Review of: "[Review] Early Real-World Evidence on the Relative SARS-CoV-2 Vaccine Effectiveness of Bivalent COVID-19 Booster Doses: a Narrative Review"

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The article is a comprehensive review of literature on the effectiveness of bivalent versus monovalent COVID-19 booster doses. I appreciate author's effort and have some comments and remarks which hopefully could make the article a better one.

1. The primary issue is that the definition of relative VE. In different studies, the ``relative'' VE appears to refer to different comparisons. In the current text, author says `the main outcome … was rVE of a bivalent booster dose compared with that of ≥ 1 monovalent vaccine doses administered.' In one study, e.g., [35], the comparison groups consist of people with different prior infection history and multiple monovalent doses but (1) received a bivalent booster on top of that and (2) received a monovalent booster on top of that. In this case, the rVE refers to bivalent versus monovalent booster, controlling for all previous infection and vaccination histories. In other studies, e.g., [31], the rVE is defined as 'odds of receiving a bivalent booster dose (after 2, 3, or 4 monovalent doses) versus not receiving a bivalent booster dose (but receiving 2, 3, or 4 monovalent doses),' i.e., the study was comparing 2 mono + bivalent versus 2 mono + nothing, 3 mono + bivalent versus 3 mono + nothing, etc. This essentially explained the drastic difference in the rRV estimates. There is little rVE in [35] but a ~30%-60% rVE in [31]. Essentially [35] is suggesting 2 mono (or 3 or 4) + bivalent booster is very similar to 2 mono (or 3 or 4) + monovalent booster, while [31] is saying boosting with bivalent is partially effective compared to not receiving any booster (on top of the same primary series).

The article will be greatly improved, in my opinion, if author could delve a little bit deeper into the precise definition of rVE in different studies and highlight these differences in both Table 1 and the discussion. In fact, I believe a better examination of this aspect could reconcile many seemingly heterogeneous findings.

2. I appreciate authors' effort in making Table 1 which is clearly informative. In addition to the rVE definition issue I mentioned above, one key difference among different studies, as author correctly pointed out, is their approach in adjusting for other confounding variables. In particular, I am concerned about the previous infection history by different strains in comparisons groups in each study. As [35] showed, a person's HR is largely affected by the previous infection history, in particular the lineage of the most recent infection. It seems to me that the confounding effect from this factor is so large that it can significantly affect the VE estimate in most studies, as most studies were not able to control for this factor. I would appreciate it if author could highlight the confounder adjusted in each study in Table 1.