Review of: "Evidence for increased breakthrough rates of SARS-CoV-2 variants of concern in BNT162b2 mRNA vaccinated individuals"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

The authors of this observational study (matched case-control) attempted to identify the cause of the failure of genetic vaccination against COVID-19. They assessed it in individuals either partial- or full-vaccinated with the BNT162b2 mRNA vaccine. They focused on possible breakthrough infections caused by other variants, i.e., B.1.1.7 and B.1.351, assigned to variants of concerns (VOCs). They tried to find out if these variants could be the main cause of the failure of the current vaccination.
There are a few notes to this study which include the following:

1) The authors reported that they documented both symptomatic and asymptomatic SARS-COV-2 positive persons. It would be very interesting to also display the results dependently of both status of positivity.

2) The authors mention a study hypothesis but the null hypothesis was not defined. Therefore, it should be important to define it and to determine the power of test and to determine if the sample size was sufficient or not.

3) Some minor notes:
a) It should be better to describe the design of published study as a matched case-control one.
b) The odds ratio is usually reported as one number - instead of 26:10 it will be better to write 2.6 including the lower limit of one-side 95% CI.
c) There is written: ... while other studies suggested neutralization remained relatively high against both B.1.1.7 and B.1.351 [12]. Because there is referred only one study the authors should supply the others (at least one another) or change the plural.
d) The authors have not established effectiveness of vaccination. Therefore, the denotation of PE (partial effectiveness) and FE (full effectiveness) should be changed to for example partial vaccination (PV) or full vaccination (FV).
e) The authors write: ... matched with an unvaccinated carrier (control) with similar demographic characteristics (date of PCR, age, sex, ethnic sector, and geographic location) to reduce bias associated with differential exposure ...
This matching is used to demonstrate the comparability of both investigated groups (case and control).
f) Te authors use "variant of concern" (VOC). Why the following is used? ... "No other variants of concern or variants of

interests, as defined by the WHO" ...

"Variants of interests" (VOI) were not defined in anywhere of manuscript. Moreover, they were not more used.

g) The authors wrote: ... "our FE cohort" ... It is not in link with the matched case-control study. The cohort should be replaced by groups or other words to prevent the misunderstanding of study design.

h) This statement: "Some subjects in this cohort may have been infected before the immunity from the boost was fully established, and it is thus possible that enhanced immunity from the boost, which develops over time [17], may more effectively prevent infection with the B.1.351 variant." is not clear.

i) It should be better explained the following: "For the analysis of B.1.351, all other variants were defined as the reference group, while for the B.1.1.7 analysis we excluded any paired observation that included B.1.3.5 (assuming ordinality of breakthrough), while any other variant was defined as the reference."

Maybe the demonstration of both results, i.e., including also B.1.351, could be displayed in supplement.

j) Some expressions should be modified: such as neutralization studies - studies focused on neutralizing antibodies etc.