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COVID-19 Updates: What We Know Now

Releases monthly

Newest Episodes:

- SHEA Spring 2022 Recap
- CDC Guidance & Influence on COVID

COVID-19 Allies in Infection Prevention

LEARNINGCE SHEA Online Education Center

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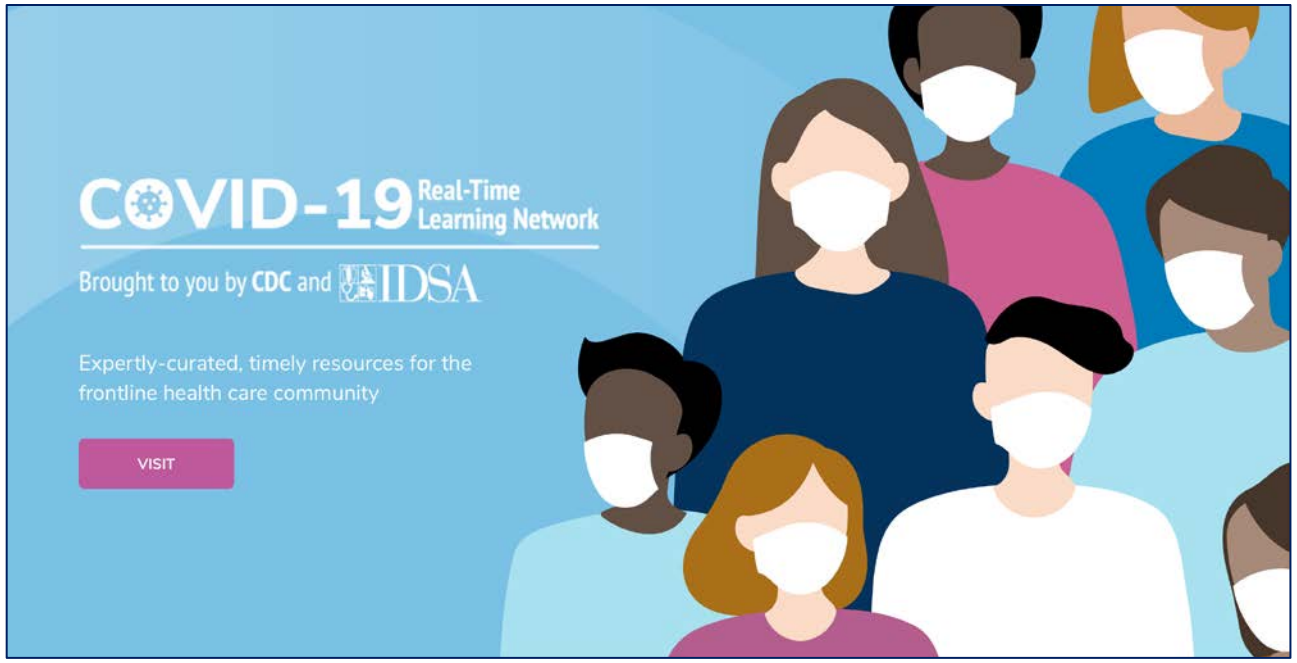
COVID-19 Real-Time Learning Network



Specialty Society Collaborators:

- American Academy of Family Physicians
- American Academy of Pediatrics
- American College of Emergency Physicians
- American College of Physicians
- American Geriatrics Society
- American Thoracic Society
- Pediatric Infectious Diseases Society
- Society for Critical Care Medicine
- Society for Healthcare Epidemiology of America
- Society of Hospital Medicine
- Society of Infectious Diseases Pharmacists

With funding from the Centers for Disease Control and Prevention, IDSA has launched the COVID-19 Real Time Learning Network, an online community that brings together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.

www.COVID19LearningNetwork.org

@RealTimeCOVID19 | #RealTimeCOVID19

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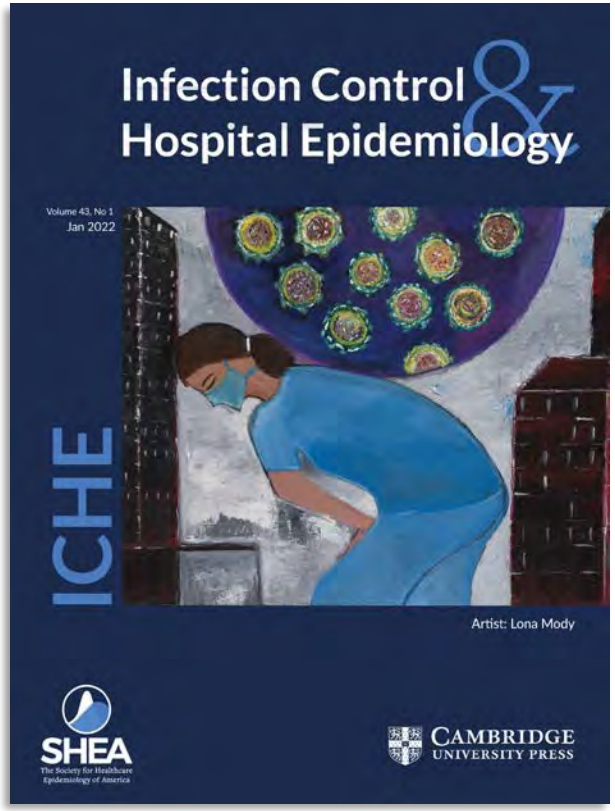
ICHE Journal – Fast Tracking COVID Article Submissions



Infection Control & Hospital Epidemiology publishes scientifically authoritative, clinically applicable, peer-reviewed research on control and evaluation of the transmission of pathogens in healthcare institutions and on the use of epidemiological principles and methods to evaluate and improve the delivery of care. Major topics covered include infection control practices, surveillance, antimicrobial stewardship, cost-benefit analyses, resource use, occupational health, and regulatory issues.

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SHEA SPRING

SEE YOU NEXT YEAR!

We hope to see you in Seattle, Washington for SHEA Spring 2023 April 12-14.


IDWeek
Save the Date
Important Dates:
• Abstract & Travel Award Submission Deadline – May 4
• Case Submission Deadline – May 4
• Registration is scheduled to open for members May 3 & nonmembers on May 31.
Join Us LIVE in Washington, DC
Oct. 19-23, 2022

SHEA Webinar

COVID-19 Town Hall Round 74

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In Case of Technical Difficulties:

- **Audio:**
  - Select one form of audio only (computer speakers or telephone connection)
  - For full participation, you will need to join by computer

- **If you are having trouble joining:**
  - Use the emailed invitation to join via the URL, or call in with the provided phone numbers

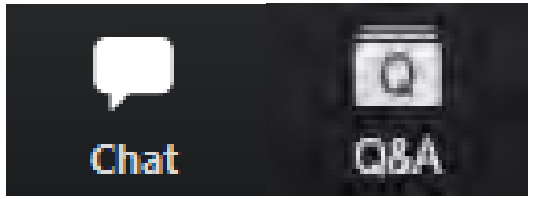
- https://support.zoom.us

Webinar Recording Access:

This webinar will be recorded and uploaded to LearningCE's [Rapid Response Program]

Streaming Live on SHEA's Facebook page

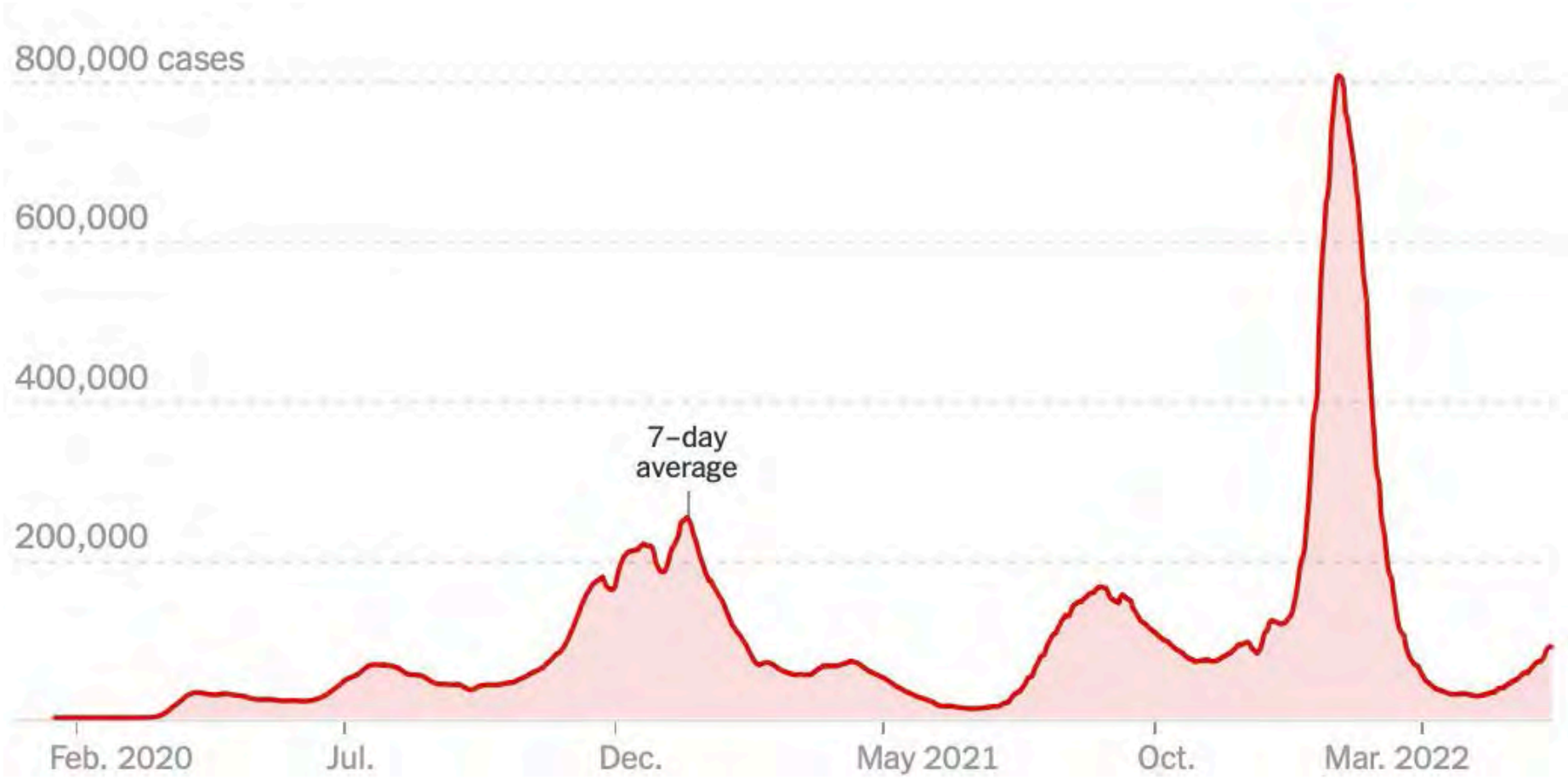
Useful Features:



- **Chat**: Talk to each other or ask SHEA Staff questions if you are having technical difficulties
- **Q&A**: Type in your question to be read aloud by SHEA Staff and answered by the Panelists

Reported COVID-19 Cases in the United States

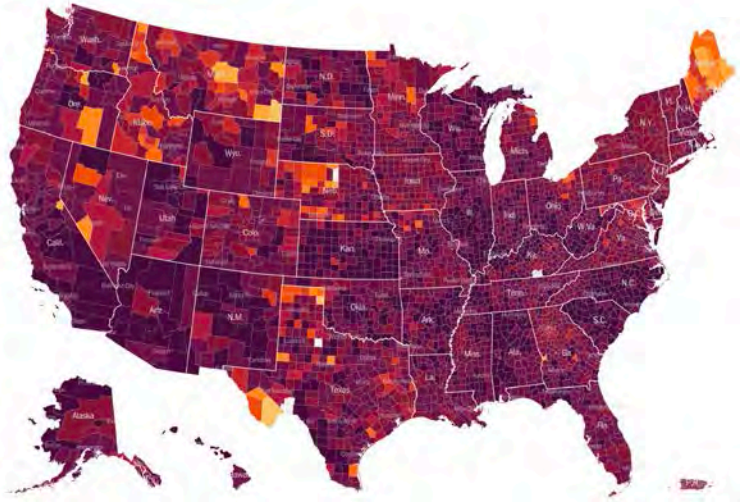
Cumulative Cases – 82,386,465



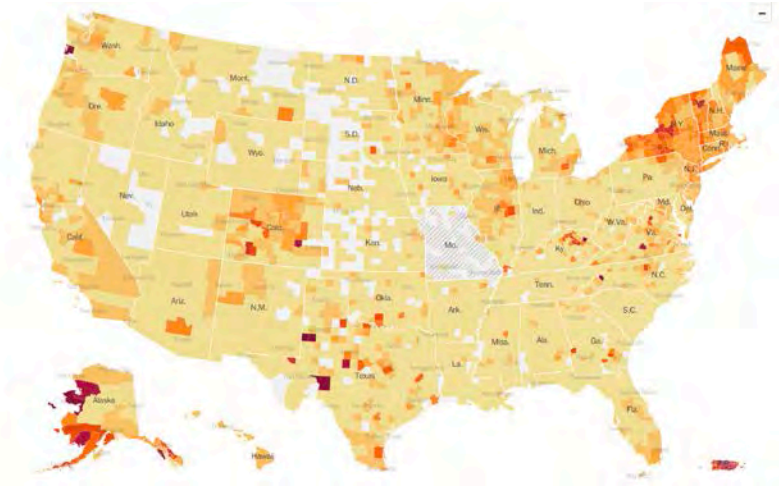
Increased by 58% from two weeks earlier

Source: New York Times 5-15-22

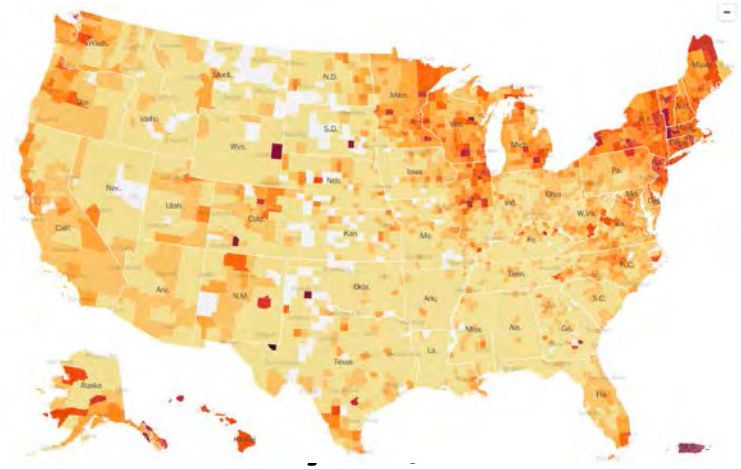
US COVID-19 HOTSPOTS



February 6, 2022

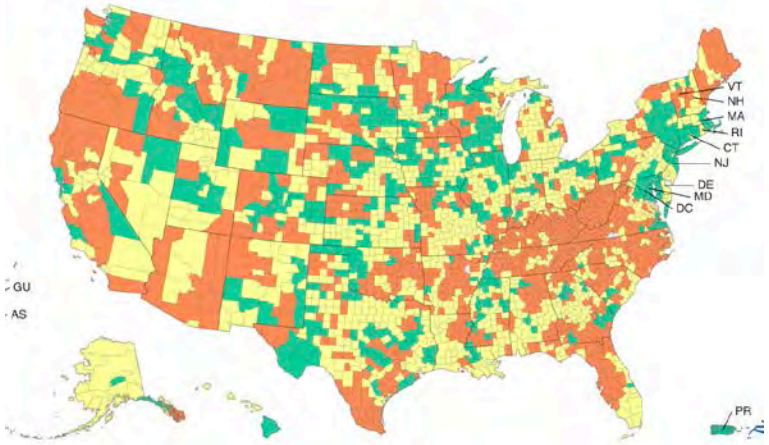


April 24, 2022

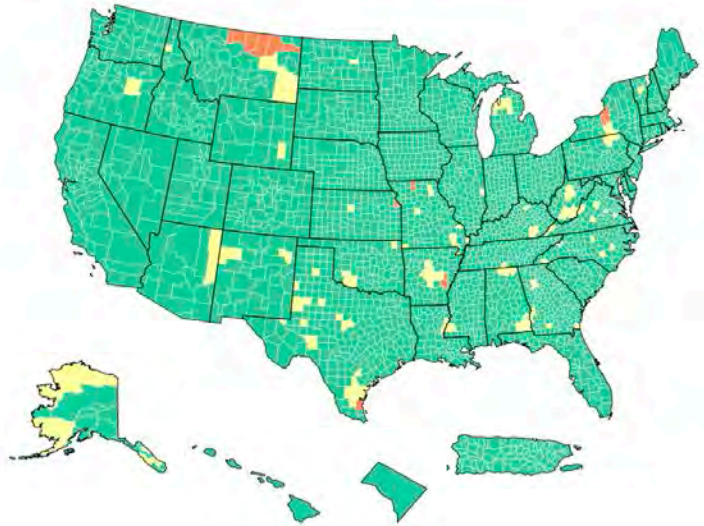


Source: New York Times 5-15-2022

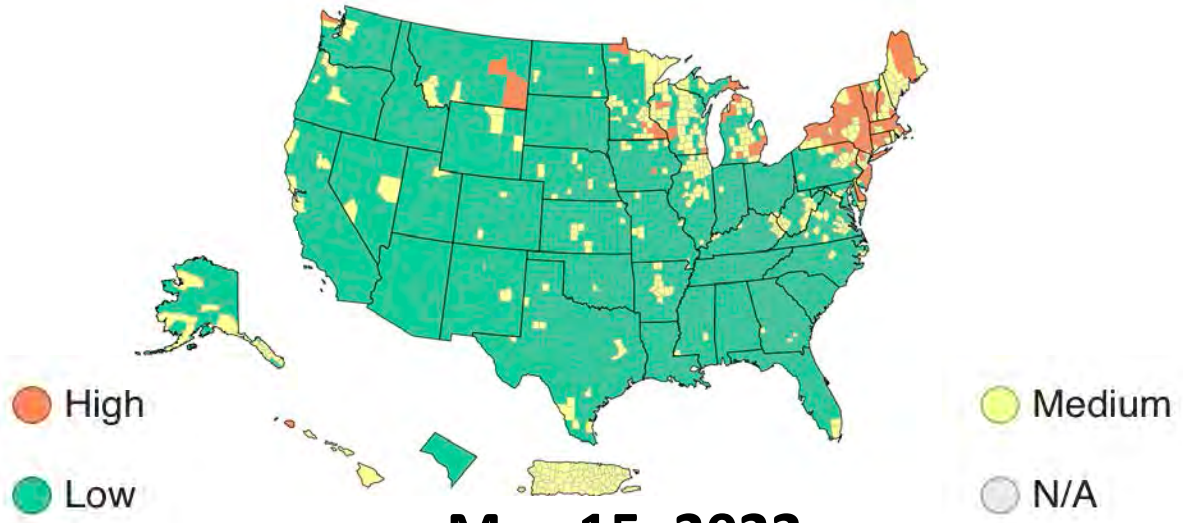
CDC COVID-19 COMMUNITY LEVELS



February 27, 2022



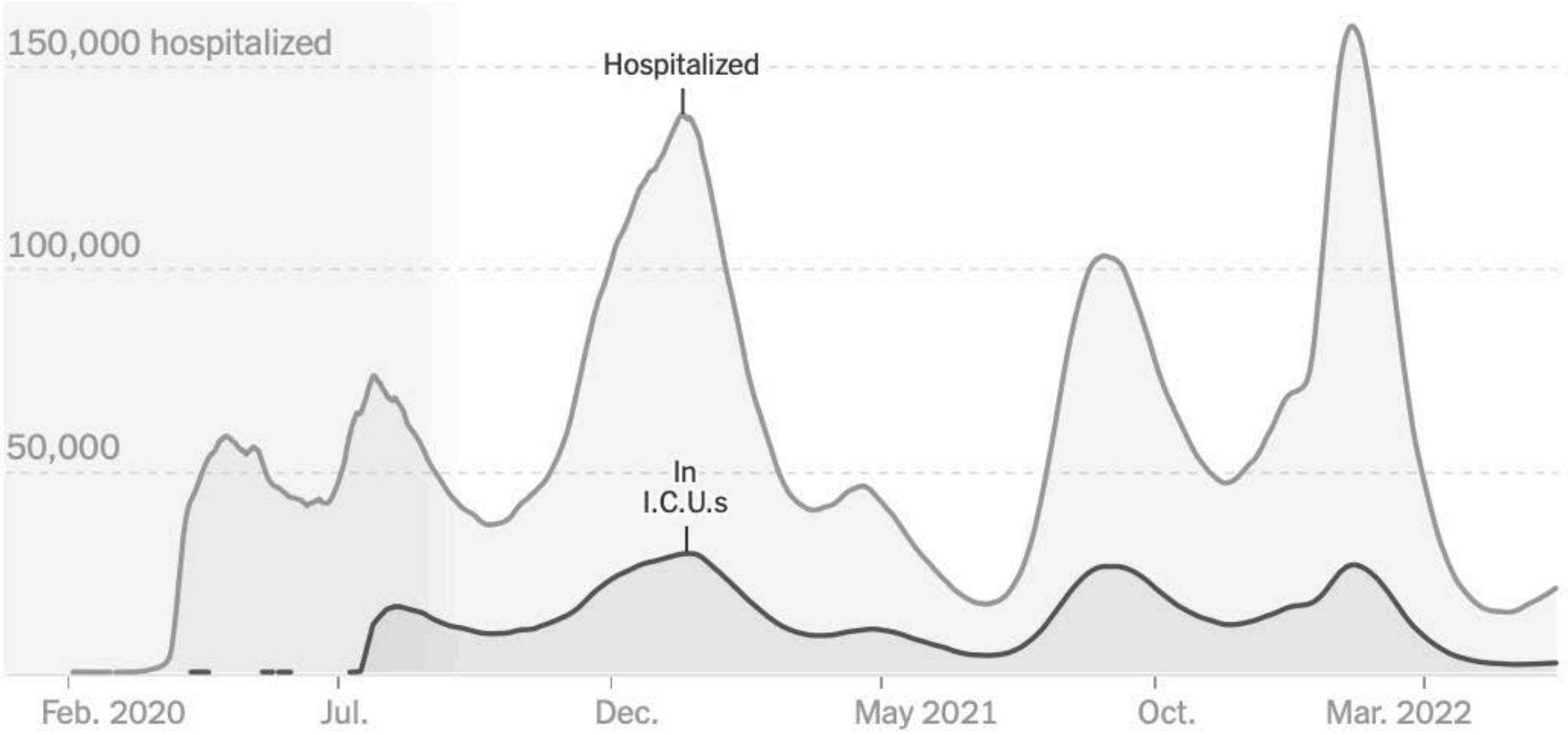
April 3, 2022



May 15, 2022

Source – https://covid.cdc.gov/covid-data-tracker/#county-view?list_select_state=all_states&list_select_county=all_counties&data-type=CommunityLevels&null=CommunityLevels

HOSPITALIZATIONS AND ICU ADMISSIONS FOR COVID-19 IN THE UNITED STATES

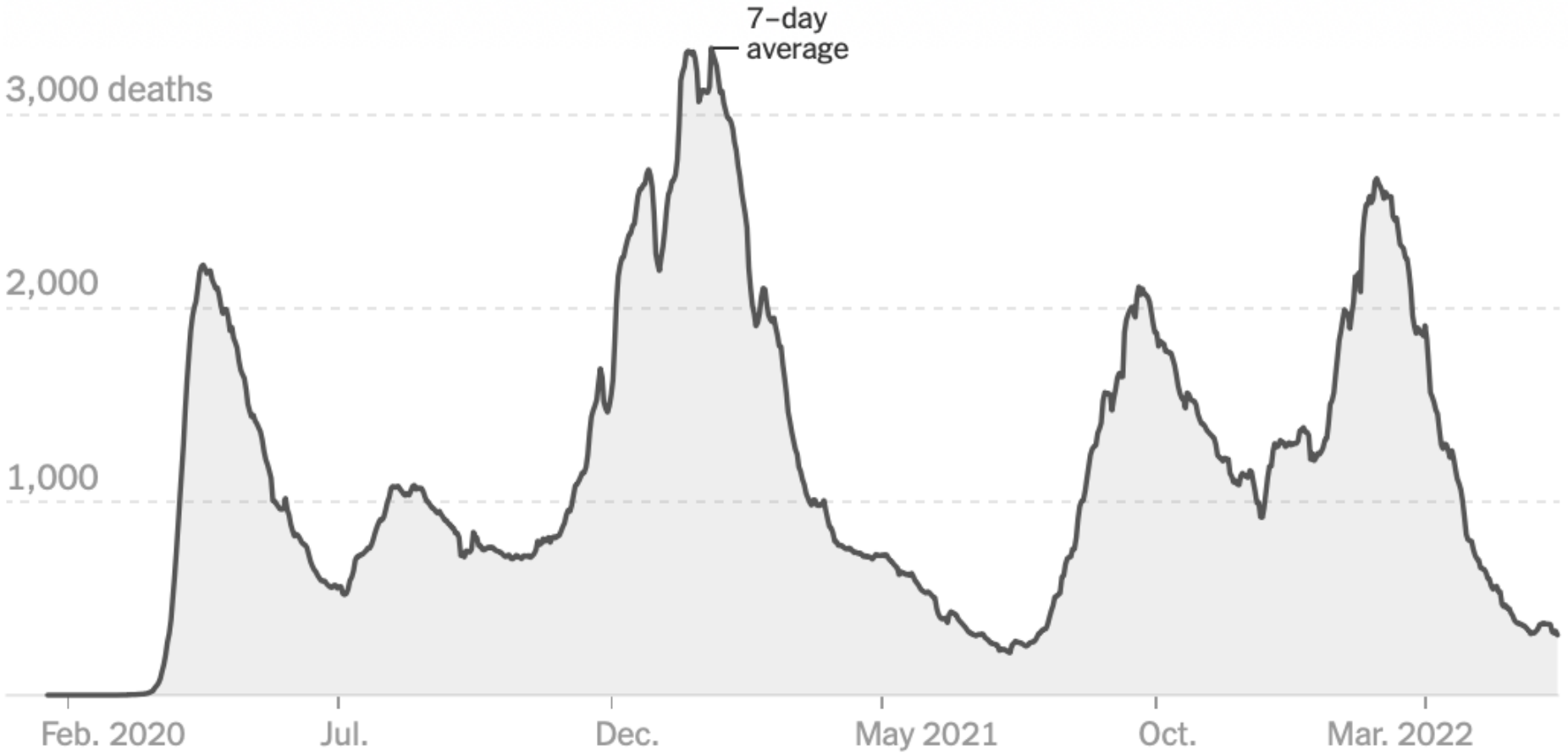


Hospitalizations Increased 21% from two weeks earlier

Source: New York Times 5-15-22

COVID-19 Deaths in the United States

Cumulative Deaths – 998,310



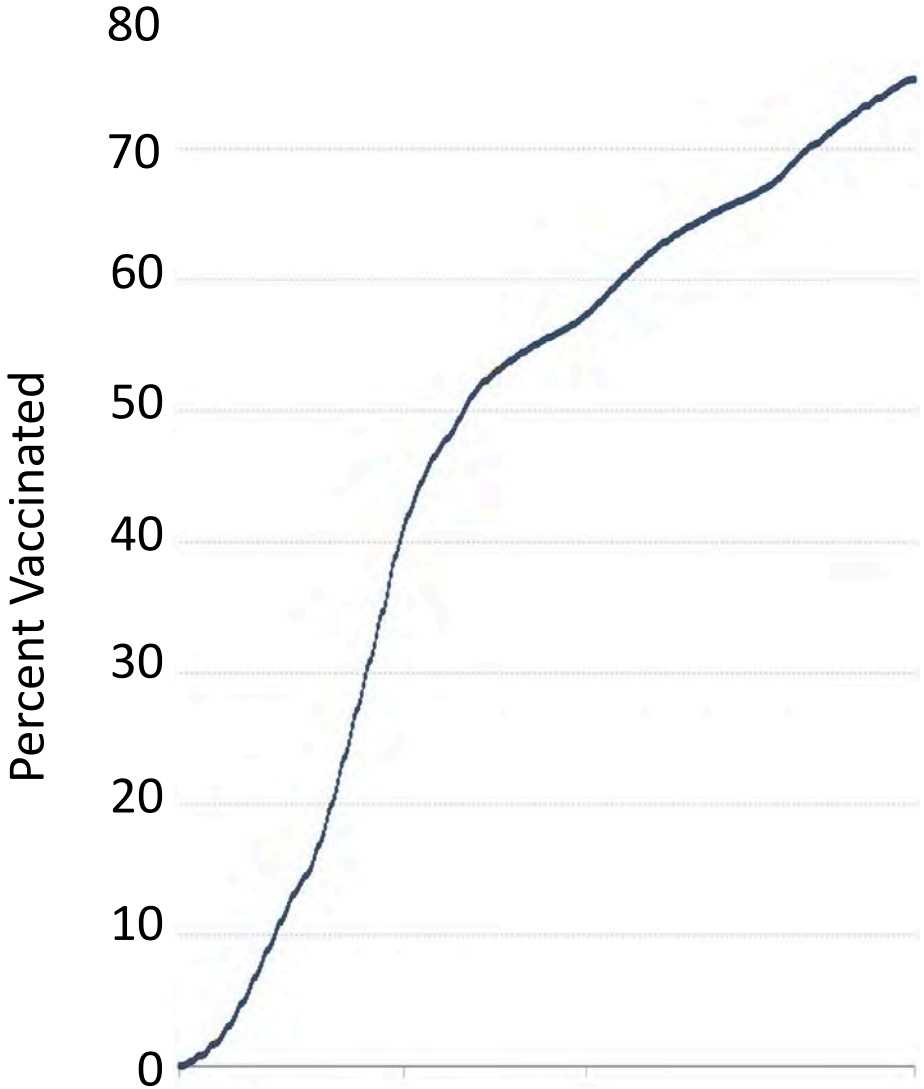
3% decrease from two weeks earlier

Source: New York Times 5-15-22

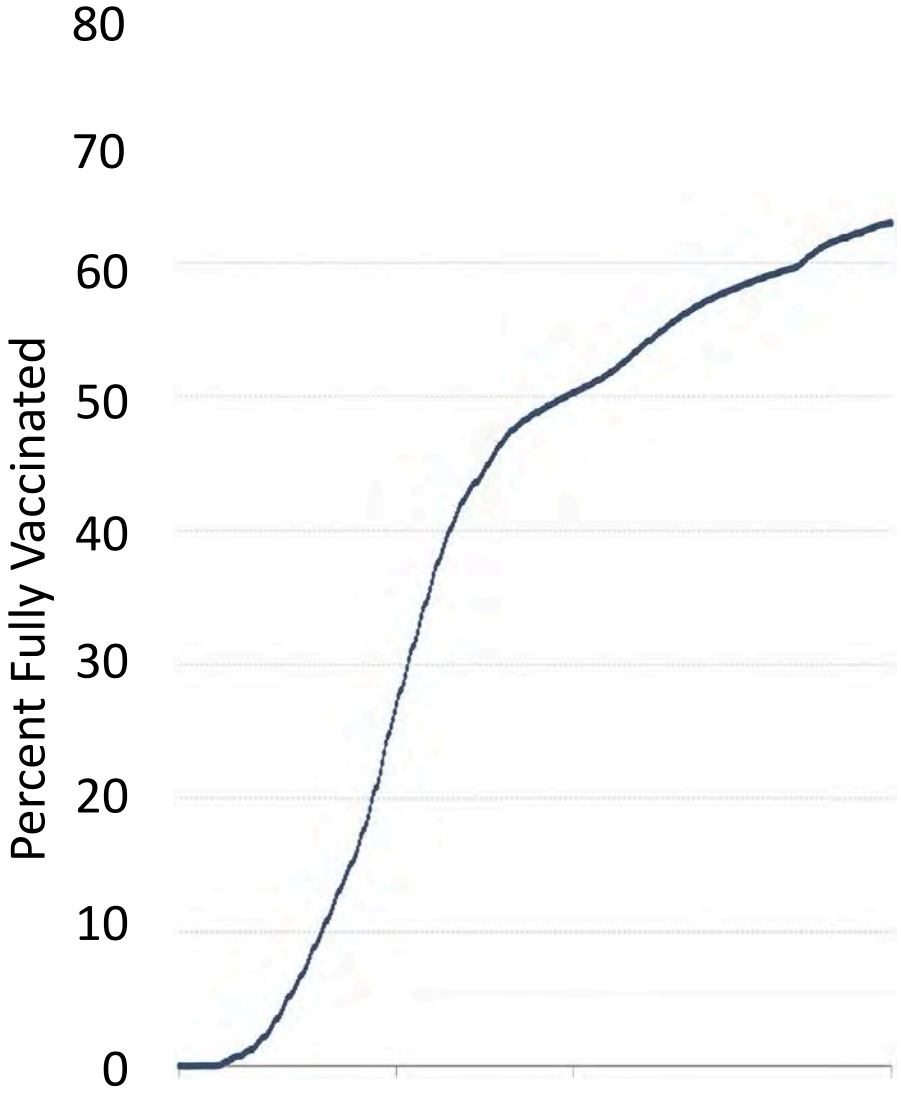
DAILY COVID-19 VACCINATIONS IN THE UNITED STATES

Source: Our World in Data 5-14-22

COVID-19 VACCINATIONS IN THE UNITED STATES



257,710,000 (77.6%)



220,460,000 (66.4%)

Source: Our World in Data 5-14-22

COVID-19 Booster Doses in the United States

Cumulative Doses Administered 102.01 M

Source: Our World in Data 5-14-22

This Week's COVID-19 News

1. A **New England Journal of Medicine** study demonstrated the efficacy of a Chinese adjuvanted receptor-binding-domain dimer peptide in preventing SARS-CoV-2 infection.
2. A paper in the **New England Journal of Medicine** describing the second phase of the trial of the Moderna vaccine in children 6 to 11 found that two 50 microgram doses were safe, immunogenic and estimated as 88% effective in preventing SARS CoV-2 infection.
3. An editorial accompanying this paper in the **New England Journal of Medicine** makes to case for continued and continuing vaccine development.
4. A **Lancet** paper found that two-years after COVID-19 infection survivors have significantly lower health status than the general population.
5. A paper in **Science** found that SARS-CoV-2 antigen challenge histories influence the speed and magnitude of antibody responses, functional cross-variant antibody repertoire composition, and longevity of protection.
6. A **Journal of Infectious Diseases** paper found that two-dose primary vaccination within the prior two months was effective in reducing severe sequelae of COVID.
7. A paper in **Clinical Infectious Diseases** noted that SARS-CoV-2 viremia is associated with COVID-19 severity and the level of viremia is predictive of clinical outcomes.
8. A preprint published in **Nature Communications** described the first SARS-CoV-2 challenge study conducted in humans and evaluated the early kinetics of infection.

References available in the chat

Panelists:

Dr. David Henderson
NIH Consultant

Dr. Sarah Haessler
Baystate Health

Dr. Kristina Bryant
University of Louisville

Dr. David Weber
UNC School of Medicine

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Paxlovid: Beware the Drug Interactions

- 54 yo woman with RA on enbrel (and 20 other regular outpatient medications including atorvastatin, mirtazipine and quetiapine)
- prescribed Paxlovid after positive COVID PCR at PCP office
- 4 days later she was brought to ED by her family with lethargy and mental status changes
- Afebrile and hemodynamically stable but minimally responsive. Labs with no leukocytosis, Cr 1.3, CK 500. COVID/RSV/Flu PCR negative on admission
- CT of head was unremarkable
- Unable to have LP initially, treated with acyclovir, vancomycin, ceftriaxone, and ampicillin
- Hospital day 2-3, had 2nd head CT and LP which were normal, and was about to get MRI and EEG, when she had some gradual improvement
- an IV infiltrated into her hand which became swollen, so she underwent CT of her hand
- ID consult for mental status changes in immunocompromised patient: identified Paxlovid drug interaction as cause of patient's symptoms

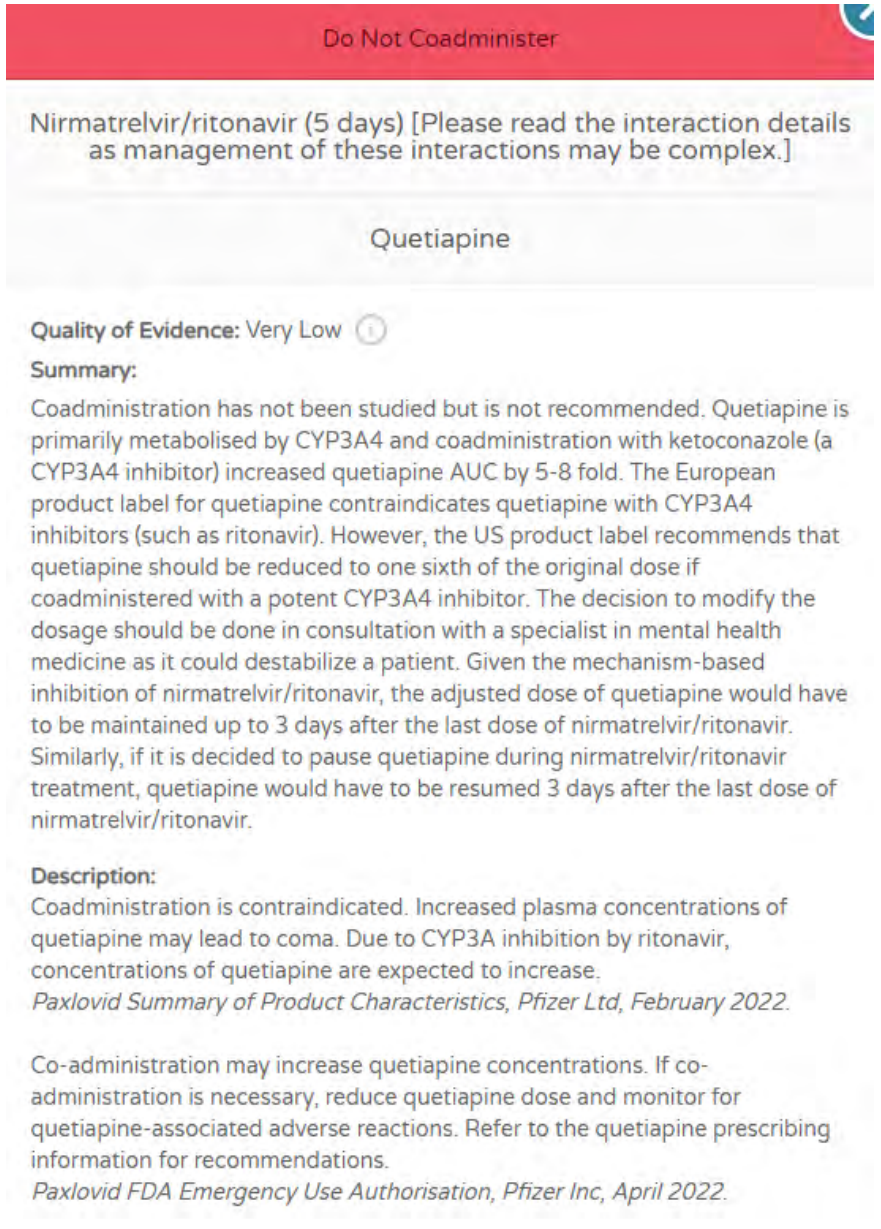
Case and slides courtesy of Jennifer Schimmel MD, 2022

Paxlovid Interaction: Downstream Consequences

- 4 day hospitalization
- 2 CT scans of the head
- Lumbar puncture
- Broad spectrum antibiotic exposure
- IV acyclovir
- IV infiltration
- CT scan of hand

Liverpool Drug Interaction Checker

https://www.covid19-druginteractions.org/checker



slides courtesy of Jennifer Schimmel MD, 2022

Executive Summary

- Nirmatrelvir/ritonavir (PAXLOVID) is the preferred treatment for most patients with mild-to-moderate COVID-19 at high risk of progression to severe disease and continues to be widely available and in adequate supply in Massachusetts
- The dose pack presentation of nirmatrelvir/ritonavir (PAXLOVID) for individuals with moderate renal impairment has been updated.

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Executive Office of Health and Human Services
Department of Public Health
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Clinical Guidance on Therapeutics for COVID-19
Issued April 26, 2022

Executive Summary

- Nirmatrelvir/ritonavir (PAXLOVID) is the preferred treatment for most patients with mild-to-moderate COVID-19 at high risk of progression to severe disease and continues to be widely available and in adequate supply in Massachusetts.
- The dose pack presentation of nirmatrelvir/ritonavir (PAXLOVID) for individuals with moderate renal impairment has been updated.

The purpose of this document is to provide guidance to health care providers on the use of therapeutics to treat COVID-19 positive individuals, as well as pre-exposure prophylaxis for immunocompromised individuals. Therapeutics should be considered for all patients with a positive test for COVID-19 who are symptomatic and at risk for moderate-to-severe disease progression. This group includes over 40 percent of all MA residents who are eligible due to heart, lung, liver, or kidney disease, diabetes, pregnancy, dementia, cancer, disability, substance use disorder, mental health disorder, age over 65, overweight/obesity and immunocompromised.

Full CDC list is here: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

At present, there are two general classes of treatment for mild-to-moderate COVID-19: antivirals and monoclonal antibodies (mAb). Presently all individuals who qualify for treatment under the applicable Emergency Use Authorization (EUA) or approval from the Food and Drug Administration (FDA), regardless of vaccination status, are eligible to receive therapeutics for mild-to-moderate COVID-19.

Providers must ensure that eligible patients have access to and receive these critical and available therapies. Treatments are available widely. Use the COVID-19 Therapeutics Locator to connect patients to locations near them.

Treatment of COVID-19 with oral antiviral therapy

The oral antiviral therapy nirmatrelvir co-packaged with ritonavir (PAXLOVID) is available under FDA EUA for the treatment of mild-to-moderate COVID-19 in adult and pediatric patients (12 years of age and older and weighing at least 40 kg). This drug is expected to retain activity against all known variants of SARS-CoV-2.

Revised 4/26/2022: Providers should ensure that they are consulting the most current version of this guidance as recommendations frequently change. Find the latest document at: https://www.mass.gov/info-details/covid-19-therapeutics-locator#clinical-therapeutics-guidance-for-covid-19-providers-

COVID-19 when given within five days of symptom onset.

Based on FDA approval, nirmatrelvir/r is indicated for treatment of COVID-19 in individuals who meet the following two criteria:

1. Individuals who have mild-to-moderate COVID-19 and a positive viral direct SARS-CoV-2 viral test (molecular or antigen)
2. Individuals who are at high risk for progression to severe COVID-19.[1]

Nirmatrelvir/r should be taken as soon as possible after the diagnosis of COVID-19, and within five days of symptom onset.

Nirmatrelvir/r is not authorized for treatment in patients requiring hospitalization due to COVID-19, pre-exposure or post-exposure prophylaxis or for use longer than five consecutive days.

The standard dose of nirmatrelvir/r is 300 mg of nirmatrelvir (two 150 mg tablets) with 100 mg of ritonavir (one 100 mg tablet), with all three tablets taken twice daily for five days. A single five-day course is dispensed in a blister pack. The nirmatrelvir dose is reduced to 150 mg of nirmatrelvir (one 150 mg tablet) with 100 mg of ritonavir (one 100 mg tablet) for moderate renal impairment (eGFR ≥30 to < 60 mL/min), with both tablets taken twice daily for five days. This presentation is available in a dose-reduced blister pack. Nirmatrelvir/r is not recommended in patients with severe renal impairment (eGFR < 30 mL/min) or severe hepatic impairment (Child-Pugh Class C).

Nirmatrelvir/r should be avoided in individuals on medications not compatible with protease inhibitors, or that cannot be temporarily held.

A second oral antiviral therapy, molnupiravir (LAGEVRIO), is available under FDA EUA for the treatment of mild-to-moderate COVID-19 in adult patients.

Molnupiravir is a nucleoside analog antiviral agent active against SARS-CoV-2. Clinical trials have shown molnupiravir to reduce severe disease by 30% compared to placebo in individuals with mild-to-moderate COVID-19 when given within 5 days of symptom onset. This drug is expected to retain activity against all known variants of SARS-CoV-2.

Molnupiravir is indicated for treatment of COVID-19 in individuals who meet the following three criteria:

1. Individuals who have mild-to-moderate COVID-19 and a positive viral direct SARS-CoV-2 viral test (molecular or antigen)
2. Individuals who are at high risk for progression to severe COVID-19.[1]
3. Individuals for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.

Revised 4/26/2022: Providers should ensure that they are consulting the most current version of the guidance on recommendations frequently change. Find the latest document at: https://www.mass.gov/info-details/covid-19-therapeutics-locator#clinical-therapeutics-guidance-for-covid-19-providers-

slides courtesy of Jennifer Schimmel MD, 2022

Management of Drug Interactions With Nirmatrelvir/Ritonavir (Paxlovid®): Resource for Clinicians

IDSA

IDSA COVID-19 TREATMENT AND MANAGEMENT GUIDELINE PANEL ON BEHALF OF THE INFECTIOUS DISEASES SOCIETY OF AMERICA

Last Updated: May 6, 2022- *Version 1.1**

Nirmatrelvir/ritonavir has FDA Emergency Use Authorization to treat mild-to-moderate COVID-19 in patients at high risk of progression to severe disease who are ≥12 years of age and weigh ≥40 kg.

In such patients, IDSA guidelines suggest nirmatrelvir/ritonavir be initiated within 5 days of symptom onset. Patients with mild-to-moderate COVID-19 who are at high risk of progression to severe disease admitted to the hospital for reasons other than COVID-19 may also receive nirmatrelvir/ritonavir. NIH guidelines also suggest nirmatrelvir/ritonavir for nonhospitalized patients with mild-to-moderate COVID-19 who are at high risk of disease progression.

Given coformulation with ritonavir as a pharmacokinetic booster, there is potential for drug interactions. The following steps can be taken to minimize the risk of drug interactions for those who are eligible and would benefit from nirmatrelvir/ritonavir treatment:

1. Obtain a complete list of the patient's current medications, including over-the-counter agents and herbal supplements.
2. Confirm that the patient is taking each medication as prescribed. If the patient is not taking a medication, discontinue the medication from their medication profile.
3. Review the FDA Paxlovid® Healthcare Provider Fact Sheet to identify any medications that the patient is currently taking that are contraindicated with nirmatrelvir/ritonavir. If the patient is taking a contraindicated medication, prescribe alternative treatment for mild to moderate COVID-19.
4. Review potential drug interactions between nirmatrelvir/ritonavir and the patient's current medications.

   Resources:

   - Liverpool COVID-19 Interactions (covid19-druginteractions.org)
   - Paxlovid® Healthcare Provider Fact Sheet
   - PAXLOVID® Patient Eligibility Screening Checklist Tool for Prescribers (fda.gov)
   - Nirmatrelvir/Ritonavir (Paxlovid®): What Prescribers and Pharmacists Need to Know - Ontario COVID-19 Science Advisory Table (covid19-sciencetable.ca)
5. Advise the patient on dose adjustments, temporary cessation of medication(s), or clinical monitoring that is needed during and after the 5 day nirmatrelvir/ritonavir treatment.
6. If relapse occurs after initial treatment and a second course of treatment is warranted, duration of therapy should be used to guide adjustments to concomitant medications.

"Version 1.1 contains the following correction: "200" has been changed to "100" in the sentence that originally read, "Among the top 200 prescribed drugs, only two have interactions so severe that nirmatrelvir/ritonavir should be avoided altogether: rivaroxaban and salmeterol."

Among the top 100 prescribed drugs, **only two have interactions so severe that nirmatrelvir/ritonavir should be avoided altogether:** rivaroxaban **and** salmeterol.

Concomitant Medication	Nirmatrelvir/Ritonavir Effect on Drug Level	Possible Effect	Recommendation During Nirmatrelvir/Ritonavir Treatment
Rivaroxaban	↑	Increased bleeding	Avoid nirmatrelvir/ritonavir
Salmeterol	↑	Increased cardiac effects	Avoid nirmatrelvir/ritonavir

The following table contains information on management of commonly prescribed medications that are known to interact with nirmatrelvir/ritonavir. This list was derived from ClinCalc's Top 200 Prescribed Medications in the United States in 2019. Please note:

- Inclusion on this list is not a contraindication to prescribe nirmatrelvir/ritonavir. Rather, additional management considerations may be necessary as shown below.
- If a drug is not on this list, it should still be checked for interactions, as it may be a less commonly prescribed medication that has interactions or is contraindicated.
- Routine lab testing for transaminases or creatinine is not needed, and clinical judgement should be used.

Concomitant Medication	Nirmatrelvir/Ritonavir Effect on Drug Level	Possible Effect	Recommendation During Nirmatrelvir/Ritonavir Treatment
Alprazolam	↑	Excess sedation	Consider dose reduction, but do not stop if chronic use
Apixaban	↑	Increased bleeding	Dose dependent: • Apixaban 2.5 mg: Avoid nirmatrelvir/ritonavir • Apixaban 5mg or 10 mg: Reduce dose by 50% until 3 days after nirmatrelvir/ritonavir
Bupropion	↓	Decreased effects	No dose adjustment required
Buspirone	↑	Increased side effects	Reduce dose or monitor for side effects
Calcium-channel blockers (amlodipine, nifedipine)	↑	Decreased blood pressure	• Continue if tolerated based on symptoms • Reduce dose if patient has low blood pressure
Calcium-channel blockers (diltiazem, verapamil)	↑	Decreased blood pressure	• Continue if tolerated • Reduce dose if patient has low blood pressure or bradycardia
Clonazepam	↑	Excess sedation	Consider dose-reduction, but do not stop if chronic use

https://urldefense.com/v3/__https://www.idsociety.org/globalassets/idsa/practice-guidelines/covid-19/treatment/idsa-paxlovid-drug-interactions-resource-5-6-22-v1.1.pdf__;!!P_vj-BUkwjF5!dCJ7ptputLLmhUdoJgDt9ZodsTmpDwgJ09ixBQmwA_PUUALuqUekvk_9U8mYu5-L-CAQ9GJ3AaxH0vH98tJGAgfb$

slides courtesy of Jennifer Schimmel MD, 2022

Example Provider Communication

Paxlovid (Nirmatrelvir/Ritonavir): Information for Prescribers

Baystate Health

1. Confirm patient meets all EUA eligibility criteria for treatment with Paxlovid

- Age >=12 and weight ≥40kg
- Positive COVID-19 test (PCR or antigen)
- Symptom onset within 5 days
- Absence of contraindications: patient does NOT have severe renal impairment (eGFR <30) or severe hepatic impairment (Child-Pugh Class C)

2. Assess drug-drug interactions

- Ritonavir is a potent CYP3A inhibitor. Prescriber must perform a comprehensive drug-drug interaction check. Use Lexicomp drug-drug interaction checker (UpToDate) or the tool provided by the University of Liverpool.
- If co-administered medications require dose adjustment provide written instructions on the Paxlovid prescription

3. Dose appropriately for renal function

- Recent creatinine is not required for patients in whom there is no clinical suspicion for renal insufficiency.
  - **eGFR >60**: 300mg nirmatrelvir (two 150mg tablets) with 100mg ritonavir (one tablet). All 3 tablets taken together twice daily for 5 days, with or without food.
  - **eGFR 30-60:** 150mg nirmatrelvir with 100mg ritonavir. Both tablets taken together twice daily for 5 days, with or without food.
  - **eGFR <30:** do not use

Dear Providers

As we face rising numbers of COVID cases, we wanted to ensure that all providers are equipped with the tools to treat mild/moderate COVID in outpatients.
Please see the summary below, as well as the attached information sheets.

1. *Preferred therapy:* **Paxlovid (nirmatrelvir/ritonavir)**

- Within 5 days of symptom onset
- 5-day course of oral therapy
- Check drug-drug interactions (www.covid19-druginteractions.org)

- Prescribe through any participating pharmacy. Free of charge, regardless of insurance status. See list of pharmacies at MA COVID-19 Therapeutics Locator

2. *If Paxlovid not appropriate or available:* **Remdesivir**

- Within 7 days of symptom onset
- 3-day course of intravenous therapy
- Refer to Gothams

3. *If neither Paxlovid nor remdesivir appropriate or available:* **Bebtelovimab (monoclonal Ab)**

slides courtesy of Jennifer Schimmel MD, 2022

COVID-19 UPDATE:
FOCUS ON SARS-CoV-2 VARIANTS, INCLUDING BA.4 AND BA.5

David J. Weber, MD, MPH, FIDSA, FSHEA, FRSM (London)
Sanders Distinguished Professor of Medicine, Pediatrics and Epidemiology
Associate Chief Medical Officer
Medical Director, Hospital Epidemiology

UNC
SCHOOL OF MEDICINE

SARS-CoV-2: EMERGING VARIANTS

- Recently emerged Omicron sublineages: BA.2.12.1, BA.2.13, BA.4 and BA.5; all contain L452 mutations and show higher transmissibility over BA.2. It is currently unknown how differences in the mutation profiles of BA.4 and BA.5, relative to BA.2, will impact on the phenotype. Changes at spike amino acids 452, 486 and 493 are likely to influence human angiotensin-converting enzyme-2 (hACE2) and antibody binding. The 452 residue is in immediate proximity to the interaction interface of the hACE2 receptor. The L452R mutation has been associated with an increased affinity for receptor binding with a resultant increased infectivity. The L452R mutation is also present in the Delta, Kappa and Epsilon variants (and L452Q in Lambda), and mutations at this position have been associated with a reduction in neutralization by monoclonal antibodies (particularly class 2 antibodies) and polyclonal sera. Mutations at this position (L452R/M/Q) have also arisen independently in at least four BA.2 sublineages in different parts of the world, most notably BA.2.12.1

Currently circulating variants of concern (VOCs):

WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Additional amino acid changes monitored°	Earliest documented samples	Date of designation
Delta	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:K417N +S:E484K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron*	B.1.1.529	GR/484A	21K, 21L, 21M	+S:R346K +S:L452R/Q +S:F486V	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

* Includes BA.1, BA.2, BA.3, BA.4, BA.5 and descendent lineages. It also includes BA.1/BA.2 circulating recombinant forms such as XE. WHO emphasizes that these descendant lineages should be monitored as distinct lineages by public health authorities and comparative assessments of their virus characteristics should be undertaken.

https://www.who.int/activities/tracking-SARS-CoV-2-variants

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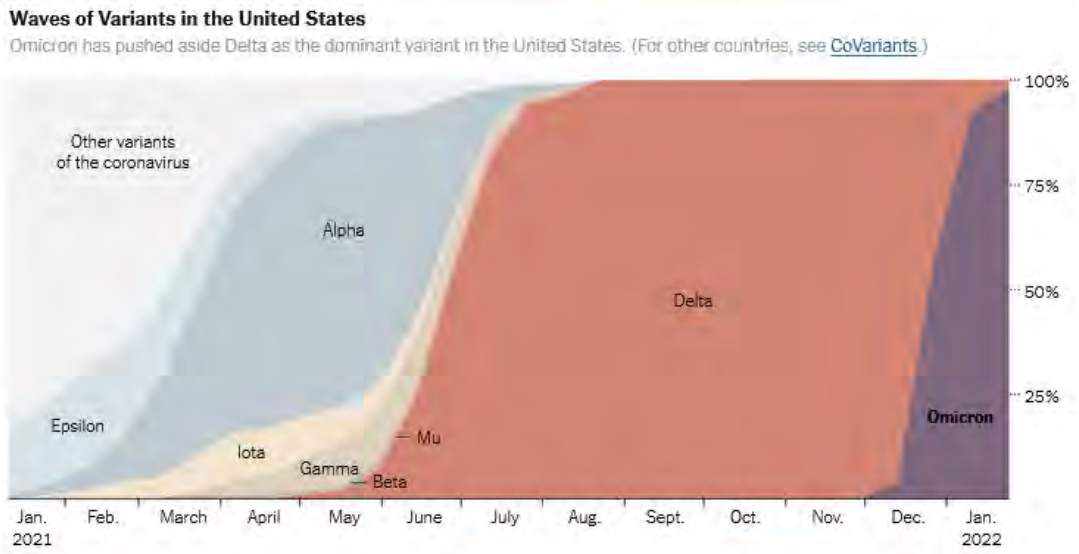
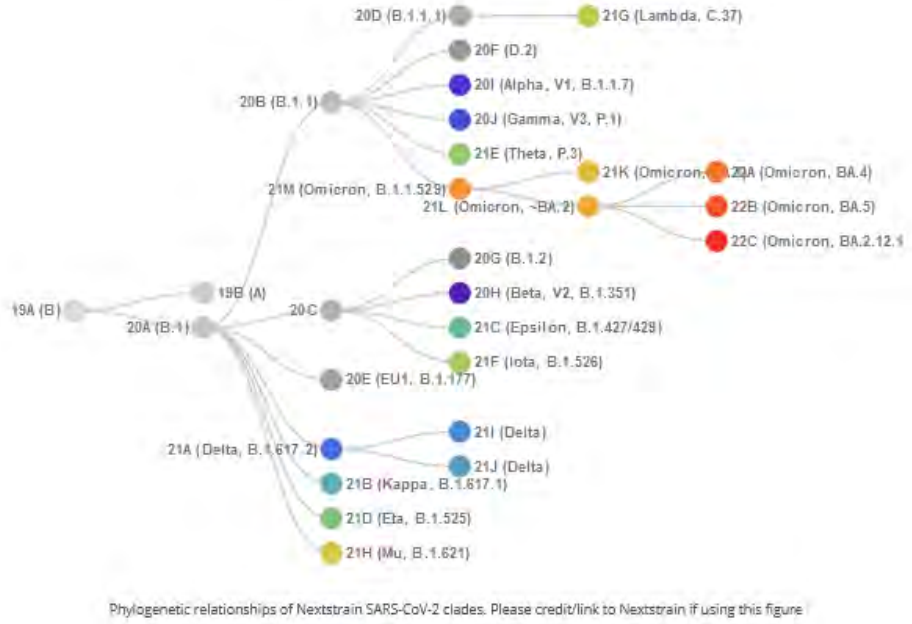
COVID-19 VARIANTS: HISTORY





Phylogenetic relationships of Nextstrain SARS-CoV-2 clades. Please credit/link to Nextstrain if using this figure

Current variants of concern

Name	Lineage	Status
Omicron	B.1.1.529	Identified in southern Africa in Nov. 2021 and spread around the world. Within a month it was dominant in the U.S.
Delta	B.1.617.2	Emerged in India in late 2020 and spread around the world. Delta carries the L452R spike mutation, among others.
Gamma	P.1	Emerged in Brazil in late 2020.
Beta	B.1.351	Emerged in South Africa in late 2020.
Alpha	B.1.1.7	Emerged in Britain in late 2020.

Current variants of interest

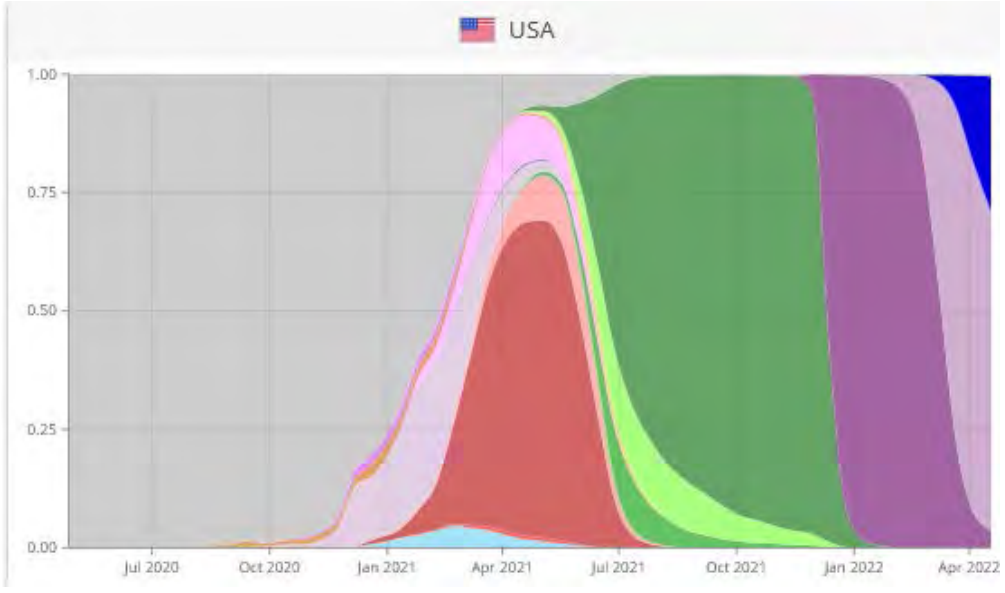
Name	Lineage	Status
Mu	B.1.621	Emerged in Colombia in early 2021.
Lambda	C.37	Emerged in Peru in late 2020.

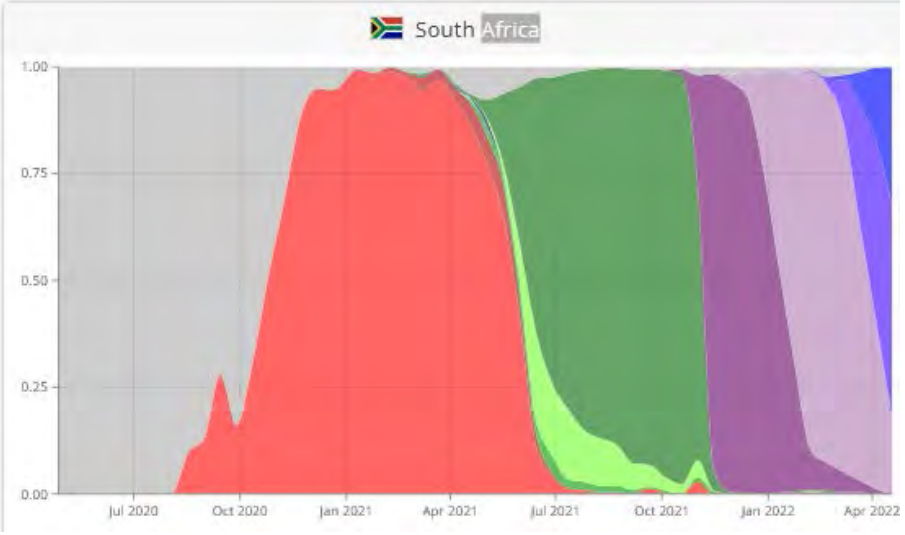
Mutations that may help the coronavirus spread

Mutation	Lineage	Status
D614G	B.1	Appeared in early 2020 and spread around the world.
N501Y	Several	A defining mutation in several lineages, including B.1.1.7 (Alpha), B.1.351 (Beta) and P.1 (Gamma). Helps the virus bind more tightly to human cells.
E484K or "Eek"	Several	Appears in several lineages. May help the virus avoid some kinds of antibodies.
K417	Several	Appears in several lineages, including B.1.351 (Beta) and P.1 (Gamma). May help the virus bind more tightly to cells.
L452R	Several	Appears in several lineages, including B.1.617.2 (Delta).

https://www.nytimes.com/interactive/2021/health/coronavirus-variant-tracker.html

SARS-CoV-2 VARIANTS PER COUNTRY





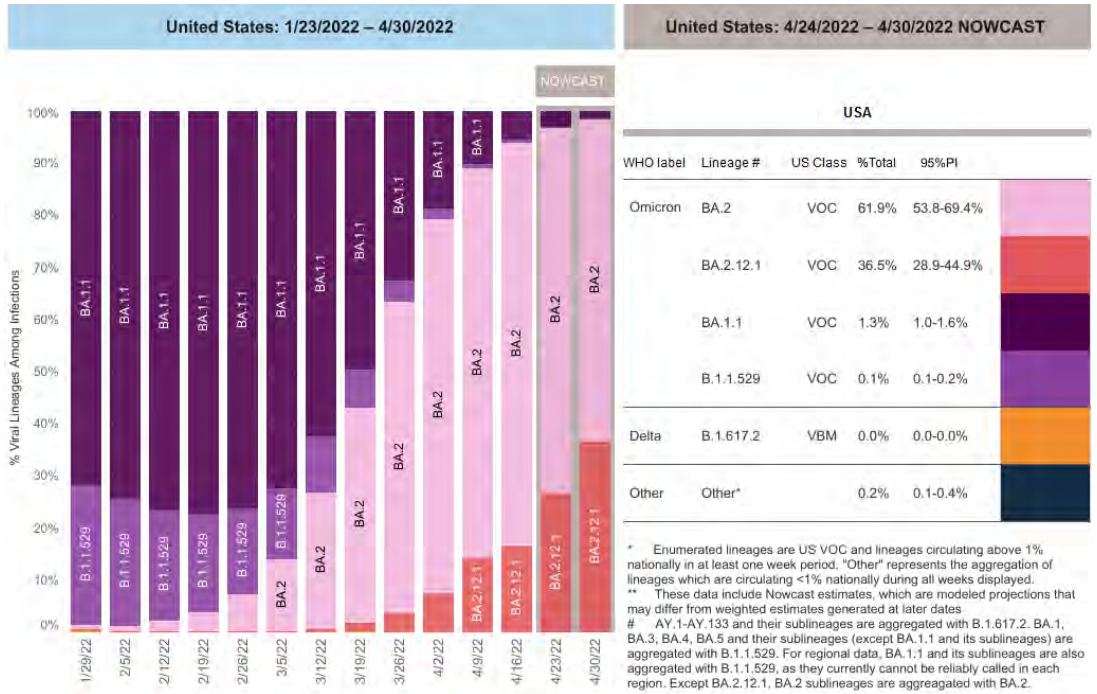
- 20I (Alpha, V1)
- 20H (Beta, V2)
- 20J (Gamma, V3)
- 21A (Delta)
- 21I (Delta)
- 21J (Delta)
- 21K (Omicron)
- 21L (Omicron)
- 22A (Omicron)
- 22B (Omicron)
- 22C (Omicron)
- 21B (Kappa)
- 21D (Eta)
- 21F (Iota)
- 21G (Lambda)
- 21H (Mu)
- 20B/S:732A
- 20A/S:126A
- 20E (EU1)
- 21C (Epsilon)
- 20A/S:439K
- S:677H.Robin1
- S:677P.Pelican
- 20A.EU2
- 20A/S:98F
- 20C/S:80Y
- 20B/S:626S
- 20B/S:1122L

Nextstrain Clade	Pango Lineage	WHO Label
20I (Alpha, V1)	B.1.1.7	α Alpha
20H (Beta, V2)	B.1.351	β Beta
20J (Gamma, V3)	P.1	γ Gamma
21A (Delta)	B.1.617.2	δ Delta
21I (Delta)		δ Delta
21J (Delta)		δ Delta
21B (Kappa)	B.1.617.1	κ Kappa
21C (Epsilon)	B.1.427, B.1.429	ε Epsilon
21D (Eta)	B.1.525	η Eta
21F (Iota)	B.1.526	ι Iota
21G (Lambda)	C.37	λ Lambda
21H (Mu)	B.1.621	μ Mu
21K (Omicron)	BA.1	o Omicron
21L (Omicron)	BA.2	o Omicron
22A (Omicron)	BA.4	o Omicron
22B (Omicron)	BA.5	o Omicron
22C (Omicron)	BA.2.12.1	o Omicron
20E (EU1)	B.1.177	
20B/S:732A	B.1.1.519	
20A/S:126A	B.1.620	
20A.EU2	B.1.160	
20A/S:439K	B.1.258	
20A/S:98F	B.1.221	
20C/S:80Y	B.1.367	
20B/S:626S	B.1.1.277	
20B/S:1122L	B.1.1.302	

21.K = BA.1
21.L = BA.2
22A = BA.4
22B = BA.5
22C = BA.2.12.1

CoVariants, GISAID
https://covariants.org/

SARS-CoV-2 Variants: US (April 30) & UNC-MC (May 5)

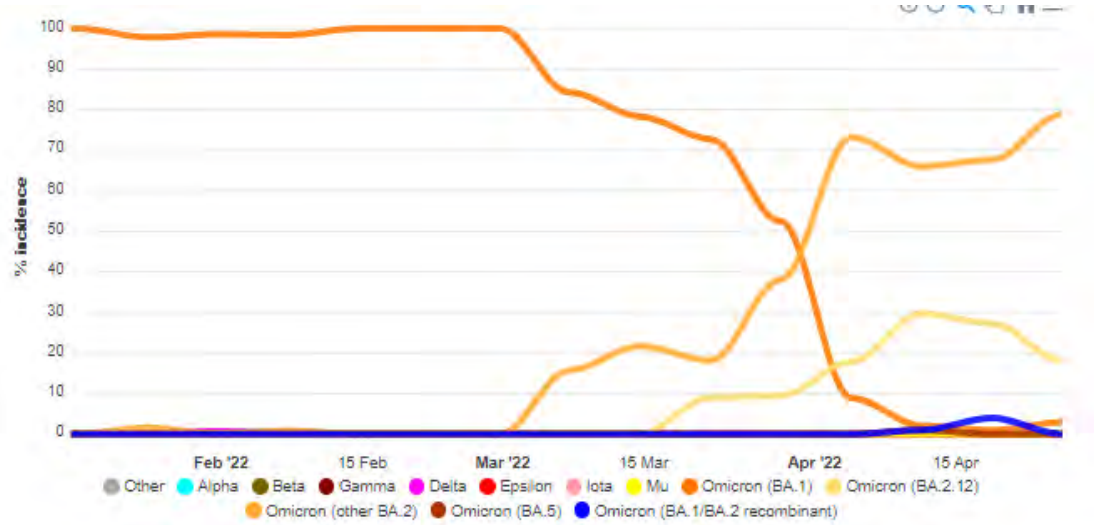


United States: 4/24/2022 – 4/30/2022 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.2	VOC	61.9%	53.8-69.4%
	BA.2.12.1	VOC	36.5%	28.9-44.9%
	BA.1.1	VOC	1.3%	1.0-1.6%
	B.1.1.529	VOC	0.1%	0.1-0.2%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.2%	0.1-0.4%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.3, BA.4, BA.5 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data, BA.1.1 and its sublineages are also aggregated with B.1.1.529, as they currently cannot be reliably called in each region. Except BA.2.12.1, BA.2 sublineages are aggreagated with BA.2.



WHO	Pango lineage	# Samples
Alpha	B.1.1.7	397
Beta	B.1.351	27
Gamma	P.1	22
Delta	B.1.617.2	56
Delta	AY	1742
Epsilon	B.1.427	7
Epsilon	B.1.429	46
Zeta	P.2	1
Eta	B.1.525	3
Theta	P.3	0
Iota	B.1.526	232
Kappa	B.1.617.1	0
Mu	B.1.621	3
Omicron (BA.1)	BA.1	1564
Omicron (BA.2.12)	BA.2.12	74
Omicron (other BA.2)	BA.2	218
Omicron (BA.5)	BA.5	1
Omicron (BA.1/BA.2 recombinant)	XE	5
	Other (non-VOI/VOC)	490
	Total samples	4888

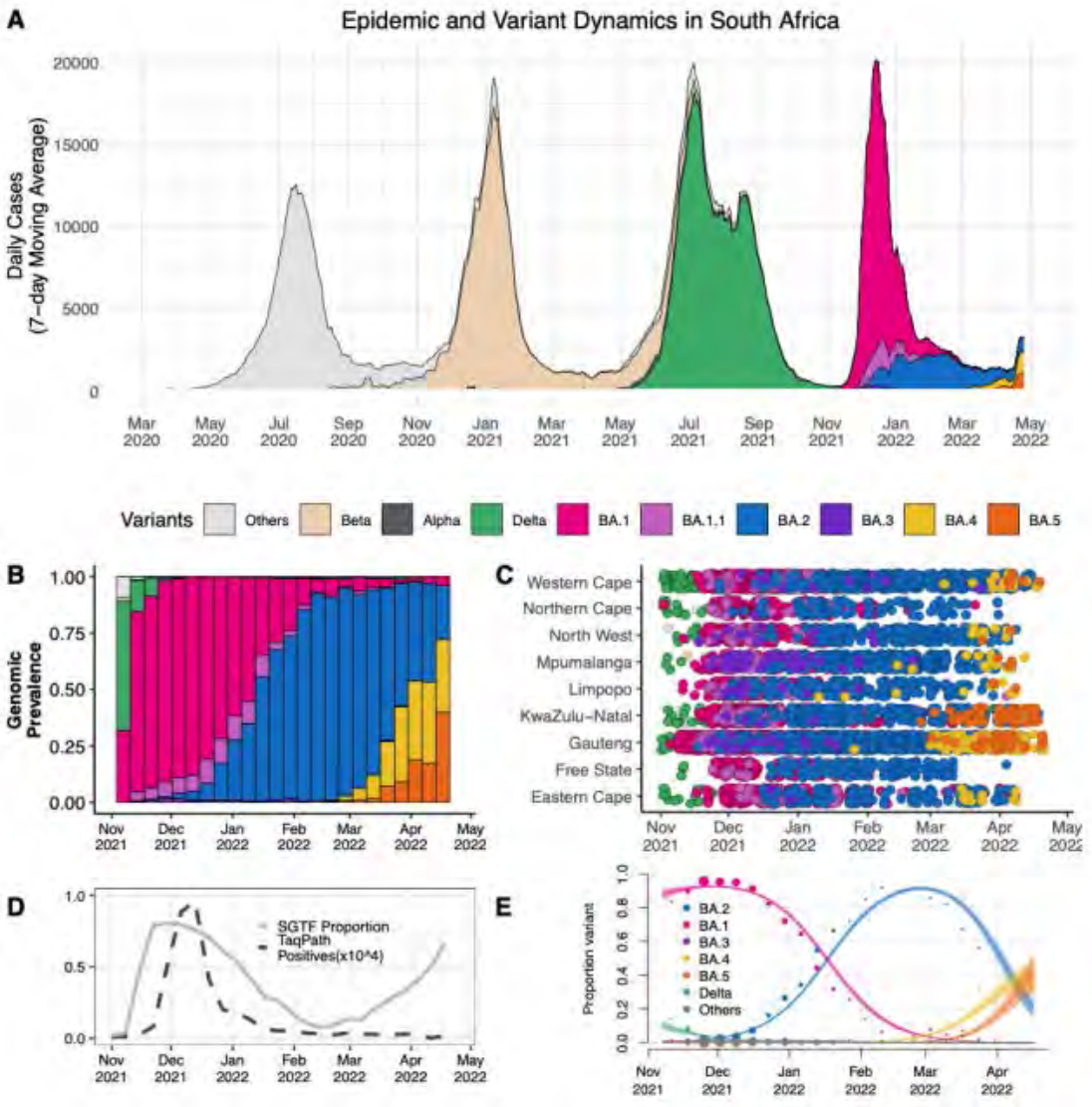
https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Variants of concern (CDC) = Omicron (B.1.1.529, BA.1, BA.1.1, BA.2, BA.3, BA.4 and BA.5 lineages)

https://www.who.int/docs/default-source/coronaviruse/2022-01-21-global-technical-brief-and-priority-action-on-omicron-sars-cov-2-variant.pdf?sfvrsn=f3ac8bc3_9&download=true

Continued Emergence and Evolution of Omicron in SA: New BA.4 and BA.5 lineages

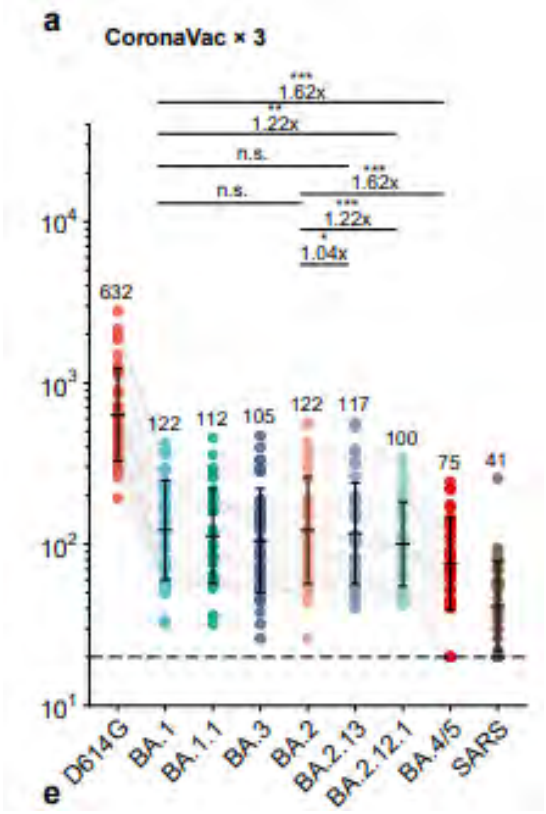
- Assessment new lineages BA.4 and BA.5, South Africa
- Results: The spike proteins of BA.4 and BA.5 are identical, and comparable to BA.2 except for the addition of 69-70del, L452R, F486V and the wild type amino acid at Q493. BA.4 and BA.5 have rapidly replaced BA.2, reaching more than 50% of sequenced cases in South Africa from the first week of April 2022 onwards. Using a multinomial logistic regression model, we estimate growth advantages for BA.4 and BA.5 of 0.08 (95% CI: 0.07-0.09) and 0.12 (95% CI: 0.09 - 0.15) per day respectively over BA.2 in South Africa. {this growth advantage is similar to that observed for BA.2 over BA.1.}
- Reasons for growth advantage: (i) an increase in its intrinsic transmissibility relative to other variants, (ii) an increase relative to other variants in its capacity to infect, and be transmitted from, previously infected and vaccinated individuals or (iii) both. Given that the transmission advantage becomes apparent approximately four months from the start of the Omicron wave, it is plausible that waning immunity (particularly that acquired from BA.1 infection) is an important contributory factor.

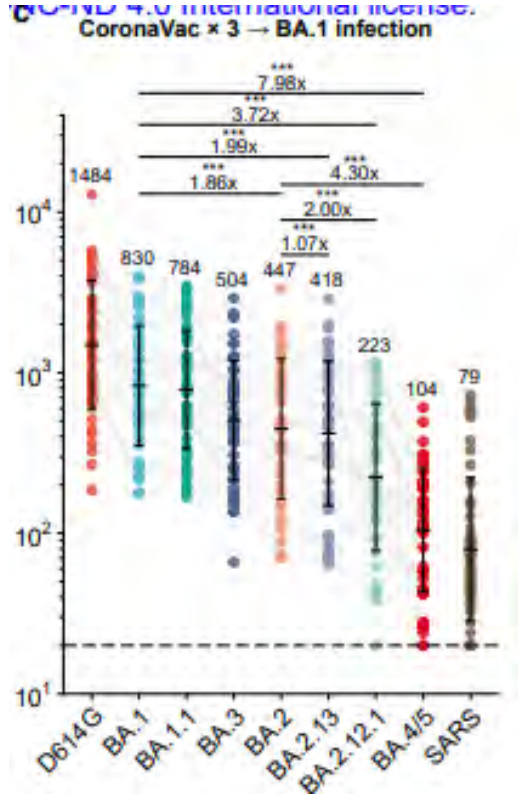


Tegally H, et al. https://krisp.org.za/manuscripts/MEDRXIV-2022-274406v1-deOliveira.pdf

BA.2.12.1, BA.4 and BA.5 escape antibodies elicited by Omicron infection

- Assessment of BA.2.12.1, BA.4, and BA.5; China
- Study showed that BA.2 sublineages, including A.2.12.1 and BA.2.13, exhibit increased ACE2-binding affinities compared to BA.1; while BA.4/BA.5 displays the weakest receptor-binding activity due to F486V and R493Q reversion. Importantly, compared to BA.2, BA.2.12.1 and BA.4/BA.5 exhibit stronger neutralization evasion against the plasma of 3-dose vaccinees and, most strikingly, of vaccinated BA.1 convalescents. As for therapeutic NAbs, LYCoV1404 (Bebtelovimab) and COV2-2130 (Cilgavimabcan) still effectively neutralize BA.2.12.1 and BA.4/BA.5, while the S371F, D405N and R408S mutations carried by BA.2/BA.4/BA.5 sublineages would undermine most broad sarbecovirus Nabs.
- Results indicate that Omicron can evolve mutations to specifically evade humoral immunity elicited by BA.1 infection. The continuous evolution of Omicron poses great challenges to SARS-CoV-2 herd immunity and suggests that BA.1-derived vaccine boosters may not be ideal for achieving broad-spectrum protection.





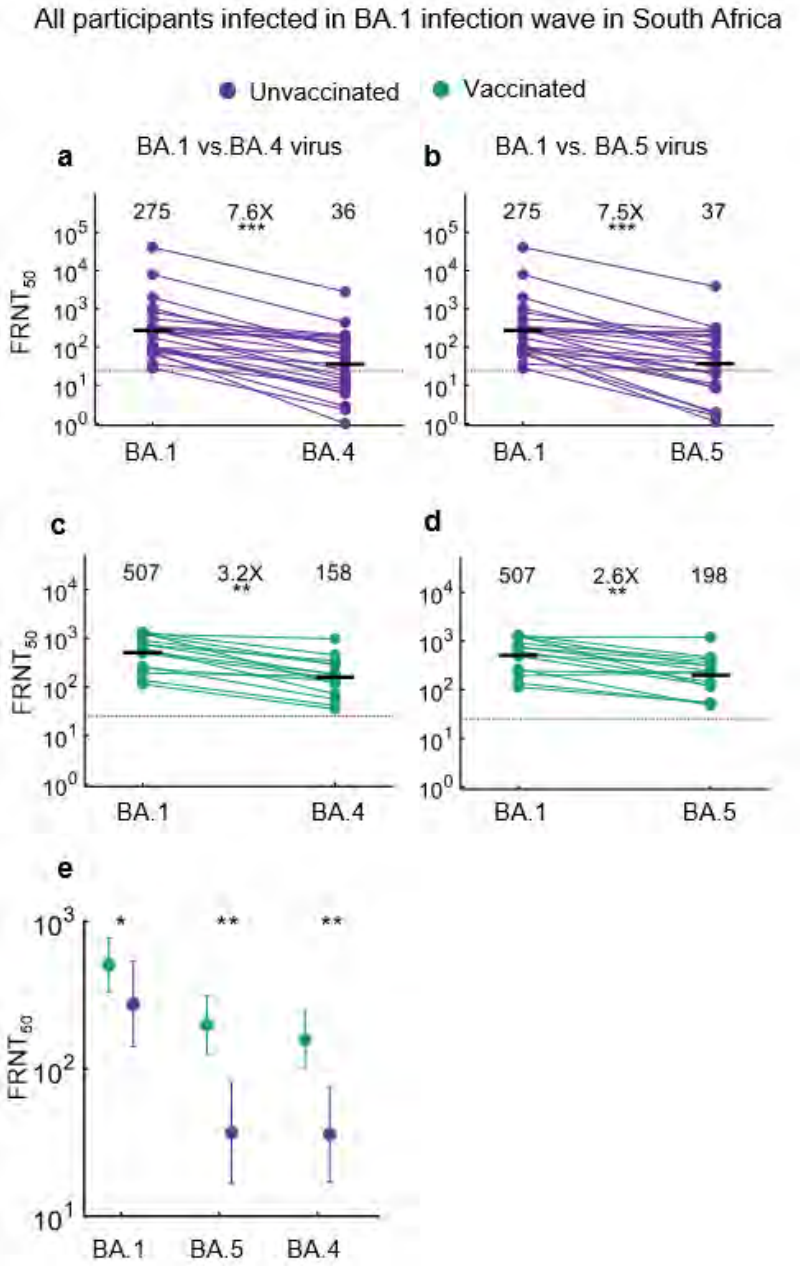
IC50 (ng/mL)	LY-CoV016	LY-CoV555	LY-CoV1404	REGN 10933	REGN 10987	COV2-2196	COV2-2130	BRII-196	BRII-198	S309	DXP-604	ADG-2	S2K146	SA58 (BD55-5840)	SA55 (BD55-5514)	LY-CoV016+ LY-CoV555	REGN10933+ REGN10987	COV2-2196+ COV2-2130	BRII-196+ BRII-198	SA55+SA58
D614G	32	15	0.7	5.6	5.7	1.6	2.5	53	1239	74	11	11	17	0.9	11	20	5.0	2.1	81	2.1
BA.1	*	*	0.6	*	*	5419	3007	7118	1171	361	285	979	11	4.4	1.7	*	*	491	1890	3.2
BA.1.1	*	*	1.8	8912	*	4764	*	8324	*	314	198	991	17	4.5	3.0	*	*	8090	*	3.3
BA.2	*	*	0.9	*	590	4312	6.3	8530	8990	918	219	*	20	12	7.2	*	821	8.2	8610	7.8
BA.3	*	*	1.1	*	*	5609	11	7833	1687	972	259	6226	16	8.1	7.1	*	*	19	2190	6.4
BA.2.13	*	*	1.0	9221	417	3591	6.6	6902	*	700	148	*	16	4.9	5.9	*	699	7.1	*	4.8
BA.2.12.1	*	*	0.8	*	499	5521	11	7620	*	989	201	*	13	5.0	5.2	*	714	18	*	5.0
BA.4/BA.5	*	*	0.9	*	520	*	23	7124	*	792	6264	*	221	3.9	5.0	*	709	40	*	4.5
SARS-CoV-1	*	*	*	*	*	*	*	*	*	31	*	1.7	108	5.6	4.4	*	*	*	*	4.6
Pangolin-GD	1125	6.8	8.6	157	84	17	*	13	*	*	7.4	5.0	14	296	5.7	10	98	27	33	7.7
RaTG13	*	*	*	*	*	*	*	16	*	*	1.1	*	3.9	*	38	*	*	*	29	49

Bebtelovimab

Cao Y, et al. https://doi.org/10.1101/2022.04.30.489997

Omicron sub-lineages BA.4/BA.5 escape BA.1 infection elicited neutralizing immunity

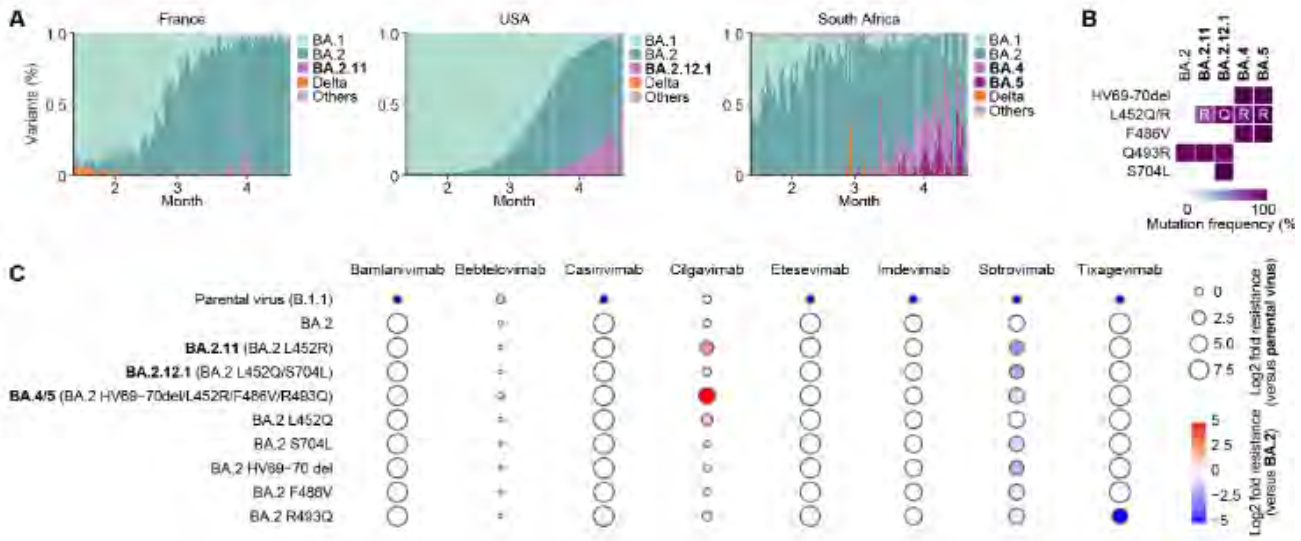
- Methods: We isolated live BA.4 and BA.5 viruses and tested them against neutralizing immunity elicited to BA.1 infection in participants who were Omicron/BA.1 infected but unvaccinated (n=24) and participants vaccinated with Pfizer or J&J vaccines with breakthrough Omicron/BA.1 infection (n=15).
- Results: In unvaccinated individuals, FRNT50, the inverse of the dilution for 50% neutralization, declined from 275 for BA.1 to 36 for BA.4 and 37 for BA.5, a 7.6 and 7.5-fold drop, respectively. In vaccinated BA.1 breakthroughs, FRNT50 declined from 507 for BA.1 to 158 for BA.4 (3.2-fold) and 198 for BA.5 (2.6-fold). Absolute BA.4 and BA.5 neutralization levels were about 5-fold higher in this group versus unvaccinated BA.1 infected participants
- Conclusion: The observed escape of
- BA.4 and BA.5 from BA.1 elicited immunity is more moderate than of BA.1 against previous immunity. However, the low absolute neutralization levels for BA.4 and BA.5, particularly in the unvaccinated group, are unlikely to protect well against symptomatic infection4.This may indicate that, based on neutralization escape, BA.4 and BA.5 have potential to result in a new infection wave.



Khan K, et al, https://doi.org/10.1101/2022.04.29.22274477

Sensitivity of novel SARS-CoV-2 Omicron subvariants, BA.2.11, BA.2.12.1,1 BA.4 and BA.5 to therapeutic monoclonal antibodies

- Background: Omicron BA.2.11, BA.2.12.119 and BA.4/5 subvariants are becoming dominant in France, US and South Africa, respectively.
- Study goal: Assess the sensitivity of these new Omicron subvariants (BA.2.11, BA.2.12.1 and BA.4/5) to eight therapeutic monoclonal antibodies (bamlanivimab, bebtelovimab, casirivimab, cilgavimab, etesevimab, imdevimab, sotrovimab and tixagevimab).
- Results: Although cilgavimab is antiviral against BA.2, BA.4/5 exhibits higher resistance to this antibody compared to BA.2. Bamlanivimab, casirivimab, tesevimab, imdevimab and tixagevimab were not functional against BA.2. Bebtelovimab was ~2-fold more effective against BA.2 and all Omicron subvariants tested than the parental virus. Omicron subvariants bearing L452R substitution including BA.2.11 and BA.4/5 were more sensitive to sotrovimab than BA.2. Cilgavimab was also antiviral against BA.2, while the L452R/; BA.4/5 exhibited ~30-fold more resistance to cilgavimab compared to BA.2



Yamasoba D, et al.
https://doi.org/10.1101/2022.05.03.490409

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