

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 (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 \rightarrow 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.

Day 57 Spike protein antibody

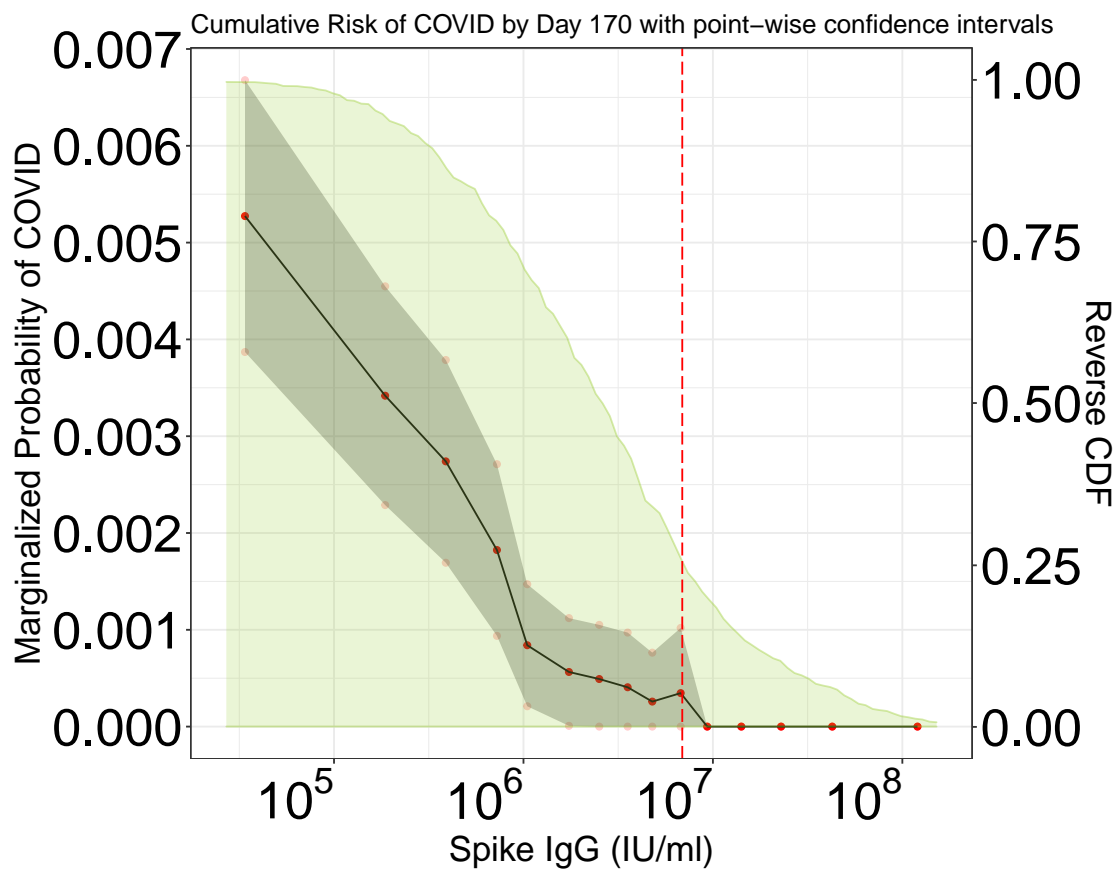


Figure 1: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.531	3.40×10^4	0.00527	0.00387	0.00668
5.588	3.87×10^5	0.00274	0.00169	0.00379
5.860	7.24×10^5	0.00182	0.00094	0.00271
6.236	1.72×10^6	0.00056	0.00001	0.00112
6.395	2.48×10^6	0.00049	0.00000	0.00105
6.677	4.75×10^6	0.00026	0.00000	0.00076
6.832	6.79×10^6	0.00035	0.00000	0.00102
7.151	1.42×10^7	0.00000	0.00000	1.00000
7.356	2.27×10^7	0.00000	0.00000	1.00000
8.081	1.21×10^8	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.

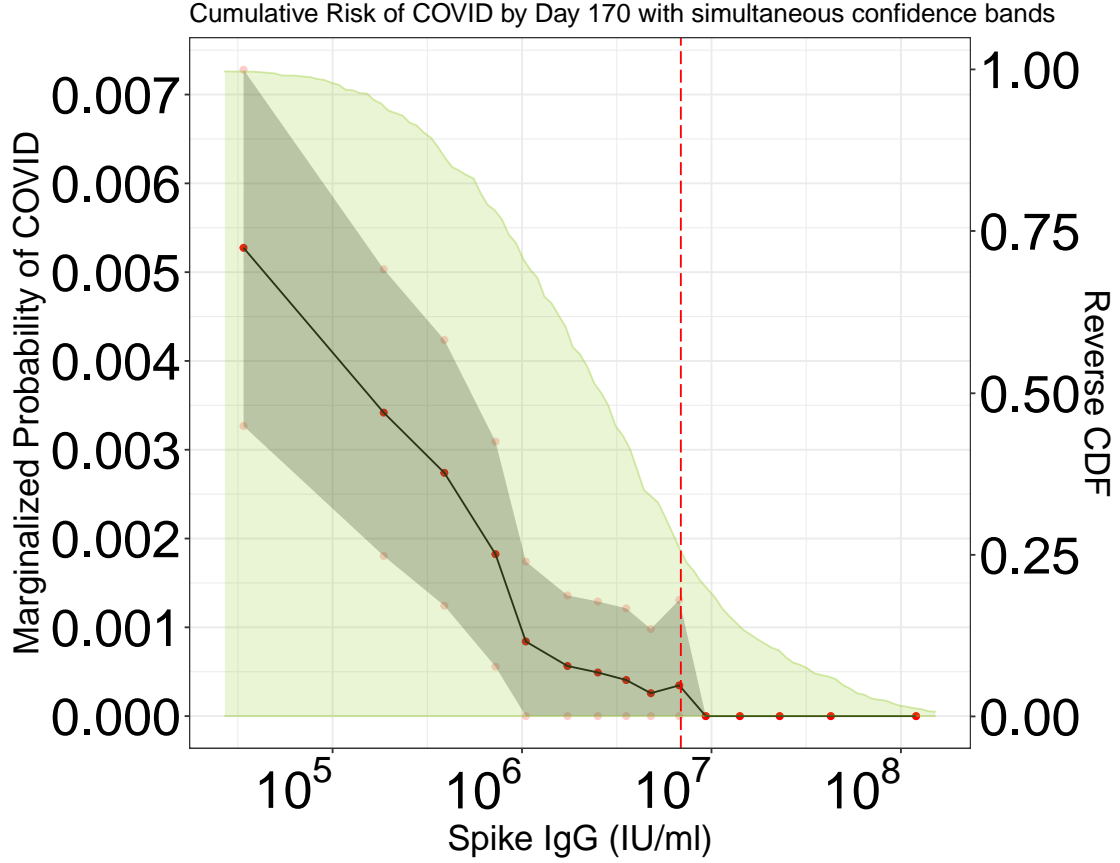


Figure 3: Adjusted threshold-response function for a range of thresholds of the Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.531	$3.40 \cdot 10^4$	0.00527	0.00327	0.00728
5.588	$3.87 \cdot 10^5$	0.00274	0.00124	0.00424
5.860	$7.24 \cdot 10^5$	0.00182	0.00056	0.00309
6.236	$1.72 \cdot 10^6$	0.00056	0.00000	0.00136
6.395	$2.48 \cdot 10^6$	0.00049	0.00000	0.00129
6.677	$4.75 \cdot 10^6$	0.00026	0.00000	0.00098
6.832	$6.79 \cdot 10^6$	0.00035	0.00000	0.00131
7.151	$1.42 \cdot 10^7$	0.00000	0.00000	1.00000
7.356	$2.27 \cdot 10^7$	0.00000	0.00000	1.00000
8.081	$1.21 \cdot 10^8$	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

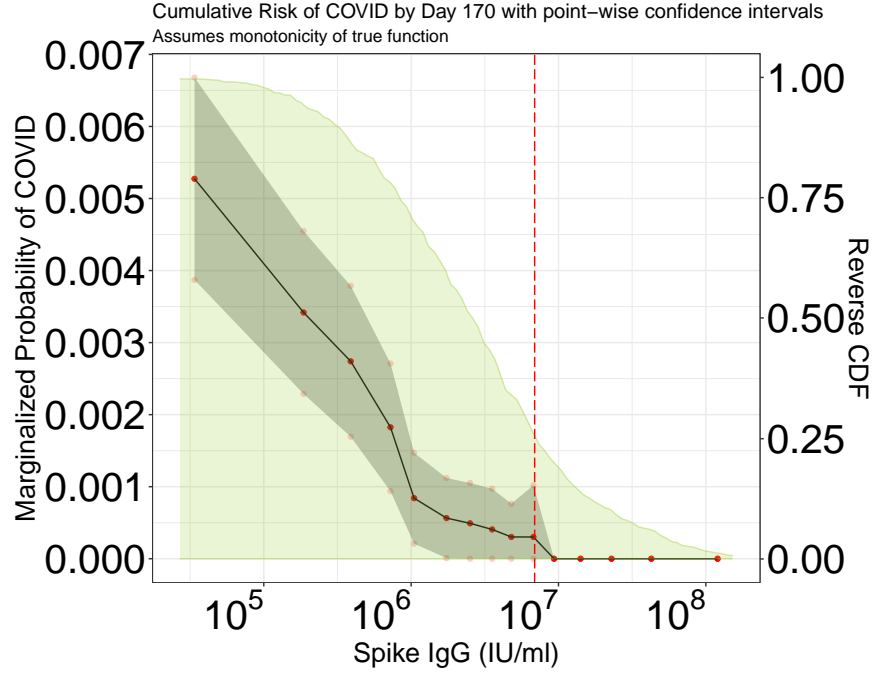


Figure 5: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after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

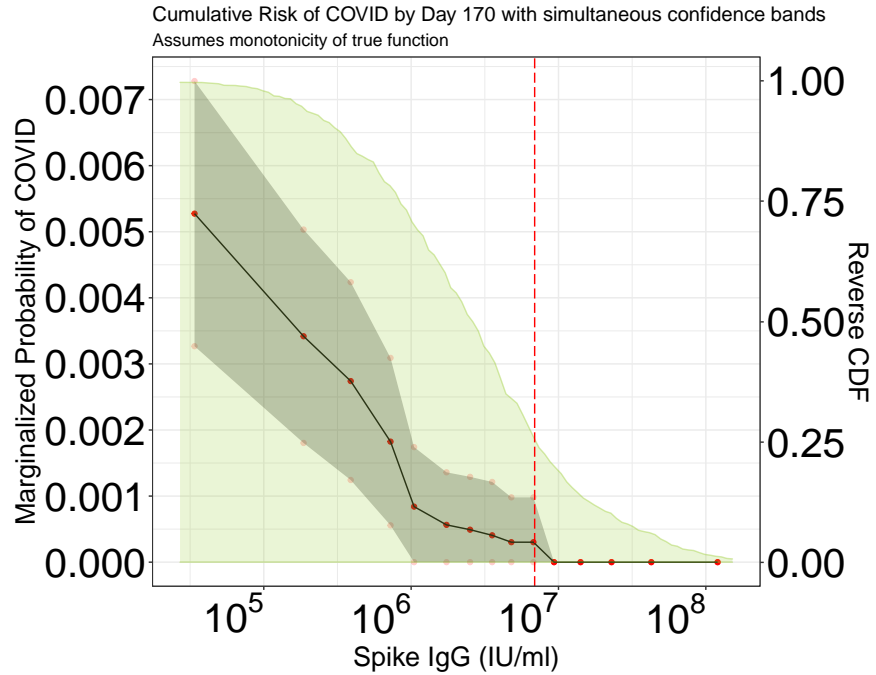


Figure 6: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

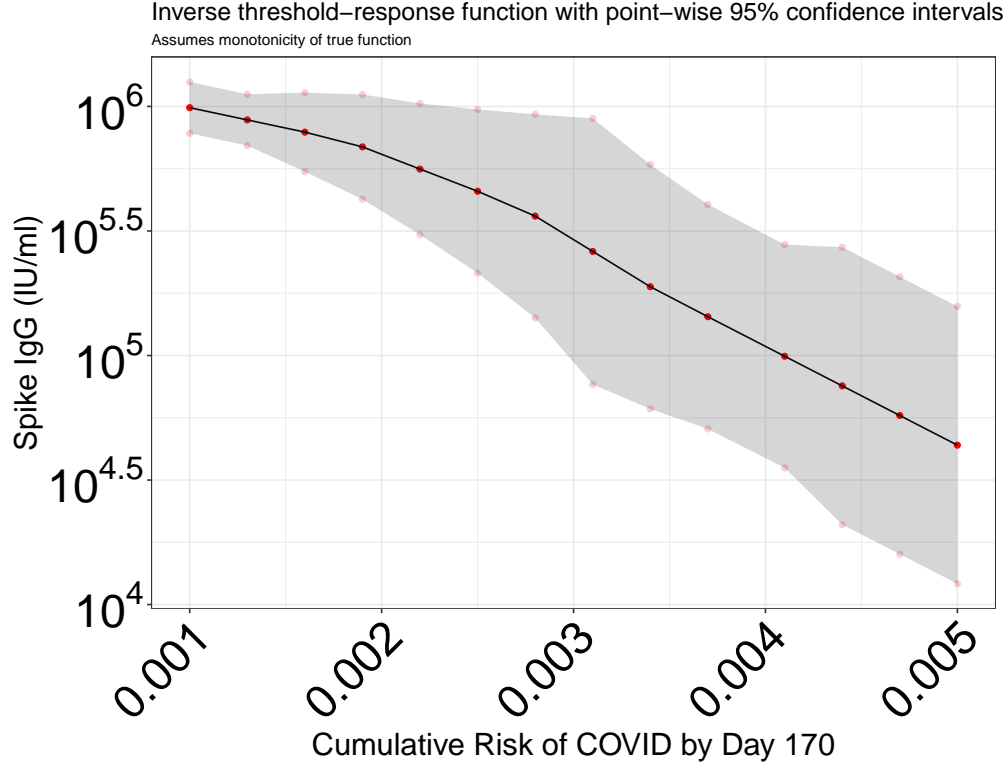


Figure 7: The inverse adjusted threshold-response function with pointwise 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.001	$1.00 \cdot 10^6$	$7.76 \cdot 10^5$	$1.26 \cdot 10^6$
0.0013	$8.91 \cdot 10^5$	$6.92 \cdot 10^5$	$1.12 \cdot 10^6$
0.0016	$7.94 \cdot 10^5$	$5.50 \cdot 10^5$	$1.15 \cdot 10^6$
0.0019	$6.92 \cdot 10^5$	$4.27 \cdot 10^5$	$1.12 \cdot 10^6$
0.0022	$5.62 \cdot 10^5$	$3.09 \cdot 10^5$	$1.02 \cdot 10^6$
0.0025	$4.57 \cdot 10^5$	$2.14 \cdot 10^5$	$9.77 \cdot 10^5$
0.0028	$3.63 \cdot 10^5$	$1.41 \cdot 10^5$	$9.33 \cdot 10^5$
0.0031	$2.63 \cdot 10^5$	$7.59 \cdot 10^4$	$8.91 \cdot 10^5$
0.0034	$1.91 \cdot 10^5$	$6.17 \cdot 10^4$	$5.89 \cdot 10^5$
0.0037	$1.45 \cdot 10^5$	$5.01 \cdot 10^4$	$4.07 \cdot 10^5$
0.0041	$1.00 \cdot 10^5$	$3.55 \cdot 10^4$	$2.82 \cdot 10^5$
0.0044	$7.59 \cdot 10^4$	$2.09 \cdot 10^4$	$2.69 \cdot 10^5$
0.0047	$5.75 \cdot 10^4$	$1.58 \cdot 10^4$	$2.09 \cdot 10^5$
0.005	$4.37 \cdot 10^4$	$1.20 \cdot 10^4$	$1.58 \cdot 10^5$

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.

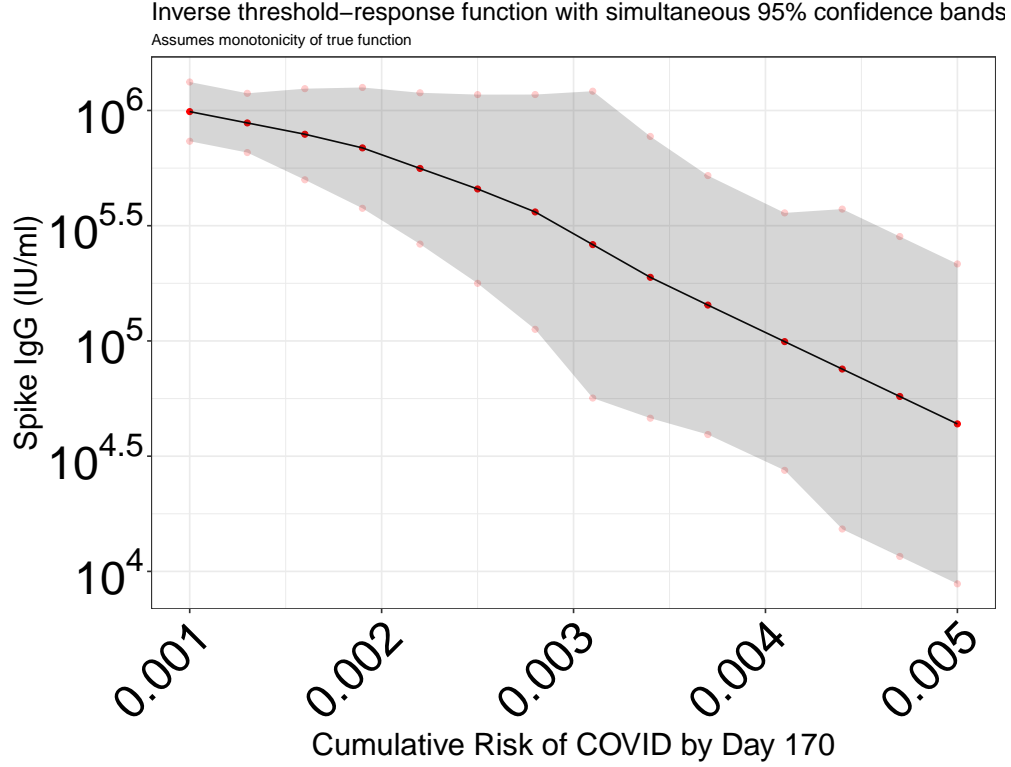


Figure 9: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with simultaneous 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.001	$1.00 \cdot 10^6$	$7.41 \cdot 10^5$	$1.32 \cdot 10^6$
0.0013	$8.91 \cdot 10^5$	$6.61 \cdot 10^5$	$1.17 \cdot 10^6$
0.0016	$7.94 \cdot 10^5$	$5.01 \cdot 10^5$	$1.23 \cdot 10^6$
0.0019	$6.92 \cdot 10^5$	$3.80 \cdot 10^5$	$1.26 \cdot 10^6$
0.0022	$5.62 \cdot 10^5$	$2.63 \cdot 10^5$	$1.20 \cdot 10^6$
0.0025	$4.57 \cdot 10^5$	$1.78 \cdot 10^5$	$1.17 \cdot 10^6$
0.0028	$3.63 \cdot 10^5$	$1.12 \cdot 10^5$	$1.17 \cdot 10^6$
0.0031	$2.63 \cdot 10^5$	$5.62 \cdot 10^4$	$1.20 \cdot 10^6$
0.0034	$1.91 \cdot 10^5$	$4.57 \cdot 10^4$	$7.76 \cdot 10^5$
0.0037	$1.45 \cdot 10^5$	$3.89 \cdot 10^4$	$5.25 \cdot 10^5$
0.0041	$1.00 \cdot 10^5$	$2.75 \cdot 10^4$	$3.63 \cdot 10^5$
0.0044	$7.59 \cdot 10^4$	$1.51 \cdot 10^4$	$3.72 \cdot 10^5$
0.0047	$5.75 \cdot 10^4$	$1.15 \cdot 10^4$	$2.82 \cdot 10^5$
0.005	$4.37 \cdot 10^4$	$8.91 \cdot 10^3$	$2.14 \cdot 10^5$

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

Day 57 RBD binding antibody

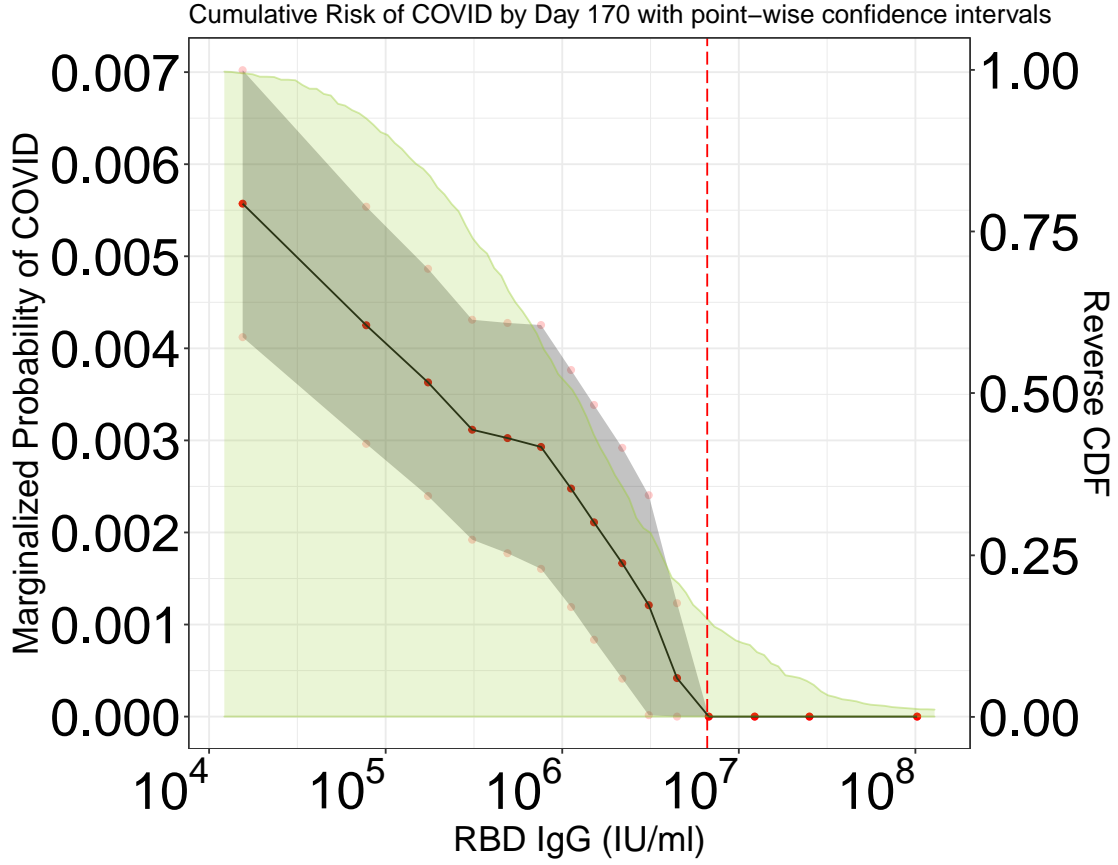


Figure 11: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.186	$1.53 \cdot 10^4$	0.00557	0.00412	0.00702
5.242	$1.75 \cdot 10^5$	0.00363	0.00240	0.00486
5.488	$3.08 \cdot 10^5$	0.00312	0.00192	0.00431
5.880	$7.59 \cdot 10^5$	0.00293	0.00161	0.00425
6.052	$1.13 \cdot 10^6$	0.00248	0.00119	0.00376
6.344	$2.21 \cdot 10^6$	0.00167	0.00041	0.00292
6.486	$3.06 \cdot 10^6$	0.00121	0.00002	0.00241
6.829	$6.75 \cdot 10^6$	0.00000	0.00000	1.00000
7.092	$1.24 \cdot 10^7$	0.00000	0.00000	1.00000
8.009	$1.02 \cdot 10^8$	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.

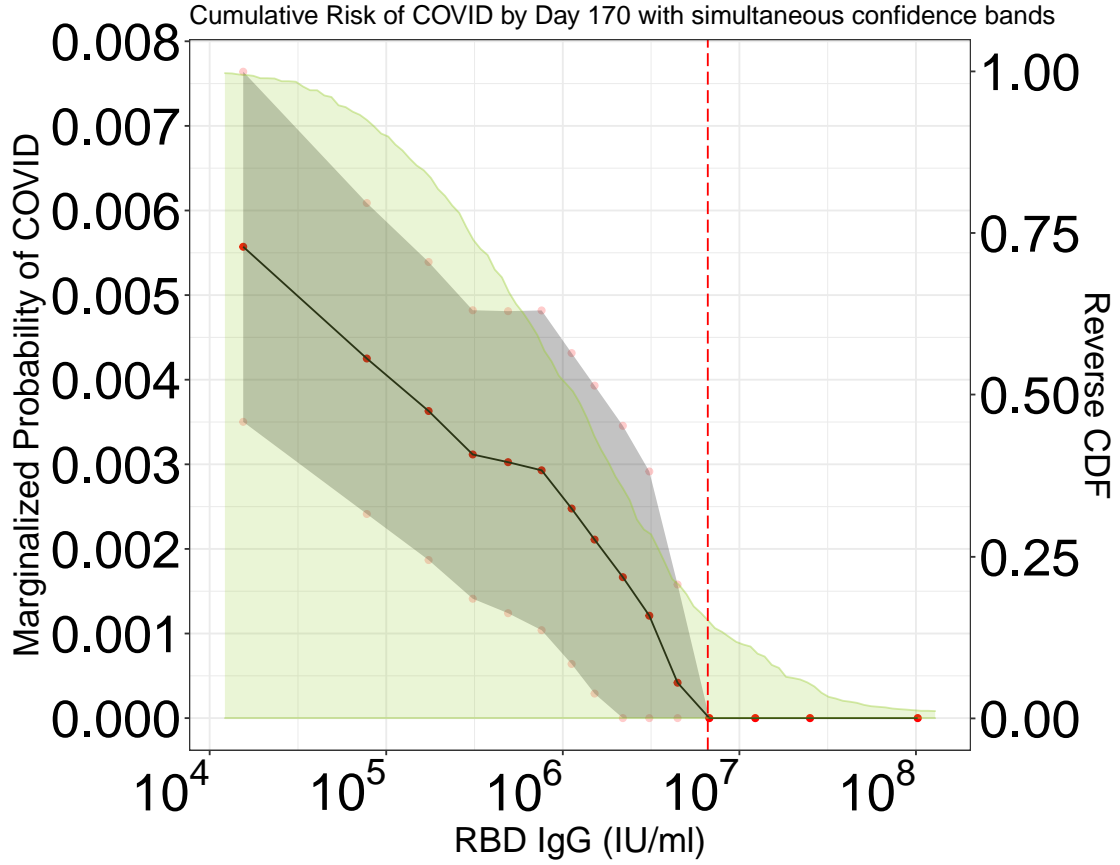


Figure 13: Adjusted threshold-response function for a range of thresholds of the RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.186	$1.53 \cdot 10^4$	0.00557	0.00350	0.00764
5.242	$1.75 \cdot 10^5$	0.00363	0.00187	0.00539
5.488	$3.08 \cdot 10^5$	0.00312	0.00141	0.00482
5.880	$7.59 \cdot 10^5$	0.00293	0.00104	0.00482
6.052	$1.13 \cdot 10^6$	0.00248	0.00064	0.00431
6.344	$2.21 \cdot 10^6$	0.00167	0.00000	0.00346
6.486	$3.06 \cdot 10^6$	0.00121	0.00000	0.00292
6.829	$6.75 \cdot 10^6$	0.00000	0.00000	1.00000
7.092	$1.24 \cdot 10^7$	0.00000	0.00000	1.00000
8.009	$1.02 \cdot 10^8$	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

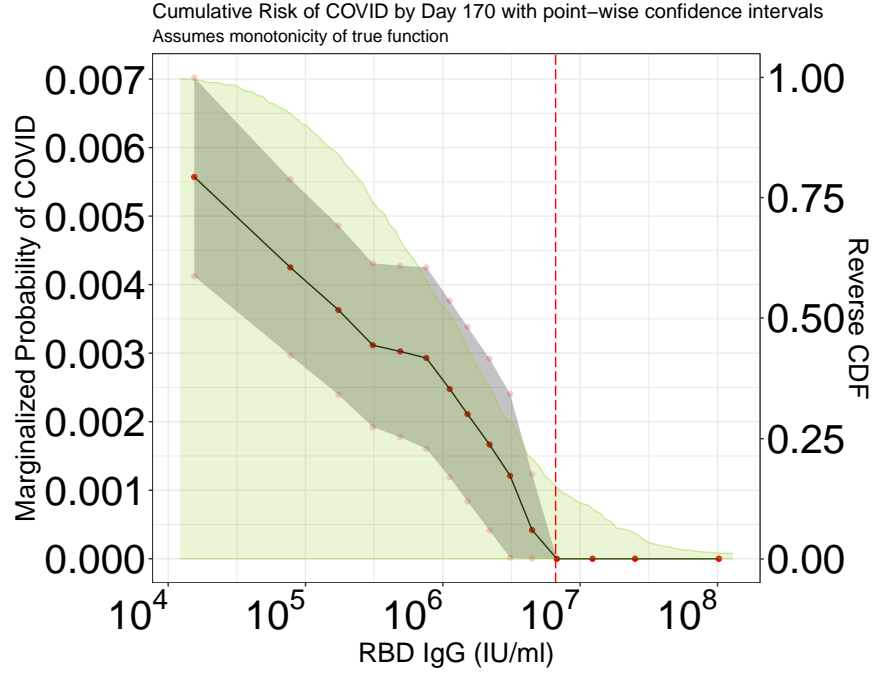


Figure 15: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after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

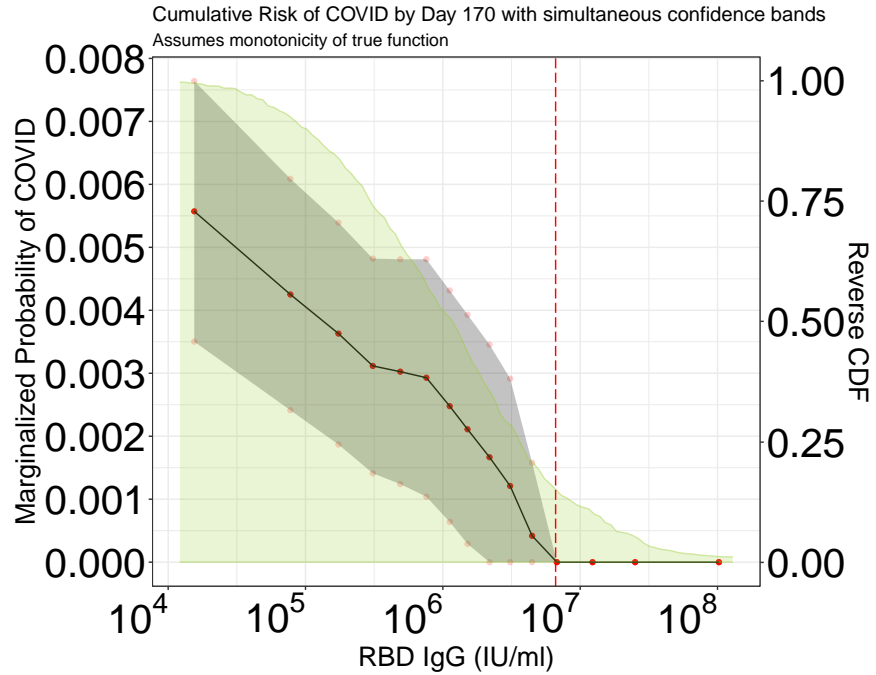


Figure 16: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after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

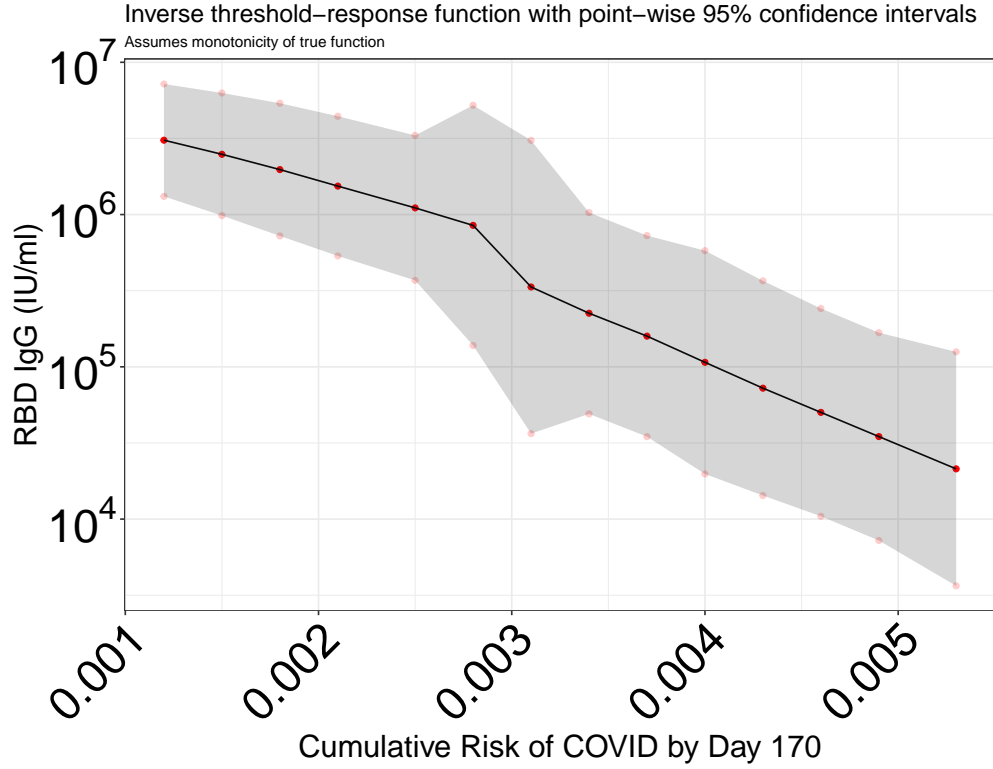


Figure 17: The inverse adjusted threshold-response function with pointwise 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.0012	3.09×10^6	1.32×10^6	7.24×10^6
0.0015	2.51×10^6	9.77×10^5	6.31×10^6
0.0018	2.00×10^6	7.24×10^5	5.37×10^6
0.0021	1.55×10^6	5.37×10^5	4.47×10^6
0.0025	1.10×10^6	3.72×10^5	3.31×10^6
0.0028	8.51×10^5	1.38×10^5	5.25×10^6
0.0031	3.31×10^5	3.63×10^4	3.09×10^6
0.0034	2.24×10^5	4.90×10^4	1.02×10^6
0.0037	1.58×10^5	3.47×10^4	7.24×10^5
0.004	1.07×10^5	2.00×10^4	5.75×10^5
0.0043	7.24×10^4	1.45×10^4	3.63×10^5
0.0046	5.01×10^4	1.05×10^4	2.40×10^5
0.0049	3.47×10^4	7.24×10^3	1.66×10^5
0.0053	2.14×10^4	3.63×10^3	1.26×10^5

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 pointwise 95% confidence intervals.

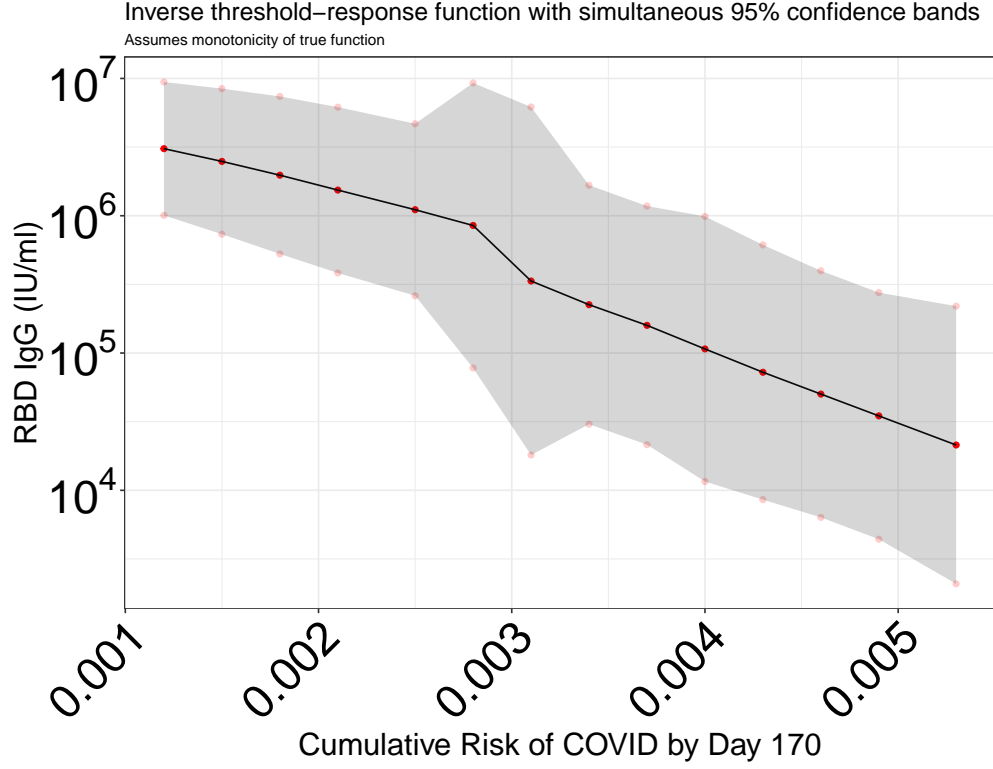


Figure 19: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with simultaneous 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.0012	3.09×10^6	1.00×10^6	9.33×10^6
0.0015	2.51×10^6	7.41×10^5	8.51×10^6
0.0018	2.00×10^6	5.25×10^5	7.41×10^6
0.0021	1.55×10^6	3.80×10^5	6.17×10^6
0.0025	1.10×10^6	2.63×10^5	4.68×10^6
0.0028	8.51×10^5	7.76×10^4	9.33×10^6
0.0031	3.31×10^5	1.82×10^4	6.17×10^6
0.0034	2.24×10^5	3.02×10^4	1.66×10^6
0.0037	1.58×10^5	2.14×10^4	1.17×10^6
0.004	1.07×10^5	1.15×10^4	1.00×10^6
0.0043	7.24×10^4	8.51×10^3	6.17×10^5
0.0046	5.01×10^4	6.31×10^3	3.98×10^5
0.0049	3.47×10^4	4.37×10^3	2.75×10^5
0.0053	2.14×10^4	2.09×10^3	2.19×10^5

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

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

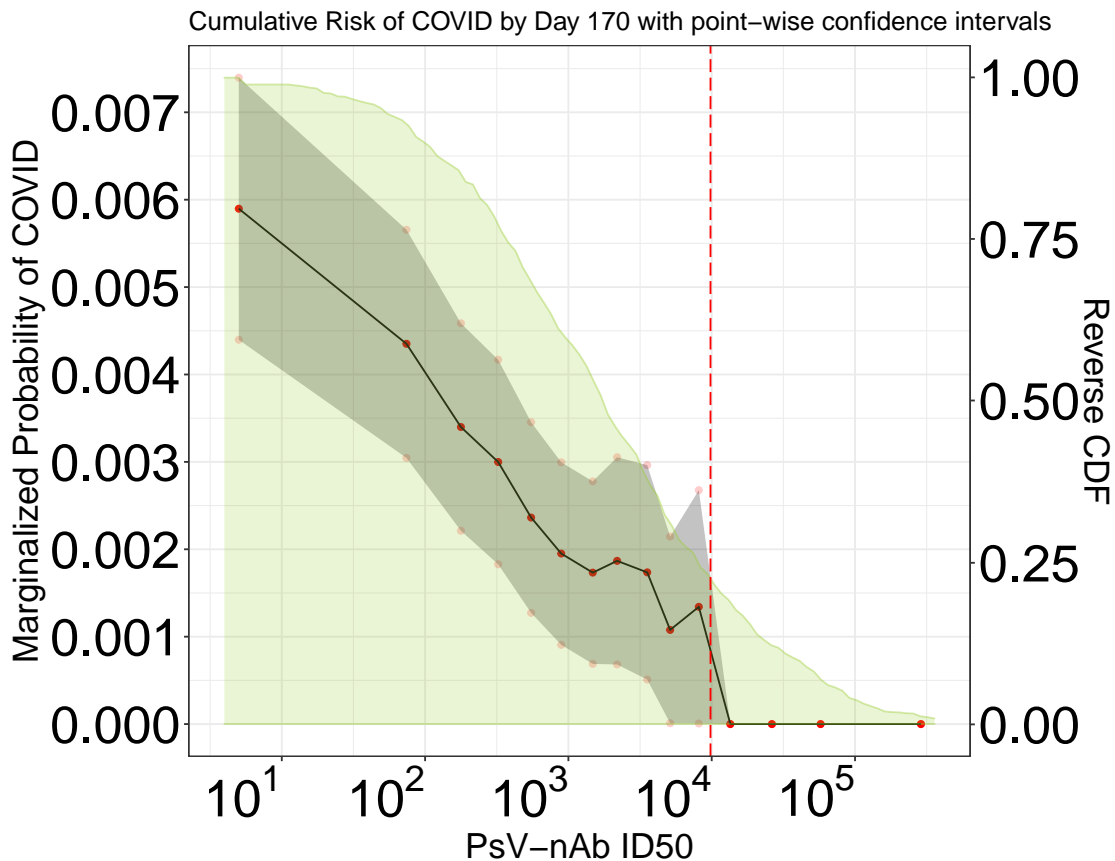


Figure 21: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 \cdot 10^0$	0.00590	0.00440	0.00740
2.253	$1.79 \cdot 10^2$	0.00340	0.00221	0.00459
2.514	$3.27 \cdot 10^2$	0.00300	0.00183	0.00417
2.954	$8.99 \cdot 10^2$	0.00195	0.00091	0.00300
3.168	$1.47 \cdot 10^3$	0.00173	0.00069	0.00278
3.551	$3.56 \cdot 10^3$	0.00174	0.00051	0.00296
3.706	$5.08 \cdot 10^3$	0.00108	0.00001	0.00215
4.128	$1.34 \cdot 10^4$	0.00000	0.00000	1.00000
4.419	$2.62 \cdot 10^4$	0.00000	0.00000	1.00000
5.455	$2.85 \cdot 10^5$	0.00000	0.00000	1.00000

Figure 22: Table of risk estimates for range of thresholds of Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals.

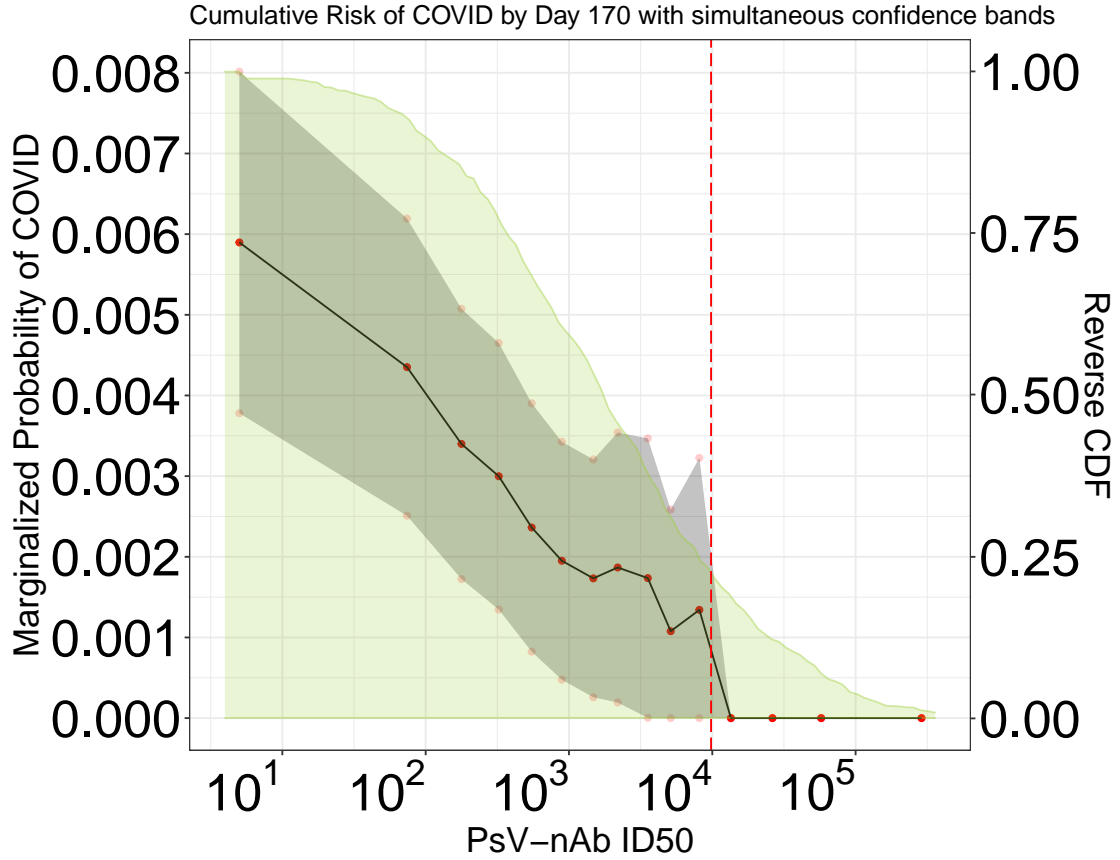


Figure 23: Adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 \cdot 10^0$	0.00590	0.00378	0.00801
2.253	$1.79 \cdot 10^2$	0.00340	0.00172	0.00507
2.514	$3.27 \cdot 10^2$	0.00300	0.00135	0.00465
2.954	$8.99 \cdot 10^2$	0.00195	0.00048	0.00343
3.168	$1.47 \cdot 10^3$	0.00173	0.00026	0.00321
3.551	$3.56 \cdot 10^3$	0.00174	0.00000	0.00347
3.706	$5.08 \cdot 10^3$	0.00108	0.00000	0.00259
4.128	$1.34 \cdot 10^4$	0.00000	0.00000	1.00000
4.419	$2.62 \cdot 10^4$	0.00000	0.00000	1.00000
5.455	$2.85 \cdot 10^5$	0.00000	0.00000	1.00000

Figure 24: Table of risk estimates for range of thresholds of Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands

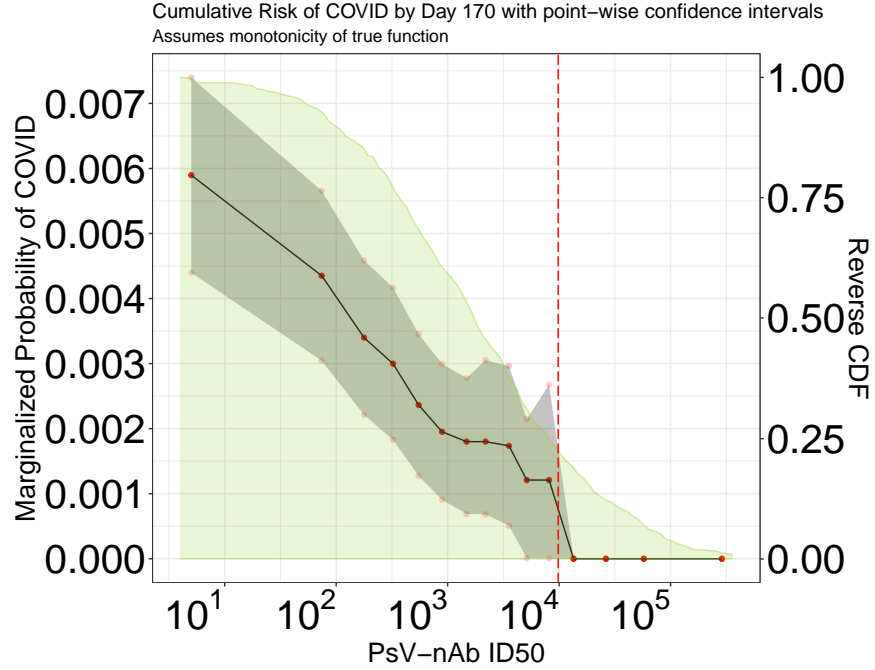


Figure 25: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

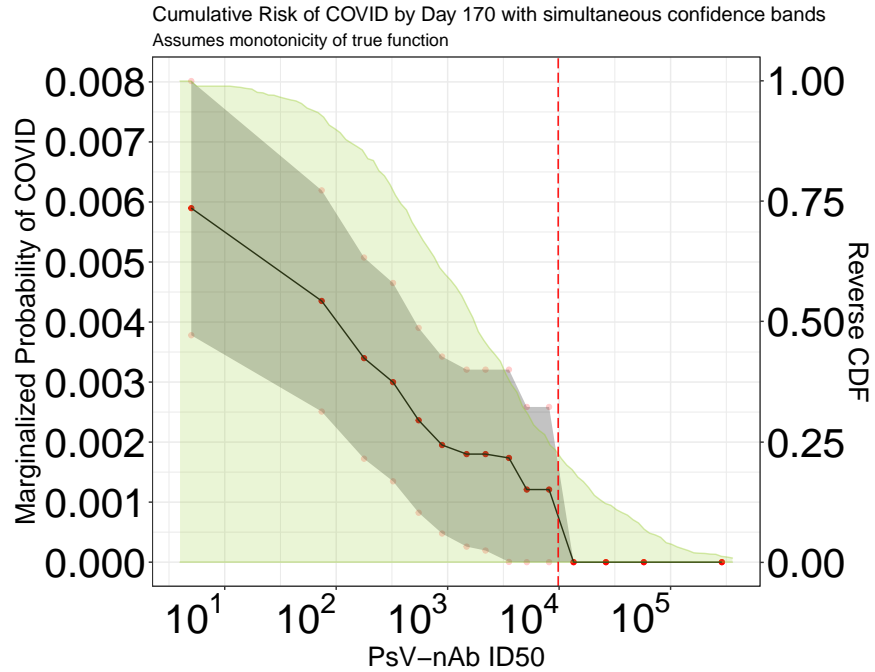


Figure 26: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

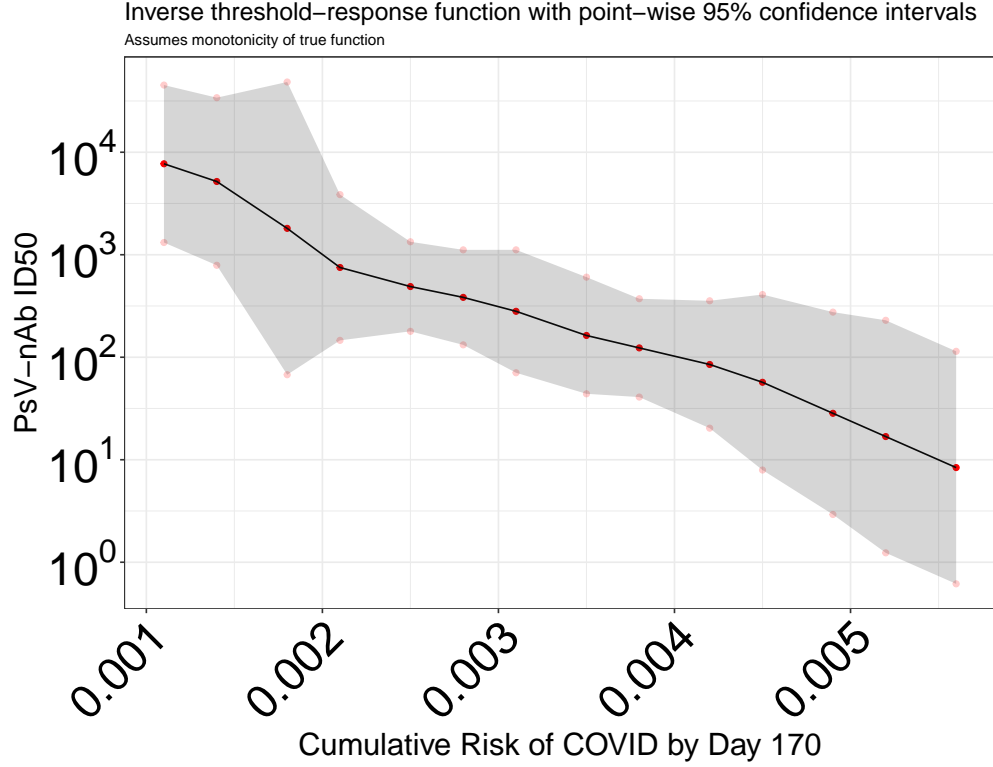


Figure 27: The inverse adjusted threshold-response function with pointwise 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.0011	$7.76 \cdot 10^3$	$1.32 \cdot 10^3$	$4.57 \cdot 10^4$
0.0014	$5.13 \cdot 10^3$	$7.94 \cdot 10^2$	$3.39 \cdot 10^4$
0.0018	$1.82 \cdot 10^3$	$6.76 \cdot 10^1$	$4.90 \cdot 10^4$
0.0021	$7.59 \cdot 10^2$	$1.45 \cdot 10^2$	$3.89 \cdot 10^3$
0.0025	$4.90 \cdot 10^2$	$1.78 \cdot 10^2$	$1.35 \cdot 10^3$
0.0028	$3.80 \cdot 10^2$	$1.32 \cdot 10^2$	$1.12 \cdot 10^3$
0.0031	$2.82 \cdot 10^2$	$7.08 \cdot 10^1$	$1.12 \cdot 10^3$
0.0035	$1.62 \cdot 10^2$	$4.37 \cdot 10^1$	$6.03 \cdot 10^2$
0.0038	$1.23 \cdot 10^2$	$4.07 \cdot 10^1$	$3.72 \cdot 10^2$
0.0042	$8.51 \cdot 10^1$	$2.04 \cdot 10^1$	$3.55 \cdot 10^2$
0.0045	$5.75 \cdot 10^1$	$7.94 \cdot 10^0$	$4.07 \cdot 10^2$
0.0049	$2.82 \cdot 10^1$	$2.95 \cdot 10^0$	$2.75 \cdot 10^2$
0.0052	$1.70 \cdot 10^1$	$1.23 \cdot 10^0$	$2.29 \cdot 10^2$
0.0056	$8.32 \cdot 10^0$	$6.17 \cdot 10^{-1}$	$1.15 \cdot 10^2$

Figure 28: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Pseudo virus-neutralizing antibody (50% titer) activity level at a range of risk levels with pointwise 95% confidence intervals.

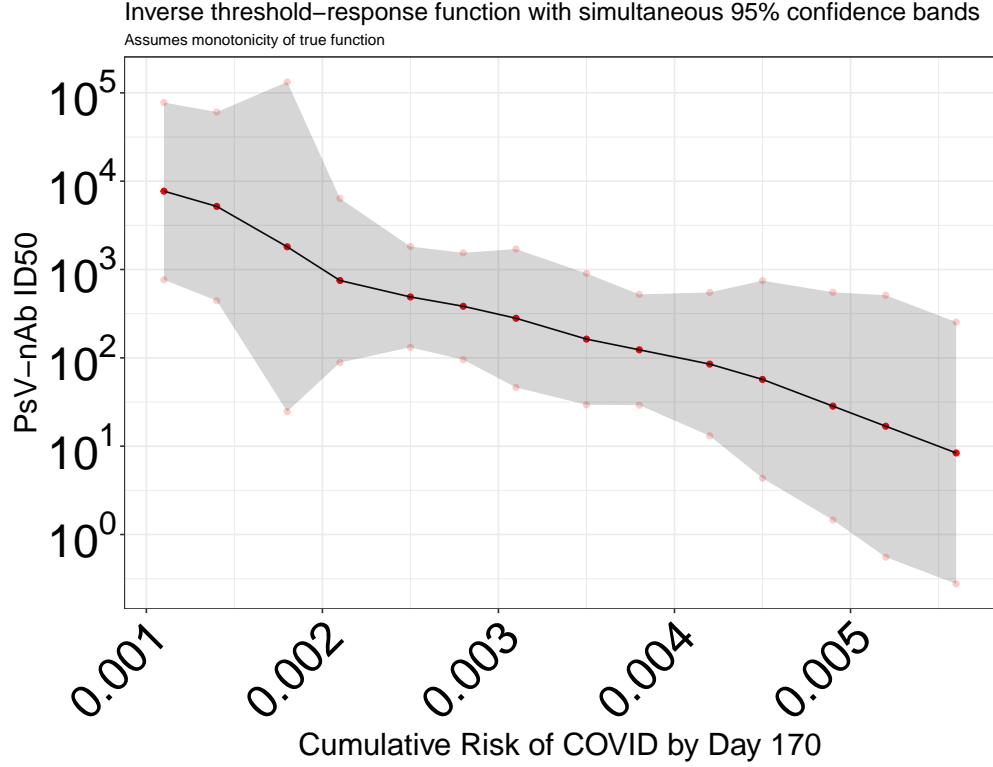


Figure 29: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with simultaneous 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.0011	7.76×10^3	7.59×10^2	7.76×10^4
0.0014	5.13×10^3	4.47×10^2	6.03×10^4
0.0018	1.82×10^3	2.45×10^1	1.32×10^5
0.0021	7.59×10^2	8.91×10^1	6.31×10^3
0.0025	4.90×10^2	1.32×10^2	1.82×10^3
0.0028	3.80×10^2	9.55×10^1	1.55×10^3
0.0031	2.82×10^2	4.57×10^1	1.70×10^3
0.0035	1.62×10^2	2.95×10^1	9.12×10^2
0.0038	1.23×10^2	2.88×10^1	5.25×10^2
0.0042	8.51×10^1	1.32×10^1	5.50×10^2
0.0045	5.75×10^1	4.37×10^0	7.41×10^2
0.0049	2.82×10^1	1.45×10^0	5.50×10^2
0.0052	1.70×10^1	5.50×10^{-1}	5.13×10^2
0.0056	8.32×10^0	2.75×10^{-1}	2.57×10^2

Figure 30: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Pseudo virus-neutralizing antibody (50% titer) activity level at a range of risk levels with simultaneous 95% confidence bands

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

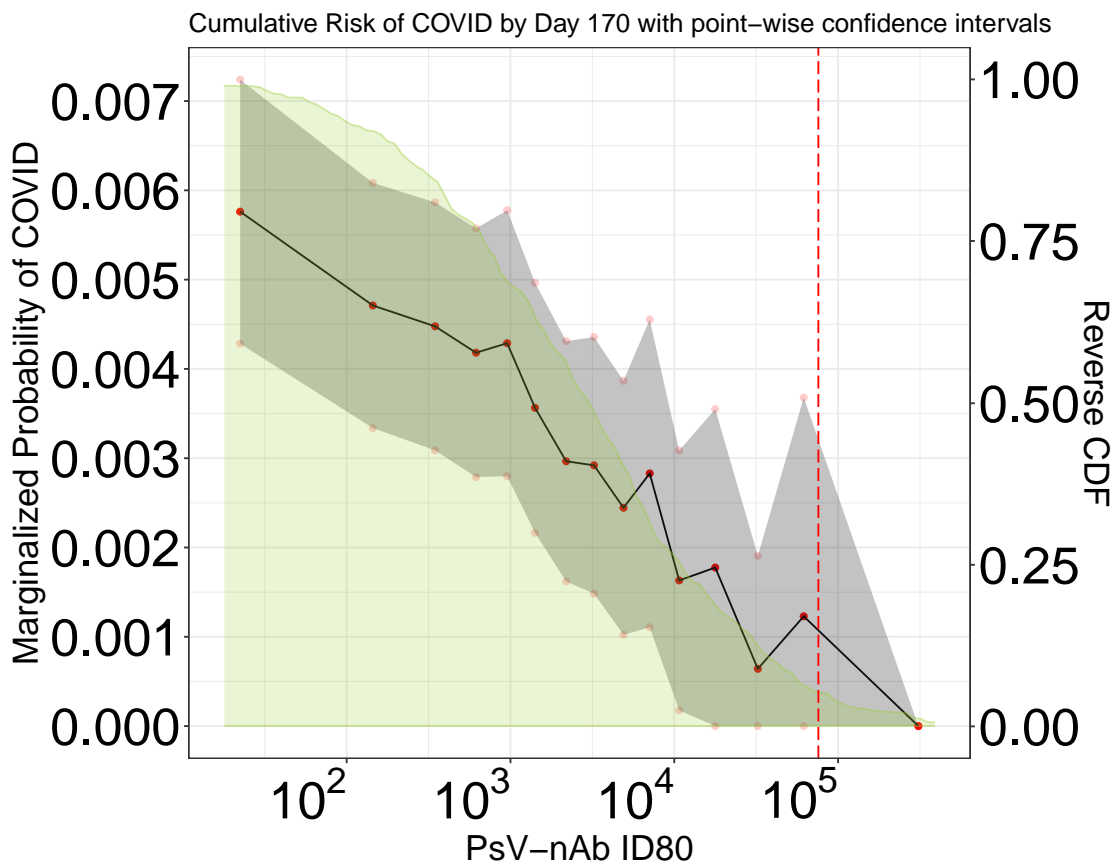


Figure 31: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.353	$2.25 \cdot 10^1$	0.00576	0.00428	0.00724
2.537	$3.44 \cdot 10^2$	0.00448	0.00309	0.00587
2.793	$6.21 \cdot 10^2$	0.00418	0.00279	0.00557
3.147	$1.40 \cdot 10^3$	0.00356	0.00216	0.00496
3.335	$2.16 \cdot 10^3$	0.00297	0.00162	0.00431
3.689	$4.89 \cdot 10^3$	0.00244	0.00102	0.00387
3.845	$7.00 \cdot 10^3$	0.00283	0.00111	0.00455
4.252	$1.79 \cdot 10^4$	0.00178	0.00000	0.00355
4.506	$3.21 \cdot 10^4$	0.00064	0.00000	0.00191
5.489	$3.08 \cdot 10^5$	0.00000	0.00000	1.00000

Figure 32: Table of risk estimates for range of thresholds of Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals.

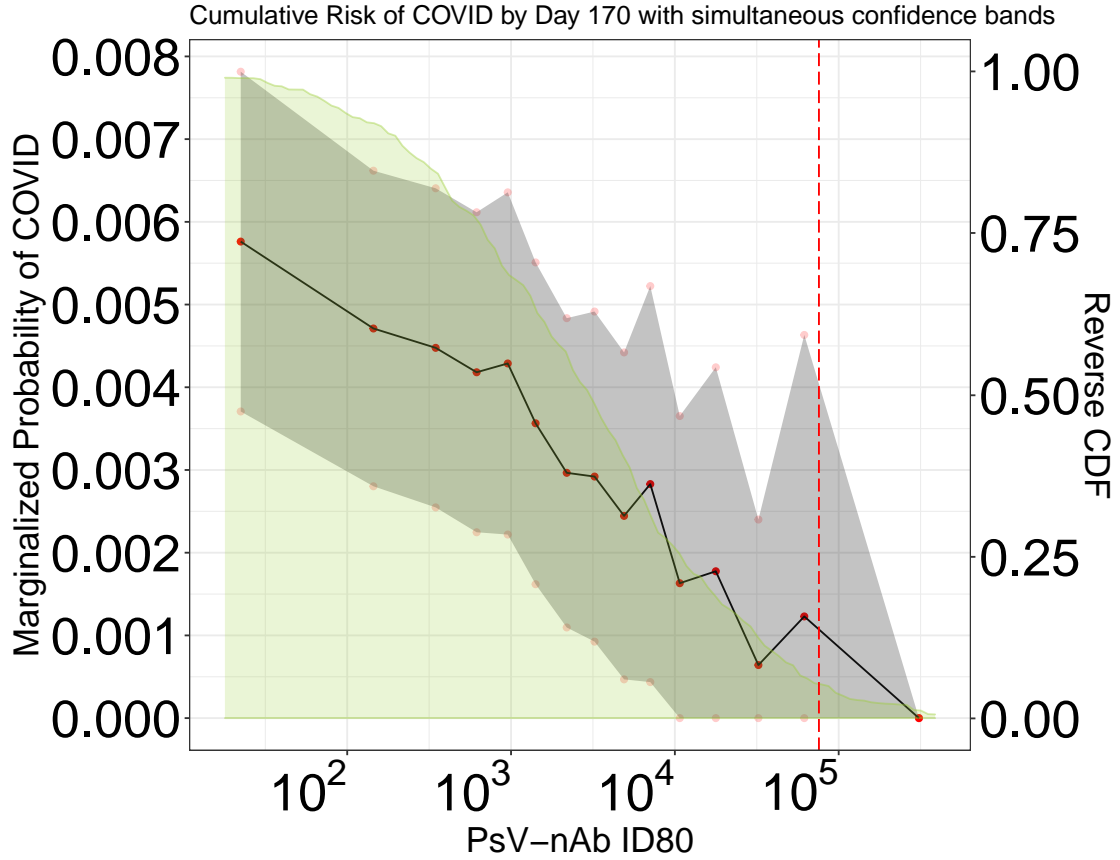


Figure 33: Adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.353	$2.25 \cdot 10^1$	0.00576	0.00371	0.00782
2.537	$3.44 \cdot 10^2$	0.00448	0.00255	0.00641
2.793	$6.21 \cdot 10^2$	0.00418	0.00225	0.00612
3.147	$1.40 \cdot 10^3$	0.00356	0.00162	0.00551
3.335	$2.16 \cdot 10^3$	0.00297	0.00110	0.00484
3.689	$4.89 \cdot 10^3$	0.00244	0.00047	0.00442
3.845	$7.00 \cdot 10^3$	0.00283	0.00044	0.00522
4.252	$1.79 \cdot 10^4$	0.00178	0.00000	0.00424
4.506	$3.21 \cdot 10^4$	0.00064	0.00000	0.00240
5.489	$3.08 \cdot 10^5$	0.00000	0.00000	1.00000

Figure 34: Table of risk estimates for range of thresholds of Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands

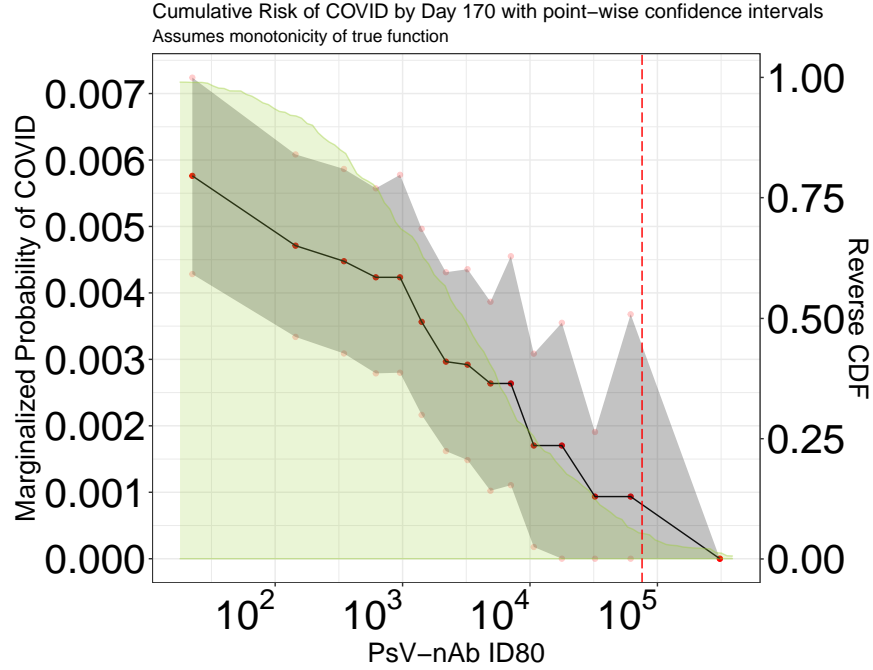


Figure 35: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

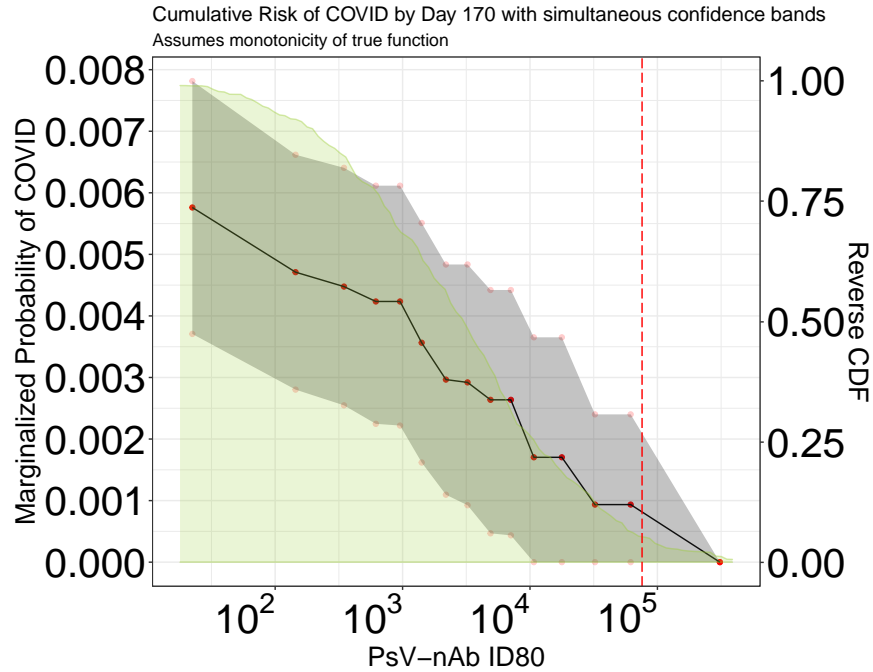


Figure 36: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

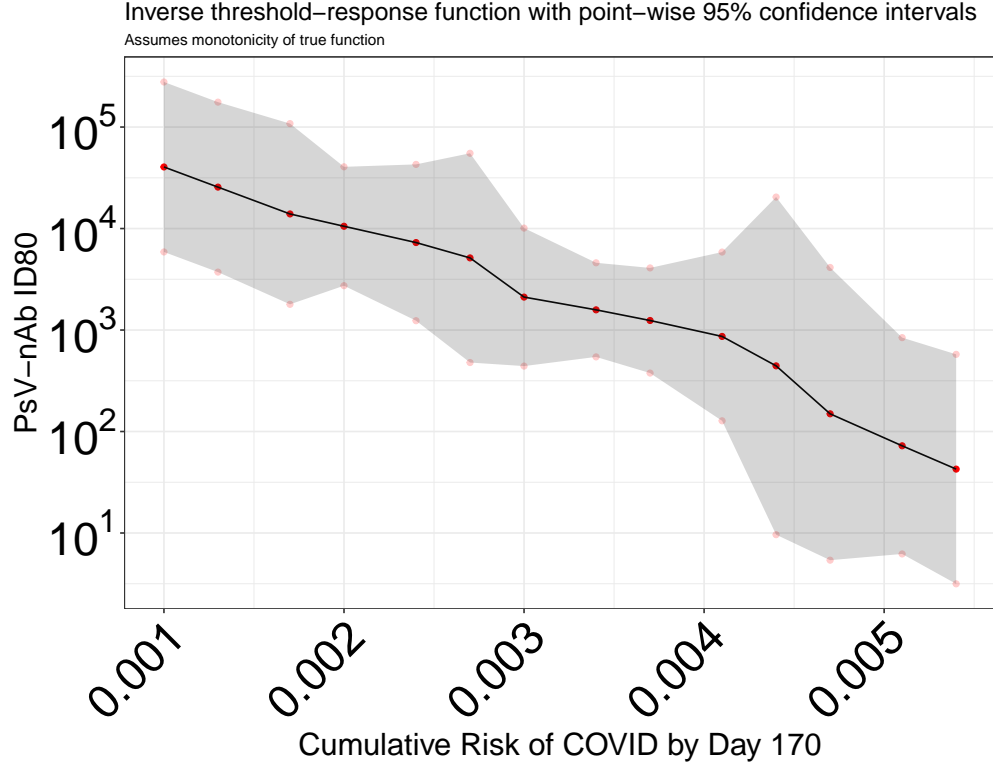


Figure 37: The inverse adjusted threshold-response function with pointwise 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.001	$4.07 \cdot 10^4$	$5.89 \cdot 10^3$	$2.75 \cdot 10^5$
0.0013	$2.57 \cdot 10^4$	$3.72 \cdot 10^3$	$1.78 \cdot 10^5$
0.0017	$1.38 \cdot 10^4$	$1.78 \cdot 10^3$	$1.07 \cdot 10^5$
0.002	$1.05 \cdot 10^4$	$2.75 \cdot 10^3$	$4.07 \cdot 10^4$
0.0024	$7.24 \cdot 10^3$	$1.23 \cdot 10^3$	$4.27 \cdot 10^4$
0.0027	$5.13 \cdot 10^3$	$4.79 \cdot 10^2$	$5.50 \cdot 10^4$
0.003	$2.09 \cdot 10^3$	$4.37 \cdot 10^2$	$1.00 \cdot 10^4$
0.0034	$1.58 \cdot 10^3$	$5.50 \cdot 10^2$	$4.57 \cdot 10^3$
0.0037	$1.23 \cdot 10^3$	$3.80 \cdot 10^2$	$4.07 \cdot 10^3$
0.0041	$8.71 \cdot 10^2$	$1.29 \cdot 10^2$	$5.89 \cdot 10^3$
0.0044	$4.47 \cdot 10^2$	$9.55 \cdot 10^0$	$2.04 \cdot 10^4$
0.0047	$1.48 \cdot 10^2$	$5.37 \cdot 10^0$	$4.17 \cdot 10^3$
0.0051	$7.24 \cdot 10^1$	$6.17 \cdot 10^0$	$8.32 \cdot 10^2$
0.0054	$4.27 \cdot 10^1$	$3.16 \cdot 10^0$	$5.75 \cdot 10^2$

Figure 38: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Pseudo virus-neutralizing antibody (80% titer) activity level at a range of risk levels with pointwise 95% confidence intervals.

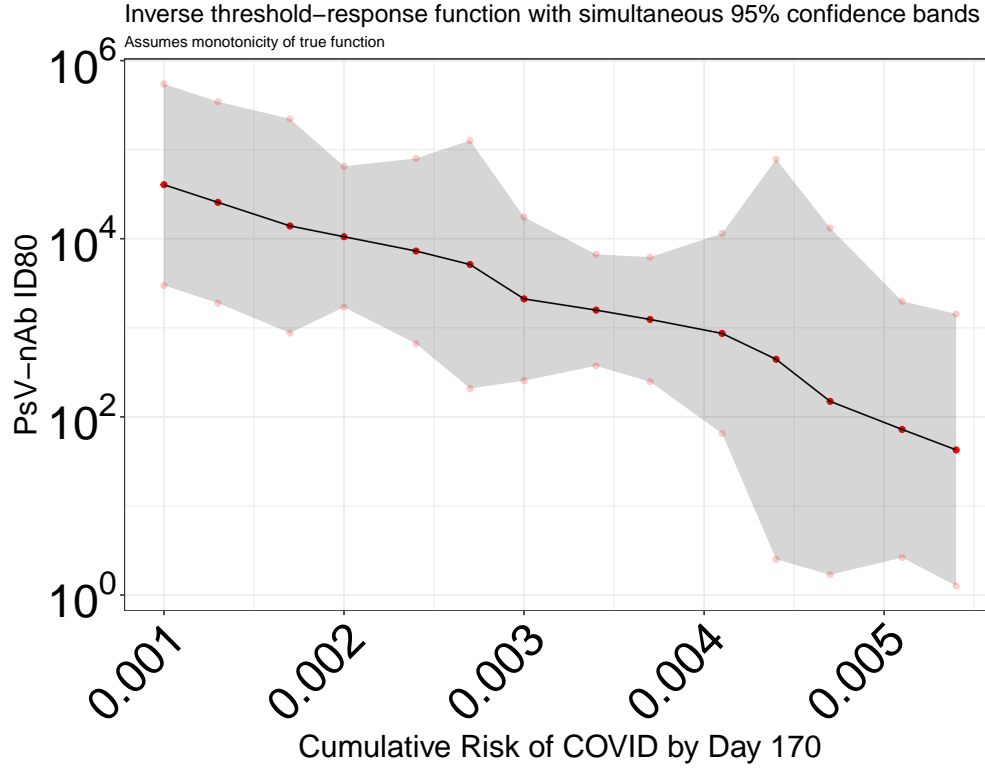


Figure 39: This analysis assumes monotonicity of the true function. The plot shows the inverse adjusted threshold-response function with simultaneous 95% confidence intervals.

Risk	Threshold est.	CI left	CI right
0.001	$4.07 \cdot 10^4$	$3.02 \cdot 10^3$	$5.50 \cdot 10^5$
0.0013	$2.57 \cdot 10^4$	$1.91 \cdot 10^3$	$3.47 \cdot 10^5$
0.0017	$1.38 \cdot 10^4$	$8.71 \cdot 10^2$	$2.24 \cdot 10^5$
0.002	$1.05 \cdot 10^4$	$1.70 \cdot 10^3$	$6.46 \cdot 10^4$
0.0024	$7.24 \cdot 10^3$	$6.61 \cdot 10^2$	$7.94 \cdot 10^4$
0.0027	$5.13 \cdot 10^3$	$2.09 \cdot 10^2$	$1.26 \cdot 10^5$
0.003	$2.09 \cdot 10^3$	$2.57 \cdot 10^2$	$1.74 \cdot 10^4$
0.0034	$1.58 \cdot 10^3$	$3.72 \cdot 10^2$	$6.61 \cdot 10^3$
0.0037	$1.23 \cdot 10^3$	$2.45 \cdot 10^2$	$6.17 \cdot 10^3$
0.0041	$8.71 \cdot 10^2$	$6.46 \cdot 10^1$	$1.15 \cdot 10^4$
0.0044	$4.47 \cdot 10^2$	$2.51 \cdot 10^0$	$7.76 \cdot 10^4$
0.0047	$1.48 \cdot 10^2$	$1.70 \cdot 10^0$	$1.32 \cdot 10^4$
0.0051	$7.24 \cdot 10^1$	$2.63 \cdot 10^0$	$2.00 \cdot 10^3$
0.0054	$4.27 \cdot 10^1$	$1.26 \cdot 10^0$	$1.45 \cdot 10^3$

Figure 40: This analysis assumes monotonicity of the true function. The table displays the estimated threshold of protection of Pseudo virus-neutralizing antibody (80% titer) activity level at a range of risk levels with simultaneous 95% confidence bands