More Analyses are Needed to Evaluate the Effectiveness of Protection by Vaccines and Previous Infection Against the Omicron Variant of SARS-CoV-2

TO THE EDITOR—We have read with interest the article "Protection by vaccines and previous infection against the Omicron variant of SARS-CoV-2" by Šmid et al [1]. Although this article presents interesting data, the analysis and interpretation appear to be only partial.

First and foremost, the authors compare vaccine (2 or 3 doses) effectiveness after 2 months to the effectiveness of protection gained through previous coronavirus disease 2019 (COVID-19) infection after 6 months. We appreciate that a new polymerase chain reaction (PCR) positivity within 2 months of a previous COVID-19 infection cannot be considered reinfection; however, this does not justify a comparison of effectiveness over the periods of 2 versus 6 months.

As vaccination effectiveness is known to decline over time much more quickly than postinfection immunity, which the authors have described in their previous work [2], it would be fair to compare the effectiveness at the same time points (2, 6, and 9 months). Selecting these time points would be practical—in many European countries, 9 months after vaccination and 6 months after COVID-19 infection are arbitrarily considered protective against new disease.

The conclusion that a booster dose provides persistent and slowly declining protection against hospitalizations and severe outcomes at 2+ months should be compared with the protection provided by infection. The first booster doses in the Czech Republic were administered in October 2021, with only about 3.5% of the population being booster vaccinated by the end of October and 14.7% by the end of November. Hence, the vast majority of the “booster 2+ months” group was booster vaccinated for 3 months or less by the end of the study period—and is compared to groups containing individuals who were fully vaccinated many months previously or who had been infected more than a year ago.

The most important outcomes, mortality and, in particular, case fatality rate, should be considered in all groups. This is omitted, even though the authors state that they have available data on deaths.

In addition, as the authors rightly state, where hospitalization rates are concerned, the “concomitant COVID-19 hospitalizations” at the time of the Omicron wave constitute a major problem. Patients admitted to the hospitals in the Czech Republic for any reason are tested for COVID-19 positivity, regardless of the reason for admission. From this perspective, intensive care unit (ICU)/oxygen therapy rates are much more reliable for evaluating events.

Figure 1. COVID-19 deaths in the 60+ years age group as a percentage of all age groups per month, in the Czech Republic, 2021 (source of data Czech Ministry of Health [3]).
due to COVID-19—but these data are not presented in the tables assessing the effect of hybrid immunity, and are not compared to protection achieved by previous infection. The generalized statement that “the best protective strategy before a coming wave is to vaccinate all individuals, whether previously vaccinated or with a previous COVID-19 infection” needs to cover the severe outcomes (oxygen therapy, ICU admissions, possibly deaths).

Moreover, the severe outcome rates (including case fatality rate) should be calculated separately for the high- and low-risk groups (note that 93.5% of all COVID-19 deaths in the Czech Republic in 2021 were in the 60+ years age group; Figure 1) [3]. A consistent vaccine effectiveness across all age groups (as assumed by the authors) is not valid. Calculations including children and young adults, whose COVID-19 hospitalization rates and severe outcomes are low, dilute the true protective effects of vaccination/previous infection. Again, the aforementioned statement about vaccinating all individuals would require a separate detailed analysis at least for the high-risk (60+ years) and low-risk groups.

In summary, this article appears to work with the available data to promote the need for vaccination and inflates the booster dose effectiveness. Unifying the time intervals, considering death as an important outcome, and calculating the results separately for high- and low-risk groups would help better interpretation of the data.

**Notes**

**Financial support.** No financial support was received for this work.

**Potential conflict of interest.** All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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