Review 1: "BNT162b2 vaccine boosts neutralizing antibodies to ancestral SARS-CoV-2 & Omicron variant in adults received 2-dose inactivated vaccine"

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RR:C19 Evidence Scale rating by reviewers:

- **Strong.** The main study claims are very well-justified by the data and analytic methods used. There is little room for doubt that the study produced has very similar results and conclusions as compared with the hypothetical ideal study. The study's main claims should be considered conclusive and actionable without reservation.

Review

Leung and colleagues report the outcome of booster mRNA vaccination in a population of 315 adults (75% above 47 years) that were immunized 6-7 months before with two doses of inactivated virus vaccine. Serum antibody neutralization increased by 27-fold and 14-fold when measured against wild-type virus and Omicron variant, respectively. Interestingly, levels of wt strain neutralizing antibodies were higher than previously reported for inactivated virus vaccine booster (21-fold increase). In this population, mRNA booster dose had an acceptable safety profile with fever and headache as the most commonly reported reactions. The study is thoughtfully executed and well described. Additionally, the report of booster vaccination in a population at risk of Covid-19 provides meaningful information on heterologous vaccination and the importance of third dose immunization to increase neutralization and putative protection against the Omicron variant.

Suggested changes:

1. Goldbatt and colleagues have recently reported the use of spike-specific IgG titer to determine vaccine protection, with a threshold of 60 antibody binding units (BAU) per mL (<https://doi.org/10.1016/j.vaccine.2021.12.006>) for non-inferiority comparison of vaccines and estimation of protection against variants of concern. Therefore, authors should include Omicron-specific IgG titer and determine BAU/mL to corroborate the putative Omicron protection of mRNA booster dose discussed in lines 165-168.
2. Please clarify in text and figure S1 that participants included in the analysis did not report SARS-CoV-2 infection between vaccination and sampling to exclude that Omicron-specific neutralizing antibodies originated from natural infection due to the rapid diffusion of this variant in the study period.
3. Please add the statistical results described in the text in figure 1.