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Concise Communication

Susceptibility of healthcare personnel with severe acute respiratory coronavirus virus 2 (SARS-CoV-2) hybrid immunity to XBB lineage reinfection

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Abstract

Among 8,678 vaccinated healthcare personnel (HCP) with previous coronavirus disease 2019 (COVID-19), by August 28, 2023, 909 (10%) had an infection of severe acute respiratory coronavirus virus 2 (SARS-CoV-2) omicron XBB variant. Reinfection risk was comparable irrespective of previous infection type except for the omicron BQ.1 variant. Bivalent vaccination had a protective effect. COVID-19 vaccines remain vital to protect HCP, including those with hybrid immunity.

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Healthcare personnel (HCP) coronavirus disease 2019 (COVID-19) vaccination protects coworkers and patients from healthcare-associated severe acute respiratory coronavirus virus 2 (SARS-CoV-2) infection and alleviates workforce shortages.[1] Federal and state COVID-19 vaccine mandates allowed many institutions to initially achieve high COVID-19 vaccination rates. However, with an end to the public health emergency in May 2023, the Centers for Medicare & Medicaid Services and many state public health departments rescinded their HCP COVID-19 immunization requirements.

In August 2022, the bivalent vaccine was approved to include the SARS-CoV-2 omicron BA.4/5 variants. By December 2022, the omicron XBB lineages replaced the previous variants as the most dominant strain.[2] Newer XBB-like lineages continued to rise and were projected to spread during the winter.[3]

In response to the continued viral evolution in September 2023, the XBB 1.5 monovalent vaccine became available for the 2023–24 season. Preliminary analysis suggested that the XBB vaccine effectively targets the circulating XBB-like lineages, and the CDC has recommended the vaccine for all persons 6 months and older.[4] Nevertheless, HCP uptake of the vaccine has remained low, and specific data on reinfection risks in previously SARS-CoV-2–infected HCP may promote vaccine acceptance in this group.[5,6]

In the present study, we assessed the occurrence of XBB reinfection in a previously described longitudinal cohort of HCP who had completed at least 2 doses of the monovalent vaccine and had at least 1 previous SARS-CoV-2 infection before the emergence of the omicron XBB variant.[2,6,7] HCP with multiple infections were stratified according to the most recent illness. Using NYC Department of Health surveillance data and timing of infection to estimate variant status, we compared these rates between prior infection variant groups. Using rate ratios, we also compared infection rates between individuals who received the bivalent vaccine versus those who did not.

Methods

Memorial Sloan Kettering Cancer Center (MSKCC) is a 514-bed tertiary-care cancer center in New York City that employs >21,000 individuals. All SARS-CoV-2–positive results, regardless of testing method, were reported through an automated electronic survey. HCP hired before November 11, 2020, were eligible for inclusion, and they were excluded on a rolling basis if employment ended, as previously described.[7] Among them, we identified eligible employees who met the following criteria: HCP with receipt of at least 2 doses of the monovalent vaccine and at least 1 previous SARS-CoV-2 infection before the emergence of the omicron XBB variant. Next, using data from December 17, 2022, to August 28, 2023, we estimated the XBB test positivity rates among groups defined by the variant type of their most recently recorded SARS-CoV-2 infection. Because limited samples were available for variant sequencing at MSKCC, concurrent regional surveillance data were used to estimate variant distributions and to calculate the likelihood that a positive test on any given day was of a particular variant type.[8] These probabilities were then used to adjust daily counts of positive tests, providing an estimated distribution of variant types for all prior positives. Test positivity rates were derived using these weighted positive test counts and rate ratios, and 95% confidence intervals (CIs) were estimated using 1,000 bootstrap iterations and the percentile method to approximate

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Table 1. Weekly Rate Ratios for XBB Infections Per Prior Variant Group[a]

Test Positivity Rates and Rate Ratios (December 17, 2022–August 28, 2023)					
Variant	Positive Tests, No.	Person Days, No.	Mean Group Size, No.	Positivity Rates (Positives/Person Days ×100)	Rate Ratios (95% CI)
Comparing pre-omicron to later variants					
XBB pre-omicron	172	464,758	1,774	0.0370	. . .
XBB prior BA1/BA2	427	1,031,069	3,935	0.0414	1.120 (0.970–1.297)
XBB prior BA4/BA5	172	526,764	2,010	0.0327	0.884 (0.743–1.057)
XBB prior BQ1	21	132,039	504	0.0159	0.430 (0.318–0.570)
Comparing bivalent vaccinated to non-bivalent vaccinated					
XBB pre-omicron					
Bivalent vaccinated	14	48,848	184	0.0287	0.755 (0.440–1.190)
No bivalent vaccine	158	415,910	1,569	0.0380	
XBB prior BA1/BA2					
Bivalent vaccinated	59	170,689	644	0.0346	0.806 (0.618–1.018)
No bivalent vaccine	369	860,380	3,247	0.0429	
XBB prior BA4/BA5					
Bivalent vaccinated	11	69,523	262	0.0158	0.449 (0.269–0.698)
No bivalent vaccine	161	457,240	1,725	0.0352	
XBB prior BQ1					
Bivalent vaccinated	2	17,633	67	0.0113	0.646 (0.0495–1.296)
No bivalent vaccine	20	114,406	432	0.0175	

Note. CI, confidence interval.
[a]Rates were calculated as daily positives divided by person days and were calculated using data from December 17, 2022, to August 28, 2023. Positive test results and person days were rounded to nearest whole numbers, and rates were rounded to 3 significant decimals. Confidence intervals were wider for groups with low prior infection rates.

confidence bounds. For analysis of the potential effect of the bivalent vaccine, test positivity rates were further stratified by those who did and did not receive the bivalent vaccine, and these were compared per variant group using rate ratios. The bivalent vaccine was offered but not mandated for HCP, and employees reported any outside vaccine records by email to a designated inbox. A statewide mandate was followed for the 2-dose primary series.

The MSKCC Institutional Review Board granted HIPAA approval to conduct the study.

Results

The XBB variant cases were first reported circulating in New York City on October 8, 2022. By December 17, 2022, 50% of reported cases were XBB infections, cocirculating mostly with variants BQ1 and BA5/BA2 (Supplementary Fig. 1 online).[8] At this date, 14,001 full-time employees were employed at the study institution and recorded at least 2 doses of a COVID-19 monovalent vaccine. Of these, 8,678 (67%) had at least 1 prior SARS-CoV-2–positive test with 490 had had >1 previous SARS-CoV-2 infection.

Distribution of infecting variants of 9,168 SARS-CoV-2–positive tests prior to this date were estimated as follows: 1,814 pre-omicron; 4,551 omicron BA.1/2; 2,065 omicron BA.4/5; 510 omicron BQ.1 and 160 XBB (68 'other type'). By August 28, 2023, an estimated 1,540 XBB infections had occurred, with 909 occurring in the subgroup with a prior positive infection on record.

Overall, the rate ratios comparing XBB test positivity rates among individuals with prior BA1/2 and BA4/5 infection versus those with a pre-omicron infection indicate comparable risk of reinfection: prior BA1/2 versus pre-omicron (RR, 1.120; 95% CI, 0.970–1.297), prior BA4/5 versus pre-omicron (RR, 0.884; 95% CI, 0.743–1.057) (Table 1 and Fig. 1). The group with prior BQ1 infection showed potentially lower risk: prior BQ1 versus pre-omicron (RR, 0.430; 95% CI, 0.318–0.570). However, BQ.1–positive test numbers were limited, and because this variant cocirculated with XBB, some XBB cases may have been misattributed to BQ1.

Bivalent vaccine uptake was low overall, and 1,374 employees had received the bivalent vaccine by December 17, 2022. Rate ratios comparing bivalent vaccinated versus not stratified by prior variant group indicated that the vaccine may have provided additional protection against reinfection with XBB, although positive numbers were low, and confidence intervals were wide (Table 1 and Supplementary Fig. 2 online).

Discussion

Our study from an established cohort of 8,678 HCP with at least 1 previous pre-XBB SARS-CoV-2 infection demonstrated a 10% (909 suspected XBB positive tests of 8,678 individuals) XBB cumulative reinfection rate as of August 28, 2023. Our variant-specific infection rate ratio analysis shows that the XBB reinfection risk for those with prior omicron BA.1/2 or omicron BA.4/5

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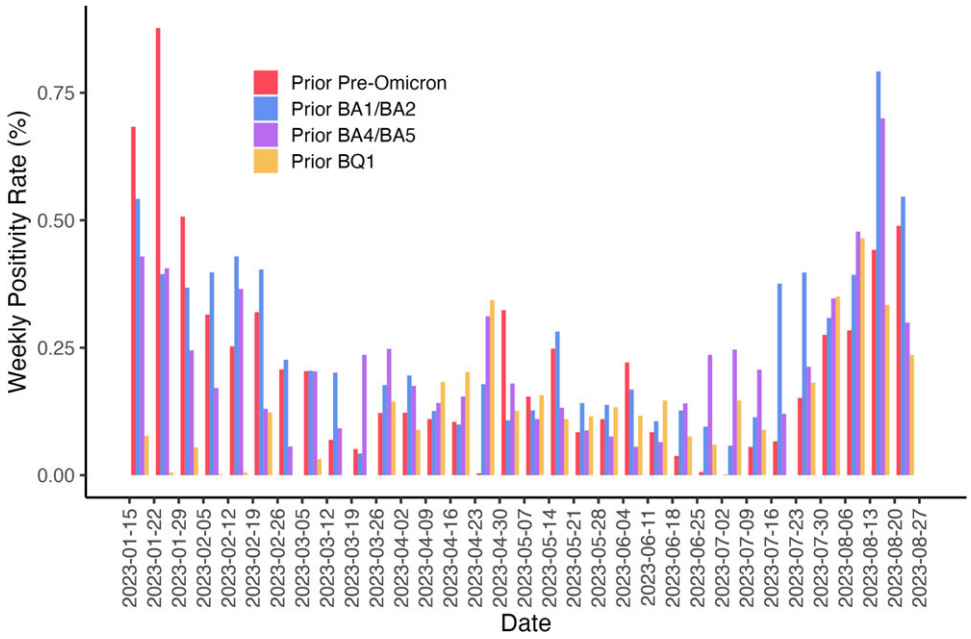

Figure 1. Weekly test positivity rates for XBB infections per prior variant group. Rate bars are calculated using a variable moving window (7–20 days) to stabilize estimates when test counts are low.

infection was comparable to those who were last infected with a pre-omicron variant. Additionally, although the bivalent vaccine had limited documented uptake in this HCP cohort, it may have provided additional benefit over protection from a prior infection alone.

COVID-19 vaccine uptake among HCP has been suboptimal.[9] The hesitancy in this group with high previous vaccine acceptance is due to a lack of data on added benefits and the perception among infected staff that additional vaccine doses are unnecessary after gaining natural or hybrid immunity.[1,9] Our study findings show that frontline HCP with hybrid immunity remain highly susceptible to XBB reinfection. Staying up-to-date with the COVID-19 vaccine is essential to restore immunity in HCP, to prevent infection with circulating variants, and to develop broad protection against severe disease and post–COVID-19 conditions. Higher vaccine uptake among HCPs ensures a safer workplace.

Our study had several limitations. First, we did not specifically examine the impact of multiple previous infections, and low vaccination uptake limited sample sizes for efficacy calculations. Additionally, there may be underreporting of infections as well as misattribution of prior variant typing due to lack of available viral sampling from the study cohort and reliance on regional genomic surveillance. Also, ~5,300 individuals were excluded from this study because they did not report COVID-19. This number was disproportionally higher than indicated on national serosurveys.[10] Overall, we do not think that this bias differentially affected groups or the study findings. Finally, we did not routinely record COVID-19 severity among HCP; thus, we were unable to provide this information.

In summary, our data indicate that HCP with hybrid immunity remain highly susceptible to reinfection from XBB and emerging XBB-like lineage infections. Despite the rapid viral evolution, vaccines protect against infection and post–COVID-19 conditions. Achieving broader cross immunity through vaccination in HCPs with previous SARS CoV-2 infection remains essential for the upcoming season to ensure that HCPs are protected against recently evolved variants and to reduce the likelihood of workplace transmission to vulnerable patients.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2023.282

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Competing interests. The authors report no potential conflicts of interest.

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