Volume 2, Issue 9, 2022

Infectious Diseases Watch

October 2, 2022

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VII Editorial: Are We Prepared for the Next Emerging Pathogen?

The US, among the wealthiest and most advanced nations in the world, remains inadequately prepared to combat new pathogens. No single agency is completely to blame, although the CDC has acknowledged there were missteps in the response to Covid-19. The price of failure can be very high. Covid-19 has killed more than one million Americans so far, and many more are dealing with long Covid. Although cases, hospitalizations and deaths are all falling, Covid-19 remains the third leading cause of death in the US in 2021 and continued to kill 400 people in the US daily. Monkeypox is spreading more slowly now and has never posed the same threat as Covid-19. However, the US has reported more monkeypox cases than any other country — 25,000, about 40 percent of the global total — and the virus is likely to persist as a constant, low-grade threat. Both outbreaks have revealed significant gaps in the public health framework for responding to emerging pathogens. This has contributed to reduced trust in our public health agencies. Add to that misinformation and the politicization of every aspect of the Covid-19 response from testing and masks to the use of vaccines has made our response more difficult.

It is not a matter of if, but when we will see the next emerging pathogen(s). This is mostly because of the rise in global travel, vaccine hesitancy, and the growing proximity of people and animals. This is the new norm! Public health in the US has always operated on a shoestring. We have underinvested in public for decades. The data systems used by the CDC and other federal agencies is out of date. The most difficult hurdle to a coordinated national response arises from the division of responsibility and resources between federal, state, and local governments, along with gaps in communications between the public health officials coordinating the response and the doctors and nurses treating the patients. The complex laws that govern health care in the US are designed to protect confidentiality and patient rights but are not designed to optimized working with the public health system and getting the public health system the data, they need in a timely manner. Generally, states are not obligated to share health data, such as the number of cases of infection or demographic details of vaccinated people, with federal authorities in a real time manner. Our systems are not interconnected. Current rules on data sharing create many hurdles. A recent example, CDC has not yet included monkeypox in its disease reporting computer system. This means state officials must manually type in data from case reports, instead of simply uploading the files. A request for testing must often be faxed to the state laboratory; the results are often routed through a state epidemiologist, then to the provider, then to the patient. In the beginning of the pandemic health care institutions were in fact faxing reports on Covid-19 to the CDC! In Houston we recognized the value of data sharing early. We have had some success. We have created a Greater Houston Health Connect for Covid-19 through UTHealth School of Public Health and the Texas Medical Center facilities shared data on admissions, test positivity,

hospitalizations, reproductive number etc., but more needs to be done. Discussions are ongoing.

Health care systems in countries like the UK and Israel rely on nationalized systems that make it much easier to collect and analyze information on cases. In many instances, we got our information and acted on it from foreign health agencies, from the UK., Israel, and South Africa. We frequently had to rely on other countries for vital information: How effective are boosters? Is the virus airborne? Do masks work?

In the end epidemics are managed by public health agencies, but it is clinicians including doctors, nurses and others who diagnose and care for patients. An efficient outbreak response relies on mutual understanding and exchange of information between the two groups which does not always occur. In Houston starting in March 2020, the Health Authorities began hosting a weekly Covid-19 conference calls with the Local Health Authorities. In August 2021 the call was expanded to include a team of top infectious diseases doctors and epidemiologists representing the major health care systems and medical schools. This collaboration has enhanced knowledge and communication and provided front line experience of professionals treating patients and who also provide guidance to not just health care, but schools, religious organizations, and businesses.

Ideally, here's how the national response to an outbreak or an emerging pathogen should occur. Reports from a clinic or any other health care entity anywhere in the country could signal a new pathogen's arrival. We have also learned how wastewater surveillance can enhance and provide an early signal a new threat like what we have seen for polio in New York State. In Houston, starting in May 2020, the Houston Health Department began working with a coalition of municipal and academic partners developed a wastewater monitoring and reporting system for the city of Houston. This information was used to shape policies and inform actions to mitigate and prevent the spread of Covid-19 at municipal, institutional, and individual levels. This report has been a regular agenda item for our weekly calls with our Local Health Authorities. In fact, the CDC has recognized the wastewater surveillance programs in Houston as NWSS Centers of Excellence. In the end all these sources of information would flow from local health departments to state and federal authorities real-time with IT systems that are interconnected. Federal officials would rapidly offer guidance for the development of tests, vaccines, and treatments. A communication plan speaking with one voice should be pushed out to key stakeholders. Outbreaks and epidemics/pandemics should be coordinated by public health agencies, but public health needs to recognize that it is clinicians such as doctors, nurses and others who actually diagnose and treat patients. An efficient outbreak response relies on mutual understanding, respect, and exchange of information between the two groups. I am proud that Houston has recognized and created such a collaboration.

Finally, to create the public health system we need will require adequate investment in our public health infrastructure, However, more money won't solve all the problems, but additional funding could help public health departments hire and train staff, update their aging data systems and invest in robust surveillance networks. We can do better, and we must act now!

General Infectious Diseases

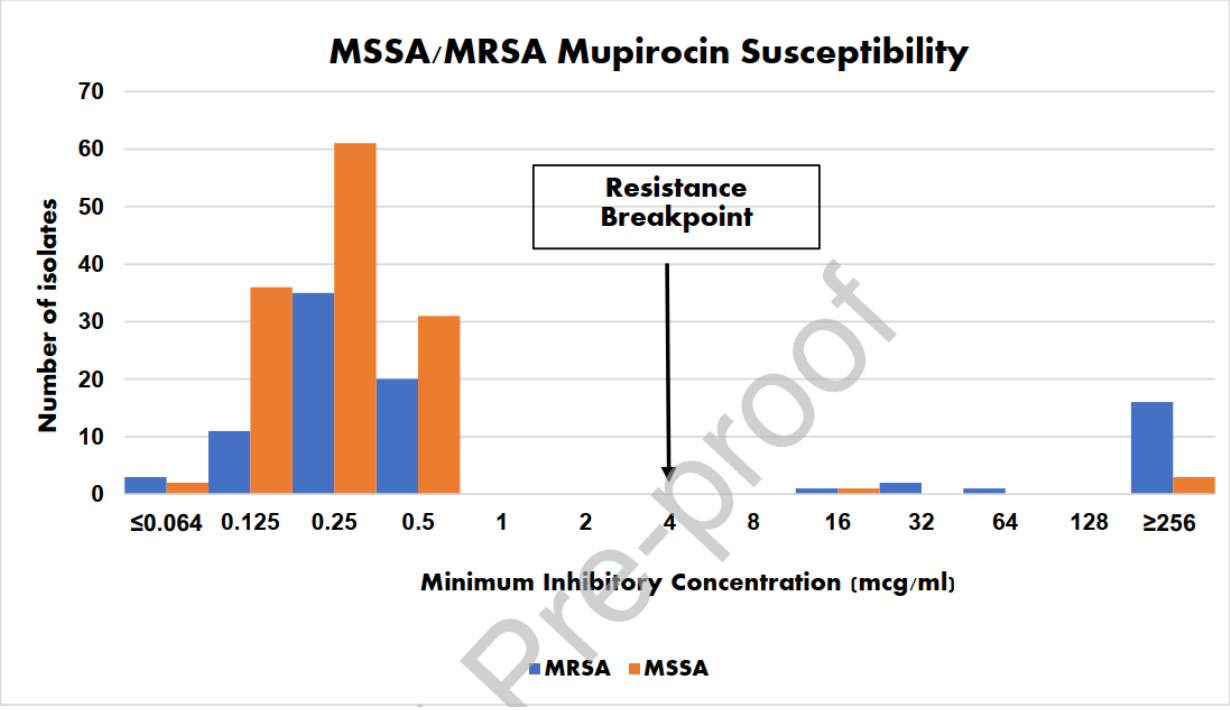
Mupirocin Susceptibility of Staphylococci 2022: Is it time for a change in MRSA decolonization protocols? Am J Infect Control published online September 14, 2022- article provided by Julia Moody

doi.org/10.1016/j.ajic.2022.08.025

S. aureus isolates were recovered from clinical and screening samples received in the microbiology laboratory. Mupirocin susceptibility was determined using e-tests and isolates were categorized as susceptible or resistant using a breakpoint MIC value of 4mcg/ml. Resistant strains were further divided into low-level resistance, with MIC values from 8 to 256 mcg/ml, and high-level resistance, with MIC values >256 mcg/ml.

223 S. aureus (SA) isolates were available from 218 patients. 5 patients had two distinctly different isolates accounting for the excess number of isolates. 60.1% of the isolates were MSSA and 39.9% were MRSA. Isolates were predominantly from outpatients (76.1%), males (55.5%), with skin and soft tissue sources (63.7%). 15.7% were nasal samples obtained in the course of pre-operative screening.

Mupirocin susceptibility was performed on all 223 SA isolates. Most of the isolates (199/223) were susceptible to mupirocin, but 24 SA strains (10.8%) were resistant to mupirocin: 22.5% of MRSA strains (20/89) but only 3.0% of MSSA strains (4/134) were mupirocin resistant. This difference is statistically significant ($p< 0.001$). Further analysis of these mupirocin-resistant isolates demonstrated high-level resistance (MIC value >256mcg/ml) in the vast majority (73.3%). Risk factors for mupirocin-resistance among MRSA cases, were in-patient collection site ($p=0.03$) and older age ($p=0.002$).



Comment: This study raises concern because most decolonization protocols for high-risk surgical procedures in patients colonized with MRSA or MSSA involve mupirocin. Based on the STOP SSI study [JAMA. 2015; 313:2162-2171] our current protocol for cardiac, joint replacements, and complicated spinal surgeries, recommends testing the nares for MRSA/MSSA. If the result is positive for MSSA/MRSA, the use of intranasal mupirocin for 5 days prior to the surgery along with CHG bathing for 5 days is recommended. With growing mupirocin resistance should we be looking at alternative intranasal agents such as povidone iodine or photodynamic therapy? Lastly do the current breakpoints accurately predict mupirocin's effect and benefit? The recent Mupirocin-Iodophor Swap Out Trial presented at ID week 2021 found universal ICU decolonization with nasal mupirocin was more effective than nasal iodophor in reducing *S. aureus* and MRSA clinical isolates when each was combined with daily CHG bathing in the ICU. In the current study the investigators did not collect detailed clinical information or prior history of antibiotic use or MRSA infection to determine if there was a relationship between these historical elements and mupirocin resistance.

Efficacy of different preoperative skin antiseptics on the incidence of surgical site infections: a systematic review, GRADE assessment, and network meta-analysis

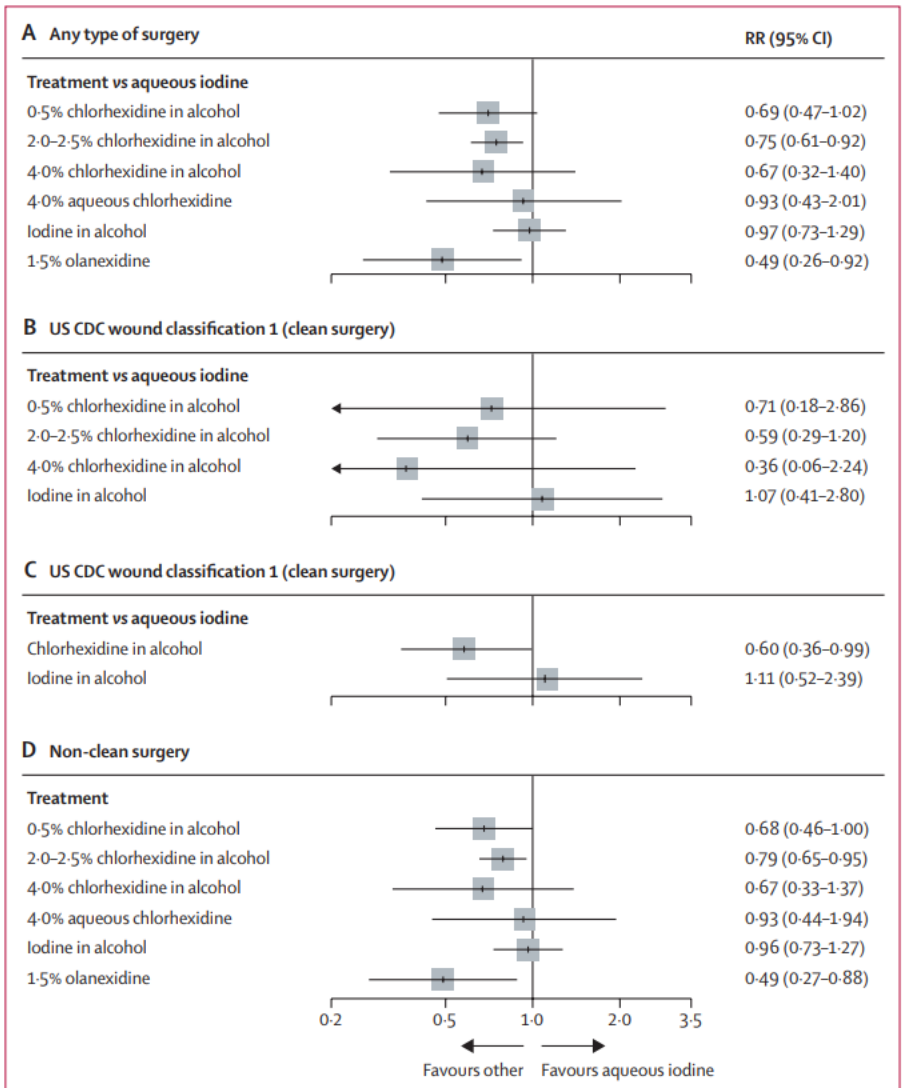
Lancet Microbe published online August 16, 2022

doi.org/10.1016/ S2666-5247(22)00187-2

The authors searched for RCTs in MEDLINE, Embase, and Cochrane CENTRAL, published up to November 23, 2021, that directly compared two or more antiseptic agents (i.e., chlorhexidine, iodine, or olanexidine) or concentrations in aqueous and alcohol-based solutions. They excluded pediatric, animal, and non-randomized studies, and studies not providing standard preoperative intravenous antibiotic prophylaxis. Studies with no SSIs in both groups were

excluded from the quantitative analysis. Two reviewers screened and reviewed eligible full texts and extracted data. The primary outcome was the occurrence of SSI (i.e., superficial, deep, and organ space). They conducted a frequentist random effects network meta-analysis to estimate the network effects of the skin preparation solutions on the prevention of SSIs. A risk-of-bias and Grading of Recommendations, Assessment, Development, and Evaluation assessment were done to determine the certainty of the evidence.

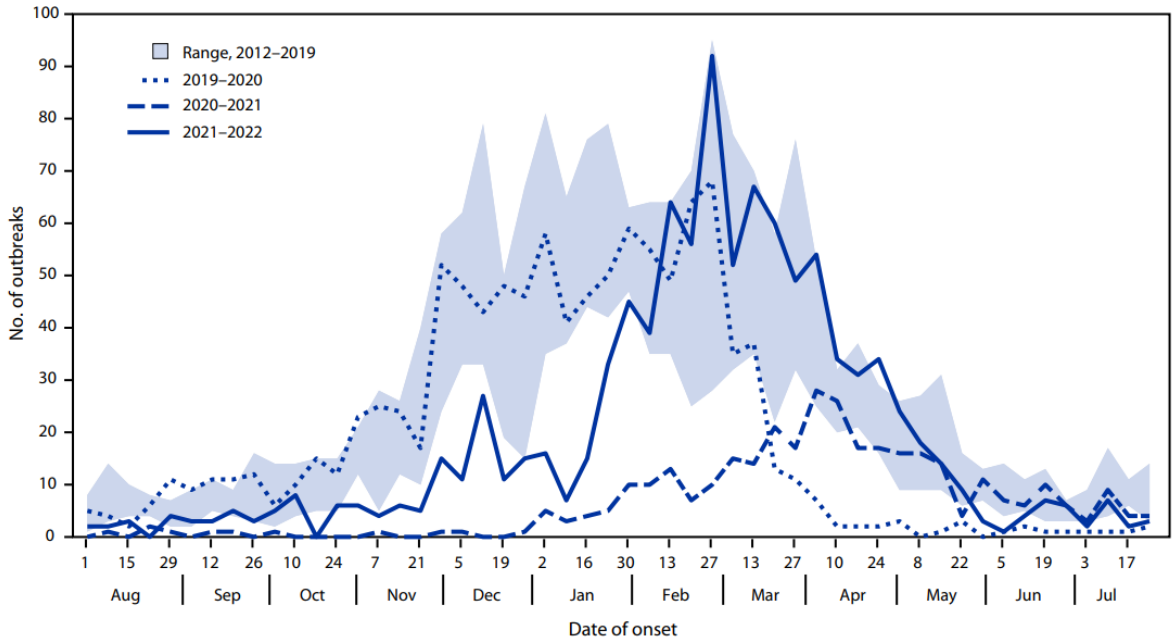
Overall, 2326 articles were identified, 33 studies were eligible for the systematic review, and 27 studies with 17,735 patients reporting 2144 SSIs (overall incidence of 12·1%) were included in the quantitative analysis. Only 2·0–2·5% chlorhexidine in alcohol (relative risk 0·75, 95% CI 0·61–0·92) and 1·5% olanexidine (0·49, 0·26–0·92) significantly reduced the rate of SSIs compared with aqueous iodine. For clean surgery, we found no difference in efficacy between different concentrations of chlorhexidine in alcohol. Seven RCTs were at high risk of bias, 24 had some concerns, and two had low risk of bias. Heterogeneity across the studies was moderate (I^2=27·5%). Five of ten studies that mentioned adverse events related to the skin preparation solutions reported no adverse events, and five reported a total of 56 mild events (mainly erythema, pruritus, dermatitis, skin irritation, or mild allergic symptoms); none reported a substantial difference in adverse events between groups.



Comment: In line with prior publications, they found a benefit of chlorhexidine in alcohol over both aqueous iodine and iodine in alcohol for the prevention of SSIs in all wound classifications, particularly 2·0–2·5% chlorhexidine in alcohol. They did not find additional benefit from 4·0% chlorhexidine in alcohol. Of interest 1·5% olanexidine showed benefit, but this was based on only one randomized controlled trial with some limitations. More RCTs regarding the efficacy of olanexidine are needed to be able to draw more reliable conclusions and before implementation in daily practice is possible. This study found an overall SSI rate of 12.1%, which is higher than the rates reported in the literature on SSI across all types of surgery. This discrepancy can be explained by the SSI rate of 20% reported by the largest included RCT conducted in seven low-income and middle-income countries. The Compendium on Strategies to Prevent Surgical Site Infections in Acute Care Hospitals: 2022 Update is being finalized and will review this issue as well.

Norovirus Outbreaks Reported Through NoroSTAT — 12 States, August 2012–July 2022 MMWR 2022;71:1222-1224

In 2012, CDC established the Norovirus Sentinel Testing and Tracking Network (NoroSTAT) to improve timeliness and completeness of surveillance for norovirus outbreaks that occur in the United States. NoroSTAT is a collaboration between CDC and 12 state health departments. In April 2020, the incidence of norovirus outbreaks in the US declined substantially, likely because of implementation of COVID-19–related nonpharmaceutical interventions, such as facility closures, social distancing, and increased hand hygiene. [J Infect Dis 2021; 224:9–13] Norovirus outbreaks in the US increased rapidly starting in January 2022, approaching prepandemic (i.e., 2012–2019) levels.

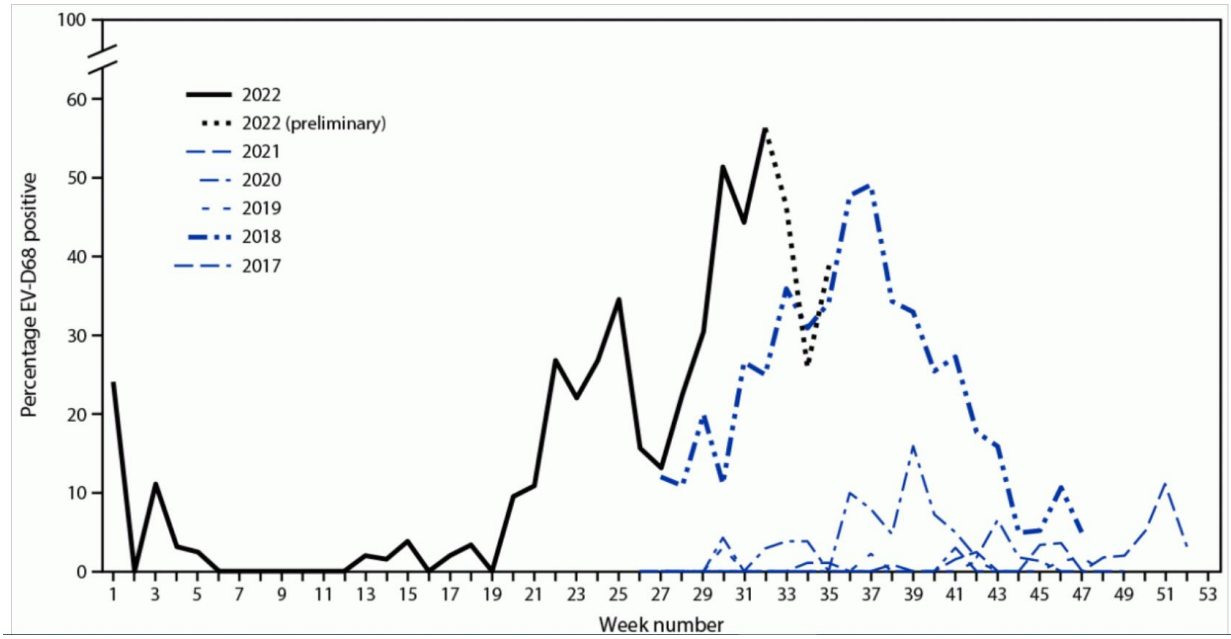


Comment: The number of norovirus outbreaks that NoroSTAT participating states reported during the 2021–2022 surveillance year was nearly three times the number reported during the 2020–2021 surveillance year. Nonpharmaceutical interventions implemented during the COVID-19 pandemic were likely effective in preventing outbreaks of other infectious diseases, including norovirus and C difficile. As the use of nonpharmaceutical interventions has relaxed, norovirus outbreak incidence has returned to levels similar to those during prepandemic surveillance years, and GII.4 viruses continue to cause the largest proportion of norovirus outbreaks.

Increase in Acute Respiratory Illnesses Among Children and Adolescents Associated with Rhinoviruses and Enteroviruses, Including Enterovirus D68 — United States, July–September 2022 MMWR early release September 27, 2022

Increases in severe respiratory illness and acute flaccid myelitis (AFM) among children and adolescents resulting from enterovirus D68 (EV-D68) infections occurred biennially in the US during 2014, 2016, and 2018, primarily in late summer and fall. Although EV-D68 annual trends are not fully understood, EV-D68 levels were lower than expected in 2020, felt to be in part because of implementation of COVID-19 mitigation measures (e.g., wearing face masks, enhanced hand hygiene, and physical distancing. In August 2022, clinicians in several

geographic areas notified CDC of an increase in hospitalizations of pediatric patients with severe respiratory illness and positive rhinovirus/enterovirus (RV/EV) test results. Surveillance data were analyzed from multiple national data sources to characterize reported trends in acute respiratory illness (ARI), asthma/reactive airway disease (RAD) exacerbations, and the percentage of positive RV/EV and EV-D68 test results during 2022 compared with previous years. During a period lasting from March 1 to Sept. 20, 2022, the New Vaccine Surveillance Network enrolled 5,633 children and adolescents with acute respiratory illness (ARI) in need of emergency care or hospitalization. As of September 20th , RV/EV was detected in 1,492 (26.4%) of these patients, among whom 260 (17.4%) had a positive EV-D68 test result. The authors also noted that the percentage of positive EV-D68 test results among children and adolescents with ARI and positive RV/EV test results increased to 56% during the week ending August 13th.



Comment: These data demonstrated an increase in ED visits by children and adolescents with ARI and asthma/RAD in late summer 2022. The percentage of positive RV/EV test results in national laboratory-based surveillance and the percentage of positive EV-D68 test results in pediatric sentinel surveillance also increased during this time. The percentage of positive EV-D68 test results during July and August 2022 was higher than during the same months in 2017 and 2019 to 2021 and similar to peak levels observed in 2018. Using ED data, ARI is a broad definition designed to capture all diagnoses related to respiratory illness, including SARS-CoV-2, influenza, pneumonia, and cough, potentially limiting specificity for identifying visits with EV-D68-associated respiratory illnesses. In addition, the COVID-19 pandemic likely affected health care–seeking behaviors and testing practices in multiple ways; these differences could affect comparability of recent data to 2019 and previous years. Finally, comparable NSSP data on hospitalizations or trends before 2018 are unavailable, as are NVSN data before 2017. Bottom line, clinicians are advised to consider EV-D68 as a possible cause of severe respiratory illness in children and adolescents, particularly those with wheezing or who require respiratory support. Past increases in EV-D68 circulation were also associated with increased reports of AFM. Providers should have a high index of clinical suspicion for AFM in patients with acute flaccid limb weakness, neurologic signs and symptoms, or neck or back pain who have a recent history of respiratory illness or fever. Given the detection of a paralytic polio case and wastewater samples positive for poliovirus in New York during summer 2022 [I am sure once

other locations begin to test for polio we will find other states with positive samples], clinicians should also test for poliovirus infection in patients suspected of having AFM because of the clinical similarity to acute flaccid paralysis caused by poliovirus.

FDA panel votes in favor of fecal transplant therapy RBX2660 for recurrent *C. difficile* infection

RBX2660n is an investigational live biotherapeutic, which can restore microbiome and bile acid composition. Vaccines and Related Biological Products Advisory Committee voted 13-4 in favor of the availability of adequate data supporting effectiveness and 12-4, with one abstention, in favor of the availability of adequate data supporting safety. The main support for the application came from the Punch CD2 and Punch CD3 trials, in which RBX2660 showed a response rate 12% higher than placebo.

Comment: Seres this month filed its rival microbiome therapeutic SER-109. SER-109 showed a greater treatment effect in its pivotal trial, albeit in a more refractory population; it is also an oral formulation versus RBX2660 an enema agent. Reviewed in ID Watch [N Engl J Med 2022;386:220-9] In patients with symptom resolution of C. difficile infection after treatment with standard-of-care antibiotics, oral administration of SER-109 was superior to placebo in reducing the risk of recurrent infection. SER-109, an investigational oral microbiome therapeutic composed of live purified Firmicutes bacterial spores.

Influenza

Influenza Vaccines 2022-3

Composition

All influenza vaccines available in the US this season are quadrivalent. Influenza A viruses are the main cause of influenza-related morbidity and mortality, especially in older adults. Influenza B illness is usually more severe in children, especially those <5 years old. [World J Clin Pediatr 2020; 9:44]

- Egg-Based Vaccines
  A/Victoria/2570/2019 (H1N1)pdm09-like
  A/Darwin/9/2021 (H3N2)-like
  B/Austria/1359417/2021 (Victoria lineage)-like
  B/Phuket/3073/2013 (Yamagata lineage)-like

- Cell Culture-Based and Recombinant Vaccines
  A/Wisconsin/588/2019 (H1N1)pdm09-like
  A/Darwin/6/2021 (H3N2)-like
  B/Austria/1359417/2021 (Victoria lineage)-like
  B/Phuket/3073/2013 (Yamagata lineage)-like

Summary

- Annual vaccination in the US against influenza A and B viruses is recommended for everyone ≥6 months old without a contraindication.
- All influenza vaccines available in the US this season are quadrivalent; they contain two influenza A and two influenza B virus antigens. (see above)
- Influenza vaccination reduces the incidence of laboratory confirmed influenza and the risk of serious complications and death associated with influenza illness.
- In adults ≥65 years old, use of a high dose, adjuvanted, or recombinant vaccine can improve immune responses and is preferentially recommended over other influenza vaccines. See summary below
- Pregnant women in any trimester should be vaccinated against influenza.
    - Vaccination protects pregnant women against influenza-associated illness, which can be especially severe during pregnancy, and protects their infants for up to 6 months after birth (not approved for use in infants <6 months old). The ACIP and ACOG recommend that pregnant women be vaccinated against influenza without regard to the trimester of pregnancy. Pregnant women should not receive the intranasal live-attenuated vaccine *(FluMist Quadrivalent)*
- The ACIP states that persons with a history of egg allergy can receive any age-appropriate influenza vaccine, but those with a history of severe egg allergy who receive an egg-based vaccine should be vaccinated in a medical setting supervised by a healthcare provider experienced in managing severe allergic reactions.
    - The recombinant vaccine *(Flublok Quadrivalent)* and the cell culture-based inactivated vaccine *(Flucelvax Quadrivalent)* do not contain egg protein. Other available influenza vaccines may contain trace amounts of egg protein (ovalbumin), but numerous studies have found that patients with a history of egg allergy are not at increased risk for a reaction to influenza vaccines that are propagated in eggs. [Ann Allergy Asthma Immunol 2018; 120:49]
- Vaccination should ideally be offered in September or October and continue to be offered as long as influenza viruses are circulating in the community.
    - Children who require 2 doses should receive the first dose as early as possible so that the second dose can be given by the end of October.
        - Children 6 months to 8 years old who are being vaccinated for the first time, whose vaccination history is not known, or who have not received at least 2 lifetime doses of a trivalent or quadrivalent influenza vaccine before July 1, 2022, should receive 2 doses at least 4 weeks apart

Vaccine Effectiveness (VE)

Influenza vaccination can reduce the incidence of laboratory-confirmed influenza and the risk of serious complications and death associated with influenza illness. [Clin Infect Dis 2017; 65:1289; Clin Infect Dis 2021; 73:e947] VE of the in preventing influenza illness depends on several factors, including the match between the vaccine composition and circulating strains.

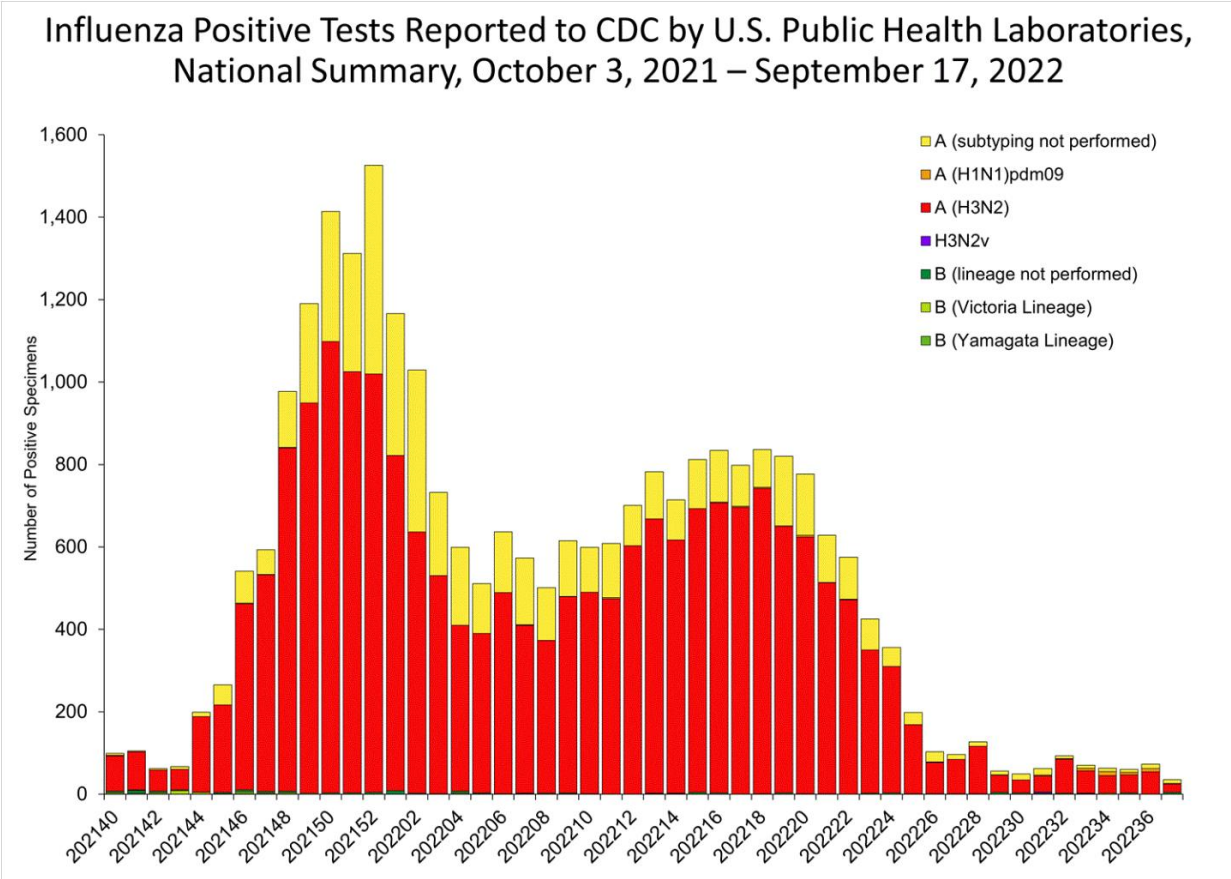
VE is greatest when the match is close, but what many are not aware even when it is suboptimal, vaccination still can still substantially reduce the risk of influenza-related hospitalization and death. [Clin Infect Dis 2014; 14:1228]

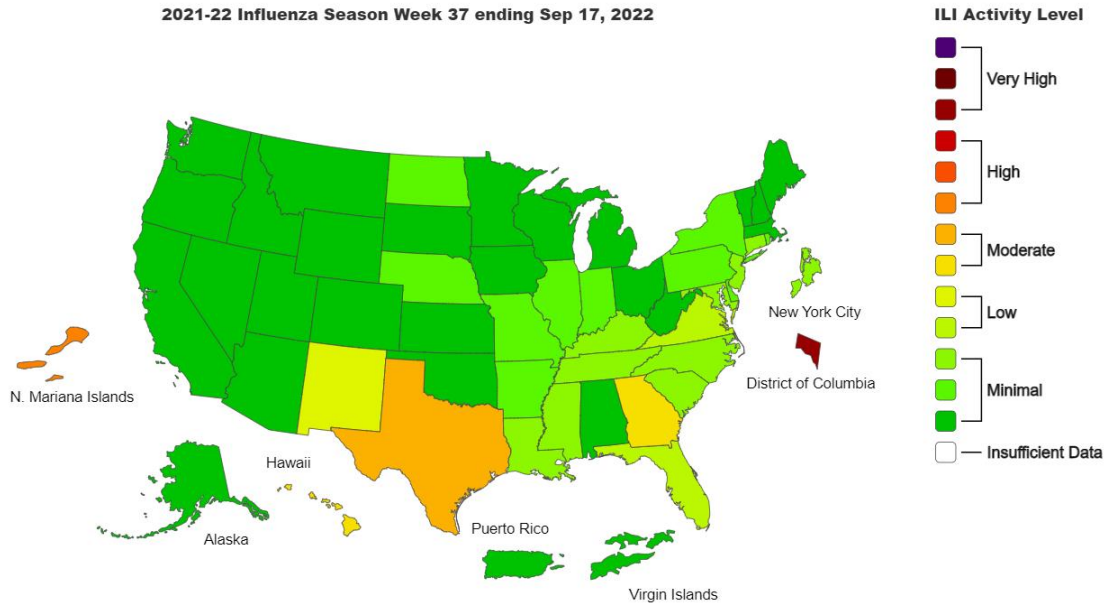
Choice of Vaccine

- For the first time, ACIP is recommending use of a high-dose, adjuvanted, or recombinant influenza vaccine over other available age-appropriate influenza vaccines in adults ≥65 years old
    - High Dose [an inactivated vaccine that contains 4 times(60 mcg) the amount of antigen included in standard dose inactivated influenza vaccines] Fluzone *High Dose*
        - In a randomized, double-blind trial in 31,989 adults ≥65 years old during 2 influenza seasons, a high dose inactivated trivalent vaccine (*Fluzone HighDose*-now quadravalent) induced significantly greater antibody responses than a standard dose inactivated trivalent vaccine and was 24% more effective in preventing laboratory-confirmed influenza illness. [N Engl J Med 2014:371:635]
        - In several other studies in adults ≥65 years old, use of a high-dose inactivated trivalent vaccine was associated with a reduced risk of respiratory-related and all-cause hospitalization and death compared to standard-dose inactivated trivalent vaccines. [Vaccine 2021; 39(Suppl 1) A:24]
    - Adjuvant Vaccine *Fluad Quadrivalent*, an adjuvanted inactivated influenza vaccine, is FDA licensed for use in persons ≥65 years old. It contains MF59, an oil-in-water emulsion of squalene oil that increases the immune response.
        - In a randomized trial in 7082 adults ≥65 years old, an adjuvanted inactivated trivalent vaccine (*Fluad*; no longer available-now quadrivalent) elicited significantly greater antibody responses against all three influenza strains than a nonadjuvanted inactivated trivalent vaccine. [Vaccine 2014; 32:5027]
        - In other trials, older adults who received an adjuvanted inactivated trivalent vaccine were less likely to develop symptomatic influenza illness or to be hospitalized for influenza or pneumonia than those who received a nonadjuvanted inactivated trivalent vaccine. [Clin Infect Dis 2021; 73:e4237]
    - Recombinant Vaccine. *Flublok Quadrivalent*, a recombinant influenza vaccine produced without the use of influenza virus or chicken eggs, contains 3 times(45 mcg) the amount of antigen included in standard dose inactivated influenza vaccines. [approved in people ≥ 18]
        - In a randomized, double-blind trial in 8604 adults ≥50 years old during the A/H3N2-predominant 2014-2015 influenza season, the recombinant quadrivalent vaccine was 30% more effective than a nonadjuvanted standard-dose inactivated quadrivalent vaccine in preventing laboratory confirmed influenza illness.]N Engl J Med 2017; 376:2427]
- Immunocompromised Individuals
    - The live attenuated influenza vaccine should not be used in immunocompromised persons.
    - Inactivated and recombinant vaccines are generally considered safe for use in such persons, but the immune response may be reduced. In two randomized trials in solid organ transplant recipients, the high-dose vaccine induced significantly greater immune responses than standard-dose vaccines. [Clin Infect Dis 2018: 66:1698]

"Twindemic" risk

Experts believe the risk is greater this year because widespread masking and other prevention measures are no longer commonplace, and there are already signs that this year's upcoming flu season will be more severe, based on the Southern Hemisphere's severe flu season, which typically runs from April to September. Australia is coming out of its worst flu season in five years. See current US activity below





Comment: It is early, but a few states are now reporting moderate flu activity. H3N2 is the predominant strain to date. Unlike the last 2 seasons, it appears influenza may make a comeback. Vaccination is still the best preventive strategy. See vaccination summary above

Does repeated influenza vaccination attenuate effectiveness? A systematic review and meta-analysis

Lancet Respir Med published online September 21, 2022

doi.org/10.1016/S2213-2600(22)00266-1

Several reports have suggested that repeated vaccination might reduce VE. The authors performed a systematic review and meta-analysis. They searched MEDLINE, EMBASE, and CINAHL Complete databases for articles published from January 1, 2016, to June 13, 2022, and Web of Science for studies published from database inception to June 13, 2022. For studies published before January 1, 2016 and reviewed published systematic reviews. Two reviewers independently screened, extracted data using a data collection form, assessed studies' risk of bias using the Risk Of Bias In Non-Randomized Studies of Interventions (ROBINS-I) and evaluated the weight of evidence by Grading of Recommendations Assessment, Development, and Evaluation (GRADE). They included observational studies and randomized controlled trials that reported vaccine effectiveness against influenza A(H1N1)pdm09, influenza A(H3N2), or influenza B using four vaccination groups: current season; previous season; current and previous seasons; and neither season (reference). For each study, they calculated the absolute difference in vaccine effectiveness (ΔVE) for current season only and previous season only versus current and previous season vaccination to estimate attenuation associated with repeated vaccination. Pooled vaccine effectiveness and ΔVE were calculated by season, age group, and overall.

They identified 4979 publications, selected 681 for full review, and included 83 in the systematic review and 41 in meta-analyses. ΔVE for vaccination in both seasons compared with the current

season was –9% (95% CI –16 to –1, I^2=0%; low certainty) for influenza A(H1N1)pdm09, –18% (–26 to –11, I^2=7%; low certainty) for influenza A(H3N2), and –7% (–14 to 0, I^2=0%; low certainty) for influenza B, indicating lower protection with consecutive vaccination. However, for all types, A subtypes and B lineages, vaccination in both seasons afforded better protection than not being vaccinated.

Comment: They estimated that vaccine effectiveness against influenza A(H1N1)pdm09 and the influenza B viruses for people vaccinated in both the current and previous seasons were, on average, slightly attenuated compared with effectiveness in people vaccinated in the current season only. Vaccine effectiveness against influenza A(H3N2) was worse overall than for influenza B and displayed a greater loss in effectiveness with repeated vaccination. However, for all types, A subtypes and B lineages, vaccination in both seasons afforded better protection than not being vaccinated. The data available in this review represents a small number of seasons and should be interpreted with caution because of strong seasonal effects and heterogeneity among seasons. Some of the reduced vaccine effectiveness in older age groups might be associated with immunosenescence. However, the results support current season vaccination regardless of previous season vaccination and suggest that vaccination in any combination of current and previous seasons provided better protection than not being vaccinated.

Monkeypox

Severe Manifestations of Monkeypox among People who are Immunocompromised Due to HIV or Other Conditions CDC September 29, 2022

Severe manifestations of monkeypox (MPXV) have been observed in the US in the current outbreak. People who are immunocompromised due to HIV or other conditions are at higher risk for severe manifestations of monkeypox than people who are immunocompetent. Because people with HIV-associated immunocompromise are at risk for severe manifestations of monkeypox, the HIV status of all sexually active adults and adolescents with suspected or confirmed monkeypox should be determined.

During the current outbreak, CDC has received reports of people with MPXV who have severe manifestations of disease, including but not limited to

- Atypical or persistent rash with coalescing or necrotic lesions, or both, some which have required extensive surgical debridement or amputation of an affected extremity.
- Lesions on a significant proportion of the total body surface area, which may be associated with edema and secondary bacterial or fungal infections among other complications.

- Lesions in sensitive areas (including mucosal surfaces such as, oropharynx, urethra, rectum, vagina) resulting in severe pain that interferes with activities of daily living.
- Bowel lesions that are exudative or cause significant tissue edema, leading to obstruction.
- Severe lymphadenopathy that can be necrotizing or obstructing (such as in airways).
- Lesions leading to stricture and scar formation resulting in significant morbidity such as urethral and bowel strictures, phimosis, and facial scarring.
- Involvement of multiple organ systems and associated comorbidities, including:
    - Oropharyngeal lesions inhibiting oral intake
    - Pulmonary involvement with nodular lesions
    - Neurologic conditions including encephalitis and transverse myelitis
    - Cardiac complications including myocarditis and pericardial disease
    - Ocular conditions including severe conjunctivitis and sight-threatening corneal ulcerations
    - Urologic involvement including urethritis and penile necrosis

Comment: In immunocompromised people, MPXV treatment should include optimizing immune function by limiting the use of immunosuppressive medications if not otherwise clinically indicated, and, for those with HIV, providing antiretroviral therapy. In addition, there are medical countermeasures that may have a role in treating severe illness, including oral and intravenous tecovirimat (TPOXX), cidofovir or brincidofovir, and vaccinia immune globulin intravenous (VIGIV), although there are limited data on effectiveness in treating human MPXV with these medical countermeasures. Decisions on whether and when to use these medical countermeasures must be made individually for each person and can depend on a variety of clinical and other parameters. Worsening, non-healing, recurrent, and new skin lesions while receiving antiviral treatment have been observed among immunocompromised people with severe manifestations of monkeypox. Clinicians are encouraged to obtain repeat lesion swabs to assess for persistent MPXV DNA. In such people, clinicians may consider continuing tecovirimat beyond 14 days, until there is clinical improvement (no more than 90 days).

Neurologic Complications of Smallpox and Monkeypox A Review JAMA Neurol published online September 20, 2022

doi:10.1001/jamaneurol.2022.3491

This was a literature review of the known neurologic complications of smallpox, which include encephalitis, transverse myelitis, and acute disseminated encephalomyelitis among others; historical complications of smallpox vaccination, including postvaccinal encephalomyelitis; and the known neurologic complications of monkeypox, which include headaches and mood disturbances, as well as rare presentations of encephalitis, transverse myelitis, and seizures. See below Of concern is the possibility of viral persistence and systemic complications in immunocompromised individuals.

Table 2. Neurologic Manifestations of Orthopox Viruses

Symptom	Smallpox	Vaccinia vaccine	Monkeypox
Headaches	+[a]	+	+
Mood disorder	–	–	+
Febrile seizures/encephalopathy	+	+	–
Viral encephalitis[b]	+	–	+
ADEM	+	+	–
Cranial neuropathy	–	+	–
Transverse myelitis	+	+	–
Acute flaccid paralysis	+	+	–
Guillain-Barré syndrome	+	+	–
Post viral cerebellar signs	+	–	–
Neuropathic pain	–	–	+

Smallpox may lead to a variety of neurologic complications. See Table 2 Headaches at onset are very common. Backaches are typical in the prodrome, affecting up to 90% of patients. Delirium or encephalopathy can accompany the disease in about 15% of patients during the febrile stage. Febrile seizures can occur in about 7% of children younger than 5 years. Encephalitis may occur in approximately1 in 500 cases of smallpox, characterized by decreased levels of consciousness. CSF is characterized by elevated opening pressure, mild lymphocytic pleocytosis, which may be neutrophilic early on, normal glucose level, and normal to mildly elevated protein level. No virus could be cultured from the CSF. Patients recovering from smallpox-related encephalitis often had dysarthria and an ataxic gait that does improve overtime, indicating possible cerebellar involvement. Similar features have been reported with varicella-zoster virus infection. In these cases, magnetic resonance imaging (MRI) shows a hyperintense signal in the cerebellum, and patients respond to high-dose corticosteroids. Because cases of smallpox predated the availability of MRIs, it remains unknown if a similar pattern may be seen with smallpox.

Very few neurologic complications of monkeypox have been described. [see ID Watch September 18, 2022, page 12] see table 2 Headache is a common presenting feature in both clades1 and2. Mood disturbance, including depression and anxiety, and neuropathic pain are frequent.36,37 The skin lesions themselves may cause painful sores and, depending on the site involved, can cause dysphagia, rectal pain with anal fissures, etc. It is not clear if some of the pain may be dermatomal—similar to that seen with varicella zoster—but the pain can be severe. Conjunctivitis occurred in approximately 20% of patients in a recent outbreak in the DRC, which could lead to decreased vision. During the brief outbreak in the Midwestern US in 2003 and propagated by a pet prairie dog, a 6-year-old girl had prodromal symptoms of headache, fever, and malaise, with a rash 2 days later. Seven days after initial symptoms, she developed decreased responsiveness, rigidity, dilated pupils, disc edema, and bilateral Babinski signs. MRI revealed meningeal enhancement, right parietal and left thalamic signal abnormality, and diffuse edema involving the cortex, thalamus, and brain stem. CSF revealed mild pleocytosis (21 cells/mm3) with a neutrophilic predominance (60%) and normal protein and glucose levels. CSF was negative for MPXV DNA by PCR testing. [J Infect Dis. 2004;190(10):1833- 1840]

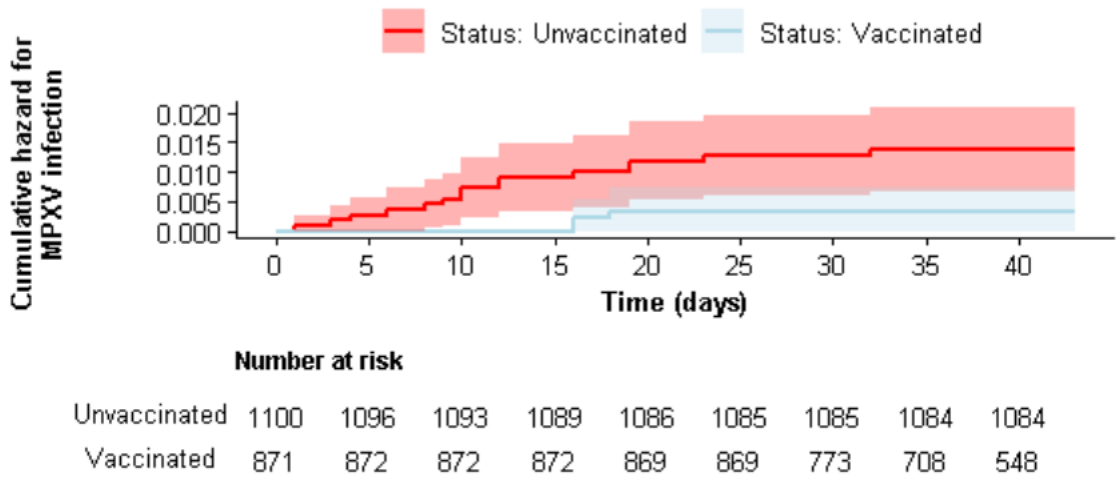
Comment: The authors conclude MPXV should be considered in high-risk populations who present with neurologic syndromes. Diagnosis may require serology and polymerase chain reaction testing of blood and spinal fluid as well as skin lesions. Antiviral therapy should be initiated early in the course of the illness.

Effectiveness of a single-dose Modified Vaccinia Ankara in Human Monkeypox: an observational study Res Sq posted September 23, 2022

doi.org/10.21203/rs.3.rs-1976861/v2

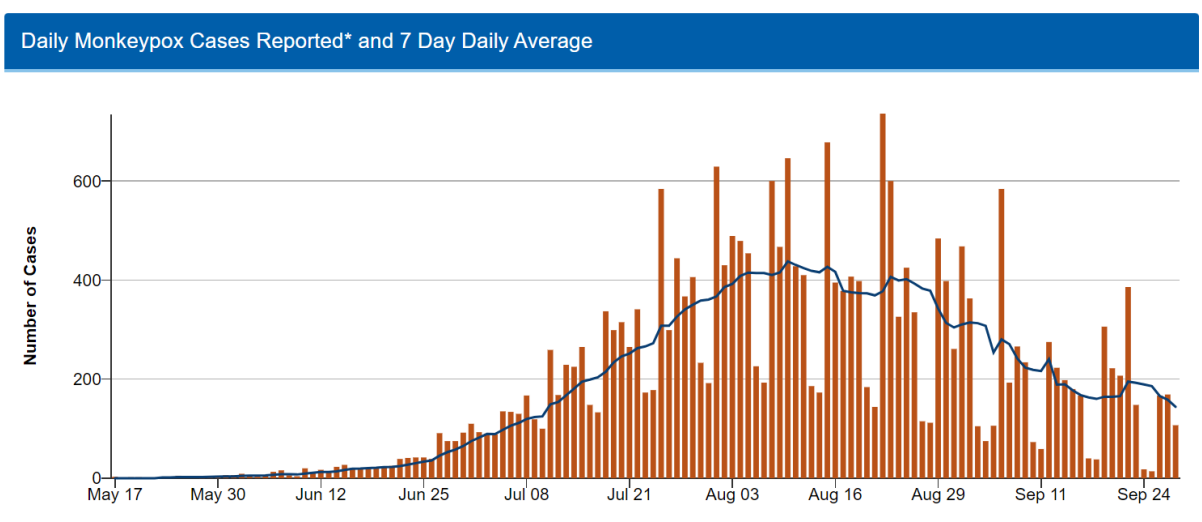
This study was based on patients eligible for monkeypox (MPXV) vaccine seen in the Clalit Health Services system between July 31 and September 12, 2022. A Cox proportional-hazards regression model with time-dependent covariates was used to estimate the association between vaccination and MPXV infections with adjustment for sociodemographic and clinical risk factors. The MVA eligibility criteria were: (a) Males aged 18 – 42 who were dispensed HIVPrEP at least for one month since January 1, 2022, or (b) Males aged 18 – 42 who were diagnosed with HIV and also were diagnosed with one or more of the following STIs since January 1, 2022: active Syphilis, Chlamydia, or Gonorrhea. Subjects who were infected with MPXV prior to the study period were excluded

Of 1,970 subjects eligible for the study, 873 (44%) were vaccinated with Jynneos (one dose) and completed at least 25 days of follow-up. Fifteen unvaccinated subjects and three vaccinated participants contracted MPXV during the study, with vaccine effectiveness estimated at 79% (95% CI [confidence interval], 24% to 94%).



Comment: The results suggest that a single dose of MVA is associated with a significantly lower risk for MPVX infection in high-risk individuals. These findings highlight that urgent MVA vaccination of high-risk individuals may contribute to the containment of the current MPXV outbreak. The primary limitation is that a low number of infections were observed during the study period. No testing for the existence of MPXV was done prior to vaccine administration. Therefore, some high-risk vaccinated individuals may have been infected (but undiagnosed) before vaccine administration. The CDC just announced preliminary results in US showing lower infections in high-risk persons even after one dose, but urge for maximum VE, a second dose should be administered. The CDC reported that unvaccinated men, between the ages 18 and 49 who were considered eligible for the vaccine, were 14 times as likely to become infected with MPXV as those who had one dose at least two weeks earlier.

Monkeypox by the numbers



Comment: Nearly four months after the first report of monkeypox in the US, the virus is continuing to decline easing fears that it may spill over into populations of older adults, pregnant women and young children. However, cases are increasing in a few states and jurisdictions, including Indiana, Virginia and Massachusetts. Black and Hispanic men make up nearly two-thirds of the infected, but only about one-fourth of those vaccinated so far.

COVID-19

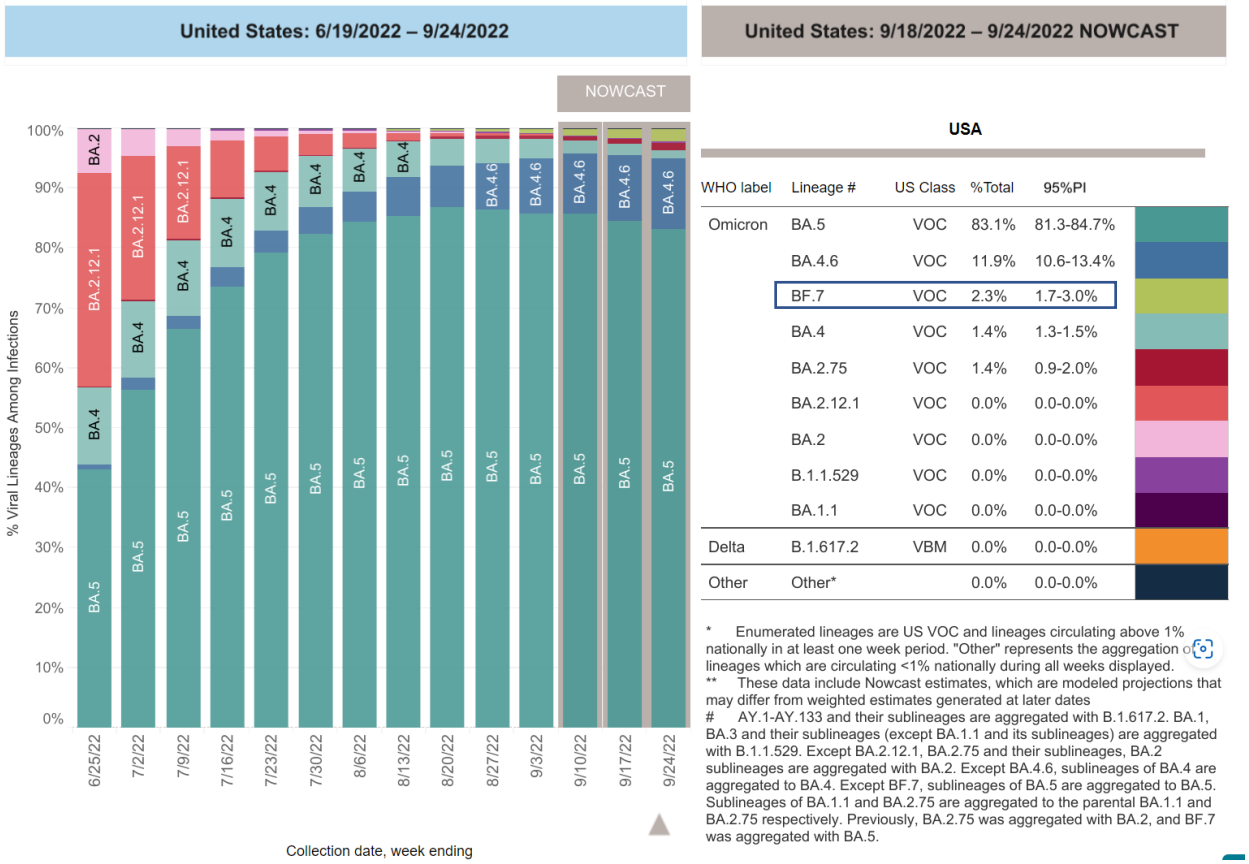
COVID-19 News

BA.5.2.1.7 (BF.7 for short)

BF.7—short for BA.5.2.1.7—comprised 2.3% of sequenced infections last week in the US., according to new data from the CDC. BF.7 has one additional genetic mutation in the spike protein compared to BA.5, its parental strain. Data indicates that this specific genetic change could reduce the efficacy of Evusheld. Other variants jockeying for the top spot right now—held by BA.5, at 83%—include BA.4.6, which comprised 12% of infections, and BA.2.75, which comprised 1.4%. Scientists are taking notice of BF.7 because it's making headway in an increasingly crowded field of Omicron subvariants. For months CDC was watching BA.2.75 but this week, BF.7 surpassed it. BF.7 is only beginning to appear in the US, but it's already taken off in other countries. BA.2.75 still predicted to overtake in many places, but BA.5.2.1.7 has similar advantage over plain BA.5, so different outcomes. The New England region has the highest proportion of BF.7 cases in the U.S. at 3.9 percent.

So far Belgium has seen the lion's share of BF.7 cases identified globally: 25%. Denmark, Germany, and France have each seen 10% of the world's identified cases so far, according to cov-lineages.org, a COVID data repository updated daily by contributors from universities in England, Scotland, and Australia, among others.

Comment: The same growth advantage in multiple countries makes it reasonable to think that BF.7 is gaining and that it's potentially more transmissible than parent BA.5. While very little is known about the severity of disease BF.7, so far all Omicron subvariants have had similar severity. It's unknown how effective the new bivalent Omicron vaccines will be against this variant.



CDC Revises Masking Guidance For Healthcare Facilities

The agency on September 23rd published the updated guidance, which says healthcare facilities that are not in communities with high levels of COVID-19 transmission no longer need to require masking for physicians, patients and visitors. This means over a quarter of counties nationwide can choose not to require masking in their facilities. The guidance still recommends universal masking during an outbreak or when caring for immunocompromised patients.

Comment: Many have voiced concerns over this new guidance. [including me] If you wait until you have an outbreak reinstituting universal masking is too late. It says continue universal masking when caring for immunocompromised patients which may mean many patients who are hospitalized. Some hospitals have stopped admission Covid-19 testing so you could have transmission from an unmask sick patient who haven't been tested for Covid-19, right next to the elderly person with underlying high-risk medical conditions or a pregnant woman. We still have employees out with Covid-19. My recommendation is to maintain universal masking in healthcare for now especially as we approach the respiratory virus season.

CDC revised its "up to date" COVID-19 vaccination September 30, 2022

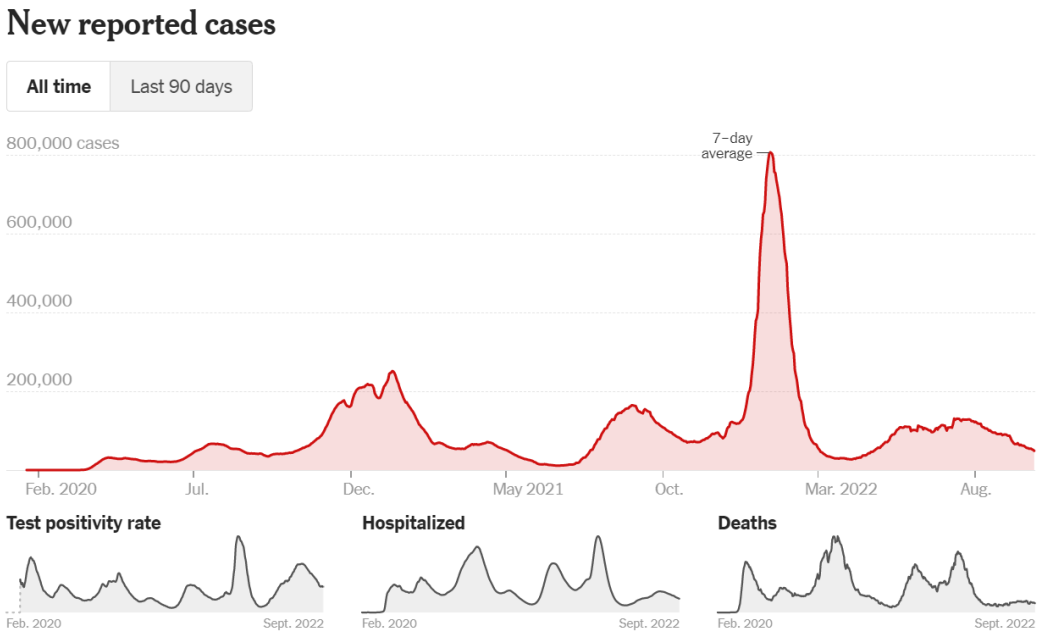
Now, "fully vaccinated" includes the following populations, per the CDC's website:

- People ages 6 months through 4 years should get all COVID-19 primary series doses
- People ages 5 years and older should get all primary series doses and the booster dose recommended for them by the CDC
    - People ages 5 to 11 years are currently recommended to get the original (monovalent) booster
    - People ages 12 years and older are recommended to receive the updated Pfizer or Moderna bivalent booster
    - This includes people who have received all primary series doses and people who have previously received one or more original boosters
    - At this time, people ages 12 to 17 years can only receive the updated Pfizer bivalent booster
- People who are moderately or severely immunocompromised have different recommendations for COVID-19 vaccines

Comment: It makes sense that if you are eligible for a booster that you receive the updated bivalent booster. The question is timing, recent infection etc. which I have commented on in prior ID Watches. It is clear that if you have had only had the primary series and have not had at least one booster you should strongly consider getting the new bivariant booster if you are 12 years old or older.

The rollout of the updated vaccine has been disappointing. Last week, only about 1.5 percent of the eligible population having received the new boosters had . The slow rollout may be attributed to the public's confusion about their eligibility and the lack of confidence is public health. Among vaccinated adults, 40 percent were not sure if the new boosters were recommended for them, according to a poll run by the Kaiser Family Foundation.

COVID-19 by the Numbers



Comment: Cases, hospitalizations, and test positivity have all fallen noticeably in recent weeks. Fewer than 60,000 cases are announced each day nationwide, the lowest level since April. Known daily cases continue to fall at the national level, but a series of regional increases threaten to halt that progress. Most Northeastern states have seen cases increase by 10 percent or more in the past two weeks. In the West, case counts are climbing in Montana, Washington and Oregon. Hospitalizations are falling nearly everywhere. At the national level, they have declined by 14 percent in the past two weeks, however, hospitalizations have begun to increase in some of these Northeastern and Western states as well**.** Deaths remain a concern nationally. More than 400 deaths are reported per day on average, more than twice as many daily deaths as are typically seen in a bad flu season.

COVID-19 Journal Review

Emotional Exhaustion Among US Health Care Workers Before and During the COVID-19 Pandemic, 2019-2021 JAMA Netw Open published online September 21, 2022 5:e2232748

doi:10.1001/jamanetworkopen.2022.32748

Emotional exhaustion was assessed using routine electronic (via email and/or access to a generic link) administration of the Safety, Communication, Organizational Reliability, Physician and Employee Burnout and Engagement (SCORE)28 survey in 2 US health care systems across 76 widely geographically dispersed hospitals before the pandemic (September 2019), after the start of the pandemic (September 2020), and after the introduction of vaccines and vaccine mandates and the rise of the Delta variant (September 2021 in the first system and December 2021 through January 2022 in the second system).

The SCORE survey assesses safety culture and workforce well-being and engagement, including an EE scale and an emotional exhaustion climate (EEclim) scale, because HCW well-being was increasingly recognized as common, expensive, and treatable. Emotional exhaustion assesses the extent to which one feels drained, overwhelmed, and unable to meet demands.

Electronic surveys were returned by 37,187 (of 49,936) HCWs in 2019, by 38 460 (of 45,268) in 2020, and by 31,475 (of 41,224) in 2021 to 2022 for overall response rates of 74.5%, 85.0%, and 76.4%, respectively. The overall sample comprised 107,122 completed surveys. Nursing was the most frequently reported role (n = 43,918 [40.9%])

From September 2019 to September 2021 through January 2022, overall %EE increased from 31.8% (95% CI, 30.0%-33.7%) to 40.4% (95% CI, 38.1%-42.8%), with a proportional increase in %EE of 26.9% (95% CI, 22.2%-31.8%). Physicians had a decrease in %EE from 31.8% (95% CI, 29.3%-34.5%) in 2019 to 28.3% (95% CI, 25.9%-31.0%) in 2020 but an increase during the second year of the pandemic to 37.8% (95% CI, 34.7%-41.3%). Nurses had an increase in %EE during the pandemic's first year, from 40.6% (95% CI, 38.4%-42.9%) in 2019 to 46.5% (95% CI, 44.0%-49.1%) in 2020 and increasing again during the second year of the pandemic to 49.2% (95% CI, 46.5%-51.9%)

Comment: These findings indicate that emotional exhaustion among health care workers, which was problematic before the pandemic, has become worse; increases in emotional exhaustion may jeopardize care quality and necessitate additional support for the workforce. The COVID-19 pandemic has likely exacerbated, the stress of how health care systems are able to meet a high demand for patient care across the health continuum. We have seen increasingly higher rates of HCW absenteeism and turnover. This report has concentrated on burnout in physicians and nurses, but what about other disciplines (e.g., respiratory therapists, pharmacists, nursing assistants, laboratory technologists) since it is likely they may be experiencing the same burnout. It is now necessary to broaden our efforts to define protective factors and establish mitigation strategies. We now must employ the lessons learned from this pandemic so that we can improve the approaches to care delivery, improve HCW training, and conduct meaningful research needed to develop strategies to promote HCW well-being and retention.

Long-term neurologic outcomes of COVID-19 Nature Med published online September 22, 2022

doi.org/10.1038/s41591-022-02001-z

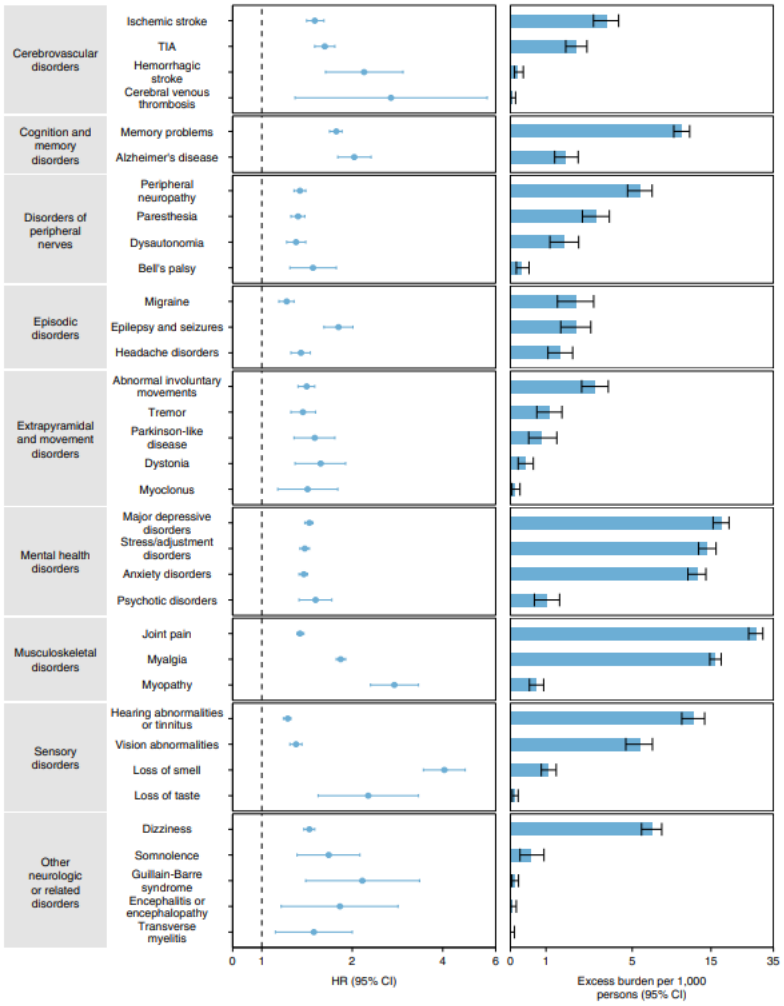
The investigators used the database of the US Department of Veterans Health Care System (VHA) to build a cohort of 154,068 individuals with COVID-19, 5,638,795 contemporary controls (consisting of veterans who were VHA users with no evidence of severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] infection) and 5,859,621 historical controls (consisting of VHA users during 2017 predating the global COVID-19 pandemic). Investigators used inverse probability weighting to balance the cohorts and estimate risks and burdens of incident neurologic disorders at 12 months following acute SARS-CoV-2 infection.

Median follow-up time in the COVID-19, contemporary control and historical control groups was 408 (interquartile range [IQR 378–500), 409 (379–505) and 409 (379–504) days, respectively. The COVID-19, contemporary control and historical control groups had 185,399, 6,808,464 and 7,071,123 person-years of follow up, respectively; altogether corresponding to 14,064,985 person-years of follow up.

Overall, study data showed increased risk of an array of neurologic disorders in comparison with contemporary controls, spanning several neurologic disease categories, including:

- cerebrovascular disorders (hazard ratio [HR] 1.50 [95% confidence interval (CI) 1.41-1.61]; burden 3.40 [95% CI 2.75-4.09] per 1,000 persons at 12 months)
- cognition and memory disorders (HR 1.80 [1.71-1.88]; burden 10.35 [9.27-11.47]),

- peripheral nervous system disorders (HR 1.34 [1.29-1.39]; burden 8.64 [7.44-9.87]).
- episodic disorders including migraine, epilepsy and seizures (HR 1.32 [1.26-1.39]; burden 4.75 [3.79, 5.76])
- extrapyramidal and movement disorders (HR 1.42 [1.34-1.50]; burden 3.98 [3.24-4.77])
- mental health disorders (HR 1.43 [1.38-1.47]; burden 25.00 [22.40-27.69])
- musculoskeletal disorders (HR 1.45 [1.42-1.48]; burden 40.09 [37.22-43.01])
- sensory disorders (HR 1.25 [1.22-1.28]; burden 17.03 [14.85-19.26])
- other neurologic or related disorders including Guillain–Barré syndrome, and encephalitis or encephalopathy (HR 1.46 [1.40-1.52]; burden 7.37 [6.41-8.38]).



Comment: The risks of incident composite neurologic outcomes were evident in all subgroups based on age, race, sex, obesity, smoking, area deprivation index, diabetes, chronic kidney disease, hyperlipidemia, hypertension and immune dysfunction. Particularly, interaction analyses between age and exposure suggested that the risks of episodic disorders, mental health disorders, musculoskeletal disorders and any neurologic disorder increased as age increased (*P* for interaction < 0.001, < 0.001, < 0.001 and = 0.003, respectively), while risks of cognition and memory disorders, sensory disorders and other neurologic or related disorders decreased as age increased (*P* for interaction = 0.001, < 0.001, < 0.001, respectively). The risks and burdens were elevated even in people who did not require hospitalization during acute

COVID-19. Limitations include a cohort comprising mostly white males. Taken together, the results provide evidence of increased risk of long-term neurologic disorders in people who had COVID-19.

Association of SARS-CoV-2 Infection With New-Onset Type 1 Diabetes Among Pediatric Patients From 2020 to 2021 JAMA Netw Open published online September 23, 2022

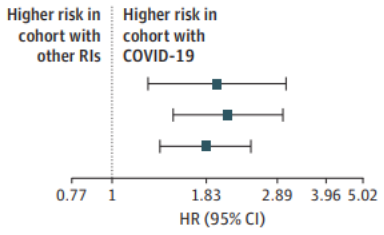
doi:10.1001/jamanetworkopen.2022.33014

Data were obtained using TriNetX Analytics Platform, a web-based database of deidentified electronic health records of more than 90 million patients, from the Global Collaborative Network, which includes 74 large health care organizations across 50 US states and 14 countries with diverse representation of geographic regions, self-reported race, age, income, and insurance types. The study population comprised pediatric patients in 2 cohorts: (1) patients aged 18 years or younger with SARS-CoV-2 infection between March 2020 and December 2021 and (2) patients aged 18 years or younger without SARS-CoV-2 infection but with non–SARS-CoV-2 respiratory infection during the same period. These cohorts were subdivided into groups aged 0 to 9 years and 10 to 18 years. Cohorts were propensity score matched for demographics and family history of diabetes. Risk of new diagnosis of T1D within 1, 3, and 6 months after infection were compared between matched cohorts using hazard ratios (HRs) and 95% CIs.

The study population included 1,091,494 pediatric patients: 314,917 with COVID-19 and 776,577 with non–COVID-19 respiratory infections. The matched cohort included 571,256 pediatric patients: 285,628 with COVID-19 and 285,628 with non–COVID-19 respiratory infections. By 6 months after COVID-19, 123 patients (0.043%) had received a new diagnosis of T1D, but only 72 (0.025%) were diagnosed with T1D within 6 months after non–COVID-19 respiratory infection. At 1, 3, and 6 months after infection, risk of diagnosis of T1D was greater among those infected with SARS-CoV-2 compared with those with non–COVID-19 respiratory infection (1 month: HR, 1.96 [95%CI, 1.26-3.06]; 3 months: HR, 2.10 [95% CI, 1.48-3.00]; 6 months: HR, 1.83 [95% CI, 1.36-2.44]) and in subgroups of patients aged 0 to 9 years, a group unlikely to develop type 2 diabetes, and 10 to 18 years. Similar increased risks were observed among children infected with SARS-CoV-2 compared with other control cohorts at 6 months (fractures: HR, 2.09 [95% CI, 1.41- 3.10]; well child visits: HR, 2.10 [95% CI, 1.61- 2.73]).

A Patients aged 0-18 y at diagnosis of infection

Time since infection, mo	Patients with type 1 diabetes, No. (%)		HR (95% CI)
	Cohort with COVID-19	Cohort with other RIs	
1	56 (0.02)	30 (0.01)	1.96 (1.26-3.06)
3	91 (0.03)	46 (0.02)	2.10 (1.48-3.00)
6	123 (0.04)	72 (0.03)	1.83 (1.36-2.44)



Comment: Of the 571,256 total participants, 123 (0.04%) were newly diagnosed with T1D, compared with 72 (0.03%) who had non-COVID respiratory infections, a 72% increase. In both age-groups 1, 3, and 6 months after infection, the risk of T1D was substantially higher for COVID-19 survivors than for those with other respiratory infections. Type 1 diabetes is considered by some as an autoimmune disease. COVID-19 has been suggested to increase autoimmune responses, and the present finding reinforces that suggestion. An observational nationwide study of 1.2 million Norwegian children in the first 2 years of the pandemic finds that 0.13% of children and teens were diagnosed as having T1D 1 month or more after COVID-19 infection, versus 0.08% in uninfected children, a 63% increase in relative risk [(abstract) EASD 2022 Stockholm, Abstract number 233]

Odds of Hospitalization for COVID-19 After 3 vs 2 Doses of mRNA COVID-19 Vaccine by Time Since Booster Dose JAMA published online September 23, 2022

doi:10.1001/jama.2022.17811

Investigators used electronic health record data to estimate the odds of COVID-related hospitalization after the receipt of only the primary vaccination series (two doses) or a third (booster) dose of an mRNA vaccine among adults admitted to hospitals in the Providence Health & Services network in one of six Western states from October 1, 2021, to July 26, 2022. During the study period, 81% of cases were attributed to the Omicron variant.

Each of the 3,062 COVID-19 patients were matched 1:4 with 12,248 control patients admitted to the hospital for non-COVID indications within 3 days of the case-patient in the same geographic region and received a second vaccine dose (Pfizer or Moderna) within 7 days of the case-patient. Average age was 70.8 years in case-patients and 67.1 in controls, and proportions of men were 52.6% and 46.7%, respectively.

Protection waned after 4 or 5 months. A multivariable analysis showed an association between a third dose and reduced odds of COVID-19 hospitalization (34.7% of case-patients vs 49.3% of controls; adjusted odds ratio [aOR], 0.41, or a 59% reduction). The odds of hospitalization depended on time since the third dose (aOR at less than 50 days, 0.24; 50 to 100 days, 0.24; 101 to 150 days, 0.47; and after 150 days, 0.72). Risk factors for COVID-19 hospitalization were age 70 years or older, male sex, cognitive impairment, chronic obstructive pulmonary disease, diabetes, impaired immune system, obesity, rheumatologic disease, history of organ transplant, and receipt of the Pfizer COVID-19 vaccine.

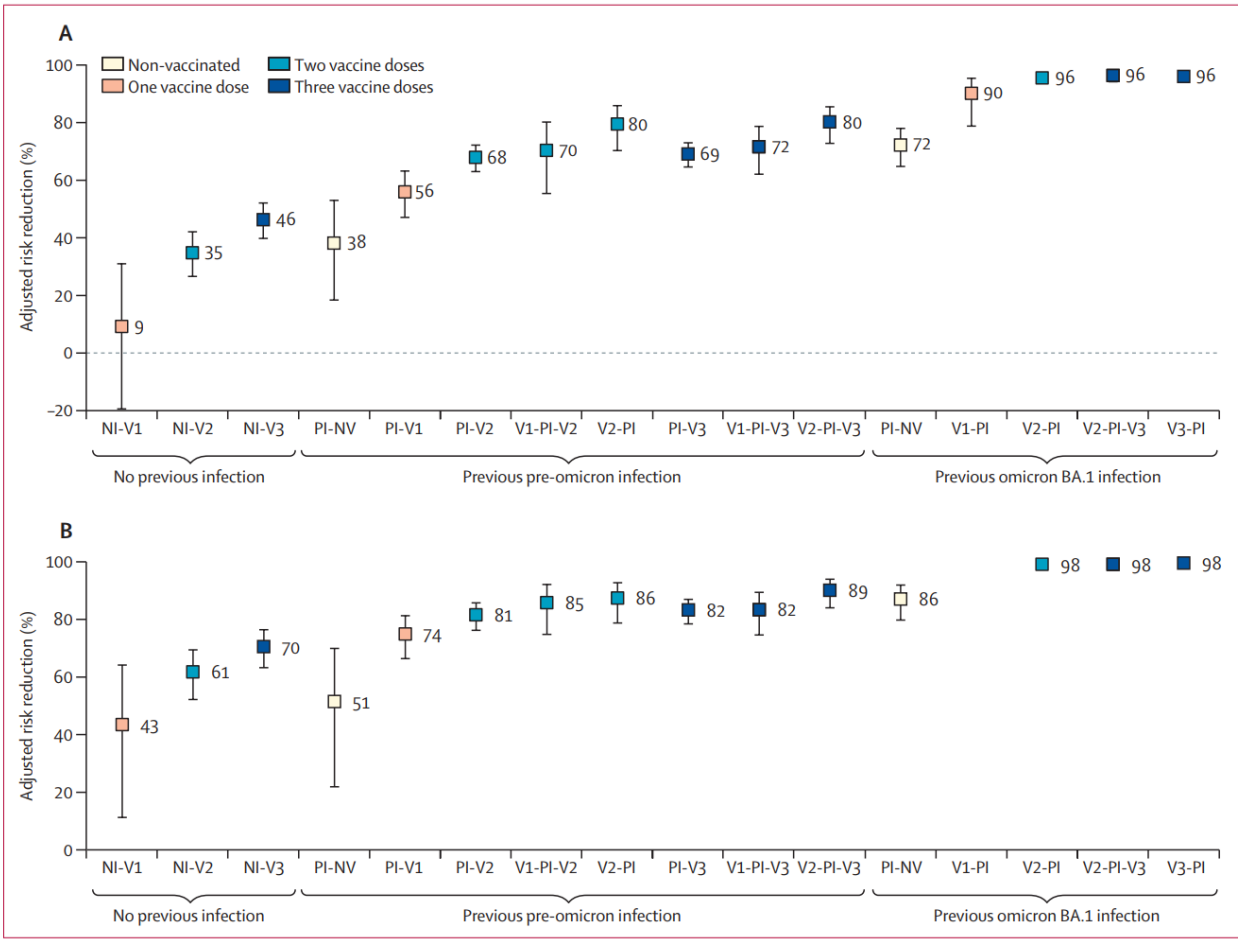
Comment: The investigators noted that studies comparing COVID-19 rates among recipients of a booster dose and their unvaccinated counterparts have found 55% to 99% lower odds of COVID-19 among those boosted. By matching cases with controls based on the date of second mRNA dose, this study was able to measure the added benefit of a booster dose to the primary series. This article shows us that even if you're fully vaccinated, there is additional protection to getting a booster dose. Compared to people who only had their initial vaccinations, people with boosters were a lot less likely to have severe Covid-19 for 4-5 months after the booster shot. Even after protection wanes over time, the overall risk of hospitalization among vaccinated patients is still quite low due in large part to T-cell function.

Protection against omicron (B.1.1.529) BA.2 reinfection conferred by primary omicron BA.1 or pre-omicron SARS-CoV-2 infection among health-care workers with and without mRNA vaccination: a test-negative case-control study Lancet Infect Dis published online September 21, 2022

doi.org/10.1016/ S1473-3099(22)00578-3

The investigators conducted a test-negative case-control study among HCWs aged 18 years or older who were tested for SARS-CoV-2 in Quebec, Canada, between March 27 and June 4, 2022, when BA.2 was the predominant variant and was presumptively diagnosed with a positive test result. They identified cases (positive test during study period) and controls (negative test during study period) using the provincial laboratory database that records all nucleic acid amplification testing for SARS-CoV-2 in Quebec and used the provincial immunization registry to determine vaccination status. Logistic regression models compared the likelihood of BA.2 infection or reinfection (second positive test ≥30 days after primary infection) among health-care workers who had previous primary infection and none to three mRNA vaccine doses versus unvaccinated health-care workers with no primary infection.

Previous omicron BA.1 infection alone was the single most protective factor against BA.2 reinfection (risk reduction of 72%) and was associated with higher protection than pre-omicron primary infection alone (38%) or even than three doses of mRNA vaccine in people with no previous infection (46%). Hybrid immunity conferred by previous omicron BA.1 primary infection plus vaccination increased estimated protection against BA.2 reinfection, similarly to 96% with two or three vaccine doses, and this protection was maintained for at least 5 months after primary infection.



Protection against any BA.2 infection (A) and symptomatic BA.2 infection (B). Logistic regression models compared participants with previous primary infection or vaccination, or both, versus unvaccinated participants without previous primary infection

Comment: The findings of substantial and sustained omicron BA.1 hybrid protection against BA.2 among health-care workers suggest that people who have had previous omicron infection and two vaccine doses might be well protected. For such individuals, additional doses might provide only marginal added benefit against subsequent omicron infections and severe outcomes. They defined reinfections on the basis of a 30-day or longer interval between positive tests, because of data documenting early BA.2 reinfections. Prolonged viral shedding might have been misclassified as reinfection, but this would tend to underestimate the protection associated with previous BA.1 infection. Asymptomatic or HCWs with minimal symptomatic infections might have been undetected before or during omicron waves, which would also lead to underestimation of the protection induced by previous infection. Due to the low COVID-19 hospitalization rate among HCWs, the effect of primary infection severity as well as effectiveness against severe outcomes could not be estimated to newly circulating omicron BA.4 and BA.5 or other sublineages requires caution. BA.4 and BA.5 differ antigenically from BA.2 and are even more distant from BA.1.24. BA.1 infection-induced neutralizing immunity seems less protective against newly dominating omicron BA.5 than BA.2,27 but preprints from epidemiological studies in Portugal and Qatar suggest that hybrid protection against BA.4 and BA.5 conferred by omicron primary infection and vaccination also remains high at 76–80%. [medRxiv; published online July 12, 2022; medRxiv; published online July 28, 2022]. The CDC

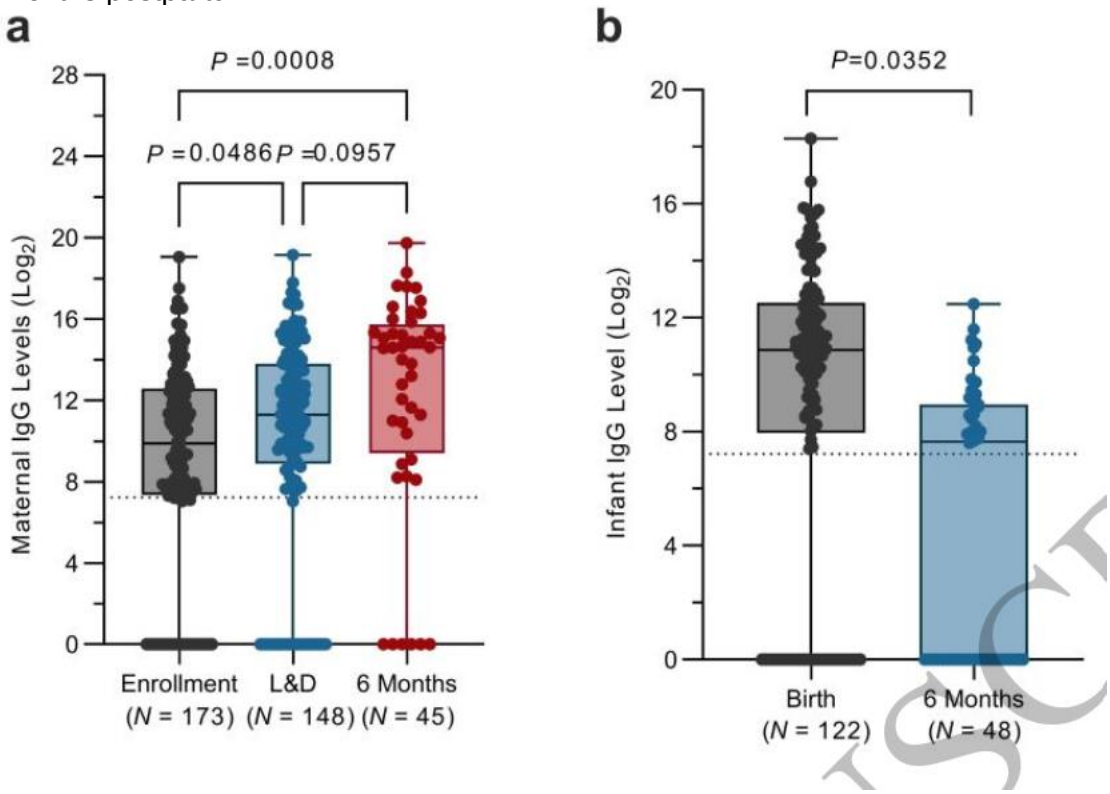
has yet to change recommendations based on hybrid or natural immunity. Perhaps available vaccine doses might be better prioritized for protecting people who are more vulnerable.

Longitudinal Evaluation of Antibody Persistence in Mother-Infant Dyads Following SARS-CoV-2 2 Infection in Pregnancy J Infect Dis published online September 9, 2022

doi.org/10.1093/infdis/jiac366

This is a longitudinal cohort of pregnant women with PCR-confirmed SARS-CoV-2 infection. Maternal/infant sera were collected at enrollment, delivery/birth, and 6 months. Anti-SARS-CoV-2 spike IgG, IgM and IgA were measured by ELISA.

256 pregnant women and 135 infants were enrolled; 148 maternal and 122 neonatal specimens were collected at delivery/birth; 45 maternal and 48 infant specimens were collected at 6 months. Sixty-eight percent of women produced all anti-SARS-CoV-2 isotypes at delivery (IgG, IgM, IgA); 96% had at least one isotype. Symptomatic disease, and vaccination prior to delivery, were associated with higher maternal IgG at L&D. Detectable IgG in infants dropped from 78% at birth to 52% at 6 months. In the multivariate analysis evaluating factors associated with detectable IgG in infants at delivery, significant predictors were 3rd trimester infection (OR 4.0), mild/moderate disease (OR 4.8), severe/critical disease (OR 6.3), and maternal vaccination prior to delivery (OR 18.8). No factors were significant in the multivariate analysis at 6 months postpartum.



Comment: This is the largest longitudinal cohort of mother-infant dyads with a history of SARS-CoV-2 in pregnancy. Their ability to follow mothers and infants up to 6 months of age allows them to monitor changes in antibody patterns over time. Second, few studies have analyzed

differential maternal and neonatal antibody responses based not only on maternal COVID-19 disease severity and timing of infection, but also subsequent vaccination following recovery. They did not have vaccinated controls without a history of SARS-CoV-2, although several other studies have addressed this question. This study adds to the growing evidence that document efficient transplacental IgG transfer following either symptomatic, natural SARS-CoV-2 infection or vaccination in pregnancy.

Methicillin-Resistant Staphylococcus aureus Bacteremia during the COVID-19 Pandemic: Trends and Distinguishing Characteristics among Patients in a Health Care System in New York City ICHE published online September 9, 2022

DOI: 10.1017/ice.2022.238

From January 2019 through March 2022, there were 216 cases of healthcare facility-onset (HCFO) MRSA bacteremia across the 11 public acute care medical centers within New York City Health and Hospitals Enterprise, a healthcare system that serves primarily low-income patients in the Bronx, Brooklyn, Manhattan, and Queens. The baseline rate of MRSA bacteremia was 0.073 per 1,000 patient-days in 2019, and during four COVID-19 surges it climbed to 0.53, 0.20, 0.51, and 0.43 infections per 1,000 patient-days. From January 202o through March 2022, the overall rate of MRSA bacteremia in patients without COVID-19 was 0.065 per 1,000 patient-days, and 0.34 per 1,000 patient-days in patients with a diagnosis of COVID-19.

Compared with patients without COVID-19, MRSA bacteremia patients with COVID-19 were older (67.2 vs 55.6 years), more likely to be Asian (31% vs 4%), less likely to be Black (13% vs 36%), and more likely to be located in an intensive care area at the time of MRSA bacteremia (58% vs 34%). In addition, 77% of the patients with COVID-19 were on mechanical ventilation, 63% were on corticosteroids, and 79% met the National Healthcare Safety Network definition of pneumonia. Mortality rates were higher for patients with COVID-19 (81% vs 34%), and only 4% of patients with HCFO MRSA bacteremia and COVID-19 were discharged home, compared with 23% of patients without COVID-19. Prolonged hospitalization and the high rates of corticosteroid use, and mechanical ventilation likely contributed to superimposed MRSA infection, as did increased use of the antibiotic ceftriaxone during the initial surge of COVID-19. They also suggest the number of central-line associated MRSA bacteremia cases may be underestimated.

Comment: The elevated rates of HCFO MRSA bacteremia during the pandemic once again emphasizes the important role of ASP and infection prevention, especially during surges of patients with COVID-19. This report is consistent with earlier publications indicating increases CLABSIs and other HAIs. A recent CDC report covered in ID Watch highlighted a significant uptick in MDROs during the pandemic.