Univariate CoR: Nonparametric Threshold Modeling

An extension of the unadjusted nonparametric threshold-searching approach developed in @Donovan, the covariate-adjusted TMLE-based approach developed by van der Laan, Zhang, Gilbert (submitted) is used to estimate the so-called threshold-response function $E_X[E[Y|S \geq s, X, A = 1]|A = 1]$ for a range of thresholds s.Here, X is a set of baseline characteristics, $A = 1$ represents the vaccine group, S is the biomarker/immune-response/correlate of interest, and Y is the indicator of COVID disease before some time point t_f. This parameter can be viewed as a causal version of the parameter $P(Y = 1|S \geq s, A = 1)$ Intuitively, the threshold-response at a given threshold is the expected probability of obtaining COVID disease if one experiences a marker/immune-response value above that threshold. The threshold-response function is estimated for each of the four Day 57 antibody markers, in each case adjusting for the baseline covariates: baseline risk score, high risk indicator, and underrepresented minority status.A parametric learner, selected via cross-validation, is used for the covariate adjustment. A number of plots and tables are reported: 1. A plot and table with risk estimates and point-wise 95% confidence intervals for the threshold-response at a grid of thresholds. 2. A plot and table with risk estimates and simultaneous 95% confidence bands for the threshold-response at a grid of thresholds.

A reverse cumulative distribution function curve estimated by the IPW NPMLE of the marker values is superimposed on the threshold-response plots and a dashed red line is added to mark the threshold value after which no more events are observed.

Plots and Tables with estimates and pointwise confidence interval for Day 57

Day 57 Spike protein binding antibody

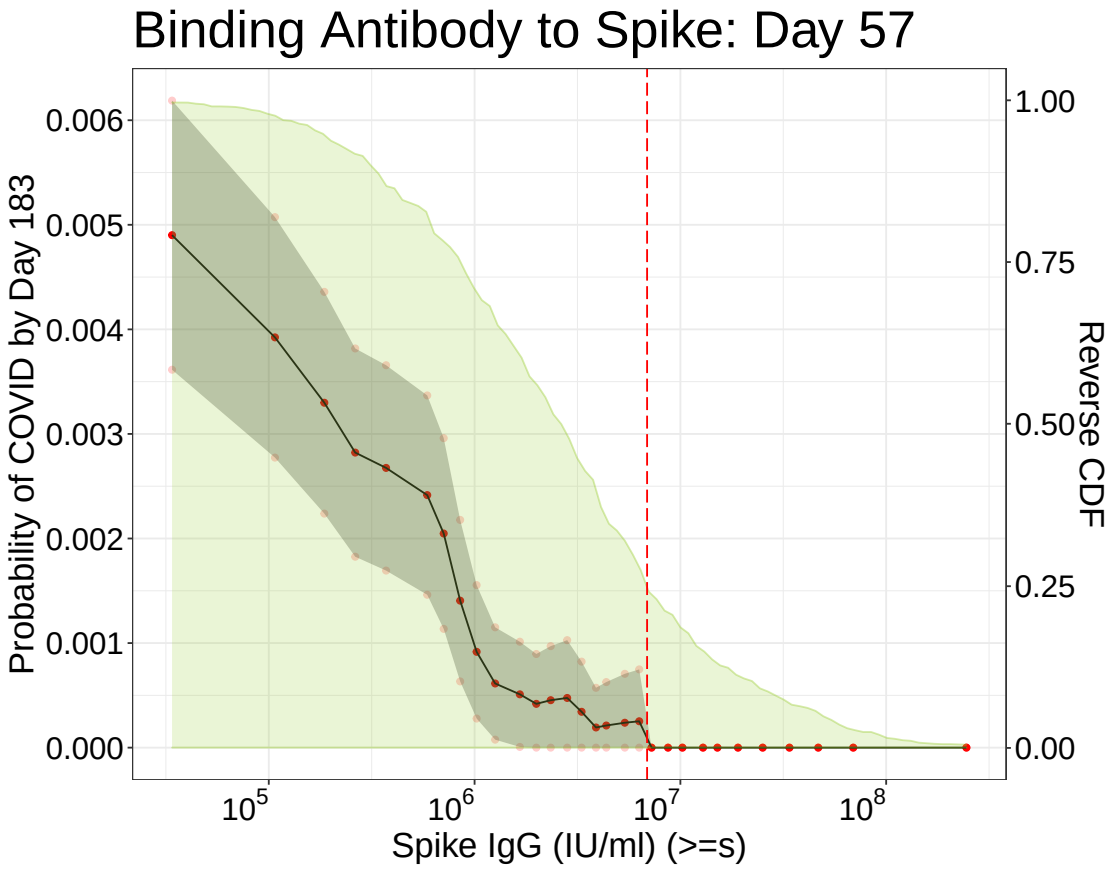

Figure 1: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1: Table of risk estimates for a range of thresholds of Day 57 Spike protein binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.530	$3.39 * 10^4$	0.00490	0.00361	0.00619
5.420	$2.63 * 10^5$	0.00282	0.00183	0.00382
5.851	$7.10 * 10^5$	0.00205	0.00114	0.00296
6.218	$1.65 * 10^6$	0.00051	0.00001	0.00101
6.453	$2.84 * 10^6$	0.00048	0.00000	0.00103
6.644	$4.41 * 10^6$	0.00021	0.00000	0.00063
6.864	$7.31 * 10^6$	0.00000	0.00000	NA
7.185	$1.53 * 10^7$	0.00000	0.00000	NA
7.525	$3.35 * 10^7$	0.00000	0.00000	NA
8.391	$2.46 * 10^8$	0.00000	0.00000	NA

Day 57 RBD binding antibody

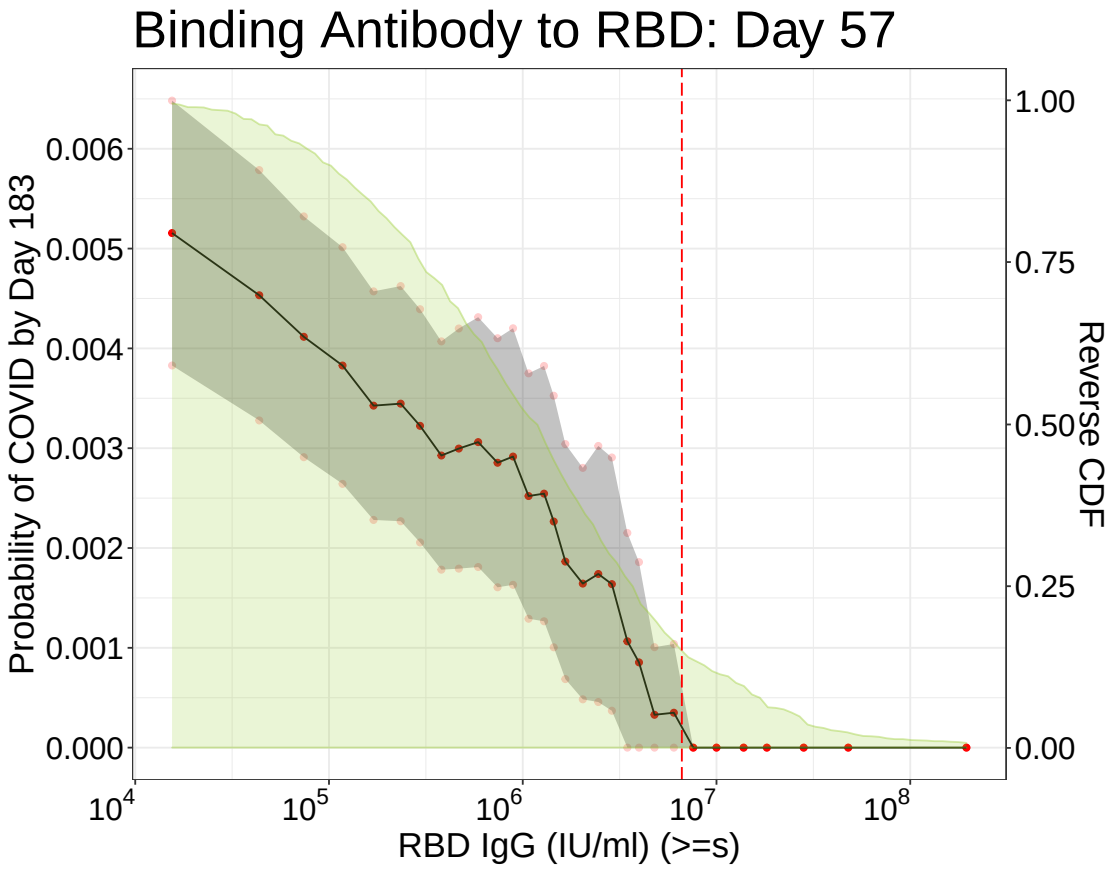

Figure 2: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 2: Table of risk estimates for a range of thresholds of Day 57 RBD binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.185	$1.53 * 10^4$	0.00516	0.00383	0.00648
5.070	$1.17 * 10^5$	0.00383	0.00264	0.00501
5.466	$2.92 * 10^5$	0.00322	0.00206	0.00439
5.865	$7.33 * 10^5$	0.00285	0.00161	0.00410
6.107	$1.28 * 10^6$	0.00254	0.00127	0.00382
6.309	$2.04 * 10^6$	0.00164	0.00048	0.00280
6.541	$3.48 * 10^6$	0.00107	0.00000	0.00215
6.879	$7.57 * 10^6$	0.00000	0.00000	NA
7.262	$1.83 * 10^7$	0.00000	0.00000	NA
8.291	$1.95 * 10^8$	0.00000	0.00000	NA

Day 57 Pseudo virus-neutralizing antibody (50% titer)

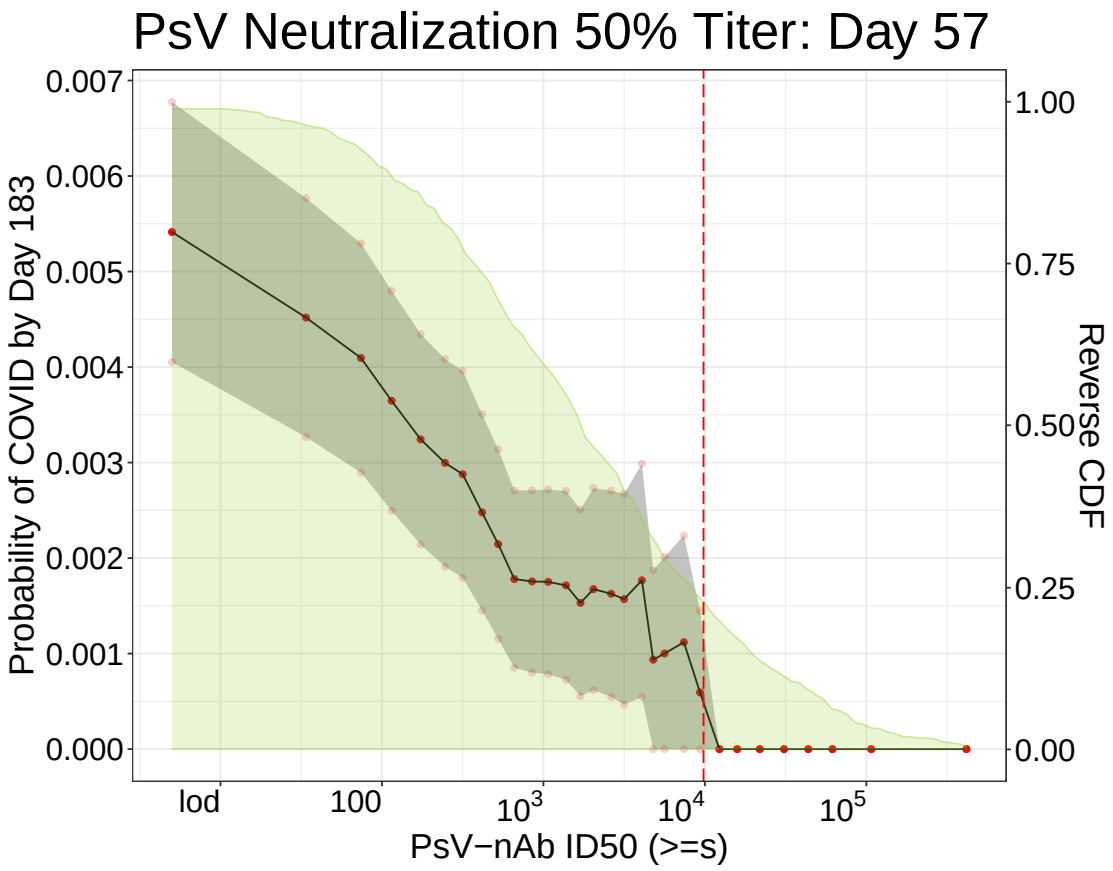

Figure 3: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 3: Table of risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00541	0.00405	0.00677
2.057	$1.14 * 10^2$	0.00365	0.00249	0.00480
2.499	$3.16 * 10^2$	0.00288	0.00179	0.00396
2.929	$8.49 * 10^2$	0.00176	0.00080	0.00271
3.230	$1.70 * 10^3$	0.00153	0.00055	0.00251
3.501	$3.17 * 10^3$	0.00157	0.00047	0.00267
3.747	$5.58 * 10^3$	0.00100	0.00000	0.00201
4.200	$1.58 * 10^4$	0.00000	0.00000	NA
4.636	$4.33 * 10^4$	0.00000	0.00000	NA
5.620	$4.17 * 10^5$	0.00000	0.00000	NA

Day 57 Pseudo virus-neutralizing antibody (80% titer)

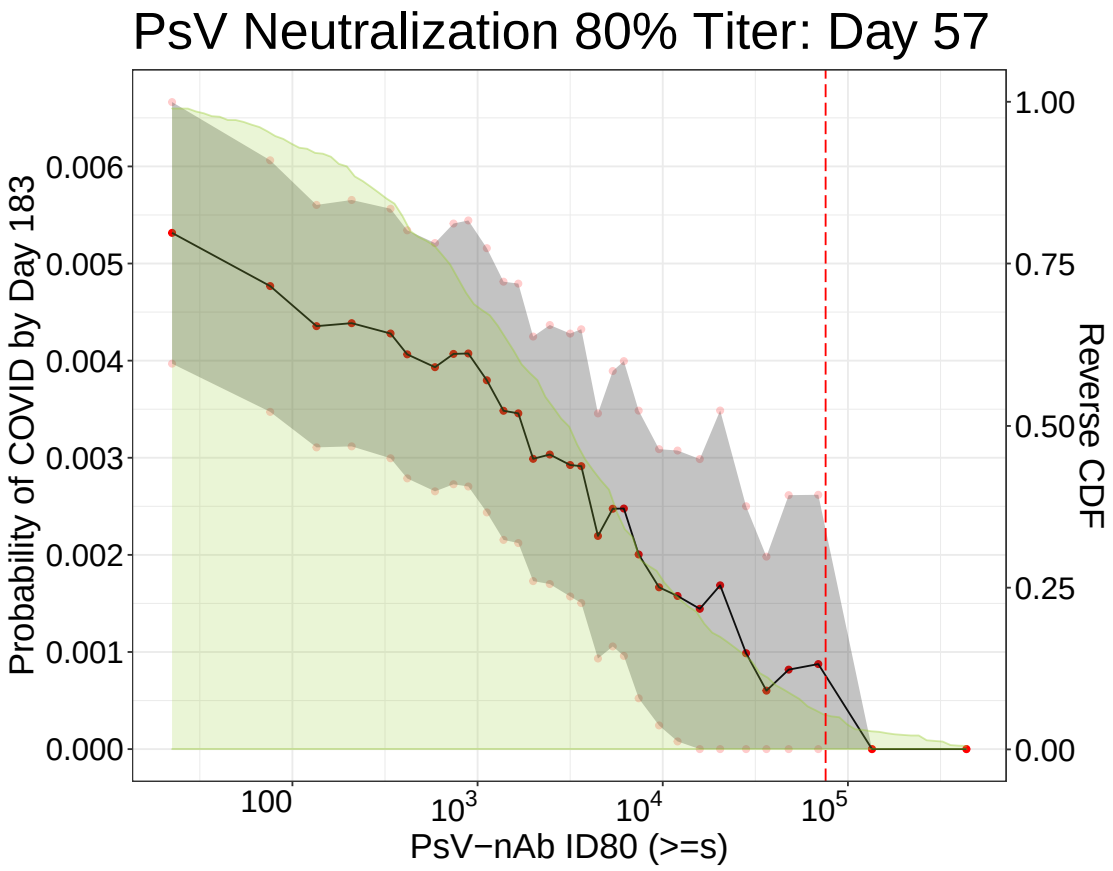

Figure 4: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4: Table of risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	$2.25 * 10^1$	0.00532	0.00397	0.00666
2.319	$2.08 * 10^2$	0.00439	0.00312	0.00565
2.772	$5.92 * 10^2$	0.00393	0.00265	0.00521
3.136	$1.37 * 10^3$	0.00348	0.00215	0.00481
3.395	$2.48 * 10^3$	0.00303	0.00170	0.00437
3.652	$4.49 * 10^3$	0.00219	0.00093	0.00346
3.875	$7.50 * 10^3$	0.00200	0.00052	0.00349
4.314	$2.06 * 10^4$	0.00169	0.00000	0.00349
4.685	$4.84 * 10^4$	0.00082	0.00000	0.00261
5.644	$4.41 * 10^5$	0.00000	0.00000	NA

Plots and Tables with estimates and pointwise confidence intervals for Day 29

Day 29 Spike protein antibody

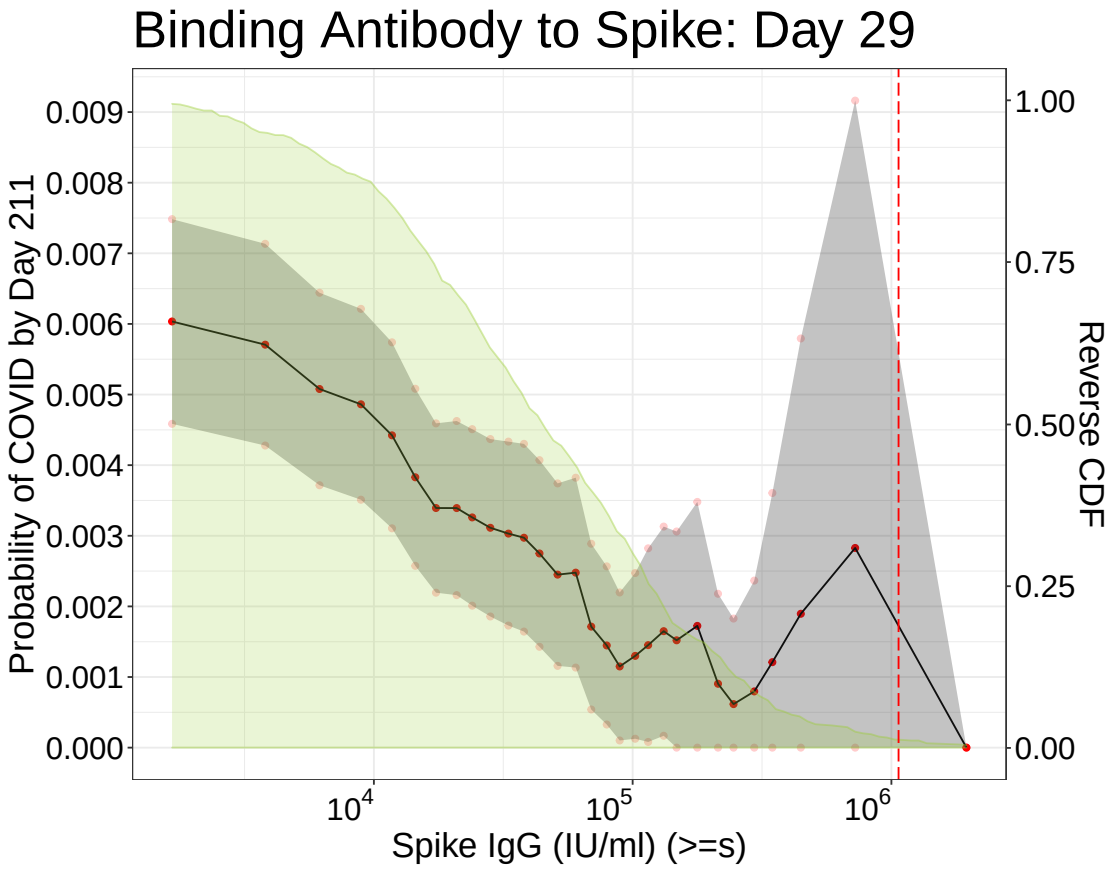

Figure 5: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 5: Table of risk estimates for a range of thresholds of Day 29 Spike protein antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
3.220	$1.66 * 10^3$	0.00603	0.00459	0.00748
3.954	$8.99 * 10^3$	0.00486	0.00351	0.00621
4.244	$1.75 * 10^4$	0.00339	0.00219	0.00459
4.522	$3.33 * 10^4$	0.00303	0.00173	0.00433
4.707	$5.09 * 10^4$	0.00245	0.00116	0.00374
4.899	$7.93 * 10^4$	0.00145	0.00033	0.00257
5.060	$1.15 * 10^5$	0.00145	0.00008	0.00282
5.327	$2.12 * 10^5$	0.00090	0.00000	0.00218
5.542	$3.48 * 10^5$	0.00121	0.00000	0.00361
6.285	$1.93 * 10^6$	0.00000	0.00000	NA

Day 29 RBD binding antibody

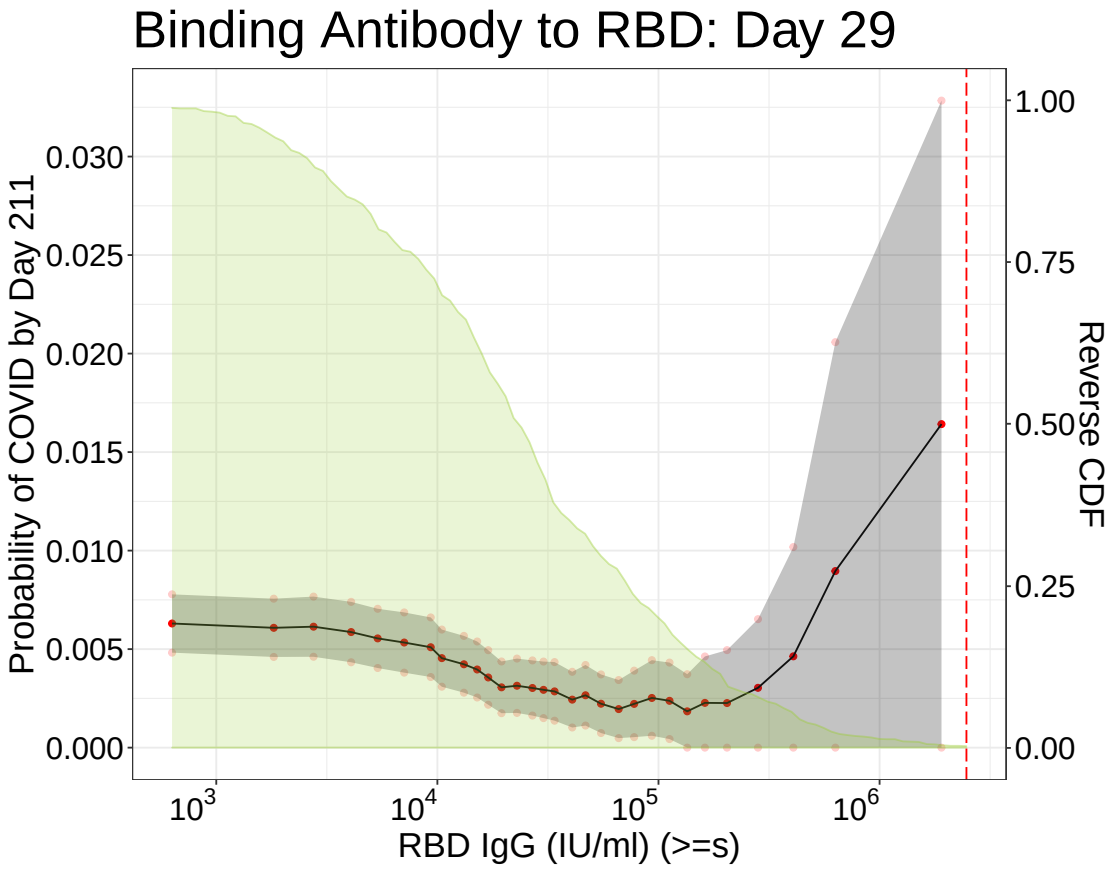

Figure 6: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 6: Table of risk estimates for a range of thresholds of Day 29 RBD binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
2.802	$6.34 * 10^2$	0.00630	0.00482	0.00778
3.605	$4.03 * 10^3$	0.00587	0.00433	0.00740
3.969	$9.31 * 10^3$	0.00510	0.00358	0.00661
4.233	$1.71 * 10^4$	0.00356	0.00218	0.00495
4.430	$2.69 * 10^4$	0.00303	0.00163	0.00443
4.606	$4.04 * 10^4$	0.00244	0.00102	0.00385
4.816	$6.55 * 10^4$	0.00196	0.00048	0.00343
5.131	$1.35 * 10^5$	0.00184	0.00000	0.00373
5.449	$2.81 * 10^5$	0.00304	0.00000	0.00652
6.281	$1.91 * 10^6$	0.01642	0.00000	0.04845

Day 29 Pseudo virus-neutralizing antibody (50% titer)

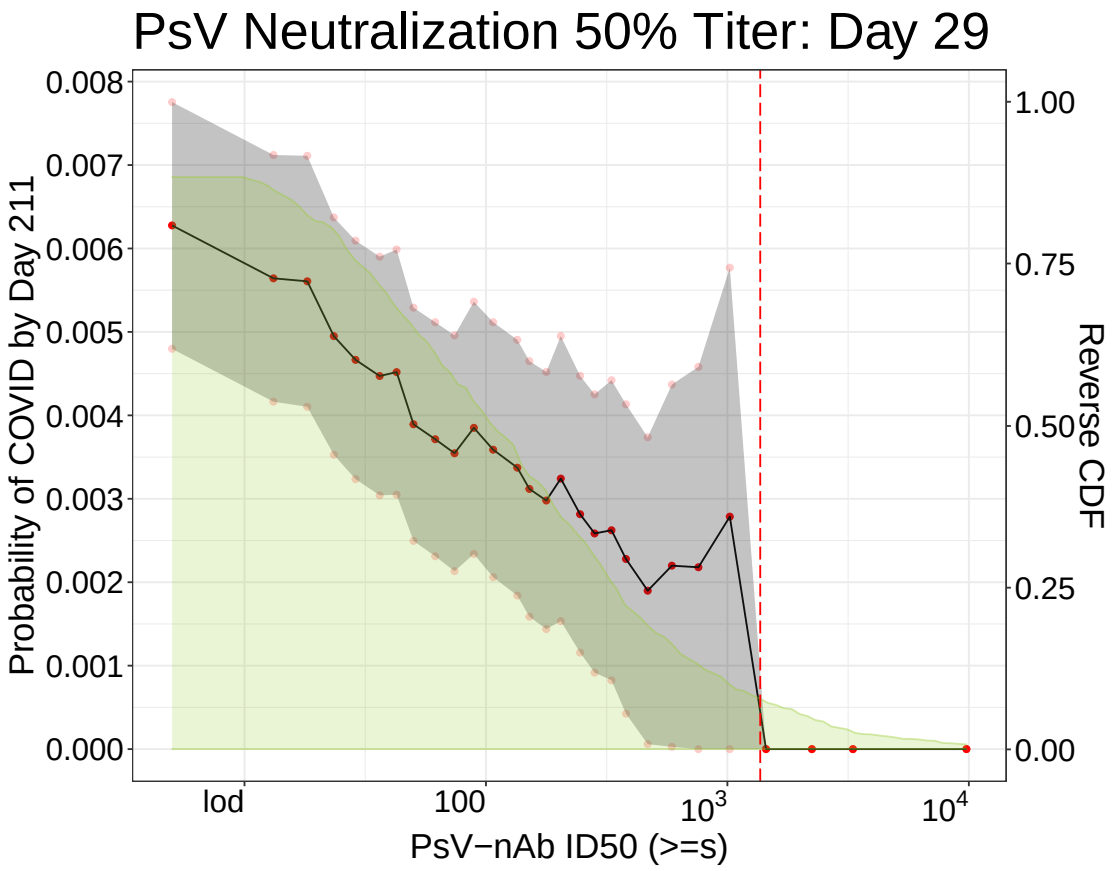

Figure 7: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 7: Table of risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00628	0.00480	0.00775
1.368	$2.33 * 10^1$	0.00495	0.00353	0.00637
1.631	$4.28 * 10^1$	0.00452	0.00305	0.00599
1.874	$7.48 * 10^1$	0.00355	0.00213	0.00496
2.127	$1.34 * 10^2$	0.00337	0.00184	0.00491
2.313	$2.06 * 10^2$	0.00324	0.00153	0.00495
2.524	$3.34 * 10^2$	0.00262	0.00082	0.00442
2.773	$5.93 * 10^2$	0.00220	0.00003	0.00437
3.165	$1.46 * 10^3$	0.00000	0.00000	NA
3.989	$9.75 * 10^3$	0.00000	0.00000	NA

Day 29 Pseudo virus-neutralizing antibody (80% titer)

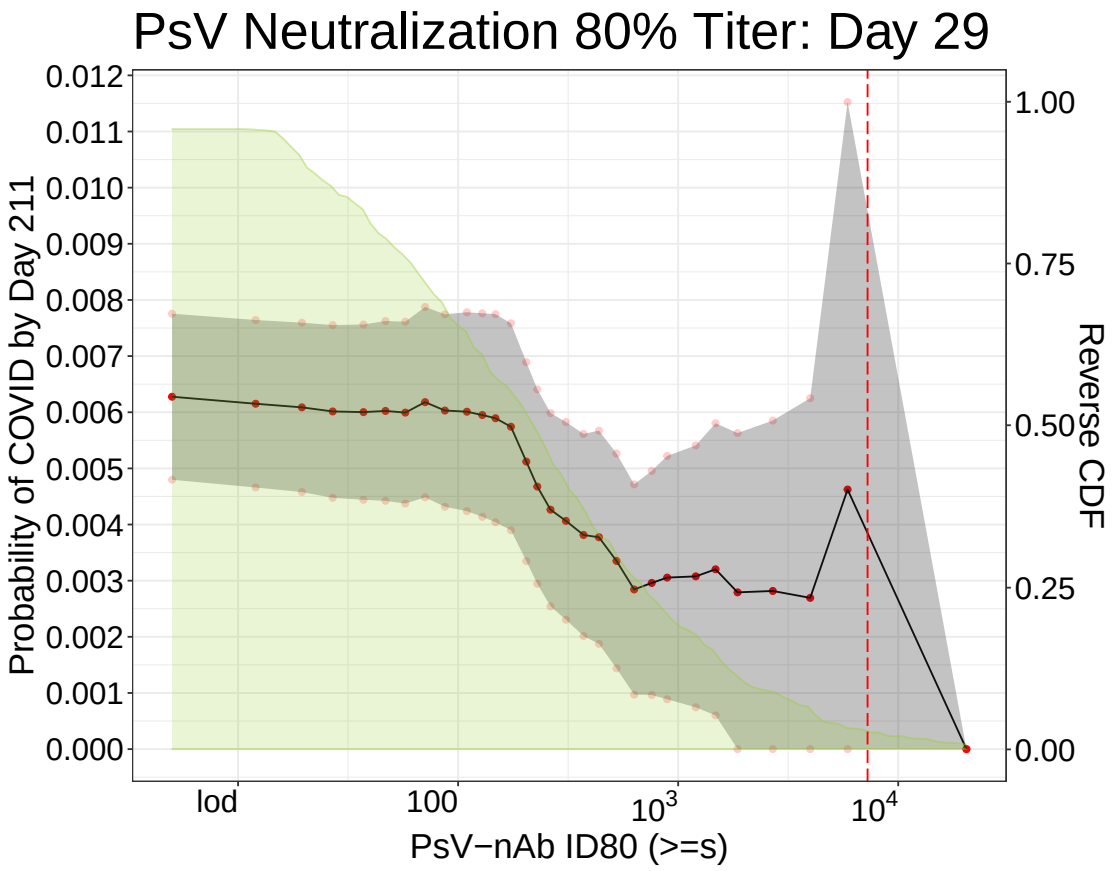

Figure 8: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 8: Table of risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00628	0.00480	0.00775
1.427	$2.67 * 10^1$	0.00601	0.00448	0.00755
1.761	$5.77 * 10^1$	0.00599	0.00437	0.00761
2.113	$1.30 * 10^2$	0.00595	0.00414	0.00776
2.310	$2.04 * 10^2$	0.00512	0.00335	0.00689
2.486	$3.06 * 10^2$	0.00406	0.00230	0.00583
2.724	$5.30 * 10^2$	0.00335	0.00144	0.00526
3.075	$1.19 * 10^3$	0.00308	0.00074	0.00541
3.426	$2.67 * 10^3$	0.00282	0.00000	0.00585
4.305	$2.02 * 10^4$	0.00000	0.00000	NA

Plots and Tables with estimates and pointwise confidence interval for Day 57 (monotone-corrected)

Day 57 Spike protein binding antibody

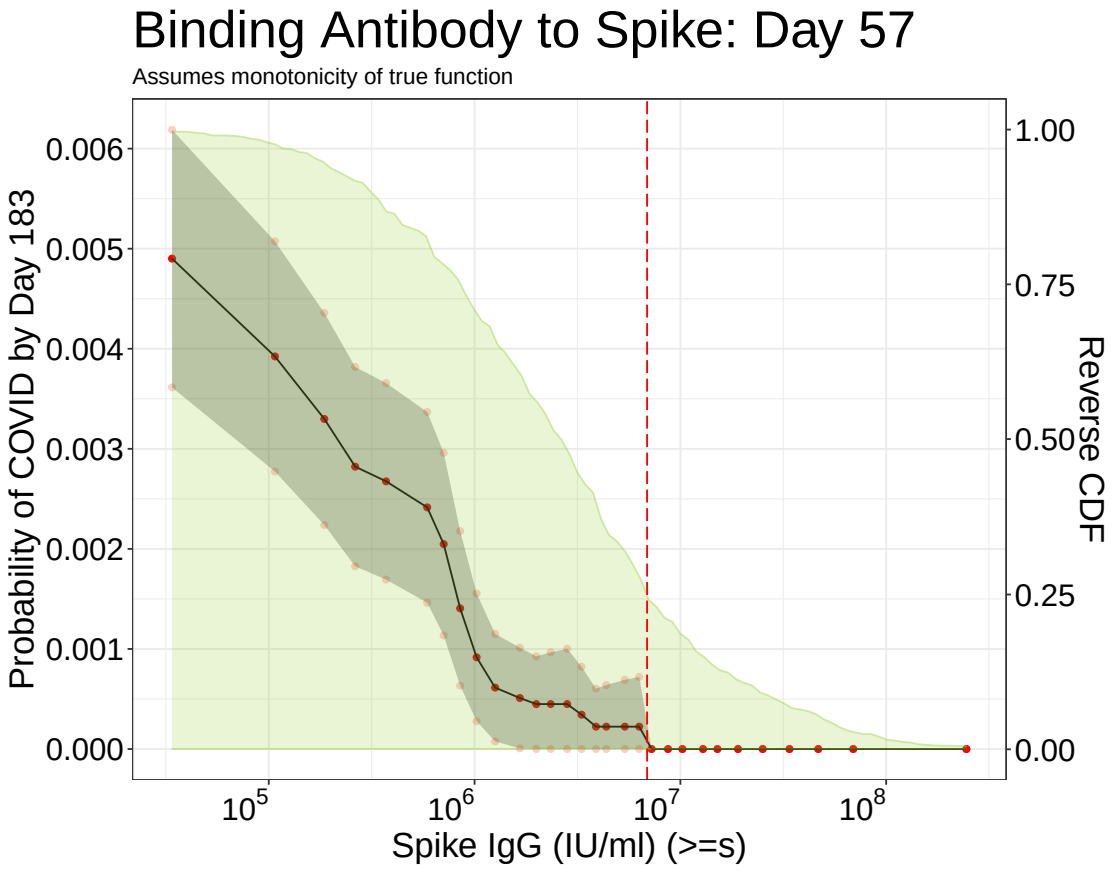

Figure 9: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 9: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Spike protein binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.530	$3.39 * 10^4$	0.00490	0.00361	0.00619
5.420	$2.63 * 10^5$	0.00282	0.00183	0.00382
5.851	$7.10 * 10^5$	0.00205	0.00114	0.00296
6.218	$1.65 * 10^6$	0.00051	0.00001	0.00101
6.453	$2.84 * 10^6$	0.00045	0.00000	0.00100
6.644	$4.41 * 10^6$	0.00022	0.00000	0.00064
6.864	$7.31 * 10^6$	0.00000	0.00000	NA
7.185	$1.53 * 10^7$	0.00000	0.00000	NA
7.525	$3.35 * 10^7$	0.00000	0.00000	NA
8.391	$2.46 * 10^8$	0.00000	0.00000	NA

Day 57 RBD binding antibody

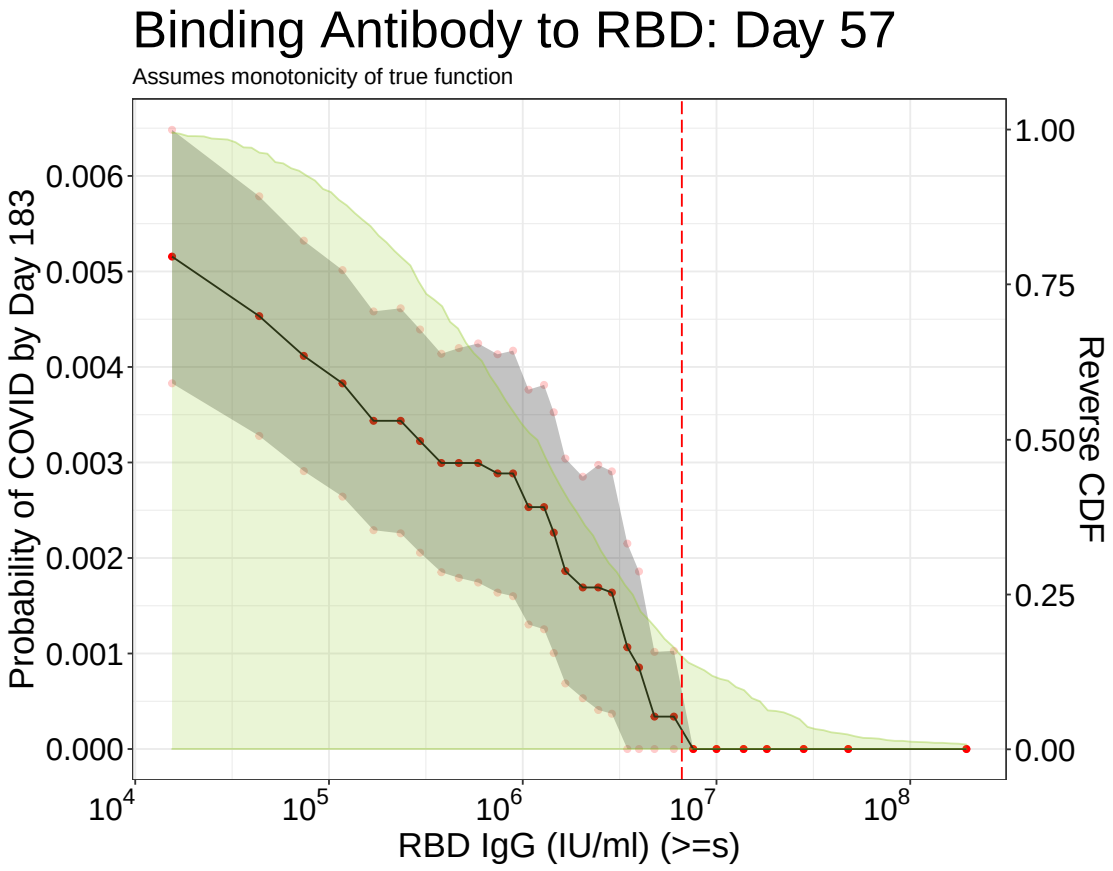

Figure 10: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 10: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 RBD binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.185	$1.53 * 10^4$	0.00516	0.00383	0.00648
5.070	$1.17 * 10^5$	0.00383	0.00264	0.00501
5.466	$2.92 * 10^5$	0.00322	0.00206	0.00439
5.865	$7.33 * 10^5$	0.00289	0.00164	0.00413
6.107	$1.28 * 10^6$	0.00253	0.00125	0.00381
6.309	$2.04 * 10^6$	0.00169	0.00053	0.00285
6.541	$3.48 * 10^6$	0.00107	0.00000	0.00215
6.879	$7.57 * 10^6$	0.00000	0.00000	NA
7.262	$1.83 * 10^7$	0.00000	0.00000	NA
8.291	$1.95 * 10^8$	0.00000	0.00000	NA

Day 57 Pseudo virus-neutralizing antibody (50% titer)

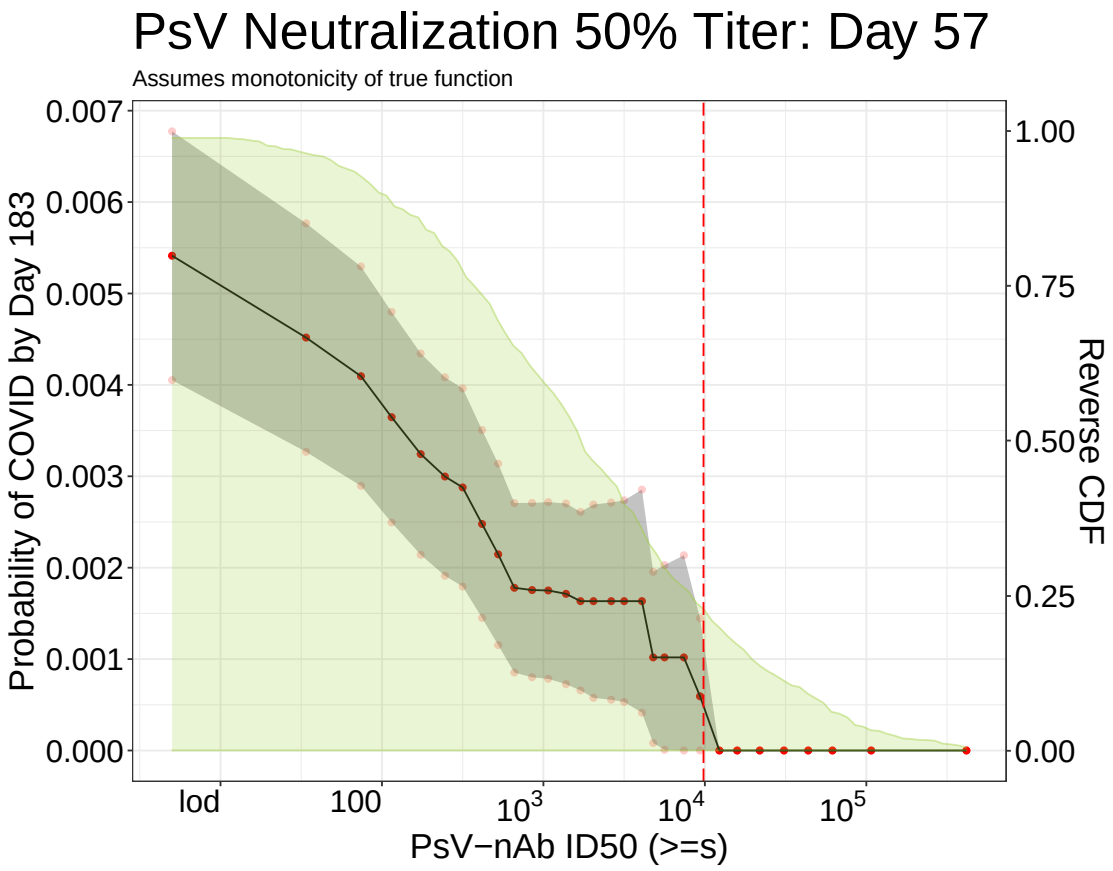

Figure 11: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 11: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00541	0.00405	0.00677
2.057	$1.14 * 10^2$	0.00365	0.00249	0.00480
2.499	$3.16 * 10^2$	0.00288	0.00179	0.00396
2.929	$8.49 * 10^2$	0.00176	0.00080	0.00271
3.230	$1.70 * 10^3$	0.00163	0.00066	0.00261
3.501	$3.17 * 10^3$	0.00163	0.00053	0.00274
3.747	$5.58 * 10^3$	0.00102	0.00001	0.00203
4.200	$1.58 * 10^4$	0.00000	0.00000	NA
4.636	$4.33 * 10^4$	0.00000	0.00000	NA
5.620	$4.17 * 10^5$	0.00000	0.00000	NA

Day 57 Pseudo virus-neutralizing antibody (80% titer)

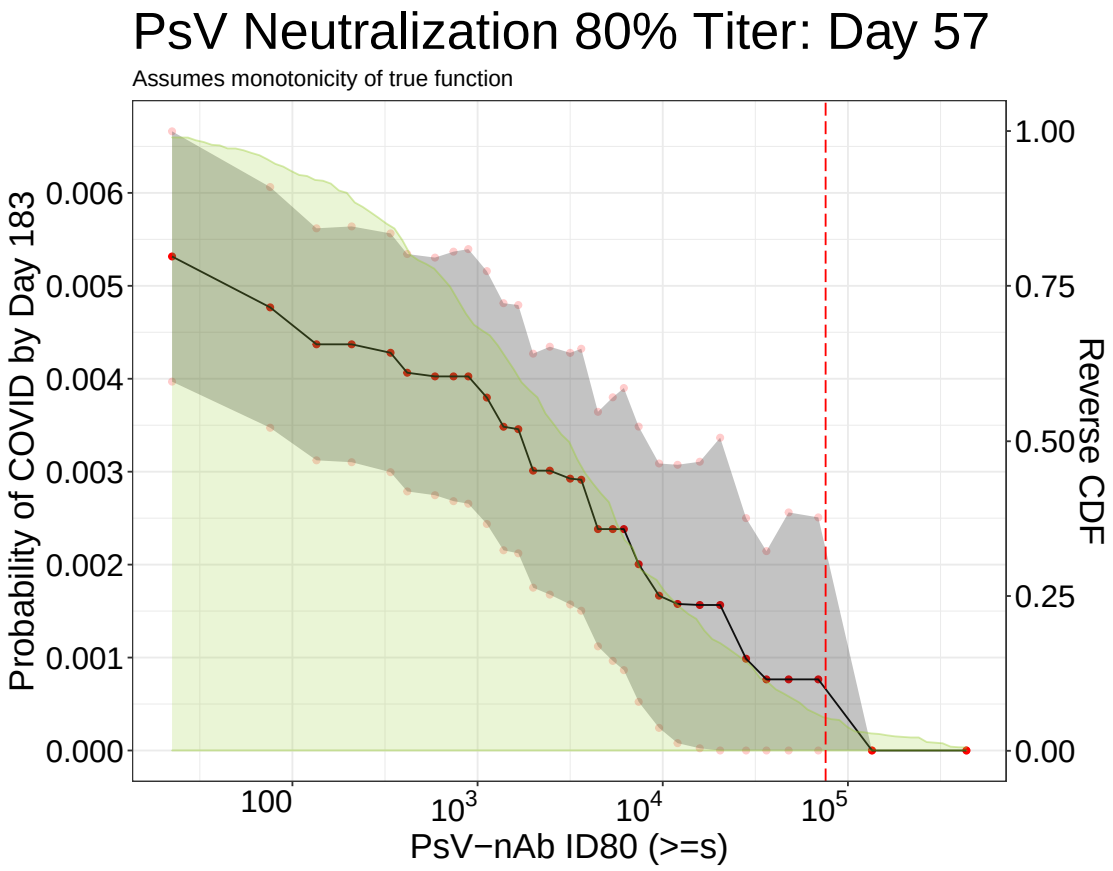

Figure 12: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 12: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	$2.25 * 10^1$	0.00532	0.00397	0.00666
2.319	$2.08 * 10^2$	0.00437	0.00310	0.00564
2.772	$5.92 * 10^2$	0.00403	0.00275	0.00530
3.136	$1.37 * 10^3$	0.00348	0.00215	0.00481
3.395	$2.48 * 10^3$	0.00301	0.00168	0.00434
3.652	$4.49 * 10^3$	0.00238	0.00112	0.00364
3.875	$7.50 * 10^3$	0.00200	0.00052	0.00349
4.314	$2.06 * 10^4$	0.00157	0.00000	0.00337
4.685	$4.84 * 10^4$	0.00077	0.00000	0.00256
5.644	$4.41 * 10^5$	0.00000	0.00000	NA

Plots and Tables with estimates and pointwise confidence intervals for Day 29 (monotone-corrected)

Day 29 Spike protein antibody

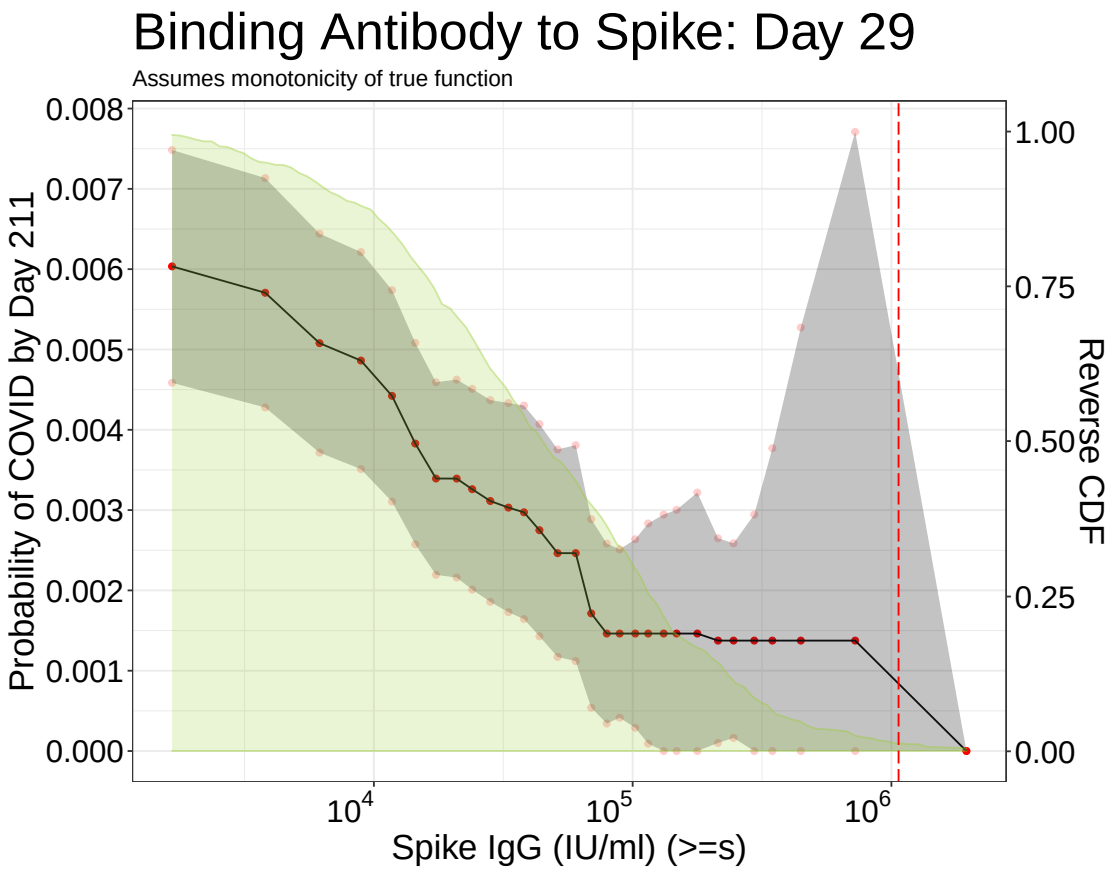

Figure 13: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 13: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Spike protein antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
3.220	$1.66 * 10^3$	0.00603	0.00459	0.00748
3.954	$8.99 * 10^3$	0.00486	0.00351	0.00621
4.244	$1.75 * 10^4$	0.00339	0.00219	0.00459
4.522	$3.33 * 10^4$	0.00303	0.00173	0.00433
4.707	$5.09 * 10^4$	0.00246	0.00117	0.00376
4.899	$7.93 * 10^4$	0.00146	0.00034	0.00258
5.060	$1.15 * 10^5$	0.00146	0.00009	0.00283
5.327	$2.12 * 10^5$	0.00137	0.00010	0.00265
5.542	$3.48 * 10^5$	0.00137	0.00000	0.00377
6.285	$1.93 * 10^6$	0.00000	0.00000	NA

Day 29 RBD binding antibody

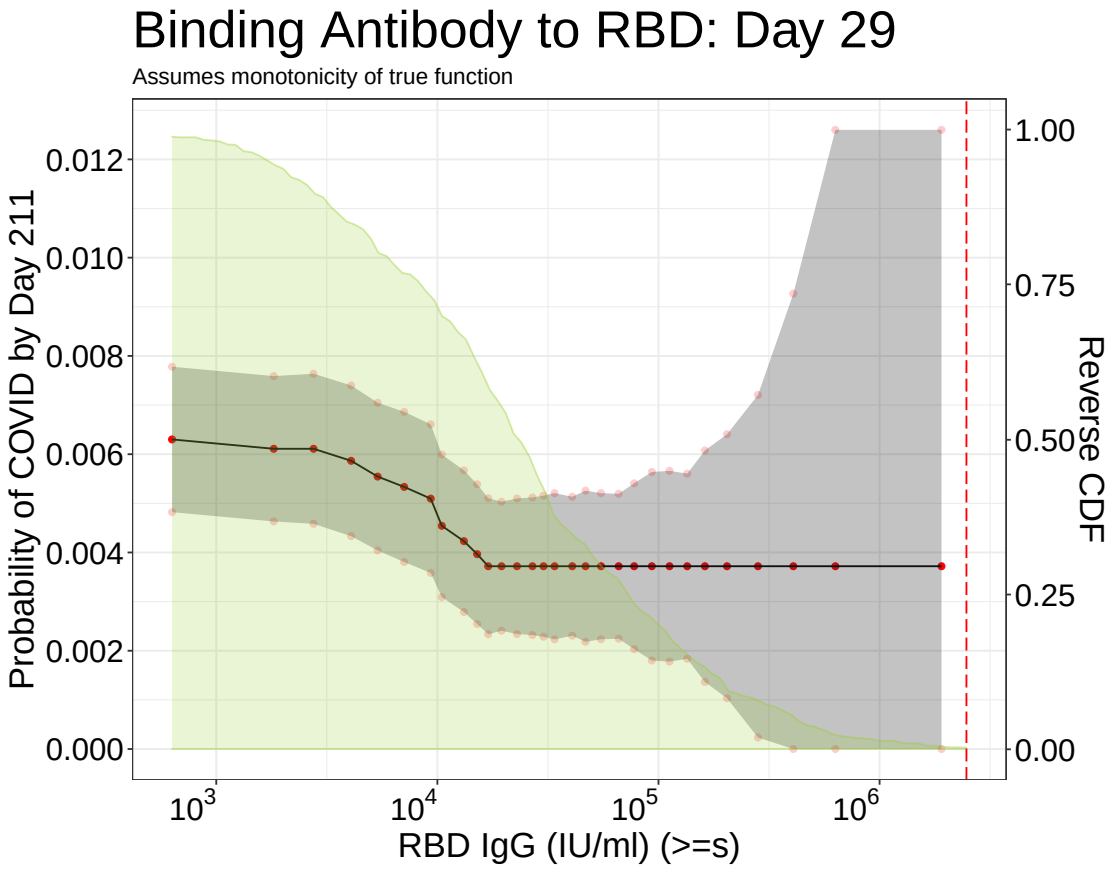

Figure 14: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 14: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 RBD binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
2.802	$6.34 * 10^2$	0.00630	0.00482	0.00778
3.605	$4.03 * 10^3$	0.00587	0.00433	0.00740
3.969	$9.31 * 10^3$	0.00510	0.00358	0.00661
4.233	$1.71 * 10^4$	0.00372	0.00234	0.00510
4.430	$2.69 * 10^4$	0.00372	0.00232	0.00512
4.606	$4.04 * 10^4$	0.00372	0.00231	0.00513
4.816	$6.55 * 10^4$	0.00372	0.00225	0.00519
5.131	$1.35 * 10^5$	0.00372	0.00184	0.00560
5.449	$2.81 * 10^5$	0.00372	0.00023	0.00721
6.281	$1.91 * 10^6$	0.00372	0.00000	0.03575

Day 29 Pseudo virus-neutralizing antibody (50% titer)

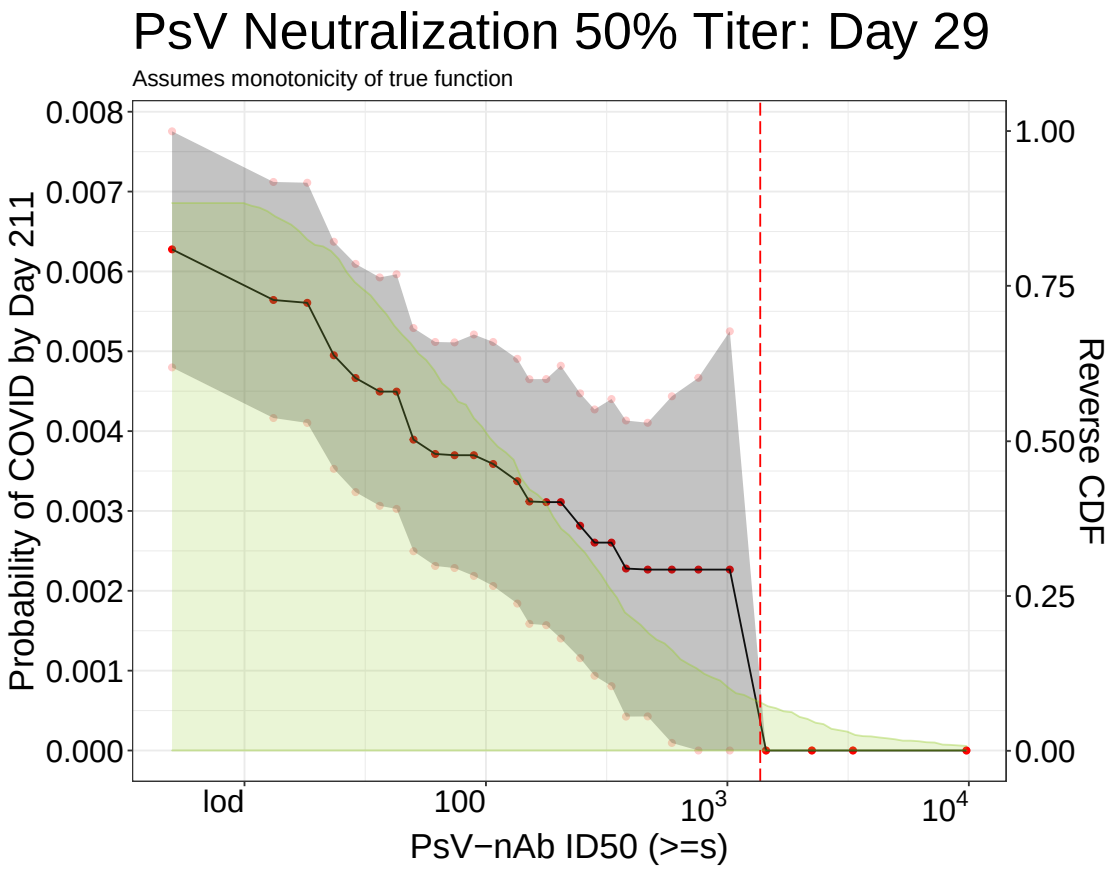

Figure 15: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 15: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00628	0.00480	0.00775
1.368	$2.33 * 10^1$	0.00495	0.00353	0.00637
1.631	$4.28 * 10^1$	0.00449	0.00303	0.00596
1.874	$7.48 * 10^1$	0.00370	0.00229	0.00511
2.127	$1.34 * 10^2$	0.00337	0.00184	0.00491
2.313	$2.06 * 10^2$	0.00311	0.00140	0.00482
2.524	$3.34 * 10^2$	0.00260	0.00081	0.00440
2.773	$5.93 * 10^2$	0.00227	0.00009	0.00444
3.165	$1.46 * 10^3$	0.00000	0.00000	NA
3.989	$9.75 * 10^3$	0.00000	0.00000	NA

Day 29 Pseudo virus-neutralizing antibody (80% titer)

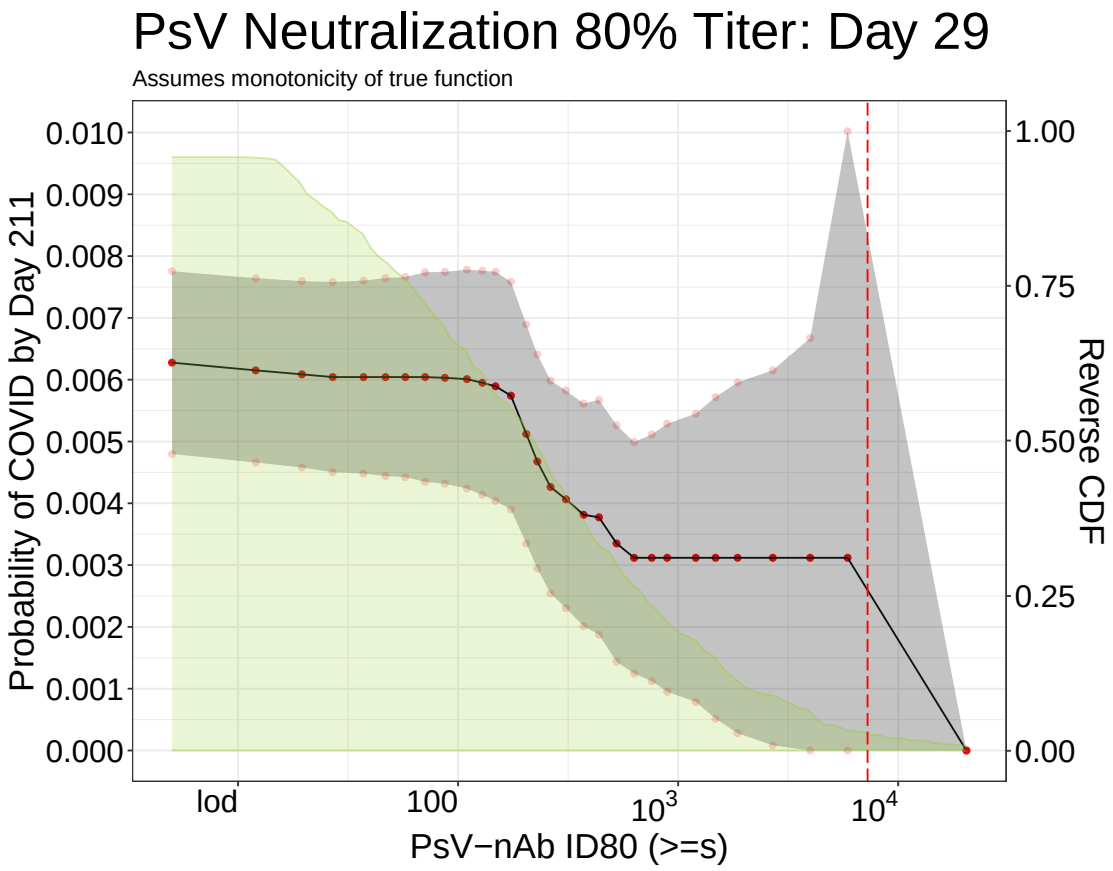

Figure 16: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 16: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00628	0.00480	0.00775
1.427	$2.67 * 10^1$	0.00604	0.00450	0.00758
1.761	$5.77 * 10^1$	0.00604	0.00442	0.00766
2.113	$1.30 * 10^2$	0.00595	0.00414	0.00776
2.310	$2.04 * 10^2$	0.00512	0.00335	0.00689
2.486	$3.06 * 10^2$	0.00406	0.00230	0.00583
2.724	$5.30 * 10^2$	0.00335	0.00144	0.00526
3.075	$1.19 * 10^3$	0.00312	0.00079	0.00545
3.426	$2.67 * 10^3$	0.00312	0.00008	0.00615
4.305	$2.02 * 10^4$	0.00000	0.00000	NA

Plots and Tables with estimates and simultaneous confidence bands for Day 57

Day 57 Spike protein binding antibody

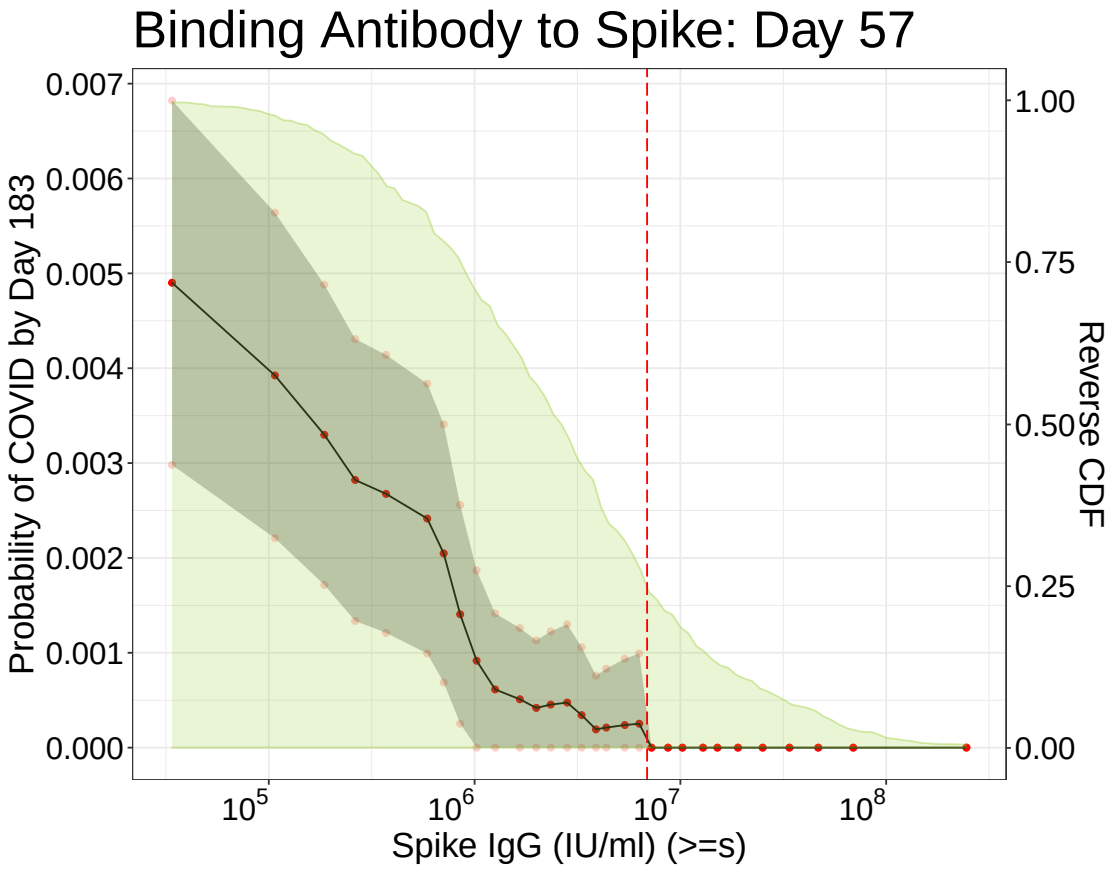

Figure 17: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 17: Table of risk estimates for a range of thresholds of Day 57 Spike protein binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.530	$3.39 * 10^4$	0.00490	0.00298	0.00682
5.420	$2.63 * 10^5$	0.00282	0.00134	0.00431
5.851	$7.10 * 10^5$	0.00205	0.00069	0.00341
6.218	$1.65 * 10^6$	0.00051	0.00000	0.00126
6.453	$2.84 * 10^6$	0.00048	0.00000	0.00130
6.644	$4.41 * 10^6$	0.00021	0.00000	0.00083
6.864	$7.31 * 10^6$	0.00000	0.00000	NA
7.185	$1.53 * 10^7$	0.00000	0.00000	NA
7.525	$3.35 * 10^7$	0.00000	0.00000	NA
8.391	$2.46 * 10^8$	0.00000	0.00000	NA

Day 57 RBD binding antibody

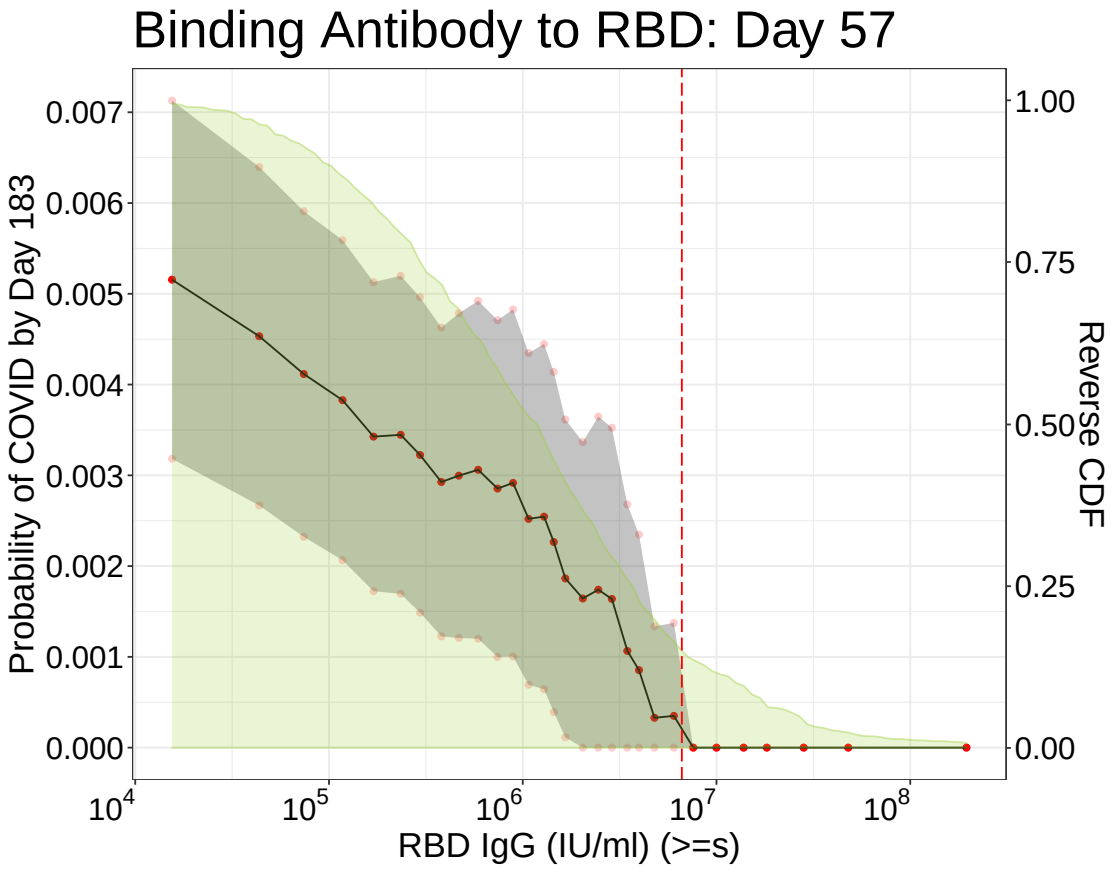

Figure 18: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 18: Table of risk estimates for a range of thresholds of Day 57 RBD binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.185	$1.53 * 10^4$	0.00516	0.00318	0.00713
5.070	$1.17 * 10^5$	0.00383	0.00207	0.00559
5.466	$2.92 * 10^5$	0.00322	0.00149	0.00496
5.865	$7.33 * 10^5$	0.00285	0.00100	0.00471
6.107	$1.28 * 10^6$	0.00254	0.00064	0.00445
6.309	$2.04 * 10^6$	0.00164	0.00000	0.00337
6.541	$3.48 * 10^6$	0.00107	0.00000	0.00268
6.879	$7.57 * 10^6$	0.00000	0.00000	NA
7.262	$1.83 * 10^7$	0.00000	0.00000	NA
8.291	$1.95 * 10^8$	0.00000	0.00000	NA

Day 57 Pseudo virus-neutralizing antibody (50% titer)

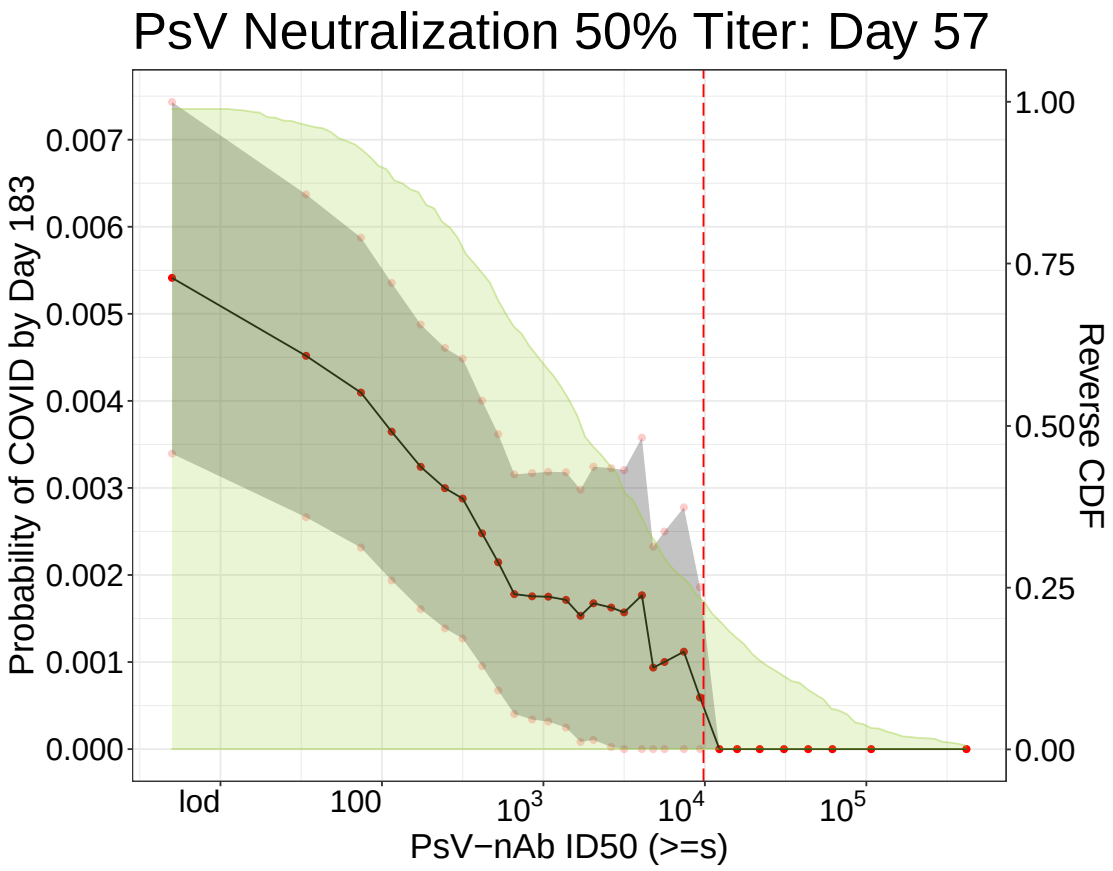

Figure 19: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 19: Table of risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00541	0.00339	0.00743
2.057	$1.14 * 10^2$	0.00365	0.00194	0.00536
2.499	$3.16 * 10^2$	0.00288	0.00127	0.00449
2.929	$8.49 * 10^2$	0.00176	0.00034	0.00317
3.230	$1.70 * 10^3$	0.00153	0.00008	0.00298
3.501	$3.17 * 10^3$	0.00157	0.00000	0.00321
3.747	$5.58 * 10^3$	0.00100	0.00000	0.00250
4.200	$1.58 * 10^4$	0.00000	0.00000	NA
4.636	$4.33 * 10^4$	0.00000	0.00000	NA
5.620	$4.17 * 10^5$	0.00000	0.00000	NA

Day 57 Pseudo virus-neutralizing antibody (80% titer)

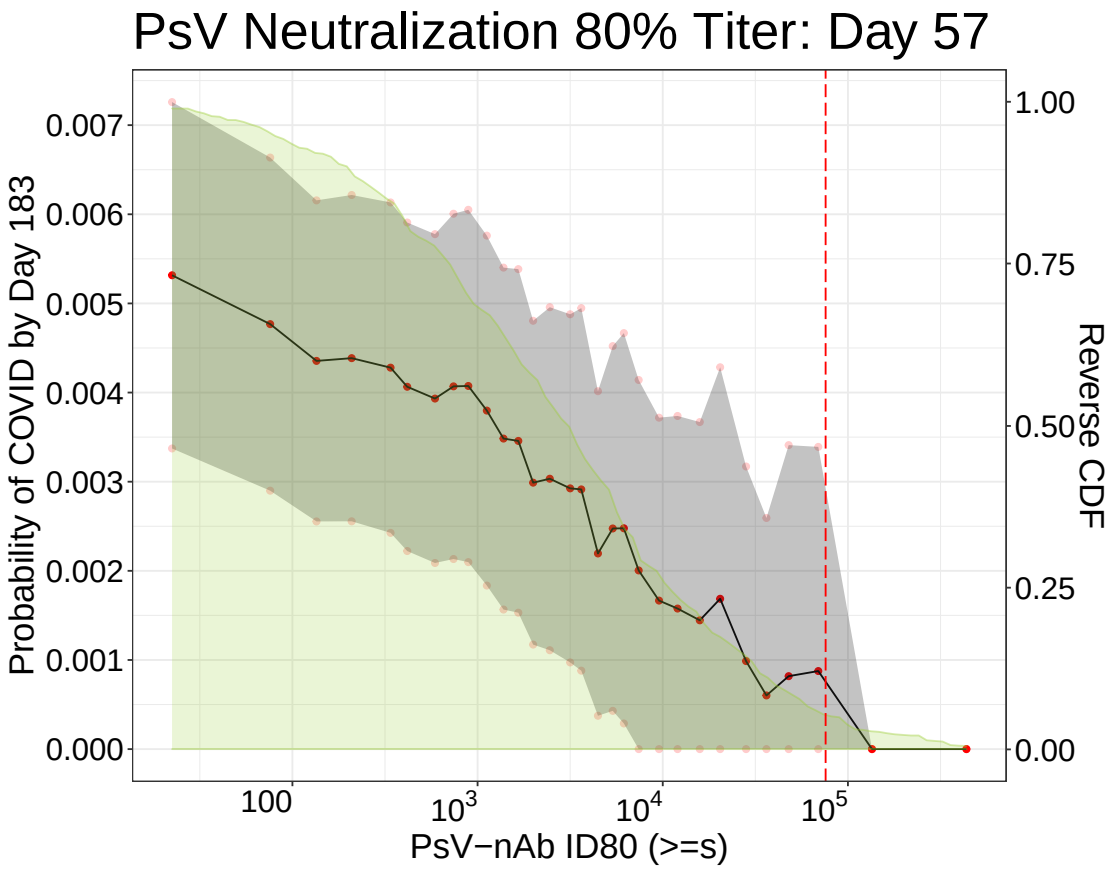

Figure 20: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 20: Table of risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	$2.25 * 10^1$	0.00532	0.00337	0.00726
2.319	$2.08 * 10^2$	0.00439	0.00256	0.00622
2.772	$5.92 * 10^2$	0.00393	0.00209	0.00578
3.136	$1.37 * 10^3$	0.00348	0.00157	0.00540
3.395	$2.48 * 10^3$	0.00303	0.00111	0.00496
3.652	$4.49 * 10^3$	0.00219	0.00037	0.00402
3.875	$7.50 * 10^3$	0.00200	0.00000	0.00414
4.314	$2.06 * 10^4$	0.00169	0.00000	0.00428
4.685	$4.84 * 10^4$	0.00082	0.00000	0.00341
5.644	$4.41 * 10^5$	0.00000	0.00000	NA

Plots and Tables with estimates and simultaneous confidence bands for Day 29

Day 29 Spike protein antibody

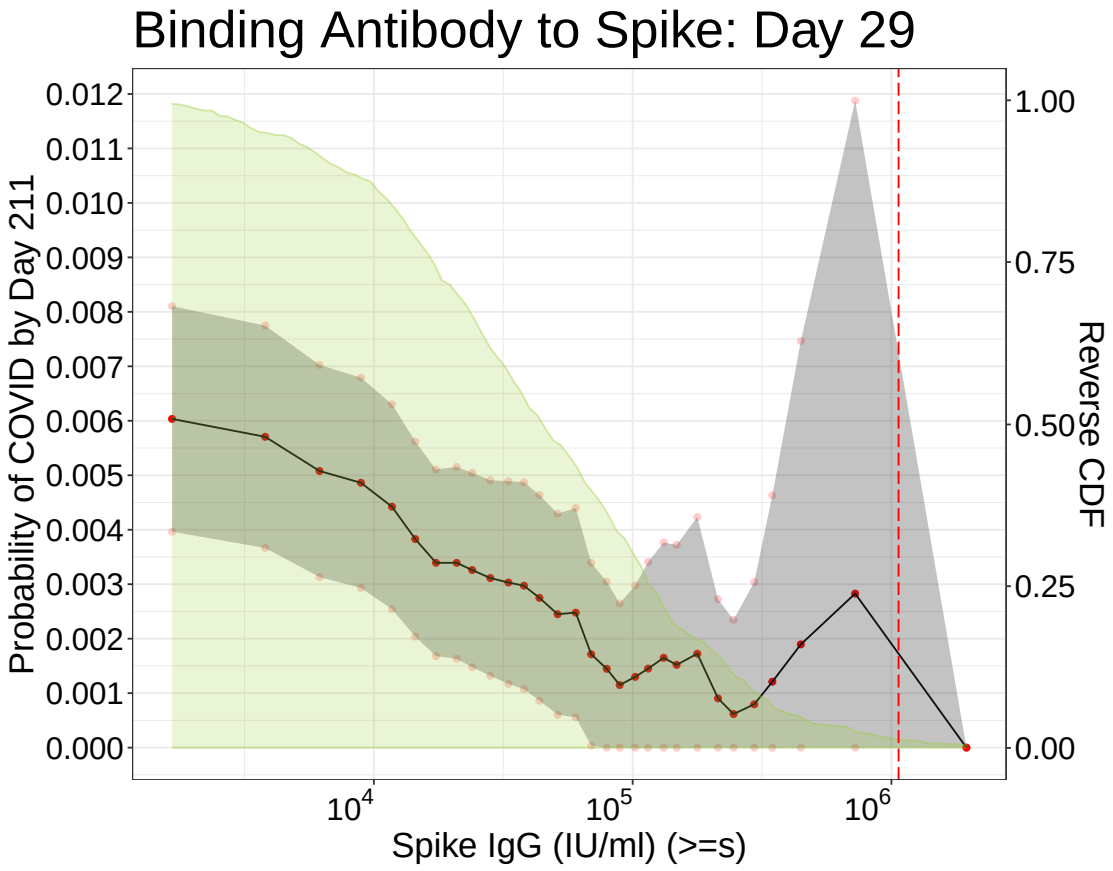

Figure 21: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 21: Table of risk estimates for a range of thresholds of Day 29 Spike protein antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
3.220	$1.66 * 10^3$	0.00603	0.00396	0.00811
3.954	$8.99 * 10^3$	0.00486	0.00293	0.00679
4.244	$1.75 * 10^4$	0.00339	0.00168	0.00511
4.522	$3.33 * 10^4$	0.00303	0.00117	0.00489
4.707	$5.09 * 10^4$	0.00245	0.00060	0.00430
4.899	$7.93 * 10^4$	0.00145	0.00000	0.00305
5.060	$1.15 * 10^5$	0.00145	0.00000	0.00341
5.327	$2.12 * 10^5$	0.00090	0.00000	0.00273
5.542	$3.48 * 10^5$	0.00121	0.00000	0.00463
6.285	$1.93 * 10^6$	0.00000	0.00000	NA

Day 29 RBD binding antibody

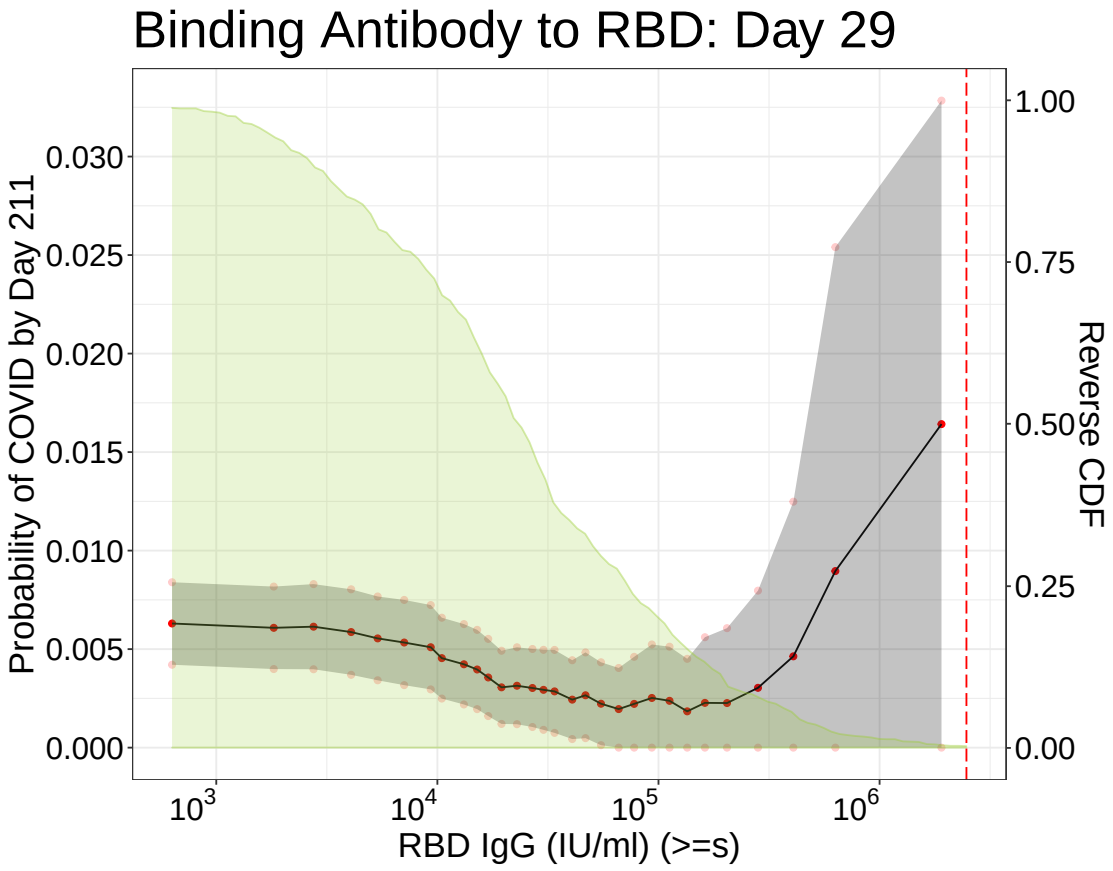

Figure 22: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 22: Table of risk estimates for a range of thresholds of Day 29 RBD binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
2.802	$6.34 * 10^2$	0.00630	0.00421	0.00839
3.605	$4.03 * 10^3$	0.00587	0.00370	0.00804
3.969	$9.31 * 10^3$	0.00510	0.00295	0.00724
4.233	$1.71 * 10^4$	0.00356	0.00160	0.00552
4.430	$2.69 * 10^4$	0.00303	0.00105	0.00501
4.606	$4.04 * 10^4$	0.00244	0.00043	0.00444
4.816	$6.55 * 10^4$	0.00196	0.00000	0.00404
5.131	$1.35 * 10^5$	0.00184	0.00000	0.00451
5.449	$2.81 * 10^5$	0.00304	0.00000	0.00797
6.281	$1.91 * 10^6$	0.01642	0.00000	0.06175

Day 29 Pseudo virus-neutralizing antibody (50% titer)

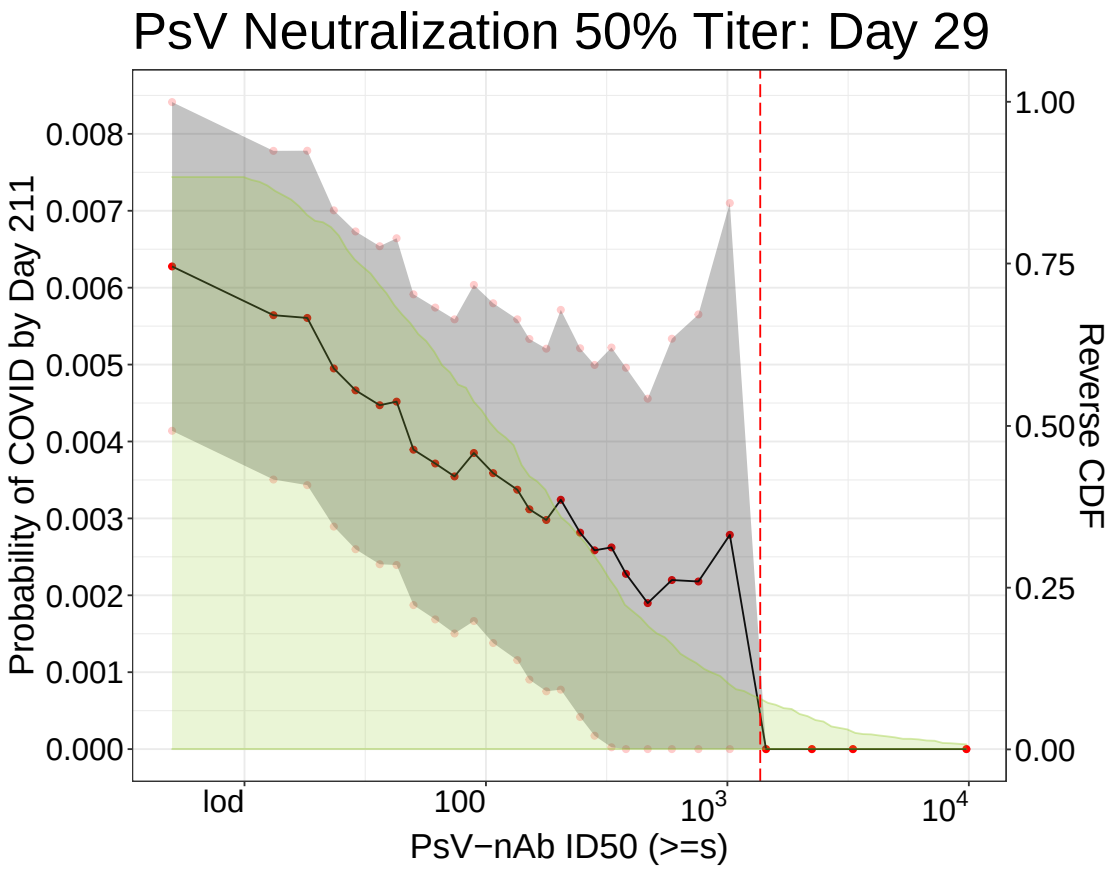

Figure 23: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 23: Table of risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00628	0.00414	0.00841
1.368	$2.33 * 10^1$	0.00495	0.00289	0.00701
1.631	$4.28 * 10^1$	0.00452	0.00239	0.00664
1.874	$7.48 * 10^1$	0.00355	0.00150	0.00559
2.127	$1.34 * 10^2$	0.00337	0.00116	0.00559
2.313	$2.06 * 10^2$	0.00324	0.00077	0.00571
2.524	$3.34 * 10^2$	0.00262	0.00002	0.00522
2.773	$5.93 * 10^2$	0.00220	0.00000	0.00534
3.165	$1.46 * 10^3$	0.00000	0.00000	NA
3.989	$9.75 * 10^3$	0.00000	0.00000	NA

Day 29 Pseudo virus-neutralizing antibody (80% titer)

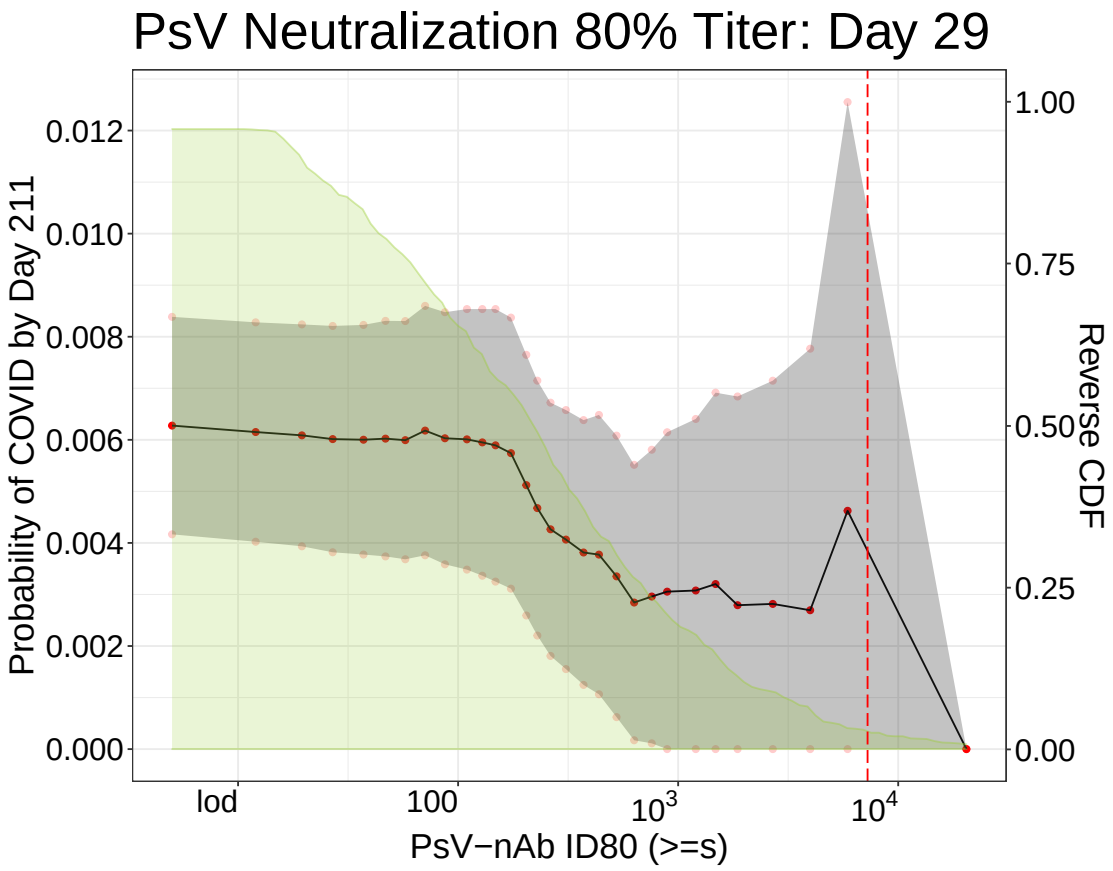

Figure 24: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 24: Table of risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00628	0.00417	0.00839
1.427	$2.67 * 10^1$	0.00601	0.00382	0.00821
1.761	$5.77 * 10^1$	0.00599	0.00368	0.00830
2.113	$1.30 * 10^2$	0.00595	0.00336	0.00854
2.310	$2.04 * 10^2$	0.00512	0.00259	0.00765
2.486	$3.06 * 10^2$	0.00406	0.00155	0.00658
2.724	$5.30 * 10^2$	0.00335	0.00062	0.00608
3.075	$1.19 * 10^3$	0.00308	0.00000	0.00641
3.426	$2.67 * 10^3$	0.00282	0.00000	0.00715
4.305	$2.02 * 10^4$	0.00000	0.00000	NA

Plots and Tables with estimates and pointwise confidence interval for Day 57 (monotone-corrected)

Day 57 Spike protein binding antibody

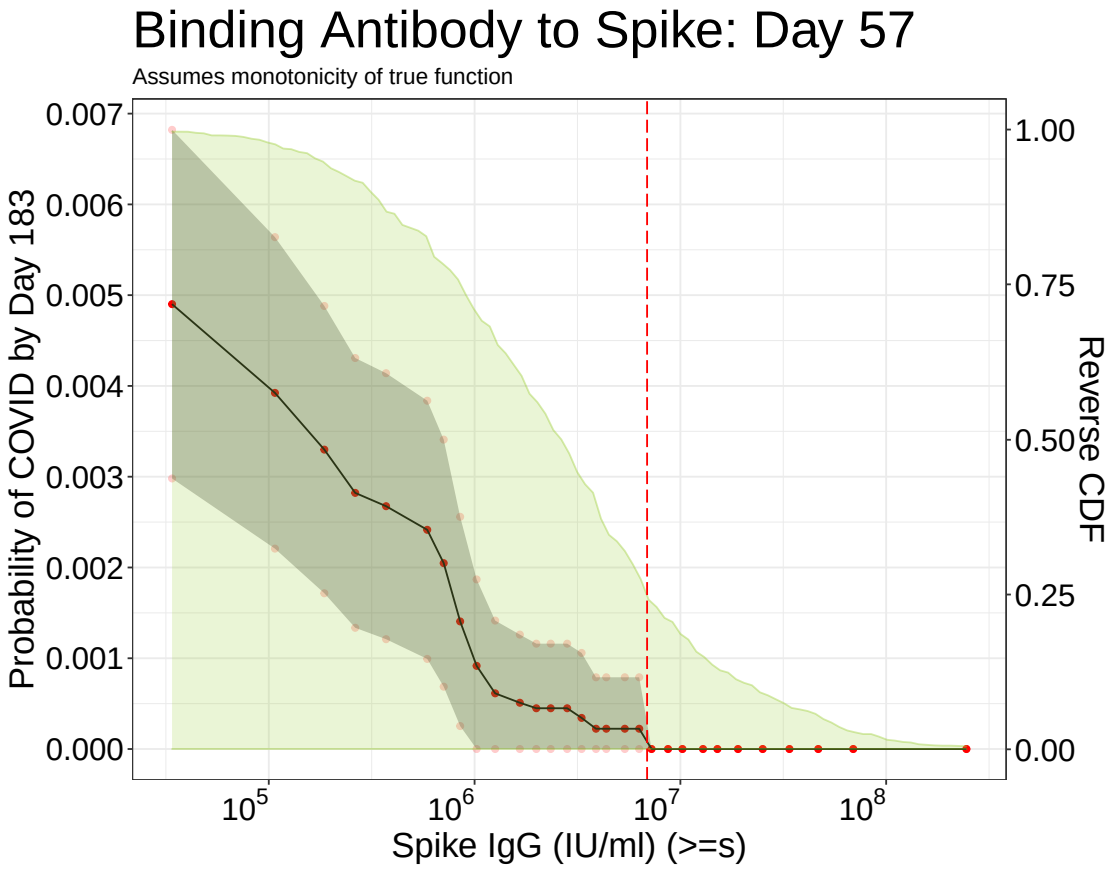

Figure 25: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 25: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Spike protein binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.530	$3.39 * 10^4$	0.00490	0.00298	0.00682
5.420	$2.63 * 10^5$	0.00282	0.00134	0.00431
5.851	$7.10 * 10^5$	0.00205	0.00069	0.00341
6.218	$1.65 * 10^6$	0.00051	0.00000	0.00126
6.453	$2.84 * 10^6$	0.00045	0.00000	0.00127
6.644	$4.41 * 10^6$	0.00022	0.00000	0.00084
6.864	$7.31 * 10^6$	0.00000	0.00000	NA
7.185	$1.53 * 10^7$	0.00000	0.00000	NA
7.525	$3.35 * 10^7$	0.00000	0.00000	NA
8.391	$2.46 * 10^8$	0.00000	0.00000	NA

Day 57 RBD binding antibody

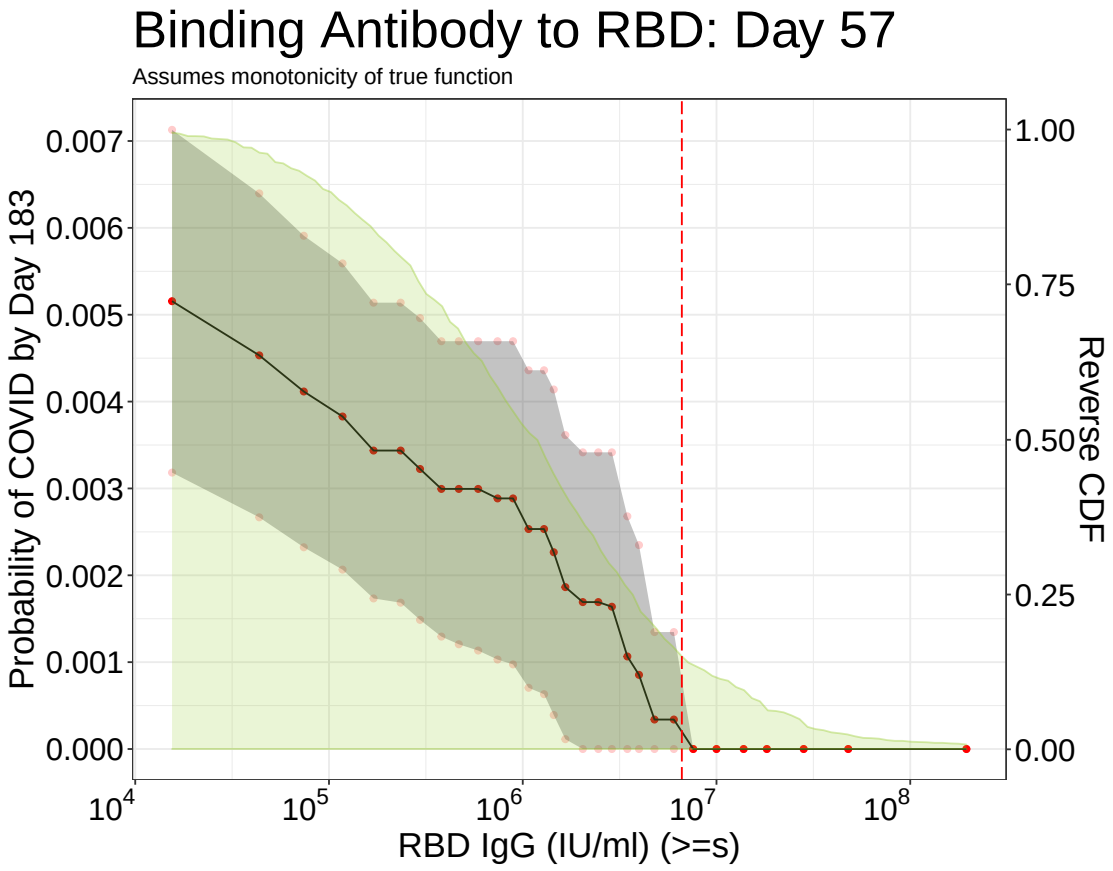

Figure 26: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 26: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 RBD binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.185	$1.53 * 10^4$	0.00516	0.00318	0.00713
5.070	$1.17 * 10^5$	0.00383	0.00207	0.00559
5.466	$2.92 * 10^5$	0.00322	0.00149	0.00496
5.865	$7.33 * 10^5$	0.00289	0.00103	0.00474
6.107	$1.28 * 10^6$	0.00253	0.00063	0.00443
6.309	$2.04 * 10^6$	0.00169	0.00000	0.00342
6.541	$3.48 * 10^6$	0.00107	0.00000	0.00268
6.879	$7.57 * 10^6$	0.00000	0.00000	NA
7.262	$1.83 * 10^7$	0.00000	0.00000	NA
8.291	$1.95 * 10^8$	0.00000	0.00000	NA

Day 57 Pseudo virus-neutralizing antibody (50% titer)

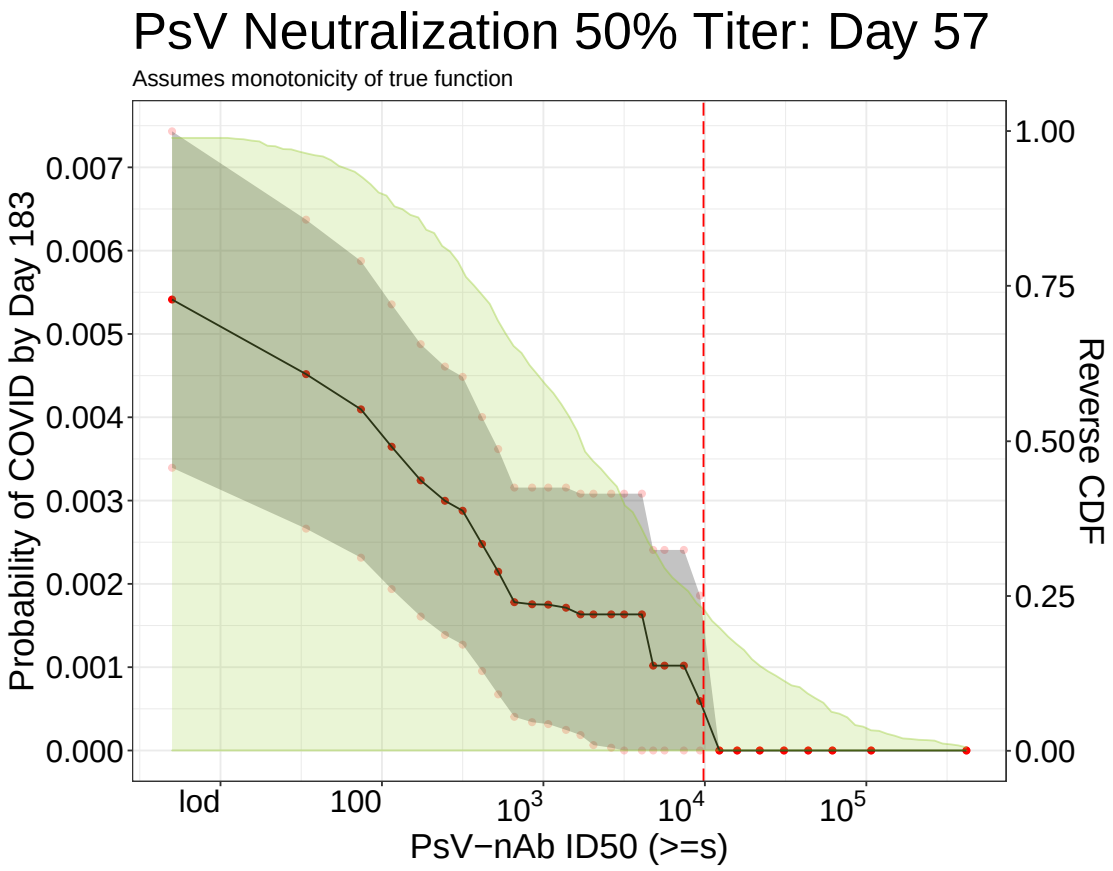

Figure 27: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 27: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00541	0.00339	0.00743
2.057	$1.14 * 10^2$	0.00365	0.00194	0.00536
2.499	$3.16 * 10^2$	0.00288	0.00127	0.00449
2.929	$8.49 * 10^2$	0.00176	0.00034	0.00317
3.230	$1.70 * 10^3$	0.00163	0.00018	0.00308
3.501	$3.17 * 10^3$	0.00163	0.00000	0.00327
3.747	$5.58 * 10^3$	0.00102	0.00000	0.00252
4.200	$1.58 * 10^4$	0.00000	0.00000	NA
4.636	$4.33 * 10^4$	0.00000	0.00000	NA
5.620	$4.17 * 10^5$	0.00000	0.00000	NA

Day 57 Pseudo virus-neutralizing antibody (80% titer)

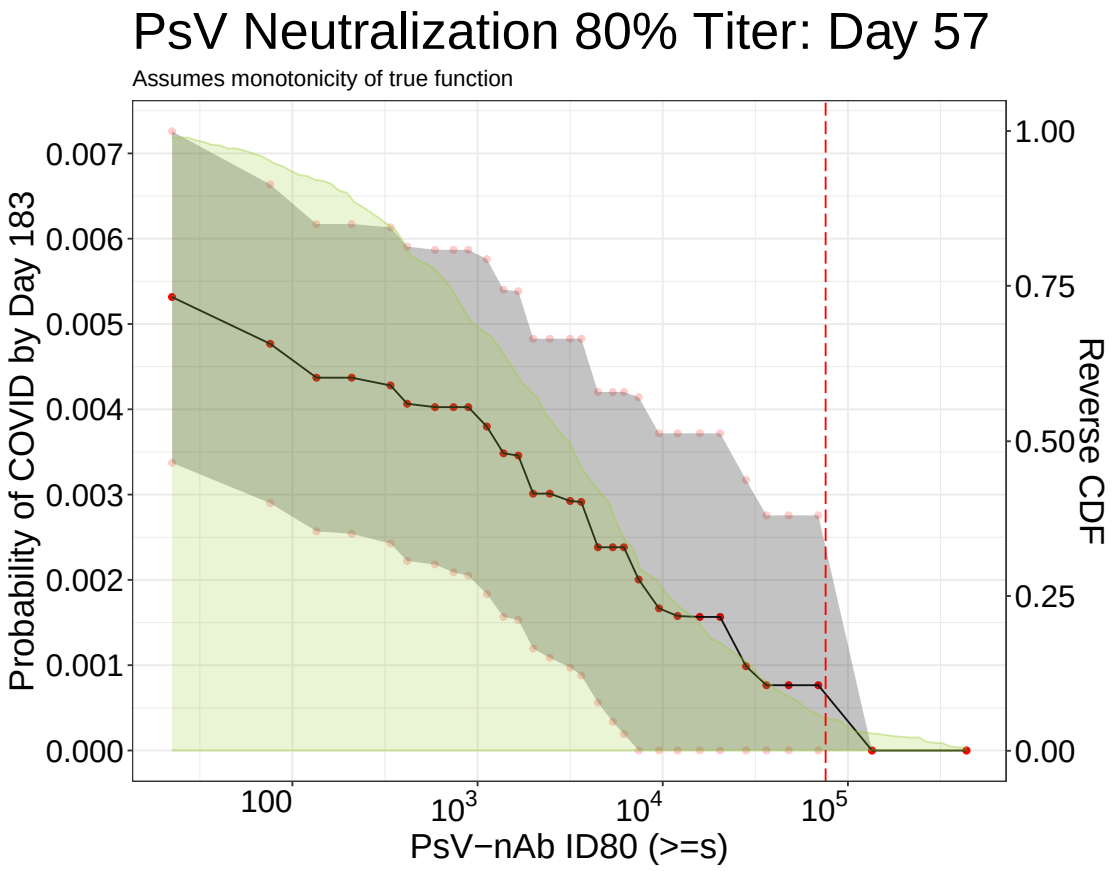

Figure 28: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 28: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	$2.25 * 10^1$	0.00532	0.00337	0.00726
2.319	$2.08 * 10^2$	0.00437	0.00254	0.00620
2.772	$5.92 * 10^2$	0.00403	0.00218	0.00587
3.136	$1.37 * 10^3$	0.00348	0.00157	0.00540
3.395	$2.48 * 10^3$	0.00301	0.00109	0.00494
3.652	$4.49 * 10^3$	0.00238	0.00056	0.00420
3.875	$7.50 * 10^3$	0.00200	0.00000	0.00414
4.314	$2.06 * 10^4$	0.00157	0.00000	0.00416
4.685	$4.84 * 10^4$	0.00077	0.00000	0.00336
5.644	$4.41 * 10^5$	0.00000	0.00000	NA

Plots and Tables with estimates and pointwise confidence intervals for Day 29 (monotone-corrected)

Day 29 Spike protein antibody

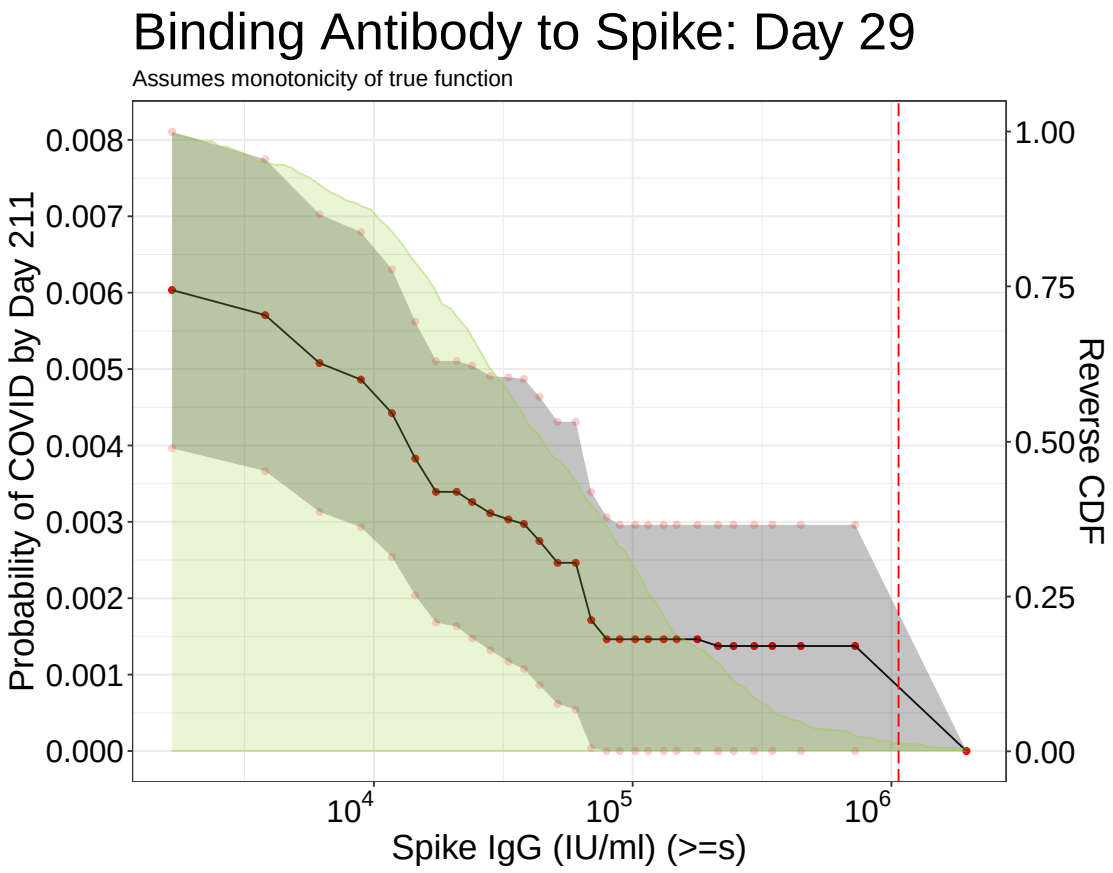

Figure 29: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 29: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Spike protein antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
3.220	$1.66 * 10^3$	0.00603	0.00396	0.00811
3.954	$8.99 * 10^3$	0.00486	0.00293	0.00679
4.244	$1.75 * 10^4$	0.00339	0.00168	0.00511
4.522	$3.33 * 10^4$	0.00303	0.00117	0.00489
4.707	$5.09 * 10^4$	0.00246	0.00062	0.00431
4.899	$7.93 * 10^4$	0.00146	0.00000	0.00306
5.060	$1.15 * 10^5$	0.00146	0.00000	0.00342
5.327	$2.12 * 10^5$	0.00137	0.00000	0.00320
5.542	$3.48 * 10^5$	0.00137	0.00000	0.00480
6.285	$1.93 * 10^6$	0.00000	0.00000	NA

Day 29 RBD binding antibody

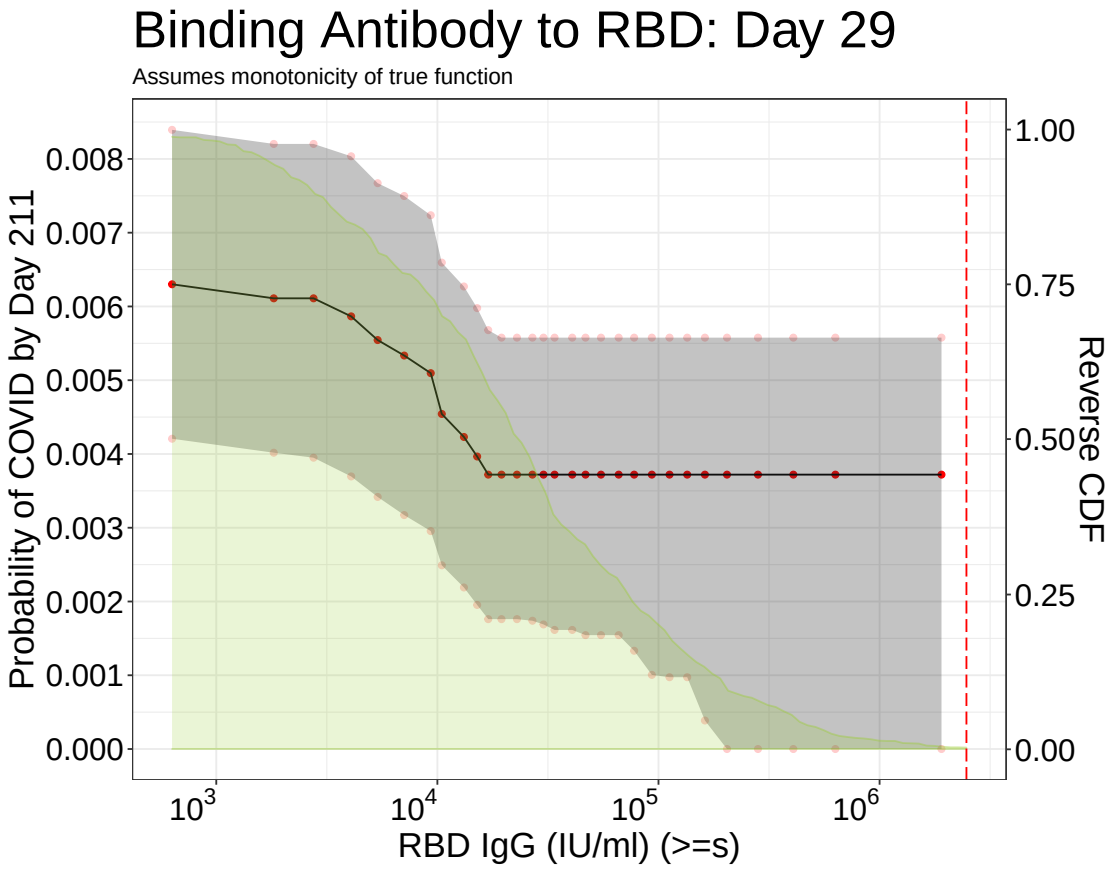

Figure 30: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 30: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 RBD binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
2.802	$6.34 * 10^2$	0.00630	0.00421	0.00839
3.605	$4.03 * 10^3$	0.00587	0.00370	0.00804
3.969	$9.31 * 10^3$	0.00510	0.00295	0.00724
4.233	$1.71 * 10^4$	0.00372	0.00176	0.00568
4.430	$2.69 * 10^4$	0.00372	0.00174	0.00570
4.606	$4.04 * 10^4$	0.00372	0.00172	0.00572
4.816	$6.55 * 10^4$	0.00372	0.00163	0.00581
5.131	$1.35 * 10^5$	0.00372	0.00105	0.00639
5.449	$2.81 * 10^5$	0.00372	0.00000	0.00865
6.281	$1.91 * 10^6$	0.00372	0.00000	0.04905

Day 29 Pseudo virus-neutralizing antibody (50% titer)

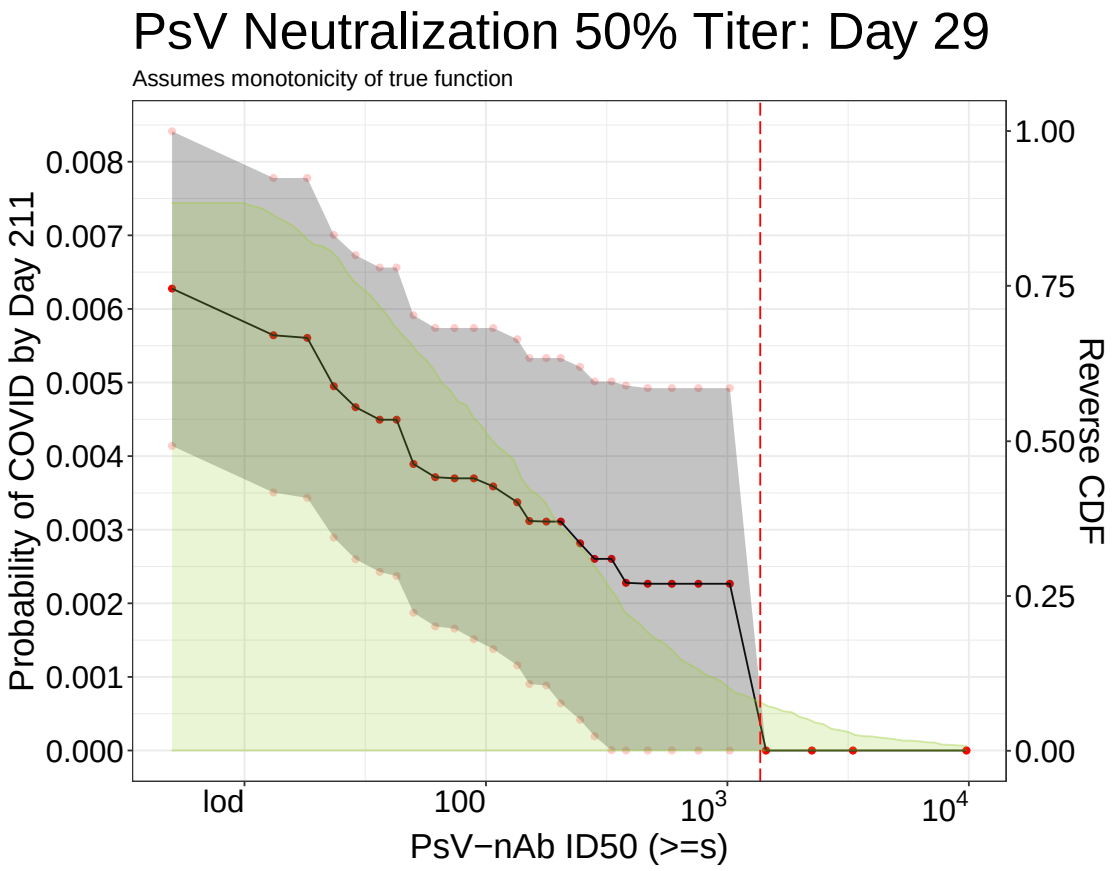

Figure 31: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 31: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00628	0.00414	0.00841
1.368	$2.33 * 10^1$	0.00495	0.00289	0.00701
1.631	$4.28 * 10^1$	0.00449	0.00237	0.00662
1.874	$7.48 * 10^1$	0.00370	0.00166	0.00574
2.127	$1.34 * 10^2$	0.00337	0.00116	0.00559
2.313	$2.06 * 10^2$	0.00311	0.00064	0.00558
2.524	$3.34 * 10^2$	0.00260	0.00000	0.00520
2.773	$5.93 * 10^2$	0.00227	0.00000	0.00540
3.165	$1.46 * 10^3$	0.00000	0.00000	NA
3.989	$9.75 * 10^3$	0.00000	0.00000	NA

Day 29 Pseudo virus-neutralizing antibody (80% titer)

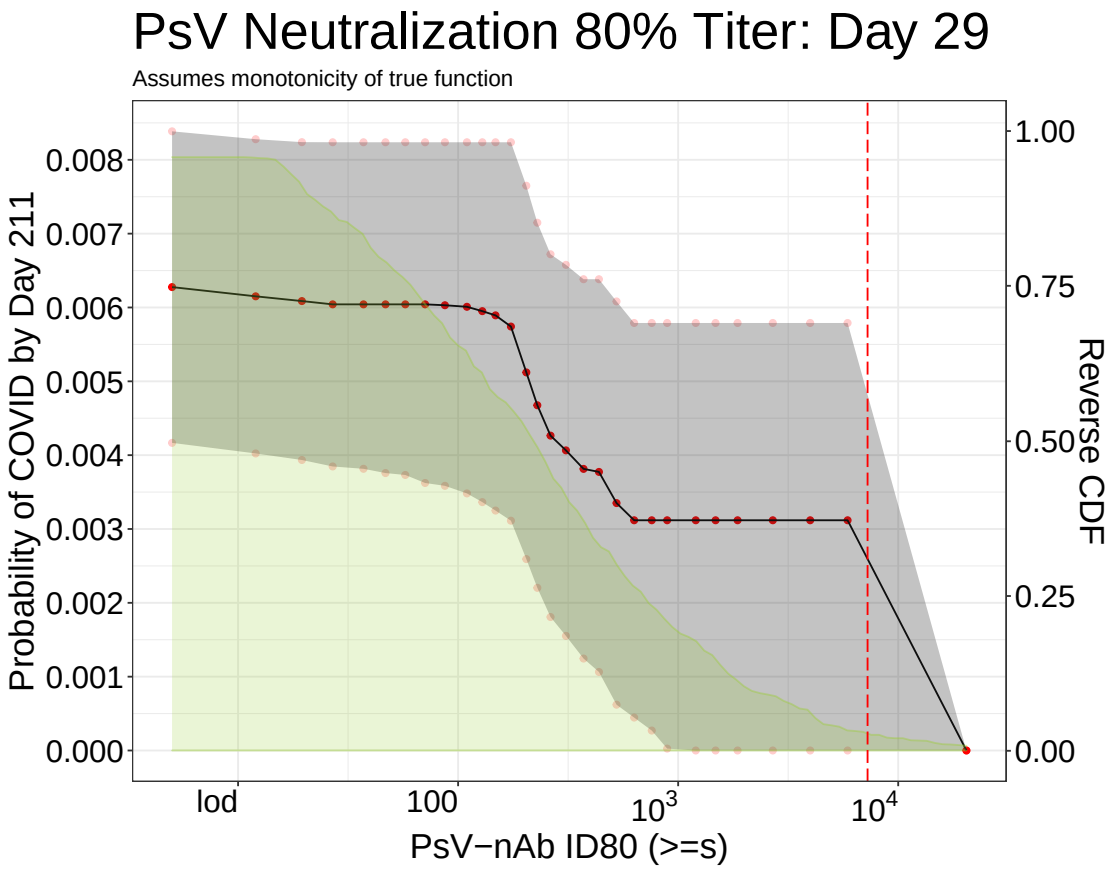

Figure 32: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 32: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00628	0.00417	0.00839
1.427	$2.67 * 10^1$	0.00604	0.00385	0.00824
1.761	$5.77 * 10^1$	0.00604	0.00373	0.00835
2.113	$1.30 * 10^2$	0.00595	0.00336	0.00854
2.310	$2.04 * 10^2$	0.00512	0.00259	0.00765
2.486	$3.06 * 10^2$	0.00406	0.00155	0.00658
2.724	$5.30 * 10^2$	0.00335	0.00062	0.00608
3.075	$1.19 * 10^3$	0.00312	0.00000	0.00645
3.426	$2.67 * 10^3$	0.00312	0.00000	0.00745
4.305	$2.02 * 10^4$	0.00000	0.00000	NA