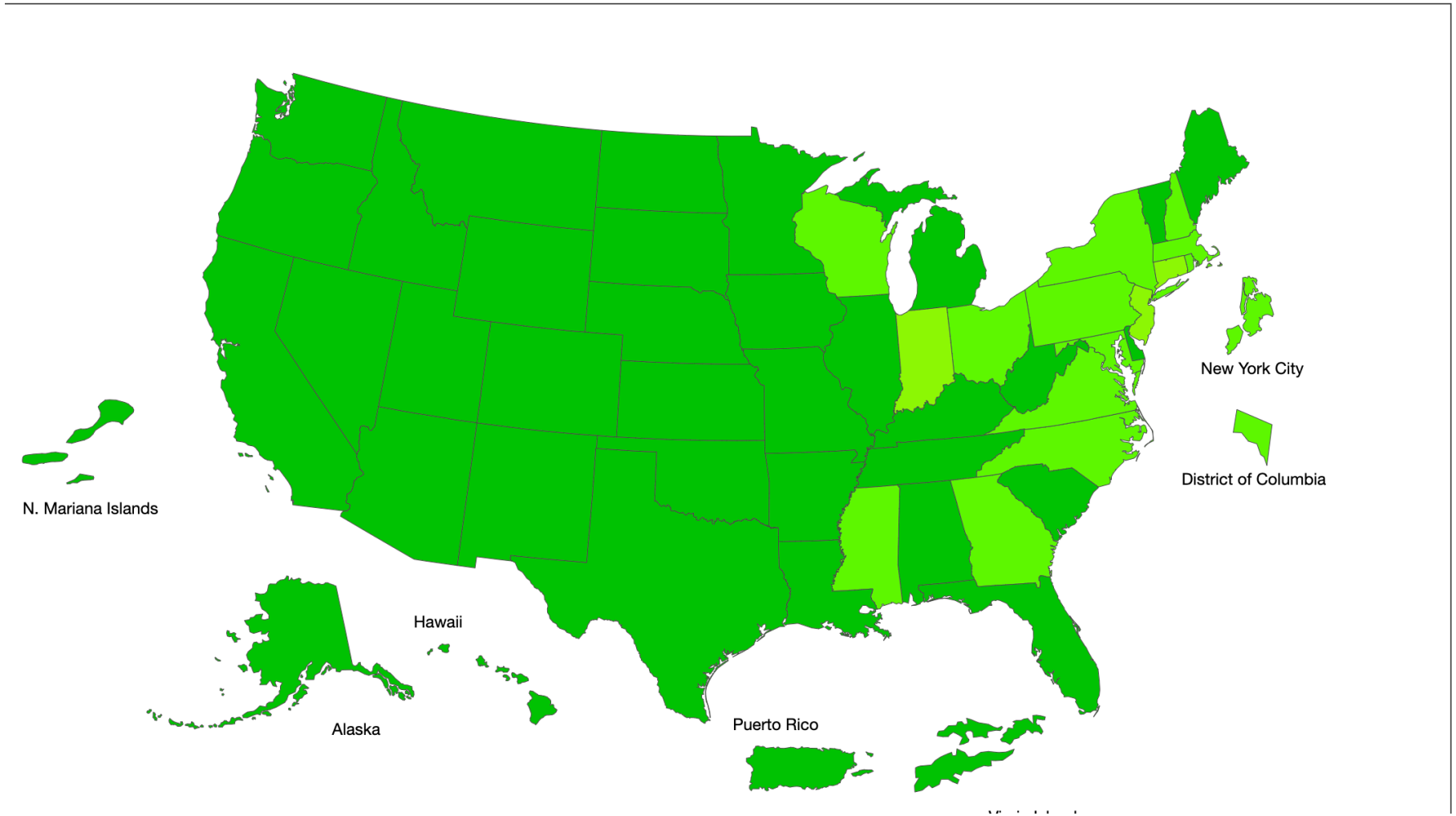
- Usually, 1/2 of hospitalized infants have a health visit in the 24 hours before admission.
- Early treatment may benefit children 2 to 5 years of age who have underlying high-risk conditions that could lead to hospitalization
- Many infants seen in the ED and sent home will be admitted within 24 hours

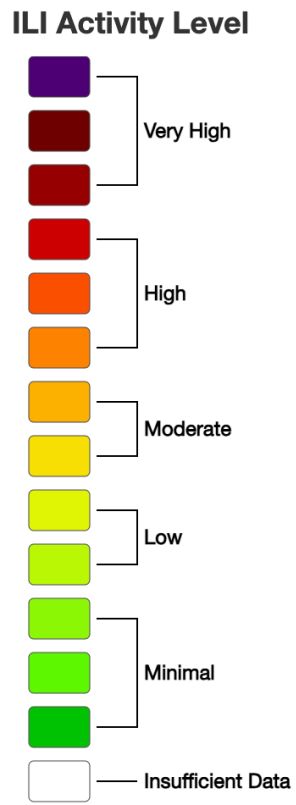
Conclusions:

- If these results are confirmed, they may portend clinical benefits in persons with severe immunosuppression, a group needing an effective RSV antiviral
- Ziresovir offers the potential to augment the recently approved maternal vaccination and monoclonal antibody approaches for reducing the burden of RSV infection in infants

Published September 25, 2024 N Engl J Med 2024;391:1155-1156 VOL. 391 NO. 12

2024-25 Influenza Season Week 40 ending Oct 05, 2024





This map uses the proportion of outpatient visits to healthcare providers for influenza-like illness to measure the ILI activity level within a state. It does not, however, measure the extent of geographic spread of flu within a state. Therefore, outbreaks occurring in a single city could cause the state to display high activity levels.

*Data collected in ILINet may disproportionately represent certain populations within a state, and therefore may not accurately depict the full picture of influenza activity for the whole state.

*Data displayed in this map are based on data collected in ILINet, whereas the State and Territorial flu activity map are based on reports from state and territorial epidemiologists. The data presented in this map is preliminary and may change as more data is received.

*Differences in the data presented by CDC and state health departments likely represent differing levels of data completeness with data presented by the state likely being the more complete.

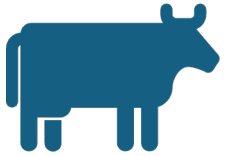
*For the data download you can use Activity Level for the number and Activity Level Label for the text description.

*This graphic notice ( ) means that you are leaving an HHS Web site.

For more information, please see CDC's Exit Notification and Disclaimer policy.

For more information on the methodology, please visit Outpatient Illness Surveillance methods section.

CDC has confirmed two human cases of H5 bird flu from specimens submitted by California



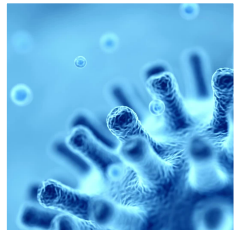
The cases occurred in people with occupational exposure to infected dairy cows.

No evidence of human-to-human transmission

CDC's risk assessment for the public continues to be low.

These are the first human cases of H5 in California

Where H5N1 outbreaks among dairy herds were first reported in August 2024.



H5N1 bird flu was detected for the first time in cows this year in the United States.

The virus is widespread in wild birds and has caused ongoing outbreaks among poultry in the United States since 2022.

It has caused rare, sporadic infections in people who work with infected animals, such as dairy cow workers and poultry workers. Including this most recent case

https://www.cdc.gov/media/releases/2024/s1003-birdflu-case-california.

CDC has confirmed two human cases of H5 bird flu from specimens submitted by California

Sixteen human cases of H5N1 have been reported in the US during 2024, bringing the total to 17 since 2022.

Cases during 2024 were reported in:

Texas (1), Michigan (2), Colorado (10), Missouri (1) and California (2).

Six of the 16 reported human cases have been linked to exposure to sick or infected **dairy cows.**

Nine cases had exposure to infected **poultry**.

The source of infection for the one case in Missouri has not been determined and serologic testing of contacts is ongoing.

https://www.cdc.gov/media/releases/2024/s1003-birdflu-case-california.

Highly pathogenic avian influenza (HPAI) A(H5) CDC Recommendations

People should avoid unprotected exposures to sick or dead animals

- Wild birds
- Poultry
- Domesticated birds
- Other wild or domesticated animals (including cows)

People should also avoid unprotected exposures

- To animal feces, bedding,
- Unpasteurized milk
- Materials that have been touched by, or close to, birds or other animals with suspected or confirmed A(H5N1) virus.

CDC has interim recommendations for

- prevention
- Monitoring
- Public health investigations of A(H5N1) virus infections in people.
- PPE recommendations

Following these recommendations

- **Is central to reducing a person's risk and containing the overall public health risk.**

For immediate release: July 25, 2024 http://www.cdc.gov/media

What are We Trying to Achieve with Respiratory Virus Vaccines?

Risk Factors* for Severe Respiratory Viral Disease

Condition	COVID-19	Influenza	RSV
Age	50+ years	<2 and 65+ years	<2 and 75+ years
Cardio-pulmonary	Yes	Yes	Yes
Renal/hepatic	Yes	Yes	Unclear
Diabetes	Yes	Yes	Yes
Congenital/Developmental Disabilities	Yes	Yes	Some
Diseases and Drugs affecting Immune Response	Yes	Yes	Yes
Multiple Conditions	Yes	Yes	Probably
Pregnancy	Yes	Yes	Not evident

https://www.cdc.gov/respiratory-viruses/risk-factors/index.html

Fall and Winter Immunization Guide

COVID-19 and Flu Updated 2024-25 Vaccines

Everyone 6 months and older

RSV Immunization to Protect Babies

Vaccine
Pregnant parents during weeks 32-36 of pregnancy during RSV season

OR

Monoclonal Antibodies
Babies entering or born during the RSV season

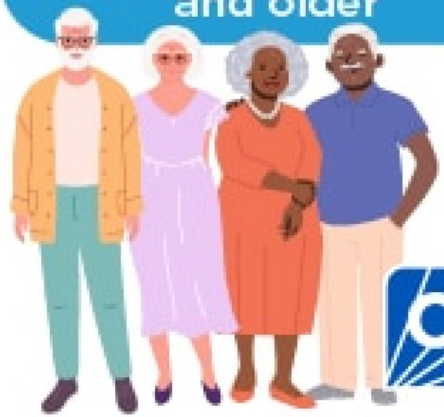
RSV Vaccine for Older Adults

(currently, older adults only need to get the RSV vaccine once; not annually)

People ages 60 and over at high risk of severe RSV

AND

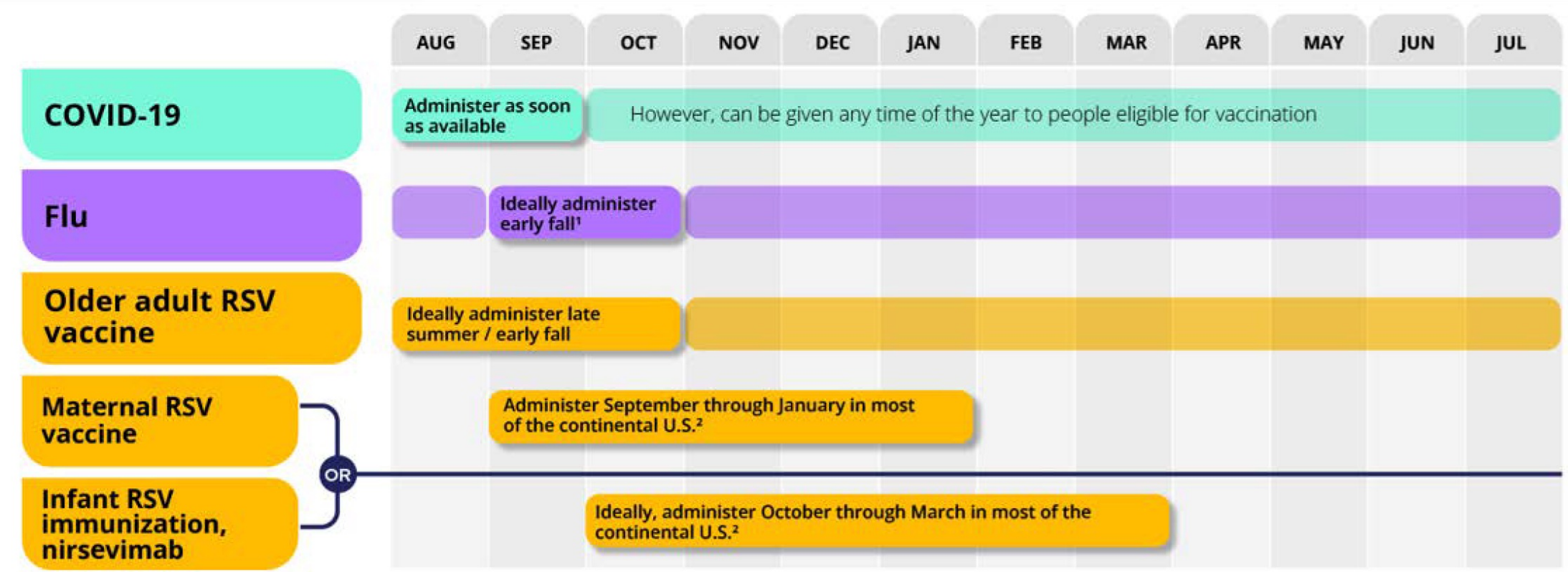
Everyone ages 75 and older



CDC

cdc.gov/respiratory-viruses/prevention/immunizations.html

Respiratory Virus Prevention



https://www.cdc.gov/respiratory-viruses/prevention/immunizations.html

Rwanda's Marburg total rises as vaccine trial launches

Lisa Schnirring, *October 7, 2024*

Topics: Marburg , Viral Hemorrhagic Fever

The health ministry in Rwanda has reported a steady rise in Marburg virus cases over the past few days, and in quickly evolving developments, the country received a shipment of investigational Marburg vaccine and began immunizing healthcare workers.

In updates over the last 3 days, Rwanda's health ministry announced the confirmation of 20 more cases and 1 more death, raising the **outbreak total** to 56 cases, which includes 12 people who have died from their infections.

Photo: Courtesy of Sabin Vaccine Institute

CDC Statement on Marburg Cases in Rwanda

For immediate release: September 30, 2024

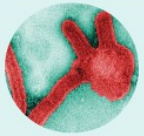
CDC is aware of	26 individuals with Marburg virus disease Eight of those individuals have died
To date	No cases of Marburg virus disease related to this outbreak have been reported in the United States The anticipated risk of Marburg virus disease to the general population in the United States is low.
Marburg virus disease	Is a rare, severe viral hemorrhagic fever similar to Ebola It can cause deadly infections in people.
Spread in several countries in Africa	By certain types of bats and from person-to-person through direct contact with people who are sick. Healthcare workers in outbreak settings are at an increased risk of infection.
Symptoms	Can appear suddenly and may include fever, rash, and severe bleeding.

https://www.cdc.gov/media/releases/2024/s0929-marburg-cases-rwanda.html

https://www.cdc.gov/marburg/about/index.html

Marburg Virus

Marburg



Marburg is a rare and deadly disease caused by infection with the Marburg virus.

- It was first discovered in 1967 in Marburg and Frankfurt, Germany.

How does Marburg spread?

People get Marburg through direct contact with:

- The body fluids (such as urine, feces, saliva, sweat, vomit, breast milk, semen, and vaginal fluids) of a person who is sick or has died from Marburg.
- Objects contaminated with body fluids of a person who is sick with or has died of Marburg.
- Infected animals (Egyptian fruit bats, monkeys).

- Marburg virus has been found in the semen of men who have recovered from Marburg virus disease
- Marburg virus is also likely present in the breast milk and other body fluids of survivors.

Can people without symptoms spread Marburg?

People recently infected with Marburg cannot spread the disease to others before symptoms appear.

After recovering from the virus, it is possible for Marburg to spread through the semen or breast milk of people without symptoms.

OUTBREAKS OF MARBURG VIRUS DISEASE

● Outbreak Location and Year

0 250 500 750 mi

Signs and symptoms of Marburg

The signs and symptoms of Marburg can appear 2-21 days after exposure. Symptoms of Marburg develop over several days and become worse over time.

Most Common

- Fever
- Aches and pains, such as severe headache, muscle and joint pain, and stomach pain
- Weakness and fatigue
- Diarrhea and vomiting

Additional Symptoms

- Unexplained hemorrhaging (bleeding or bruising)
- Red eyes
- Skin rash
- Hiccups (late stage)

Who is at high risk for becoming infected with Marburg?

- Health workers who do not use proper infection control while caring for Marburg patients, and family and friends in close contact with Marburg patients.

- People who have close contact with bats and or their urine/droppings, or spend time where bats congregate (such as caves, mines, abandoned buildings).
- Marburg poses little risk to travelers or the general public who have not cared for or been in close contact (within 3 feet) with someone sick with Marburg.

Who is at risk of severe illness from Marburg?

Pregnant women, children, and those who are late in the course of illness are at higher risk of dying from Marburg.


Questions?