

Estimated half-life of SARS-CoV-2 anti-spike antibodies more than double the half-life of anti-nucleocapsid antibodies in healthcare workers

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Dear editor:

Lumley et al. studied the duration, and dynamics of SARS-CoV-2 antibody responses in 452 individual healthcare workers (HCW) over a 6-month period [1]. SARS-CoV-2 IgG anti-nucleocapsid (N) antibodies started to decline within one month after first positive PCR with an estimated half-life of 85 days and an estimated 50% of HCW becoming seronegative after 7 months. Confirming these results, we recently reported that 61.1% of mild SARS-CoV-2 infected patients became seronegative within 6 months after first positive PCR [2]. Anti-spike (S) antibodies, in contrast, remained positive up to 7 months in an estimated 94% of participants. The authors were unable to determine whether the longer anti-spike response was due to slower waning or higher initial antibody levels since most results were above the upper limit of quantification of their assay [1].

We report antibody levels for anti-S and anti-N in 118 individual HCW with a previous SARS-CoV-2 infection. Participants were sampled 1-3 months (28-103 days) and 7-10 months (209-315 days) after positive PCR. Seroconversion for anti-S and anti-N typically occurs within 28 days after positive PCR [3]. Antibodies were measured on Abbott Architect with the SARS-CoV-2 IgG (anti-N) and IgG II Quant (anti-S) assays using the manufacturer's cut-offs for positivity of 1.4 S/CO and 50 AU/mL, respectively. The median age was 48 years old (range 20-62), with 88.1% women. Most participants experienced mild disease and only six participants were briefly hospitalized.

At 1-3 months, 98.3% were positive for anti-S compared to 85.6% for anti-N ($p < 0.01$ with Fisher's exact test). At 7-10 months, 92.4% of patients were still positive for anti-S compared to only 17.8% for anti-N ($p < 0.01$). To estimate the antibody half-life, we used a simple linear regression model (RStudio version 1.3.1093) correlating the \log_{10} antibody level to days after positive PCR. Only patients who tested positive for anti-N ($n=101$) or anti-S ($n=116$) 1-3 months after PCR were included to estimate half-life. The computed mean half-life was 76.4 days for anti-N [95% confidence interval (CI): 68.3-86.7] compared to 198.8 days for anti-S [CI: 143.6-323.0] with an estimated 50% of patients becoming seronegative for anti-N 201.2 [CI: 179.9-228.3] days after positive PCR compared to 803.2 [CI: 580.2-1305.0] days for anti-S. We also calculated the half-life by dividing the \log_{10} antibody level difference between the paired samples by the number of days between the

two samples for each patient. The results were normally distributed for anti-S and anti-N (Shapiro-Wilk test) and the estimated mean half-life was 74.8 days [CI: 70.1-80.1] for anti-N and 197.2 days [CI: 172.4-230.4] for anti-S.

Our results confirm a recent study that reported more than 90% anti-S seropositivity up to 8 months after positive PCR [4]. This could have implications on the estimated duration of the antibody response after vaccination which appears to be similar to the antibody response after infection during the first 8 weeks [5]. Of note, anti-N antibodies wane significantly slower in moderate to critical COVID-19 patients [2]. Further studies are needed to determine the dynamics of anti-S antibodies in these patients.

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NOTES

Author contributions

PV conceived the study. JVE, LGr, PV, conducted experiments and drafted the manuscript. LGo aided in collecting data and all authors critically reviewed the manuscript.

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Conflicts of interest

The authors report no conflicts of interest.

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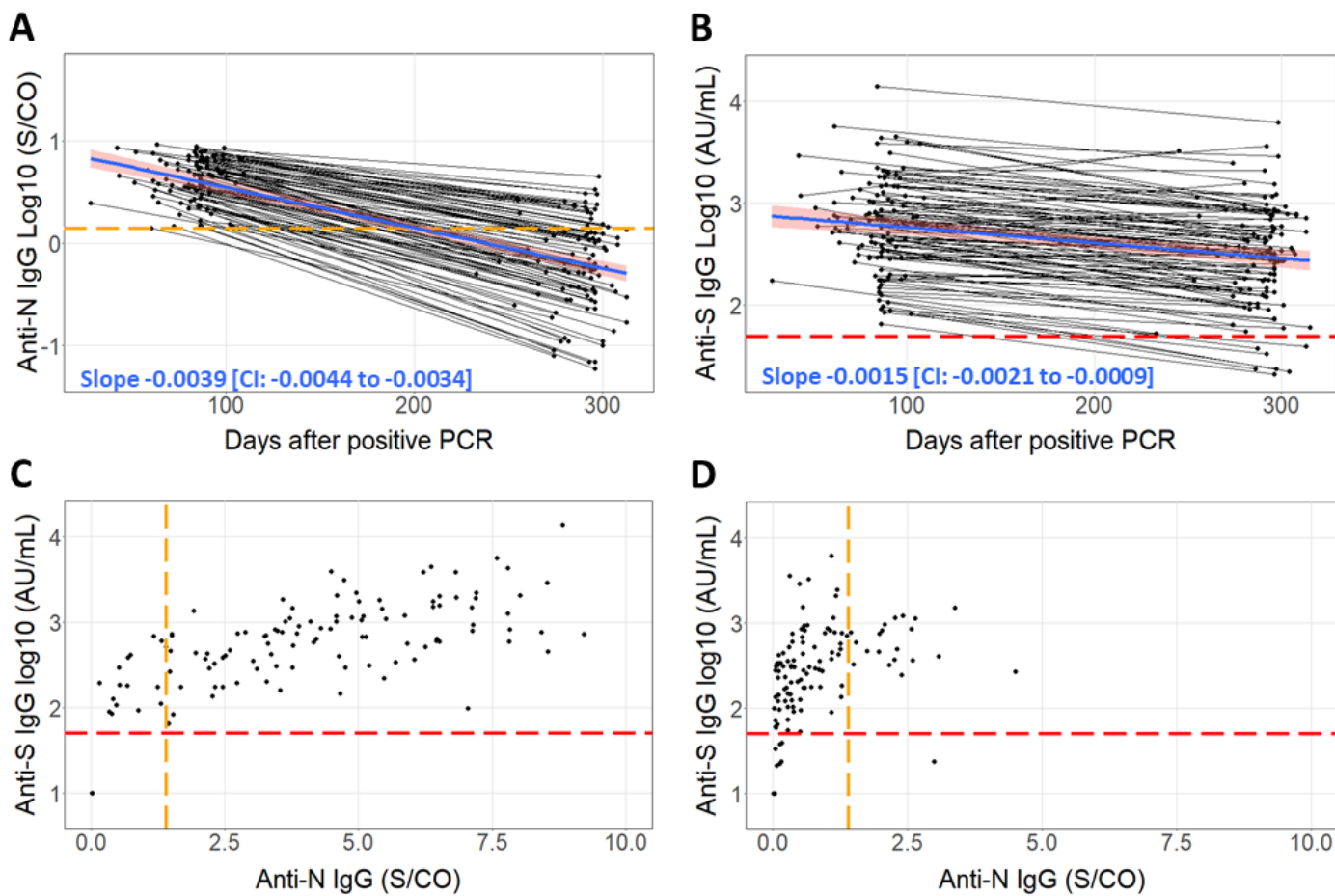
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Figure legend:

Figure 1: Longitudinal evolution of SARS-CoV-2 antibody titers against nucleocapsid (panel A) and spike (panel B) and correlation between both antibody levels 1-3 months (panel C) and 7-10 months (panel D) after positive PCR in 118 health care workers. S: spike, N: nucleocapsid, S/CO: signal-to-cut-off, AU: arbitrary units. Thick blue line represents line of best fit (red: 95% confidence interval). Dashed orange and red lines represent the manufacturer's cut-offs for positivity for anti-N (1.4 S/CO) and anti-S (50 AU/mL), respectively.

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Figure 1



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