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Infectious Diseases Watch

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General Infectious Diseases

2022 SPECIAL REPORT July 2022
COVID-19 U.S. IMPACT ON ANTIMICROBIAL RESISTANCE

Key Takeaways:

- The report, *COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022*, concludes that the threat of AR infections is not only still present but has gotten worse in the U.S.—with **resistant hospital-onset infections and deaths both increasing at least 15%** during the first year of the pandemic.
- **More than 29,400 people died from AR infections** commonly associated with healthcare during the first year of the pandemic. Of these, **nearly 40% of the people** got the infection while they were in the hospital. The burden of resistance is likely much higher, but the pandemic caused data gaps.
- For many **community-associated pathogens,** infection and death data **were delayed or unavailable** as many clinics and healthcare facilities had limited services, served fewer patients, or closed their doors entirely in the face of challenges from COVID-19.

Available data show an alarming increase in resistant infections starting during hospitalization, growing at least 15% from 2019 to 2020.

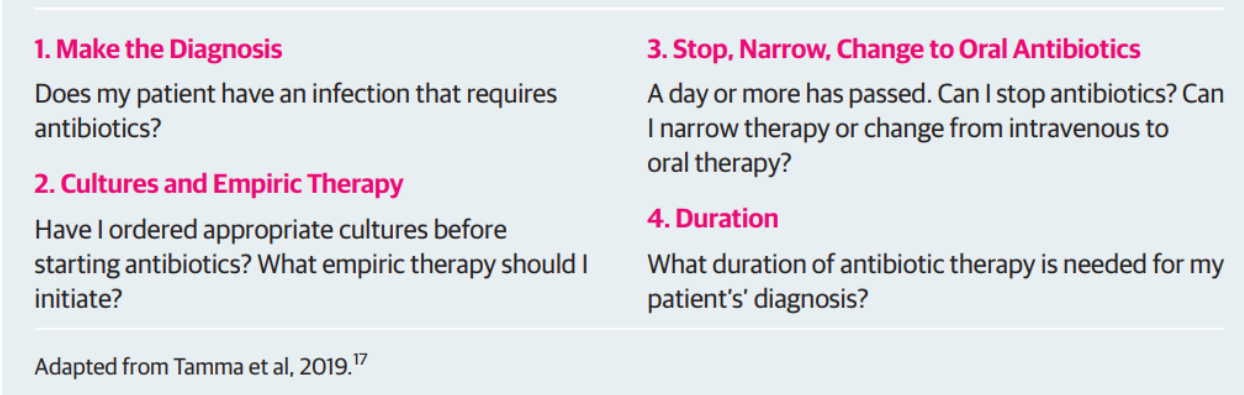
- Carbapenem-resistant *Acinetobacter* (↑78%)
- Antifungal-resistant *Candida auris* (↑60%)*
- Carbapenem-resistant Enterobacterales (↑35%)
- Antifungal-resistant *Candida* (↑26%)
- ESBL-producing Enterobacterales (↑32%)
- Vancomycin-resistant Enterococcus (↑14%)
- Multidrug-resistant *P. aeruginosa* (↑32%)
- Methicillin-resistant *Staphylococcus aureus* (↑13%)

Comment: The findings in this report are disappointing because prior to the pandemic, the progress was being made against AMR and HAIs. More than 90% of US hospitals had implemented an antibiotic stewardship program, and rates of HAIs had been in decline since 2015. Data from 2012 through 2017 show that US deaths from AMR fell by 18% overall and by 30% in hospitals. In the last issue of ID Watch I reviewed the HAI rates during year two of the pandemic. [ICHE may 20, 2022] Device related HAIs and MDROs have continued to increase. When Covid-19 cases increased in hospitals so did HAIs and antibiotic use. During surges hospitals treated sicker patients who required frequent and longer use of catheters and ventilators. We must continue to invest in prevention-focused interventions that we know work, such as accurate rapid diagnostics, effective infection prevention, and expansion of innovative

strategies to combat antimicrobial resistance. These include new vaccines to combat infections that can develop antimicrobial resistance, and new decolonizing strategies to stop the spread of antimicrobial-resistant organisms by carriers.

Assessment of Changes in Visits and Antibiotic Prescribing During the Agency for Healthcare Research and Quality Safety Program for Improving Antibiotic Use and the COVID-19 Pandemic JAMA Netw Open . 2022;5(7):e2220512. doi:10.1001/jamanetworkopen.2022.20512

Based on AHRQ's Four Moments of Antibiotic Decision Making framework, the AHRQ Safety Program uses webinars, audio presentations, educational tools, and office hours to establish an antibiotic stewardship infrastructure and culture.



Participating clinics selected clinical and administrative leads to oversee implementation of the program, and those leads were encouraged to hold monthly staff meetings to review practice-level data on antibiotic prescribing and educational materials. To evaluate the program, the investigators looked at monthly data submitted by the participating clinics during a baseline period (September through November 2019) and the intervention period (December 2019 through November 2020). The primary outcome was antibiotic prescriptions per 100 acute respiratory infection (ARI) visits, with a secondary outcome of antibiotic prescriptions per 100 visits. Data on total visits and ARI visits were also collected.

Of the 467 practices that enrolled in the program, 389 remained until its completion and 292 submitted complete data for analysis. The data covered more than 6.5 million visits to 5,483 clinicians. Participants included urgent care clinics (35%), primary care practices (28%), pediatric urgent care clinics (13%), federally supported practices (12%), pediatric-only clinics (7%), and other clinics (5%).

Overall, antibiotic prescribing declined from 18.2% of visits at baseline to 9.5% of visits at the end of the program (absolute decline –8.7%; 95% confidence interval [CI], –9.9% to –7.6%). A total of 87% of practices reduced antibiotic prescribing per 100 visits, with the decrease more evident for urgent care and pediatric practices. Antibiotic prescriptions for ARI visits declined from 39.2% at baseline to 24.7% at the end of the program (absolute reduction, –14.5%; 95% CI, –16.8% to –12.2%), with urgent care practices seeing the steepest declines. A total of 80% of practices reduced antibiotic prescribing per 100 ARI visits.

Although the study period coincided with the early months of the COVID-19 pandemic, which saw patient visits per practice per month decline substantially (from 1,624 at baseline to 906 in

April 2020), by the end of the study, all practice types had returned to baseline visit rates. The investigators also note that the decline in prescribing was per visit, so it was not as affected by patient volume.

Figure 2. Acute Respiratory Infection (ARI) Visits and Antibiotic Prescriptions per 100 ARI Visits Over Time

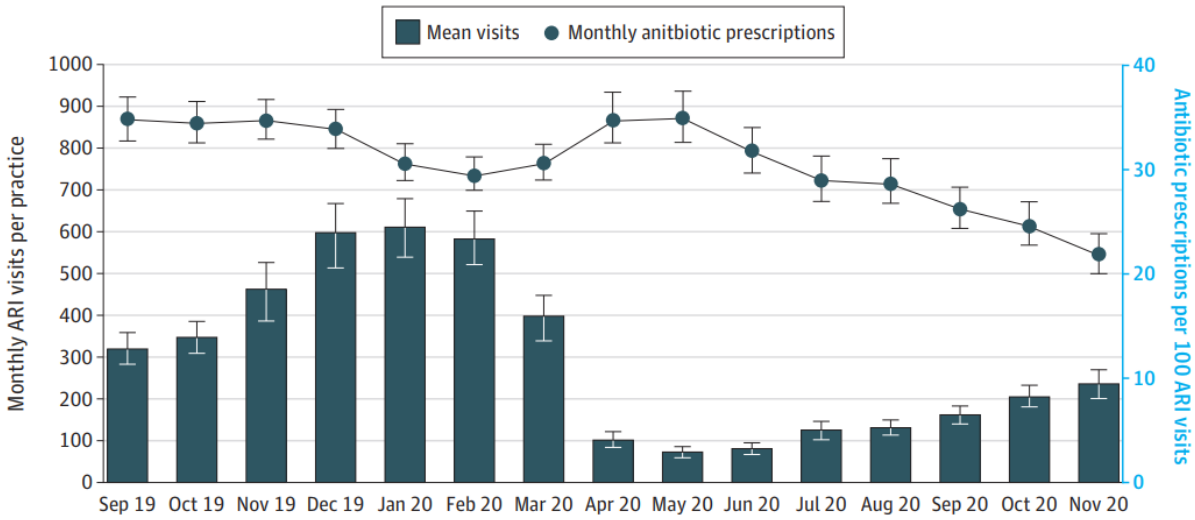
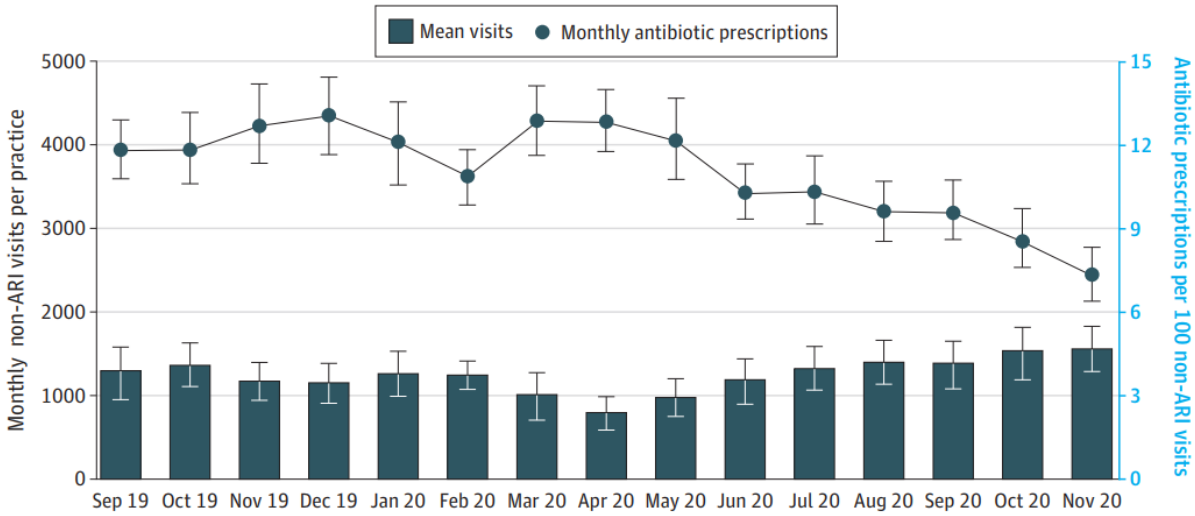


Figure 3. Non-Acute Respiratory Infection (ARI) Visits and Antibiotic Prescriptions per 100 Non-ARI Visits Over Time



Comment: In this study of US ambulatory care sites, the AHRQ Safety Program successfully launched and retained engagement in AS in a national collaboration of ambulatory care practices, despite challenges posed by the COVID-19 pandemic. There was a significant decrease in antibiotic prescribing per 100 visits and per 100 ARI visits. Addressing behavior and communication and empowering frontline staff to take part in AS was an important consideration when establishing ambulatory AS. Despite the findings, it was difficult to distinguish the

association of the COVID-19 pandemic with antibiotic prescriptions from the association of the program with antibiotic prescriptions since there was no control group was used. Because data abstraction tools were built before the COVID-19 pandemic, data were not collected about COVID-19 diagnoses and no *ICD-10* codes were included for COVID-19. In addition, the focus was on prescriptions, so delayed prescriptions (i.e., an antibiotic prescription provided to a patient for an antibiotic-inappropriate condition with instructions to not fill the prescription unless they were still feeling poorly after several days) would have been counted. Despite these potential limitations, the results of this project shows that with appropriate supports and tools we can reduce unnecessary OP antibiotics. It would be nice to be able to go back in one year to see if these gains have been sustained.

Clinical Spectrum of Children with Acute Hepatitis of Unknown Cause N Engl J Med published online July 13, 2022

DOI: 10.1056/NEJMoa2206704

A Case Series of Children with Acute Hepatitis and Human Adenovirus Infection published online July 13, 2022

DOI: 10.1056/NEJMoa2206294

The first article comes from Birmingham in the UK. The UK uses three referral centers, including the one in Birmingham, to centralize the care of patients who may undergo liver transplantation. This article reported on 44 children who received treatment at the Birmingham liver center and whose conditions were consistent with the confirmed case definition of the UK Health Security Agency (e.g., non-A–E acute hepatitis without a metabolic, inherited or genetic, congenital, or mechanical cause in a child ≤10 years of age with a serum aminotransferase [ALT or AST] level >500 IU per liter); the median age of patients in the cohort was 4 years. The majority of the patients presented with jaundice and gastrointestinal symptoms. Six of the patients had progression to liver failure and underwent liver transplantation. Common presenting features were jaundice (in 93% of the children), vomiting (in 54%), and diarrhea (in 32%). Among the 30 patients who underwent molecular testing for human adenovirus, 27 (90%) were positive. Fulminant liver failure developed in 6 patients (14%), all of whom received a liver transplant. None of the patients died. All the children, including the 6 who received liver transplants, were discharged home.

In the study from the US report there were nine patients from various locations in Alabama who were treated at children's hospital in Birmingham AL and who had presenting signs and ages similar to those in the UK cohort, although the US investigators used different criteria for aminotransferase levels (>250 U per liter for ALT and >440 U per liter for AST).
Three of the patients had progression to liver failure, and two of these patients underwent liver transplantation. Eight (89%) of the patients with hepatitis of unknown cause tested positive for human adenovirus Liver biopsies indicated mild-to-moderate active hepatitis in 6 children but did not show evidence of human adenovirus on immunohistochemical examination or electron microscopy. PCR testing of liver tissue for human adenovirus was positive in 3 children (50%). Sequencing of specimens from 5 children showed three distinct human adenovirus type 41 hexon variants.

Comment: Of interest is the discovery that all 9 of the children in the US case series and 27 of the 30 children who underwent molecular testing in the UK study tested positive for human adenovirus type 41. Serum viral loads in the patients with progression to liver failure were

substantially higher than those in the patients who spontaneously recovered. Is there sufficient evidence that human adenovirus 41 is a new cause of pediatric hepatitis/liver failure? In the US there has not been an increase in reported cases of adenoviral hepatitis.[MMWR 2022;71:797-802] In addition, , none of the histologic evaluations have revealed evidence of hepatocellular adenoviral infection, which is different from immunocompromised patients. Adenoviral infections are exceedingly common during childhood, and human adenovirus 41 is known to cause acute gastroenteritis, although not in association with liver failure to my knowledge. [Sci Adv 2021;7:eabe0974] Without evidence of adenovirus-mediated tissue damage, studies to date are not yet sufficient to link human adenovirus 41 as a firm cause of acute hepatitis that can lead to liver failure.

CDC Recommends High Dose or Adjuvant Flu Vaccine for Seniors

The CDC director has approved a new guideline that indicates that adults aged 65 and older should preferentially receive one of the higher-dose or adjuvanted influenza vaccines over standard-dose or unadjuvanted flu vaccines. The recommendation was made June 22 by majority vote of the ACIP. ACIP voted to preferentially recommend the use of higher dose flu vaccines (Fluzone High-Dose vaccine and Flublok recombinant vaccine) or adjuvanted flu vaccine (Fluad vaccine) over standard-dose unadjuvanted flu vaccines.

Comment: In the last decade, CDC had not recommended any one flu vaccine over another for any age group, and there is still no preferential recommendation for people younger than 65. Based on known immunesenescence and antibody studies, many of us had already recommended high-dose or adjuvant vaccine for our patient >65. I am not sure why it took so long form ACIP to finally change their recommendation.

Polio in US

The New York Department of Health on Thursday reported a case of polio in a resident of the state's Rockland County. This case marks the first in the U.S. in nearly a decade. he is sequencing showed revertant polio Sabin type 2 virus.

Comment: This is indicative that transmission was probably from an individual who received the OPV, which is no longer authorized or administered in the U.S., where only the IPV has been given since 2000. This also suggests that the virus probably originated outside of the U.S. where OPV is still being administered, since revertant strains cannot emerge from inactivated vaccines. The person infected had not been vaccinated for polio and is part of the Jewish ultraorthodox community known for their low vaccination rates.

Monkeypox

VII Perspective

The monkeypox outbreak is now a global health emergency. [see below] The US response to this public health emergency has been inconsistent and slow at times, but overall better than the initial response to SARS-CoV-2. They have expanded testing and now after significant pushback have made it easier to order tecovirimat. But more needs to be done.

Monkeypox is not a new disease. It was discovered in the early 1970s and for years has been well-described by public health in West and Central Africa, where the disease has been present for decades. There are tests to diagnose it, vaccines to prevent it, treatments to improve symptoms and clinical outcomes.

In early June, we seemed overconfidence. US officials told us Monkeypod spread very differently than SARS-CoV-2. It is not as contagious as Covid so many believed we were going to be able to keep it from spreading. They were wrong. While this outbreak thus far has mostly affected men who have sex with men, it is possible it could begin spreading in settings where there is no close or physical contact. [US just reported the first two pediatric cases]In addition, Monkeypox, unlike smallpox, can also infect animals, providing new mammalian reservoirs for the infection, which also becomes a possibility as this current outbreak continues to grow.

How did this happen? First, the rollout of monkeypox testing was initially conservative, routed through state health departments. As stated earlier the CDC did respond by allowing major commercial diagnostic companies to perform the initial test as well.

Next, one of the key vaccines against monkeypox, the two-dose Jynneos vaccine has been in short supply, far below the volume needed for a full vaccination campaign — even though the US has access to most of the world's stockpile. When monkeypox was first detected in the US in May, the administration announced that the US had enough smallpox vaccine (also approved for monkeypox) in the Strategic National Stockpile (SNS), however, most of the stockpiled doses consisted of the older ACAM2000 vaccine, which was deployed on May 23. But that vaccine carries the risk of myocarditis (1 in 175 vaccinees) and pain at the injection site, which can fester and further spread the virus with close contact. Plus, people with compromised immune systems cannot safely receive the older vaccine. Jynneos carries fewer risks, but only 2,400 doses were in the SNS at the onset of the outbreak, per the US Department of HHS. On May 20 HHS's Biomedical Advance Research and Development Authority (BARDA) requested 36,000 Jynneos doses from Bavarian Nordic, followed by another request for the same number on June 10. Finally in early July, the FDA inspected 786,000 doses of Jynneos at Bavarian Nordic's Danish finish-and-fill facility to ship to the US after it approves the inspection at the end of the month and about 5 million more for delivery in mid-2023. HHS said it has now fast-tracked the FDA application and inspection, which was originally scheduled for this fall.

Controlling the growing international monkeypox outbreak will in part based on the availability of millions of vaccine doses. But the vaccines are in very limited supply, with people from all over the US reporting waiting in long lines only to be turned away from clinics. This echoes the bumpy COVID-19 vaccine rollout. If we used ring and contact racing early on, vaccinated high risk groups, we could have blunted the number of cases. Doctors also complained about the burden of paperwork required to access US stockpiles of key drugs to treat the infections, but this is now being addressed. [see below]

Monkeypox, reminds us again that it does not work to wait for an outbreak to order the tests, vaccines, and treatments to manage the situation, because drug and vaccine supply chains can take months to years to fill the emergency orders needed now. This brings me to my last point: The White House announced last week that they are creating a division within the Department of HHS that will focus on health disasters such as a pandemic. Instead, what we should do is to fix the problems at the CDC and the FDA, and give them the resources they need to get the job done. This announcement gives the impression, rightly or wrongly, that in creating a new entity and passing a critical responsibility to a new untested government entity in the midst of

two public health crises reflects the lack of trust in the CDC and FDA. Does this make sense? You decide

WHO declares monkeypox a global health emergency Monkeypox Update

For the second time in as many months, the World Health Organization (WHO) convened a meeting today to determine if the ongoing global outbreak of monkeypox infections warrants a public health emergency of international concern (PHEIC). The answer was YES

During opening remarks, WHO Director-General Tedros Adhanom Ghebreyesus, PhD, said worldwide cases are mostly still in men who have sex with men (MSM).

"This transmission pattern represents both an opportunity to implement targeted public health interventions, and a challenge because in some countries, the communities affected face life-threatening discrimination."

As of today, 75 countries have reported more than 16,500 cases. Europe remains the epicenter of the monkeypox outbreak; according to data from the WHO, Europe has 10,064 cases from 36 countries. Spain, the United Kingdom, and Germany have the bulk of the cases. However, the US now has the second-highest tally at nearly 2,900. There has been one intensive care unit admission, but no deaths have been reported.

In the US, the outbreak continues to grow, with the CDC adding 215 more monkeypox cases to its total mid-week, raising the number to over 2,900.North Dakota has become the latest state to report an initial case of the virus.

Comment: This transmission pattern represents an opportunity to implement targeted public health interventions. [See next 4 articles] The outbreak can be contained if countries work with communities of men who have sex with men, while stressing we should avoid stigmatizing this group.

Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients, Barcelona, Spain, May to June 2022 Eurosurveillance published online July 14, 2022 . Euro Surveill. 2022;27(28):pii=2200503.

doi.org/10.2807/1560-7917.ES.2022.27.28.2200503

The investigators tested 147 clinical samples collected at different time points from 12 patients by real-time PCR. MPX DNA was detected in saliva from all cases, sometimes with high viral loads. [low Ct] Other samples were frequently positive: rectal swab (11/12 cases), nasopharyngeal swab (10/12 cases), semen (7/9 cases), urine (9/12 cases) and feces (8/12 cases).

Comment: This is a small study, but the results contribute to helping to improve our understanding of the complex transmission enigma and underline other immediate areas for research such as the infectivity of bodily fluids, the frequency of secondary and asymptomatic cases or the impact of social and behavioral factors affecting viral transmission. The outbreak disproportionately impacts men who had sex with men. The preliminary results from this study may help explain non travel related transmission. Like many studies with Covid-19, the investigators use Ct to estimated viral loads.

Demographic and clinical characteristics of confirmed human monkeypox virus cases in individuals attending a sexual health centre in London, UK: an observational analysis Lancet Infect Dis published online July 1, 2022

doi.org/10.1016/ S1473-3099(22)00411-X

Previously most monkeypox (MPX) cases occurred in Africa, but in recent months, an outbreak of MPX has been recognized in Europe, the US, and other countries outside of Africa. This paper summarizes a UK case series which provides impiortant information about the characteristics of this outbreak.

Between May 14 and May 25, 2022, MPX was diagnosed in 54 individuals seen at four sexual health clinics in London. All identified as men who have sex with men (MSM). The following features were notable:

- 57% reported fevers.
- 94% had anogenital lesions and 56% had lymphadenopathy (mainly inguinal).
- One quarter had a concurrent sexually transmitted infection.
- Five individuals (9%) were hospitalized (four for anogenital cellulitis and one with disseminated vesicles, facial cellulitis, and pain). No deaths occurred.
- Thirteen individuals (24%) had HIV; all were on ART and had normal CD4 cell counts; 11 had undetectable HIV RNA and the others had just begun ART.
- Skin lesions at >3 sites were present in 22% of those without HIV and 54% of those with HIV.

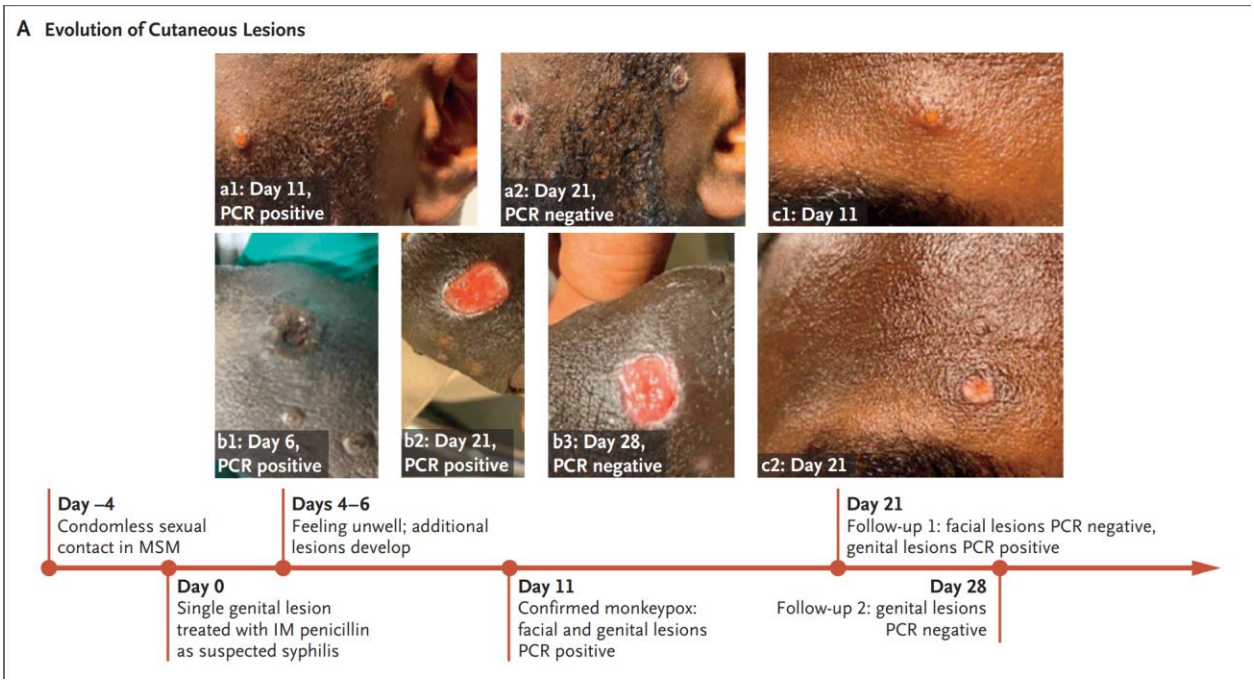
Comment: The investigators found a high proportion of concomitant STIs and frequent anogenital symptoms, suggesting transmissibility through local inoculation during close skin-to-skin or mucosal contact, during sexual activity. Further studies to clarify routes of transmission and viral distribution in the population are urgently needed to inform infection control policies, contact tracing, prevention and education policies, and strategies to prevent ongoing viral circulation, given the high risk of further outbreaks in global settings. Lastly, patients suspected of MPX should be tested for other STIs.

Monkeypox Virus Infection in Humans across 16 Countries — April–June 2022 N Engl J Med published online July 21, 2022

DOI: 10.1056/NEJMoa2207323

The investigators report 528 infections diagnosed between April 27 and June 24, 2022, at 43 sites in 16 countries. Overall, 98% of the persons with infection were gay or bisexual men, 75% were White, and 41% had HIV; the median age was 38 years. Transmission was suspected to have occurred through sexual activity in 95% of the persons with infection. In this case series, 95% of the persons presented with a rash (with 64% having <10 lesions), 73% had anogenital lesions, and 41% had mucosal lesions (with 54 having a single genital lesion). Common systemic features preceding the rash included fever (62%), lethargy (41%), myalgia (31%), and headache (27%); lymphadenopathy was also common (reported in 56%). Concomitant sexually transmitted infections were reported in 109 of 377 persons (29%) who were tested. Among the 23 persons with a clear exposure history, the median incubation period was 7 days (range, 3 to

20). Monkeypox virus DNA was detected in 29 of the 32 persons in whom seminal fluid was analyzed. No deaths were reported.



Comment: The strong likelihood of sexual transmission is supported by the findings of primary genital, anal, and oral mucosal lesions, which may represent the inoculation site. Monkeypox virus DNA that was detectable by PCR in seminal fluid in 29 of the 32 cases in which seminal fluid was tested further supports this hypothesis. However, whether semen is capable of transmitting infection remains to be investigated. [See article above] This series is an observational case series in which infection was confirmed with various PCR platforms. Persons in this case series had symptoms that led them to seek medical care, which implies that persons who were asymptomatic, had milder symptoms, or were presymptomatic could have been missed.

Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective cohort study Lancet posted online July 18, 2022

In this study 91.7% of patients were men who have sex with men (MSM), and detailed sexual history showed that those who reported having anal-receptive intercourse had longer incubation periods (8 vs 6 days) and higher rate of systemic symptoms before the rash (62.0% vs 27.6%) and presented more frequently with proctitis (32.9% vs 6.9%) than MSM who did not engage in this type of sexual practice. Viral load was higher in skin lesion swabs than in pharyngeal specimens (CT-value 22 vs 33, p<0·001). Overall, the median time from the onset of lesions to the formation of a dry crust was 10 2 days (IQR 7-13).

Comment: All these articles identify MSM as the most significant risk factor. The investigators also believe that compared to pharyngeal swabs, lesion swabs show much higher viral loads, suggesting close contact is likely to be the dominant transmission route in the current outbreak.

Using TPOXX (Tecovirimat) for Treatment of Monkeypox

CDC, in partnership with FDA, has made it easier for healthcare providers to provide tecovirimat (TPOXX) treatment to patients with monkeypox under the expanded access investigational new drug (EA-IND). The streamlined process allows healthcare providers to start treatment before the paperwork is submitted, and reduces the number of required forms, patient samples, photos, and gives patients the option to see their doctor virtually.

TPOXX is available through the Strategic National Stockpile. To request TPOXX, clinicians and care facility pharmacists can contact their state/territorial health department or CDC (Emergency Operations Center 770-488-7100; Poxvirus@cdc.gov)

Treatment with TPOXX can begin upon receipt of the medication and after obtaining informed consent. No pre-registration is required for clinicians or facilities. Forms requested under the EA-IND can all be returned to CDC **after** treatment begins.

They have reduced number of case report forms from 6 forms (17 pages) to 2 forms (6 pages) Changed all patient assessments to virtual (via telemedicine) or in-person Reduced required assessment and follow-up visit to 3 time points that could be done via telemedicine visits. No longer require photos of lesions

Comment: This change is welcomed. The paperwork etc. is still significant, but treatment can begin before paperwork is submitted.

COVID-19

COVID-19 News

ECDC and EMA update recommendations on additional booster doses of mRNA COVID-19 vaccines July 12, 2022

The European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency (EMA) now are recommending a second booster doses of mRNA COVID-19 vaccines be considered for people between 60 and 79 years old and people with medical conditions putting them at high risk of severe disease.

In April 2022, both agencies recommended that people over 80 years of age be considered for a second booster. The agencies noted at the time that it might be necessary to consider second boosters in people between 60 and 79 years old and vulnerable persons of any age if there was a resurgence of infections.

Europe is now experiencing a wave associated with increasing rates of hospital and ICU admissions, therefore public health authorities are now recommending people between 60 and 79 as well as vulnerable persons of any age for a second booster. The agencies stated these could be administered at least four months after the previous one, with a focus on people who have received a previous booster more than 6 months ago. The agencies said at the moment, there is no clear evidence to support giving a second booster dose to people below 60 years of age who are not at higher risk of severe disease.

Novavax Given EUA by FDA and CDC

Finally, after two years of development, the vaccine has finally overcome manufacturing problems to become the fourth vaccine to earn clearance in the US. Advisers to the CDC will meet next week and are expected to discuss who should get the Novavax vaccine.

Novavax's vaccine, given in doses spread three weeks apart, works differently from mRNA vaccines. It provokes an immune response with nanoparticles made up of proteins from the surface of SARS-CoV-2. . Similar protein-based vaccines have been widely used around the world for decades.

Comment: It is hoped that its vaccine will appeal to people who have spurned the shots from Pfizer and Moderna, which use mRNA technology. However, the authorization comes with a warning that Novavax's vaccine is linked to an elevated but small risk of myocarditis and pericarditis. In their review of Novavax's data, FDA reviewers identified six cases of the side effect in about 40,000 trial volunteers. In a related development, the European Medicines Agency on Thursday identified severe allergic reactions as a potential side effect of the Novavax vaccine.

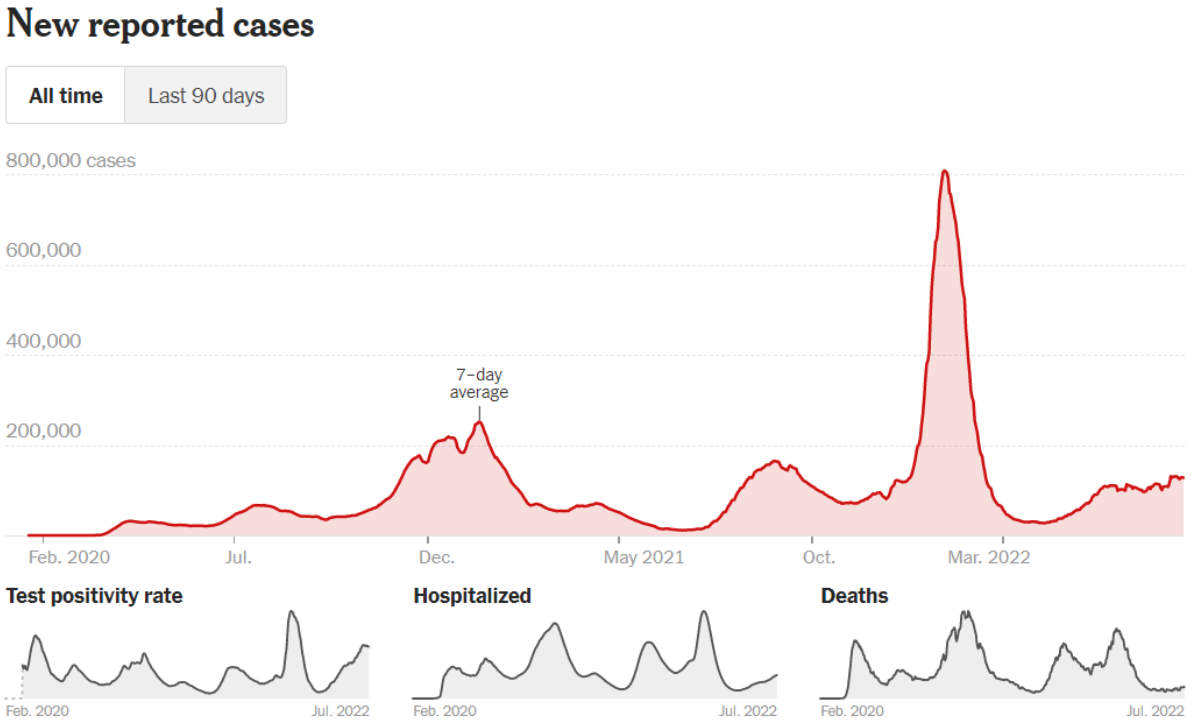
IDSA Treatment Guidelines Update Ivermectin June 30, 2022

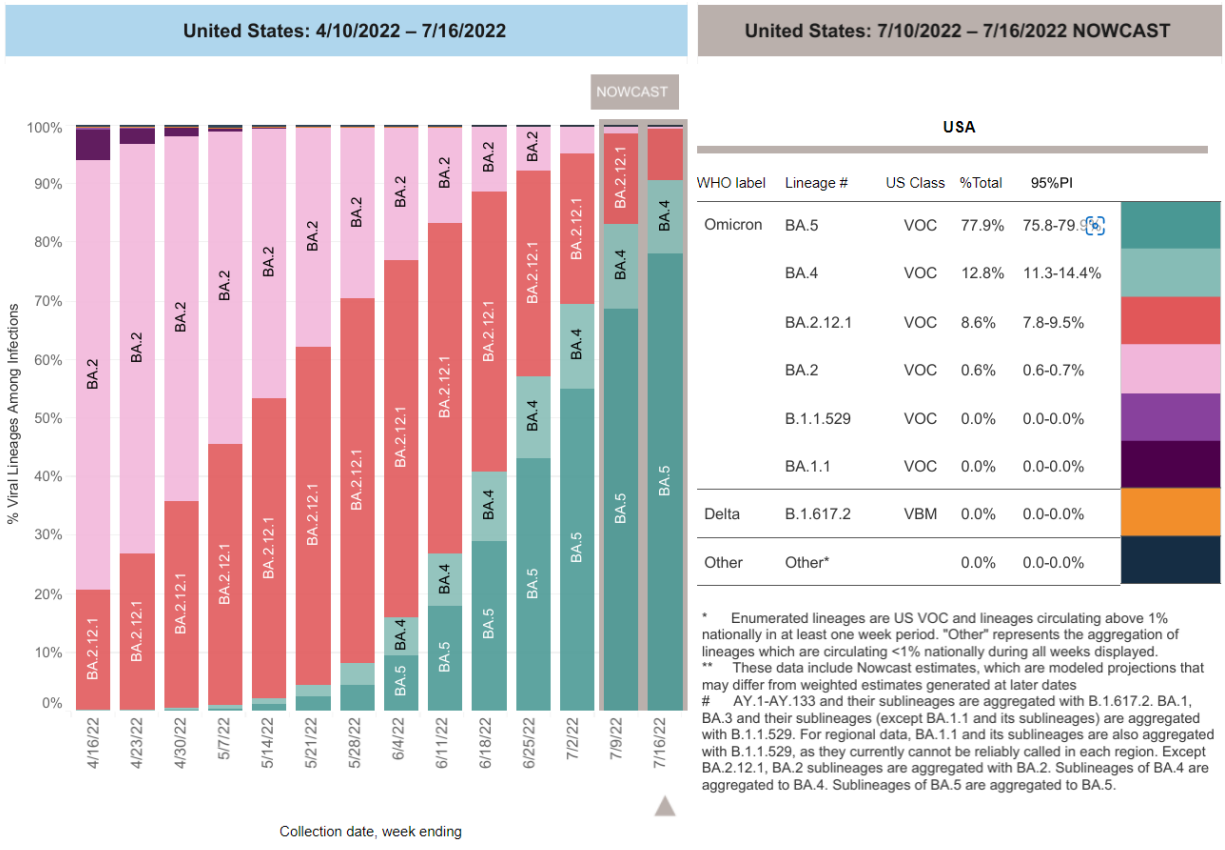
Recommendation 1: In hospitalized patients with COVID-19, the IDSA panel suggests against ivermectin. (Conditional recommendation††, Very low certainty of evidence)

Recommendation 2: In ambulatory persons with COVID-19, the IDSA panel recommends against ivermectin. (Strong recommendation, Moderate certainty of evidence)

Comment: These recommendations are based on recent studies and should help clarify any doubts about the use of ivermectin.

COVID-19 by the Numbers





USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	77.9%	75.8-79.[illegible]
	BA.4	VOC	12.8%	11.3-14.4%
	BA.2.12.1	VOC	8.6%	7.8-9.5%
	BA.2	VOC	0.6%	0.6-0.7%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data, BA.1.1 and its sublineages are also aggregated with B.1.1.529, as they currently cannot be reliably called in each region. Except BA.2.12.1, BA.2 sublineages are aggregated with BA.2. Sublineages of BA.4 are aggregated to BA.4. Sublineages of BA.5 are aggregated to BA.5.

Comment: Cases, hospitalizations and deaths are all higher than they have been at so far this summer as the BA.5 variant continues to spread across the US now accounting for 80% of cases. Compared with prior surges, hospitalizations and deaths are still well below prior peaks. The BA.5 variant is highly contagious (approaching measles) and immune evasive. Fortunately multiple studies still show the Omicron variants are less severe.

COVID-19 Journal Review

Seroconversion and outcomes after initial and booster COVID-19 vaccination in adults with hematologic malignancies Cancer published online July 11, 2022

doi.org/10.1002/cncr.34354

Brown University researchers led the study, which involved analysis of SARS-CoV-2 antibody levels and COVID-19 outcomes in the sera of 378 patients with hematologic cancers after initial and booster vaccine doses. Patients who have blood cancers such as multiple myeloma, leukemia, and lymphoma are at high risk for poor vaccine immune response and severe COVID-19 outcomes. Patients had received boosters after either the two-dose Pfizer/BioNTech or Moderna COVID-19 vaccine, or the one-dose Johnson & Johnson COVID-19 version.

Of the 378 patients, 181 (48%) had detectable SARS-CoV-2 antibodies in their sera (seroconverted) after initial vaccination. Patients with active cancer or who had recently received an immune-cell–depleting monoclonal antibody were the least likely to produce an immune response.

Among the 85 patients whose immune systems didn't respond to initial vaccination, 48 (56%) developed antibodies after a booster vaccine dose. The results were similar for patients who were and weren't receiving active treatment (53% vs 58%).

By the end of February 2022, 33 patients (8.8%) later tested positive for COVID-19, and 3 died of their infections (0.8%). While postvaccination seroconversion and the incidence of infection weren't significantly associated, no patient with detectable SARS-CoV-2 antibodies died of COVID-19, and none of the 25 given tixagevimab-cilgavimab combination (Evusheld) tested positive for the virus.

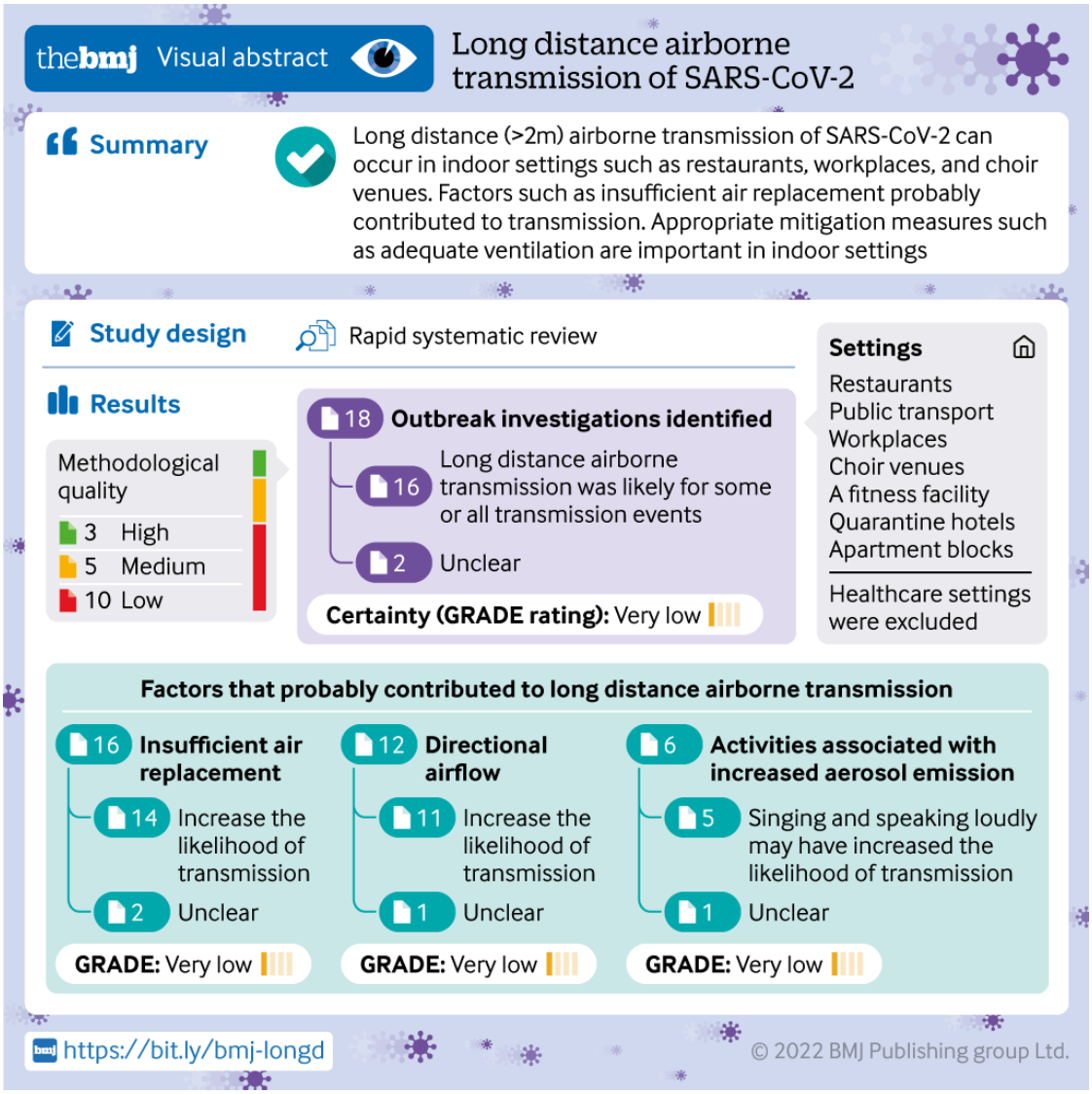
Comment: The findings underscore the importance of encouraging COVID-19 vaccine booster doses and checking antibody levels in patients with blood cancer to identify who might benefit from Evusheld. This is real world evidence that these actions can save lives.

Long distance airborne transmission of SARS-CoV-2: rapid systematic review BMJ 2022;377:e068743

doi.org/10.1136/ bmj-2021-068743

This is a systematic review using data sources Medline, Embase, medRxiv, Arxiv, and WHO COVID-19 Research Database for studies published from 27 July 2020 to 19 January 2022; existing relevant rapid systematic review for studies published from 1 January 2020 to 27 July 2020; and citation analysis in Web of Science and Cocites.

22 reports relating to 18 studies were identified (methodological quality was high in three, medium in five, and low in 10); all the studies were outbreak investigations. Long distance airborne transmission was likely to have occurred for some or all transmission events in 16 studies and was unclear in two studies (GRADE: very low certainty). In the 16 studies, one or more factors plausibly increased the likelihood of long-distance airborne transmission, particularly insufficient air replacement (very low certainty), directional air flow (very low certainty), and activities associated with increased emission of aerosols, such as singing or speaking loudly (very low certainty). In 13 studies, the primary cases were reported as being asymptomatic, presymptomatic, or around symptom onset at the time of transmission. Although some of the included studies were well conducted outbreak investigations, they remain at risk of bias owing to study design and do not always provide the level of detail needed to fully assess transmission routes.



Comment: This analysis confirms that long distance airborne transmission of SARS-CoV-2 might occur in indoor settings such as restaurants, workplaces, and venues for choirs, and identified factors such as inadequate ventilation that probably contributed to transmission.

These results strengthen the need for mitigation strategies especially in indoor settings, particularly the use of adequate ventilation. With BA.5 the importance of adequate ventilation in indoors settings is even more important.

Effectiveness of 2, 3, and 4 COVID-19 mRNA Vaccine Doses Among Immunocompetent Adults During Periods when SARS-CoV-2 Omicron BA.1 and BA.2/BA.2.12.1 Sublineages Predominated — VISION Network, 10 States, December 2021–June 2022 MMWR 2022; 71:July 15 early release

Overall, the study revealed that when BA.1 was the predominant variant, VE for two doses was 61% against COVID-19-associated hospitalizations but increased to between 85% and 92% after receipt of a third or booster dose.

After BA.2/BA.2.12.1 became predominant, vaccine effectiveness (VE) for two doses was 24% against COVID-19-associated hospitalizations and increased to 52% to 69% after a third dose. According to the study, similar trends were seen among ED and urgent care encounters, with lower VE during BA.2/BA.2.12.1 prevalence and higher VE with three or four doses compared with the initial two dose series.

Additional data showed that VE against COVID-19-associated hospitalization among adults aged 50 years or older — for whom second boosters are authorized — during BA.2/BA.2.12.1 was 55% more than 4 months after a booster dose and increased to 80% more than a week after the fourth dose.

Comment: Immunocompetent persons should receive recommended COVID-19 booster doses to prevent moderate to severe COVID-19, including a first booster dose for all eligible persons and second dose for adults aged ≥50 years at least 4 months after an initial booster dose. Booster doses should be obtained immediately when persons become eligible. No genetic characterization was available for SARS-CoV-2–positive specimens; therefore, date of testing was used to ascribe likely sublineage, and BA.2 and BA.2.12.1 sublineages were combined, given their overlap in circulation. This report did not assess VE against the most severe COVID-19–associated disease (e.g., respiratory failure) because of smaller numbers of these cases. This report was before BA.4 and BA.5, therefore, VE should continue to be monitored in the setting of newly emerging sublineages and variants. Lastly the duration of any protection needs to be measured as well.