

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 . 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: 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.

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.

Day 57 Spike protein antibody

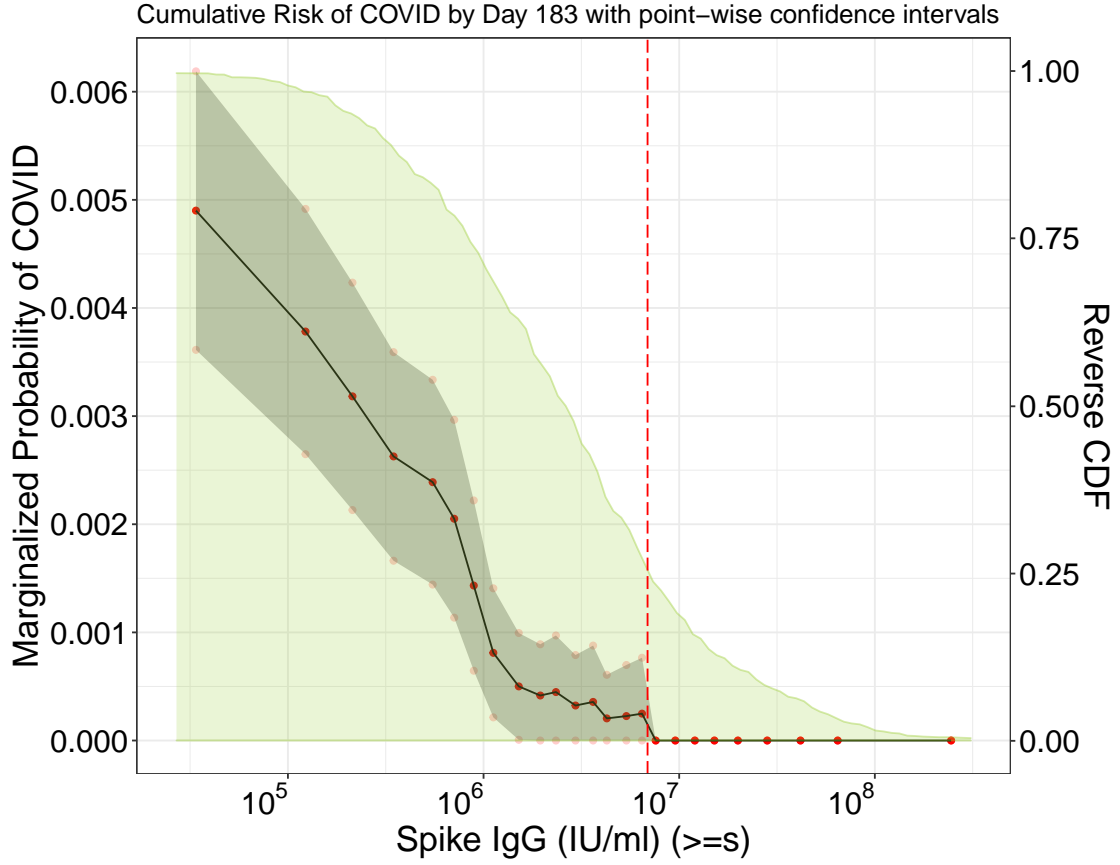


Figure 1: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.530	3.39×10^4	0.00490	0.00361	0.00619
5.540	3.47×10^5	0.00263	0.00166	0.00359
5.853	7.13×10^5	0.00205	0.00114	0.00297
6.182	1.52×10^6	0.00050	0.00001	0.00099
6.472	2.96×10^6	0.00032	0.00000	0.00079
6.628	4.25×10^6	0.00020	0.00000	0.00061
6.880	7.59×10^6	0.00000	0.00000	NA
7.184	1.53×10^7	0.00000	0.00000	NA
7.449	2.81×10^7	0.00000	0.00000	NA
8.391	2.46×10^8	0.00000	0.00000	NA

Figure 2: Table of risk estimates for range of thresholds of Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals.

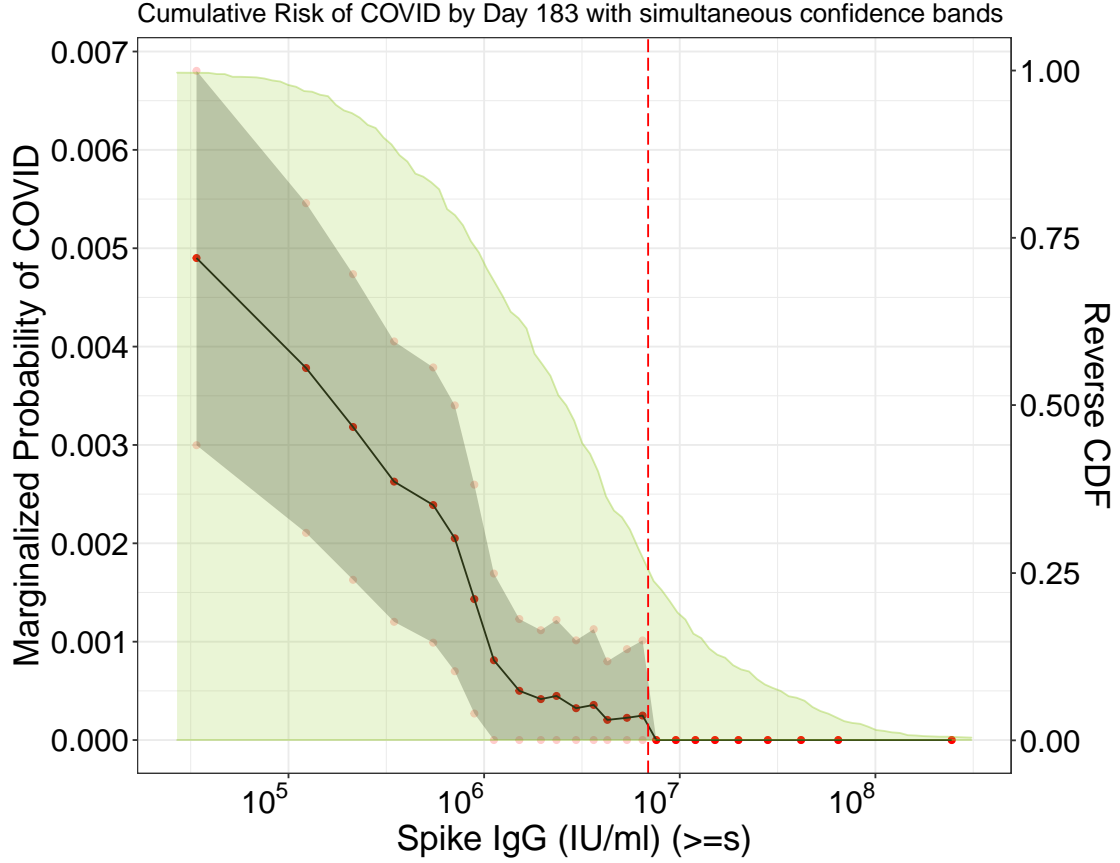


Figure 3: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.530	3.39×10^4	0.00490	0.0030	0.00680
5.540	3.47×10^5	0.00263	0.0012	0.00405
5.853	7.13×10^5	0.00205	0.0007	0.00340
6.182	1.52×10^6	0.00050	0.0000	0.00123
6.472	2.96×10^6	0.00032	0.0000	0.00101
6.628	4.25×10^6	0.00020	0.0000	0.00080
6.880	7.59×10^6	0.00000	0.0000	NA
7.184	1.53×10^7	0.00000	0.0000	NA
7.449	2.81×10^7	0.00000	0.0000	NA
8.391	2.46×10^8	0.00000	0.0000	NA

Figure 4: Table of risk estimates for range of thresholds of Day 57 Spike protein antibody activity levels with simultaneous 95% confidence bands

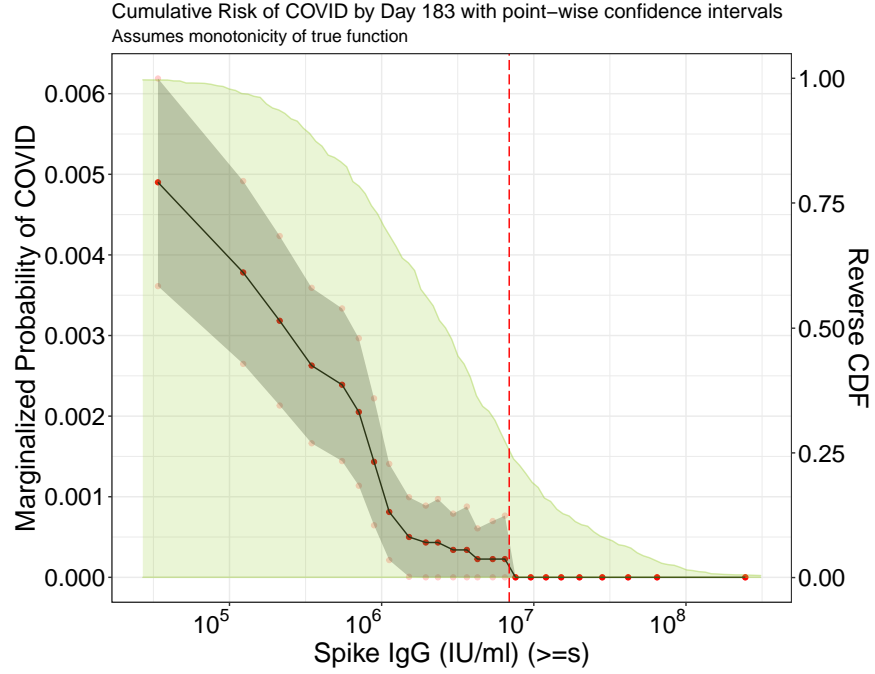


Figure 5: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

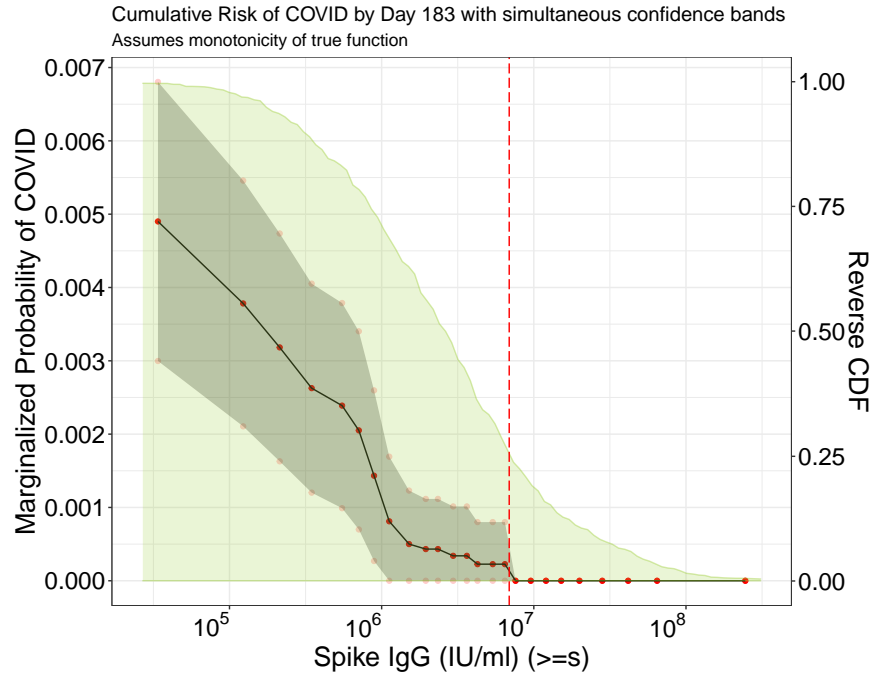


Figure 6: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Day 57 RBD binding antibody

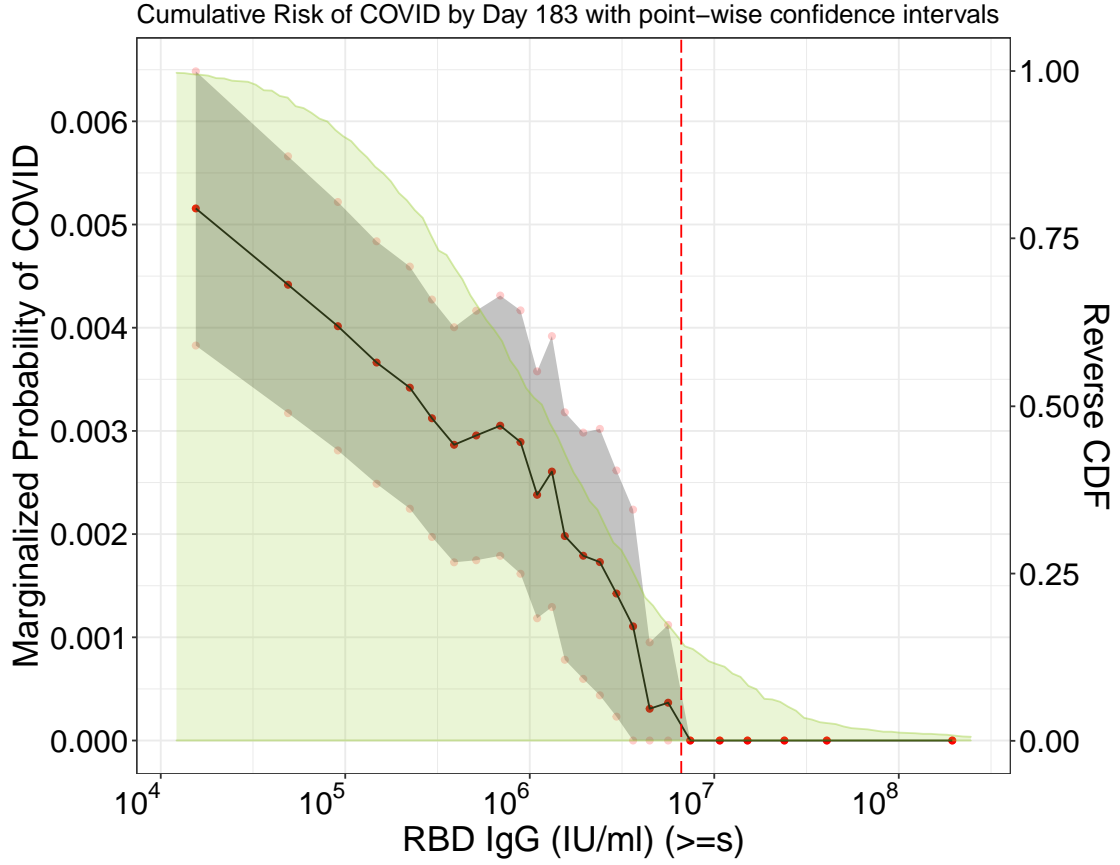


Figure 7: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.185	$1.53 \cdot 10^4$	0.00516	0.00383	0.00648
5.172	$1.49 \cdot 10^5$	0.00366	0.00249	0.00484
5.469	$2.94 \cdot 10^5$	0.00312	0.00197	0.00427
5.841	$6.93 \cdot 10^5$	0.00305	0.00179	0.00431
6.125	$1.33 \cdot 10^6$	0.00261	0.00129	0.00392
6.286	$1.93 \cdot 10^6$	0.00179	0.00060	0.00298
6.559	$3.62 \cdot 10^6$	0.00111	0.00000	0.00224
6.868	$7.38 \cdot 10^6$	0.00000	0.00000	NA
7.178	$1.51 \cdot 10^7$	0.00000	0.00000	NA
8.291	$1.95 \cdot 10^8$	0.00000	0.00000	NA

Figure 8: Table of risk estimates for range of thresholds of Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals.

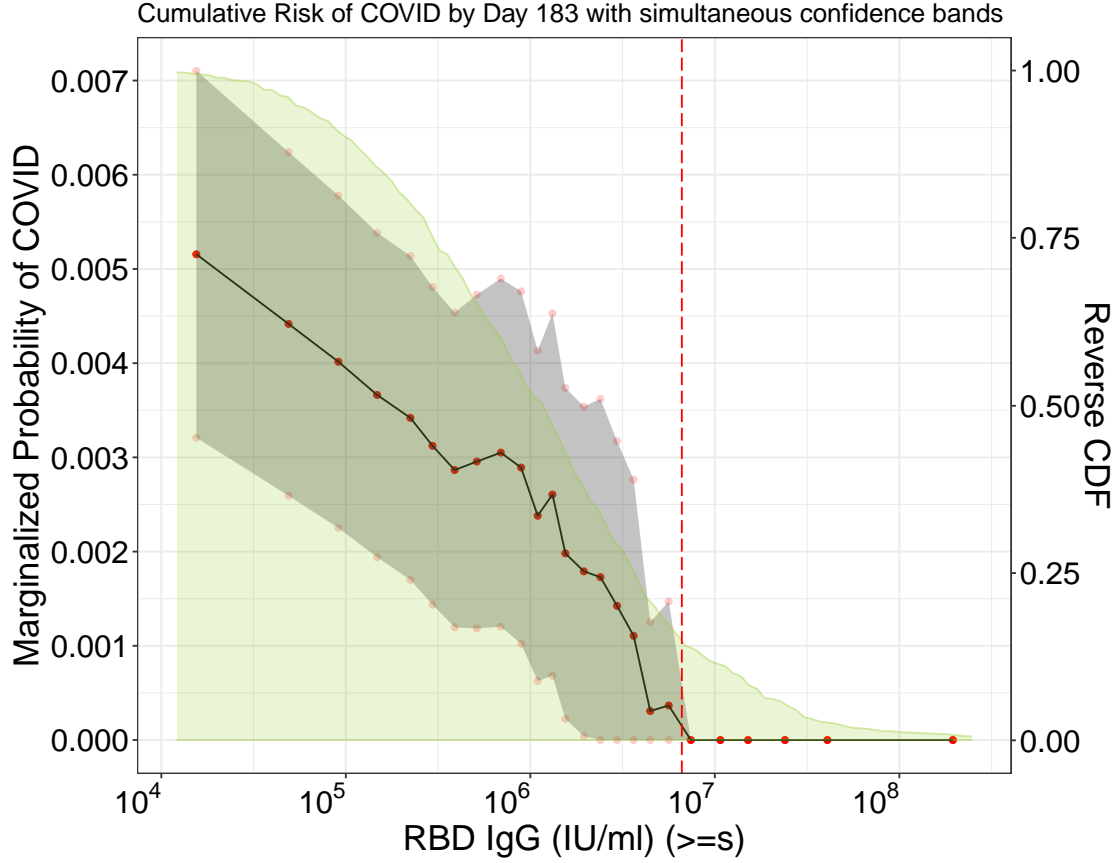


Figure 9: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.185	$1.53 \cdot 10^4$	0.00516	0.00321	0.00710
5.172	$1.49 \cdot 10^5$	0.00366	0.00194	0.00538
5.469	$2.94 \cdot 10^5$	0.00312	0.00144	0.00481
5.841	$6.93 \cdot 10^5$	0.00305	0.00120	0.00490
6.125	$1.33 \cdot 10^6$	0.00261	0.00068	0.00453
6.286	$1.93 \cdot 10^6$	0.00179	0.00004	0.00354
6.559	$3.62 \cdot 10^6$	0.00111	0.00000	0.00276
6.868	$7.38 \cdot 10^6$	0.00000	0.00000	NA
7.178	$1.51 \cdot 10^7$	0.00000	0.00000	NA
8.291	$1.95 \cdot 10^8$	0.00000	0.00000	NA

Figure 10: Table of risk estimates for range of thresholds of Day 57 RBD binding antibody activity levels with simultaneous 95% confidence bands

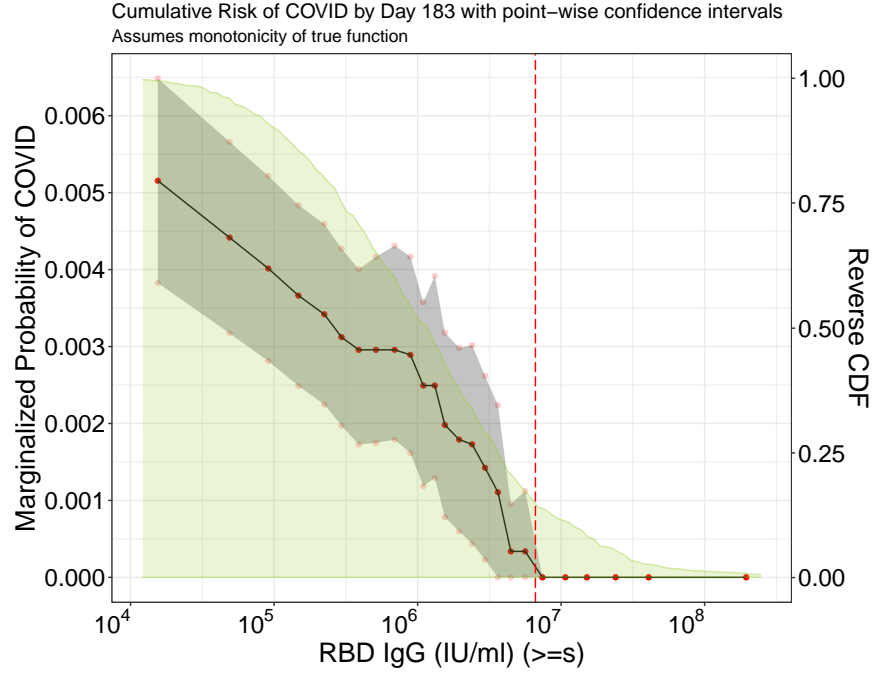


Figure 11: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

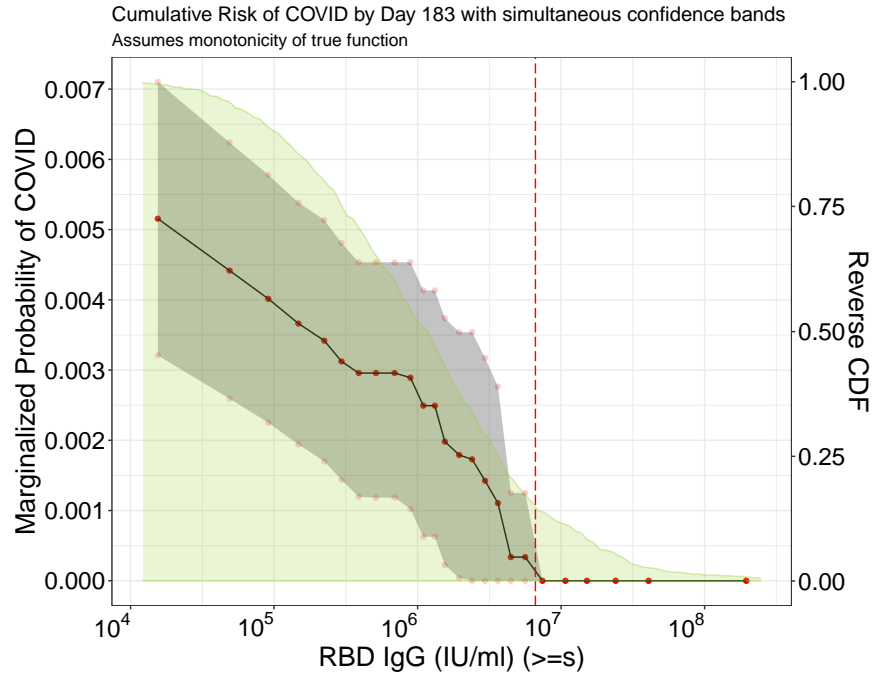


Figure 12: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

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

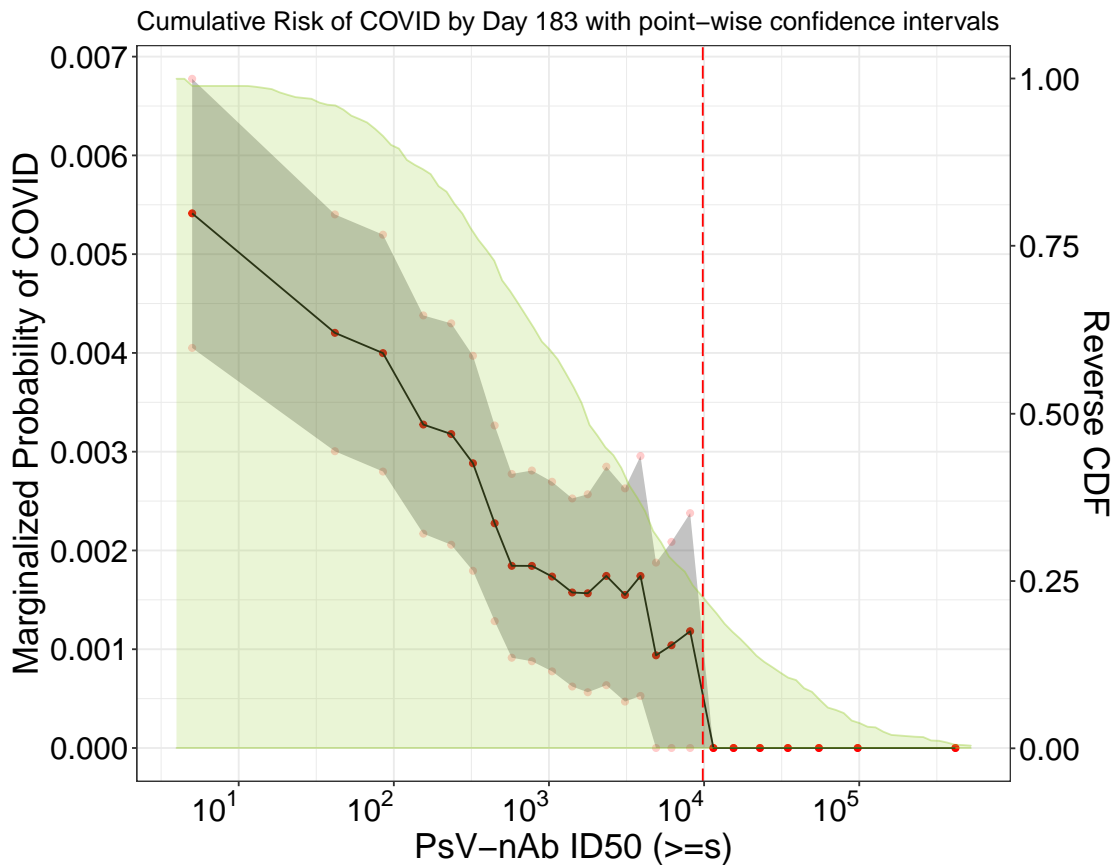


Figure 13: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00×10^0	0.00541	0.00405	0.00678
2.187	1.54×10^2	0.00327	0.00217	0.00438
2.510	3.24×10^2	0.00288	0.00179	0.00397
2.891	7.78×10^2	0.00184	0.00088	0.00281
3.248	1.77×10^3	0.00157	0.00056	0.00257
3.489	3.08×10^3	0.00155	0.00047	0.00263
3.787	6.12×10^3	0.00104	0.00000	0.00209
4.187	1.54×10^4	0.00000	0.00000	NA
4.543	3.49×10^4	0.00000	0.00000	NA
5.620	4.17×10^5	0.00000	0.00000	NA

Figure 14: Table of risk estimates for range of thresholds of Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals.

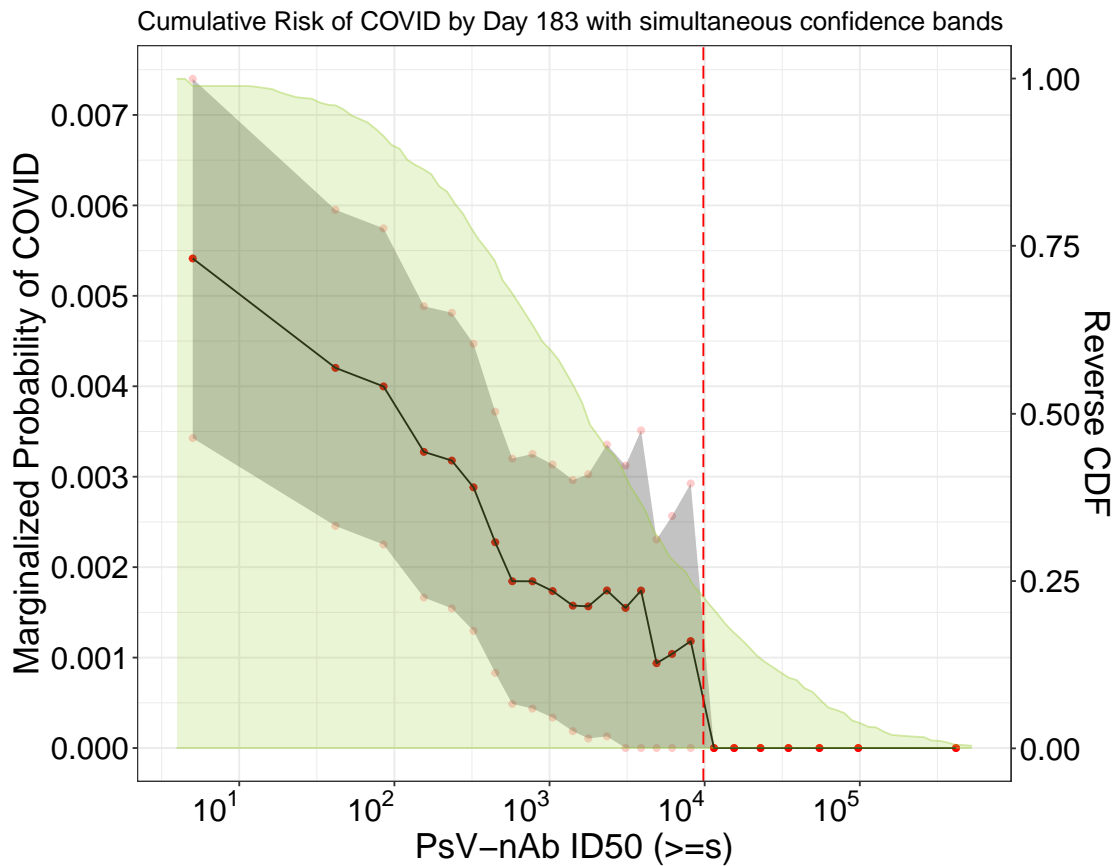


Figure 15: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 \cdot 10^0$	0.00541	0.00343	0.00740
2.187	$1.54 \cdot 10^2$	0.00327	0.00166	0.00489
2.510	$3.24 \cdot 10^2$	0.00288	0.00130	0.00447
2.891	$7.78 \cdot 10^2$	0.00184	0.00044	0.00325
3.248	$1.77 \cdot 10^3$	0.00157	0.00011	0.00303
3.489	$3.08 \cdot 10^3$	0.00155	0.00000	0.00312
3.787	$6.12 \cdot 10^3$	0.00104	0.00000	0.00257
4.187	$1.54 \cdot 10^4$	0.00000	0.00000	NA
4.543	$3.49 \cdot 10^4$	0.00000	0.00000	NA
5.620	$4.17 \cdot 10^5$	0.00000	0.00000	NA

Figure 16: Table of risk estimates for range of thresholds of Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands

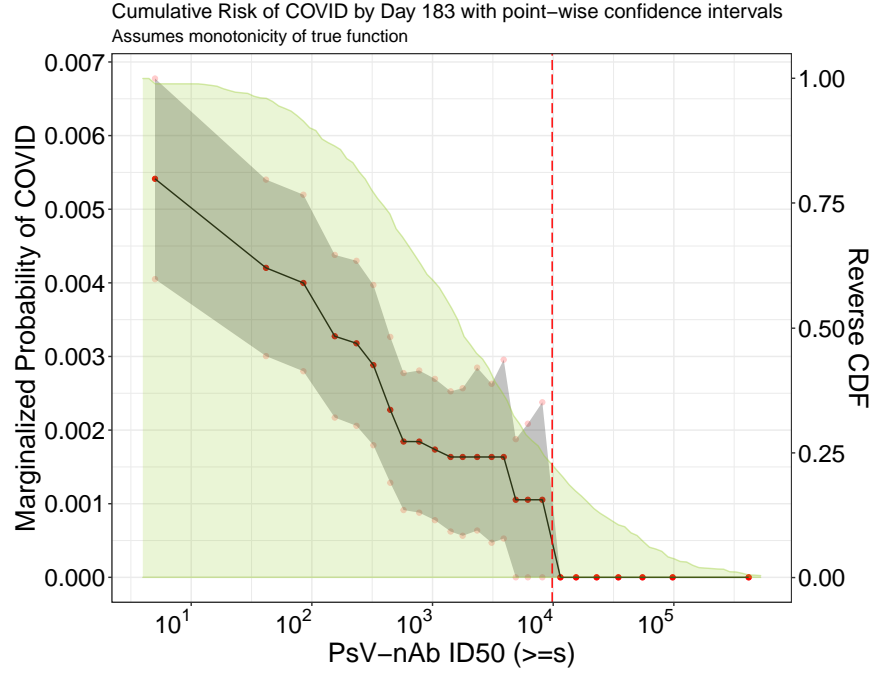


Figure 17: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

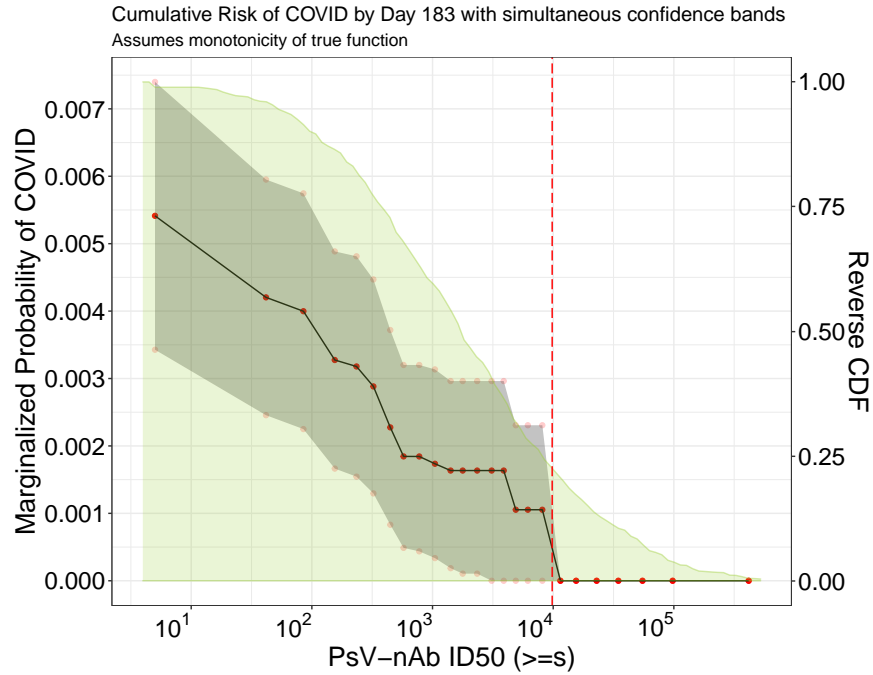


Figure 18: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

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

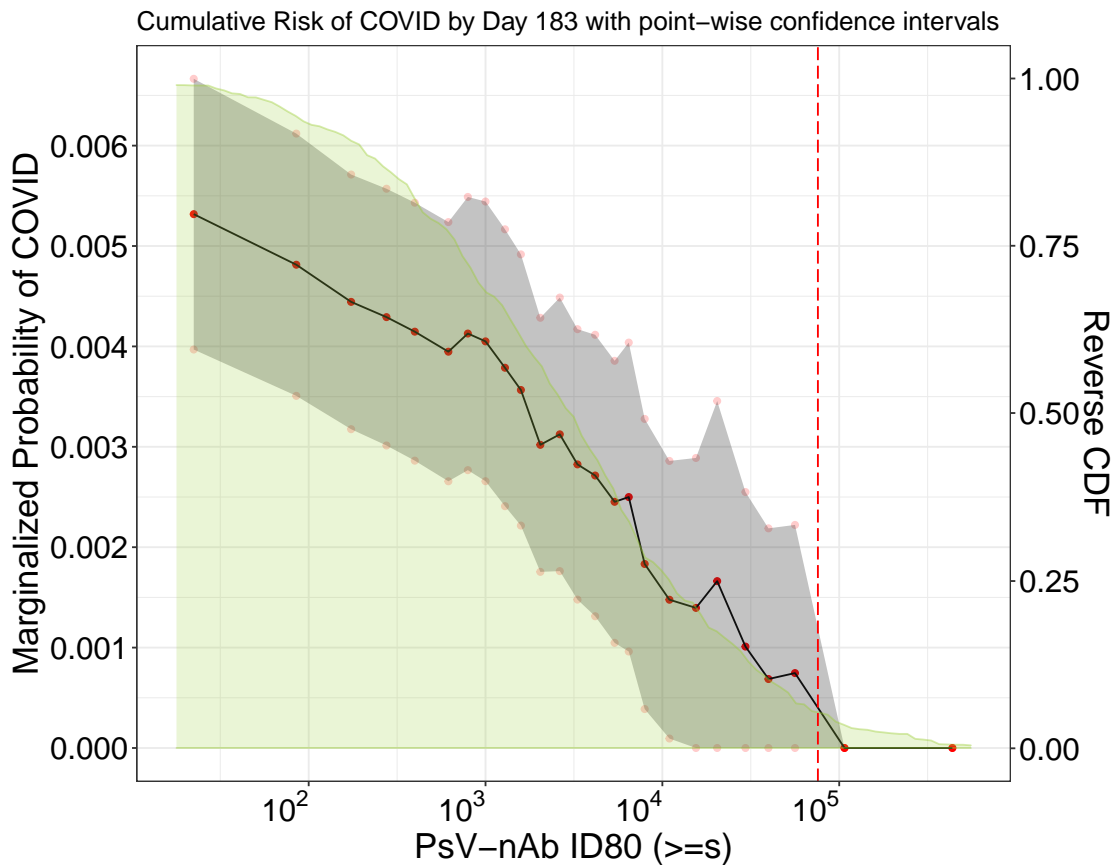


Figure 19: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	$2.25 \cdot 10^1$	0.00532	0.00397	0.00667
2.441	$2.76 \cdot 10^2$	0.00429	0.00301	0.00557
2.789	$6.15 \cdot 10^2$	0.00395	0.00266	0.00524
3.111	$1.29 \cdot 10^3$	0.00379	0.00241	0.00517
3.421	$2.64 \cdot 10^3$	0.00312	0.00176	0.00449
3.623	$4.20 \cdot 10^3$	0.00271	0.00131	0.00412
3.900	$7.94 \cdot 10^3$	0.00183	0.00039	0.00328
4.309	$2.04 \cdot 10^4$	0.00166	0.00000	0.00346
4.598	$3.96 \cdot 10^4$	0.00069	0.00000	0.00219
5.644	$4.41 \cdot 10^5$	0.00000	0.00000	NA

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

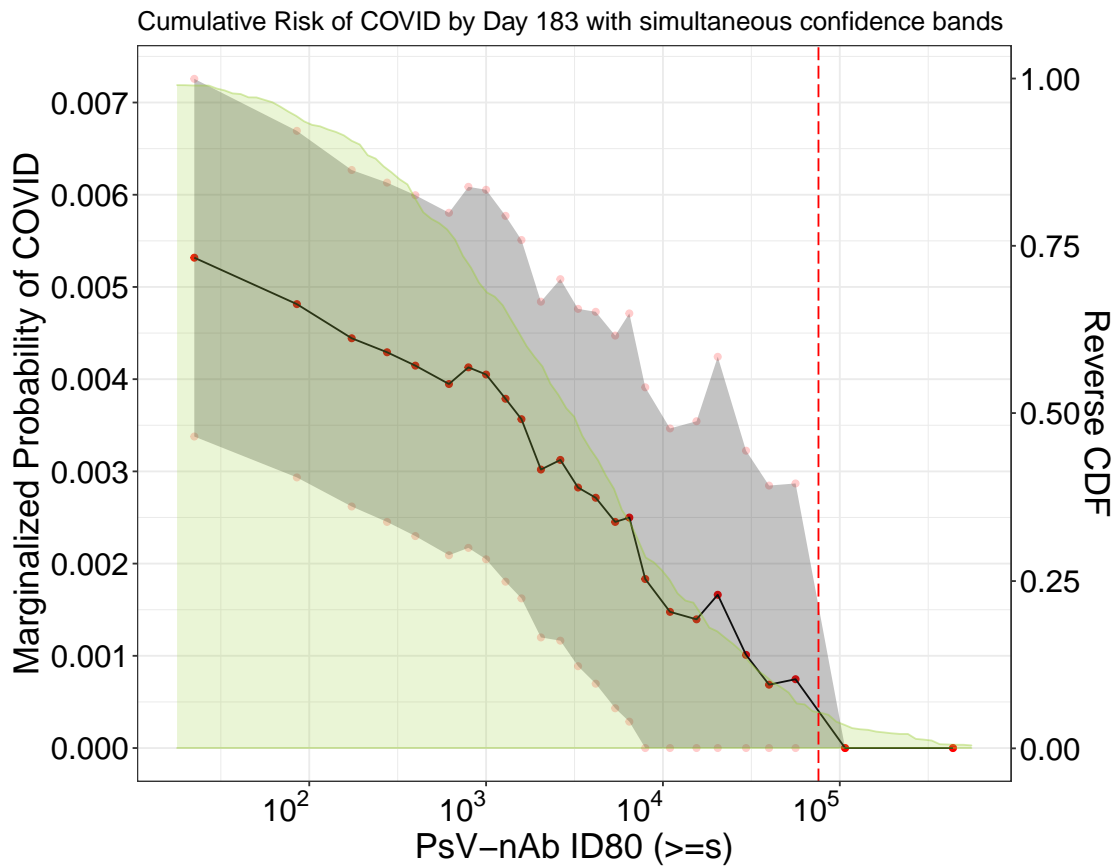


Figure 21: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	$2.25 \cdot 10^1$	0.00532	0.00338	0.00726
2.441	$2.76 \cdot 10^2$	0.00429	0.00245	0.00613
2.789	$6.15 \cdot 10^2$	0.00395	0.00209	0.00580
3.111	$1.29 \cdot 10^3$	0.00379	0.00180	0.00577
3.421	$2.64 \cdot 10^3$	0.00312	0.00116	0.00508
3.623	$4.20 \cdot 10^3$	0.00271	0.00070	0.00473
3.900	$7.94 \cdot 10^3$	0.00183	0.00000	0.00391
4.309	$2.04 \cdot 10^4$	0.00166	0.00000	0.00424
4.598	$3.96 \cdot 10^4$	0.00069	0.00000	0.00285
5.644	$4.41 \cdot 10^5$	0.00000	0.00000	NA

Figure 22: Table of risk estimates for range of thresholds of Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands

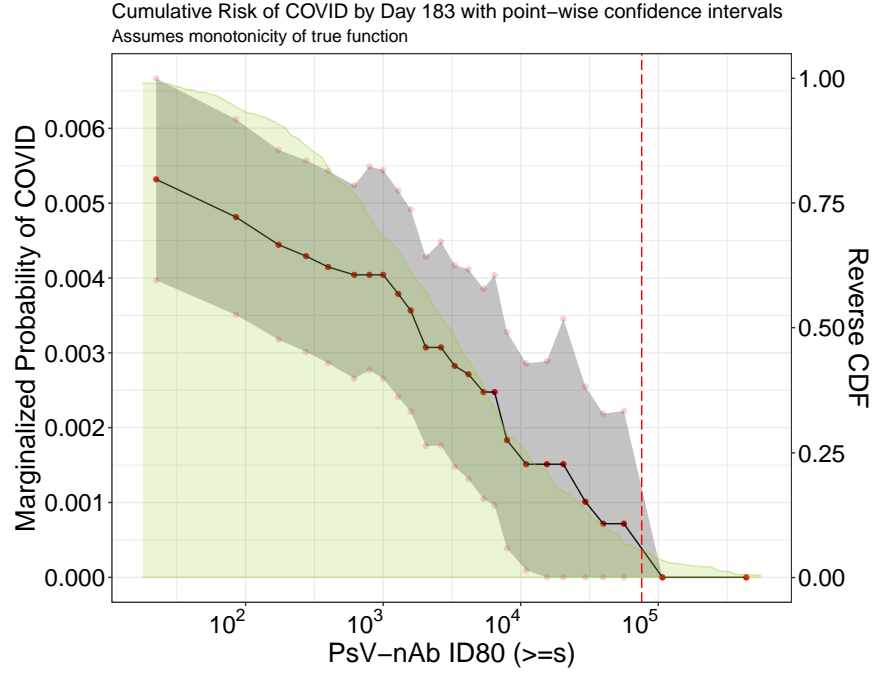


Figure 23: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

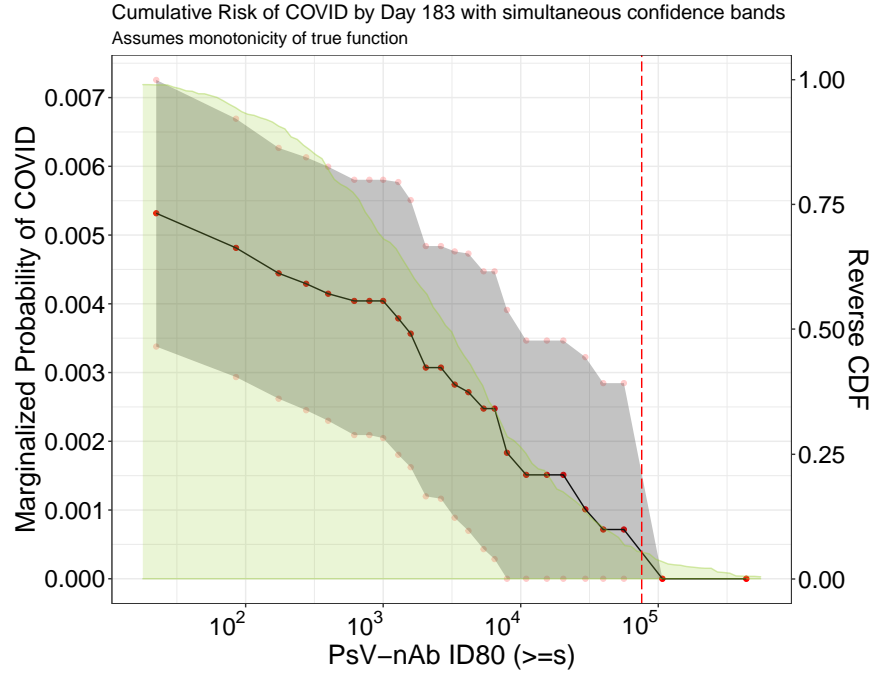


Figure 24: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Day 29 Spike protein antibody

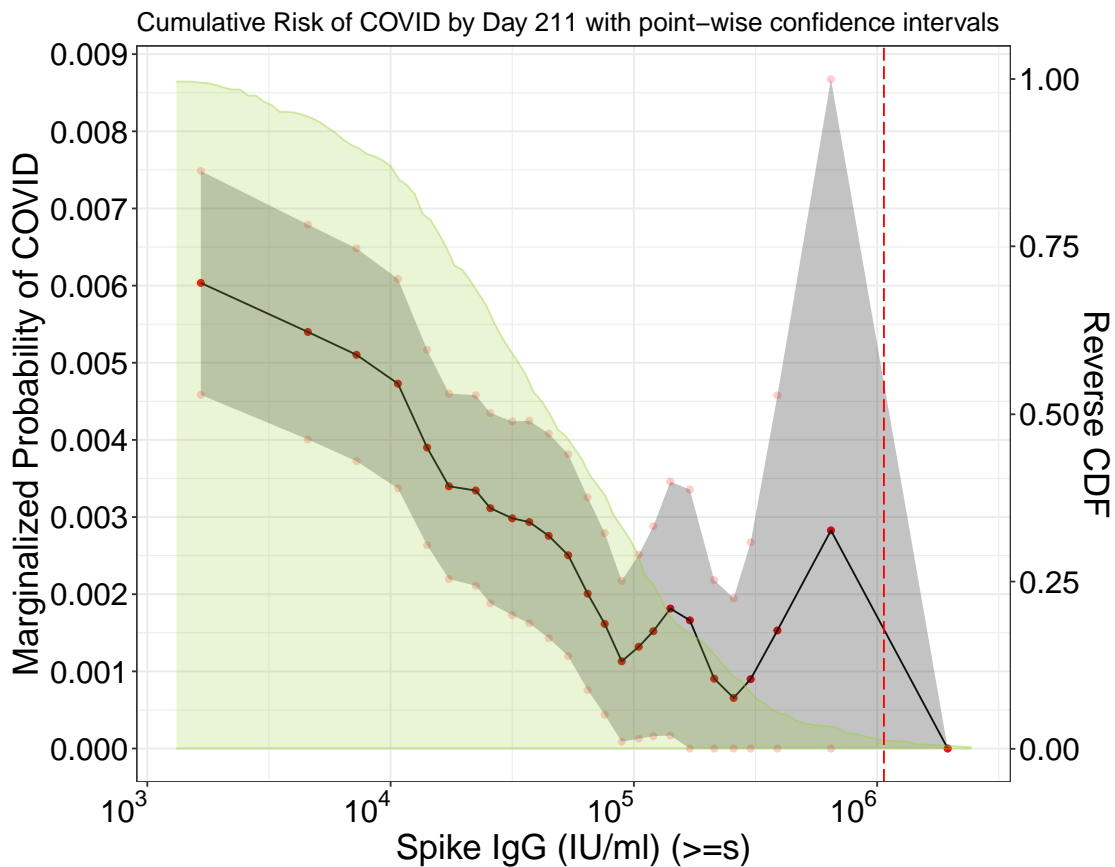


Figure 25: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
3.220	1.66×10^3	0.00603	0.00458	0.00749
4.030	1.07×10^4	0.00473	0.00337	0.00609
4.244	1.75×10^4	0.00340	0.00220	0.00460
4.503	3.18×10^4	0.00298	0.00173	0.00424
4.729	5.36×10^4	0.00251	0.00120	0.00381
4.884	7.66×10^4	0.00162	0.00044	0.00279
5.082	1.21×10^5	0.00152	0.00016	0.00288
5.326	2.12×10^5	0.00091	0.00000	0.00218
5.484	3.05×10^5	0.00090	0.00000	0.00267
6.285	1.93×10^6	0.00000	0.00000	NA

Figure 26: Table of risk estimates for range of thresholds of Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals.

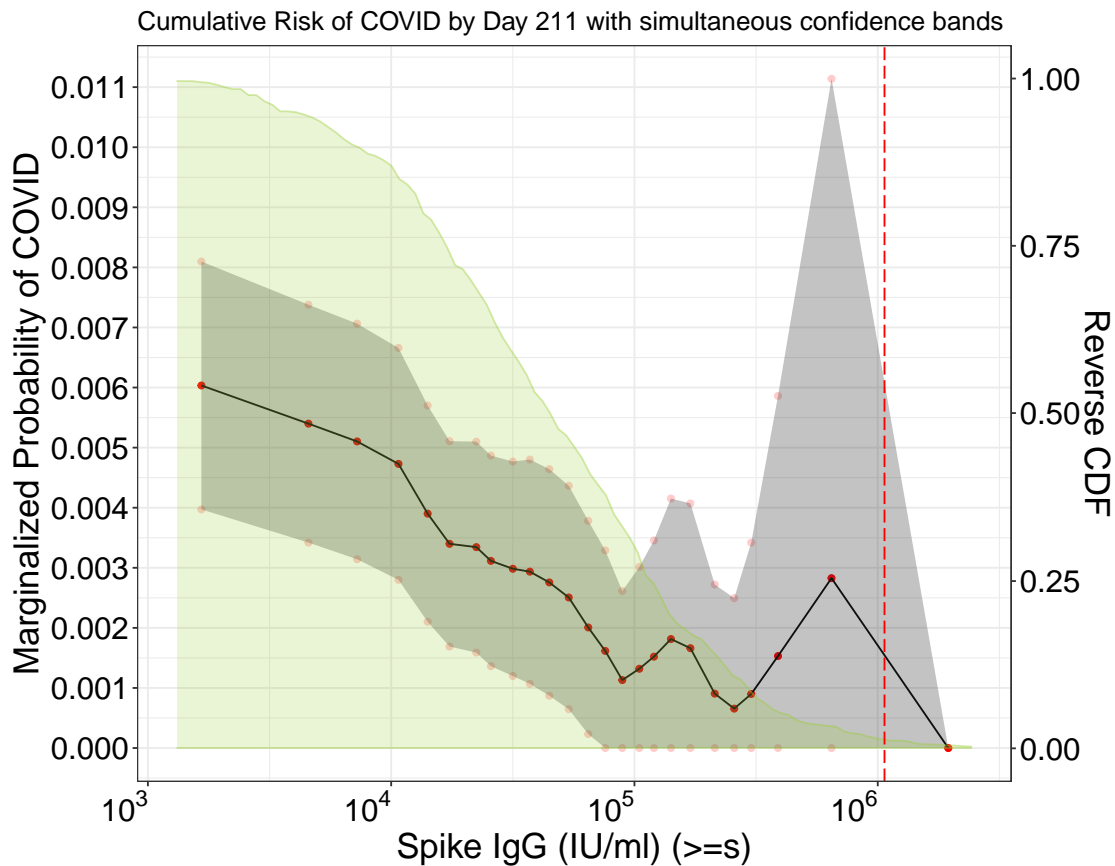


Figure 27: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
3.220	$1.66 \cdot 10^3$	0.00603	0.00397	0.00810
4.030	$1.07 \cdot 10^4$	0.00473	0.00280	0.00666
4.244	$1.75 \cdot 10^4$	0.00340	0.00169	0.00511
4.503	$3.18 \cdot 10^4$	0.00298	0.00120	0.00477
4.729	$5.36 \cdot 10^4$	0.00251	0.00065	0.00437
4.884	$7.66 \cdot 10^4$	0.00162	0.00000	0.00329
5.082	$1.21 \cdot 10^5$	0.00152	0.00000	0.00346
5.326	$2.12 \cdot 10^5$	0.00091	0.00000	0.00272
5.484	$3.05 \cdot 10^5$	0.00090	0.00000	0.00342
6.285	$1.93 \cdot 10^6$	0.00000	0.00000	NA

Figure 28: Table of risk estimates for range of thresholds of Day 29 Spike protein antibody activity levels with simultaneous 95% confidence bands

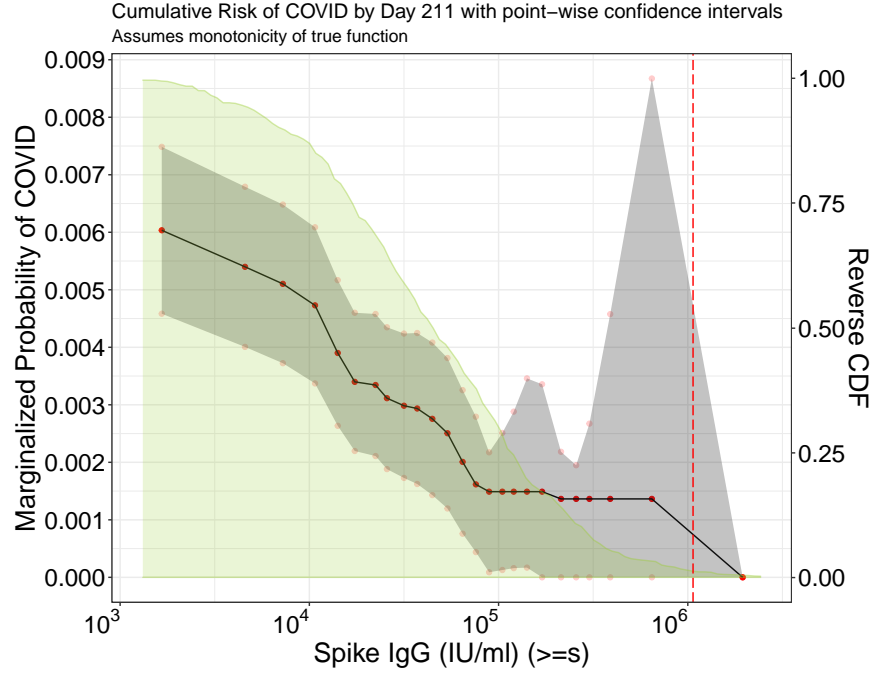


Figure 29: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

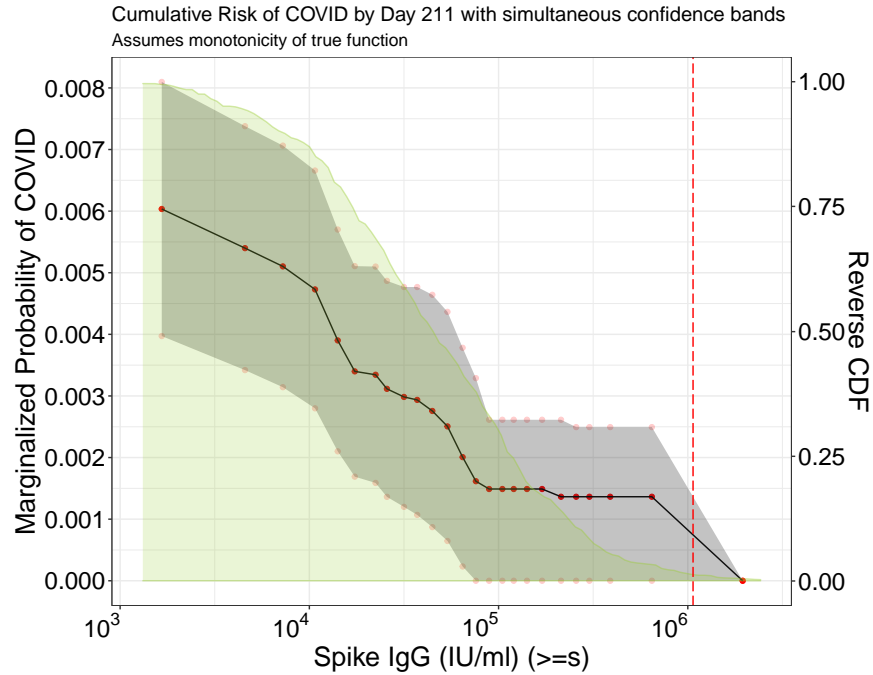


Figure 30: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Day 29 RBD binding antibody

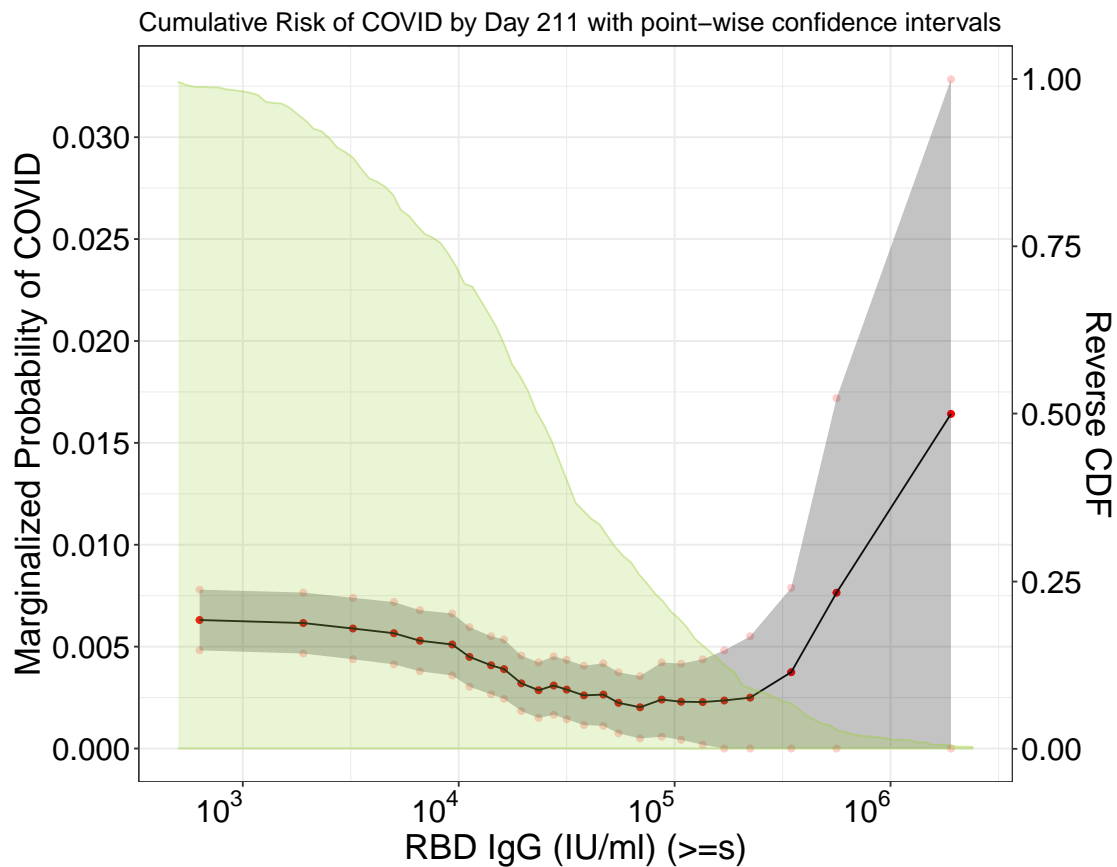


Figure 31: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
2.802	$6.34 \cdot 10^2$	0.00631	0.00482	0.00780
3.701	$5.02 \cdot 10^3$	0.00566	0.00413	0.00719
3.970	$9.33 \cdot 10^3$	0.00511	0.00359	0.00663
4.215	$1.64 \cdot 10^4$	0.00390	0.00244	0.00535
4.443	$2.77 \cdot 10^4$	0.00309	0.00166	0.00452
4.579	$3.79 \cdot 10^4$	0.00261	0.00115	0.00406
4.835	$6.84 \cdot 10^4$	0.00202	0.00050	0.00355
5.127	$1.34 \cdot 10^5$	0.00228	0.00019	0.00438
5.351	$2.24 \cdot 10^5$	0.00250	0.00000	0.00551
6.281	$1.91 \cdot 10^6$	0.01642	0.00000	0.04849

Figure 32: Table of risk estimates for range of thresholds of Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals.

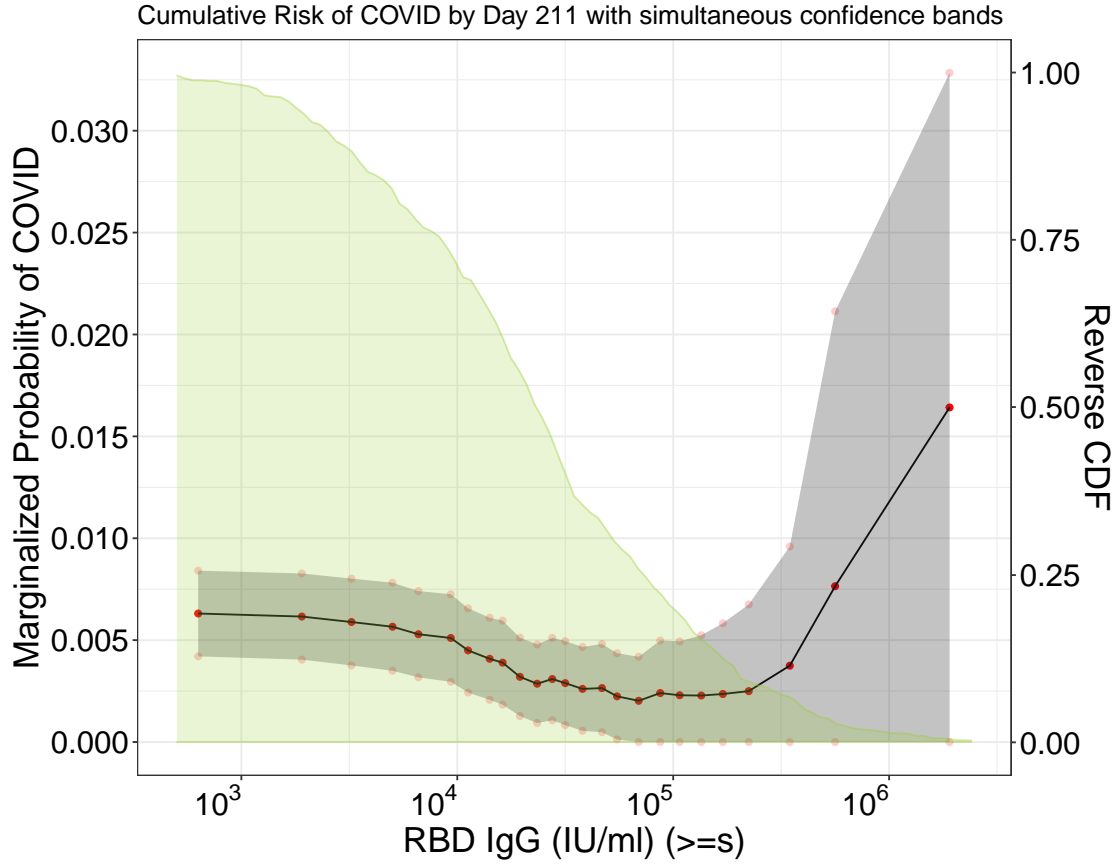


Figure 33: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
2.802	$6.34 \cdot 10^2$	0.00631	0.00420	0.00841
3.701	$5.02 \cdot 10^3$	0.00566	0.00350	0.00782
3.970	$9.33 \cdot 10^3$	0.00511	0.00296	0.00725
4.215	$1.64 \cdot 10^4$	0.00390	0.00183	0.00596
4.443	$2.77 \cdot 10^4$	0.00309	0.00107	0.00512
4.579	$3.79 \cdot 10^4$	0.00261	0.00055	0.00466
4.835	$6.84 \cdot 10^4$	0.00202	0.00000	0.00418
5.127	$1.34 \cdot 10^5$	0.00228	0.00000	0.00524
5.351	$2.24 \cdot 10^5$	0.00250	0.00000	0.00675
6.281	$1.91 \cdot 10^6$	0.01642	0.00000	0.06172

Figure 34: Table of risk estimates for range of thresholds of Day 29 RBD binding antibody activity levels with simultaneous 95% confidence bands

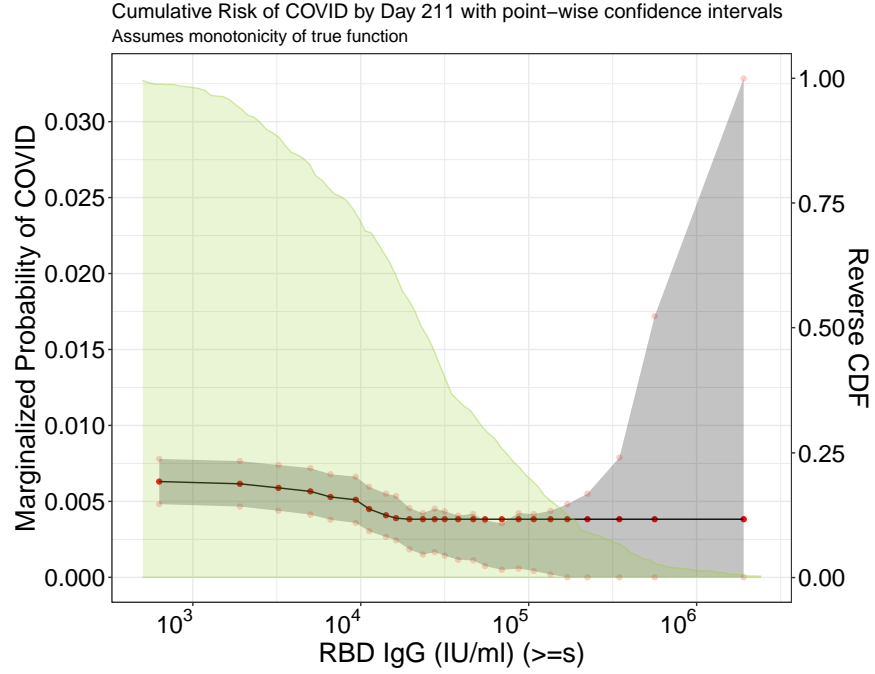


Figure 35: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

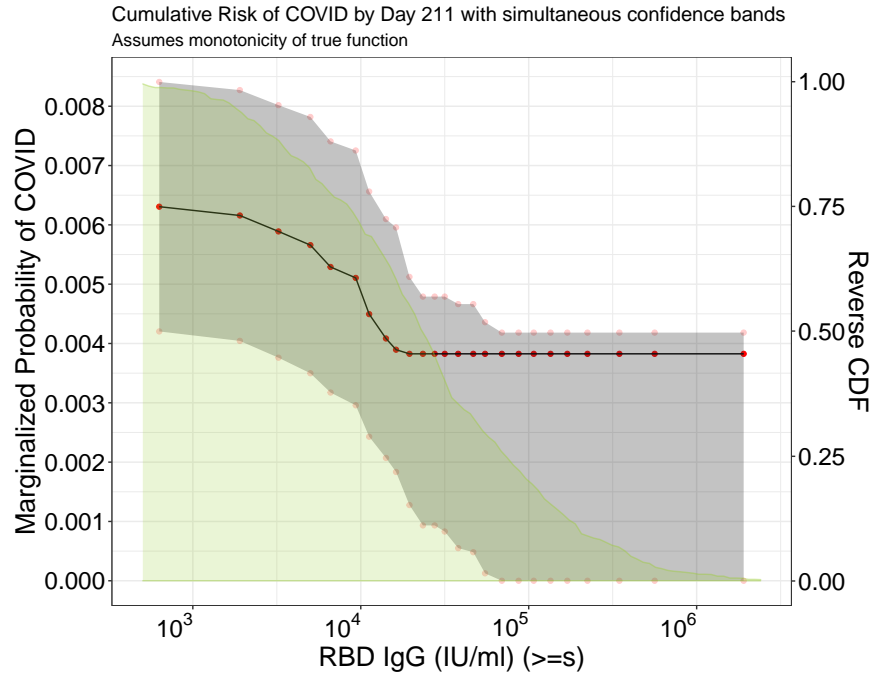


Figure 36: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

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

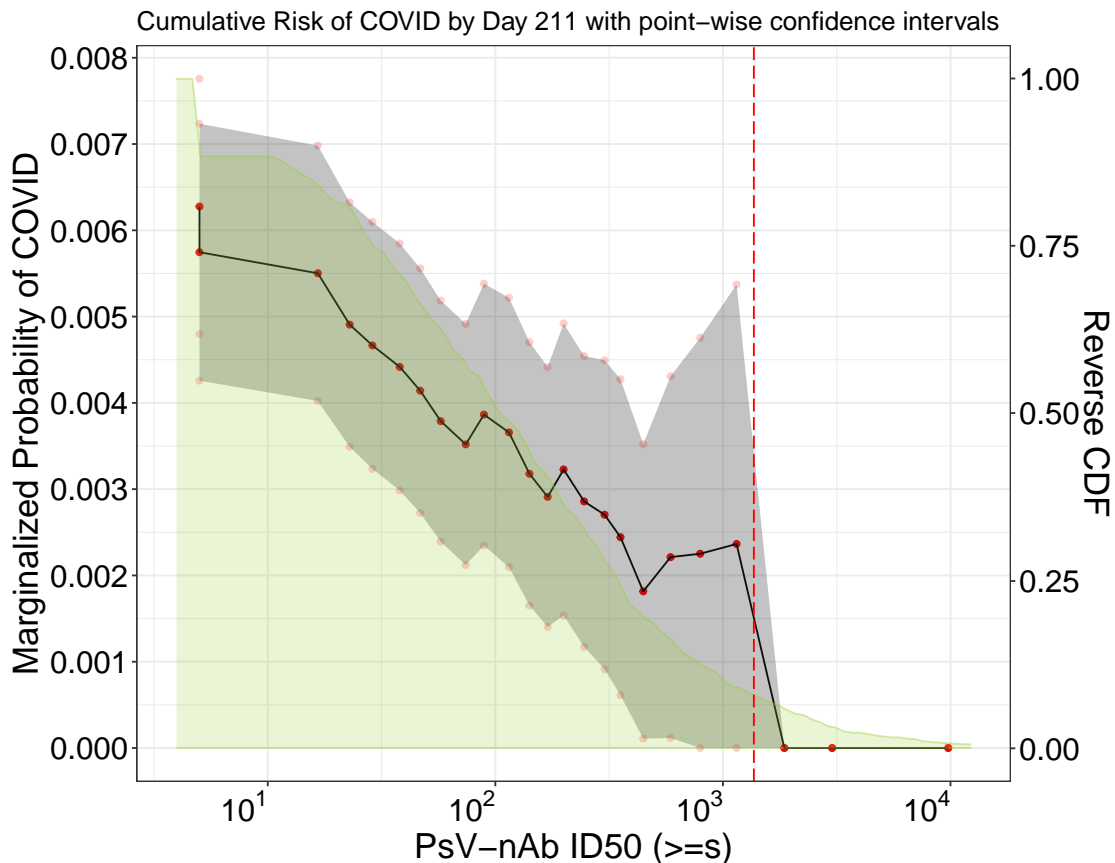


Figure 37: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00×10^0	0.00628	0.00480	0.00776
1.356	2.27×10^1	0.00491	0.00349	0.00632
1.575	3.76×10^1	0.00442	0.00299	0.00585
1.868	7.38×10^1	0.00352	0.00212	0.00492
2.055	1.14×10^2	0.00366	0.00210	0.00522
2.303	2.01×10^2	0.00323	0.00154	0.00492
2.481	3.03×10^2	0.00270	0.00091	0.00449
2.770	5.89×10^2	0.00221	0.00012	0.00431
3.056	1.14×10^3	0.00236	0.00000	0.00537
3.989	9.75×10^3	0.00000	0.00000	NA

Figure 38: Table of risk estimates for range of thresholds of Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals.

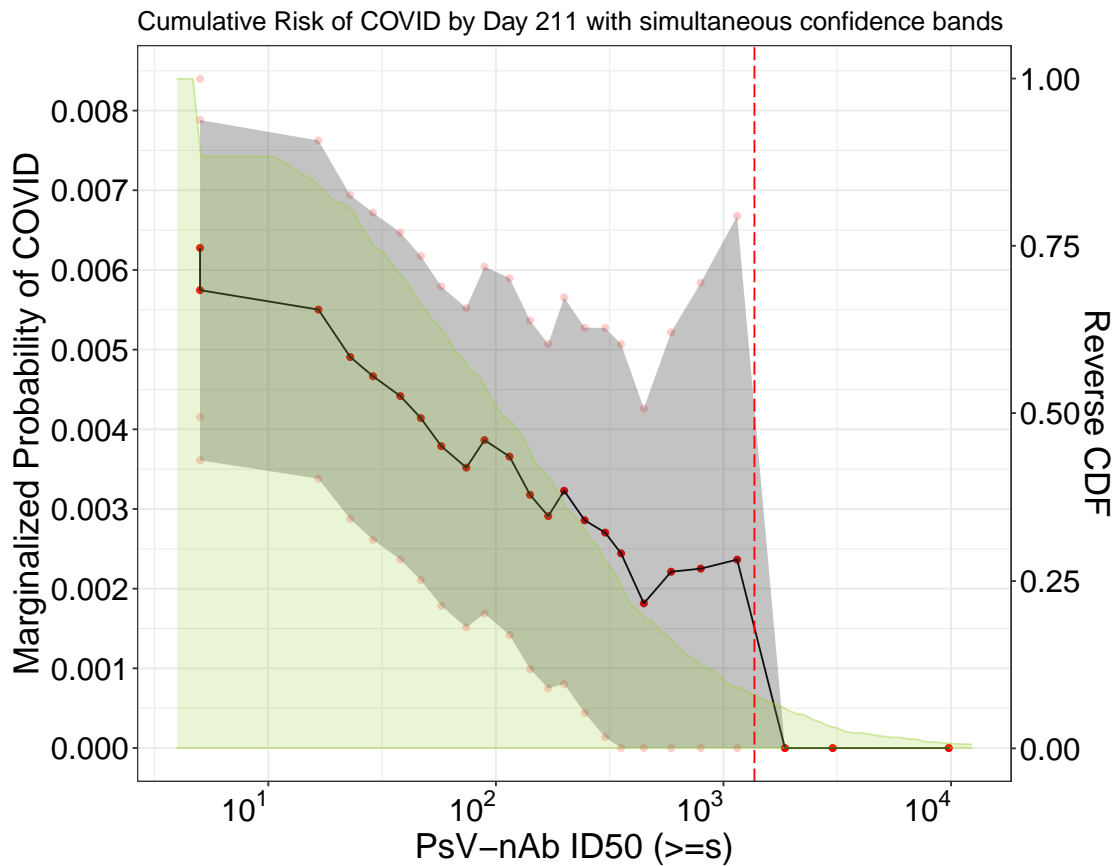


Figure 39: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 \cdot 10^0$	0.00628	0.00415	0.00840
1.356	$2.27 \cdot 10^1$	0.00491	0.00287	0.00694
1.575	$3.76 \cdot 10^1$	0.00442	0.00236	0.00647
1.868	$7.38 \cdot 10^1$	0.00352	0.00152	0.00552
2.055	$1.14 \cdot 10^2$	0.00366	0.00142	0.00590
2.303	$2.01 \cdot 10^2$	0.00323	0.00080	0.00565
2.481	$3.03 \cdot 10^2$	0.00270	0.00014	0.00527
2.770	$5.89 \cdot 10^2$	0.00221	0.00000	0.00522
3.056	$1.14 \cdot 10^3$	0.00236	0.00000	0.00668
3.989	$9.75 \cdot 10^3$	0.00000	0.00000	NA

Figure 40: Table of risk estimates for range of thresholds of Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands

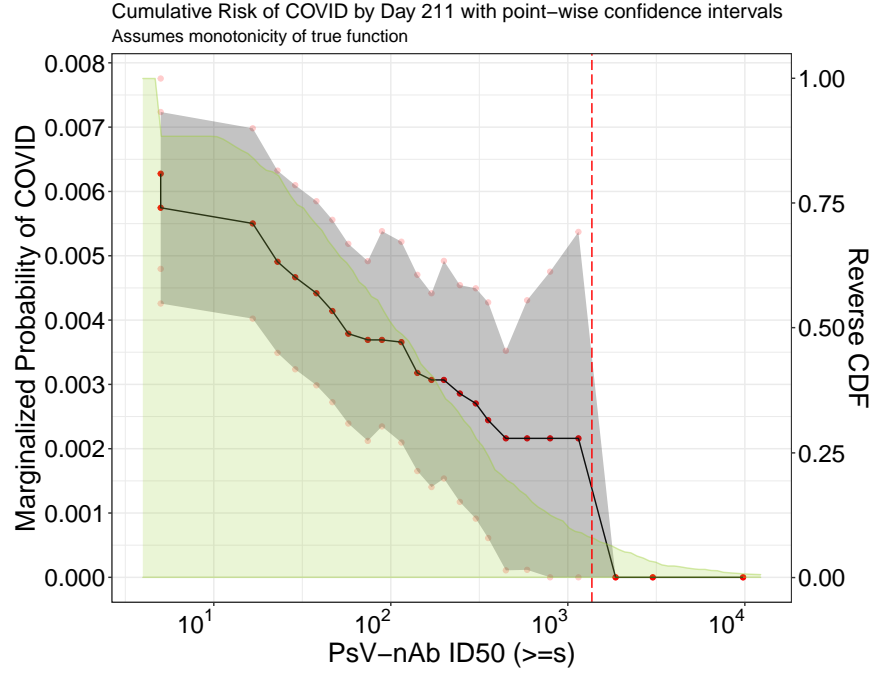


Figure 41: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

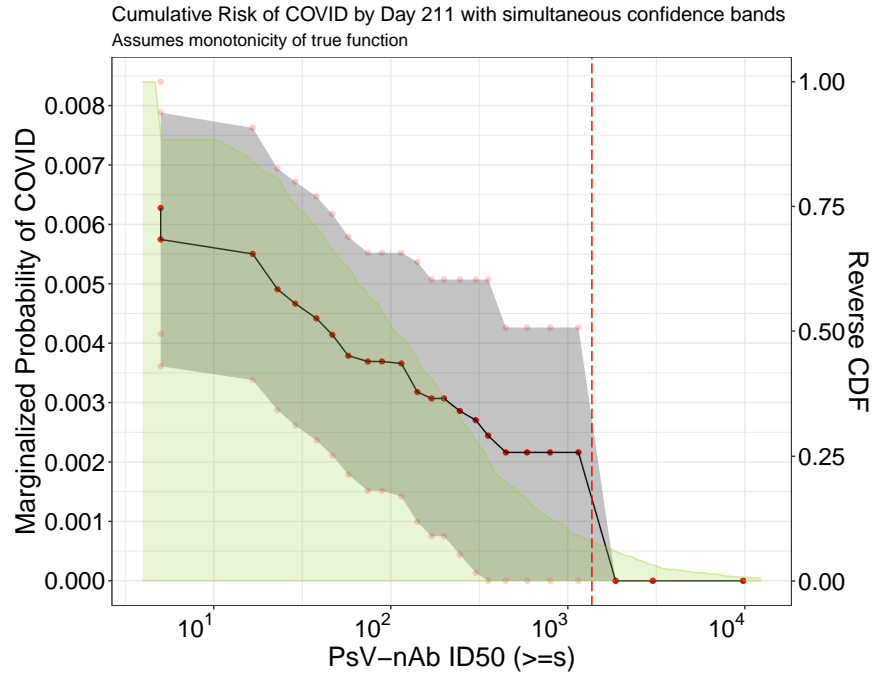


Figure 42: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

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

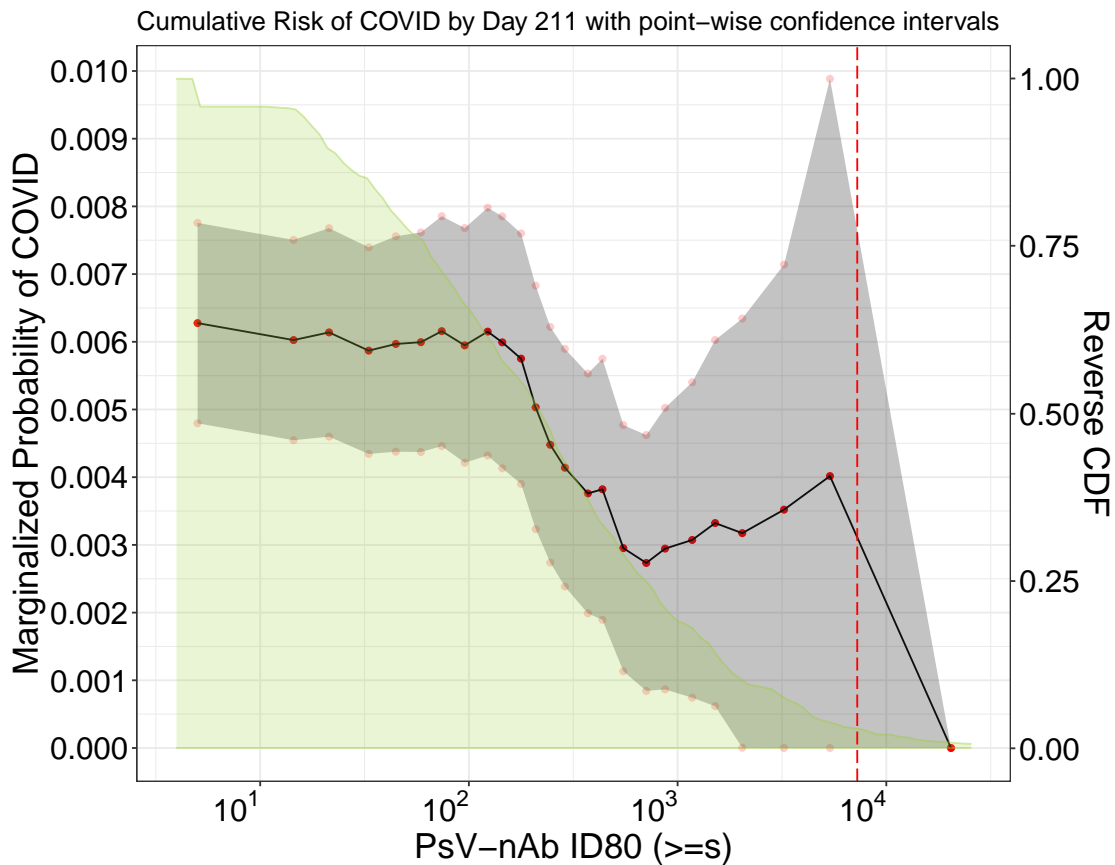


Figure 43: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 \cdot 10^0$	0.00628	0.00480	0.00776
1.515	$3.27 \cdot 10^1$	0.00587	0.00434	0.00740
1.765	$5.82 \cdot 10^1$	0.00599	0.00437	0.00762
2.088	$1.22 \cdot 10^2$	0.00615	0.00432	0.00798
2.324	$2.11 \cdot 10^2$	0.00503	0.00323	0.00683
2.462	$2.90 \cdot 10^2$	0.00414	0.00238	0.00590
2.744	$5.55 \cdot 10^2$	0.00295	0.00113	0.00477
3.070	$1.17 \cdot 10^3$	0.00307	0.00074	0.00540
3.314	$2.06 \cdot 10^3$	0.00317	0.00000	0.00634
4.305	$2.02 \cdot 10^4$	0.00000	0.00000	NA

Figure 44: Table of risk estimates for range of thresholds of Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals.

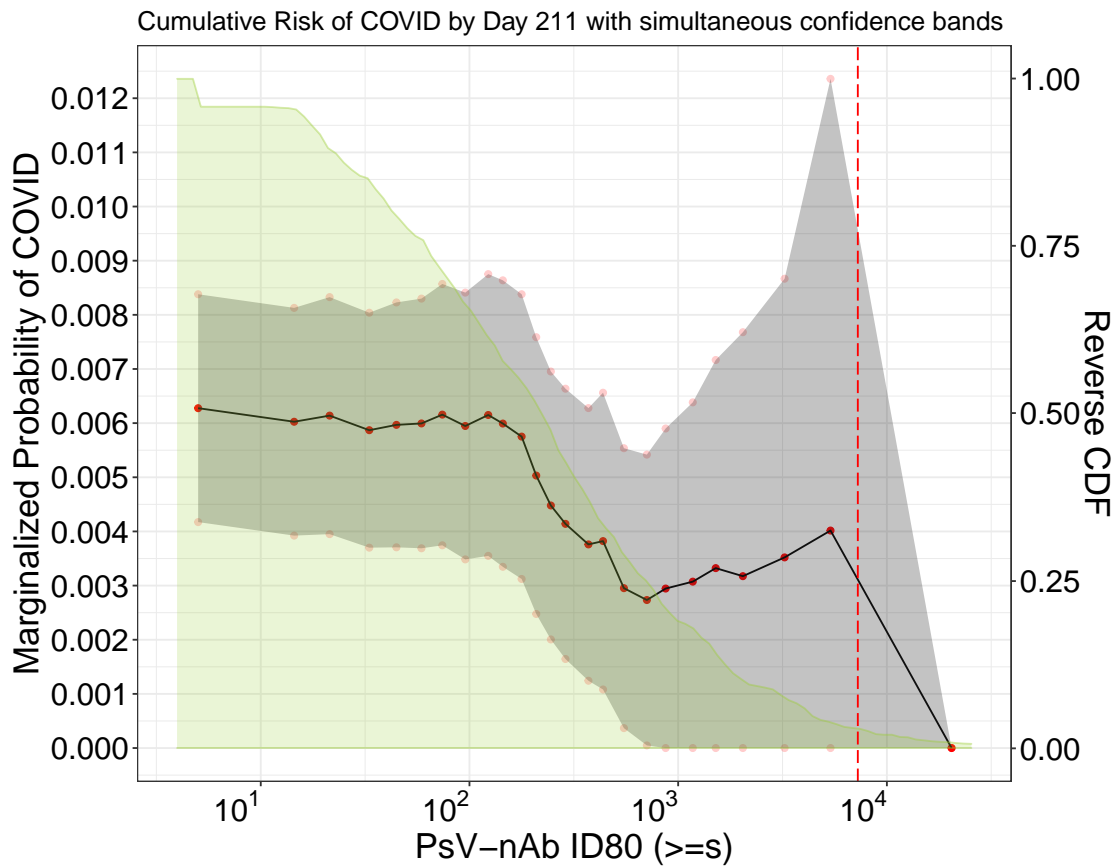


Figure 45: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 \cdot 10^0$	0.00628	0.00417	0.00838
1.515	$3.27 \cdot 10^1$	0.00587	0.00370	0.00804
1.765	$5.82 \cdot 10^1$	0.00599	0.00369	0.00830
2.088	$1.22 \cdot 10^2$	0.00615	0.00355	0.00875
2.324	$2.11 \cdot 10^2$	0.00503	0.00248	0.00759
2.462	$2.90 \cdot 10^2$	0.00414	0.00164	0.00664
2.744	$5.55 \cdot 10^2$	0.00295	0.00037	0.00554
3.070	$1.17 \cdot 10^3$	0.00307	0.00000	0.00638
3.314	$2.06 \cdot 10^3$	0.00317	0.00000	0.00768
4.305	$2.02 \cdot 10^4$	0.00000	0.00000	NA

Figure 46: Table of risk estimates for range of thresholds of Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands

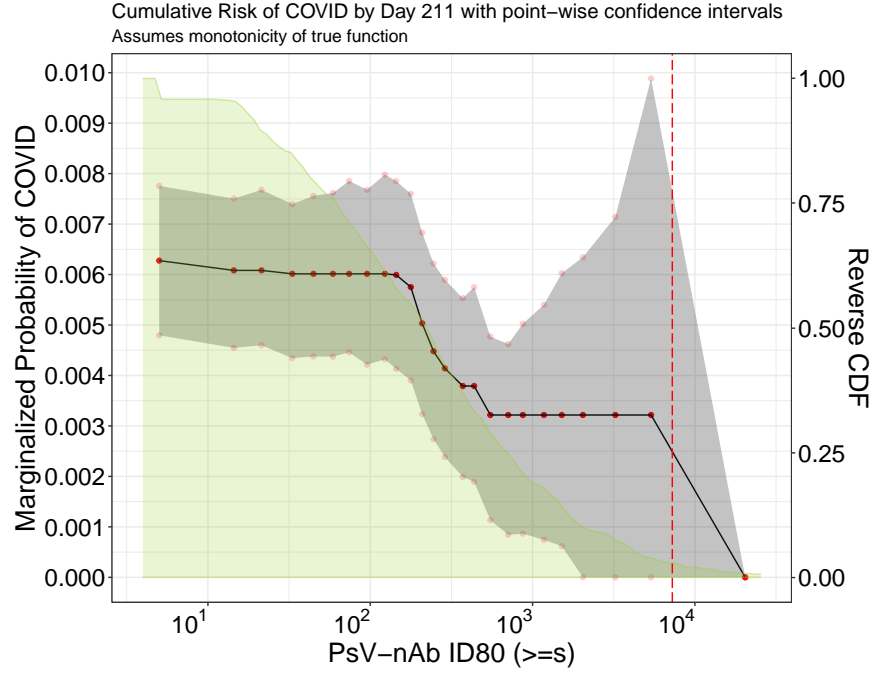


Figure 47: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

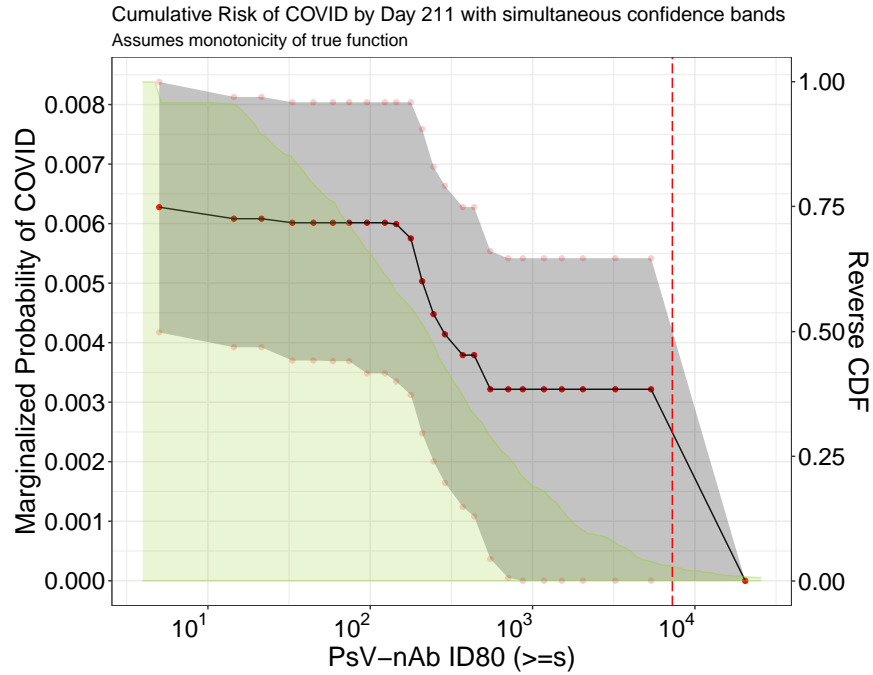


Figure 48: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.