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

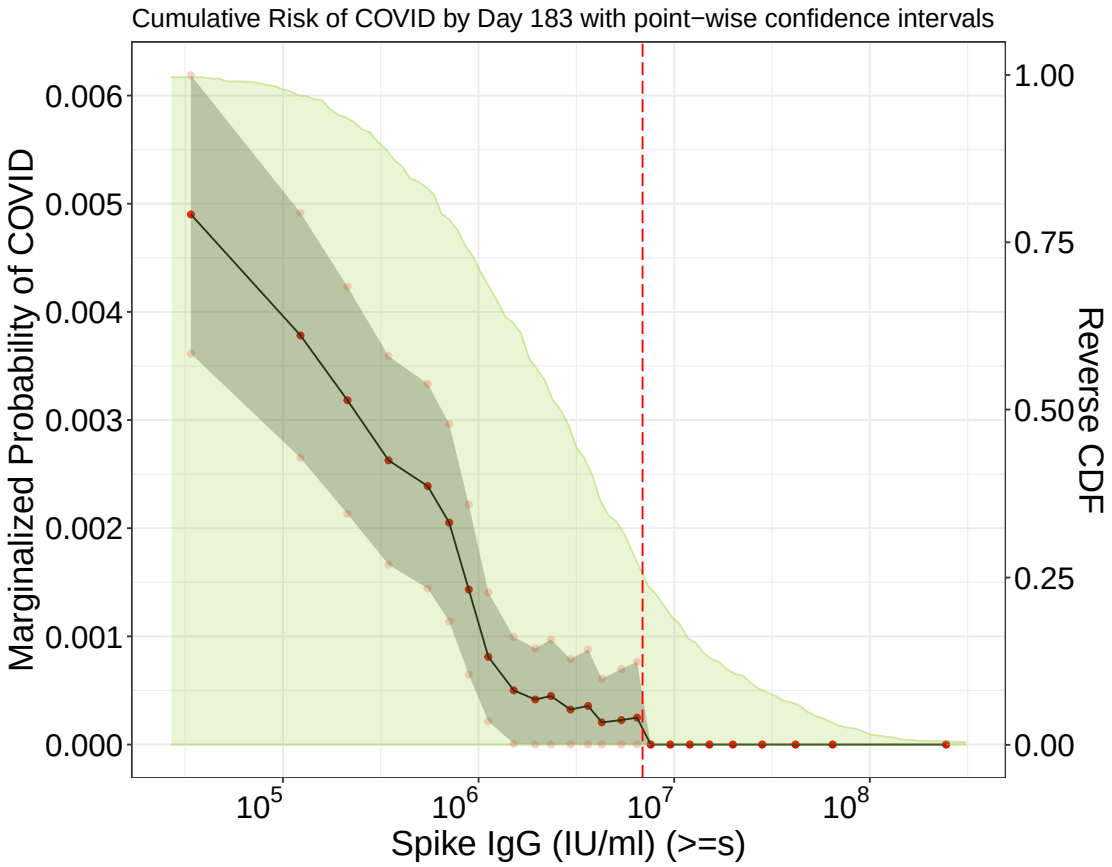

Figure 1: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

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	0.00296
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.

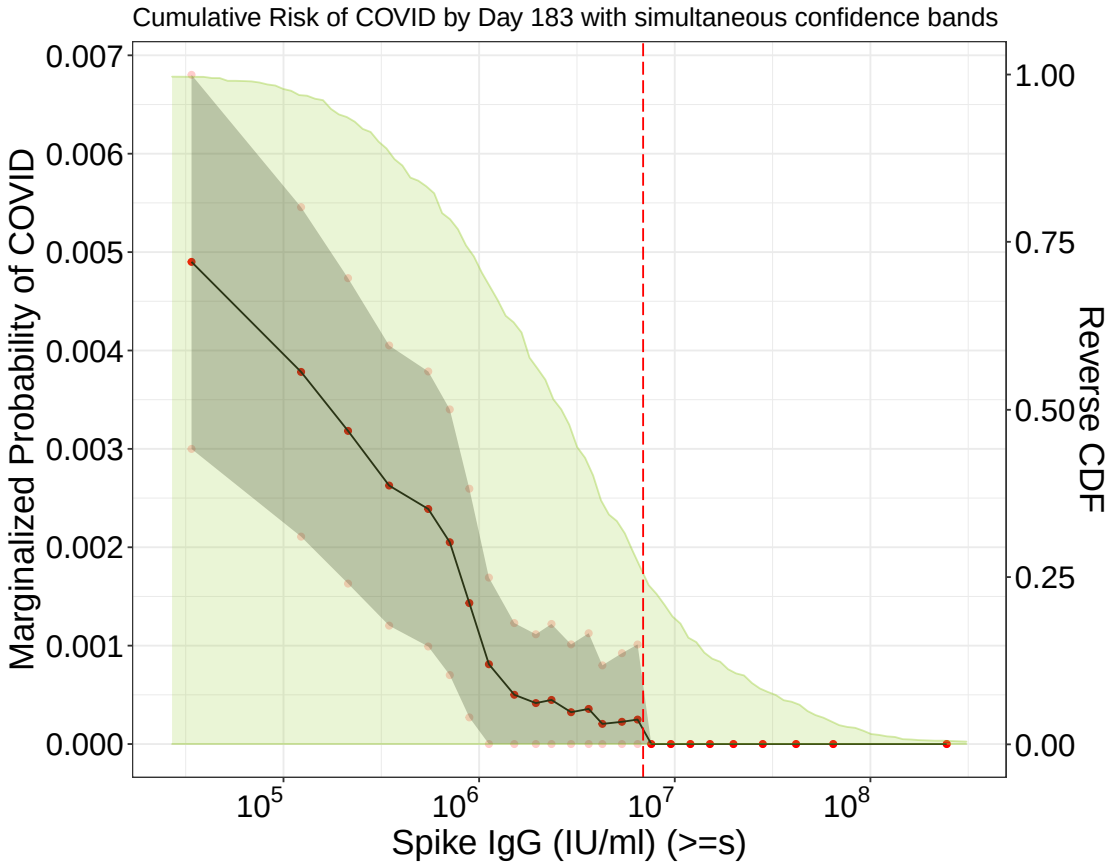

Figure 3: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

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

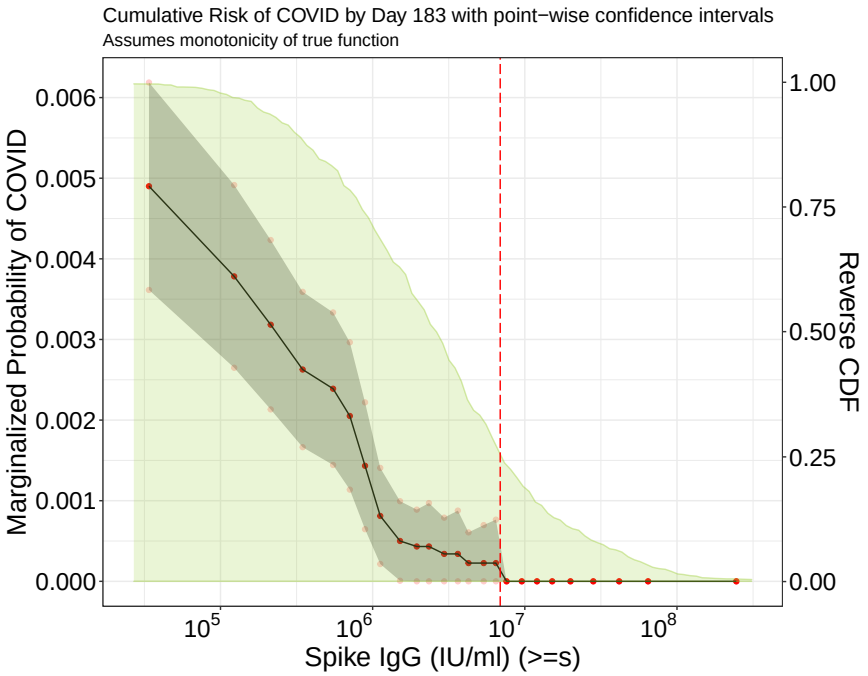

Figure 5: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

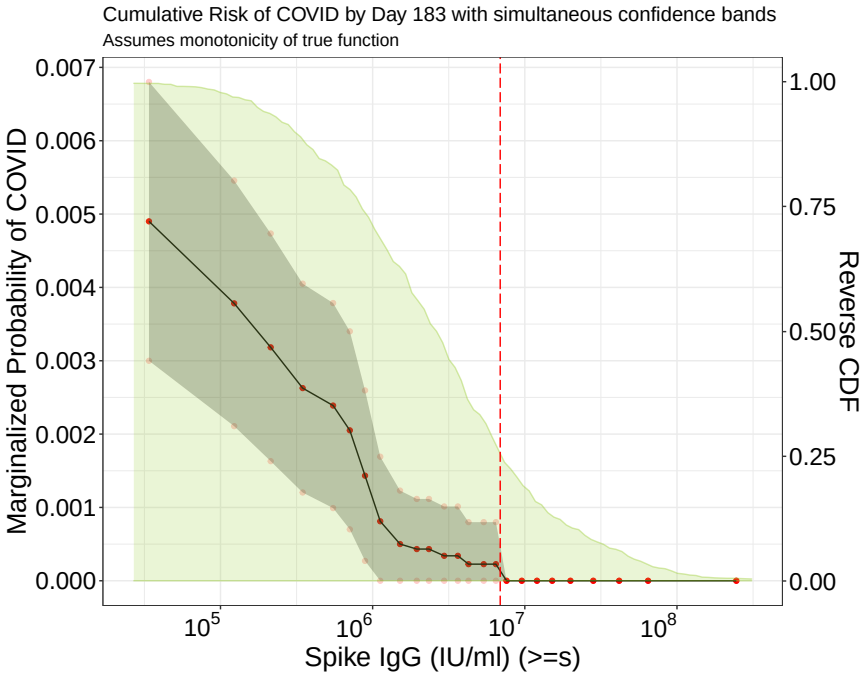

Figure 6: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

Day 57 RBD binding antibody

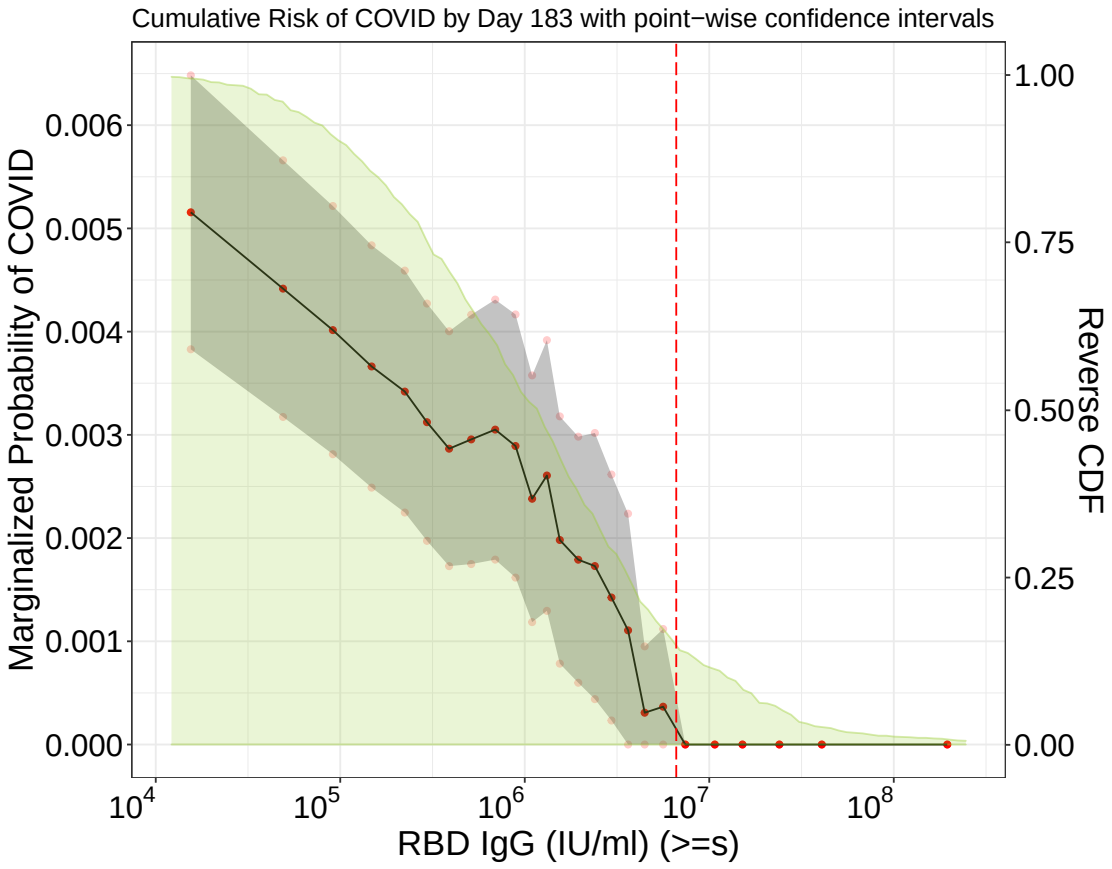

Figure 7: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

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

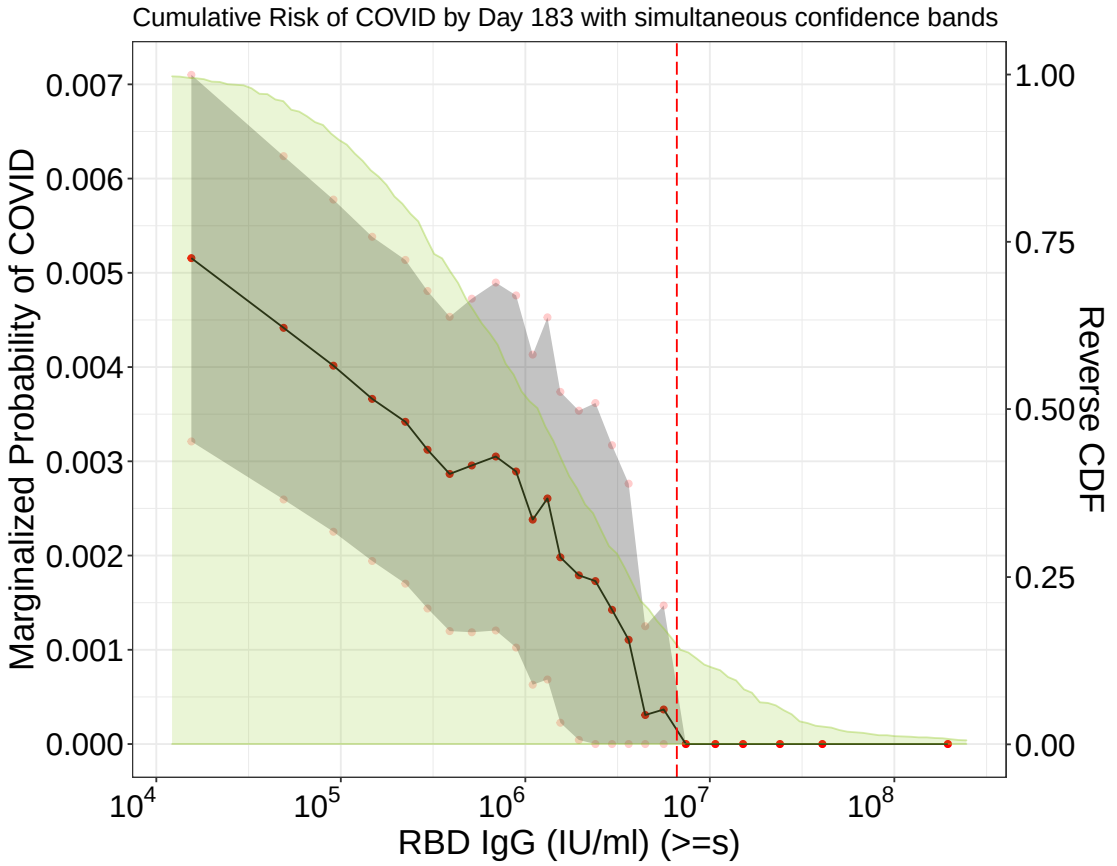

Figure 9: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

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

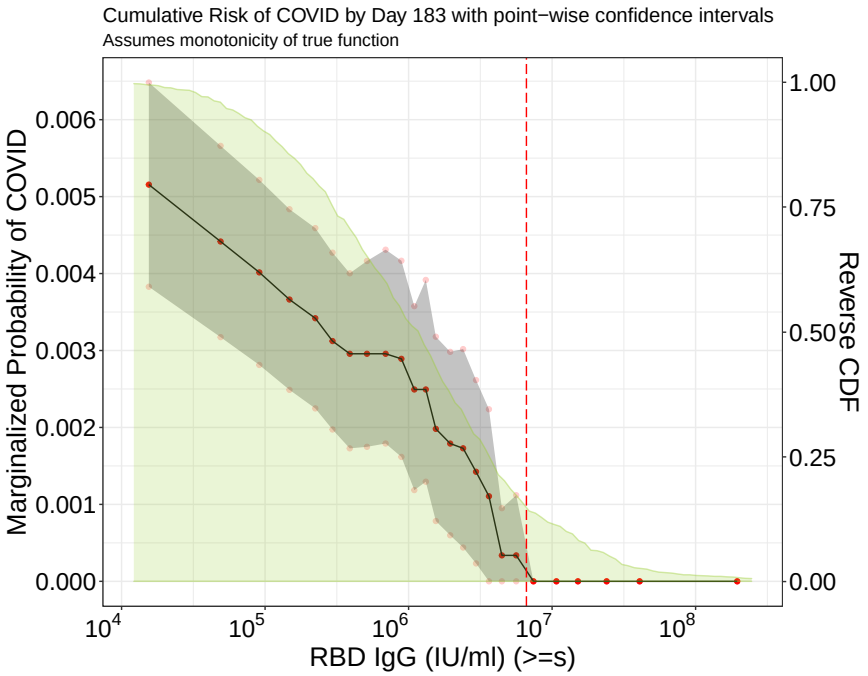

Figure 11: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

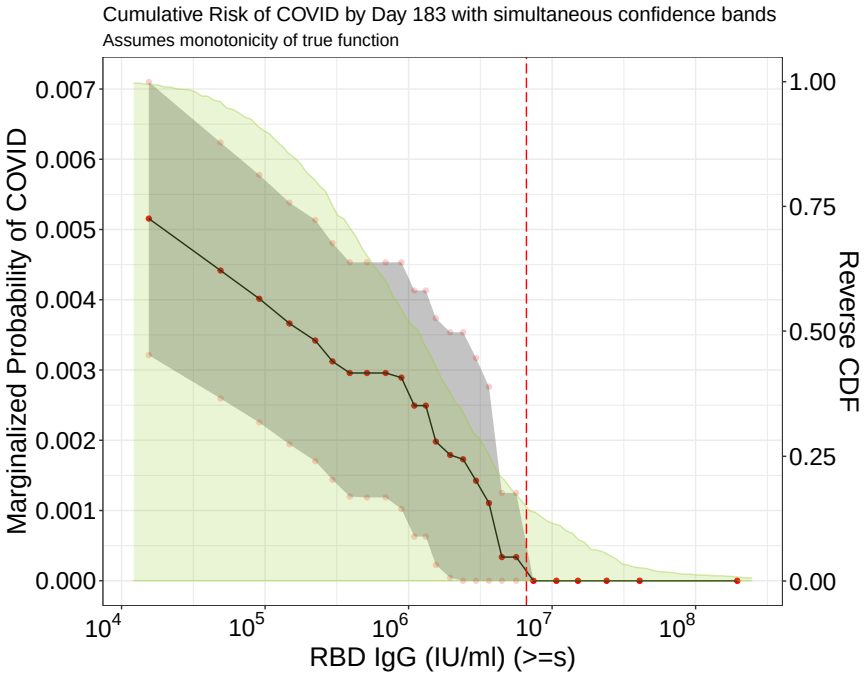

Figure 12: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

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

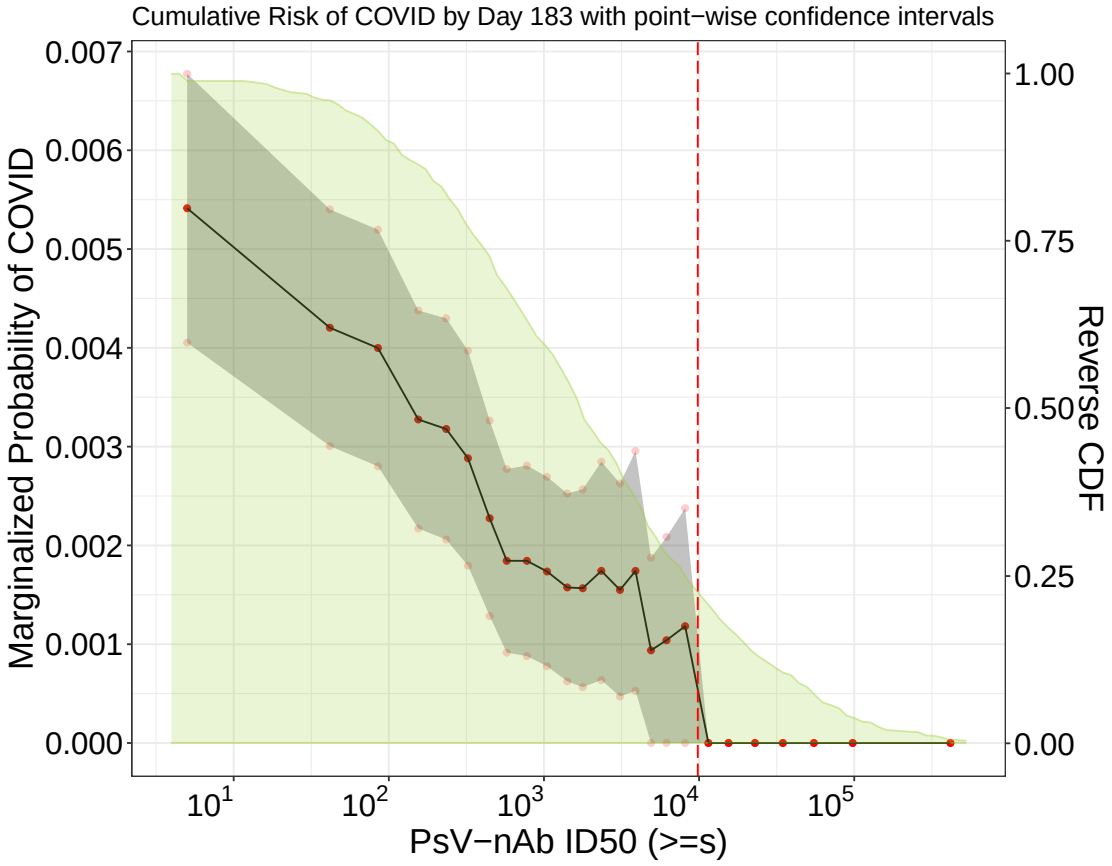

Figure 13: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00541	0.00405	0.00677
2.187	1.54*10^2	0.00327	0.00217	0.00438
2.510	3.24*10^2	0.00288	0.00180	0.00397
2.891	7.78*10^2	0.00184	0.00088	0.00281
3.248	1.77*10^3	0.00157	0.00057	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.

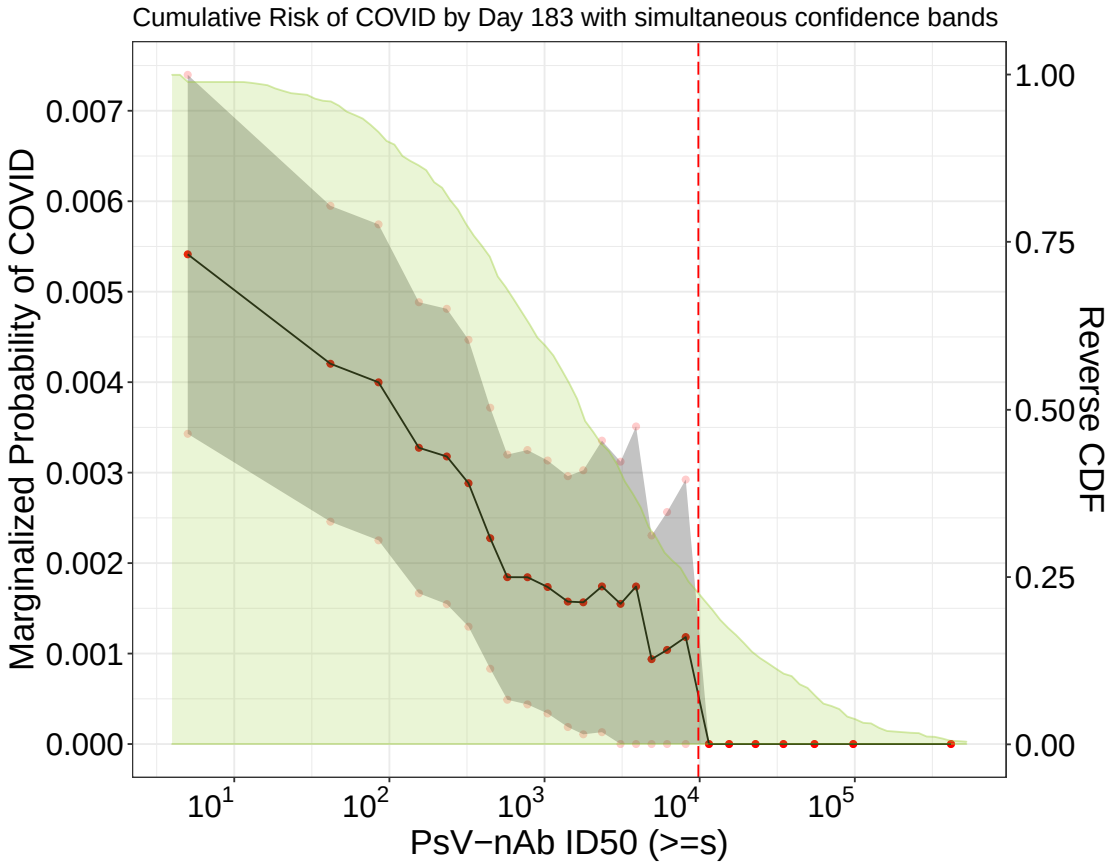

Figure 15: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00541	0.00343	0.00740
2.187	1.54*10^2	0.00327	0.00167	0.00488
2.510	3.24*10^2	0.00288	0.00130	0.00447
2.891	7.78*10^2	0.00184	0.00044	0.00325
3.248	1.77*10^3	0.00157	0.00011	0.00303
3.489	3.08*10^3	0.00155	0.00000	0.00312
3.787	6.12*10^3	0.00104	0.00000	0.00256
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 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

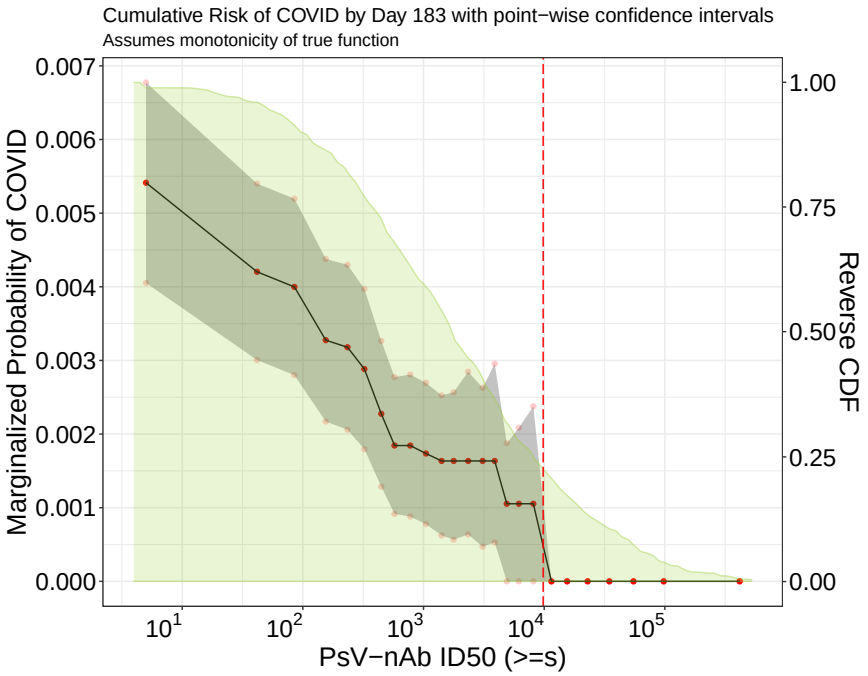

Figure 17: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed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

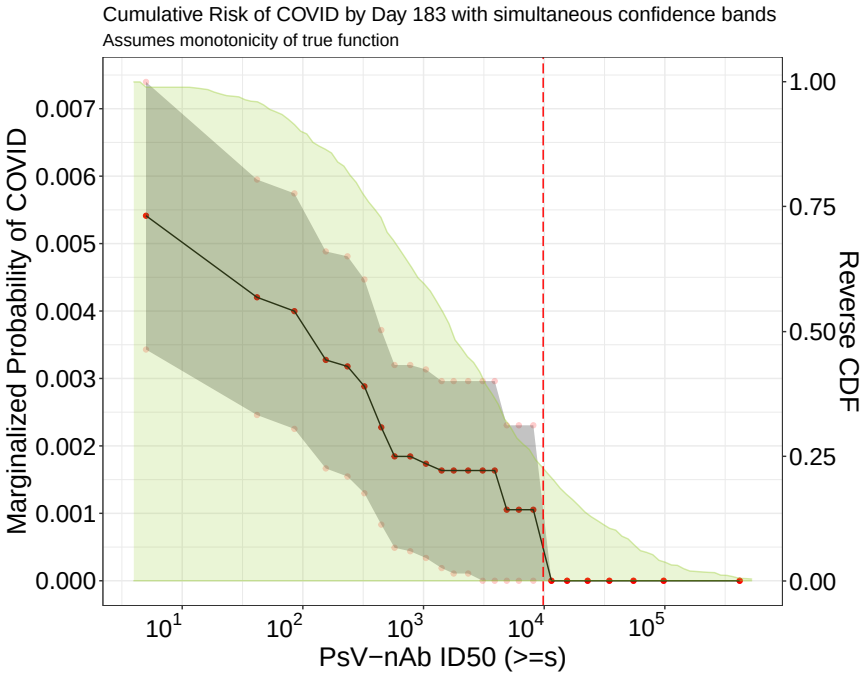

Figure 18: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence intervals. The dashed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

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

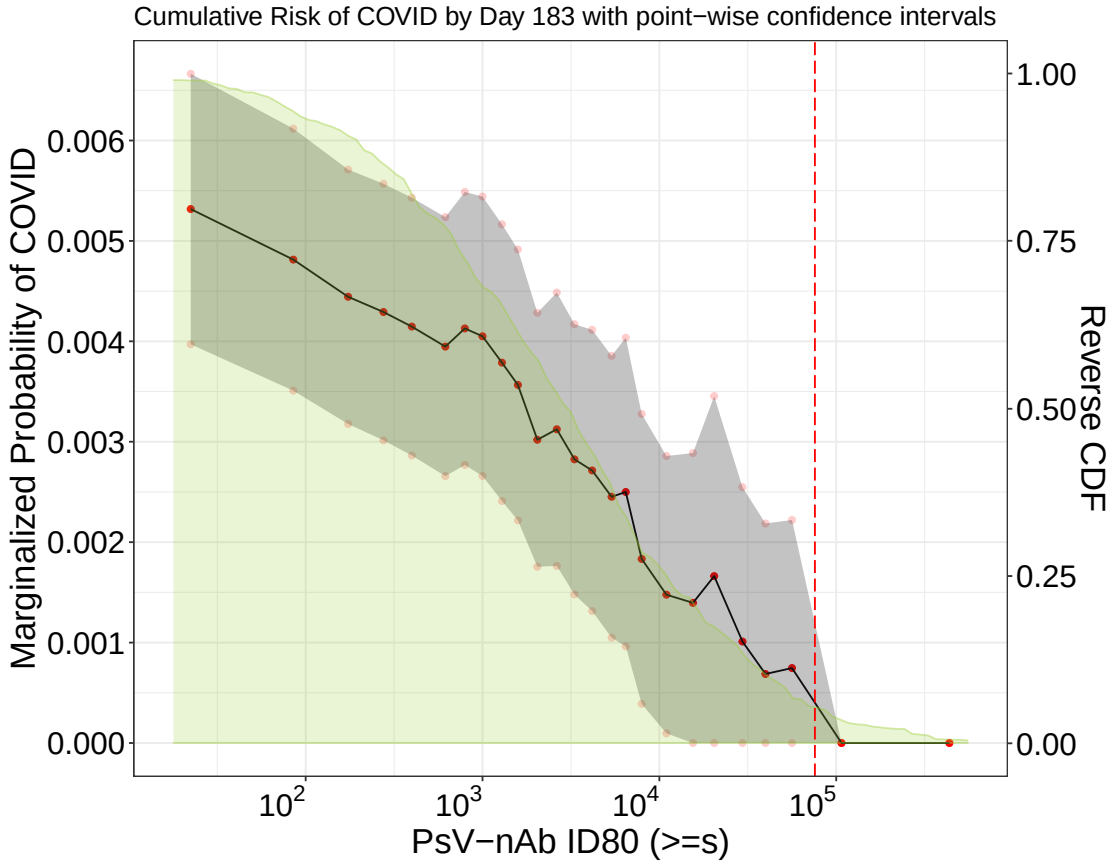

Figure 19: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	2.25*10^1	0.00532	0.00397	0.00666
2.441	2.76*10^2	0.00429	0.00301	0.00557
2.789	6.15*10^2	0.00395	0.00266	0.00524
3.111	1.29*10^3	0.00379	0.00241	0.00517
3.421	2.64*10^3	0.00312	0.00176	0.00449
3.623	4.20*10^3	0.00271	0.00131	0.00411
3.900	7.94*10^3	0.00183	0.00039	0.00328
4.309	2.04*10^4	0.00166	0.00000	0.00345
4.598	3.96*10^4	0.00069	0.00000	0.00219
5.644	4.41*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.

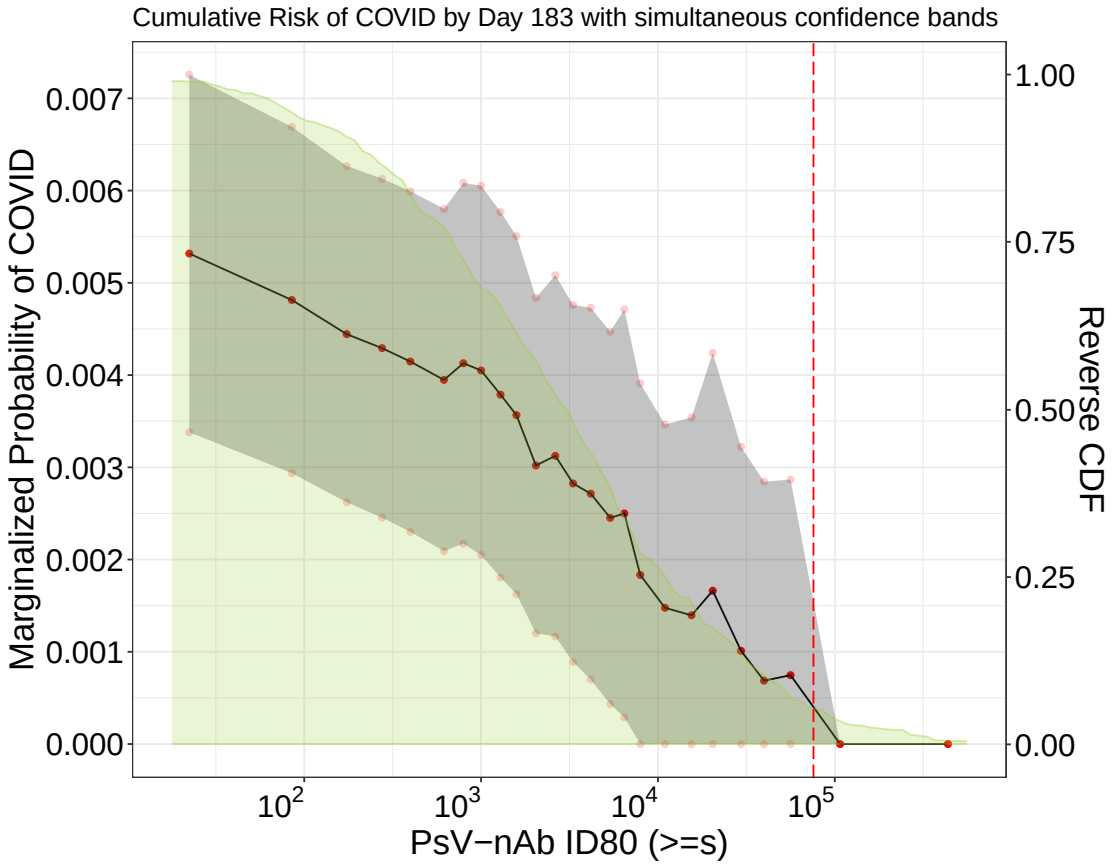

Figure 21: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	2.25*10^1	0.00532	0.00338	0.00725
2.441	2.76*10^2	0.00429	0.00245	0.00613
2.789	6.15*10^2	0.00395	0.00209	0.00580
3.111	1.29*10^3	0.00379	0.00181	0.00577
3.421	2.64*10^3	0.00312	0.00117	0.00508
3.623	4.20*10^3	0.00271	0.00070	0.00473
3.900	7.94*10^3	0.00183	0.00000	0.00391
4.309	2.04*10^4	0.00166	0.00000	0.00424
4.598	3.96*10^4	0.00069	0.00000	0.00284
5.644	4.41*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

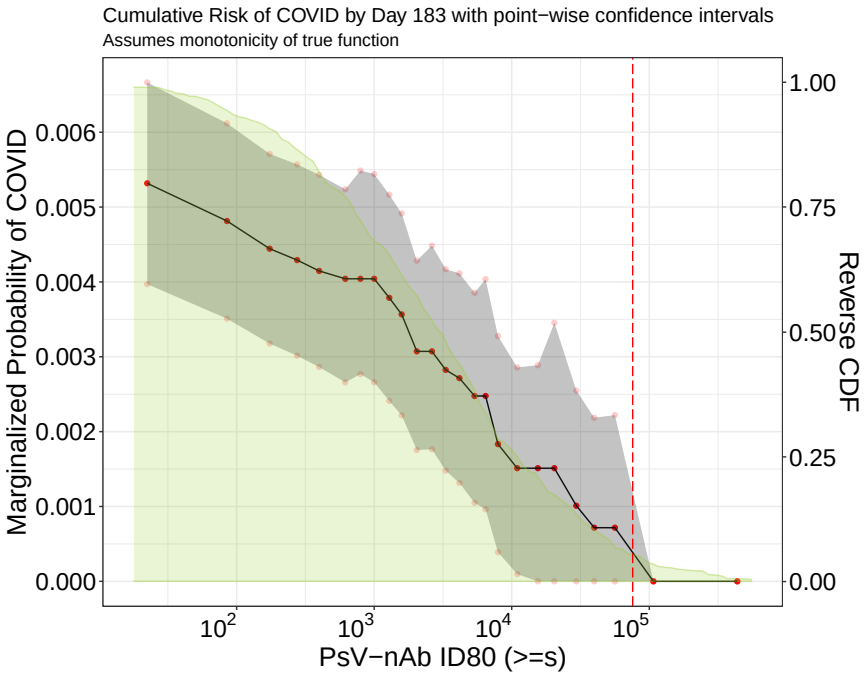

Figure 23: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed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

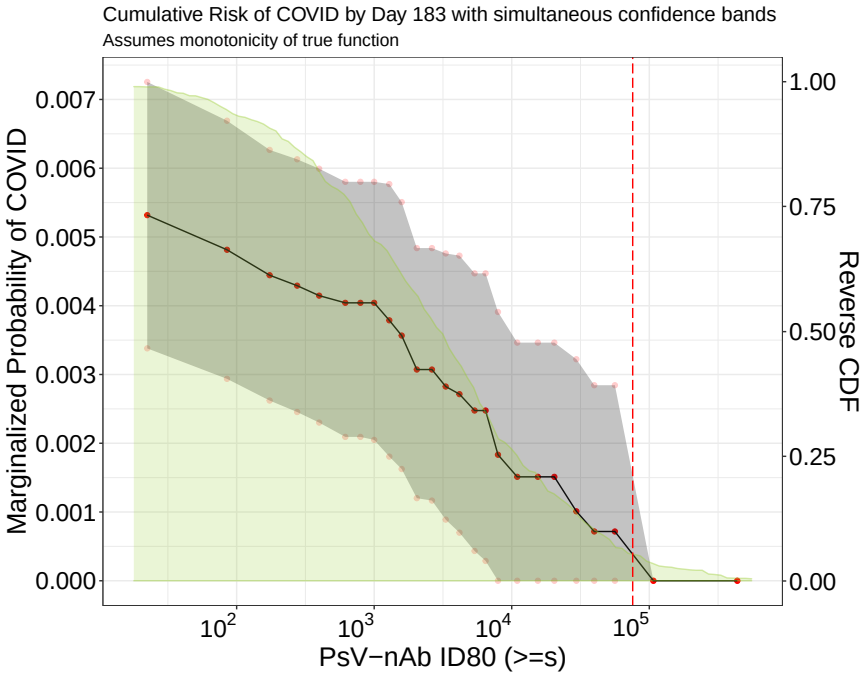

Figure 24: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence intervals. The dashed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

Day 29 Spike protein antibody

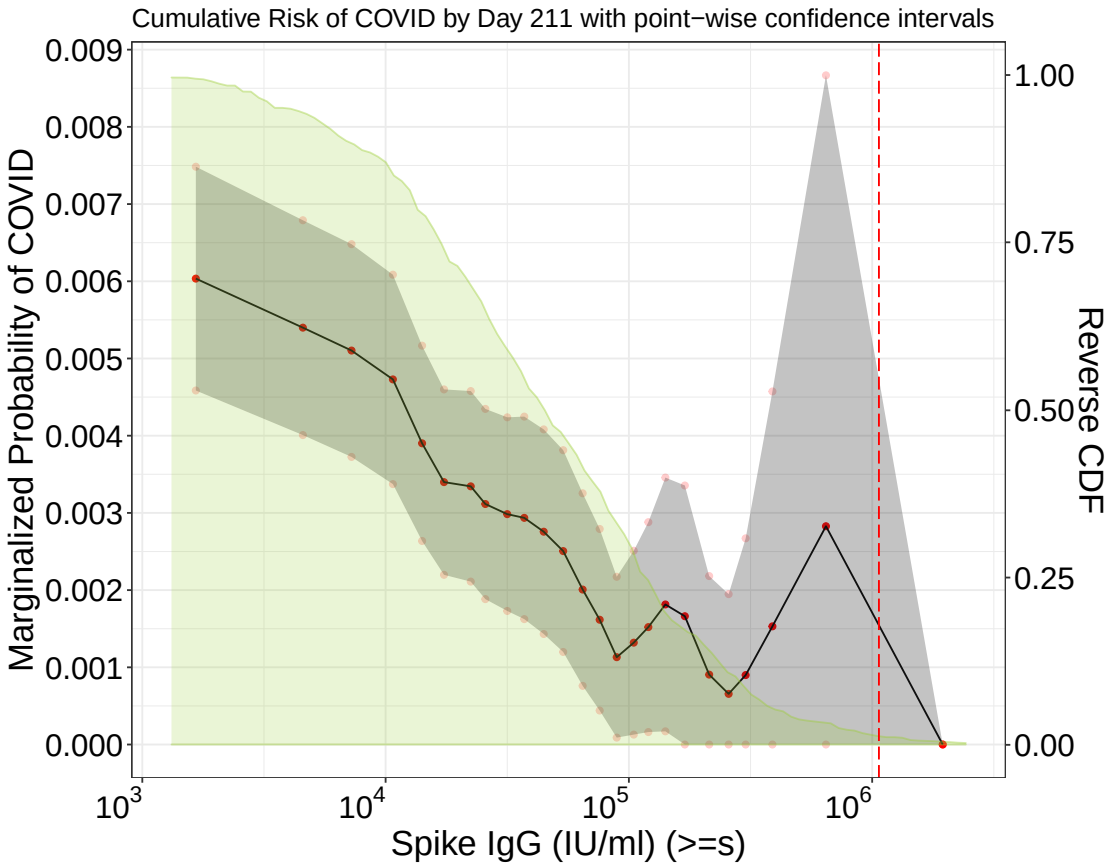

Figure 25: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
3.220	1.66*10^3	0.00603	0.00459	0.00748
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.

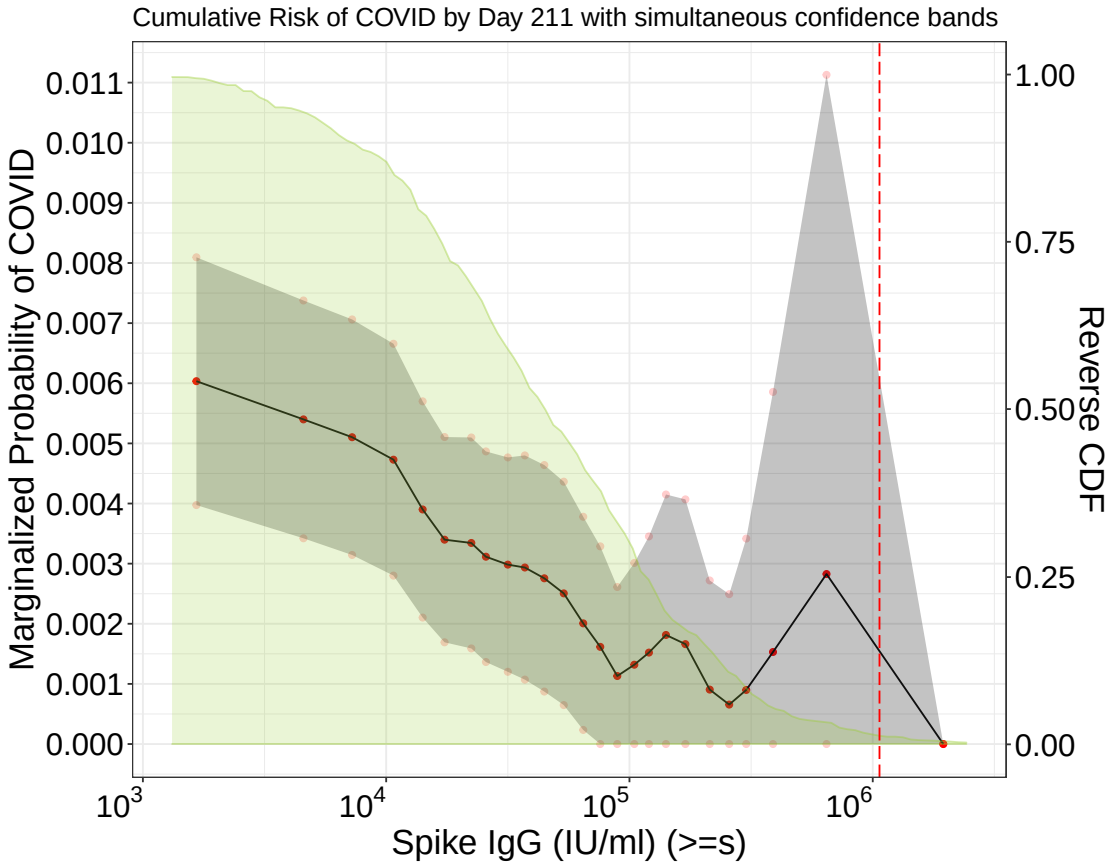

Figure 27: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
3.220	1.66*10^3	0.00603	0.00397	0.00809
4.030	1.07*10^4	0.00473	0.00280	0.00666
4.244	1.75*10^4	0.00340	0.00169	0.00511
4.503	3.18*10^4	0.00298	0.00120	0.00477
4.729	5.36*10^4	0.00251	0.00065	0.00436
4.884	7.66*10^4	0.00162	0.00000	0.00329
5.082	1.21*10^5	0.00152	0.00000	0.00345
5.326	2.12*10^5	0.00091	0.00000	0.00272
5.484	3.05*10^5	0.00090	0.00000	0.00342
6.285	1.93*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

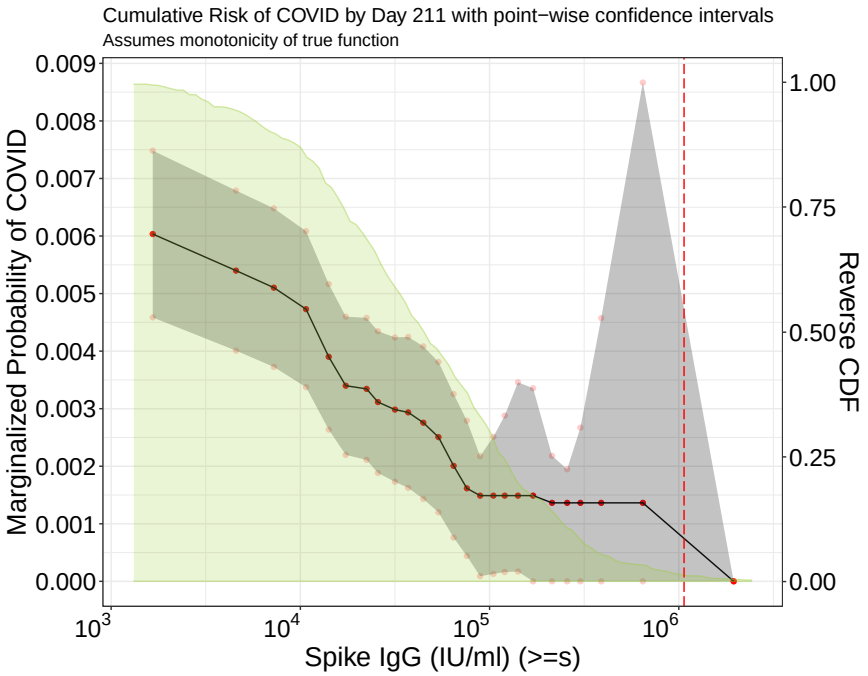

Figure 29: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

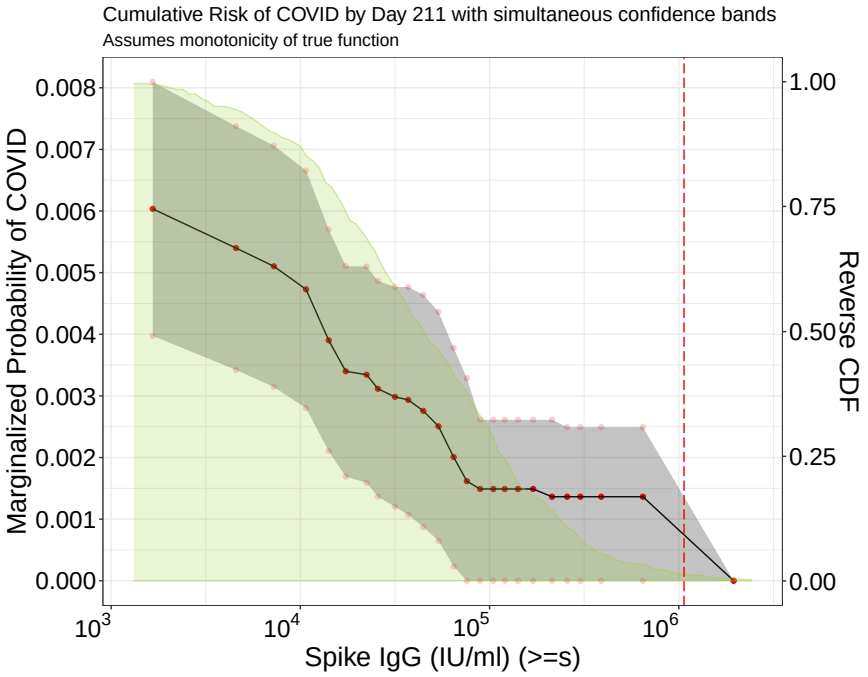

Figure 30: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

Day 29 RBD binding antibody

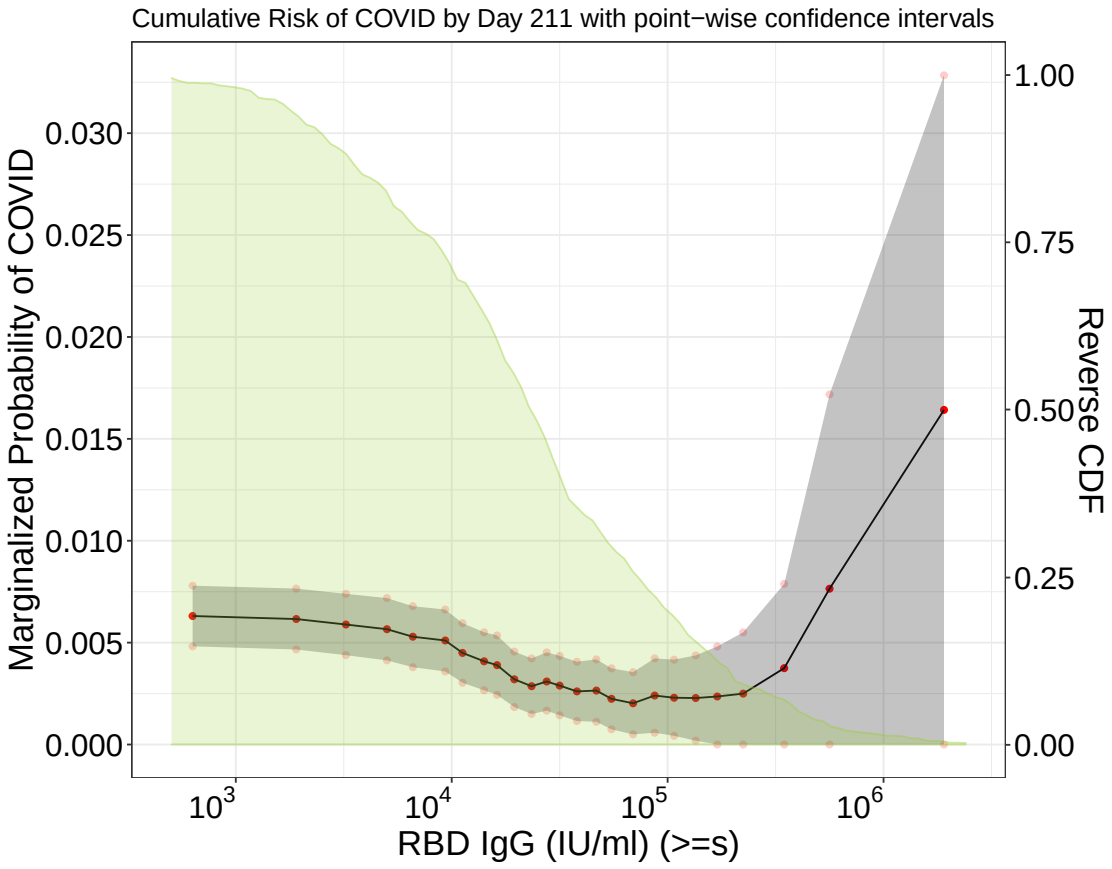

Figure 31: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
2.802	6.34*10^2	0.00631	0.00482	0.00779
3.701	5.02*10^3	0.00566	0.00413	0.00719
3.970	9.33*10^3	0.00511	0.00359	0.00662
4.215	1.64*10^4	0.00390	0.00244	0.00535
4.443	2.77*10^4	0.00309	0.00166	0.00452
4.579	3.79*10^4	0.00261	0.00115	0.00406
4.835	6.84*10^4	0.00202	0.00050	0.00355
5.127	1.34*10^5	0.00228	0.00019	0.00437
5.351	2.24*10^5	0.00250	0.00000	0.00551
6.281	1.91*10^6	0.01642	0.00000	0.04845

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

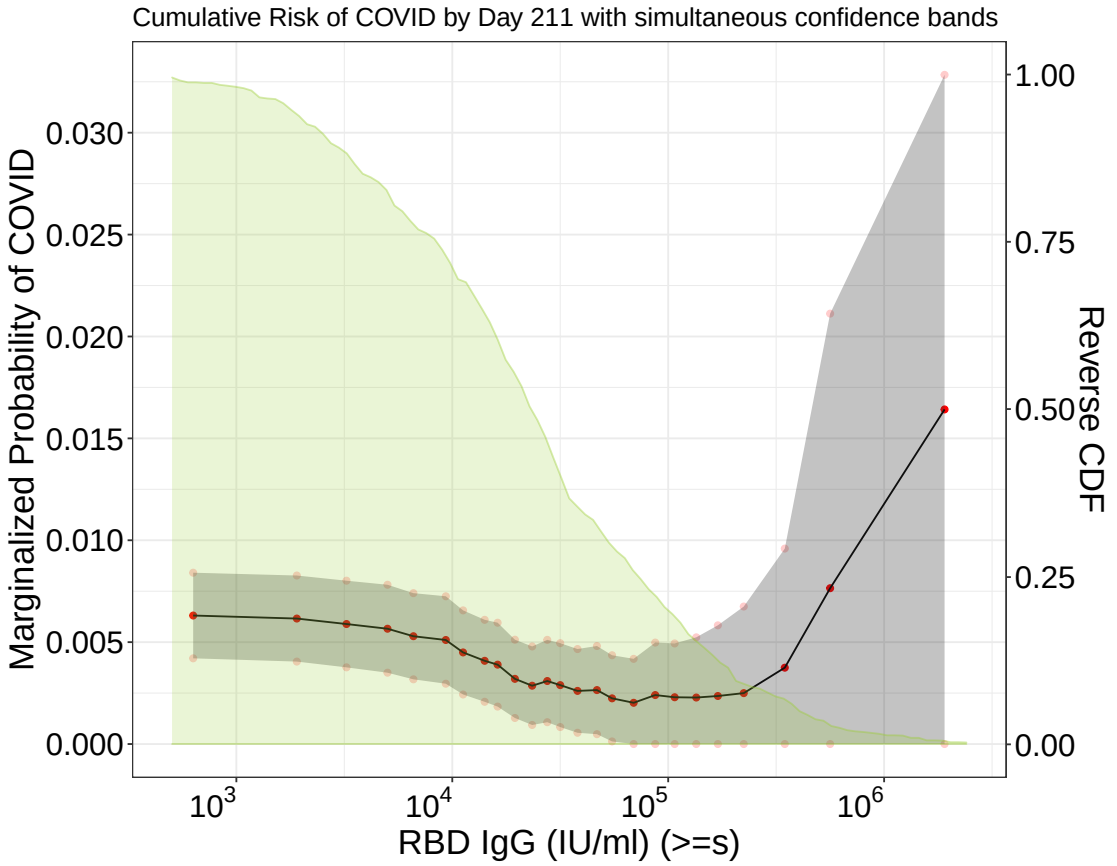

Figure 33: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
2.802	6.34*10^2	0.00631	0.00421	0.00841
3.701	5.02*10^3	0.00566	0.00350	0.00782
3.970	9.33*10^3	0.00511	0.00296	0.00725
4.215	1.64*10^4	0.00390	0.00184	0.00595
4.443	2.77*10^4	0.00309	0.00107	0.00511
4.579	3.79*10^4	0.00261	0.00055	0.00466
4.835	6.84*10^4	0.00202	0.00000	0.00418
5.127	1.34*10^5	0.00228	0.00000	0.00524
5.351	2.24*10^5	0.00250	0.00000	0.00675
6.281	1.91*10^6	0.01642	0.00000	0.06168

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

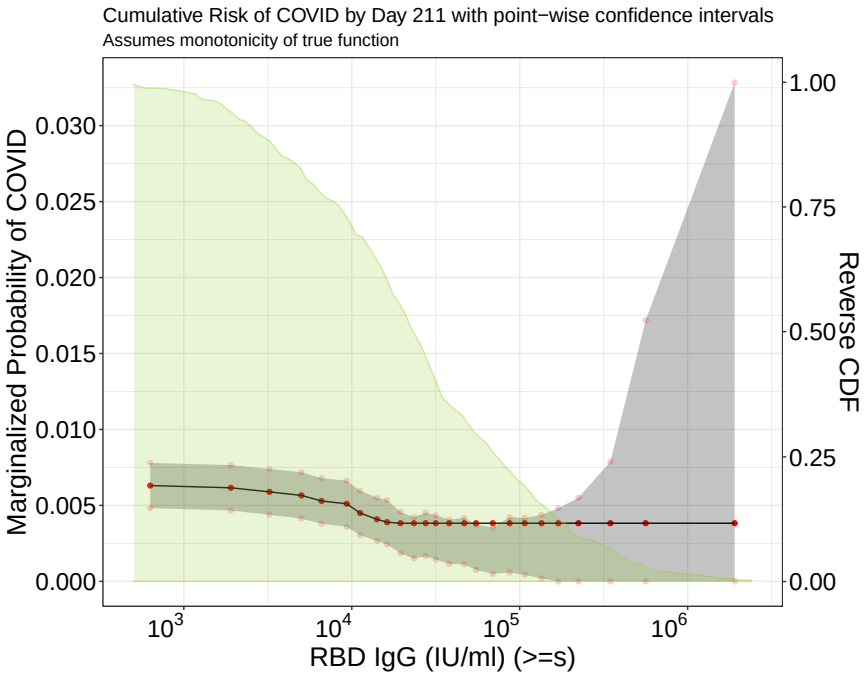

Figure 35: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold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

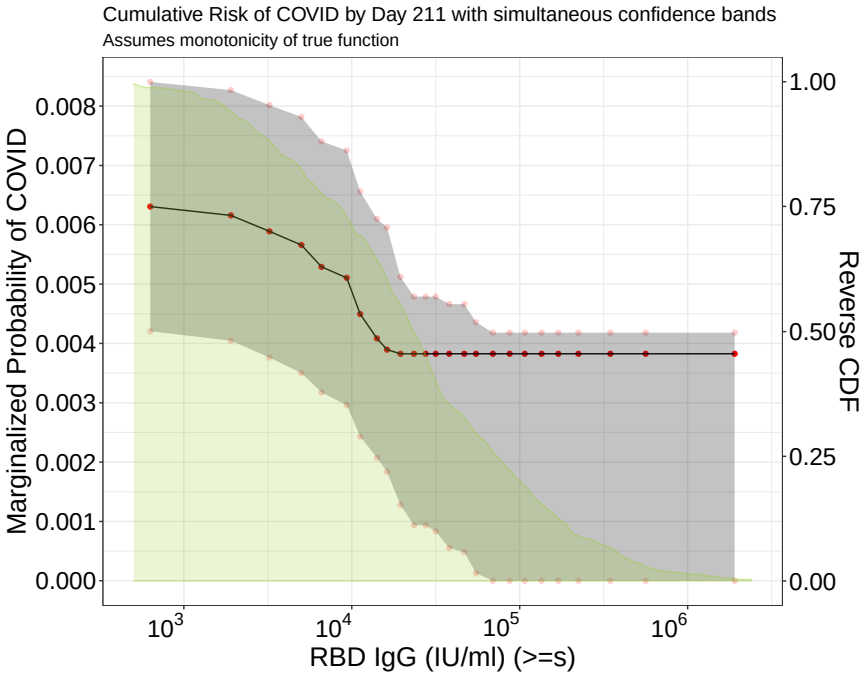

Figure 36: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold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

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

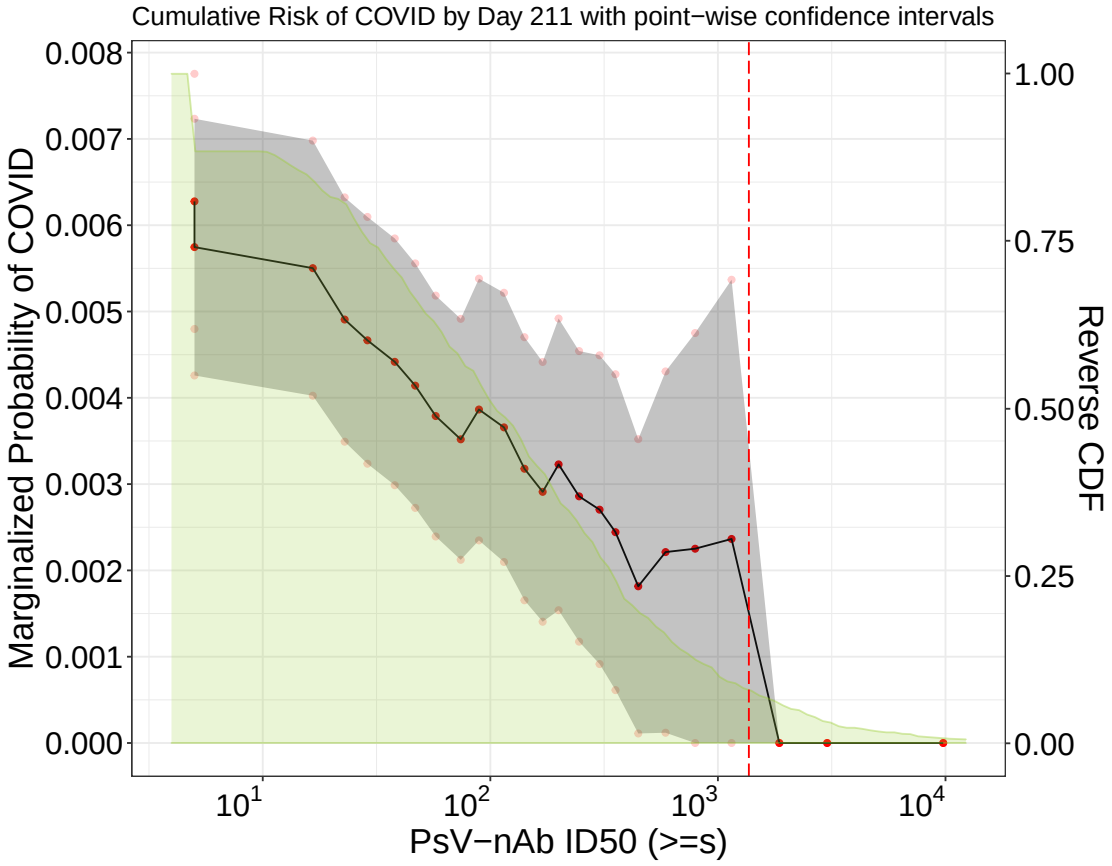

Figure 37: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00628	0.00480	0.00775
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.

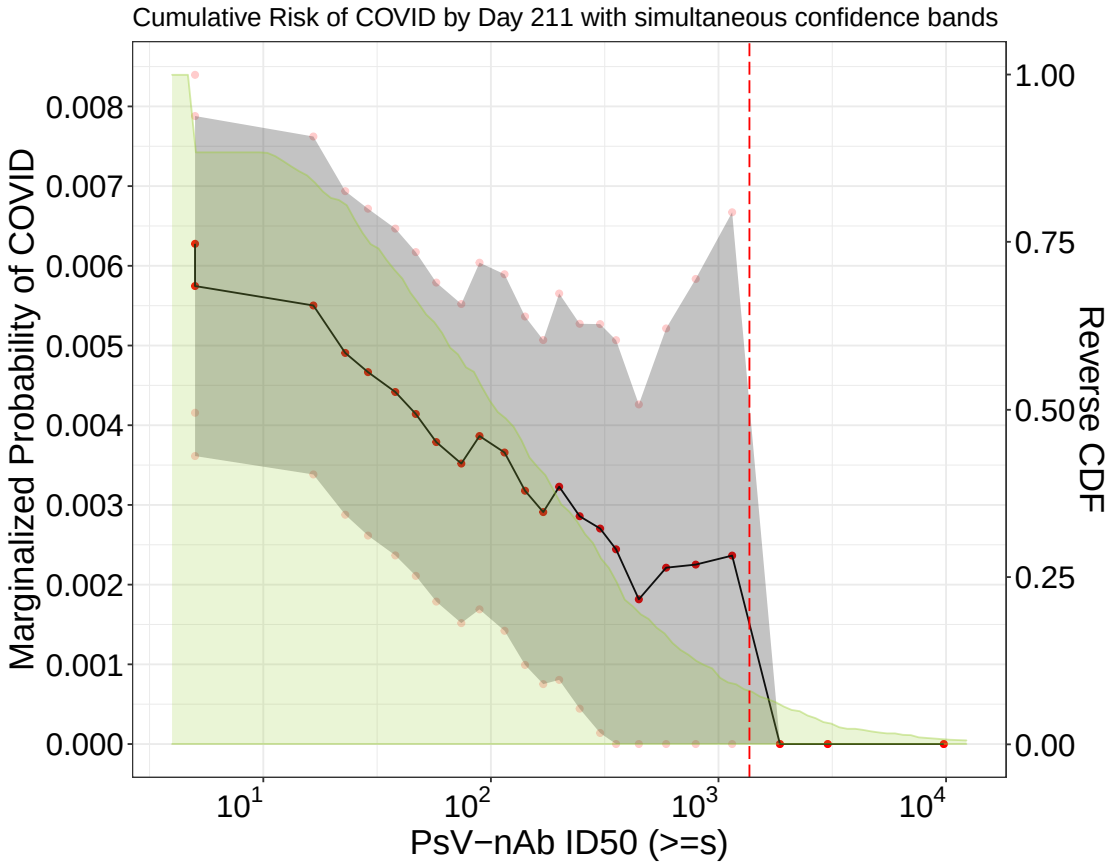

Figure 39: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00628	0.00416	0.00840
1.356	2.27*10^1	0.00491	0.00288	0.00694
1.575	3.76*10^1	0.00442	0.00237	0.00647
1.868	7.38*10^1	0.00352	0.00152	0.00552
2.055	1.14*10^2	0.00366	0.00142	0.00589
2.303	2.01*10^2	0.00323	0.00080	0.00565
2.481	3.03*10^2	0.00270	0.00014	0.00527
2.770	5.89*10^2	0.00221	0.00000	0.00521
3.056	1.14*10^3	0.00236	0.00000	0.00667
3.989	9.75*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

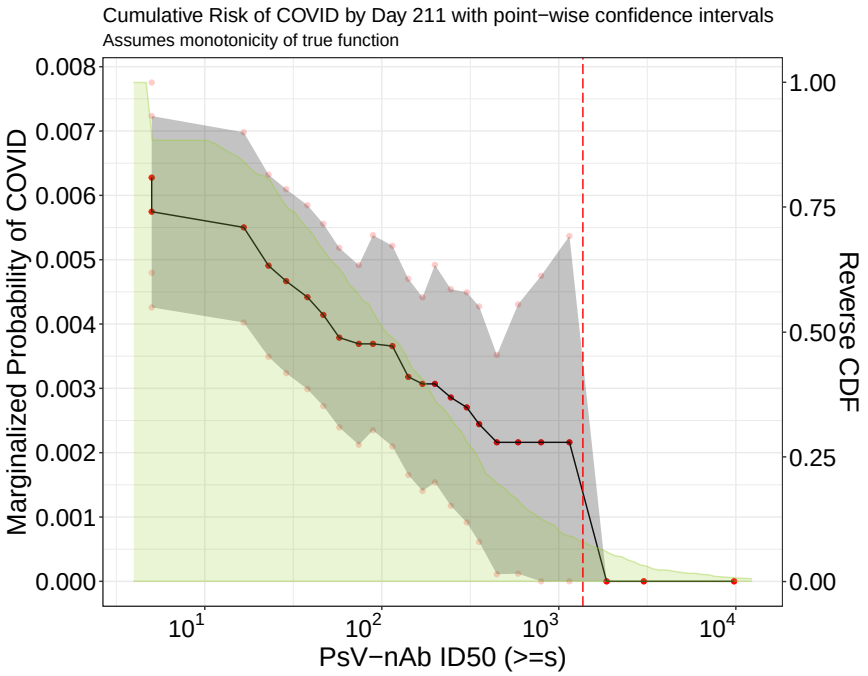

Figure 41: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed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

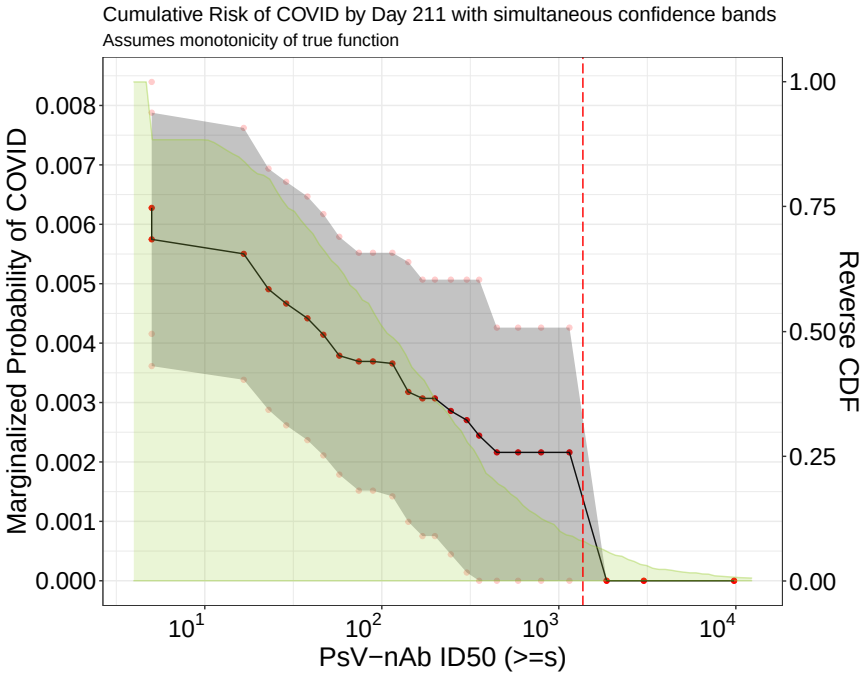

Figure 42: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence intervals. The dashed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

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

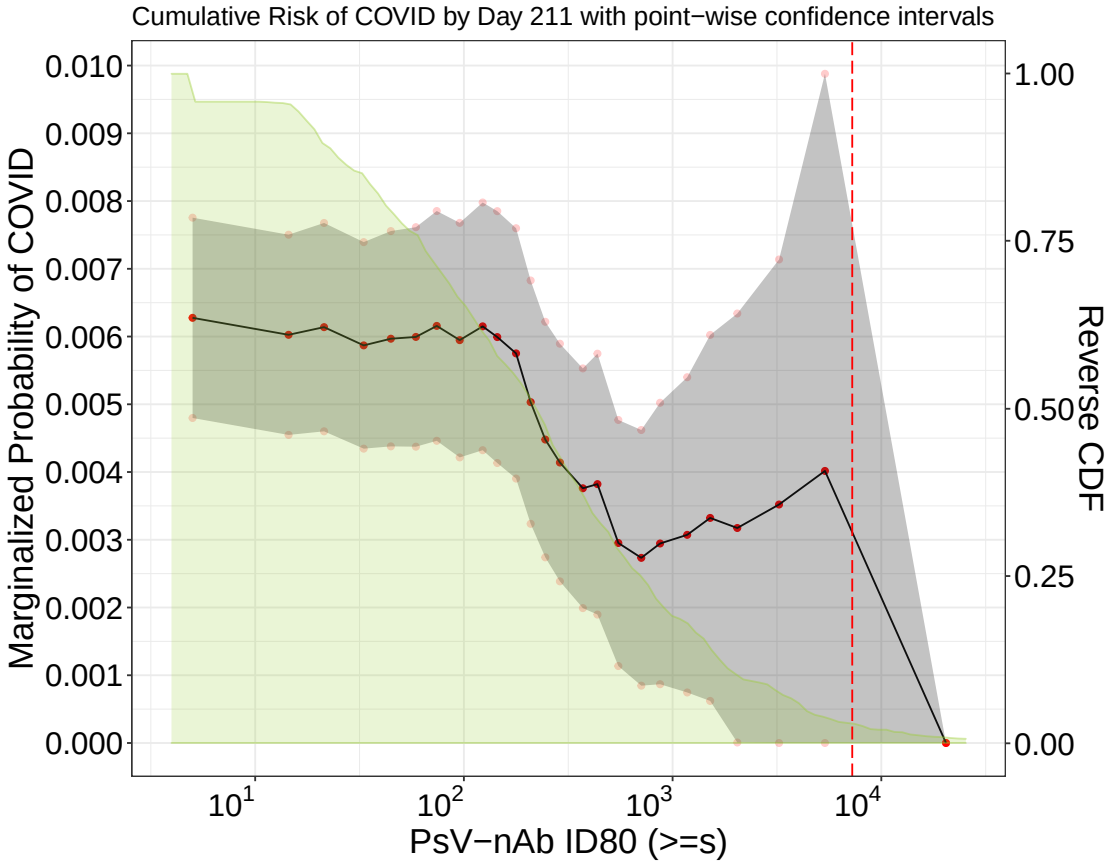

Figure 43: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00628	0.00480	0.00775
1.515	3.27*10^1	0.00587	0.00435	0.00739
1.765	5.82*10^1	0.00599	0.00437	0.00761
2.088	1.22*10^2	0.00615	0.00432	0.00798
2.324	2.11*10^2	0.00503	0.00324	0.00683
2.462	2.90*10^2	0.00414	0.00239	0.00589
2.744	5.55*10^2	0.00295	0.00114	0.00477
3.070	1.17*10^3	0.00307	0.00075	0.00540
3.314	2.06*10^3	0.00317	0.00001	0.00634
4.305	2.02*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.

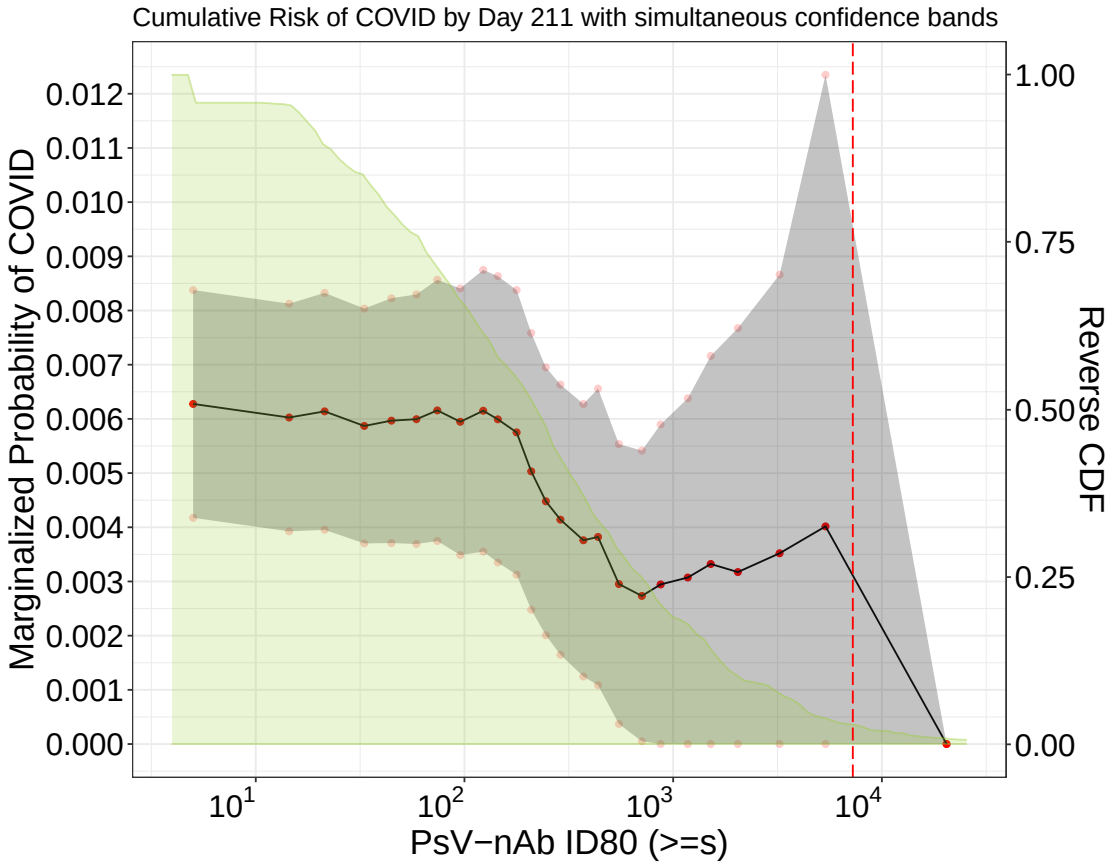

Figure 45: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

log10-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	5.00*10^0	0.00628	0.00417	0.00838
1.515	3.27*10^1	0.00587	0.00370	0.00804
1.765	5.82*10^1	0.00599	0.00369	0.00830
2.088	1.22*10^2	0.00615	0.00355	0.00875
2.324	2.11*10^2	0.00503	0.00248	0.00758
2.462	2.90*10^2	0.00414	0.00165	0.00663
2.744	5.55*10^2	0.00295	0.00037	0.00553
3.070	1.17*10^3	0.00307	0.00000	0.00638
3.314	2.06*10^3	0.00317	0.00000	0.00767
4.305	2.02*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

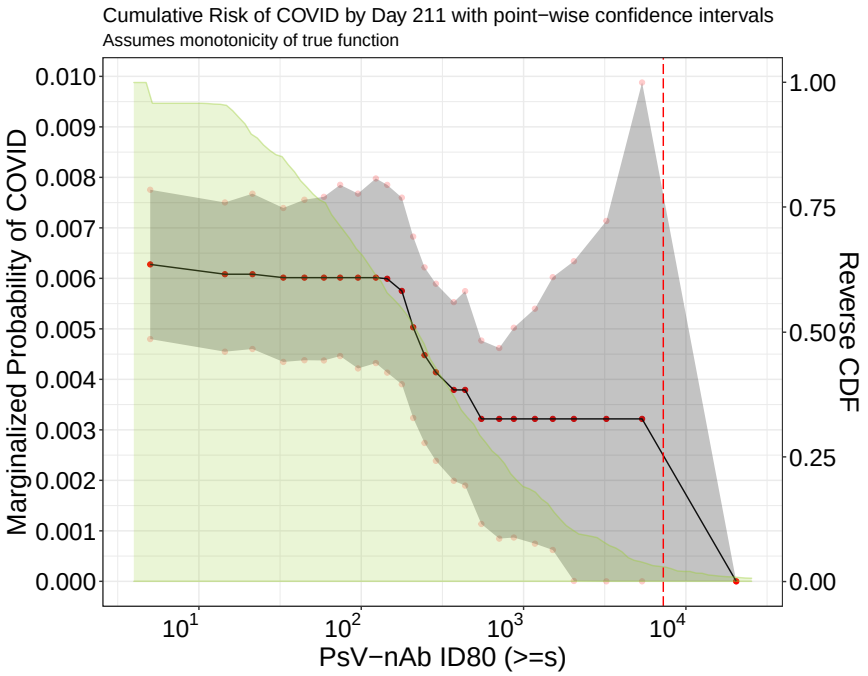

Figure 47: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed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

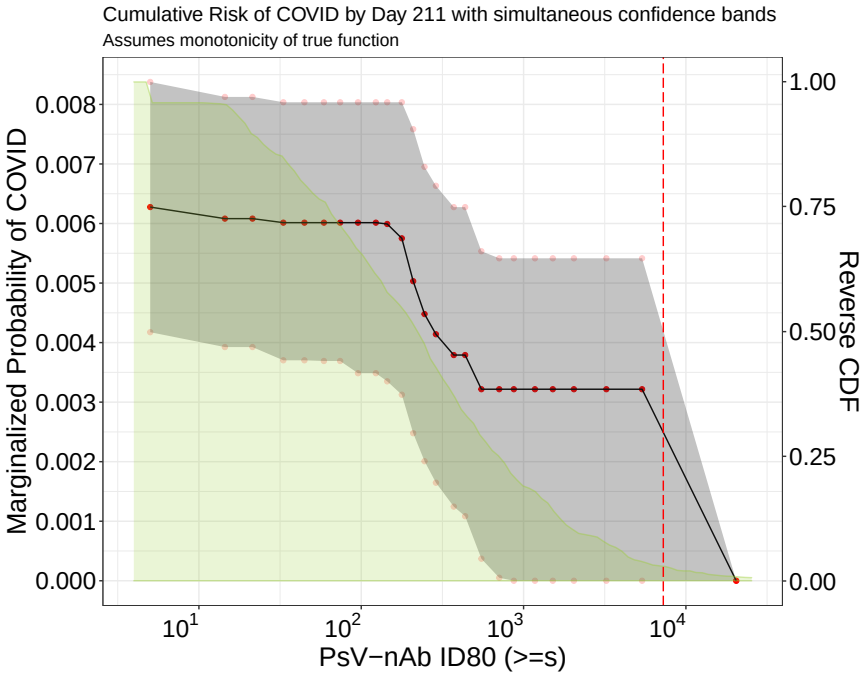

Figure 48: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence intervals. The dashed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