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Supplemental information

Impact of hybrid immunity booster vaccination and Omicron breakthrough infection on SARS-CoV-2 VOCs cross-neutralization

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Figure S1

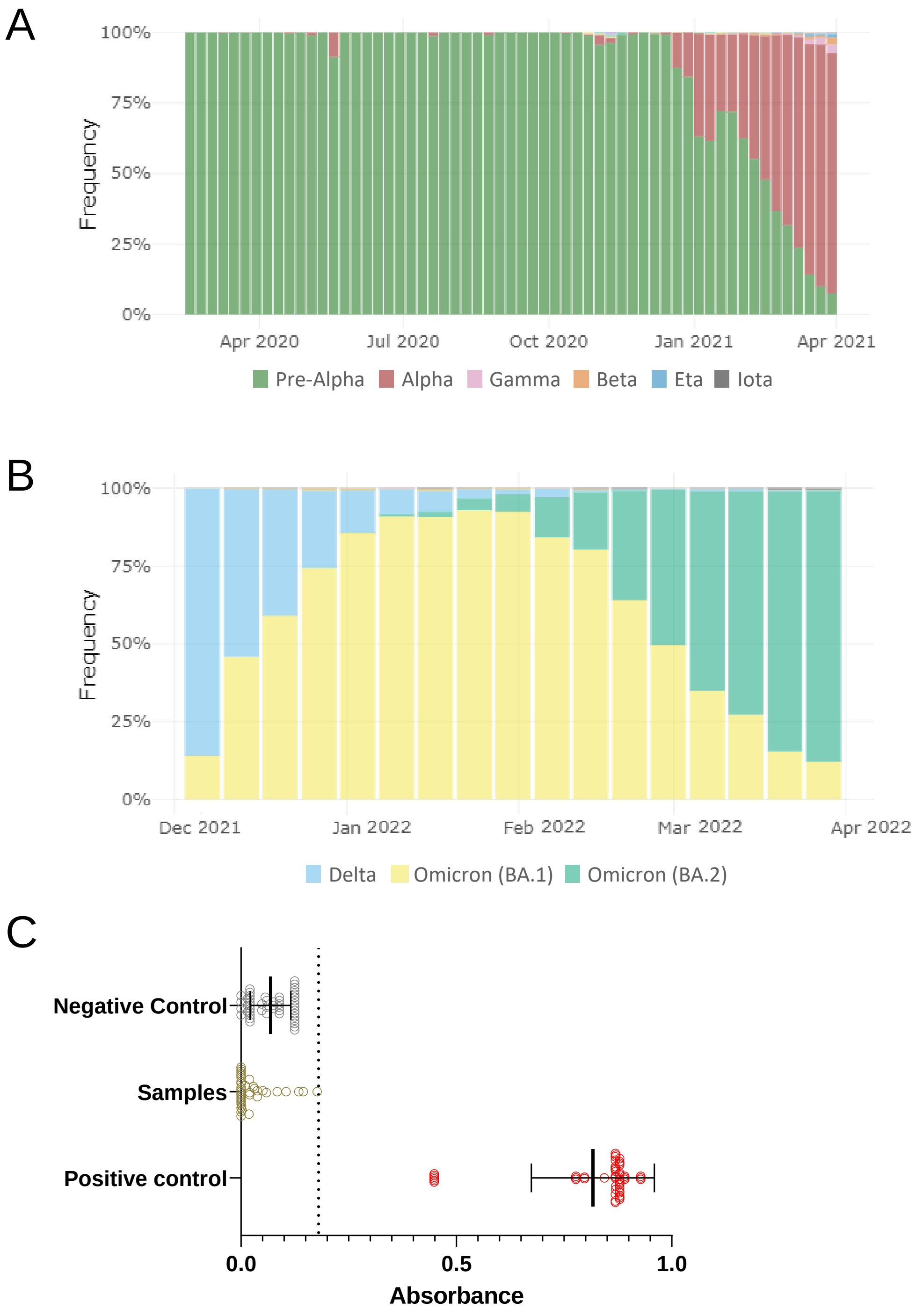

Figure S1. Participants infection history and nucleocapsid test (related to STAR Methods: study overview and subjects).

A. Temporal identification of circulating SARS-CoV-2 variants and their frequency in Catalonia Spain between March 2020 and March 2021 (source: http://covidtag.paseq.org/).

B. Temporal identification of circulating SARS-CoV-2 variants and their frequency in Catalonia Spain between December 2021 and March 2022 (source: http://covidtag.paseq.org/).

C. Anti-nucleocapsid protein IgG quantification for the status confirmation of uninfected participants. Threshold for positivity was calculated as the mean of negative controls + 2 standard deviations. Error bars indicate standard deviations. All uninfected participants were below threshold.

Figure S2

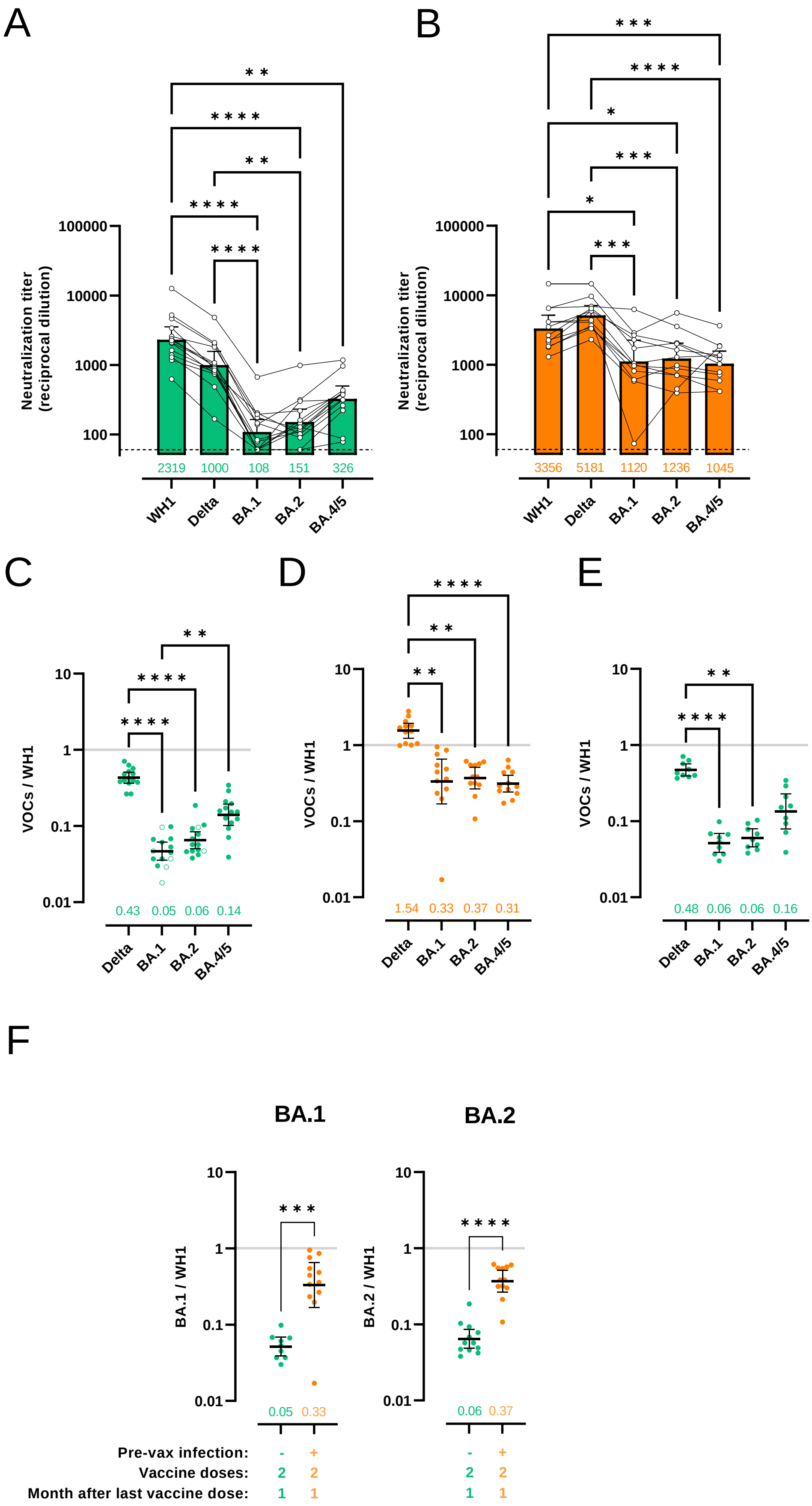
A
B
C
D
E
F
Neutralization titer (reciprocal dilution)
100000
10000
1000
100
WH1
Delta
BA.1
BA.2
BA.4/5
2319
1000
108
151
326
3356
5181
1120
1236
1045
* *
* * * *
* * *
*
VOCs / WH1
10
1
0.1
0.01
0.43
0.05
0.06
0.14
1.54
0.33
0.37
0.31
0.48
0.06
0.06
0.16
BA.1
BA.2
BA.1 / WH1
BA.2 / WH1
0.05
0.33
0.06
0.37
Pre-vax infection:
Vaccine doses:
Month after last vaccine dose:
-
+
2
2
1
1

Figure S2. Direct comparison of variants neutralizing titers and ratios within -/2/- and +/2/- groups at 1 month after last vaccine dose (Related to Figure 1).

A/B. raw ID_{50} (reciprocal dilutions) titers against the indicated variant spikes for -/2/- (A.) and +/2/- (B.) participants. Horizontal bars and numbers indicate ID_{50} geometric means (GMT) for each variant and error bars indicate 95% confidence intervals. At the bottom are fold changes for the indicated comparisons. Only significant *p* values are indicated for comparisons between all variants (Friedman test with Dunn's multiple comparison, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$). Dashed lines indicate the assay lower limit of detection (60 reciprocal dilutions).

C/D/E. Ratio of WH1 ID50 over the indicated VOC ID50 calculated for spikes for -/2/- (C.) and +/2/- (D.) participants. E. is a reanalysis of C. excluding non-responders. Horizontal bars indicate ratio geometric means for each variant and error bars indicate 95% confidence intervals. Bottom numbers indicate fold reduction compared to WH1. Significant p values are indicated for comparisons between all variants (Friedman test with Dunn's multiple comparison, ** $p < 0.01$, **** $p < 0.0001$)

F. Re-analysis of Figure 1C for variant BA.1 and BA.2 excluding non-responders.

Figure S3

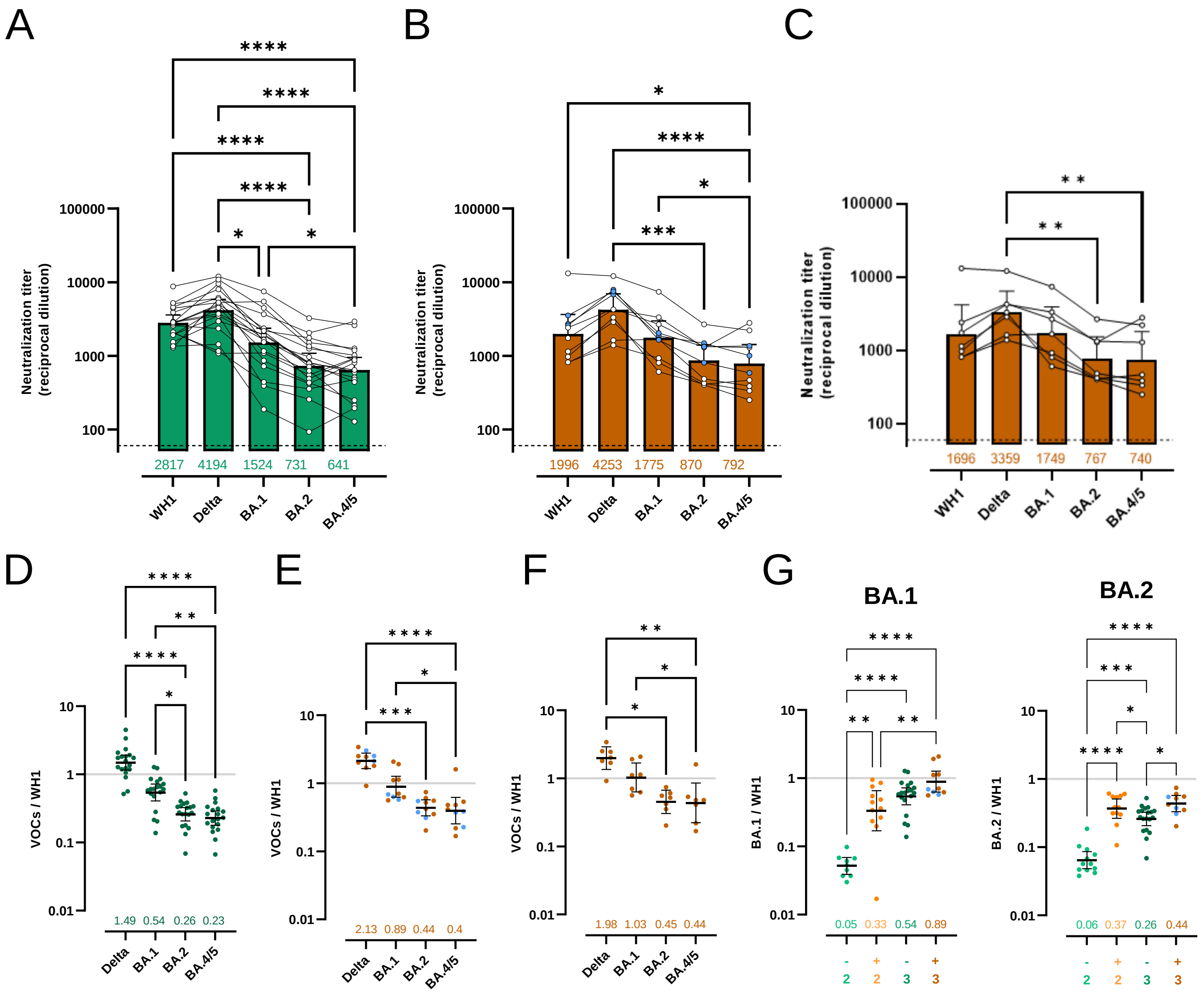

Figure S3. Direct comparison of variants neutralizing titers and ratios within -/3/- and +/3/- groups (related to Figure 2).

A/B/C. raw ID_{50} (reciprocal dilutions) titers against the indicated variant spikes for -/3/- (A.) and +/3/- (B.) participants. C. is a reanalysis of B. excluding participants who received only 1 dose as part of full vaccine schedule (highlighted in blue in B.). Horizontal bars and numbers indicate ID_{50} geometric means (GMT) for each variant and error bars indicate 95% confidence intervals. At the bottom are fold changes for the indicated comparisons. Significant *p* values are indicated for comparisons between all variants (Friedman test with Dunn's multiple comparison, * $p < 0.05$, *** $p < 0.001$, **** $p < 0.0001$). Dashed lines indicate the assay lower limit of detection (60 reciprocal dilutions).

D/E/F. Ratio of WH1 ID_{50} over the indicated VOC ID_{50} calculated for spikes for -/3/- (D.) and +/3/- (E.) participants**.** F. is a reanalysis of E. excluding participants who received only 1 dose as part of full vaccine schedule (highlighted in blue in D.). Horizontal bars indicate ratio geometric means for each variant and error bars indicate 95% confidence intervals. Bottom numbers indicate fold reduction compared to WH1. Significant *p* values are indicated for comparisons between all variants (Friedman test with Dunn's multiple comparison, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$)

G. Re-analysis of Figure 2C for variant BA.1 and BA.2 excluding non-responders.

Figure S4

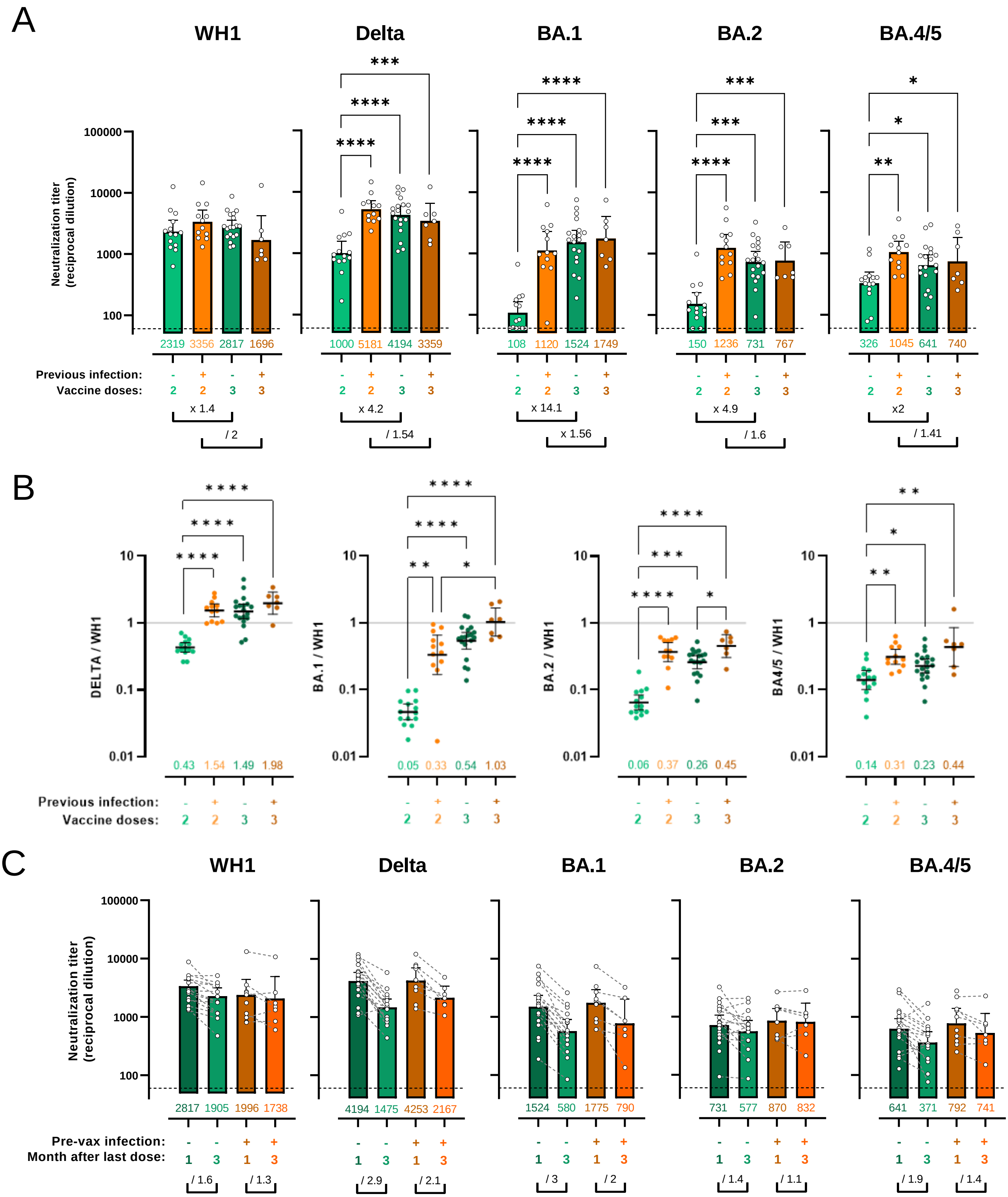

Figure S4. Additional stratified analyses and 3 months follow up on participants who received a booster vaccines (related to Figure 2).

A/B. Reanalyses of Figure 2B and C, respectively, excluding participants who only received 1 dose as part of full vaccine schedule.

C. Follow-up neutralization titers about 1 month (=Figure 2B) and 3 month after booster vaccine.

Figure S5

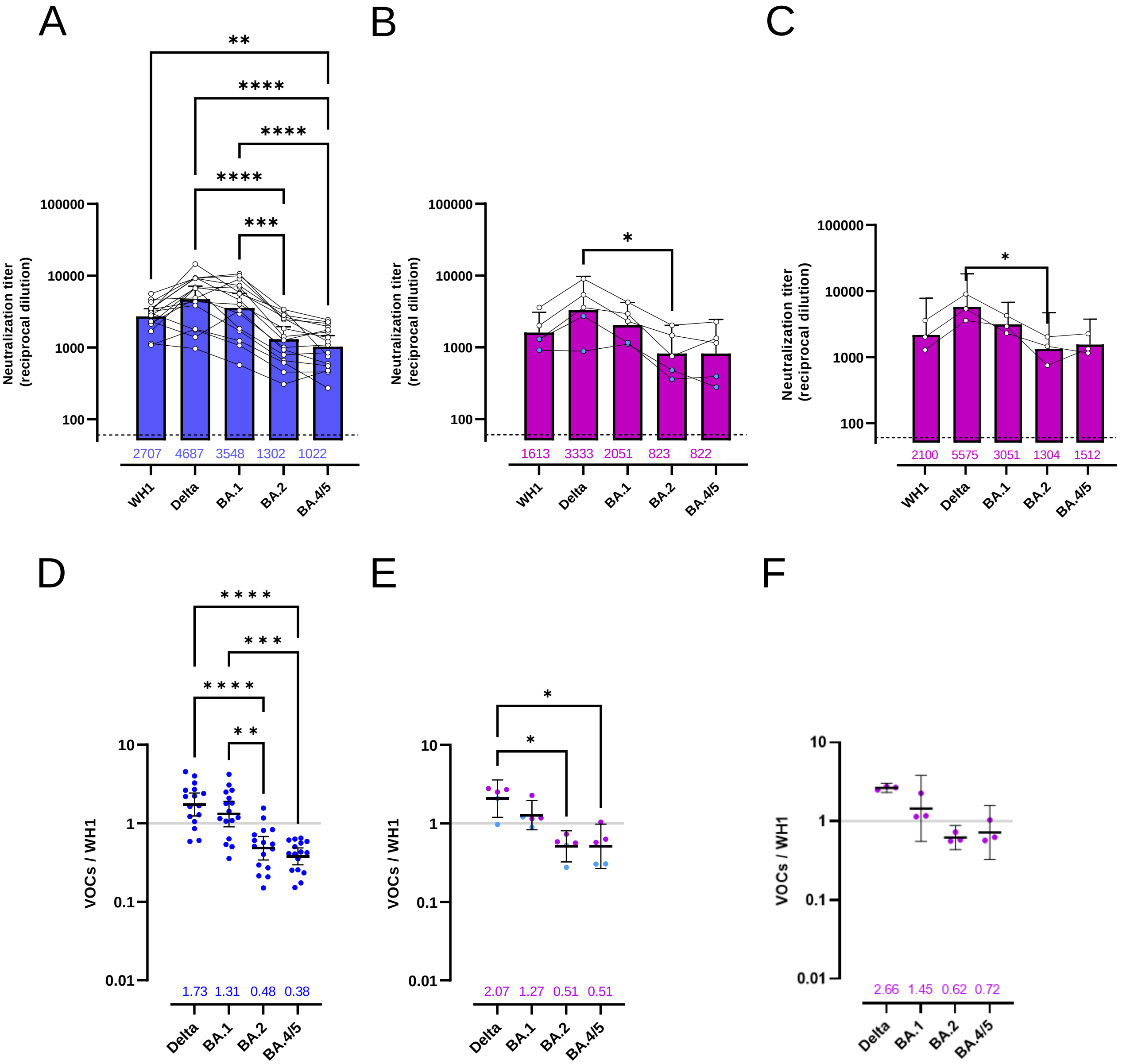

Figure S5. Direct comparison of variants neutralizing titers and ratios within -/3/+ and +/3/+ groups (related to Figure 3).

A/B/C. raw ID_{50} (reciprocal dilutions) titers against the indicated variant spikes for -/3/+ (A.) and +/3/+ (B.) participants. **C.** is a reanalysis of B. excluding participants who received only 1 dose as part of full vaccine schedule (highlighted in blue in B.). Horizontal bars and numbers indicate ID_{50} geometric means (GMT) for each variant and error bars indicate 95% confidence intervals. At the bottom are fold changes for the indicated comparisons. Significant *p* values are indicated for comparisons between all variants (Friedman test with Dunn's multiple comparison, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$). Dashed lines indicate the assay lower limit of detection (60 reciprocal dilutions).

D/E/F. Ratio of WH1 ID_{50} over the indicated VOC ID_{50} calculated for spikes for -/3/+ (D.) and +/3/+ (E.) participants**. F.** is a reanalysis of E. excluding participants who received only 1 dose as part of full vaccine schedule (highlighted in blue in E.). Horizontal bars indicate ratio geometric means for each variant and error bars indicate 95% confidence intervals. Bottom numbers indicate fold reduction compared to WH1. Significant *p* values are indicated for comparisons between all variants (Friedman test with Dunn's multiple comparison, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$)

Figure S6

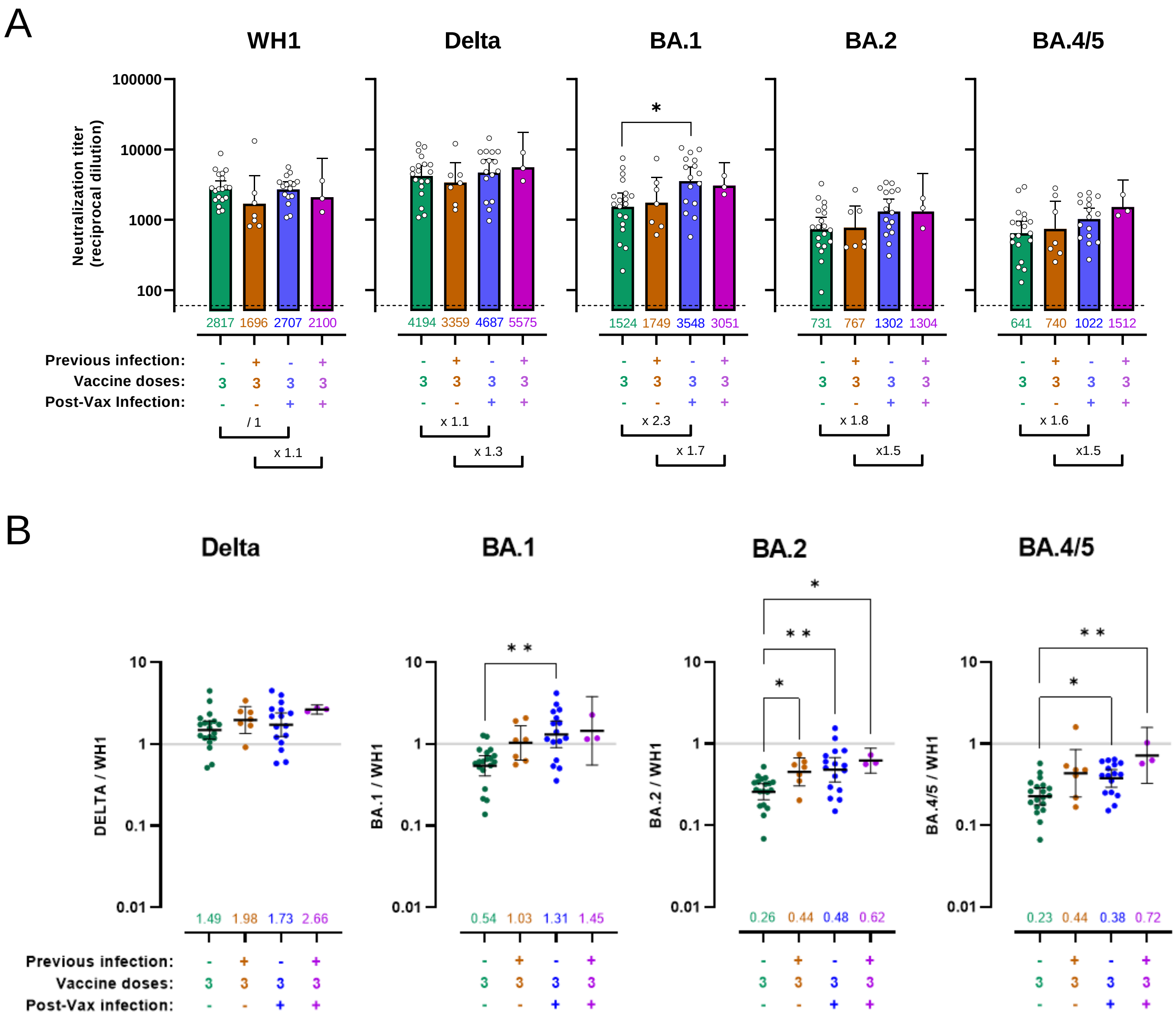

Figure S6. Additional stratified analyses (related to Figure 3).
A/B. Reanalyses of Figure 3B and 3C, respectively, excluding participants who only received 1 dose as part of full vaccine schedule.