Date: September 27, 2024

Dear Editor:

We are pleased to submit an Original Article manuscript entitled: **“Protective effectiveness of SARS-CoV-2 infection risk between hybrid and vaccine-induced immunity against the omicron variant.”** for consideration of publication in *BMJ Global Health*.

Immunogenicity research indicates that the effectiveness of vaccines might decline over time, although it is not clear how this reduction translates to protective effectiveness against breakthrough infections. We examined the antibody decay trend and associated infection risks across age groups between hybrid and vaccine-induced immune populations based on community-based nationwide surveillance after the Omicron wave in South Korea.

We utilized data from a nationwide community-based cohort, with repeated antibody testing in August and December 2022, alongside detailed demographic and clinical characterization. The objectives of this research are threefold: First, we assessed the trajectory of S antibody waning following the last immunological event, comparing hybrid and vaccine-induced immunity across different age subgroups. Second, we evaluated the age-specific protective efficacy of the hybrid and vaccine immunity groups over time, specifically focusing on the probability of remaining free from COVID-19 infection. Third, we examined the age-specific association between S antibody levels and the probability of remaining infection-free between hybrid and vaccine-induced immunity groups.

Our findings highlight that children and their household members without booster vaccination and previous infection and elderly aged >65 (who are more likely to rely upon vaccination to increase immunity and might have waned) might need more proactive vaccination efforts to maintain protection [31]. These findings could guide targeted booster campaigns or tailored communication strategies to increase uptake, considering age and the timing of past vaccinations and infections. As we expect an increase in the number of people with hybrid immunity with new variants over time, the definition of high-risk individuals or key risk factors with and without previous infection may change over time. For public health authorities, these findings highlight the need for **continuous surveillance** of infection rates post-vaccination/infection and possibly adjusting booster guidelines based on observed immune waning rather than fixed timelines. As we transition to endemicity, there is the potential need for altered vaccine formulations to track viral variants, the need to identify immune correlates of protection, and the public health challenges of using various tools to counter breakthrough infections, including boosters in an era of global vaccine shortages.

We hope that you will consider our work for publication in *BMJ Global Health*. This manuscript represents original work that is not being considered for publication elsewhere nor has not been previously published. All authors have seen and approved the contents of the submitted manuscript and contributed significantly to the work. As the corresponding author, I have full access to all aspects of the research – from the study design to manuscript development – and take full responsibility for all the contents of this manuscript. All authors have nothing to disclose.

We look forward to your editorial decision.

Sincerely,

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