COVID-19 Update
April 19, 2023

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Outline

COVID-19

- USA COVID-19 stats and variants update
- Treatment updates
- Vaccine updates

RSV and Influenza updates

COVID-19 USA STATS

Daily Update for the United States

Cases

New Cases (Weekly Total)

101,437

Case Trends

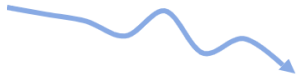
Feb 2023 Apr 2023

Deaths

New Deaths (Weekly Total)

1,327

Death Trends



Feb 2023 Apr 2023

Hospitalizations

New Admissions (Daily Avg)

1,850

Admission Trends

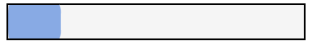
Mar 2023 Apr 2023

Vaccinations

% with Updated Booster Dose

16.7%

Total Population

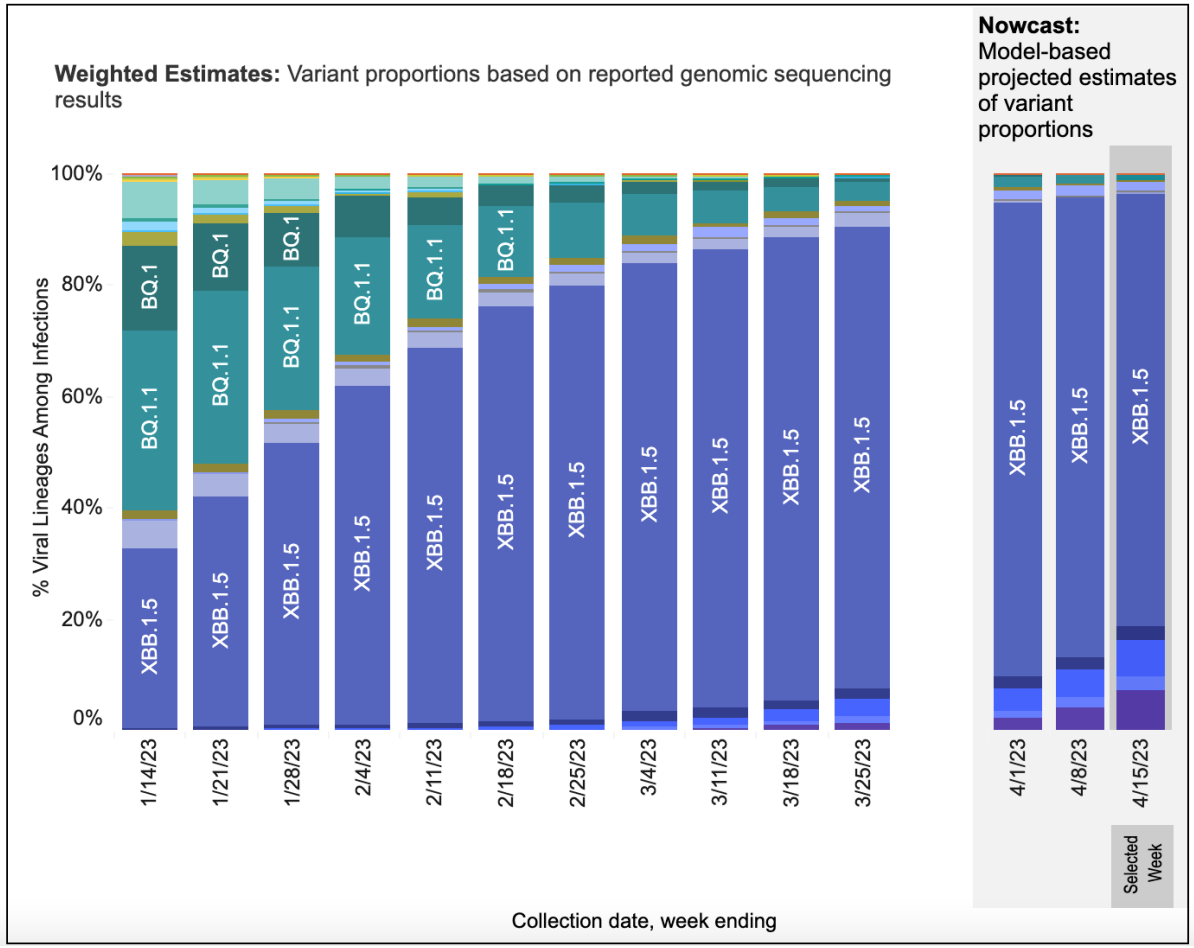


Total Cases	Total Deaths	Current Hospitalizations	Total Updated Booster Doses
104,348,746	1,128,404	11,279	55,577,285

CDC | Data as of: April 14, 2023 4:02 PM ET. Posted: April 14, 2023 5:00 PM ET

Weighted and Nowcast Estimates in United States for Weeks of 1/8/2023 – 4/15/2023

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



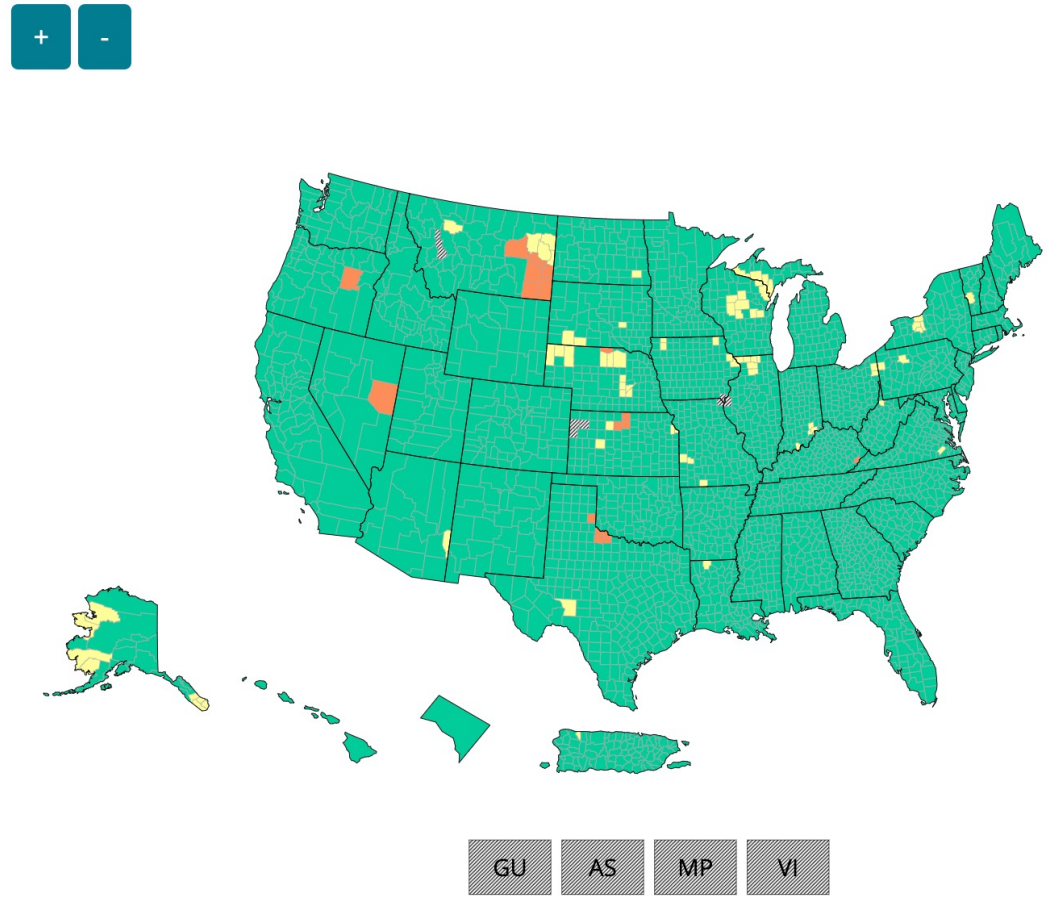
Nowcast Estimates in United States for 4/9/2023 – 4/15/2023

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	XBB.1.5	VOC	78.0%	73.6-81.8%
	XBB.1.16	VOC	7.2%	4.5-11.3%
	XBB.1.9.1	VOC	6.5%	4.8-8.8%
	XBB.1.9.2	VOC	2.5%	1.5-4.1%
	XBB.1.5.1	VOC	2.4%	1.8-3.1%
	FD.2	VOC	1.7%	0.9-3.2%
	BQ.1.1	VOC	1.0%	0.6-1.5%
	CH.1.1	VOC	0.3%	0.2-0.5%
	XBB	VOC	0.3%	0.2-0.3%
	BQ.1	VOC	0.1%	0.1-0.2%
	BN.1	VOC	0.0%	0.0-0.0%
	BA.5	VOC	0.0%	0.0-0.0%
	BA.2.75	VOC	0.0%	0.0-0.0%
	BF.7	VOC	0.0%	0.0-0.0%
	BA.2	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
	BA.5.2.6	VOC	0.0%	0.0-0.0%
	BF.11	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.4.6	VOC	0.0%	0.0-0.0%
Other	Other*		0.1%	0.0-0.1%

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

COVID-19 Community Levels in US by County



COVID-19 Community Levels in US by County

	Total	Percent	% Change
High	17	0.53%	0.13%
Medium	79	2.46%	– 1.05%
Low	3117	97.01%	0.93%

How are COVID-19 Community Levels calculated?

As of April 13, 2023, there are 17 (0.5%) counties, districts, or territories with a high COVID-19 Community Level, 79 (2.5%) with a medium Community Level, and 3,117 (96.8%) with a low Community Level. Compared with last week, the number of counties, districts, or territories in the high level increased by 0.1%, in the medium level decreased by 0.9%, and in the low level increased by 0.7%. Overall, 25 out of 52 jurisdictions** had high- or medium-level counties this week.

https://www.cdc.gov/coronavirus/2019-ncov/your-health/covid-by-county.html

Individual an Community-Level Prevention Strategies

Individual-Level Prevention Steps You Can Take Based on Your COVID-19 Community Level

LOW, MEDIUM, AND HIGH

At all COVID-19 Community Levels:

- Stay up to date on vaccination, including recommended booster doses.
- Maintain ventilation improvements.
- Avoid contact with people who have suspected or confirmed COVID-19.
- Follow recommendations for isolation if you have suspected or confirmed COVID-19.
- Follow the recommendations for what to do if you are exposed to someone with COVID-19.
- If you are at high risk of getting very sick, talk with a healthcare provider about additional prevention actions.

MEDIUM AND HIGH

When the COVID-19 Community Level is Medium or High:

- If you are at high risk of getting very sick, wear a high-quality mask or respirator (e.g., N95) when indoors in public
- If you have household or social contact with someone at high risk for getting very sick, consider self-testing to detect infection before contact, and consider wearing a high-quality mask when indoors with them

HIGH

When the COVID-19 Community Level is High:

- Wear a high-quality mask or respirator.
- If you are at high risk of getting very sick, consider avoiding non-essential indoor activities in public where you could be exposed.

Community-Level Prevention Strategies

LOW, MEDIUM, AND HIGH

At all COVID-19 Community Levels:

- Promote equitable access to vaccination, testing, masks and respirators, treatment and prevention medications, community outreach, and support services.
- Ensure access to testing, including through point-of-care and at-home tests for all people.
- Maintain ventilation improvements.
- Provide communications and messaging to encourage isolation among people who test positive.

MEDIUM AND HIGH

When the COVID-19 Community Level is Medium or High:

- Implement screening testing in high-risk settings where screening testing is recommended.

HIGH

When the COVID-19 Community Level is High:

- Implement healthcare surge support as needed.

https://www.cdc.gov/coronavirus/2019-ncov/your-health/covid-by-county.html

End of COVID-19 Public Health Emergency: Related Changes 4/17/23

What is changing for Isolation and Personal Protective Equipment (PPE) for COVID-19 Infection	• **Nothing** will change for isolation and PPE required for patients with COVID-19 infection. • Guidelines for isolation and PPE have not changed based on CDC recommendations.

What is required for patients with COVID-19 infection?	• Patients with COVID-19 infection, whether symptomatic or asymptomatic, will still require:
	  • Single room with air scrubber or airborne isolation infection room [AIIR]
	  • Appropriate PPE (gowns, gloves, N95 mask, eye protection, and bouffant)

Outpatient setting:	• Single room • Appropriate PPE (gowns, gloves, N95 mask, eye protection, and bouffant)

COVID-19 and Mask Use: What is Changing?

What's changing?

- Universal Masking will no longer be required in clinical settings.
- However, anyone can still choose to use masks when interacting with patients and colleagues.

When is masking still required?

- When patients are on specific types of isolation precautions
  - *Airborne: N95 mask*
  - *Droplet: procedure mask*
- When you have respiratory symptoms and are working
- When patients ask you to wear a mask

When is masking still strongly recommended?

- When caring for patients who are immunocompromised (examples: heme-oncology patients, renal transplant patients)
- When influenza, RSV, and COVID-19 levels rise within the community again
- When unit or area outbreaks occur.

COVID-19 Testing: What is changing

COVID-19 Testing will no longer be required for patients

- At the time of admission to the hospital
- Before surgical procedures

When is COVID-19 testing still required?

- For any patients who are admitted with any COVID-19 symptoms (including pneumonia)
- When required for placement after hospitalization
- Testing may be required again at the time of admission based on levels of community transmission and disease severity

When is COVID-19 testing recommended?

- For inpatients who develop COVID-19 symptoms
- Maybe considered for patients at high risk for complications with COVID-19 infection:
- Perioperatively (e.g., patients ≥ 70 years or with underlying comorbidities) **or**
- Prior to initiation of chemotherapy, transplant or immunosuppression

Which of the Following Statements are True

A. In patients who are critically ill due to COVID-19, ACE inhibitors and ARBs should not be initiated as a treatment for COVID-19

B. Initiation of an ACE inhibitor or ARB among critically ill patients with COVID 19 may worsen the outcome

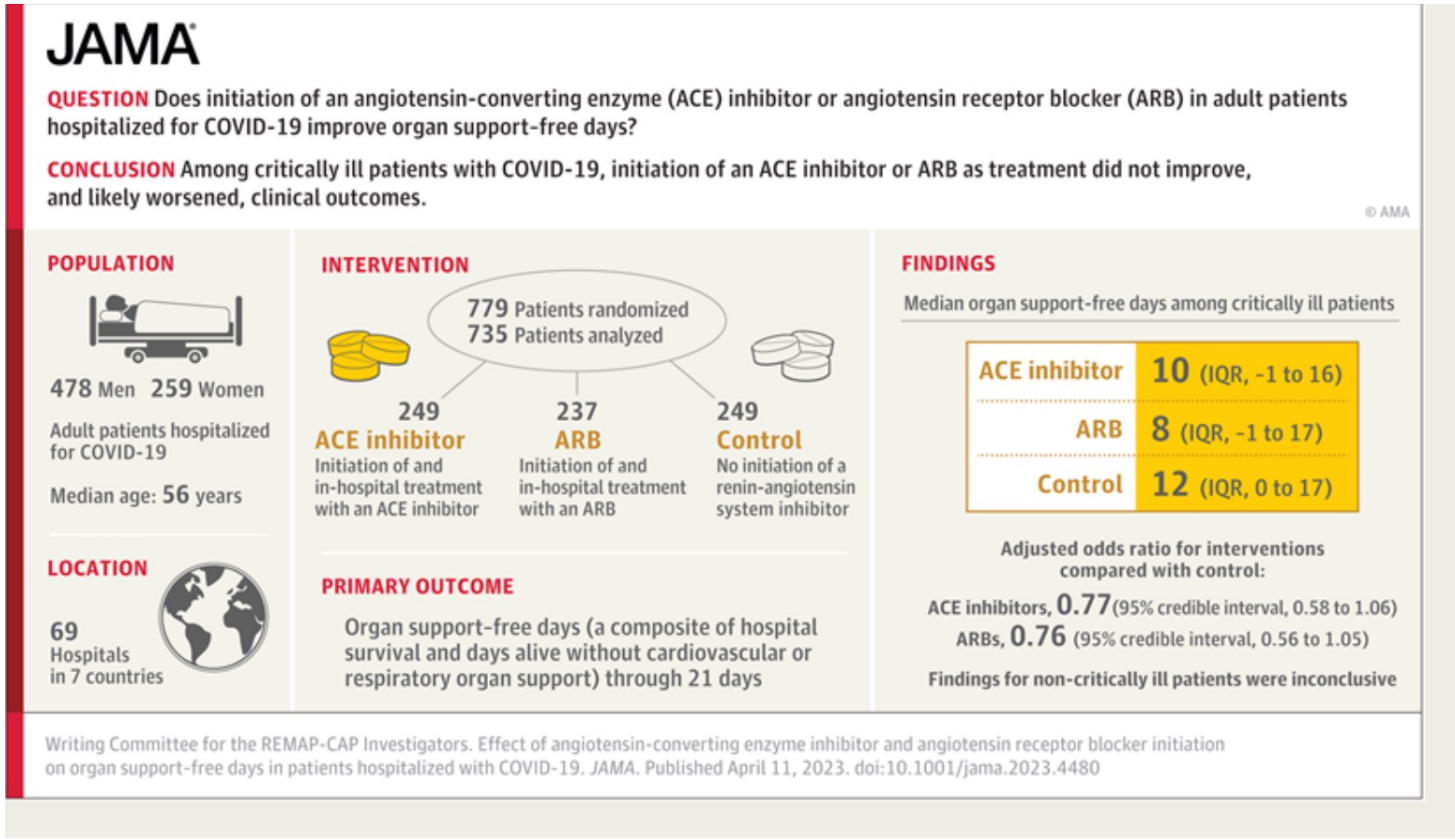
C. Treatment with an ACE inhibitor or ARBs do not need to be stopped in non–critically ill patients with COVID-19.

D. A and B are correct

E. All are correct

Effect of Angiotensin-Converting Enzyme Inhibitor and Angiotensin Receptor Blocker Initiation on Organ Support–Free Days in Patients Hospitalized With COVID-19A Randomized Clinical Trial

In this randomized clinical trial that included 779 patients, initiation of an ACE inhibitor or ARB did not improve organ support–free days. Among critically ill patients, there was a 95% probability that treatments worsened this outcome.



Writing Committee for the REMAP-CAP Investigators. *JAMA.* 2023;329(14):1183–1196. doi:10.1001/jama.2023.4480

Renin-Angiotensin System Modulation With Synthetic Angiotensin (1-7) and Angiotensin II Type 1 Receptor–Biased Ligand in Adults With COVID-19Two Randomized Clinical Trials

Question

- Among adults hospitalized with severe COVID-19, does treatment with synthetic angiotensin (1-7) (TXA-127) or an angiotensin II type 1 receptor–biased ligand (TRV-027) improve clinical outcomes?

Findings

- In 2 placebo-controlled, randomized clinical trials, the number of days alive and free from supplemental oxygen during the 28 days after trial enrollment (oxygen-free days) was not significantly different from placebo for TXA-127 (adjusted odds ratio, 0.88) or TRV-027 (adjusted odds ratio, 0.74).

Meaning

- These findings do not support the hypothesis that pharmacological modulation of the renin-angiotensin system with exogenous administration of synthetic angiotensin (1-7) or blockade of the angiotensin II type 1 receptor results in clinical benefit for patients with severe COVID-19.

BMJMED 2023;2:e000385. doi:10.1136/ bmjmed-2022-000385

JAMA Network™

From: **Renin-Angiotensin System Modulation With Synthetic Angiotensin (1-7) and Angiotensin II Type 1 Receptor–Biased Ligand in Adults With COVID-19: Two Randomized Clinical Trials**

JAMA. 2023;329(14):1170-1182. doi:10.1001/jama.2023.3546

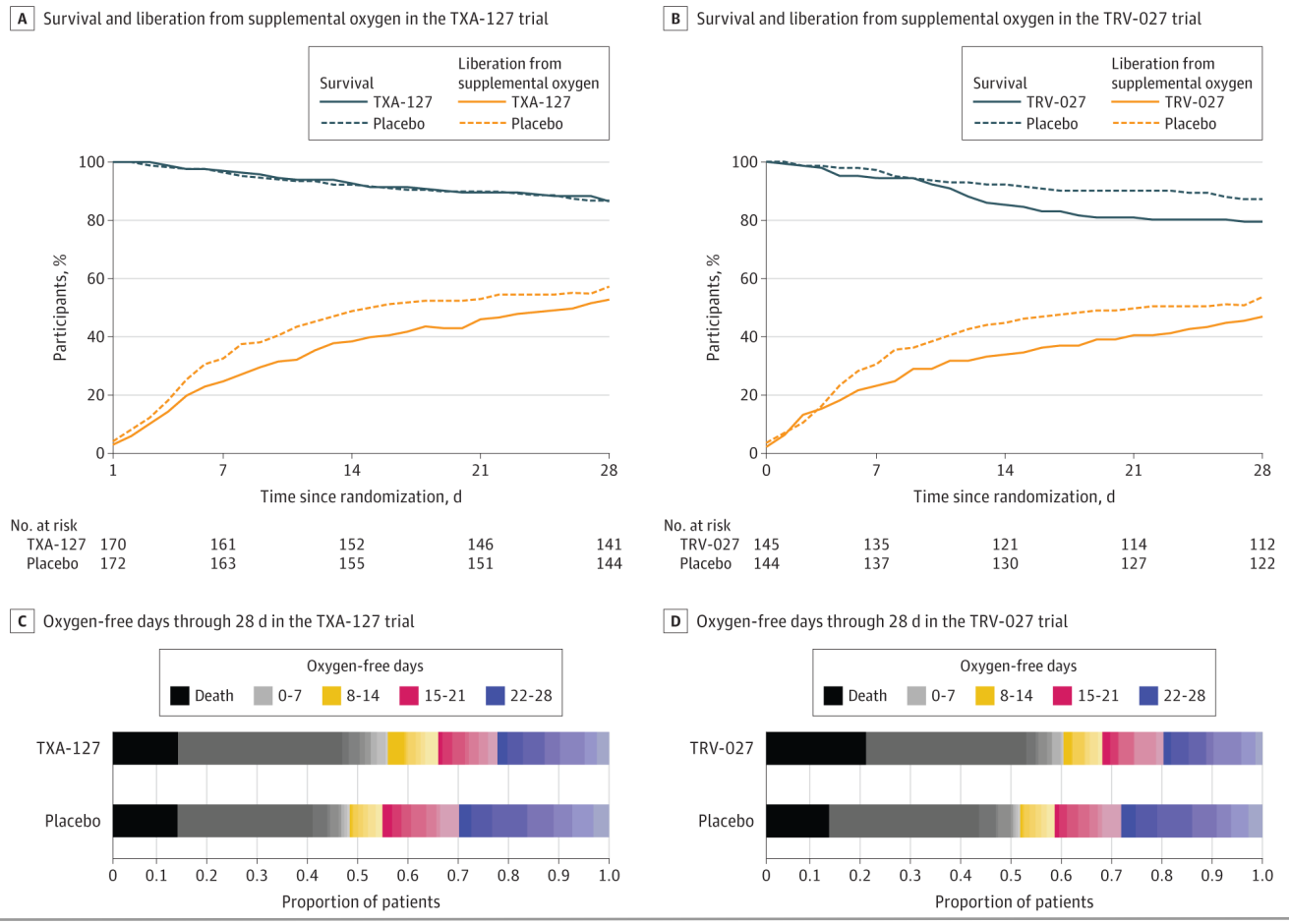


Figure Legend:

Primary Outcome of Oxygen-Free Days Between Randomization and Day 28 in the TXA-127 Trial and in the TRV-027 Trial

The day of randomization was study day 0.

The total sample size was 343 patients in the TXA-127 trial.

The total sample size was 290 patients in the TRV-027 trial.

Patients were followed up until the earlier of death or day 28.

The numbers at risk shown in panels A and B are the numbers of patients who were not deceased, withdrawn, or lost to follow-up.

The plots in panels C and D display the proportion of patients in each of the 30 levels (range, –1 to 28 days) of the oxygen-free days ordinal scale at day 28.

The oxygen-free days outcome demonstrated null results for TXA-127 vs placebo and TRV-027 vs placebo with point estimates in the direction of inferiority for the TXA-127 trial (adjusted OR, 0.88 [95% credible interval, 0.59 to 1.30]) and for the TRV-027 trial (adjusted OR, 0.74 [95% credible interval, 0.48 to 1.13]).

Which of the Following Statements are True

A. In patients who are critically ill due to COVID-19, ACE inhibitors and ARBs should not be initiated as a treatment for COVID-19

B. Initiation of an ACE inhibitor or ARB among critically ill patients with COVID 19 may worsen the outcome

C. Treatment with an ACE inhibitor or ARBs do not need to be stopped in non–critically ill patients with COVID-19.

D. A and B are correct

E. All are correct

FDA authorizes Gohibic (vilobelimab) injection under EUA for the treatment of COVID-19

Indications

- Adult patients with COVID-19 that are in hospitalized within 48 hours of receiving invasive mechanical ventilation or ECMO

Mechanism of action

- It is a complement inhibitor

Impact:

- Patients randomized to vilobelimab had a lower mortality rate by day 28 and 60 compared to the placebo arm

The recommended dosage of Gohibic is:

- 800 mg administered by intravenous infusion after dilution, given up to six times over the treatment period.

The most common adverse reactions were:

- Pneumonia, sepsis, delirium, pulmonary embolism, hypertension, pneumothorax, deep vein thrombosis, herpes simplex, enterococcal infection, bronchopulmonary aspergillosis, hepatic enzyme increased, urinary tract infection, hypoxia, thrombocytopenia, pneumomediastinum, respiratory tract infection, supraventricular tachycardia, constipation, and rash. Serious infections due to bacterial, fungal, or viral pathogens have been reported in patients with COVID-19 receiving Gohibic.

https://www.fda.gov/drugs/drug-safety-and-availability/fda-authorizes-gohibic-vilobelimab-injection-treatment-covid-19

Triple combination therapy with two antivirals and monoclonal antibodies for persistent or relapsed SARS-cov-2 infection in immunocompromised patients

Introduction:

- Severely immunocompromised patients are at risk for prolonged or relapsed COVID-19 leading to increased morbidity and mortality.

Objectives

- Evaluate the efficacy and safety of combination treatment in immunocompromised COVID-19 patients.

Methods:

- All immunocompromised patients with prolonged/relapsed COVID-19 treated with combination therapy with two antivirals (remdesivir plus nirmatrelvir/ritonavir, or molnupiravir in case of renal failure) plus, if available, anti-spike monoclonal antibodies (Mabs), between February and October 2022.
- The main outcomes were virological response at day 14 (negative SARS-CoV-2 swab) and virological and clinical response (alive, asymptomatic, with negative SARS-CoV-2 swab) at day 30 and the last follow-up.

Triple combination therapy with two antivirals and monoclonal antibodies for persistent or relapsed SARS-cov-2 infection in immunocompromised patients

***Results*: 22 patients (Omicron variant in 17/18) were included:**

- The majority (18)received two antivirals and Mabs and 4 received two antivirals only;
- The majority (91%) received nirmatrelvir/ritonavir plus remdesivir.
- Nineteen (86%) patients had hematological malignancy, 15 (68%) had received anti-CD20 therapy.
- All were symptomatic; 8 (36%) required oxygen.

Response rate at day 14, 30 and last follow-up was, respectively, 75% , 73% and 82%.

- Day 14 and 30 response rates were significantly higher when combination therapy included Mabs.
- Higher number of vaccine doses was associated with better final outcome.
- Two patients (9%) developed severe side effects: bradycardia leading to remdesivir discontinuation and myocardial infarction.

***Conclusion*:**

- Combination therapy including two antivirals (mainly remdesivir and nirmatrelvir/ritonavir) and Mabs was associated with high rate of virological and clinical response in immunocompromised patients with prolonged/relapsed COVID-19.

DOI: 10.1093/cid/ciad181

COVID-19 convalescent plasma utilization in the United States: data from the National Inpatient Sample

Early in the pandemic, CCP was transfused to patients in about a fifth of COVID-19 hospitalizations.

Most CCP was provided to patients with advanced disease; at the time, it was not yet known that CCP is optimally effective in those with early rather than late, severe disease.

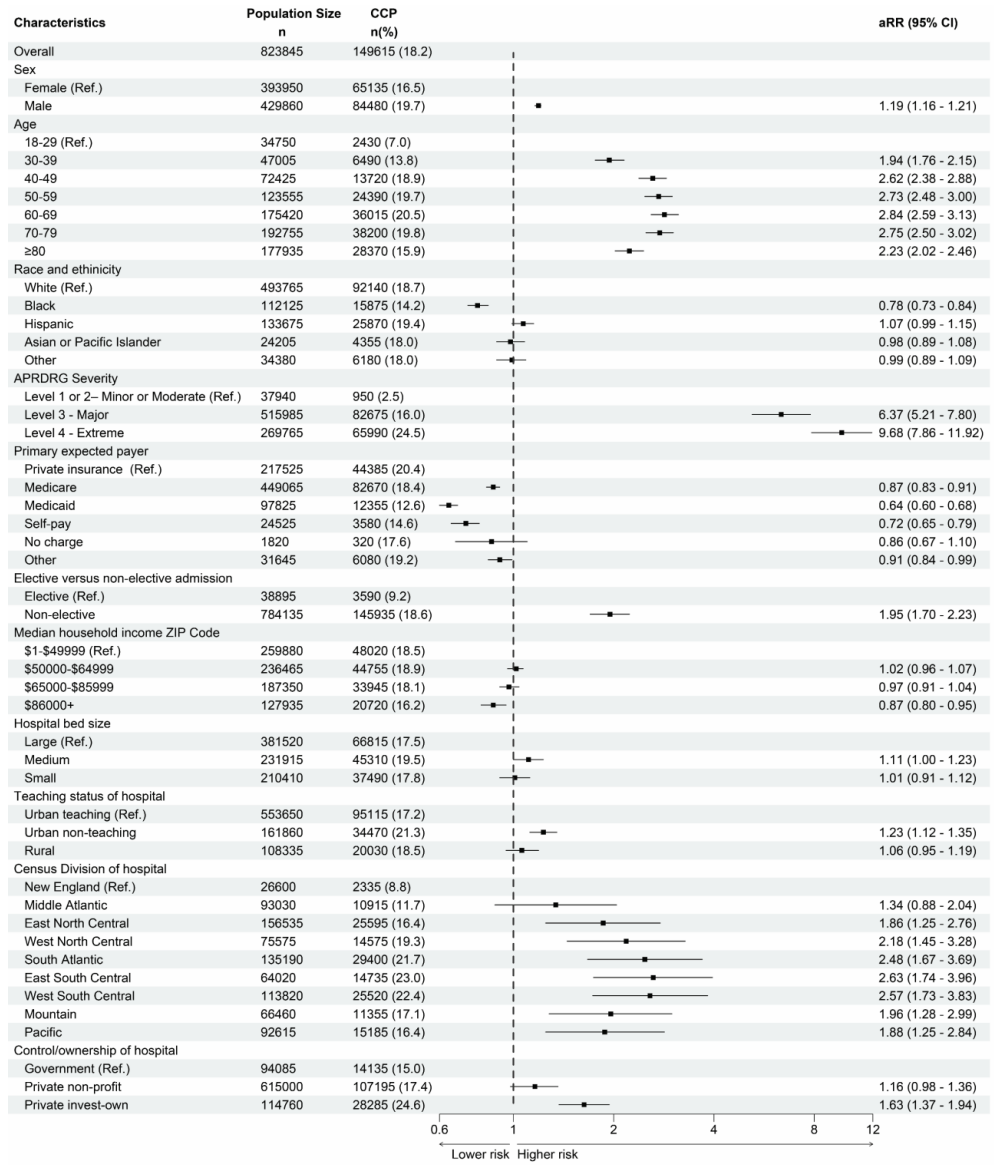
The findings also show the variability in access, availability and clinical practice, whereby geography, insurance, race and ethnicity could have had an impact on whether a given patient was transfused with CCP.

Female

Black

Medicare
Medicaid
Self pay

Geography



Characteristics	Population Size n	CCP n(%)	aRR (95% CI)
Overall	823845	149615 (18.2)	
Sex			
Female (Ref.)	393950	65135 (16.5)	
Male	429860	84480 (19.7)	1.19 (1.16 - 1.21)
Age			
18-29 (Ref.)	34750	2430 (7.0)	
30-39	47005	6490 (13.8)	1.94 (1.76 - 2.15)
40-49	72425	13720 (18.9)	2.62 (2.38 - 2.88)
50-59	123555	24390 (19.7)	2.73 (2.48 - 3.00)
60-69	175420	36015 (20.5)	2.84 (2.59 - 3.13)
70-79	192755	38200 (19.8)	2.75 (2.50 - 3.02)
≥80	177935	28370 (15.9)	2.23 (2.02 - 2.46)
Race and ethinicity			
White (Ref.)	493765	92140 (18.7)	
Black	112125	15875 (14.2)	0.78 (0.73 - 0.84)
Hispanic	133675	25870 (19.4)	1.07 (0.99 - 1.15)
Asian or Pacific Islander	24205	4355 (18.0)	0.98 (0.89 - 1.08)
Other	34380	6180 (18.0)	0.99 (0.89 - 1.09)
APRDRG Severity			
Level 1 or 2– Minor or Moderate (Ref.)	37940	950 (2.5)	
Level 3 - Major	515985	82675 (16.0)	6.37 (5.21 - 7.80)
Level 4 - Extreme	269765	65990 (24.5)	9.68 (7.86 - 11.92)
Primary expected payer			
Private insurance (Ref.)	217525	44385 (20.4)	
Medicare	449065	82670 (18.4)	0.87 (0.83 - 0.91)
Medicaid	97825	12355 (12.6)	0.64 (0.60 - 0.68)
Self-pay	24525	3580 (14.6)	0.72 (0.65 - 0.79)
No charge	1820	320 (17.6)	0.86 (0.67 - 1.10)
Other	31645	6080 (19.2)	0.91 (0.84 - 0.99)
Elective versus non-elective admission			
Elective (Ref.)	38895	3590 (9.2)	
Non-elective	784135	145935 (18.6)	1.95 (1.70 - 2.23)
Median household income ZIP Code			
$1-$49999 (Ref.)	259880	48020 (18.5)	
$50000-$64999	236465	44755 (18.9)	1.02 (0.96 - 1.07)
$65000-$85999	187350	33945 (18.1)	0.97 (0.91 - 1.04)
$86000+	127935	20720 (16.2)	0.87 (0.80 - 0.95)
Hospital bed size			
Large (Ref.)	381520	66815 (17.5)	
Medium	231915	45310 (19.5)	1.11 (1.00 - 1.23)
Small	210410	37490 (17.8)	1.01 (0.91 - 1.12)
Teaching status of hospital			
Urban teaching (Ref.)	553650	95115 (17.2)	
Urban non-teaching	161860	34470 (21.3)	1.23 (1.12 - 1.35)
Rural	108335	20030 (18.5)	1.06 (0.95 - 1.19)
Census Division of hospital			
New England (Ref.)	26600	2335 (8.8)	
Middle Atlantic	93030	10915 (11.7)	1.34 (0.88 - 2.04)
East North Central	156535	25595 (16.4)	1.86 (1.25 - 2.76)
West North Central	75575	14575 (19.3)	2.18 (1.45 - 3.28)
South Atlantic	135190	29400 (21.7)	2.48 (1.67 - 3.69)
East South Central	64020	14735 (23.0)	2.63 (1.74 - 3.96)
West South Central	113820	25520 (22.4)	2.57 (1.73 - 3.83)
Mountain	66460	11355 (17.1)	1.96 (1.28 - 2.99)
Pacific	92615	15185 (16.4)	1.88 (1.25 - 2.84)
Control/ownership of hospital			
Government (Ref.)	94085	14135 (15.0)	
Private non-profit	615000	107195 (17.4)	1.16 (0.98 - 1.36)
Private invest-own	114760	28285 (24.6)	1.63 (1.37 - 1.94)

DOI: 10.1093/cid/ciad185 3

Updated WHO Guidance for Prioritizing COVID-19 Vaccines

Strategic Advisory Group of Experts on Immunization (SAGE), part of the World Health Organization (WHO).

The recommendations reflect

- The impact of circulating Omicron variants as well as current population immunity due to previous infection and vaccination

SAGE recommends an additional booster 6 or 12 months after the last dose to those in a high priority group:

- Older adults
- People with underlying conditions or who are immunocompromised
- Frontline health care workers
- In addition, it suggests that pregnant people obtain another booster dose if they received their last 1 more than 6 months before.

SAGE does not recommend:

- Routine use of additional boosters for healthy adults younger than 50 to 60 years, although their use is safe.

Sage suggests that:

- Although primary and booster doses are safe and effective for healthy children between age 6 months and 17 years, countries should consider their disease burden, cost-effectiveness, as well as other health priorities when choosing whether to vaccinate this group.

JAMA. Published online April 12, 2023. doi:10.1001/jama.2023.6256

Evaluation of Preferred Language and Timing of COVID-19 Vaccine Uptake and Disease Outcomes

Question

- Are there linguistic disparities in COVID-19 vaccine uptake and disease outcomes based on self-reported preferred language and interpreter need?

Findings

- In this cohort study of 851 410 individuals between December 2020 and March 2022, self-identified language preference other than English and limited English proficiency, as measured by interpreter need, were both associated with delayed time to first vaccine dose and increased rates of COVID-19–associated hospitalization and death among specific language preference groups.
- Marked temporal clusters were observed for COVID-19 vaccination uptake, hospitalizations, and deaths associated with primary series vaccine eligibility, booster availability, and COVID-19 variants.

Meaning

- The findings of this study suggest that disaggregated data collection of preferred language and interpreter need is essential to identify and address barriers to care to improve health disparities in the US

JAMA Netw Open. 2023;6(4):e237877. doi:10.1001/jamanetworkopen.2023.7877

F.D.A. Authorizes Another Bivalent Covid Booster Shot for People Over 65

Why?

- COVID-19 still claims 1,300 per week
- C.D.C. data also show that only 43 percent of people over 65 have received an Omicron booster shot, and just 20 percent of those 18 and older

Who:

- Adults who are 65 and over
- People with compromised immune systems.

What variants does it target:

- Omicron variants of the coronavirus.
- It has the same formula that was released to protect people from the Omicron variant of the virus.
- An updated vaccine is expected later this year.
- The F.D.A. said it intended to make decisions about the recommended vaccine schedule for people younger than 65 after a June advisory meeting.

When:

- People who are 65 and older who have not had a bivalent booster shot in at least four months may get another one.
- For those who are immunocompromised, additional doses of the bivalent vaccine can be given two months after the last shot.
- Those who are unvaccinated can get a single dose of the bivalent booster, the agency said.

Effectiveness of BNT162b2 after extending the primary series dosing interval in children and adolescents aged 5–17

Introduction:

- Extended intervals between the first and second doses of mRNA Covid-19 vaccines may reduce the risk of myocarditis in children and adolescents.
- However, vaccine effectiveness after this extension remains unclear.

Methods

- From January 1 to August 15, 2022 a population based nested case-control study of children and adolescents aged 5–17 years who had received two doses of BNT162b2 in Hong Kong was studied

Results

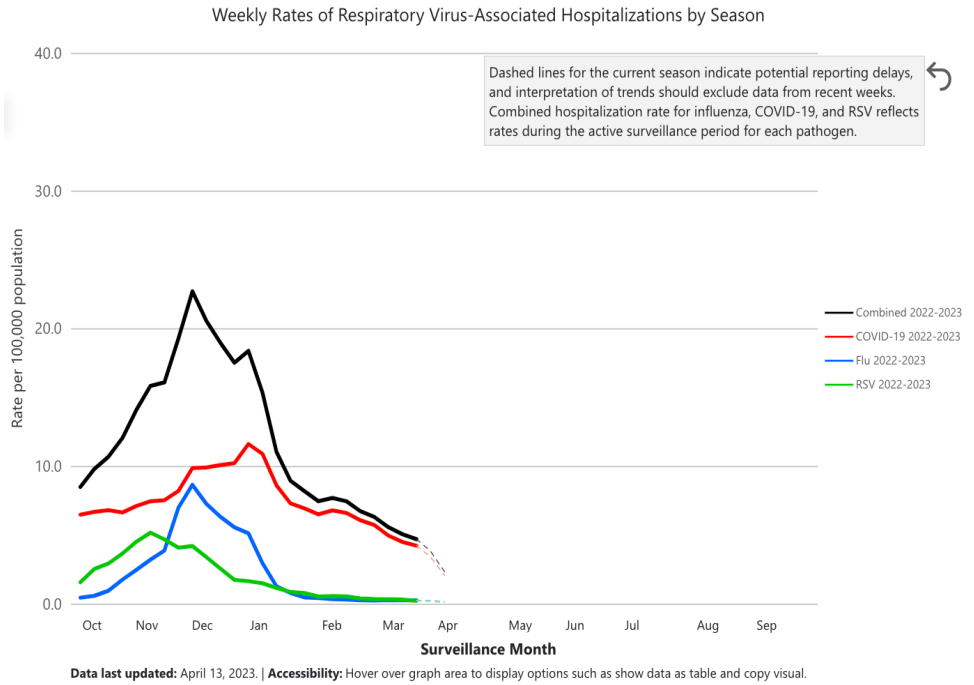
- 5396 Covid-19 cases and 202 Covid-19 related hospitalizations were identified and matched with 21,577 and 808 controls, respectively.
- For vaccine recipients with extended intervals [≥28 days, adjusted odds ratio 0.718, 95% Confidence Interval: 0.619, 0.833] there was a 29.2%-reduced risk of Covid-19 infection compared to those with regular intervals (21–27 days).
- If the threshold was set at eight weeks, the risk reduction was estimated at 43.5% (aOR 0.565, 95% CI: 0.456, 0.700).

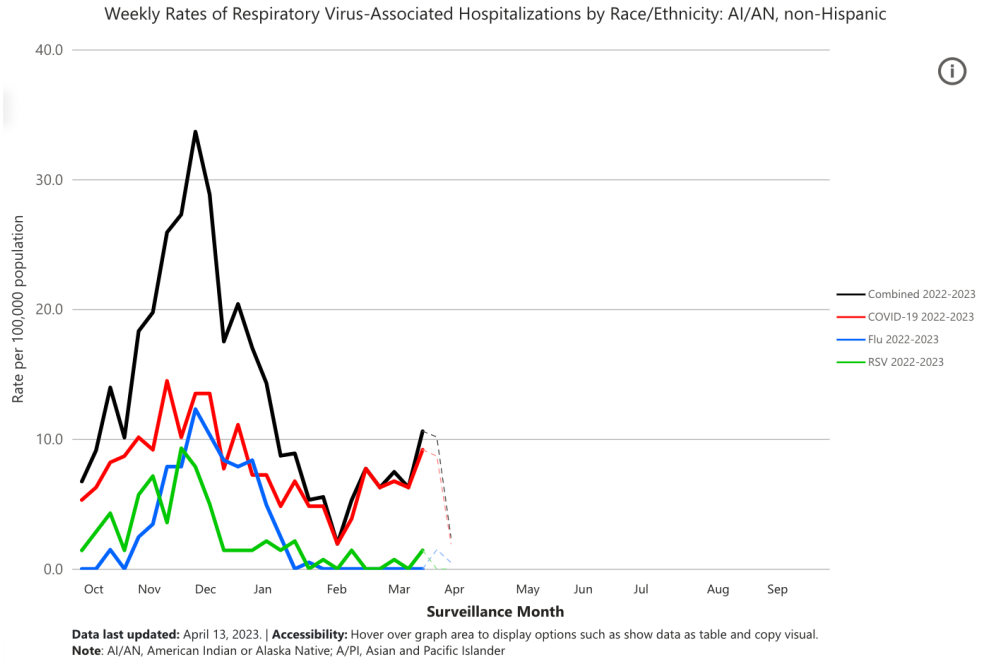
Conclusion:

- Longer dosing intervals for children and adolescents should be considered.

https://doi.org/10.1038/s41467-023-37556-z

RESP-NET Interactive Dashboard





The Respiratory Virus Hospitalization Surveillance Network (RESP-NET) comprises three platforms that conduct population-based surveillance for laboratory-confirmed hospitalizations associated with COVID-19, Influenza, and Respiratory Syncytial Virus (RSV) among children and adults. While RESP-NET does not collect data on all hospitalizations caused by respiratory illnesses, it can describe hospitalizations caused by three viruses that account for a large proportion of these hospitalizations. Surveillance is conducted through a network of acute care hospitals in select counties in 13 states. The surveillance platforms for COVID-19, Influenza, and RSV (known as COVID-NET, FluSurv-NET, and RSV-NET, respectively) cover more than 29 million people and include an estimated 8-10% of the U.S. population.

https://www.cdc.gov/surveillance/resp-net/dashboard.html

Which of the Following Statements are True

A. In an older population hospitalization for COVID-19 is associated with higher mortality compared to hospitalization for seasonal influenza

B. Death rates among people hospitalized for COVID-19 have decreased over time

C. Death rates among people hospitalized for COVID-19 is greater among unvaccinated individuals compared with those vaccinated or boosted

D. A and C are correct

E. All are correct

Risk of Death in Patients Hospitalized for COVID-19 vs Seasonal Influenza in Fall-Winter 2022-2023

In a VA population in fall-winter 2022-2023, being hospitalized for COVID-19 vs seasonal influenza was associated with an increased risk of death.

- This finding should be interpreted in the context of a 2 to 3 times greater number of people being hospitalized for COVID-19 vs influenza in the US in this period.

The difference in mortality rates between COVID-19 and influenza appears to have decreased since early in the pandemic;

- Death rates among people hospitalized for COVID-19 were 17% to 21% in 2020 vs 6% in this study
- Death rates for those hospitalized for influenza were 3.8% in 2020 vs 3.7% in this study.

The decline in death rates among people hospitalized for COVID-19 may be due to:

- Changes in SARS-CoV-2 variant
- Increased immunity levels (from vaccination and prior infection)
- Improved clinical care

The increased risk of death was greater among unvaccinated individuals compared with those vaccinated or boosted

- Findings that highlight the importance of vaccination in reducing risk of COVID-19 death.

Study limitations include:

- The older and predominantly male VA population may limit generalizability to broader populations.
- The results may not reflect risk in nonhospitalized individuals.
- The analyses did not examine causes of death, and residual confounding cannot be ruled out.

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	Death rate at 30 d, % (95% CI)		Excess deaths at 30 d, % (95% CI)	Hazard ratio (95% CI)	*P* value for interaction
	COVID-19	Influenza			
Age, y					
≤65	1.29 (0.77-1.82)	1.33 (0.46-2.20)	-0.04 (-1.06 to 0.98)	0.97 (0.45-2.11)	Reference
>65	6.42 (5.85-6.98)	3.66 (2.77-4.54)	2.76 (1.71 to 3.81)	1.78 (1.37-2.31)	.10
COVID-19 vaccination status					
Unvaccinated	8.75 (7.46-10.01)	3.86 (3.09-4.63)	4.88 (3.39 to 6.37)	2.32 (1.80-3.00)	Reference
1 or 2 doses of vaccine	6.23 (5.22-7.23)	3.79 (3.03-4.56)	2.44 (1.17 to 3.70)	1.66 (1.28-2.17)	.009
Boosted	5.18 (4.55-5.79)	3.77 (3.00-4.53)	1.41 (0.43 to 2.39)	1.38 (1.09-1.76)	<.001
SARS-CoV-2 infection					
Primary infection	6.14 (5.58-6.69)	3.76 (2.99-4.51)	2.38 (1.44 to 3.32)	1.65 (1.32-2.08)	Reference
Reinfection	5.11 (4.11-6.09)	3.85 (3.08-4.62)	1.26 (0.00 to 2.52)	1.34 (1.01-1.78)	.15
Outpatient COVID-19 antiviral treatment					
No	6.03 (5.53-6.53)	3.75 (2.99-4.51)	2.28 (1.37 to 3.19)	1.63 (1.30-2.04)	Reference
Yes	4.81 (2.49-7.07)	3.81 (3.04-4.57)	1.01 (-1.41 to 3.42)	1.27 (0.75-2.16)	.42
Overall	5.97 (5.48-6.46)	3.75 (2.98-4.50)	2.23 (1.32 to 3.13)	1.61 (1.29-2.02)	

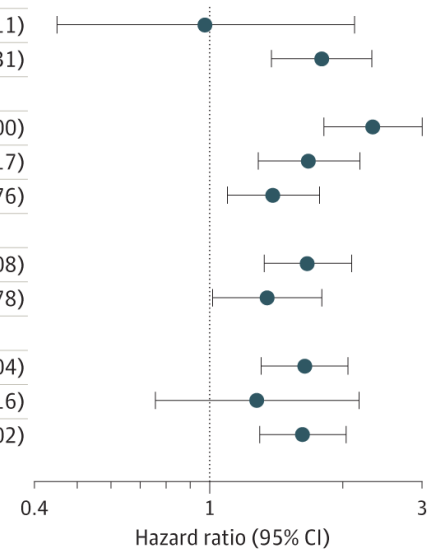

Figure Legend:

Hazard Ratio, Death Rates, and Percentage of Excess Deaths in COVID-19 Compared With Seasonal Influenza. Comparison conducted in overall cohort by age (≤65, >65 years) and by COVID-19 vaccination status (unvaccinated, 1-2 doses of vaccine, and boosted), SARS-CoV-2 infection status (with primary SARS-CoV-2 infection and reinfection), and outpatient COVID-19 antiviral treatment (yes or no), compared with overall seasonal influenza. Outpatient COVID-19 antiviral treatment included nirmatrelvir-ritonavir, molnupiravir, or remdesivir.

Which of the Following Statements are True

A. In an older population hospitalization for COVID-19 is associated with higher mortality compared to hospitalization for seasonal influenza

B. Death rates among people hospitalized for COVID-19 have decreased over time

C. Death rates among people hospitalized for COVID-19 is greater among unvaccinated individuals compared with those vaccinated or boosted

D. A and C are correct

E. All are correct

questions