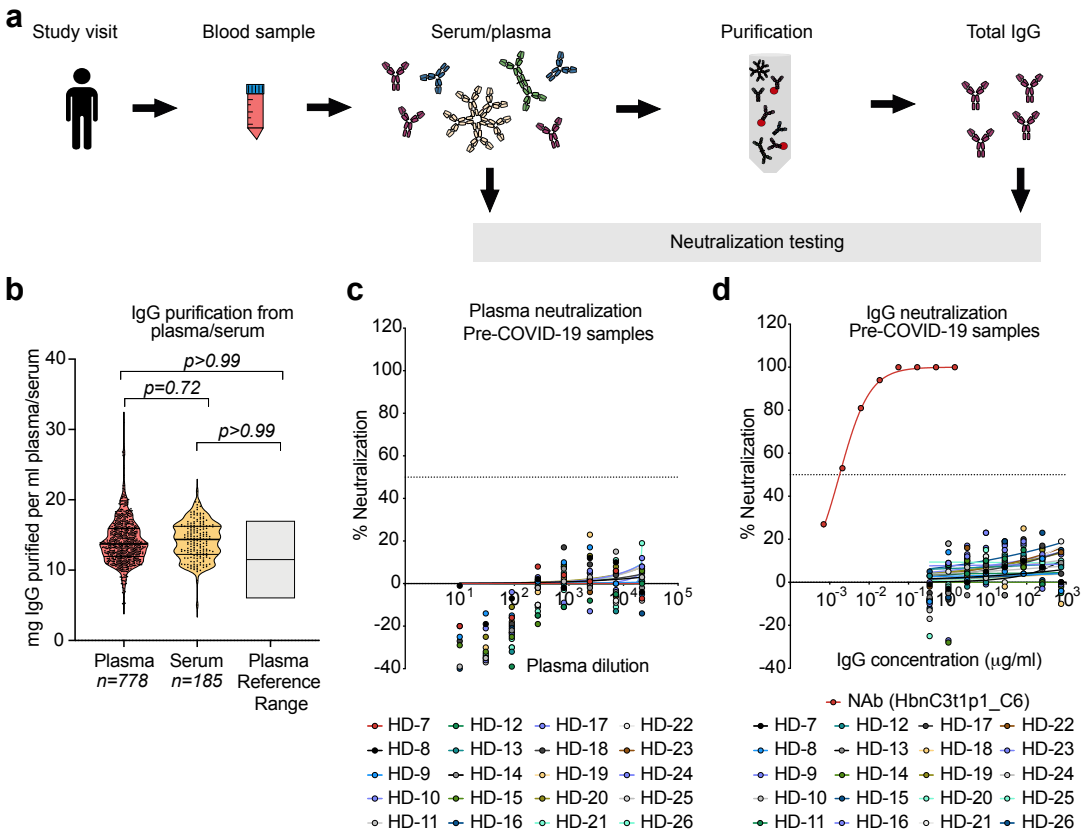
Extended data for manuscript:

Kinetics and correlates of the neutralizing antibody response to SARS-CoV-2

Extended data figures

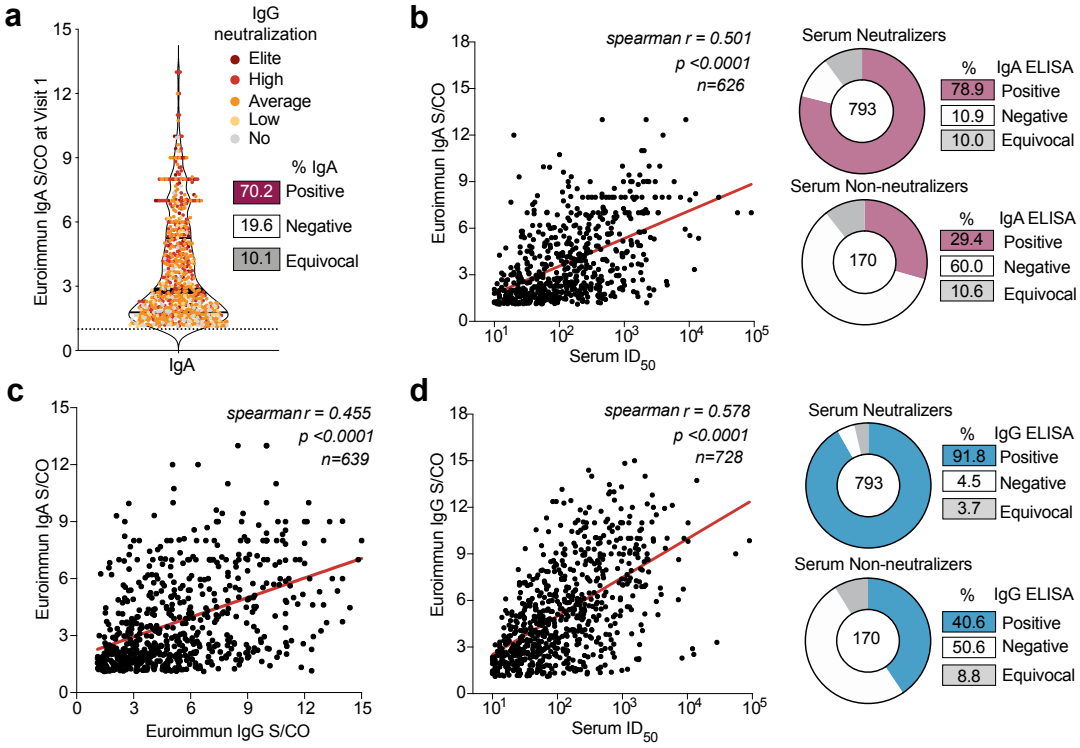
Supplementary Tables

Extended Data Figure 1



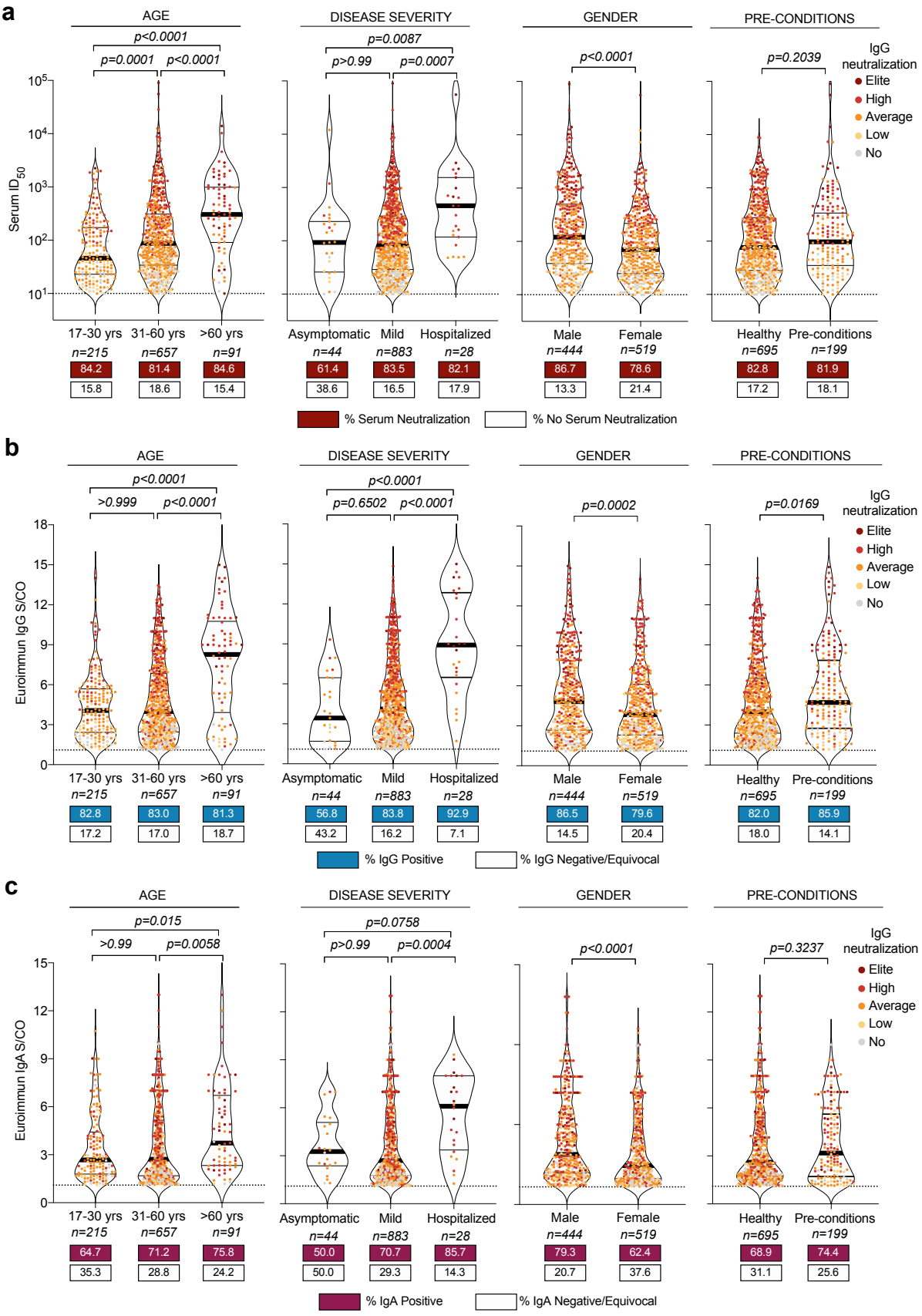
Extended Data Figure 1: Samples used for analysis of SARS-CoV-2 antibody response
a, Illustration depicting processing of blood samples and IgG purification from plasma or serum samples. **b**, Plot analyzing the efficiency of IgG purification from plasma or serum as compared to clinical reference range. Statistical testing performed with Kruskal-Wallis test. Validation of the pseudovirus neutralization test against SARS-2-S Wu01 pseudovirus using Pre-COVID-19 plasma (**c**) and IgG (**d**) samples with a neutralizing monoclonal antibody as positive control.

Extended data figure 2



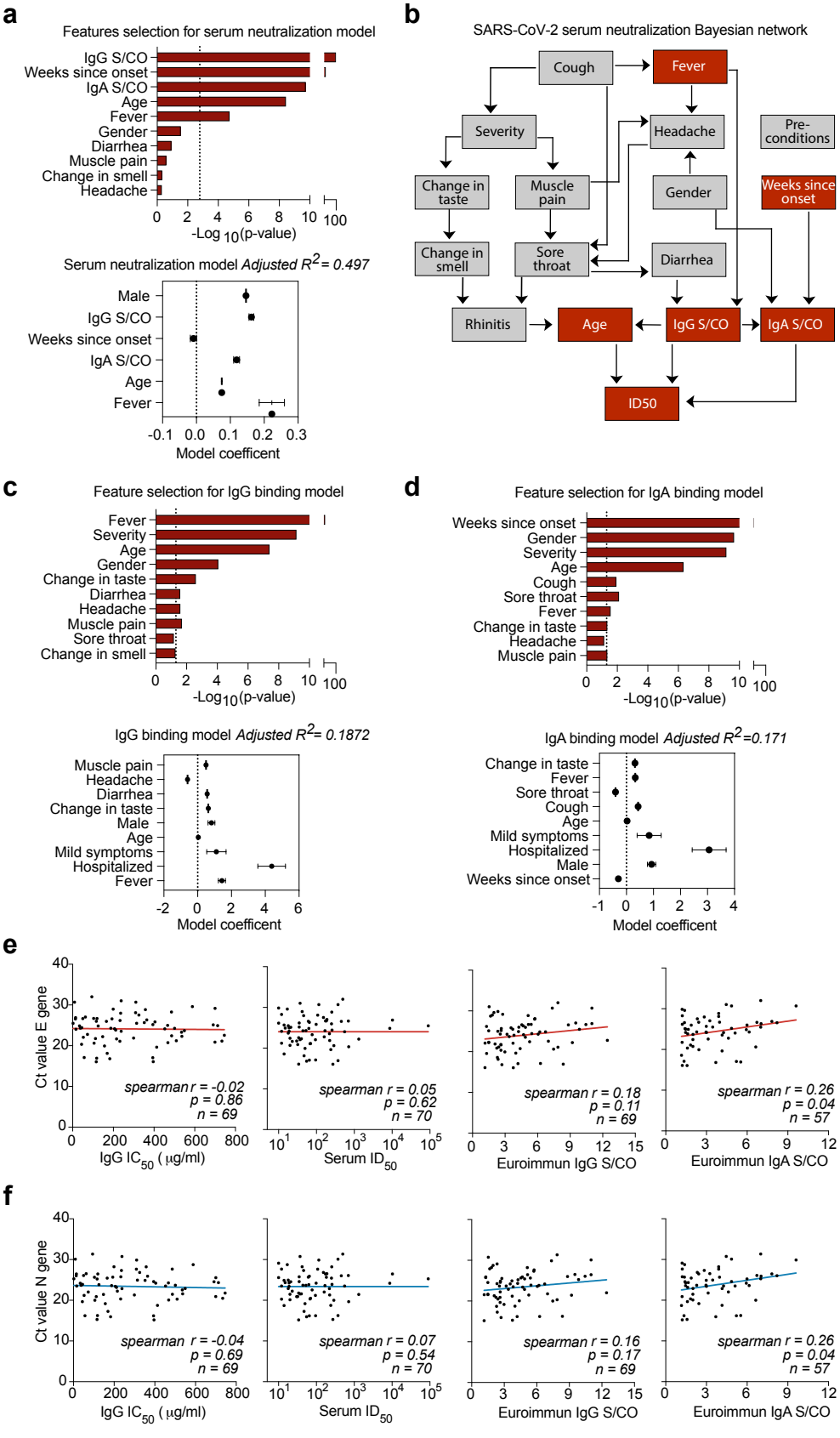
Extended Data Figure 2: Correlation between neutralization and serology results
a, violin plot of Euroimmun ELISA signal over cut-off (S/CO) ratios for anti-spike IgA. Dotted line represents the limit of detection (S/CO=1.1) of the assay. **b**, Spearman correlation plot between Euroimmun IgA S/CO and serum ID50 values at study visit 1. Euroimmun IgA S/CO and serum ID50 values at study visit 1. Pie charts illustrating the fraction of serum neutralizers and non-neutralizers and their corresponding Euroimmun IgA ELISA result for comparison. **c**, Spearman correlation plot of Euroimmun IgG S/CO ratios vs. IgA S/CO ratios at study visit 1. **d**, Spearman correlation plot between Euroimmun IgG S/CO and serum ID50 values at study visit 1. Pie charts illustrating the fraction of serum neutralizers and non-neutralizers and their corresponding Euroimmun IgG ELISA result for comparison.

Extended data figure 3



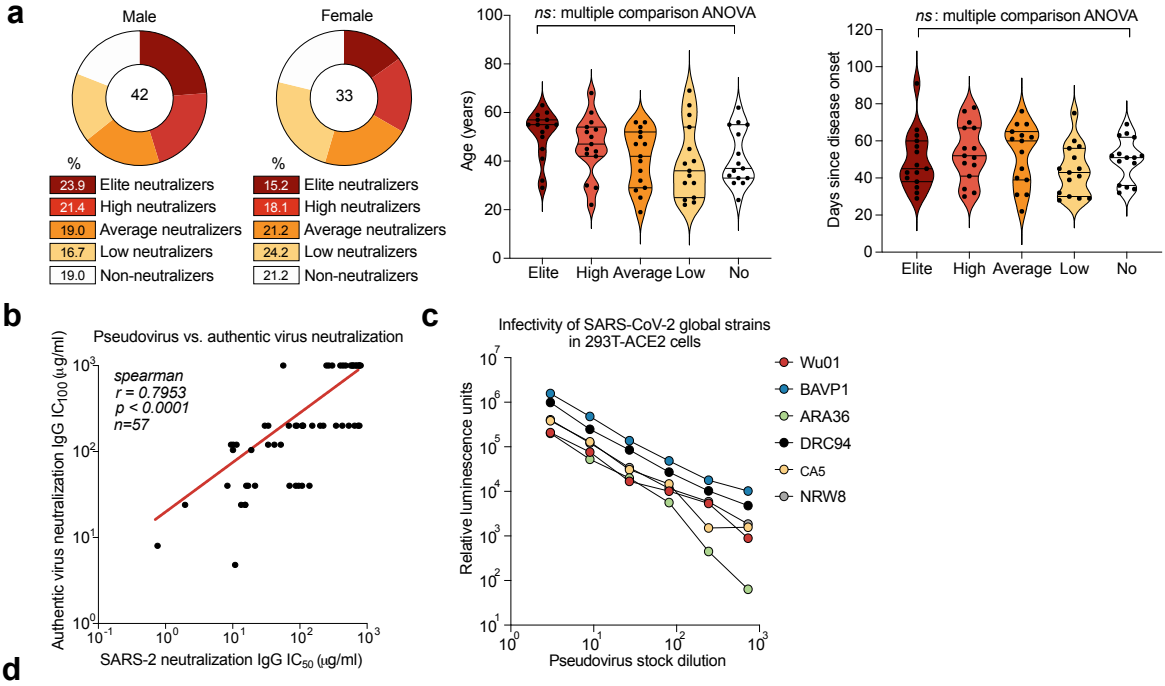
Extended Data Figure 3: Corelates of anti-SARS-CoV-2 antibody titers
a, violin plots depicting serum neutralization at study visit 1 against Wu01 pseudovirus, subdivided based on age, disease severity, gender and pre-conditions. Dotted line represents the limit of detection (1:10 dilution) of the assay. **b**, violin plots depicting Euroimmun IgG ELISA S/CO at study visit 1, subdivided based on age, disease severity, gender and pre-conditions. Dotted line represents the limit of detection (S/CO=1.1) of the assay. **c**, violin plots depicting Euroimmun IgA ELISA S/CO at study visit 1, subdivided based on age, disease severity, gender and pre-conditions. Dotted line represents the limit of detection (S/CO=1.1) of the assay. **a, b** and **c** Statistical analysis was performed using Kruskal-Wallis and Mann-Whitney tests.

Extended Data Figure 4



Extended Data Figure 4: Statistical predication of SARS-CoV-2 antibody responses
a, multiple linear regression model and model coefficients for predicting serum neutralization using the features: Euroimmun S/CO, gender, age, disease severity, pre-conditions, weeks since infection and the 9 reported symptoms. **b**, Bayesian network of the features predicting serum ID50 are plotted using the bnlearn R package. The graph connects the features which are predictive of each other with serum ID50 as sink. **c** and **d**, Multiple linear regression model for predicting IgG and IgA ratios using the features: gender, age, disease severity, pre-conditions, weeks since infection and the 9 reported symptoms. Plots on the right depicts model coefficients to study the goodness of fit of the corresponding final models. Spearman correlation plot for diagnostic naso-/oro-pharyngeal swab Ct values for E-gene (**e**) or N-gene (**f**) vs. IgG IC50, serum ID50, anti-spike IgG and anti-spike IgA values at study visit 1.

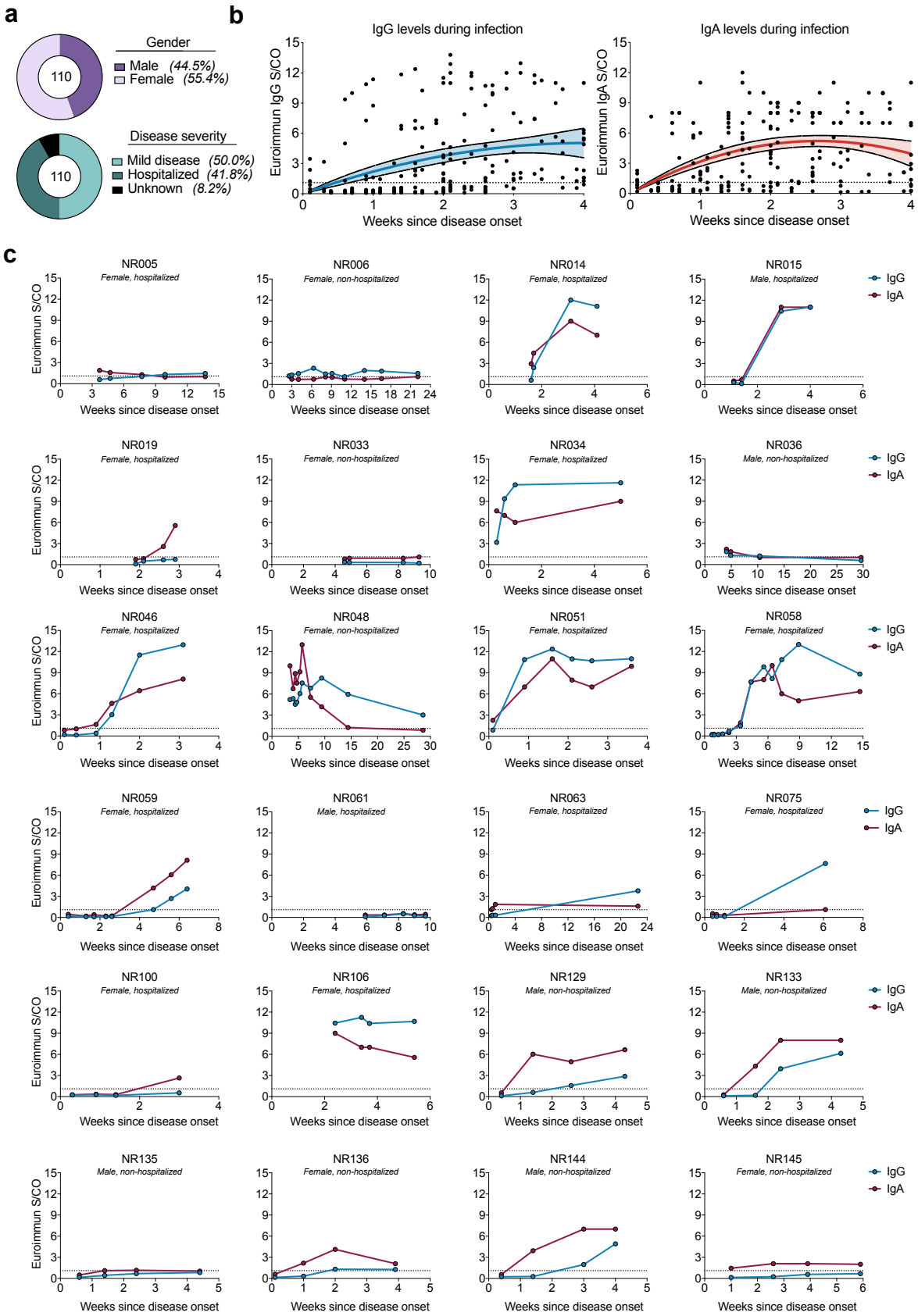
Extended Data Figure 5



Extended Data Figure 5: Neutralization of different strains by SARS-CoV-2 elite-neutralizers

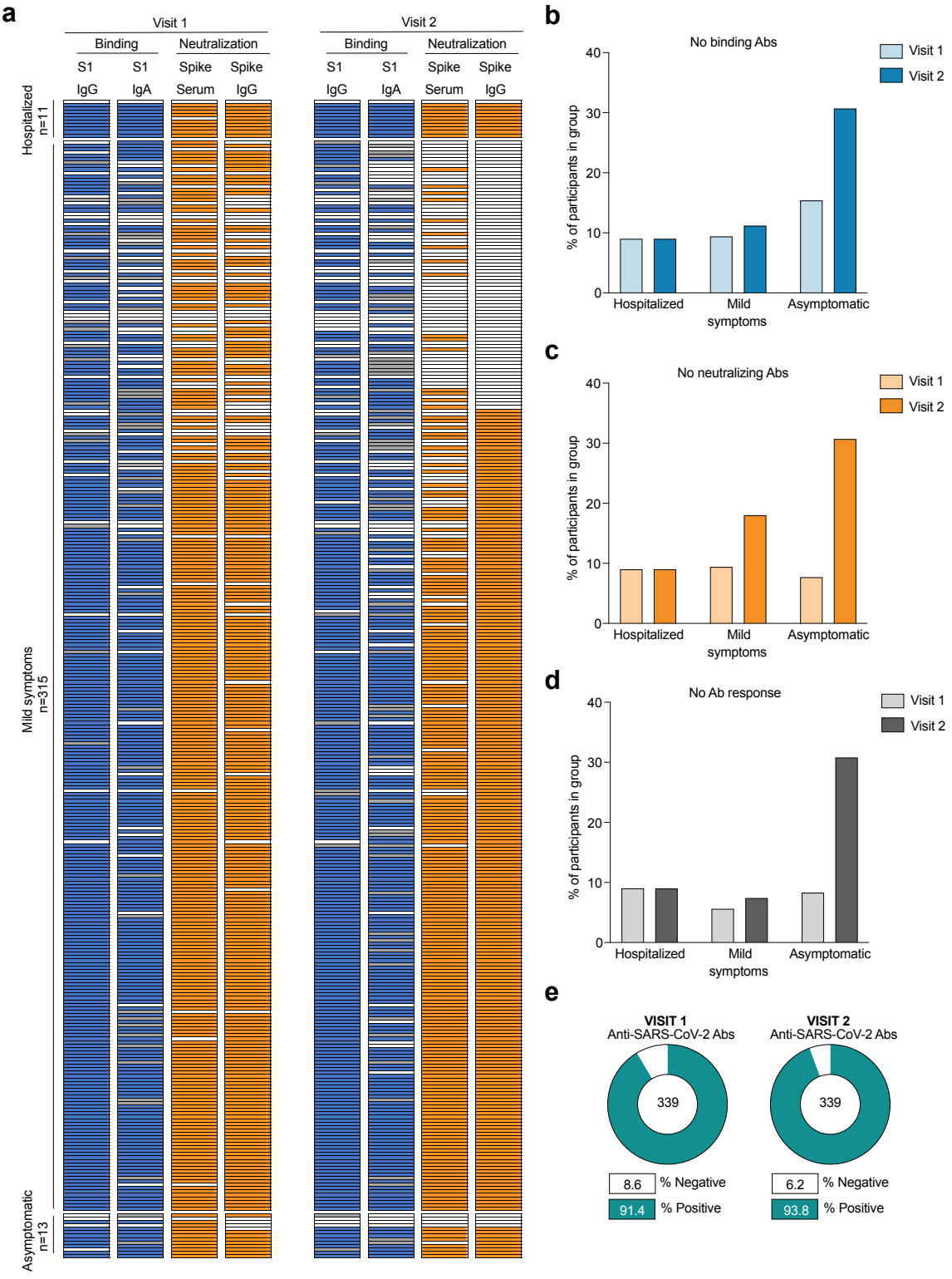
a, plots for the distribution of gender, age and time since infection for the 15 individuals selected randomly from the five IgG neutralization categories: elite-, high-, average-, low-, and non-neutralizers (n=75 total). Statistical testing performed with Kruskal-Wallis test using Dunn's multiple comparisons. ***b***, Spearman correlation of IgG IC50 against SARS-2-S pseudovirus and SARS-2 authentic virus. **c**, Relative infectivity of SARS-CoV-2 global strain pseudovirus in 293T-ACE2 cells. **d**, Sequence alignment of the spike amino acid sequence of the 6 global SARS-CoV-2 strains and SARS-1 used for pseudovirus neutralization assays in this study.

Extended data figure 6



Extended Data Figure 6: Antibody kinetics in the early phase of SARS-CoV-2 infection
a, Pie charts indicating distribution of gender and disease severity in individuals who were longitudinally monitored starting from the early phase of infection. **b**, Plots depicting IgG and IgA ratios over time in individuals (n=107). Dotted line represents the limit of detection (S/CO=1.1) of the Euroimmun ELISA. Statistical analysis was performed using a second order polynomial quadratic equation (R2=0.128 for IgG and R2=0.140 for IgA) with 95% confidence interval shading (IgG in blue and IgA in red) of the best line. **c**, Individual plots depicting IgG (blue) and IgA (red) levels over time. Gender and disease severity are indicated within each plot. Dotted line represents the limit of detection (S/CO=1.1) of the Euroimmun ELISA.

Extended data figure 7



Extended Data Figure 7: Changes in Ab response against SARS-CoV-2 over time
a, plot depicting SARS-CoV-2 S1 binding and Wu01 pseudovirus neutralization of 339 individuals at visit 1 and visit 2 with each row representing 1 individual. Bar graphs showing change in fraction of individuals negative for anti-spike Abs (**b**), anti-spike NAbs (**c**) or any Ab response (**d**). **e**, pie chart evaluating the total presence if Ab response between visit 1 and 2 for all individuals.

Supplementary Table 1:Study cohort demographics, clinical information and antibody measurements

Study cohort

Study cohort demographics ***n=963***

Gender		Age	
Male	**Female**	**Median**	**Range**
(n=) / (%)	*(n=) / (%)*	*(years)*	*(years)*
444 / 46.1%	519 / 53.9%	44	18-79

Study cohort clinical information

Asymptomatic	**Symptomatic**	**Unknown**
(n=) / (%)	*(n=) / (%)*	*(n=) / (%)*
44 / 4.5%	911 / 94.6%	8 / 0.8%

Fever	**Cough**	**Sore throat**	**Rhinitis**	**Muscle ache**	**Headache**	**Diarrhea**	**Change in taste**	**Change in smell**
(n=) / (%)	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*
428 / 44.4%	613 / 63.7%	353 / 36.7%	332 / 34.5%	508 / 52.8%	507 / 52.6%	182 / 18.9%	563 / 58.5%	517 / 53.7%

Not hospitalized	**Hospitalized**	**ICU**	**Unknown**
(n=) / (%)	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*
927 / 96.3%	28 / 2.9%	7 / 0.7%	8 / 0.8%

Pre-conditions	**No pre-conditions**	**Unknown**
(n=) / (%)	*(n=) / (%)*	*(n=) / (%)*
224 / 23.3%	695 / 72.2%	44 / 4.6%

Respiratory	**Heart**	**Kidney**	**Clotting**	**Cancer**	**Diabetes**	**Hypertension**	**Auto-immune**	**Other**
(n=) / (%)	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*	*(n=) / (%)*
53 / 5.5%	14 / 1.5%	5 / 0.5%	11 / 1.1%	24 / 2.5%	12 / 1.2%	73 / 7.6%	33 / 3.4%	33 / 3.4 %

Study Visit 1

Neutralization analyse ***n=963***

Time since disease onset	Serum/plasma ID50				Total IgG IC50			
Median	**Geo. Mean**	**Range**	**Neutralizer**	**Non-neutralizer**	**Geo. Mean**	**Range**	**Neutralizer**	**Non-neutralizer**
(weeks)	*(dilution)*	*(dilution)*	*(n=)*	*(n=)*	*(ug/ml)*	*(ug/ml)*	*(n=)*	*(n=)*
7.3	111,3	10-90092	793	170	161	0.7-745.6	760	203

ELISA analyses ***n=963***

Time since disease onset	IgG				IgA			
Median	**Geo. Mean**	**Pos**	**Neg**	**Equivocal**	**Geo. Mean**	**Pos**	**Neg**	**Equivocal**
(weeks)	*(S/CO)*	*(n=)*	*(n=)*	*(n=)*	*(S/CO)*	*(n=)*	*(n=)*	*(n=)*
7.3	4,1	797	122	44	3,0	676	189	98

Study Visit 2

Neutralization analyse ***n=342***

Time since disease onset	Serum/plasma ID50				Total IgG IC50			
Median	**Geo. Mean**	**Range**	**Neutralizer**	**Non-neutralizer**	**Geo. Mean**	**Range**	**Neutralizer**	**Non-neutralizer**
(weeks)	*(dilution)*	*(dilution)*	*(n=)*	*(n=)*	*(ug/ml)*	*(ug/ml)*	*(n=)*	*(n=)*
17,3	64,3	10-5826	241	101	186,2	13.6-750	256	86

ELISA analyses ***n=616***

Time since disease onset	IgG			
Median	**Geo. Mean**	**Pos**	**Neg**	**Equivocal**
(weeks)	*(S/CO)*	*(n=)*	*(n=)*	*(n=)*
18,8	3,4	479	100	37

Study Visit 3

ELISA analyses ***n=430***

Time since disease onset	IgG			
Median	**Geo. Mean**	**Pos**	**Neg**	**Equivocal**
(weeks)	*(S/CO)*	*(n=)*	*(n=)*	*(n=)*
30,1	2,9	322	74	35

Study Visit 4

ELISA analyses ***n=137***

Time since disease onset	IgG			
Median	**Geo. Mean**	**Pos**	**Neg**	**Equivocal**
(weeks)	*(S/CO)*	*(n=)*	*(n=)*	*(n=)*
37,9	3,0	100	28	9