

Results of Studies Evaluating the Impact of SARS-CoV-2 Variants of Concern on COVID-19 Vaccines: An Ongoing Systematic Review

Overview of neutralizing antibody responses in recipients of variant-containing vs. ancestral virus-based vaccines

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Methods for Inclusion in Analysis

The studies included in the plots below were identified as part of an ongoing systematic review of studies evaluating the impact of SARS-CoV-2 variants of concern on COVID-19 vaccine performance which began on March 15, 2021. Studies that report fold reductions in neutralization for SARS-CoV-2 variants relative to the index (ancestral) strain or that report data that enable the calculation of fold reductions in neutralization are included in the review. Methods for the review are available [here](#).

For the assessment of the performance of variant-containing vaccines relative to index-based vaccines, studies meeting the following criteria were included:

- Reported fold reductions in neutralizing antibody titers against Omicron subvariants relative to the ancestral strain or provided data allowing for the calculation of fold reductions
- Reported results for variant-adapted vaccines containing antigens of Omicron sub-variants (i.e. vaccines containing other antigens (e.g., Beta or Delta) were excluded as they are not currently in clinical use)
- Provided neutralization data for at least one variant-based vaccine *and* an index-based vaccine

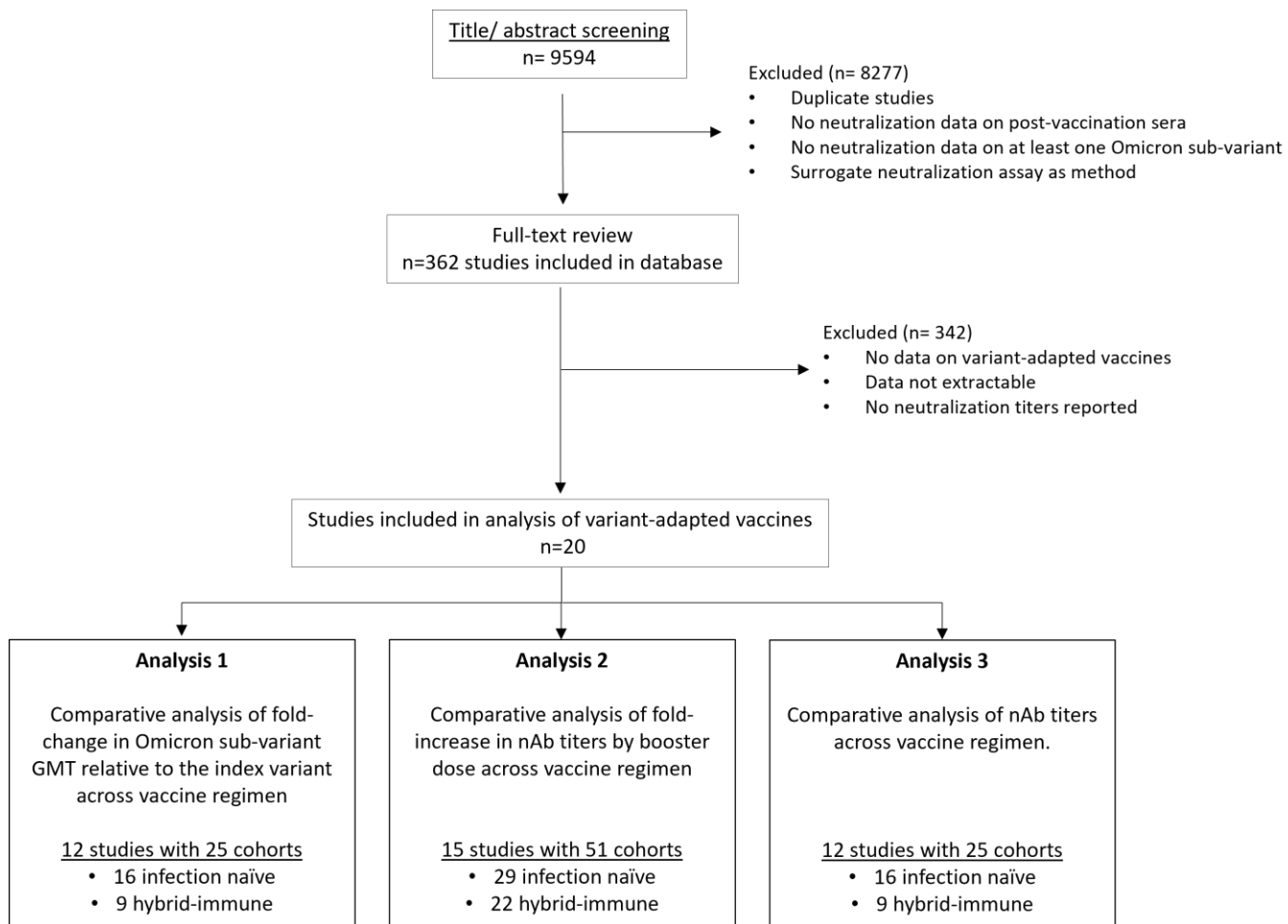
At the time this analysis was performed, 20 of 362 studies were eligible for inclusion. The identification of included studies is shown in the figure below.

Because variant-adapted vaccines are most commonly used as a fourth booster dose, neutralizing antibody responses after the fourth dose are displayed. Because neutralization results can vary substantially across studies due to differences in methodology, only within-study paired observations were included in this analysis. That is, only relative results from within the same study (fold-differences between index-based and variant-adapted vaccines or differences in titer-increase between the two) are shown. Connecting lines indicate paired observations from the same cohorts.

Every data point in the plots represents one cohort (studies can contain multiple cohorts). Numbers across the top of the plots represent mean-fold changes or mean GMT.

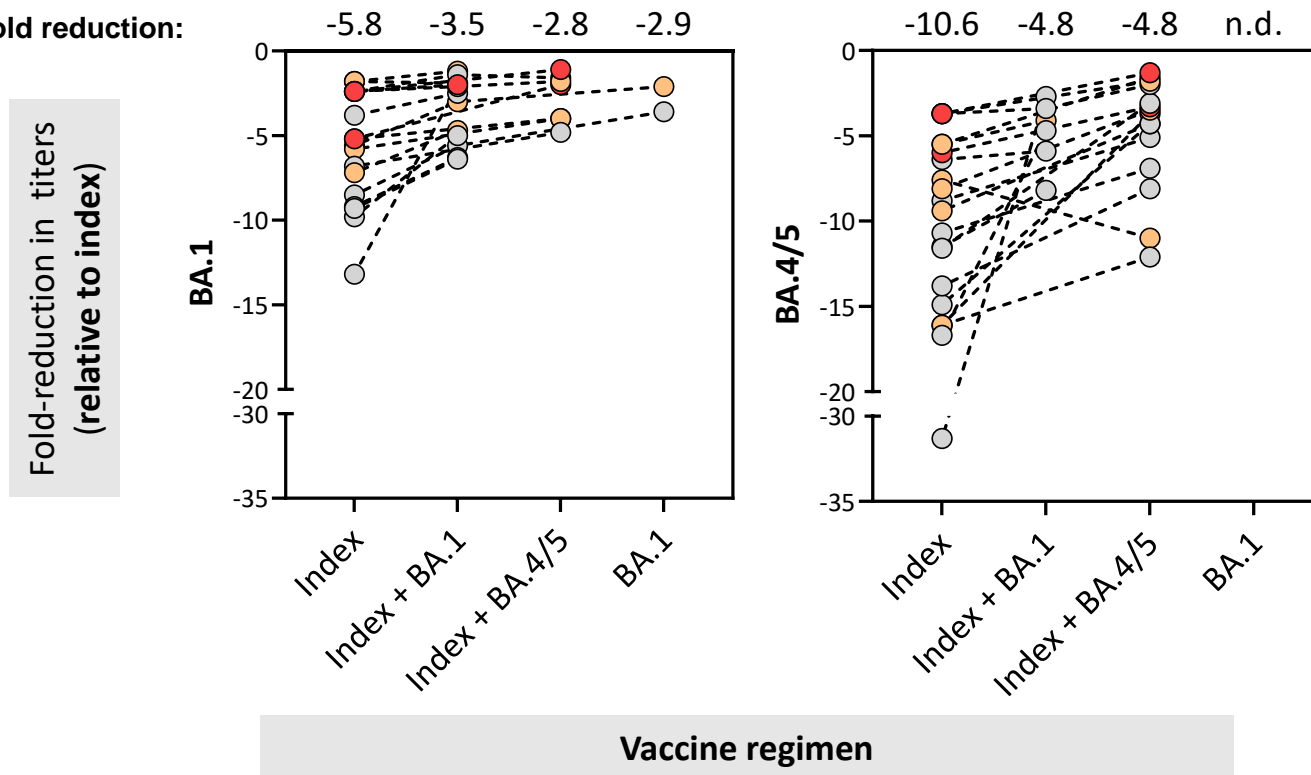
Because hybrid immunity (pre- or post-vaccination infection with SARS-CoV-2) plays an important role in post-vaccination immunity, infection status of the cohorts is color-coded within the plots. Grey indicates no previous-infection, orange indicates cohorts with pre-Omicron infection, and red refers to cohorts infected with any Omicron sub-variant. This applies also to cohorts in which only a portion have been previously infected.

For any questions, comments, or suggestions about this document, please contact Melissa Higdon: mhigdon@jhu.edu.



Mean Fold Reduction in Neutralizing Antibody Titers against Omicron BA.1 or BA.4/5 Following a Second Booster Dose, Relative to Index (Ancestral) Strain: Variant-adapted vs. Index-based vaccines

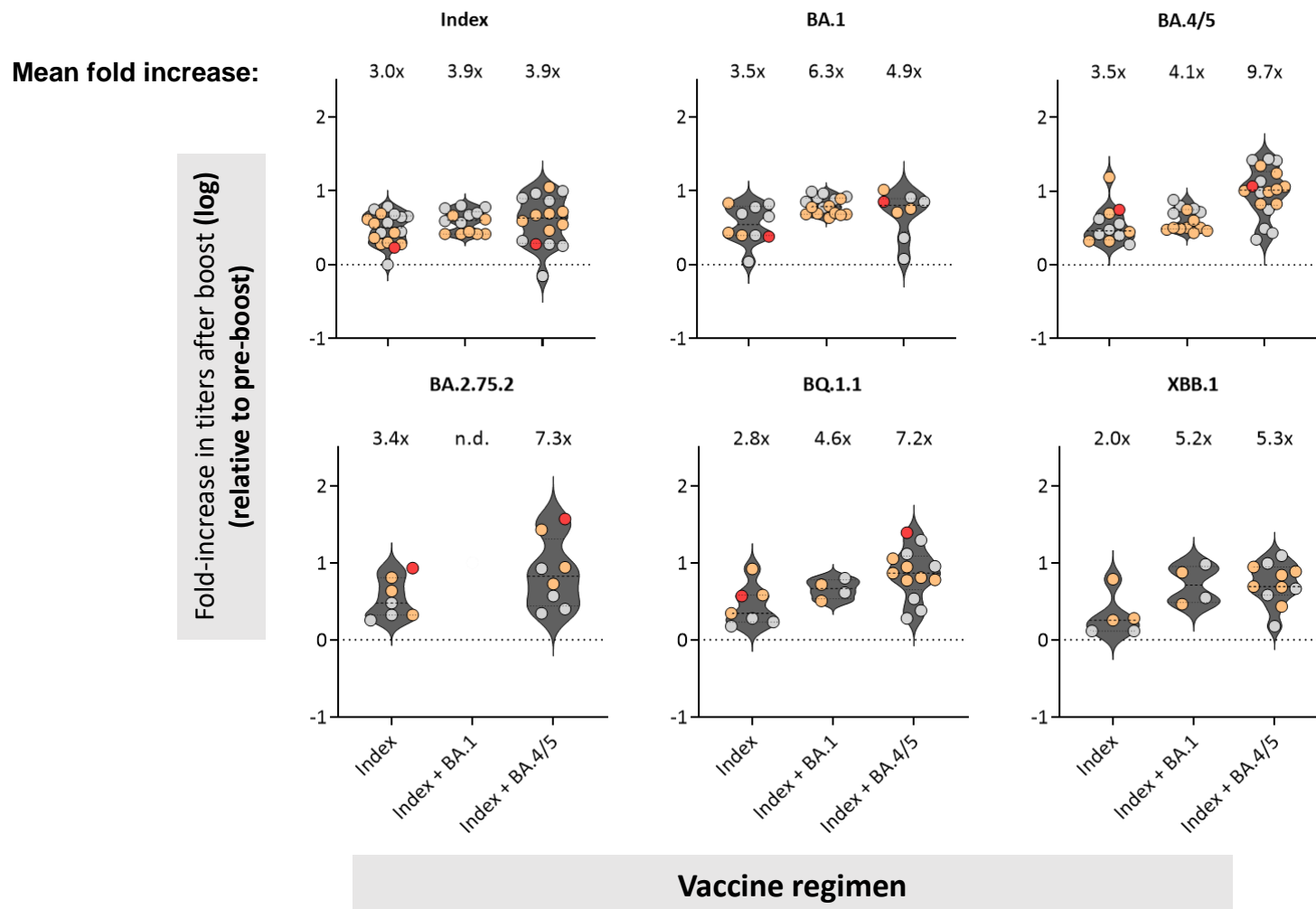
Mean fold reduction:



- Reductions in neutralizing antibodies against BA.1 and BA.4/5 sub-variants relative to the index strain are smaller for variant-adapted vaccines than for the monovalent, index-based vaccines, suggesting better performance of the variant-adapted vaccines.

Index = monovalent ancestral vaccines; Index + BA.1 = bivalent ancestral/omicron BA.1 vaccines; Index + BA.4/5 = bivalent ancestral/omicron BA.4/5 vaccines; BA.1 = monovalent omicron BA.1 vaccines

Fold Increases in Neutralizing Antibody titers Post Second Booster vaccination (Relative to Pre-Boost) by Omicron sub-variant: Variant-adapted vs. Index-based vaccines

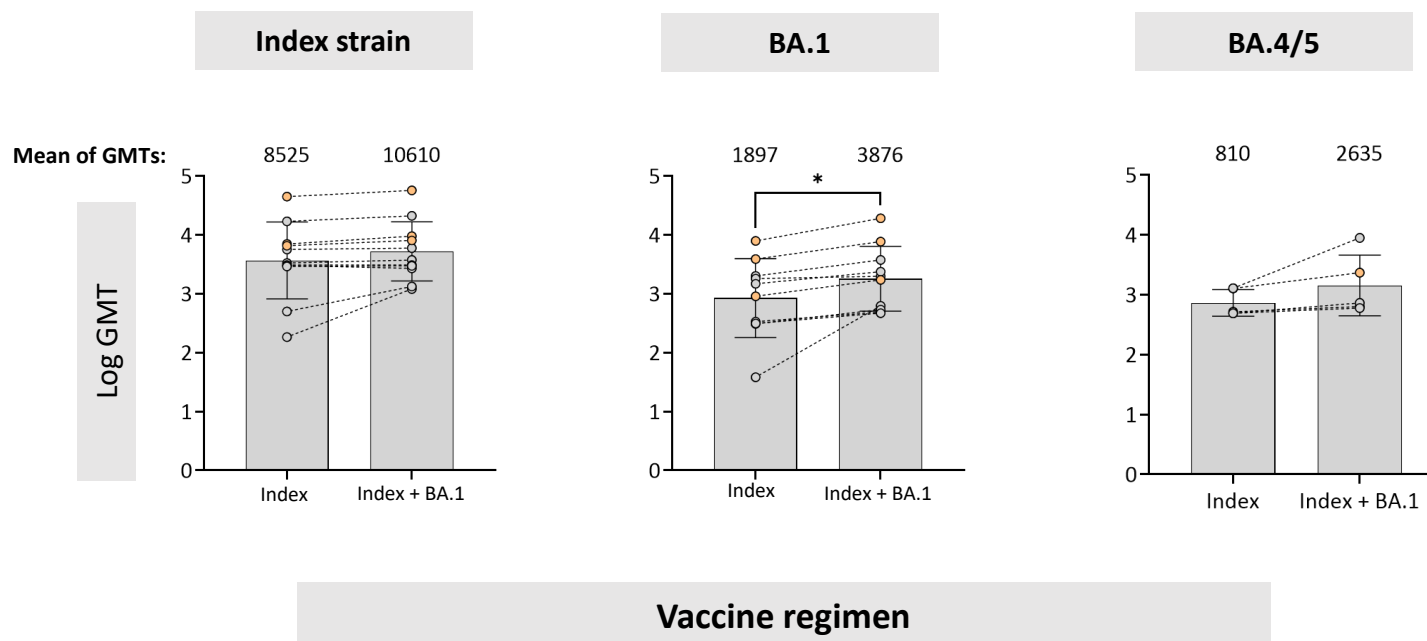


- Compared to monovalent, index strain-based vaccines, variant-adapted vaccines exhibit larger increases in neutralizing antibodies against various Omicron sub-variants upon booster vaccination.

Index = monovalent ancestral vaccines; Index + BA.1 = bivalent ancestral/omicron BA.1 vaccines; Index + BA.4/5 = bivalent ancestral/omicron BA.4/5 vaccines

Geometric Mean Titers (GMT) Following a Second Booster Dose by Omicron sub-variant: Variant-adapted vs. Index-based vaccines

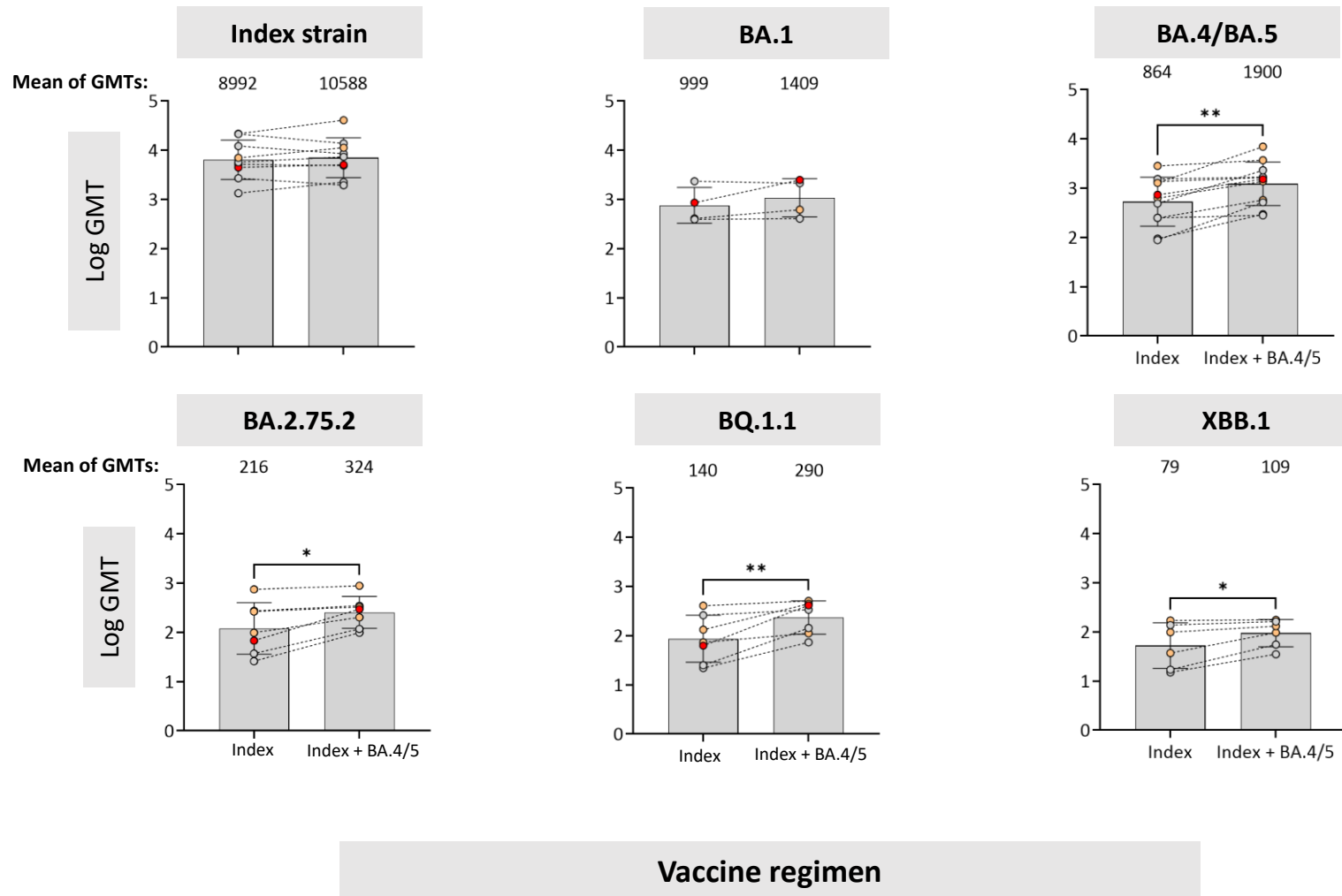
Monovalent Index Vaccines vs. Bivalent Index/Omicron BA.1 Vaccines



- Evidence suggests Omicron BA.1-adapted vaccines notably increase titers against Omicron BA.1 and potentially other Omicron sub-variants compared to monovalent index strain-based vaccines.
- Currently, no data are available for BA.1-adapted vaccines against novel sub-variants (BA.2.75.2, BQ.1.1, XBB.1)

Index = monovalent ancestral vaccines; Index + BA.1 = bivalent ancestral/omicron BA.1 vaccines; Index + BA.4/5 = bivalent ancestral/omicron BA.4/5 vaccines

Monovalent Index Vaccines vs. Bivalent Index/Omicron BA.4/BA.5 Vaccines



- Evidence suggests Omicron BA.4/5-adapted vaccines notably increase titers against all Omicron sub-variants compared to monovalent index stain-based vaccines.

Index = monovalent ancestral vaccines; Index + BA.1 = bivalent ancestral/omicron BA.1 vaccines; Index + BA.4/5 = bivalent ancestral/omicron BA.4/5 vaccines