Infectious Diseases Watch

January 10, 2022

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General Infectious Diseases

Rapid Assessment and Containment of Candida auris Transmission in Postacute Care Settings—Orange County, California, 2019 Ann Intern Med 2021;174:1554-62

doi:10.7326/M21-2013

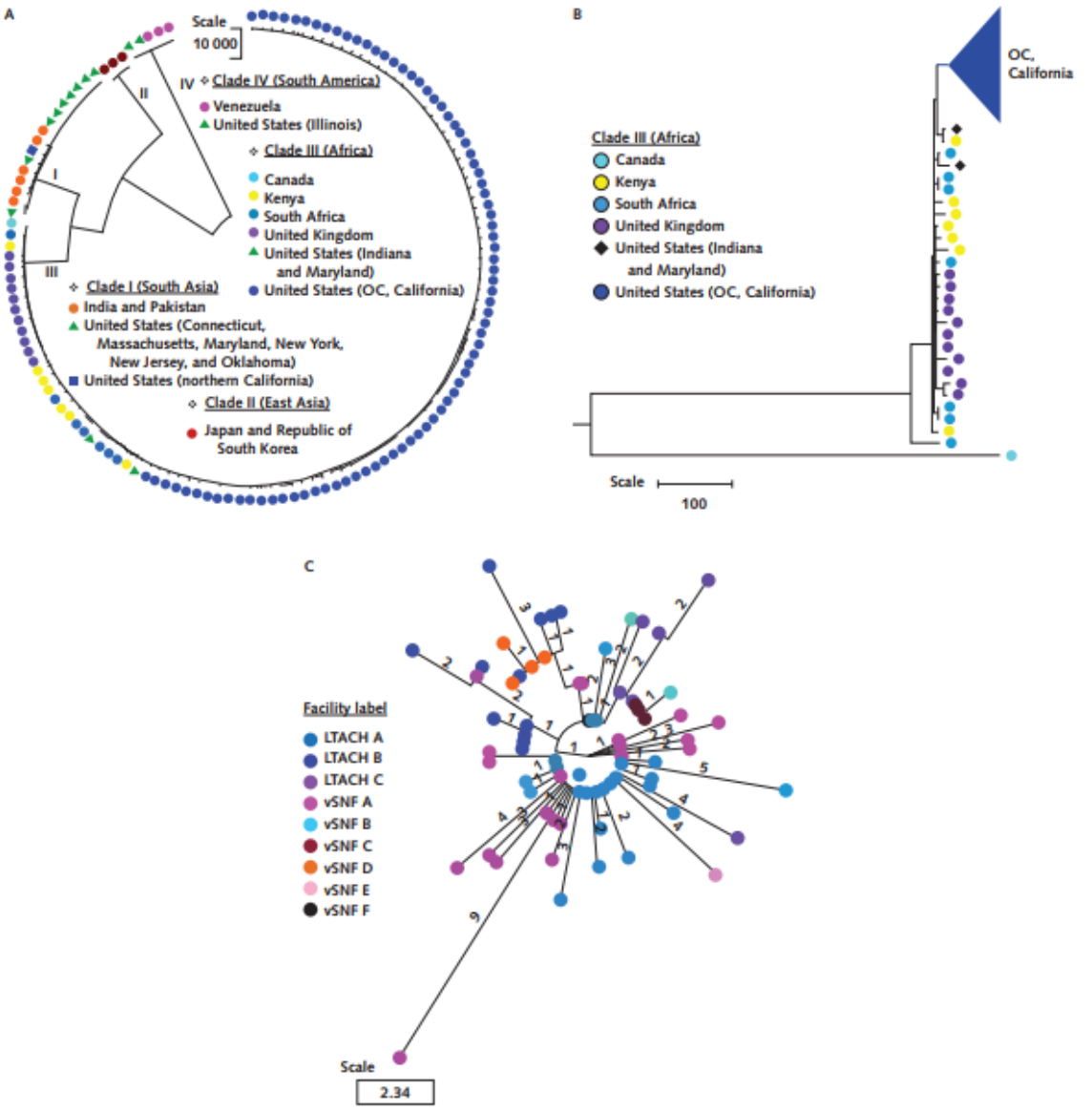
In 2018, a laboratory serving LTACHs in southern California began identifying species of Candida that were detected in urine specimens to enhance surveillance of C auris. C auris was identified in February 2019 in a patient in an Orange County LTACH. Further investigation identified C auris at 3 additional facilities.

Point prevalence surveys (PPSs), post discharge testing for C auris detection, and assessments of infection control were done from March to October 2019. In facilities where C auris was detected, PPSs were repeated every 2 weeks. Antifungal susceptibility testing and whole genome sequencing were performed to assess isolate relatedness. Initial PPSs involved collecting both axilla–groin and nasal screening swabs from all patients without known C auris who were residing in the facility, including new admissions. Any facility with a PPS that identified 1 or more new C auris screening cases had subsequent PPSs performed every 2 weeks with axilla–groin screening swab to detect new C auris positivity among patients with a previously negative result or among patients who were newly admitted.

Initial PPSs at 17 facilities identified 44 additional patients with C auris in 3 (100%) LTACHs and 6 (43%) SNFs, with the first BSI reported in May 2019. By October 2019, a total of 182 patients with C auris were identified by serial PPSs and discharge testing. Of 81 isolates that were sequenced, all were clade III and highly related. Assessments of infection prevention practices identified gaps in hand hygiene, transmission-based precautions, and environmental cleaning. The outbreak was contained to 2 facilities by October 2019. Surveillance showed that only 1 of 44 patient colonization events was identified by nasal swabbing. Limiting screening to a single combined axilla–groin swab may be the more cost-effective and efficient.

A total of 137 Orange County isolates that were tested. All were azole resistant and echinocandin susceptible. Amphotericin B resistance testing, done on 136 of these isolates, identified that 10 (7.4%) were resistant.

Figure 2. Whole-genome sequencing results of *Candida auris* isolates, OC, California, 2019.



Comment: After C auris was detected in 4 facilities in Orange County, the authors conducted repeated point prevalence surveys and comprehensive assessment of infection prevention practices and provided support for all LTACHs and SNFs. This enhanced surveillance method allowed them to gauge the extent of C auris burden 3 months before the first positive clinical culture result was found. By that time, outbreak containment was already well under way, resulting in the reduced mortality and morbidity. Since most patients in SNFs and LTACHs are confined to their beds, this limited direct patient-to-patient transmission. However, acquisition can occur from the environment or health care personnel and visitors, or also from previous acute care stays. Two of the study facilities still had ongoing, but greatly reduced, transmission of C auris despite an effective intervention and dramatic improvement of adherence to infection prevention measures. Access to whole-genome sequencing and accurate resistance testing is also critical in understanding the epidemiology of C auris outbreaks, and in the case of the current study, it showed a close relationship between all isolated strains. The investigators

postulated that this outbreak likely resulted from a single introduction to the region followed by undetected transmission in local facilities before the first case was identified through enhanced laboratory surveillance. All investigation isolates from Orange County were clonal and differed by fewer than 11 SNPs. Although the outbreak was controlled during this investigation, with sustained containment through December 2019, C auris screening and clinical cases increased in Orange County and surrounding areas in southern California during the COVID-19 pandemic. This study serves as a warning of how much of an effort is needed to contain transmission of C auris in these settings and of why prevention and early intervention are by far the preferred goal in containing this difficult pathogen. Acute care hospitals were not assessed.

Optimizing the Management of Uncomplicated Gram-negative Bloodstream Infections: Consensus Guidance Using a Modified Delphi Process OFID October 2021 Highlights

https://academic.oup.com/ofid/article/8/10/ofab434/6355731

Literature on the recommended durations of antibiotic therapy, the use of oral antibiotic therapy, and the need for repeat blood cultures remain limited for gram-negative bloodstream infections (GN-BSI). The authors convened a panel of infectious diseases specialists to develop a consensus definition of uncomplicated gram-negative bloodstream infections to guide clinicians with management decisions.

13 infectious diseases specialists (7 physicians and 6 pharmacists) from across the United States participated in the consensus process (Delphi Process).

Uncomplicated gram-negative bloodstream infections are defined as the following (the panel suggests all 4 conditions must be met):

1. Bloodstream infection confirmed to be secondary to 1 of the following sources
    a. Urinary tract infection
    b. Intra-abdominal or biliary infections
    c. Catheter-related bloodstream infection
    d. Pneumonia (without structural lung disease, empyema/abscess, cystic fibrosis)
    e. Skin and soft tissue infection
2. Source control (i.e., removal of any infected hardware, catheters, or devices and near complete drainage of infected fluid collections, as well as imaging assurance [as needed] of no residual or metastatic sites of infection)
3. Patients *without* immunocompromise and risk for opportunistic infections (e.g., recent solid organ transplant recipients; expected prolonged neutropenia with ANC <500 cells/mL during the GN-BSI treatment course; recent CD4 cell count <200 cells/mL; chronic corticosteroids and/or immunomodulator therapy); select immunocompromised patients such as those on stable immunomodulatory therapy may be considered on a case-by-case basis
4. Clinical improvement within 72 hours of effective antibiotic treatment—at a minimum includes defervescence and hemodynamic stability

Role of bacterial pathogens and resistance phenotype in defining uncomplicated GN-BSI

Disagreement exists as to whether uncomplicated GN-BSI should be limited to Enterobacterales or also extend to include glucose-nonfermenting gram-negative rods (e.g., *Pseudomonas aeruginosa*). Next was a discussion on the management of GN-BSI with resistance phenotypes such as ESBLs or CRE given very limited data. Ultimately, the consensus was to not distinguish the specific organism (e.g., *E. coli* vs *P. aeruginosa*) or the resistance phenotype in the definition of uncomplicated GN-BSI as management would be based on the day *effective* therapy was initiated, even if that was not the same day that antibiotic therapy was initiated.

Duration of treatment

Patients with uncomplicated GN-BSI, regardless of the gram-negative organism or resistance phenotype, can generally be treated with a 7-day course of effective therapy.

Patients with uncomplicated GN-BSI can be treated with oral antibiotics if all of the following criteria are all met:

1. Clinical improvement observed on effective intravenous therapy
    a. If effective oral therapy was started initially and appropriate clinical response is achieved, oral therapy can continue for the duration of the treatment course
2. Underlying source is confirmed
3. Susceptibility testing confirms that oral antibiotic options are available
4. The patient has an intact and functional gastrointestinal tract

Repeat blood cultures

Repeat blood cultures to document clearance are generally not necessary in uncomplicated gram-negative bloodstream infections except:

1. Patients without an appropriate clinical response within 72 hours
2. Patients with clinical concern for an endovascular infection or endocarditis
3. Situations where there is limited or no source control

Comment: I found this publication to be very useful. The authors point out and I agree that the translation of evidence in practice is frequently delayed especially if there are no professional society guidelines. In the absence of professional guidelines for the management of uncomplicated GN-BSI, the use of a Delphi approach can be useful in developing interim recommendations. Further research will be needed to evaluate the association made by the panel and clinical outcomes, particularly related to immunocompromised patients, infections with gram-negative organisms other than Enterobacterales, and the role of oral beta-lactam therapy.

COVID-19

FDA Action

The FDA authorized Pfizer's COVID-19 booster shots for 12- to 15-year-olds.

The FDA also shortened the length of time between the completion of a primary vaccination series and receiving a Pfizer booster dose from six months to five months for everyone 12 and older and authorized a third dose for certain immunocompromised children 5 to 11, such as solid organ transplant recipients. FDA just updated the EUA for Moderna's COVID-19 vaccine, allowing for a 5-month interval between the second primary series' dose and a booster.

Comment: Nearly 66 percent of Americans 5 and older had been fully vaccinated as of January 5th. Meanwhile, only about 36 percent of adults 18 and older had received their booster and 25% of children aged 5-11 have been fully vaccinated. Only 53% of teenagers are vaccinated. I again raise the issue on the role of prior infection as an important factor that still has not been addressed by the CDC. I cannot understand why at this point in the pandemic we do not have enough information that could guide recommendations. The Pfizer vaccine is the only vaccine approved for use in children in the United States. Also, all the discussion around booster is a distraction. I think Paul Offit said it best: "This is a disease of the unvaccinated and I just think that boosting is largely a detour that is not going to have a big impact on this pandemic. I just feel like we've given up on the unvaccinated."

The National Institutes of Health (NIH) COVID-19 Treatment Panel has released recommendations that include an order of preference for which therapeutics to use to treat nonhospitalized patients with mild to moderate COVID-19 who are at high risk of severe disease progression. January 5, 2022

The panel recommendations include therapeutics in the following order of preference:

- Nirmatrelvir with ritonavir (Paxlovid)
    - Nirmatrelvir is an orally bioavailable protease inhibitor that is active against M^{PRO}, a viral protease that plays an essential role in viral replication by cleaving the 2 viral polyproteins. It has demonstrated antiviral activity against all coronaviruses that are known to infect humans. Nirmatrelvir is packaged with ritonavir (as Paxlovid), a strong cytochrome P450 (CYP) 3A4 inhibitor and pharmacokinetic boosting agent. Ritonavir is required to increase nirmatrelvir concentrations to the target therapeutic ranges.
    - Nirmatrelvir 300 mg with ritonavir 100 mg (Paxlovid) orally twice daily for 5 days, initiated as soon as possible and within 5 days of symptom onset in those aged ≥12 years and weighing ≥40 kg **(Alla).** The dose should be reduced to nirmatrelvir 150 mg and ritonavir 100 mg twice daily in patients with moderate renal impairment (i.e., those with an estimated glomerular filtration rate [eGFR] of ≥30 to <60 mL/min). Ritonavir-boosted nirmatrelvir (Paxlovid) **is not**

recommended in patients with an eGFR of <30 mL/min until more data are available.
    - Ritonavir-boosted nirmatrelvir (Paxlovid) has significant and complex drug-drug interactions, primarily due to the ritonavir component of the combination.
- Sotrovimab.
    - sotrovimab is the only available anti-SARS-CoV-2 MCA that has activity against the Omicron variant
    - Sotrovimab 500 mg as a single IV infusion, administered as soon as possible and within 10 days of symptom onset in those aged ≥12 years and weighing ≥40 kg who live in areas with a high prevalence of the Omicron VOC **(AIIa)**.
- Remdesivir
    - Remdesivir 200 mg IV on Day 1, followed by remdesivir 100 mg IV daily on Days 2 and 3, initiated as soon as possible and within 7 days of symptom onset in those aged ≥12 years and weighing ≥40 kg **(BIIa)**.
    - Because remdesivir requires IV infusion for 3 consecutive days, there may be logistical constraints to administering remdesivir in many settings.
- Molnupiravir.
    - Molnupiravir 800 mg orally twice daily for 5 days, initiated as soon as possible and within 5 days of symptom onset in those aged ≥18 years **ONLY** when none of the above options can be used **(CIIa)**.
    - The FDA EUA states that molnupiravir is not recommended for use in pregnant patients due to concerns about the instances of fetal toxicity observed during animal studies.

Comment: Clearly Sotrovimab and Paxlovid are the preferred therapeutics for early treatment of patients at high risk for progression to severe disease. The challenge is supply. (See comments below)

NIH: The COVID-19 Treatment Guidelines Panel's Statement on Tixagevimab Plus Cilgavimab (Evusheld) for Pre-Exposure Prophylaxis for SARS-CoV-2 Infection

January 5, 2022

The COVID-19 Treatment Guidelines Panel recommends using tixagevimab plus cilgavimab as SARS-CoV-2 PrEP for adults and adolescents (aged ≥12 years and weighing ≥40 kg) who do not have SARS-CoV-2 infection, who have not been recently exposed to an individual with SARS-CoV-2 infection, AND who:

- Are moderately to severely immunocompromised and may have an inadequate immune response to COVID-19 vaccination **(BIIa)**; *or*
- Are not able to be fully vaccinated with any available COVID-19 vaccines due to a documented history of severe adverse reactions to a COVID-19 vaccine or any of its components **(AIIa)**.

If supplies of tixagevimab plus cilgavimab are limited, priority should be given to those who are at the highest risk for severe COVID-19.

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

Comment: As we enter year 3 of the pandemic, we now have more tools, but some new lifesaving therapeutics are in limited supply. We are being forced in a position of deciding which patients will get these treatments and who will not. We are all rushing to develop algorithms to help allocate limited therapeutics for sotrovimab and Paxlovid. The updated NIH Guidelines now include priorities for pre-exposure prophylaxis tixagevimab plus cilgavimab for patients at highest risk for severe disease. (See above) It is very frustrating that as physicians we cannot provide optimal care to all of our patients due to limited lifesaving treatments and testing. We need an operation warp speed for therapeutics.

CDC: Definition of fully vaccinated 'is not changing' January 5, 2022

CDC says it has no plans to require a booster shot for people to be considered fully vaccinated against COVID-19. Individuals are considered fully vaccinated against COVID-19 if they've received their primary series. That definition is not changing instead the language will ask persons to stay “up to date” on their Covid-19 vaccinations.

Israel Preliminary Data Second Booster (Fourth Shot)

Researchers from Israel reported promising preliminary findings from a study on fourth COVID-19 vaccine shots, which suggest the second booster produces a fivefold increase in antibody levels. Researchers had recently released preliminary findings on safety, noting that the side effect profile was similar to that of third doses. Recent data from Israel indicated significant waning in protection as soon as 3 months after the third COVID-19 vaccine dose!

Comment: I think we need to look at vaccinations differently. We have known that neutralizing antibodies do wane over time, but we also know that T-cell and B-cell memory lasts much longer and does protect against severe disease and death against all variants. This memory stays intact after just two doses. I agree with Paul Offit. (See above)

Overview of COVID-19 Isolation for K-12 Schools January 6, 2022

Overview of COVID-19 Quarantine for K-12 School January 6, 2022

Those who are infected or have symptoms of Covid-19 must isolate regardless of vaccination status. Students, teachers and staff can end isolation after five days after their initial positive test or the onset of symptoms (Day 0), or if they are fever-free for 24 hours without using fever-reducing medication and their symptoms have improved. The CDC said people should continue to wear a well-fitting mask around others at home and in public for five more days after the end of the initial five-day isolation period.

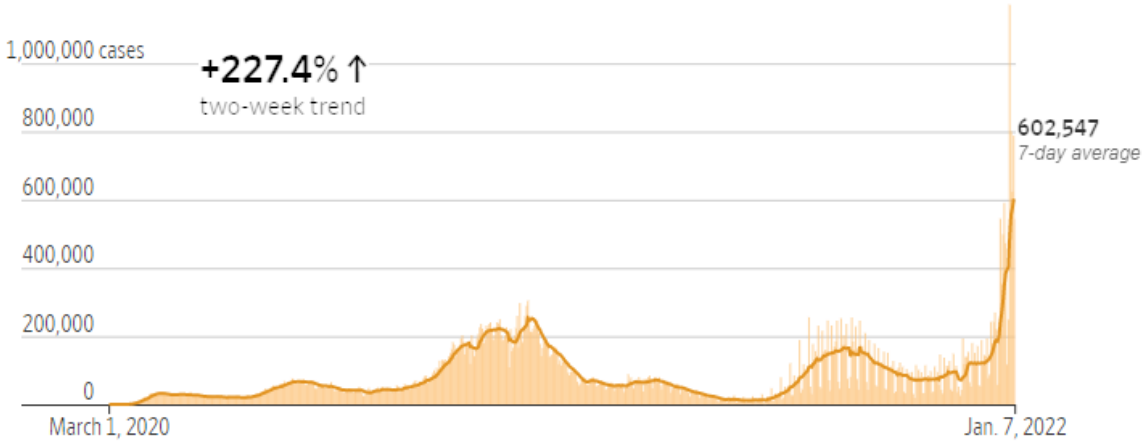
Students, teachers and staff 18 years or older who have been in close contact with someone with Covid-19 should quarantine for at least five days if they haven't been boosted or had a recently confirmed infection. If they do not develop symptoms, get tested at least 5 days after they last had close contact with someone with COVID-19. If they test negative, they can leave home, but continue to wear a well-fitting mask when around others at home and in public until 10 days after their last close contact with someone with COVID-19 People who are 18 or older who are fully vaccinated, including boosters; those who are 5-17 years old who are fully vaccinated; and those who have had confirmed Covid-19 within the last 90 days don't need to quarantine after an exposure.

Comment: This is similar to general public guidance, but the question is, why were they not released BEFORE school started. I have same concerns about not testing infected people at 5 days before ending isolation.

COVID-19 By the Numbers

Daily reported Covid-19 cases in the U.S.

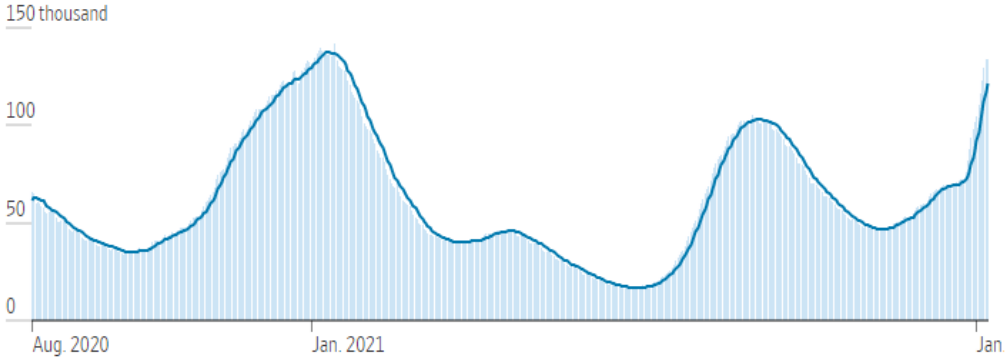
— Seven-day rolling average



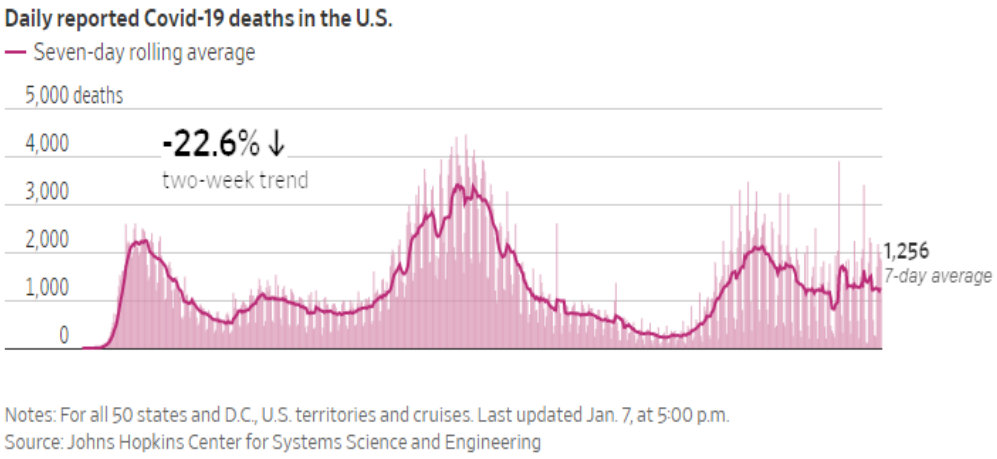
Note: For all 50 states and D.C., U.S. territories and cruises. Last updated Jan. 7, at 5:00 p.m.
Source: Johns Hopkins Center for Systems Science and Engineering

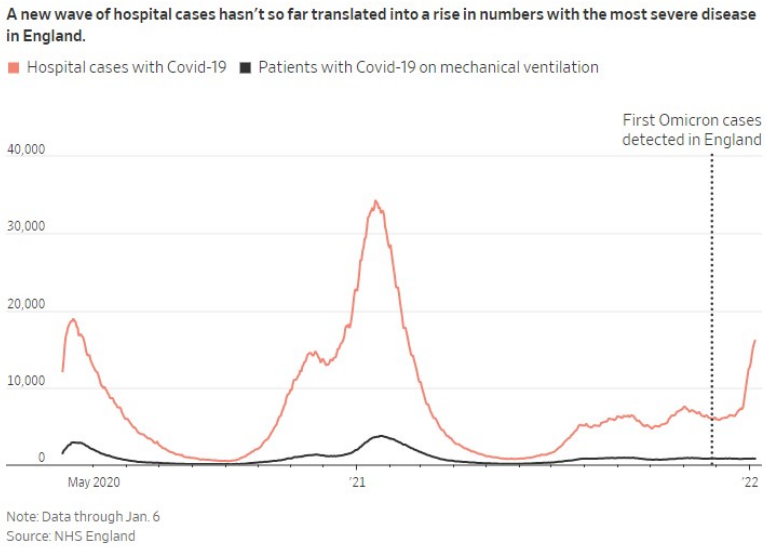
Number of Covid-19 patients hospitalized in the U.S.

■ Seven-day rolling average



Note: Last updated Jan. 7
Source: U.S. Department of Health & Human Services





Comment:

First a word about children. The number of hospitalized young children infected with SARS-Cv-2 rose precipitously last week to the highest levels since the beginning of the pandemic. The increase was observed in children who were 4 and younger, who are not eligible for vaccination, and the data included children who were admitted to hospitals for reasons other than Covid. But the data do not show a similar steep rise in SARS-CoV-2 infections among hospitalized children of other ages. More than four in 100,000 children ages 4 and younger admitted to hospitals were infected with the coronavirus as of Jan. 1 — double the rate reported a month ago and about three times the rate this time last year. By contrast, the rate of hospitalized 5- to 11-year-

olds with Covid-19 was 0.6 per 100,000, roughly the same figure reported over past many months. Officials were considering the possibility that Omicron may not be as mild in young children as it is older children. Children infected with the variant are still at much less risk of becoming severely ill compared with adults, and even young children seem less likely to need ventilators than those admitted during previous surges. Another challenge is only 16 percent of children from 5 to 11 had been fully vaccinated Fewer than 25 percent of children from 5 to 11, and just over 60 percent of adolescents from 12 to 17, have received at least one dose let alone a booster. (see article below on vaccine protection against MIC-S below)

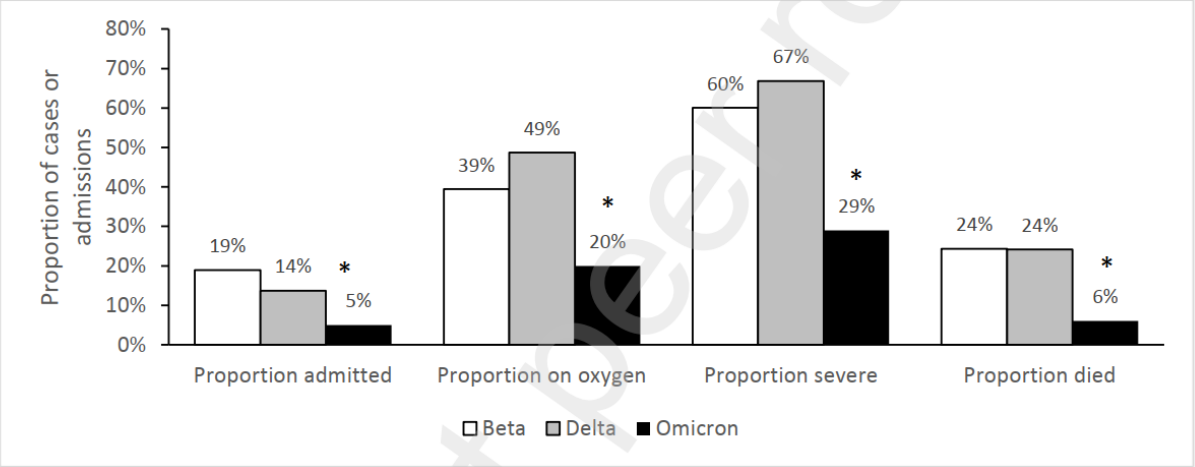
More and more public health officials are shifting to hospitalization, ICU admissions, and deaths as more meaningful measures. With Omicron we are beginning to learn that not only does it appears milder but looking at hospitalization may be misleading since over 50% of COVID-19 hospitalizations are not due to COVID-19 or related symptoms. To have a meaningful measure we need to count only admissions for COVID-19 symptoms which at present is not readily available. Lastly based on graphs above, we are seeing fewer ICU admissions and deaths with Omicron in the US. I also included the graph from the UK which uses mechanical ventilation as an indicator of severity. Below I share an article from South Africa under review showing the same pattern including a much lower mortality rate with Omicron compared to other variants.

COVID-19 Journal Review

Clinical severity of COVID-19 patients admitted to hospitals in Gauteng, South Africa during the Omicron-dominant fourth wave Lancet submission January 2022

The investigators described the clinical severity of patients hospitalized with SARS-CoV-2 infection during the first four weeks of the Omicron-dominated fourth wave and compare this to the fist 4 weeks of the beta and delta waves.

There were 41,046, 33,423, and 133,551 SARS-CoV-2 cases in the second, third and fourth waves respectively. About 4.9% of cases were admitted to hospital during the fourth wave compared to 18.9% and 13.7% during the second and third waves ($p<0.001$). During the fourth wave, 28.8% of admissions were severe disease compared to 60% and 67% in the beta and delta waves ($p<0.001$). Admitted patients in the Omicron wave were 73% less likely to have severe disease than patient admitted during the delta wave. [aOR 0.27 CI 0.25-0.31]



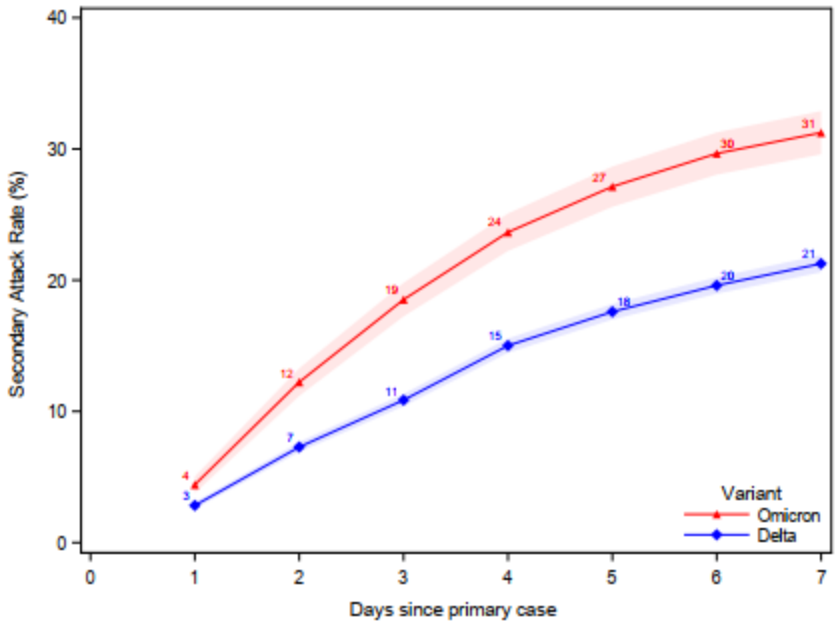
Comment: The proportion of cases admitted were less severe during the first four weeks of the Omicron wave in South Africa. This is probably multifactorial: a less-virulent virus, higher immunity from prior infection(s) and/or vaccination may be important contributors. To date, this experience is similar to the UK experience and the early US experience. (see above)

SARS-CoV-2 Omicron VOC Transmission in Danish Households medRxiv published online December 27, 2021

doi.org/10.1101/2021.12.27.21268278

Investigators analyzed transmission data collected from nearly 12,000 infected households in Denmark, including 2,225 households with an Omicron infection. Overall, there were 6,397 secondary infections in the week after the first infection in the house.

After accounting for other risk factors. comparing households infected with the Omicron to Delta, they found a 1.17 (95%-CI: 0.99-1.38) times higher secondary attack rate (SAR) for unvaccinated, 2.61 times (95%-CI: 2.34-2.90) higher for fully vaccinated and 3.66 (95%-CI: 2.65-5.05) times higher for booster-vaccinated individuals, demonstrating strong evidence of immune evasiveness of the Omicron. Booster-vaccinated people were nearly 3.7 times more likely to get infected in the Omicron households than in the Delta households. Looking only at Omicron households, however, booster-vaccinated people were 56% less likely to become infected compared to vaccinated people who had not received a booster.



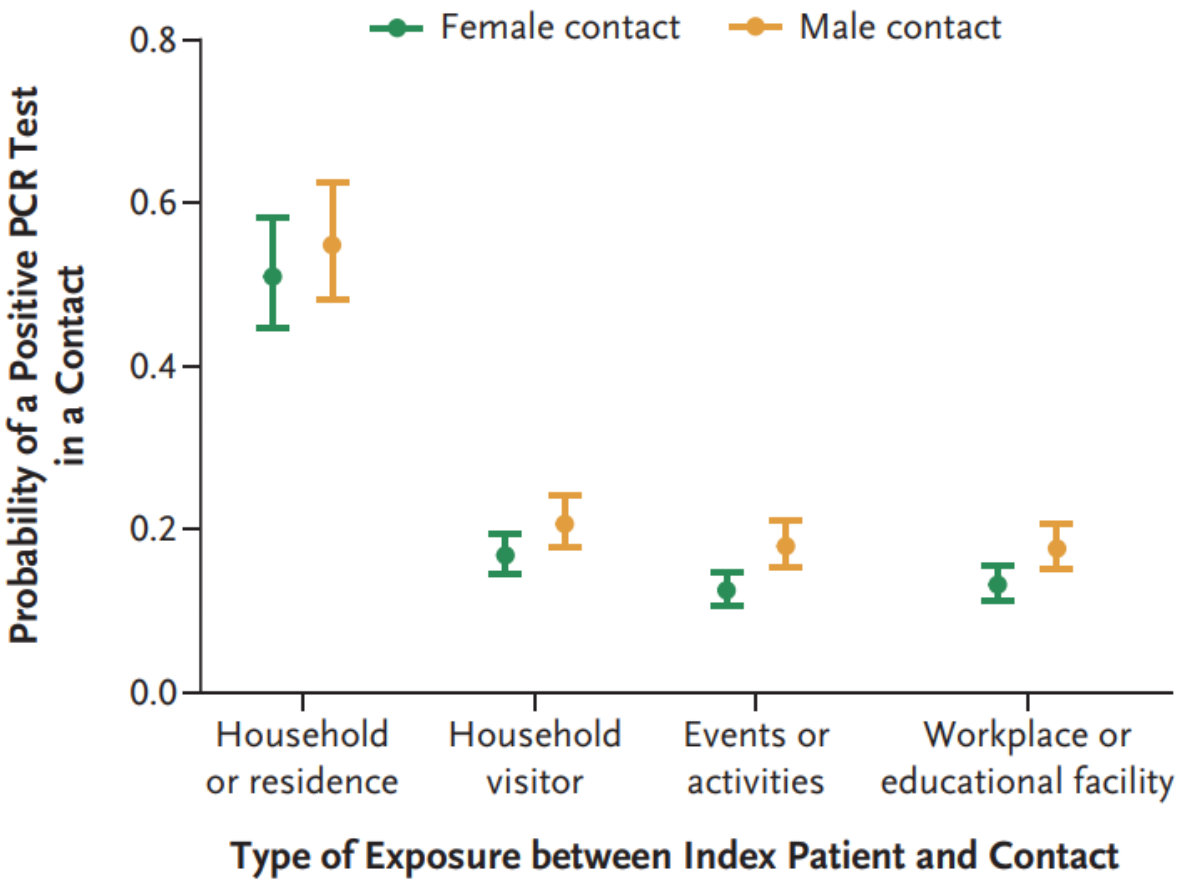
Comment: The odds that vaccinated people will catch the virus if a household member becomes infected are nearly three to four times higher with Omicron than with Delta, but booster doses did reduce that risk. These findings confirm that the rapid spread of the Omicron is partly due to the immune evasiveness and increase in the basic transmissibility. See next article

Effect of Covid-19 Vaccination on Transmission of Alpha and Delta Variants N Engl J Med published online January 5, 2022

DOI: 10.1056/NEJMoa2116597

The investigators used contact-testing data from England to perform a retrospective observational cohort study involving adult contacts of SARS-CoV-2–infected adult index patients. They used multivariable Poisson regression to investigate associations between transmission and the vaccination status of index patients and contacts and to determine how these associations varied with the alpha and delta variants and time since the second vaccination.

They found that both the Pfizer and AZ vaccines were associated with reduced onward transmission of SARS-CoV-2 from index patients who became infected despite vaccination. However, in index patients who were vaccinated with Pfizer and probably in those who were vaccinated with AZ, reductions in transmission of the delta variant were smaller than reductions in transmission of the alpha variant. In population-based studies, vaccines have continued to provide protection against infection with the delta variant, but to a lesser degree than against infection with the alpha variant. Vaccination was associated with higher Ct values (lower viral loads) of the alpha variant and, to a smaller extent, with higher Ct values of the delta variant. Higher Ct values were associated with less transmission.



Comment: Ct values at diagnosis are probably imperfectly representative of viral loads at transmission, despite the relationship observed between Ct values and transmission, because viral loads are dynamic over time. Vaccination may also act by facilitating faster clearance of viable infectious virions, [Lancet Infect Dis 2021 October 29] but they may leave viral fragments behind that still are PCR +. Studies of this possibility and of how antigen assays perform after vaccination could lead to improvement in diagnostic tests after vaccination. (See next article) In order to minimize bias introduced by differences in testing behavior arising for multiple reasons, including the vaccination status of contacts, they included only contacts who had undergone PCR testing. Therefore, we cannot estimate secondary attack rates according to the vaccination status of patients and contacts, and the absolute protective effects of vaccination on transmission may be underestimated because vaccine-protected, uninfected contacts may not have sought testing. Their approach is also unlikely to eliminate bias, particularly if test-seeking behavior is related to perceived vaccine efficacy, given the nonspecificity of many symptoms of Covid-19

Rapid Diagnostic Testing for SARS-CoV-2 N Engl J Med published online January 7, 2022 summary

DOI: 10.1056/NEJMcp2117115

1. Symptomatic persons should undergo testing as soon as possible, quarantine while awaiting test results, and consider retesting if they have a negative RDT, particularly if they have a high pretest probability of infection
2. Asymptomatic persons with a known exposure to SARS-CoV-2 should undergo testing 5 to 7 days after exposure, and if the RDT is negative, they should undergo testing again 2 days later.
3. Persons with a known exposure to SARS-CoV-2 who are not fully vaccinated should quarantine while awaiting test results, and persons who test positive should isolate, contact a health care provider or public health department, and inform close contacts about the infection.
4. Testing should be considered in asymptomatic persons who have been in a setting where the risk of transmission is high, such as in an airplane or at a sporting event
5. Molecular NAATs detect the presence of viral gene targets, including the *N*, *S*, and *E* genes and the open reading frame 1ab *(ORF 1ab)*
6. Antigen-based tests, also called immunoassays, detect domains of the surface proteins, including the nucleocapsid, spike, and receptor binding domains, that are specific to SARS-CoV-2.
7. NAATs are generally more sensitive than antigen-based tests because they amplify target genomic sequences.

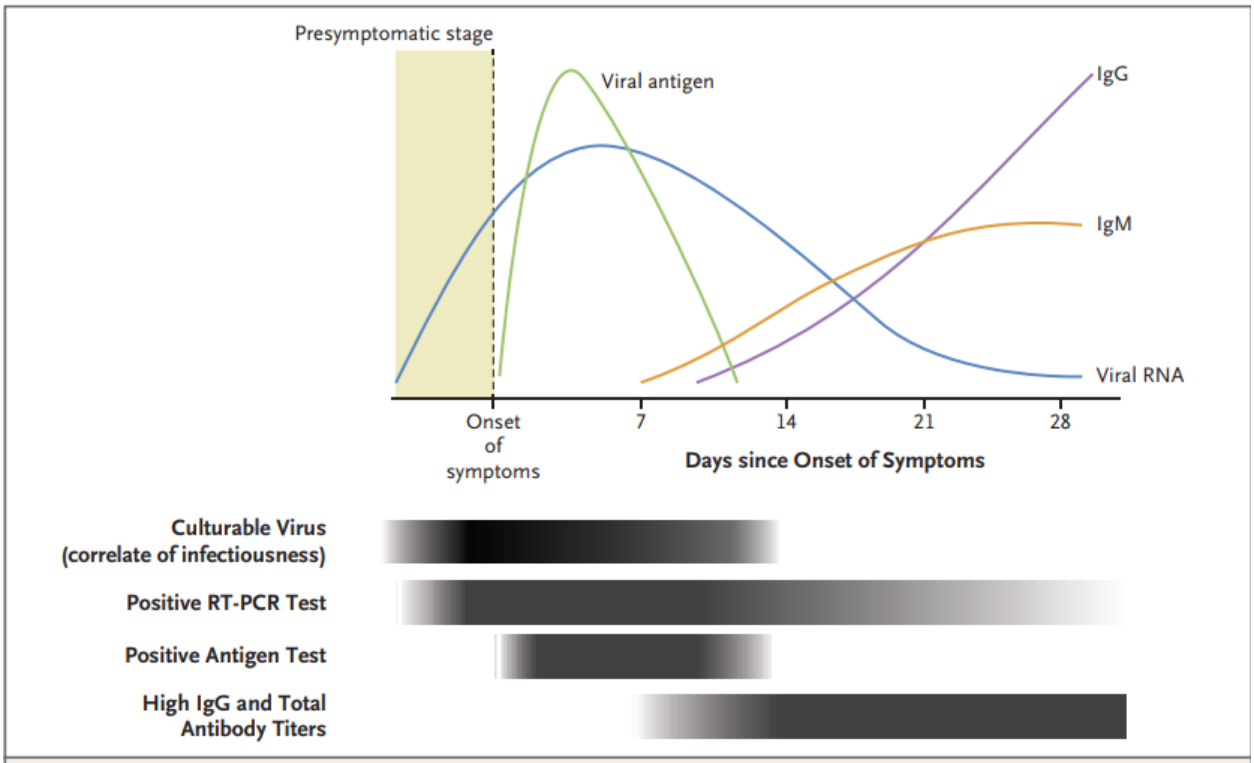


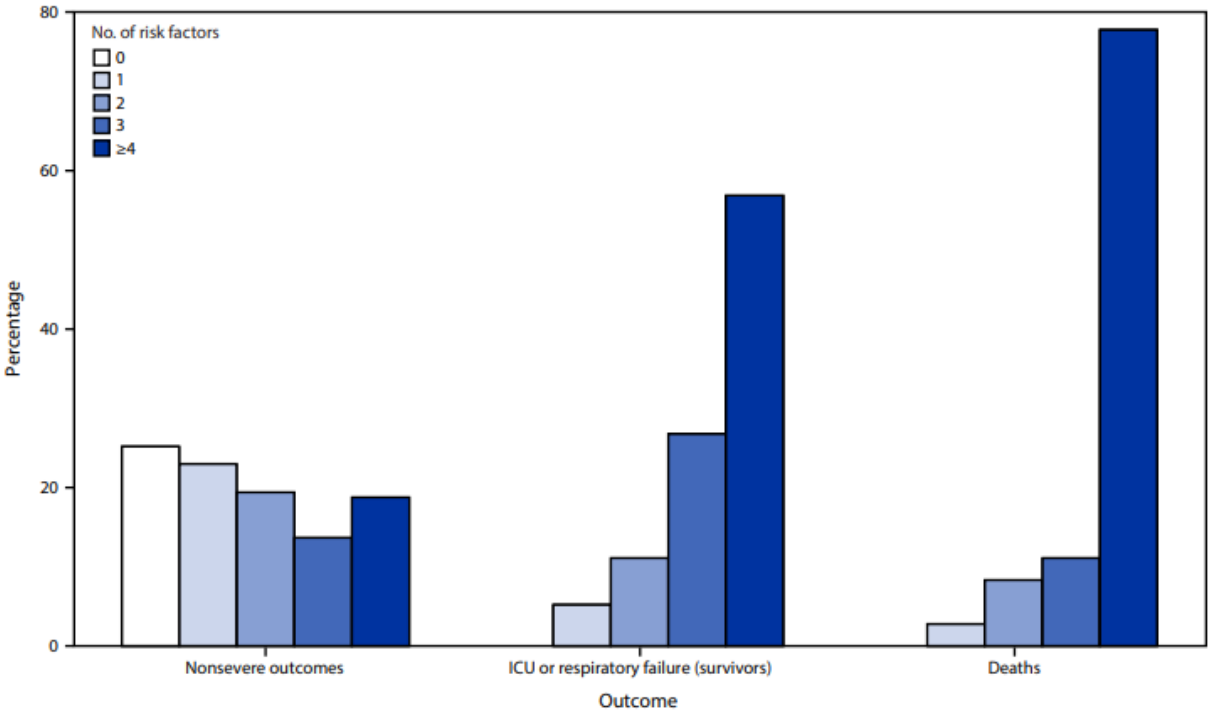
Figure 1. Pathophysiology and Timeline of Viremia, Antigenemia, and Immune Response during Acute SARS-CoV-2 Infection.

Comment: The figure above speaks for itself and very nicely summarizes testing including comparing to cultural virus. Antigen-based assays remain positive for 5 to 12 days after symptom onset and perform better in persons with a high viral load, which correlates with disease severity and death. Thus, antigen-based tests may correlate better with replication competent SARS-CoV-2 than molecular tests and may provide information about potential

transmissibility. Like therapeutics we do not have enough tests. Until we do have enough tests, we will have to triage their use to critical infrastructure like healthcare, emergency services, public transportation, and schools.

Risk Factors for Severe COVID-19 Outcomes Among Persons Aged ≥18 Years Who Completed a Primary COVID-19 Vaccination Series — 465 Health Care Facilities, United States, December 2020–October 2021 MMWR January 7, 2022

Among 1,228,664 persons who completed primary vaccination during December 2020–October 2021, severe COVID-19–associated outcomes (0.015%) or death (0.0033%) were rare. Risk factors for severe outcomes included age ≥65 years, immunosuppressed, and six other underlying conditions. All persons with severe outcomes had at least one risk factor; 78% of persons who died had at least four.



Abbreviation: ICU = intensive care unit.
* Outcome totals: nonsevere = 2,057; ICU/respiratory failure = 153; deaths = 36.
† All persons in the ICU or respiratory failure (survivors) and deceased groups had at least one risk factor.

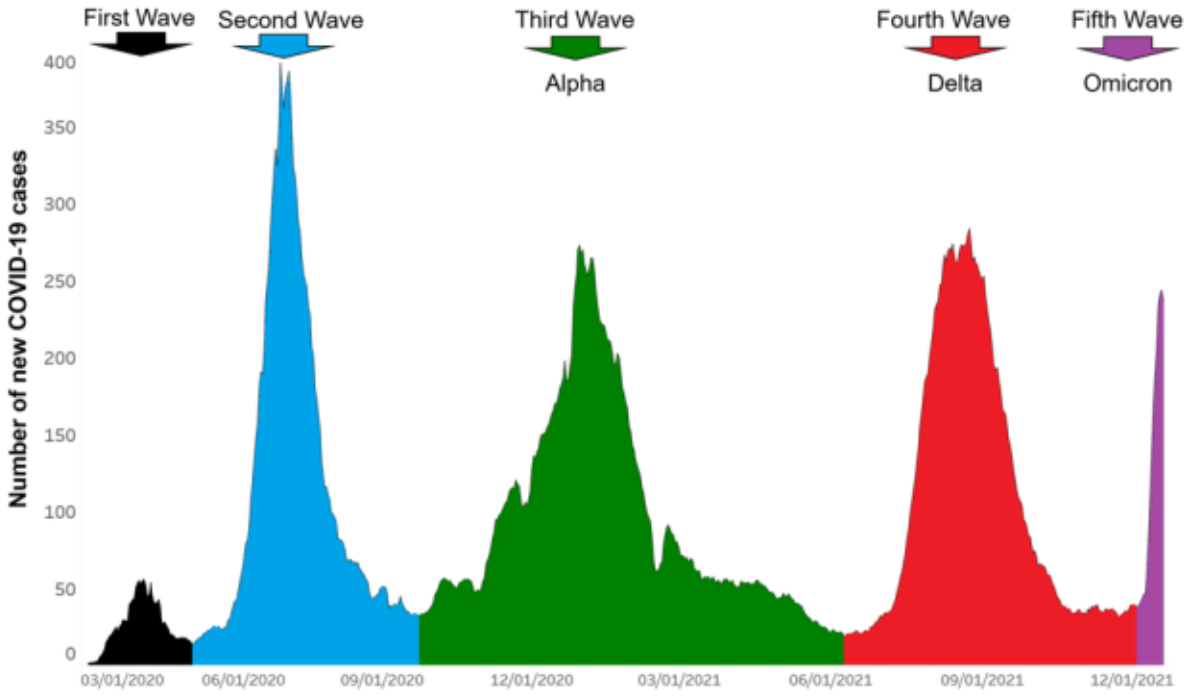
Comment: These findings are consistent with studies that have shown that COVID-19 vaccination significantly lowers the likelihood of COVID-19–associated hospitalization and death. Risk for a severe COVID-19 outcome after primary vaccination was higher among persons aged ≥65 years, were immunosuppressed, or had one of six other underlying conditions (DM, COPD, CKD, liver disease, obesity, cardiac disease); all persons with severe COVID-19 outcomes after primary vaccination had at least one risk factor. Population-wide data also demonstrated that COVID-19 hospitalization and death are more frequent among Hispanic, non-Hispanic Black, and non-Hispanic American Indian or Alaska Native persons than among non-Hispanic White persons. This might be explained by higher levels of SARS-CoV-2 exposure, reduced access to care, and higher rates of poorly controlled underlying conditions.

This report supports the strong recommendation to vaccination. If you are unvaccinated, you are 10X more likely to test positive for SARS-CoV-2 and 20X more likely to die compared to fully vaccinated people.

Early signals of significantly increased vaccine breakthrough, decreased hospitalization rates, and less severe disease in patients with COVID-19 caused by the Omicron variant of SARS-CoV-2 in Houston, Texas medRxiv posted January 4, 2022

doi.org/10.1101/2021.12.30.21268560

This report highlights genome sequencing study of SARS-CoV-2 in the Houston Methodist Healthcare System which identified 1,313 symptomatic patients with infections caused by Omicron from late November 2021 through December 20, 2021. Omicron very rapidly increased in only three weeks to cause 90% of all new COVID-19 cases with an estimated case doubling time of 1.8 days! Compared to patients infected with either Alpha or Delta variants in Houston Methodist Healthcare System, Omicron patients were significantly younger, had significantly increased vaccine "breakthrough" rates, and were significantly less likely to be hospitalized. Omicron patients required less intense respiratory support and had a shorter length of hospital stay, consistent with decreased disease severity.



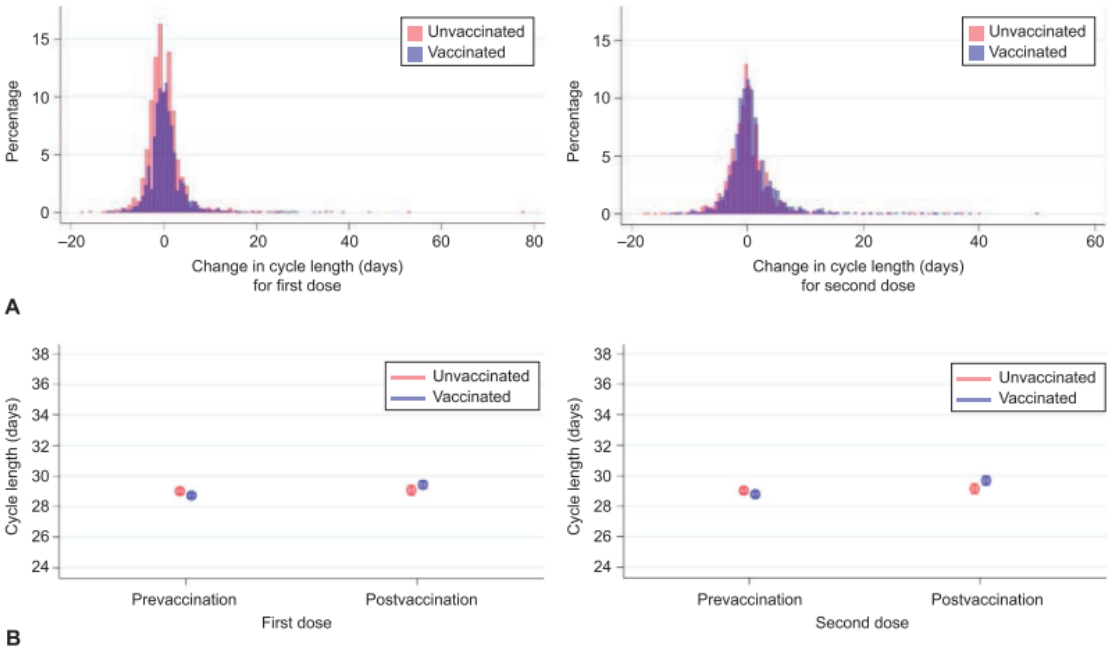
	Omicron	Delta	Total	
Admission Data				
Admitted	193 (14.7%)	6749 (43.0%)	6942 (40.8%)	*P*<0.0001 Fisher's exact test Odds Ratio: 0.228 (95% CI 0.195-0.267)
Not Admitted	1120 (85.3%)	8933 (57.0%)	10053 (59.2%)	
Median LOS (Days) (Discharged patients only)	3.0	5.4	5.3	*P*<0.0001 Mann-Whitney
Mortality				
Alive	1302 (99.2%)	14855 (94.7%)	16157 (95.1%)	*P*<0.0001 Fisher's exact test Odds Ratio: 0.152 (95% CI 0.083-0.276)
Deceased	11 (0.8%)	827 (5.3%)	838 (4.9%)	

Comment: Although the numbers are small, the observation of this early study confirms studies from South Africa and UK. They found Omicron rapidly increased as a cause of COVID-19 and spread throughout the Houston metroplex in a very short period of time, far faster than any other SARS-CoV-2 variant to date. The recent data from CDC mirrors the rapid spread of Omicron across the US now at >95% (see above). They also found Omicron caused more vaccine breakthrough cases than the Alpha or Delta but fewer admissions, deaths, and shorter LOS. In addition, Omicron patients were significantly younger than Alpha or Delta patients. (See above) Because Houston Methodist has sequenced the genome of approximately 90% of SARS-CoV-2 in the Houston Methodist Healthcare System for almost two years, they have had the advantage of continuously monitoring the epidemiology of this virus in a major US metroplex.

Association Between Menstrual Cycle Length and Coronavirus Disease 2019 (COVID-19) Vaccination OB GYN published online January 5, 2022

A team of scientists analyzed cycles of nearly 4,000 women through a fertility tracking app - some of which were vaccinated, and others were unvaccinated. They evaluated 23,754 menstrual cycles prospectively reported by 3,959 U.S. individuals to determine whether COVID-19 vaccination is associated with menstrual cycle disturbances during cycles when vaccination occurs. Included individuals had normal prevaccination menstrual cycle lengths. Everyone contributed six consecutive cycles of data. For those who received a COVID-19 vaccination, they included three prevaccine cycles and three post–first vaccine dose, inclusive of the vaccination cycle. They included six consecutive cycles for those who remained unvaccinated.

After adjusting for confounders, they found that normally cycling individuals experienced small variations in cycle length regardless of vaccination status. Statistically significant differences existed between vaccination status groups, but the change in cycle length was less than 1 day, which is below the reportable difference in the menstrual cycle tracking application and is not clinically significant. The average increase in women's cycles after the first vaccine dose was 0.64-day (about 15.36 hours), and 0.79-day (about 18.96 hours) following the second dose. However, a subgroup of app users who received two vaccine doses in the same menstrual cycle (358 users) had a larger average increase in cycle length of two days.



Comment: The investigators hypothesized since mRNA vaccines create a robust immune response or stressor, this could temporarily affect the hypothalamic-pituitary-ovarian axis if timed correctly. They claim their findings for individuals who received two doses in a single cycle supports this hypothesis. This study may not be generalizable to the US population given the selection of Natural Cycles users (more likely to be White, college educated, and have lower BMIs than national distributions) and women enrolled were not using hormonal contraception. Their results also suggest that individuals receiving two doses in a single cycle return to baseline cycle length quickly. This study did not address other questions such as other possible changes in menstrual cycles, such as menstrual symptoms, unscheduled bleeding, and changes in the quality and quantity of menstrual bleeding.

Risk for Newly Diagnosed Diabetes >30 Days After SARS-CoV-2 Infection Among Persons Aged <18 years — United States, March 1, 2020–June 28, 2021 MMWR January 7, 2022

To evaluate the risk for any new diabetes diagnosis (type 1, type 2, or other diabetes) >30 days after acute infection with SARS-CoV-2, CDC estimated diabetes incidence among patients aged <18 with diagnosed COVID-19 from retrospective cohorts constructed using IQVIA health care claims data from March 1, 2020, through February 26, 2021, and compared it with incidence among patients matched by age and sex 1) who did not receive a COVID-19 diagnosis during the pandemic, or 2) who received a prepandemic non–COVID-19 acute respiratory infection (ARI) diagnosis.

Among these patients, diabetes incidence was significantly higher among those with COVID-19 than among those without COVID-19 in both databases 1)(IQVIA: hazard ratio [HR] = 2.66,

95% CI = 1.98–3.56; HR = 1.31, 95% CI = 1.20–1.44) and 2) with non–COVID-19 ARI in the prepandemic period,(HR = 2.16, 95% CI = 1.64–2.86).

Comment: Persons aged <18 with COVID-19 were more likely to receive a new diabetes diagnosis 30 days after infection than were those without COVID-19 and those with prepandemic acute respiratory infections. Non–SARS-CoV-2 respiratory infection was not associated with an increased risk for diabetes. The COVID-19 pandemic has disproportionately affected people with diabetes, who are at increased risk of severe COVID-19. Increases in the number of type 1 diabetes diagnoses [Diabetes Care 2020;43:e170–1] and increased frequency and severity of diabetic ketoacidosis (DKA) at the time of diabetes diagnosis [JAMA 2020;324:801–4] have been reported in European pediatric populations The present analyses lacked information on covariates that could have affected the association between COVID-19 and incident diabetes, including prediabetes, race/ethnicity, and obesity status. Nonetheless, this study suggests an increased risk for diabetes among persons aged <18 years with COVID-19, which is supported by independent studies in adult. [Diabetes Obes Metab 2021;23:870–4] Evidence of increased pediatric type 1 diabetes has been reported during the COVID-19 pandemic as well. [Diabetes Care 2020;43:e170–1] Of interest the increases were seen both among those who had been ill with Covid, and those who were asymptomatic but tested positive.

Effectiveness of BNT162b2 (Pfizer-BioNTech) mRNA Vaccination Against Multisystem Inflammatory Syndrome in Children Among Persons Aged 12–18 Years — United States, July–December 2021 MMWR January 7, 2022

Pfizer vaccine is currently the only authorized vaccine for use in children and adolescents aged 5–15 years under. Recent evidence suggests that COVID-19 vaccination is associated with lower MIS-C incidence among adolescents [JAMA 2021.doi.org/10.1001/jama.2021.232628]; however, VE of the 2-dose Pfizer regimen against MIS-C has not been evaluated. This study used a test-negative case-control design, commonly used for postauthorization VE evaluations. Patients were hospitalized at 24 participating sites in the Overcoming COVID-19 Network, a collaboration between CDC and approximately 70 pediatric hospitals nationwide to assess COVID-19 complications in children and young adults. Given that children aged 5–11 years were not recommended to receive the Pfizer vaccine until November 2, 2021, this analysis focused on persons aged 12–18 years.

Estimated effectiveness of 2 doses of Pfizer vaccine against MIS-C was 91% (95% CI = 78%–97%). Among critically ill MIS-C case-patients requiring life support, all were unvaccinated.

Comment: Vaccination was highly effective in preventing MIS-C in persons aged 12–18 years. These findings further support on vaccinating eligible children.