Volume 1, Issue 18, 2022

Infectious Diseases Watch

May 2, 2022, 2022

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General Infectious Disease

Impact of Oral Metronidazole, Vancomycin, and Fidaxomicin on Host Shedding and Environmental Contamination With *Clostridioides difficile*

Clin Infect Dis 2022;74:648–56

DOI: 10.1093/cid/ciab473

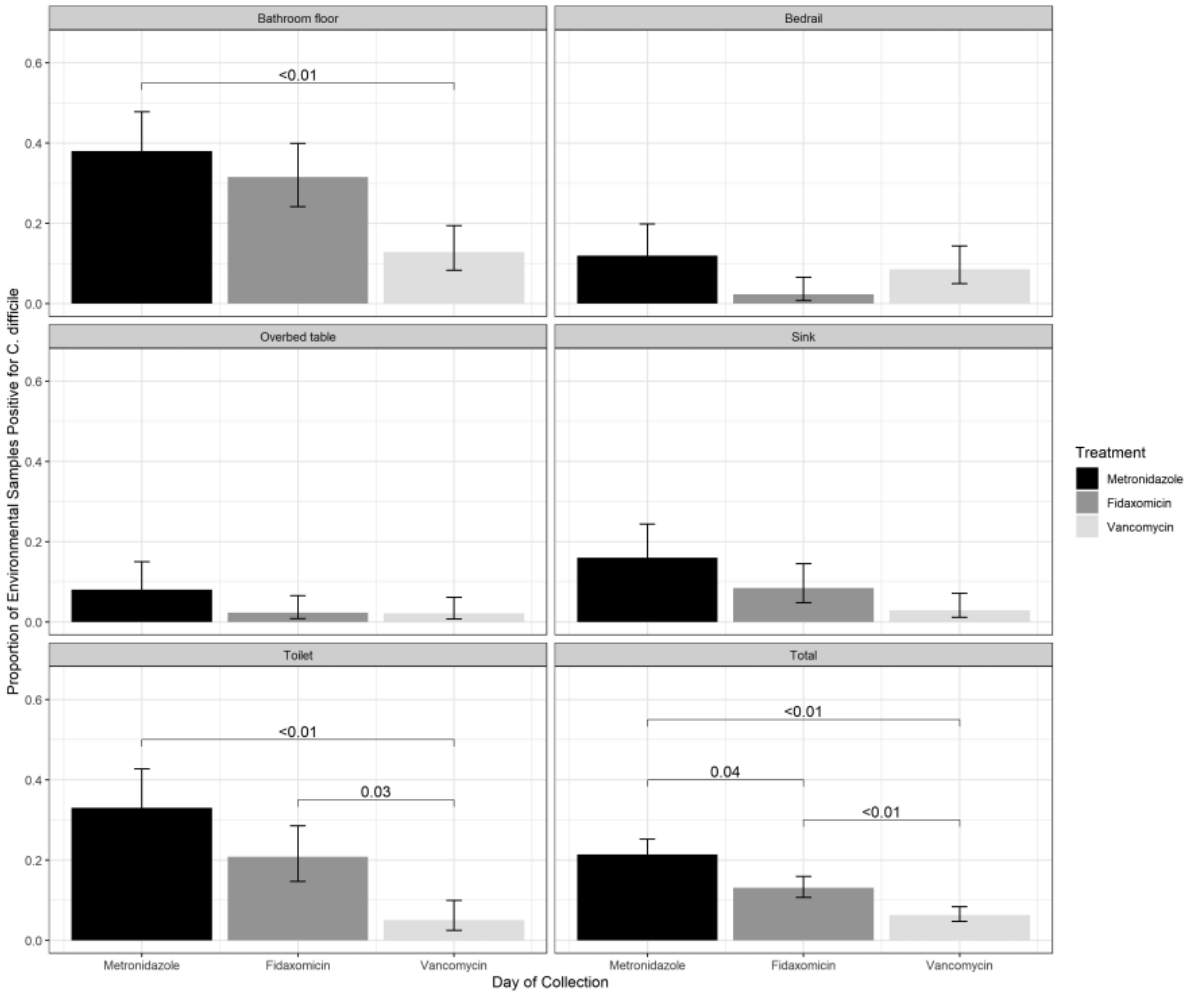
This is a prospective, unblinded, randomized controlled trial of hospitalized adults with *C. difficile* infection. Patients were randomized 1:1:1 to receive fidaxomicin, oral vancomycin, or metronidazole. (metronidazole 500 mg orally every 6 hours, vancomycin 125 mg orally every 6 hours, or fidaxomicin 200 mg orally every 12 hours). Treatment was provided for a minimum of 10 days after enrollment. The primary outcome was change in environmental contamination rate during treatment. Secondary outcomes included stool shedding, total burden of contamination, and molecular relatedness of stool versus environmental *C. difficile* isolates.

Inpatients with >3 loose stools in a 24-hour period, a positive *C. difficile* nucleic acid amplification test result, and mild to moderate infection at the time of enrollment were eligible for inclusion. Severity was defined in accordance with the 2010 IDSA guidelines, current at the time the protocol was written.

Cultures were acquired from 5 prespecified high-touch environmental surfaces in the room, with 5 replicates per site. The 5 prespecified environmental surfaces included the bed rail, overbed table, sink, toilet seat, and bathroom floor. Cultures were obtained from these sources starting on the day of enrollment (day 0), on days 3 and 7 after admission, at the end of each subsequent week (day 14, 21, etc.), and on the day of discharge. Environmental cultures were collected from each room, using Rodac plates with Dey/Engley neutralizing agar and *C. difficile* selective agar (Becton-Dickinson BBL). During the study period, rooms of patients with *C. difficile* underwent daily and terminal cleaning with a hypochlorite containing sporicidal disinfectant, in accordance with existing hospital protocols. The sole exception was bathroom floors, where bleach was incompatible with floor wax. Stool samples were collected starting the day of enrollment (day 0), on days 3 and 7 after admission, at the end of each subsequent week (day 14, 21, etc.), and on the day of discharge. They performed ribotyping on all viable *C. difficile* isolates to assess whether environmental strains matched *C. difficile* shed by study subjects.

Of 33 patients enrolled, 31 (94%) completed the study. Fidaxomicin (-0.36 log10 colony-forming units [CFUs]/d [95% confidence interval (CI), -.52 to -.19]; $P < .01$) and vancomycin (-0.17 log10

CFUs/d [-.34 to -.01]; *P* = .05) were associated with more rapid decline in *C. difficile* shedding than metronidazole (-0.01 log10 CFUs/d [95% CI, -.10 to .08). Both vancomycin (6.3% [95% CI, 4.7–8.3) and fidaxomicin (13.1% [10.7–15.9]) were associated with lower rates of environmental contamination than metronidazole (21.4% [18.0– 25.2]). With specific modeling of within-subject change over time, fidaxomicin (adjusted odds ratio, 0.83 [95% CI, .70–.99]; *P* = .04) was associated with more rapid decline in environmental contamination than vancomycin or metronidazole. Overall, 207 of 233 environmental *C. difficile* isolates (88.8%) matched patient stool isolates by ribotyping, without significant difference by treatment. *C. difficile* was isolated from ≥1 environmental surface for 23 of 31 included patients (74%). Contamination rates varied by surface, with the toilet (76 of 430 [17.7%]) and bathroom floor (116 of 429 [27.0%]) the most frequently contaminated.



Comment: Fidaxomicin, and to a lesser extent vancomycin, reduces *C. difficile* shedding and contamination of the hospital. This was a small trial and limited in duration and was unblinded. The particularly high contamination rates observed on the bathroom floor also probably reflect cleaning practices: nonsporicidal agents were used on bathroom floors owing to incompatibility with floor wax. With consistent reductions in both stool shedding and environmental

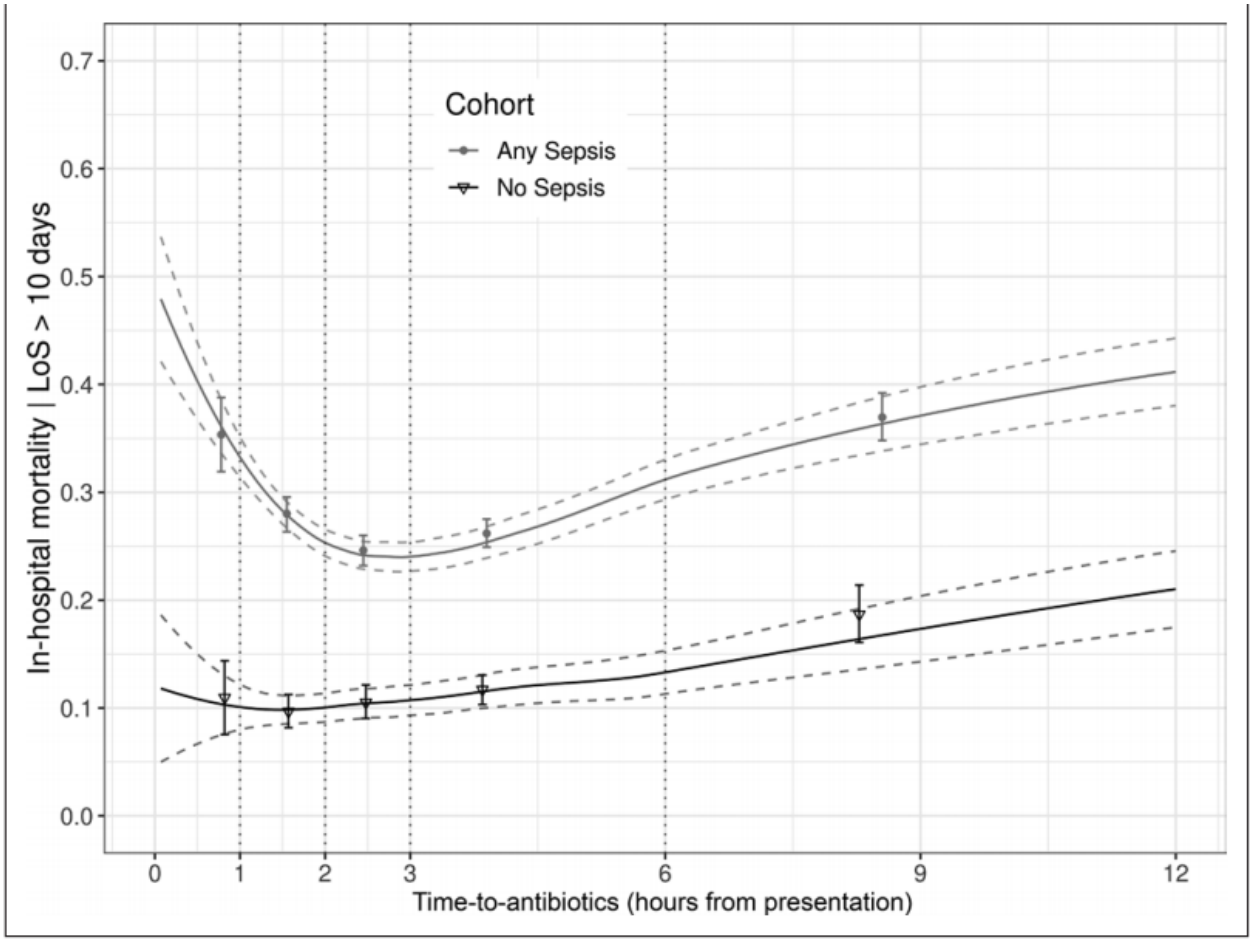
contamination, both fidaxomicin and vancomycin have potential benefits for preventing *C. difficile* transmission that metronidazole lacks. Interestingly, while vancomycin was associated with the lowest overall contamination rate, fidaxomicin was associated with more rapid within-subject reduction in shedding and environmental contamination over time. Whether these reflect clinically meaningful differences remains unclear. Larger studies are needed to confirm the impact on healthcare-associated *C. difficile* transmission rates.

Patient Heterogeneity and the J-Curve Relationship Between Time-to-Antibiotics and the Outcomes of Patients Admitted With Bacterial Infection Crit Care Med 2022; 799-809

DOI: 10.1097/CCM.0000000000005429

The investigators conducted a retrospective analysis of 18,315 patients with presumed severe bacterial illness (defined by a blood culture order, IV antibiotics, and continuation of at least 5 days of antibiotics or until death or discharge with a full antibiotic course) admitted to a seven-hospital network between October 2010 and December 2016, and identified those with and without evidence of sepsis, defined by the presence of either SIRS criteria or acute organ dysfunction. Models were constructed to describe the probability of administering antibiotics at different time intervals based on patient and clinical characteristics, and the risk-adjusted association between time-to-antibiotics and outcomes was assessed using detailed propensity matching. The primary outcome was a composite of in-hospital death or length of stay greater than 10 days; the latter outcome was included to capture potential harms associated with delayed antibiotics in patients at low baseline risk for mortality.

The first major finding was the observation of a “J-shaped curve” relationship between time-to-antibiotics and the composite outcome, such that the unadjusted rate of death or prolonged length of stay was elevated for patients who received antibiotics within the first hour of hospital presentation, decreased for those who received antibiotics in the next 3 hours, then increased steadily after 4 hours. Looking at their paper, it makes sense that patients who received antibiotics immediately after arrival to the hospital tended to have higher acuity (as marked by shock, tachypnea, fever or hypothermia, and/or elevated lactate), whereas patients who received antibiotics later were more likely to have a chronic illness, but initially without shock etc. The second main finding is that after detailed propensity matching, earlier time-to-antibiotics was associated with better risk-adjusted outcomes in all patients, including those with and without SIRS and organ dysfunction, compared to antibiotics given later than 2.5 hours after presentation.



Comment: In an editorial the authors state the observation that the timeliness of antibiotics is not random, but rather is strongly influenced by patient characteristics and clinical presentation, is logical, but nonetheless a very important contribution to the literature. "It makes complete sense that most clinicians will not hesitate to administer broad-spectrum antibiotics to patients who present in extremis if infection is a possibility, especially if they present with fever or other obvious signs of infection. Conversely, clinicians will likely be more judicious for less seriously ill patients who present with ambiguous syndromes for which infection may not be high on the differential; furthermore, it is easy to understand why the lack of a clear diagnosis at presentation may be more common in complex patients with chronic comorbidities." The other important finding in this study is that early antibiotics may improve outcomes not just in patients with sepsis, but in all patients with serious bacterial infections requiring hospitalization. "Efforts to improve early antibiotic administration for any patient with possible bacterial infection must be balanced against their potential to drive further inappropriate use, especially as recent data indicate that a third or more of patients treated empirically with broad-spectrum IV antibiotics are unlikely in retrospect to have had bacterial infections (Crit Care Med 2021; 49:e1144–e1150). Furthermore, most patients who do have confirmed bacterial infections are very unlikely to have resistant organisms and could be treated perfectly adequately with relatively narrow-spectrum antibiotics."

COVID-19

COVID-19 News

FDA Grants Full Approval To Remdesivir (RDV) For Treatment Of COVID-19 In Children Aged 28 Days And Older

Last week, the FDA granted the first full approval for treating COVID-19 in children aged 28 days and older with RDV. This comes months after the agency expanded the drug's EUA use to also include children below 12 years of age weighing at least 3.5 kilograms. The full approval is applicable to children who are hospitalized or have mild-to-moderate disease and are at high risk of severe COVID-19.

Comment: This change from EUA to full approval is welcomed.

Moderna Asks FDA to Clear Its Covid Vaccine for children < 6

Moderna has asked the FDA to authorize the use of its Covid-19 vaccine in children ages 6 months to 5 years old. Covid-related hospitalization rates for children in the U.S. rose sharply during the winter surge of Covid-19 cases caused by the Omicron, according to the CDC.(see article below) In January, weekly Covid-19 hospitalization rates of children under 5 peaked at about 14.5 per 100,000 children, which was about five times the peak rate during the Delta variant surge, the CDC said. The study found the vaccine was 43.7% effective against symptomatic Covid-19 infections in children ages 6 months to 2 years, and 37.5% effective in those ages 2 to 5. Most side effects, like injection-site pain and fever, were mild or moderate, Moderna said. The company observed no new safety concerns, and there were no deaths, myocarditis or cases of an inflammatory syndrome in children reported in the study,

Comment: The FDA is expected to convene a public meeting of a panel of outside vaccine advisers within weeks to consider Moderna's request. The risk of severe Covid-19 is much lower in children than in older adults, but there is still a level of risk that public health specialists say warrants vaccination. Only about 28% of children ages 5 to 11 and 59% of adolescents 12 to 17 have received the full primary vaccination series of two doses. The efficacy rates in children are lower than the 94% efficacy Moderna's vaccine demonstrated against symptomatic disease in a large study of adults in 2020. But that study was conducted before the more-transmissible Omicron variant, and Moderna said the efficacy in adults against symptomatic disease caused by Omicron is comparable to the rates seen in the pediatric study.

Other FDA News

- FDA will review Novavax's vaccine for adults 18 and over on June 7, 2022.
- The FDA will discuss Moderna and Pfizer vaccines for children under age 5 either June 8, 21, or 22, 2022
- The FDA will also meet on June 28, 2022, to discuss whether the current vaccines need to be redesigned to target mutations of the virus. Both Pfizer and Moderna are looking at vaccines that target omicron variant as well as the ancestral strain.

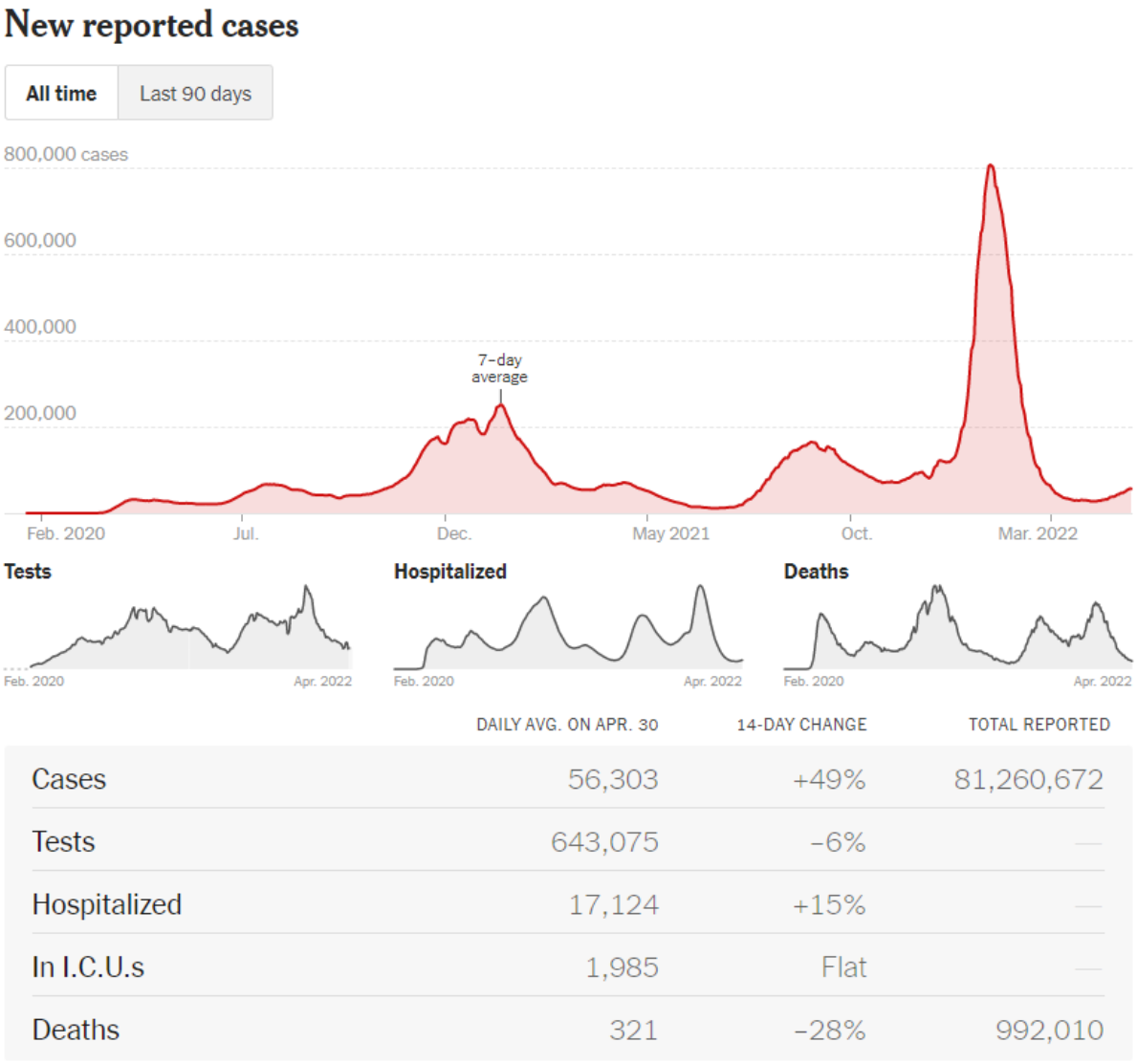
Comment: Novavax vaccine produces spike protein using the genetic code for spike putting into a baculovirus that infects insect cells which then produces copies of the spike that are purified for the vaccine. The vaccine also uses an adjuvant. The protein technology has been used in past vaccines. The adjuvant has been licensed for other vaccines including shingles. June promises to be a very busy month for the FDA.

Pfizer's Covid Drug Fails to Show Benefit as Preventive Therapy

Friday Pfizer announced that nirmatrelvir/ritonavir (Paxlovid), failed to meet its primary goal of significantly reducing the risk of Covid-19 infection in adults exposed to the virus through a household contact.

Comment: The result of this study was a big disappointment. Given the results of early treatment and the antiviral effects of nirmatrelvir/ritonavir, I would have expected a positive result for postexposure prophylaxis in households. I do not know the vaccination status and any precautions, demographics etc. of the study yet.

COVID-19 by the Numbers



	DAILY AVG. ON APR. 30	14-DAY CHANGE	TOTAL REPORTED
Cases	56,303	+49%	81,260,672
Tests	643,075	-6%	—
Hospitalized	17,124	+15%	—
In I.C.U.s	1,985	Flat	—
Deaths	321	-28%	992,010

Comment: Covid-19 cases and hospitalizations are rising in a majority of American states; however, the US remains at its lowest level since last summer, and hospitalizations, despite recent increases, are nearly as low as they have been at any point in the pandemic. Meanwhile deaths continue to decline.

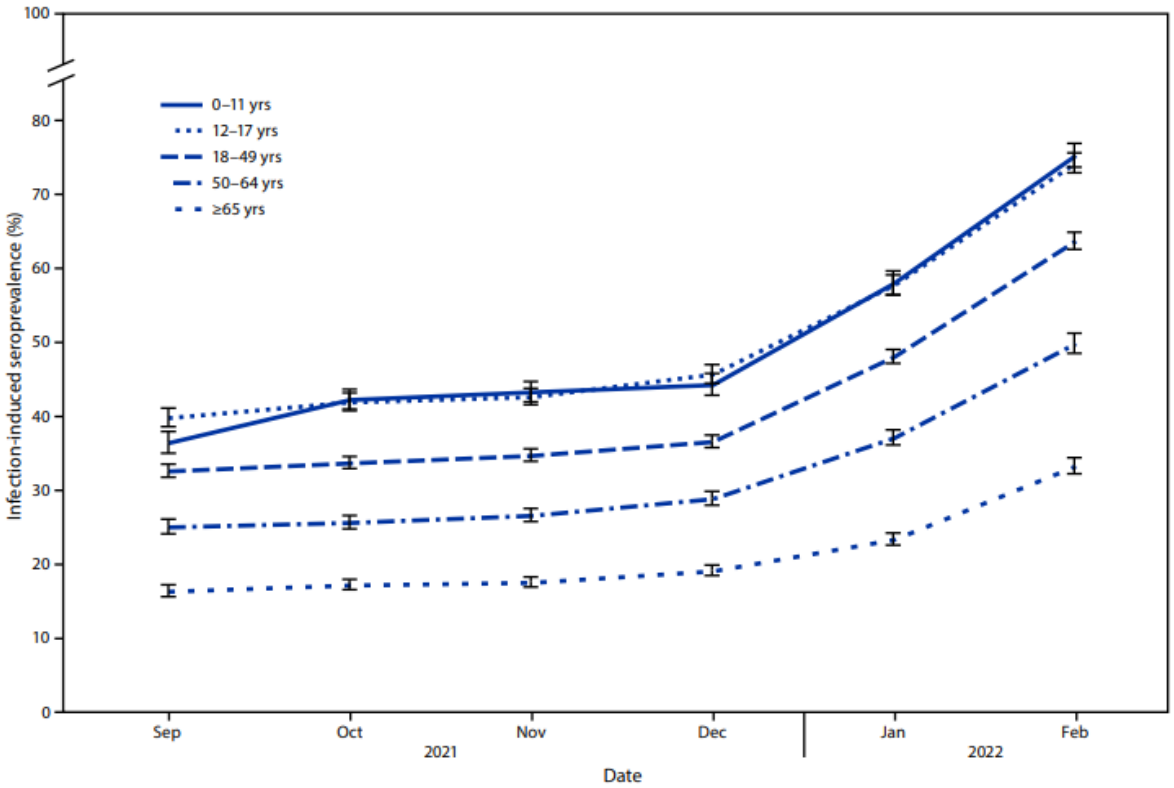
COVID-19 Journal Review

Seroprevalence of Infection-Induced SARS-CoV-2 Antibodies — United States, September 2021–February 2022 MMWR early release April 26, 2022

Following the record surge in COVID-19 cases during the Omicron wave, some 58% of the U.S. population overall and more than 75% of younger children have been infected with SARS-CoV-2 since the start of the pandemic, according to a US nationwide blood survey released last Tuesday. Investigators looked for antibodies against the viral nucleocapsid (N) protein, which would not be induced by any of the vaccines authorized in the U.S. and are therefore presumed to be present only after an infection

This is the first time in which more than half of the US population has been infected with the SARS-CoV-2 virus at least once and demonstrates the impact of the Omicron surge. Before Omicron arrived in December of 2021, a third of the US population had evidence of a prior SARS-CoV-2 infection. Omicron drove up infections in every age group, according to the new data, but children and adolescents, many of whom remain unvaccinated, had the highest rates of infection, while people 65 and older – a more heavily vaccinated population - had the lowest.

During the December 2021 to February 2022 period - when Omicron cases were surging in the US - 75.2% of children aged 11 and younger had infection-related antibodies in their blood, up from 44.2% in the prior three-month period. Among those 12-17, 74.2% carried antibodies, up from 45.6% from September to December 2021.

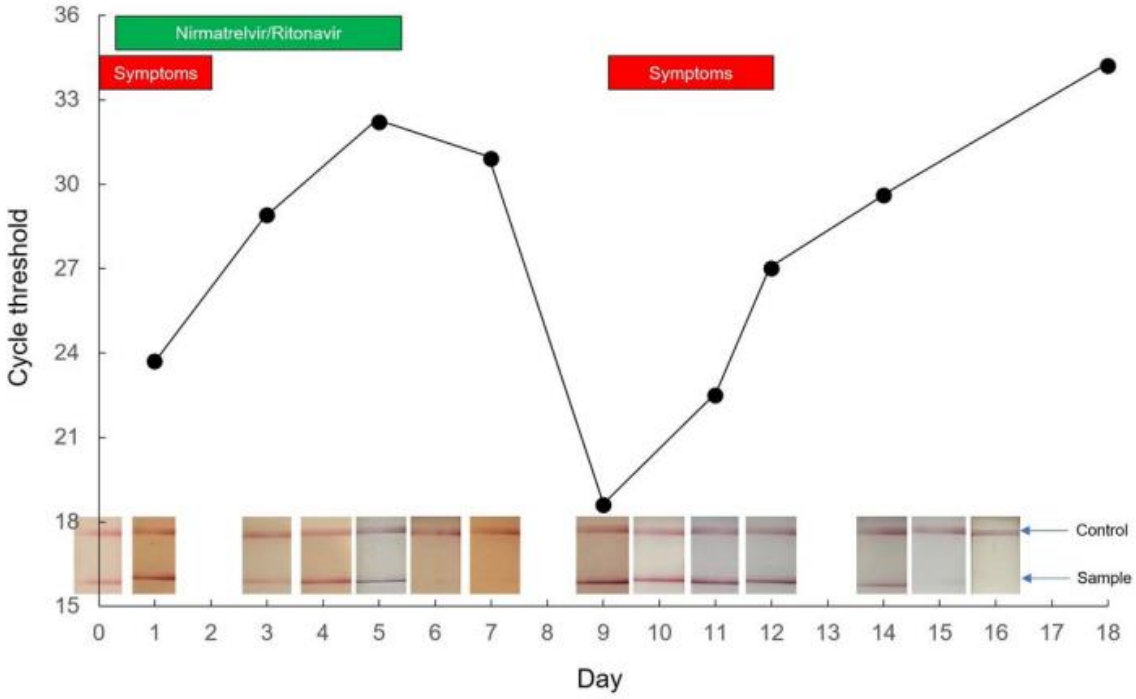


Comment: The investigators used of a convenience sample, which may limit generalizability. The findings also might underestimate the cumulative number of SARS-CoV-2 infections because infections after vaccination might result in lower anti-N titers, and screening for anti-nucleocapsid antibodies cannot account for reinfections. In addition, if we add vaccinated with natural infections, the percent of immunity in the US is much higher. More than 66% of the U.S. population is fully vaccinated against COVID-19, and nearly 46% of adults have had at least one booster, according to latest CDC data.

Rapid Relapse of Symptomatic SARS-CoV-2 Infection Following Early Suppression with Nirmatrelvir/Ritonavir (NM/R) Res Square posted April 26, 2022

doi.org/10.21203/rs.3.rs-1588371/v1

Initiation of NM/R treatment on Day 0 in a 71-year-old vaccinated and boosted male resulted in rapid resolution of COVID-19 symptoms followed one week later by the development of typical cold symptoms. SARS-CoV-2 viral load fluctuated in parallel with symptoms, with two distinct peaks on Day 1 and Day 9 of illness. No other respiratory pathogens were identified. Viral samples demonstrated sequence identity for the omicron subvariant BA.1 on Days 1, 7, and 11.



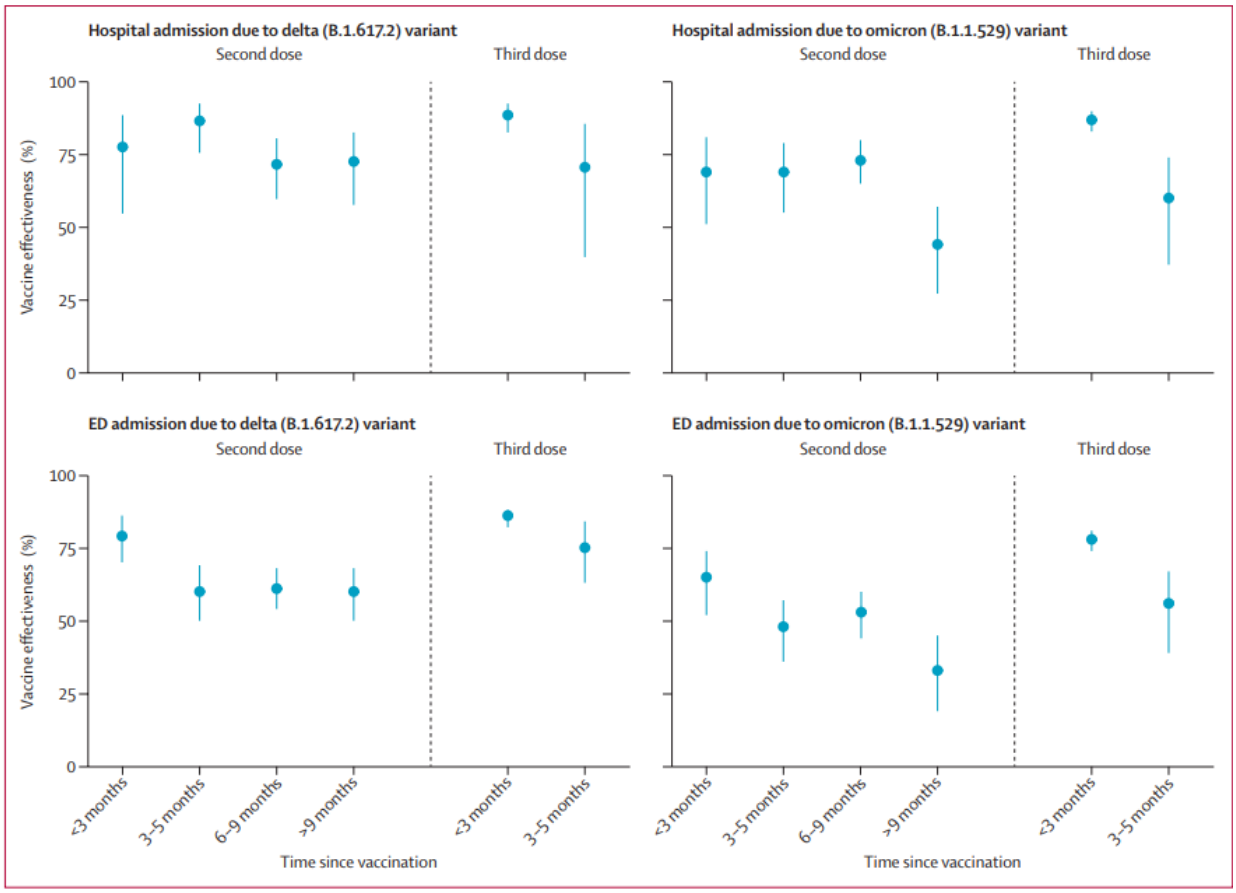
Comment: Little is known about the rebound cases, including how frequently they occur and whether the highly transmissible omicron variant plays a role. Several similar cases have been described on Twitter and medical blogs. Bottom line: Physicians should be aware that that if people have symptoms worsening after Paxlovid, it's probably still Covid. Researchers are planning to study how often and why SARS-CoV-2 levels rebound in some Covid-19 patients who have completed a five-day course of treatment.

Durability of BNT162b2 vaccine against hospital and emergency department admissions due to the omicron and delta variants in a large health system in the USA: a test-negative case–control study Lancet Resp Med published online April 22, 2022

doi.org/10.1016/ S2213-2600(22)00101-1

This is a case–control study with a test-negative design. The investigators analyzed electronic health records of members of Kaiser Permanente Southern California (KPSC) from Dec 1, 2021, to Feb 6, 2022. Vaccine effectiveness was calculated in KPSC patients aged 18 years and older admitted to hospital or an emergency department (without a subsequent hospital admission) with a diagnosis of acute respiratory infection and tested for SARS-CoV-2 via PCR. Adjusted vaccine effectiveness was estimated with odds ratios from adjusted logistic regression models.

Analyses were done for 11,123 hospital or emergency department admissions. In adjusted analyses, effectiveness of two doses of the Pfizer vaccine against the omicron variant was 41% (95% CI 21−55) against hospital admission and 31% (16−43) against emergency department admission at 9 months or longer after the second dose. After three doses, effectiveness of the Pfizer vaccine against hospital admission due to the omicron variant was 85% (95% CI 80−89) at less than 3 months but fell to 55% (28−71) at 3 months or longer, although the confidence intervals were wide. Against emergency department admission, the effectiveness of three doses of the Pfizer vaccine against the omicron variant was 77% (72−81) at less than 3 months but fell to 53% (36−66) at 3 months or longer. Trends in waning against SARS-CoV-2 outcomes due to the delta variant were generally similar, but with higher effectiveness estimates at each timepoint than those seen for the omicron variant. Stratification of vaccine effectiveness by age group showed similar trends as with all ages but revealed slightly higher vaccine effectiveness estimates among individuals aged 65 years and older versus those aged 18−64 years.

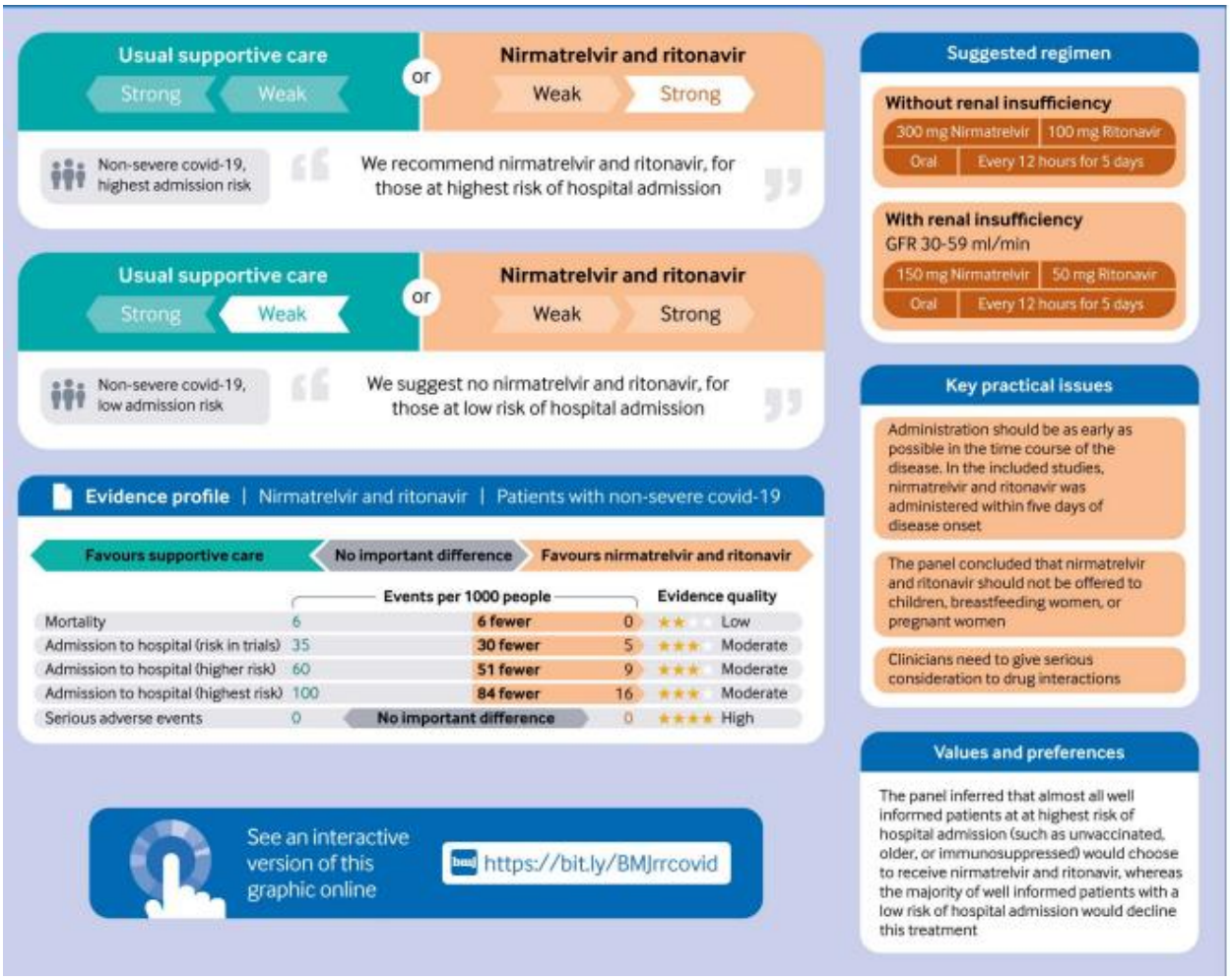


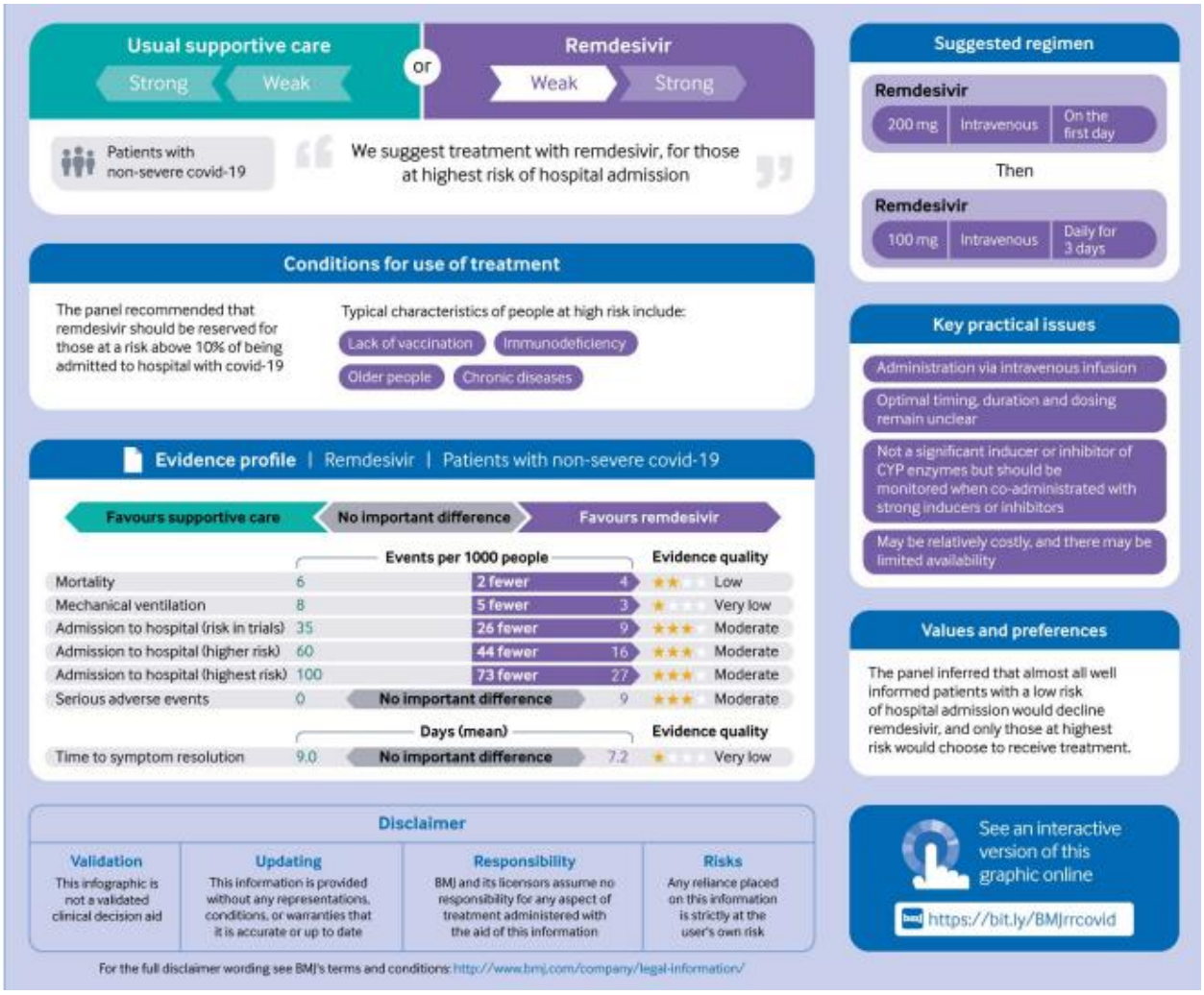
Comment: Three doses of Pfizer vaccine conferred high protection against hospital and emergency department admission due to both the delta and omicron variants in the first 3 months after vaccination. However, after 3 months of a third dose, waning was apparent against SARS-CoV-2 outcomes due to the omicron variant, including hospital admission. Although waning was observed, effectiveness of two and three doses against hospital admission was generally higher than that seen for the less severe endpoint of emergency department admission across all timepoints. Previous reports have shown that T-cell immunity has a role in the prevention of severe SARS-CoV-2 infection. Since this was an observational study, there might be residual confounders driven by differences in the likelihood of exposure to SARS-CoV-2 between vaccinated and unvaccinated individuals. Although investigators attempted to control for previous SARS-CoV-2 infection, they were not able to assess previous infections among those who do not seek testing at KPSC. If undocumented previous infection was more likely in unvaccinated individuals, for example, this could contribute to underestimation of vaccine effectiveness, which might be more likely in the omicron era. As we have seen some emergency department or hospital admissions were “with COVID-19” rather than “for COVID-19.” This could lead to spurious findings of waning against severe outcomes if in fact vaccine breakthroughs were only incidental infections among patients admitted to hospital for something other than COVID-19. In the future, additional doses of current, adapted, or novel COVID-19 vaccines might be needed to maintain high protection against severe SARS-CoV-2 infection to reduce future SARS-CoV-2 outbreaks. This study was funded by Pfizer.

A living WHO Guideline on Drugs for Covid-19 BMJ 2020;370:m3379

doi.org/10.1136/bmj.m3379

The WHO update their guidelines to strongly recommends administering nirmatrelvir/ritonavir to patients with non-severe COVID-19 who are at highest risk for hospitalization. Also, WHO issued a conditional recommendation for the use of remdesivir for the same patient population.




Usual supportive care
Strong
Weak
or
Remdesivir
Weak
Strong
Patients with non-severe covid-19
We suggest treatment with remdesivir, for those at highest risk of hospital admission
Conditions for use of treatment
The panel recommended that remdesivir should be reserved for those at a risk above 10% of being admitted to hospital with covid-19
Typical characteristics of people at high risk include:
Lack of vaccination
Immunodeficiency
Older people
Chronic diseases
Evidence profile | Remdesivir | Patients with non-severe covid-19
Favours supportive care
No important difference
Favours remdesivir
Events per 1000 people
Evidence quality
Mortality 6 2 fewer 4 Low
Mechanical ventilation 8 5 fewer 3 Very low
Admission to hospital (risk in trials) 35 26 fewer 9 Moderate
Admission to hospital (higher risk) 60 44 fewer 16 Moderate
Admission to hospital (highest risk) 100 73 fewer 27 Moderate
Serious adverse events 0 No important difference 9 Moderate
Days (mean)
Evidence quality
Time to symptom resolution 9.0 No important difference 7.2 Very low
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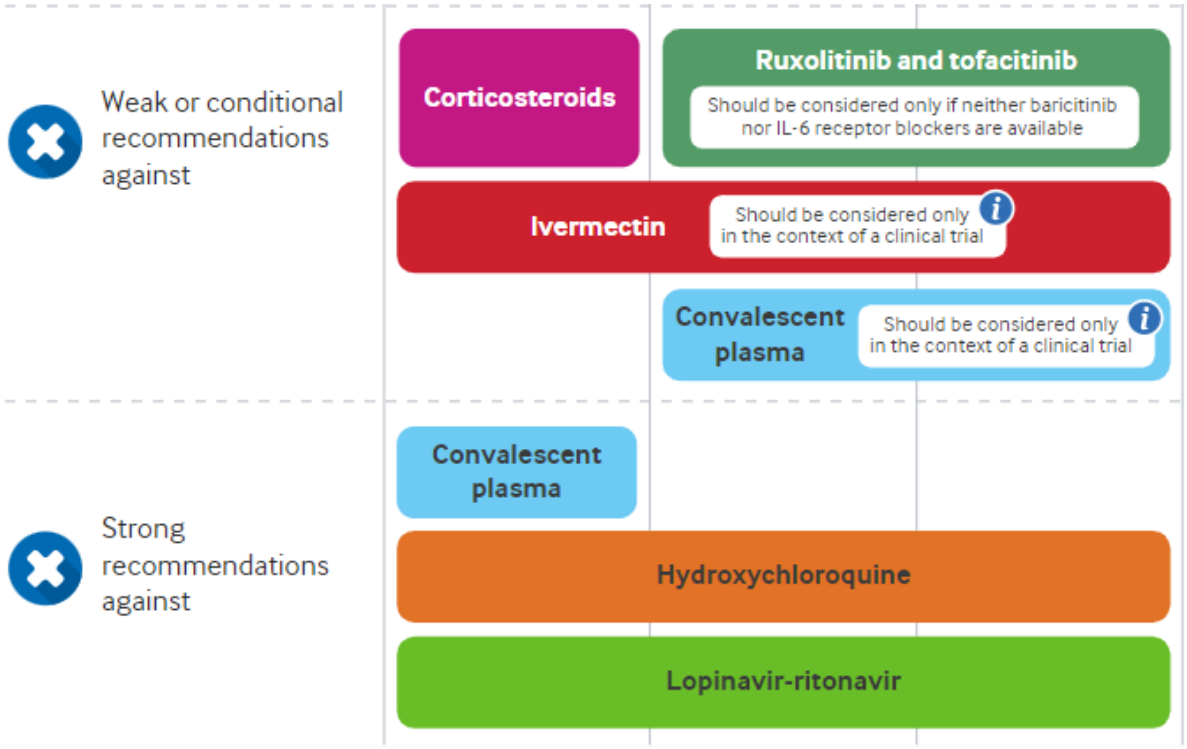
Suggested regimen
Remdesivir
200 mg
Intravenous
On the first day
Then
Remdesivir
100 mg
Intravenous
Daily for 3 days
Key practical issues
Administration via intravenous infusion
Optimal timing, duration and dosing remain unclear
Not a significant inducer or inhibitor of CYP enzymes but should be monitored when co-administrated with strong inducers or inhibitors
May be relatively costly, and there may be limited availability
Values and preferences
The panel inferred that almost all well informed patients with a low risk of hospital admission would decline remdesivir, and only those at highest risk would choose to receive treatment.
See an interactive version of this graphic online
https://bit.ly/BMJrrcovid


Population
This recommendation applies only to people with these characteristics:
Patients with confirmed covid-19
Disease severity
Non-severe
Severe
Critical
Absence of signs of severe or critical disease
Oxygen saturation <90% on room air
Signs of pneumonia
Signs of severe respiratory distress
Requires life sustaining treatment
Acute respiratory distress syndrome
Sepsis
Septic shock
Interventions
Strong recommendations in favour
Corticosteroids
IL-6 receptor blockers
or
Baricitinib
Depending on availability as well as clinical and contextual factors
Nirmatrelvir and ritonavir
Weak or conditional recommendations in favour
Molnupiravir
Mitigation strategies to reduce potential harms should be implemented
Sotrovimab
Remdesivir
For those with highest risk of hospital admission
Casirivimab and imdevimab
Evidence of limited efficacy against Omicron BA1 variant
Casirivimab and imdevimab
For those with seronegative status for SARS-CoV-2 antibodies
Use the interactive multiple comparison tool to compare and choose treatments
MATCH-IT



Hospitalizations of Children Aged 5–11 Years with Laboratory-Confirmed COVID-19 — COVID-NET, 14 States, March 2020–February 2022 MMWR April 22, 2022

The investigators describe characteristics of COVID-19–associated hospitalizations among 1,475 U.S. children aged 5–11 years throughout the pandemic, focusing on the period of early Omicron predominance (December 19, 2021–February 28, 2022). Among 397 children hospitalized during the Omicron-predominant period, 87% were unvaccinated, 30% had no underlying medical conditions, and 19% were admitted to an intensive care unit. The cumulative hospitalization rate during the Omicron-predominant period was 2.1 times as high among unvaccinated children (19.1 per 100,000 population) as among vaccinated children

Comment: Consistent with other studies, this analysis demonstrated that the Omicron-predominant period was associated with less severe disease among hospitalized children. However, both population-based peak hospitalization and ICU admission rates were higher during the Omicron-predominant period compared with those during the Delta-predominant period, likely because of the high Rt of the Omicron variant which led to a greater number of persons infected. This study found that some underlying medical conditions, including asthma and immunocompromising conditions, were not associated with increased risk for severe COVID-19. This analysis based on vaccination status may be biased toward the null because partially vaccinated children were grouped with unvaccinated children. In addition, primary reason for admission was not always clear, and medical charts might not completely capture underlying conditions, potentially resulting in misclassification. Finally, COVID-NET catchment areas include approximately 10% of the U.S. population; thus, these findings which may not be generalizable to the rest of the US.

Comparison of Home Antigen Testing With RT-PCR and Viral Culture During the Course of SARS-CoV-2 Infection JAMA Intern Med published online April 29, 2022

doi:10.1001/jamainternmed.2022.1827

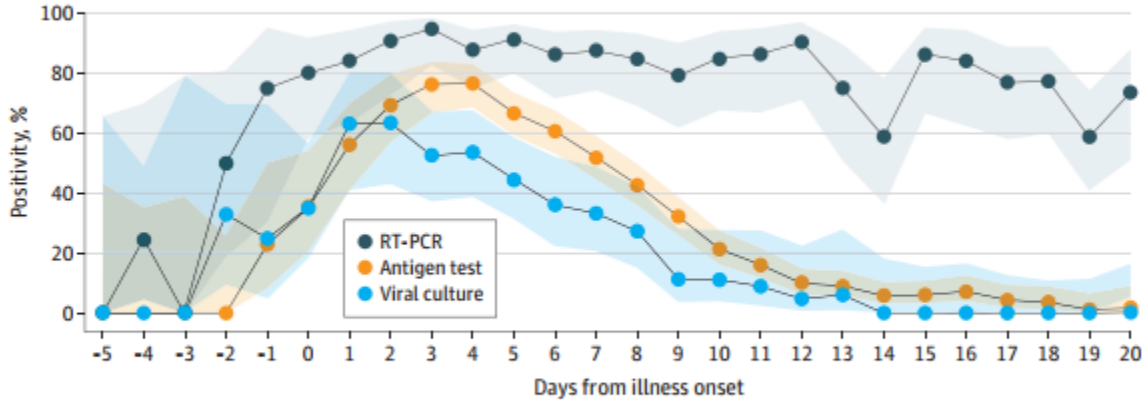
The study, led by the CDC COVID-19 Response Team, studied test sensitivity in 225 adults and children from 107 households who tested positive for COVID-19 in San Diego County, California, and metropolitan Denver from January to May 2021.

Participants used antigen tests for 15 days and had at least one same-day PCR test and viral culture. A total of 3,044 antigen tests and 642 PCR tests were performed. Average participant age was 29 years, 52% were female, and 91% had COVID-19 symptoms.

Antigen tests were less sensitive than PCR, but more sensitive than viral culture. During the first few days of illness, antigen test sensitivity was 50% (95% confidence interval [CI], 45% to 55%). Overall antigen test sensitivity was 64% (95% CI, 56% to 70%) and 84% (95% CI, 75% to 90%) compared to PCR and viral culture, respectively.

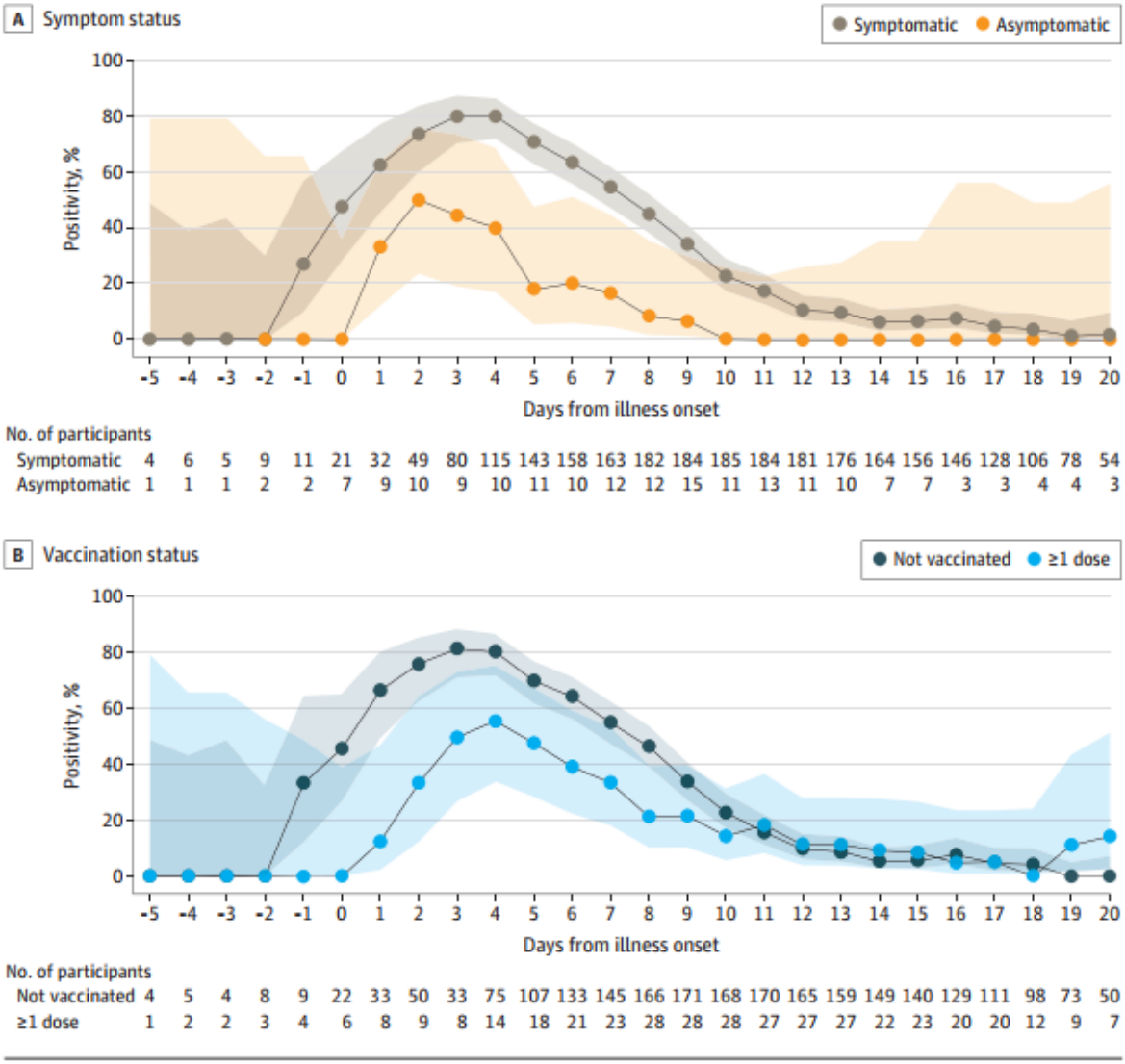
Sensitivity of the antigen tests peaked at 77% (95% CI, 69% to 83%) 4 days after symptom onset and was 81% to 85% on a second test 1 or 2 days later. PCR positivity peaked at 95% 3 days after illness onset, while viral cultures peaked at 64% on day 2. Six days after symptom onset, antigen test positivity was 61% (95% CI, 53% to 68%), falling to less than 20% by day 11.

Figure 1. Daily Percentage of Positive SARS-CoV-2 Tests in Participants With Reverse Transcription–Polymerase Chain Reaction (RT-PCR)–Confirmed Infection



No. of participants																									
RT-PCR	2	4	1	6	4	20	19	22	38	41	47	36	40	33	29	27	22	21	16	17	22	19	26	31	29	19
Antigen test	5	7	6	11	13	28	41	59	89	125	154	168	175	194	199	196	197	192	186	171	163	149	131	110	82	57
Viral culture	2	4	1	6	4	20	19	22	38	41	47	36	39	33	27	27	22	21	16	17	21	19	26	31	29	19

Figure 2. Daily Percentage of Positive Home Antigen Tests by Symptom Status and Vaccination Status



Comment: The investigators noted that antigen test performance may differ in vaccinated and unvaccinated people and among infections with different SARS-CoV-2 variants. Most participants were symptomatic and household contacts of a known COVID-19 case. Therefore, results may not be generalizable for use of home antigen tests to screen individuals who are asymptomatic or without a known exposure to SARS-CoV-2. Almost all symptomatic cases experienced mild disease, so diagnostic performance for severe disease could not be assessed. Not all specimens were sent for culture; some specimens that were assumed to be culture negative based on Ct values and prior studies may have been misclassified. Regardless, the findings, could help clarify the recommended length of isolation after COVID-19 diagnosis.

Daily longitudinal sampling of SARS-CoV-2 infection reveals substantial heterogeneity in infectiousness Nat Microbiol 2022; 7: 640–652

doi.org/10.1038/s41564-022-01105-z

Led by scientists from the Los Alamos National Laboratory and the University of Illinois, the study tracked daily SARS-CoV-2 viral loads in university staff and students' saliva and nose starting within 24 hours of diagnosis for up to 14 days early in the pandemic.

The team used rapid antigen COVID-19 tests, polymerase chain reaction (PCR) tests, and viral culture to determine loads of live (infectious) SARS-CoV-2 and noninfectious viral RNA. The researchers used mathematical models to estimate viral replication and clearance rates and overall infectiousness for each participant. Participants had a median age of 28 years and were primarily White; none had been vaccinated against COVID-19, because vaccines weren't available at that time

Some participants shed live SARS-CoV-2 for only a day or two, while others did so for up to 9 days. Based on that finding, they predicted that those people who are shedding virus for more than a week are going to be a much greater risk of transmission than someone who only has live virus detectable for a day or two.

Viral loads often peaked in saliva days before they did so in nasal swabs, which the researchers said indicates that saliva may be the better sample for early COVID-19 diagnosis. The Alpha variant's viral loads and clearance dynamics didn't differ significantly from those of previous strains, which the study authors said suggests that higher viral loads or delayed clearance cannot alone explain Alpha's higher transmissibility in relation to the wild-type virus.

When the researchers integrated the area under the infectious virus load curve over the course of disease to estimate infectiousness, they found a broad range of individual infectiousness, with a greater than 57-fold difference between the most and least infectious.

Comment: Daily infectious SARS-CoV-2 virus shedding varied substantially among 60 newly diagnosed asymptomatic or mildly ill COVID-19 patients early in the pandemic, suggesting that individual differences in viral dynamics may account for "superspreading," according to a first-of-its-kind modeling study.