Infectious Diseases Watch

January 17, 2022

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VII Perspective: COVID-19: The 2022 Crisis

As Omicron races across the globe, we are comforted by the news that Omicron appears to be milder than previous variants; however, there is another crisis unfolding with far reaching impact: burnout of HCWs.

Burnout is defined as "a syndrome of emotional exhaustion, loss of meaning in work, feelings of ineffectiveness, and a tendency to view people as objects rather than as human beings" (SAGE Open 2017;7). This definition was updated in 2019 by the WHO which defined burnout as a syndrome resulting from chronic workplace stress that has not been successfully managed and is characterized by feelings of exhaustion, depersonalization, negativity, and reduced productivity (asamonitor.pub/3D3oxM4). Burnout has been disproportionately higher in health care workers than the general workforce during the pandemic.

When I think back to April 2020 when my community was first hit by COVID-19, we went into lockdown(stay at home) and as a HCW we rushed between patients severely ill, many placed on mechanical ventilation and many of them died. PPE, testing, and other supplies were in short supply, and I had to be issued an N-95 masks and face shield by the charge nurse and told to reuse for the rest of the day. Putting on PPE was laborious and by the end of the day we were all exhausted, physically, and mentally. We had no therapeutics or vaccines at the time as our ICUs filled. Our knowledge of this unique virus was very limited and frankly we felt fearful and helpless.

Over the next year the knowledge gap narrowed. We now have more tools. We have some effective therapeutics including steroids, remdesivir, inflammatory inhibitors, MCA, and oral antivirals although in short supply. We have learned administering heated oxygen at high flow rates substantially improves patient outcomes, but the greatest intervention has come from effective vaccines. Unfortunately, only 2/3 of American have been fully vaccinated and only 30% who are eligible have received a booster. The politics of fear and the messaging have been disappointing.

Despite these advances, these tools have not been enough to slow the rapid number of Omicron patients we are now seeing. And even though nearly all my patients now are experiencing milder illness compared to April and July 2020 and January and August 2021, they still take up the same amount of space in a hospital bed. Right now, all patients with COVID-19 still require isolation and use of PPE which is labor intensive. And yes, even though about 50% patients are incidentally found to have the virus, they still require isolation.

What's in critically short supply now are health care providers. Ten of thousands of HCW are now out due to COVID-19 infections. Some hospitals are near the breaking point. In Houston, up to 10% of HCWs are out because of COVID-19 and 20% due to burnout. Updated guidance from the CDC that shortens isolation time after testing positive for the virus has allowed health care workers to return to work earlier. This may help, but severe staffing shortages have led to contingency plans that allow providers who may still be potentially contagious to treat patients. Fewer providers mean fewer available beds and services which means triaging who gets care. These are terrible decisions to make two years into the pandemic.

Exhausted by long hours and staffing shortages, traumatized by the magnitude of death from COVID-19, many HCWs including physicians are rethinking their careers. There are also reports of abuse against the medical staff. A recent survey of over 6000 nurses by the American Association of Critical-Care Nurses found that two-thirds said the pandemic had prompted them to consider leaving the profession. The share of nurses who said they were likely to leave their positions in the coming year rose to 32% in a survey conducted in November and December up from 22% last February. A Washington Post-Kaiser Family Foundation survey found that 20%-30% of front-line health care workers are considering leaving the profession including physicians. (asamonitor.pub/3n0ylRm) Since February 2020, 30% of U.S. health care workers have either lost their jobs (12%) or quit (18%). Turnover and burnout in healthcare can have life-or-death repercussions. Studies have shown during surges heavy nurse workloads and staffing shortages can lead to mistakes and lapses in care leading to poor outcomes. Hospitals have tried offering bonuses to new hires and bringing on traveling nurses who work on a contract basis, earning much higher hourly rates, but these practices aren't sustainable. In fact, many experienced nurses have opted to become a traveling nurse due to the higher salary forcing hospitals in turn to hire travelers which may also impact outcomes. As I wrote in last week's Infectious Diseases Watch how frustrating it has been that we cannot provide optimal care to all of our patients due to limited lifesaving treatments and testing. The feeling that pushes many to leave is one of not being able to do the job we were trained to do and providing care for patients the way we believe we should. Some have called this "moral distress." The scars from COVID-19 will linger far longer than the pandemic. We must start to address this now or I fear our healthcare system will suffer irreparable damage.

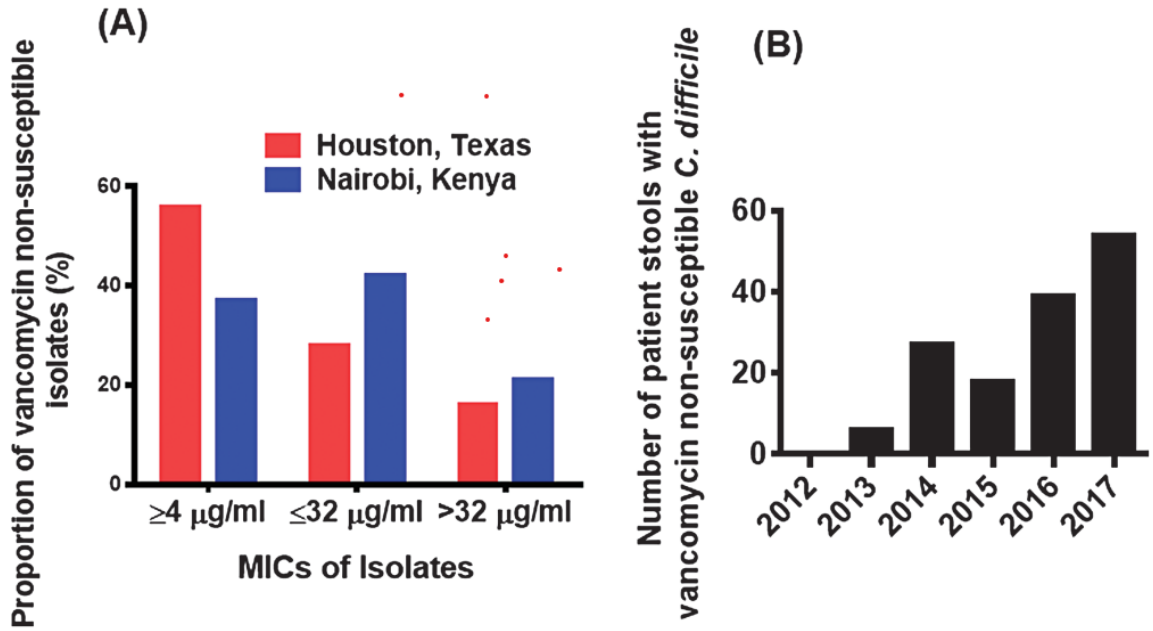
General Infectious Diseases

Emergence of Clinical *Clostridioides difficile* Isolates With Decreased Susceptibility to Vancomycin Clin Infect Dis 2022;74:120–6

doi.org/10.1093/cid/ciaa912

Stool samples from patients with CDI were collected from 438 and 98 patients at a large university hospital in Houston, Texas, and Nairobi, Kenya, respectively. The stools were examined for the presence of vancomycin and metronidazole nonsusceptible *C. difficile* using broth dilution culture, Etest, polymerase chain reaction (PCR), WGS, and *in vivo* testing in a CDI mouse model. To identify stool samples containing nonsusceptible *C. difficile* isolates, samples were plated on CDPA only and CDPA containing either 8 µg/mL of metronidazole or 4 µg/mL of vancomycin based on breakpoint concentrations published by CLSI. 7-week-old C57BL/6 mice (n = 12 in each group) were administered a cocktail of antibiotics for 7 days in their drinking water. The antibiotics included kanamycin (40 mg/kg), gentamicin (3.5 mg/kg), colistin (4.2 mg/kg), metronidazole (21.5 mg/kg), and vancomycin (4.5 mg/kg). One day after the antibiotic treatment, mice were administered 1 mg/kg clindamycin by intraperitoneal injection. Twenty-four hours following the clindamycin treatment, mice were infected with 106 spores of either vancomycin susceptible R20291 strain or a vancomycin nonsusceptible isolate (from a Houston patient with MIC >16 µg/mL) in a suspension of 250 µL PBS by oral gavage. The infected mice were treated twice daily by oral gavage with and without vancomycin (20 mg/kg) beginning 24 hours postinfection for 4 days. The mice were observed twice daily for 14 days postinfection and scored based on 3 main endpoint parameters as previously reported

Of the Houston stool samples, 114/438 (26%) had vancomycin nonsusceptible *C. difficile* isolates and 128/438 (29%) were metronidazole nonsusceptible. Similarly, 66 out of 98 (67%) and 83/98 (85%) of the Nairobi patients harbored vancomycin and metronidazole nonsusceptible isolates, respectively. Vancomycin treatment of a CDI mouse model infected with a vancomycin nonsusceptible isolate failed to eradicate the infection. Whole-genome sequencing analyses did not identify *vanA* genes, suggesting a different mechanism of resistance.



Comment: *C. difficile* strains exhibiting reduced susceptibility to vancomycin are currently circulating in patient populations and growing. The spread of strains resistance to vancomycin, a first-line antibiotic for CDI, could pose a serious therapeutic challenge. Routine susceptibility testing may be necessary. Metronidazole is poorly bioavailable in the colon, with fecal

concentrations ranging from 0.8 to 24.2 µg/g stool, possibly explaining metronidazole decreased efficacy in treating CDI. On the other hand, fecal concentrations of oral vancomycin are much higher, ranging from 520 to 2200 µg/g stool. However, *in vivo* data indicated that vancomycin was suboptimal in treating mice infected with a vancomycin nonsusceptible isolate. Given very high levels of vancomycin in GI human gut, is this finding clinically relevant in humans since studies to date show equal efficacy in treating CDIs?

In 2021, ACG [Am J Gastroenterol published May 18, 2022] updated their treatment guidelines.

1. Recommends that oral vancomycin 125 mg 4 times daily for 10 d be used to treat an initial episode of nonsevere CDI (strong recommendation, low quality of evidence)

2. They recommend that oral fidaxomicin 200 mg twice daily for 10 d be used for an initial episode of nonsevere CDI (strong recommendation, moderate quality of evidence)

3. They recommend fidaxomicin for patients experiencing a first recurrence after an initial course of vancomycin or metronidazole (conditional recommendation, moderate quality of evidence).

The recent IDSA/SHEA guidelines published in 2018 [Clin Infect Dis 2018;66: e1–48]. recommended either vancomycin or fidaxomicin in nonsevere CDI. Fidaxomicin has been demonstrated to be generally equivalent to vancomycin, but studies demonstrated decreased recurrence rates. Although vancomycin is less expensive, lower recurrence rates of fidaxomicin may make fidaxomicin a cost-effectiveness strategy. More data is necessary to determine if we are seeing widespread vancomycin resistance that impacts response to therapy.

Optimal Urine Culture Diagnostic Stewardship Practice– Results from an Expert Modified-Delphi Procedure Clin Infect Dis published online November 29, 2021

doi.org/10.1093/cid/ciab987

Urine cultures are nonspecific for infection and often lead to misdiagnosis of UTI and unnecessary antibiotics. Diagnostic stewardship is a critical component for an effective antimicrobial stewardship program. Diagnostic stewardship provides guidance that modifies test ordering, processing, and reporting to optimize diagnosis and treatment. This paper aimed to develop expert guidance on best practices for urine culture diagnostic stewardship.

165 questions were reviewed with the panel reaching agreement on 104, leading to 18 overarching guidance statements. Below are the recommendations.

Appropriate Practices:

1. Require documentation of signs or symptoms of UTI to obtain a urine culture, which includes dysuria or flank pain
2. Replace stand-alone urine culture orders with conditional reflex urine cultures*+
3. Implement best practice alerts to discourage ordering urine cultures in the absence of signs or symptoms of UTI*
4. Automatically cancel repeat urine cultures within 5 days of a positive culture (during the same hospital admission and 7 days for long-term care residents)

Inappropriate Practices:

1. Include urine cultures in standard order sets for:
   - ED evaluation
   - Hospital admission
   - Inpatient pre-op
   - Assessment of altered mental status
   - Assessment of falls in long-term care
2. Order urine cultures in response to change in urine characteristics

Appropriate Practices:

1. Use elevated urine WBC count as a criterion to reflex to urine culture when a clinician orders a urine culture (all settings)
2. Require documentation of collection site method (i.e. clean catch) prior to processing urine cultures

Inappropriate Practices:

1. Automatically reflex routine urinalyses to urine cultures for abnormal findings when a urine culture was not specifically requested by the ordering clinician

Appropriate Practices:

1. In urine culture reports, to:
   - Inform clinicians that even high colony counts (i.e.> 100,000 CFU) may not represent true infection in the absence of symptoms or signs‡
   - Nudge clinicians to not treat asymptomatic bacteriuria‡
   - Nudge clinicians to not to treat mixed flora‡
   - Differentiate typical uropathogens versus contaminants‡
2. Withhold urine culture results (including organism identification and antibiotic susceptibilities) when there are more than two unique bacterial strains identified in culture
3. Preferentially report only IDSA-recommended antibiotics if organism is susceptible
4. Withhold fluoroquinolone susceptibilities unless there is resistance to preferred oral antibiotics

Inappropriate Practices:

1. Nudge clinicians not to treat if there are less than 100,000 CFU of bacteria
2. Withhold information about urine culture organism identification or antibiotic susceptibilities unless the clinician contacts the clinical microbiology laboratory

Patients without Urinary Catheters		
Appropriate Dysuria, suprapubic pain, flank pain, Costovertebral angle (CVA) tenderness, or septic shock	**Uncertain** Fever or systemic leukocytosis with no other known cause	**Inappropriate** Altered mental status, or change in urine characteristics (color, sediment, smell)

Patients with Urinary Catheters		
Appropriate Dysuria, suprapubic pain flank pain, Costovertebral angle (CVA) tenderness, or septic shock	**Uncertain** Fever, systemic leukocytosis with no other known cause, or delirium*	**Inappropriate** Change in urine characteristics (color, sediment, smell)

Comment: Using a rigorous modified Delphi approach with a diverse expert panel, they identified the best practices for diagnostic stewardship for urine culturing This is a very useful paper to address unnecessary and inappropriate ordering of urine cultures which I think should be adopted immediately. Clinicians often feel pressured to treat a positive urine culture results rather than treating the patient.

Effect of 7 vs 14 Days of Antibiotic Therapy on Resolution of Symptoms Among Afebrile Men With Urinary Tract Infection A Randomized Clinical Trial

JAMA 2021;326:324-33

Studies on UTI in men lacks a defined optimal treatment duration. This study set out to determine whether 7 days of treatment is noninferior to 14 days when using ciprofloxacin or trimethoprim/sulfamethoxazole (TMP/SMX) to treat urinary tract infection (UTI) in afebrile men.

This trial was a randomized, double-blind, placebo-controlled noninferiority trial of afebrile men with presumed symptomatic UTI treated with ciprofloxacin or TMP/SMX at 2 US Veterans Affairs medical centers. The prespecified primary outcome was resolution of UTI symptoms by 14 days after completion of active antibiotic treatment. A noninferiority margin of 10% was selected. [standard] Other than the requirement that participants be afebrile, trial inclusion criteria encompassed both simple cystitis and complicated UTI. Inclusion criteria of costovertebral angle tenderness, flank pain, and perineal pain would suggest infection possibly extending beyond the bladder.

Symptom resolution occurred in 122/131 (93.1%) participants in the 7-day group vs 111/123 (90.2%) in the 14-day group (difference, 2.9% [1-sided 97.5% CI, –5.2% to]), meeting the noninferiority criterion. In the secondary as-randomized analysis, symptom resolution occurred in 125/136 (91.9%) participants in the 7-day group vs 123/136 (90.4%) in the 14-day group (difference, 1.5% [1-sided 97.5% CI, –5.8% to]) Recurrence of UTI symptoms occurred in 13/131 (9.9%) participants in the 7-day group vs 15/123 (12.9%) in the 14-day group (difference, –3.0% [95% CI, –10.8% to 6.2%]; *P* = .70). Adverse events occurred in 28/136 (20.6%) participants in the 7-day group vs 33/136 (24.3%) in the 14-day group.

Comment: The findings support the use of a 7-day course of ciprofloxacin or TMP/SMX as an alternative to a 14-day course for treatment of afebrile men with suspected UTI. Many of the study patients had important comorbidities, such as prior UTIs, BPH, and urinary incontinence. Therefore, participants represented the types of patients who would be considered for empirical UTI treatment in routine clinical practice. A limitation of the trial is that the 254 patients included in the as-treated analysis fell short of the target 290 needed to provide 85% power for detecting a between-group difference; thus, the trial may have failed to detect a true, but small, difference between treatment groups. Larger trials and evaluation of other antimicrobial regimens are needed especially given increase resistance to both FQ and TMP/SMX.

COVID-19

COVID-19 News

From NIH

Comparing Cold, Flu, Allergies, and COVID-19				
Symptoms	**Cold**	**Flu**	**Airborne Allergy**	**COVID-19**
Fever	Rare	Usual, high (100–102 °F), sometimes higher, especially in young children); lasts 3–4 days	Never	Common
Headache	Uncommon	Common	Uncommon	Common
General Aches, Pains	Slight	Usual; often severe	Never	Common
Fatigue, Weakness	Sometimes	Usual, can last up to 3 weeks	Sometimes	Common
Extreme Exhaustion	Never	Usual, at the beginning of the illness	Never	Common
Stuffy, Runny Nose	Common	Sometimes	Common	Common
Sneezing	Usual	Sometimes	Usual	Rarely
Sore Throat	Common	Sometimes	Sometimes	Common
Cough	Common	Common, can become severe	Sometimes	Common, dry cough
Chest Discomfort	Mild to moderate	Common	Rare, except for those with allergic asthma	Common; can cause trouble breathing or persistent pain or pressure in the chest that calls for immediate emergency care
Loss of Taste or Smell	Rarely	Rarely	Rarely	Common

CDC: Updated Guidance Masks and Respirators January 14, 2022

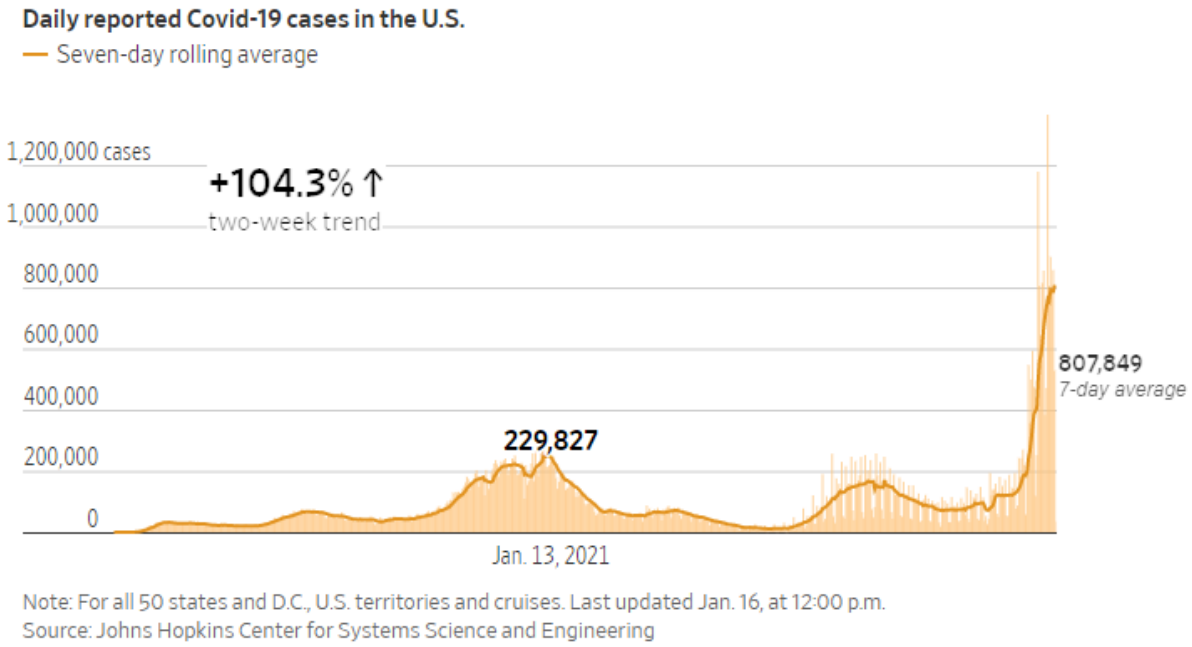
- Masking is a critical public health tool for preventing spread of COVID-19, and it is important to remember that any mask is better than no mask.
- To protect yourself and others from COVID-19, CDC continues to recommend that you wear the most protective mask you can that fits well and that you will wear consistently.
- Masks and respirators are effective at reducing transmission of SARS-CoV-2, when worn consistently and correctly.
- Some masks and respirators offer higher levels of protection than others, and some may be harder to tolerate or wear consistently than others. It is most important to wear a well-fitted mask or respirator correctly that is comfortable for you and that provides good protection.
- While all masks and respirators provide some level of protection, properly fitted respirators provide the highest level of protection. Wearing a highly protective mask or respirator may be most important for certain higher risk situations, or by some people at increased risk for severe disease.
- Ways to have better fit and extra protection with cloth and disposable masks
    - Wear two masks (disposable mask underneath AND cloth mask on top)
    - Combine either a cloth mask or disposable mask with a fitter or brace
    - Knot and tuck ear loops of a 3-ply mask where they join the edge of the mask

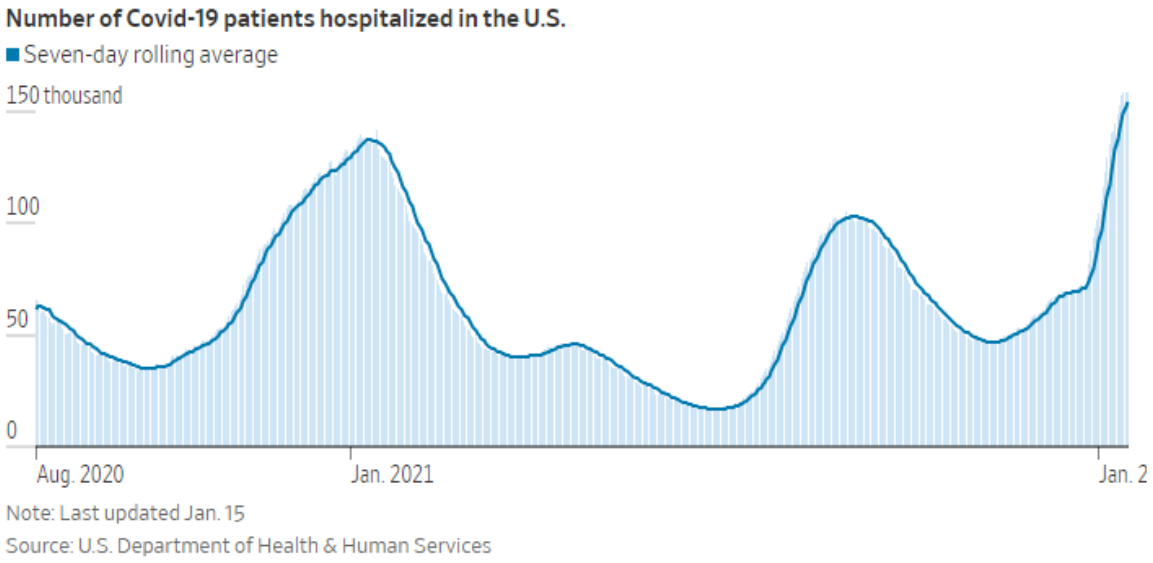
Comment: The CDC on Friday clarified its stance on various kinds of masks, finally acknowledging that the cloth masks frequently worn by Americans do not offer as much protection as surgical masks or respirators. The change comes as infections with the highly contagious Omicron variant continues to spread. Some experts have said that cloth masks are inadequate to protect from this variant and have urged the CDC to recommend a higher level of mask. According to the CDC's new description of masks, loosely woven cloth products provide the least protection and layered finely woven products offer more. Well-fitting disposable surgical masks and KN95s — are more protective than all cloth masks, and well-fitting respirators, including N95s, offer the highest level of protection. CDC concludes with urging Americans to "wear the most protective mask you can that fits well and that you will wear consistently." While the higher-quality masks provide better protection, they can be uncomfortable to wear and expensive. Therefore, the best mask that you wear is the one you will wear and the one you can keep on all day long and tolerate in public indoor settings.

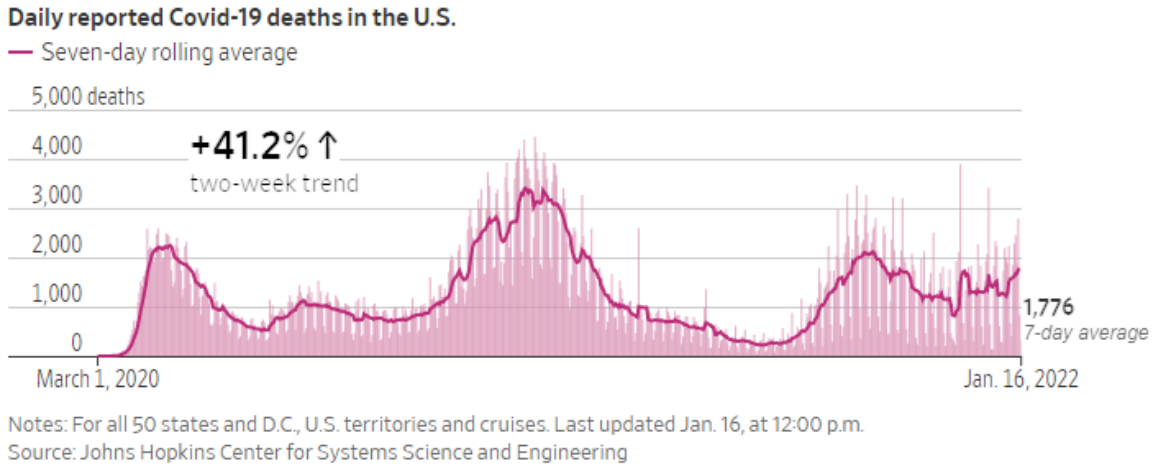
COVID-19 by the Numbers

1. As of Jan. 12, the nation's seven-day case average was 782,766, a 33.2 percent increase from the previous week's average.
2. The current seven-day hospitalization average for Jan. 5-11 is 20,637, a 24.5 percent increase from the previous week's average. This increase is significantly less than the 60.2 percent jump in hospitalizations the CDC reported Jan. 7.

3. The current seven-day death average is 1,729, up 36.8 percent from the previous week's average. This increase in deaths has accelerated since Jan. 7, when the CDC reported a 14.4 percent jump in deaths compared to the week prior.
4. As of Jan. 13, about 248 million people — 74.7 percent of the total U.S. population — have received at least one dose of the COVID-19 vaccine, and more than 208.6 million people, or 62.8 percent of the population, have received both doses. About 78.1 million booster doses in fully vaccinated people have been reported, up from 72.3 million the week prior.
5. Based on projections for the week ending Jan. 8, the CDC estimates the omicron variant accounts for 98.3 percent of all U.S. COVID-19 cases, with the delta variant accounting for the remaining 1.7 percent of cases.







Comment: Cases appear to have peaked and maybe comikng down in states hit first with Omicron. As expected death did increase over the last 1-2 weeks, many of deaths may be due to Delta before Omicron. Not all deaths were directly due to Covid-19, but exact numbers are not available.

Journal Review

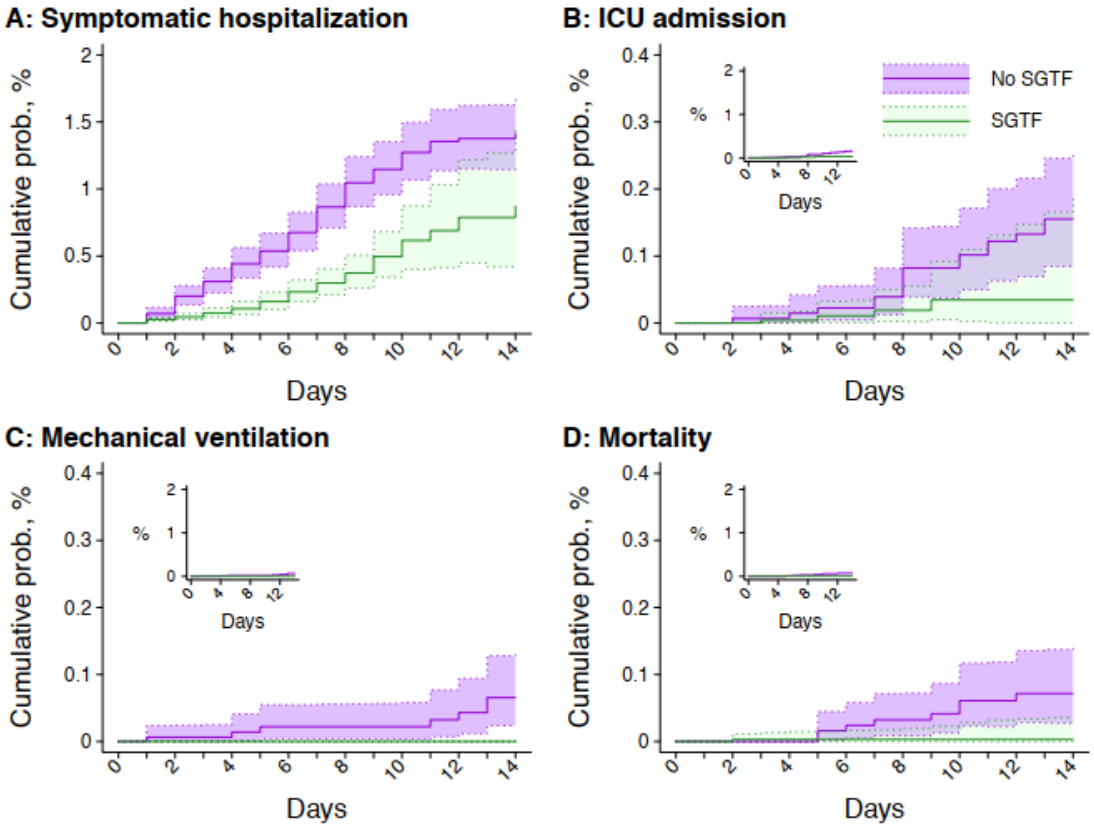
Clinical outcomes among patients infected with Omicron (B.1.1.529) SARS-CoV-2 variant in southern California medRxiv posted January 11, 2022

doi.org/10.1101/2022.01.11.22269045

Investigators from Kaiser Permanente of Southern California (KPSC) and the CDC analyzed EHR data on 69,279 COVID-19 patients treated between Nov. 30, 2021, and Jan. 1, 2022. About 52,000 patients had Omicron infections, and nearly 17,000 had Delta infections.

PCR testing for SARS-CoV-2 occurred in a variety of clinical settings within KPSC during the study period. A majority of tests conducted in outpatient settings are submitted to regional laboratories, where >90% of samples are processed using the ThermoFisher TaqPath COVID-19 Combo Kit. Samples collected in hospitals are processed by either these regional laboratories or by in-house hospital laboratories, which use the ThermoFisher TaqPath COVID-19 Comboo Kit as well as the Roche cobas 8800 system for diagnostic testing. Previous evidence has indicated that the Δ69-70 amino acid deletion in the spike (S) protein of Omicron variant specimens [S gene target failure (SGTF)] causes a failure in PCR probes targeting the S gene, whereas the Orf1ab and nucleocapsid (N) probes retain sensitivity; in contrast, SGTF is rare in Delta variant SARS-CoV-2 infections. They therefore considered S gene target SGTF in PCR-positive specimens processed using the ThermoFisher TaqPath COVID-19 Comboo Kit to serve as a proxy for Omicron variant infections. They did validate the concordance of SGTF with Omicron variant identification by tabulating the number of Omicron and non-Omicron variant infections identified over this period using whole genome sequencing and viral lineage designation among cases whose tests did or did not exhibit SGTF.

The investigators found patients with Omicron infections were half as likely to require hospitalization. Just 0.5 percent of Omicron patients were hospitalized, compared to 1.3 percent of those with Delta infections. Of those hospitalized with Omicron, none were put on ventilators. Median duration of hospital stay was 3.4 (2.8-4.1) days shorter for hospitalized cases with Omicron variant infections as compared to hospitalized patients with Delta variant infections, reflecting a 69.6% (64.0-74.5%) reduction in hospital length of stay.



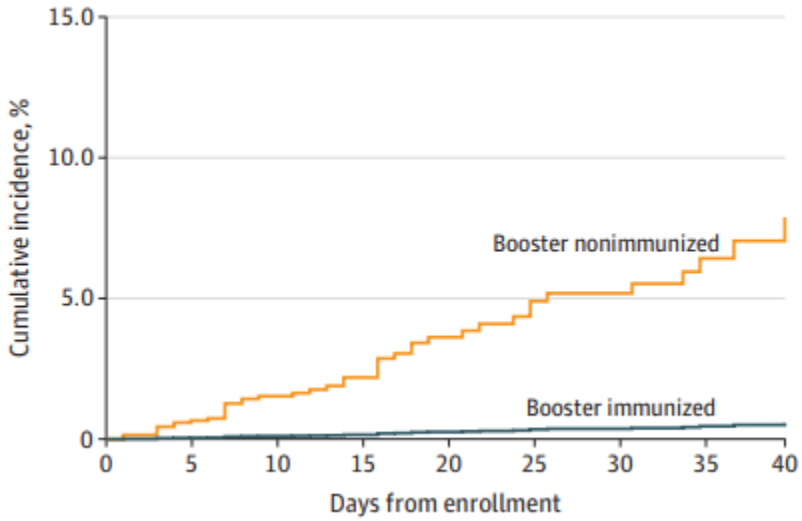
Comment: The investigators confirmed two aspects of comparative severity of Omicron vs. Delta variant infections: the risk of progression to severe endpoints among diagnosed cases, and the risk of progression to acute respiratory symptoms among those first diagnosed before symptoms onset. The results of this study are similar to the study from Houston reviewed in last week's Infectious Diseases Watch. [the current study had much higher numbers] While milder disease is associated with the Omicron variant is an encouraging finding, evidence of higher transmissibility of Omicron variant and infection in vaccinated persons remain a concern.

Association of a Third Dose of BNT162b2 Vaccine With Incidence of SARS-CoV-2 Infection Among Health Care Workers in Israel JAMA published online January 10, 2022

doi:10.1001/jama.2021.23641

This is a prospective cohort study conducted at a tertiary medical center in Israel. The study cohort included 1928 immunocompetent HCWs who were previously vaccinated with a 2-dose series of Pfizer, and had enrolled between August 8 and 19, 2021, with final follow-up reported through September 20, 2021. Screening for SARS-CoV-2 infection was performed every 14 days. Anti–spike protein receptor binding domain IgG titers were determined at baseline and 1 month after enrollment. Cox regression with time-dependent analysis was used to estimate hazard ratios of SARS-CoV-2 infection between booster-immunized status and 2-dose vaccinated (booster-nonimmunized) status.

Among 1928 participants, the median age was 44 years and 1381 were women (71.6%). Participants completed the 2-dose vaccination series a median of 210 days before study enrollment. A total of 1650 participants (85.6%) received the booster dose. During a median follow-up of 39 days, SARS-CoV-2 infection occurred in 44 participants (incidence rate, 60.2 per 100 000 person-days); 31 (70.5%) were symptomatic. Five SARS-CoV-2 infections occurred in booster-immunized participants and 39 in booster-nonimmunized participants (incidence rate, 12.8 vs 116 per 100 000 person-days, respectively). In a time-dependent Cox regression analysis, the adjusted hazard ratio of SARS-CoV-2 infection for booster-immunized vs booster-nonimmunized participants was 0.07 (95% CI, 0.02-0.20).



Comment: Among health care workers at a single center in Israel who were previously vaccinated with a 2-dose series of Pfizer, administration of a booster dose compared with not receiving one was associated with a significantly lower rate of SARS-CoV-2 infection over a median of 39 days of follow-up. The short follow-up and the relatively young and healthy population in the study limit the generalizability of the results. Booster vaccine doses reduce the risk of infection therefore, boosters should hopefully decrease transmission. (See next article)

High Rate of Asymptomatic Carriage Associated with Variant Strain Omicron

medRxiv posted December 27, 2021

doi.org/10.1101/2021.12.20.21268130

In early December 2021, a clinical trial, designed to evaluate efficacy of the Moderna vaccine among persons living with HIV (PLWH), began enrolling participants. Nasal swabs are routinely obtained at the initial vaccination visit, which requires participants to be clinically well to receive their initial jab. Of the initial 230 participants enrolled between December 2 and December 17, 2021, 71 (31%) were PCR positive for SARS-CoV-2: all of whom were subsequently confirmed by S gene dropout to be Omicron; 48% of the tested samples had cycle threshold (CT) values <25 and 18% less than 20, indicative of high titers of asymptomatic shedding. Asymptomatic carriage rates were similar in SARS-CoV-2 seropositive and seronegative persons (27%

respectively). These data are in stark contrast to COVID-19 vaccine studies conducted pre-Omicron, where the SARS-CoV-2 PCR positivity rate at the first vaccination visit ranged from <1%-2.4%, including a cohort of over 1,200 PLWH largely enrolled in South Africa during the Beta outbreak. They also evaluated asymptomatic carriage in a sub study of the Sisonke vaccine trial conducted in South African health care workers, which indicated 2.6% asymptomatic carriage during the Beta and Delta outbreaks and subsequently rose to 16% in both PLWH and PHLWH during the Omicron period.

Comment: These findings strongly suggest that Omicron has a much higher rate of asymptomatic disease than other variants and this high prevalence of asymptomatic infection is likely a contributing factor in the widespread, rapid dissemination of the variant globally, even among populations with high prior rates of SARS-CoV-2 infection and/or vaccination.

Direct Comparison of SARS Co-V-2 Nasal RT- PCR and Rapid Antigen Test (BinaxNOWTM) at a Community Testing Site During an Omicron Surge medRxiv posted January 10, 2022 article provided by Josh Septimus

doi.org/10.1101/2022.01.08.22268954

This report includes data collected January 3-4, 2022, at a free, outdoor, walk- up testing and vaccine site situated in an outdoor parking lot in the heart of the Mission Cultural District in San Francisco. Persons seeking testing provided demographics, symptoms and onset date, vaccination status, reason for testing and informed consent. RT-PCR using probes specific to N and E genes were performed on the nasal swabs collected in DNA/RNA Shield (Zymo Research) with an internal human positive control (RNAse P). The assay limit of detection is 100 viral copies/mL; cycle thresholds less than 40 were considered positive

731 persons sought COVID-19 testing at a walk-up San Francisco community site in January 2022. Simultaneous nasal rapid antigen testing (BinaxNOW) and RT-PCR testing was performed. There were 296 (40.5%) positive tests by RT-PCR; 97% of a random sample were the omicron variant. Sensitivity of a single antigen test was 95.2% (95% CI 92-98%); 82.1% (95% CI 77-87%) and 65.2% (95% CI 60-70%) for Ct threshold of < 30, < 35 and no threshold, respectively. When stratified by asymptomatic versus symptomatic BinaxNOW had greater sensitivity with symptoms especially with Ct<30. (see below)

Population	BinaxNOW Performance	All Persons	Symptom Onset ≤ 7 Days	Asymptomatic or Symptom Onset > 7 Days Ago
All ages (N = 731) Value (95% CI)	**Ct = 30 cutoff**			
	Sensitivity	95.2% (177/186; 91.8 – 97.9)	97.6% (123/126; 94.6 – 100)	89.8% (43/59; 81.4 – 96.6)
	Specificity	96.5% (526/545; 94.9 – 98.0)	96.4% (160/166; 93.2 – 98.8)	96.5% (362/375; 94.5 – 98.2)
	Ct = 35 cutoff			
	Sensitivity	82.1% (193/235; 77.2 – 86.8)	84.2% (128/152; 78.2 – 89.8)	78.0% (64/82; 68.7 – 86.7)
	Specificity	99.4% (493/496; 98.6 – 100)	99.3% (139/140; 97.7 – 100)	99.4% (350/352; 98.6 – 100)
	No Ct Cutoff			
	Sensitivity	65.2% (193/296; 59.7 – 70.6)	74.0% (128/173; 67.2 – 80.3)	52.5% (64/122; 43.5 – 61.5)
	Specificity	99.3% (432/435; 98.4 – 100)	99.2% (118/119; 97.2 – 100)	99.4% (310/312; 98.3 – 100)

Comment: A single BinaxNow rapid antigen test detected 95% of high viral load omicron cases from nasal specimens. (Ct<30) This cross- sectional analysis confirms that the BinaxNOW rapid antigen test detects omicron with a sensitivity similar to that observed for prior variants. The assay rapidly identifies persons with highest levels of virus, and thus those likely to pose the greatest risk for transmission. As we reflect on new CDC guidance on isolation, adding a rapid antigen at 5 days before returning to work in healthcare would have been a welcome addition.

Effectiveness of BNT162b2 Vaccine against Critical Covid-19 in Adolescents N Engl J Med published online January 12, 2022

DOI: 10.1056/NEJMoa2117995

The investigators screened admission logs for eligible case patients with laboratory confirmed Covid-19 at 31 hospitals in 23 states between July 1 and October 25, 2021. They used a case–control, test-negative design to assess VE against Covid-19 resulting in hospitalization, admission to an intensive care unit (ICU), the use of life-supporting interventions (mechanical ventilation, vasopressors, and ECMO), or death. They estimated VE by comparing the odds of antecedent full vaccination (two doses of Pfizer) in case patients as compared with two hospital-based control groups: patients who had Covid-19–like symptoms but negative results on testing for SARS-CoV-2 (test-negative) and patients who did not have Covid-19–like symptoms (syndrome negative).

A total of 445 case patients 12 to 18 years old and 777 controls were enrolled after the emergence of the Delta variant. Seventeen case patients (4%) and 282 controls (36%) had received two doses of the Pfizer vaccine. Among case patients, 180 (40%) were admitted to an intensive care unit (ICU), and 127 (29%) needed life support. Of all ICU patients, only two were

fully vaccinated. Overall vaccine effectiveness (VE) against hospitalization was 94% (95% confidence interval [CI], 90 to 96).

Among uninfected controls with COVID-like symptoms, VE was 95% (95% CI, 91 to 97), while it was 94% (95% CI, 89 to 96) among uninfected controls with no symptoms. VE was 98% against ICU admission and 98% against requiring life support. Seven patients died, and 13 required extracorporeal membrane oxygen, all of whom were unvaccinated. Three-quarters of the COVID-19 patients had underlying chronic illnesses, and nearly half were Black or Hispanic (24% and 25%, respectively).

Table 2. Clinical Outcomes and Covid-19 Severity among Hospitalized Case Patients, According to Vaccination Status.*

Variable	Unvaccinated (N=427)	Fully or Partially Vaccinated (N=18)
Severe Covid-19 — no. (%)†	194 (45)	2 (11)
ICU admission — no. (%)	178 (42)	2 (11)
Life-threatening illness with life support — no. (%)‡	126 (30)	1 (6)
Invasive mechanical ventilation — no./total no. (%)	48/425 (11)	1/18 (6)
Noninvasive mechanical ventilation (BiPAP or CPAP) — no./total no. (%)	90/423 (21)	1/18 (6)
Vasoactive infusions — no./total no. (%)	38/426 (9)	1/18 (6)
Extracorporeal membrane oxygenation — no./total no. (%)	13/425 (3)	0
Patients with discharge data — no./total no. (%)	407/427 (95)	18/18 (100)
Median length of hospital stay (IQR)§	5 (2–7)	4 (1–5)
Death before discharge — no./total no. (%)	7/407 (2)	0

Comment: In this real-world study when Delta was dominant, they found that the vaccine was highly effective against Covid-19 hospitalization and critical illness, including among patients with underlying risk factors for severe illness. Vaccination prevented nearly all life-threatening Covid-19 illness in this age group. Unfortunately, <25% of US children aged 5 to 11 years had received at least one COVID-19 vaccine and just over 60% of adolescents have received at least one dose.

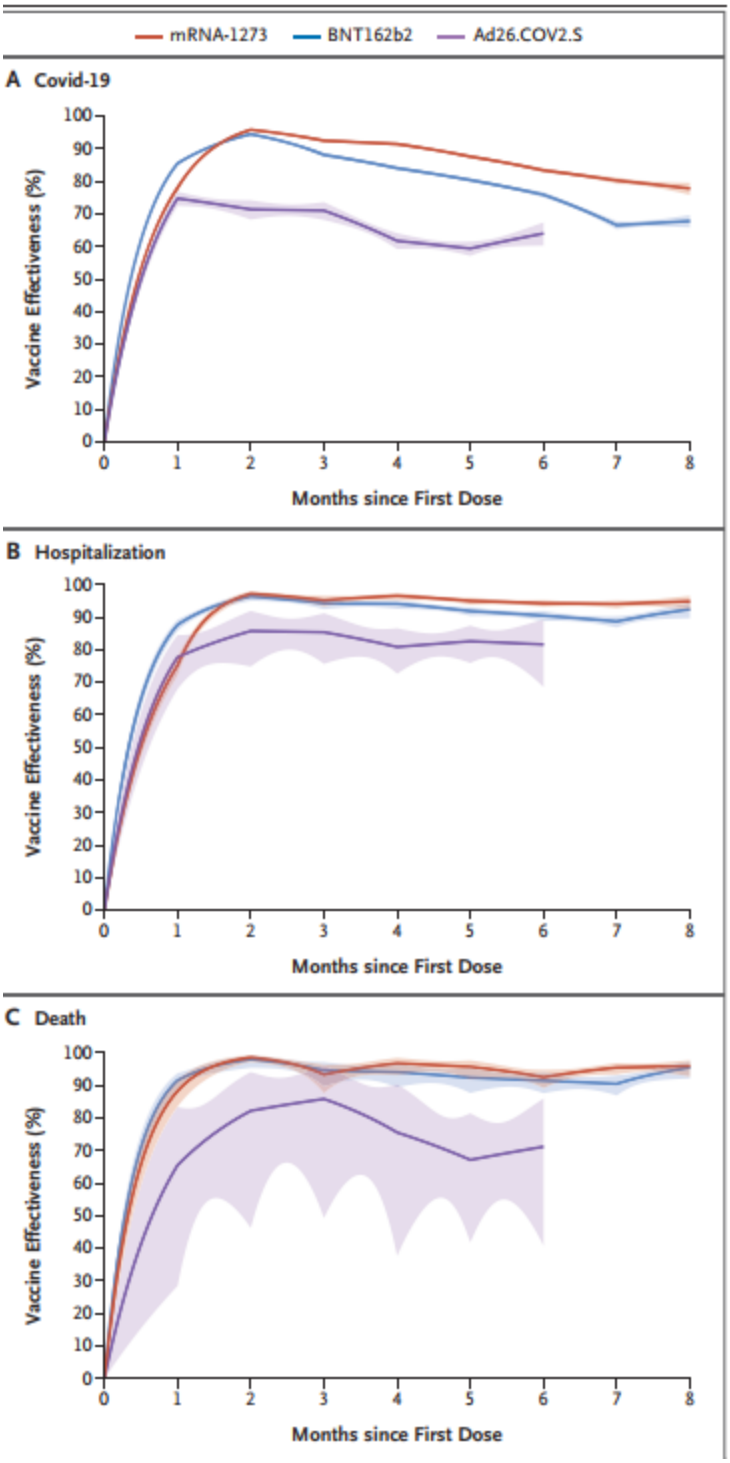
Effectiveness of Covid-19 Vaccines over a 9-Month Period in North Carolina N Engl J Med published online January 12, 2022

DOI: 10.1056/NEJMoa2117128

The investigators extracted data regarding Covid-19–related vaccination and outcomes during a 9-month period (December 11, 2020, to September 8, 2021) for approximately 10.6 million North Carolina residents by linking data from the North Carolina Covid-19 Surveillance System and the Covid-19 Vaccine Management System. They used a Cox regression model to estimate the effectiveness of the Pfizer, Moderna, J&J vaccines in reducing the current risks of Covid-19, hospitalization, and death, as a function of time elapsed since vaccination.

Two months after receipt of the first Pfizer or Moderna COVID-19 vaccine, estimated VE against symptomatic or asymptomatic infection was 94.5% (95% CI, 94.1 to 94.9) and 95.9% (95% CI, 95.5 to 96.2), respectively, declining to 66.6% (95% CI, 65.2 to 67.8) and 80.3% (95% CI, 79.3 to 81.2), respectively, by 7 months. Estimated VE among patients who received the Pfizer or Moderna vaccine early fell by roughly 15 and 10 percentage points, respectively, from mid-June to mid-July, when the Delta variant became dominant. Among recipients of the one-dose J&J vaccine, VE against infection was 74.8% (95% CI, 72.5 to 76.9) at 1 month, dropping to 59.4% (95% CI, 57.2 to 61.5) at 5 months.

VE against hospitalization or death after two doses of the Pfizer vaccine peaked at 96.4% (95% CI, 95.1 to 97.4) at 2 months and was still at 88.7% (95% CI, 86.9 to 90.3) at 7 months. Moderna two-dose effectiveness peaked at 97.2% (95% CI, 96.1 to 98.0) at 2 months and was still 94.1% (95% CI, 92.7 to 95.2) at 7 months. VE of the J&J vaccine peaked at 85.8% (95% CI, 74.9 to 91.9) at 2 months and remained higher than 80% through 6 months. All three vaccines were better at preventing hospitalization and death over time than at preventing infection, although the Pfizer and Moderna vaccines offered more protection than J&J. (see next article)



Comment: All three vaccines were better at preventing hospitalization and death over time than at preventing infection, although the Pfizer and Moderna vaccines offered more protection than J&J. This study suggests that waning immunity is leading to breakthrough COVID-19 infections, but vaccines-maintained effectiveness against hospitalization and severe disease 9 months after the first injection. This study was observational and thus was limited by

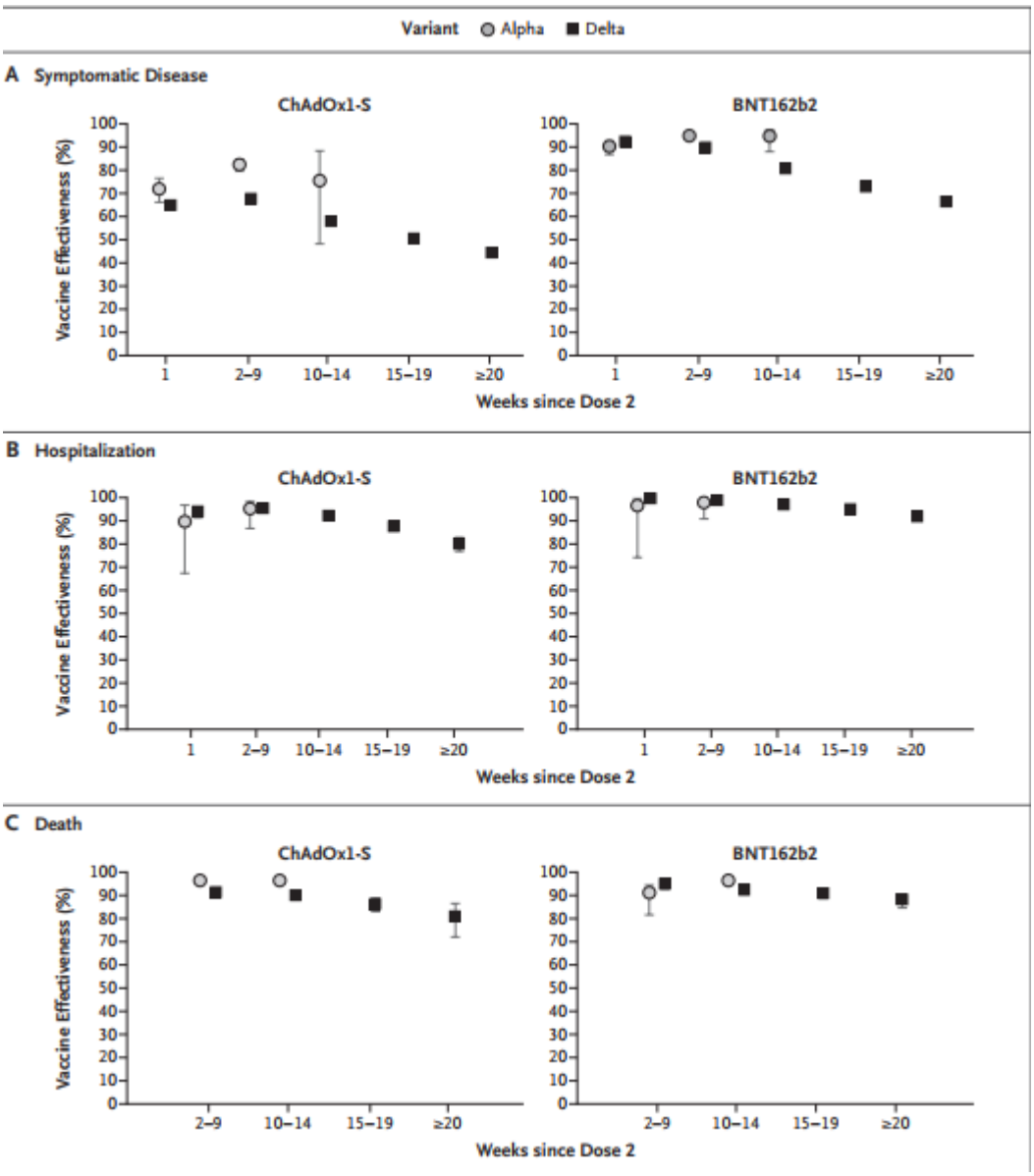
confounding bias. They did adjust for measured confounders (age, sex, race or ethnic group, geographic region, and county-level vaccination rate). See next article

Duration of Protection against Mild and Severe Disease by Covid-19 Vaccines N Engl J Med published online January 12, 2022

DOI: 10.1056/NEJMoa2115481

The investigators used a test-negative case–control design to estimate vaccine effectiveness against symptomatic Covid-19 and related hospitalization and death in England. Effectiveness of the AZ and Pfizer vaccines was assessed according to participant age and status with regard to coexisting conditions and over time since receipt of the second vaccine dose to investigate waning of effectiveness separately for the Alpha and Delta variants.

VE against symptomatic disease caused by the Delta variant peaked in the early weeks after the second dose, then declined by 20 weeks to 44.3% (95% CI, 43.2 to 45.4) for AstraZeneca and 66.3% (95% CI, 65.7 to 66.9) for Pfizer. Waning VE against infection with symptoms was greater in patients 65 years and older than in those 40 to 64. VE against hospitalization with infection with the Delta variant was 80.0% (95% CI, 76.8 to 82.7) with AstraZeneca and 91.7% (95% CI, 90.2 to 93.0) with Pfizer 20 weeks or more after vaccination. Similarly, VE against death due to the Delta variant for the AstraZeneca vaccine was 84.8% (95% CI, 76.2 to 90.3) and 91.9% for Pfizer (95% CI, 88.5 to 94.3).



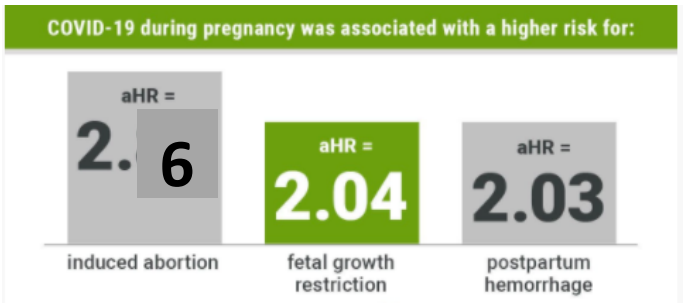
Comment: This study and the one above and others confirm VE against symptomatic disease wanes over time, but protection against hospitalization and death was sustained at high levels for at least 20 weeks or longer after receipt of the second dose. The test negative case–control study design is observational and, therefore, subject to potential bias. The estimates of vaccine effectiveness relate to the population of persons who seek testing and were successfully matched to the NIMS database, so they may not be representative of the whole population. All of these articles confirm that despite waning VE against symptomatic disease, vaccination maintains significant protection against severe disease and death.

SARS-CoV-2 infection during pregnancy and associated perinatal health outcomes: a national US cohort study J Infect Dis published online December 27, 2022

DOI: 10.1093/infdis/jiab626

The investigators conducted a national cohort study using de-identified administrative claims data for 78,283 pregnancies with estimated conception before 30 April 2020 and pregnancy end after 11 March 2020. They identified maternal infections using diagnostic and laboratory testing data.

2,655 (3.4%) had documented SARS-CoV-2 infection; 3.4% required admission to ICU, MV, or ECMO. Covid-19 infection during pregnancy was not associated with risk of miscarriage, antepartum hemorrhage, or stillbirths, but associated with a 2-3 fold higher risk of induced abortion [aHR 2.6 CI 1.17-5.78], c-section [aHR 1.99 CI 1.71,2.31], clinician-initiated preterm birth [2.88, CI 1.93, 4.30], spontaneous preterm birth [aHR 1.79 CI 1.37-2.34], fetal growth restriction [aHR 2.04, CI 1.72-2.43], and postpartum hemorrhage [aHR 2.03 CI 1.6-2.63]



Comment: Based on this large cohort, Covid-19 infection during pregnancy was associated with increased risk of poor pregnancy outcomes. This study confirms other studies which all demonstrates similar findings. Several studies have identified higher rates of maternal mortality associated with SARS-CoV-2 infection during pregnancy, and this remains an important maternal health outcome for consideration in future studies. The maternal mortality rate was higher in this study than the national average. The database for this study was commercially insured pregnant women which may not be generalizable for the entire population. This study supports vaccination in pregnancy.