Univariate CoR: Nonparametric Threshold Modeling

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getwd()
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## [1] "/Users/larsvanderlaan/correlates_reporting/cor_threshold"
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Absolute risk analysis by antibody biomarker threshold

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 (in progress) 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. 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 $-->$ age, 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.

3. A plot and table with threshold estimates and simultaneous 95% confidence bands for the inverse threshold-response at a grid of risk values.

A histogram 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.

For the estimates and inference of the threshold of protection at each risk level (based on the inverse threshold-response function, item 3) to be correct, we assume monotonicity of the true function $s \mapsto E_X[E[Y|S \geq s, X, A = 1]|A = 1]$. If the threshold-response function estimate does not seem to have a monotonic trend then the inverse threshold-response estimates and inference should be interpreted with caution.
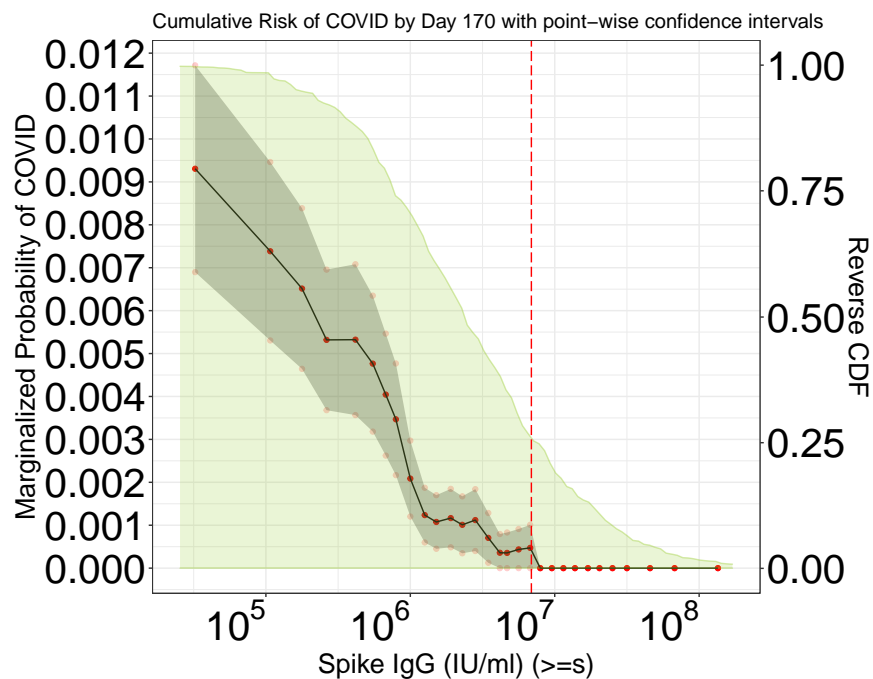
Spike protein antibody

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

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.505	3.20*10^4	0.01034	0.00787	0.01282
5.507	3.21*10^5	0.00569	0.00392	0.00747
5.893	7.82*10^5	0.00382	0.00239	0.00526
6.122	1.32*10^6	0.00102	0.00037	0.00167
6.432	2.70*10^6	0.00085	0.00022	0.00148
6.689	4.89*10^6	0.00026	0.00000	0.00062
6.961	9.14*10^6	0.00000	0.00000	1.00000
7.144	1.39*10^7	0.00000	0.00000	1.00000
7.465	2.92*10^7	0.00000	0.00000	1.00000
8.131	1.35*10^8	0.00000	0.00000	1.00000

Figure 2: Table of risk estimates for range of thresholds of Spike protein antibody activity levels with point-wise 95% confidence intervals.
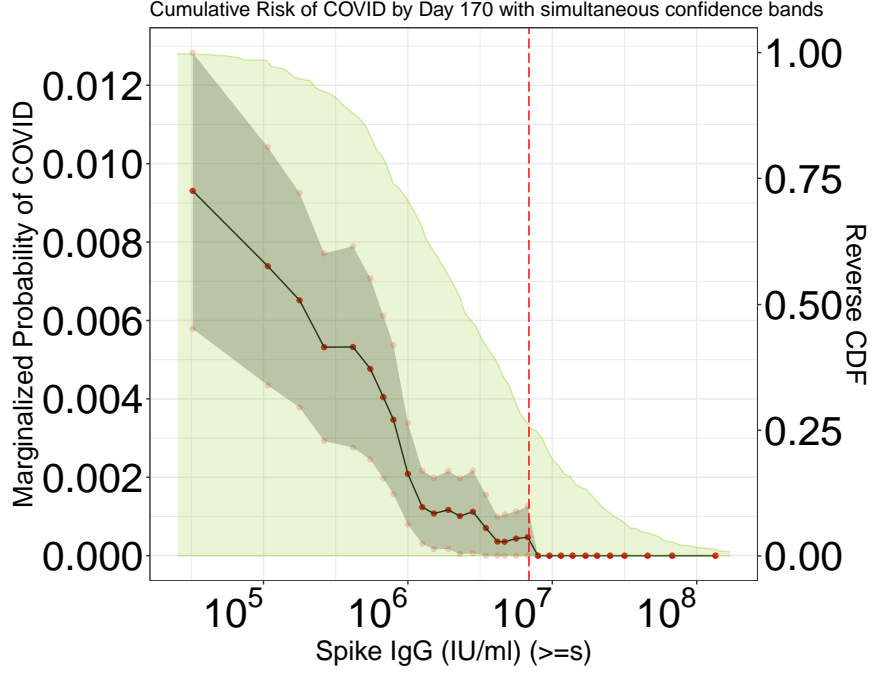
Figure 3: Adjusted threshold-response function for a range of thresholds of the Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.505	$3.20*10^4$	0.01034	0.00668	0.01401
5.507	$3.21*10^5$	0.00569	0.00307	0.00832
5.893	$7.82*10^5$	0.00382	0.00170	0.00595
6.122	$1.32*10^6$	0.00102	0.00005	0.00198
6.432	$2.70*10^6$	0.00085	0.00000	0.00178
6.689	$4.89*10^6$	0.00026	0.00000	0.00079
6.961	$9.14*10^6$	0.00000	0.00000	1.00000
7.144	$1.39*10^7$	0.00000	0.00000	1.00000
7.465	$2.92*10^7$	0.00000	0.00000	1.00000
8.131	$1.35*10^8$	0.00000	0.00000	1.00000

Figure 4: Table of risk estimates for range of thresholds of Spike protein antibody activity levels with simultaneous 95% confidence bands
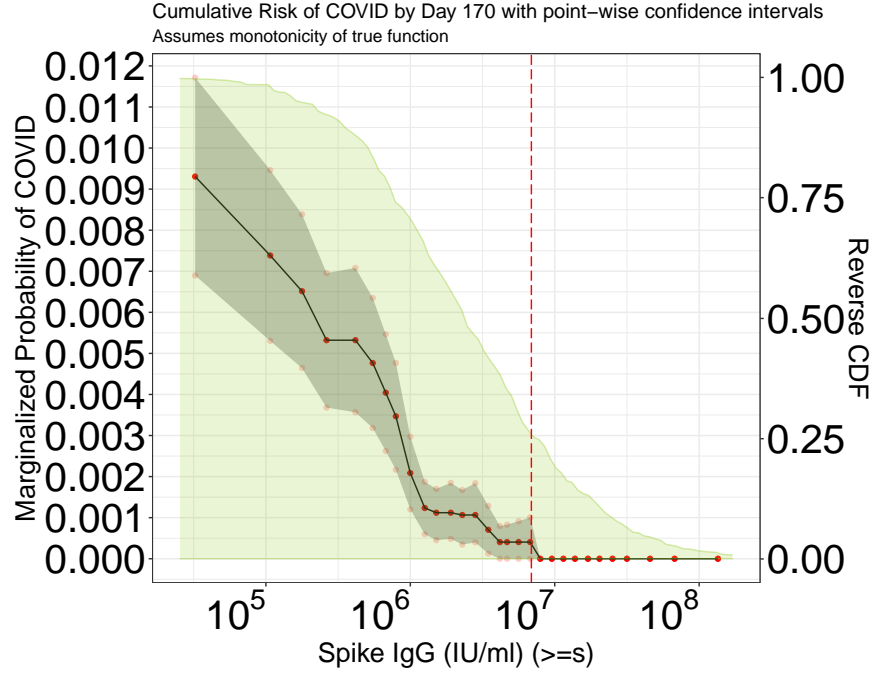
Figure 5: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
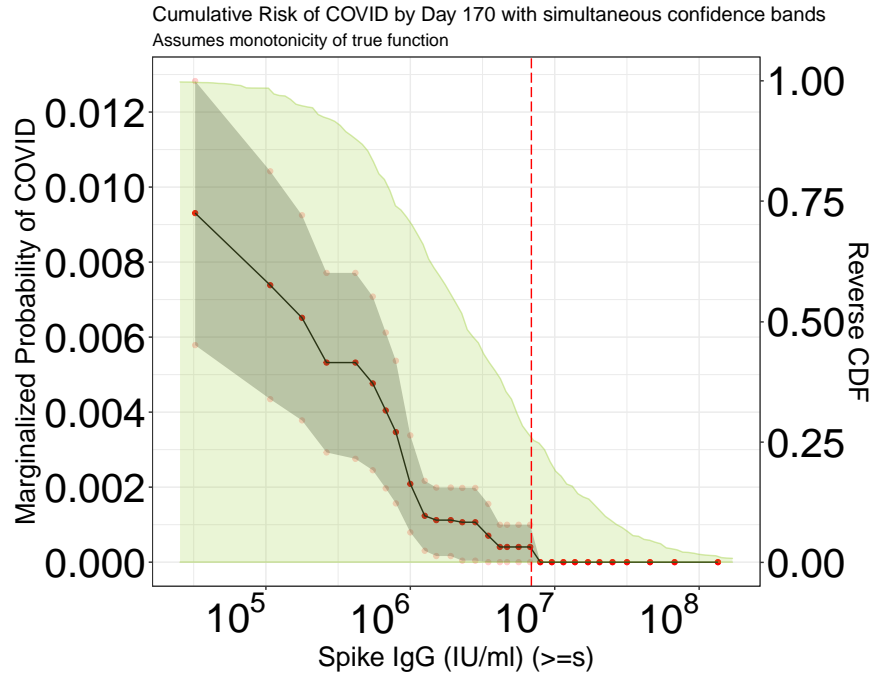

Figure 6: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
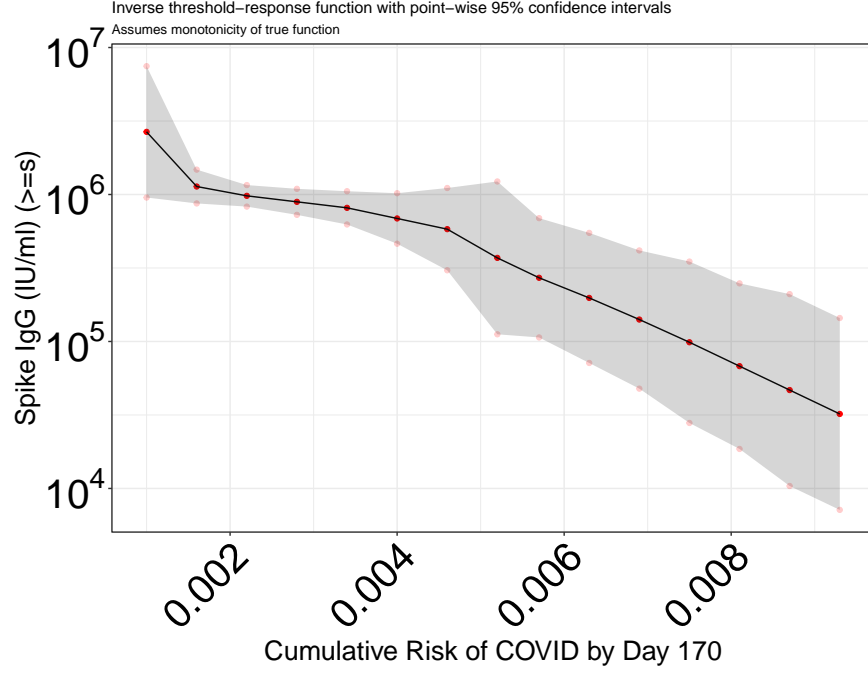
Figure 7: The inverse adjusted threshold-response function with pointwise 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.001	2.69*10^6	9.55*10^5	7.41*10^6
0.0016	1.12*10^6	8.71*10^5	1.48*10^6
0.0022	9.77*10^5	8.32*10^5	1.15*10^6
0.0028	8.91*10^5	7.24*10^5	1.10*10^6
0.0034	8.13*10^5	6.31*10^5	1.05*10^6
0.004	6.92*10^5	4.68*10^5	1.02*10^6
0.0046	5.75*10^5	3.02*10^5	1.10*10^6
0.0052	3.72*10^5	1.12*10^5	1.23*10^6
0.0057	2.69*10^5	1.07*10^5	6.92*10^5
0.0063	2.00*10^5	7.08*10^4	5.50*10^5
0.0069	1.41*10^5	4.79*10^4	4.17*10^5
0.0075	9.77*10^4	2.82*10^4	3.47*10^5
0.0081	6.76*10^4	1.86*10^4	2.51*10^5
0.0087	4.68*10^4	1.05*10^4	2.09*10^5
0.0093	3.24*10^4	7.08*10^3	1.45*10^5

Figure 8: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Spike protein antibody activity level at a range of risk levels with pointwise 95% confidence intervals.
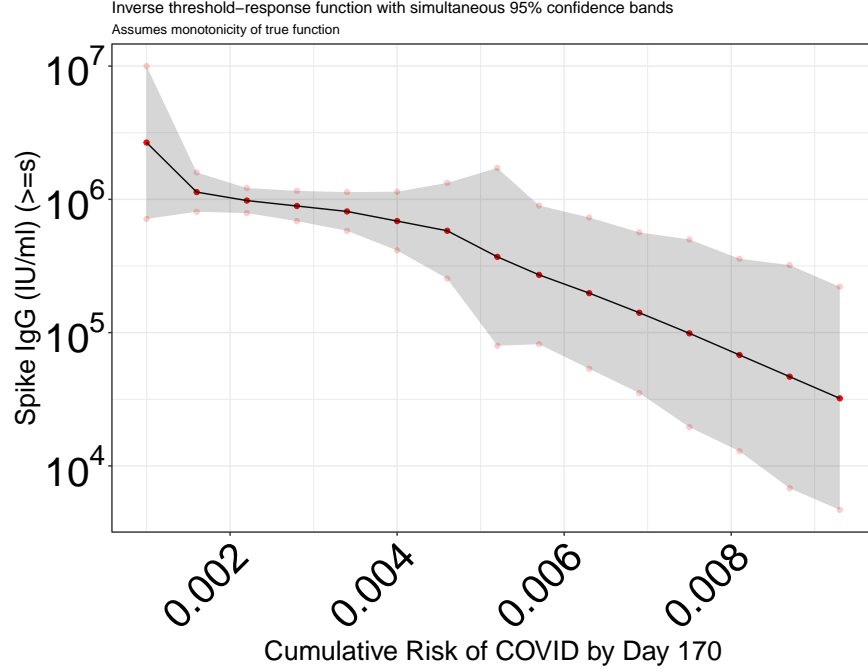
Figure 9: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with simultaneous 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.001	2.69*10^6	7.08*10^5	1.00*10^7
0.0016	1.12*10^6	8.13*10^5	1.58*10^6
0.0022	9.77*10^5	7.94*10^5	1.20*10^6
0.0028	8.91*10^5	6.92*10^5	1.15*10^6
0.0034	8.13*10^5	5.75*10^5	1.12*10^6
0.004	6.92*10^5	4.17*10^5	1.15*10^6
0.0046	5.75*10^5	2.57*10^5	1.32*10^6
0.0052	3.72*10^5	7.94*10^4	1.74*10^6
0.0057	2.69*10^5	8.13*10^4	8.91*10^5
0.0063	2.00*10^5	5.37*10^4	7.24*10^5
0.0069	1.41*10^5	3.55*10^4	5.62*10^5
0.0075	9.77*10^4	1.95*10^4	5.01*10^5
0.0081	6.76*10^4	1.29*10^4	3.55*10^5
0.0087	4.68*10^4	6.76*10^3	3.24*10^5
0.0093	3.24*10^4	4.68*10^3	2.19*10^5

Figure 10: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Spike protein antibody activity level at a range of risk levels with simultaneous 95% confidence bands

Receptor binding domain (RBD) binding antibody

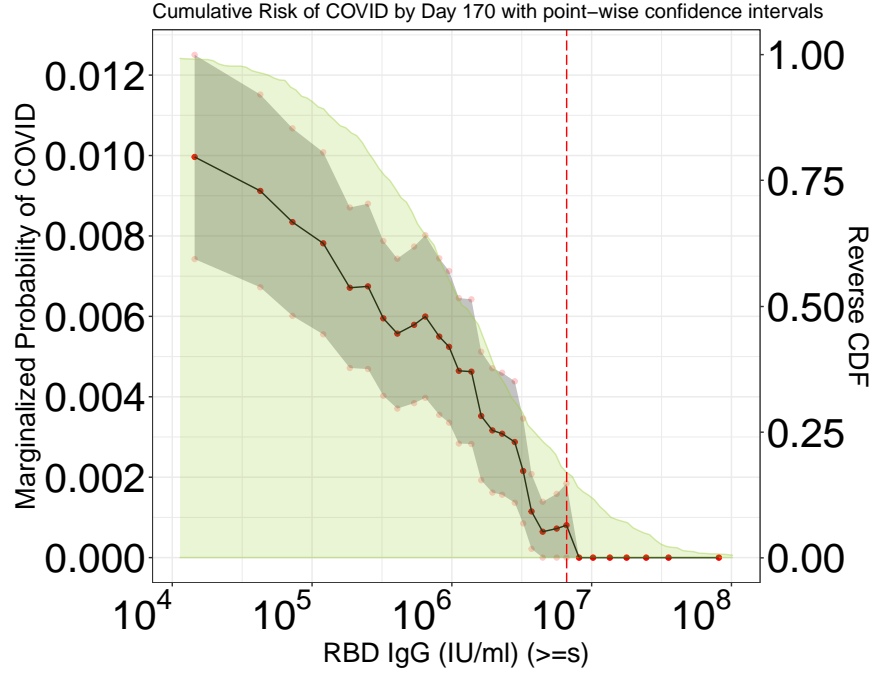Cumulative Risk of COVID by Day 170 with point−wise confidence intervals

Figure 11: Adjusted threshold-response function for a range of thresholds of the RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.155	1.43*10^4	0.00996	0.00742	0.01250
5.084	1.21*10^5	0.00782	0.00555	0.01008
5.515	3.27*10^5	0.00595	0.00402	0.00788
5.914	8.20*10^5	0.00550	0.00355	0.00744
6.139	1.38*10^6	0.00462	0.00283	0.00642
6.360	2.29*10^6	0.00308	0.00156	0.00460
6.575	3.76*10^6	0.00115	0.00022	0.00208
6.910	8.13*10^6	0.00000	0.00000	1.00000
7.251	1.78*10^7	0.00000	0.00000	1.00000
7.907	8.07*10^7	0.00000	0.00000	1.00000

Figure 12: Table of risk estimates for range of thresholds of RBD binding antibody activity levels with point-wise 95% confidence intervals
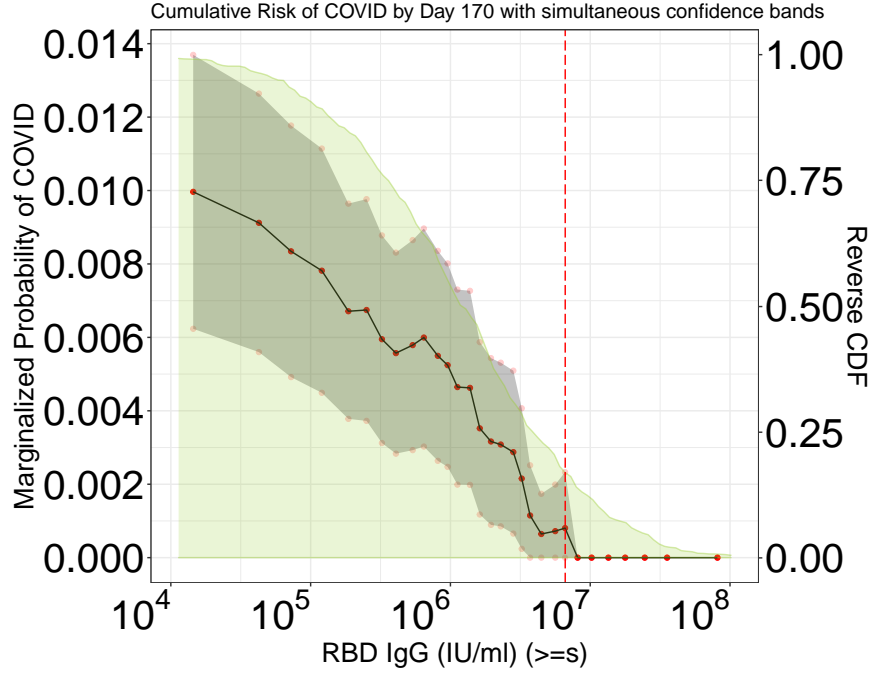
Figure 13: Adjusted threshold-response function for a range of thresholds of the RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.155	1.43*10^4	0.00996	0.00623	0.01369
5.084	1.21*10^5	0.00782	0.00449	0.01114
5.515	3.27*10^5	0.00595	0.00312	0.00878
5.914	8.20*10^5	0.00550	0.00264	0.00836
6.139	1.38*10^6	0.00462	0.00198	0.00727
6.360	2.29*10^6	0.00308	0.00085	0.00531
6.575	3.76*10^6	0.00115	0.00000	0.00252
6.910	8.13*10^6	0.00000	0.00000	1.00000
7.251	1.78*10^7	0.00000	0.00000	1.00000
7.907	8.07*10^7	0.00000	0.00000	1.00000

Figure 14: Table of risk estimates for range of thresholds of RBD binding antibody activity levels with simultaneous 95% confidence bands.
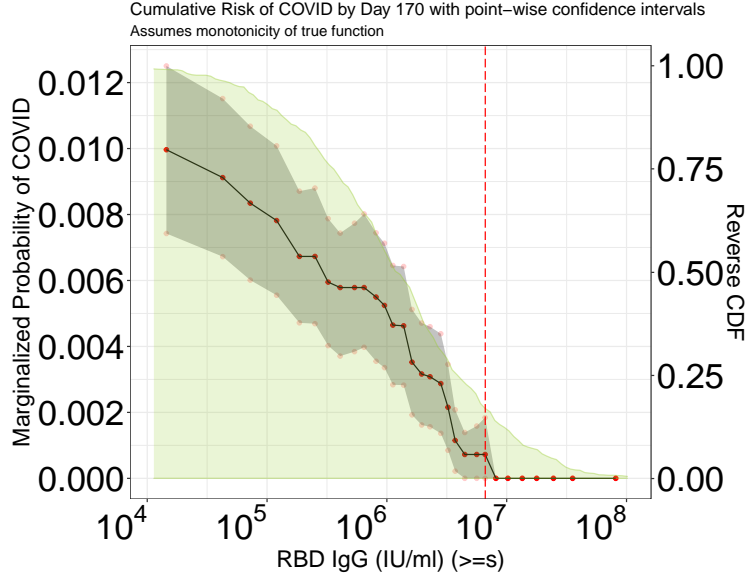
Figure 15: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
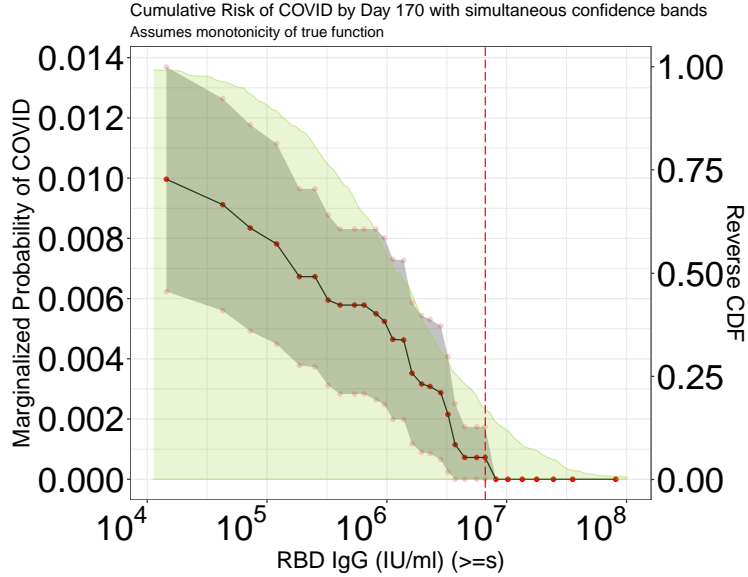

Figure 16: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
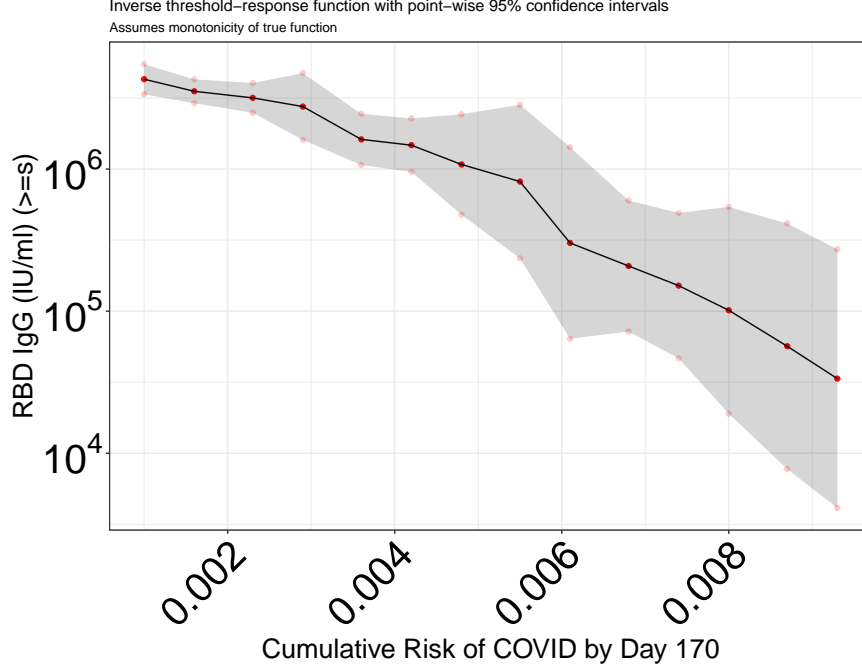
Figure 17: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with point-wise 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.001	4.27*10^6	3.39*10^6	5.50*10^6
0.0016	3.55*10^6	2.88*10^6	4.27*10^6
0.0023	3.16*10^6	2.51*10^6	4.07*10^6
0.0029	2.75*10^6	1.62*10^6	4.68*10^6
0.0036	1.62*10^6	1.07*10^6	2.45*10^6
0.0042	1.48*10^6	9.55*10^5	2.29*10^6
0.0048	1.07*10^6	4.79*10^5	2.45*10^6
0.0055	8.13*10^5	2.34*10^5	2.82*10^6
0.0061	3.02*10^5	6.46*10^4	1.41*10^6
0.0068	2.09*10^5	7.24*10^4	6.03*10^5
0.0074	1.51*10^5	4.68*10^4	4.90*10^5
0.008	1.02*10^5	1.91*10^4	5.37*10^5
0.0087	5.62*10^4	7.76*10^3	4.17*10^5
0.0093	3.39*10^4	4.17*10^3	2.75*10^5

Figure 18: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of RBD binding antibody activity level at a range of risk levels with point-wise 95% confidence intervals.
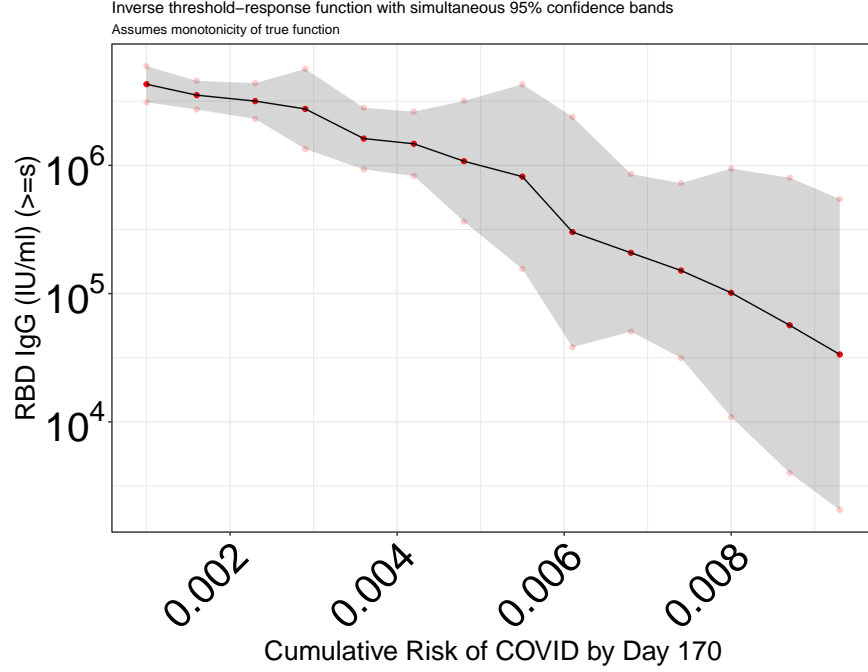
Figure 19: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with simultaneous 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.001	4.27*10^6	3.09*10^6	5.89*10^6
0.0016	3.55*10^6	2.75*10^6	4.57*10^6
0.0023	3.16*10^6	2.29*10^6	4.37*10^6
0.0029	2.75*10^6	1.35*10^6	5.62*10^6
0.0036	1.62*10^6	9.33*10^5	2.82*10^6
0.0042	1.48*10^6	8.32*10^5	2.63*10^6
0.0048	1.07*10^6	3.63*10^5	3.16*10^6
0.0055	8.13*10^5	1.55*10^5	4.27*10^6
0.0061	3.02*10^5	3.80*10^4	2.40*10^6
0.0068	2.09*10^5	5.01*10^4	8.51*10^5
0.0074	1.51*10^5	3.16*10^4	7.24*10^5
0.008	1.02*10^5	1.10*10^4	9.55*10^5
0.0087	5.62*10^4	3.98*10^3	7.94*10^5
0.0093	3.39*10^4	2.04*10^3	5.50*10^5

Figure 20: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of RBD binding antibody activity level at a range of risk levels with simultaneous 95% confidence bands.
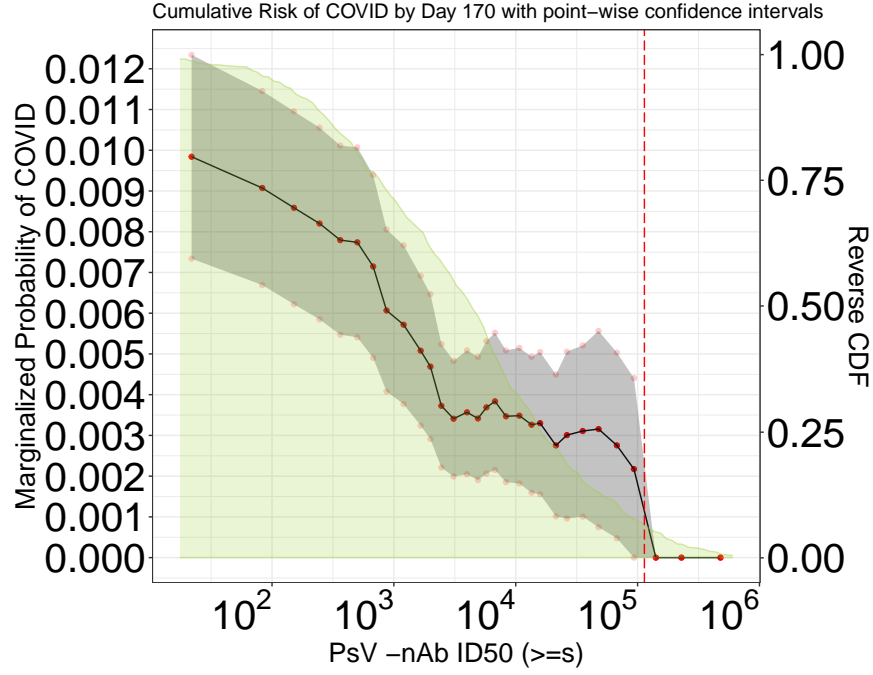
Pseudo-neutralizing antibody (50% titer)

Figure 21: Adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.345	2.21*10^1	0.00984	0.00734	0.01234
2.395	2.48*10^2	0.00820	0.00585	0.01056
2.833	6.81*10^2	0.00715	0.00490	0.00939
3.296	1.98*10^3	0.00469	0.00291	0.00647
3.601	3.99*10^3	0.00357	0.00205	0.00509
3.832	6.79*10^3	0.00384	0.00215	0.00552
4.127	1.34*10^4	0.00326	0.00159	0.00493
4.553	3.57*10^4	0.00311	0.00101	0.00521
4.971	9.35*10^4	0.00217	0.00000	0.00441
5.679	4.78*10^5	0.00000	0.00000	1.00000

Figure 22: Table of risk estimates for range of thresholds of Pseudo virus-neutralizing antibody activity levels with point-wise 95% confidence intervals.
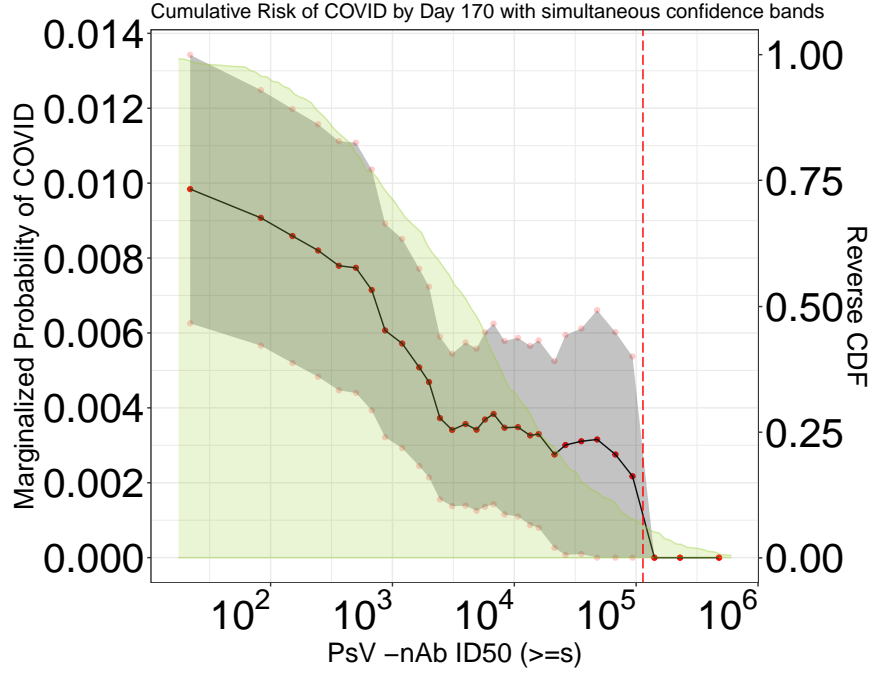
Figure 23: Adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.345	2.21*10^1	0.00984	0.00626	0.01343
2.395	2.48*10^2	0.00820	0.00483	0.01157
2.833	6.81*10^2	0.00715	0.00393	0.01036
3.296	1.98*10^3	0.00469	0.00214	0.00724
3.601	3.99*10^3	0.00357	0.00139	0.00575
3.832	6.79*10^3	0.00384	0.00142	0.00625
4.127	1.34*10^4	0.00326	0.00087	0.00566
4.553	3.57*10^4	0.00311	0.00010	0.00612
4.971	9.35*10^4	0.00217	0.00000	0.00537
5.679	4.78*10^5	0.00000	0.00000	1.00000

Figure 24: Table of risk estimates for range of thresholds of Pseudo virus-neutralizing antibody activity levels with simultaneous 95% confidence bands.
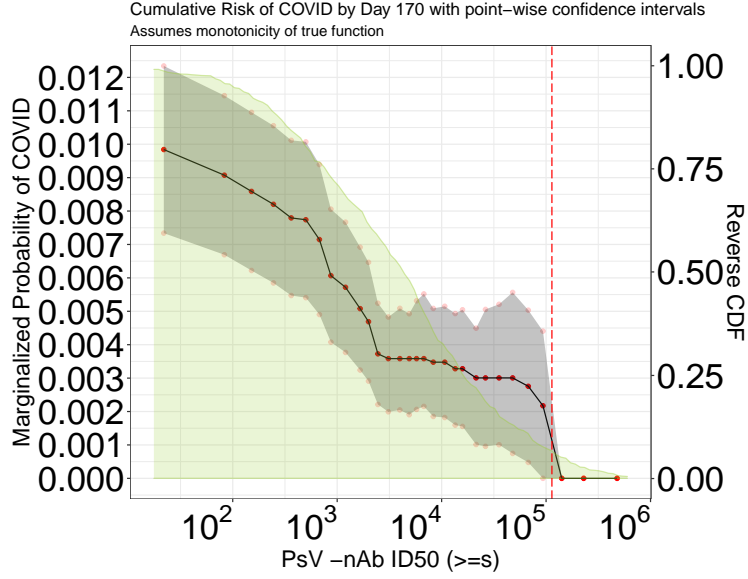
Figure 25: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
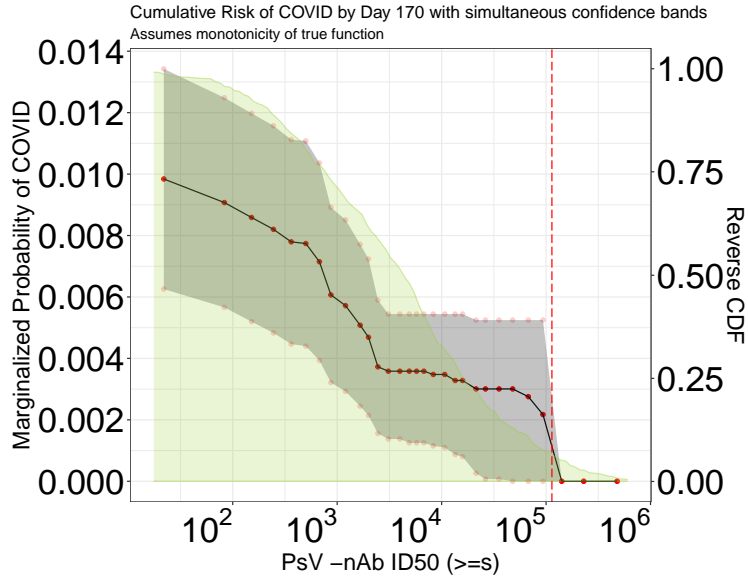

Figure 26: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
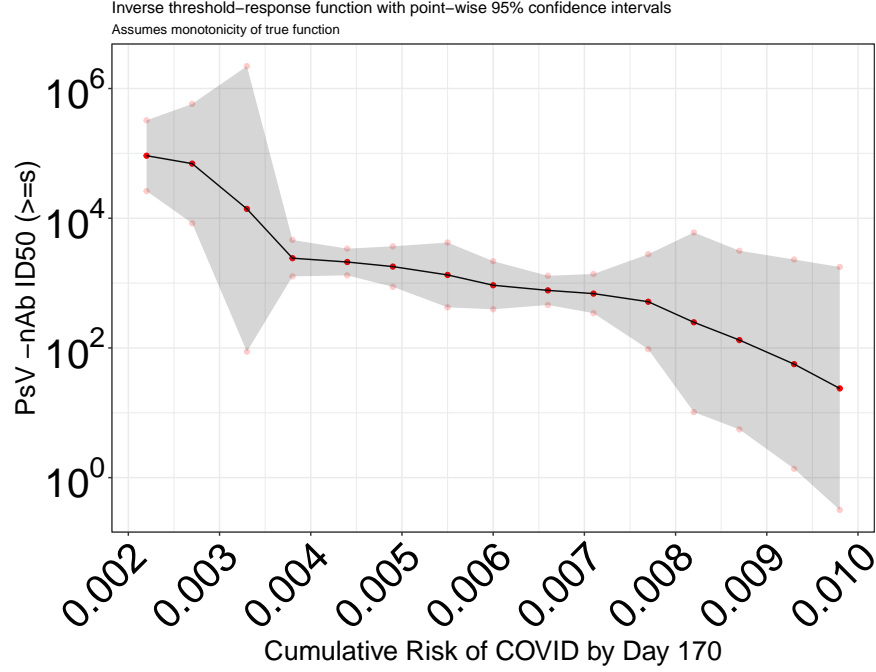
Figure 27: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with point-wise 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.0022	9.12*10^4	2.63*10^4	3.24*10^5
0.0027	6.92*10^4	8.32*10^3	5.75*10^5
0.0033	1.38*10^4	8.71*10^1	2.19*10^6
0.0038	2.40*10^3	1.26*10^3	4.57*10^3
0.0044	2.09*10^3	1.32*10^3	3.39*10^3
0.0049	1.78*10^3	8.71*10^2	3.72*10^3
0.0055	1.35*10^3	4.27*10^2	4.27*10^3
0.006	9.33*10^2	3.98*10^2	2.19*10^3
0.0066	7.76*10^2	4.57*10^2	1.29*10^3
0.0071	6.92*10^2	3.47*10^2	1.38*10^3
0.0077	5.13*10^2	9.55*10^1	2.82*10^3
0.0082	2.51*10^2	1.02*10^1	6.03*10^3
0.0087	1.32*10^2	5.50*10^0	3.16*10^3
0.0093	5.62*10^1	1.38*10^0	2.29*10^3
0.0098	2.40*10^1	3.16e-01	1.78*10^3

Figure 28: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Pseudo virus-neutralizing antibody activity level at a range of risk levels with point-wise 95% confidence intervals
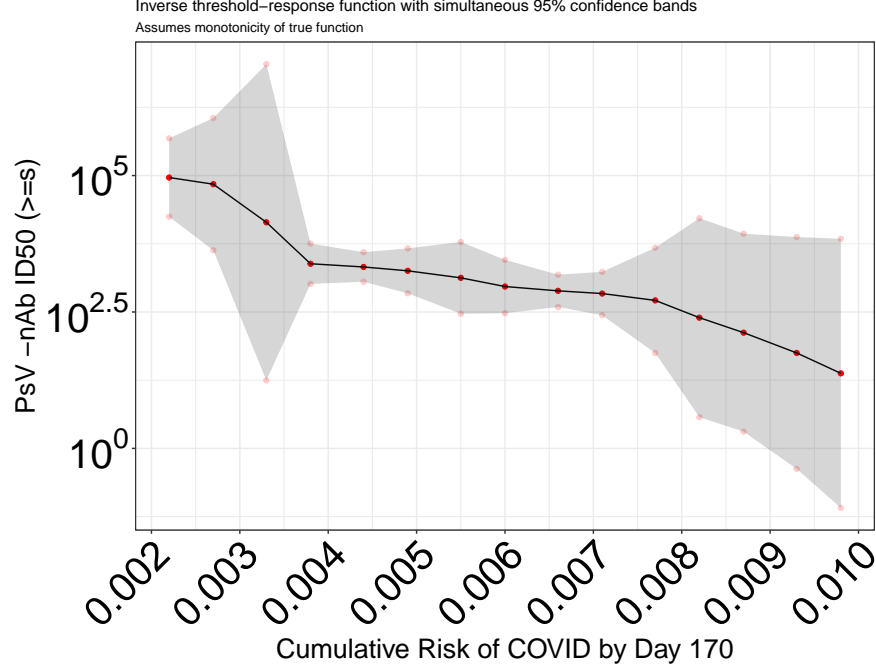
Figure 29: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with simultaneous 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.0022	9.12*10^4	1.78*10^4	4.79*10^5
0.0027	6.92*10^4	4.27*10^3	1.12*10^6
0.0033	1.38*10^4	1.78*10^1	1.10*10^7
0.0038	2.40*10^3	1.02*10^3	5.62*10^3
0.0044	2.09*10^3	1.12*10^3	3.98*10^3
0.0049	1.78*10^3	6.92*10^2	4.68*10^3
0.0055	1.35*10^3	2.95*10^2	6.03*10^3
0.006	9.33*10^2	3.02*10^2	2.88*10^3
0.0066	7.76*10^2	3.89*10^2	1.51*10^3
0.0071	6.92*10^2	2.75*10^2	1.74*10^3
0.0077	5.13*10^2	5.62*10^1	4.79*10^3
0.0082	2.51*10^2	3.72*10^0	1.66*10^4
0.0087	1.32*10^2	2.04*10^0	8.51*10^3
0.0093	5.62*10^1	4.27e-01	7.41*10^3
0.0098	2.40*10^1	8.13e-02	6.92*10^3

Figure 30: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Pseudo virus-neutralizing antibody activity level at a range of risk levels with simultaneous 95% confidence bands.

Pseudo-neutralizing antibody (80% titer)

Cumulative Risk of COVID by Day 170 with point–wise confidence intervals
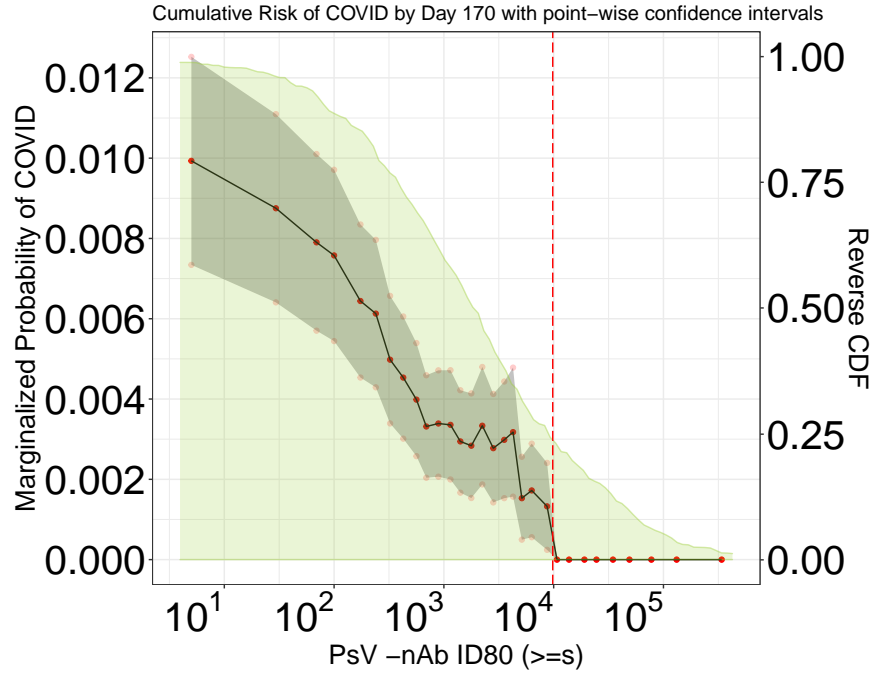

Figure 31: Adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.697	4.98*10^0	0.00993	0.00734	0.01252
2.000	1.00*10^2	0.00758	0.00544	0.00971
2.514	3.27*10^2	0.00498	0.00339	0.00657
2.947	8.85*10^2	0.00339	0.00207	0.00471
3.245	1.76*10^3	0.00284	0.00153	0.00414
3.551	3.56*10^3	0.00298	0.00153	0.00444
3.804	6.37*10^3	0.00172	0.00056	0.00289
4.277	1.89*10^4	0.00000	0.00000	1.00000
4.691	4.91*10^4	0.00000	0.00000	1.00000
5.528	3.37*10^5	0.00000	0.00000	1.00000

Figure 32: Table of risk estimates for range of thresholds of Pseudo virus-neutralizing antibody activity levels with point-wise 95% confidence intervals.
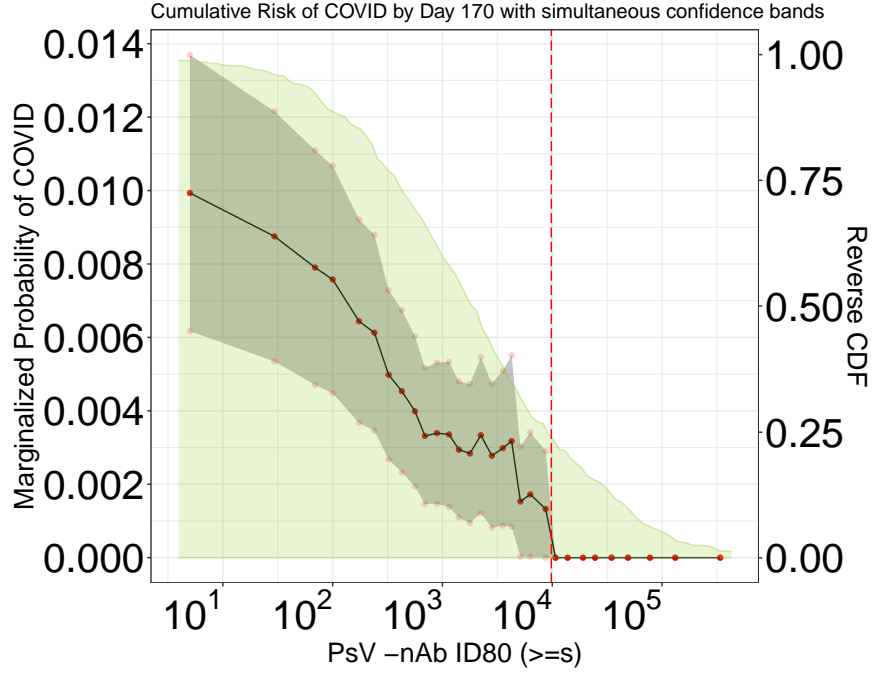
Figure 33: Adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.697	4.98*10^0	0.00993	0.00617	0.01370
2.000	1.00*10^2	0.00758	0.00448	0.01068
2.514	3.27*10^2	0.00498	0.00267	0.00729
2.947	8.85*10^2	0.00339	0.00147	0.00531
3.245	1.76*10^3	0.00284	0.00094	0.00473
3.551	3.56*10^3	0.00298	0.00087	0.00509
3.804	6.37*10^3	0.00172	0.00003	0.00342
4.277	1.89*10^4	0.00000	0.00000	1.00000
4.691	4.91*10^4	0.00000	0.00000	1.00000
5.528	3.37*10^5	0.00000	0.00000	1.00000

Figure 34: Table of risk estimates for range of thresholds of Pseudo virus-neutralizing antibody activity levels with simultaneous 95% confidence bands
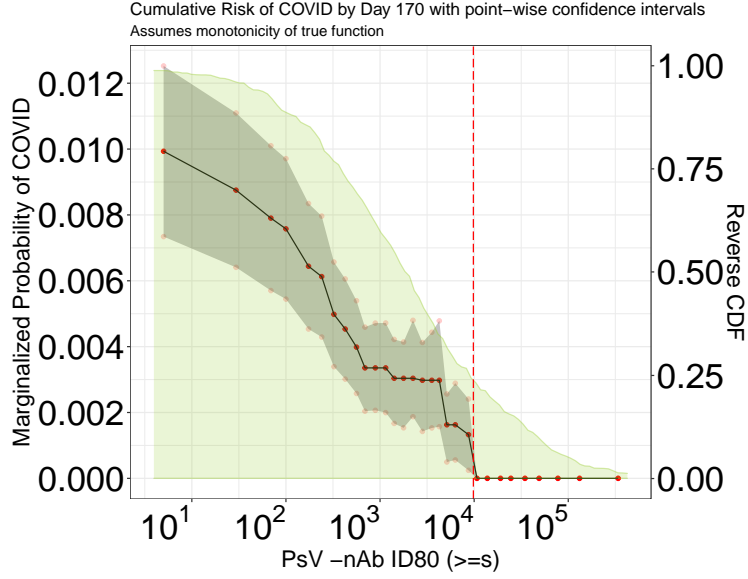
Figure 35: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
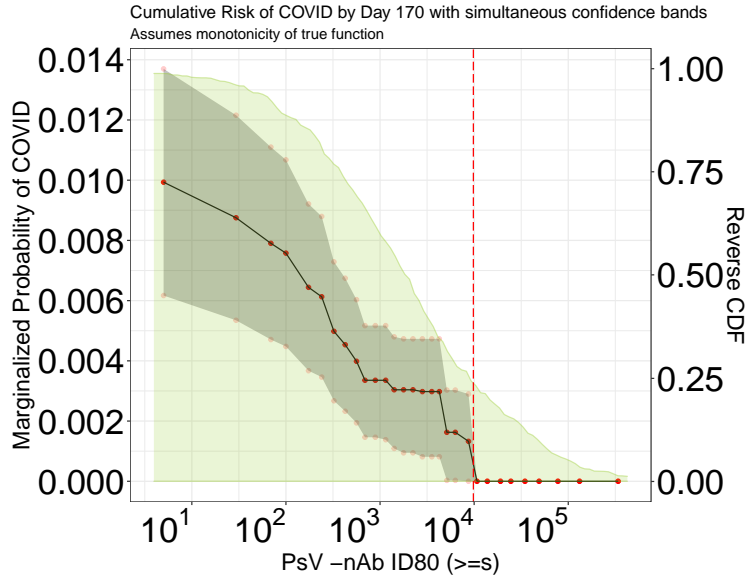

Figure 36: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
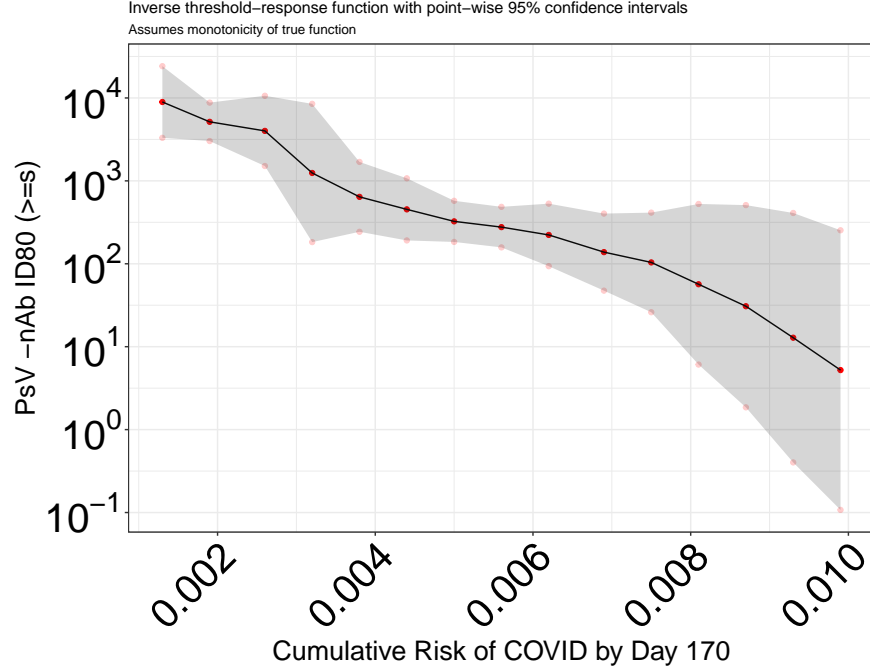
Figure 37: The inverse adjusted threshold-response function with 95% point-wise confidence bands.

Risk	Threshold est.	CI left	CI right
0.0013	8.91*10^3	3.31*10^3	2.40*10^4
0.0019	5.13*10^3	3.02*10^3	8.71*10^3
0.0026	3.98*10^3	1.51*10^3	1.07*10^4
0.0032	1.26*10^3	1.82*10^2	8.51*10^3
0.0038	6.46*10^2	2.45*10^2	1.70*10^3
0.0044	4.57*10^2	1.91*10^2	1.07*10^3
0.005	3.24*10^2	1.82*10^2	5.75*10^2
0.0056	2.75*10^2	1.58*10^2	4.90*10^2
0.0062	2.24*10^2	9.33*10^1	5.37*10^2
0.0069	1.38*10^2	4.79*10^1	4.07*10^2
0.0075	1.05*10^2	2.63*10^1	4.17*10^2
0.0081	5.62*10^1	6.03*10^0	5.25*10^2
0.0087	3.09*10^1	1.86*10^0	5.13*10^2
0.0093	1.29*10^1	3.98e-01	4.07*10^2
0.0099	5.25*10^0	1.07e-01	2.51*10^2

Figure 38: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Pseudo virus-neutralizing antibody activity level at a range of risk levels with 95% point-wise confidence intervals.
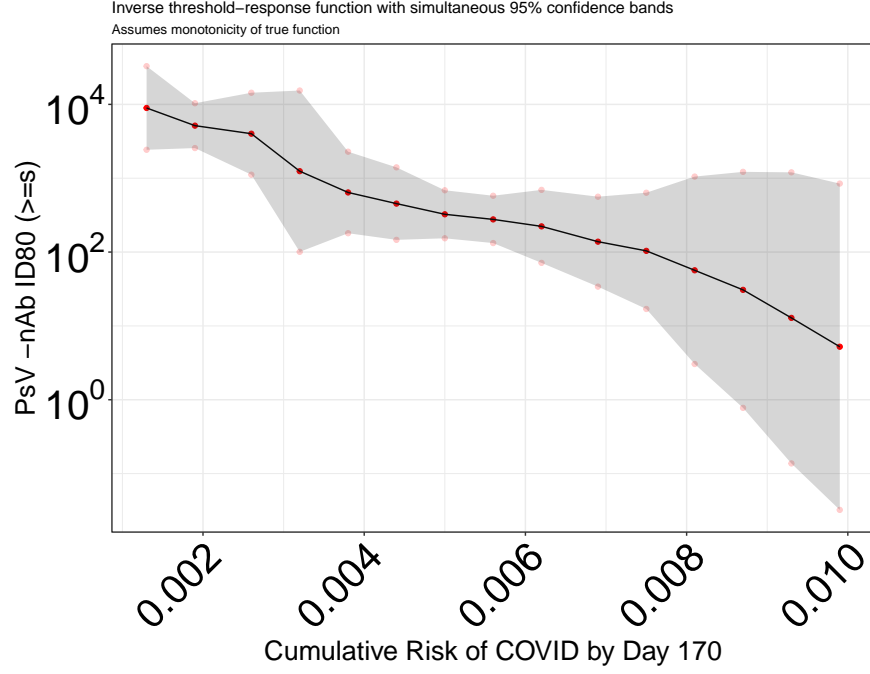
Figure 39: The inverse adjusted threshold-response function with 95% simultaneous confidence bands.

Risk	Threshold est.	CI left	CI right
0.0013	8.91*10^3	2.45*10^3	3.31*10^4
0.0019	5.13*10^3	2.57*10^3	1.05*10^4
0.0026	3.98*10^3	1.12*10^3	1.45*10^4
0.0032	1.26*10^3	1.00*10^2	1.55*10^4
0.0038	6.46*10^2	1.82*10^2	2.29*10^3
0.0044	4.57*10^2	1.48*10^2	1.41*10^3
0.005	3.24*10^2	1.55*10^2	6.92*10^2
0.0056	2.75*10^2	1.32*10^2	5.75*10^2
0.0062	2.24*10^2	7.08*10^1	6.92*10^2
0.0069	1.38*10^2	3.39*10^1	5.62*10^2
0.0075	1.05*10^2	1.70*10^1	6.31*10^2
0.0081	5.62*10^1	3.02*10^0	1.05*10^3
0.0087	3.09*10^1	7.76e-01	1.23*10^3
0.0093	1.29*10^1	1.38e-01	1.20*10^3
0.0099	5.25*10^0	3.24e-02	8.51*10^2

Figure 40: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Pseudo virus-neutralizing antibody activity level at a range of risk levels with 95% simultaneous confidence intervals.

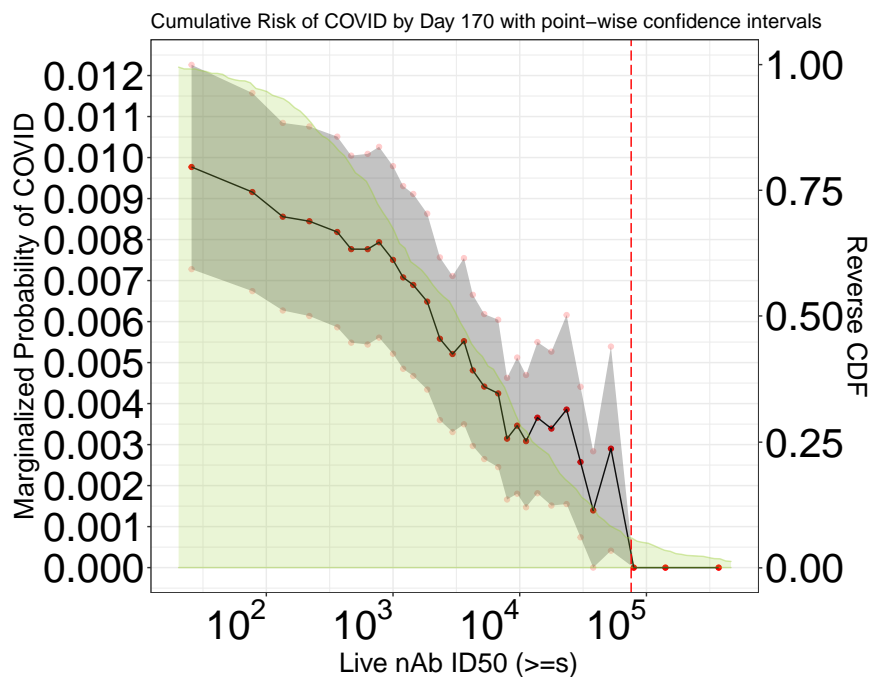**Live virus-neutralizing antibody (50% titer)**

Figure 41: Adjusted threshold-response function for a range of thresholds of the Live virus-neutralizing antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.408	2.56*10^1	0.00977	0.00728	0.01226
2.341	2.19*10^2	0.00845	0.00614	0.01076
2.796	6.25*10^2	0.00777	0.00544	0.01009
3.162	1.45*10^3	0.00689	0.00467	0.00911
3.470	2.95*10^3	0.00521	0.00331	0.00711
3.723	5.28*10^3	0.00442	0.00265	0.00618
3.983	9.62*10^3	0.00346	0.00180	0.00512
4.373	2.36*10^4	0.00385	0.00155	0.00616
4.719	5.24*10^4	0.00290	0.00041	0.00539
5.568	3.70*10^5	0.00000	0.00000	1.00000

Figure 42: Table of risk estimates for range of thresholds of Live virus-neutralizing antibody activity levels with point-wise 95% point-wise intervals.
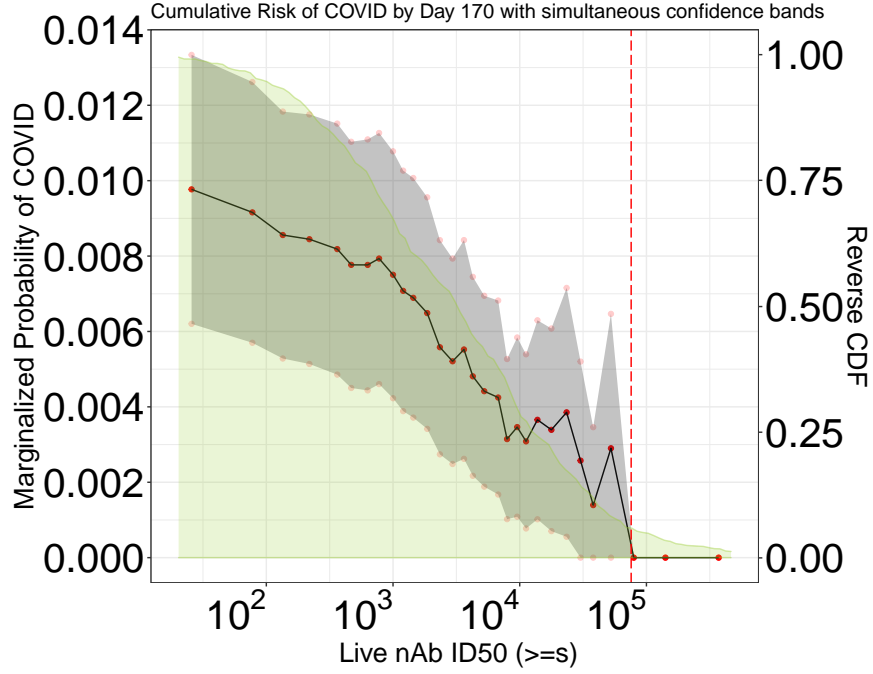
Figure 43: Adjusted threshold-response function for a range of thresholds of the Live virus-neutralizing antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.408	2.56*10^1	0.00977	0.00620	0.01334
2.341	2.19*10^2	0.00845	0.00514	0.01176
2.796	6.25*10^2	0.00777	0.00444	0.01109
3.162	1.45*10^3	0.00689	0.00371	0.01007
3.470	2.95*10^3	0.00521	0.00248	0.00793
3.723	5.28*10^3	0.00442	0.00188	0.00695
3.983	9.62*10^3	0.00346	0.00109	0.00584
4.373	2.36*10^4	0.00385	0.00055	0.00716
4.719	5.24*10^4	0.00290	0.00000	0.00647
5.568	3.70*10^5	0.00000	0.00000	1.00000

Figure 44: Table of risk estimates for range of thresholds of Live virus-neutralizing antibody activity levels with simultaneous 95% confidence bands.
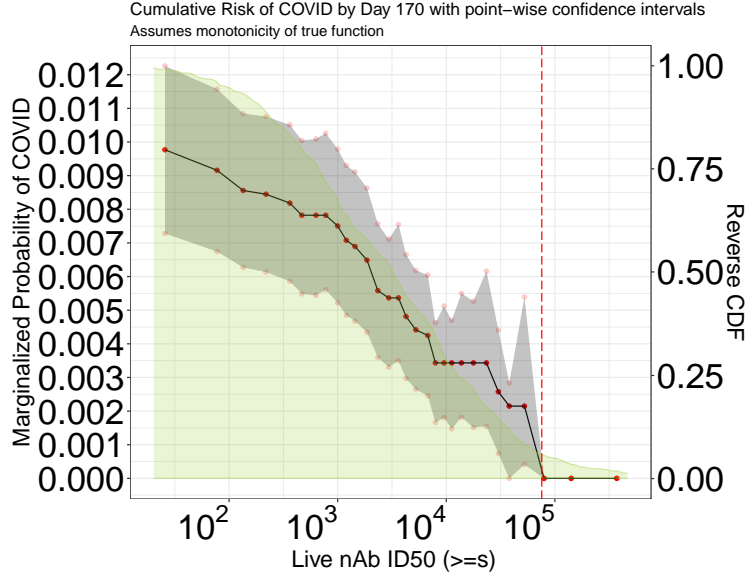
Figure 45: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Live virus-neutralizing antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
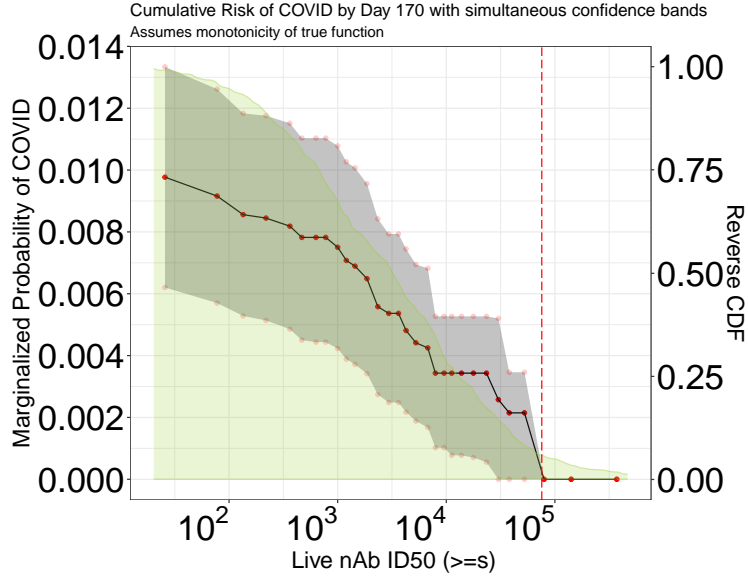

Figure 46: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Live virus-neutralizing antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
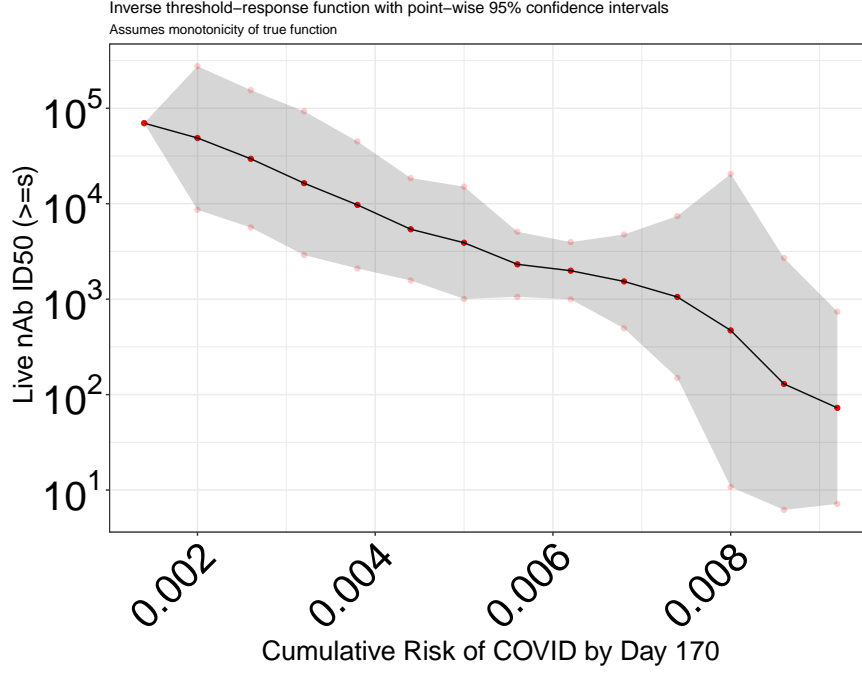
Figure 47: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with point-wise 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.0014	6.92*10^4	6.92*10^4	6.92*10^4
0.002	4.90*10^4	8.71*10^3	2.75*10^5
0.0026	2.95*10^4	5.62*10^3	1.55*10^5
0.0032	1.62*10^4	2.88*10^3	9.33*10^4
0.0038	9.77*10^3	2.09*10^3	4.47*10^4
0.0044	5.37*10^3	1.58*10^3	1.86*10^4
0.005	3.89*10^3	1.00*10^3	1.51*10^4
0.0056	2.29*10^3	1.05*10^3	5.13*10^3
0.0062	2.00*10^3	1.00*10^3	3.98*10^3
0.0068	1.55*10^3	4.90*10^2	4.79*10^3
0.0074	1.05*10^3	1.51*10^2	7.41*10^3
0.008	4.68*10^2	1.07*10^1	2.04*10^4
0.0086	1.29*10^2	6.17*10^0	2.69*10^3
0.0092	7.24*10^1	7.08*10^0	7.41*10^2

Figure 48: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Live virus-neutralizing antibody activity level at a range of risk levels with point-wise 95% confidence intervals
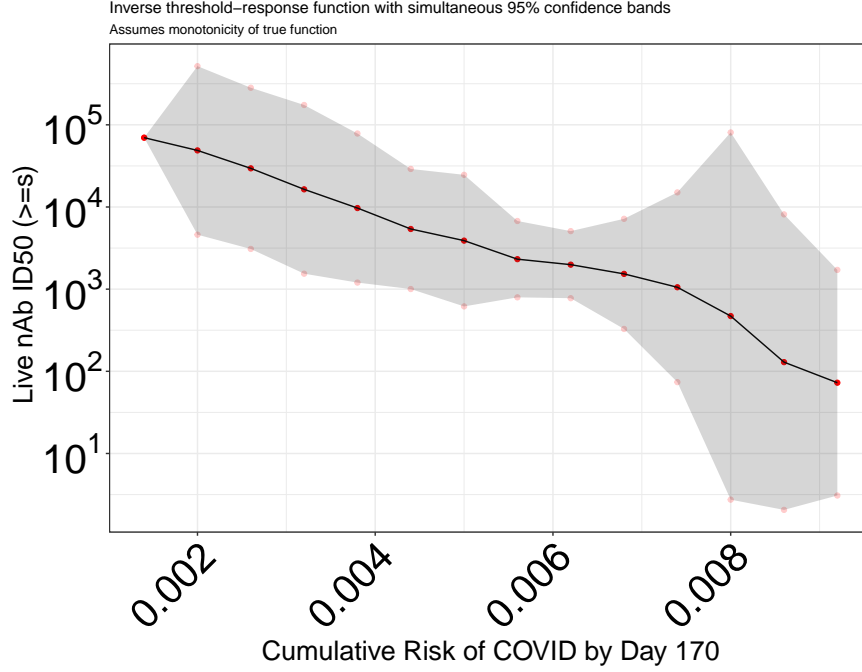
Figure 49: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with simultaneous 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.0014	6.92*10^4	6.92*10^4	6.92*10^4
0.002	4.90*10^4	4.57*10^3	5.13*10^5
0.0026	2.95*10^4	3.09*10^3	2.82*10^5
0.0032	1.62*10^4	1.55*10^3	1.74*10^5
0.0038	9.77*10^3	1.20*10^3	7.76*10^4
0.0044	5.37*10^3	1.00*10^3	2.88*10^4
0.005	3.89*10^3	6.17*10^2	2.45*10^4
0.0056	2.29*10^3	7.94*10^2	6.76*10^3
0.0062	2.00*10^3	7.76*10^2	5.13*10^3
0.0068	1.55*10^3	3.31*10^2	7.24*10^3
0.0074	1.05*10^3	7.41*10^1	1.51*10^4
0.008	4.68*10^2	2.75*10^0	8.13*10^4
0.0086	1.29*10^2	2.04*10^0	8.13*10^3
0.0092	7.24*10^1	3.09*10^0	1.70*10^3

Figure 50: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Live virus-neutralizing antibody activity level at a range of risk levels with simultaneous 95% confidence bands

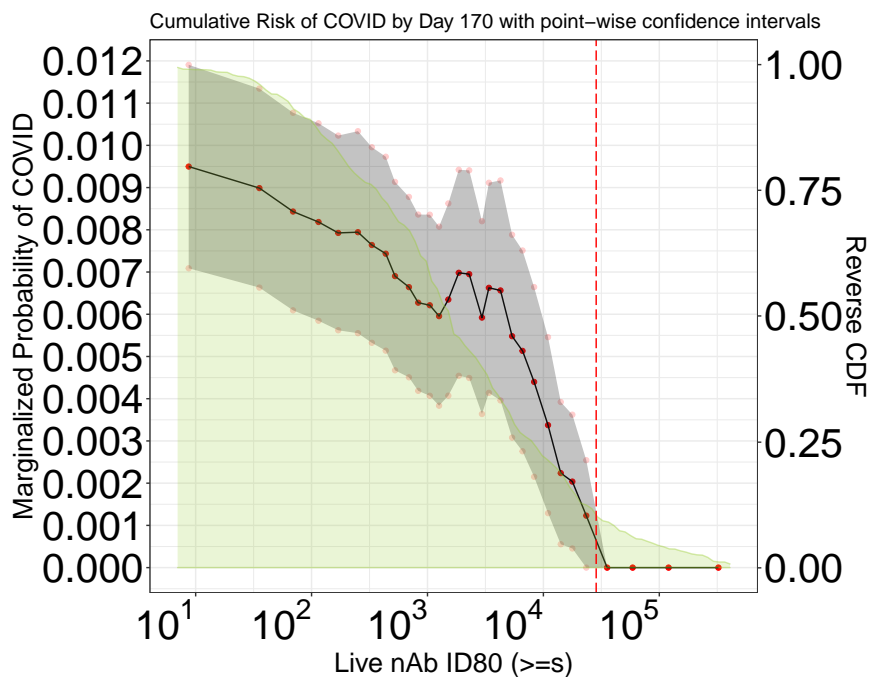**Live virus-neutralizing antibody (80% titer)**

Figure 51: Adjusted threshold-response function for a range of thresholds of the Live virus-neutralizing antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.944	8.79*10^0	0.00950	0.00709	0.01191
2.061	1.15*10^2	0.00818	0.00585	0.01052
2.520	3.31*10^2	0.00764	0.00532	0.00996
2.924	8.39*10^2	0.00627	0.00419	0.00836
3.185	1.53*10^3	0.00635	0.00407	0.00862
3.473	2.97*10^3	0.00592	0.00364	0.00820
3.732	5.40*10^3	0.00548	0.00308	0.00788
4.150	1.41*10^4	0.00224	0.00055	0.00392
4.549	3.54*10^4	0.00000	0.00000	1.00000
5.510	3.24*10^5	0.00000	0.00000	1.00000

Figure 52: Table of risk estimates for range of thresholds of Live virus-neutralizing antibody activity levels with point-wise 95% confidence intervals.
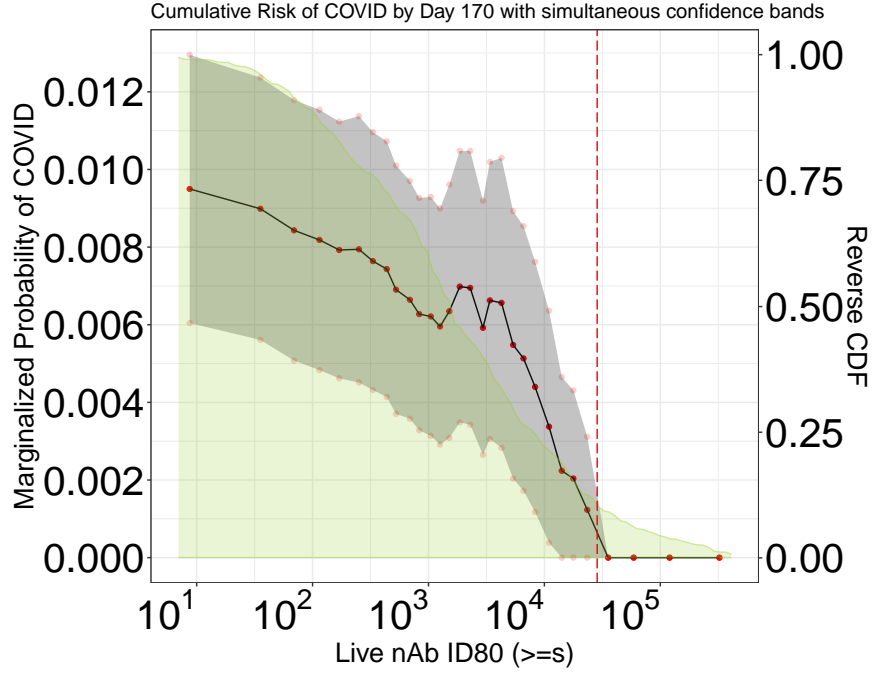
Figure 53: Adjusted threshold-response function for a range of thresholds of the Live virus-neutralizing antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.944	8.79*10^0	0.00950	0.00604	0.01295
2.061	1.15*10^2	0.00818	0.00483	0.01154
2.520	3.31*10^2	0.00764	0.00432	0.01096
2.924	8.39*10^2	0.00627	0.00328	0.00927
3.185	1.53*10^3	0.00635	0.00308	0.00961
3.473	2.97*10^3	0.00592	0.00265	0.00919
3.732	5.40*10^3	0.00548	0.00204	0.00893
4.150	1.41*10^4	0.00224	0.00000	0.00465
4.549	3.54*10^4	0.00000	0.00000	1.00000
5.510	3.24*10^5	0.00000	0.00000	1.00000

Figure 54: Table of risk estimates for range of thresholds of Live virus-neutralizing antibody activity levels with simultaneous 95% confidence bands.
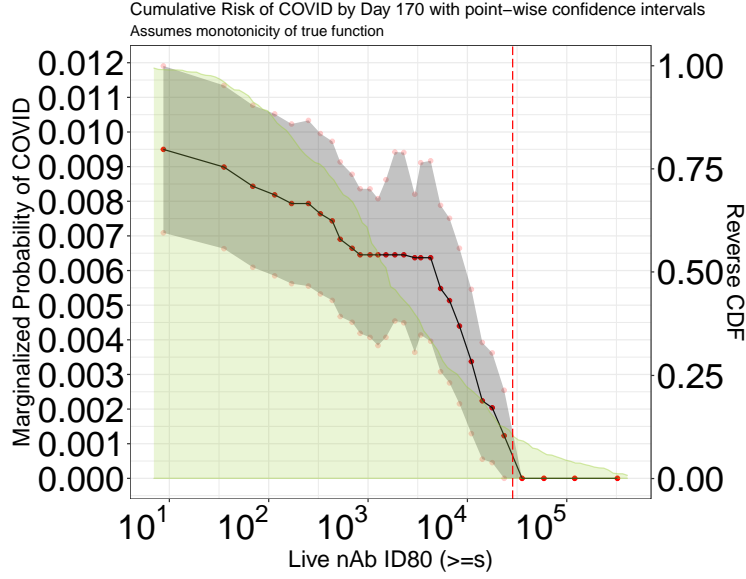
Figure 55: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated adjusted threshold-response function for a range of thresholds of the Live virus-neutralizing antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
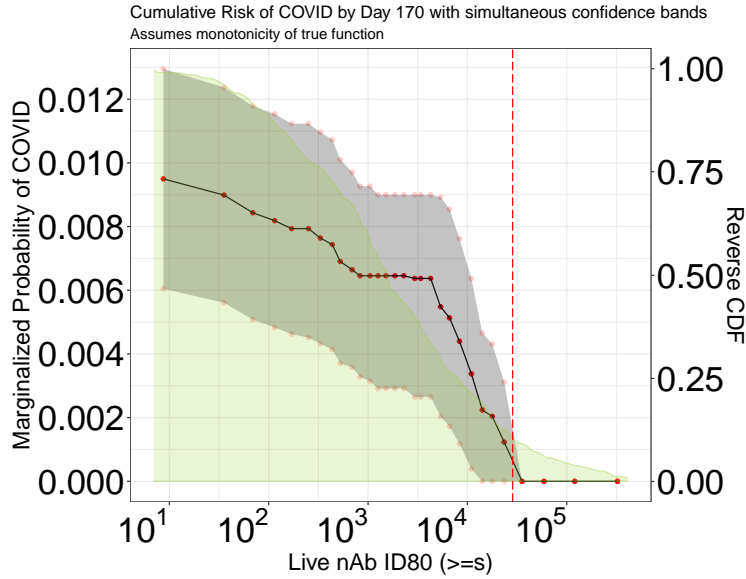

Figure 56: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Live virus-neutralizing antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.
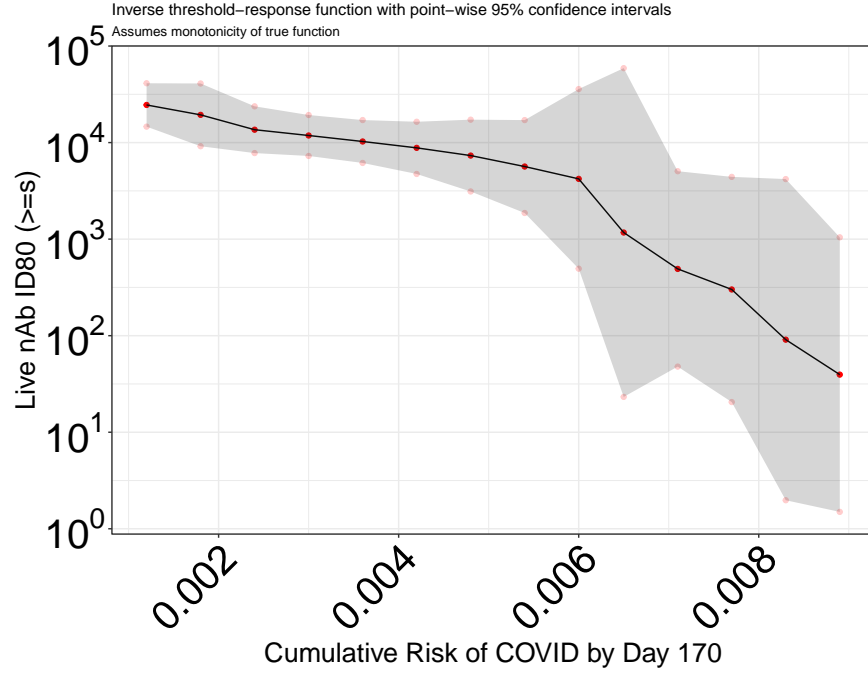
Figure 57: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with point-wise 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.0012	$2.45*10^4$	$1.48*10^4$	$4.07*10^4$
0.0018	$1.95*10^4$	$9.12*10^3$	$4.07*10^4$
0.0024	$1.35*10^4$	$7.76*10^3$	$2.40*10^4$
0.003	$1.17*10^4$	$7.24*10^3$	$1.95*10^4$
0.0036	$1.02*10^4$	$6.17*10^3$	$1.70*10^4$
0.0042	$8.91*10^3$	$4.79*10^3$	$1.66*10^4$
0.0048	$7.41*10^3$	$3.09*10^3$	$1.74*10^4$
0.0054	$5.62*10^3$	$1.86*10^3$	$1.70*10^4$
0.006	$4.17*10^3$	$4.90*10^2$	$3.55*10^4$
0.0065	$1.17*10^3$	$2.34*10^1$	$5.89*10^4$
0.0071	$4.90*10^2$	$4.79*10^1$	$5.01*10^3$
0.0077	$3.02*10^2$	$2.04*10^1$	$4.37*10^3$
0.0083	$9.12*10^1$	$2.00*10^0$	$4.17*10^3$
0.0089	$3.98*10^1$	$1.48*10^0$	$1.05*10^3$

Figure 58: This analysis assumes monotonicity of the true function. The table shows the estimated threshold of protection of Live virus-neutralizing antibody activity level at a range of risk levels with point-wise 95% confidence intervals.
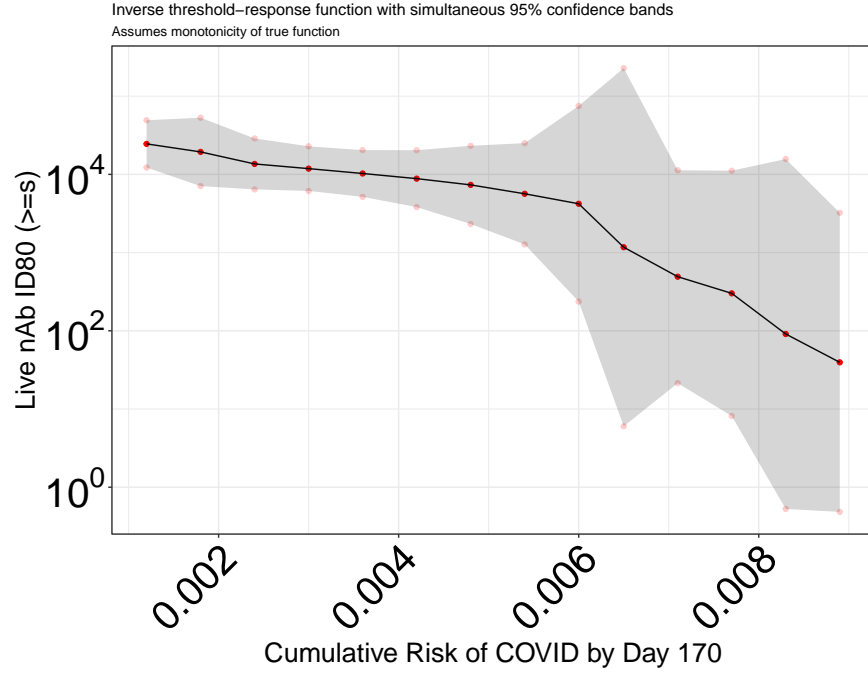
Figure 59: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with simultaneous 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.0012	2.45*10^4	1.23*10^4	4.90*10^4
0.0018	1.95*10^4	7.08*10^3	5.25*10^4
0.0024	1.35*10^4	6.46*10^3	2.88*10^4
0.003	1.17*10^4	6.17*10^3	2.29*10^4
0.0036	1.02*10^4	5.13*10^3	2.04*10^4
0.0042	8.91*10^3	3.80*10^3	2.04*10^4
0.0048	7.41*10^3	2.34*10^3	2.34*10^4
0.0054	5.62*10^3	1.26*10^3	2.51*10^4
0.006	4.17*10^3	2.34*10^2	7.59*10^4
0.0065	1.17*10^3	6.03*10^0	2.29*10^5
0.0071	4.90*10^2	2.14*10^1	1.12*10^4
0.0077	3.02*10^2	8.13*10^0	1.12*10^4
0.0083	9.12*10^1	5.25e-01	1.58*10^4
0.0089	3.98*10^1	4.79e-01	3.24*10^3

Figure 60: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Live virus-neutralizing antibody activity level at a range of risk levels with simultaneous 95% confidence bands.