

# Beta variant infection combined with vaccination broadens neutralizing immunity against Omicron subvariants

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## 1. Background

- Current Omicron sub-lineages have extensive escape of vaccine elicited neutralization and one potential approach to broaden vaccine elicited immunity is to design multivalent vaccines incorporating variant sequences (Cele, et al. 2022; Corbett et al. 2021).
- Would Beta variant elicited immunity combined with vaccination offer broader protection?

### Aim of the study

To assess whether individuals infected with the Beta variant and vaccinated with Pfizer BNT162b2 have broader immunity to Omicron sub-lineages

## 2. Methods

All participants infected in Beta infection wave in South Africa

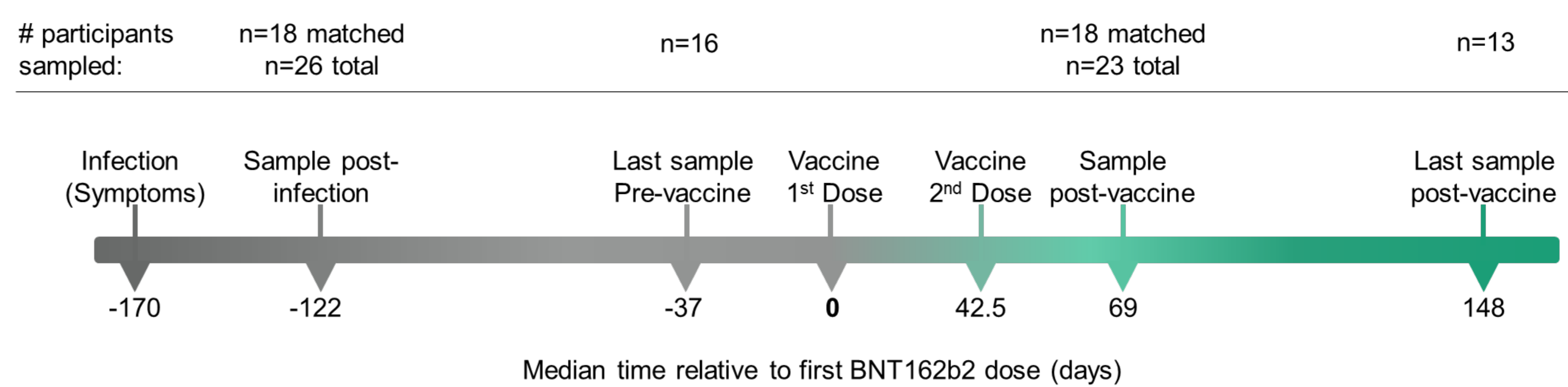


Fig. 1: Study design and participants.

- To quantify neutralization, we used a live virus neutralization assay (LVNA).
- We report the geometric mean titer (GMT) focus reduction neutralization test value (FRNT50) for each participant group.

## 3. Results

### Vaccine effect on Beta and Omicron/BA.1 neutralization

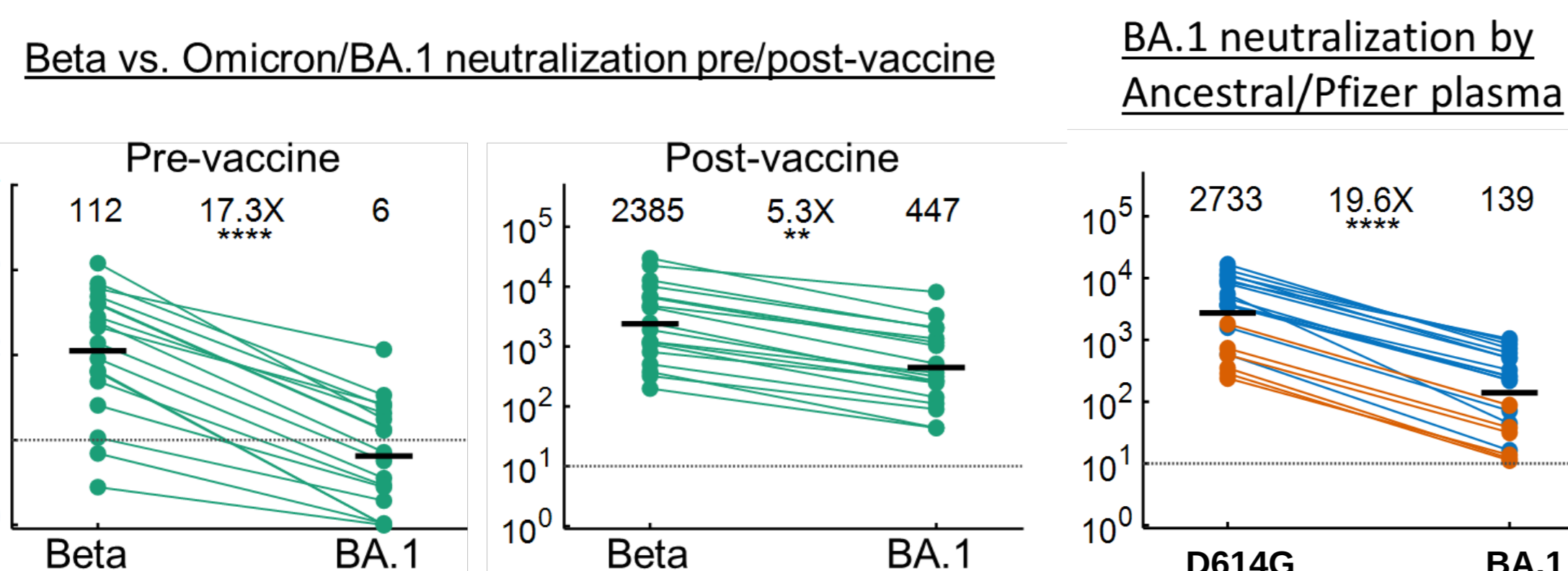
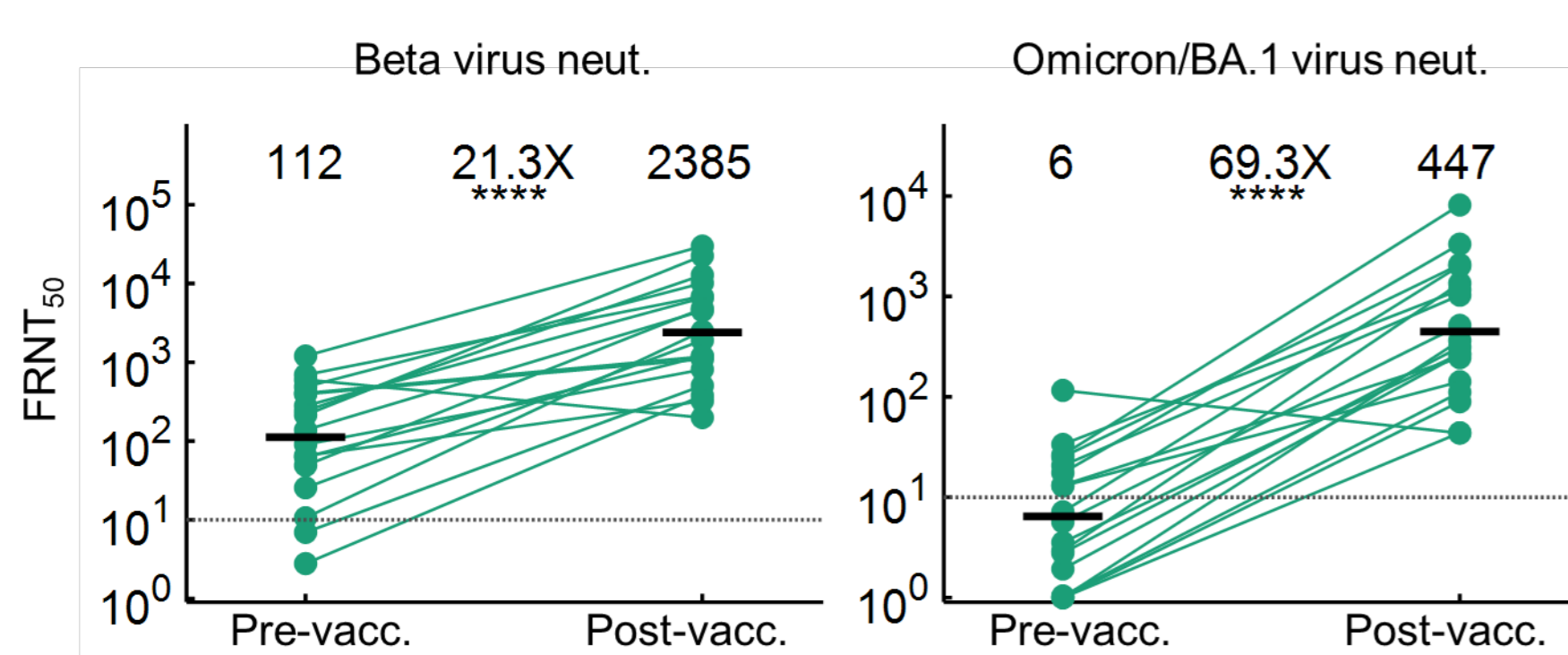


Fig. 2: Neutralization of the Beta and Omicron (BA.1) variants by Beta infected participants before and after Pfizer vaccination.

- Vaccination increases neutralization capacity of the Beta and Omicron/BA.1 variant.
- Pre-vaccination, Omicron/BA.1 neutralization was 17.3-fold lower than Beta virus.
- In contrast, the fold-drop between Beta and Omicron/BA.1 neutralization post-vaccination was 5.3.
- These results contrast with BNT162b2 vaccination in combination with ancestral virus infection, where we observed a 19.6-fold drop in Omicron/BA.1 neutralization relative to ancestral virus.

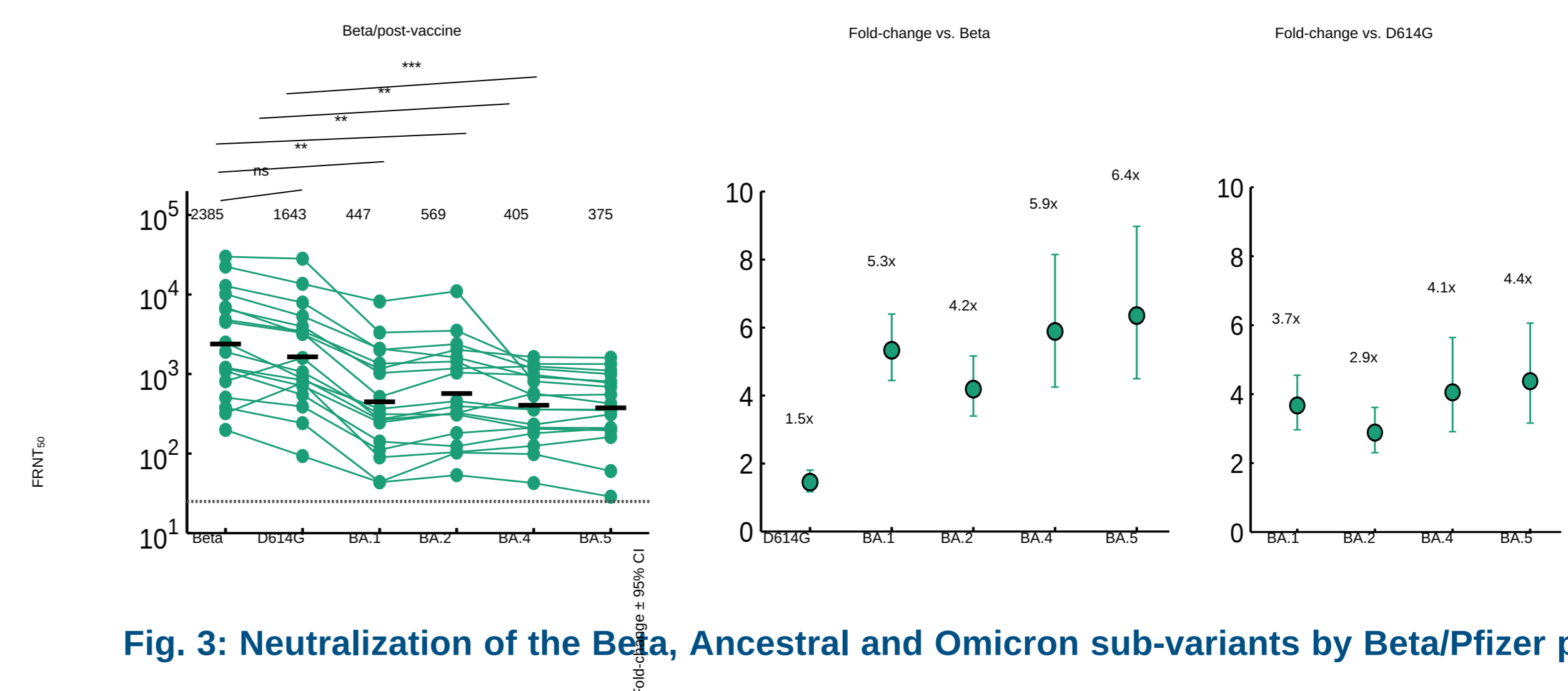


Fig. 3: Neutralization of the Beta, Ancestral and Omicron sub-variants by Beta/Pfizer plasma.

- Similarly, to BA.1, cross-neutralization of Omicron/BA.2, BA.4, and BA.5 post-vaccination was only 4.2, 5.9, and 6.4-fold lower relative to Beta (Fig 3).
- Ancestral virus led to a 1.5-fold decline and fold-drop for BA.1 was lower when compared to ancestral virus relative to the Beta virus.
- Lower escape was retained when we examined samples taken ~6 months post-vaccination (Fig 4).

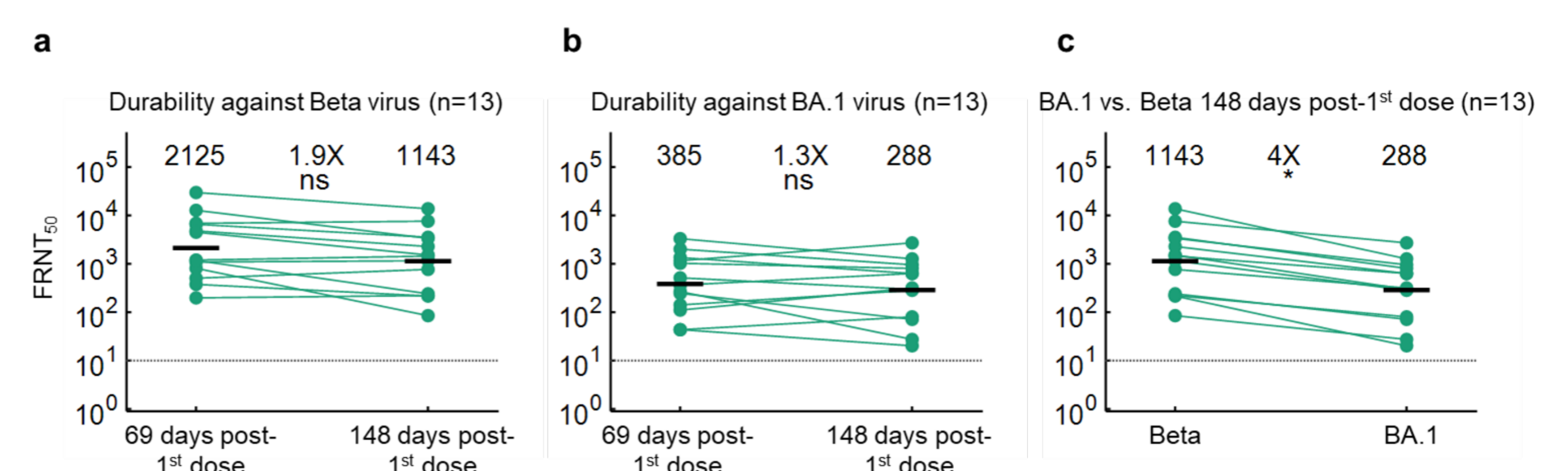


Fig. 4: Neutralization of the Beta and Omicron/BA.1 variant by matched samples from peak vaccine response and ~5 months post vaccination.

## 4. Discussion & Conclusion

- The degree of Omicron BA.1 escape in Beta infected participants before BNT162b2 vaccination or in vaccinated but not Beta infected participants are consistent with previous work (Khan, et al. 2022).
- Escape of Omicron sub-lineages from BNT162b2 elicited immunity was attenuated when vaccination was combined with Beta infection.
- Ancestral/BNT162b2 hybrid immunity did not have a similar effect.
- These results are one line of evidence which supports testing multivalent vaccines incorporating the Beta variant sequence.

## 5. References

- Cele, S. et al. Omicron extensively but incompletely escapes Pfizer BNT162b2 neutralization. *Nature* 602, 654–656 (2022).
- Corbett, K. S. et al. Protection against SARS-CoV-2 Beta variant in mRNA-1273 vaccine-boostered nonhuman primates. *Science* 374, 1343 – 1353 (2021).
- Khan, K. et al. Omicron sub-lineages BA.4/BA.5 escape BA.1 infection elicited neutralizing immunity. *Nature communications* 13:4686 (2022).