COVID-19 Updates: What We Know Now

Newest Episodes:
• To Mask or Not to Mask as Part of Standard Precautions?
TUNE IN TO THE SHEA JOURNALS PODCASTS

AVAILABLE ON:

- iHeartRadio
- Spotify
- Apple Podcasts
- SoundCloud
- Stitcher
With funding from the Centers for Disease Control and Prevention, IDSA has launched the COVID-19 Real Time Learning Network, an online community that brings together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.

www.COVID19LearningNetwork.org
@RealTimeCOVID19 | #RealTimeCOVID19
Prevention

An online learning module designed with frontline healthcare personnel in mind.

PreventionCHKC.org
Infection Control & Hospital Epidemiology publishes scientifically authoritative, clinically applicable, peer-reviewed research on control and evaluation of the transmission of pathogens in healthcare institutions and on the use of epidemiological principles and methods to evaluate and improve the delivery of care. Major topics covered include infection control practices, surveillance, antimicrobial stewardship, cost-benefit analyses, resource use, occupational health, and regulatory issues.

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COVID-19 Town Hall
Round 88
House Keeping Items

- Technical difficulties? Visit: https://support.zoom.us
- Webinar recording, PowerPoint presentation, and references available LearningCE’s Rapid Response Program
- Streaming Live on SHEA's Facebook page
- Zoom Q&A and Chat
SHEA Town Hall 88
Overview
SARS-CoV-2 Variants, US, CDC

Weighted Estimates: Variant proportions based on reported genomic sequencing results

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* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one 2-week period. *Other* represents the aggregation of lineages which are circulating <1% nationally during all 2-week periods displayed.

# BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, XBB and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.2.75.2, CH.1.1 and BN.1, BA.2.75 sublineages are aggregated with BA.2.75. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, BQ.1, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. Except the lineages shown and their sublineages, sublineages of XBB are aggregated to XBB. Except XBB.1.5.1, XBB.1.5.10 and FD.2, sublineages of XBB.1.5 are aggregated to XBB.1.5. Except XBB.1.16.1, sublineages of XBB.1.16 are aggregated to XBB.1.16. For all the other lineages listed, their sublineages are aggregated to the listed parental lineages respectively. Previously, XBB.1.5.10 was aggregated to XBB.1.5. Lineages BA.2.75.2, XBB, XBB.1.5, XBB.1.5.1, FD.2, XBB.1.9.1, XBB.1.9.2, XBB.1.16, XBB.1.16.1, XBB.2.3, BN.1, BA.4.6, BF.7, BQ.11, BA.5.2.6, BQ.1.1 and XBB.1.5.10 contain the spike substitution R346T.
REPORTED COVID-19 CASES IN THE UNITED STATES

Sources: Our World in Data: https://ourworldindata.org/covid-cases 5-23-2023
US COVID-19 HOTSPOTS

February 6, 2022

February 12, 2023

May 19, 2023

June 23, 2023

Hospitalizations decreased 22.1% from our last Town Hall
ICU admissions decreased 9.3% from our last Town Hall

Source: New York Times –
COVID-19 HOSPITAL ADMISSIONS IN THE UNITED STATES, BY AGE

Daily hospitalizations decreased 24.3% from our last Town Hall

Source: New York Times 6-23-2023
COVID-19 DEATHS IN THE UNITED STATES

Cumulative Deaths – 1,132,206

84.5% decrease from our last Town Hall

INFLUENZA ACTIVITY BY STATE IN THE UNITED STATES

January 8, 2023

March 17, 2023

May 6, 2023

May 6, 2023

Source: CDC https://www.cdc.gov/flu/weekly/usmap.htm 3-17-23
PERCENTAGE OF OUTPATIENT VISITS FOR INFLUENZA-LIKE ILLNESS

This Month’s Emerging Infectious Disease News


2. A Lancet systematic review found evidence of efficacy and effectiveness of inactivated COVID vaccines but noted that many studies had significant design issues.

3. Another Lancet study demonstrated efficacy of the mRNA vaccines against omicron infection and severe outcomes in children younger than 12 years and also found that bivalent boosters were more effective than monovalent boosters.

4. A JAMA Pediatrics study used near real-time monitoring of outcomes to demonstrate the efficacy of the Pfizer-BioNTech vaccine in children aged 5-17.

5. A JAMA Internal Medicine systematic review and meta-analysis found that female sex, older age, higher body mass index, smoking, preexisting comorbidities, and previous hospitalization or ICU admission were risk factors for developing Long COVID.

6. A Bavarian study published in JAMA found that a diagnosis of COVID-19 in children was associated with an increased incidence of type 1 diabetes.

7. Another JAMA study found 37 symptoms across multiple pathophysiological domains identified as present more often in SARS-CoV-2–infected participants at 6 months or more after infection, providing an approach both to the definition and the diagnosis of Long-COVID.

8. The CDC’s Advisory Committee on Immunization Practices recommended administration of RSV vaccine for individuals 60 and older, especially for those with comorbidities, in consultation with their providers.

References available in the chat
9. A study in *JAMA Network Open* found no evidence for an increased risk of spontaneous abortion among mRNA booster vaccine recipients who were between 6 and 19 weeks of gestation at the time of boosting.

10. A study published in *JAMA Internal Medicine* provided evidence for the benefit of the routine use of high-dose prophylactic anticoagulation for patients who have severe hypoxemic COVID-19 pneumonia.

11. Another *JAMA Internal Medicine* study found that discontinuation of routine admission COVID testing in hospitals in England and Scotland was associated with significant increases in hospital-onset SARS-CoV-2 infections relative to community-onset infections.

12. A study in *Clinical Infectious Diseases* found that commercial preparations of intravenous immunoglobulin contain significant titers of antibodies against SARS-CoV-2.

13. A survey of 25 acute-care hospitals published in *Infection Control and Hospital Epidemiology* found significant deviation from CDC guidance about HCP returning to work after COVID; many have HCPs return to work earlier than recommended.

14. An *FDA Advisory Committee* recommended that manufacturers produce a booster dose targeting the XBB.1.5 strain, and that this vaccine be used in the fall as a monovalent vaccine.

15. A fascinating study published in *Lancet Microbe* described a SARS-CoV-2 human challenge study. The results provided evidence for the concept of superspreading and implicated the nose as the primary source of expelled virus.

*References available in the chat*
Panelists:

Dr. David Henderson
NIH

Dr. Clare Rock
Johns Hopkins Medicine

Dr. Kristina Bryant
University of Louisville

Dr. David Weber
UNC School of Medicine
COVID-19 UPDATE:
FOCUS ON EVOLUTION OF SARS-CoV-2 VARIANTS

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Associate Chief Medical Officer
Medical Director, Hospital Epidemiology
University of North Carolina, Chapel Hill, NC

Disclosures: Consultancy; Pfizer, Merck, PDI, BD, Germitec, Wellair
All drugs/vaccines issues discussed consistent with FDA approvals or authorizations
SARS-CoV-2 Variants: Current Summary

• XBB.1 first reported from India in August 2022; XBB.1.5 first reported from US (NY, CT) in late October 2022; XBB.1: Recombinant of BA.2.10.1 and BA.2.75 sublineages; evidence pointing at a higher reinfection risk, as compared to other circulating Omicron sublineages

• Spike proteins of XBB.1.16, XBB.1.5 and XBB.2.3 are similar with few amino acid differences, and available studies suggest little to no further immune evasion from these new substitutions in the XBB.1.16 spike compared to XBB.1.5

• Epidemiology, US
  • The sublineages XBB.1.5, XBB.1.16 and XBB.2.3 carry an additional spike mutation in a key antigenic site (i.e. R346T); these sublineages show a significant growth advantage over other circulating Omicron sublineages in many settings
  • Rapid increase of XBB.1, XBB.1.5 and XBB.1.16 – subvariants with greatest escape from vaccines and natural immunity (also not impacted by Evusheld or Bebtelovimab); similar severity of disease (lower severity than delta)

• The current trajectory of virus evolution suggests that XBB.1.16 could be dominant by fall 2023 but that XBB.2.3 and other XBB sublineages could also continue to increase in proportion as the virus evolves

• Alternative therapy to monoclonal antibodies: Remdesivir (IV x 3 days) {Remdesivir resistance report in 2 kidney transplant recipients}^  
• Best evidence suggests that antivirals (e.g., Remdesivir, Paxlovid, Molnupivir) retain activity against all variants

• Bivalent COVID-19 vaccine elicits lower neutralizing antibodies to XBB than other SARS-CoV-2 variants and Omicron sublineages but is superior to monovalent vaccines including persons who have had 2 boosters (i.e., 4 doses)

• Only ~17% of Americans 5+ have received bivalent booster; ~43% of persons 65 years and older

Hogan JI, et al. Clin Infect Dis 2022;Sept 26,ciac769
FDA, 15 June 2023
COVID-19 AND SARS-CoV-2 OVER TIME, US
Spread Of New Variants A Key Driver Of Surges

Key issues in assessing impact of new variants: Escape from immunity (natural and vaccine), transmissibility and virulence


Summary

What is already known about this topic?

CDC has used genomic surveillance to monitor trends in circulating U.S. SARS-CoV-2 variants since December 2020, including the emergence of the Omicron variant at the end of 2021.

What is added by this report?

Weekly estimates of variant proportions during January 2, 2022–May 13, 2023, identified the emergence and subsequent predominance of multiple Omicron lineages in the United States, including BA.2, BA.2.12.1, BA.5, and XBB.1.5. Repeated independent substitutions in the spike protein suggested convergent evolution related to immune evasion. Analytic methods for variant proportion estimation have been updated as numbers of cases and sequenced specimens have declined.

What are implications for public health practice?

Ongoing genomic surveillance can identify emerging SARS-CoV-2 variants and guide vaccine and therapeutic development and use.

Ma KC, et al. MMWR 2023;72:651
CURRENT SARS-CoV-2 VARIANTS, US

https://covid.cdc.gov/covid-data-tracker/#variant-proportions
SARS-CoV-2 VARIANTS: TRANSMISSIBILITY AND VIRULENCE

Fig 1. Qualitative plot of different VOC variants of the disease of Covid-19

Jabraeilian H, Jamali Y. https://doi.org/10.1101/2023.06.13.23291332
Enhanced transmissibility of XBB.1.5 is contributed by both strong ACE2 binding and antibody evasion

SARS-CoV-2 recombinant subvariant XBB.1.5 is growing rapidly in the United States, carrying an additional Ser486Pro substitution compared to XBB.1 and outcompeting BQ.1.1 and other XBB sublineages. The underlying mechanism for such high transmissibility remains unclear. Here we show that XBB.1.5 exhibits a substantially higher hACE2-binding affinity compared to BQ.1.1 and XBB/XBB.1. Convalescent plasma samples from BA.1, BA.5, and BF.7 breakthrough infection are significantly evaded by both XBB.1 and XBB.1.5, with XBB.1.5 displaying slightly weaker immune evasion capability than XBB.1. Evusheld and Bebtelovimab could not neutralize XBB.1/XBB.1.5, while Sotrovimab remains weakly reactive and notably, SA55 is still highly effective. The fact that XBB.1 and XBB.1.5 showed comparable antibody evasion but distinct transmissibility suggests enhanced receptor-binding affinity would indeed lead to higher growth advantages. The strong hACE2 binding of XBB.1.5 could also enable its tolerance of further immune escape mutations, which should be closely monitored.

Yue C, et al  https://www.biorxiv.org/content/10.1101/2023.01.03.522427v2.full.pdf
A turning point in COVID-19 severity and fatality during the pandemic: National Cohort Study, Qatar

Results: The cumulative incidence of severe, critical, or fatal COVID-19 after 3.14 years of follow-up was 0.45% (95% CI: 0.43-0.47%). The incidence rate for severe, critical, or fatal COVID-19 throughout the pandemic was 1.43 (95% CI: 1.35-1.50) per 1,000 person-years. In the pre-omicron phase, first omicron wave, and combined phases, it was 2.01 (95% CI: 1.90-2.13), 3.70 (95% CI: 3.25-4.22), and 2.18 (95% CI: 2.07-2.30) per 1,000 person-years, respectively. The post-first omicron phase saw a drastic drop to 0.10 (95% CI: 0.08-0.14) per 1,000 person-years, a 95.4% reduction. Among all severe, critical, and fatal cases, 99.5% occurred during the primary infection. In the post-first omicron phase, the incidence rate of fatal COVID-19 decreased by 90.0% compared to earlier stages. Both severity and fatality exhibited an exponential increase with age and a linear increase with the number of coexisting conditions.


Figure 1. COVID-19 acute-care and ICU bed hospitalizations and COVID-19 severity and criticality among Qataris throughout the pandemic. A) Comparison of the number of new COVID-19 admissions into acute-care hospital beds and the number of new severe COVID-19 cases according to the WHO definition for COVID-19 severity. B) Comparison of the number of new COVID-19 admissions into ICU hospital beds and the number of new critical COVID-19 cases according to the WHO definition for COVID-19 criticality.
Severity of SARS-CoV-2 Omicron XBB subvariants in Singapore

Abstract
Several XBB subvariants such as XBB.1.5, XBB.1.9, XBB.1.16 and XBB.2.3 co-circulate in Singapore. Despite the different viral properties of XBB.1.16 as compared to other XBB subvariants, comparison on their severity is limited. In this study, we investigate the outcomes of hospitalization and severe COVID-19 infection in individuals infected with different XBB subvariants, adjusted for potential confounders such as age and vaccination history. Overall, our preliminary analysis showed no difference in the severity of different XBB variants.

https://www.medrxiv.org/content/10.1101/2023.05.04.23289510v1

Figure 1 Probability of infection outcomes for different XBB subvariants and vaccination history; (A) severe infection in those aged 60 and above, (B) hospitalisation in those aged 60 and above, (C) severe infection in those aged below 60, (D) hospitalisation in those age below 60. Results were not statistically significant.
Bivalent COVID-19 vaccine antibody responses to Omicron variants suggest that responses to divergent variants would be improved with matched vaccine antigens

We compared neutralizing antibody responses to BA.4/5, BQ.1.1, XBB, and XBB.1.5 Omicron SARS-CoV-2 variants after a bivalent or ancestral COVID-19 mRNA booster vaccine or post-vaccination infection. We found that the bivalent booster elicited moderately high antibody titers against BA.4/5 that were approximately two-fold higher against all Omicron variants than titers elicited by the monovalent booster. The bivalent booster elicited low but similar titers against both XBB and XBB.1.5 variants. These findings inform risk assessments for future COVID-19 vaccine recommendations and suggest that updated COVID-19 vaccines containing matched vaccine antigens to circulating divergent variants may be needed.

Bivalent mRNA-1273.214 vaccine effectiveness against SARS-CoV-2 omicron XBB* infections

Qatar introduced COVID-19 bivalent vaccination for persons ≥12 years old using the 50-μg mRNA-1273.214 vaccine combining SARS-CoV-2 ancestral and omicron BA.1 strains. We estimated effectiveness of this bivalent vaccine against SARS-CoV-2 infection using a matched, retrospective, cohort study. Matched cohorts included 11,482 persons in the bivalent cohort and 56,806 persons in the no-recent-vaccination cohort. During follow-up, 65 infections were recorded in the bivalent cohort and 406 were recorded in the no-recent vaccination cohort. None progressed to severe, critical, or fatal COVID-19. Cumulative incidence of infection was 0.80% (95% CI: 0.61-1.07%) in the bivalent cohort and 1.00% (95% CI: 0.89-1.11%) in the no-recent-vaccination cohort, 150 days after the start of follow-up. Incidence during follow-up was dominated by omicron XBB* subvariants including XBB, XBB.1, XBB.1.5, XBB.1.9.1, XBB.1.9.2, XBB.1.16, and XBB.2.3. The adjusted hazard ratio comparing incidence of infection in the bivalent cohort to that in the no-recent-vaccination cohort was 0.75 (95% CI: 0.57-0.97). Bivalent vaccine effectiveness against infection was 25.2% (95% CI: 2.6-42.6%). Effectiveness was 21.5% (95% CI: -8.2-43.5%) among persons with no prior infection and 33.3% (95% CI: -4.6-57.6%) among persons with prior infection. mRNA-1273.214 reduced incidence of SARS-CoV-2 infection, but the protection was modest at only 25%. The modest protection may have risen because of XBB* immune evasion or immune imprinting effects, or combination of both.

VACCINE EFFECTIVENESS, CASES AND DEATHS, US

In March 2023, people ages 18 years and older and vaccinated with an updated (bivalent) booster had:

- 5.1x lower risk of dying from COVID-19 compared to unvaccinated people, and
- 1.1x lower risk of dying from COVID-19 compared to people vaccinated without the updated (bivalent) booster.
Durability of Bivalent Boosters against Omicron Subvariants

Bivalent vaccines are associated with a lower risk of infection or severe infection with the BQ.1–BQ.1.1 and XBB–XBB.1.5 subvariants. The effectiveness was higher against hospitalization and death than against infection and waned gradually from its peak over time.

Lin DG, et al. NEJM 2023;21 April
Methods: This modeling study used person-level data from the California Department of Public Health on COVID-19 cases, hospitalizations, deaths, and vaccine administration from July 23, 2022 to January 23, 2023.

Results: For both bivalent vaccines and nirmatrelvir-ritonavir, the most efficient strategy (based on NNT) for averting severe COVID-19 was targeting the 75+ years group. We predicted that perfect coverage of bivalent boosters in the 75+ years group would avert 3,920 hospitalizations (95%UI: 2,491-4,882; 7.8% total averted; NNT 387) and 1,074 deaths (95%UI: 774-1,355; 16.2% total averted; NNT 1,410). Perfect uptake of nirmatrelvir-ritonavir in the 75+ years group would avert 5,644 hospitalizations (95%UI: 3,947-6,826; 11.2% total averted; NNT 11) and 1,669 deaths (95%UI: 1,053-2,038; 25.2% total averted; NNT 35).
CONCLUSIONS

• Since the onset of the COVID-19 pandemic there have been five variants of concern (VOC) designated by WHO: Alpha, Beta, Gamma, Delta, and Omicron (currently predominant variant). No new COV circulating worldwide.

• Omicron
  • Current predominant sublineages: XBB
  • Increased infectivity
  • Increased escape from monoclonal antibodies (no currently FDA approved products effective), natural immunity and vaccines
  • Reduced virulence

• The totality of available evidence suggests that a monovalent XBB-lineage vaccine is warranted for the 2023–2024 vaccination campaign. Current sublineages under consideration include XBB.1.5, XBB.1.16, or XBB.2.3. (FDA, 15 June 2023)

• Public health interventions (vaccine, antivirals) should focus on risk groups for severe COVID-19 (>65 years of age, co-morbidities)

• Transmissibility and virulence can be independent attributes of microbes. There is no assurance that future variants may not evolve with both higher transmissibility (required to displace current variants) and virulence

• Monitoring for new variants: Sequencing isolates from hospitalized patients and wastewater monitoring (although wastewater monitoring has some challenges)