Supplementary Material

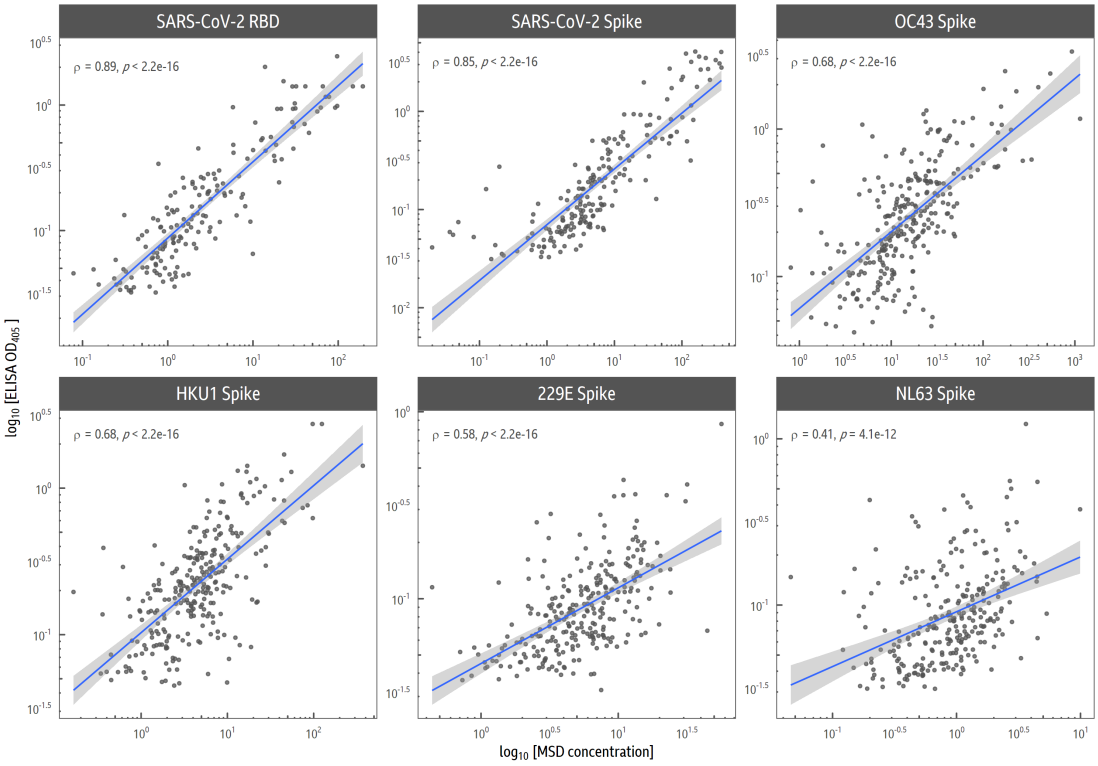


Figure S1: Correlation of MSD VPLEX and ELISA data. The correlation of results across the two assays for the SARS-CoV-2 full-length spike and RBD domains, along with endemic coronavirus spike antigens is shown with Spearman's Rank correlations.

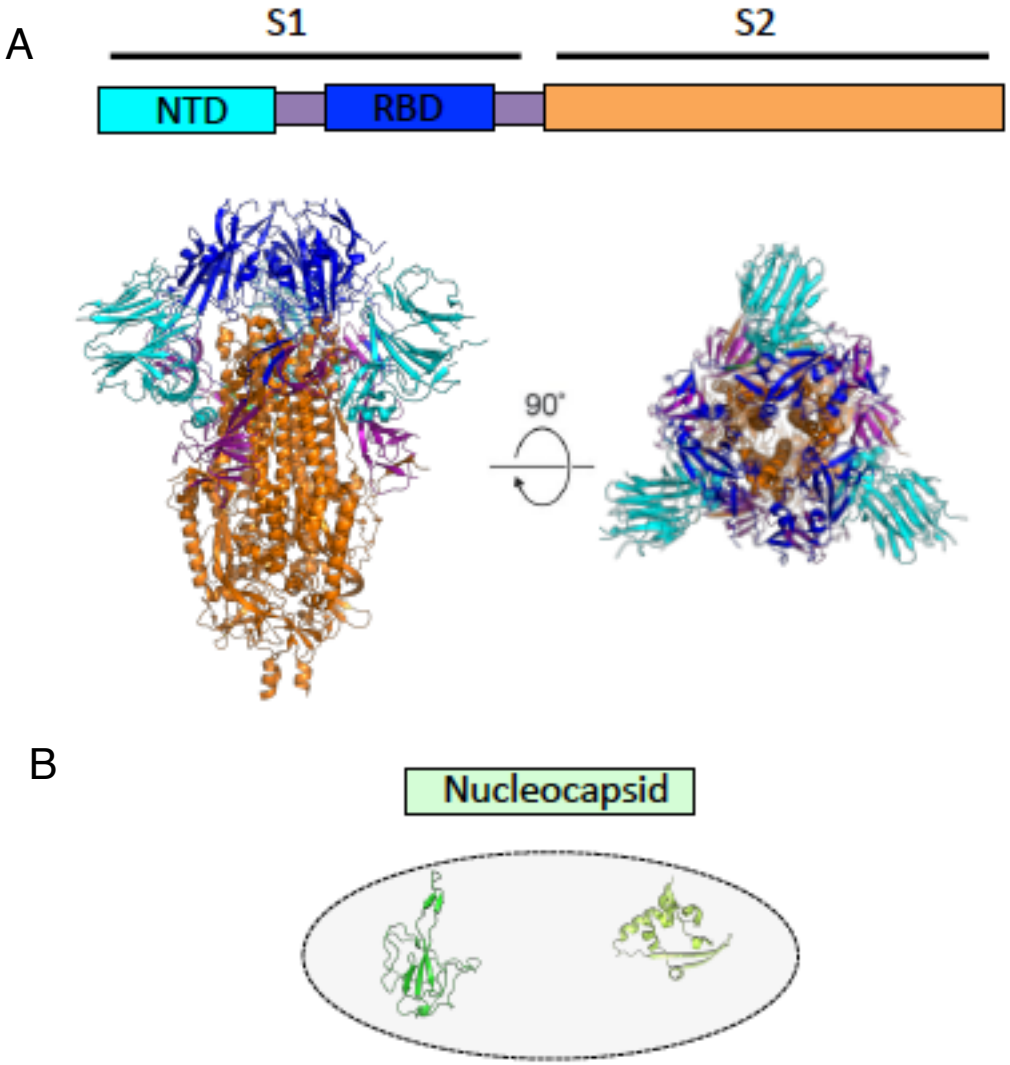
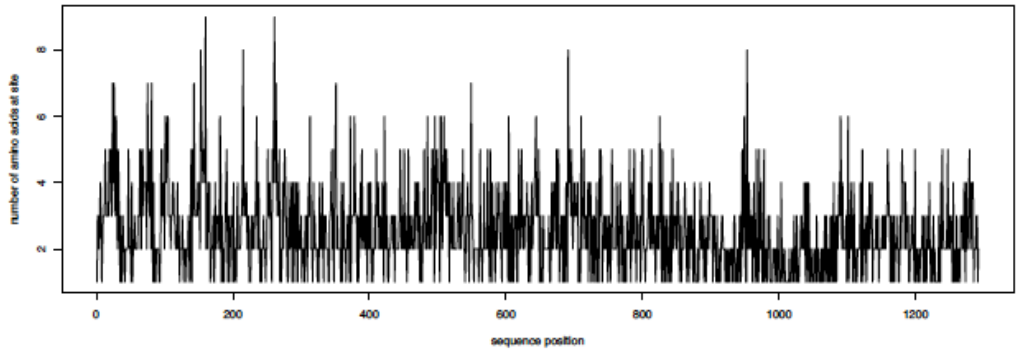


Figure S2. A schematic of the subunits and domains of the SARS-CoV-2 spike protein and SARS-CoV-2 nucleocapsid used in the MSD V-PLEX assay and ELISAs. (**A) Various regions and subunits of the spike were analysed.** Variable regions such as the N-terminal (NTD) and receptor-binding domain (RBD) in the S1 subunit of the spike protein, in addition to the more conserved S2 subunit were analysed.. (**B) A second antigen was also assessed, the SARS-CoV-2 nucleocapsid, which was not subdivided into domains.** A full crystal structure exists for the SARS-CoV-2 spike, whilst only partial structures of the N-terminal and RNA binding domain regions of the SARS-CoV-2 nucleocapsid exist. These are shown above.

A



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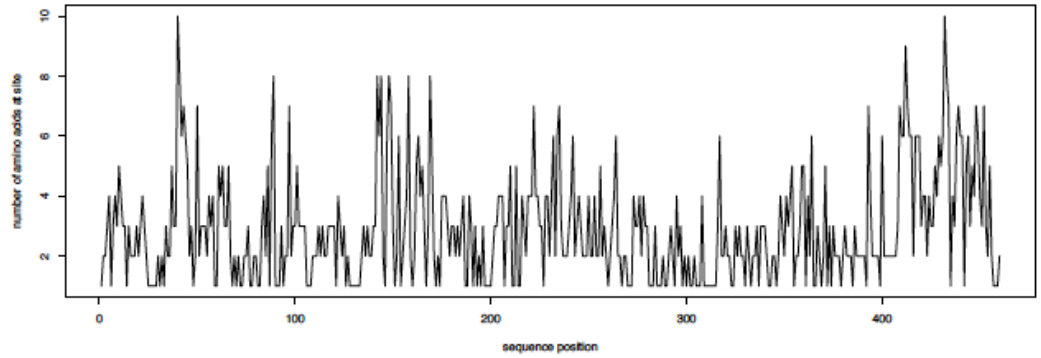
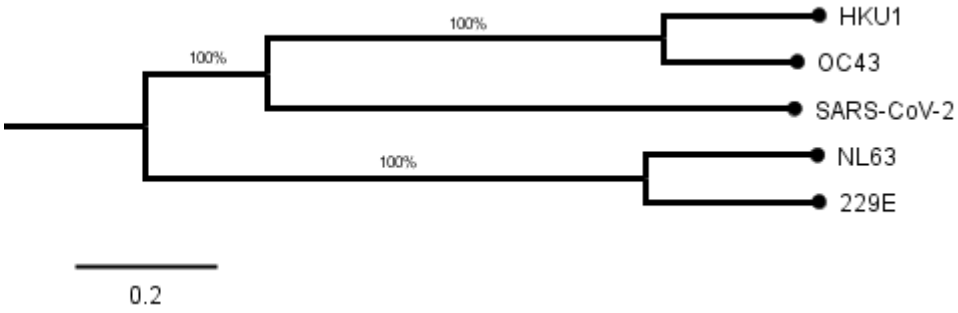


Figure S3. Variability of aligned beta-HCoV spike and nucleocapsid proteins. (**A) Variability analysis of spike protein**: 3,653 SARS-CoV-2, 100 HCoV-HKU1 and 100 HCoV-OC43 spike sequences. (**B) Variability analysis of nucleocapsid protein:** 4,845 SARS-CoV-2, 100 HCoV-HKU1 and 100 HCoV-OC43 nucleocapsid sequences. Further information regarding the analysis can be found in the Methods section.

Spike proteins



Nucleocapsid proteins

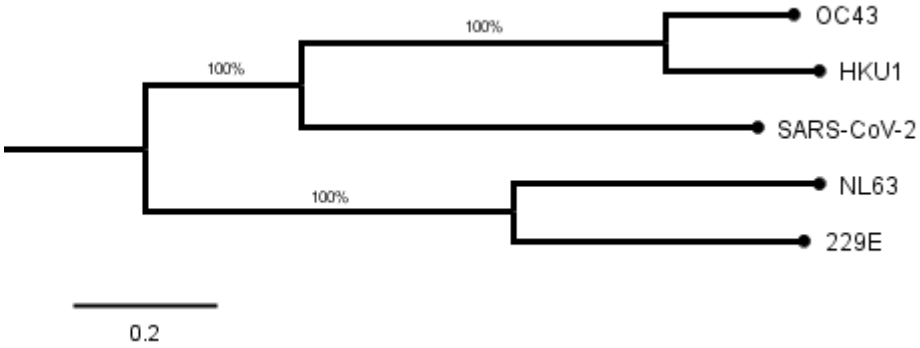


Figure S4: Phylogenetic analysis of coronavirus spike and nucleocapsid protein consensus sequences.

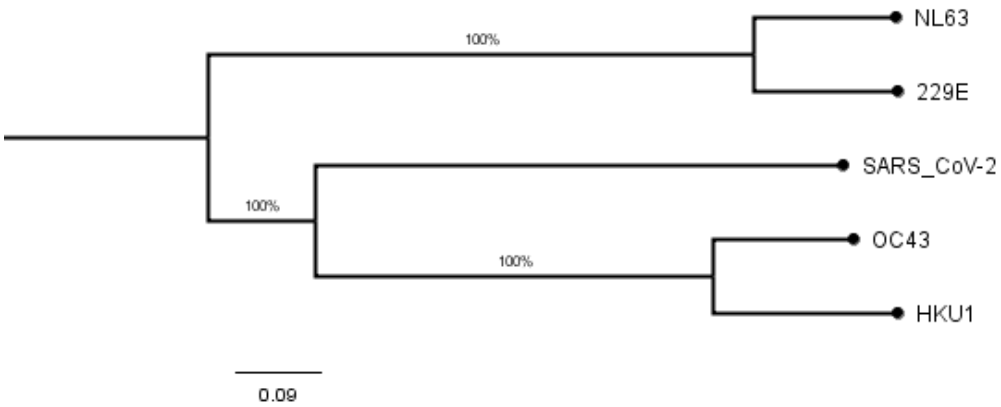


Figure S5: Phylogenetic analysis of coronavirus spike S2 subunit consensus sequences.

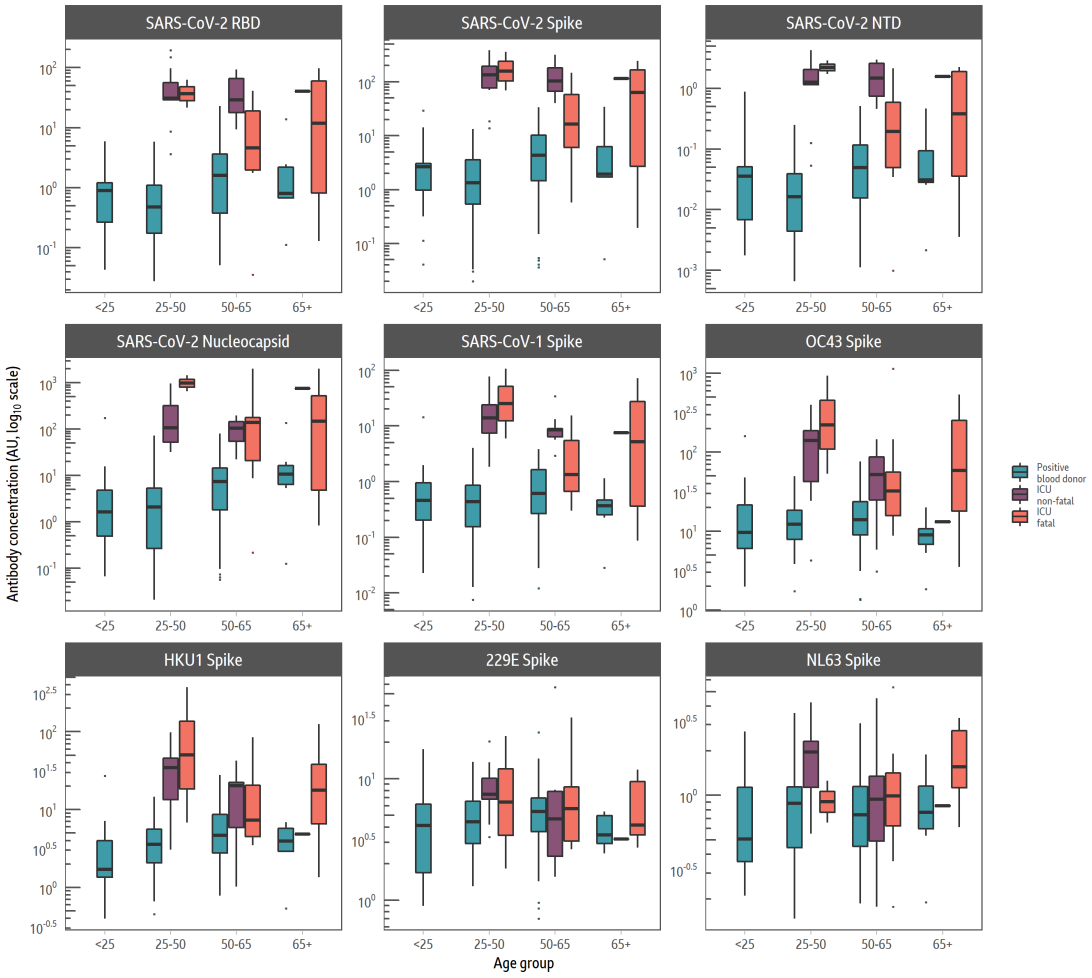


Figure S6: IgG antibody responses categorised by age in the different groups.

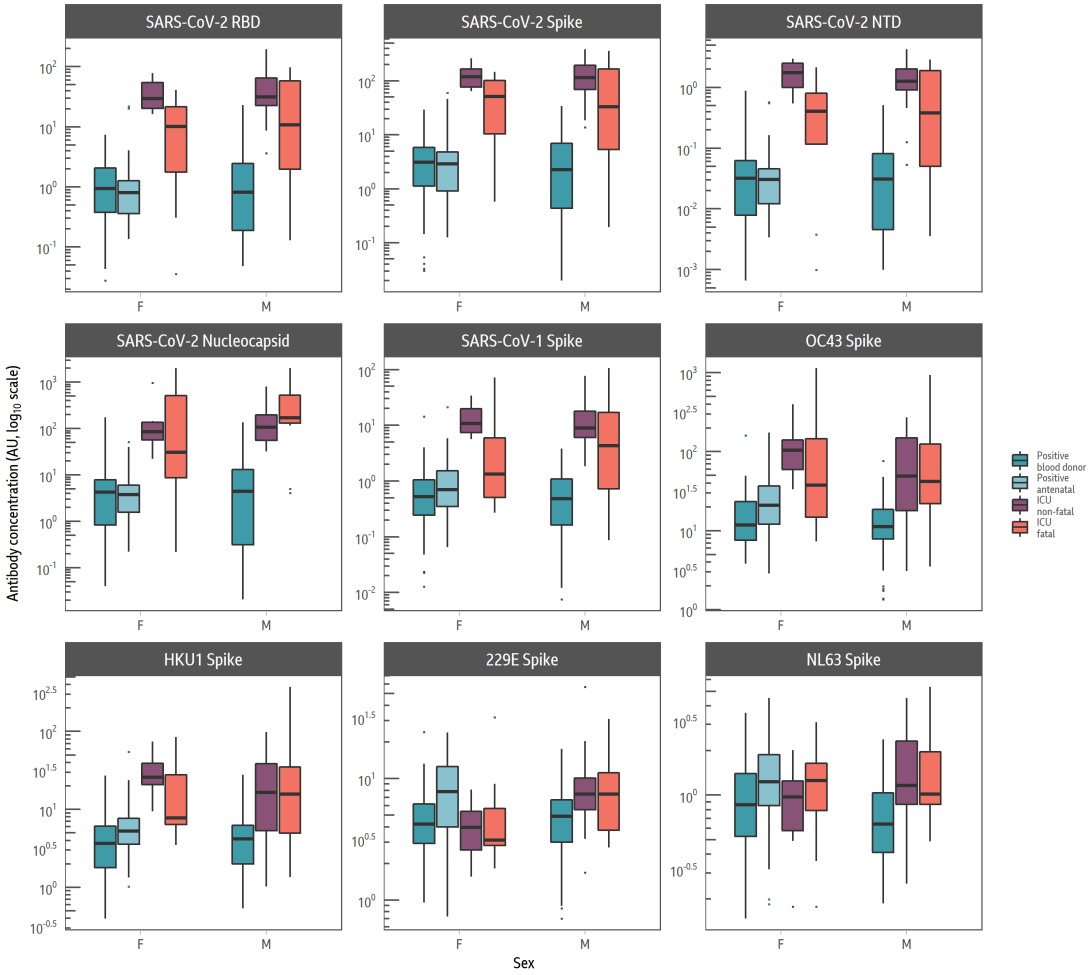


Figure S7: IgG antibody responses categorised by sex in the different groups.

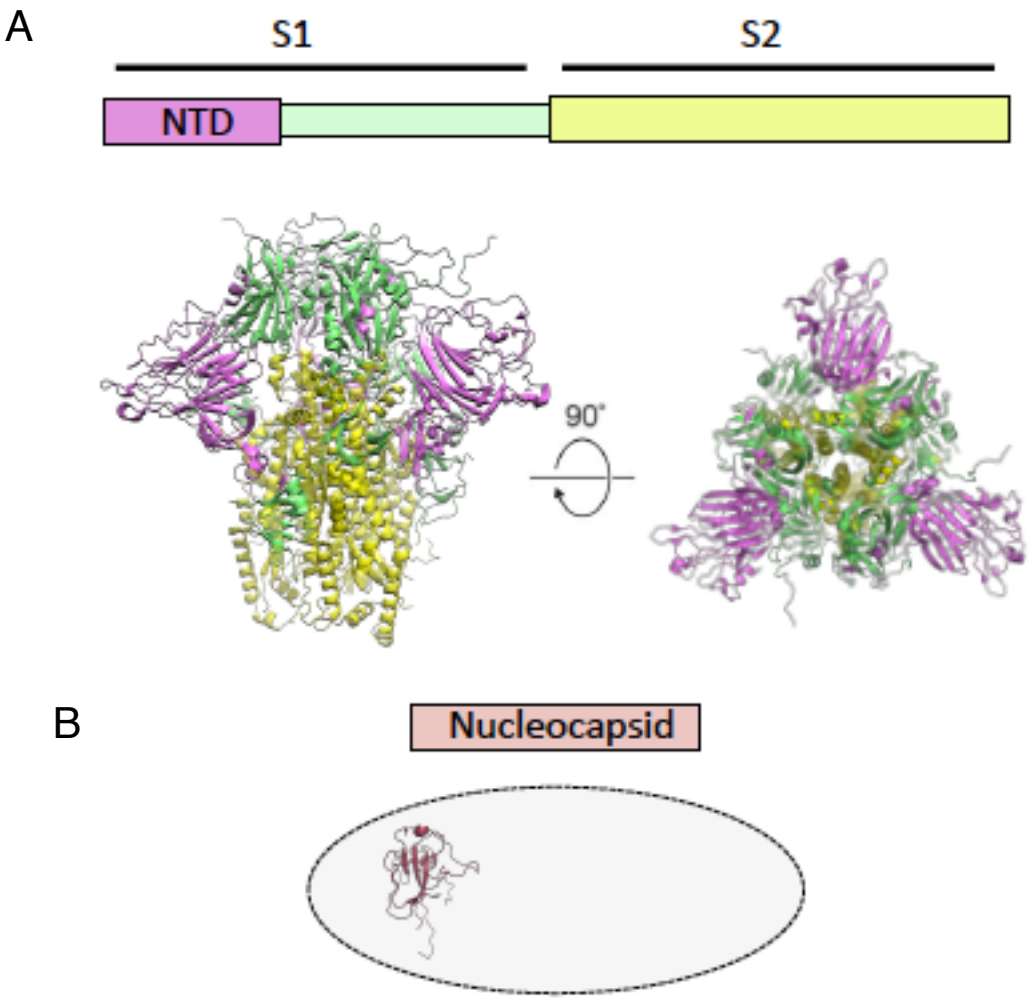


Figure S8. A schematic of the subunits and domains of the HCoV-OC43 spike protein and HCoV-OC43 nucleocapsid used in ELISAs. **(A) Various domains and subunits of the HCoV-OC43 spike were analysed.** Variable regions such as the N-terminal (NTD) in the S1 subunit of the spike protein in addition to the more conserved S2 subunit were analysed. **(B) A second antigen, the HCoV-OC43 nucleocapsid, was analysed which was not subdivided into domains.** A full crystal structure exists for the HCoV-OC43 spike, whilst only a partial structure of the N-terminal domain exists.

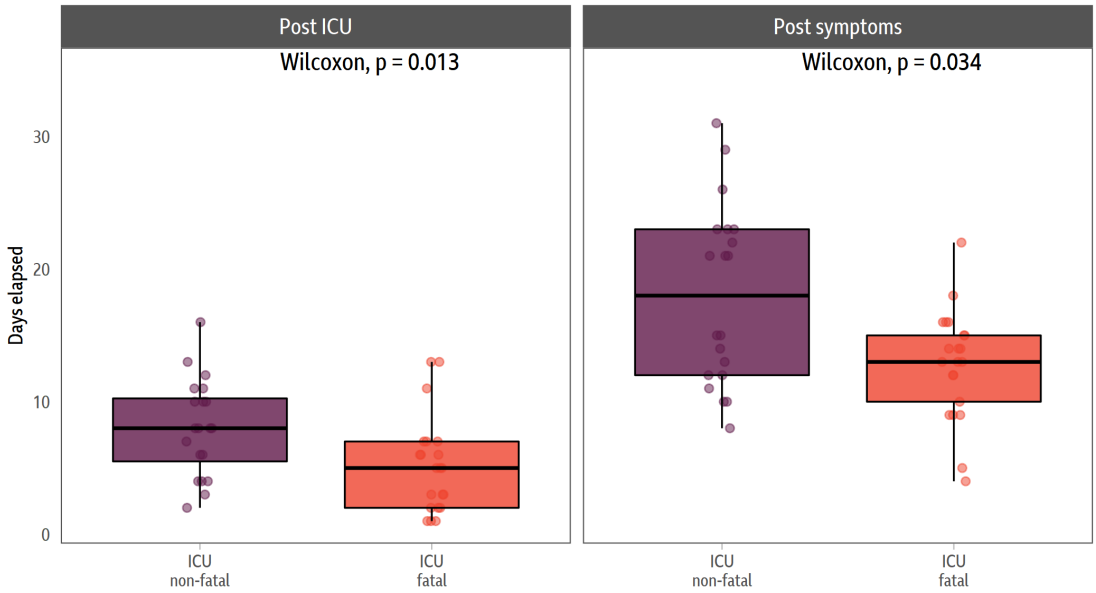


Figure S9: Days from post-symptomatic and entry to ICU in the fatal and non-fatal groups. In both instances there is statistically significant differences.

Antigens	Adjusted R-squared for the fatal ICU cohort	P-value for the fatal ICU cohort	Adjusted R-squared for the non-fatal ICU cohort	P-value for the non-fatal ICU cohort
OC43 spike & SARS-CoV-2 Spike	0.66	6*10-6	0.04	0.81
HKU spike & SARS-CoV-2 Spike	0.597	0.0002	0.05	0.69
OC43 spike & SARS-CoV-2 RBD	0.496	0.0002	0.07	0.42
HKU spike & SARS-CoV-2 RBD	0.42	0.001	0.1	0.296

Table S1. Adjusted R-squared, and p-values for the slope of the antigen in age-adjusted linear models based on those in Figure 4.

Antigens	Adjusted R-squared for the fatal ICU cohort	P-value for the fatal ICU cohort	Adjusted R-squared for the non-fatal ICU cohort	P-value for the non-fatal ICU cohort
OC43 S2 &SARS-CoV-2 Spike	0.66	1.5*10-5	0.13	0.16
OC43 S2 &SARS-CoV-2 Nucleocapsid	0.396	0.0011	0.07	0.37
OC43 Nucleocapsid & SARS-CoV-2 Nucleocapsid	-0.03	0.865	-0.06	0.35
OC43 Nucleocapsid & SARS-CoV-2 Spike	-0.02	0.77	-0.09	0.61
OC43 S1 & SARS-CoV-2 Spike	0.179	0.099	-0.02	0.99
OC43 S1 & SARS-CoV-2 Nucleocapsid	0.11	0.25	0.015	0.38
OC43 NTD & SARS-CoV-2 Nucleocapsid	-0.04	0.28	0.13	0.51
OC43 NTD & SARS-CoV-2 Nucleocapsid	-0.04	0.3	0.11	0.77

Table S2. Adjusted R-squared, and p-values for the slope of the antigen in age-adjusted linear models based on those in Figure 5.

Supplementary Materials

Methods Table 1: Protein sequences used in ELISAs

Protein	Expressed in	Provider	Reference
HCoV-HKU1 spike	Insect cells	Sino Biological	
HCoV-OC43 spike	Insect cells	Sino Biological	
HCoV-NL63 spike	Insect cells	Sino Biological	
HCoV-229E spike	Insect cells	Sino Biological	
SARS-CoV-2 spike	HEK 293T	Produced in-house	Amanat *et al.* 2020 (44)
SARS-CoV-2 RBD	HEK 293T	Produced in-house	Amanat *et al.* 2020 (44)
SARS-CoV-2 S2 subunit	HEK 293T	Sino Biological	
HCoV-OC43 S1 subunit	HEK 293T	Sino Biological	
HCoV-OC43 S2 subunit	Insect cells	Sino Biological	
HCoV-OC43 N protein	*Escherichia coli*	The Native Antigen Company	

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