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.

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

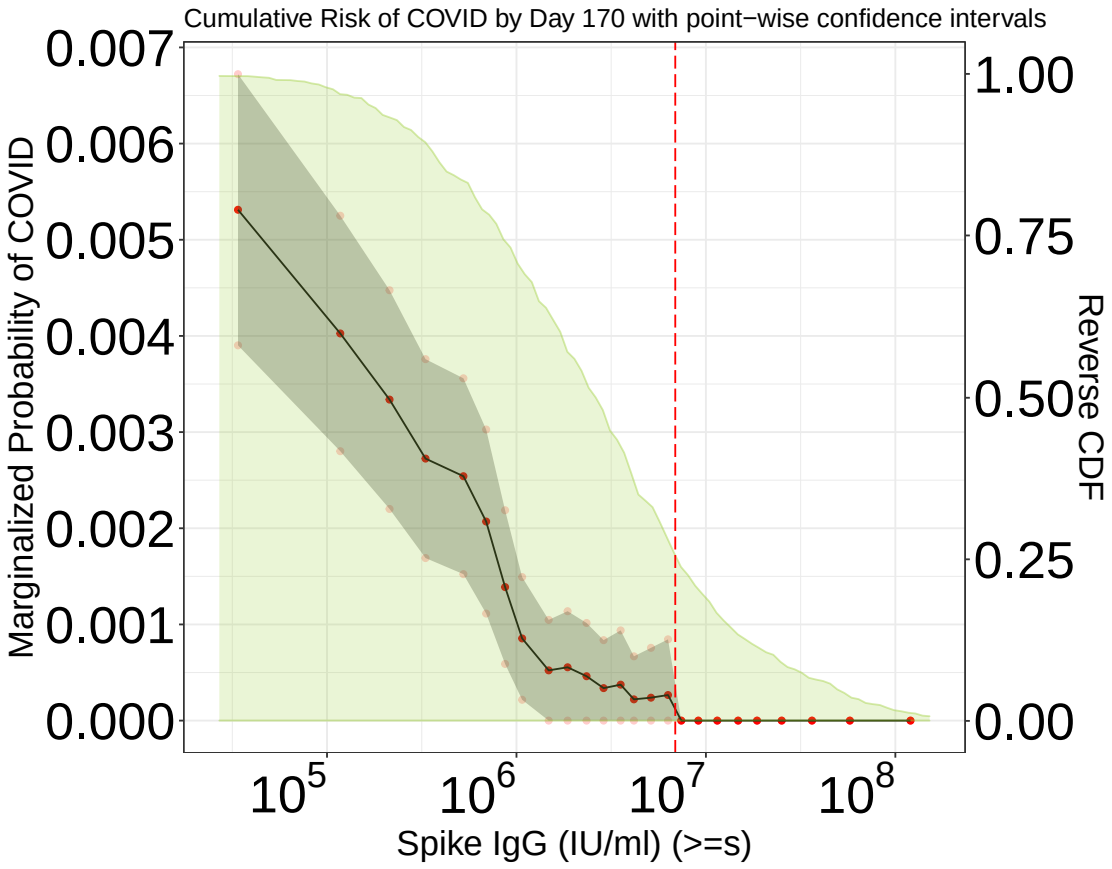

Figure 1: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.531	3.40*10^4	0.00531	0.00390	0.00672
5.524	3.34*10^5	0.00272	0.00169	0.00376
5.836	6.85*10^5	0.00207	0.00111	0.00303
6.169	1.48*10^6	0.00052	0.00000	0.00105
6.462	2.90*10^6	0.00034	0.00000	0.00084
6.621	4.18*10^6	0.00022	0.00000	0.00067
6.870	7.41*10^6	0.00000	0.00000	1.00000
7.166	1.47*10^7	0.00000	0.00000	1.00000
7.402	2.52*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 Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals.

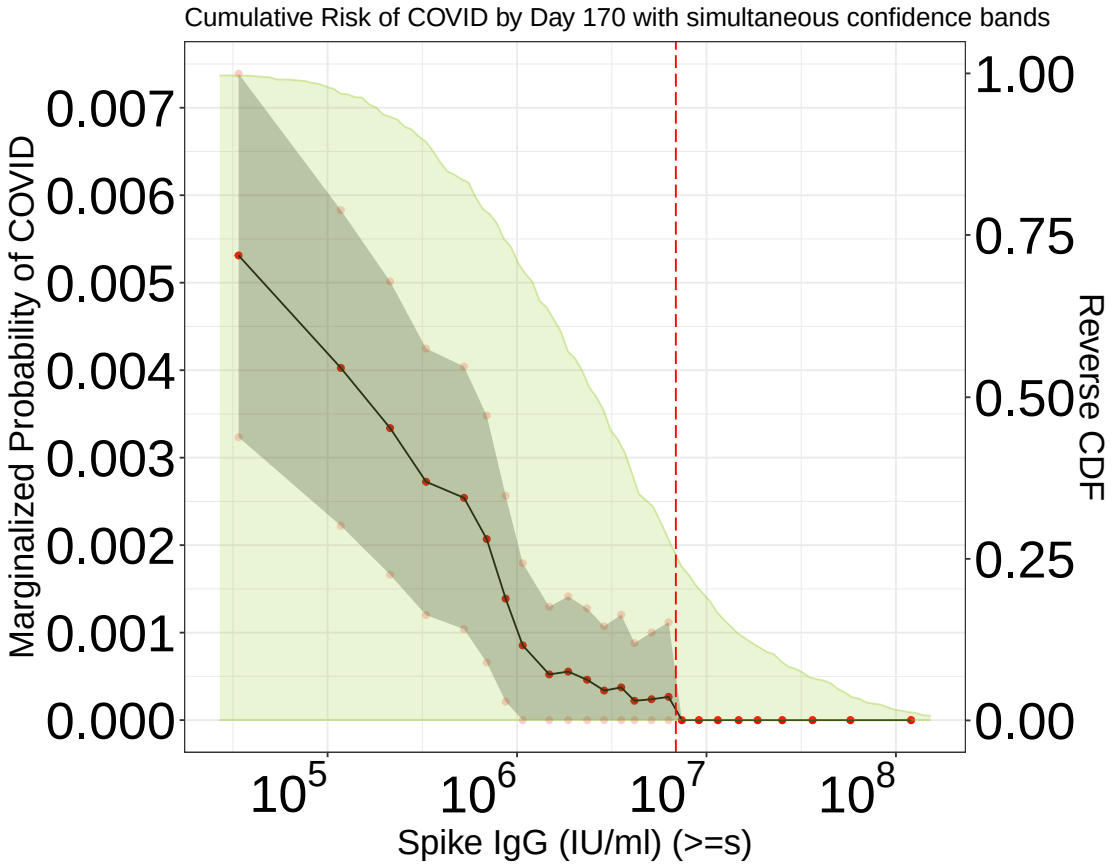

Figure 3: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.531	3.40*10^4	0.00531	0.00323	0.00739
5.524	3.34*10^5	0.00272	0.00120	0.00425
5.836	6.85*10^5	0.00207	0.00066	0.00348
6.169	1.48*10^6	0.00052	0.00000	0.00130
6.462	2.90*10^6	0.00034	0.00000	0.00107
6.621	4.18*10^6	0.00022	0.00000	0.00088
6.870	7.41*10^6	0.00000	0.00000	1.00000
7.166	1.47*10^7	0.00000	0.00000	1.00000
7.402	2.52*10^7	0.00000	0.00000	1.00000
8.081	1.21*10^8	0.00000	0.00000	1.00000

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

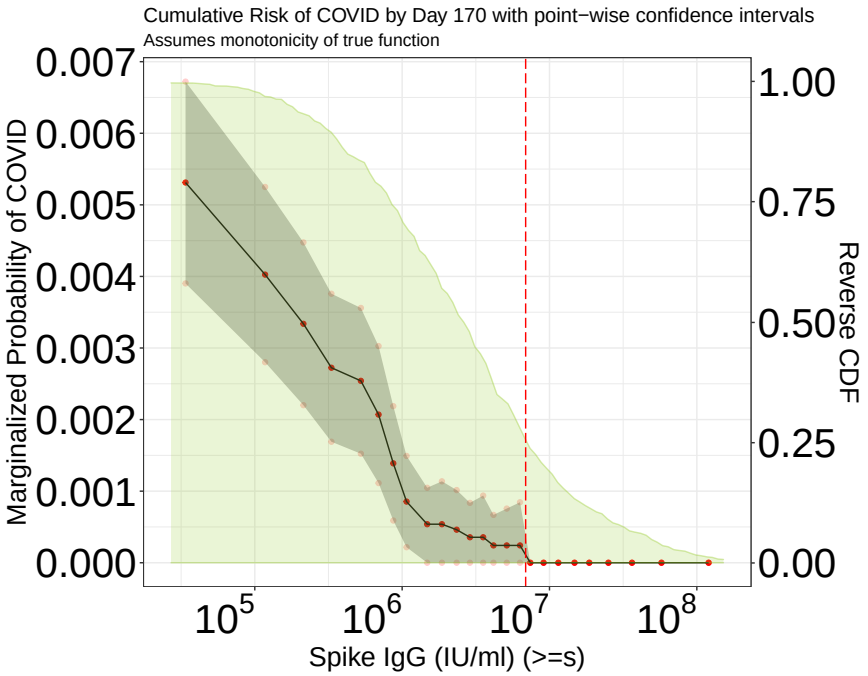

Figure 5: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

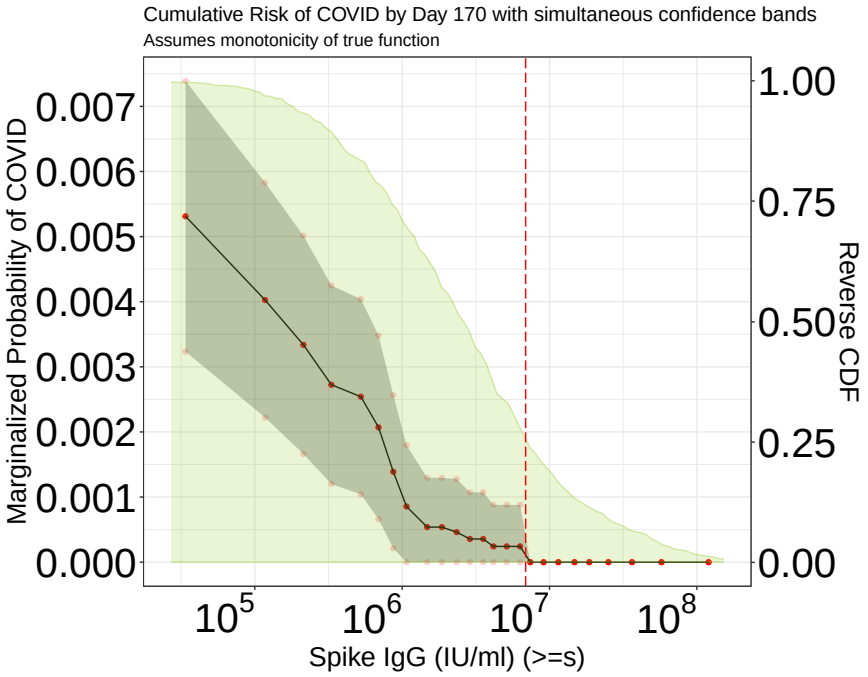

Figure 6: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

Day 57 RBD binding antibody

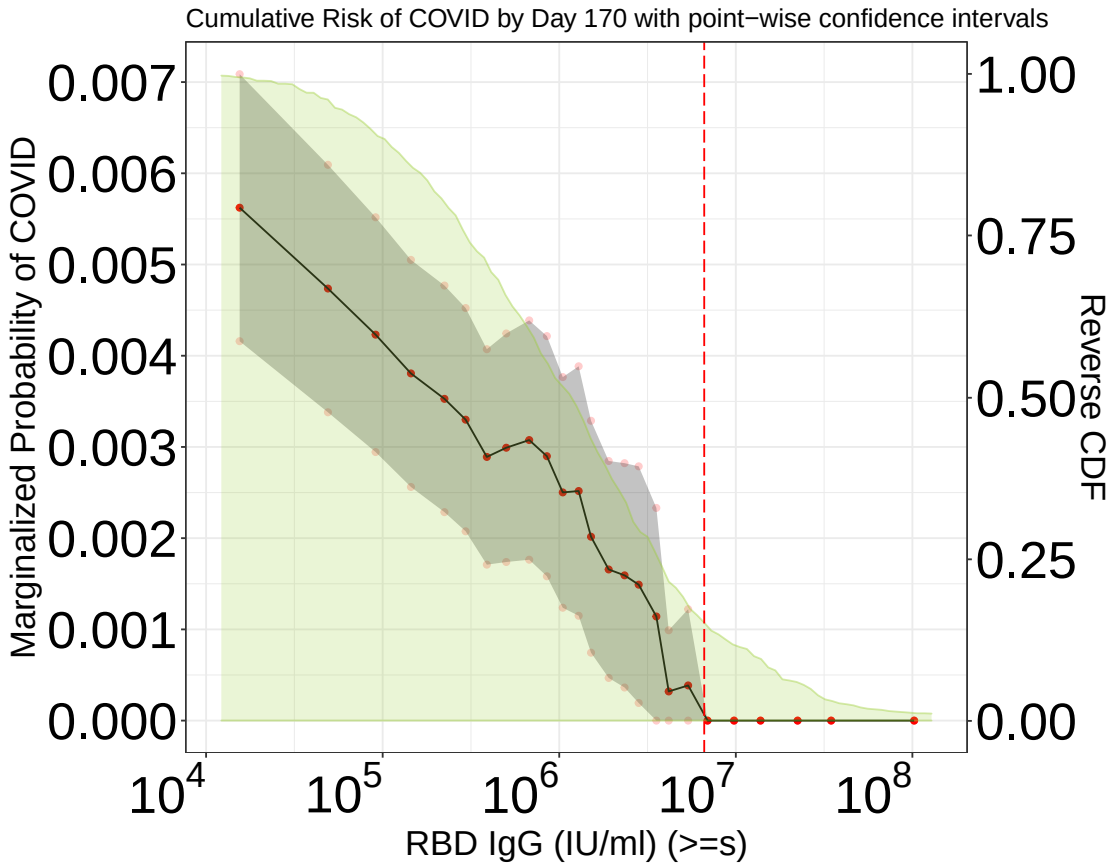

Figure 7: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.186	1.53*10^4	0.00562	0.00416	0.00709
5.165	1.46*10^5	0.00381	0.00256	0.00505
5.466	2.92*10^5	0.00330	0.00208	0.00452
5.828	6.73*10^5	0.00308	0.00176	0.00439
6.110	1.29*10^6	0.00252	0.00115	0.00388
6.276	1.89*10^6	0.00166	0.00047	0.00285
6.549	3.54*10^6	0.00114	0.00000	0.00233
6.837	6.87*10^6	0.00000	0.00000	1.00000
7.144	1.39*10^7	0.00000	0.00000	1.00000
8.009	1.02*10^8	0.00000	0.00000	1.00000

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

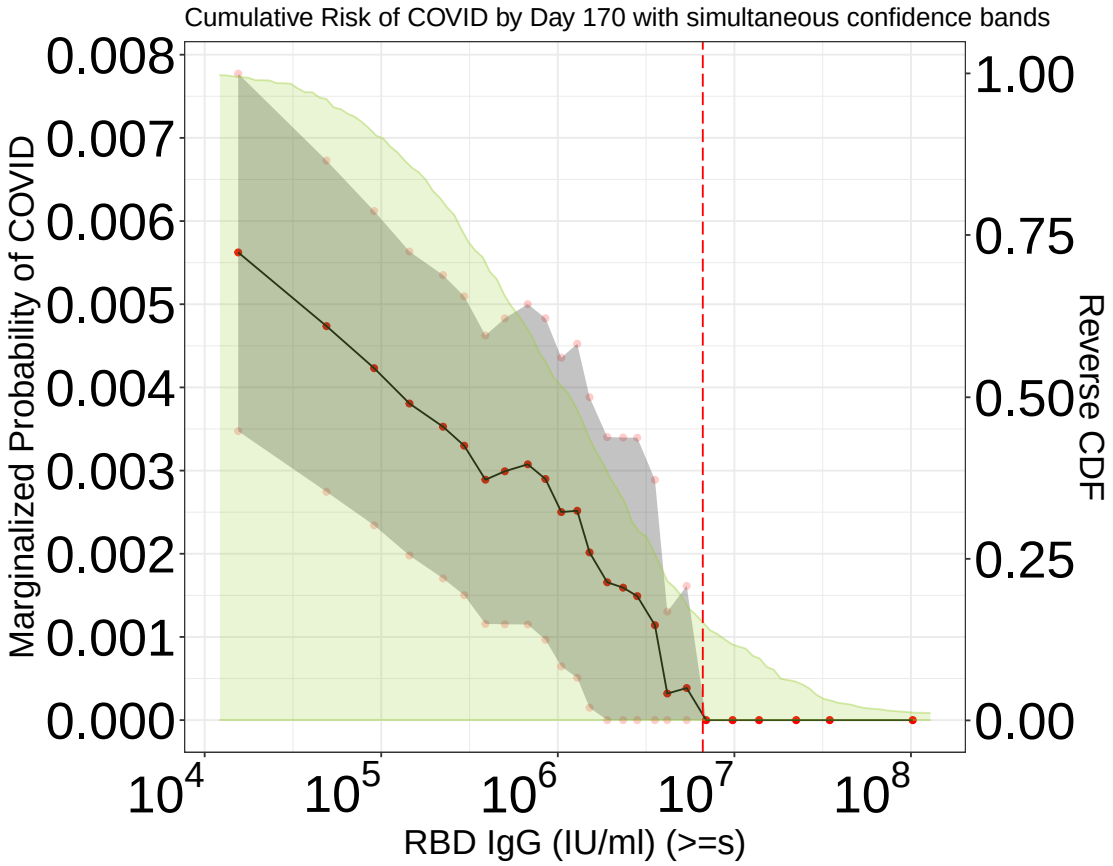

Figure 9: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
4.186	1.53*10^4	0.00562	0.00347	0.00777
5.165	1.46*10^5	0.00381	0.00198	0.00563
5.466	2.92*10^5	0.00330	0.00150	0.00510
5.828	6.73*10^5	0.00308	0.00115	0.00500
6.110	1.29*10^6	0.00252	0.00051	0.00452
6.276	1.89*10^6	0.00166	0.00000	0.00340
6.549	3.54*10^6	0.00114	0.00000	0.00289
6.837	6.87*10^6	0.00000	0.00000	1.00000
7.144	1.39*10^7	0.00000	0.00000	1.00000
8.009	1.02*10^8	0.00000	0.00000	1.00000

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

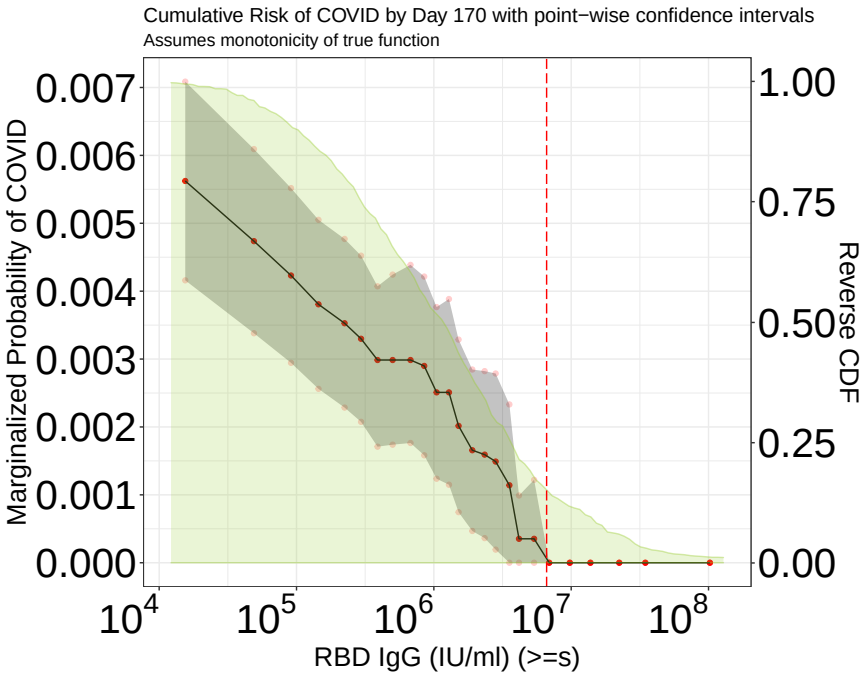

Figure 11: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

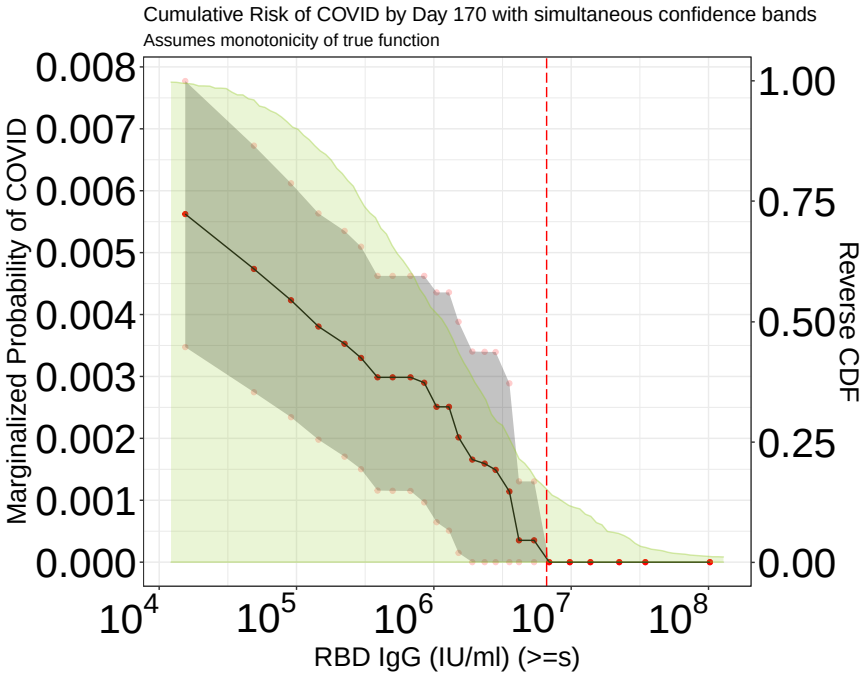

Figure 12: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

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

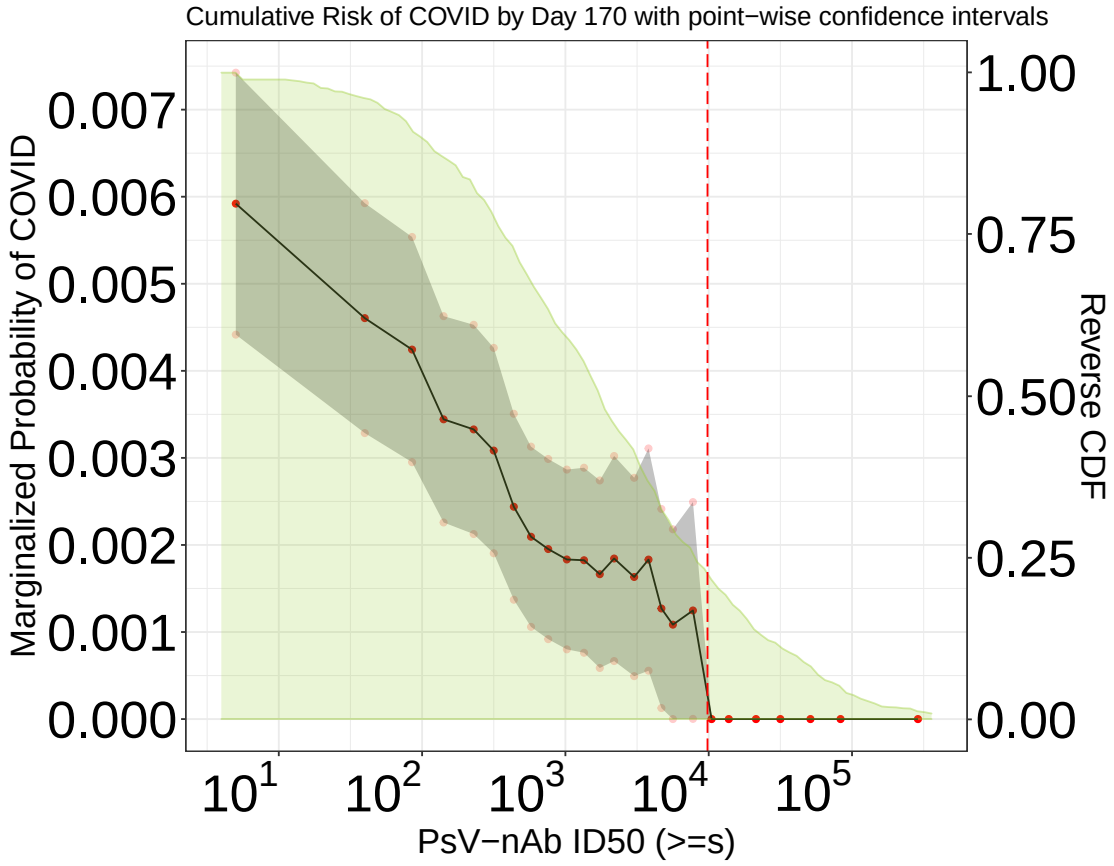

Figure 13: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00592	0.00442	0.00742
2.148	1.41*10^2	0.00344	0.00226	0.00463
2.495	3.13*10^2	0.00308	0.00190	0.00426
2.878	7.55*10^2	0.00195	0.00092	0.00299
3.239	1.73*10^3	0.00166	0.00059	0.00274
3.479	3.01*10^3	0.00163	0.00049	0.00277
3.753	5.66*10^3	0.00108	0.00000	0.00218
4.144	1.39*10^4	0.00000	0.00000	1.00000
4.501	3.17*10^4	0.00000	0.00000	1.00000
5.455	2.85*10^5	0.00000	0.00000	1.00000

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.

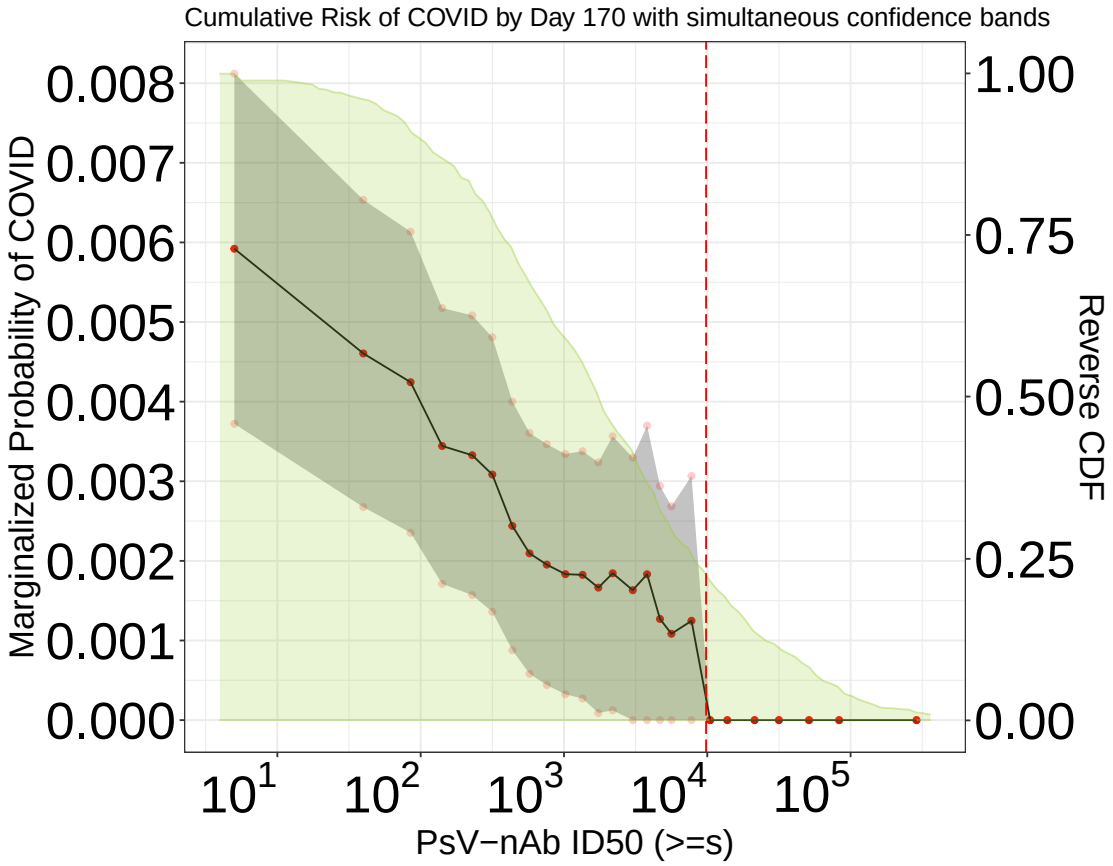

Figure 15: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00592	0.00372	0.00812
2.148	1.41*10^2	0.00344	0.00171	0.00517
2.495	3.13*10^2	0.00308	0.00136	0.00481
2.878	7.55*10^2	0.00195	0.00044	0.00347
3.239	1.73*10^3	0.00166	0.00009	0.00324
3.479	3.01*10^3	0.00163	0.00000	0.00330
3.753	5.66*10^3	0.00108	0.00000	0.00269
4.144	1.39*10^4	0.00000	0.00000	1.00000
4.501	3.17*10^4	0.00000	0.00000	1.00000
5.455	2.85*10^5	0.00000	0.00000	1.00000

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

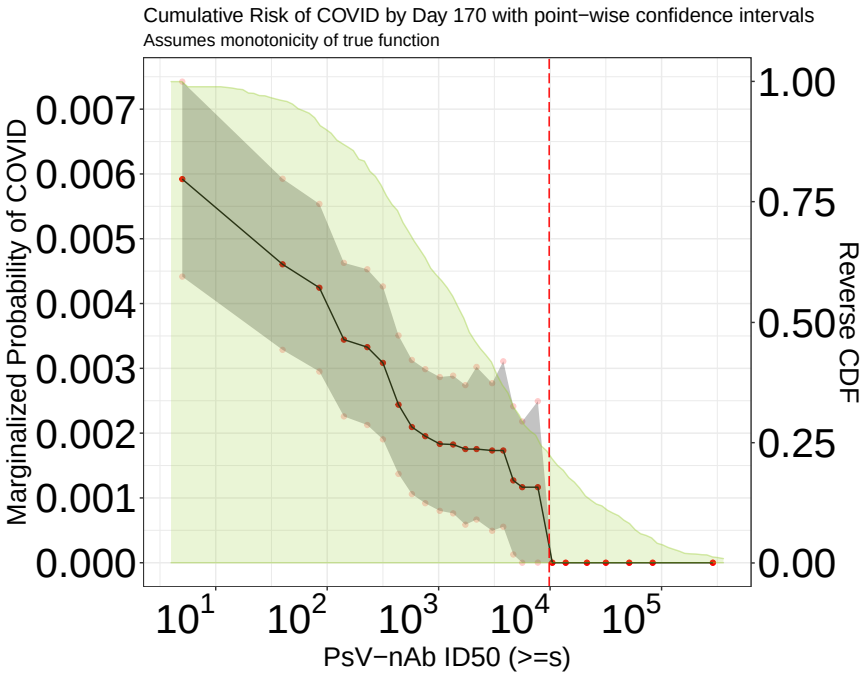

Figure 17: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed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

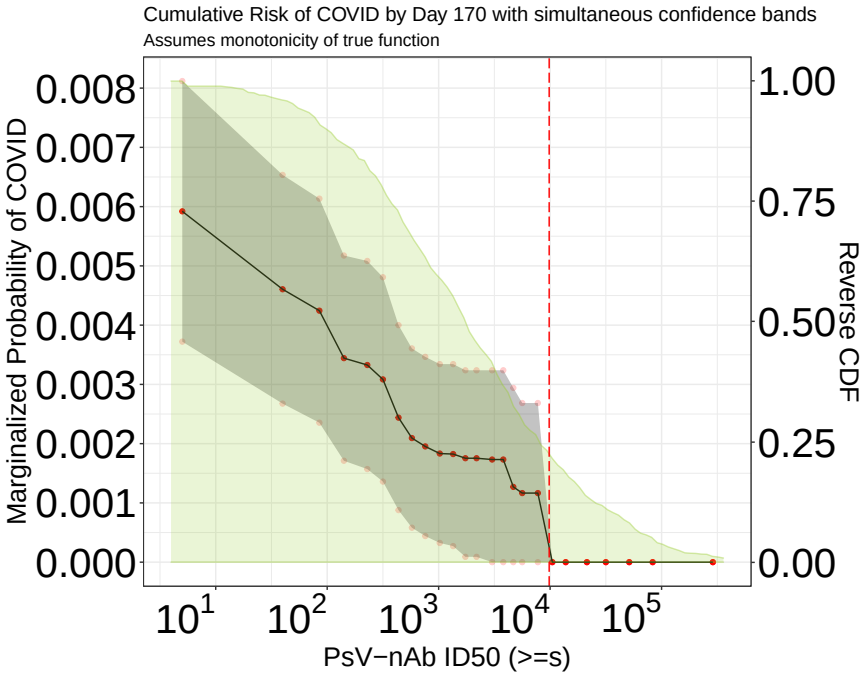

Figure 18: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence intervals. The dashed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

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

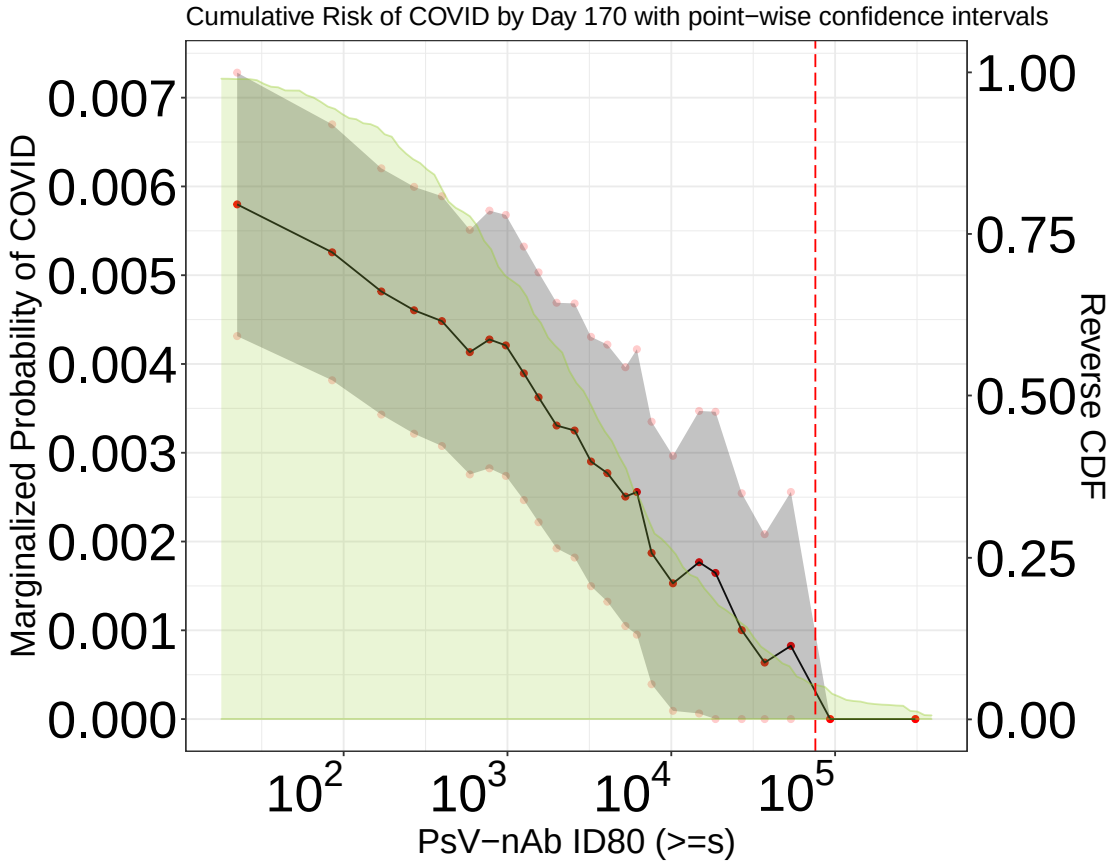

Figure 19: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.353	2.25*10^1	0.00580	0.00431	0.00728
2.430	2.69*10^2	0.00460	0.00321	0.00600
2.766	5.83*10^2	0.00413	0.00276	0.00551
3.104	1.27*10^3	0.00389	0.00247	0.00532
3.410	2.57*10^3	0.00325	0.00182	0.00468
3.611	4.08*10^3	0.00277	0.00132	0.00422
3.883	7.64*10^3	0.00187	0.00039	0.00335
4.266	1.85*10^4	0.00165	0.00000	0.00346
4.567	3.69*10^4	0.00064	0.00000	0.00208
5.489	3.08*10^5	0.00000	0.00000	1.00000

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.

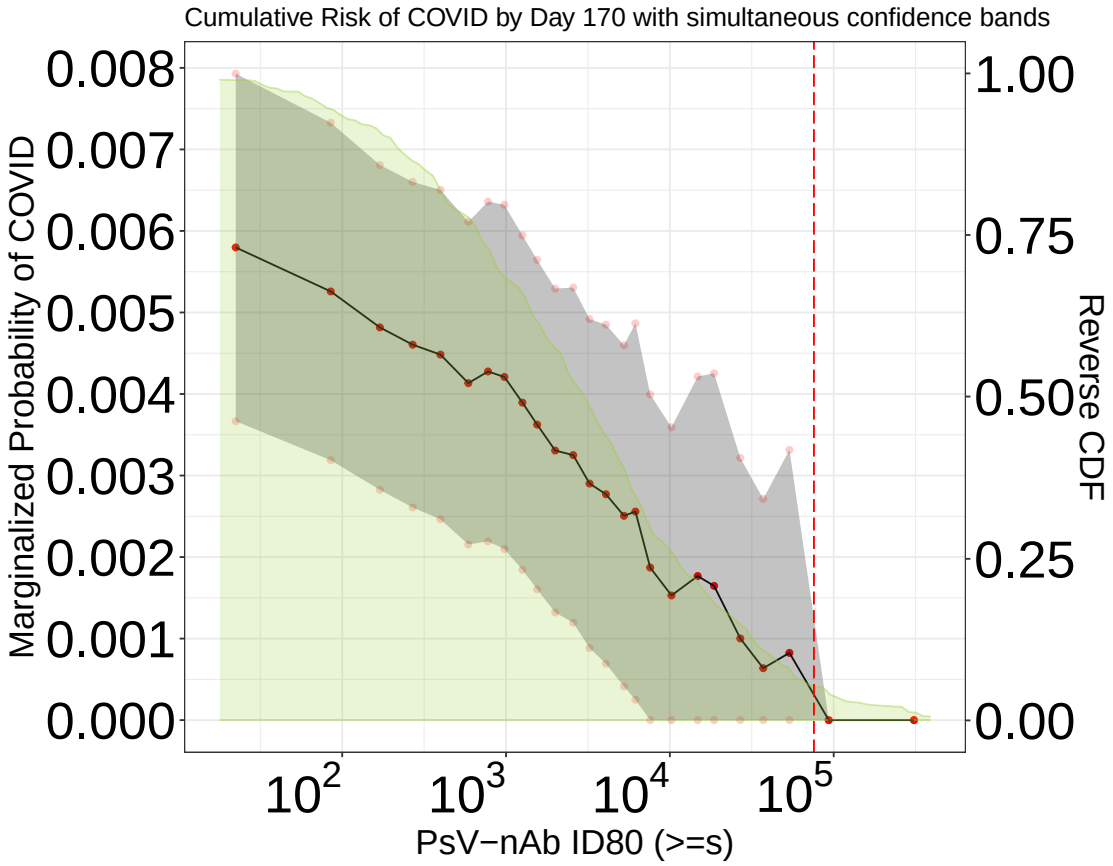

Figure 21: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.353	2.25*10^1	0.00580	0.00367	0.00793
2.430	2.69*10^2	0.00460	0.00261	0.00660
2.766	5.83*10^2	0.00413	0.00215	0.00611
3.104	1.27*10^3	0.00389	0.00184	0.00595
3.410	2.57*10^3	0.00325	0.00120	0.00531
3.611	4.08*10^3	0.00277	0.00069	0.00485
3.883	7.64*10^3	0.00187	0.00000	0.00399
4.266	1.85*10^4	0.00165	0.00000	0.00425
4.567	3.69*10^4	0.00064	0.00000	0.00271
5.489	3.08*10^5	0.00000	0.00000	1.00000

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

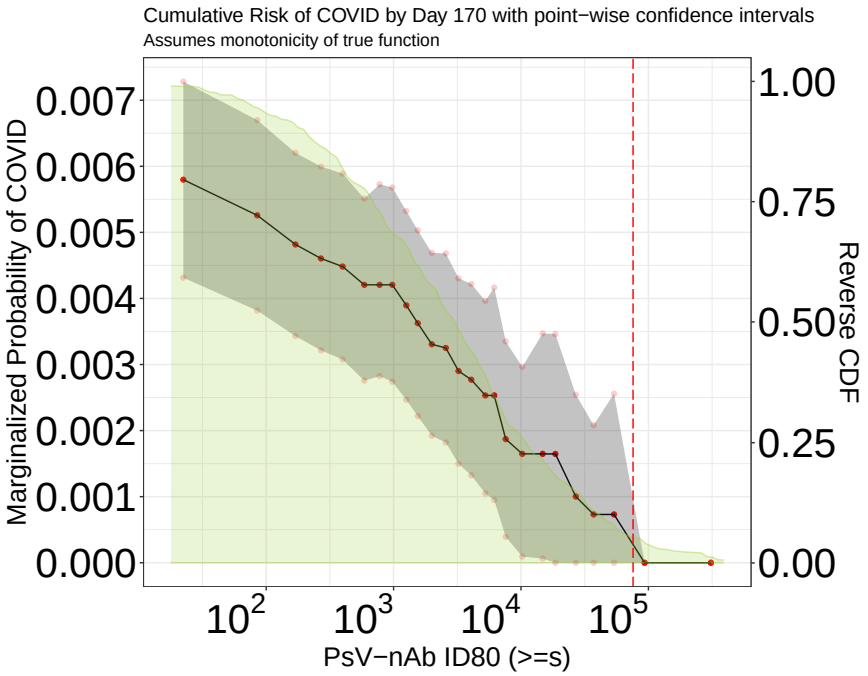

Figure 23: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed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

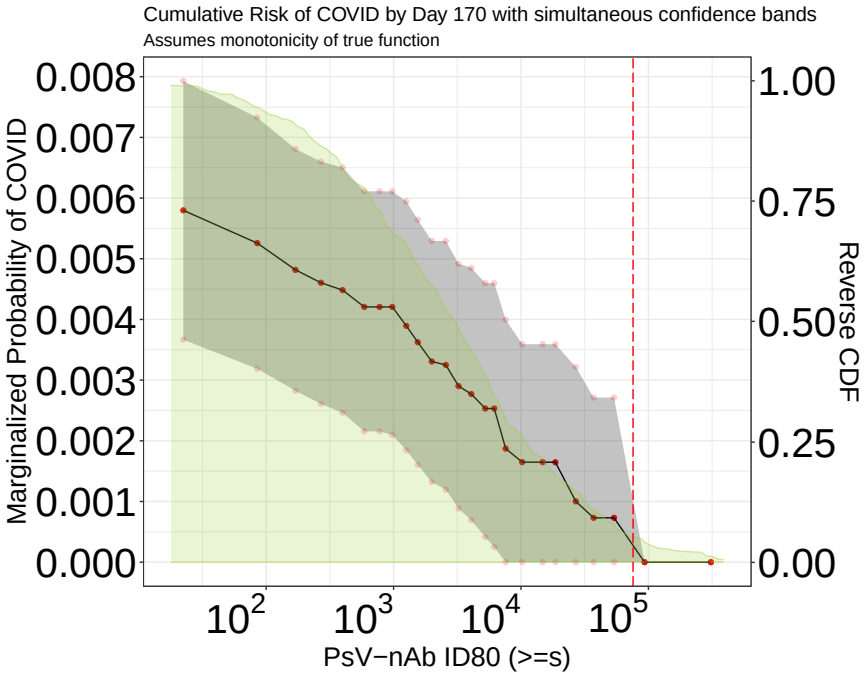

Figure 24: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence intervals. The dashed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

Day 29 Spike protein antibody

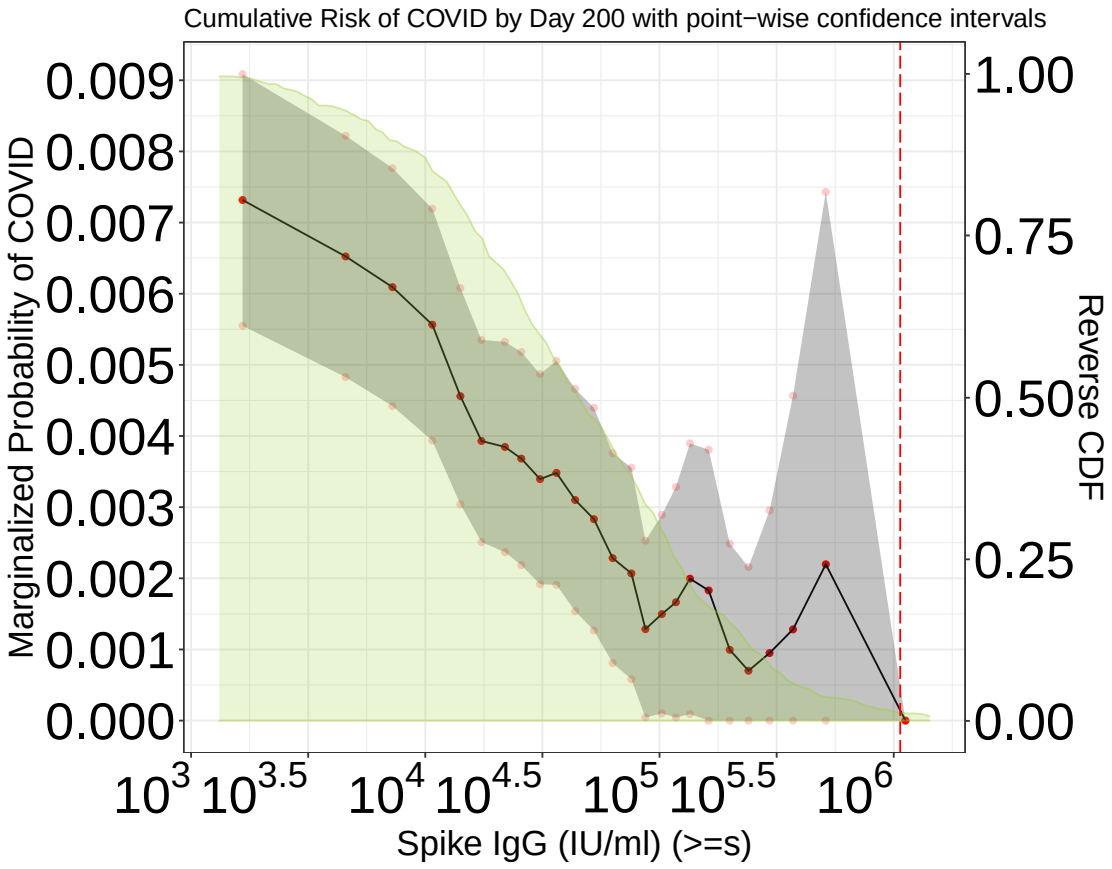

Figure 25: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
3.221	1.66*10^3	0.00732	0.00555	0.00909
4.026	1.06*10^4	0.00556	0.00393	0.00719
4.243	1.75*10^4	0.00393	0.00251	0.00535
4.487	3.07*10^4	0.00339	0.00192	0.00487
4.717	5.21*10^4	0.00283	0.00127	0.00440
4.875	7.50*10^4	0.00207	0.00058	0.00356
5.069	1.17*10^5	0.00166	0.00004	0.00328
5.303	2.01*10^5	0.00099	0.00000	0.00249
5.473	2.97*10^5	0.00095	0.00000	0.00295
6.053	1.13*10^6	0.00000	0.00000	1.00000

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

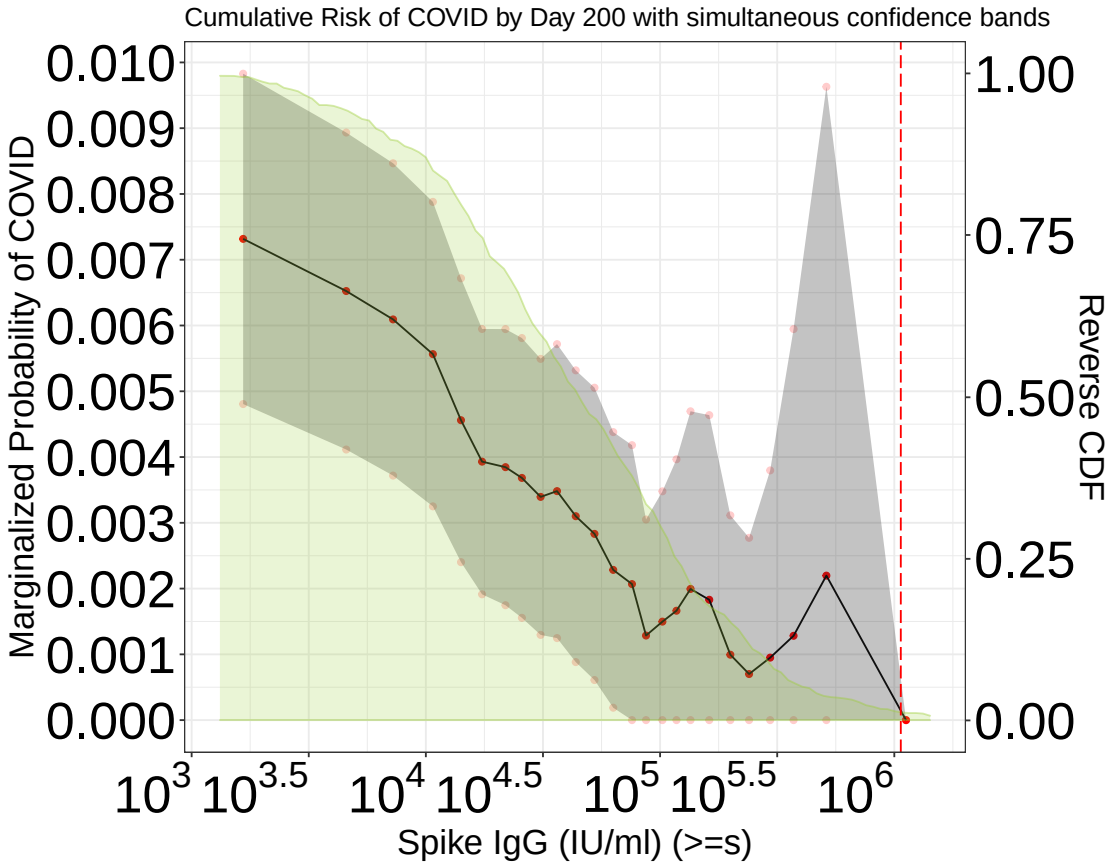

Figure 27: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
3.221	1.66*10^3	0.00732	0.00481	0.00983
4.026	1.06*10^4	0.00556	0.00325	0.00788
4.243	1.75*10^4	0.00393	0.00191	0.00595
4.487	3.07*10^4	0.00339	0.00130	0.00549
4.717	5.21*10^4	0.00283	0.00061	0.00505
4.875	7.50*10^4	0.00207	0.00000	0.00418
5.069	1.17*10^5	0.00166	0.00000	0.00397
5.303	2.01*10^5	0.00099	0.00000	0.00311
5.473	2.97*10^5	0.00095	0.00000	0.00380
6.053	1.13*10^6	0.00000	0.00000	1.00000

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

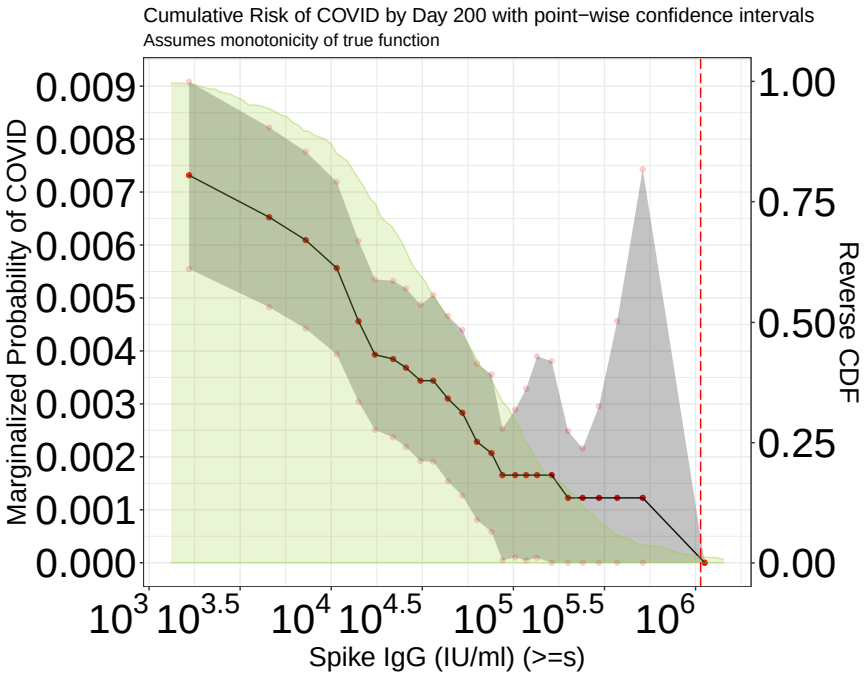

Figure 29: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

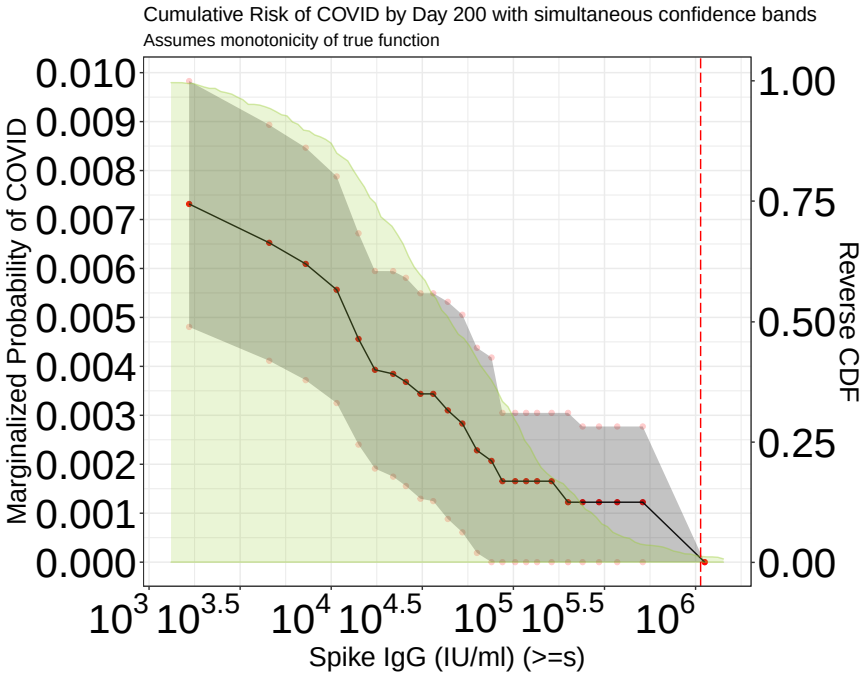

Figure 30: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

Day 29 RBD binding antibody

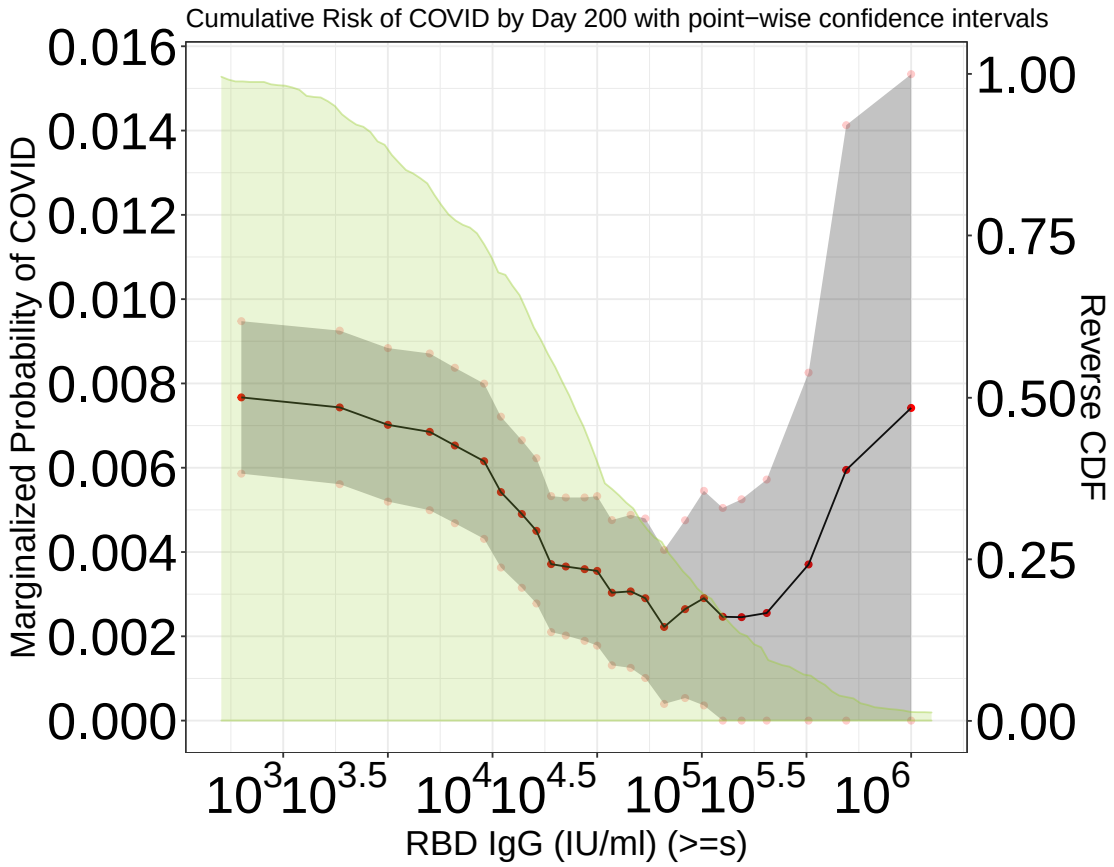

Figure 31: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
2.804	6.37*10^2	0.00767	0.00586	0.00948
3.697	4.98*10^3	0.00685	0.00499	0.00871
3.959	9.10*10^3	0.00615	0.00431	0.00800
4.208	1.61*10^4	0.00450	0.00278	0.00623
4.437	2.74*10^4	0.00359	0.00189	0.00529
4.565	3.67*10^4	0.00303	0.00131	0.00476
4.821	6.62*10^4	0.00222	0.00040	0.00405
5.098	1.25*10^5	0.00246	0.00000	0.00505
5.312	2.05*10^5	0.00255	0.00000	0.00572
5.998	9.95*10^5	0.00742	0.00000	0.02071

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

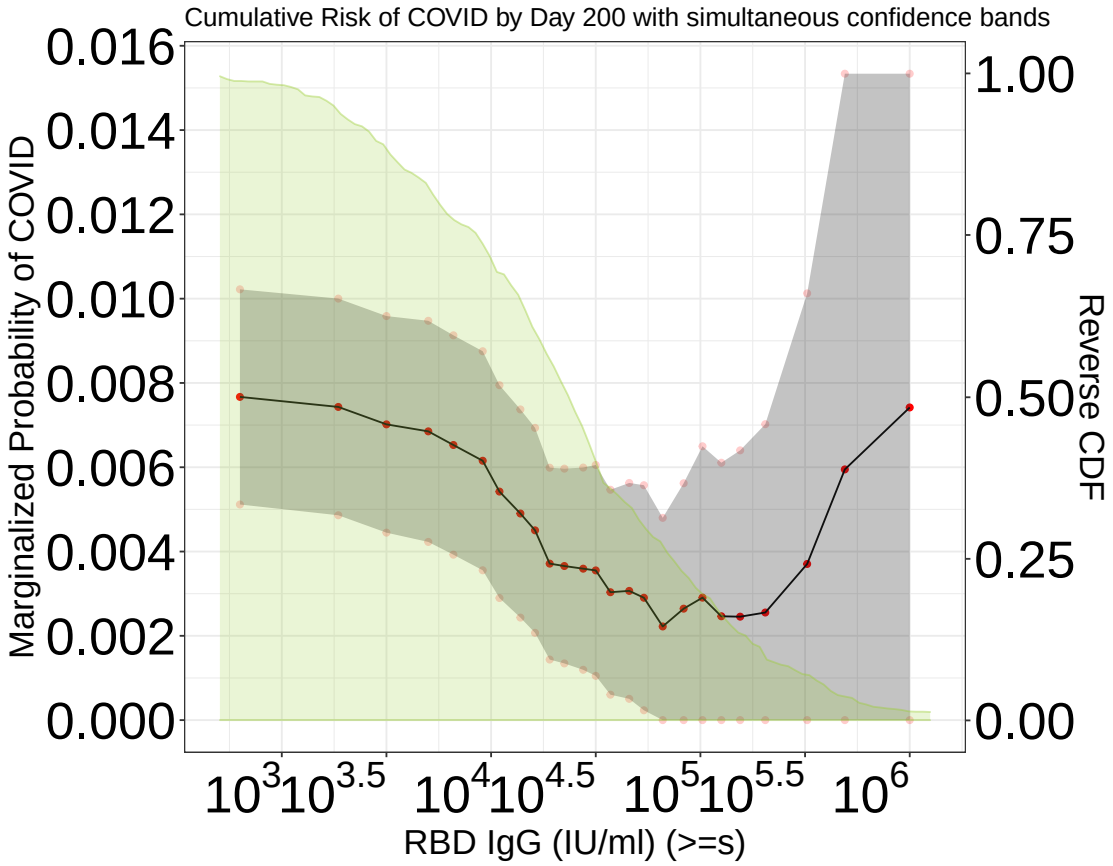

Figure 33: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
2.804	6.37*10^2	0.00767	0.00512	0.01022
3.697	4.98*10^3	0.00685	0.00423	0.00947
3.959	9.10*10^3	0.00615	0.00355	0.00875
4.208	1.61*10^4	0.00450	0.00207	0.00694
4.437	2.74*10^4	0.00359	0.00119	0.00599
4.565	3.67*10^4	0.00303	0.00060	0.00547
4.821	6.62*10^4	0.00222	0.00000	0.00480
5.098	1.25*10^5	0.00246	0.00000	0.00611
5.312	2.05*10^5	0.00255	0.00000	0.00702
5.998	9.95*10^5	0.00742	0.00000	0.02618

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

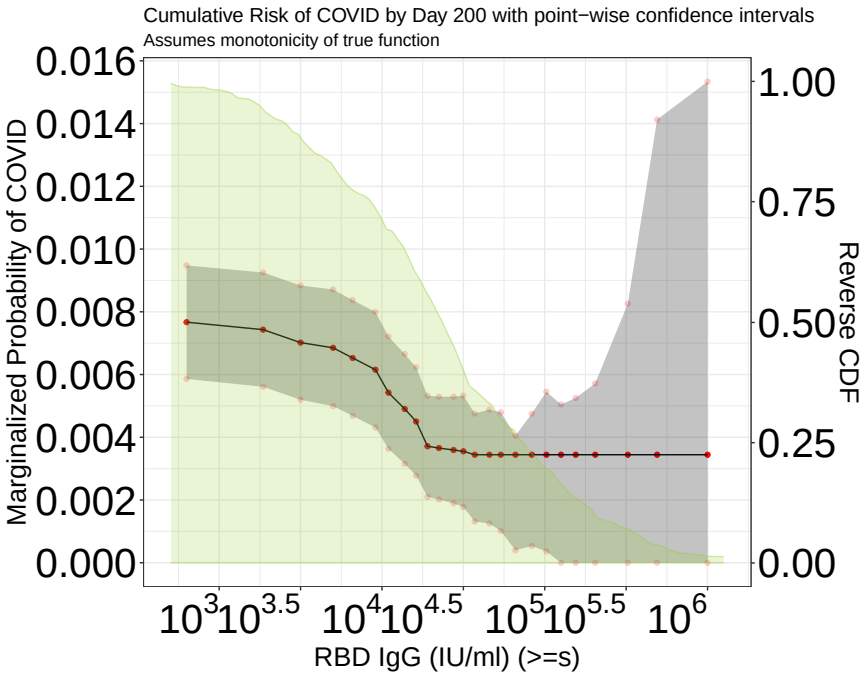

Figure 35: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

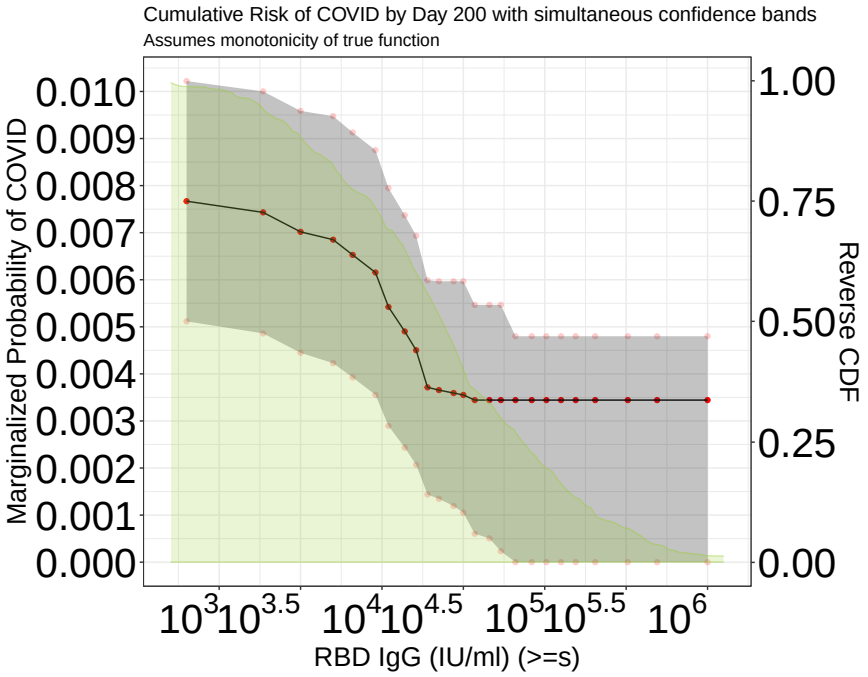

Figure 36: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

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

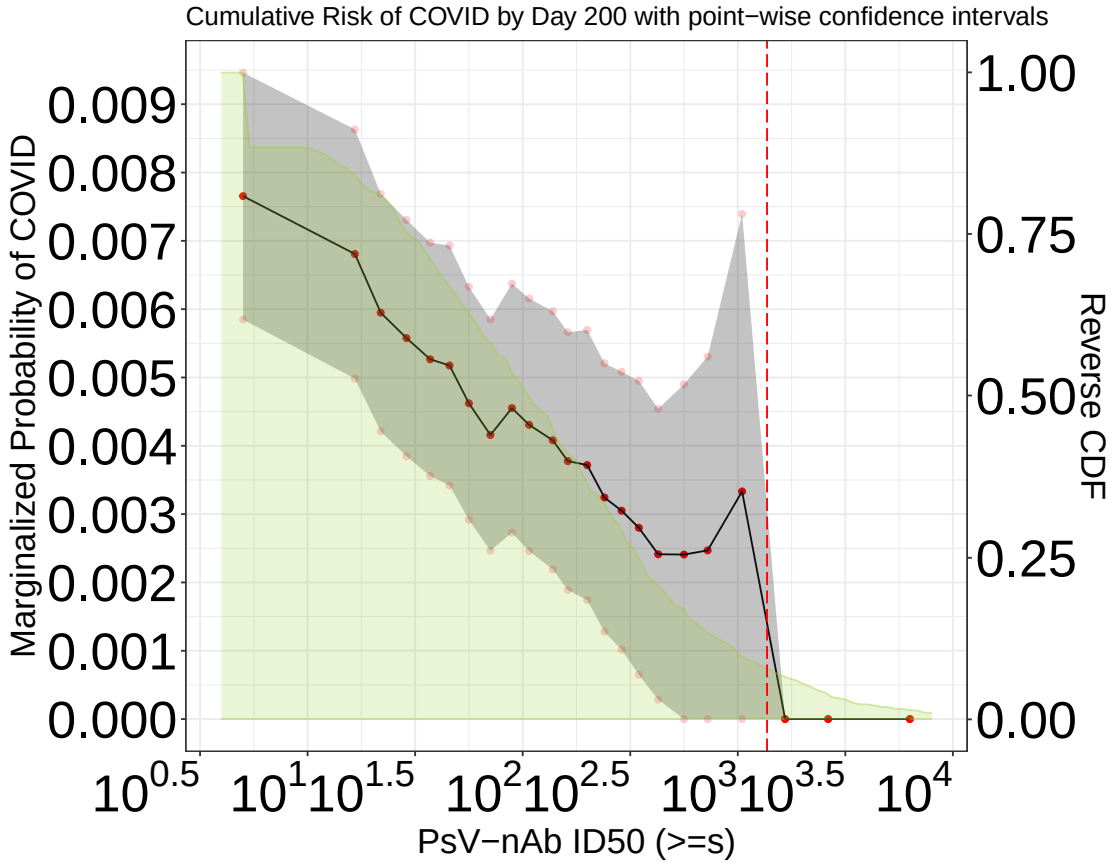

Figure 37: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00765	0.00585	0.00946
1.341	2.19*10^1	0.00595	0.00421	0.00769
1.663	4.60*10^1	0.00518	0.00342	0.00693
1.848	7.05*10^1	0.00416	0.00246	0.00585
2.138	1.37*10^2	0.00408	0.00219	0.00597
2.296	1.98*10^2	0.00372	0.00174	0.00570
2.540	3.47*10^2	0.00280	0.00065	0.00495
2.753	5.66*10^2	0.00241	0.00000	0.00490
3.217	1.65*10^3	0.00000	0.00000	1.00000
3.801	6.32*10^3	0.00000	0.00000	1.00000

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.

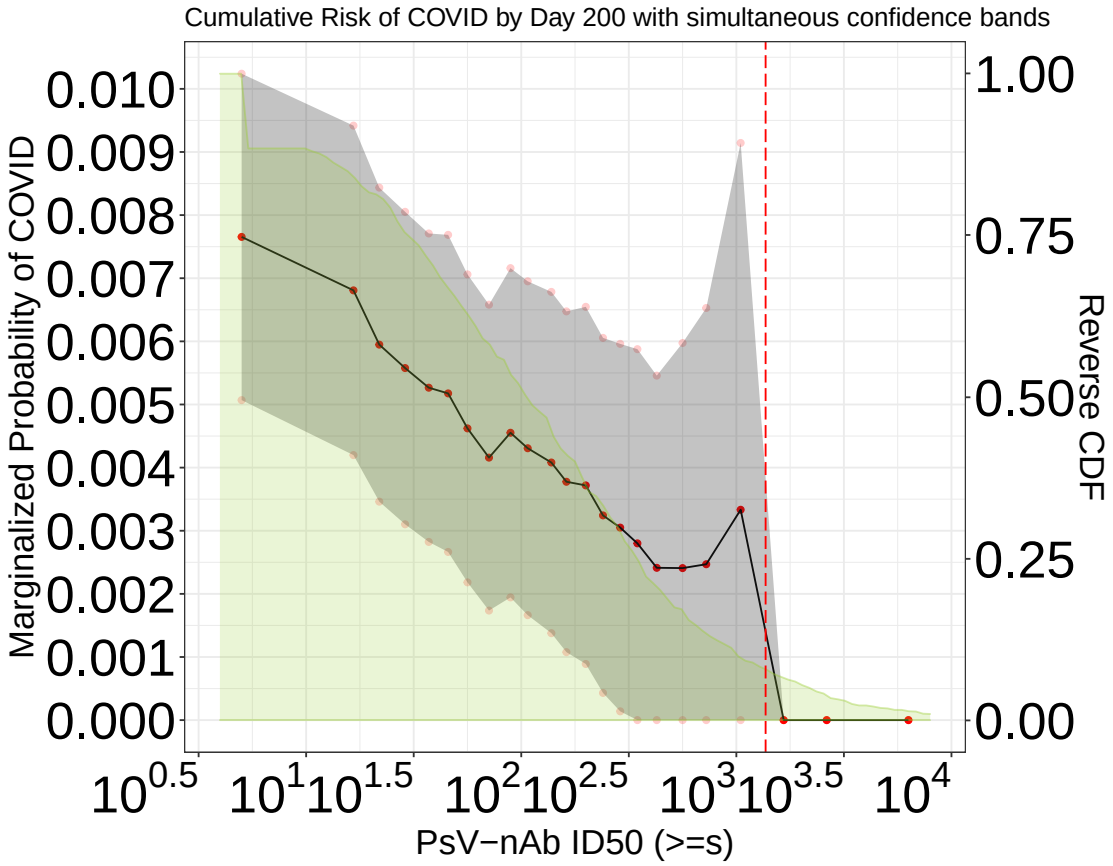

Figure 39: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00765	0.00507	0.01024
1.341	2.19*10^1	0.00595	0.00346	0.00844
1.663	4.60*10^1	0.00518	0.00266	0.00769
1.848	7.05*10^1	0.00416	0.00174	0.00658
2.138	1.37*10^2	0.00408	0.00138	0.00678
2.296	1.98*10^2	0.00372	0.00089	0.00655
2.540	3.47*10^2	0.00280	0.00000	0.00588
2.753	5.66*10^2	0.00241	0.00000	0.00597
3.217	1.65*10^3	0.00000	0.00000	1.00000
3.801	6.32*10^3	0.00000	0.00000	1.00000

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

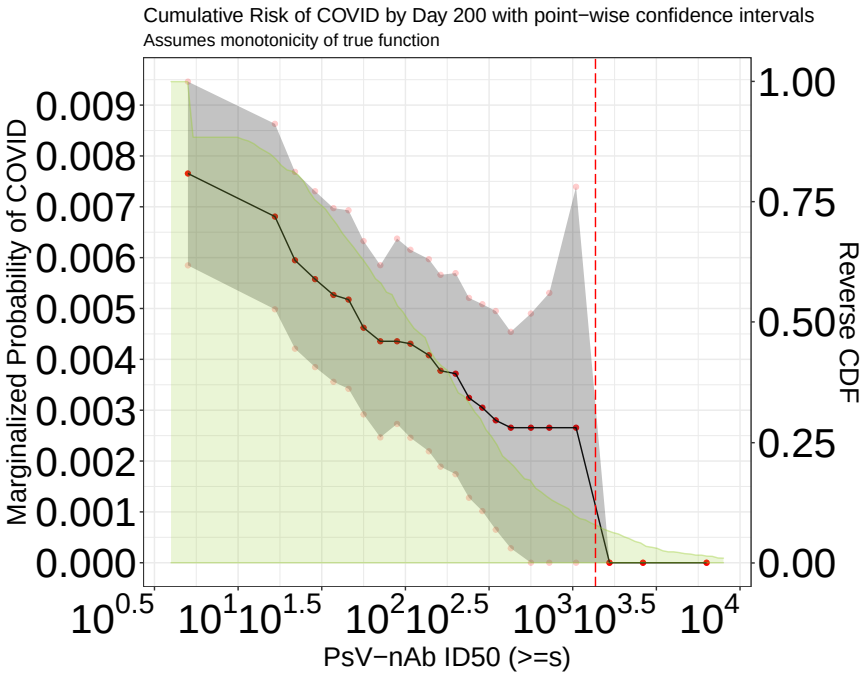

Figure 41: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed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

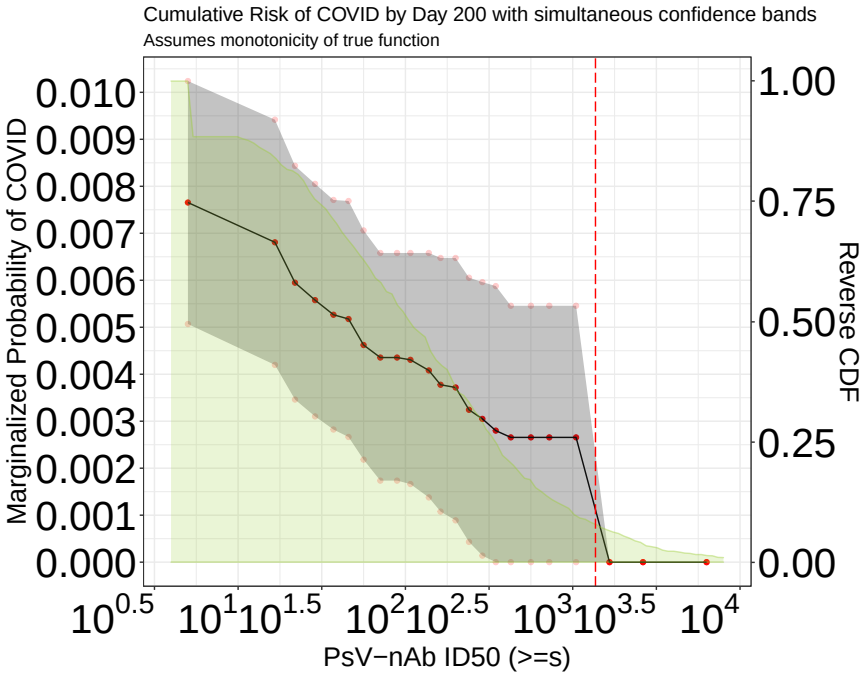

Figure 42: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence intervals. The dashed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

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

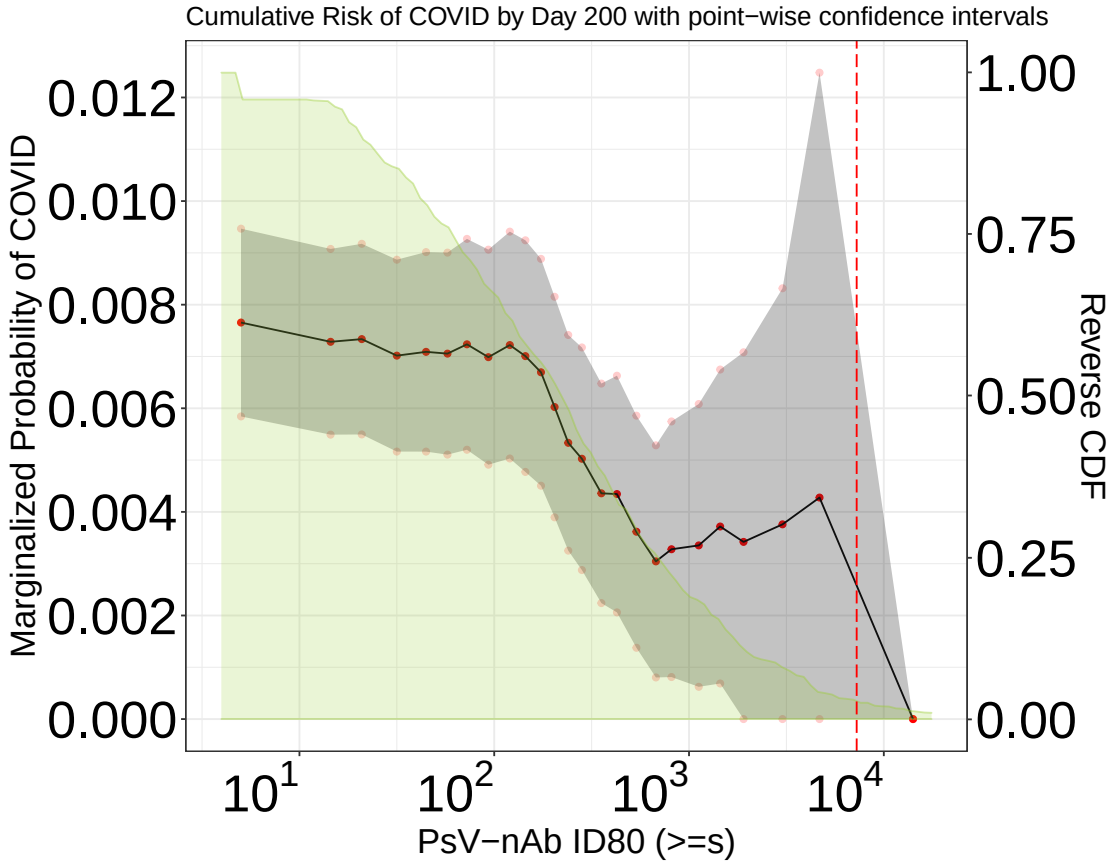

Figure 43: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00766	0.00584	0.00947
1.502	3.18*10^1	0.00702	0.00516	0.00887
1.759	5.74*10^1	0.00706	0.00511	0.00901
2.077	1.19*10^2	0.00722	0.00503	0.00941
2.314	2.06*10^2	0.00602	0.00389	0.00815
2.449	2.81*10^2	0.00503	0.00288	0.00717
2.730	5.37*10^2	0.00362	0.00138	0.00586
3.045	1.11*10^3	0.00335	0.00062	0.00608
3.275	1.88*10^3	0.00342	0.00000	0.00708
4.145	1.40*10^4	0.00000	0.00000	1.00000

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.

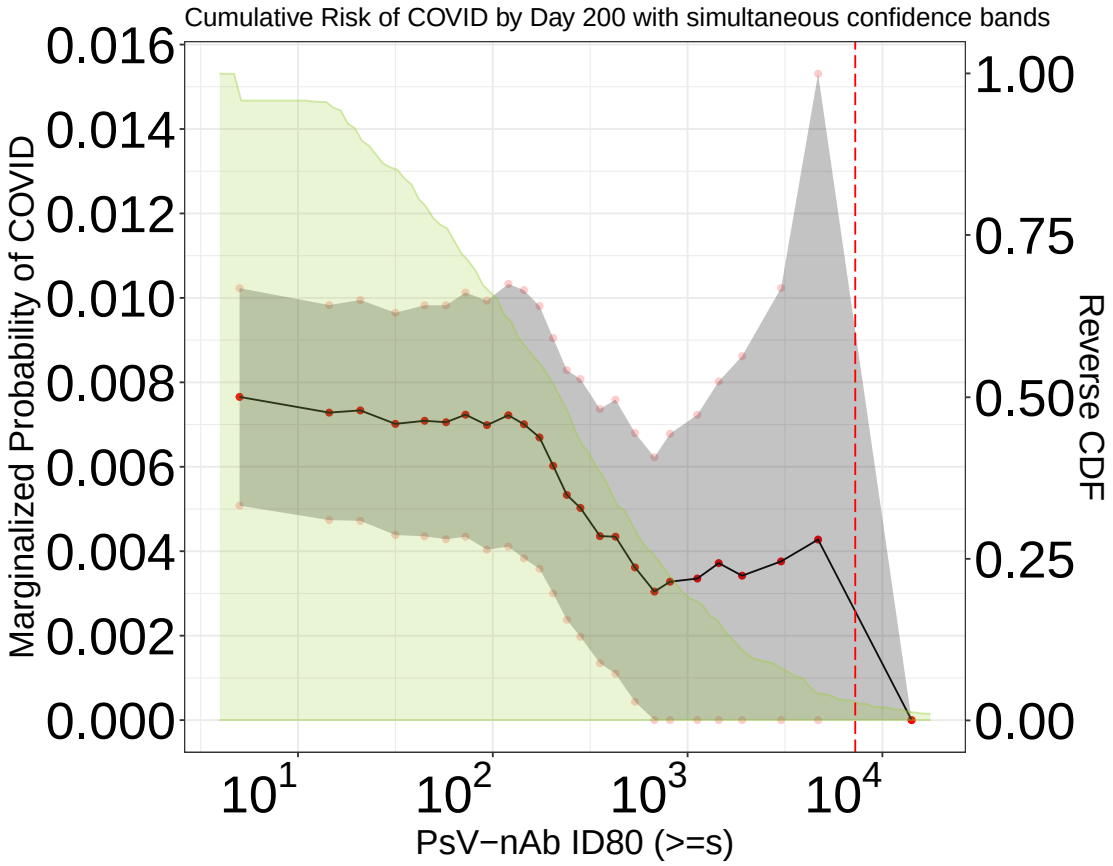

Figure 45: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00766	0.00508	0.01023
1.502	3.18*10^1	0.00702	0.00438	0.00965
1.759	5.74*10^1	0.00706	0.00428	0.00983
2.077	1.19*10^2	0.00722	0.00411	0.01033
2.314	2.06*10^2	0.00602	0.00300	0.00905
2.449	2.81*10^2	0.00503	0.00197	0.00808
2.730	5.37*10^2	0.00362	0.00043	0.00680
3.045	1.11*10^3	0.00335	0.00000	0.00723
3.275	1.88*10^3	0.00342	0.00000	0.00862
4.145	1.40*10^4	0.00000	0.00000	1.00000

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

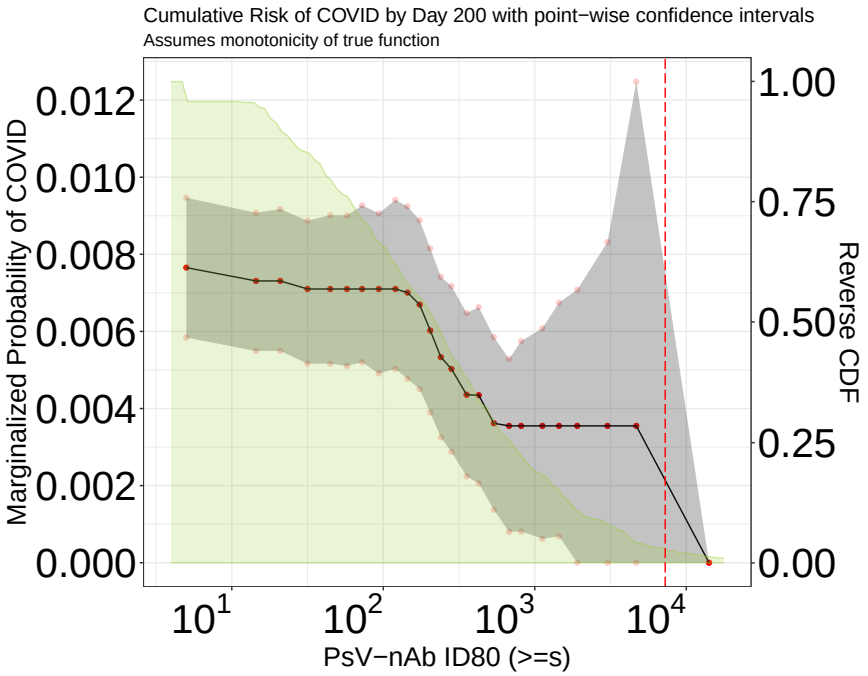

Figure 47: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed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

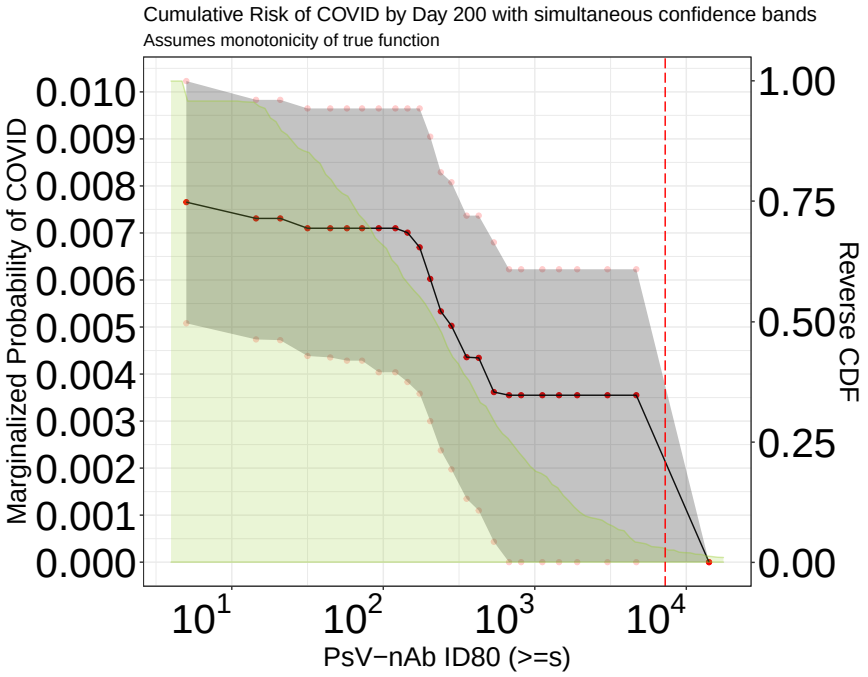

Figure 48: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence intervals. The dashed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