COVID-19 Series for Free & Charitable Clinics

May 12, 2022

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AT THE FOREFRONT UChicago Medicine

Vaccinate with Confidence

A National Strategy to Reinforce Confidence in COVID-19 Vaccines

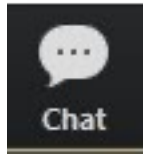
CDC's Strategy: **Empower Healthcare Personnel**: Promote confidence among healthcare personnel in their decisions to get vaccinated and recommend the vaccination to their patients.

Project Goal: Build and reinforce COVID-19 vaccine confidence among healthcare personnel in the safety net sector and, in turn, the patients they serve.

Partnerships: **The National Association of Free and Charitable Clinics** and **15 State Associations** and Federally Qualified Health Centers (FQHCs) in Puerto Rico and the U.S. Virgin Islands.

How: Provide tailored COVID-19 vaccine information to the free and charitable clinic sector through various channels and **give the FCC sector a direct line of communication to CDC**.

Reminders:

- Please use your first name and clinic name when you join the session
- Use the “chat” feature to ask questions 

- Please remember to mute your microphone 

- If you can’t connect audio via computer or you lose computer audio at anytime, you can call in to session at **(408) 638-0968, Meeting ID 932-6566-2201##**
- This activity has been approved for AMA PRA Category 1 Credit™ & Nursing CEUs

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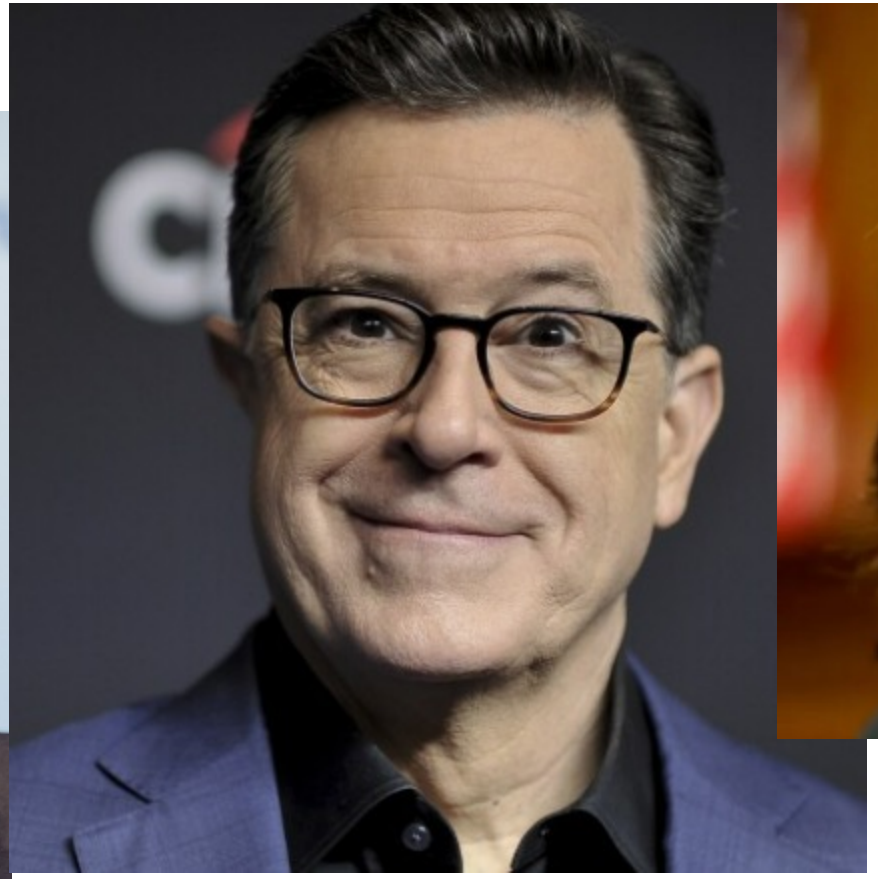
Disclosures

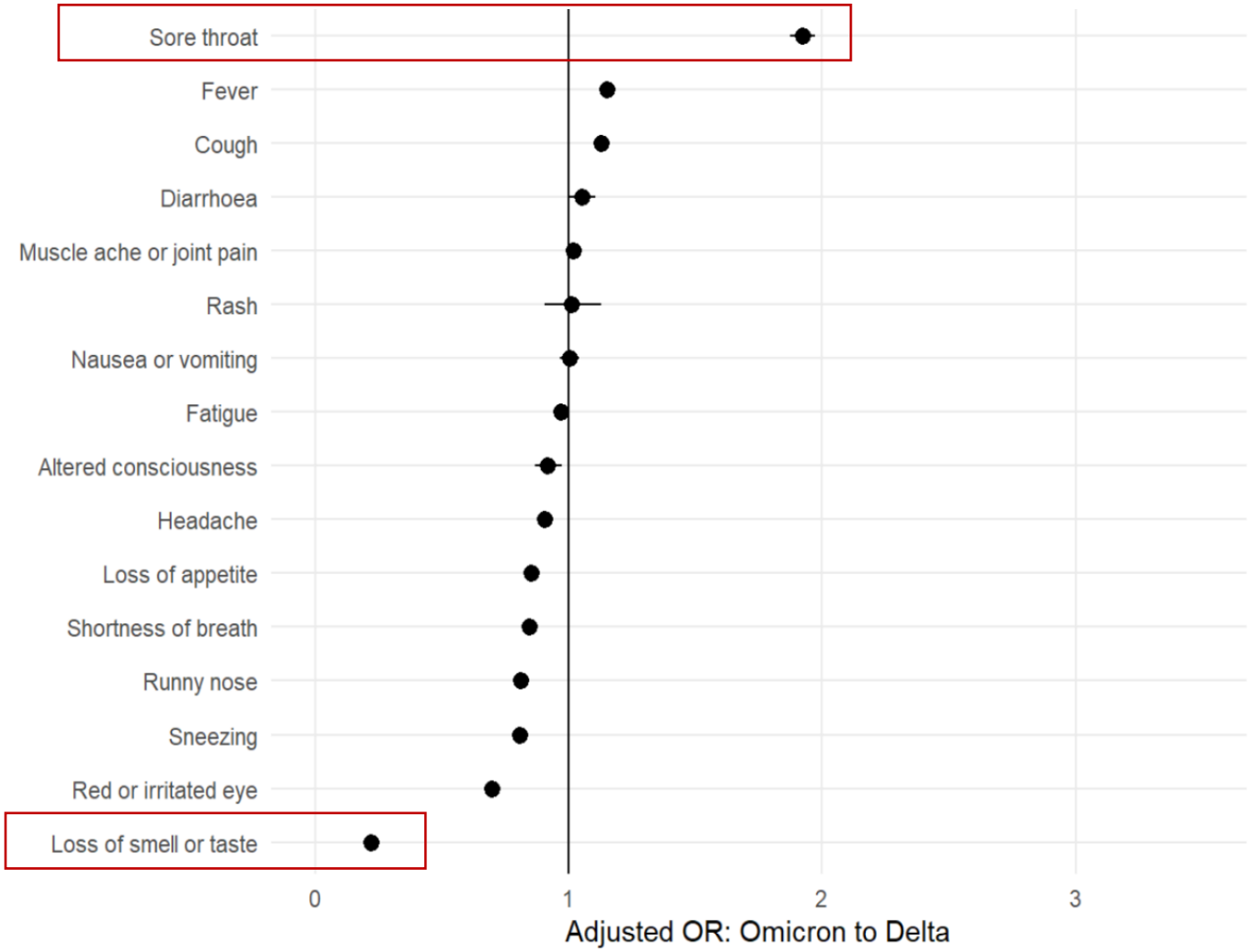
- We have no relevant financial interests to disclose.

Personal Experience Bias?

At least I am in good company!



Clinical presentation differs for Omicron?

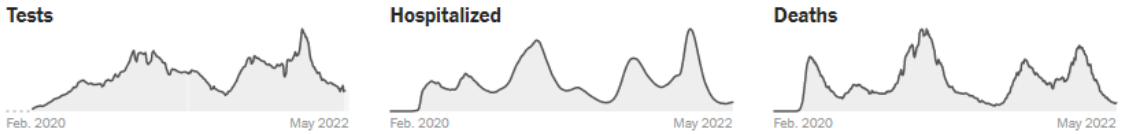


[UK Health Security Agency: Technical briefing 34]

Coronavirus in the U.S.: Latest Map and Case Count

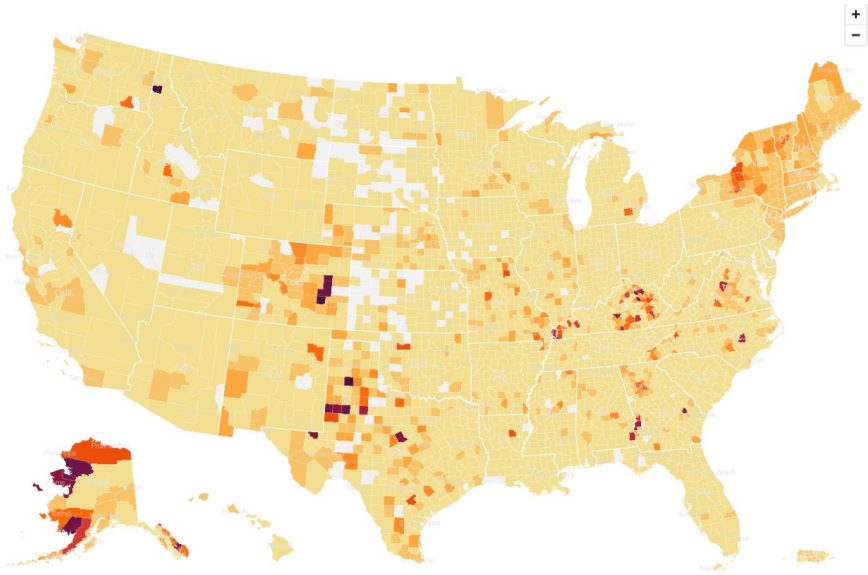
New reported cases

All time | Last 90 days

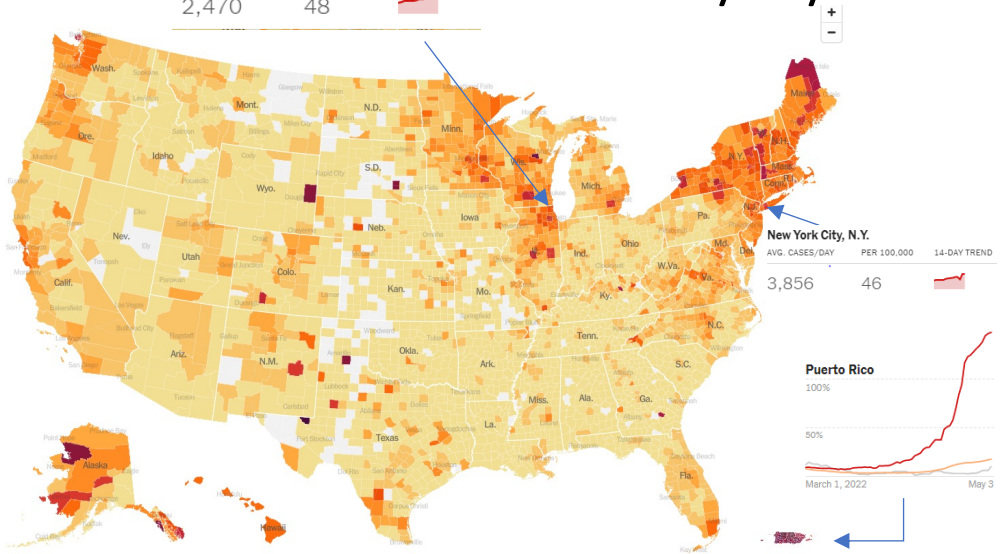


	DAILY AVG. ON MAY 3	14-DAY CHANGE	TOTAL REPORTED
Cases	62,428	+50%	81,440,777
Tests	643,075	−12%	—
Hospitalized	17,532	+18%	—
In I.C.U.s	1,994	+4%	—
Deaths	340	−17%	993,088

4/5/22

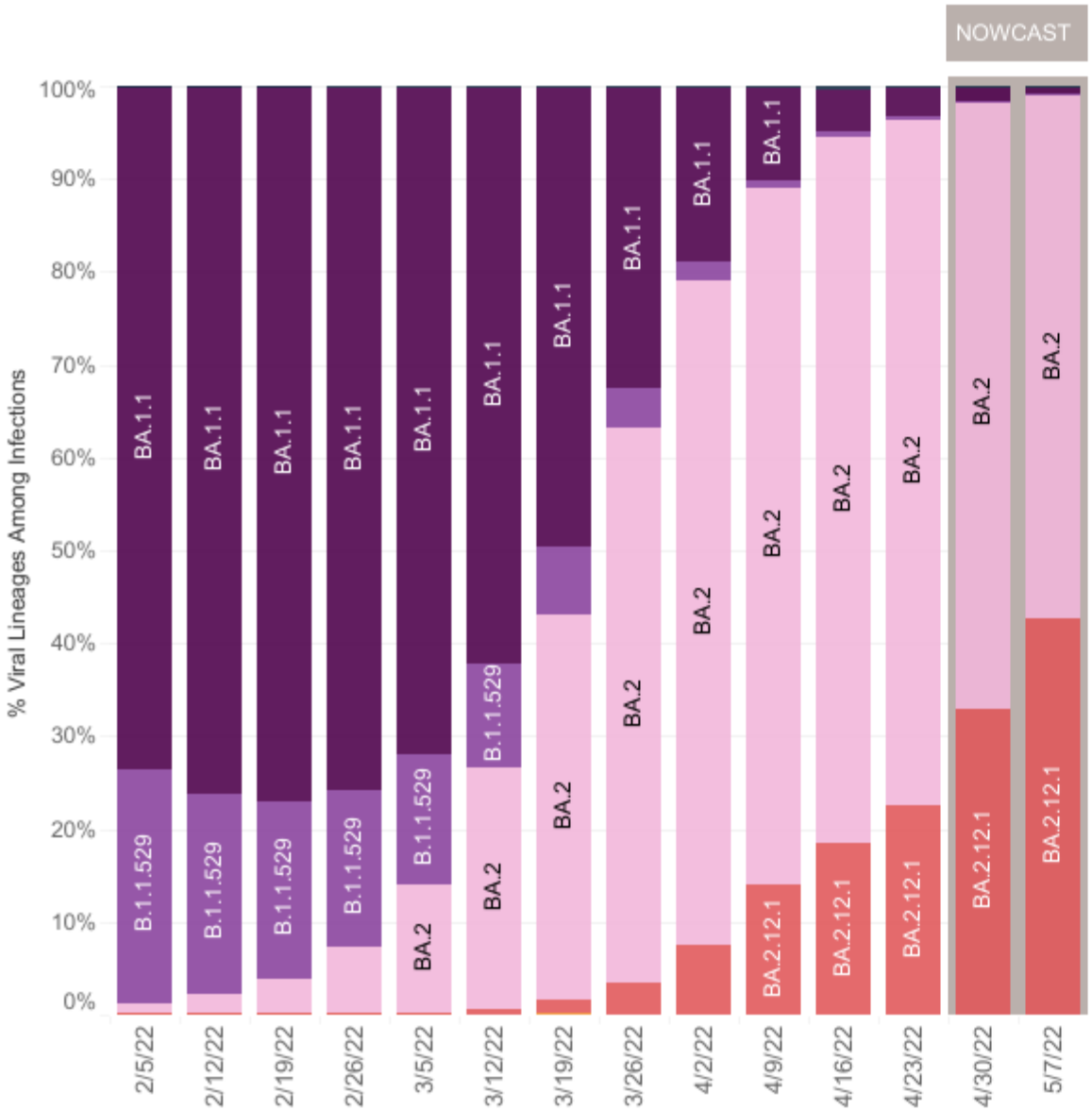


5/11/22



https://www.nytimes.com/interactive/2021/us/coronavirus-us-cases.html

United States: 1/30/2022 – 5/7/2022



United States: 5/1/2022 – 5/7/2022 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.2	VOC	56.4%	49.3-63.3%
	BA.2.12.1	VOC	42.6%	35.6-49.9%
	BA.1.1	VOC	0.6%	0.5-0.8%
	B.1.1.529	VOC	0.2%	0.1-0.4%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.2%	0.1-0.3%

* 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.

Feature	BA.1	BA.2	BA.2.12.1	BA.4 and BA.5
Transmissibility Increase	Reference	30% increase	25% over BA.2	~10% over BA.2
Immune Escape	Reference	+	+++	+++
Ability to infect cells	Reference	+	++	Like BA.1
Key Mutations	Reference	T367A, D405N, R408S	L452Q	L452R, F486V, R493Q, Δ 69-70
Cross-Immunity w/ BA.1	Reference	Mostly preserved	Reduced	Reduced
Resistance to Monoclonal Antibodies	Reference	++	+++	+++
Places Where Dominant	Outcompeted	>100 countries	United States Region 2	South Africa
3-Shot Vaccine Effectiveness vs Hospitalization*	81% (95% CI 75,85)	83% (95% CI 71,91)	TBD	TBD
2-Shot Vaccine Effectiveness vs Hospitalization^	32% (95% CI 11,49)	50% (95% CI 7,73)	TBD	TBD

*UKHSA reports, up to 70 days, ^ past 6 months, TBD-to be determined

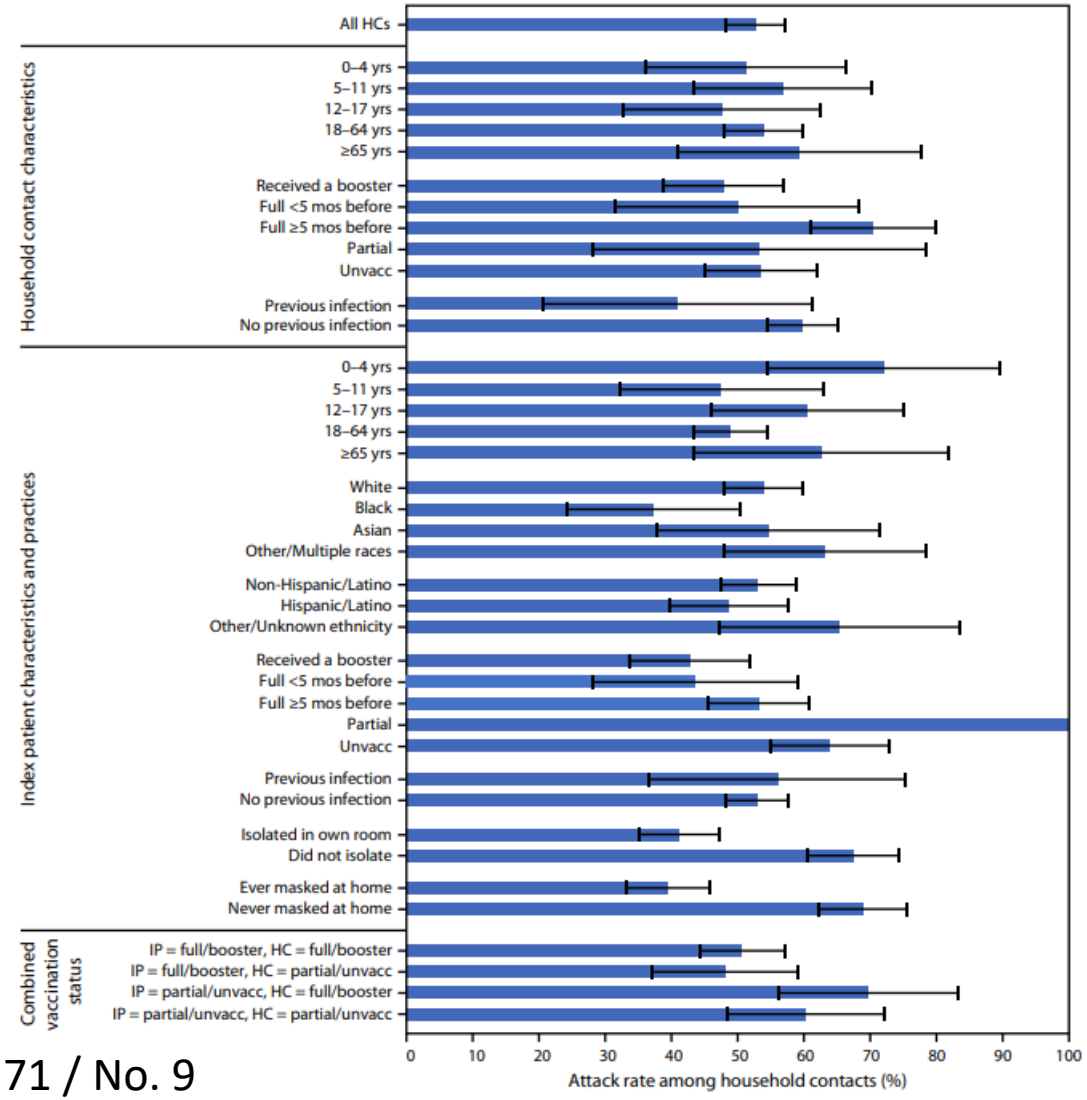
@erictopol

There are estimates that more than 60% of the world's population has been exposed to Omicron and over 65% of the world's population has received at least one dose of the vaccine per IHME at the University of Washington.

SARS-CoV-2 B.1.1.529 (Omicron) Variant Transmission Within Households — November 2021–February 2022

- Omicron infection resulted in high ARs among household contacts in this investigation, particularly among those who lived with index patients who were not vaccinated or who did not practice prevention measures (isolating or ever wearing a mask at home)
- AR in this investigation is consistent with the range of ARs observed in other Omicron transmission studies, and higher than those associated with some other SARS-CoV-2 variants
- ARs were consistently high across household contact and index patient age groups, including those aged 0–4 years, further highlight young children's potential contribution to household transmission of SARS-CoV-2, as well as their ongoing susceptibility to infection when SARS-CoV-2 is introduced in the home

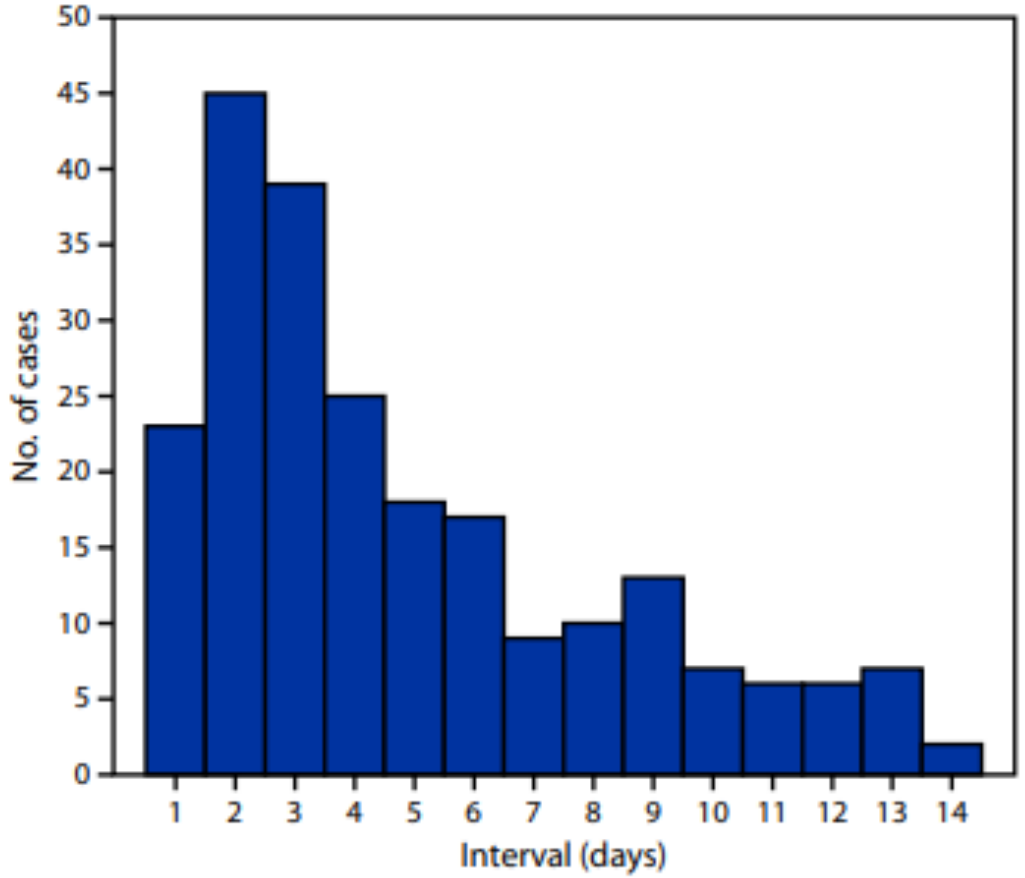
FIGURE 2. SARS-CoV-2 infection attack rates* among household contacts (N = 431) with known case status, by household contact characteristics,†,§ index patient characteristics and practices,†,¶,¶ and combined vaccination status** — four U.S. jurisdictions, November 2021–February 2022



Transmission occurs quickly, but risk lingers

- Transmission occurred within 67.8% (124 of 183) of households, and the overall AR among household contacts with known status was 52.7% (227 of 431)
- Similar ARs were observed across age groups for household contacts, including those aged 0–4 years (51.2%, 21 of 41). ARs were high across all household contact vaccination categories but lowest among those who received a booster dose (47.8%, 54 of 113) or were fully vaccinated

FIGURE 1. Interval[§,†] between index patient onset date and household contact onset date — four U.S. jurisdictions, November 2021–February 2022



Fourth Dose Likely Helps

- A fourth dose of the BNT162b2 vaccine was effective in reducing the short-term risk of Covid-19–related outcomes among persons who had received a third dose at least 4 months earlier.

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Fourth Dose of BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting

Magen O et al. DOI: 10.1056/NEJMoa2201688

CLINICAL PROBLEM

Emergence of the B.1.1.529 (omicron) variant of SARS-CoV-2 in late 2021 led to the largest waves of Covid-19 to date. Some policymakers considered recommending a fourth dose of Covid-19 vaccine for high-risk populations, but evidence on the effectiveness of four doses as compared with three is sparse.

OBSERVATIONAL STUDY

Data Source: Electronic records from the largest health care organization in Israel were used to examine the relative effectiveness of four doses of the BNT162b2 mRNA vaccine (Pfizer–BioNTech) as compared with three doses among adults 60 years of age or older. A total of 182,122 persons who received a fourth dose between January 3 and February 18, 2022, when the omicron variant was predominant, were matched to persons who had received a third dose at least 4 months earlier but had not yet received a fourth dose.

Outcomes Measured: Five outcomes were examined, including polymerase chain reaction (PCR)–confirmed SARS-CoV-2 infection, symptomatic infection, Covid-19–related hospitalization, severe Covid-19, and Covid-19–related death.

RESULTS

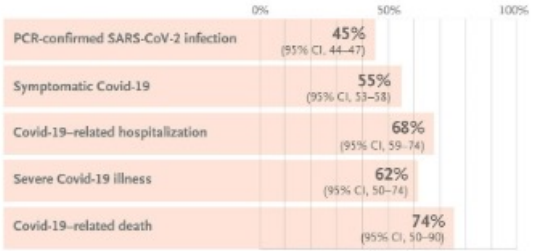
For all outcomes studied, four doses of BNT162b2 were more effective than three during days 7 to 30 after the fourth dose. Outcomes were similar in analyses limited to days 14 to 30 after the fourth dose.

LIMITATIONS AND REMAINING QUESTIONS

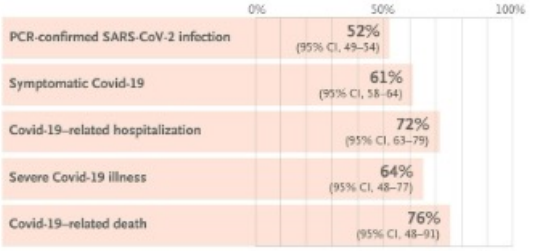
- The follow-up time was short, so longer-term effectiveness of a fourth dose could not be assessed.
- Given the observational nature of the study, there was potential for confounding.
- Most participants were drawn from the older Israeli population.

Links: Full Article | NEJM Quick Take

Relative Vaccine Effectiveness of Fourth Dose of BNT162b2 vs. Third Dose Days 7–30 after Fourth Dose



Relative Vaccine Effectiveness of Fourth Dose of BNT162b2 vs. Third Dose Days 14–30 after Fourth Dose

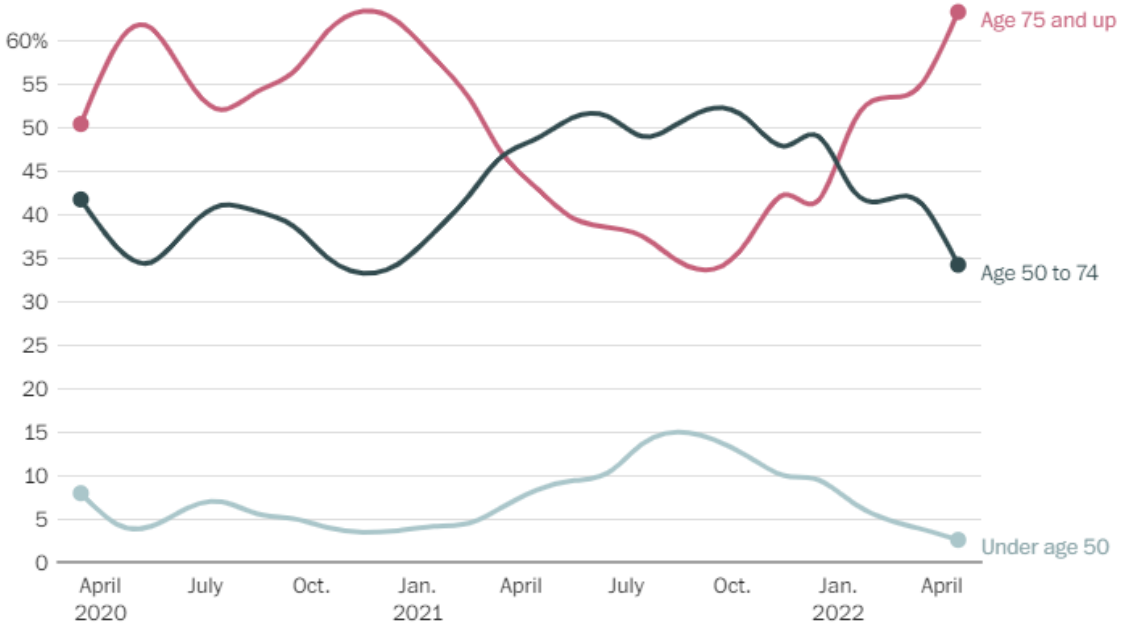


CONCLUSIONS

A fourth dose of the BNT162b2 vaccine, as compared with a third dose given at least 4 months earlier, appeared to improve short-term protection against PCR-confirmed SARS-CoV-2 infection, symptomatic illness, Covid-19–related hospitalization, severe Covid-19, and Covid-19–related death.

Oldest seniors are again the majority of covid-19 deaths

During the delta variant's surge, most of the deaths were people under age 75. After the arrival of the omicron variant, the deaths are again mostly among people 75 or older.



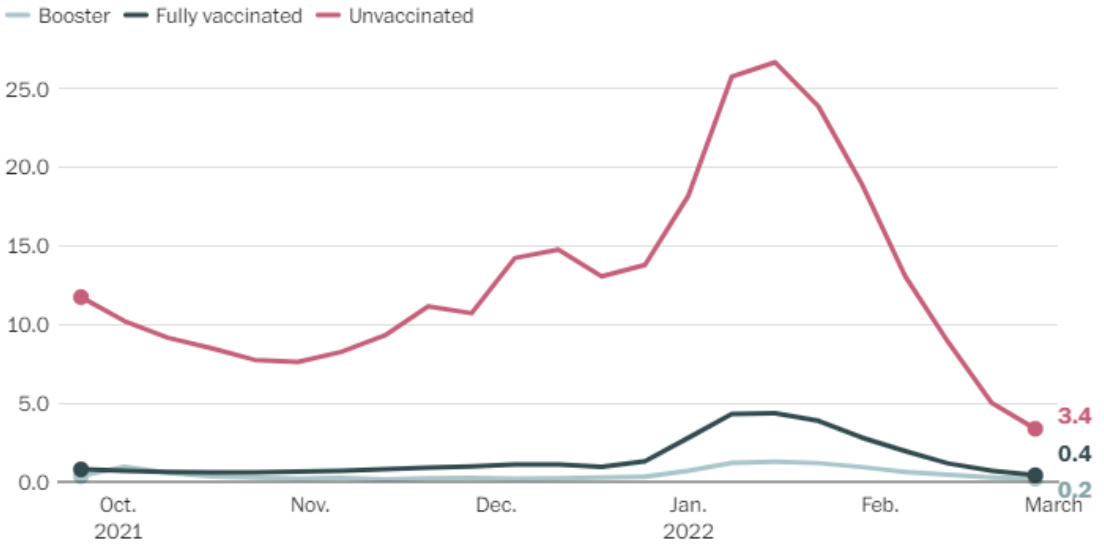
Share of deaths in that month for each age group

Source: Centers for Disease Control and Prevention

DAN KEATING / THE WASHINGTON POST

Unvaccinated still die at a much higher rate

The share of deaths among vaccinated people has risen, but the rate of death is still many times higher among unvaccinated people. In January and February, unvaccinated people died at about seven times the rate of the fully vaccinated and 20 times the rate of people with boosters, according to a study of deaths among the vaccinated from 23 state and county health departments.



Rate of deaths per 100,000 people

Source: Centers for Disease Control and Prevention

DAN KEATING / THE WASHINGTON POST

A key explanation for the rise in deaths among the vaccinated is that covid-19 fatalities are again concentrated among the elderly. Nearly two-thirds of the people who died during the omicron surge were 75 and older compared with a third during the delta wave. Seniors are overwhelmingly immunized, but vaccines are less effective and their potency wanes over time in older age groups.

https://www.washingtonpost.com/health/2022/04/29/covid-deaths-unvaccinated-boosters/

Paxlovid – Why aren’t we using it?

- Some doctors feel uncomfortable prescribing such a new drug
- Others worry about contraindications with medications for other conditions.
- Or they question whether a patient really qualifies as "high risk."
- Some may not even realize Paxlovid is much more available than it was initially

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

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

Concomitant Medication	Nirmatrelvir/ Ritonavir Effect on Drug Level	Possible Effect	Recommendation During Nirmatrelvir/Ritonavir Treatment
Trazodone	↑	Sedation, hypotension	No dose adjustment required; consider reducing dose if risk for falls
Warfarin	**Variable**	Unpredictable effects on INR	Monitor INR for dose adjustment
Valsartan	↑	Hypotension	No dose adjustment required; consider reducing dose if risk of hypotension

Nirmatrelvir/Ritonavir Renal Dosing Guide:

Estimated Glomerular Filtration Rate (eGFR)*	Nirmatrelvir Dose	Ritonavir Dose
> 60 mL/min	300 mg every 12 hours x 5 days	100 mg every 12 hours x 5 days
≥ 30 to < 60 mL/min	150 mg every 12 hours x 5 days	100 mg every 12 hours x 5 days
< 30 mL/min	Nirmatrelvir/ritonavir not recommended	

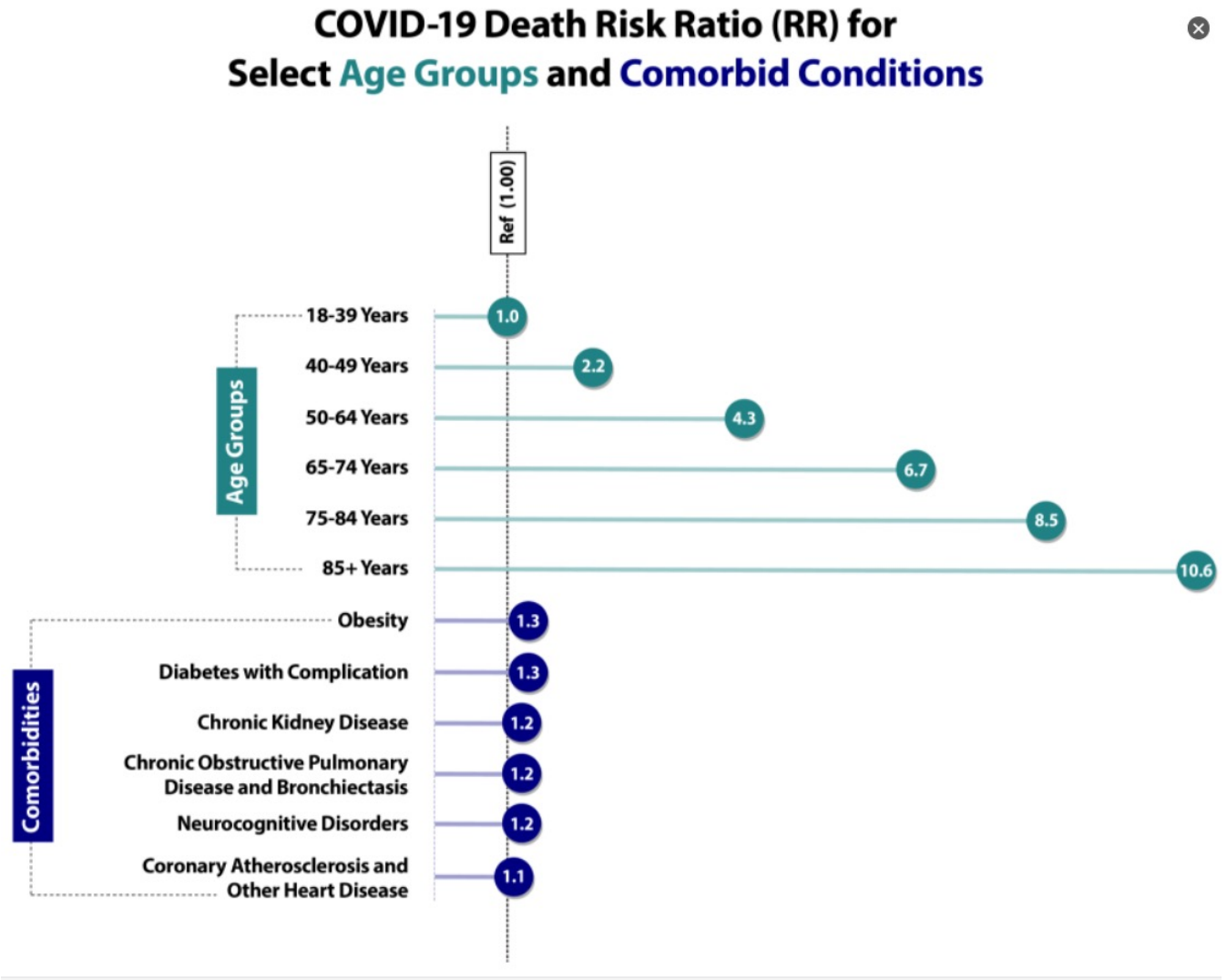
* eGFR calculated by CKD-EPI Creatinine Equation (eGFR Calculator | National Kidney Foundation)

Concomitant Medication	Nirmatrelvir/ Ritonavir Effect on Drug Level	Possible Effect	Recommendation During Nirmatrelvir/Ritonavir Treatment
Clopidogrel	↓	Increased clotting	• Avoid nirmatrelvir/ritonavir for 6 weeks after coronary stenting • Other patients: No change
Diazepam	↑	Excess sedation	Consider dose reduction, but do not stop if chronic use
Hormonal contraceptives with ethinyl estradiol	↓	Lack of contraceptive efficacy	Recommend nonhormonal contraception until one menstrual cycle after nirmatrelvir/ritonavir
Hydrocodone Oxycodone (with or without acetaminophen)	↑	Increased opioid side effects, sedation	Consider reducing frequency of dosing or reduced dose of hydrocodone/oxycodone
Isosorbide mononitrate	↓	Decreased active drug	No dose adjustment required
Paroxetine	↓	Decreased effects	No dose adjustment required
Quetiapine	↑	Increased effects	Reduce dose of quetiapine to one-sixth of the original dose during nirmatrelvir/ritonavir treatment
Risperidone	↑	Increased toxicity	No dose adjustment; monitor for adverse effects
Rivaroxaban	↑	Increased bleeding	Avoid nirmatrelvir/ritonavir
Salmeterol	↑	Increased cardiac effects	Avoid nirmatrelvir/ritonavir
Statins (HMG-CoA reductase inhibitors)	↑ **most statins**	Increased toxicity	Hold statins during nirmatrelvir/ritonavir course and for 5 days after
Steroids, inhaled or nasal	↑	Increased toxicity	No dose adjustment required
Steroids, oral	↑	Increased toxicity	No specific adjustment; consider reducing the dose
Tamsulosin	↑	Hypotension, orthostasis	Dose-dependent: • Tamsulosin 0.4 mg: No change (monitor blood pressure) • Tamsulosin 0.8 mg: Consider holding or decrease to 0.4 mg
Tramadol	↓	Decreased effects, increased side effects	No dose adjustment required

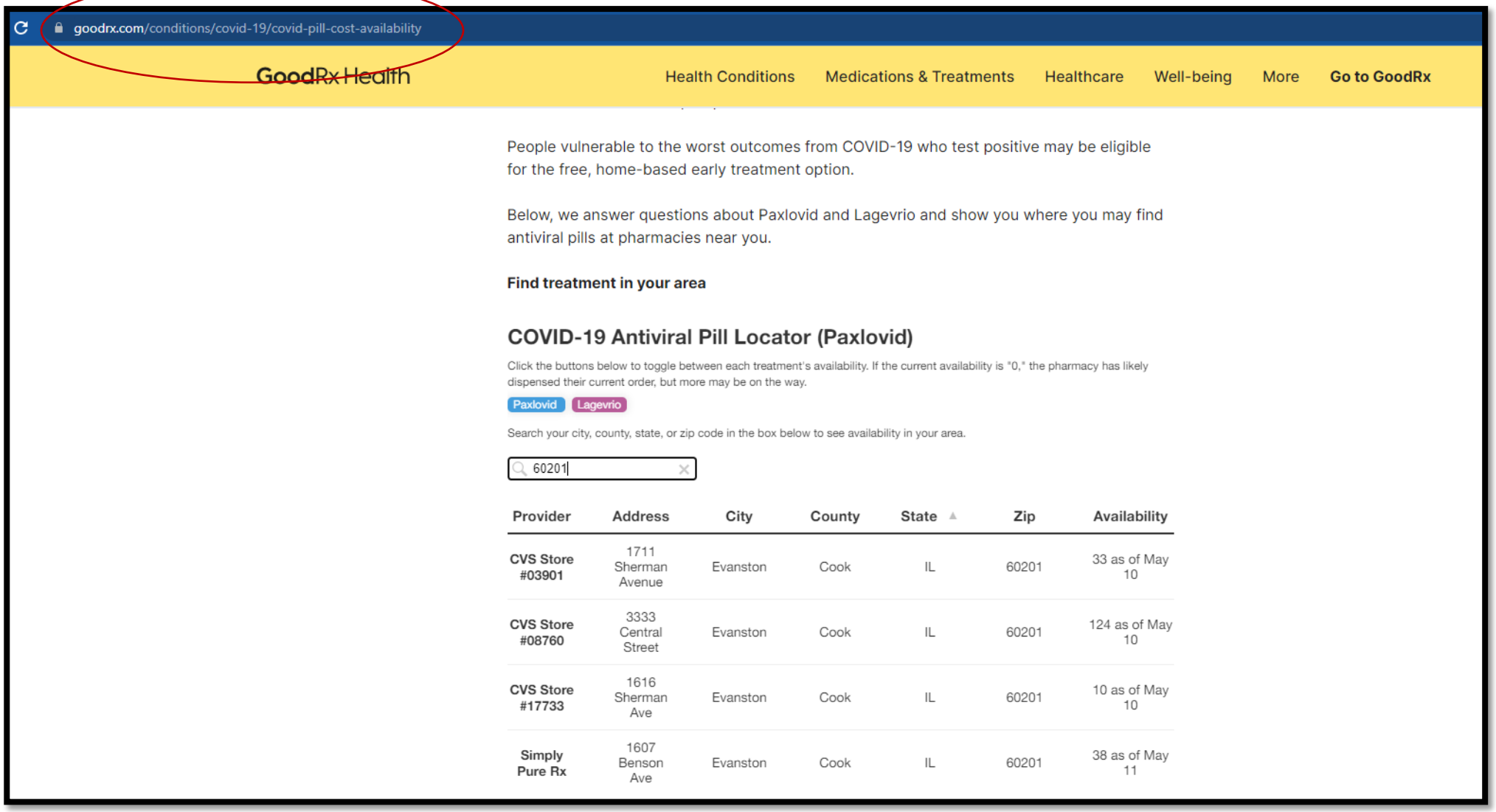
https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/management-of-drug-interactions-with-nirmatrelvirritonavir-paxlovid/

Who Should be Considered for Treatment?

Tier	Risk Group
1	• Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status (see Immunocompromising Conditions below); *or* • Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors).
2	• Unvaccinated individuals not included in Tier 1 who are at risk of severe disease (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors)
3	• Vaccinated individuals at high risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with clinical risk factors) **Note:** Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients within this tier in this situation should be prioritized for treatment.
4	• Vaccinated individuals at risk of severe disease (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors) **Note:** Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients within this tier in this situation should be prioritized for treatment.

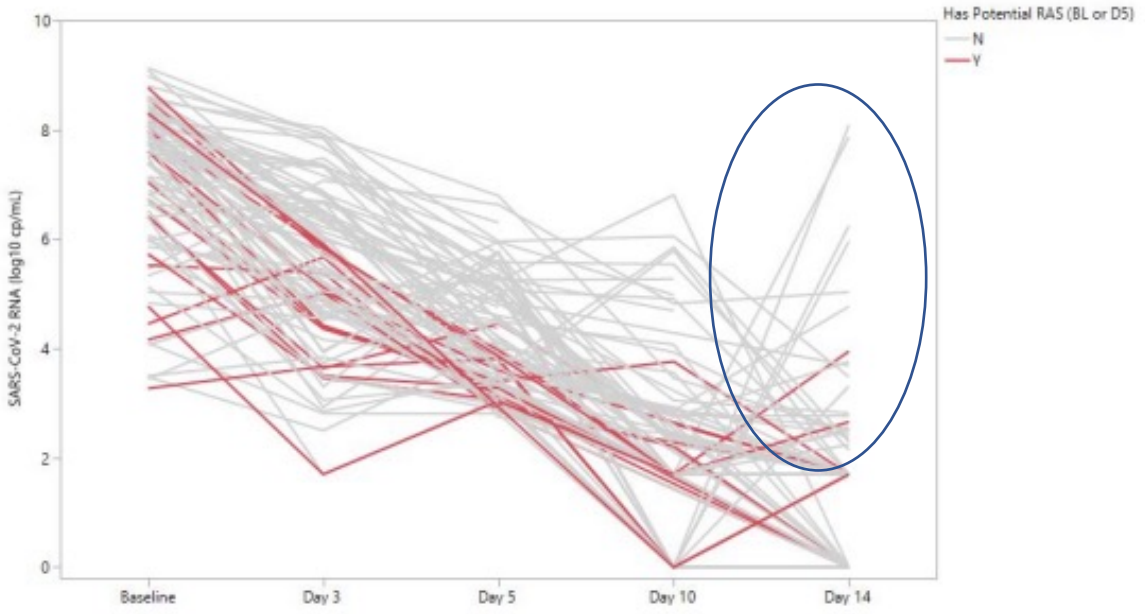


Where to find Paxlovid?



Relapses After Paxlovid?

- Sequencing of SARS-CoV-2 from these cases did not demonstrate resistance mutations either at baseline or at relapse that correlated with resistance. Currently there are no clear signals of baseline or treatment-emergent NIR resistance from the preliminary analyses of clinical trial EPIC-HR.
- What to do? Treat longer? New medication? Continue to isolate?
- Seems to be uncommon, but need to understand which patients may relapse



Source: FDA analysis.

Paxlovid does not work as prevention

- In a 2,957-subject trial testing whether Paxlovid could also work preventively, researchers found that the risk of developing an infection declined by 32% in subjects who received Paxlovid for five days compared with people who got a placebo, and declined 37% in people who received treatment for 10 days
- The results weren't statistically significant and failed the study's primary endpoint
- Per Pfizer: "While we are disappointed in the outcome of this particular study, these results do not impact the strong efficacy and safety data we've observed in our earlier trial for the treatment of Covid-19 patients at high risk of developing severe illness, and we are pleased to see the growing global use of Paxlovid in that population"

https://www.wsj.com/articles/pfizers-covid-19-pill-failed-study-testing-its-preventative-use-11651276069

FDA Authorizes First COVID-19 Diagnostic Test Using Breath Samples

- InspectIR COVID-19 Breathalyzer was validated in a large study of 2,409 individuals, including those with and without symptoms. 91.2% sensitivity and 99.3% specificity
- A population with only 4.2% of individuals who are positive for the virus, the test had a negative predictive value of 99.6%
- The test performed with similar sensitivity in a follow-up clinical study focused on the Omicron variant.
- The InspectIR COVID-19 Breathalyzer uses a technique called gas chromatography gas mass-spectrometry (GC-MS) to separate and identify chemical mixtures and rapidly detect five Volatile Organic Compounds (VOCs) associated with SARS-CoV-2 infection in exhaled breath
- Each instrument (size of small suitcase) can be used to evaluate approximately 160 samples per day (20 per hour).

Near 1 million deaths due to COVID-19

Questions?

Thank you!

Next Session: Thursday, June 16th ,12-1:15pm CST

Resources & recording of the session

https://www.echo-chicago.org/resources/covid19/

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