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. <!–
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.

Day 57 Spike protein antibody

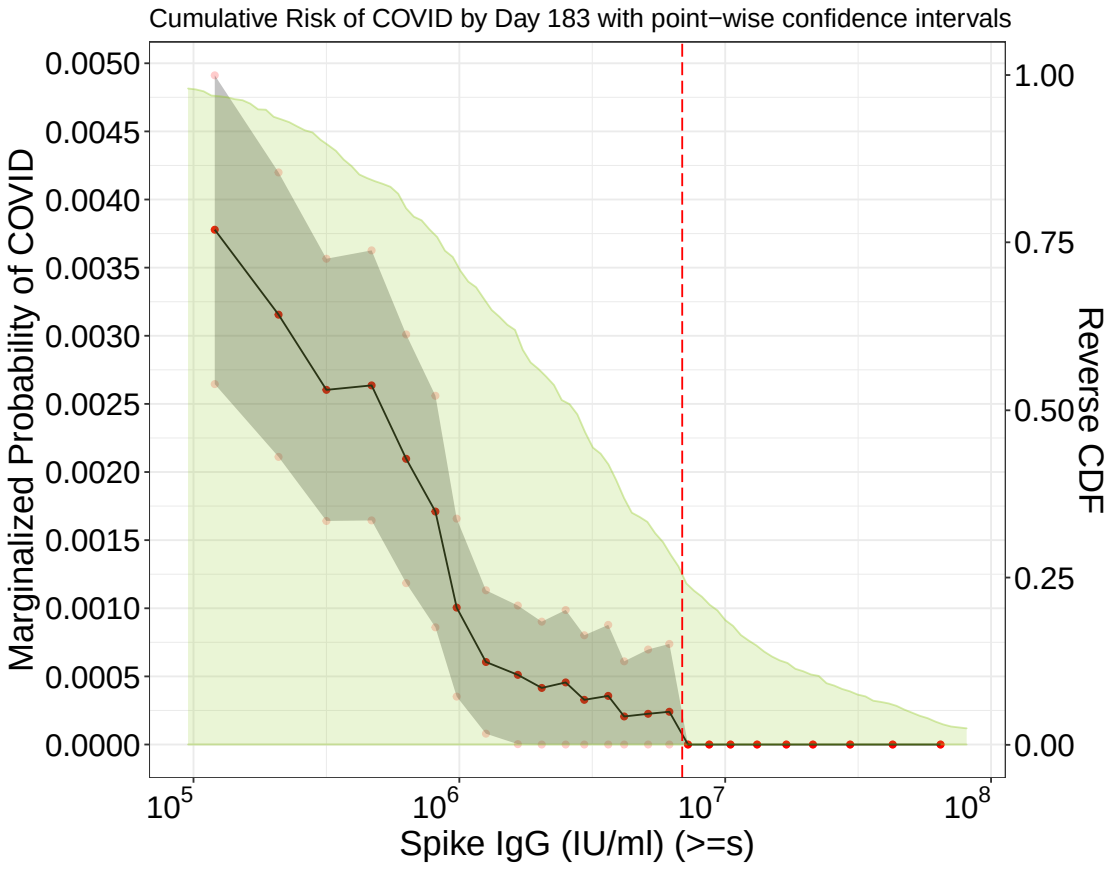

Figure 1: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
5.080	1.20*10^5	0.00378	0.00265	0.00491
5.667	4.65*10^5	0.00264	0.00164	0.00363
5.915	8.22*10^5	0.00171	0.00086	0.00256
6.223	1.67*10^6	0.00051	0.00000	0.00102
6.475	2.99*10^6	0.00033	0.00000	0.00080
6.623	4.20*10^6	0.00021	0.00000	0.00061
6.857	7.19*10^6	0.00000	0.00000	NA
7.122	1.32*10^7	0.00000	0.00000	NA
7.330	2.14*10^7	0.00000	0.00000	NA
7.808	6.43*10^7	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.

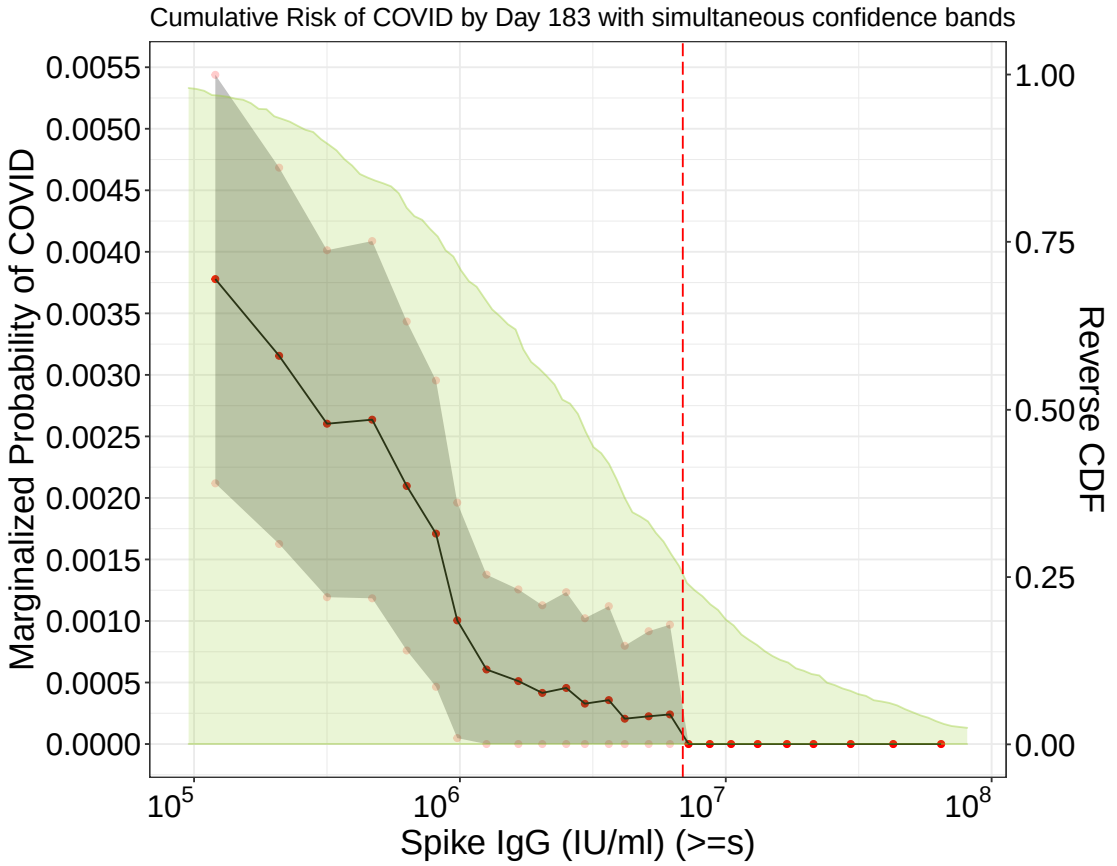

Figure 3: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
5.080	1.20*10^5	0.00378	0.00212	0.00544
5.667	4.65*10^5	0.00264	0.00118	0.00409
5.915	8.22*10^5	0.00171	0.00047	0.00295
6.223	1.67*10^6	0.00051	0.00000	0.00126
6.475	2.99*10^6	0.00033	0.00000	0.00102
6.623	4.20*10^6	0.00021	0.00000	0.00080
6.857	7.19*10^6	0.00000	0.00000	NA
7.122	1.32*10^7	0.00000	0.00000	NA
7.330	2.14*10^7	0.00000	0.00000	NA
7.808	6.43*10^7	0.00000	0.00000	NA

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

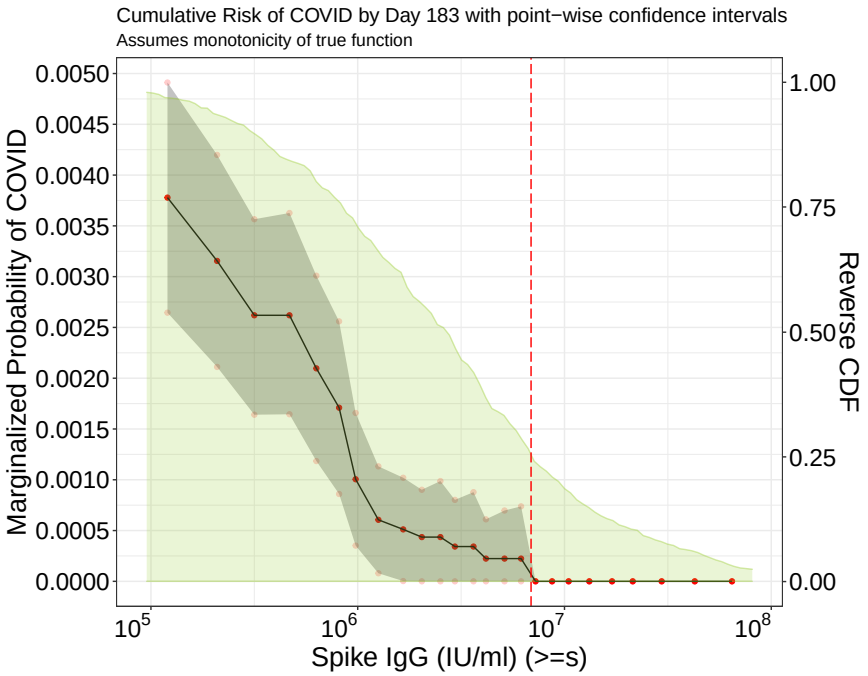

Figure 5: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

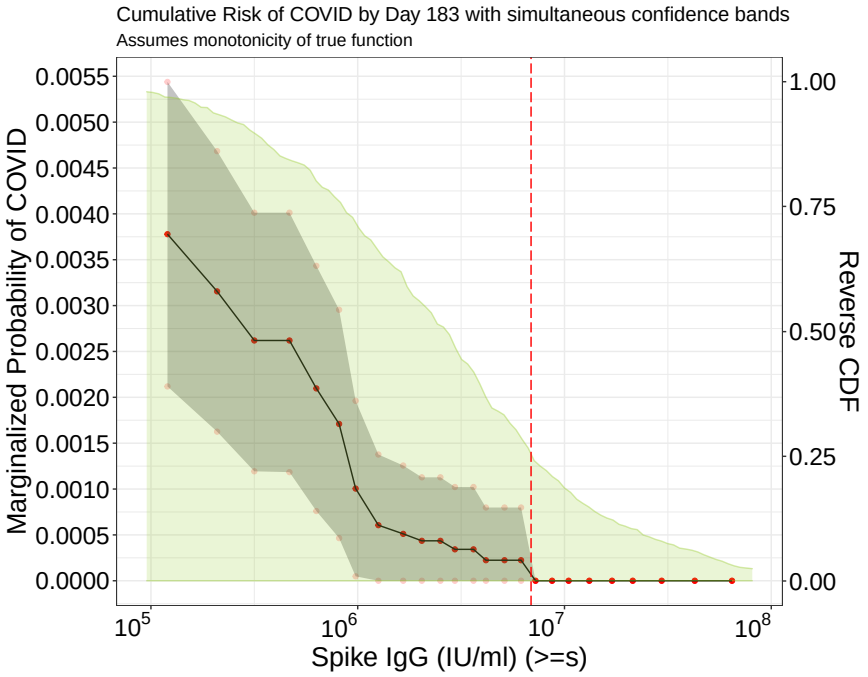

Figure 6: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

Day 57 RBD binding antibody

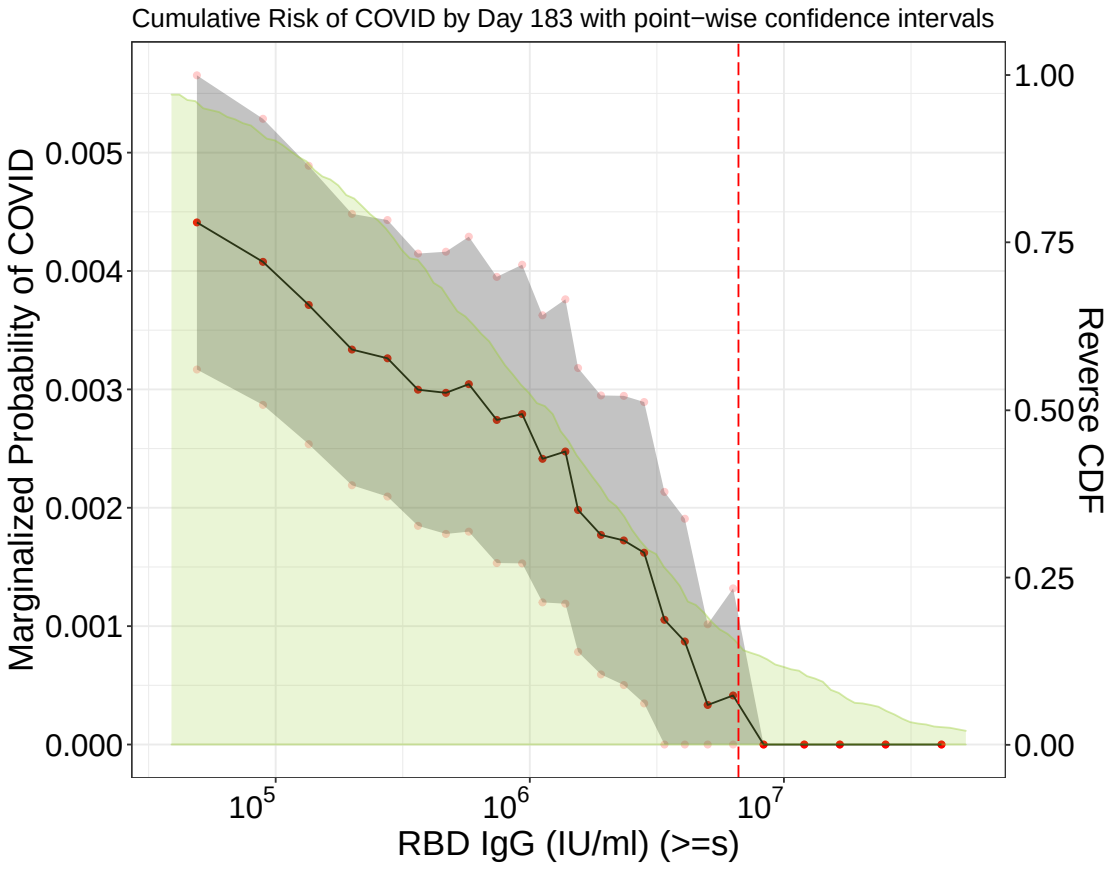

Figure 7: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.690	4.90*10^4	0.00441	0.00317	0.00565
5.300	2.00*10^5	0.00334	0.00219	0.00448
5.558	3.61*10^5	0.00300	0.00185	0.00415
5.871	7.43*10^5	0.00274	0.00153	0.00395
6.137	1.37*10^6	0.00248	0.00119	0.00376
6.280	1.91*10^6	0.00177	0.00059	0.00295
6.531	3.40*10^6	0.00105	0.00000	0.00213
6.803	6.35*10^6	0.00041	0.00000	0.00132
7.083	1.21*10^7	0.00000	0.00000	NA
7.616	4.13*10^7	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.

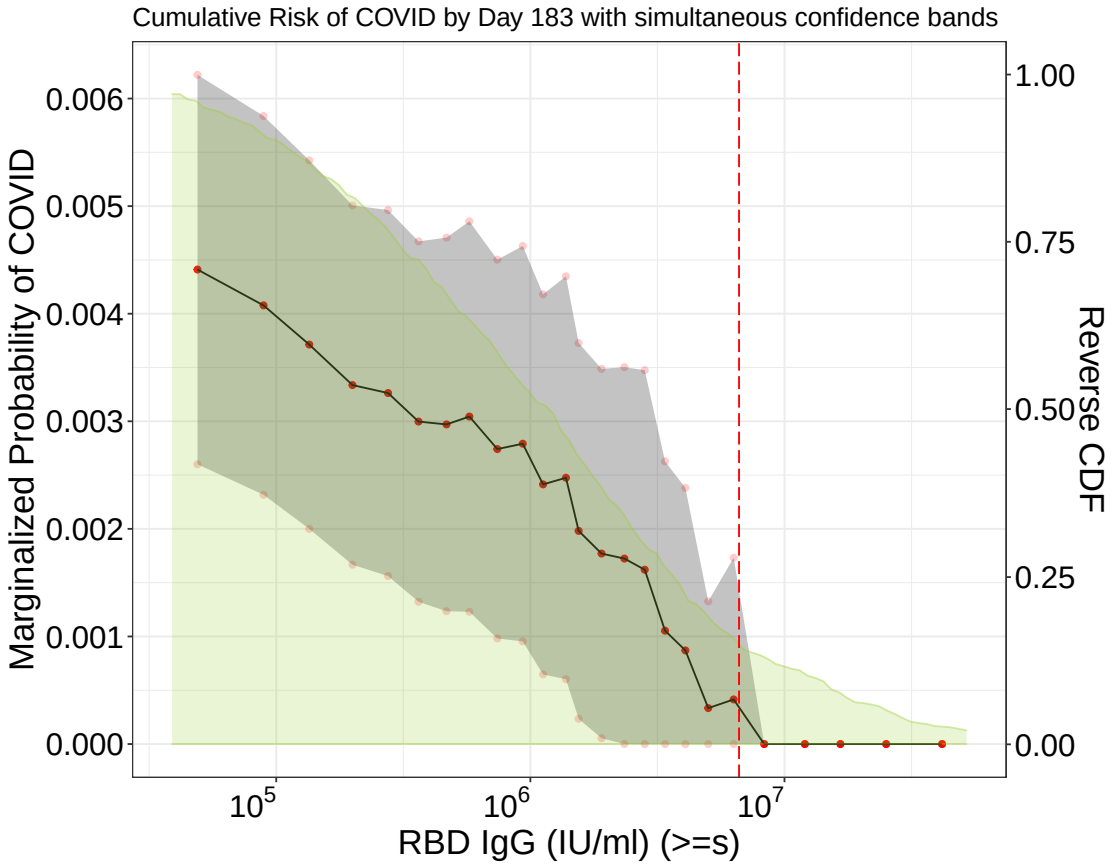

Figure 9: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.690	4.90*10^4	0.00441	0.00260	0.00622
5.300	2.00*10^5	0.00334	0.00167	0.00501
5.558	3.61*10^5	0.00300	0.00132	0.00467
5.871	7.43*10^5	0.00274	0.00098	0.00450
6.137	1.37*10^6	0.00248	0.00060	0.00435
6.280	1.91*10^6	0.00177	0.00005	0.00349
6.531	3.40*10^6	0.00105	0.00000	0.00263
6.803	6.35*10^6	0.00041	0.00000	0.00173
7.083	1.21*10^7	0.00000	0.00000	NA
7.616	4.13*10^7	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

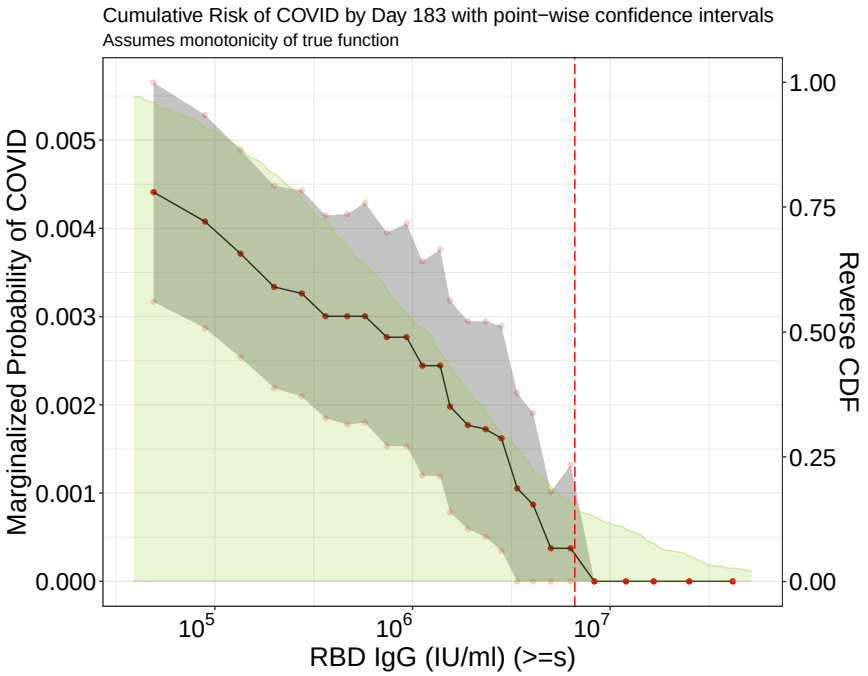

Figure 11: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

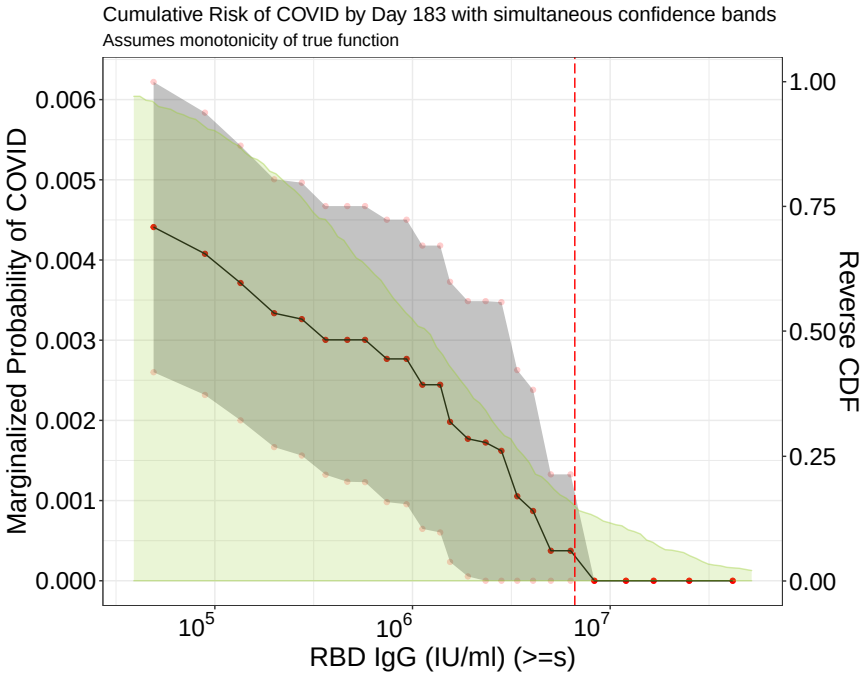

Figure 12: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

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

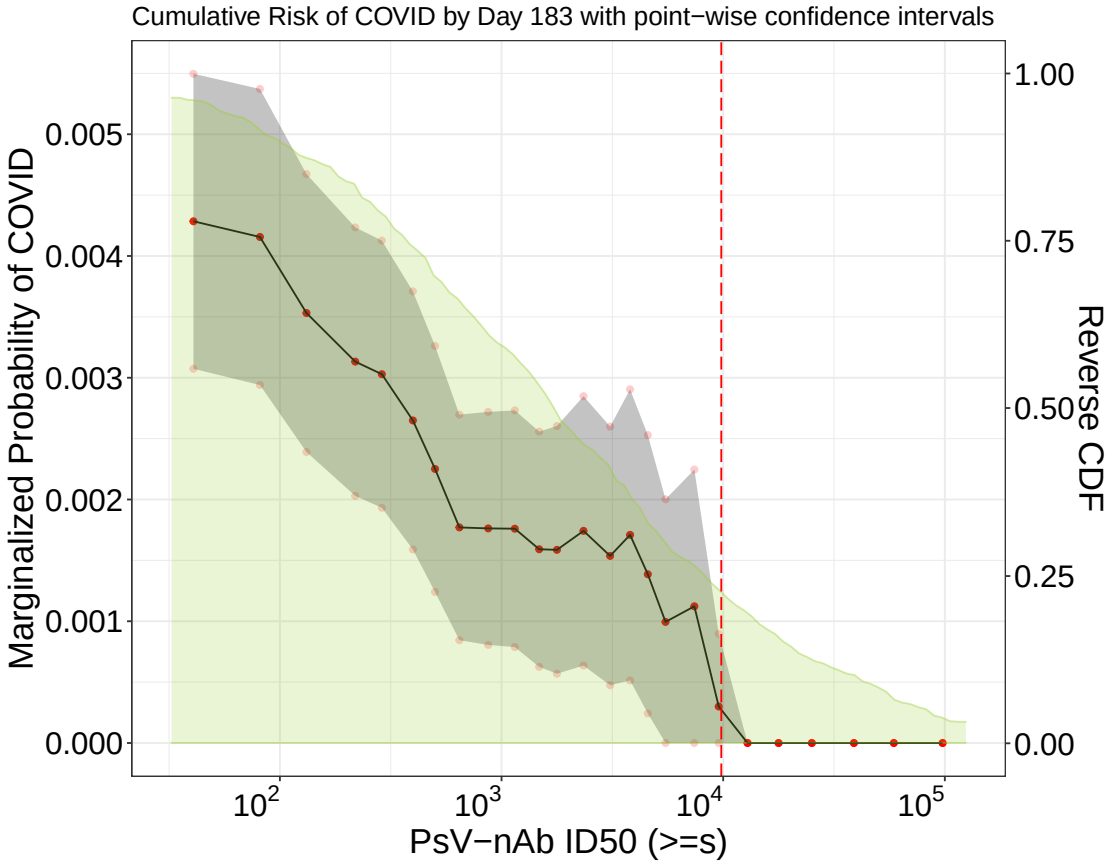

Figure 13: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.611	4.08*10^1	0.00429	0.00307	0.00550
2.345	2.21*10^2	0.00313	0.00203	0.00423
2.595	3.94*10^2	0.00265	0.00159	0.00371
2.935	8.61*10^2	0.00176	0.00081	0.00272
3.254	1.79*10^3	0.00159	0.00057	0.00260
3.485	3.05*10^3	0.00154	0.00047	0.00260
3.739	5.48*10^3	0.00099	0.00000	0.00200
4.112	1.29*10^4	0.00000	0.00000	NA
4.404	2.54*10^4	0.00000	0.00000	NA
4.995	9.89*10^4	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.

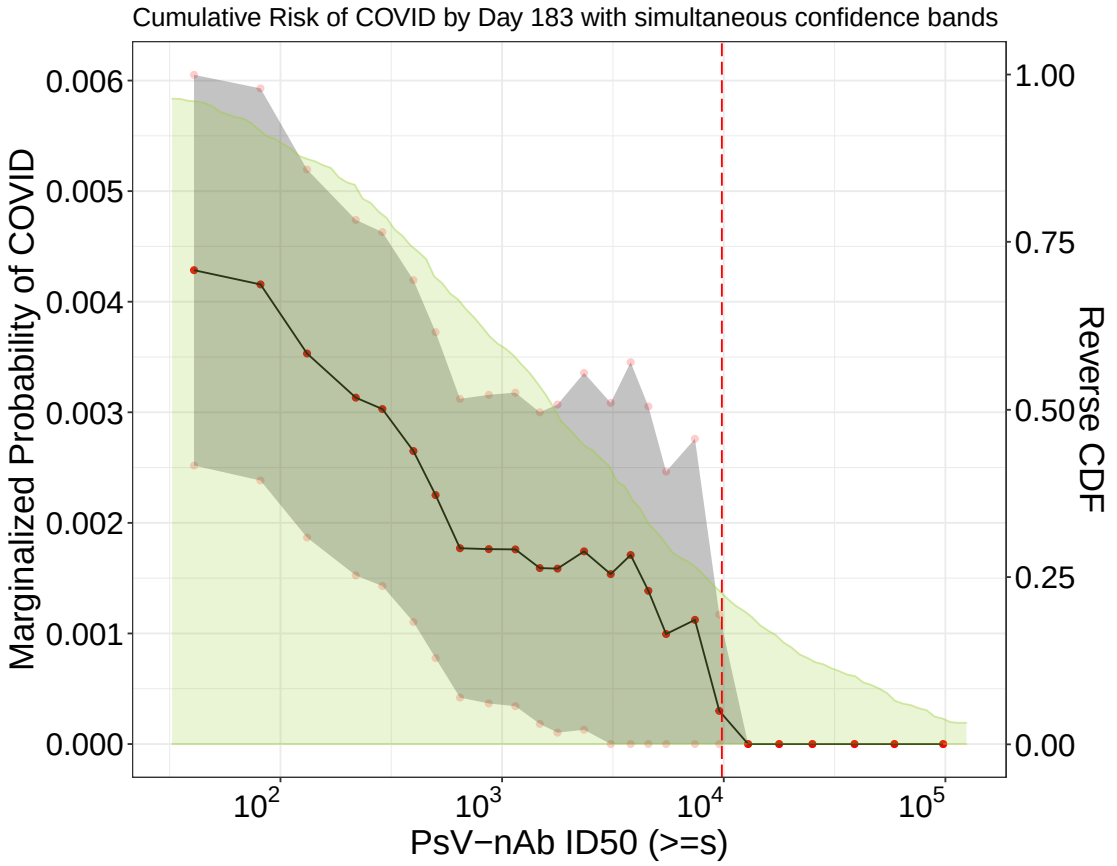

Figure 15: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.611	4.08*10^1	0.00429	0.00252	0.00605
2.345	2.21*10^2	0.00313	0.00152	0.00474
2.595	3.94*10^2	0.00265	0.00110	0.00420
2.935	8.61*10^2	0.00176	0.00037	0.00316
3.254	1.79*10^3	0.00159	0.00010	0.00307
3.485	3.05*10^3	0.00154	0.00000	0.00309
3.739	5.48*10^3	0.00099	0.00000	0.00246
4.112	1.29*10^4	0.00000	0.00000	NA
4.404	2.54*10^4	0.00000	0.00000	NA
4.995	9.89*10^4	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

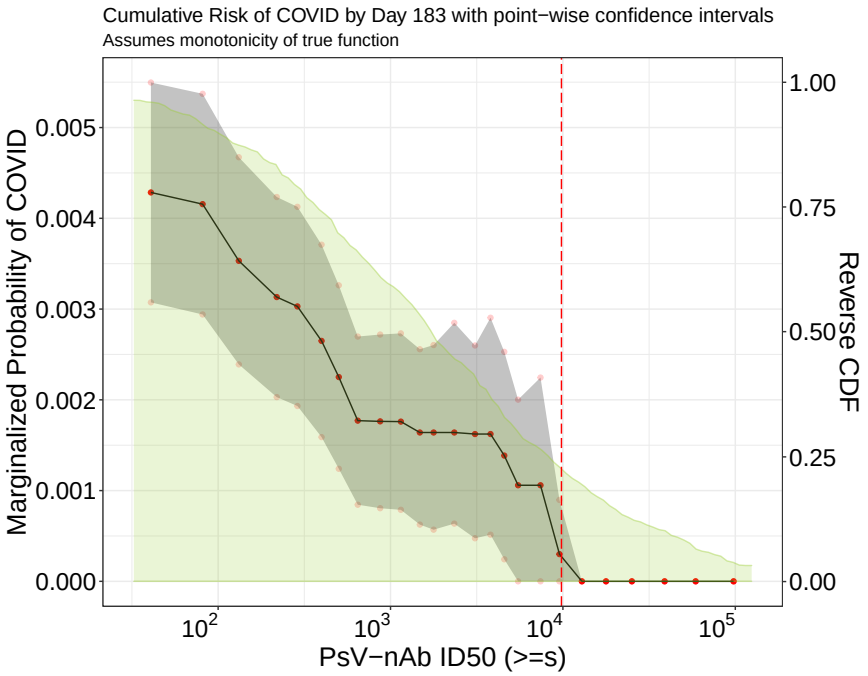

Figure 17: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed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

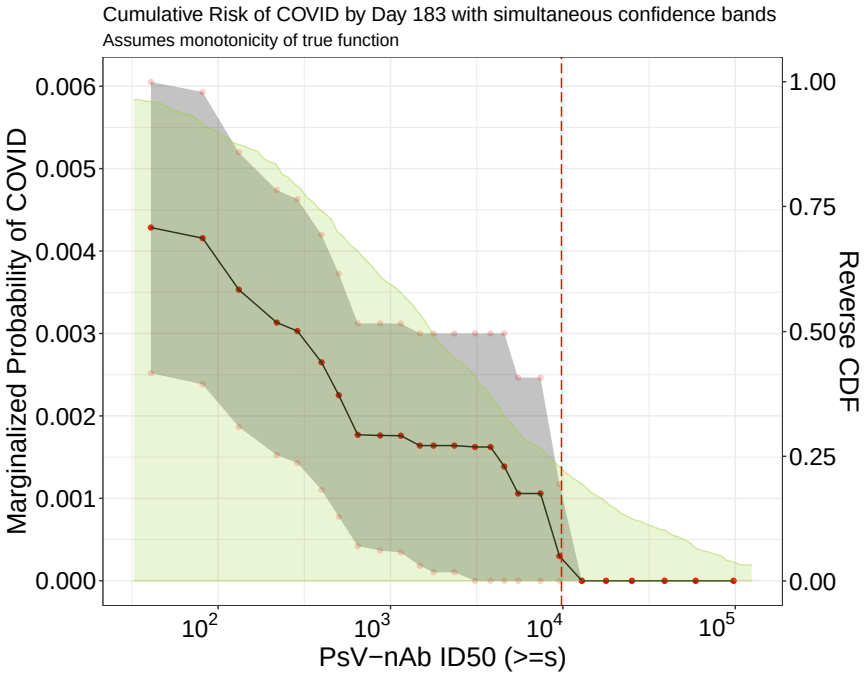

Figure 18: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence intervals. The dashed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

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

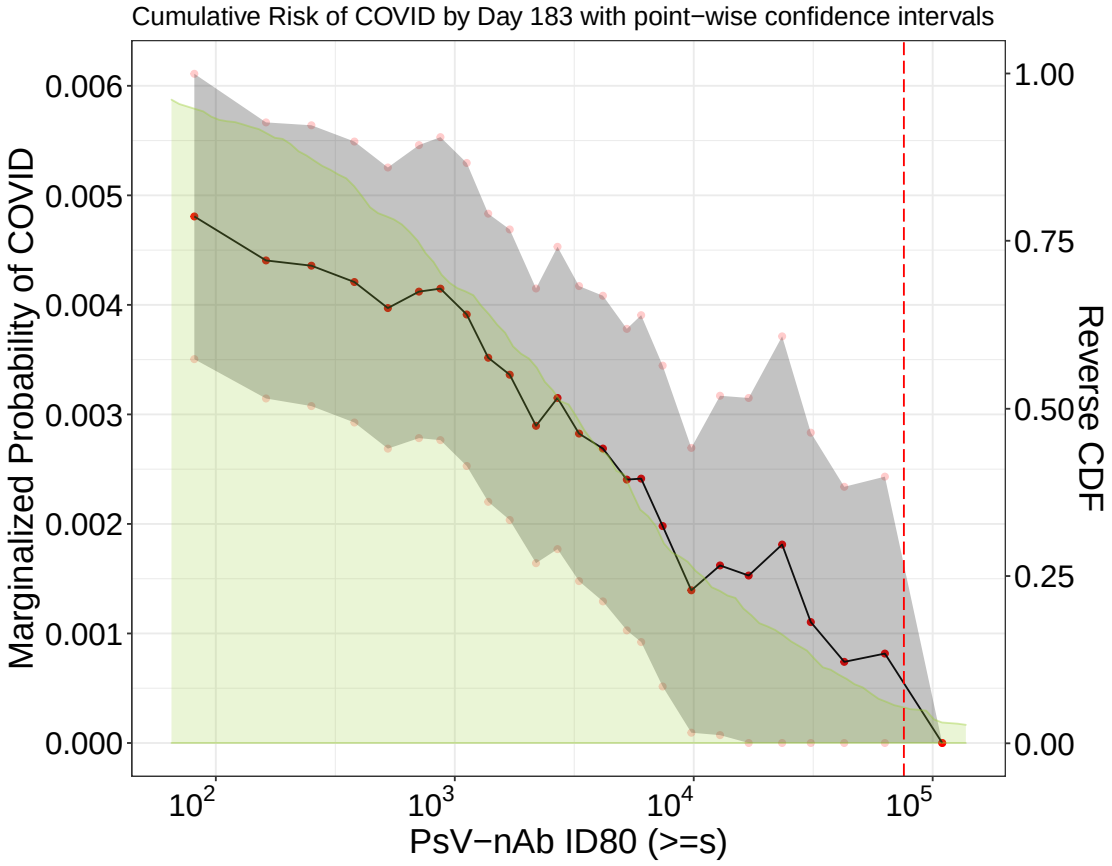

Figure 19: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.914	8.20*10^1	0.00481	0.00350	0.00611
2.579	3.79*10^2	0.00421	0.00293	0.00549
2.851	7.10*10^2	0.00412	0.00278	0.00546
3.142	1.39*10^3	0.00352	0.00220	0.00483
3.429	2.69*10^3	0.00315	0.00177	0.00453
3.619	4.16*10^3	0.00269	0.00129	0.00408
3.871	7.43*10^3	0.00198	0.00052	0.00345
4.234	1.71*10^4	0.00153	0.00000	0.00315
4.491	3.10*10^4	0.00110	0.00000	0.00283
5.039	1.09*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.

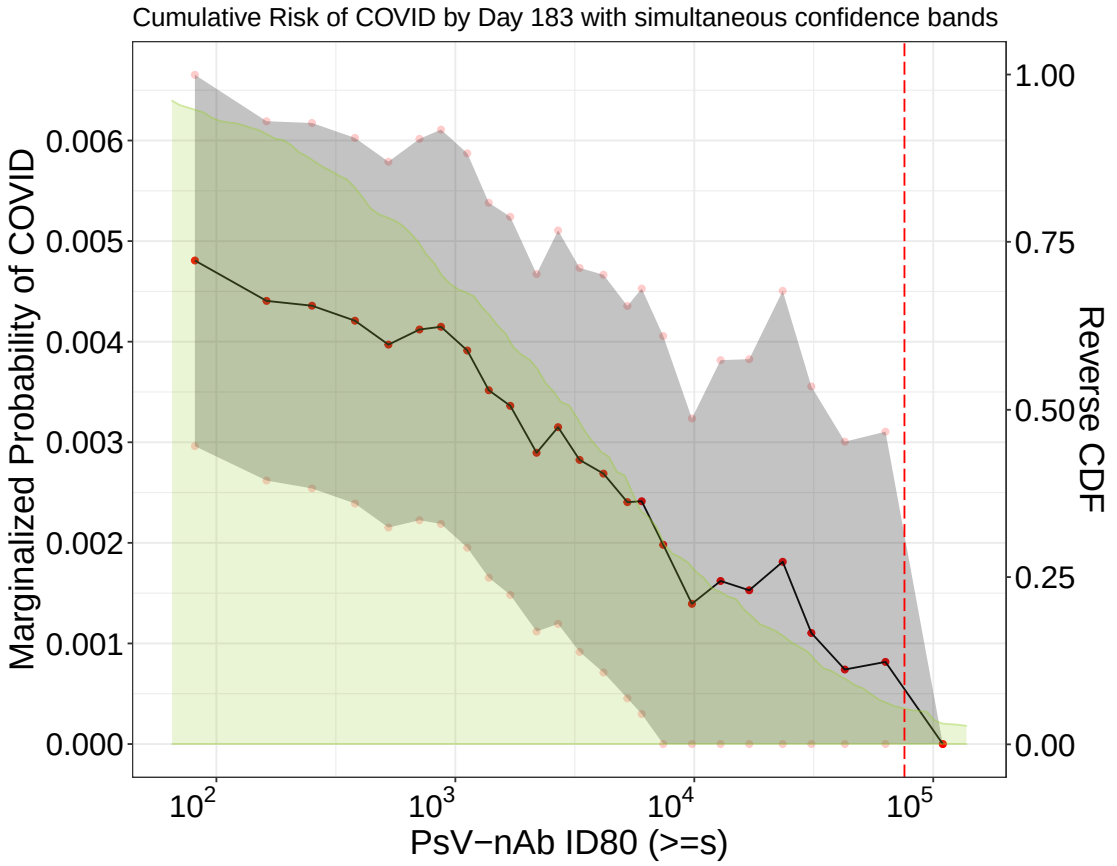

Figure 21: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.914	8.20*10^1	0.00481	0.00296	0.00665
2.579	3.79*10^2	0.00421	0.00239	0.00603
2.851	7.10*10^2	0.00412	0.00223	0.00602
3.142	1.39*10^3	0.00352	0.00165	0.00538
3.429	2.69*10^3	0.00315	0.00119	0.00511
3.619	4.16*10^3	0.00269	0.00071	0.00467
3.871	7.43*10^3	0.00198	0.00000	0.00406
4.234	1.71*10^4	0.00153	0.00000	0.00383
4.491	3.10*10^4	0.00110	0.00000	0.00355
5.039	1.09*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

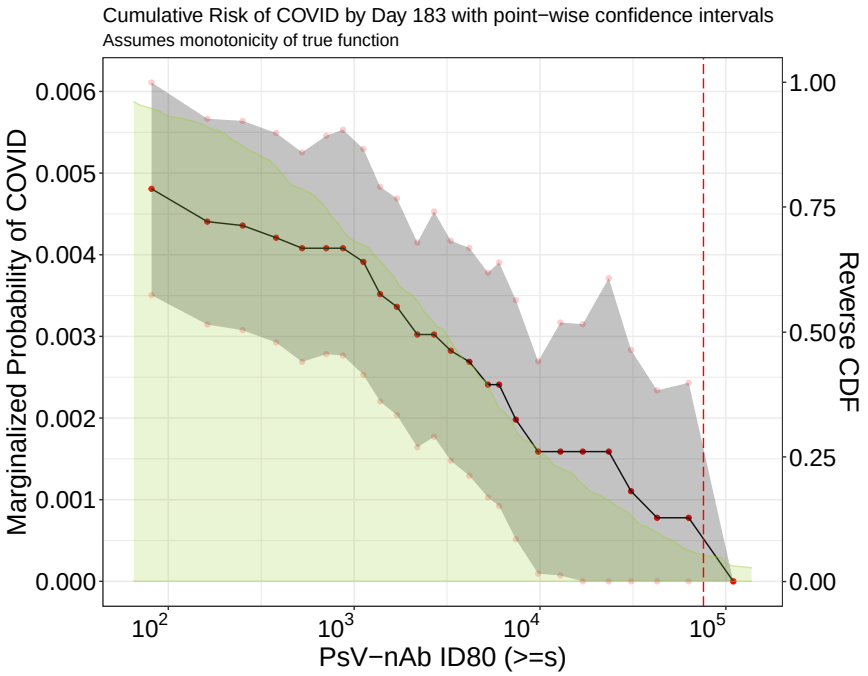

Figure 23: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed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

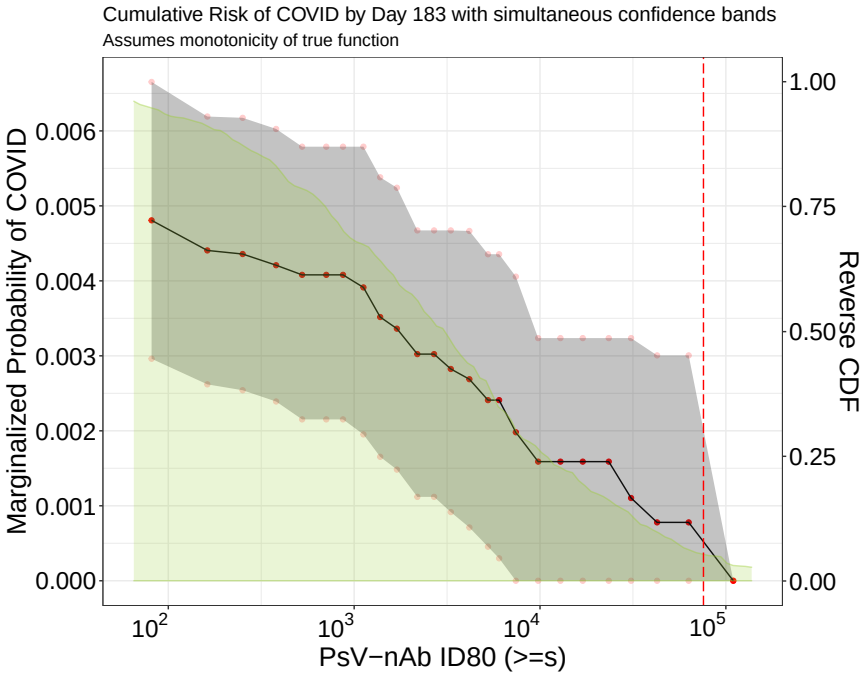

Figure 24: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence intervals. The dashed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

Day 29 Spike protein antibody

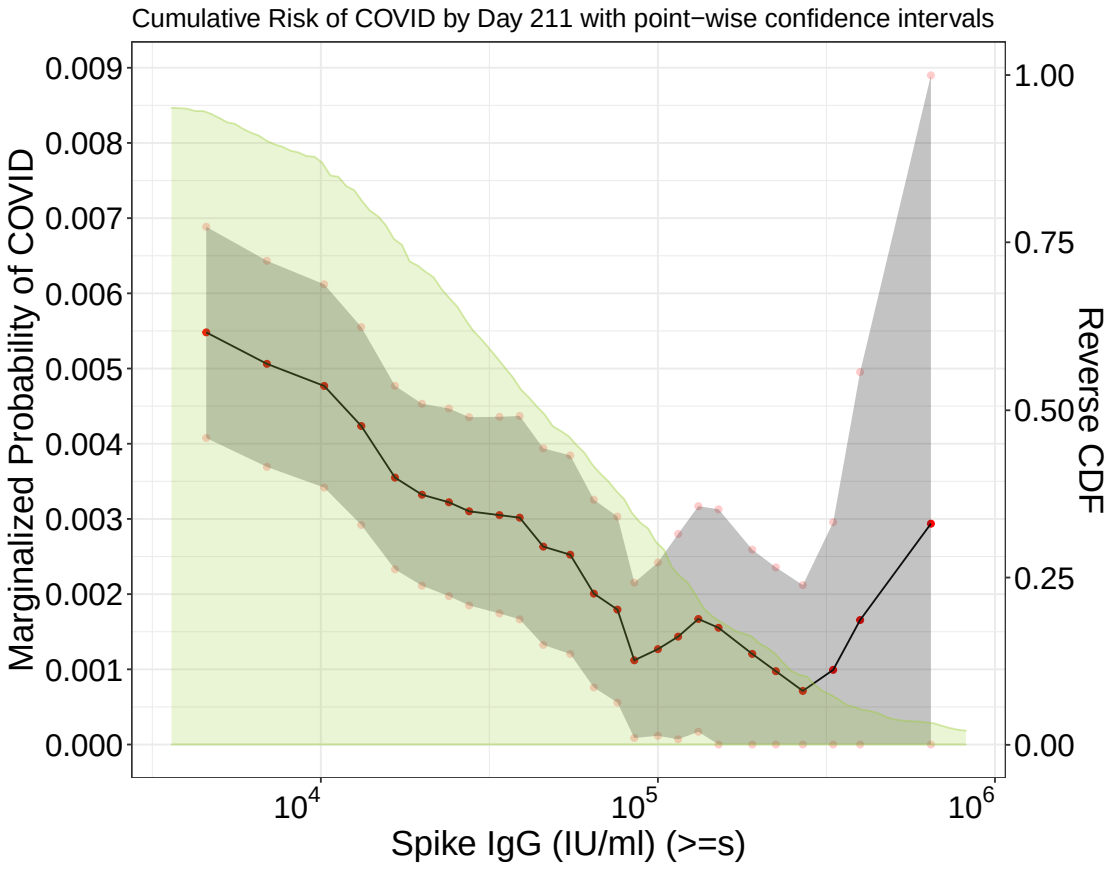

Figure 25: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
3.657	4.54*10^3	0.00548	0.00408	0.00689
4.124	1.33*10^4	0.00424	0.00292	0.00555
4.299	1.99*10^4	0.00332	0.00211	0.00453
4.526	3.36*10^4	0.00305	0.00174	0.00436
4.736	5.45*10^4	0.00252	0.00120	0.00384
4.880	7.59*10^4	0.00179	0.00056	0.00303
5.059	1.15*10^5	0.00143	0.00007	0.00280
5.278	1.90*10^5	0.00120	0.00000	0.00259
5.434	2.72*10^5	0.00071	0.00000	0.00212
5.814	6.52*10^5	0.00294	0.00000	0.00890

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

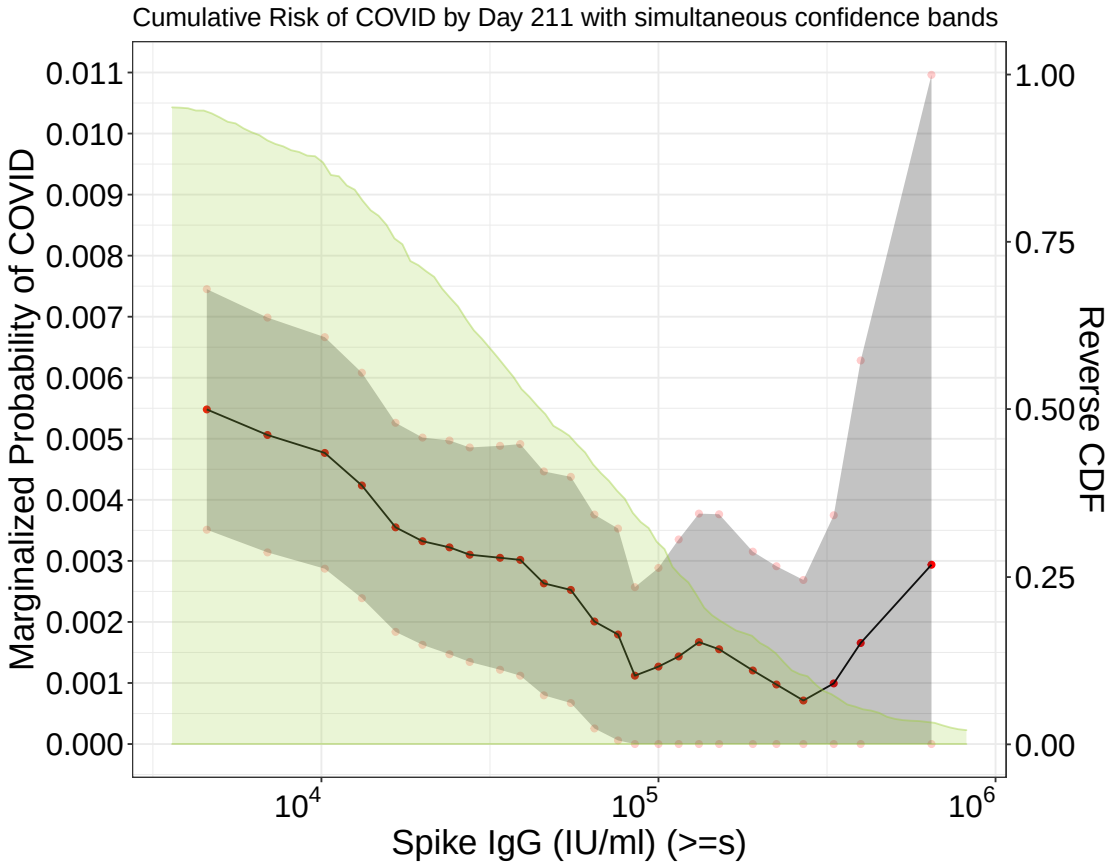

Figure 27: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
3.657	4.54*10^3	0.00548	0.00351	0.00745
4.124	1.33*10^4	0.00424	0.00239	0.00608
4.299	1.99*10^4	0.00332	0.00162	0.00502
4.526	3.36*10^4	0.00305	0.00122	0.00489
4.736	5.45*10^4	0.00252	0.00067	0.00438
4.880	7.59*10^4	0.00179	0.00006	0.00353
5.059	1.15*10^5	0.00143	0.00000	0.00335
5.278	1.90*10^5	0.00120	0.00000	0.00315
5.434	2.72*10^5	0.00071	0.00000	0.00269
5.814	6.52*10^5	0.00294	0.00000	0.01130

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

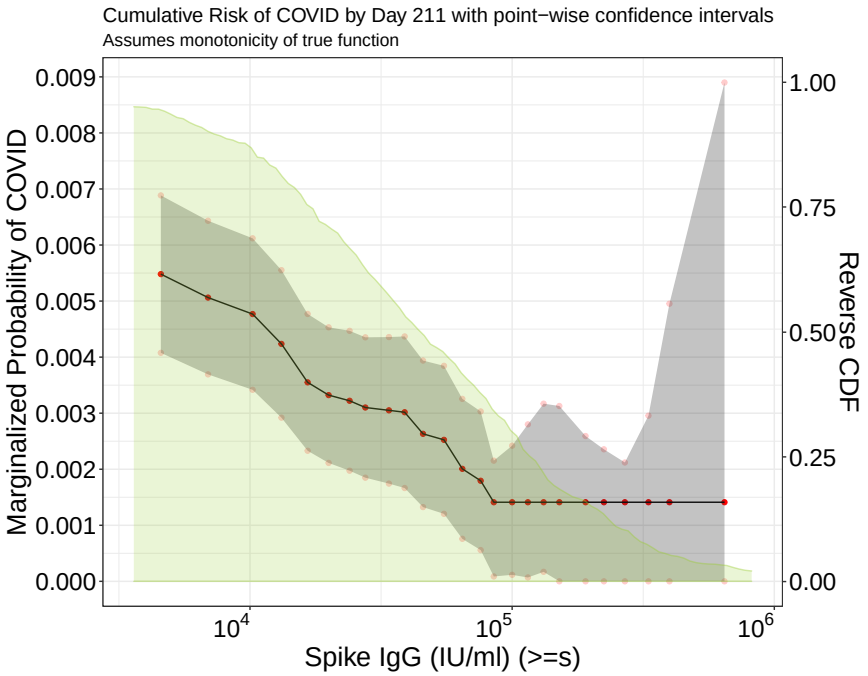

Figure 29: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

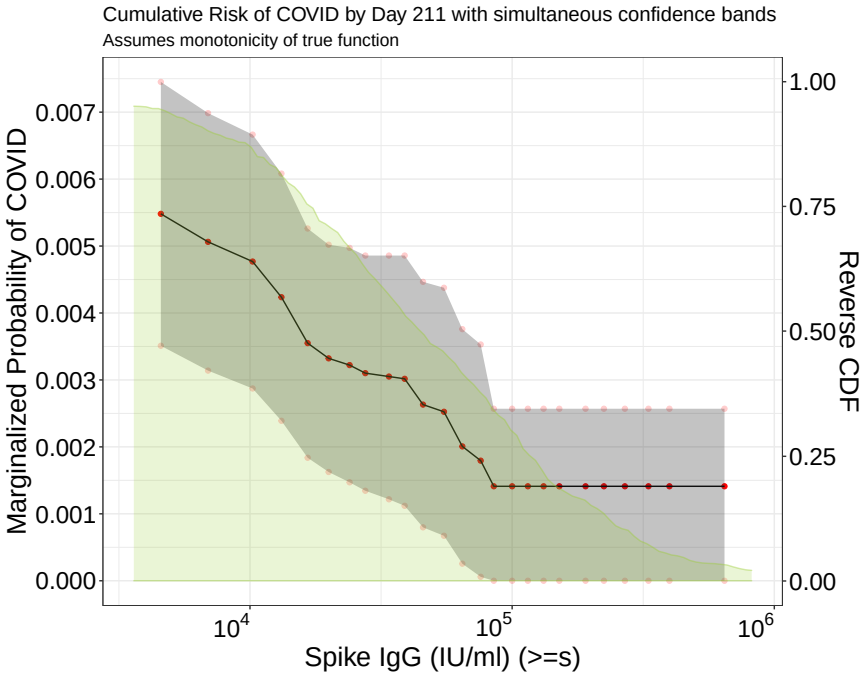

Figure 30: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

Day 29 RBD binding antibody

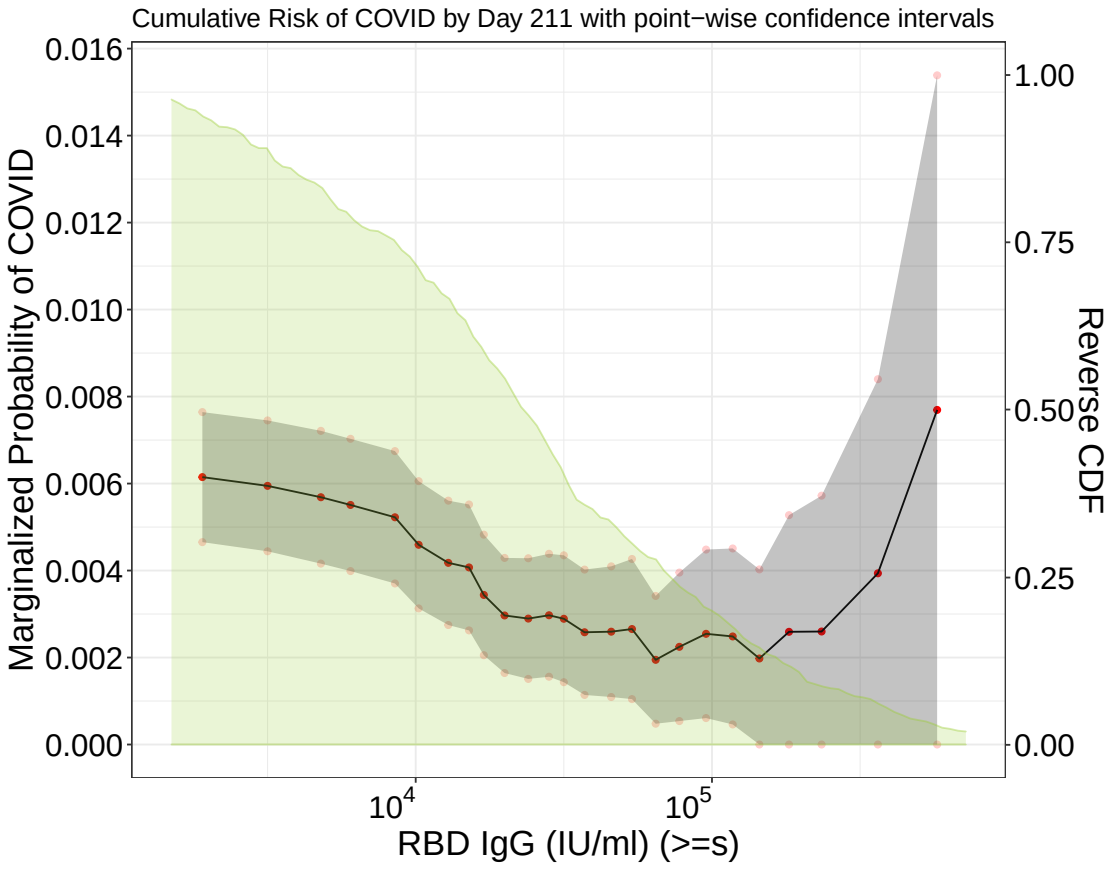

Figure 31: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
3.276	1.89*10^3	0.00615	0.00465	0.00764
3.779	6.01*10^3	0.00551	0.00399	0.00703
4.009	1.02*10^4	0.00459	0.00313	0.00605
4.235	1.72*10^4	0.00344	0.00205	0.00483
4.453	2.84*10^4	0.00297	0.00156	0.00439
4.568	3.70*10^4	0.00258	0.00114	0.00402
4.813	6.50*10^4	0.00195	0.00048	0.00342
5.067	1.17*10^5	0.00248	0.00046	0.00451
5.258	1.81*10^5	0.00259	0.00000	0.00527
5.757	5.71*10^5	0.00769	0.00000	0.01744

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

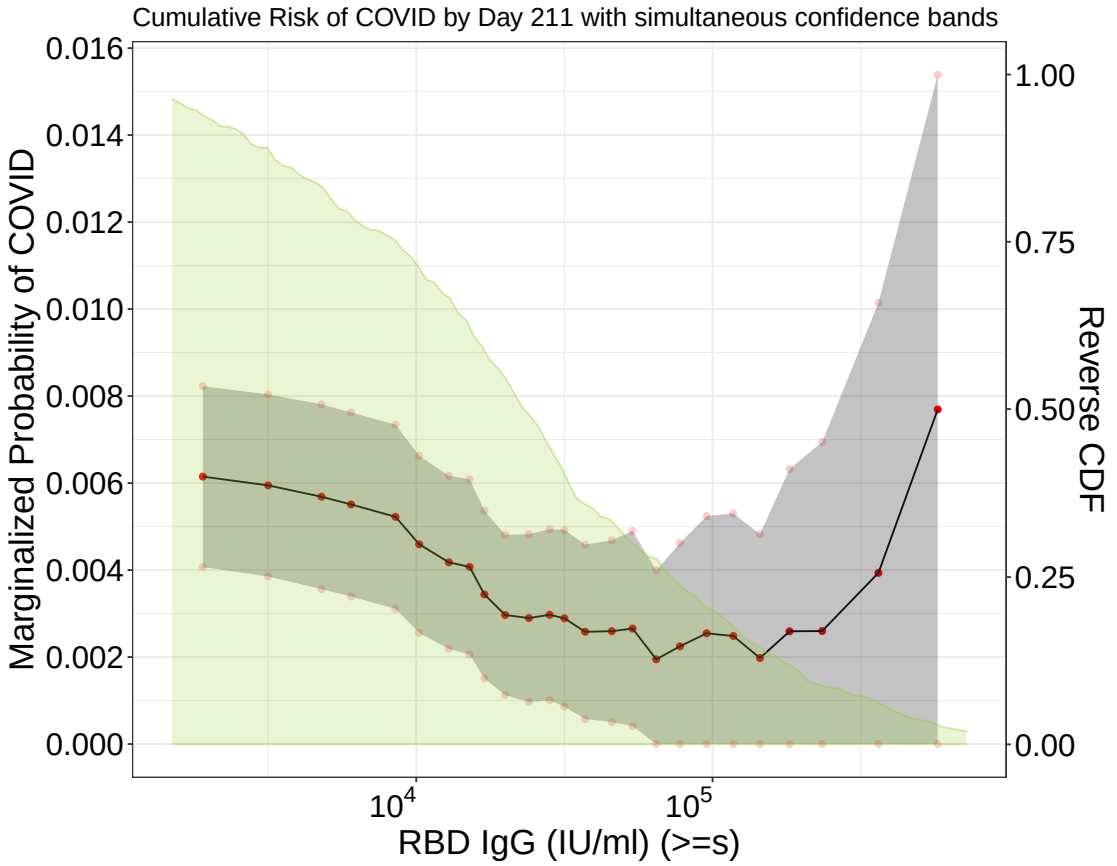

Figure 33: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
3.276	1.89*10^3	0.00615	0.00407	0.00823
3.779	6.01*10^3	0.00551	0.00339	0.00762
4.009	1.02*10^4	0.00459	0.00256	0.00663
4.235	1.72*10^4	0.00344	0.00151	0.00537
4.453	2.84*10^4	0.00297	0.00101	0.00494
4.568	3.70*10^4	0.00258	0.00058	0.00459
4.813	6.50*10^4	0.00195	0.00000	0.00399
5.067	1.17*10^5	0.00248	0.00000	0.00530
5.258	1.81*10^5	0.00259	0.00000	0.00632
5.757	5.71*10^5	0.00769	0.00000	0.02125

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

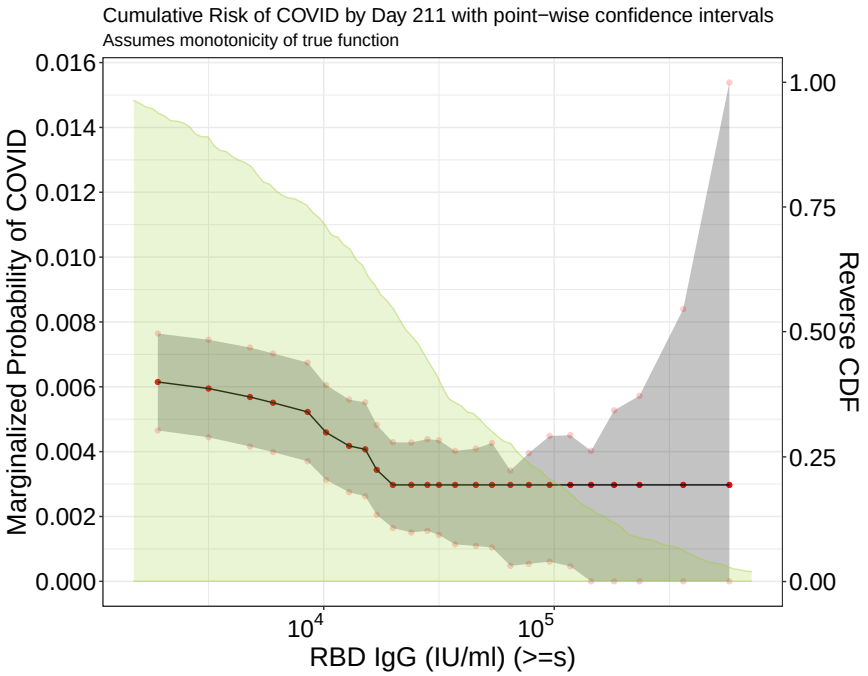

Figure 35: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

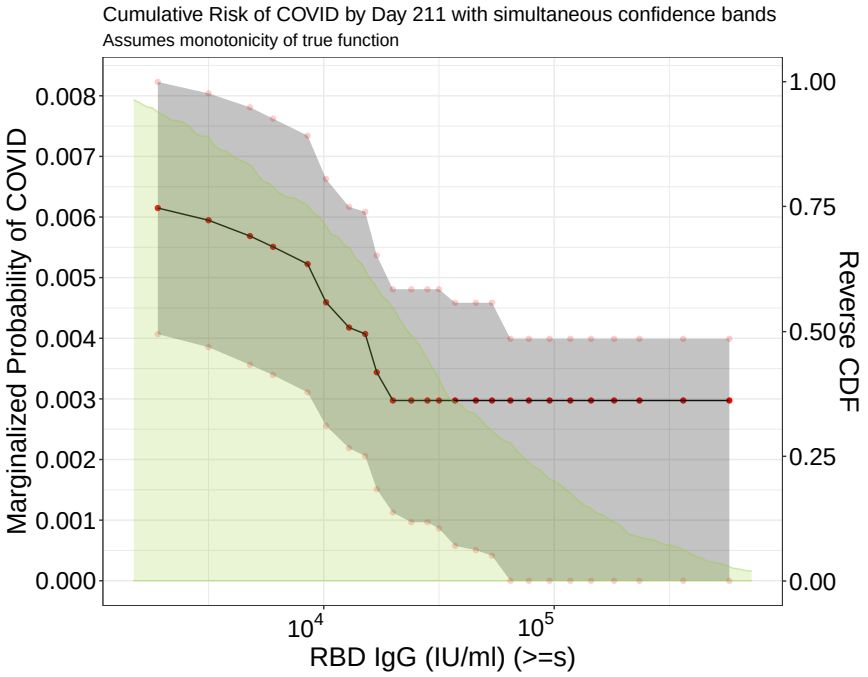

Figure 36: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

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

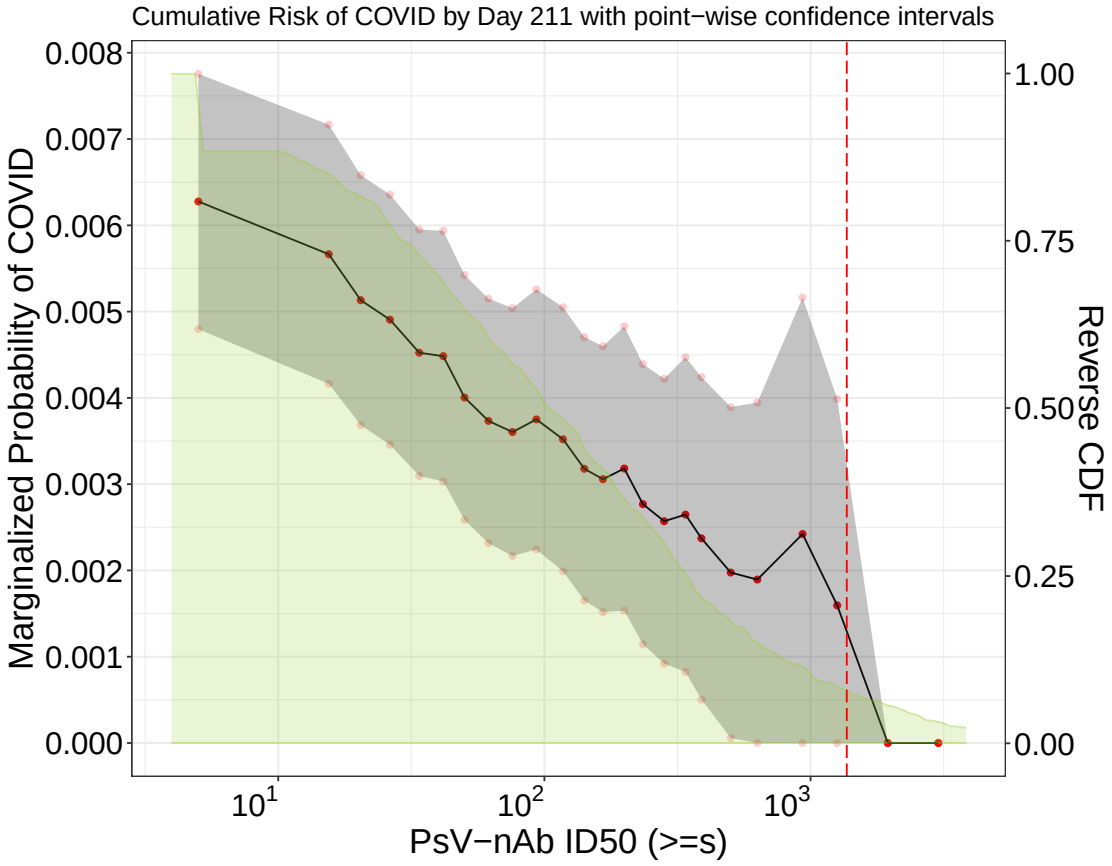

Figure 37: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00628	0.00480	0.00776
1.425	2.66*10^1	0.00491	0.00346	0.00636
1.618	4.15*10^1	0.00448	0.00303	0.00594
1.882	7.62*10^1	0.00360	0.00217	0.00504
2.070	1.17*10^2	0.00352	0.00199	0.00505
2.296	1.98*10^2	0.00318	0.00153	0.00483
2.447	2.80*10^2	0.00257	0.00092	0.00422
2.703	5.05*10^2	0.00198	0.00006	0.00389
2.965	9.23*10^2	0.00242	0.00000	0.00516
3.483	3.04*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.

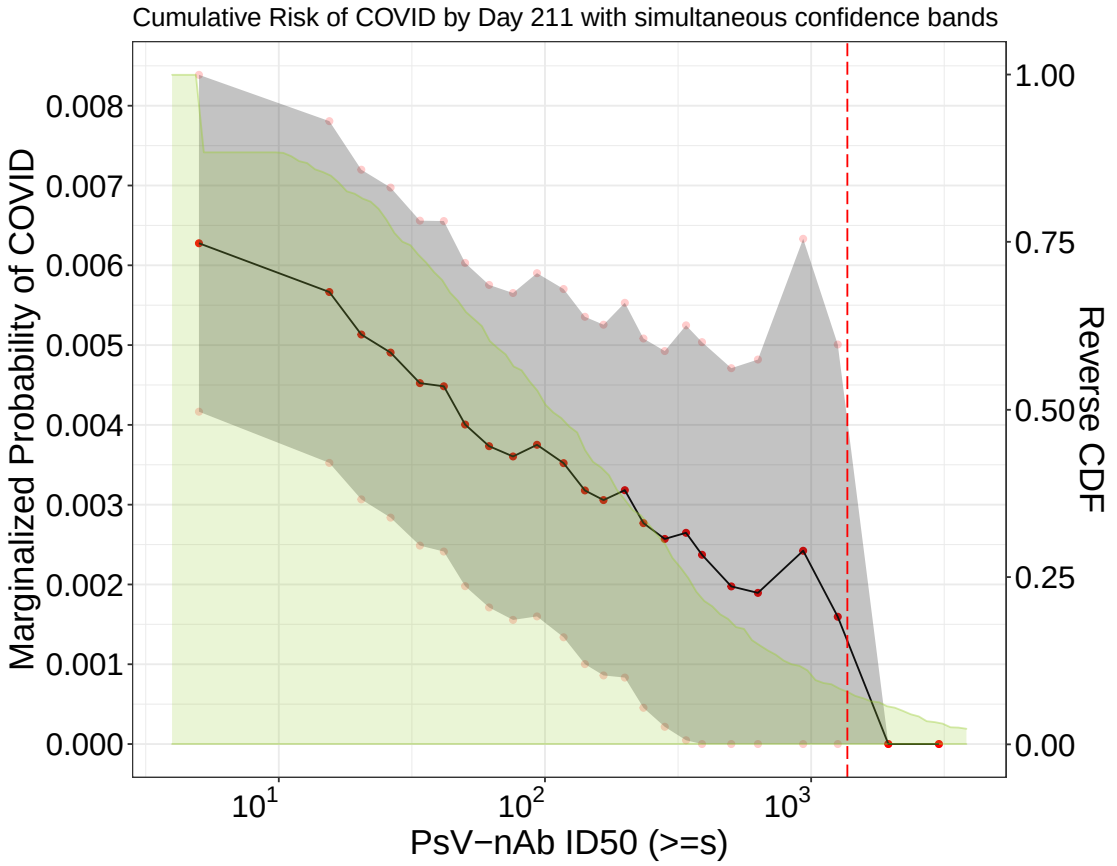

Figure 39: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00628	0.00417	0.00839
1.425	2.66*10^1	0.00491	0.00284	0.00697
1.618	4.15*10^1	0.00448	0.00241	0.00655
1.882	7.62*10^1	0.00360	0.00156	0.00565
2.070	1.17*10^2	0.00352	0.00134	0.00570
2.296	1.98*10^2	0.00318	0.00083	0.00553
2.447	2.80*10^2	0.00257	0.00022	0.00493
2.703	5.05*10^2	0.00198	0.00000	0.00471
2.965	9.23*10^2	0.00242	0.00000	0.00633
3.483	3.04*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

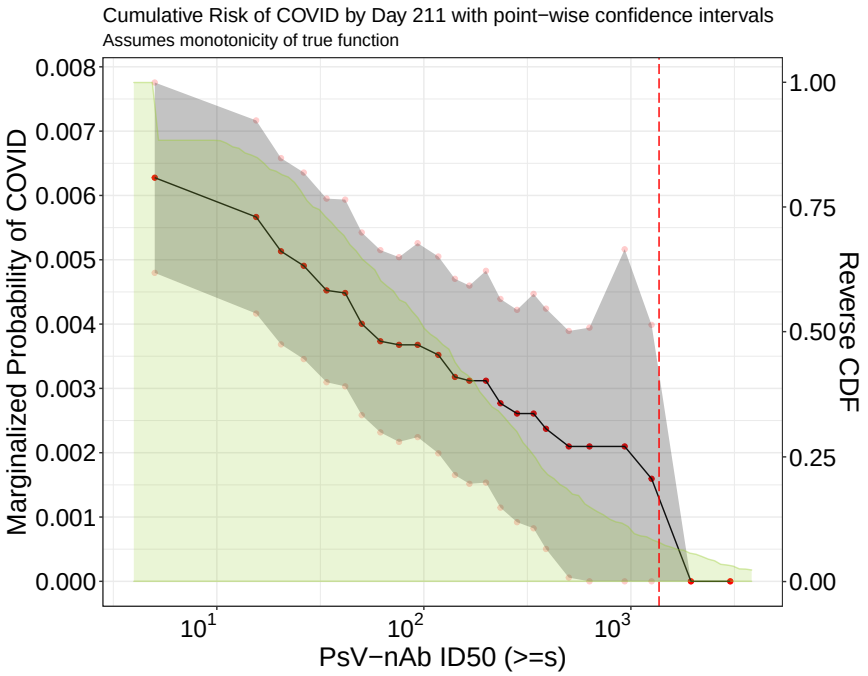

Figure 41: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed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

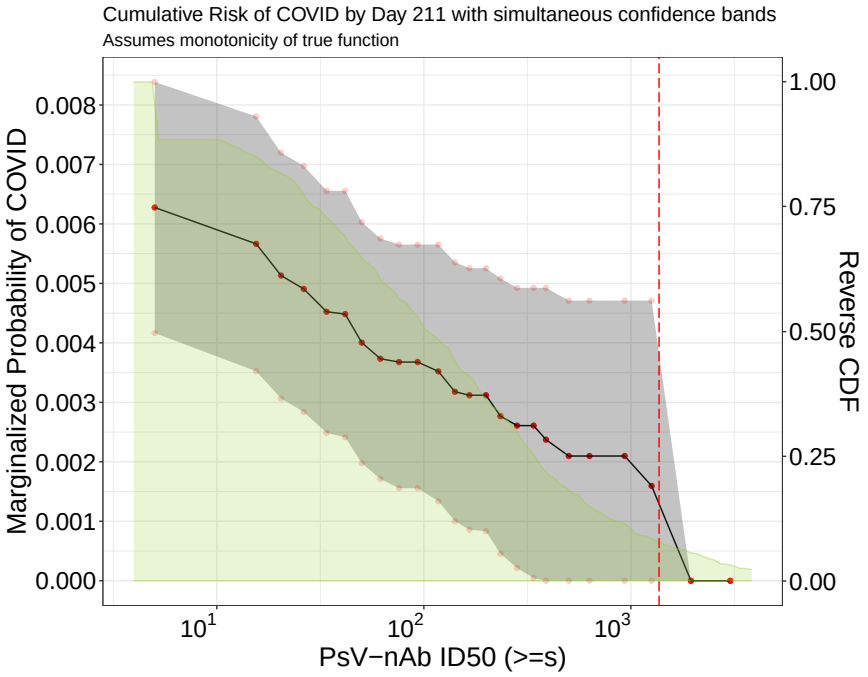

Figure 42: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence intervals. The dashed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

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

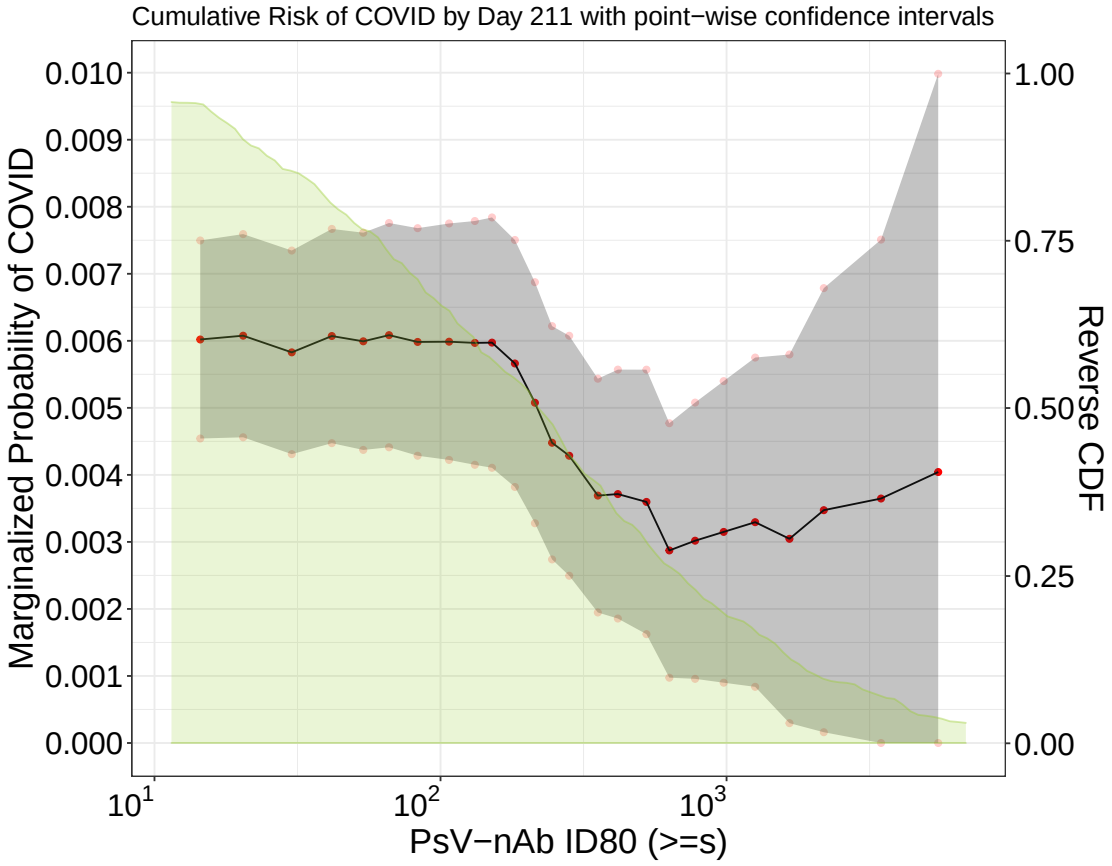

Figure 43: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.159	1.44*10^1	0.00602	0.00454	0.00750
1.620	4.17*10^1	0.00607	0.00447	0.00767
1.825	6.68*10^1	0.00608	0.00441	0.00776
2.118	1.31*10^2	0.00597	0.00415	0.00779
2.332	2.15*10^2	0.00508	0.00328	0.00687
2.451	2.82*10^2	0.00429	0.00250	0.00608
2.716	5.20*10^2	0.00360	0.00162	0.00557
2.987	9.71*10^2	0.00315	0.00090	0.00540
3.217	1.65*10^3	0.00305	0.00030	0.00580
3.737	5.46*10^3	0.00404	0.00000	0.00998

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.

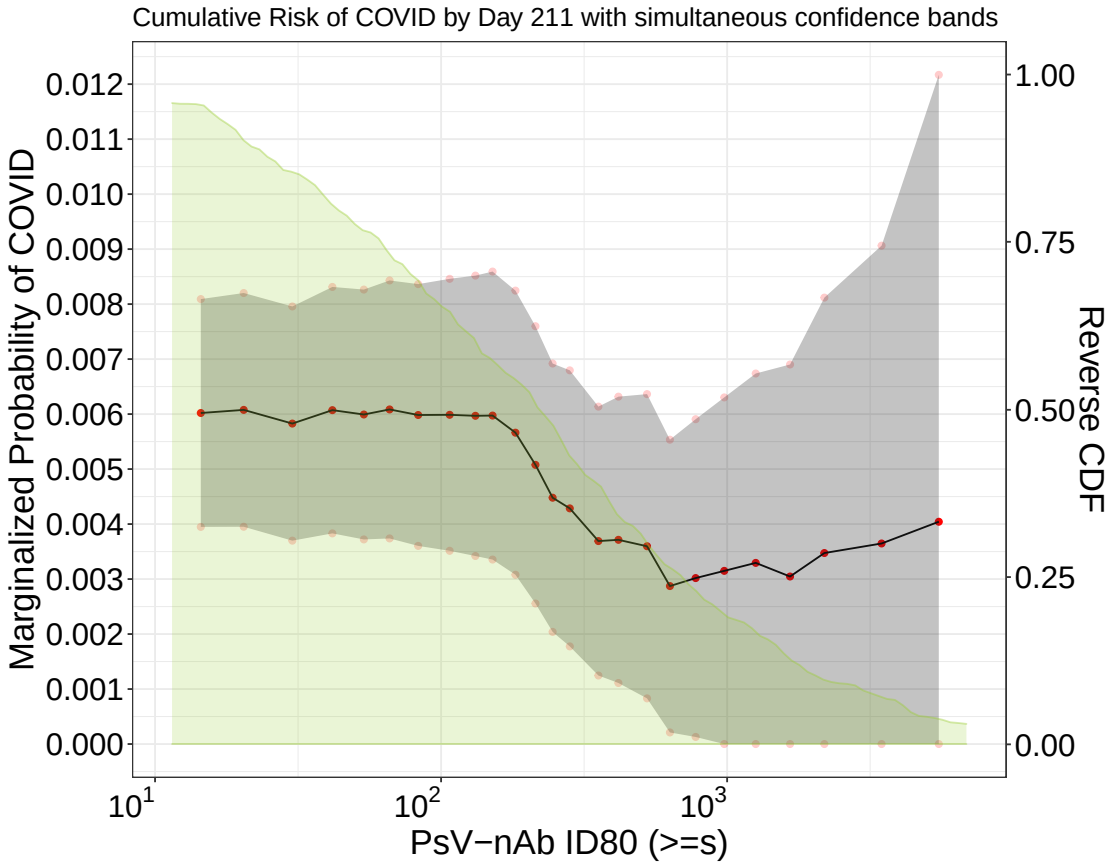

Figure 45: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.159	1.44*10^1	0.00602	0.00395	0.00809
1.620	4.17*10^1	0.00607	0.00383	0.00831
1.825	6.68*10^1	0.00608	0.00374	0.00843
2.118	1.31*10^2	0.00597	0.00342	0.00852
2.332	2.15*10^2	0.00508	0.00256	0.00760
2.451	2.82*10^2	0.00429	0.00178	0.00680
2.716	5.20*10^2	0.00360	0.00083	0.00636
2.987	9.71*10^2	0.00315	0.00000	0.00630
3.217	1.65*10^3	0.00305	0.00000	0.00690
3.737	5.46*10^3	0.00404	0.00000	0.01237

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

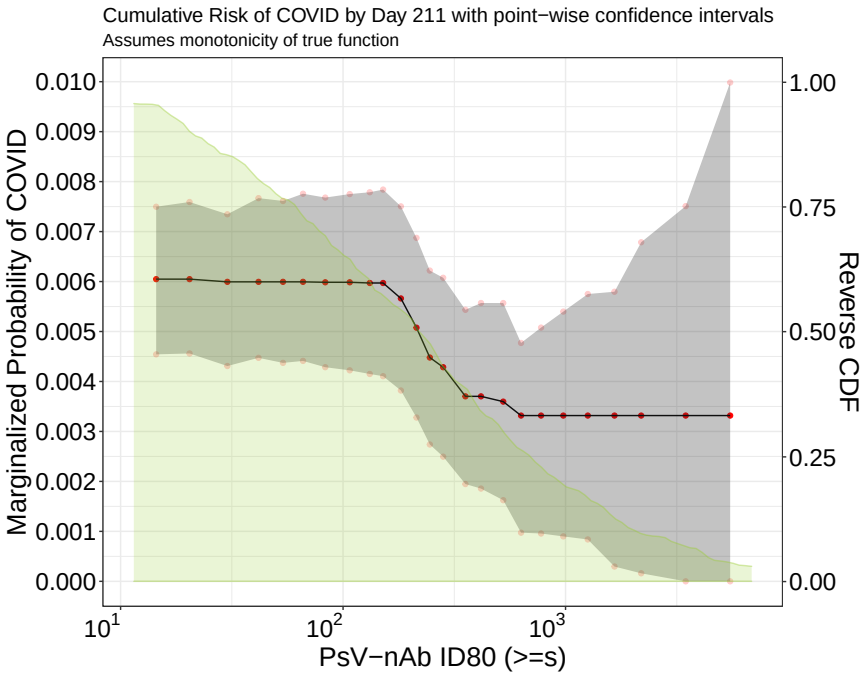

Figure 47: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed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

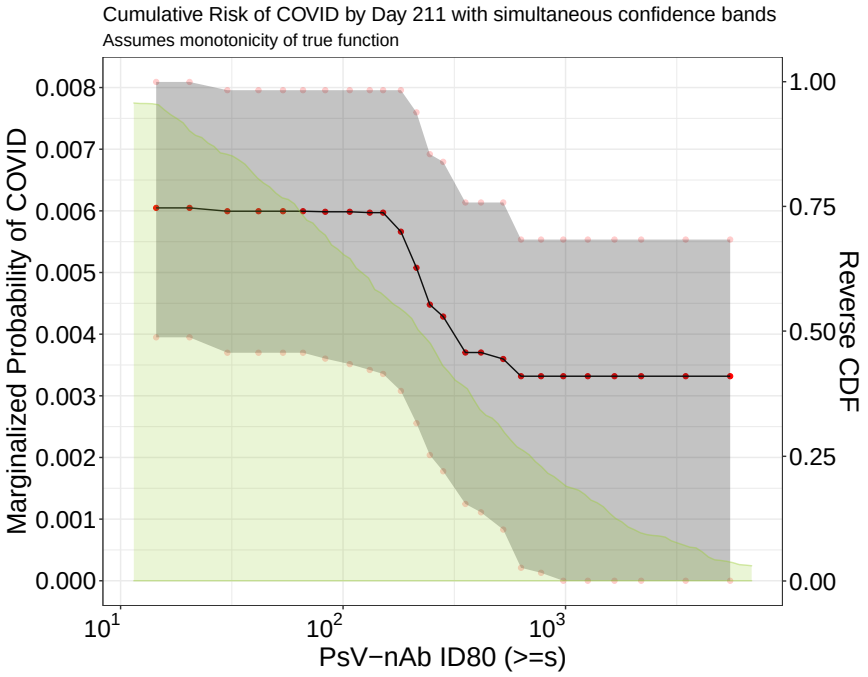

Figure 48: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence intervals. The dashed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