COVID-19 Correlates of Risk Analysis Report

COVID-19 Prevention Network (CoVPN) Biostatistics Team

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Chapter 1

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Figure 1.67: (Mock data) violinplots of Pseudovirus Neutralization ID50: baseline negative placebo arm by age (2 timepoints)

Figure 1.68: (Mock data) violinplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm by age (2 timepoints)

Figure 1.69: (Mock data) violinplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by age (2 timepoints)

Figure 1.70: (Mock data) violinplots of Pseudovirus Neutralization ID80: baseline negative vaccine arm by age (2 timepoints)

Figure 1.71: (Mock data) lineplots of Binding Antibody to Spike: baseline negative placebo arm by age (3 timepoints)

Figure 1.72: (Mock data) lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age (3 timepoints)

Figure 1.73: (Mock data) lineplots of Binding Antibody to RBD: baseline negative placebo arm by age (3 timepoints)

Figure 1.74: (Mock data) lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age (3 timepoints)

Figure 1.75: (Mock data) lineplots of Pseudovirus Neutralization ID50: baseline negative placebo arm by age (3 timepoints)

Figure 1.76: (Mock data) lineplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm by age (3 timepoints)

Figure 1.77: (Mock data) lineplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by age (3 timepoints)

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Figure 1.80: (Mock data) violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age (3 timepoints)

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Figure 1.82: (Mock data) violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age (3 timepoints)

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Figure 1.86: (Mock data) violinplots of Pseudovirus Neutralization ID80: baseline negative vaccine arm by age (3 timepoints)

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Figure 1.155: (Mock data) lineplots of Pseudovirus Neutralization ID50: baseline negative placebo arm by sex assigned at birth (2 timepoints)

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Figure 1.157: (Mock data) lineplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by sex assigned at birth (2 timepoints)

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Figure 1.160: (Mock data) violinplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth (2 timepoints)

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Figure 1.164: (Mock data) violinplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm by sex assigned at birth (2 timepoints)

Figure 1.165: (Mock data) violinplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by sex assigned at birth (2 timepoints)

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Figure 1.170: (Mock data) lineplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth (3 timepoints)

Figure 1.171: (Mock data) lineplots of Pseudovirus Neutralization ID50: baseline negative placebo arm by sex assigned at birth (3 timepoints)

Figure 1.172: (Mock data) lineplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm by sex assigned at birth (3 timepoints)

Figure 1.173: (Mock data) lineplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by sex assigned at birth (3 timepoints)

Figure 1.174: (Mock data) lineplots of Pseudovirus Neutralization ID80: baseline negative vaccine arm by sex assigned at birth (3 timepoints)

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Figure 1.177: (Mock data) violinplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth (3 timepoints)

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Figure 1.180: (Mock data) violinplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm by sex assigned at birth (3 timepoints)

Figure 1.181: (Mock data) violinplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by sex assigned at birth (3 timepoints)

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Figure 1.187: (Mock data) lineplots of Pseudovirus Neutralization ID50: baseline negative placebo arm by race and ethnic group (2 timepoints)

Figure 1.188: (Mock data) lineplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm by race and ethnic group (2 timepoints)

Figure 1.189: (Mock data) lineplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by race and ethnic group (2 timepoints)

Figure 1.190: (Mock data) lineplots of Pseudovirus Neutralization ID80: baseline negative vaccine arm by race and ethnic group (2 timepoints)

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Figure 1.192: (Mock data) violinplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group (2 timepoints)

Figure 1.193: (Mock data) violinplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group (2 timepoints)

Figure 1.194: (Mock data) violinplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group (2 timepoints)

Figure 1.195: (Mock data) violinplots of Pseudovirus Neutralization ID50: baseline negative placebo arm by race and ethnic group (2 timepoints)

Figure 1.196: (Mock data) violinplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm by race and ethnic group (2 timepoints)

Figure 1.197: (Mock data) violinplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by race and ethnic group (2 timepoints)

Figure 1.198: (Mock data) violinplots of Pseudovirus Neutralization ID80: baseline negative vaccine arm by race and ethnic group (2 timepoints)

Figure 1.199: (Mock data) lineplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group (3 timepoints)

Figure 1.200: (Mock data) lineplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group (3 timepoints)

Figure 1.201: (Mock data) lineplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group (3 timepoints)

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Figure 1.203: (Mock data) lineplots of Pseudovirus Neutralization ID50: baseline negative placebo arm by race and ethnic group (3 timepoints)

Figure 1.204: (Mock data) lineplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm by race and ethnic group (3 timepoints)

Figure 1.205: (Mock data) lineplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by race and ethnic group (3 timepoints)

Figure 1.206: (Mock data) lineplots of Pseudovirus Neutralization ID80: baseline negative vaccine arm by race and ethnic group (3 timepoints)

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Figure 1.208: (Mock data) violinplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group (3 timepoints)

Figure 1.209: (Mock data) violinplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group (3 timepoints)

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Figure 1.213: (Mock data) violinplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by race and ethnic group (3 timepoints)

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Figure 1.215: (Mock data) lineplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group (2 timepoints)

Figure 1.216: (Mock data) lineplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group (2 timepoints)

Figure 1.217: (Mock data) lineplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group (2 timepoints)

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Figure 1.219: (Mock data) lineplots of Pseudovirus Neutralization ID50: baseline negative placebo arm by dichotomous classification of race and ethnic group (2 timepoints)

Figure 1.220: (Mock data) lineplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm by dichotomous classification of race and ethnic group (2 timepoints)

Figure 1.221: (Mock data) lineplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by dichotomous classification of race and ethnic group (2 timepoints)

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Figure 1.223: (Mock data) violinplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group (2 timepoints)

Figure 1.224: (Mock data) violinplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group (2 timepoints)

Figure 1.225: (Mock data) violinplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group (2 timepoints)

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Figure 1.233: (Mock data) lineplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group (3 timepoints)

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Figure 1.244: (Mock data) violinplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm by dichotomous classification of race and ethnic group (3 timepoints)

Figure 1.245: (Mock data) violinplots of Pseudovirus Neutralization ID80: baseline negative placebo arm by dichotomous classification of race and ethnic group (3 timepoints)

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Figure 1.248: (Mock data) scatterplots of Binding Antibody to Spike: baseline negative vaccine arm at day 29

Figure 1.249: (Mock data) scatterplots of Binding Antibody to Spike: baseline negative vaccine arm at day 57

Figure 1.250: (Mock data) scatterplots of Binding Antibody to RBD: baseline negative vaccine arm at day 1

Figure 1.251: (Mock data) scatterplots of Binding Antibody to RBD: baseline negative vaccine arm at day 29

Figure 1.252: (Mock data) scatterplots of Binding Antibody to RBD: baseline negative vaccine arm at day 57

Figure 1.253: (Mock data) scatterplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm at day 1

Figure 1.254: (Mock data) scatterplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm at day 29

Figure 1.255: (Mock data) scatterplots of Pseudovirus Neutralization ID50: baseline negative vaccine arm at day 57

Figure 1.256: (Mock data) scatterplots of Pseudovirus Neutralization ID80: baseline negative vaccine arm at day 1

Figure 1.257: (Mock data) scatterplots of Pseudovirus Neutralization ID80: baseline negative vaccine arm at day 29

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Figure 1.260: (Mock data) scatterplots of Binding Antibody to Spike: by arm at day 29

Figure 1.261: (Mock data) scatterplots of Binding Antibody to Spike: by arm at day 57

Figure 1.262: (Mock data) scatterplots of Binding Antibody to RBD: by arm at day 1

Figure 1.263: (Mock data) scatterplots of Binding Antibody to RBD: by arm at day 29

Figure 1.264: (Mock data) scatterplots of Binding Antibody to RBD: by arm at day 57

Figure 1.265: (Mock data) scatterplots of Pseudovirus Neutralization ID50: by arm at day 1

Figure 1.266: (Mock data) scatterplots of Pseudovirus Neutralization ID50: by arm at day 29

Figure 1.267: (Mock data) scatterplots of Pseudovirus Neutralization ID50: by arm at day 57

Figure 1.268: (Mock data) scatterplots of Pseudovirus Neutralization ID80: by arm at day 1

Figure 1.269: (Mock data) scatterplots of Pseudovirus Neutralization ID80: by arm at day 29

Figure 1.270: (Mock data) scatterplots of Pseudovirus Neutralization ID80: by arm at day 57

Chapter 2

Day 57 Univariate CoR: Cox Models of Risk

The main regression model is the Cox proportional hazards model. All plots are made with Cox models fit unless specified otherwise.

2.1 Hazard ratios

Table 2.1: Inference for Day 57 antibody marker covariate-adjusted correlates of risk of COVID in the vaccine group: Hazard ratios per 10-fold increment in the marker*

Mock Immunologic Marker	No. cases / No. at-risk**	HR per 10-fold incr. Pt. Est.	95% CI	P-value (2-sided)	q-value	FWER
Spike IgG (IU/ml)	72/13,254	0.08	(0.05-0.13)	<0.001	<0.001	<0.001
RBD IgG (IU/ml)	72/13,254	0.17	(0.12-0.24)	<0.001	<0.001	<0.001
PsV-nAb ID50	72/13,254	0.23	(0.18-0.31)	<0.001	<0.001	<0.001
PsV-nAb ID80	72/13,254	0.37	(0.27-0.51)	<0.001	<0.001	<0.001

*Baseline covariates adjusted for: age in years, at risk or not, community of color or not . Average follow-up time 172 days, maximum follow-up time 185 days.
**No. at-risk = number of per-protocol baseline negative vaccine recipients at-risk for COVID; no. cases = number of this cohort with an observed COVID endpoints starting 7 days post Day 57 visit.

Table 2.2: Inference for Day 57 antibody marker covariate-adjusted correlates of risk of COVID in the vaccine group: Hazard ratios for Middle vs. Upper tertile vs. Lower tertile*

Mock Immunologic Marker	Tertile	No. cases / No. at-risk**	Attack rate	Haz. Ratio Pt. Est.	Haz. Ratio 95% CI	P-value (2-sided)	Overall P-value***	Overall q-value	Overall FWER
Spike IgG (IU/ml)	Lower	66/4,422	0.0149	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	4/4,409	0.0009	0.03	(0.01-0.10)	<0.001			
	Upper	1/4,423	0.0002	0.00	(0.00-0.03)	<0.001			
RBD IgG (IU/ml)	Lower	46/4,432	0.0104	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	18/4,378	0.0041	0.23	(0.12-0.42)	<0.001			
	Upper	8/4,444	0.0018	0.06	(0.02-0.12)	<0.001			
PsV-nAb ID50	Lower	56/4,458	0.0126	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	8/4,380	0.0018	0.09	(0.04-0.20)	<0.001			
	Upper	7/4,415	0.0016	0.05	(0.02-0.12)	<0.001			
PsV-nAb ID80	Lower	39/4,420	0.0088	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	21/4,373	0.0048	0.46	(0.25-0.83)	0.010			
	Upper	11/4,460	0.0025	0.17	(0.08-0.36)	<0.001			
Placebo		713/13,271	0.0537						

*Baseline covariates adjusted for: age in years, at risk or not, community of color or not . Average follow-up time 172 days, maximum follow-up time 185 days. Cutpoints: Spike IgG (IU/ml) [6.1, 6.72), RBD IgG (IU/ml) [5.71, 6.38), PsV-nAb ID50 [2.8, 3.64), PsV-nAb ID80 [3.1, 3.82).
**No. at-risk = number of per-protocol baseline negative vaccine recipients at-risk for COVID at 7 days post Day 57 visit; no. cases = number of this cohort with an observed COVID endpoints.
***Generalized Wald-test p-value of the null hypothesis that the hazard rate is constant across the Lower, Middle, and Upper tertile groups.

Figure 2.1: Forest plots of hazard ratios per 10-fold increase in the marker among baseline seronegative vaccine recipients and subgroups with 95% point-wise confidence intervals.

Figure 2.2: Forest plots of hazard ratios per 10-fold increase in the Day 57 binding Ab to spike markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

Figure 2.3: Forest plots of hazard ratios per 10-fold increase in the Day 57 binding Ab to RBD markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

Figure 2.4: Forest plots of hazard ratios per 10-fold increase in the Day 57 pseudo neut ID50 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

Figure 2.5: Forest plots of hazard ratios per 10-fold increase in the Day 57 pseudo neut ID80 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

2.2 Marginalized risk and controlled vaccine efficacy plots

Figure 2.6: Marginalized cumulative risk by Day 172 as functions of Day 57 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 172 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

Figure 2.7: Marginalized cumulative risk by Day 172 as functions of Day 57 markers above a threshold ($\geq s$) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 172 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

Figure 2.8: Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

Figure 2.9: Marginalized cumulative incidence rate curves for trichotomized Day 57 markers among baseline seronegative vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

Chapter 3

Day 29 Univariate CoR: Cox Models of Risk

The main regression model is the Cox proportional hazards model. All plots are made with Cox models fit unless specified otherwise.

3.1 Hazard ratios

Table 3.1: Inference for Day 29 antibody marker covariate-adjusted correlates of risk of COVID in the vaccine group: Hazard ratios per 10-fold increment in the marker*

Mock Immunologic Marker	No. cases / No. at-risk**	HR per 10-fold incr. Pt. Est.	95% CI	P-value (2-sided)	q-value	FWER
Spike IgG (IU/ml)	83/13,271	0.09	(0.05-0.15)	<0.001	<0.001	<0.001
RBD IgG (IU/ml)	83/13,271	0.25	(0.16-0.38)	<0.001	<0.001	<0.001
PsV-nAb ID50	83/13,271	0.32	(0.23-0.45)	<0.001	<0.001	<0.001
PsV-nAb ID80	83/13,271	0.57	(0.43-0.76)	<0.001	<0.001	<0.001

*Baseline covariates adjusted for: age in years, at risk or not, community of color or not . Average follow-up time 200 days, maximum follow-up time 213 days.
**No. at-risk = number of per-protocol baseline negative vaccine recipients at-risk for COVID; no. cases = number of this cohort with an observed COVID endpoints starting 7 days post Day 29 visit.

Table 3.2: Inference for Day 29 antibody marker covariate-adjusted correlates of risk of COVID in the vaccine group: Hazard ratios for Middle vs. Upper tertile vs. Lower tertile*

Mock Immunologic Marker	Tertile	No. cases / No. at-risk**	Attack rate	Haz. Ratio Pt. Est.	Haz. Ratio 95% CI	P-value (2-sided)	Overall P-value***	Overall q-value	Overall FWER
Spike IgG (IU/ml)	Lower	55/4,408	0.0125	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	23/4,431	0.0052	0.24	(0.13-0.42)	<0.001			
	Upper	5/4,432	0.0011	0.02	(0.01-0.07)	<0.001			
RBD IgG (IU/ml)	Lower	46/4,420	0.0104	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	25/4,425	0.0056	0.34	(0.19-0.61)	<0.001			
	Upper	12/4,426	0.0027	0.09	(0.04-0.19)	<0.001			
PsV-nAb ID50	Lower	47/4,392	0.0107	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	24/4,465	0.0054	0.34	(0.20-0.60)	<0.001			
	Upper	12/4,414	0.0027	0.13	(0.06-0.26)	<0.001			
PsV-nAb ID80	Lower	31/4,409	0.0070	1	N/A	N/A	0.002	<0.001	<0.001
	Middle	35/4,435	0.0079	0.94	(0.55-1.61)	0.815			
	Upper	17/4,427	0.0038	0.33	(0.17-0.65)	0.001			
Placebo		821/13,299	0.0617						

*Baseline covariates adjusted for: age in years, at risk or not, community of color or not . Average follow-up time 200 days, maximum follow-up time 213 days. Cutpoints: Spike IgG (IU/ml) [4.4, 4.95), RBD IgG (IU/ml) [4.13, 4.66), PsV-nAb ID50 [1.67, 2.38), PsV-nAb ID80 [1.99, 2.64).
**No. at-risk = number of per-protocol baseline negative vaccine recipients at-risk for COVID at 7 days post Day 29 visit; no. cases = number of this cohort with an observed COVID endpoints.
***Generalized Wald-test p-value of the null hypothesis that the hazard rate is constant across the Lower, Middle, and Upper tertile groups.

Figure 3.1: Forest plots of hazard ratios per 10-fold increase in the marker among baseline seronegative vaccine recipients and subgroups with 95% point-wise confidence intervals.

Figure 3.2: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to spike markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

Figure 3.3: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to RBD markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

Figure 3.4: Forest plots of hazard ratios per 10-fold increase in the Day 29 pseudo neut ID50 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

Figure 3.5: Forest plots of hazard ratios per 10-fold increase in the Day 29 pseudo neut ID80 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

3.2 Marginalized risk and controlled vaccine efficacy plots

Figure 3.6: Marginalized cumulative risk by Day 200 as functions of Day 29 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 200 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

Figure 3.7: Marginalized cumulative risk by Day 200 as functions of Day 29 markers above a threshold ($\geq s$) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 200 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

Figure 3.8: Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

Figure 3.9: Marginalized cumulative incidence rate curves for trichotomized Day 29 markers among baseline seronegative vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

Chapter 4

Univariate CoR: Nonparametric Threshold Modeling

An extension of the unadjusted nonparametric threshold-searching approach developed in Donovan, Hudgens, and Gilbert (2019), the covariate-adjusted TMLE-based approach developed by van der Laan, Zhang, Gilbert (submitted) 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/covariate-adjusted 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: 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
2. A plot and table with risk estimates and simultaneous 95% confidence bands
3. Monotone-corrected versions of 1 and 2.

A reverse cumulative distribution function curve estimated by the IPW NPMLE 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.

4.1 Plots and Tables with estimates and pointwise confidence interval for Day 57

4.1.1 Day 57 Spike protein binding antibody

Figure 4.1: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.1: Table of risk estimates for a range of thresholds of Day 57 Spike protein binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.530	$3.39 * 10^4$	0.00489	0.00360	0.00618
5.420	$2.63 * 10^5$	0.00281	0.00182	0.00381
5.851	$7.10 * 10^5$	0.00204	0.00113	0.00296
6.218	$1.65 * 10^6$	0.00051	0.00000	0.00102
6.453	$2.84 * 10^6$	0.00049	0.00000	0.00105
6.644	$4.41 * 10^6$	0.00022	0.00000	0.00065
6.864	$7.31 * 10^6$	0.00000	0.00000	NA
7.185	$1.53 * 10^7$	0.00000	0.00000	NA
7.525	$3.35 * 10^7$	0.00000	0.00000	NA
8.391	$2.46 * 10^8$	0.00000	0.00000	NA

4.1.2 Day 57 RBD binding antibody

Figure 4.2: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.2: Table of risk estimates for a range of thresholds of Day 57 RBD binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.185	$1.53 * 10^4$	0.00514	0.00381	0.00647
5.070	$1.17 * 10^5$	0.00382	0.00263	0.00501
5.466	$2.92 * 10^5$	0.00321	0.00205	0.00437
5.865	$7.33 * 10^5$	0.00285	0.00161	0.00409
6.107	$1.28 * 10^6$	0.00254	0.00125	0.00382
6.309	$2.04 * 10^6$	0.00164	0.00048	0.00280
6.541	$3.48 * 10^6$	0.00106	0.00000	0.00215
6.879	$7.57 * 10^6$	0.00000	0.00000	NA
7.262	$1.83 * 10^7$	0.00000	0.00000	NA
8.291	$1.95 * 10^8$	0.00000	0.00000	NA

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

Figure 4.3: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.3: Table of risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00540	0.00404	0.00676
2.057	$1.14 * 10^2$	0.00362	0.00248	0.00477
2.499	$3.16 * 10^2$	0.00287	0.00179	0.00395
2.929	$8.49 * 10^2$	0.00175	0.00080	0.00270
3.230	$1.70 * 10^3$	0.00154	0.00056	0.00252
3.501	$3.17 * 10^3$	0.00161	0.00049	0.00273
3.747	$5.58 * 10^3$	0.00101	0.00000	0.00204
4.200	$1.58 * 10^4$	0.00000	0.00000	NA
4.636	$4.33 * 10^4$	0.00000	0.00000	NA
5.620	$4.17 * 10^5$	0.00000	0.00000	NA

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

Figure 4.4: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.4: Table of risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	$2.25 * 10^1$	0.00530	0.00396	0.00665
2.319	$2.08 * 10^2$	0.00437	0.00310	0.00564
2.772	$5.92 * 10^2$	0.00394	0.00266	0.00521
3.136	$1.37 * 10^3$	0.00346	0.00214	0.00479
3.395	$2.48 * 10^3$	0.00302	0.00170	0.00434
3.652	$4.49 * 10^3$	0.00221	0.00095	0.00346
3.875	$7.50 * 10^3$	0.00200	0.00053	0.00347
4.314	$2.06 * 10^4$	0.00169	0.00000	0.00347
4.685	$4.84 * 10^4$	0.00082	0.00000	0.00251
5.644	$4.41 * 10^5$	0.00000	0.00000	NA

4.2 Plots and Tables with estimates and pointwise confidence intervals for Day 29

4.2.1 Day 29 Spike protein antibody

Figure 4.5: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.5: Table of risk estimates for a range of thresholds of Day 29 Spike protein antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
3.221	$1.66 * 10^3$	0.00602	0.00456	0.00747
3.955	$9.02 * 10^3$	0.00484	0.00349	0.00618
4.243	$1.75 * 10^4$	0.00339	0.00218	0.00460
4.520	$3.31 * 10^4$	0.00302	0.00173	0.00430
4.707	$5.09 * 10^4$	0.00261	0.00127	0.00394
4.898	$7.91 * 10^4$	0.00144	0.00032	0.00255
5.060	$1.15 * 10^5$	0.00143	0.00008	0.00277
5.327	$2.12 * 10^5$	0.00091	0.00000	0.00221
5.541	$3.48 * 10^5$	0.00135	0.00000	0.00407
6.285	$1.93 * 10^6$	0.00000	0.00000	NA

4.2.2 Day 29 RBD binding antibody

Figure 4.6: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.6: Table of risk estimates for a range of thresholds of Day 29 RBD binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
2.804	$6.37 * 10^2$	0.00628	0.00480	0.00776
3.596	$3.94 * 10^3$	0.00583	0.00431	0.00736
3.962	$9.16 * 10^3$	0.00506	0.00356	0.00656
4.231	$1.70 * 10^4$	0.00368	0.00227	0.00509
4.430	$2.69 * 10^4$	0.00304	0.00162	0.00446
4.605	$4.03 * 10^4$	0.00248	0.00102	0.00394
4.815	$6.53 * 10^4$	0.00200	0.00047	0.00353
5.129	$1.35 * 10^5$	0.00236	0.00008	0.00465
5.445	$2.79 * 10^5$	0.00307	0.00000	0.00649
6.281	$1.91 * 10^6$	0.01460	0.00000	0.04713

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

Figure 4.7: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.7: Table of risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00625	0.00477	0.00773
1.364	$2.31 * 10^1$	0.00493	0.00349	0.00637
1.630	$4.27 * 10^1$	0.00449	0.00303	0.00594
1.870	$7.41 * 10^1$	0.00355	0.00215	0.00495
2.126	$1.34 * 10^2$	0.00353	0.00198	0.00508
2.310	$2.04 * 10^2$	0.00326	0.00156	0.00496
2.524	$3.34 * 10^2$	0.00266	0.00088	0.00445
2.772	$5.92 * 10^2$	0.00220	0.00004	0.00435
3.160	$1.45 * 10^3$	0.00000	0.00000	NA
3.988	$9.73 * 10^3$	0.00000	0.00000	NA

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

Figure 4.8: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.8: Table of risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00625	0.00477	0.00773
1.416	$2.61 * 10^1$	0.00597	0.00445	0.00749
1.761	$5.77 * 10^1$	0.00595	0.00434	0.00757
2.113	$1.30 * 10^2$	0.00589	0.00410	0.00768
2.309	$2.04 * 10^2$	0.00509	0.00330	0.00689
2.485	$3.05 * 10^2$	0.00405	0.00229	0.00581
2.718	$5.22 * 10^2$	0.00335	0.00145	0.00524
3.074	$1.19 * 10^3$	0.00306	0.00076	0.00537
3.425	$2.66 * 10^3$	0.00281	0.00000	0.00580
4.304	$2.01 * 10^4$	0.00000	0.00000	NA

4.3 Plots and Tables with estimates and pointwise confidence interval for Day 57 (monotone-corrected)

4.3.1 Day 57 Spike protein binding antibody

Figure 4.9: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.9: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Spike protein binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.530	$3.39 * 10^4$	0.00489	0.00360	0.00618
5.420	$2.63 * 10^5$	0.00281	0.00182	0.00381
5.851	$7.10 * 10^5$	0.00204	0.00113	0.00296
6.218	$1.65 * 10^6$	0.00051	0.00000	0.00102
6.453	$2.84 * 10^6$	0.00046	0.00000	0.00102
6.644	$4.41 * 10^6$	0.00023	0.00000	0.00066
6.864	$7.31 * 10^6$	0.00000	0.00000	NA
7.185	$1.53 * 10^7$	0.00000	0.00000	NA
7.525	$3.35 * 10^7$	0.00000	0.00000	NA
8.391	$2.46 * 10^8$	0.00000	0.00000	NA

4.3.2 Day 57 RBD binding antibody

Figure 4.10: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.10: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 RBD binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.185	$1.53 * 10^4$	0.00514	0.00381	0.00647
5.070	$1.17 * 10^5$	0.00382	0.00263	0.00501
5.466	$2.92 * 10^5$	0.00321	0.00205	0.00437
5.865	$7.33 * 10^5$	0.00288	0.00164	0.00412
6.107	$1.28 * 10^6$	0.00252	0.00124	0.00381
6.309	$2.04 * 10^6$	0.00169	0.00052	0.00285
6.541	$3.48 * 10^6$	0.00106	0.00000	0.00215
6.879	$7.57 * 10^6$	0.00000	0.00000	NA
7.262	$1.83 * 10^7$	0.00000	0.00000	NA
8.291	$1.95 * 10^8$	0.00000	0.00000	NA

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

Figure 4.11: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.11: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00540	0.00404	0.00676
2.057	$1.14 * 10^2$	0.00362	0.00248	0.00477
2.499	$3.16 * 10^2$	0.00287	0.00179	0.00395
2.929	$8.49 * 10^2$	0.00175	0.00080	0.00270
3.230	$1.70 * 10^3$	0.00165	0.00067	0.00263
3.501	$3.17 * 10^3$	0.00165	0.00053	0.00278
3.747	$5.58 * 10^3$	0.00103	0.00001	0.00206
4.200	$1.58 * 10^4$	0.00000	0.00000	NA
4.636	$4.33 * 10^4$	0.00000	0.00000	NA
5.620	$4.17 * 10^5$	0.00000	0.00000	NA

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

Figure 4.12: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.12: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	$2.25 * 10^1$	0.00530	0.00396	0.00665
2.319	$2.08 * 10^2$	0.00436	0.00309	0.00563
2.772	$5.92 * 10^2$	0.00402	0.00274	0.00529
3.136	$1.37 * 10^3$	0.00346	0.00214	0.00479
3.395	$2.48 * 10^3$	0.00299	0.00168	0.00431
3.652	$4.49 * 10^3$	0.00238	0.00113	0.00364
3.875	$7.50 * 10^3$	0.00200	0.00053	0.00347
4.314	$2.06 * 10^4$	0.00157	0.00000	0.00335
4.685	$4.84 * 10^4$	0.00078	0.00000	0.00247
5.644	$4.41 * 10^5$	0.00000	0.00000	NA

4.4 Plots and Tables with estimates and pointwise confidence intervals for Day 29 (monotone-corrected)

4.4.1 Day 29 Spike protein antibody

Figure 4.13: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.13: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Spike protein antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
3.221	$1.66 * 10^3$	0.00602	0.00456	0.00747
3.955	$9.02 * 10^3$	0.00484	0.00349	0.00618
4.243	$1.75 * 10^4$	0.00339	0.00218	0.00460
4.520	$3.31 * 10^4$	0.00302	0.00173	0.00430
4.707	$5.09 * 10^4$	0.00261	0.00127	0.00394
4.898	$7.91 * 10^4$	0.00145	0.00034	0.00257
5.060	$1.15 * 10^5$	0.00145	0.00011	0.00280
5.327	$2.12 * 10^5$	0.00138	0.00008	0.00267
5.541	$3.48 * 10^5$	0.00138	0.00000	0.00409
6.285	$1.93 * 10^6$	0.00000	0.00000	NA

4.4.2 Day 29 RBD binding antibody

Figure 4.14: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.14: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 RBD binding antibody levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
2.804	$6.37 * 10^2$	0.00628	0.00480	0.00776
3.596	$3.94 * 10^3$	0.00583	0.00431	0.00736
3.962	$9.16 * 10^3$	0.00506	0.00356	0.00656
4.231	$1.70 * 10^4$	0.00370	0.00229	0.00511
4.430	$2.69 * 10^4$	0.00370	0.00228	0.00512
4.605	$4.03 * 10^4$	0.00370	0.00224	0.00516
4.815	$6.53 * 10^4$	0.00370	0.00217	0.00523
5.129	$1.35 * 10^5$	0.00370	0.00142	0.00598
5.445	$2.79 * 10^5$	0.00370	0.00029	0.00712
6.281	$1.91 * 10^6$	0.00370	0.00000	0.03623

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

Figure 4.15: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.15: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00625	0.00477	0.00773
1.364	$2.31 * 10^1$	0.00493	0.00349	0.00637
1.630	$4.27 * 10^1$	0.00447	0.00302	0.00593
1.870	$7.41 * 10^1$	0.00369	0.00229	0.00509
2.126	$1.34 * 10^2$	0.00353	0.00198	0.00508
2.310	$2.04 * 10^2$	0.00312	0.00142	0.00482
2.524	$3.34 * 10^2$	0.00263	0.00085	0.00442
2.772	$5.92 * 10^2$	0.00227	0.00011	0.00442
3.160	$1.45 * 10^3$	0.00000	0.00000	NA
3.988	$9.73 * 10^3$	0.00000	0.00000	NA

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

Figure 4.16: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.16: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00625	0.00477	0.00773
1.416	$2.61 * 10^1$	0.00601	0.00449	0.00753
1.761	$5.77 * 10^1$	0.00601	0.00439	0.00762
2.113	$1.30 * 10^2$	0.00589	0.00410	0.00768
2.309	$2.04 * 10^2$	0.00509	0.00330	0.00689
2.485	$3.05 * 10^2$	0.00405	0.00229	0.00581
2.718	$5.22 * 10^2$	0.00335	0.00145	0.00524
3.074	$1.19 * 10^3$	0.00312	0.00082	0.00542
3.425	$2.66 * 10^3$	0.00312	0.00013	0.00611
4.304	$2.01 * 10^4$	0.00000	0.00000	NA

4.5 Plots and Tables with estimates and simultaneous confidence bands for Day 57

4.5.1 Day 57 Spike protein binding antibody

Figure 4.17: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.17: Table of risk estimates for a range of thresholds of Day 57 Spike protein binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.530	$3.39 * 10^4$	0.00489	0.00297	0.00682
5.420	$2.63 * 10^5$	0.00281	0.00133	0.00430
5.851	$7.10 * 10^5$	0.00204	0.00068	0.00341
6.218	$1.65 * 10^6$	0.00051	0.00000	0.00126
6.453	$2.84 * 10^6$	0.00049	0.00000	0.00133
6.644	$4.41 * 10^6$	0.00022	0.00000	0.00086
6.864	$7.31 * 10^6$	0.00000	0.00000	NA
7.185	$1.53 * 10^7$	0.00000	0.00000	NA
7.525	$3.35 * 10^7$	0.00000	0.00000	NA
8.391	$2.46 * 10^8$	0.00000	0.00000	NA

4.5.2 Day 57 RBD binding antibody

Figure 4.18: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.18: Table of risk estimates for a range of thresholds of Day 57 RBD binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.185	$1.53 * 10^4$	0.00514	0.00317	0.00711
5.070	$1.17 * 10^5$	0.00382	0.00205	0.00559
5.466	$2.92 * 10^5$	0.00321	0.00148	0.00494
5.865	$7.33 * 10^5$	0.00285	0.00101	0.00469
6.107	$1.28 * 10^6$	0.00254	0.00063	0.00445
6.309	$2.04 * 10^6$	0.00164	0.00000	0.00337
6.541	$3.48 * 10^6$	0.00106	0.00000	0.00268
6.879	$7.57 * 10^6$	0.00000	0.00000	NA
7.262	$1.83 * 10^7$	0.00000	0.00000	NA
8.291	$1.95 * 10^8$	0.00000	0.00000	NA

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

Figure 4.19: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.19: Table of risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00540	0.00339	0.00742
2.057	$1.14 * 10^2$	0.00362	0.00193	0.00532
2.499	$3.16 * 10^2$	0.00287	0.00127	0.00446
2.929	$8.49 * 10^2$	0.00175	0.00035	0.00315
3.230	$1.70 * 10^3$	0.00154	0.00009	0.00299
3.501	$3.17 * 10^3$	0.00161	0.00000	0.00327
3.747	$5.58 * 10^3$	0.00101	0.00000	0.00253
4.200	$1.58 * 10^4$	0.00000	0.00000	NA
4.636	$4.33 * 10^4$	0.00000	0.00000	NA
5.620	$4.17 * 10^5$	0.00000	0.00000	NA

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

Figure 4.20: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.20: Table of risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	$2.25 * 10^1$	0.00530	0.00336	0.00725
2.319	$2.08 * 10^2$	0.00437	0.00254	0.00620
2.772	$5.92 * 10^2$	0.00394	0.00210	0.00578
3.136	$1.37 * 10^3$	0.00346	0.00155	0.00538
3.395	$2.48 * 10^3$	0.00302	0.00112	0.00492
3.652	$4.49 * 10^3$	0.00221	0.00040	0.00402
3.875	$7.50 * 10^3$	0.00200	0.00000	0.00412
4.314	$2.06 * 10^4$	0.00169	0.00000	0.00425
4.685	$4.84 * 10^4$	0.00082	0.00000	0.00326
5.644	$4.41 * 10^5$	0.00000	0.00000	NA

4.6 Plots and Tables with estimates and simultaneous confidence bands for Day 29

4.6.1 Day 29 Spike protein antibody

Figure 4.21: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.21: Table of risk estimates for a range of thresholds of Day 29 Spike protein antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
3.221	$1.66 * 10^3$	0.00602	0.00394	0.00809
3.955	$9.02 * 10^3$	0.00484	0.00291	0.00676
4.243	$1.75 * 10^4$	0.00339	0.00166	0.00512
4.520	$3.31 * 10^4$	0.00302	0.00118	0.00486
4.707	$5.09 * 10^4$	0.00261	0.00070	0.00452
4.898	$7.91 * 10^4$	0.00144	0.00000	0.00303
5.060	$1.15 * 10^5$	0.00143	0.00000	0.00335
5.327	$2.12 * 10^5$	0.00091	0.00000	0.00276
5.541	$3.48 * 10^5$	0.00135	0.00000	0.00524
6.285	$1.93 * 10^6$	0.00000	0.00000	NA

4.6.2 Day 29 RBD binding antibody

Figure 4.22: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.22: Table of risk estimates for a range of thresholds of Day 29 RBD binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
2.804	$6.37 * 10^2$	0.00628	0.00418	0.00838
3.596	$3.94 * 10^3$	0.00583	0.00367	0.00799
3.962	$9.16 * 10^3$	0.00506	0.00293	0.00719
4.231	$1.70 * 10^4$	0.00368	0.00168	0.00568
4.430	$2.69 * 10^4$	0.00304	0.00102	0.00505
4.605	$4.03 * 10^4$	0.00248	0.00041	0.00455
4.815	$6.53 * 10^4$	0.00200	0.00000	0.00417
5.129	$1.35 * 10^5$	0.00236	0.00000	0.00560
5.445	$2.79 * 10^5$	0.00307	0.00000	0.00792
6.281	$1.91 * 10^6$	0.01460	0.00000	0.06073

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

Figure 4.23: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.23: Table of risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00625	0.00412	0.00839
1.364	$2.31 * 10^1$	0.00493	0.00286	0.00701
1.630	$4.27 * 10^1$	0.00449	0.00239	0.00658
1.870	$7.41 * 10^1$	0.00355	0.00153	0.00556
2.126	$1.34 * 10^2$	0.00353	0.00130	0.00576
2.310	$2.04 * 10^2$	0.00326	0.00081	0.00571
2.524	$3.34 * 10^2$	0.00266	0.00009	0.00524
2.772	$5.92 * 10^2$	0.00220	0.00000	0.00531
3.160	$1.45 * 10^3$	0.00000	0.00000	NA
3.988	$9.73 * 10^3$	0.00000	0.00000	NA

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

Figure 4.24: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 4.24: Table of risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00625	0.00414	0.00837
1.416	$2.61 * 10^1$	0.00597	0.00380	0.00814
1.761	$5.77 * 10^1$	0.00595	0.00365	0.00826
2.113	$1.30 * 10^2$	0.00589	0.00333	0.00845
2.309	$2.04 * 10^2$	0.00509	0.00253	0.00765
2.485	$3.05 * 10^2$	0.00405	0.00154	0.00656
2.718	$5.22 * 10^2$	0.00335	0.00064	0.00605
3.074	$1.19 * 10^3$	0.00306	0.00000	0.00635
3.425	$2.66 * 10^3$	0.00281	0.00000	0.00708
4.304	$2.01 * 10^4$	0.00000	0.00000	NA

4.7 Plots and Tables with estimates and pointwise confidence interval for Day 57 (monotone-corrected)

4.7.1 Day 57 Spike protein binding antibody

Figure 4.25: Adjusted threshold-response function for a range of thresholds of the Day 57 Spike protein binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.25: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Spike protein binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.530	$3.39 * 10^4$	0.00489	0.00297	0.00682
5.420	$2.63 * 10^5$	0.00281	0.00133	0.00430
5.851	$7.10 * 10^5$	0.00204	0.00068	0.00341
6.218	$1.65 * 10^6$	0.00051	0.00000	0.00126
6.453	$2.84 * 10^6$	0.00046	0.00000	0.00130
6.644	$4.41 * 10^6$	0.00023	0.00000	0.00087
6.864	$7.31 * 10^6$	0.00000	0.00000	NA
7.185	$1.53 * 10^7$	0.00000	0.00000	NA
7.525	$3.35 * 10^7$	0.00000	0.00000	NA
8.391	$2.46 * 10^8$	0.00000	0.00000	NA

4.7.2 Day 57 RBD binding antibody

Figure 4.26: Adjusted threshold-response function for a range of thresholds of the Day 57 RBD binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.26: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 RBD binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
4.185	$1.53 * 10^4$	0.00514	0.00317	0.00711
5.070	$1.17 * 10^5$	0.00382	0.00205	0.00559
5.466	$2.92 * 10^5$	0.00321	0.00148	0.00494
5.865	$7.33 * 10^5$	0.00288	0.00104	0.00472
6.107	$1.28 * 10^6$	0.00252	0.00061	0.00443
6.309	$2.04 * 10^6$	0.00169	0.00000	0.00341
6.541	$3.48 * 10^6$	0.00106	0.00000	0.00268
6.879	$7.57 * 10^6$	0.00000	0.00000	NA
7.262	$1.83 * 10^7$	0.00000	0.00000	NA
8.291	$1.95 * 10^8$	0.00000	0.00000	NA

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

Figure 4.27: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.27: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00540	0.00339	0.00742
2.057	$1.14 * 10^2$	0.00362	0.00193	0.00532
2.499	$3.16 * 10^2$	0.00287	0.00127	0.00446
2.929	$8.49 * 10^2$	0.00175	0.00035	0.00315
3.230	$1.70 * 10^3$	0.00165	0.00020	0.00310
3.501	$3.17 * 10^3$	0.00165	0.00000	0.00331
3.747	$5.58 * 10^3$	0.00103	0.00000	0.00254
4.200	$1.58 * 10^4$	0.00000	0.00000	NA
4.636	$4.33 * 10^4$	0.00000	0.00000	NA
5.620	$4.17 * 10^5$	0.00000	0.00000	NA

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

Figure 4.28: Adjusted threshold-response function for a range of thresholds of the Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.28: Table of monotone-corrected risk estimates for a range of thresholds of Day 57 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
1.352	$2.25 * 10^1$	0.00530	0.00336	0.00725
2.319	$2.08 * 10^2$	0.00436	0.00253	0.00619
2.772	$5.92 * 10^2$	0.00402	0.00218	0.00586
3.136	$1.37 * 10^3$	0.00346	0.00155	0.00538
3.395	$2.48 * 10^3$	0.00299	0.00109	0.00489
3.652	$4.49 * 10^3$	0.00238	0.00057	0.00419
3.875	$7.50 * 10^3$	0.00200	0.00000	0.00412
4.314	$2.06 * 10^4$	0.00157	0.00000	0.00413
4.685	$4.84 * 10^4$	0.00078	0.00000	0.00322
5.644	$4.41 * 10^5$	0.00000	0.00000	NA

4.8 Plots and Tables with estimates and pointwise confidence intervals for Day 29 (monotone-corrected)

4.8.1 Day 29 Spike protein antibody

Figure 4.29: Adjusted threshold-response function for a range of thresholds of the Day 29 Spike protein antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.29: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Spike protein antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
3.221	$1.66 * 10^3$	0.00602	0.00394	0.00809
3.955	$9.02 * 10^3$	0.00484	0.00291	0.00676
4.243	$1.75 * 10^4$	0.00339	0.00166	0.00512
4.520	$3.31 * 10^4$	0.00302	0.00118	0.00486
4.707	$5.09 * 10^4$	0.00261	0.00070	0.00452
4.898	$7.91 * 10^4$	0.00145	0.00000	0.00305
5.060	$1.15 * 10^5$	0.00145	0.00000	0.00337
5.327	$2.12 * 10^5$	0.00138	0.00000	0.00322
5.541	$3.48 * 10^5$	0.00138	0.00000	0.00526
6.285	$1.93 * 10^6$	0.00000	0.00000	NA

4.8.2 Day 29 RBD binding antibody

Figure 4.30: Adjusted threshold-response function for a range of thresholds of the Day 29 RBD binding antibody levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.30: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 RBD binding antibody levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
2.804	$6.37 * 10^2$	0.00628	0.00418	0.00838
3.596	$3.94 * 10^3$	0.00583	0.00367	0.00799
3.962	$9.16 * 10^3$	0.00506	0.00293	0.00719
4.231	$1.70 * 10^4$	0.00370	0.00170	0.00570
4.430	$2.69 * 10^4$	0.00370	0.00169	0.00572
4.605	$4.03 * 10^4$	0.00370	0.00163	0.00577
4.815	$6.53 * 10^4$	0.00370	0.00153	0.00587
5.129	$1.35 * 10^5$	0.00370	0.00047	0.00694
5.445	$2.79 * 10^5$	0.00370	0.00000	0.00855
6.281	$1.91 * 10^6$	0.00370	0.00000	0.04984

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

Figure 4.31: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.31: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (50% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00625	0.00412	0.00839
1.364	$2.31 * 10^1$	0.00493	0.00286	0.00701
1.630	$4.27 * 10^1$	0.00447	0.00238	0.00657
1.870	$7.41 * 10^1$	0.00369	0.00167	0.00571
2.126	$1.34 * 10^2$	0.00353	0.00130	0.00576
2.310	$2.04 * 10^2$	0.00312	0.00067	0.00557
2.524	$3.34 * 10^2$	0.00263	0.00006	0.00521
2.772	$5.92 * 10^2$	0.00227	0.00000	0.00538
3.160	$1.45 * 10^3$	0.00000	0.00000	NA
3.988	$9.73 * 10^3$	0.00000	0.00000	NA

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

Figure 4.32: Adjusted threshold-response function for a range of thresholds of the Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. The estimates and confidence intervals are adjusted using the assumption that the true threshold-response is nonincreasing.

Table 4.32: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Pseudo virus-neutralizing antibody (80% titer) levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
0.699	$5.00 * 10^0$	0.00625	0.00414	0.00837
1.416	$2.61 * 10^1$	0.00601	0.00383	0.00818
1.761	$5.77 * 10^1$	0.00601	0.00370	0.00831
2.113	$1.30 * 10^2$	0.00589	0.00333	0.00845
2.309	$2.04 * 10^2$	0.00509	0.00253	0.00765
2.485	$3.05 * 10^2$	0.00405	0.00154	0.00656
2.718	$5.22 * 10^2$	0.00335	0.00064	0.00605
3.074	$1.19 * 10^3$	0.00312	0.00000	0.00641
3.425	$2.66 * 10^3$	0.00312	0.00000	0.00739
4.304	$2.01 * 10^4$	0.00000	0.00000	NA