COVID-19 Update
January 18, 2023

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Outline

USA COVID-19 stats and variants update

COVID-19 Screening

Antiviral treatment update

Other Updates: Post-COVID, Vaccines, Steroids

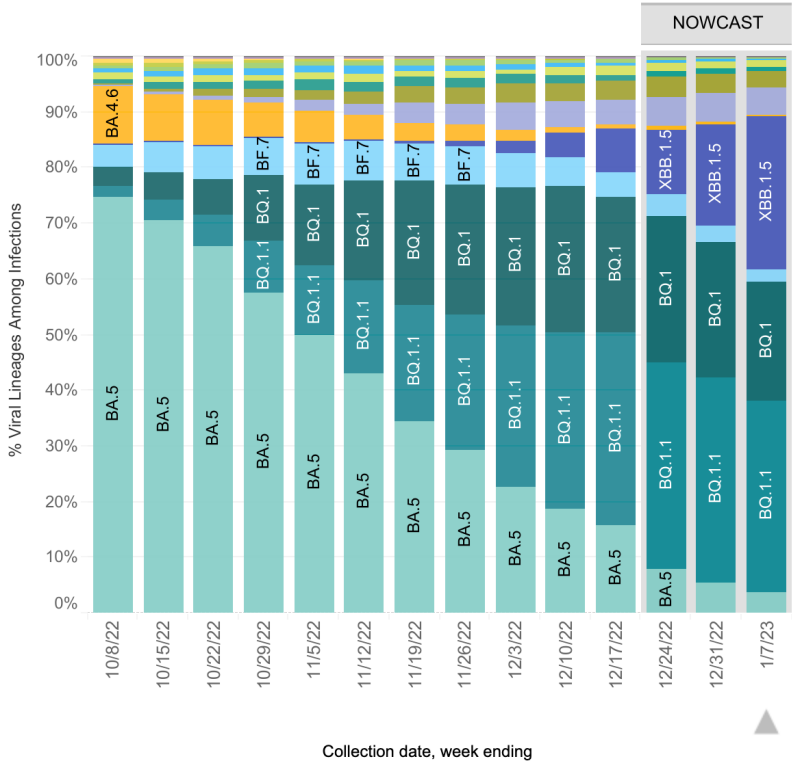
USA COVID-19 Variant Proportions January 7,2023

United States: 1/1/2023 – 1/7/2023 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BQ.1.1	VOC	34.4%	26.7-43.0%
	XBB.1.5	VOC	27.6%	14.0-46.5%
	BQ.1	VOC	21.4%	16.1-27.7%
	XBB	VOC	4.9%	4.0-6.1%
	BA.5	VOC	3.7%	2.7-5.0%
	BN.1	VOC	3.0%	2.1-4.1%
	BF.7	VOC	2.2%	1.6-3.0%
	BA.2.75	VOC	1.3%	0.9-2.0%
	BA.5.2.6	VOC	0.7%	0.5-0.9%
	BA.2	VOC	0.3%	0.2-0.5%
	BF.11	VOC	0.3%	0.2-0.4%
	BA.4.6	VOC	0.2%	0.2-0.3%
	BA.2.75.2	VOC	0.1%	0.1-0.1%
	BA.4	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.2.12.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.1%

United States: 10/2/2022 – 1/7/2023



* 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

\# BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, BA.2.75.2, BN.1,XBB and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, BF.11, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. Except XBB.1.5, sublineages of XBB are aggregated to XBB. For all the lineages listed in the above table, their sublineages are aggregated to the listed parental lineages respectively. Previously, XBB.1.5 was aggregated to XBB. Lineages BA.2.75.2, XBB, XBB.1.5, BN.1, BA.4.6, BF.7, BF.11, BA.5.2.6 and BQ.1.1 contain the spike substitution R346T.

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

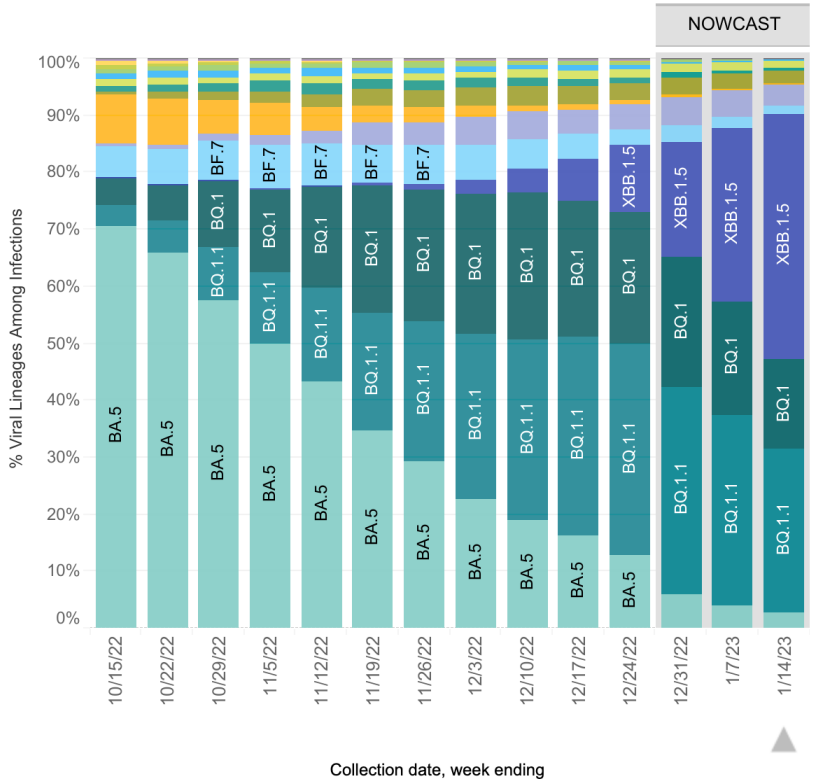
USA COVID-19 Variant Proportions January 14, 2023

United States: 1/8/2023 – 1/14/2023 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	XBB.1.5	VOC	43.0%	26.4-61.1%
	BQ.1.1	VOC	28.8%	20.5-38.7%
	BQ.1	VOC	15.9%	11.0-22.2%
	XBB	VOC	3.9%	3.0-5.1%
	BA.5	VOC	2.6%	1.8-3.7%
	BN.1	VOC	2.1%	1.5-3.1%
	BF.7	VOC	1.4%	0.9-2.1%
	BA.2.75	VOC	1.3%	0.8-1.9%
	BA.5.2.6	VOC	0.5%	0.3-0.8%
	BA.2	VOC	0.2%	0.1-0.4%
	BF.11	VOC	0.2%	0.1-0.3%
	BA.4.6	VOC	0.1%	0.1-0.2%
	BA.2.75.2	VOC	0.1%	0.0-0.1%
	BA.1.1	VOC	0.0%	0.0-0.0%
	BA.4	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.2.12.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

United States: 10/9/2022 – 1/14/2023



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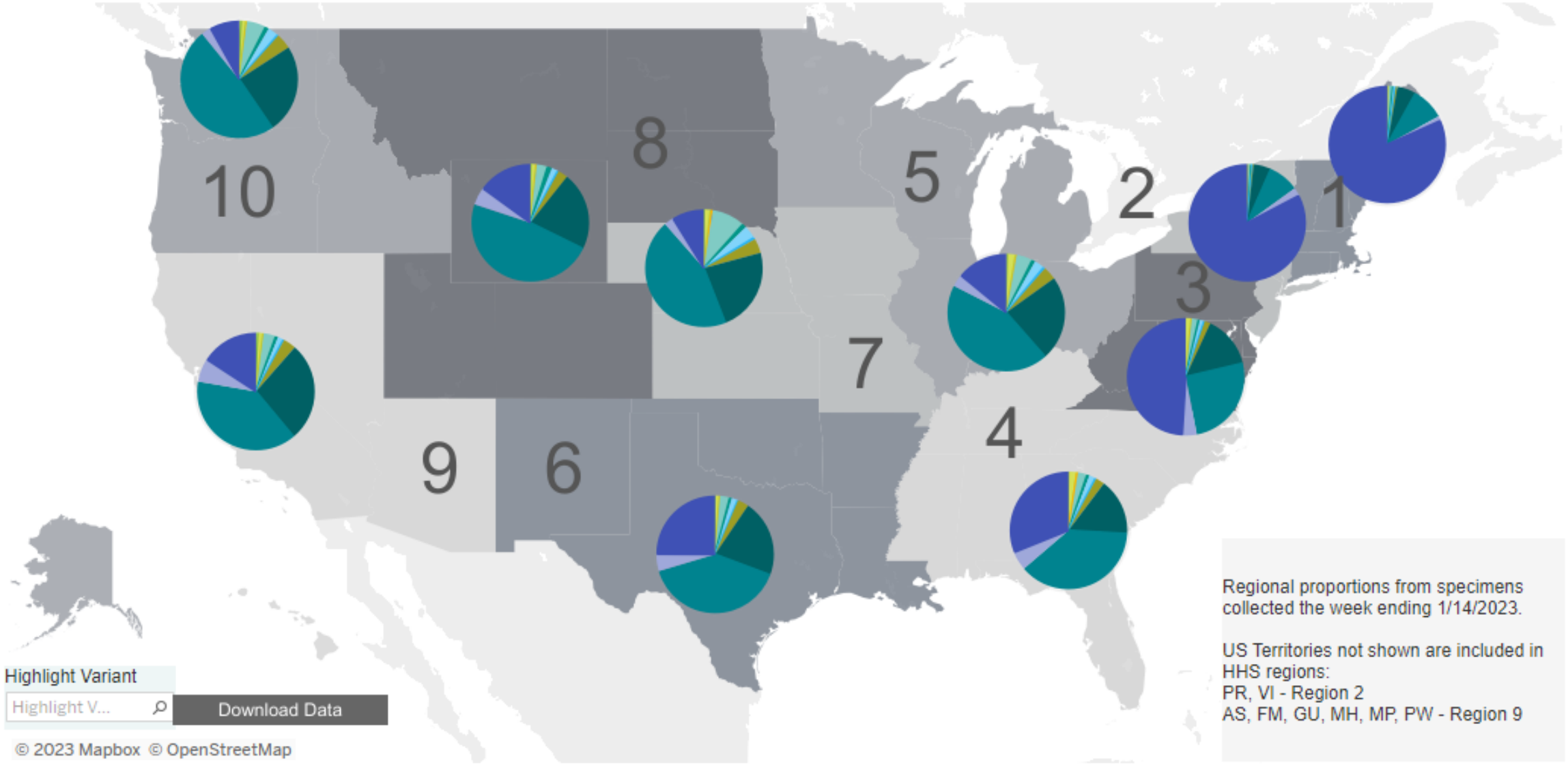
https://covid.cdc.gov/covid-data-tracker/#variant-proportions

United States: 1/8/2023 – 1/14/2023 NOWCAST



Highlight Variant

Highlight V...

Download Data

Regional proportions from specimens collected the week ending 1/14/2023.

US Territories not shown are included in HHS regions:
PR, VI - Region 2
AS, FM, GU, MH, MP, PW - Region 9

Lineages called using pangolin v4.1.3, pangolin-data v1.17 and usher v.0.5.4.

Updated January 13, 2023

The COVID-19 Treatment Guidelines Panel's Statement on Tixagevimab Plus Cilgavimab (Evusheld) as Pre-Exposure Prophylaxis of COVID-19 Last Updated: January 10, 2023

The prevalence of SARS-CoV-2 Omicron subvariants likely to be resistant to tixagevimab plus cilgavimab (Evusheld) has been rapidly increasing in the United States.

- These subvariants are BA.2.75.2, BA.4.6, BA.5.2.6, BF.7, BF.11, BQ.1, BQ.1.1, and XBB.1
- In addition, the XBB.1.5 subvariant is not anticipated to be neutralized by tixagevimab plus cilgavimab
- As of January 6, 2023, the overall prevalence of these Omicron subvariants is estimated to be more than 91%.

Tixagevimab plus cilgavimab is authorized by the Food and Drug Administration (FDA) for preexposure prophylaxis (PrEP) of COVID-19

- In people who are not expected to mount an adequate immune response to COVID-19 vaccination or people with contraindications for COVID-19 vaccination.

Due to the high prevalence of resistant Omicron subvariants in the United States, tixagevimab plus cilgavimab is unlikely to be effective at preventing COVID-19 in the vast majority of individuals, although it is still authorized by the FDA for COVID-19 PrEP.

- However, given the lack of alternative PrEP options, clinicians could still administer tixagevimab plus cilgavimab after considering an individual patient's risks and the regional prevalence of the resistant subvariants.

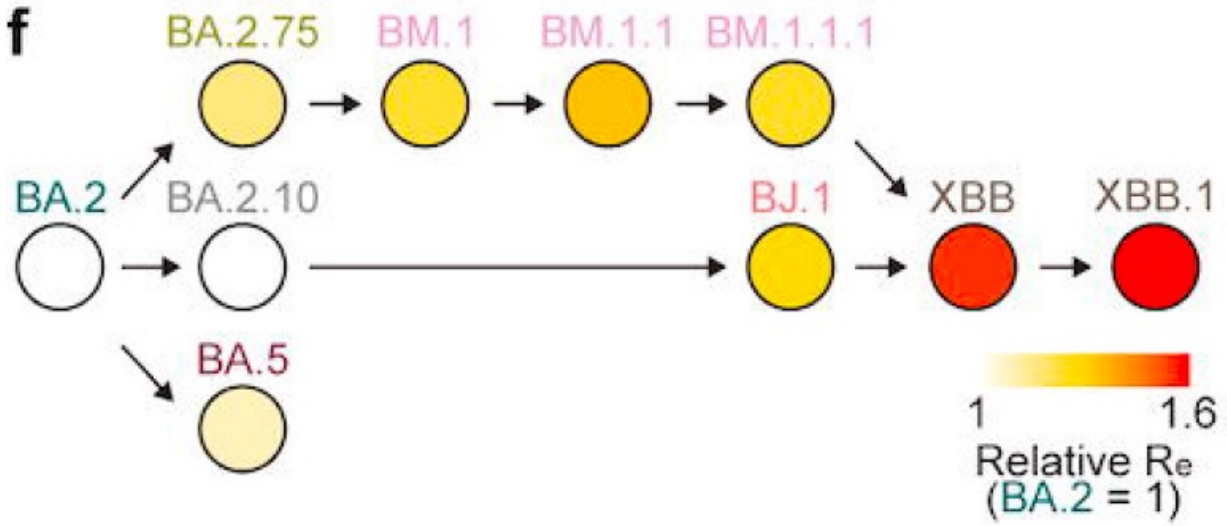
Regardless of their use of tixagevimab plus cilgavimab, it is crucial that these high-risk patients:

- Keep up to date with COVID-19 vaccination and boosters, unless contraindicated.
- Take precautions to avoid infection. • Be tested for SARS-CoV-2 if they experience signs and symptoms consistent with COVID-19 and, if infected, promptly seek medical attention.

https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-evusheld/

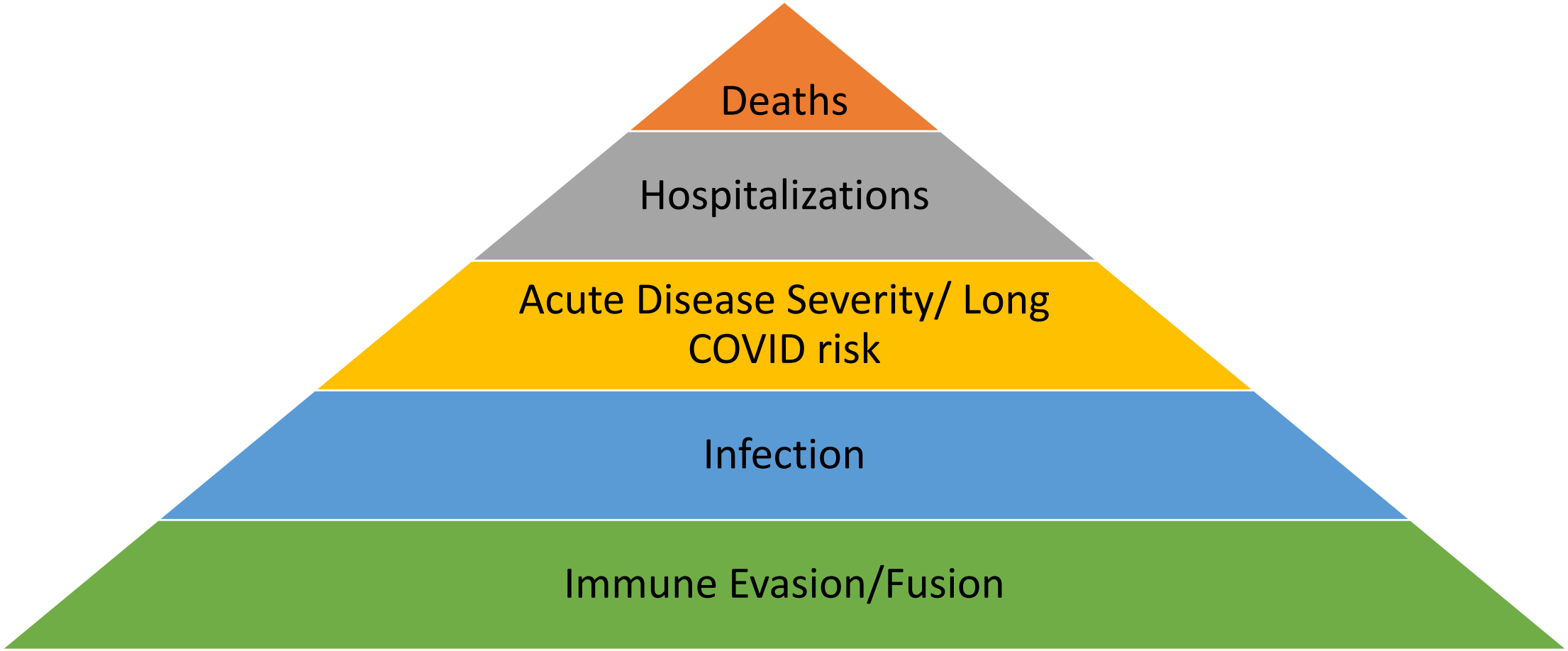
Virological characteristics of the SARS-C 1 oV-2 XBB variant derived from 2 recombination of two Omicron subvariants

- Phylogenetic analysis suggests that Omicron subvariant XBB emerged
  - During the summer of 2022 around India
  - Recombination of two co-circulating BA.2 lineages, BJ.1 and BM.1.1.1 (a progeny of BA.2.75)
- **XBB is the resistant variant to BA.2.75 breakthrough infection sera and is more fusogenic than BA.2.75.**
  - The recombination is located in the RBD of the spike protein
- The intrinsic pathogenicity of XBB in hamsters is comparable to or even lower than that of BA.2.75.
- **This is the first documented SARS-CoV-2 variant increasing its fitness through recombination rather than single mutations.**

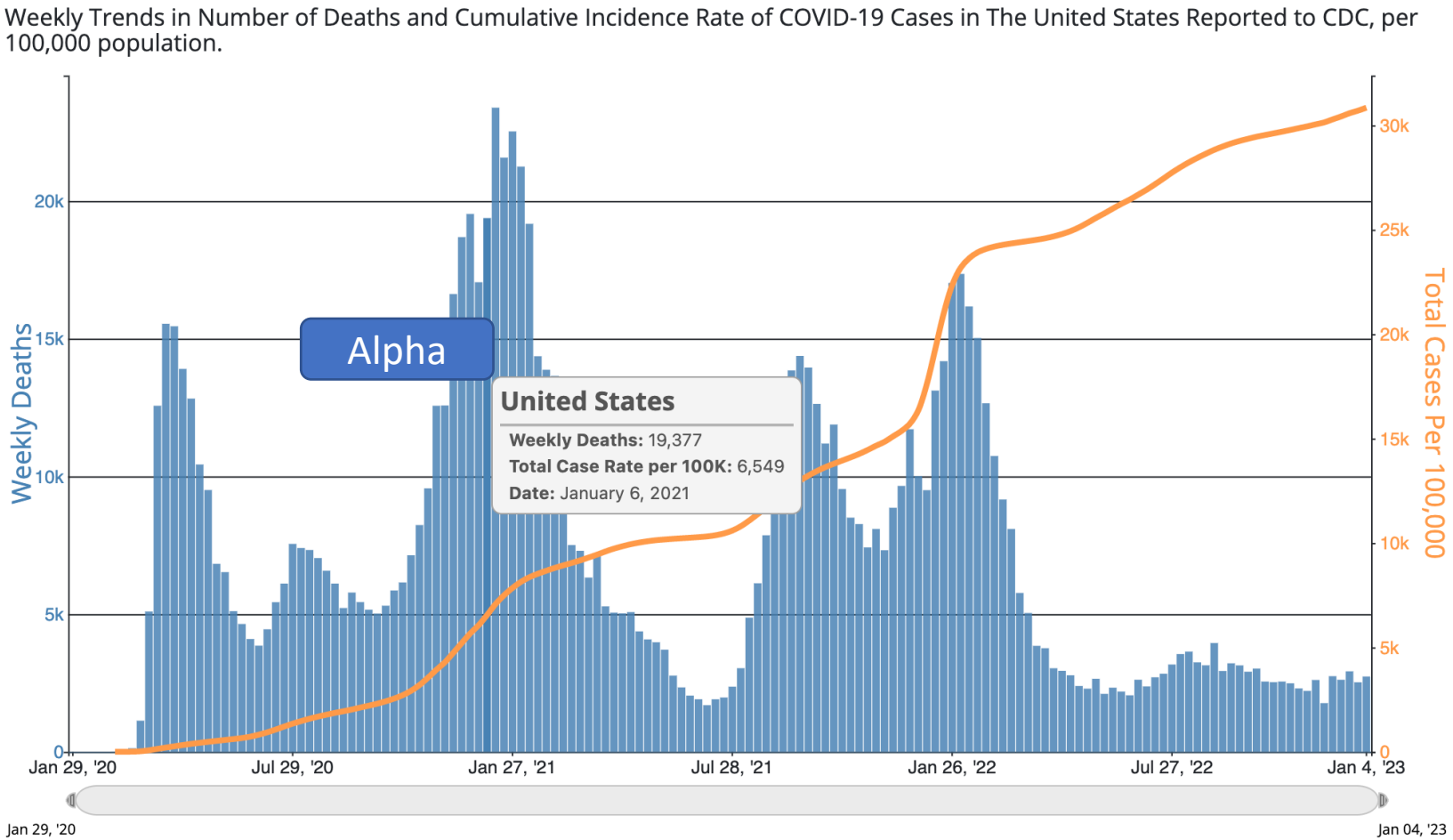


Preprint: bioRxiv preprint doi: https://doi.org/10.1101/2022.12.27.521986; this version posted December 27, 2022.

SARS-CoV-2 Variants: Impact Measurements



Trends in Number of COVID-19 Cases and Deaths in the US Reported to CDC



https://covid.cdc.gov/covid-data-tracker/#trends_weeklydeaths_totalcasesper100k_00

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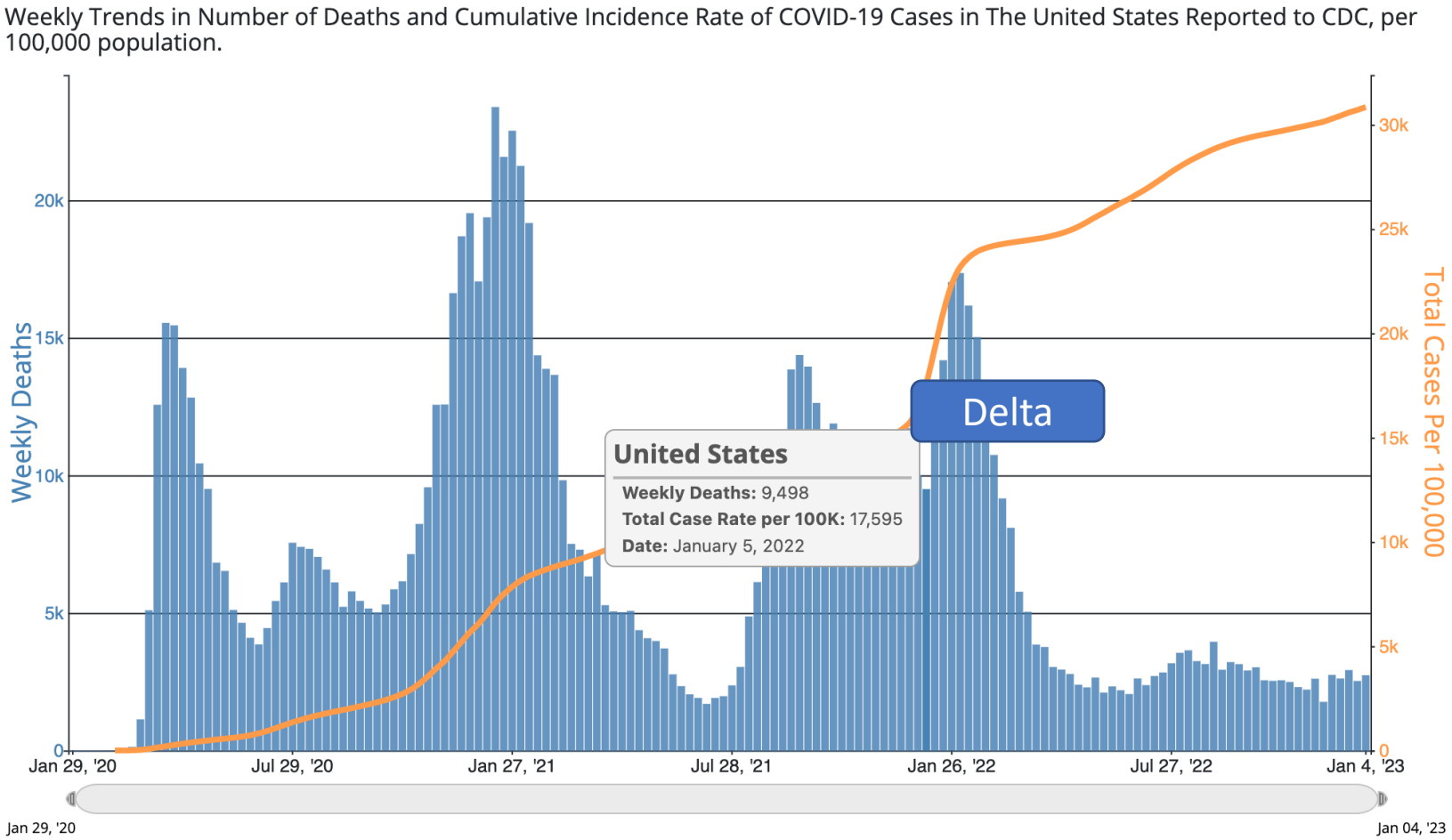

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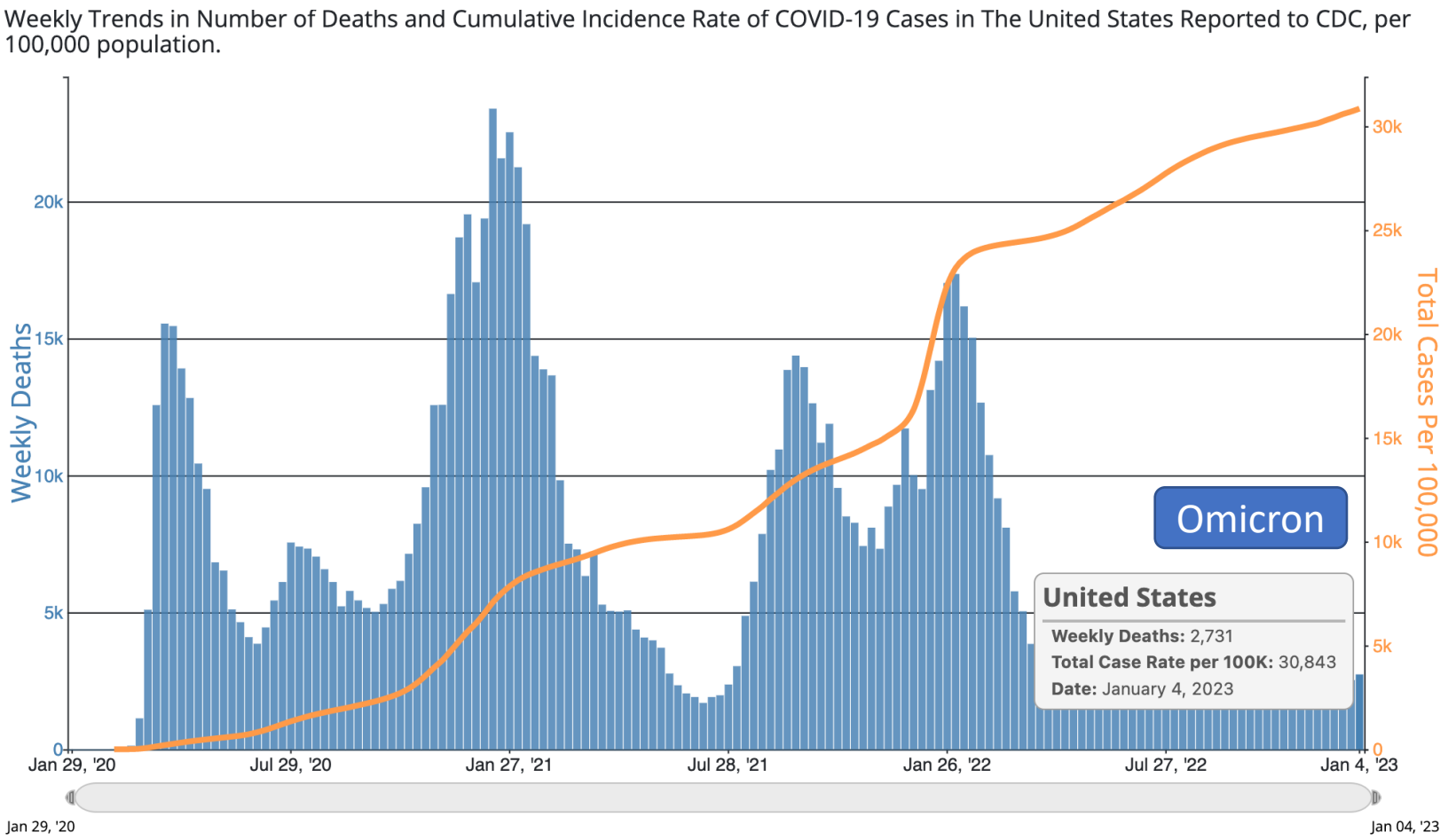

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Other Updates: Post-COVID, Vaccines, Steroids

Canine real-time detection of SARS-CoV- 2infections in the context of a mass screening event

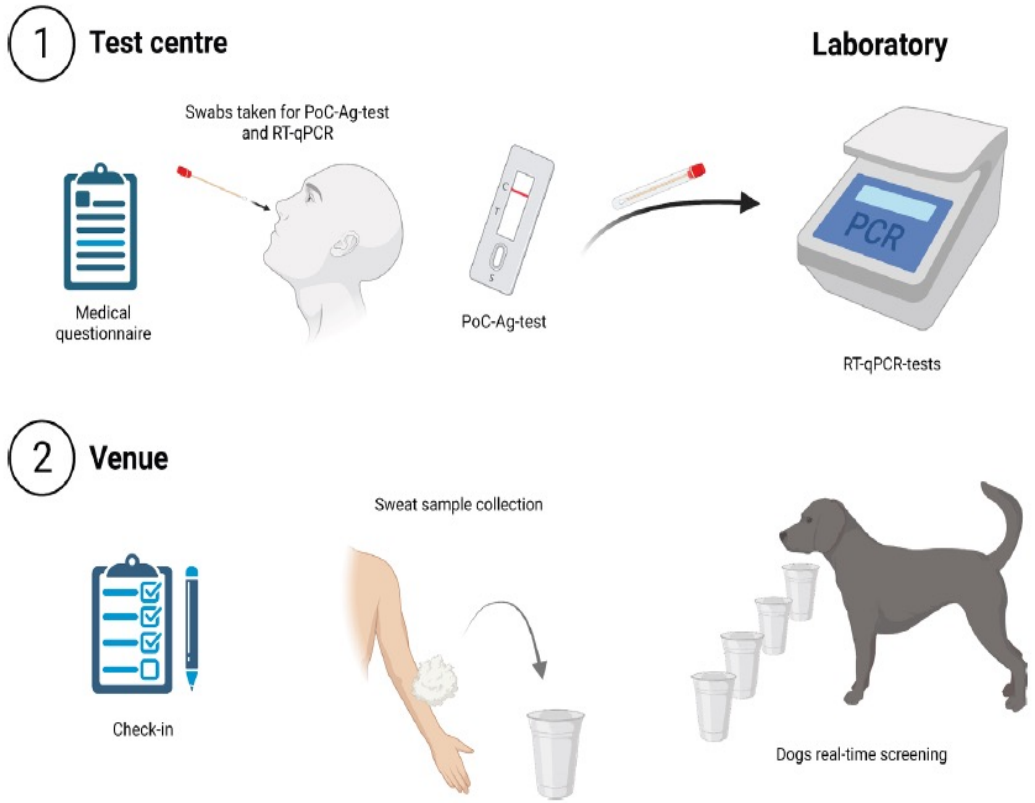

Figure 1 Schematic representation for test procedure (created with BioRender.com). PoC, point of care.

Four public concerts (Sep/Oct 2021)

- Included 2802 participants

Inclusion criteria:

- Book free, personalized tickets, be at least 18 years old
- At the day of study, attend the same certified COVID-19 test center were SARS-CoV- 2 PoC-antigen test and an RT-qPCR test.
  - If PoC-antigen positive could not concert area, but two sweat samples obtained and sent to the venue

Survey given to all participants to obtain:

- Demographics, vaccination status, previous COVID-19 infection, comorbidities, presence of Long Covid, Medications etc.

In general, a dog needed only one to two seconds to sniff one sample in a line-up.

- The search of a line-up with 40 samples took a dog about 40–60s.
- Including sample collection, line-up loading and unloading, it took approximately 3 min to perform a line-up with 40 sample

ten Hagen NA, Twele F, Meller S, et al. BMJ Global Health 2022;7:e010276. doi:10.1136/bmjgh-2022-010276

Results and Conclusions

Dogs achieved a sensitivity of **81.58%** (95% CI 66.58% to 90.78%)

Dogs achieved a specificity of **99.93%** (95% CI 99.74% to 99.99%)

- During the presentation of samples from the 2802 participants, dogs had two false positive indications and the PoC-antigen test was false positive for one participant, respectively.

Rate of diagnostic concordant results of SARS-CoV-2 detection dogs was 99.68%.

At a low prevalence of 0.2%, the canine test would achieve a PPV of 70.02% and an NPV of 99.96%.

- Higher than a POC antigen test (PPV of 5.07% and a NPV of 99.96%).
- This would result in 94.93% of positive test results being false positive, whereas the canine test would only produce 29.98%

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Trained scent detection dogs are able to discriminate samples from SARS-CoV-2 infected individuals to samples from SARS-CoV-2 negative individuals using different body fluids as well as to samples from other viral infections.

WHAT THIS STUDY ADDS

⇒ SARS-CoV-2 scent detection dogs achieved high diagnostic accuracies in a real-life scenario and demonstrated their feasibility as a diagnostic tool for screening at public events.

⇒ The dogs' performance was not affected by the participants' vaccination status, disease and medication history, and previous SARS-CoV-2 infection.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Medical scent detection dogs can become an affordable rapid diagnostic tool in addition to the use of point of care-antigen and PCR-based tests.

⇒ At public events where high-throughput screening is required, SARS-CoV-2 detection dogs can provide a rapid and reliable screening option.

"The use of medical scent detection dogs can become an affordable rapid diagnostic tool in addition to the use of PoC-antigen and PCR-based tests. Especially in areas or countries, which lack test infrastructure or limited financial means, medical scent detection dogs provide an additional opportunity to control the ongoing COVID-19 and possibly future pandemics."

ten Hagen NA, Twele F, Meller S, et al. BMJ Global Health 2022;7:e010276. doi:10.1136/bmjgh-2022-010276

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Therapeutic Management of Nonhospitalized Adults With Mild to Moderate COVID-19 Who Do Not Require Supplemental Oxygen

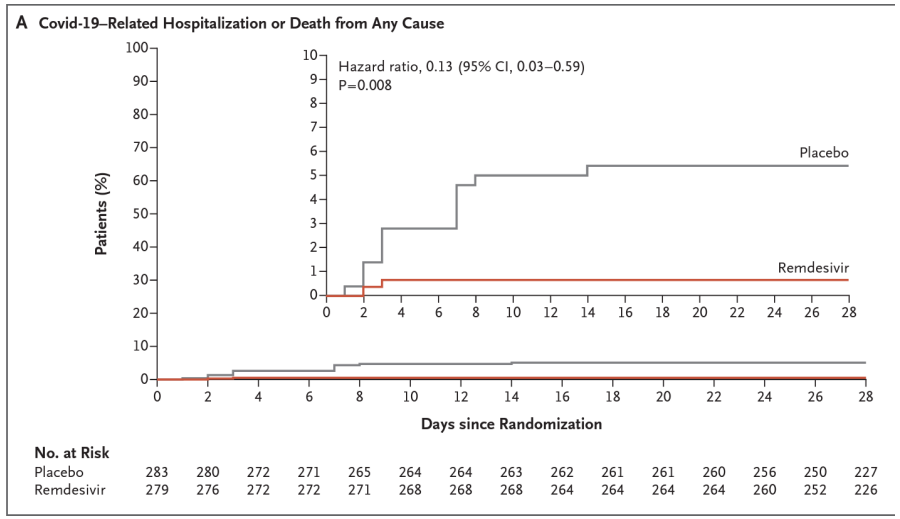
Patient Disposition	Panel's Recommendations
All Patients	• All patients should be offered symptom management **(AIII)**. • The Panel recommends against the use of **dexamethasone**[a] or **other systemic corticosteroids** in the absence of another indication **(AIIb)**.
Patients Who Are at High Risk of Progressing to Severe COVID-19[b]	*Preferred therapies. Listed in order of preference:* • **Ritonavir-boosted nirmatrelvir (Paxlovid)**[c,d] **(AIIa)** • **Remdesivir**[d,e] **(BIIa)** *Alternative therapy. For use when the preferred therapies are not available, feasible to use, or clinically appropriate:* • **Molnupiravir**[d,f,g] **(CIIa)**
Each recommendation in the Guidelines receives 2 ratings that reflect the strength of the recommendation and the quality of the evidence that supports it. See Guidelines Development for more information.	

COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed 01/07/2023.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 27, 2022 VOL. 386 NO. 4

Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients



Oral Remdesivir Analogues

Several oral analogues of remdesivir have been developed

- GS-621763
- ATV006
- VV116

VV116 is a deuterated remdesivir hydrobromide with:

- Oral bioavailability
- Potent activity against SARS-CoV-2 in studies in animals
- Satisfactory safety and side-effect profiles in phase 1 trials.

VV116 versus Nirmatrelvir–Ritonavir for Oral Treatment of Covid-19: METHODS

Design

- **Phase 3, noninferiority, observer-blinded, randomized**
- Outbreak caused by the B.1.1.529 (omicron) variant
- **Symptomatic adults with mild-to-moderate Covid-19 with a high risk of progression**
- Assigned to receive a 5-day course of either VV116 or nirmatrelvir–ritonavir.

The primary end point was:

- **Time to sustained clinical recovery through day 28.**
- Sustained clinical recovery was defined as the alleviation of all Covid-19–related target symptoms for 2 consecutive days.

NEJM.org. December 28, 2022, DOI: 10.1056/NEJMoa2208822

VV116 versus Nirmatrelvir–Ritonavir for Oral Treatment of Covid-19: RESULTS

- Shown are participants who underwent randomization and received at least one dose of VV116 or nirmatrelvir–ritonavir.
- Participants were grouped according to treatment assignment. Percentages may not total 100 because of rounding.
- Covid-19 denotes coronavirus disease 2019, IQR interquartile range, RT-PCR reverse-transcriptase–polymerase chain reaction, and SARS-CoV-2 severe acute respiratory syndromeccoronavirus 2.
- † Ethnic group was reported by the participant.
- ‡ Symptom scores range from 0 to 3 (with higher scores indicating greater severity) for each of 11 symptoms; total symptom scores range from 0 to 33.
- § Obesity was defined as a body-mass index of 25 or higher in accordance with World Health Organization (WHO) criteria for adult Asians.
- ¶ Data were available for 291 participants in the VV116 group and 307 participants in the nirmatrelvir–ritonavir group.

NEJM.org. December 28, 2022, DOI: 10.1056/NEJMoa2208822

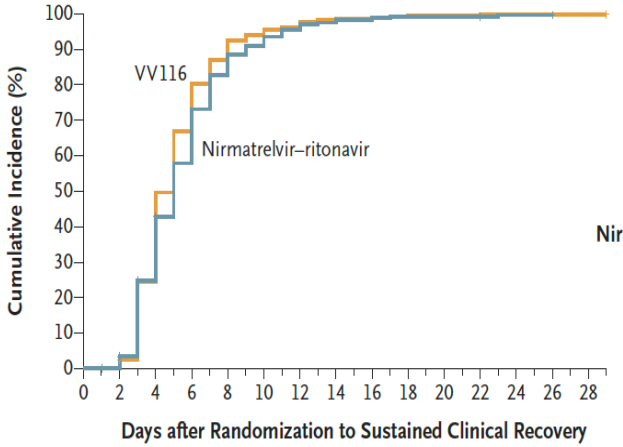
Table 1. Demographic and Clinical Characteristics of the Full Analysis Population.*

Characteristic	VV116 (N=384)	Nirmatrelvir–Ritonavir (N=387)	Total (N=771)
Median age at randomization (range) — yr	53.0 (18–94)	53.0 (18–91)	53.0 (18–94
Sex — no. (%)			
Male	185 (48.2)	199 (51.4)	384 (49.8)
Female	199 (51.8)	188 (48.6)	387 (50.2)
Ethnic group — no. (%)†			
Han	384 (100)	385 (99.5)	769 (99.7)
Other	0	2 (0.5)	2 (0.3)
Vaccination status — no. (%)			
Unvaccinated	94 (24.5)	93 (24.0)	187 (24.3)
Standard course	117 (30.5)	121 (31.3)	238 (30.9)
Boosted course	173 (45.1)	173 (44.7)	346 (44.9)
Covid-19 severity — no. (%)			
Mild	355 (92.4)	355 (91.7)	710 (92.1)
Moderate	29 (7.6)	32 (8.3)	61 (7.9)
Covid-19–related symptoms			
Median time from onset of first symptom to first dose (IQR) — days	4 (3–5)	4 (3–5)	4 (3–5)
Median total score for Covid-19–related target symptoms (IQR) — points‡	3.0 (3.0–5.0)	3.0 (2.0–5.0)	3.0 (2.0–5.0
Risk factors for severe illness from Covid-19 — no. (%)			
Age of ≥60 yr	144 (37.5)	147 (38.0)	291 (37.7)
Cardiovascular disease, including hypertension	129 (33.6)	142 (36.7)	271 (35.1)
Obesity§	124 (32.3)	130 (33.6)	254 (32.9)
Current smoking	46 (12.0)	50 (12.9)	96 (12.5)
Diabetes mellitus	35 (9.1)	43 (11.1)	78 (10.1)
Chronic lung disease	21 (5.5)	23 (5.9)	44 (5.7)
Active cancer	15 (3.9)	17 (4.4)	32 (4.2)
Chronic kidney disease	2 (0.5)	9 (2.3)	11 (1.4)
Immunosuppressive disease or use of immunosuppressive treatment	0	1 (0.3)	1 (0.1)
Virology			
Median time from first RT-PCR confirmation of SARS-CoV-2 to first dose (IQR) — days	4 (3–5)	4 (3–5)	4 (3–5)
Median SARS-CoV-2 RNA cycle-threshold value from naso-pharyngeal swab (IQR)¶	21.5 (18.5–25.6)	21.9 (18.9–26.1)	21.7 (18.6–25

VV116 versus Nirmatrelvir–Ritonavir for Oral Treatment of Covid-19: RESULTS

- **822 participants underwent randomization**
  - 771 received VV116 (384 participants) or nirmatrelvir–ritonavir (387 participants).
- The noninferiority of VV116 to nirmatrelvir–ritonavir with respect to the time to sustained clinical recovery was established
  - In the primary analysis (hazard ratio, 1.17; 95% confidence interval [CI], 1.01 to 1.35) and was maintained in the final analysis (median, 4 days with VV116 and 5 days with nirmatrelvir–ritonavir; hazard ratio, 1.17; 95% CI, 1.02 to 1.36).
- **Time to a first negative SARS-CoV-2 test did not differ** substantially between the two groups.
- No participants in either group had died or had had progression to severe Covid-19 by day 28.
- **The incidence of adverse events was lower in the VV116 group** than in the nirmatrelvir–ritonavir group (67.4% vs. 77.3%)

Sustained Clinical Recovery, Per Protocol Population



	No. of Participants	No. of Events (%)	25th Percentile (95% CI)	Median
			days	*days*
VV116	371	366 (98.7)	4.0 (3.0–4.0)	5.0
Nirmatrelvir–Ritonavir	358	352 (98.3)	4.0 (3.0–4.0)	5.0

Hazard ratio, 1.17 (95% CI, 1.01–1.35)

No. at Risk																
VV116	371	371	277	122	48	22	14	6	5	3	2	2	1	1	1	1
Nirmatrelvir–ritonavir	358	357	267	149	61	32	16	9	6	3	3	3	1	1	0	0

NEJM.org. December 28, 2022, DOI: 10.1056/NEJMoa2208822

Nirmatrelvir Plus Ritonavir for Early COVID-19 in a Large U.S. Health System: A Population-Based Cohort Study

Background:

- The clinical impact of nirmatrelvir plus ritonavir among vaccinated populations is uncertain.

Objective:

- To assess whether nirmatrelvir plus ritonavir reduces risk for hospitalization or death among outpatients with early COVID-19 in the setting of prevalent SARS-CoV-2 immunity and immune-evasive SARS-CoV-2 lineages.

Design:

- Population-based cohort study analyzed to emulate a clinical trial.

Setting:

- Health care system (1.5 million patients) in Massachusetts and New Hampshire during the Omicron wave (1 January to 17 July 2022).

Patients:

- 44,551 nonhospitalized adults (90.3% with ≥3 vaccine doses) aged 50 years or older with COVID-19 and no contraindications for nirmatrelvir plus ritonavir.

Measurements:

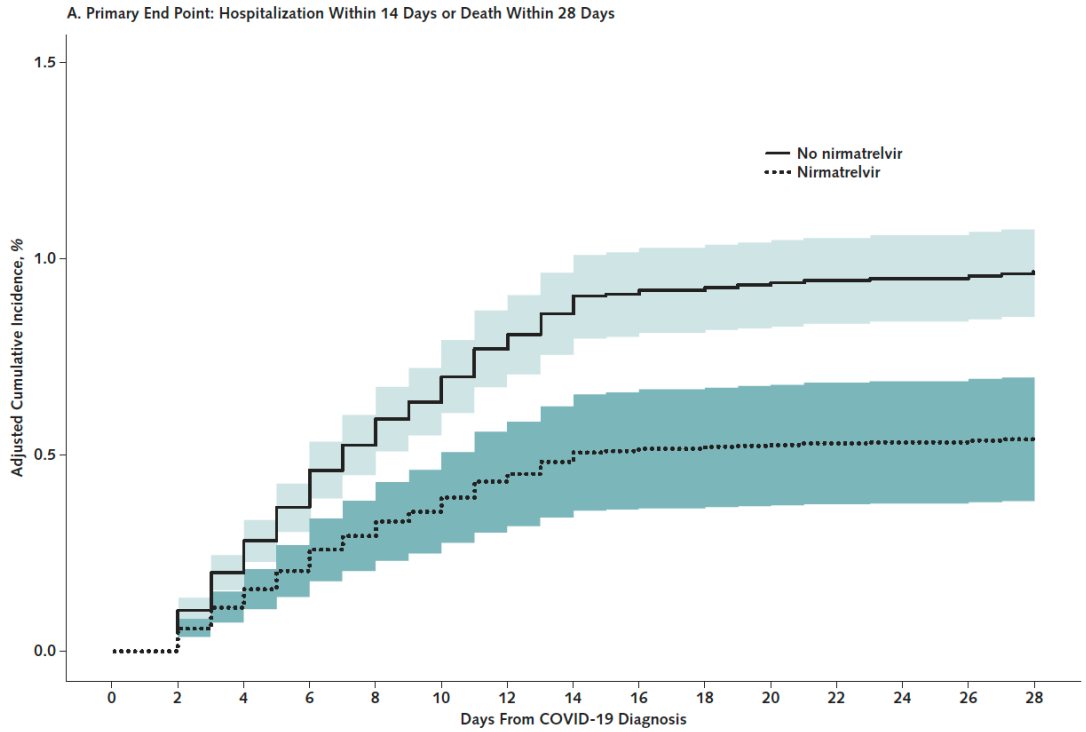
- The primary outcome was a composite of hospitalization within 14 days or death within 28 days of a COVID-19 diagnosis.

Published at Annals.org on 13 December 2022. doi:10.7326/M22-2141

Nirmatrelvir Plus Ritonavir for Early COVID-19 in a Large U.S. Health System: A Population-Based Cohort Study

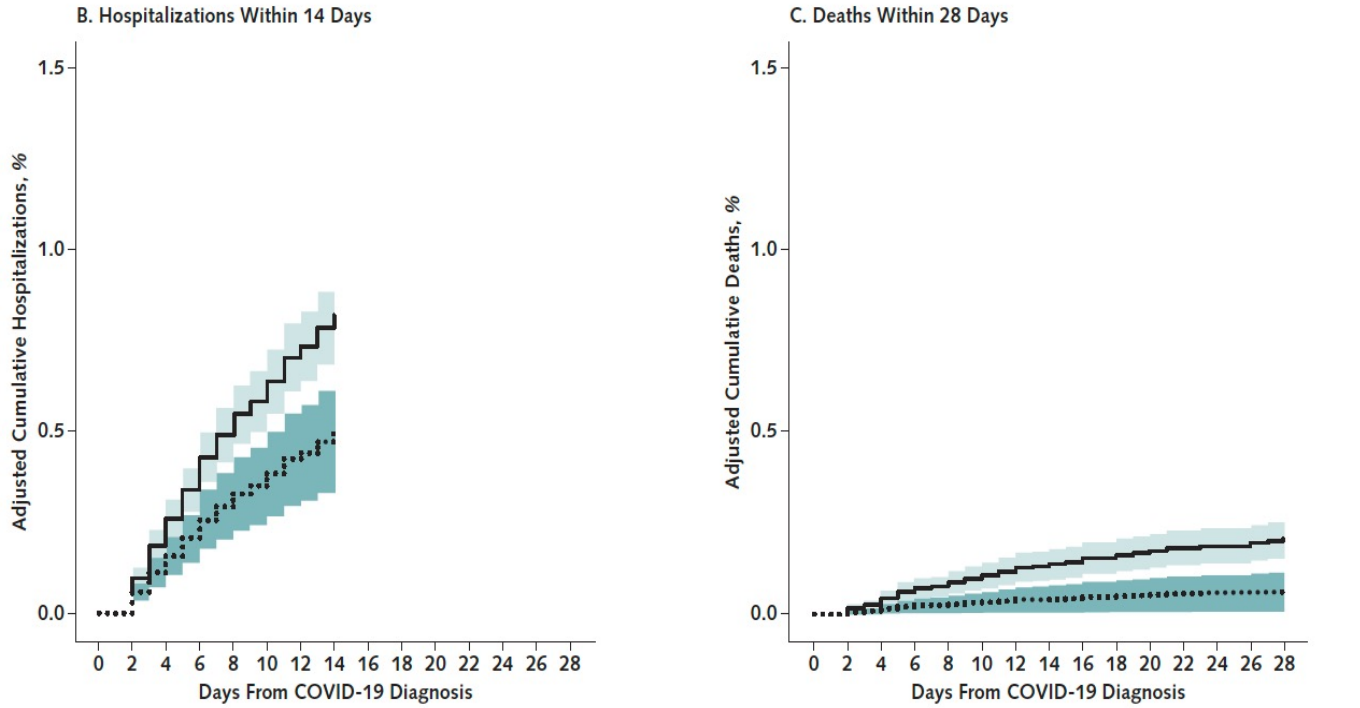
Results:

- During the study period **12,541 (28.1%)** patients were prescribed nirmatrelvir plus ritonavir, and **32 010 (71.9%)** were not.
- Patients prescribed nirmatrelvir plus ritonavir were more likely to be older, have more comorbidities, and be vaccinated.
- **The composite outcome of hospitalization or death occurred in**
  - 69 (0.55%) patients who were prescribed Nirmatrelvir plus ritonavir and
  - 310 (0.97%) who were not (adjusted risk ratio, 0.56 [95% CI, 0.42 to 0.75]).
- **Recipients of Nirmatrelvir plus ritonavir had lower risk for**
  - Hospitalization (adjusted risk ratio, 0.60 [CI, 0.44 to 0.81]) and
  - Death (adjusted risk ratio, 0.29 [CI, 0.12 to 0.71])



Published at Annals.org on 13 December 2022. doi:10.7326/M22-2141

Nirmatrelvir Plus Ritonavir for Early COVID-19 in a Large U.S. Health System: A Population-Based Cohort Study



Patients with hospitalization or death on the day of diagnosis or the next calendar day are not considered outpatients and were excluded. The primary end point (hospitalization within 14 days or death within 28 days of diagnosis) is shown in panel A. Hospitalization (*B*) and death (*C*) are secondary end points.

The overall risk for hospitalization or death was already low (1%) after an outpatient diagnosis of COVID-19, but nirmatrelvir plus ritonavir reduced this risk further.

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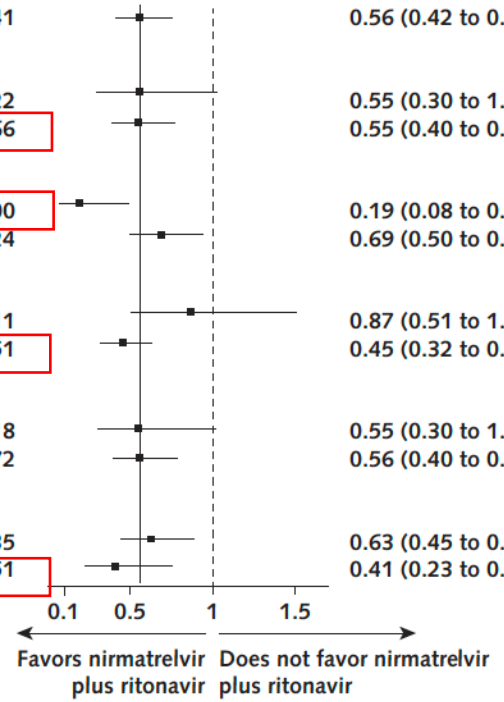
Subgroup analysis comparing cumulative incidence of hospitalization or death among patients who were prescribed nirmatrelvir plus ritonavir and those who were not.

Subgroup	Nirmatrelvir Plus Ritonavir	No Nirmatrelvir Plus Ritonavir	Hospitalization or Death, %		Risk Difference, %	Relative Risk (95% CI)
			Nirmatrelvir Plus Ritonavir	No Nirmatrelvir Plus Ritonavir		
All	12 541	32 010	0.52	0.93	−0.41	0.56 (0.42 to 0.75)
Age						
50–64y	5885	18 931	0.27	0.49	−0.22	0.55 (0.30 to 1.03)
≥65 y	6656	13 079	0.82	1.48	−0.66	0.55 (0.40 to 0.77)
Vaccination status						
Not fully vaccinated	682	3633	0.48	2.48	−2.00	0.19 (0.08 to 0.49)
Vaccinated	11 859	28 377	0.53	0.77	−0.24	0.69 (0.50 to 0.94)
Vaccination timing						
Last vaccine <20 wk prior	2621	10 517	0.79	0.91	−0.11	0.87 (0.51 to 1.50)
Last vaccine >20 wk prior	9920	21 493	0.43	0.94	−0.51	0.45 (0.32 to 0.64)
Monoclonal Antibody Screening Score						
≤3	6608	18 944	0.23	0.41	−0.18	0.55 (0.30 to 1.02)
≥4	5933	13 066	0.92	1.63	−0.72	0.56 (0.40 to 0.78)
Obesity status						
No obesity (BMI <30 kg/m^2)	8368	21 215	0.60	0.96	−0.35	0.63 (0.45 to 0.89)
Obesity (BMI ≥30 kg/m^2)	4173	10 795	0.36	0.88	−0.51	0.41 (0.23 to 0.75)



Estimates, risk differences, and CIs were calculated with an inverse probability–weighted model performed within each stratum. BMI = body mass index.

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Nirmatrelvir Plus Ritonavir for Early COVID-19 in a Large U.S. Health System: A Population-Based Cohort Study

Limitation:

- Potential residual confounding due to differential access to COVID-19 vaccines, diagnostic tests, and treatment.

Conclusion:

- The overall risk for hospitalization or death was already low (1%) after an outpatient diagnosis of COVID-19, but nirmatrelvir plus ritonavir reduced this risk further.

Primary Funding Source:

- National Institutes of Health.

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Molnupiravir plus usual care versus usual care alone as early treatment for adults with COVID-19 at increased risk of adverse outcomes (PANORAMIC): an open-label, platform-adaptive randomized controlled trial

Background

- The safety, effectiveness, and cost-effectiveness of molnupiravir, has not been established in vaccinated patients at increased risk of COVID-19 morbidity and mortality

AIMS:

- To establish whether the addition of molnupiravir to usual care reduced hospital admissions and deaths associated with COVID-19 in this population.

Methods (UK-based, national, multicenter, open-label, multigroup, prospective, RCT)

- **Eligible participants were:**
  - Aged 50 years or older—or aged 18 years or older with comorbidities, symptomatic with confirmed COVID-19 for 5 days or fewer in the community**.**
- **Participants were randomly assigned:**
  - (1:1) to receive 800 mg molnupiravir twice daily for 5 days plus usual care or usual care only.
  - Randomization, was stratified by age (<50 years *vs* ≥50 years) and vaccination status (yes *vs* no).
- **The primary outcome was all-cause hospitalization or death within 28 days of randomization**
  - Other COVID-19 outcomes were tracked via a self-completed online daily diary for 28 days after randomization.

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Molnupiravir plus usual care versus usual care alone as early treatment for adults with COVID-19 at increased risk of adverse outcomes (PANORAMIC): an open-label, platform-adaptive randomized controlled trial

Findings

- **Between 12/21- 4/22, 26 411 participants were randomly assigned**
  - 12 821 to molnupiravir plus usual care (12 529 included in the analysis)
  - 12 962 to usual care alone (12 529 included in the analysis)
  - 628 to other treatment groups (which will be reported separately)
  - The mean age was 56·6 years and (94%) had had at least three doses of a SARS-CoV-2 vaccine
- **Hospitalizations or deaths were recorded in:**
  - *105 (1%) of 12 529* participants in the molnupiravir plus usual care group versus
  - *98 (1%) of 12 525* in the usual care group (aOR 1·06)
- **Serious adverse events were recorded for:**
  - 50/12,774 (0·4%) in the molnupiravir plus usual care group and for (None judged to be related to molnupiravir)
  - 45/12,934 (0·3%) in the usual care group

Interpretation

- **Molnupiravir did not reduce the frequency of COVID-19-associated hospitalizations or death among high-risk vaccinated adults in the community.**

Thelancet.com Published online December 22, 2022 https://doi.org/10.1016/S0140-6736(22)02597-1

Outline

USA COVID-19 stats and variants update

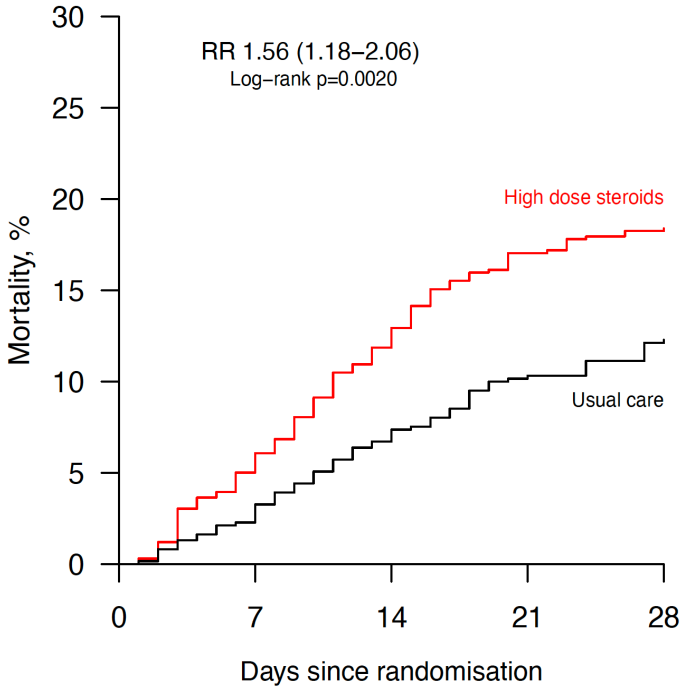
COVID-19 Screening

Antiviral treatment update

Other Updates: Post-COVID, Vaccines, Steroids

Higher dose corticosteroids in hospitalised COVID-19patients with hypoxia but not requiring ventilatory support (RECOVERY): a randomised, controlled,open-label, platform trial

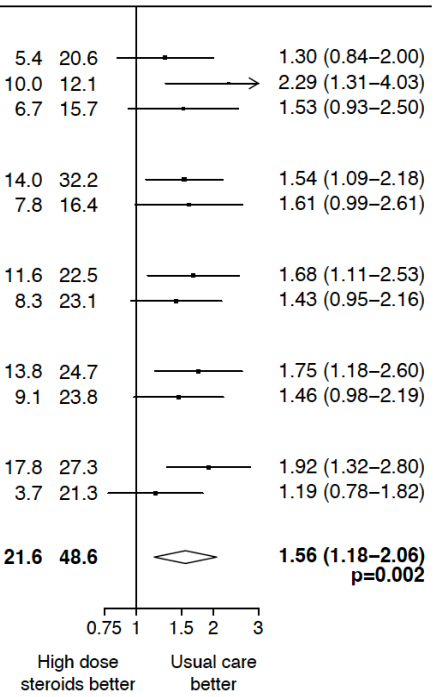
Effect of allocation to high dose steroids vs usual care on 28–daymortality in patients receiving no oxygen or simple oxygen only



Number at risk					
High dose steroids	659	617	572	545	536
Usual care	613	590	565	547	535

Effect of allocation to high dose steroids vs usual care on 28–day mortality n patients receiving no oxygen or simple oxygen only, by other baseline characteristics

	High dose steroids	Usual care	O–E	V	RR (95% CI)
Age, years (χ^2_1= 0.3; p=0.56)					
<70	48/426 (11%)	35/395 (9%)	5.4	20.6	1.30 (0.84–2.00)
≥70 <80	34/128 (27%)	15/123 (12%)	10.0	12.1	2.29 (1.31–4.03)
≥80	39/105 (37%)	25/95 (26%)	6.7	15.7	1.53 (0.93–2.50)
Sex (χ^2_1= 0.0; p=0.89)					
Men	79/393 (20%)	51/376 (14%)	14.0	32.2	1.54 (1.09–2.18)
Women	42/266 (16%)	24/236 (10%)	7.8	16.4	1.61 (0.99–2.61)
Ethnicity (χ^2_1=0.3; p=0.60)					
White	56/227 (25%)	35/226 (15%)	11.6	22.5	1.68 (1.11–2.53)
Black, Asian and Minority Ethnic	56/371 (15%)	37/340 (11%)	8.3	23.1	1.43 (0.95–2.16)
Country (χ^2_1= 0.4; p=0.53)					
UK	61/249 (24%)	39/263 (15%)	13.8	24.7	1.75 (1.18–2.60)
Other countries	60/410 (15%)	36/350 (10%)	9.1	23.8	1.46 (0.98–2.19)
Days since symptom onset (χ^2_1= 2.7; p=0.10)					
≤7	74/384 (19%)	36/346 (10%)	17.8	27.3	1.92 (1.32–2.80)
>7	47/275 (17%)	39/267 (15%)	3.7	21.3	1.19 (0.78–1.82)
All participants	**121/659 (18%)**	**75/613 (12%)**	**21.6**	**48.6**	**1.56 (1.18–2.06) p=0.002**



Preprint. medRxiv preprint doi: https://doi.org/10.1101/2022.12.16.22283578; this version posted December 17, 2022.

Long-term cardiovascular outcomes of COVID-19

Objective:

- Estimate risks and 1-year burdens of a set of pre-specified incident cardiovascular outcomes

Population

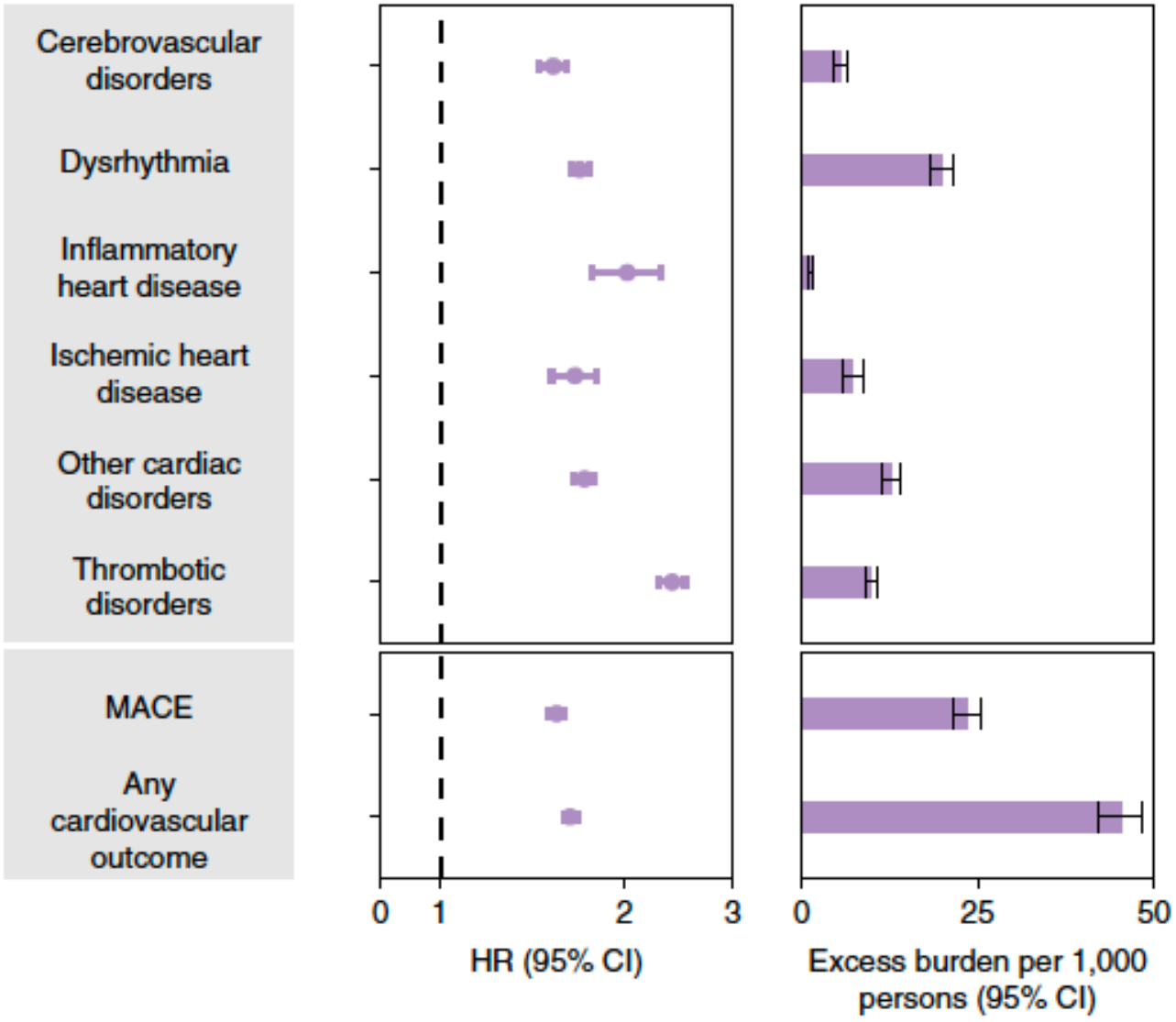
- National healthcare databases from the US Department of Veterans Affairs
- Cohort of 153,760 individuals with COVID-19,
- Control cohorts with 5,637,647 (contemporary controls)
- Control cohorts with 5,859,411 (historical controls)

Beyond the first 30 days after infection, individuals with COVID-19 are at increased risk of incident cardiovascular disease

- Cerebrovascular disorders
- Dysrhythmias
- Ischemic and non-ischemic heart disease
- Pericarditis
- Myocarditis
- Heartfailure
- Thromboembolic disease

Nature Medicine I VOL 28 I March 2022 I 583–590 I www.nature.com/naturemedic

Risks and 12-month burdens of incident post-acute COVID-19 composite cardiovascular outcomes compared with the contemporary control cohort.



Nature Medicine | VOL 28 | March 2022 | 583–590 |
www.nature.com/naturemedic

Long-term cardiovascular outcomes of COVID-19

These risks and burdens were evident even among individuals who were not hospitalized during the acute phase of the infection

The risk increased in a graded fashion according to the care setting during the acute phase (**non-hospitalized, hospitalized and admitted to intensive care).**

These results provide evidence that the risk and 1-year burden of cardiovascular disease in survivors of acute COVID-19 are substantial.

Care pathways of those surviving the acute episode of COVID-19 should include attention to cardiovascular health and disease.

Nature Medicine I VOL 28 I March 2022 I 583–590 I www.nature.com/naturemedic

Comparative effectiveness of third doses of mRNA-based COVID-19 vaccines in US veterans

Objective:

- Compare effectiveness BNT162b2 or mRNA-1273 for a range of COVID-19

Methods

- Emulated a target trial using electronic health records of US veterans who received a third dose of either BNT162b2 or mRNA-1273 vaccines between 20 October 2021 and 8 February 2022, during a period that included Delta- and Omicron-variant waves.
- Eligible veterans had previously completed an mRNA vaccine primary series.
- Patients were matched recipients of each vaccine in a 1:1 ratio according to recorded risk factors.
- Each vaccine group included 65,196 persons.

The excess number of events over 16 weeks per 10,000 persons for BNT162b2 compared with mRNA- 1273 was:

- 45.4 (95% CI: 19.4, 84.7) for documented infection
- 3.7 (2.2, 14.1) for symptomatic COVID-19
- 10.6 (5.1, 19.7) for COVID-19 hospitalization
- 2.0 (–3.1, 6.3) for COVID-19 intensive care unit admission
- 0.2 (–2.2, 4.0) for COVID-19 death.

Between 1/1/2022 and 3/1/2022, a period with Omicron-variant predominance, the excess number of events over 9 weeks per 10,000 persons for BNT162b2 compared with mRNA-1273 was

- 63.2 (95% CI: 15.2, 100.7) for documented infection

The 16-week risks of COVID-19 outcomes were low after a third dose of mRNA-1273 or BNT162b2

- Risks were lower with mRNA-1273 than with BNT162b2, particularly for documented infection.

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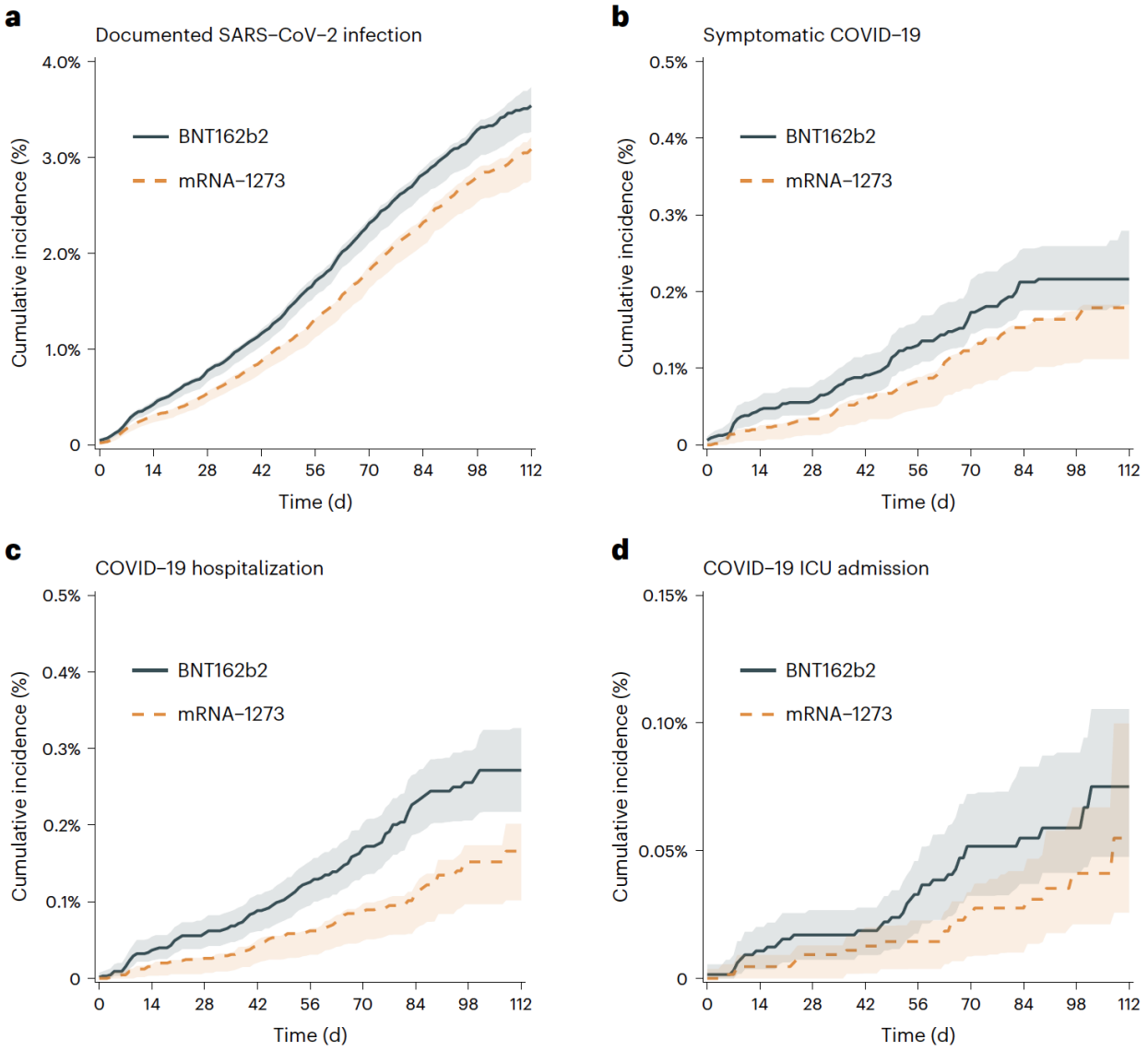
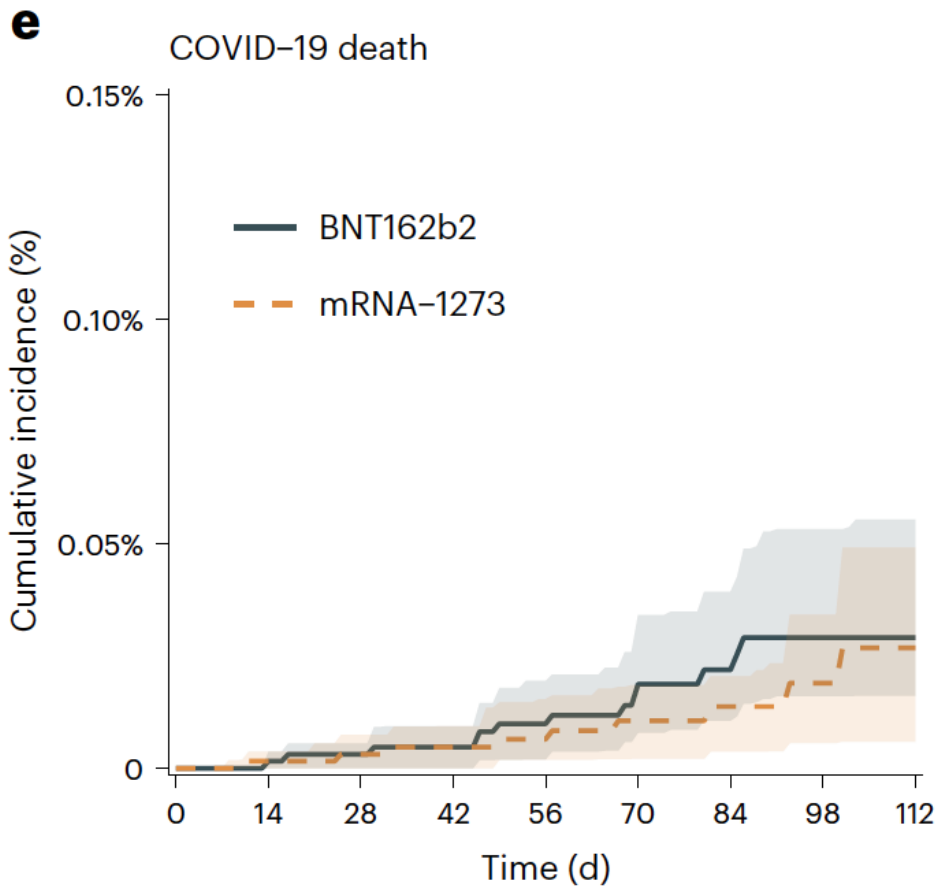
Cumulative incidence of Covid-19 outcomes during a period spanning Delta- and Omicron-variant predominance (20 October 2021 to 15 February 2022)

Documented SARS-CoV-2 infection (a), symptomatic COVID-19 (b), COVID-19 hospitalization (c), COVID-19 ICU admission (d) and COVID-19 deaths



nature microbiology
https://Article doi.org/10.1038/s41564-022-01272-z

Cumulative incidence of Covid-19 outcomes during a period spanning Delta- and Omicron-variant predominance (20 October 2021 to 15 February 2022)



- Solid blue line represents the risk curve for BNT162b2
- Dashed orange line represents the risk curve for mRNA-1273
- Shaded areas represent pointwise 95% confidence intervals.

nature microbiology
https://Article doi.org/10.1038/s41564-022-01272-z

Lessons Learned

Omicron subvariant XBB

- Evolved from recombination of two co-circulating BA.2 lineages
- It is more fit than previous variants, but clinical outcome data is still lacking
- EVUSHELD does not confer protection

Use of canines for mass COVID-19 screening could be an option

Nirmatrelvir-Ritonavir decreases mortality in individuals 50 years and older regardless of vaccination status

- The subgroups with most benefit are those who received vaccines > 20 weeks before the infection
- The unvaccinated

Experimental antiviral oral remdesivir

- Is not inferior to nirmatrelvir-ritonavir in time to symptom resolution and has less side effects

Molnupiravir did not reduce the frequency of COVID-19-associated hospitalizations or death among high-risk vaccinated adults

High dose steroids in hospitalized patients can increase mortality

Post COVID-19 Cardiovascular Complications are common beyond the first 30 days after infection

The 16-week risks of COVID-19 outcomes were low after a third dose of mRNA-1273 or BNT162b2

- Risks were lower with mRNA-1273 than with BNT162b2, particularly for documented infection.