The magnitude and durability of the antibody response to mRNA-based vaccination among SARS-CoV-2 seronegative and seropositive healthcare personnel

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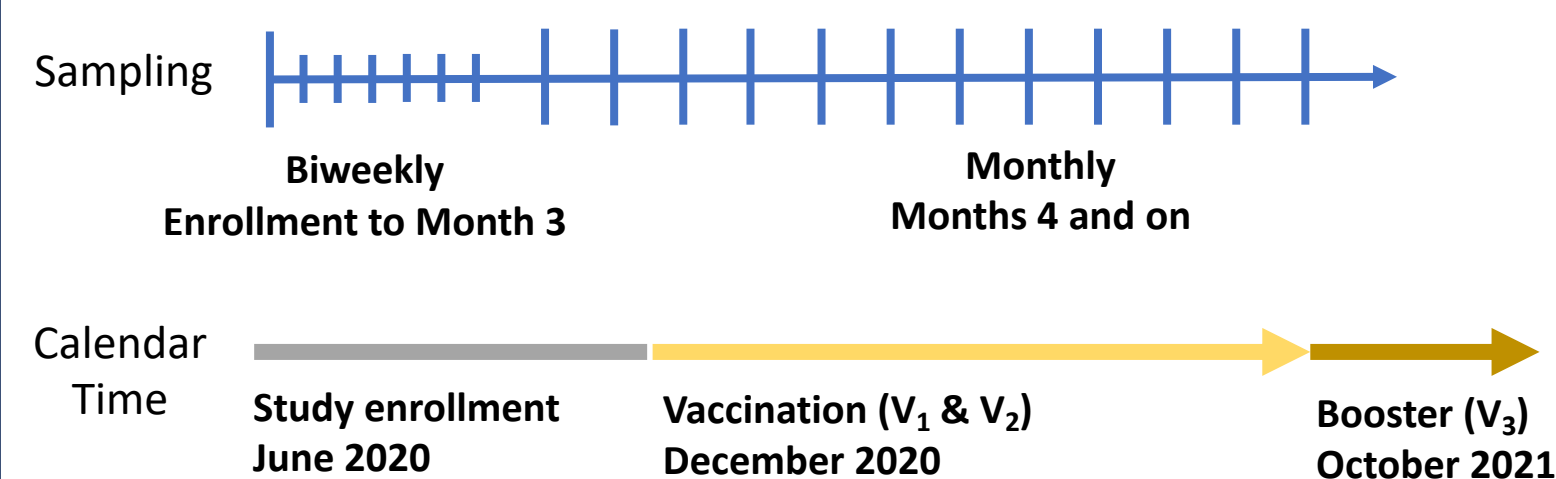[6]Department of Microbiology and Immunology, UNC SOM

Introduction

- The impact of natural infection on vaccination response has not been fully studied.
- We conducted a longitudinal study of healthcare personnel (HCP) with antibody testing up to 5 months before and 13 months after mRNA vaccination.
- We assessed whether natural infection prior to vaccination was associated with differences in the response to mRNA-based vaccines.

Study Design/Methods

Sampling

Biweekly Enrollment to Month 3 | Monthly Months 4 and on

Calendar Time

Study enrollment June 2020 | Vaccination (V₁ & V₂) December 2020 | Booster (V₃) October 2021

- For all samples, we measured total immunoglobulin (Ig) and IgG antibodies specific to the receptor binding domain (RBD) of the SARS-CoV-2 spike protein by ELISA[4] and calculated a positive to negative ratio (P/N) from the sample OD measurements.
- We measured live virus neutralization by pre- and post-vaccination samples from seropositive individuals and post-vaccination seronegative individuals matched by sex, age, and time from vaccination using a Nanoluciferase-expressing reporter D614G SARS-CoV-2 virus on the Nano-Glo® Luciferase Assay System.[5]
- Infection prior to vaccination was defined as positive total Ig RBD-spike antibody or SARS-CoV-2 polymerase chain reaction (PCR)
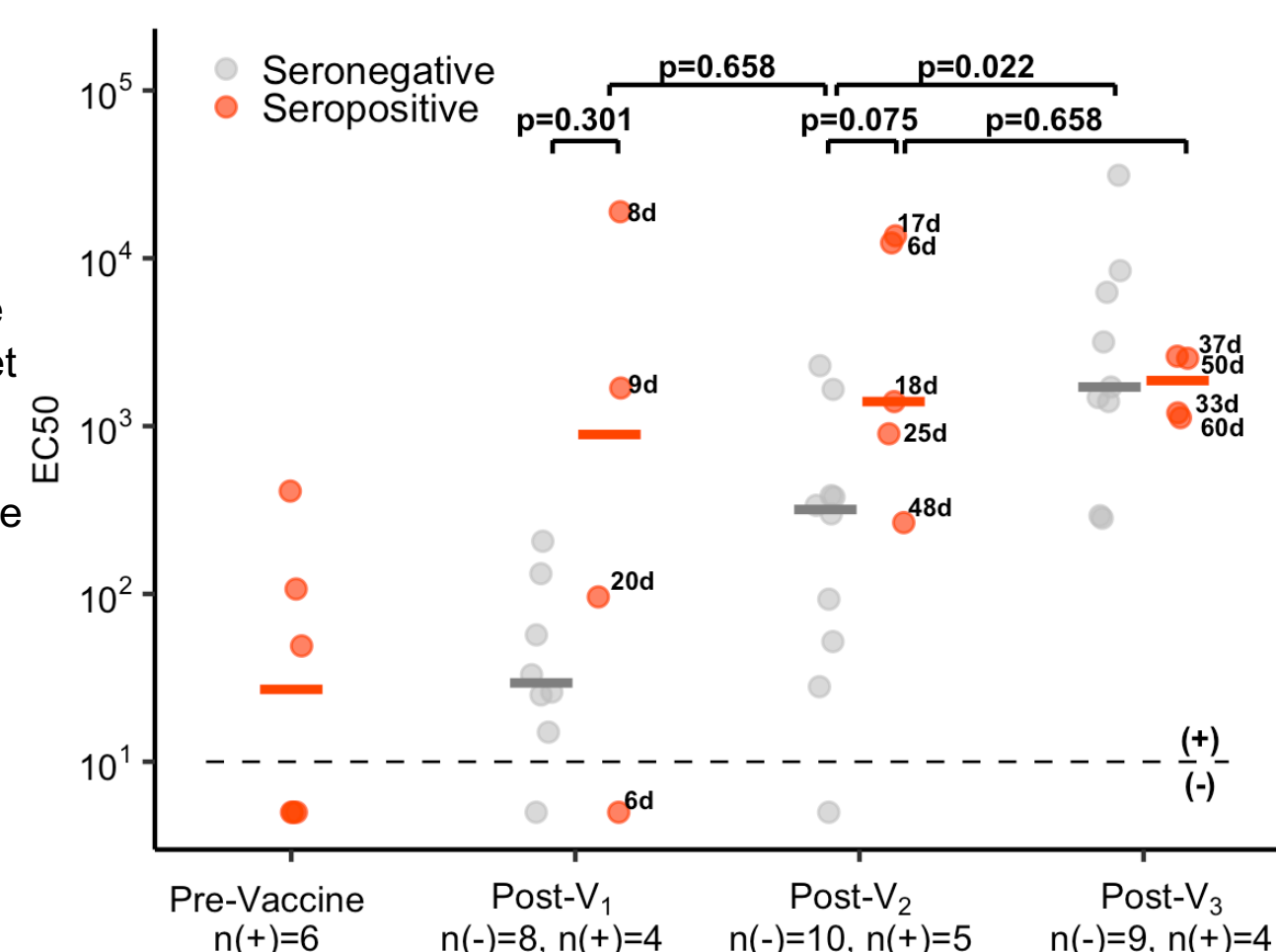
Results

Study cohort

- 192 HCP enrolled between July 2020 and Jan 2021 and followed through February 2022. Median follow-up period was 4.5 months (Q1-Q3: 2.5-10.5 months) and the median samples per participant was 7.
- Ten (5%) were seropositive prior to vaccination; five (3%) had antibodies at baseline (prevalent seropositive) and five (3%) developed antibodies prior to vaccination (incident seropositive) (Table 1).
- 99 participants had paired antibody measurements before and after at least one vaccine dose.

Characteristics	Full cohort (n=192)	Pre- and post-vaccine (n=99)[a]	Post V₃ (n=34)
Age, median (Q1, Q3)	36 (31-44)	38 (31-46)	41 (36-47)
Female sex, n (%)	131 (68)	65 (66)	20 (41)
Total Ig Antibody Serostatus prior to vaccination, n (%)			
Seronegative	182 (95)	93 (92)	30 (88)
Seropositive	10 (5)	6 (6)	4 (12)
At baseline	5 (3)	4 (4)	3 (9)
In follow up	5 (3)	2 (2)	1 (3)
Vaccinations received, n (%)			
None	1 (0.5)	N/A	N/A
2 doses	141 (74)	51 (52)	N/A
3 doses	50 (26)	48 (48)	34 (100)

Table 1. Demographics, serostatus, and vaccinations for the total study population and the sub-sample of participants with pre- and post-vaccination antibody measurements. [a]Post-vaccine refers to after at least one dose.

Figure 1 . Total Ig responses at vaccination timepoints by serostatus. Total Ig positive P/N cut-off = 2.57.

Figure 2. IgG subtype responses at vaccination timepoints by serostatus. IgG positive P/N cut-off = 2.40.
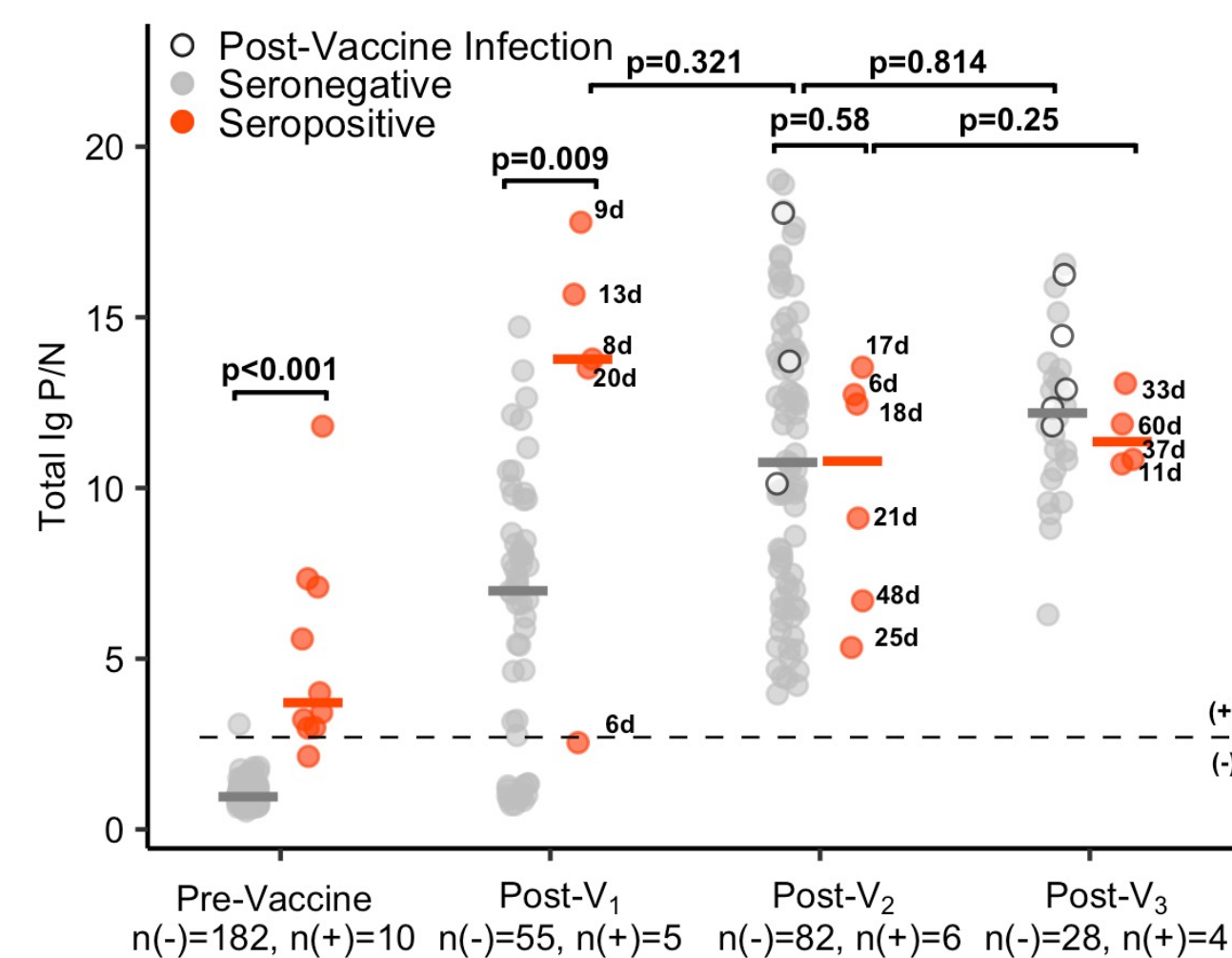
Figure 3. SARS-CoV-2 D614G live virus neutralization titers seropositive HCP and a subset of seronegative HCP. The dotted line represents the limit of detection and starting dilution, 1:10.
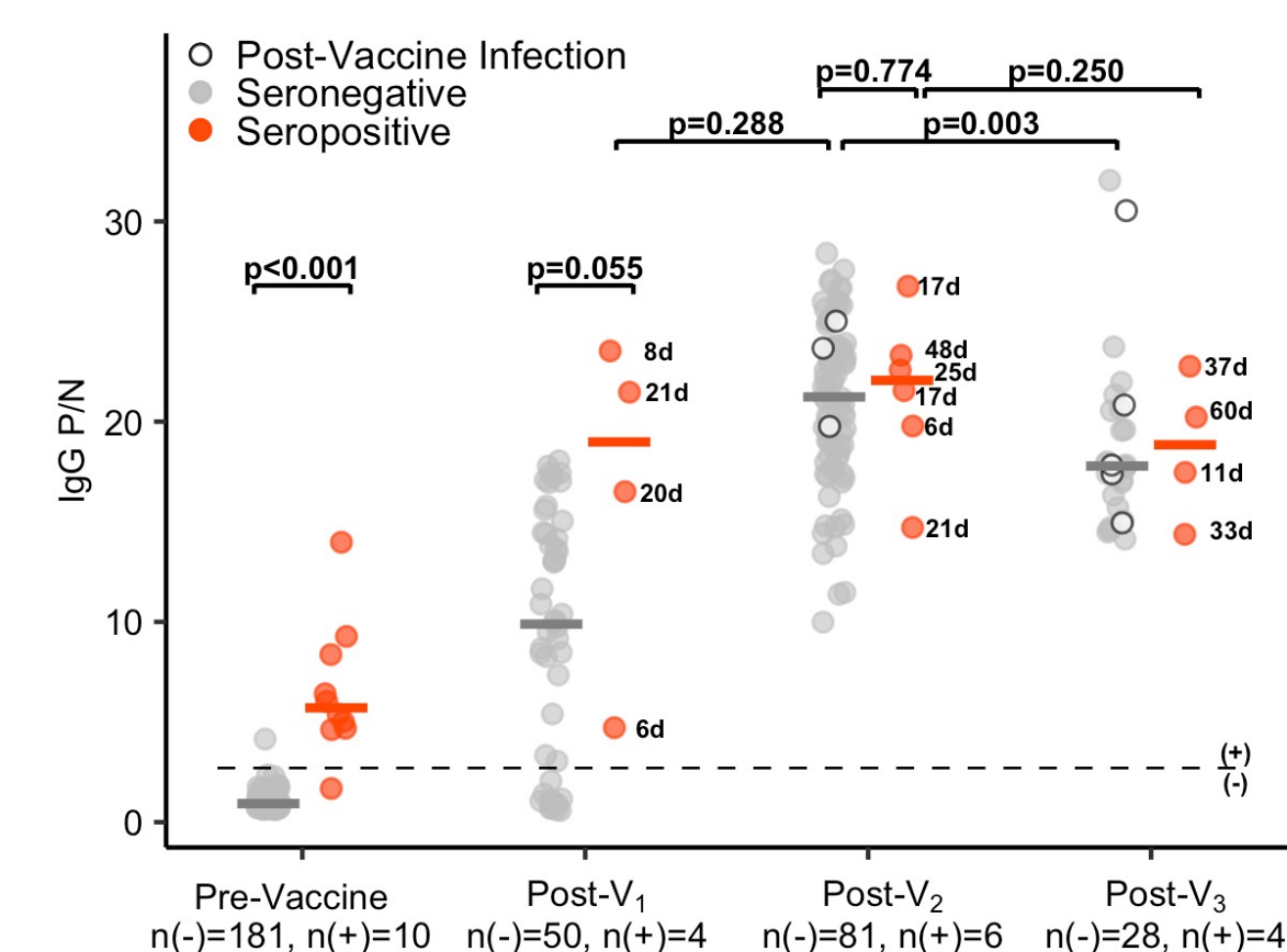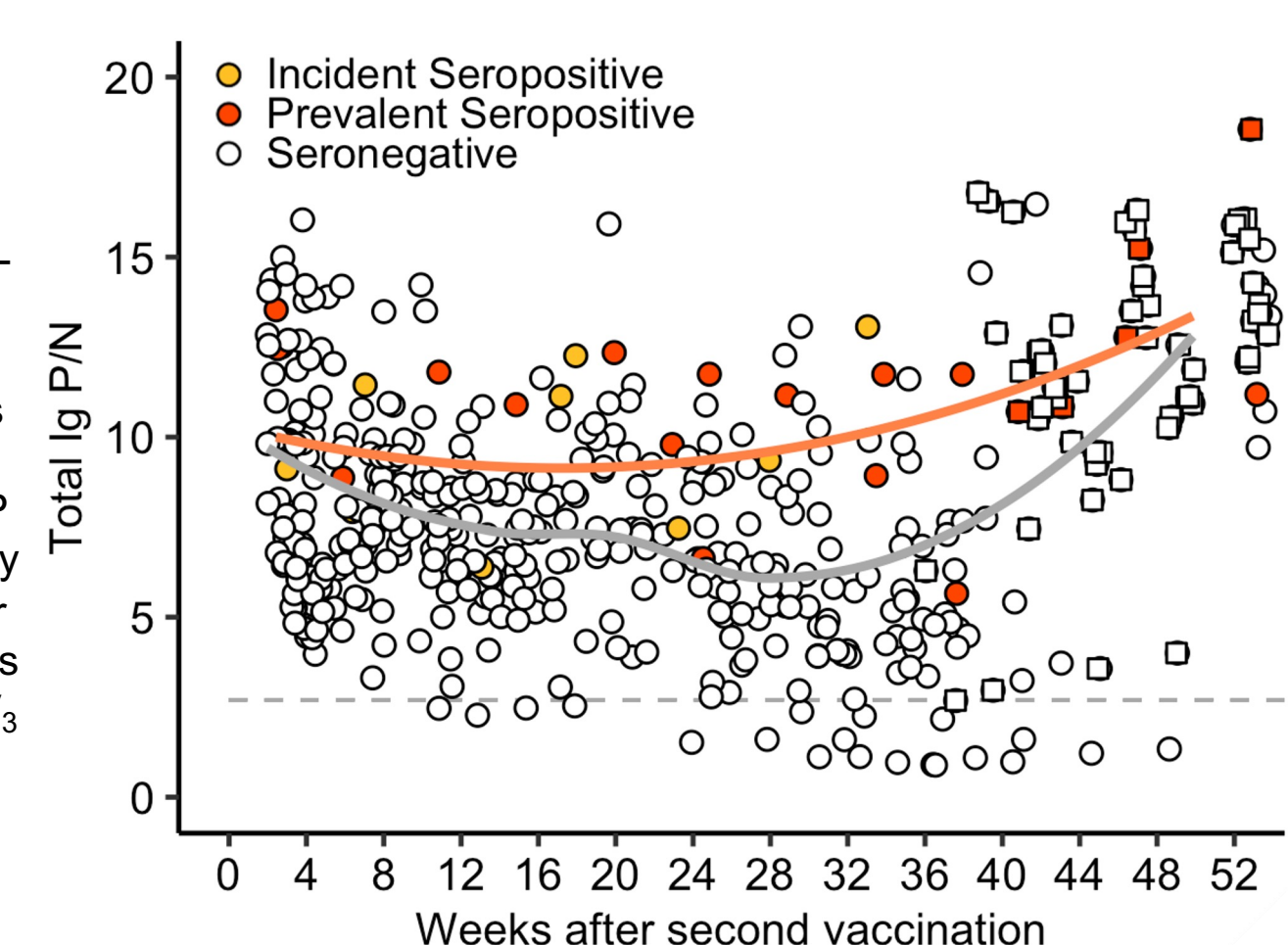

Figure 4. All total Ig measurements after 5 days post-V₂. The orange line represents the Loess curves for both incident and prevalent SP HCP and the grey line the Loess for SN HCP. Squares represent Post-V₃ samples.

Key Findings

- The antibody response to the first dose was almost two-fold higher in individuals who were seropositive prior to vaccination, although neutralization titers were more variable.
- The response to subsequent vaccine doses did not differ by serostatus prior to vaccination.
- The antibody response induced by vaccination appeared to wane over time, but generally persisted for 8-9 months regardless of serostatus prior to vaccination. However, the overall decline in antibody titers post-V₂ appeared to be more pronounced in seronegative participants.

Discussion

- This study provides frequent antibody measurements over long duration throughout pre- and post-vaccination timepoints but is limited by sample size of seropositive participants.
- These results suggest that immunity against SARS-CoV-2 prior to vaccination plays a role in maintaining higher circulating Ab titers and corroborates studies that show prior infection may significantly prime the immune response to a first dose.[6-13] Yet, the impacts on later doses may be minimal.
- Larger studies examining the moderating impacts of initial and future infections on vaccination response are needed.

References