

COVID-19 Correlates of Risk Analysis Report

COVID-19 Prevention Network (CoVPN) Biostatistics Team

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Chapter 1

Univariate CoR: Nonparametric Threshold Modeling

An extension of the unadjusted nonparametric threshold-searching approach developed in (???), 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.

1.0.1 Day 57 Spike protein antibody

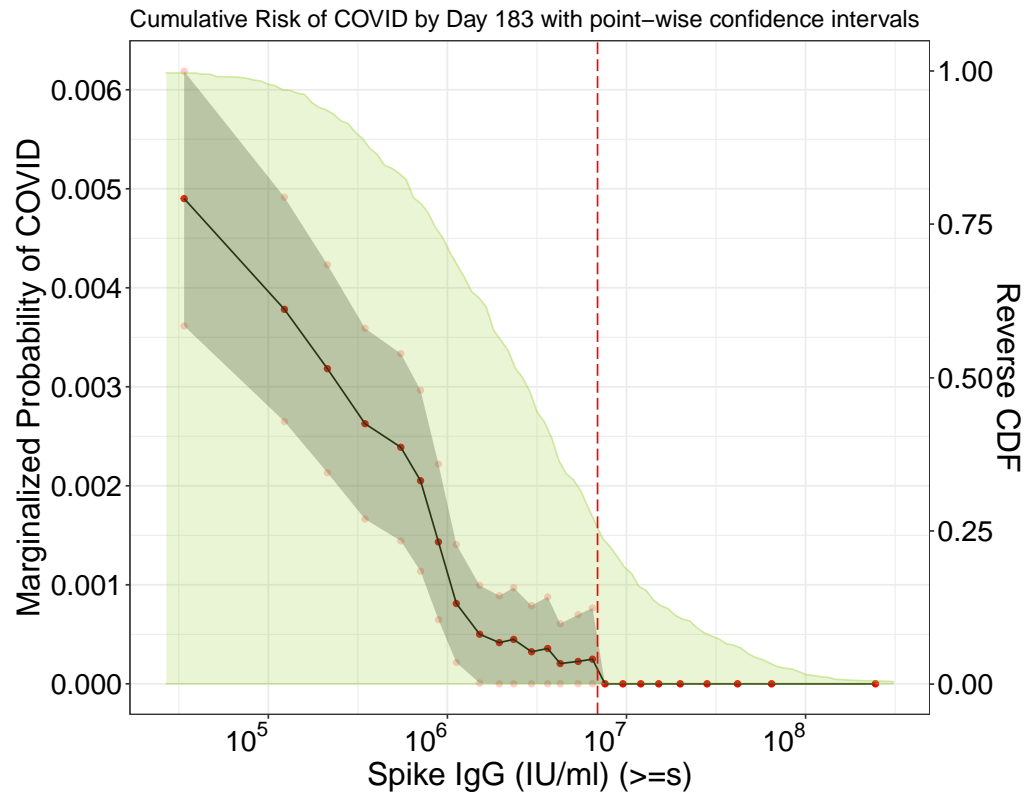


Figure 1.1: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.1: Table of risk estimates for range of thresholds of Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals.

\log_{10} -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

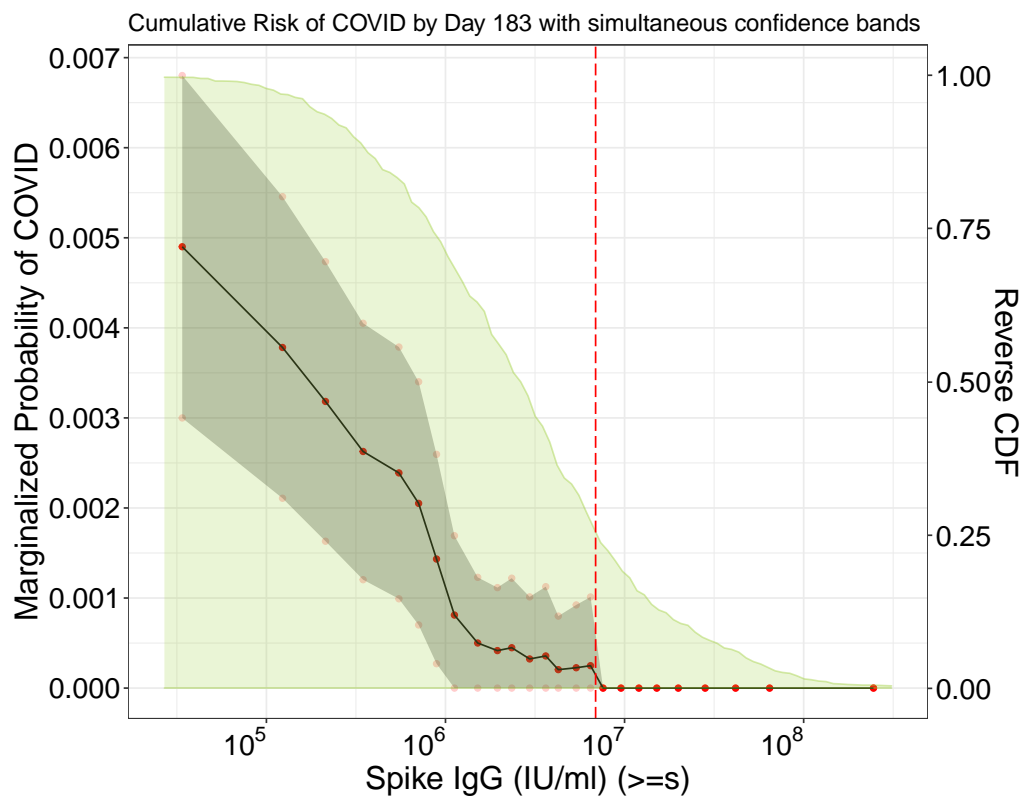


Figure 1.2: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.2: Table of risk estimates for range of thresholds of Day 57 Spike protein antibody activity levels with point-wise 95% simultaneous confidence intervals.

\log_{10} -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

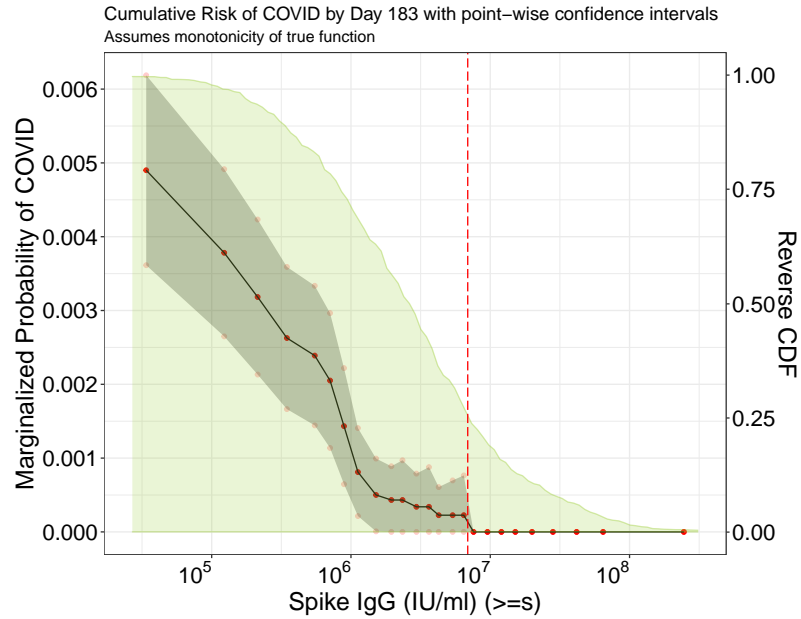


Figure 1.3: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

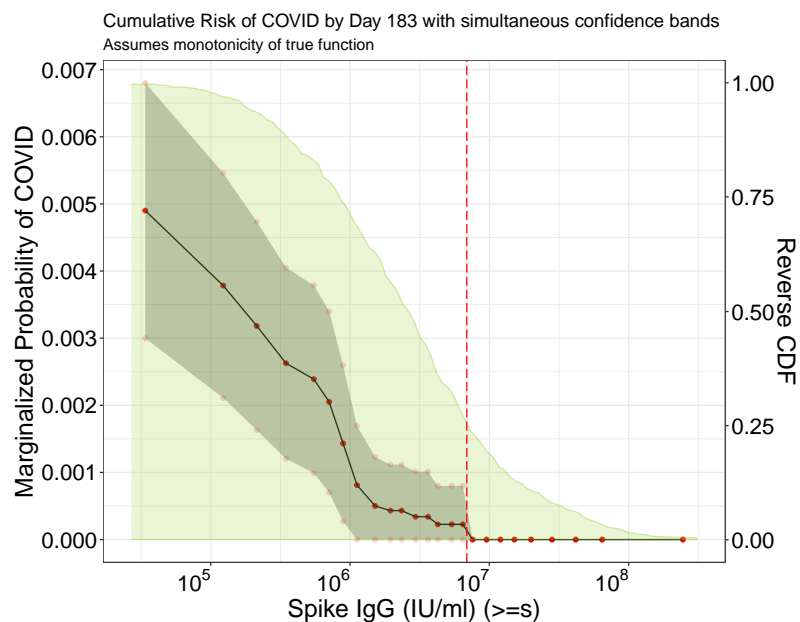


Figure 1.4: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

1.0.2 Day 57 RBD binding antibody

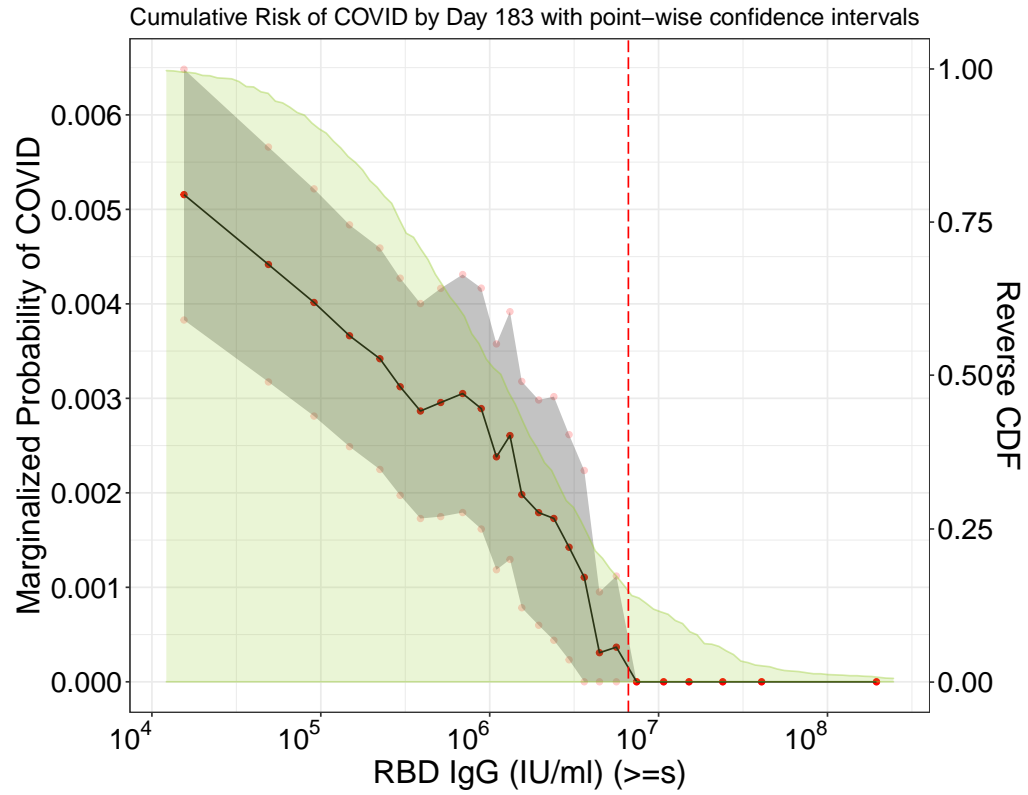


Figure 1.5: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.3: Table of risk estimates for range of thresholds of Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals.

\log_{10} -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

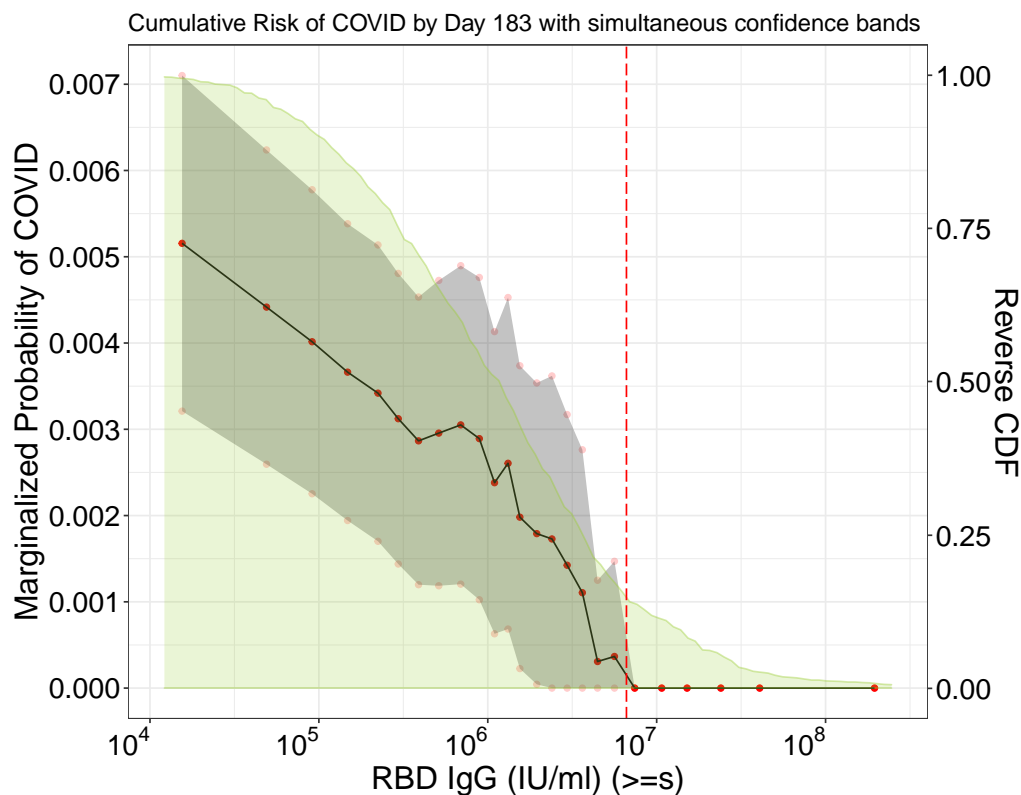


Figure 1.6: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.4: Table of risk estimates for range of thresholds of Day 57 RBD binding antibody activity levels with point-wise 95% simultaneous confidence intervals.

\log_{10} -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

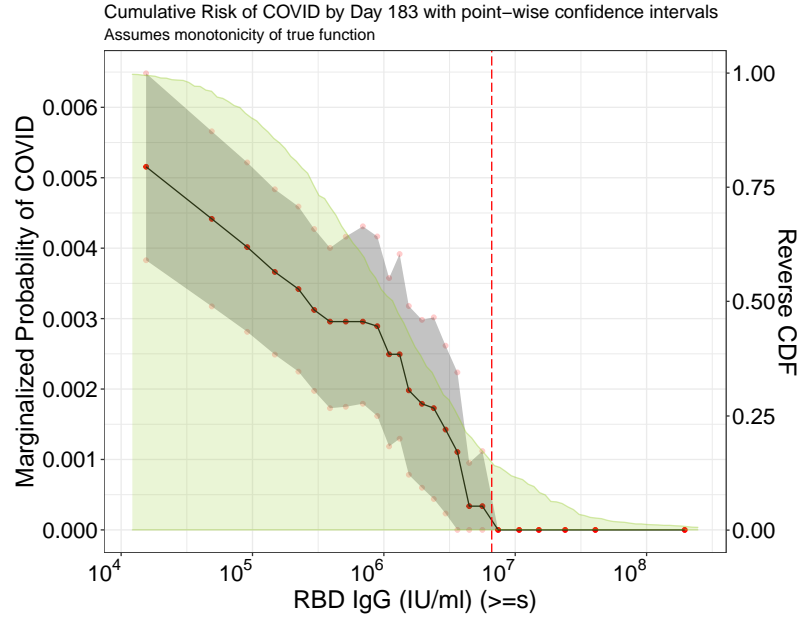


Figure 1.7: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

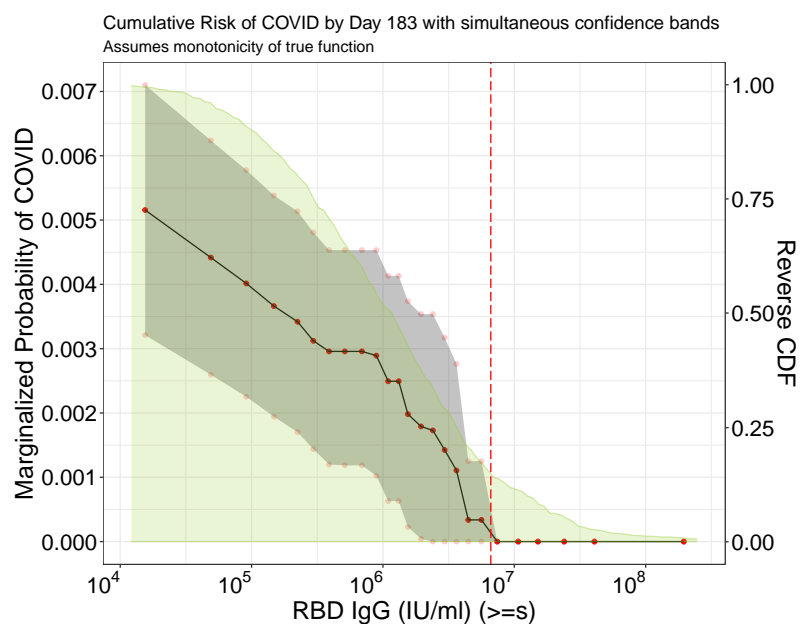


Figure 1.8: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

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

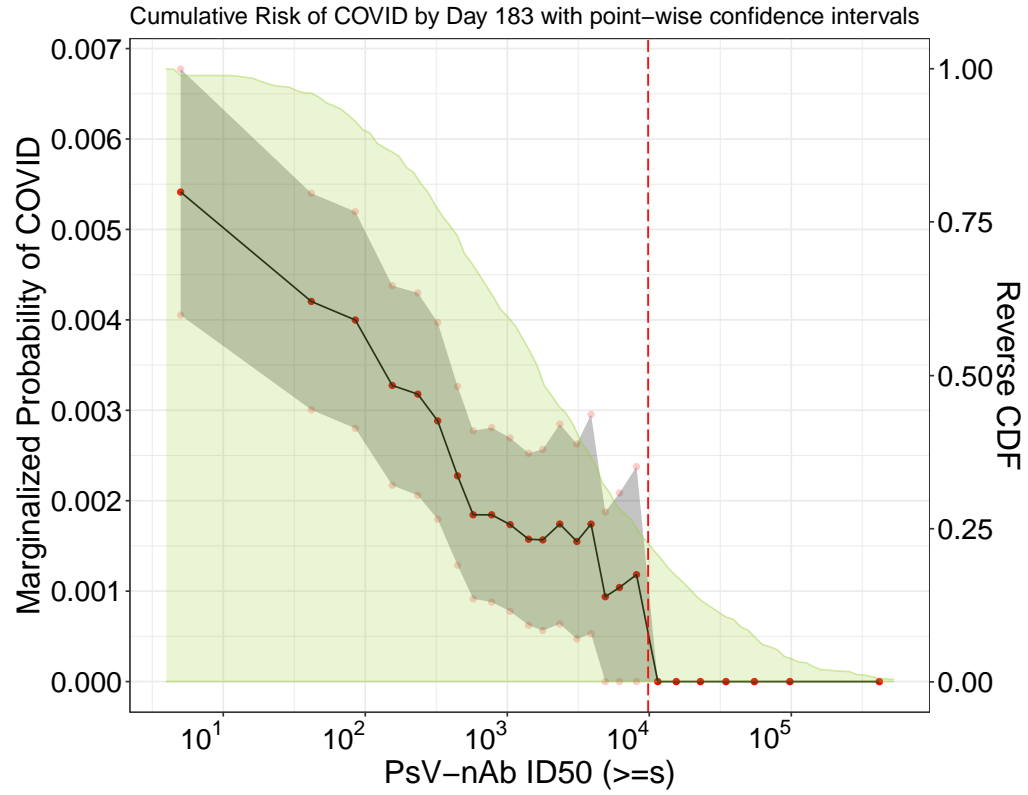


Figure 1.9: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.5: 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.

\log_{10} -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

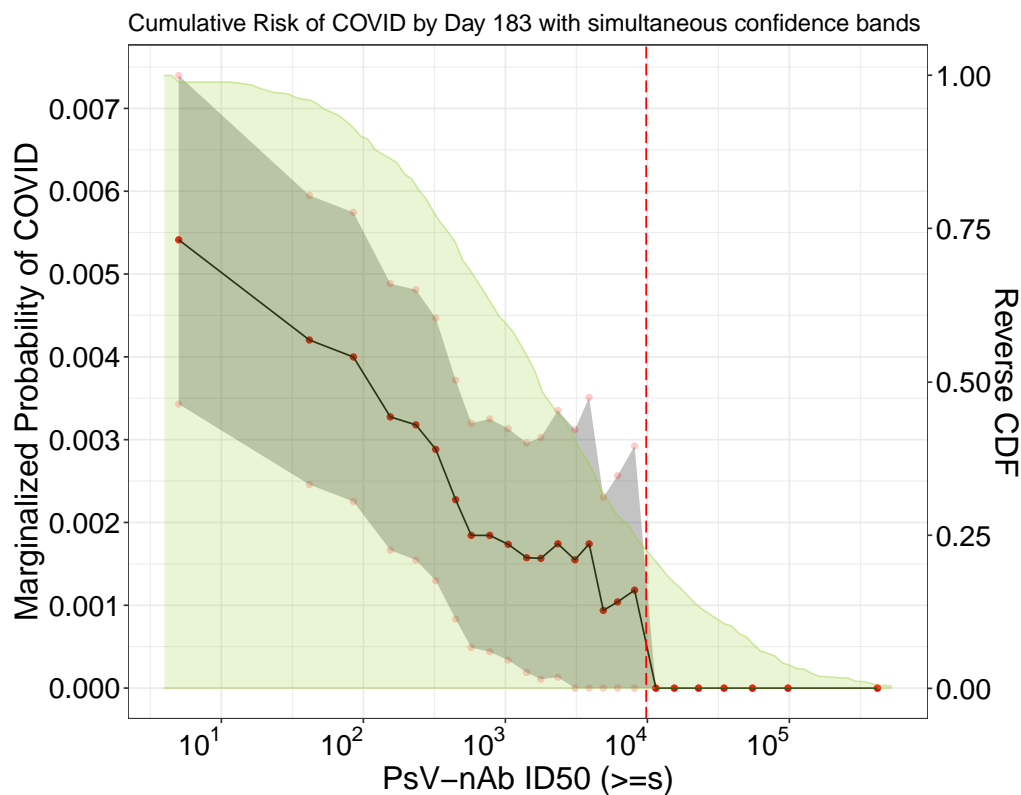


Figure 1.10: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.6: Table of risk estimates for range of thresholds of Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% simultaneous confidence intervals.

\log_{10} -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

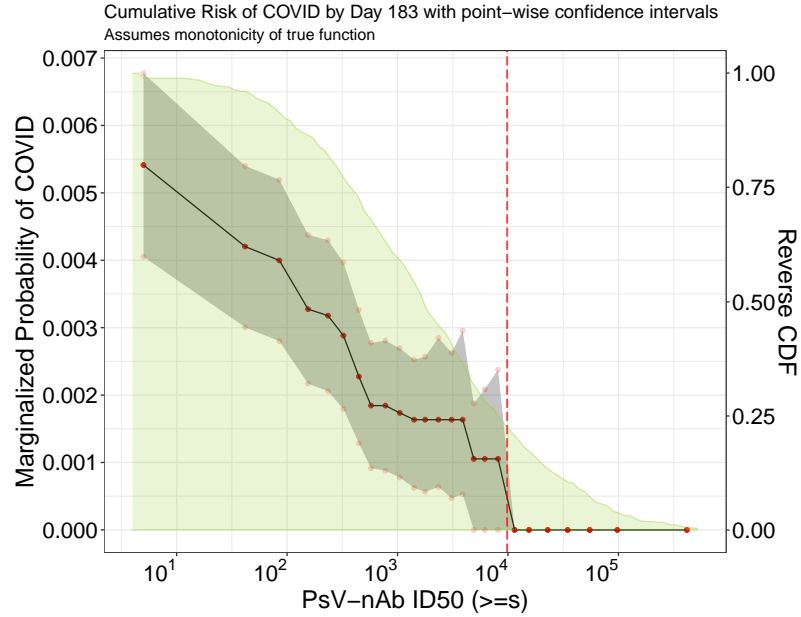


Figure 1.11: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

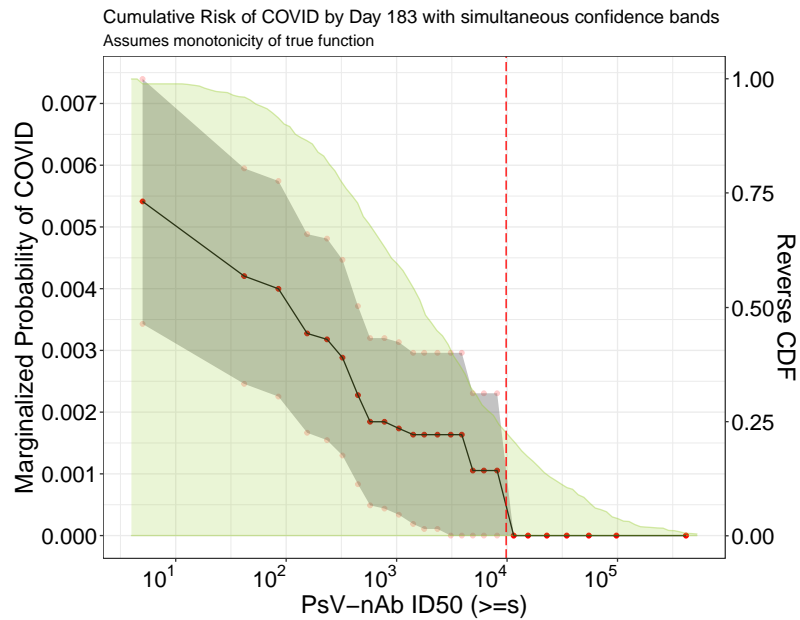


Figure 1.12: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

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

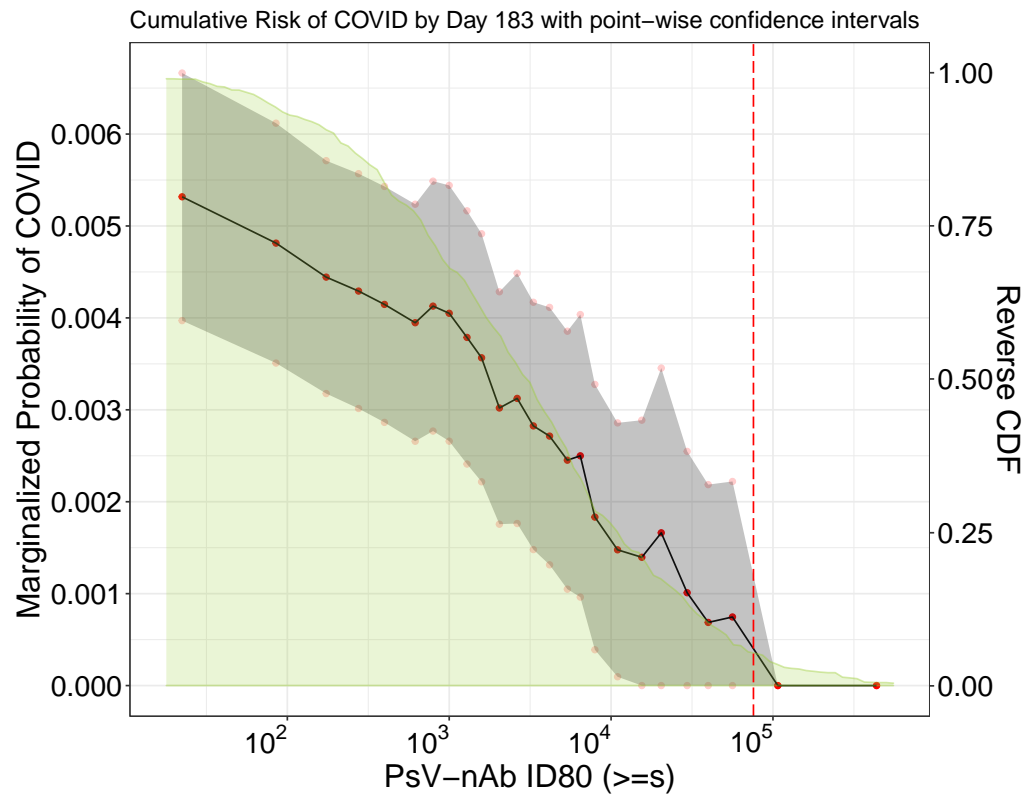


Figure 1.13: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.7: 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.

\log_{10} -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

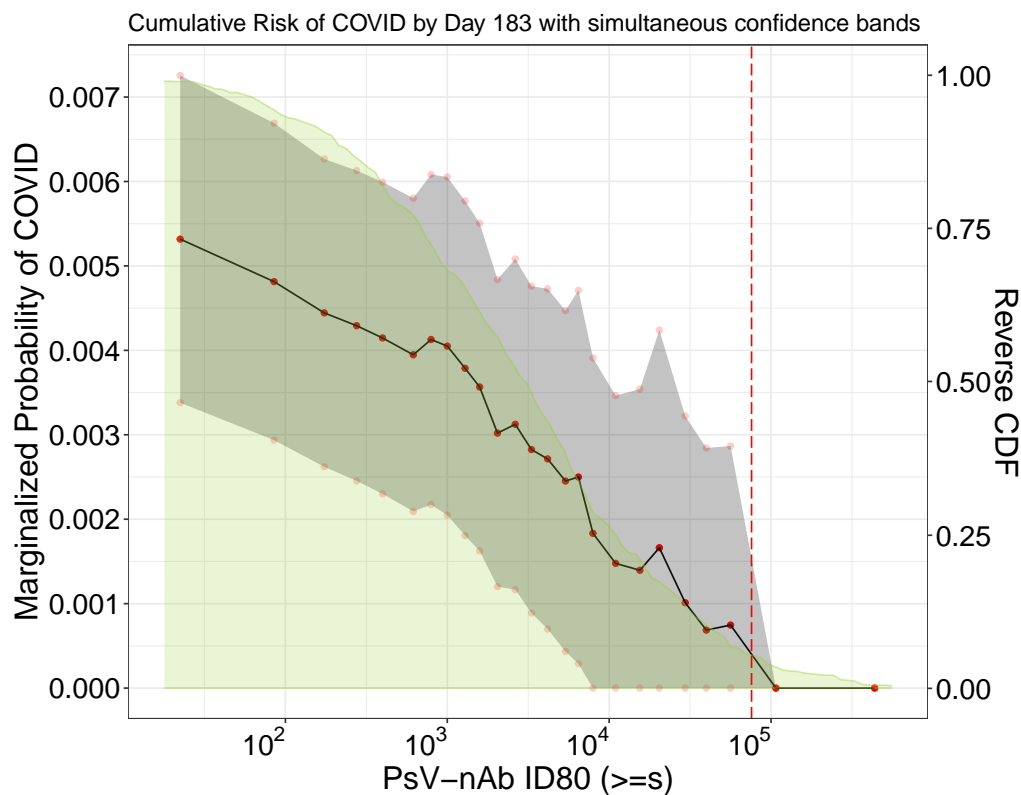


Figure 1.14: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.8: Table of risk estimates for range of thresholds of Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% simultaneous confidence intervals.

\log_{10} -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

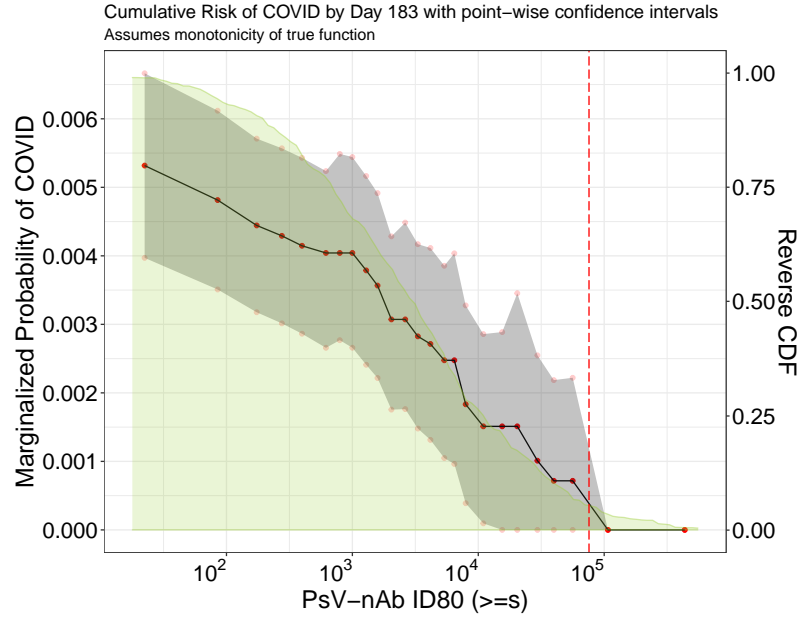


Figure 1.15: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

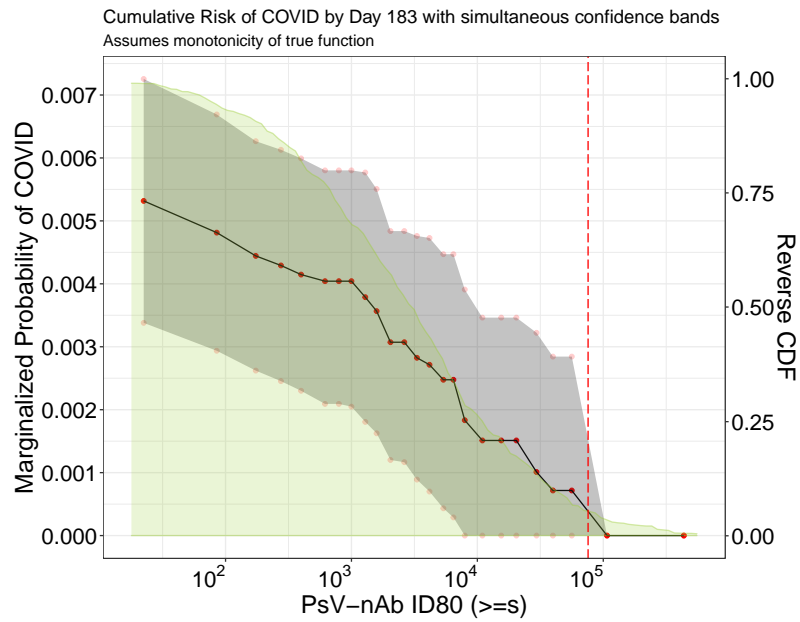


Figure 1.16: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

1.0.5 Day 29 Spike protein antibody

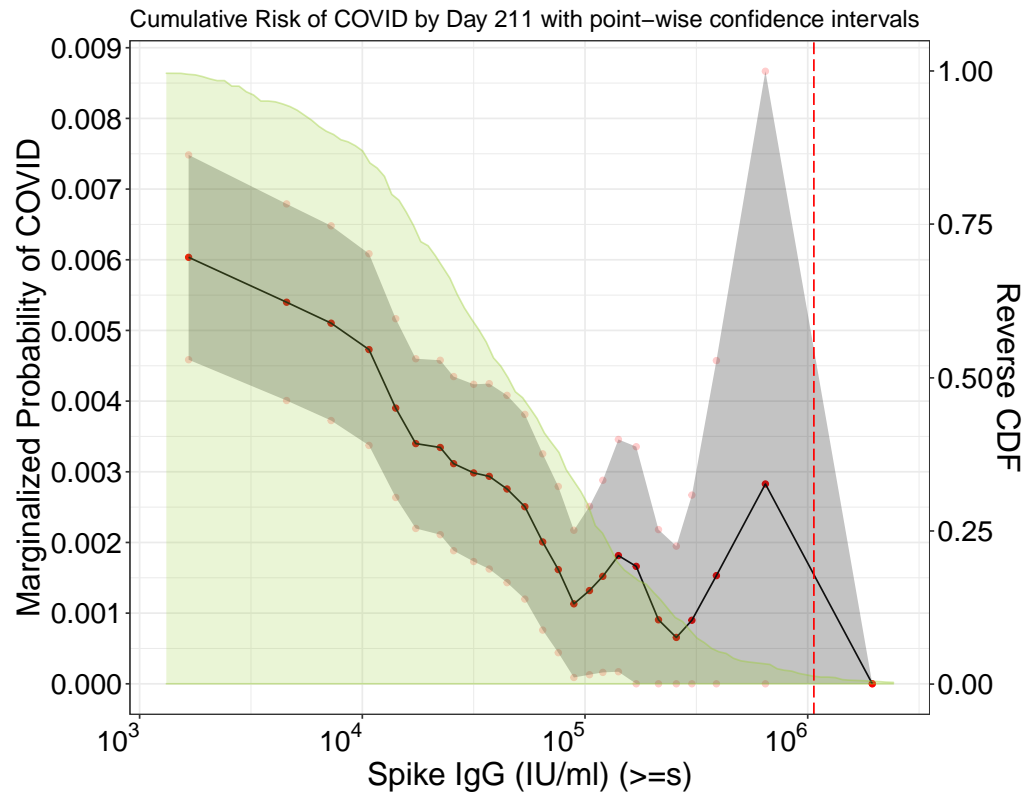


Figure 1.17: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.9: Table of risk estimates for range of thresholds of Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals.

\log_{10} -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

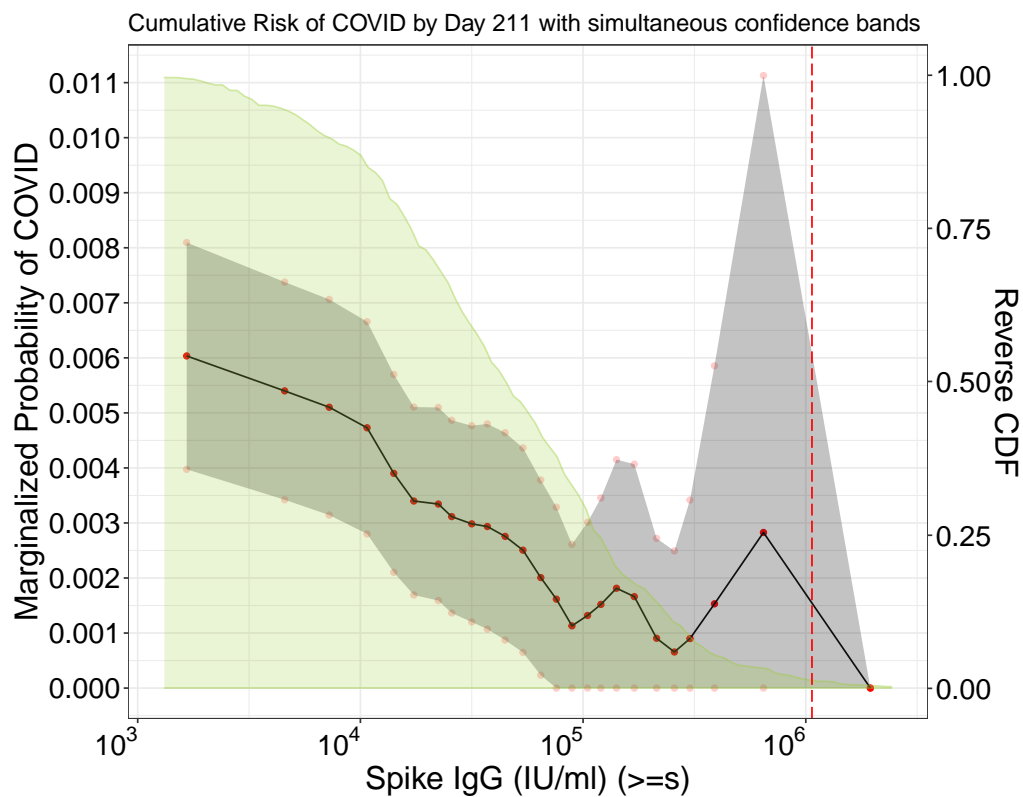


Figure 1.18: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.10: Table of risk estimates for range of thresholds of Day 29 Spike protein antibody activity levels with point-wise 95% simultaneous confidence intervals.

\log_{10} -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

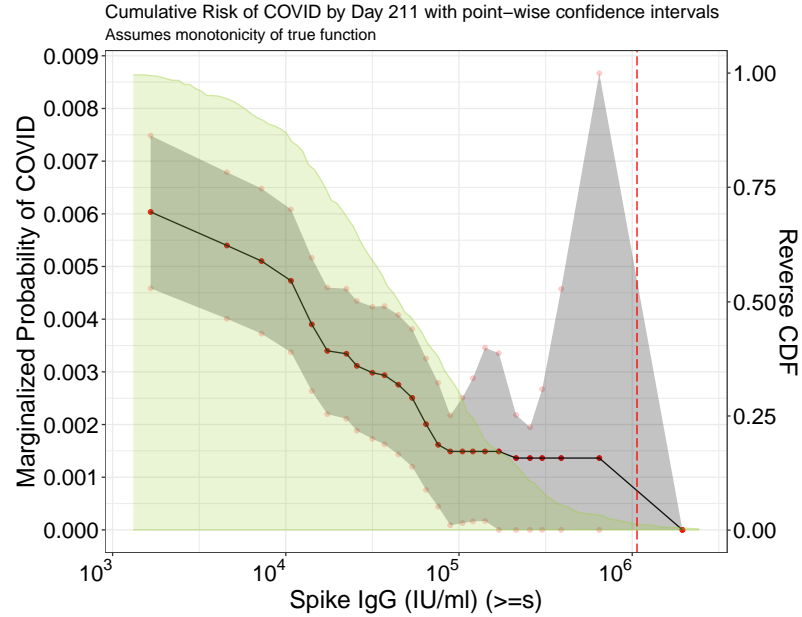


Figure 1.19: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

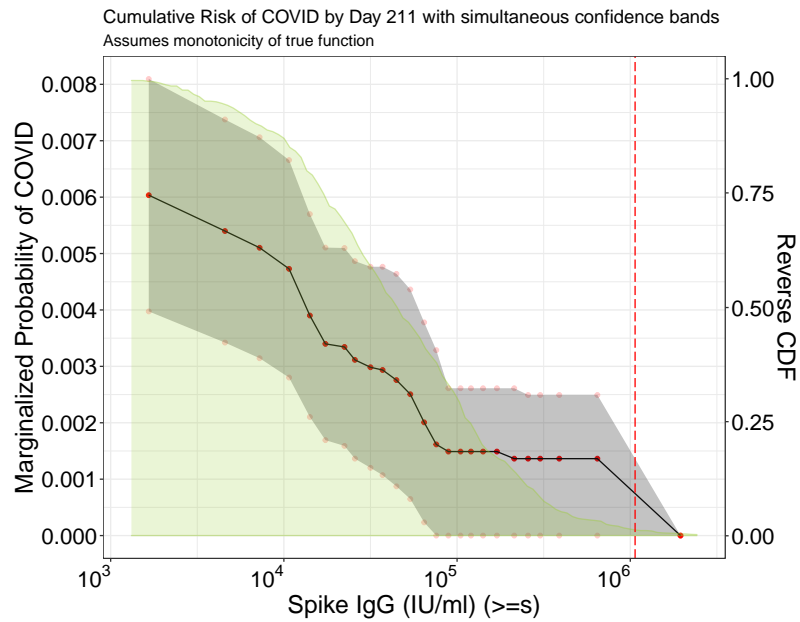


Figure 1.20: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

1.0.6 Day 29 RBD binding antibody

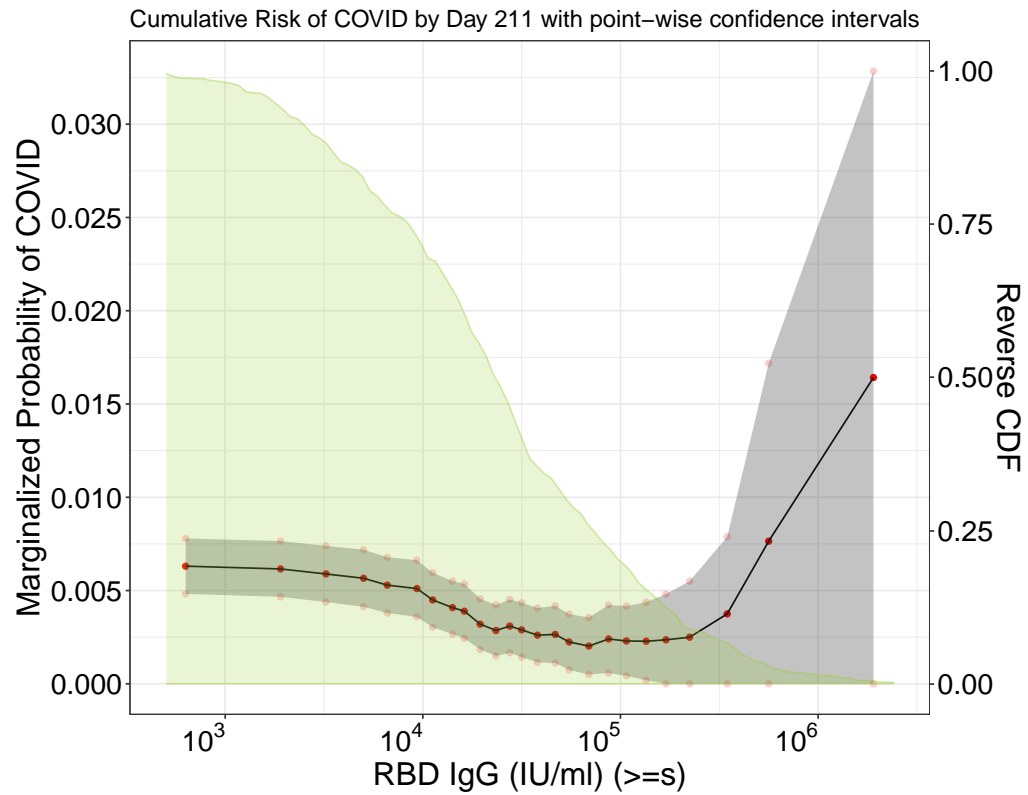


Figure 1.21: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.11: Table of risk estimates for range of thresholds of Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals.

\log_{10} -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

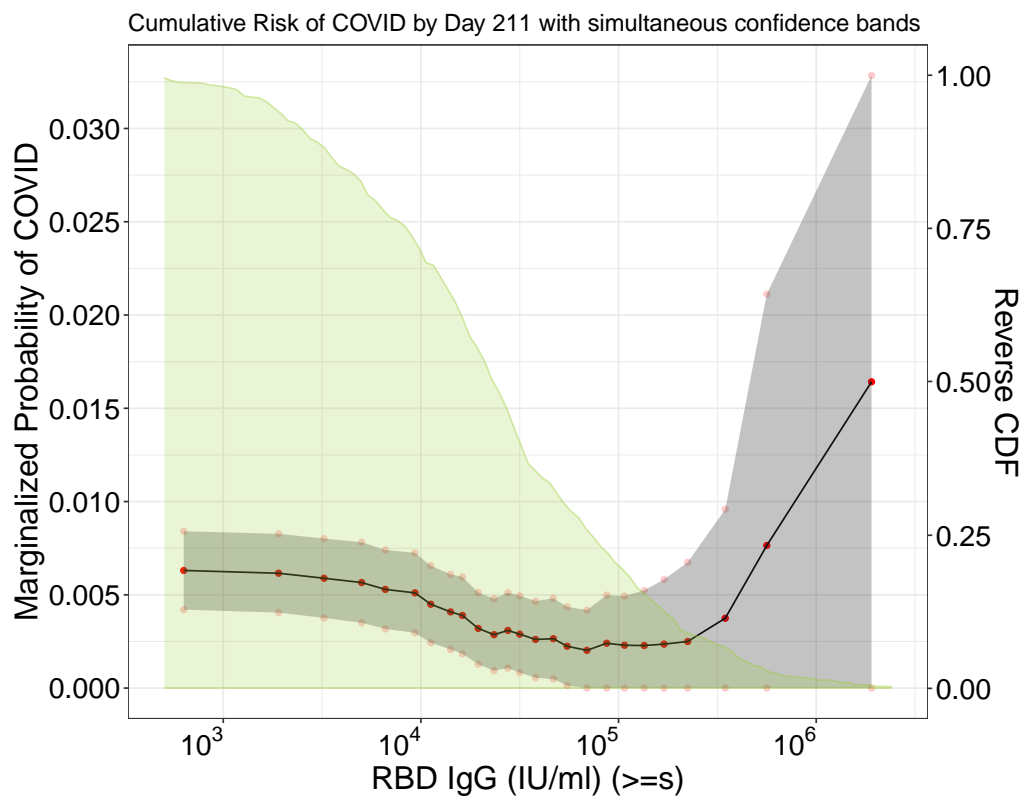


Figure 1.22: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.12: Table of risk estimates for range of thresholds of Day 29 RBD binding antibody activity levels with point-wise 95% simultaneous confidence intervals.

\log_{10} -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

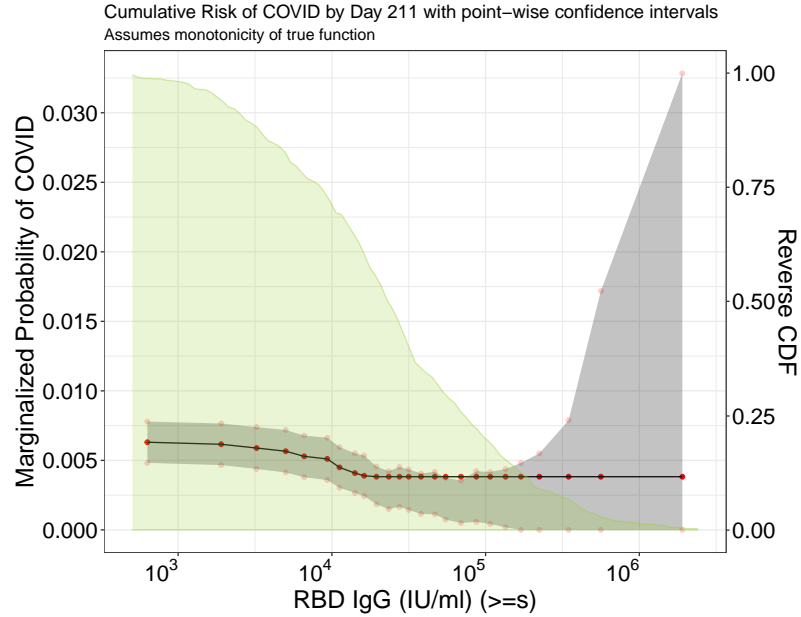


Figure 1.23: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

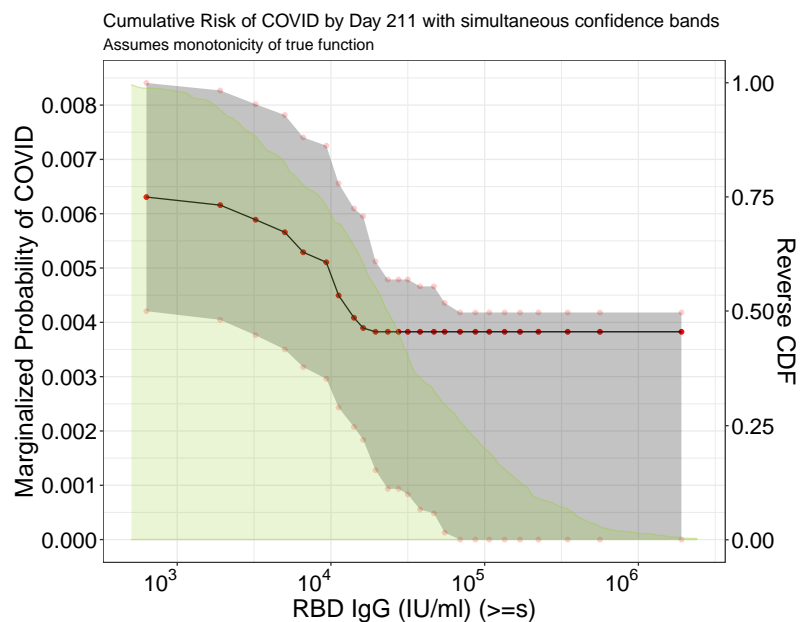


Figure 1.24: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

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

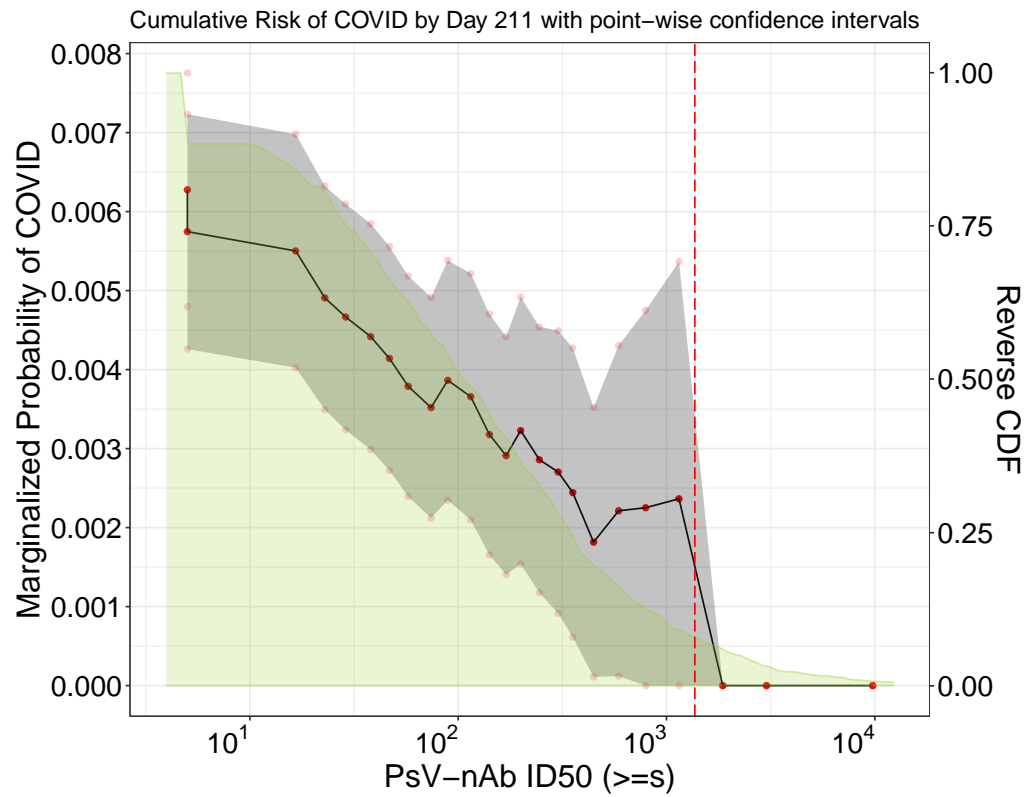


Figure 1.25: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.13: 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.

\log_{10} -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

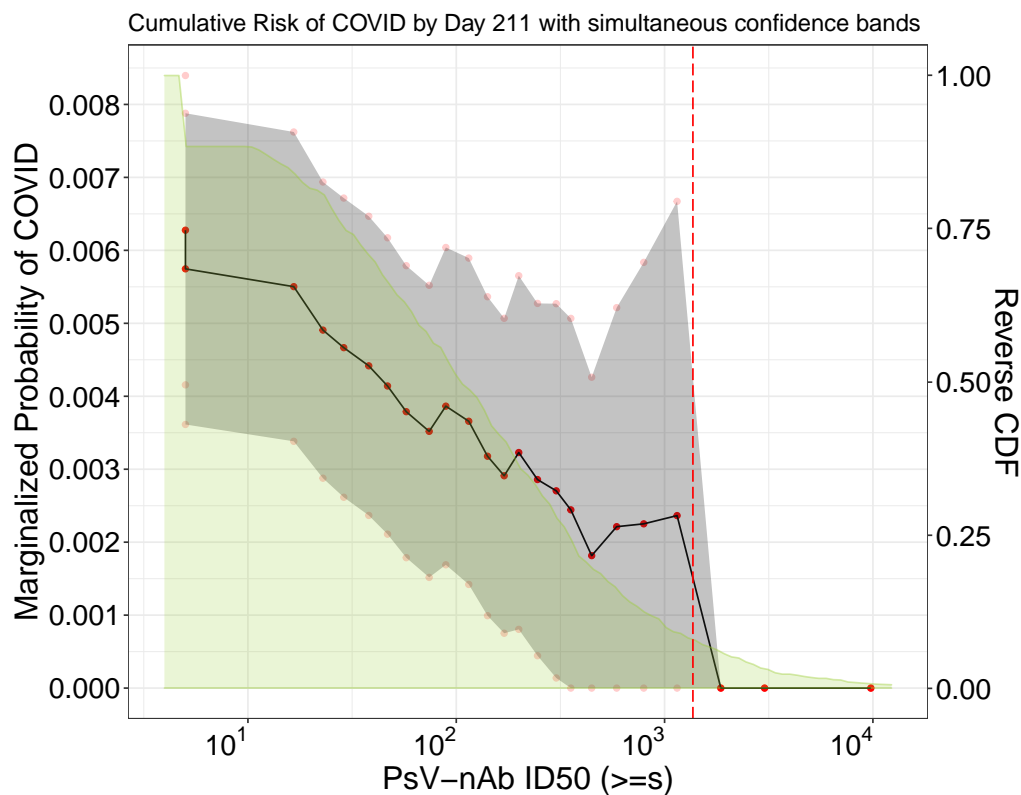


Figure 1.26: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.14: Table of risk estimates for range of thresholds of Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% simultaneous confidence intervals.

\log_{10} -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

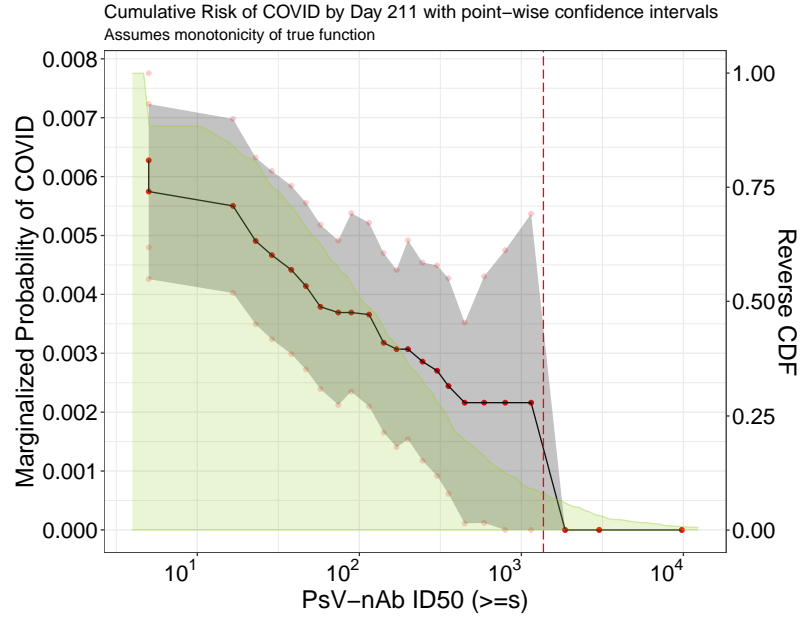


Figure 1.27: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

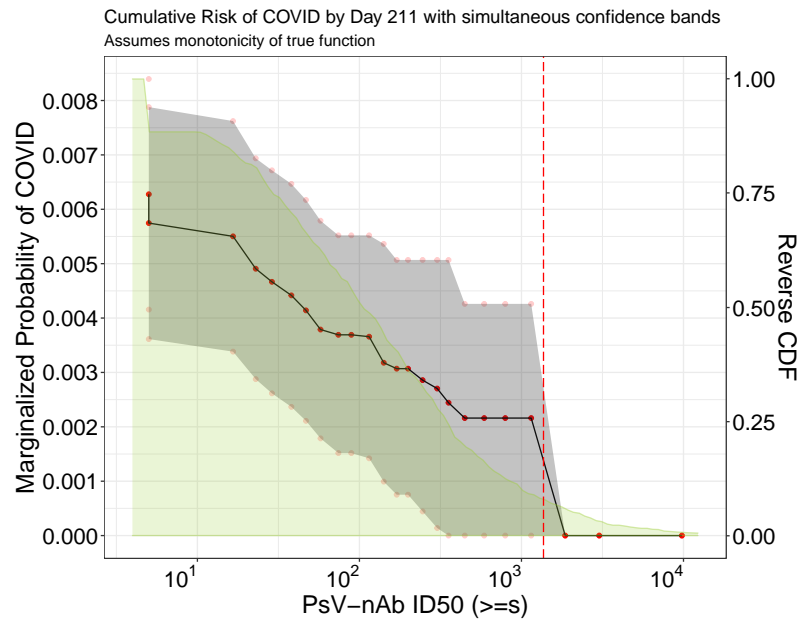


Figure 1.28: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

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

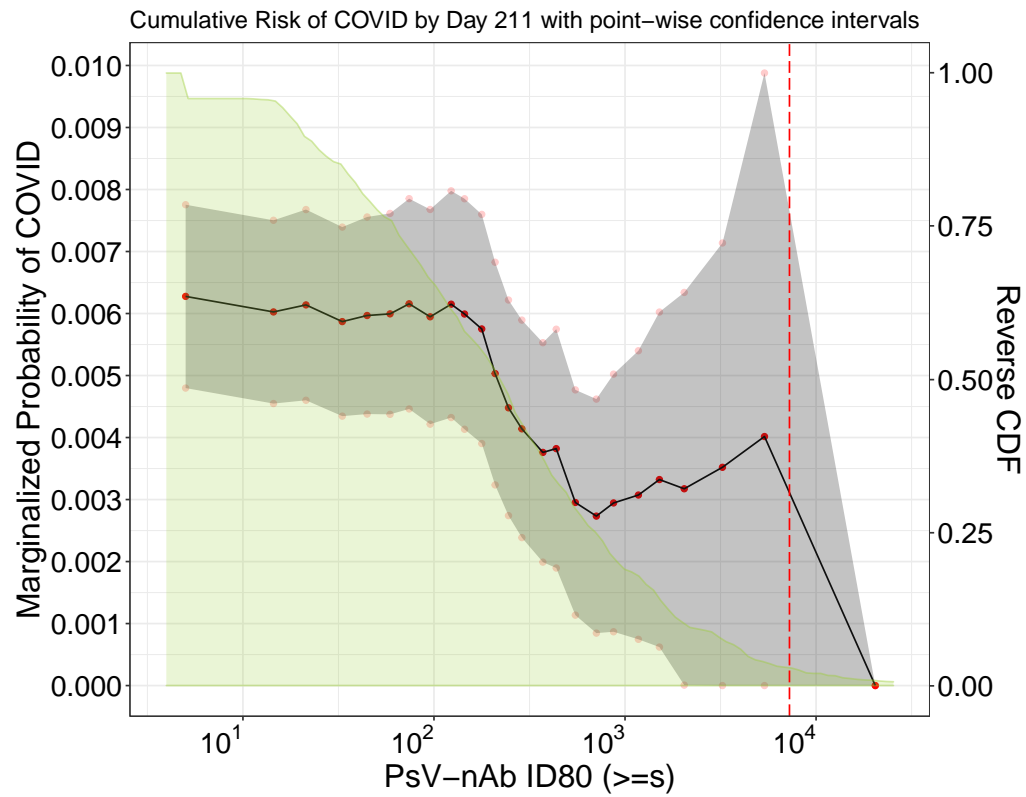


Figure 1.29: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.15: 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.

\log_{10} -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

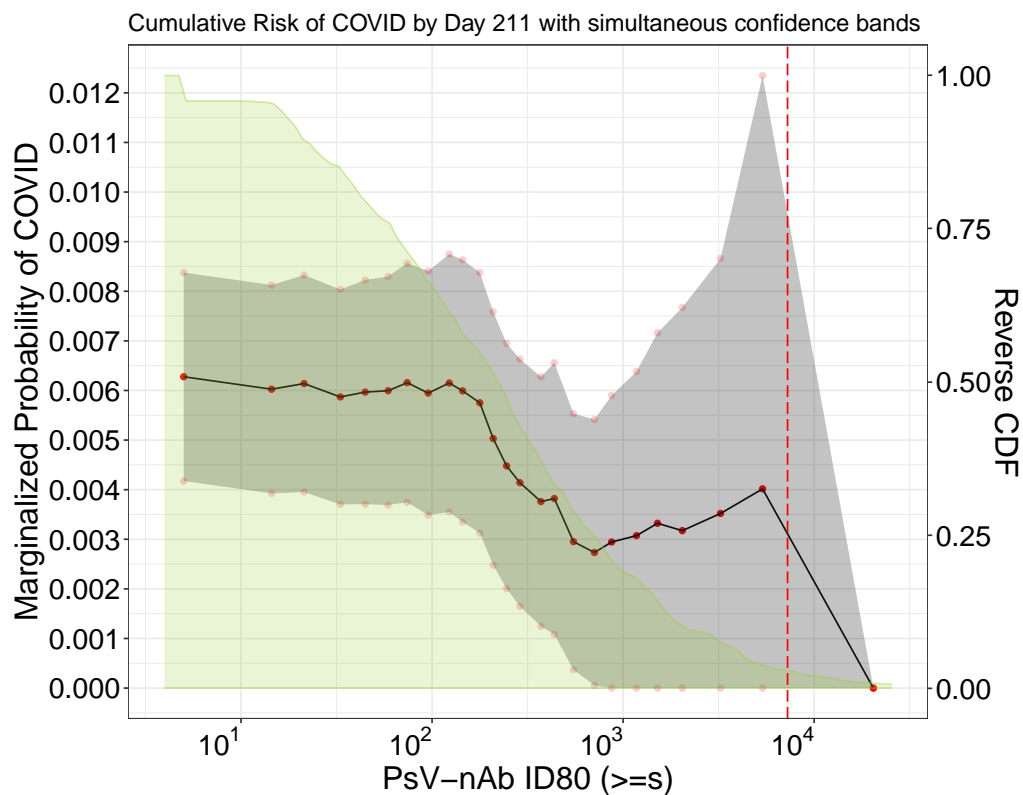


Figure 1.30: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence bands. The dashed red line marks the threshold after which no more COVID events are observed.

Table 1.16: Table of risk estimates for range of thresholds of Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% simultaneous confidence intervals.

\log_{10} -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

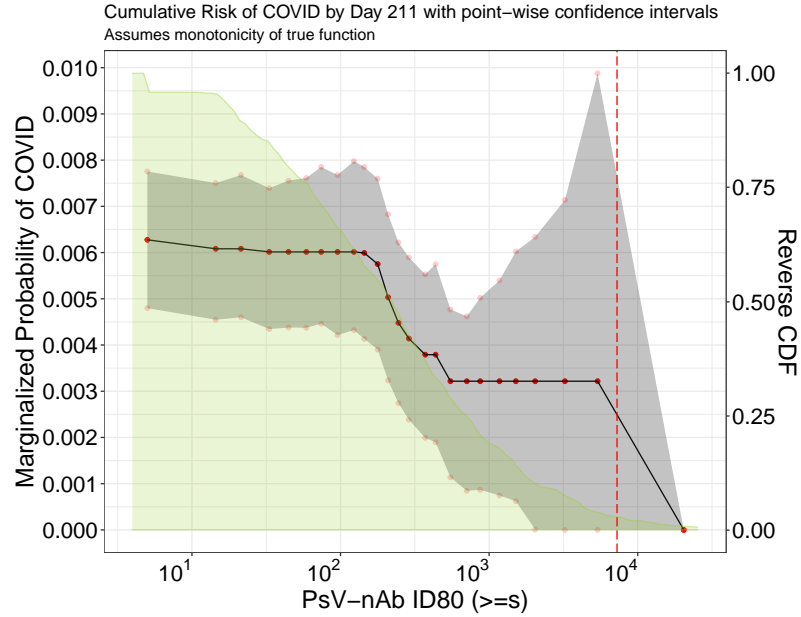


Figure 1.31: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with point-wise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

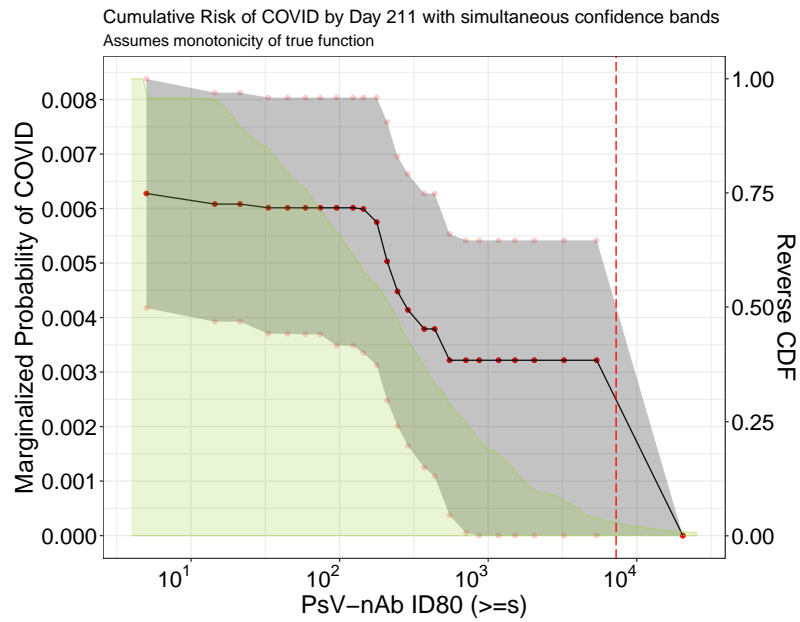


Figure 1.32: Assuming nonincreasing monotonicity of the true function, the plot shows the estimated (monotone) adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) activity levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.