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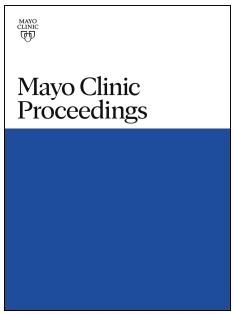

Immunity Acquired From the First Wave of COVID-19 Against Reinfections Up to Omicron Predominance

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Letter to the Editor

Immunity Acquired From the First Wave of COVID-19 Against Reinfections Up to Omicron Predominance

To the Editor: The protective effects of prior infection with SARS-CoV-2 against re-infection are of great public health interest. Among the limited literature covering delta and omicron variant predominance, a nation-wide study in Qatar shows the protective effects derived from prior infection are 92% and 56% against the delta and omicron variants, respectively.[1] Malato et al. found a previous infection could have 50–75% protective effects against the most recent BA.5 variant re-infection, with the greatest protection from previous BA.1/BA.2 omicron infection.[2] Cerqueira-Silva et al., on the other hand, found a relatively low (28.9%) protective effect of past infection against omicron infection, although better against severe outcomes (85.6%).[3] However, these existing studies may have misclassified individuals having contracted SARS-CoV-2 but without symptoms and not having a diagnostic test as lacking prior infection. Therefore, we conducted this study to follow a cohort of healthcare workers (HCWs) in a Massachusetts-based healthcare system with baseline serology testing results available during the first wave of the pandemic,[4] accounting for potential confounders (i.e., age, sex, ethnicity,[5] and the time from taking serology test to getting the first COVID-19 vaccine dose). Because the HCWs had received vaccines with various efficacies, we adjusted for their intention to be vaccinated instead of treating vaccination as a time-dependent

variable.

Each HCW was followed from the date of serology testing to his/her termination date, the date of a subsequent positive PCR assay, or February 28, 2022 (about 1.5 years follow-up). Those with either a positive baseline IgG, IgM or IgA were considered seropositive and compared to seronegative staff. The Kaplan-Meier survival curve was used to delineate the infection-free trends across the groups (Figure). After visually inspecting the log(–log) plot, we built the Schemper's weighted Cox regression models for survival analyses to account for the non-proportionality and further adjusted for potential confounders. The study was exempted for human subjects research by the Cambridge Health Alliance Institutional Review Board (4/29/202-003).

Among 176 eligible HCWs, the eighty-six (48.9%) seropositives were younger (44.7± 11.7 vs. 48.3± 11.9, P=.04), more likely to be men (27.9% vs. 12.2%, P=.02), ethnic minority (white: 30.2% vs. 53.3%, P<.001), and tended to get their first COVID-19 vaccine dose later (time to first shot: 282.6± 99.9 vs. 203.0± 80.2 days, P<.001). After adjusting for potential confounders, HCWs with baseline positive serology results had a reduced hazard ratio, 0.13 (95% CI: 0.05- 0.39), for contracting SARS-CoV-2 throughout the follow-up period. The findings remained robust after excluding those with equivocal serology results at baseline.

While limited by a lack of statistical power that prevents us from performing stratified analyses for different variant predominance, unmeasured confounding such as household

situation and testing behaviors, and different serology tests to determine the baseline serology results (there were two labs using different assay techniques), our study highlights the protective effects of immunity conferred by infection throughout periods covering the variants of interest, in agreement with existing literature, while using serology results in the first wave as a more rigorous measure to determine prior infection status.

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Figure. The Kaplan-Meier curve for the COVID-19 infection-free person-days across the populations based on their baseline serology testing results in the first wave