

This paper is based on 2 sources

- the various recent preprints comparing increase in neutralization titers after booster with ancestral or variant-specific boosters.
- the previous work by Khoury where the relation between neutralization titers and protection against infection and disease was calculated, based on original phase 3 trials.

Findings:

1) Neutralisation titers increase after booster with

- Ancestral strain = 11 X
- Variant strain = 16.6 X (= 1.51 X more than ancestral
- No significant difference in homologous versus non-homologous variant

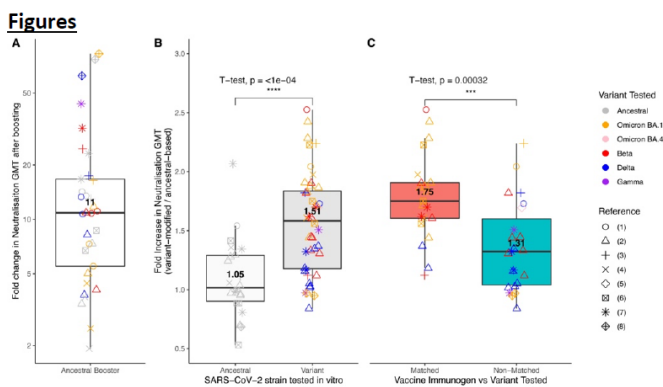


Figure 1 Aggregated neutralisation data on boosting with both ancestral-based and variant-modified vaccines. (A) Fold change in neutralisation titres after boosting with an ancestral-based vaccine. Change in titres against different tested variants are depicted in different colours. (B) Improvement in neutralisation titres (shown as fold increase) when boosting with a variant-modified vaccine compared to an ancestral-based vaccine. Improvement is shown when testing against the ancestral SARS-CoV-2 variant in-vitro (left), and when testing against other variants in-vitro (right). (C) Fold increase in neutralisation titres after boosting with a variant-modified vaccine compared to an ancestral-based vaccine depending on whether the variant tested in-vitro matched the vaccine immunogen (red, left) or did not match (blue, right) the vaccine immunogen. For panels B and C, t-tests were performed on the log10-transformed values.

2) Clinical protection: in a population that is still 50 % protected against symptomatic infection and 86.6 % against severe disease because of previously acquired immunity (by vaccination and/or infection).

Additional protection by booster:

- Against *symptomatic* disease
 - o Ancestral booster: 50 → 85.6 %
 - o Variant booster: 50 → 90.2 %
- Against *severe* disease
 - o Ancestral: 86.6 → 98 %
 - o Variant: 86.6 → 98.8 %

If the basal level of protection is lower (because of waning) the additional gain of a booster is higher (up to 15 %) and the difference between variant or ancestral booster is more important

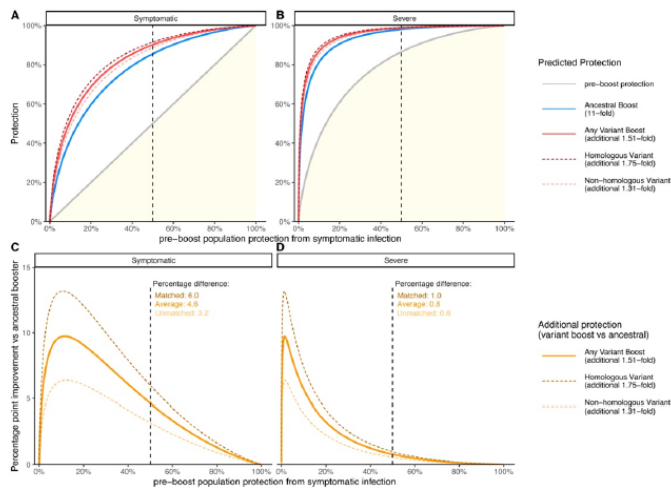


Figure 2 Estimated improved protection from a variant-modified booster over an ancestral-based booster. (A and B) Levels of protection against symptomatic (A) and severe (B) COVID-19 after either no booster (grey), an ancestral-based booster (blue) or a variant-modified booster (red) for varying levels of pre-boost population protection from symptomatic infection. Solid red line shows protection for any variant-modified vaccine, dashed red lines show protection for a matched variant-modified vaccine (dark red) and non-matched variant-modified vaccine (light red). (C and D) Average improvement in protection from symptomatic (C) and severe (D) COVID-19 for a variant-modified vaccine over an ancestral-based vaccine over the six months following boosting. Solid line shows protection for any variant-modified vaccine, dashed lines show protection for a matched variant-modified vaccine (dark orange) and non-matched variant-modified vaccine (light orange). Text at the top of panel C and D indicate the percentage point improvement in protection over an ancestral-based booster when the pre-boost population protection against symptomatic disease is 50%.

Conclusion:

- The main gain is by booster, but an additional gain from variant specific booster
- The importance of this additional gain depends on the basal immunity

Clearly, this modeling needs to be confirmed in clinical trials / observations

It applies only on the presently known variants.