COVID-19 Correlates of Risk Analysis Report

MockENSEMBLE Study

USG COVID-19 Response Biostatistics Team

September 27, 2021

Contents

1 Disclaimers **13**

2 Summary Tables **15**

2.1 Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Negative Per-Protocol Cohort . . . 15

2.2 Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Positive Per-Protocol Cohort . . . 17

2.3 Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort in U.S. . . . 19

2.4 Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort in Latin America and South Africa . . . 20

2.5 Antibody levels in the baseline SARS-CoV-2 negative per-protocol cohort (vaccine recipients) 21

3 Graphical Descriptions of Antibody Marker Data **23**

3.1 Boxplots . . . 23

3.2 Weighted RCDF plots . . . 26

3.3 Weighted RCDF plots of threshold correlate concentration for vaccine efficacy . . . 29

3.4 Spaghetti plots . . . 32

3.5 Violin and line plots . . . 33

3.6 Scatter plots . . . 257

4 Graphical Descriptions of Time to Event Data **269**

5 Day D29 Univariate CoR: Cox Models of Risk **271**

5.1 Hazard ratios . . . 271

5.2 Marginalized risk and controlled vaccine efficacy plots . . . 275

6 Day D29start1 Univariate CoR: Cox Models of Risk **289**

6.1 Hazard ratios . . . 289

6.2 Marginalized risk and controlled vaccine efficacy plots . . . 293

7 Univariate CoR: Nonparametric Threshold Modeling (>=s) 307

7.1 Plots and Tables with estimates and pointwise confidence intervals for Day 29 308

7.2 Plots and Tables with estimates and pointwise confidence intervals for Day 29 (monotone-corrected) 311

7.3 Plots and Tables with estimates and pointwise confidence intervals for Day 29 (monotone-corrected) (events after 1 day post dose) 314

7.4 Plots and Tables with estimates and pointwise confidence intervals for Day 29 (monotone-corrected) (counting events after 1 day post dose) 317

7.5 Plots and Tables with estimates and simultaneous confidence intervals for Day 29 (monotone-corrected) 320

7.6 Plots and Tables with estimates and simultaneous confidence intervals for Day 29 (monotone-corrected) 323

7.7 Plots and Tables with estimates and simultaneous confidence intervals for Day 29 (monotone-corrected) (counting events after 1 day post dose) 326

7.8 Plots and Tables with estimates and simultaneous confidence intervals for Day 29 (monotone-corrected) (counting events after 1 day post dose) 329

8 Univariate CoR: Nonparametric Threshold Modeling (<=s) 333

9 Day D29 Univariate CoR: Nonlinear modeling 335

10 Day D29start1 Univariate CoR: Nonlinear modeling 337

11 Appendix 339

List of Tables

2.1 Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Negative Per-Protocol Cohort . . . 15

2.2 Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Positive Per-Protocol Cohort . . . 17

2.3 Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort in U.S. . . . 19

2.4 Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort in Latin America and South Africa . . . 20

2.5 Antibody levels in the baseline SARS-CoV-2 negative per-protocol cohort (vaccine recipients) 21

5.1 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* . . . 271

5.2 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* . . . 272

5.3 Analysis of Day 29 markers (upper vs. lower tertile) as a CoR and a controlled risk CoP. . . 275

5.4 Marginalized cumulative risk by Day 149 as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates). . . . 279

5.5 Controlled VE as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 149 days post Day 29 was 0.009 in vaccine recipients compared to 0.027 in placebo recipients, with cumulative vaccine efficacy 67.4% (95% CI 64.4 to 71.5%). 280

5.6 Controlled VE with sensitivity analysis as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates). . . . 281

5.7 Marginalized cumulative risk by Day 149 as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates). . . . 285

5.8 Controlled VE as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 149 days post Day 29 was 0.009 in vaccine recipients compared to 0.027 in placebo recipients, with cumulative vaccine efficacy 67.4% (95% CI 64.4 to 71.5%). 286

5.9 Controlled VE with sensitivity analysis as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates). . . . 287

6.1 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* 289

6.2 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* 290

6.3 Analysis of Day 29 markers (upper vs. lower tertile) as a CoR and a controlled risk CoP. . . 293

6.4 Marginalized cumulative risk by Day 149 as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates). 297

6.5 Controlled VE as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 1 to 149 days post Day 29 was 0.009 in vaccine recipients compared to 0.027 in placebo recipients, with cumulative vaccine efficacy 67.4% (95% CI 64.3 to 71.1%). 298

6.6 Controlled VE with sensitivity analysis as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates). 299

6.7 Marginalized cumulative risk by Day 149 as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates). 303

6.8 Controlled VE as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 1 to 149 days post Day 29 was 0.009 in vaccine recipients compared to 0.027 in placebo recipients, with cumulative vaccine efficacy 67.4% (95% CI 64.3 to 71.1%). 304

6.9 Controlled VE with sensitivity analysis as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates). 305

7.1 Table of risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with pointwise 95% confidence intervals. 309

7.2 Table of risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with pointwise 95% confidence intervals. 310

7.3 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with pointwise 95% confidence intervals. 312

7.4 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with pointwise 95% confidence intervals. 313

7.5 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with pointwise 95% confidence intervals. 315

7.6 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with pointwise 95% confidence intervals. 316

7.7 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with pointwise 95% confidence intervals. 318

7.8 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with pointwise 95% confidence intervals. 319

7.9 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals. 321

7.10 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals. 322

7.11 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals. 324

7.12 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals. 325

7.13 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals. 327

7.14 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals. 328

7.15 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals. 330

7.16 Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals. 331

List of Figures

3.1 Boxplots of D29 Ab markers: vaccine arm. The three dashed lines in each figure are ULOQ, LLOQ, and LLOD, from top to bottom respectively. 24

3.2 Boxplots of D29 fold-rise over D1 Ab markers: vaccine arm. 25

3.3 RCDF plots for D29 Ab markers by treatment arm. 27

3.4 RCDF plots for D29 fold-rise over D1 Ab markers by treatment arm. 28

3.5 Marker RCDF of D29 anti-Spike binding Ab: vaccine arm 30

3.6 Marker RCDF of D29 anti-RBD binding Ab: vaccine arm 31

3.7 Spaghetti Plots of Marker Trajectory: vaccine arm 32

5.1 Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to spike markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 7 days post Day 29. 273

5.2 Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to RBD markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 7 days post Day 29. 273

5.3 Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to spike markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 7 days post Day 29. 274

5.4 Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to RBD markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 7 days post Day 29. 274

5.5 Marginalized cumulative risk curves (=s). ‡ Count cases starting 7 days post Day 29. 276

5.6 Controlled VE curves (=s). ‡ Count cases starting 7 days post Day 29. 277

5.7 Marginalized cumulative risk curves and controlled VE curves (>=s). ‡ Count cases starting 7 days post Day 29. 278

5.8 Marginalized cumulative risk curves (=s). ‡ Count cases starting 7 days post Day 29. 282

5.9 Controlled VE curves (=s). ‡ Count cases starting 7 days post Day 29. 283

5.10 Marginalized cumulative risk curves and controlled VE curves (>=s). ‡ Count cases starting 7 days post Day 29. 284

6.1 Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to spike markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 1 days post Day 29. 291

6.2 Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to RBD markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 1 days post Day 29. 291

6.3 Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to spike markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 1 days post Day 29. 292

6.4 Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to RBD markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 1 days post Day 29. 292

6.5 Marginalized cumulative risk curves (=s). ‡ Count cases starting 1 days post Day 29. 294

6.6 Controlled VE curves (=s). ‡ Count cases starting 1 days post Day 29. 295

6.7 Marginalized cumulative risk curves and controlled VE curves (>=s). ‡ Count cases starting 1 days post Day 29. 296

6.8 Marginalized cumulative risk curves (=s). ‡ Count cases starting 1 days post Day 29. 300

6.9 Controlled VE curves (=s). ‡ Count cases starting 1 days post Day 29. 301

6.10 Marginalized cumulative risk curves and controlled VE curves (>=s). ‡ Count cases starting 1 days post Day 29. 302

7.1 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. 309

7.2 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed. 310

7.3 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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. 312

7.4 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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. 313

7.5 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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. 315

7.6 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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. 316

7.7 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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. 318

7.8 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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. 319

7.9 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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. 321

7.10 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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. 322

7.11 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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. 324

7.12 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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. 325

7.13 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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. 327

7.14 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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. 328

7.15 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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. 330

7.16 Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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. 331

9.1 Marginalized risk as functions of Day 29 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands (5 replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: baseline risk score, Region (US, South Africa, Latin America). The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 0.3, 1.6, 2.4, 15 for bAb Spike, bAb RBD, PsV nAb ID50, PsV nAb ID80, respectively. ‡ Count cases starting 7 days post Day 29. 335

MOCK

10.1 Marginalized risk as functions of Day 29 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands (5 replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: baseline risk score, Region (US, South Africa, Latin America). The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 0.3, 1.6, 2.4, 15 for bAb Spike, bAb RBD, PsV nAb ID50, PsV nAb ID80, respectively. ‡ Count cases starting 1 days post Day 29. 337

MOCK

Chapter 1

Disclaimers

The data presented in the analysis are provided to NIAID in accordance with Clinical Trial Agreement between the parties. The study was funded in part by BARDA under Government Contract No. 75A50120C00034.

Statistical Analysis Plan

The SAP is available at https://doi.org/10.6084/m9.figshare.13198595

Reproducibility Notice

This project integrates the virtual environments framework provided by the `renv` package for computational reproducibility. By taking this approach, all results are generated using a consistent versioning of both R and several R packages. This version of the report was built with R version 4.0.4 (2021-02-15), pandoc version 2.2, and the following R packages:

package	version	source
bookdown	0.21.7	Github (rstudio/bookdown@0cec2fd)
bslib	0.2.4.9002	Github (rstudio/bslib@c7835c2)
data.table	1.14.0	CRAN (R 4.0.4)
delayed	0.4.0	Github (tlverse/delayed@f415340)
devtools	2.3.2	CRAN (R 4.0.4)
dplyr	1.0.5	CRAN (R 4.0.4)
ggplot2	3.3.3	CRAN (R 4.0.4)
hal9001	0.4.0	Github (tlverse/hal9001@b41ed5d)
haldensify	0.1.5	Github (nhejazi/haldensify@16350cc)
here	1.0.1	CRAN (R 4.0.4)
kableExtra	1.3.4	CRAN (R 4.0.4)
knitr	1.31	CRAN (R 4.0.4)
latex2exp	0.5.0	CRAN (R 4.0.4)
mvtnorm	1.1-1	CRAN (R 4.0.4)
origami	1.0.3	CRAN (R 4.0.4)
readr	1.4.0	CRAN (R 4.0.4)
rmarkdown	2.7.4	Github (rstudio/rmarkdown@a11240d)
skimr	2.1.3	CRAN (R 4.0.4)
sl3	1.4.3	Github (tlverse/sl3@982f4d6)
stringr	1.4.0	CRAN (R 4.0.4)
SuperLearner	2.0-28	CRAN (R 4.0.4)
svyVGAM	1.0	CRAN (R 4.0.4)
tibble	3.1.1	CRAN (R 4.0.4)

MOCK

package	version	source
tidyr	1.1.3	CRAN (R 4.0.4)
txshift	0.3.6	Github (nhejazi/txshift@c0f572a)
VGAM	1.1-5	CRAN (R 4.0.4)
xtable	1.8-4	CRAN (R 4.0.4)

To get started with using this project and its `renv` package library, we first recommend briefly reviewing the `renv` collaboration guide.

MOCK

Chapter 2

Summary Tables

2.1 Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Negative Per-Protocol Cohort

Table 2.1: Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Negative Per-Protocol Cohort

Characteristics	Vaccine (N = 913)	Placebo (N = 109)	Total (N = 1022)
Age			
Age 18 - 59	453 (49.6%)	54 (49.5%)	507 (49.6%)
Age $\geq$ 60	460 (50.4%)	55 (50.5%)	515 (50.4%)
Mean (Range)	56.1 (18.0, 85.0)	55.8 (18.0, 85.0)	56.1 (18.0, 85.0)
BMI			
Underweight BMI $<$ 18.5	14 (1.5%)	2 (1.8%)	16 (1.6%)
Normal 18.5 $\leq$ BMI $<$ 25	174 (19.1%)	27 (24.8%)	201 (19.7%)
Overweight 25 $\leq$ BMI $<$ 30	368 (40.3%)	45 (41.3%)	413 (40.4%)
Obese BMI $\geq$ 30	357 (39.1%)	35 (32.1%)	392 (38.4%)
Risk for Severe Covid-19			
At-risk	454 (49.7%)	53 (48.6%)	507 (49.6%)
Not at-risk	459 (50.3%)	56 (51.4%)	515 (50.4%)
Age, Risk for Severe Covid-19			
Age 18 - 59 At-risk	226 (24.8%)	26 (23.9%)	252 (24.7%)
Age 18 - 59 Not at-risk	227 (24.9%)	28 (25.7%)	255 (25.0%)
Age $\geq$ 60 At-risk	228 (25.0%)	27 (24.8%)	255 (25.0%)
Age $\geq$ 60 Not at-risk	232 (25.4%)	28 (25.7%)	260 (25.4%)
Sex			
Female	497 (54.4%)	54 (49.5%)	551 (53.9%)
Male	416 (45.6%)	55 (50.5%)	471 (46.1%)
Hispanic or Latino ethnicity			
Hispanic or Latino	374 (41.0%)	44 (40.4%)	418 (40.9%)
Not Hispanic or Latino	477 (52.2%)	56 (51.4%)	533 (52.2%)
Not reported and unknown	62 (6.8%)	9 (8.3%)	71 (6.9%)
Race			
White	375 (41.1%)	47 (43.1%)	422 (41.3%)

MOCK

Table 2.1: *(continued)*

Characteristics	Vaccine (N = 913)	Placebo (N = 109)	Total (N = 1022)
Black or African American	332 (36.4%)	38 (34.9%)	370 (36.2%)
Asian	18 (2.0%)	2 (1.8%)	20 (2.0%)
American Indian or Alaska Native	149 (16.3%)	18 (16.5%)	167 (16.3%)
Native Hawaiian or Other Pacific Islander	2 (0.2%)		2 (0.2%)
Multiracial	25 (2.7%)	2 (1.8%)	27 (2.6%)
Not reported and unknown	12 (1.3%)	2 (1.8%)	14 (1.4%)
Underrepresented Minority Status in the U.S.			
URM	227 (24.9%)	28 (25.7%)	255 (25.0%)
Non-URM	227 (24.9%)	28 (25.7%)	255 (25.0%)
Country			
United States	454 (49.7%)	56 (51.4%)	510 (49.9%)
Argentina	45 (4.9%)	5 (4.6%)	50 (4.9%)
Brazil	78 (8.5%)	15 (13.8%)	93 (9.1%)
Chile	13 (1.4%)	1 (0.9%)	14 (1.4%)
Columbia	64 (7.0%)	3 (2.8%)	67 (6.6%)
Mexico	9 (1.0%)	1 (0.9%)	10 (1.0%)
Peru	19 (2.1%)	1 (0.9%)	20 (2.0%)
South Africa	231 (25.3%)	27 (24.8%)	258 (25.2%)
HIV Infection			
Negative	848 (92.9%)	100 (91.7%)	948 (92.8%)
Positive	65 (7.1%)	9 (8.3%)	74 (7.2%)

This table summarizes characteristics of per-protocol participants in the immunogenicity subcohort, which was randomly sampled from the study cohort. The sampling was The sampling was stratified by strata defined by enrollment characteristics: Assigned randomization arm × Baseline SARS-CoV-2 seronegative vs. seropositive × Randomization strata. The U.S. subcohort includes 8 baseline demographic strata; the Latin America and South Africa subcohorts each include 4 baseline demographic strata.

MOCK

2.2 Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Positive Per-Protocol Cohort

Table 2.2: Demographic and Clinical Characteristics at Baseline in the Baseline SARS-CoV-2 Positive Per-Protocol Cohort

Characteristics	Vaccine (N = 283)	Placebo (N = 280)	Total (N = 563)
Age			
Age 18 - 59	141 (49.8%)	139 (49.6%)	280 (49.7%)
Age $\geq$ 60	142 (50.2%)	141 (50.4%)	283 (50.3%)
Mean (Range)	56.1 (18.0, 85.0)	56.4 (18.0, 85.0)	56.3 (18.0, 85.0)
BMI			
Underweight BMI $<$ 18.5		2 (0.7%)	2 (0.4%)
Normal 18.5 $\leq$ BMI $<$ 25	62 (21.9%)	45 (16.1%)	107 (19.0%)
Overweight 25 $\leq$ BMI $<$ 30	112 (39.6%)	114 (40.7%)	226 (40.1%)
Obese BMI $\geq$ 30	109 (38.5%)	119 (42.5%)	228 (40.5%)
Risk for Severe Covid-19			
At-risk	140 (49.5%)	141 (50.4%)	281 (49.9%)
Not at-risk	143 (50.5%)	139 (49.6%)	282 (50.1%)
Age, Risk for Severe Covid-19			
Age 18 - 59 At-risk	69 (24.4%)	69 (24.6%)	138 (24.5%)
Age 18 - 59 Not at-risk	72 (25.4%)	70 (25.0%)	142 (25.2%)
Age $\geq$ 60 At-risk	71 (25.1%)	72 (25.7%)	143 (25.4%)
Age $\geq$ 60 Not at-risk	71 (25.1%)	69 (24.6%)	140 (24.9%)
Sex			
Female	160 (56.5%)	154 (55.0%)	314 (55.8%)
Male	123 (43.5%)	126 (45.0%)	249 (44.2%)
Hispanic or Latino ethnicity			
Hispanic or Latino	106 (37.5%)	105 (37.5%)	211 (37.5%)
Not Hispanic or Latino	164 (58.0%)	152 (54.3%)	316 (56.1%)
Not reported and unknown	13 (4.6%)	23 (8.2%)	36 (6.4%)
Race			
White	108 (38.2%)	108 (38.6%)	216 (38.4%)
Black or African American	111 (39.2%)	94 (33.6%)	205 (36.4%)
Asian	5 (1.8%)	10 (3.6%)	15 (2.7%)
American Indian or Alaska Native	49 (17.3%)	48 (17.1%)	97 (17.2%)
Native Hawaiian or Other Pacific Islander		1 (0.4%)	1 (0.2%)
Multiracial	9 (3.2%)	15 (5.4%)	24 (4.3%)
Not reported and unknown	1 (0.4%)	4 (1.4%)	5 (0.9%)
Underrepresented Minority Status in the U.S.			
URM	71 (25.1%)	70 (25.0%)	141 (25.0%)
Non-URM	71 (25.1%)	71 (25.4%)	142 (25.2%)
Country			
United States	142 (50.2%)	141 (50.4%)	283 (50.3%)
Argentina	11 (3.9%)	16 (5.7%)	27 (4.8%)
Brazil	29 (10.2%)	30 (10.7%)	59 (10.5%)
Chile	1 (0.4%)	1 (0.4%)	2 (0.4%)
Columbia	20 (7.1%)	13 (4.6%)	33 (5.9%)
Mexico	4 (1.4%)	5 (1.8%)	9 (1.6%)

MOCK

Table 2.2: *(continued)*

Characteristics	Vaccine (N = 283)	Placebo (N = 280)	Total (N = 563)
Peru	6 (2.1%)	5 (1.8%)	11 (2.0%)
South Africa	70 (24.7%)	69 (24.6%)	139 (24.7%)
HIV Infection			
Negative	265 (93.6%)	266 (95.0%)	531 (94.3%)
Positive	18 (6.4%)	14 (5.0%)	32 (5.7%)

This table summarizes characteristics of per-protocol participants in the immunogenicity subcohort, which was randomly sampled from the study cohort. The sampling was The sampling was stratified by strata defined by enrollment characteristics: Assigned randomization arm × Baseline SARS-CoV-2 seronegative vs. seropositive × Randomization strata. The U.S. subcohort includes 8 baseline demographic strata; the Latin America and South Africa subcohorts each include 4 baseline demographic strata.

MOCK

2.3 Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort in U.S.

Table 2.3: Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort in U.S.

Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort in U.S.
Sample Sizes (N=793 Participants) (Janssen Trial)

	Baseline SARS-CoV-2 Negative								Baseline SARS-CoV-2 Positive							
	1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8
Vaccine																
Day 29 Cases	6	8	7	6	6	11	8	16	0	0	0	0	0	0	0	0
Non-Cases	56	56	58	56	56	55	57	58	0	0	0	0	0	0	0	0
Placebo																
Day 29 Cases	16	34	17	27	28	39	14	47	0	0	0	0	0	0	0	0
Non-Cases	6	5	7	5	7	7	7	7	0	0	0	0	0	0	0	0

Demographic covariate strata:
1. US Underrepresented minority, Age 18-59, Absence of comorbidities
2. US Underrepresented minority, Age 18-59, Presence of comorbidities
3. US Underrepresented minority, Age $\geq$ 60, Absence of comorbidities
4. US Underrepresented minority, Age $\geq$ 60, Presence of comorbidities
5. US White non-Hisp, Age 18-59, Absence of comorbidities
6. US White non-Hisp, Age 18-59, Presence of comorbidities
7. US White non-Hisp, Age $\geq$ 60, Absence of comorbidities
8. US White non-Hisp, Age $\geq$ 60, Presence of comorbidities

Observed = Numbers of participants sampled into the subcohort within baseline covariate strata.
Estimated = Estimated numbers of participants in the whole per-protocol cohort within baseline covariate strata, calculated using inverse probability weighting.

MOCK

2.4 Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort in Latin America and South Africa

Table 2.4: Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort in Latin America and South Africa

Sample Sizes of Random Subcohort Strata Plus All Other Cases Outside the Random Subcohort in Latin America and South Africa
Sample Sizes (N=792 Participants) (Janssen Trial)

	Baseline SARS-CoV-2 Negative								Baseline SARS-CoV-2 Positive							
	9	10	11	12	13	14	15	16	9	10	11	12	13	14	15	16
Vaccine																
Day 29 Cases	14	20	11	16	9	7	6	11	0	0	0	0	0	0	0	0
Non-Cases	56	57	58	54	56	57	58	58	0	0	0	0	0	0	0	0
Placebo																
Day 29 Cases	43	57	42	59	18	17	16	25	0	0	0	0	0	0	0	0
Non-Cases	7	6	7	6	7	6	7	7	0	0	0	0	0	0	0	0

Demographic covariate strata:
9. Latin America, Age 18-59, Absence of comorbidities
10. Latin America, Age 18-59, Presence of comorbidities
11. Latin America, Age $\geq$ 60, Absence of comorbidities
12. Latin America, Age $\geq$ 60, Presence of comorbidities
13. South Africa, Age 18-59, Absence of comorbidities
14. South Africa, Age 18-59, Presence of comorbidities
15. South Africa, Age $\geq$ 60, Absence of comorbidities
16. South Africa, Age $\geq$ 60, Presence of comorbidities

Observed = Numbers of participants sampled into the subcohort within baseline covariate strata.
Estimated = Estimated numbers of participants in the whole per-protocol cohort within baseline covariate strata, calculated using inverse probability weighting.

MOCK

2.5 Antibody levels in the baseline SARS-CoV-2 negative per-protocol cohort (vaccine recipients)

Table 2.5: Antibody levels in the baseline SARS-CoV-2 negative per-protocol cohort (vaccine recipients)

		Baseline SARS-CoV-2 Negative Vaccine Recipients							
		Cases*			Non-Cases/Control			Comparison	
Visit	Marker	N	Resp rate	GMT/GMC	N	Resp rate	GMT/GMC	Resp Rate Difference	GMTR/GMCR
Day 29	Anti RBD IgG (BAU/ml)	161	76.8/167 = 46.0% (38.4%, 53.8%)	11.56 (9.30, 14.36)	902	10436.4/19036 = 54.8% (51.2%, 58.4%)	16.49 (14.91, 18.25)	-0.09 (-0.17, 0)	0.70 (0.55, 0.89)
Day 29	Anti Spike IgG (BAU/ml)	161	57/167 = 34.2% (27.2%, 41.9%)	6.06 (5.00, 7.34)	902	9147.2/19036 = 48.1% (44.5%, 51.6%)	9.35 (8.51, 10.29)	-0.14 (-0.22, -0.05)	0.65 (0.52, 0.80)
Day 29	Anti N IgG (BAU/ml)	161	4.1/167 = 2.5% (0.9%, 6.5%)	1.10 (0.86, 1.41)	902	1149.5/19036 = 6.0% (4.7%, 7.7%)	1.41 (1.25, 1.60)	-0.04 (-0.06, 0.01)	0.78 (0.59, 1.03)

Cases for Day 29 markers are baseline negative per-protocol vaccine recipients with the symptomatic infection COVID-19 primary endpoint diagnosed starting 7 days after the Day 29 study visit. Non-cases/Controls are baseline negative per-protocol vaccine recipients sampled into the random subcohort with no COVID-19 endpoint diagnosis by the time of data-cut.
N is the number of cases sampled into the subcohort within baseline covariate strata.
The denominator in Resp Rate is the number of participants in the whole per-protocol cohort within baseline covariate strata, calculated using inverse probability weighting.

MOCK

MOCK

Chapter 3

Graphical Descriptions of Antibody Marker Data

3.1 Boxplots

MOCK

MOCK

Figure 3.1: Boxplots of D29 Ab markers: vaccine arm. The three dashed lines in each figure are ULOQ, LLOQ, and LLOD, from top to bottom respectively.

MOCK

Figure 3.2: Boxplots of D29 fold-rise over D1 Ab markers: vaccine arm.

3.2 Weighted RCDF plots

MOCK

MOCK

Figure 3.3: RCDF plots for D29 Ab markers by treatment arm.

MOCK

Figure 3.4: RCDF plots for D29 fold-rise over D1 Ab markers by treatment arm.

3.3 Weighted RCDF plots of threshold correlate concentration for vaccine efficacy

MOCK

Figure 3.5: Marker RCDF of D29 anti-Spike binding Ab: vaccine arm

MOCK

Figure 3.6: Marker RCDF of D29 anti-RBD binding Ab: vaccine arm

MOCK

3.4 Spaghetti plots

Figure 3.7: Spaghetti Plots of Marker Trajectory: vaccine arm

3.5 Violin and line plots

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.1: lineplots of Binding Antibody to Spike: baseline negative placebo arm (version 1)

MOCK

Figure 2.5.2: lineplots of Binding Antibody to Spike: baseline negative vaccine arm (version 1)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.3: lineplots of Binding Antibody to RBD: baseline negative placebo arm (version 1)

MOCK

Figure 2.5.4: lineplots of Binding Antibody to RBD: baseline negative vaccine arm (version 1)

MOCK

Figure 2.5.5: violinplots of Binding Antibody to Spike: baseline negative placebo arm (version 1)

MOCK

Figure 2.5.6: violinplots of Binding Antibody to Spike: baseline negative vaccine arm (version 1)

MOCK

Figure 2.5.7: violinplots of Binding Antibody to RBD: baseline negative placebo arm (version 1)

MOCK

Figure 2.5.8: violinplots of Binding Antibody to RBD: baseline negative vaccine arm (version 1)

MOCK

Figure 2.5.9: lineplots of Binding Antibody to Spike: baseline negative placebo arm (version 2)

MOCK

Figure 2.5.10: lineplots of Binding Antibody to Spike: baseline negative vaccine arm (version 2)

MOCK

Figure 2.5.11: lineplots of Binding Antibody to RBD: baseline negative placebo arm (version 2)

MOCK

Figure 2.5.12: lineplots of Binding Antibody to RBD: baseline negative vaccine arm (version 2)

MOCK

Figure 2.5.13: violinplots of Binding Antibody to Spike: baseline negative placebo arm (version 2)

MOCK

Figure 2.5.14: violinplots of Binding Antibody to Spike: baseline negative vaccine arm (version 2)

MOCK

Figure 2.5.15: violinplots of Binding Antibody to RBD: baseline negative placebo arm (version 2)

MOCK

Figure 2.5.16: violinplots of Binding Antibody to RBD: baseline negative vaccine arm (version 2)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.17: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age (version 1)

MOCK

Figure 2.5.18: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age (version 1)

MOCK

Figure 2.5.19: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age (version 1)

MOCK

Figure 2.5.20: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age (version 1)

MOCK

Figure 2.5.21: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age (version 1)

MOCK

Figure 2.5.22: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age (version 1)

MOCK

Figure 2.5.23: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age (version 1)

MOCK

Figure 2.5.24: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age (version 1)

MOCK

Figure 2.5.25: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age (version 2)

MOCK

Figure 2.5.26: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age (version 2)

MOCK

Figure 2.5.27: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age (version 2)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.28: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age (version 2)

MOCK

Figure 2.5.29: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age (version 2)

MOCK

Figure 2.5.30: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age (version 2)

MOCK

Figure 2.5.31: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age (version 2)

MOCK

Figure 2.5.32: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age (version 2)

MOCK

Figure 2.5.33: lineplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition (version 1)

MOCK

Figure 2.5.34: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition (version 1)

MOCK

Figure 2.5.35: lineplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition (version 1)

MOCK

Figure 2.5.36: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition (version 1)

MOCK

Figure 2.5.37: violinplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition (version 1)

MOCK

Figure 2.5.38: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition (version 1)

MOCK

Figure 2.5.39: violinplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition (version 1)

MOCK

Figure 2.5.40: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition (version 1)

MOCK

Figure 2.5.41: lineplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition (version 2)

MOCK

Figure 2.5.42: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition (version 2)

MOCK

Figure 2.5.43: lineplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition (version 2)

MOCK

Figure 2.5.44: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition (version 2)

MOCK

Figure 2.5.45: violinplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition (version 2)

MOCK

Figure 2.5.46: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition (version 2)

MOCK

Figure 2.5.47: violinplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition (version 2)

MOCK

Figure 2.5.48: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition (version 2)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.49: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition (version 1)

MOCK

Figure 2.5.50: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition (version 1)

MOCK

Figure 2.5.51: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition (version 1)

MOCK

Figure 2.5.52: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition (version 1)

MOCK

Figure 2.5.53: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition (version 1)

MOCK

Figure 2.5.54: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition (version 1)

MOCK

Figure 2.5.55: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition (version 1)

MOCK

Figure 2.5.56: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition (version 1)

Figure 2.5.57: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition (version 2)

Figure 2.5.58: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition (version 2)

MOCK

Figure 2.5.59: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition (version 2)

Figure 2.5.60: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition (version 2)

MOCK

Figure 2.5.61: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition (version 2)

MOCK

Figure 2.5.62: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition (version 2)

Figure 2.5.63: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition (version 2)

MOCK

Figure 2.5.64: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition (version 2)

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.65: lineplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth (version 1)

MOCK

Figure 2.5.66: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth (version 1)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.67: lineplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth (version 1)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.68: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth (version 1)

MOCK

Figure 2.5.69: violinplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth (version 1)

MOCK

Figure 2.5.70: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth (version 1)

MOCK

Figure 2.5.71: violinplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth (version 1)

MOCK

Figure 2.5.72: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth (version 1)

MOCK

Figure 2.5.73: lineplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth (version 2)

MOCK

Figure 2.5.74: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth (version 2)

MOCK

Figure 2.5.75: lineplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth (version 2)

MOCK

Figure 2.5.76: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth (version 2)

MOCK

Figure 2.5.77: violinplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth (version 2)

MOCK

Figure 2.5.78: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth (version 2)

MOCK

Figure 2.5.79: violinplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth (version 2)

MOCK

Figure 2.5.80: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth (version 2)

MOCK

Figure 2.5.81: lineplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group (version 1)

MOCK

Figure 2.5.82: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group (version 1)

MOCK

Figure 2.5.83: lineplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group (version 1)

MOCK

Figure 2.5.84: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group (version 1)

MOCK

Figure 2.5.85: violinplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group (version 1)

MOCK

Figure 2.5.86: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group (version 1)

MOCK

Figure 2.5.87: violinplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group (version 1)

MOCK

Figure 2.5.88: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group (version 1)

MOCK

Figure 2.5.89: lineplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group (version 2)

MOCK

Figure 2.5.90: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group (version 2)

MOCK

Figure 2.5.91: lineplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group (version 2)

MOCK

Figure 2.5.92: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group (version 2)

MOCK

Figure 2.5.93: violinplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group (version 2)

MOCK

Figure 2.5.94: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group (version 2)

MOCK

Figure 2.5.95: violinplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group (version 2)

MOCK

Figure 2.5.96: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group (version 2)

MOCK

Figure 2.5.97: lineplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

MOCK

Figure 2.5.98: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

MOCK

Figure 2.5.99: lineplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

MOCK

Figure 2.5.100: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

MOCK

Figure 2.5.101: violinplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

MOCK

Figure 2.5.102: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

MOCK

Figure 2.5.103: violinplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 1)

MOCK

Figure 2.5.104: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 1)

MOCK

Figure 2.5.105: lineplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

MOCK

Figure 2.5.106: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.107: lineplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

MOCK

Figure 2.5.108: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

MOCK

Figure 2.5.109: violinplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

MOCK

Figure 2.5.110: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

MOCK

Figure 2.5.111: violinplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group (version 2)

MOCK

Figure 2.5.112: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group (version 2)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.113: lineplots of Binding Antibody to Spike: baseline negative placebo arm severe only (version 1)

MOCK

Figure 2.5.114: lineplots of Binding Antibody to Spike: baseline negative vaccine arm severe only (version 1)

MOCK

Figure 2.5.115: lineplots of Binding Antibody to RBD: baseline negative placebo arm severe only (version 1)

MOCK

Figure 2.5.116: lineplots of Binding Antibody to RBD: baseline negative vaccine arm severe only (version 1)

MOCK

Figure 2.5.117: violinplots of Binding Antibody to Spike: baseline negative placebo arm severe only (version 1)

MOCK

Figure 2.5.118: violinplots of Binding Antibody to Spike: baseline negative vaccine arm severe only (version 1)

MOCK

Figure 2.5.119: violinplots of Binding Antibody to RBD: baseline negative placebo arm severe only (version 1)

MOCK

Figure 2.5.120: violinplots of Binding Antibody to RBD: baseline negative vaccine arm severe only (version 1)

MOCK

Figure 2.5.121: lineplots of Binding Antibody to Spike: baseline negative placebo arm severe only (version 2)

MOCK

Figure 2.5.122: lineplots of Binding Antibody to Spike: baseline negative vaccine arm severe only (version 2)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.123: lineplots of Binding Antibody to RBD: baseline negative placebo arm severe only (version 2)

MOCK

Figure 2.5.124: lineplots of Binding Antibody to RBD: baseline negative vaccine arm severe only (version 2)

MOCK

Figure 2.5.125: violinplots of Binding Antibody to Spike: baseline negative placebo arm severe only (version 2)

MOCK

Figure 2.5.126: violinplots of Binding Antibody to Spike: baseline negative vaccine arm severe only (version 2)

MOCK

Figure 2.5.127: violinplots of Binding Antibody to RBD: baseline negative placebo arm severe only (version 2)

MOCK

Figure 2.5.128: violinplots of Binding Antibody to RBD: baseline negative vaccine arm severe only (version 2)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.129: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age severe only (version 1)

MOCK

Figure 2.5.130: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age severe only (version 1)

MOCK

Figure 2.5.131: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age severe only (version 1)

MOCK

Figure 2.5.132: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age severe only (version 1)

MOCK

Figure 2.5.133: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age severe only (version 1)

MOCK

Figure 2.5.134: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age severe only (version 1)

MOCK

Figure 2.5.135: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age severe only (version 1)

MOCK

Figure 2.5.136: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age severe only (version 1)

MOCK

Figure 2.5.137: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age severe only (version 2)

MOCK

Figure 2.5.138: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age severe only (version 2)

MOCK

Figure 2.5.139: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age severe only (version 2)

MOCK

Figure 2.5.140: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age severe only (version 2)

MOCK

Figure 2.5.141: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age severe only (version 2)

MOCK

Figure 2.5.142: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age severe only (version 2)

MOCK

Figure 2.5.143: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age severe only (version 2)

MOCK

Figure 2.5.144: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age severe only (version 2)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.145: lineplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition severe only (version 1)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.146: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition severe only (version 1)

MOCK

Figure 2.5.147: lineplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition severe only (version 1)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.148: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition severe only (version 1)

MOCK

Figure 2.5.149: violinplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition severe only (version 1)

MOCK

Figure 2.5.150: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition severe only (version 1)

MOCK

Figure 2.5.151: violinplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition severe only (version 1)

MOCK

Figure 2.5.152: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition severe only (version 1)

MOCK

Figure 2.5.153: lineplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition severe only (version 2)

MOCK

Figure 2.5.154: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition severe only (version 2)

MOCK

Figure 2.5.155: lineplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition severe only (version 2)

MOCK

Figure 2.5.156: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition severe only (version 2)

MOCK

Figure 2.5.157: violinplots of Binding Antibody to Spike: baseline negative placebo arm by risk condition severe only (version 2)

MOCK

Figure 2.5.158: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by risk condition severe only (version 2)

MOCK

Figure 2.5.159: violinplots of Binding Antibody to RBD: baseline negative placebo arm by risk condition severe only (version 2)

MOCK

Figure 2.5.160: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by risk condition severe only (version 2)

MOCK

MOCK

Figure 2.5.161: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition severe only (version 1)

MOCK

Figure 2.5.162: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition severe only (version 1)

MOCK

Figure 2.5.163: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition severe only (version 1)

MOCK

Figure 2.5.164: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition severe only (version 1)

MOCK

Figure 2.5.165: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition severe only (version 1)

MOCK

Figure 2.5.166: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition severe only (version 1)

MOCK

Figure 2.5.167: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition severe only (version 1)

MOCK

Figure 2.5.168: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition severe only (version 1)

Figure 2.5.169: lineplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition severe only (version 2)

MOCK

Figure 2.5.170: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition severe only (version 2)

MOCK

MOCK

Figure 2.5.171: lineplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition severe only (version 2)

MOCK

Figure 2.5.172: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition severe only (version 2)

MOCK

Figure 2.5.173: violinplots of Binding Antibody to Spike: baseline negative placebo arm by age and risk condition severe only (version 2)

MOCK

Figure 2.5.174: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by age and risk condition severe only (version 2)

MOCK

Figure 2.5.175: violinplots of Binding Antibody to RBD: baseline negative placebo arm by age and risk condition severe only (version 2)

MOCK

Figure 2.5.176: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by age and risk condition severe only (version 2)

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.177: lineplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth severe only (version 1)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.178: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth severe only (version 1)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.179: lineplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth severe only (version 1)

MOCK

Figure 2.5.180: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth severe only (version 1)

MOCK

Figure 2.5.181: violinplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth severe only (version 1)

MOCK

Figure 2.5.182: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth severe only (version 1)

MOCK

Figure 2.5.183: violinplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth severe only (version 1)

MOCK

Figure 2.5.184: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth severe only (version 1)

MOCK

Figure 2.5.185: lineplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth severe only (version 2)

MOCK

Figure 2.5.186: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth severe only (version 2)

MOCK

Figure 2.5.187: lineplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth severe only (version 2)

MOCK

Figure 2.5.188: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth severe only (version 2)

MOCK

Figure 2.5.189: violinplots of Binding Antibody to Spike: baseline negative placebo arm by sex assigned at birth severe only (version 2)

MOCK

Figure 2.5.190: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by sex assigned at birth severe only (version 2)

MOCK

Figure 2.5.191: violinplots of Binding Antibody to RBD: baseline negative placebo arm by sex assigned at birth severe only (version 2)

MOCK

Figure 2.5.192: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by sex assigned at birth severe only (version 2)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.193: lineplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group severe only (version 1)

MOCK

Figure 2.5.194: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group severe only (version 1)

MOCK

Figure 2.5.195: lineplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group severe only (version 1)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.196: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group severe only (version 1)

MOCK

Figure 2.5.197: violinplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group severe only (version 1)

MOCK

Figure 2.5.198: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group severe only (version 1)

MOCK

Figure 2.5.199: violinplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group severe only (version 1)

MOCK

Figure 2.5.200: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group severe only (version 1)

MOCK

Figure 2.5.201: lineplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group severe only (version 2)

MOCK

Figure 2.5.202: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group severe only (version 2)

MOCK

Figure 2.5.203: lineplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group severe only (version 2)

MOCK

Figure 2.5.204: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group severe only (version 2)

MOCK

Figure 2.5.205: violinplots of Binding Antibody to Spike: baseline negative placebo arm by race and ethnic group severe only (version 2)

MOCK

Figure 2.5.206: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by race and ethnic group severe only (version 2)

MOCK

Figure 2.5.207: violinplots of Binding Antibody to RBD: baseline negative placebo arm by race and ethnic group severe only (version 2)

MOCK

Figure 2.5.208: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by race and ethnic group severe only (version 2)

MOCK

Figure 2.5.209: lineplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group severe only (version 1)

MOCK

Figure 2.5.210: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group severe only (version 1)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.211: lineplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group severe only (version 1)

MOCK

Figure 2.5.212: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group severe only (version 1)

MOCK

Figure 2.5.213: violinplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group severe only (version 1)

MOCK

Figure 2.5.214: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group severe only (version 1)

MOCK

Figure 2.5.215: violinplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group severe only (version 1)

MOCK

Figure 2.5.216: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group severe only (version 1)

MOCK

Figure 2.5.217: lineplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group severe only (version 2)

MOCK

Figure 2.5.218: lineplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group severe only (version 2)

MOCK

All data points for cases are shown. Non−Case data points are shown for all eligible participants or for a random sample of 100 eligible participants, whichever is larger

Figure 2.5.219: lineplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group severe only (version 2)

MOCK

Figure 2.5.220: lineplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group severe only (version 2)

MOCK

Figure 2.5.221: violinplots of Binding Antibody to Spike: baseline negative placebo arm by dichotomous classification of race and ethnic group severe only (version 2)

MOCK

Figure 2.5.222: violinplots of Binding Antibody to Spike: baseline negative vaccine arm by dichotomous classification of race and ethnic group severe only (version 2)

MOCK

Figure 2.5.223: violinplots of Binding Antibody to RBD: baseline negative placebo arm by dichotomous classification of race and ethnic group severe only (version 2)

MOCK

Figure 2.5.224: violinplots of Binding Antibody to RBD: baseline negative vaccine arm by dichotomous classification of race and ethnic group severe only (version 2)

MOCK

3.6 Scatter plots

Figure 2.6.1: scatterplots of Binding Antibody to Spike vs Age: baseline negative vaccine arm at day 1

Figure 2.6.2: scatterplots of Binding Antibody to Spike vs Age: baseline negative vaccine arm at day 29

Figure 2.6.3: scatterplots of Binding Antibody to RBD vs Age: baseline negative vaccine arm at day 1

Figure 2.6.4: scatterplots of Binding Antibody to RBD vs Age: baseline negative vaccine arm at day 29

Figure 2.6.5: scatterplots of Binding Antibody to Spike vs Age: by arm at day 1

Figure 2.6.6: scatterplots of Binding Antibody to Spike vs Age: by arm at day 29

Figure 2.6.7: scatterplots of Binding Antibody to RBD vs Age: by arm at day 1

Figure 2.6.8: scatterplots of Binding Antibody to RBD vs Age: by arm at day 29

Figure 2.6.9: scatterplots of Binding Antibody to Spike vs Days Since the Day 1 Visit: baseline negative vaccine arm at Day 1 and Day 29

MOCK

Figure 2.6.10: scatterplots of Binding Antibody to RBD vs Days Since the Day 1 Visit: baseline negative vaccine arm at Day 1 and Day 29

Figure 2.6.11: scatterplots of Binding Antibody to Spike vs Days Since the Day 1 Visit: by arm at Day 1 and Day 29

MOCK

Figure 2.6.12: scatterplots of Binding Antibody to RBD vs Days Since the Day 1 Visit: by arm at Day 1 and Day 29

Chapter 4

Graphical Descriptions of Time to Event Data

This page is empty.

MOCK

MOCK

Chapter 5

Day D29 Univariate CoR: Cox Models of Risk

MOCK

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

5.1 Hazard ratios

Table 5.1: 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*

MockENSEMBLE Immunologic Marker	No. cases / No. at-risk**	HR per 10-fold incr. Pt. Est.	95% CI	P-value (2-sided)	q-value ***	FWER
Anti Spike IgG (BAU/ml)	167/19,203	0.41	(0.31-0.54)	<0.001	<0.001	<0.001
Anti RBD IgG (BAU/ml)	167/19,203	0.52	(0.40-0.67)	<0.001	<0.001	<0.001

*Baseline covariates adjusted for: riskscore + as.factor(Region). Maximum failure event time 149 days.
**No. at-risk = estimated number in the population for analysis, i.e. baseline negative per-protocol vaccine recipients not experiencing the COVID endpoint through 6 days post Day 29 visit; no. cases = number of this cohort with an observed COVID endpoint.
***q-value and FWER (family-wide error rate) are computed over the set of p-values both for quantitative markers and categorical markers using the Westfall and Young permutation method (10 replicates).
‡ Count cases starting 7 days post Day 29.

Table 5.2: 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*

MockENSEMBLE 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
Anti Spike IgG (BAU/ml)	Lower	77/6,435	0.0120	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	58/6,363	0.0091	0.61	(0.41-0.91)	0.015			
	Upper	32/6,406	0.0050	0.27	(0.17-0.42)	<0.001			
Anti RBD IgG (BAU/ml)	Lower	69/6,414	0.0108	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	61/6,419	0.0095	0.73	(0.50-1.09)	0.124			
	Upper	36/6,370	0.0057	0.36	(0.23-0.56)	<0.001			
Placebo		513/19,233	0.0267						

*Baseline covariates adjusted for: riskscore + as.factor(Region). Maximum failure event time 149 days. Cutpoints: Anti Spike IgG (BAU/ml) [0.73, 1.25), Anti RBD IgG (BAU/ml) [0.94, 1.54), all on the log10 scale.
**No. at-risk = estimated number in the population for analysis, i.e. baseline negative per-protocol vaccine recipients not experiencing the COVID endpoint through 6 days post Day 29 visit; no. cases = number of this cohort with an observed COVID endpoint.
***Generalized Wald-test p-value of the null hypothesis that the hazard rate is constant across the Lower, Middle, and Upper tertile groups.
† q-value and FWER (family-wide error rate) are computed over the set of p-values both for quantitative markers and categorical markers using the Westfall and Young permutation method (10 replicates).
‡ Count cases starting 7 days post Day 29.

MOCK

Figure 5.1: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to spike markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 7 days post Day 29.

MOCK

Figure 5.2: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to RBD markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 7 days post Day 29.

Figure 5.3: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to spike markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 7 days post Day 29.

MOCK

Figure 5.4: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to RBD markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 7 days post Day 29.

5.2 Marginalized risk and controlled vaccine efficacy plots

Table 5.3: Analysis of Day 29 markers (upper vs. lower tertile) as a CoR and a controlled risk CoP.

	marginalized risk ratio $RR_M(0,1)$		controlled risk ratio $RR_C(0,1)$[1]		e(0,1)[2]	
	Point Est.	95% CI	Point Est.	95% CI	Point Est.	95% CI UL
Anti Spike IgG (BAU/ml)	0.27	0.16–0.40	0.36	0.22–0.53	6.9	4.5
Anti RBD IgG (BAU/ml)	0.36	0.24–0.60	0.48	0.32–0.81	4.9	2.7

[1]Conservative (upper bound) estimate assuming unmeasured confounding at level $RR_{UD}(0,1) = RR_{EU}(0,1) = 2$ and thus $B(0,1) = 4/3$.
[2]E-values are computed for upper tertile ($s = 1$) vs. lower tertile ($s = 0$) biomarker subgroups after controlling for baseline risk score, meeting the protocol randomization stratification criterion for being at heightened risk of COVID (yes or no), strata(Region); UL = upper limit.
‡ Count cases starting 7 days post Day 29.

MOCK

(a) Marginalized cumulative incidence rate curves for trichotomized Day 29 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

(b) Marginalized cumulative risk by Day 149 as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 5.5: Marginalized cumulative risk curves (=s). ‡ Count cases starting 7 days post Day 29.

MOCK

(a) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

(b) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 5.6: Controlled VE curves (=s). ‡ Count cases starting 7 days post Day 29.

MOCK

(a) Marginalized cumulative risk by Day 149 post Day 29 visit as functions of Day 29 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

(b) Controlled VE as functions of Day 29 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 5.7: Marginalized cumulative risk curves and controlled VE curves (>=s). ‡ Count cases starting 7 days post Day 29.

MOCK

Table 5.4: Marginalized cumulative risk by Day 149 as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.2	.0409 (.0265,.0699)	1	.0187 (.0151,.0250)	7	.0095 (.0086,.0103)	41	.0049 (.0040,.0059)
0	.0397 (.0260,.0674)	1	.0182 (.0148,.0241)	8	.0093 (.0084,.0100)	43	.0048 (.0038,.0058)
0	.0387 (.0254,.0650)	1	.0177 (.0145,.0232)	8	.0090 (.0082,.0097)	47	.0047 (.0037,.0057)
0	.0376 (.0249,.0627)	2	.0172 (.0142,.0224)	9	.0088 (.0079,.0094)	50	.0046 (.0036,.0056)
0	.0366 (.0244,.0605)	2	.0172 (.0142,.0223)	9	.0088 (.0079,.0094)	54	.0044 (.0034,.0055)
0	.0356 (.0240,.0583)	2	.0167 (.0140,.0215)	10	.0085 (.0077,.0091)	54	.0044 (.0034,.0054)
0	.0346 (.0235,.0563)	2	.0163 (.0137,.0207)	11	.0083 (.0074,.0088)	58	.0043 (.0033,.0053)
0	.0337 (.0230,.0543)	2	.0158 (.0134,.0200)	11	.0080 (.0072,.0085)	63	.0042 (.0032,.0052)
0	.0327 (.0226,.0523)	2	.0154 (.0131,.0192)	12	.0078 (.0070,.0083)	67	.0041 (.0030,.0051)
0	.0318 (.0221,.0504)	2	.0150 (.0129,.0187)	13	.0076 (.0068,.0081)	73	.0040 (.0029,.0050)
0	.0310 (.0217,.0486)	2	.0150 (.0129,.0185)	13	.0076 (.0067,.0081)	78	.0038 (.0028,.0049)
0	.0301 (.0213,.0469)	2	.0145 (.0126,.0179)	14	.0074 (.0065,.0079)	84	.0037 (.0027,.0048)
0	.0293 (.0208,.0452)	3	.0141 (.0124,.0172)	15	.0072 (.0063,.0077)	91	.0036 (.0026,.0047)
0	.0285 (.0204,.0436)	3	.0137 (.0121,.0166)	16	.0070 (.0061,.0076)	98	.0035 (.0025,.0046)
0	.0277 (.0200,.0420)	3	.0134 (.0119,.0160)	18	.0068 (.0059,.0074)	105	.0034 (.0024,.0045)
0	.0269 (.0196,.0405)	3	.0130 (.0117,.0154)	18	.0067 (.0058,.0073)	113	.0033 (.0023,.0045)
1	.0262 (.0192,.0390)	3	.0130 (.0116,.0153)	19	.0066 (.0057,.0072)	122	.0032 (.0022,.0044)
1	.0255 (.0188,.0376)	3	.0126 (.0114,.0148)	21	.0064 (.0055,.0071)	132	.0032 (.0022,.0043)
1	.0248 (.0185,.0362)	4	.0123 (.0112,.0143)	22	.0062 (.0053,.0069)	142	.0031 (.0021,.0042)
1	.0241 (.0181,.0349)	4	.0119 (.0109,.0138)	24	.0061 (.0052,.0068)	153	.0030 (.0020,.0041)
1	.0234 (.0177,.0337)	4	.0116 (.0106,.0133)	26	.0059 (.0050,.0067)	164	.0029 (.0019,.0040)
1	.0228 (.0174,.0324)	5	.0113 (.0103,.0128)	28	.0057 (.0048,.0065)	177	.0028 (.0019,.0040)
1	.0222 (.0171,.0313)	5	.0110 (.0100,.0124)	30	.0056 (.0046,.0064)	191	.0027 (.0018,.0039)
1	.0215 (.0167,.0301)	5	.0107 (.0097,.0119)	31	.0055 (.0045,.0063)	205	.0027 (.0017,.0038)
1	.0210 (.0164,.0290)	6	.0104 (.0094,.0115)	32	.0054 (.0044,.0063)	221	.0026 (.0016,.0037)
1	.0204 (.0161,.0280)	6	.0102 (.0092,.0112)	35	.0053 (.0043,.0061)	238	.0025 (.0016,.0037)
1	.0198 (.0157,.0269)	6	.0101 (.0092,.0111)	37	.0051 (.0041,.0060)	500	.0019 (.0011,.0030)
1	.0193 (.0154,.0260)	7	.0098 (.0089,.0107)	40	.0050 (.0040,.0059)	1000	.0015 (.0008,.0025)

MOCA

Table 5.5: Controlled VE as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 149 days post Day 29 was 0.009 in vaccine recipients compared to 0.027 in placebo recipients, with cumulative vaccine efficacy 67.4% (95% CI 64.4 to 71.5%).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.2	-0.4918 (-1.5405,.0746)	1	0.3349 (0.1241,.4822)	8	0.6712 (0.6409,.7108)	50	0.8334 (0.8061,.8709)
0	-0.4512 (-1.4509,.0929)	1	0.3534 (0.1562,.4924)	9	0.6802 (0.6522,.7193)	54	0.8375 (0.8095,.8752)
0	-0.4117 (-1.3643,.1108)	2	0.3713 (0.1872,.5025)	9	0.6804 (0.6525,.7195)	54	0.8380 (0.8099,.8758)
0	-0.3732 (-1.2805,.1284)	2	0.3718 (0.1882,.5028)	10	0.6893 (0.6636,.7279)	58	0.8426 (0.8137,.8804)
0	-0.3357 (-1.1996,.1457)	2	0.3887 (0.2170,.5124)	11	0.6980 (0.6745,.7360)	63	0.8470 (0.8174,.8849)
0	-0.2993 (-1.1214,.1626)	2	0.4056 (0.2454,.5221)	11	0.7064 (0.6849,.7439)	67	0.8512 (0.8210,.8892)
0	-0.2638 (-1.0458,.1791)	2	0.4221 (0.2723,.5316)	12	0.7146 (0.6951,.7515)	73	0.8554 (0.8245,.8934)
0	-0.2292 (-0.9728,.1954)	2	0.4381 (0.2982,.5409)	13	0.7207 (0.7026,.7573)	78	0.8595 (0.8280,.8974)
0	-0.1956 (-0.9023,.2113)	2	0.4507 (0.3184,.5482)	13	0.7225 (0.7049,.7590)	84	0.8634 (0.8314,.9013)
0	-0.1628 (-0.8342,.2270)	2	0.4537 (0.3233,.5500)	14	0.7303 (0.7144,.7662)	91	0.8672 (0.8348,.9050)
0	-0.1310 (-0.7684,.2423)	2	0.4689 (0.3474,.5589)	15	0.7378 (0.7235,.7732)	98	0.8709 (0.8380,.9085)
0	-0.0999 (-0.7049,.2573)	3	0.4836 (0.3708,.5677)	16	0.7451 (0.7324,.7802)	105	0.8745 (0.8412,.9120)
0	-0.0698 (-0.6436,.2720)	3	0.4980 (0.3932,.5763)	18	0.7522 (0.7399,.7872)	113	0.8780 (0.8444,.9153)
0	-0.0404 (-0.5844,.2864)	3	0.5119 (0.4149,.5847)	18	0.7555 (0.7426,.7904)	122	0.8815 (0.8475,.9185)
0	-0.0118 (-0.5273,.3006)	3	0.5255 (0.4358,.5929)	19	0.7592 (0.7456,.7940)	132	0.8848 (0.8505,.9215)
0	0.0160 (-0.4721,.3145)	3	0.5258 (0.4364,.5931)	21	0.7659 (0.7512,.8006)	142	0.8880 (0.8534,.9245)
1	0.0431 (-0.4189,.3280)	3	0.5387 (0.4560,.6010)	22	0.7724 (0.7566,.8070)	153	0.8911 (0.8563,.9273)
1	0.0694 (-0.3675,.3414)	4	0.5515 (0.4755,.6089)	24	0.7788 (0.7618,.8132)	164	0.8942 (0.8592,.9301)
1	0.0950 (-0.3179,.3544)	4	0.5640 (0.4943,.6170)	26	0.7850 (0.7669,.8197)	177	0.8972 (0.8620,.9327)
1	0.1200 (-0.2701,.3672)	4	0.5761 (0.5124,.6252)	28	0.7910 (0.7718,.8263)	191	0.9000 (0.8647,.9352)
1	0.1442 (-0.2240,.3798)	5	0.5879 (0.5290,.6335)	30	0.7968 (0.7767,.8326)	205	0.9028 (0.8674,.9376)
1	0.1678 (-0.1795,.3921)	5	0.5993 (0.5448,.6436)	31	0.7998 (0.7792,.8358)	221	0.9056 (0.8700,.9400)
1	0.1908 (-0.1365,.4042)	5	0.6105 (0.5600,.6535)	32	0.8025 (0.7813,.8387)	238	0.9082 (0.8726,.9422)
1	0.2131 (-0.0951,.4160)	6	0.6213 (0.5748,.6635)	35	0.8080 (0.7857,.8445)	500	0.9309 (0.8956,.9608)
1	0.2348 (-0.0552,.4276)	6	0.6290 (0.5851,.6708)	37	0.8134 (0.7899,.8502)	1000	0.9470 (0.9134,.9727)
1	0.2560 (-0.0167,.4389)	6	0.6319 (0.5891,.6736)	40	0.8186 (0.7941,.8556)	7.3	.6521 (.6162,.6928)
1	0.2766 (0.0205,.4501)	7	0.6421 (0.6029,.6833)	41	0.8196 (0.7949,.8566)	191	.9000 (.8647,.9352)
1	0.2966 (0.0563,.4610)	7	0.6521 (0.6162,.6928)	43	0.8237 (0.7981,.8608)	1000	.9470 (.9134,.9727)
1	0.3160 (0.0908,.4717)	8	0.6618 (0.6290,.7019)	47	0.8286 (0.8022,.8659)		

MOCK

Table 5.6: Controlled VE with sensitivity analysis as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.2	.0818 (-0.5637,.4304)	1	.4246 (0.2422,.5520)	8	.6713 (0.6411,.7109)	50	.8126 (0.7819,.8548)
0	.0947 (-0.5289,.4341)	1	.4353 (0.2631,.5567)	9	.6802 (0.6522,.7193)	54	.8158 (0.7841,.8586)
0	.1076 (-0.4946,.4379)	2	.4459 (0.2836,.5616)	9	.6804 (0.6525,.7195)	54	.8162 (0.7843,.8590)
0	.1203 (-0.4609,.4417)	2	.4462 (0.2843,.5617)	10	.6892 (0.6635,.7278)	58	.8197 (0.7867,.8631)
0	.1330 (-0.4277,.4455)	2	.4564 (0.3038,.5664)	11	.6976 (0.6741,.7357)	63	.8231 (0.7889,.8670)
0	.1456 (-0.3950,.4493)	2	.4669 (0.3231,.5713)	11	.7056 (0.6841,.7432)	67	.8264 (0.7911,.8708)
0	.1581 (-0.3629,.4532)	2	.4773 (0.3417,.5763)	12	.7132 (0.6936,.7504)	73	.8296 (0.7932,.8744)
0	.1706 (-0.3312,.4571)	2	.4876 (0.3600,.5813)	13	.7189 (0.7007,.7557)	78	.8327 (0.7953,.8779)
0	.1829 (-0.3001,.4610)	2	.4958 (0.3744,.5853)	13	.7206 (0.7028,.7572)	84	.8358 (0.7973,.8813)
0	.1952 (-0.2694,.4650)	2	.4978 (0.3779,.5863)	14	.7275 (0.7115,.7638)	91	.8387 (0.7993,.8846)
0	.2074 (-0.2393,.4690)	2	.5080 (0.3955,.5914)	15	.7342 (0.7198,.7701)	98	.8416 (0.8012,.8877)
0	.2196 (-0.2097,.4730)	3	.5181 (0.4128,.5966)	16	.7406 (0.7278,.7763)	105	.8443 (0.8030,.8908)
0	.2316 (-0.1806,.4771)	3	.5282 (0.4298,.6018)	18	.7468 (0.7342,.7825)	113	.8470 (0.8048,.8937)
0	.2436 (-0.1520,.4812)	3	.5382 (0.4464,.6070)	18	.7496 (0.7364,.7854)	122	.8497 (0.8066,.8966)
0	.2555 (-0.1238,.4853)	3	.5481 (0.4627,.6123)	19	.7527 (0.7388,.7885)	132	.8522 (0.8083,.8994)
0	.2673 (-0.0962,.4895)	3	.5484 (0.4632,.6125)	21	.7584 (0.7433,.7942)	142	.8547 (0.8099,.9021)
1	.2790 (-0.0690,.4937)	3	.5579 (0.4788,.6177)	22	.7639 (0.7474,.7997)	153	.8572 (0.8115,.9046)
1	.2907 (-0.0424,.4980)	4	.5677 (0.4945,.6231)	24	.7691 (0.7514,.8050)	164	.8596 (0.8131,.9072)
1	.3023 (-0.0162,.5023)	4	.5775 (0.5099,.6289)	26	.7742 (0.7552,.8107)	177	.8619 (0.8146,.9096)
1	.3138 (0.0096,.5066)	4	.5871 (0.5251,.6350)	28	.7791 (0.7589,.8164)	191	.8641 (0.8161,.9120)
1	.3252 (0.0348,.5109)	5	.5967 (0.5391,.6414)	30	.7838 (0.7624,.8218)	205	.8664 (0.8176,.9142)
1	.3365 (0.0596,.5153)	5	.6062 (0.5526,.6498)	31	.7862 (0.7642,.8246)	221	.8685 (0.8190,.9165)
1	.3478 (0.0840,.5198)	5	.6157 (0.5659,.6581)	32	.7883 (0.7656,.8271)	238	.8706 (0.8204,.9186)
1	.3590 (0.1079,.5242)	6	.6251 (0.5791,.6669)	35	.7927 (0.7686,.8321)	500	.8892 (0.8327,.9371)
1	.3701 (0.1314,.5288)	6	.6319 (0.5884,.6734)	37	.7970 (0.7714,.8370)	1000	.9034 (0.8421,.9502)
1	.3812 (0.1544,.5333)	6	.6345 (0.5920,.6759)	40	.8011 (0.7742,.8417)	7.3	.6521 (.6162,.6928)
1	.3921 (0.1770,.5379)	7	.6438 (0.6047,.6848)	41	.8019 (0.7747,.8425)	191	.9000 (.8647,.9352)
1	.4030 (0.1991,.5426)	7	.6530 (0.6172,.6936)	43	.8050 (0.7769,.8461)	1000	.9470 (.9134,.9727)
1	.4138 (0.2209,.5472)	8	.6622 (0.6295,.7023)	47	.8089 (0.7794,.8505)		

MODEL

(a) Marginalized cumulative incidence rate curves for trichotomized Day 29 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

(b) Marginalized cumulative risk by Day 149 as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 5.8: Marginalized cumulative risk curves (=s). ‡ Count cases starting 7 days post Day 29.

MOCK

(a) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

(b) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 5.9: Controlled VE curves (=s). ‡ Count cases starting 7 days post Day 29.

MOCK

(a) Marginalized cumulative risk by Day 149 post Day 29 visit as functions of Day 29 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

(b) Controlled VE as functions of Day 29 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 5.10: Marginalized cumulative risk curves and controlled VE curves (>=s). ‡ Count cases starting 7 days post Day 29.

MOCK

Table 5.7: Marginalized cumulative risk by Day 149 as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.8	.0205 (.0145,.0299)	3	.0136 (.0114,.0170)	13	.0093 (.0083,.0102)	52	.0063 (.0053,.0073)
1	.0202 (.0144,.0293)	4	.0134 (.0113,.0167)	14	.0091 (.0081,.0100)	55	.0062 (.0052,.0073)
1	.0199 (.0143,.0287)	4	.0132 (.0112,.0164)	15	.0090 (.0080,.0098)	58	.0061 (.0051,.0072)
1	.0196 (.0141,.0281)	4	.0132 (.0112,.0163)	15	.0089 (.0079,.0098)	61	.0060 (.0050,.0071)
1	.0193 (.0140,.0275)	4	.0130 (.0111,.0160)	16	.0089 (.0079,.0097)	65	.0059 (.0049,.0071)
1	.0190 (.0139,.0270)	4	.0128 (.0110,.0157)	17	.0087 (.0078,.0095)	69	.0058 (.0048,.0070)
1	.0187 (.0138,.0264)	5	.0126 (.0109,.0153)	18	.0086 (.0076,.0093)	71	.0058 (.0048,.0070)
1	.0185 (.0136,.0259)	5	.0124 (.0108,.0150)	19	.0085 (.0075,.0092)	72	.0058 (.0047,.0069)
1	.0182 (.0135,.0253)	5	.0122 (.0107,.0147)	20	.0083 (.0074,.0091)	76	.0057 (.0046,.0069)
1	.0179 (.0134,.0248)	5	.0120 (.0106,.0144)	21	.0082 (.0072,.0089)	81	.0056 (.0045,.0068)
1	.0176 (.0133,.0243)	5	.0119 (.0106,.0143)	22	.0081 (.0071,.0088)	85	.0055 (.0044,.0067)
1	.0174 (.0132,.0238)	6	.0118 (.0105,.0141)	23	.0080 (.0070,.0087)	90	.0054 (.0044,.0067)
2	.0171 (.0130,.0233)	6	.0117 (.0104,.0138)	23	.0079 (.0069,.0086)	90	.0054 (.0044,.0067)
2	.0168 (.0129,.0228)	6	.0115 (.0103,.0135)	24	.0078 (.0068,.0086)	95	.0053 (.0043,.0066)
2	.0166 (.0128,.0224)	7	.0113 (.0101,.0132)	26	.0077 (.0067,.0085)	100	.0053 (.0042,.0066)
2	.0163 (.0127,.0219)	7	.0111 (.0100,.0130)	27	.0076 (.0066,.0084)	106	.0052 (.0041,.0065)
2	.0161 (.0126,.0214)	7	.0110 (.0098,.0127)	29	.0075 (.0065,.0083)	112	.0051 (.0040,.0064)
2	.0158 (.0125,.0210)	8	.0108 (.0097,.0124)	30	.0074 (.0064,.0082)	118	.0050 (.0039,.0064)
2	.0156 (.0124,.0206)	8	.0106 (.0095,.0122)	32	.0073 (.0062,.0081)	121	.0050 (.0039,.0064)
2	.0154 (.0123,.0201)	9	.0105 (.0094,.0119)	34	.0071 (.0061,.0080)	125	.0049 (.0038,.0063)
2	.0151 (.0121,.0197)	9	.0103 (.0092,.0117)	36	.0070 (.0060,.0079)	132	.0049 (.0038,.0063)
2	.0149 (.0120,.0193)	10	.0102 (.0091,.0115)	37	.0070 (.0060,.0078)	139	.0048 (.0037,.0062)
3	.0147 (.0119,.0189)	10	.0101 (.0090,.0114)	38	.0069 (.0059,.0078)	147	.0047 (.0036,.0062)
3	.0145 (.0119,.0187)	10	.0100 (.0089,.0113)	40	.0068 (.0058,.0077)	155	.0046 (.0035,.0061)
3	.0145 (.0118,.0185)	11	.0099 (.0088,.0110)	42	.0067 (.0057,.0076)	163	.0046 (.0035,.0061)
3	.0142 (.0117,.0181)	11	.0097 (.0087,.0108)	44	.0066 (.0056,.0076)	173	.0045 (.0034,.0060)
3	.0140 (.0116,.0178)	12	.0096 (.0085,.0106)	47	.0065 (.0055,.0075)	500	.0033 (.0022,.0050)
3	.0138 (.0115,.0174)	13	.0094 (.0084,.0104)	49	.0064 (.0054,.0074)	1000	.0027 (.0017,.0045)

MOCA

Table 5.8: Controlled VE as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 7 to 149 days post Day 29 was 0.009 in vaccine recipients compared to 0.027 in placebo recipients, with cumulative vaccine efficacy 67.4% (95% CI 64.4 to 71.5%).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.8	.2502 (-0.0878,.4929)	4	.5109 (0.3933,.6051)	15	.6716 (0.6398,.7166)	61	.7798 (0.7498,.8194)
1	.2615 (-0.0655,.4973)	4	.5181 (0.4054,.6086)	15	.6740 (0.6428,.7188)	65	.7831 (0.7522,.8226)
1	.2727 (-0.0436,.5018)	4	.5184 (0.4059,.6088)	16	.6766 (0.6462,.7211)	69	.7864 (0.7546,.8258)
1	.2837 (-0.0222,.5062)	4	.5257 (0.4182,.6125)	17	.6816 (0.6524,.7255)	71	.7886 (0.7562,.8279)
1	.2945 (-0.0011,.5106)	4	.5329 (0.4303,.6161)	18	.6864 (0.6585,.7298)	72	.7897 (0.7570,.8290)
1	.3052 (0.0194,.5149)	5	.5400 (0.4421,.6197)	19	.6912 (0.6640,.7341)	76	.7929 (0.7593,.8321)
1	.3157 (0.0396,.5192)	5	.5470 (0.4535,.6233)	20	.6959 (0.6694,.7383)	81	.7961 (0.7616,.8351)
1	.3260 (0.0594,.5235)	5	.5538 (0.4643,.6268)	21	.7005 (0.6747,.7425)	85	.7992 (0.7639,.8385)
1	.3362 (0.0788,.5277)	5	.5606 (0.4749,.6303)	22	.7051 (0.6798,.7465)	90	.8023 (0.7662,.8419)
1	.3463 (0.0977,.5319)	5	.5640 (0.4802,.6323)	23	.7096 (0.6843,.7505)	90	.8024 (0.7664,.8421)
1	.3561 (0.1163,.5361)	6	.5673 (0.4853,.6343)	23	.7107 (0.6854,.7515)	95	.8053 (0.7685,.8451)
1	.3659 (0.1345,.5402)	6	.5739 (0.4955,.6384)	24	.7140 (0.6887,.7545)	100	.8082 (0.7707,.8483)
2	.3755 (0.1524,.5443)	6	.5803 (0.5054,.6425)	26	.7184 (0.6931,.7584)	106	.8112 (0.7728,.8515)
2	.3849 (0.1699,.5483)	7	.5867 (0.5152,.6466)	27	.7227 (0.6974,.7624)	112	.8141 (0.7748,.8545)
2	.3943 (0.1870,.5523)	7	.5930 (0.5248,.6505)	29	.7269 (0.7016,.7667)	118	.8169 (0.7768,.8575)
2	.4034 (0.2038,.5563)	7	.5992 (0.5342,.6547)	30	.7311 (0.7058,.7709)	121	.8180 (0.7776,.8587)
2	.4125 (0.2203,.5602)	8	.6053 (0.5434,.6592)	32	.7352 (0.7099,.7751)	125	.8197 (0.7788,.8605)
2	.4214 (0.2364,.5641)	8	.6113 (0.5525,.6637)	34	.7392 (0.7140,.7792)	132	.8224 (0.7808,.8633)
2	.4302 (0.2521,.5680)	9	.6172 (0.5613,.6681)	36	.7432 (0.7180,.7832)	139	.8252 (0.7827,.8662)
2	.4388 (0.2676,.5718)	9	.6230 (0.5700,.6728)	37	.7448 (0.7196,.7848)	147	.8278 (0.7847,.8689)
2	.4473 (0.2828,.5756)	10	.6288 (0.5785,.6780)	38	.7471 (0.7217,.7871)	155	.8305 (0.7866,.8716)
2	.4557 (0.2976,.5794)	10	.6315 (0.5825,.6804)	40	.7509 (0.7251,.7909)	163	.8330 (0.7885,.8743)
3	.4639 (0.3121,.5831)	10	.6344 (0.5868,.6831)	42	.7547 (0.7285,.7947)	173	.8356 (0.7903,.8769)
3	.4694 (0.3218,.5856)	11	.6400 (0.5950,.6881)	44	.7585 (0.7318,.7984)	500	.8784 (0.8240,.9190)
3	.4721 (0.3264,.5868)	11	.6455 (0.6030,.6931)	47	.7622 (0.7350,.8021)	1000	.9001 (0.8430,.9385)
3	.4801 (0.3403,.5905)	12	.6509 (0.6109,.6979)	49	.7658 (0.7382,.8057)	12	.6509 (.6109,.6979)
3	.4880 (0.3540,.5941)	13	.6562 (0.6186,.7027)	52	.7694 (0.7414,.8092)	1000	.9001 (.8430,.9385)
3	.4957 (0.3674,.5977)	13	.6614 (0.6261,.7074)	55	.7729 (0.7446,.8126)		(,)
3	.5034 (0.3805,.6013)	14	.6666 (0.6333,.7120)	58	.7764 (0.7474,.8160)		

MOCK

Table 5.9: Controlled VE with sensitivity analysis as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.8	.4282 (.1705,.6133)	4	.5504 (.4423,.6369)	15	.6718 (.6400,.7168)	61	.7652 (.7333,.8074)
1	.4325 (.1812,.6137)	4	.5547 (.4506,.6384)	15	.6741 (.6430,.7188)	65	.7677 (.7346,.8100)
1	.4367 (.1918,.6142)	4	.5549 (.4510,.6385)	16	.6767 (.6462,.7211)	69	.7701 (.7358,.8125)
1	.4410 (.2023,.6147)	4	.5594 (.4596,.6400)	17	.6816 (.6524,.7255)	71	.7717 (.7367,.8141)
1	.4452 (.2128,.6152)	4	.5639 (.4682,.6416)	18	.6864 (.6584,.7298)	72	.7724 (.7370,.8149)
1	.4495 (.2232,.6157)	5	.5685 (.4767,.6433)	19	.6910 (.6638,.7340)	76	.7747 (.7382,.8173)
1	.4538 (.2335,.6163)	5	.5730 (.4850,.6450)	20	.6955 (.6689,.7380)	81	.7770 (.7394,.8197)
1	.4581 (.2437,.6169)	5	.5776 (.4928,.6467)	21	.6999 (.6740,.7419)	85	.7792 (.7404,.8224)
1	.4624 (.2539,.6175)	5	.5822 (.5007,.6485)	22	.7041 (.6788,.7457)	90	.7814 (.7415,.8251)
1	.4667 (.2639,.6181)	5	.5845 (.5046,.6496)	23	.7082 (.6828,.7493)	90	.7815 (.7416,.8253)
1	.4710 (.2740,.6188)	6	.5868 (.5085,.6508)	23	.7092 (.6838,.7502)	95	.7835 (.7425,.8278)
1	.4753 (.2839,.6195)	6	.5914 (.5162,.6533)	24	.7122 (.6867,.7529)	100	.7855 (.7435,.8304)
2	.4797 (.2938,.6203)	6	.5960 (.5239,.6559)	26	.7160 (.6905,.7563)	106	.7876 (.7444,.8329)
2	.4840 (.3036,.6211)	7	.6007 (.5316,.6585)	27	.7198 (.6942,.7599)	112	.7895 (.7451,.8353)
2	.4883 (.3133,.6219)	7	.6053 (.5392,.6611)	29	.7234 (.6978,.7637)	118	.7915 (.7458,.8377)
2	.4927 (.3230,.6227)	7	.6100 (.5467,.6639)	30	.7269 (.7013,.7674)	121	.7922 (.7461,.8387)
2	.4971 (.3325,.6236)	8	.6146 (.5542,.6673)	32	.7304 (.7047,.7710)	125	.7934 (.7465,.8401)
2	.5015 (.3421,.6245)	8	.6193 (.5617,.6706)	34	.7337 (.7080,.7745)	132	.7952 (.7472,.8424)
2	.5059 (.3515,.6254)	9	.6240 (.5691,.6740)	36	.7370 (.7111,.7779)	139	.7971 (.7478,.8447)
2	.5103 (.3609,.6264)	9	.6287 (.5765,.6778)	37	.7383 (.7124,.7793)	147	.7989 (.7484,.8469)
2	.5147 (.3702,.6274)	10	.6335 (.5838,.6821)	38	.7401 (.7140,.7812)	155	.8006 (.7490,.8490)
2	.5191 (.3794,.6284)	10	.6357 (.5873,.6841)	40	.7432 (.7165,.7844)	163	.8023 (.7496,.8512)
3	.5235 (.3886,.6295)	10	.6382 (.5911,.6864)	42	.7462 (.7190,.7876)	173	.8040 (.7501,.8532)
3	.5265 (.3948,.6302)	11	.6430 (.5984,.6907)	44	.7491 (.7214,.7906)	500	.8319 (.7567,.8880)
3	.5280 (.3977,.6306)	11	.6477 (.6056,.6950)	47	.7520 (.7237,.7936)	1000	.8459 (.7578,.9052)
3	.5324 (.4068,.6317)	12	.6525 (.6127,.6994)	49	.7548 (.7259,.7965)	12	.6509 (.6109,.6979)
3	.5369 (.4157,.6329)	13	.6573 (.6199,.7037)	52	.7575 (.7281,.7993)	1000	.9001 (.8430,.9385)
3	.5414 (.4246,.6342)	13	.6621 (.6269,.7080)	55	.7601 (.7302,.8021)		(,)
3	.5459 (.4335,.6354)	14	.6670 (.6337,.7124)	58	.7627 (.7320,.8048)		

MOCA

MOCK

Chapter 6

Day D29start1 Univariate CoR: Cox Models of Risk

MOCK

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

6.1 Hazard ratios

Table 6.1: 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*

MockENSEMBLE Immunologic Marker	No. cases / No. at-risk**	HR per 10-fold incr. Pt. Est.	95% CI	P-value (2-sided)	q-value ***	FWER
Anti Spike IgG (BAU/ml)	167/19,244	0.41	(0.31-0.54)	<0.001	<0.001	<0.001
Anti RBD IgG (BAU/ml)	167/19,244	0.52	(0.40-0.67)	<0.001	<0.001	<0.001

*Baseline covariates adjusted for: riskscore + as.factor(Region). Maximum failure event time 149 days.
**No. at-risk = estimated number in the population for analysis, i.e. baseline negative per-protocol vaccine recipients not experiencing the COVID endpoint through Day 29 visit; no. cases = number of this cohort with an observed COVID endpoint.
***q-value and FWER (family-wide error rate) are computed over the set of p-values both for quantitative markers and categorical markers using the Westfall and Young permutation method (10 replicates).
‡ Count cases starting 1 days post Day 29.

Table 6.2: 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*

MockENSEMBLE 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
Anti Spike IgG (BAU/ml)	Lower	77/6,447	0.0119	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	58/6,377	0.0091	0.61	(0.41-0.91)	0.015			
	Upper	32/6,420	0.0050	0.27	(0.17-0.42)	<0.001			
Anti RBD IgG (BAU/ml)	Lower	69/6,427	0.0107	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	61/6,432	0.0095	0.73	(0.50-1.09)	0.124			
	Upper	36/6,385	0.0056	0.36	(0.23-0.56)	<0.001			
Placebo		513/19,268	0.0266						

*Baseline covariates adjusted for: riskscore + as.factor(Region). Maximum failure event time 149 days. Cutpoints: Anti Spike IgG (BAU/ml) [0.73, 1.25), Anti RBD IgG (BAU/ml) [0.94, 1.54), all on the log10 scale.
**No. at-risk = estimated number in the population for analysis, i.e. baseline negative per-protocol vaccine recipients not experiencing the COVID endpoint through Day 29 visit; no. cases = number of this cohort with an observed COVID endpoint.
***Generalized Wald-test p-value of the null hypothesis that the hazard rate is constant across the Lower, Middle, and Upper tertile groups.
† q-value and FWER (family-wide error rate) are computed over the set of p-values both for quantitative markers and categorical markers using the Westfall and Young permutation method (10 replicates).
‡ Count cases starting 1 days post Day 29.

MOCK

Figure 6.1: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to spike markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 1 days post Day 29.

MOCK

Figure 6.2: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to RBD markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 1 days post Day 29.

Figure 6.3: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to spike markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 1 days post Day 29.

MOCK

Figure 6.4: Forest plots of hazard ratios per 10-fold increase in the Day 29 binding Ab to RBD markers among baseline negative vaccine recipients (top row) and different subpopulations with 95% point-wise confidence intervals. ‡ Count cases starting 1 days post Day 29.

6.2 Marginalized risk and controlled vaccine efficacy plots

Table 6.3: Analysis of Day 29 markers (upper vs. lower tertile) as a CoR and a controlled risk CoP.

	marginalized risk ratio $RR_M(0,1)$		controlled risk ratio $RR_C(0,1)$[1]		e(0,1)[2]	
	Point Est.	95% CI	Point Est.	95% CI	Point Est.	95% CI UL
Anti Spike IgG (BAU/ml)	0.27	0.17–0.39	0.36	0.22–0.52	6.9	4.6
Anti RBD IgG (BAU/ml)	0.36	0.24–0.60	0.48	0.32–0.80	5.0	2.7

[1]Conservative (upper bound) estimate assuming unmeasured confounding at level $RR_{UD}(0,1) = RR_{EU}(0,1) = 2$ and thus $B(0,1) = 4/3$.
[2]E-values are computed for upper tertile ($s = 1$) vs. lower tertile ($s = 0$) biomarker subgroups after controlling for baseline risk score, meeting the protocol randomization stratification criterion for being at heightened risk of COVID (yes or no), strata(Region); UL = upper limit.
‡ Count cases starting 1 days post Day 29.

MOCK

(a) Marginalized cumulative incidence rate curves for trichotomized Day 29 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

(b) Marginalized cumulative risk by Day 149 as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 6.5: Marginalized cumulative risk curves (=s). ‡ Count cases starting 1 days post Day 29.

MOCK

(a) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

(b) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 6.6: Controlled VE curves (=s). ‡ Count cases starting 1 days post Day 29.

MOCK

(a) Marginalized cumulative risk by Day 149 post Day 29 visit as functions of Day 29 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

(b) Controlled VE as functions of Day 29 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =0.3.

Figure 6.7: Marginalized cumulative risk curves and controlled VE curves (>=s). ‡ Count cases starting 1 days post Day 29.

MOCK

Table 6.4: Marginalized cumulative risk by Day 149 as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.2	.0408 (.0276,.0717)	1	.0187 (.0155,.0253)	7	.0095 (.0087,.0103)	41	.0049 (.0039,.0059)
0	.0397 (.0270,.0692)	1	.0182 (.0152,.0244)	8	.0092 (.0084,.0099)	43	.0048 (.0038,.0058)
0	.0386 (.0265,.0667)	1	.0177 (.0149,.0235)	8	.0090 (.0081,.0096)	47	.0047 (.0036,.0057)
0	.0375 (.0260,.0643)	2	.0172 (.0146,.0226)	9	.0087 (.0079,.0093)	50	.0046 (.0035,.0055)
0	.0365 (.0254,.0620)	2	.0172 (.0146,.0226)	9	.0087 (.0079,.0093)	54	.0044 (.0034,.0054)
0	.0355 (.0249,.0598)	2	.0167 (.0143,.0218)	10	.0085 (.0076,.0090)	54	.0044 (.0034,.0054)
0	.0345 (.0244,.0576)	2	.0162 (.0140,.0209)	11	.0083 (.0074,.0088)	58	.0043 (.0032,.0053)
0	.0336 (.0239,.0555)	2	.0158 (.0137,.0202)	11	.0080 (.0072,.0085)	63	.0042 (.0031,.0052)
0	.0327 (.0234,.0535)	2	.0154 (.0134,.0194)	12	.0078 (.0069,.0083)	67	.0041 (.0030,.0051)
0	.0318 (.0229,.0516)	2	.0150 (.0131,.0188)	13	.0076 (.0068,.0081)	73	.0040 (.0029,.0050)
0	.0309 (.0225,.0497)	2	.0149 (.0131,.0187)	13	.0076 (.0067,.0081)	78	.0038 (.0028,.0049)
0	.0301 (.0220,.0479)	2	.0145 (.0128,.0180)	14	.0074 (.0065,.0079)	84	.0037 (.0027,.0048)
0	.0292 (.0216,.0461)	3	.0141 (.0125,.0173)	15	.0072 (.0063,.0077)	91	.0036 (.0026,.0047)
0	.0284 (.0211,.0445)	3	.0137 (.0122,.0167)	16	.0070 (.0061,.0076)	98	.0035 (.0025,.0046)
0	.0277 (.0207,.0428)	3	.0133 (.0120,.0160)	18	.0068 (.0059,.0074)	105	.0034 (.0024,.0045)
0	.0269 (.0203,.0413)	3	.0130 (.0117,.0155)	18	.0067 (.0058,.0073)	113	.0033 (.0023,.0044)
1	.0262 (.0199,.0398)	3	.0130 (.0117,.0154)	19	.0066 (.0057,.0073)	122	.0032 (.0022,.0043)
1	.0254 (.0194,.0383)	3	.0126 (.0114,.0149)	21	.0064 (.0055,.0071)	132	.0031 (.0021,.0042)
1	.0247 (.0191,.0369)	4	.0123 (.0111,.0143)	22	.0062 (.0053,.0069)	142	.0031 (.0020,.0042)
1	.0241 (.0187,.0355)	4	.0119 (.0108,.0138)	24	.0060 (.0051,.0068)	153	.0030 (.0020,.0041)
1	.0234 (.0183,.0342)	4	.0116 (.0105,.0133)	26	.0059 (.0049,.0067)	164	.0029 (.0019,.0040)
1	.0227 (.0179,.0330)	5	.0113 (.0102,.0128)	28	.0057 (.0047,.0065)	177	.0028 (.0018,.0039)
1	.0221 (.0175,.0317)	5	.0109 (.0100,.0124)	30	.0056 (.0046,.0064)	191	.0027 (.0017,.0038)
1	.0215 (.0172,.0306)	5	.0106 (.0097,.0119)	31	.0055 (.0045,.0063)	205	.0027 (.0017,.0038)
1	.0209 (.0168,.0294)	6	.0103 (.0094,.0115)	32	.0054 (.0044,.0063)	221	.0026 (.0016,.0037)
1	.0203 (.0165,.0284)	6	.0101 (.0092,.0112)	35	.0052 (.0042,.0061)	238	.0025 (.0016,.0036)
1	.0198 (.0162,.0273)	6	.0101 (.0092,.0111)	37	.0051 (.0041,.0060)	500	.0019 (.0011,.0029)
1	.0192 (.0158,.0263)	7	.0098 (.0089,.0107)	40	.0050 (.0039,.0059)	1000	.0014 (.0007,.0024)

MOCA

Table 6.5: Controlled VE as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 1 to 149 days post Day 29 was 0.009 in vaccine recipients compared to 0.027 in placebo recipients, with cumulative vaccine efficacy 67.4% (95% CI 64.3 to 71.1%).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.2	-0.4889 (-1.5891,.0375)	1	0.3363 (0.1177,.4709)	8	0.6719 (0.6386,.7101)	50	0.8337 (0.8072,.8723)
0	-0.4484 (-1.4967,.0571)	1	0.3547 (0.1497,.4817)	9	0.6808 (0.6502,.7184)	54	0.8379 (0.8106,.8766)
0	-0.4089 (-1.4073,.0764)	2	0.3726 (0.1805,.4923)	9	0.6811 (0.6504,.7186)	54	0.8384 (0.8111,.8771)
0	-0.3705 (-1.3210,.0952)	2	0.3731 (0.1815,.4927)	10	0.6899 (0.6619,.7269)	58	0.8429 (0.8149,.8817)
0	-0.3331 (-1.2376,.1137)	2	0.3899 (0.2102,.5027)	11	0.6986 (0.6729,.7350)	63	0.8473 (0.8187,.8862)
0	-0.2967 (-1.1570,.1318)	2	0.4068 (0.2389,.5128)	11	0.7070 (0.6836,.7428)	67	0.8516 (0.8224,.8905)
0	-0.2613 (-1.0792,.1495)	2	0.4233 (0.2665,.5228)	12	0.7152 (0.6940,.7504)	73	0.8557 (0.8260,.8946)
0	-0.2268 (-1.0041,.1668)	2	0.4393 (0.2931,.5326)	13	0.7213 (0.7017,.7560)	78	0.8598 (0.8295,.8986)
0	-0.1932 (-0.9315,.1839)	2	0.4518 (0.3139,.5407)	13	0.7231 (0.7040,.7578)	84	0.8637 (0.8330,.9024)
0	-0.1605 (-0.8614,.2005)	2	0.4548 (0.3188,.5427)	14	0.7308 (0.7136,.7655)	91	0.8675 (0.8364,.9061)
0	-0.1287 (-0.7938,.2168)	2	0.4700 (0.3436,.5526)	15	0.7384 (0.7230,.7729)	98	0.8712 (0.8397,.9097)
0	-0.0977 (-0.7285,.2328)	3	0.4847 (0.3675,.5623)	16	0.7457 (0.7320,.7801)	105	0.8748 (0.8429,.9131)
0	-0.0676 (-0.6655,.2485)	3	0.4990 (0.3905,.5717)	18	0.7528 (0.7400,.7871)	113	0.8783 (0.8461,.9165)
0	-0.0383 (-0.6047,.2639)	3	0.5129 (0.4127,.5810)	18	0.7560 (0.7427,.7903)	122	0.8817 (0.8492,.9196)
0	-0.0098 (-0.5461,.2789)	3	0.5265 (0.4333,.5900)	19	0.7597 (0.7458,.7939)	132	0.8850 (0.8523,.9227)
0	0.0180 (-0.4895,.2936)	3	0.5268 (0.4339,.5903)	21	0.7664 (0.7515,.8004)	142	0.8882 (0.8553,.9257)
1	0.0450 (-0.4349,.3080)	3	0.5396 (0.4527,.5989)	22	0.7729 (0.7570,.8071)	153	0.8914 (0.8582,.9285)
1	0.0713 (-0.3822,.3222)	4	0.5524 (0.4714,.6075)	24	0.7792 (0.7622,.8141)	164	0.8944 (0.8611,.9312)
1	0.0969 (-0.3314,.3360)	4	0.5649 (0.4895,.6160)	26	0.7854 (0.7674,.8208)	177	0.8974 (0.8639,.9339)
1	0.1217 (-0.2824,.3496)	4	0.5770 (0.5069,.6243)	28	0.7914 (0.7724,.8273)	191	0.9002 (0.8667,.9364)
1	0.1459 (-0.2352,.3629)	5	0.5887 (0.5238,.6344)	30	0.7972 (0.7773,.8336)	205	0.9030 (0.8694,.9388)
1	0.1695 (-0.1896,.3759)	5	0.6002 (0.5401,.6444)	31	0.8002 (0.7797,.8368)	221	0.9058 (0.8720,.9412)
1	0.1924 (-0.1457,.3887)	5	0.6113 (0.5559,.6541)	32	0.8029 (0.7819,.8396)	238	0.9084 (0.8746,.9434)
1	0.2147 (-0.1034,.4011)	6	0.6221 (0.5711,.6636)	35	0.8084 (0.7863,.8455)	500	0.9311 (0.8978,.9617)
1	0.2364 (-0.0626,.4134)	6	0.6297 (0.5817,.6705)	37	0.8138 (0.7907,.8511)	1000	0.9471 (0.9155,.9734)
1	0.2575 (-0.0232,.4254)	6	0.6326 (0.5858,.6732)	40	0.8190 (0.7949,.8567)	7.3	.6528 (.6137,.6922)
1	0.2780 (0.0146,.4371)	7	0.6429 (0.5999,.6828)	41	0.8200 (0.7957,.8578)	191	.9002 (.8667,.9364)
1	0.2980 (0.0502,.4486)	7	0.6528 (0.6137,.6922)	43	0.8240 (0.7991,.8621)	1000	.9471 (.9155,.9734)
1	0.3174 (0.0846,.4599)	8	0.6625 (0.6264,.7013)	47	0.8290 (0.8032,.8673)		

MOCK

Table 6.6: Controlled VE with sensitivity analysis as functions of Day 29 Anti Spike IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.2	.0836 (-0.5936,.4076)	1	.4258 (0.2367,.5422)	8	.6720 (0.6388,.7102)	50	.8130 (0.7831,.8564)
0	.0965 (-0.5574,.4118)	1	.4364 (0.2574,.5474)	9	.6808 (0.6502,.7184)	54	.8162 (0.7854,.8601)
0	.1093 (-0.5219,.4161)	2	.4470 (0.2777,.5526)	9	.6811 (0.6504,.7186)	54	.8166 (0.7857,.8606)
0	.1220 (-0.4868,.4204)	2	.4473 (0.2784,.5527)	10	.6899 (0.6618,.7268)	58	.8201 (0.7881,.8646)
0	.1347 (-0.4524,.4247)	2	.4575 (0.2977,.5578)	11	.6982 (0.6725,.7347)	63	.8235 (0.7904,.8685)
0	.1473 (-0.4185,.4290)	2	.4680 (0.3173,.5630)	11	.7062 (0.6828,.7421)	67	.8268 (0.7927,.8722)
0	.1598 (-0.3851,.4334)	2	.4783 (0.3365,.5683)	12	.7139 (0.6925,.7492)	73	.8300 (0.7949,.8758)
0	.1722 (-0.3523,.4378)	2	.4886 (0.3553,.5737)	13	.7195 (0.6997,.7545)	78	.8331 (0.7971,.8793)
0	.1846 (-0.3200,.4422)	2	.4969 (0.3702,.5785)	13	.7211 (0.7018,.7561)	84	.8361 (0.7992,.8827)
0	.1968 (-0.2883,.4467)	2	.4989 (0.3738,.5796)	14	.7281 (0.7107,.7631)	91	.8390 (0.8012,.8860)
0	.2090 (-0.2571,.4512)	2	.5090 (0.3920,.5856)	15	.7348 (0.7192,.7698)	98	.8419 (0.8032,.8891)
0	.2211 (-0.2264,.4557)	3	.5191 (0.4097,.5915)	16	.7412 (0.7273,.7763)	105	.8447 (0.8051,.8922)
0	.2331 (-0.1963,.4602)	3	.5292 (0.4272,.5975)	18	.7473 (0.7343,.7824)	113	.8474 (0.8070,.8952)
0	.2451 (-0.1667,.4648)	3	.5391 (0.4443,.6035)	18	.7501 (0.7365,.7852)	122	.8500 (0.8088,.8981)
0	.2570 (-0.1377,.4694)	3	.5490 (0.4604,.6096)	19	.7532 (0.7390,.7883)	132	.8526 (0.8106,.9009)
0	.2688 (-0.1091,.4740)	3	.5493 (0.4608,.6097)	21	.7589 (0.7435,.7940)	142	.8551 (0.8123,.9036)
1	.2805 (-0.0811,.4787)	3	.5589 (0.4756,.6157)	22	.7644 (0.7479,.7998)	153	.8575 (0.8140,.9062)
1	.2921 (-0.0536,.4833)	4	.5686 (0.4906,.6218)	24	.7696 (0.7519,.8060)	164	.8599 (0.8157,.9087)
1	.3037 (-0.0265,.4881)	4	.5783 (0.5053,.6279)	26	.7747 (0.7557,.8119)	177	.8622 (0.8173,.9112)
1	.3151 (0.0000,.4928)	4	.5880 (0.5198,.6340)	28	.7795 (0.7594,.8175)	191	.8644 (0.8188,.9136)
1	.3265 (0.0260,.4976)	5	.5976 (0.5340,.6423)	30	.7842 (0.7630,.8230)	205	.8666 (0.8203,.9158)
1	.3379 (0.0515,.5024)	5	.6071 (0.5480,.6506)	31	.7866 (0.7647,.8257)	221	.8688 (0.8218,.9181)
1	.3491 (0.0766,.5073)	5	.6165 (0.5618,.6588)	32	.7888 (0.7662,.8282)	238	.8709 (0.8233,.9202)
1	.3603 (0.1012,.5122)	6	.6259 (0.5754,.6669)	35	.7932 (0.7693,.8332)	500	.8895 (0.8362,.9385)
1	.3714 (0.1253,.5171)	6	.6327 (0.5850,.6731)	37	.7974 (0.7723,.8381)	1000	.9036 (0.8460,.9514)
1	.3824 (0.1489,.5220)	6	.6353 (0.5887,.6755)	40	.8015 (0.7751,.8429)	7.3	.6528 (.6137,.6922)
1	.3934 (0.1720,.5270)	7	.6445 (0.6018,.6843)	41	.8023 (0.7757,.8438)	191	.9002 (.8667,.9364)
1	.4042 (0.1940,.5321)	7	.6537 (0.6147,.6930)	43	.8055 (0.7779,.8476)	1000	.9471 (.9155,.9734)
1	.4150 (0.2155,.5371)	8	.6629 (0.6269,.7016)	47	.8093 (0.7806,.8521)		

MODEL

(a) Marginalized cumulative incidence rate curves for trichotomized Day 29 markers among vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

(b) Marginalized cumulative risk by Day 149 as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 6.8: Marginalized cumulative risk curves (=s). ‡ Count cases starting 1 days post Day 29.

MOCK

(a) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

(b) Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 6.9: Controlled VE curves (=s). ‡ Count cases starting 1 days post Day 29.

MOCK

(a) Marginalized cumulative risk by Day 149 post Day 29 visit as functions of Day 29 markers above a threshold ($\geq s$) among vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required, 10 replicates). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

(b) Controlled VE as functions of Day 29 markers (>=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates). Histograms of the immunological markers in the vaccine arm are overlaid. lod =1.6.

Figure 6.10: Marginalized cumulative risk curves and controlled VE curves (>=s). ‡ Count cases starting 1 days post Day 29.

MOCK

Table 6.7: Marginalized cumulative risk by Day 149 as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.8	.0205 (.0146,.0284)	3	.0136 (.0114,.0165)	13	.0093 (.0082,.0101)	52	.0063 (.0055,.0074)
1	.0202 (.0145,.0279)	4	.0134 (.0113,.0162)	14	.0091 (.0081,.0099)	55	.0062 (.0054,.0073)
1	.0199 (.0144,.0273)	4	.0132 (.0112,.0159)	15	.0090 (.0080,.0097)	58	.0061 (.0053,.0072)
1	.0196 (.0142,.0268)	4	.0132 (.0112,.0159)	15	.0089 (.0080,.0096)	61	.0060 (.0052,.0072)
1	.0193 (.0141,.0263)	4	.0130 (.0111,.0156)	16	.0088 (.0079,.0095)	65	.0059 (.0051,.0071)
1	.0190 (.0140,.0257)	4	.0128 (.0110,.0153)	17	.0087 (.0078,.0094)	69	.0058 (.0050,.0071)
1	.0187 (.0139,.0252)	5	.0126 (.0109,.0150)	18	.0086 (.0076,.0093)	71	.0058 (.0050,.0070)
1	.0184 (.0137,.0247)	5	.0124 (.0107,.0147)	19	.0084 (.0075,.0091)	72	.0057 (.0049,.0070)
1	.0181 (.0136,.0242)	5	.0122 (.0106,.0144)	20	.0083 (.0074,.0090)	76	.0057 (.0048,.0069)
1	.0179 (.0135,.0238)	5	.0120 (.0104,.0141)	21	.0082 (.0073,.0089)	81	.0056 (.0047,.0069)
1	.0176 (.0134,.0233)	5	.0119 (.0104,.0139)	22	.0081 (.0072,.0087)	85	.0055 (.0046,.0068)
1	.0173 (.0133,.0228)	6	.0118 (.0103,.0138)	23	.0079 (.0070,.0086)	90	.0054 (.0045,.0067)
2	.0171 (.0131,.0224)	6	.0116 (.0102,.0135)	23	.0079 (.0070,.0086)	90	.0054 (.0045,.0067)
2	.0168 (.0130,.0219)	6	.0115 (.0100,.0133)	24	.0078 (.0069,.0085)	95	.0053 (.0044,.0067)
2	.0166 (.0129,.0215)	7	.0113 (.0099,.0130)	26	.0077 (.0068,.0084)	100	.0052 (.0044,.0066)
2	.0163 (.0128,.0211)	7	.0111 (.0098,.0127)	27	.0076 (.0067,.0083)	106	.0052 (.0043,.0066)
2	.0161 (.0127,.0206)	7	.0110 (.0096,.0125)	29	.0075 (.0066,.0082)	112	.0051 (.0042,.0065)
2	.0158 (.0126,.0202)	8	.0108 (.0095,.0122)	30	.0073 (.0065,.0081)	118	.0050 (.0041,.0065)
2	.0156 (.0125,.0198)	8	.0106 (.0094,.0120)	32	.0072 (.0064,.0080)	121	.0050 (.0041,.0064)
2	.0153 (.0123,.0194)	9	.0105 (.0092,.0117)	34	.0071 (.0063,.0080)	125	.0049 (.0040,.0064)
2	.0151 (.0122,.0191)	9	.0103 (.0091,.0115)	36	.0070 (.0062,.0079)	132	.0049 (.0039,.0063)
2	.0149 (.0121,.0187)	10	.0101 (.0090,.0113)	37	.0070 (.0061,.0079)	139	.0048 (.0039,.0063)
3	.0146 (.0120,.0183)	10	.0101 (.0089,.0112)	38	.0069 (.0061,.0078)	147	.0047 (.0038,.0062)
3	.0145 (.0119,.0181)	10	.0100 (.0089,.0111)	40	.0068 (.0060,.0077)	155	.0046 (.0037,.0062)
3	.0144 (.0119,.0179)	11	.0098 (.0087,.0109)	42	.0067 (.0059,.0077)	163	.0046 (.0036,.0061)
3	.0142 (.0118,.0176)	11	.0097 (.0086,.0107)	44	.0066 (.0058,.0076)	173	.0045 (.0036,.0061)
3	.0140 (.0117,.0172)	12	.0095 (.0085,.0105)	47	.0065 (.0057,.0075)	500	.0033 (.0024,.0051)
3	.0138 (.0115,.0169)	13	.0094 (.0084,.0103)	49	.0064 (.0056,.0074)	1000	.0027 (.0018,.0046)

MOCA

Table 6.8: Controlled VE as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).Overall cumulative incidence from 1 to 149 days post Day 29 was 0.009 in vaccine recipients compared to 0.027 in placebo recipients, with cumulative vaccine efficacy 67.4% (95% CI 64.3 to 71.1%).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.8	.2517 (-0.0244,.4906)	4	.5119 (0.4153,.6052)	15	.6723 (0.6406,.7153)	61	.7802 (0.7491,.8108)
1	.2630 (-0.0042,.4952)	4	.5191 (0.4261,.6087)	15	.6747 (0.6436,.7172)	65	.7836 (0.7515,.8140)
1	.2741 (0.0157,.4996)	4	.5193 (0.4265,.6089)	16	.6773 (0.6465,.7194)	69	.7869 (0.7538,.8176)
1	.2851 (0.0352,.5041)	4	.5266 (0.4375,.6125)	17	.6822 (0.6521,.7234)	71	.7891 (0.7554,.8199)
1	.2959 (0.0543,.5085)	4	.5338 (0.4483,.6160)	18	.6871 (0.6575,.7274)	72	.7902 (0.7562,.8210)
1	.3065 (0.0730,.5128)	5	.5409 (0.4589,.6196)	19	.6919 (0.6629,.7313)	76	.7934 (0.7585,.8244)
1	.3170 (0.0914,.5172)	5	.5479 (0.4693,.6233)	20	.6965 (0.6682,.7352)	81	.7965 (0.7608,.8279)
1	.3274 (0.1094,.5214)	5	.5548 (0.4794,.6271)	21	.7012 (0.6734,.7390)	85	.7996 (0.7630,.8313)
1	.3375 (0.1270,.5257)	5	.5615 (0.4894,.6307)	22	.7057 (0.6786,.7427)	90	.8027 (0.7651,.8347)
1	.3476 (0.1443,.5299)	5	.5649 (0.4944,.6326)	23	.7102 (0.6836,.7464)	90	.8029 (0.7652,.8349)
1	.3574 (0.1613,.5341)	6	.5682 (0.4992,.6344)	23	.7113 (0.6849,.7473)	95	.8057 (0.7672,.8381)
1	.3672 (0.1779,.5382)	6	.5748 (0.5088,.6380)	24	.7146 (0.6886,.7500)	100	.8087 (0.7692,.8413)
2	.3768 (0.1943,.5423)	6	.5812 (0.5183,.6422)	26	.7190 (0.6935,.7541)	106	.8116 (0.7713,.8445)
2	.3862 (0.2103,.5463)	7	.5876 (0.5275,.6471)	27	.7233 (0.6983,.7581)	112	.8145 (0.7733,.8476)
2	.3955 (0.2259,.5504)	7	.5939 (0.5366,.6519)	29	.7275 (0.7026,.7620)	118	.8173 (0.7753,.8507)
2	.4046 (0.2413,.5546)	7	.6000 (0.5455,.6566)	30	.7316 (0.7068,.7659)	121	.8184 (0.7761,.8519)
2	.4137 (0.2564,.5587)	8	.6061 (0.5542,.6613)	32	.7357 (0.7109,.7697)	125	.8201 (0.7773,.8537)
2	.4226 (0.2712,.5628)	8	.6121 (0.5628,.6662)	34	.7398 (0.7150,.7735)	132	.8228 (0.7793,.8567)
2	.4313 (0.2857,.5668)	9	.6180 (0.5712,.6710)	36	.7437 (0.7190,.7771)	139	.8255 (0.7812,.8595)
2	.4399 (0.2999,.5708)	9	.6238 (0.5794,.6757)	37	.7453 (0.7206,.7786)	147	.8282 (0.7832,.8624)
2	.4484 (0.3138,.5748)	10	.6295 (0.5872,.6803)	38	.7476 (0.7229,.7808)	155	.8308 (0.7851,.8651)
2	.4568 (0.3275,.5787)	10	.6323 (0.5906,.6826)	40	.7515 (0.7266,.7843)	163	.8334 (0.7870,.8679)
3	.4650 (0.3409,.5826)	10	.6352 (0.5943,.6849)	42	.7553 (0.7299,.7878)	173	.8360 (0.7888,.8705)
3	.4705 (0.3498,.5852)	11	.6407 (0.6012,.6895)	44	.7590 (0.7333,.7913)	500	.8787 (0.8225,.9131)
3	.4731 (0.3540,.5865)	11	.6462 (0.6081,.6939)	47	.7627 (0.7365,.7947)	1000	.9003 (0.8415,.9330)
3	.4811 (0.3669,.5903)	12	.6516 (0.6148,.6983)	49	.7663 (0.7394,.7980)	12	.6516 (.6148,.6983)
3	.4890 (0.3795,.5941)	13	.6569 (0.6214,.7027)	52	.7699 (0.7418,.8013)	1000	.9003 (.8415,.9330)
3	.4968 (0.3919,.5978)	13	.6621 (0.6280,.7069)	55	.7734 (0.7443,.8045)		(,)
3	.5044 (0.4039,.6015)	14	.6673 (0.6344,.7111)	58	.7768 (0.7467,.8077)		

MOCK

Table 6.9: Controlled VE with sensitivity analysis as functions of Day 29 Anti RBD IgG (BAU/ml) (=s) among baseline negative vaccine recipients with 95% bootstrap point-wise confidence intervals (10 replicates).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.8	.4294 (.2188,.6116)	4	.5513 (.4624,.6371)	15	.6725 (.6408,.7154)	61	.7657 (.7325,.7983)
1	.4336 (.2283,.6120)	4	.5556 (.4697,.6385)	15	.6748 (.6437,.7173)	65	.7682 (.7338,.8008)
1	.4378 (.2377,.6125)	4	.5558 (.4700,.6385)	16	.6774 (.6466,.7194)	69	.7706 (.7350,.8036)
1	.4421 (.2471,.6130)	4	.5603 (.4775,.6400)	17	.6822 (.6521,.7234)	71	.7722 (.7358,.8054)
1	.4463 (.2563,.6135)	4	.5648 (.4850,.6416)	18	.6870 (.6575,.7273)	72	.7729 (.7362,.8063)
1	.4506 (.2656,.6140)	5	.5694 (.4924,.6432)	19	.6917 (.6627,.7311)	76	.7752 (.7373,.8090)
1	.4549 (.2747,.6146)	5	.5739 (.4998,.6450)	20	.6962 (.6678,.7348)	81	.7775 (.7384,.8118)
1	.4592 (.2839,.6152)	5	.5785 (.5072,.6469)	21	.7005 (.6727,.7384)	85	.7797 (.7394,.8146)
1	.4634 (.2929,.6158)	5	.5831 (.5145,.6489)	22	.7047 (.6775,.7418)	90	.7818 (.7403,.8173)
1	.4677 (.3019,.6165)	5	.5854 (.5182,.6499)	23	.7088 (.6821,.7452)	90	.7820 (.7403,.8174)
1	.4721 (.3109,.6172)	6	.5876 (.5218,.6509)	23	.7098 (.6832,.7460)	95	.7839 (.7411,.8199)
1	.4764 (.3198,.6179)	6	.5922 (.5290,.6529)	24	.7128 (.6866,.7484)	100	.7860 (.7419,.8225)
2	.4807 (.3286,.6186)	6	.5969 (.5363,.6556)	26	.7166 (.6909,.7521)	106	.7880 (.7427,.8251)
2	.4850 (.3374,.6194)	7	.6015 (.5434,.6590)	27	.7204 (.6952,.7556)	112	.7900 (.7434,.8276)
2	.4894 (.3462,.6203)	7	.6061 (.5506,.6624)	29	.7240 (.6988,.7590)	118	.7919 (.7441,.8300)
2	.4937 (.3549,.6212)	7	.6108 (.5577,.6658)	30	.7275 (.7023,.7623)	121	.7927 (.7444,.8309)
2	.4981 (.3635,.6223)	8	.6154 (.5647,.6693)	32	.7309 (.7057,.7655)	125	.7938 (.7448,.8324)
2	.5025 (.3721,.6233)	8	.6201 (.5718,.6731)	34	.7343 (.7090,.7687)	132	.7957 (.7454,.8347)
2	.5069 (.3806,.6244)	9	.6248 (.5788,.6768)	36	.7375 (.7122,.7717)	139	.7975 (.7461,.8370)
2	.5113 (.3891,.6255)	9	.6295 (.5857,.6806)	37	.7388 (.7134,.7730)	147	.7993 (.7467,.8392)
2	.5157 (.3975,.6266)	10	.6342 (.5924,.6844)	38	.7407 (.7153,.7747)	155	.8011 (.7472,.8414)
2	.5201 (.4058,.6278)	10	.6365 (.5953,.6862)	40	.7437 (.7181,.7776)	163	.8028 (.7478,.8436)
3	.5245 (.4142,.6290)	10	.6390 (.5985,.6882)	42	.7467 (.7205,.7804)	173	.8045 (.7483,.8457)
3	.5275 (.4197,.6299)	11	.6437 (.6045,.6920)	44	.7497 (.7229,.7832)	500	.8323 (.7546,.8798)
3	.5289 (.4224,.6303)	11	.6485 (.6106,.6959)	47	.7525 (.7252,.7859)	1000	.8463 (.7555,.8966)
3	.5334 (.4306,.6316)	12	.6533 (.6167,.6998)	49	.7553 (.7271,.7885)	12	.6516 (.6148,.6983)
3	.5378 (.4388,.6329)	13	.6580 (.6227,.7037)	52	.7580 (.7285,.7910)	1000	.9003 (.8415,.9330)
3	.5423 (.4469,.6342)	13	.6629 (.6288,.7076)	55	.7606 (.7299,.7935)		(,)
3	.5468 (.4549,.6356)	14	.6677 (.6348,.7115)	58	.7632 (.7312,.7959)		

MOCA

MOCK

Chapter 7

Univariate CoR: Nonparametric Threshold Modeling (>=s)

MOCK

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 $E_X[E[Y \mid S \geq s, X, A = 1] \mid A = 1]$ 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 $P(Y = 1 \mid S \geq s, A = 1)$. 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 restrictive but flexible specification of the Highly Adaptive Lasso estimator 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.

The blue dots on the plots represent the risk predictions at marker values where there was an observed COVID-19 case.

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

MOCK

7.1.1 Day 29 bindSpike

Figure 7.1: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

MOCK

Table 7.1: Table of risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.813	$1.54 * 10^1$	0.00852	0.00653	0.01052
0.187	$1.54 * 10^0$	0.00794	0.00587	0.01002
0.341	$2.19 * 10^0$	0.00775	0.00569	0.00981
0.509	$3.23 * 10^0$	0.00720	0.00516	0.00925
0.789	$6.15 * 10^0$	0.00696	0.00470	0.00922
0.958	$9.08 * 10^0$	0.00655	0.00374	0.00935
1.113	$1.30 * 10^1$	0.00581	0.00243	0.00919
1.264	$1.84 * 10^1$	0.00539	0.00152	0.00927
1.491	$3.10 * 10^1$	0.00386	0.00033	0.00739
1.610	$4.07 * 10^1$	0.00479	0.00015	0.00942
1.729	$5.36 * 10^1$	0.00432	0.00000	0.00878
2.377	$2.38 * 10^2$	0.00000	NA	NA
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

7.1.2 Day 29 bindRBD

Figure 7.2: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD levels with pointwise 95% confidence intervals. The dashed red line marks the threshold after which no more COVID events are observed.

Table 7.2: Table of risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.099	$7.96 * 10^1$	0.00853	0.00653	0.01052
0.436	$2.73 * 10^0$	0.00825	0.00617	0.01033
0.585	$3.85 * 10^0$	0.00828	0.00608	0.01048
0.739	$5.48 * 10^0$	0.00782	0.00556	0.01009
0.998	$9.95 * 10^0$	0.00740	0.00508	0.00972
1.187	$1.54 * 10^1$	0.00672	0.00396	0.00948
1.370	$2.34 * 10^1$	0.00599	0.00288	0.00910
1.562	$3.65 * 10^1$	0.00576	0.00183	0.00969
1.852	$7.11 * 10^1$	0.00636	0.00111	0.01162
1.955	$9.02 * 10^1$	0.00419	0.00103	0.00735
2.081	$1.21 * 10^2$	0.00478	0.00000	0.01446
2.237	$1.73 * 10^2$	0.00478	0.00000	0.01446
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

MOCK

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

MOCK

7.2.1 Day 29 bindSpike

Figure 7.3: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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.

MOCK

Table 7.3: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.813	$1.54 * 10^1$	0.00853	0.00654	0.01052
0.187	$1.54 * 10^0$	0.00794	0.00587	0.01002
0.341	$2.19 * 10^0$	0.00775	0.00569	0.00981
0.509	$3.23 * 10^0$	0.00720	0.00516	0.00925
0.789	$6.15 * 10^0$	0.00691	0.00465	0.00917
0.958	$9.08 * 10^0$	0.00653	0.00373	0.00933
1.113	$1.30 * 10^1$	0.00581	0.00243	0.00919
1.264	$1.84 * 10^1$	0.00539	0.00152	0.00927
1.491	$3.10 * 10^1$	0.00438	0.00085	0.00791
1.610	$4.07 * 10^1$	0.00438	0.00000	0.00901
1.729	$5.36 * 10^1$	0.00432	0.00000	0.00878
2.377	$2.38 * 10^2$	0.00000	NA	NA
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

7.2.2 Day 29 bindRBD

Figure 7.4: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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 7.4: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.099	$7.96 * 10^1$	0.00853	0.00653	0.01052
0.436	$2.73 * 10^0$	0.00825	0.00617	0.01033
0.585	$3.85 * 10^0$	0.00825	0.00605	0.01045
0.739	$5.48 * 10^0$	0.00782	0.00556	0.01009
0.998	$9.95 * 10^0$	0.00740	0.00508	0.00972
1.187	$1.54 * 10^1$	0.00672	0.00396	0.00948
1.370	$2.34 * 10^1$	0.00599	0.00288	0.00910
1.562	$3.65 * 10^1$	0.00585	0.00192	0.00978
1.852	$7.11 * 10^1$	0.00585	0.00059	0.01111
1.955	$9.02 * 10^1$	0.00448	0.00132	0.00764
2.081	$1.21 * 10^2$	0.00448	0.00000	0.01417
2.237	$1.73 * 10^2$	0.00448	0.00000	0.01417
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

MOCK

7.3 Plots and Tables with estimates and pointwise confidence intervals for Day 29 (monotone-corrected) (events after 1 day post dose)

MOCK

7.3.1 Day 29 bindSpike (counting events after 1 day post dose)

Figure 7.5: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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.

MOCK

Table 7.5: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.813	$1.54 * 10^1$	0.00851	0.00652	0.01049
0.187	$1.54 * 10^0$	0.00793	0.00586	0.01000
0.341	$2.19 * 10^0$	0.00774	0.00569	0.00979
0.509	$3.23 * 10^0$	0.00720	0.00516	0.00923
0.789	$6.15 * 10^0$	0.00690	0.00465	0.00914
0.958	$9.08 * 10^0$	0.00650	0.00371	0.00928
1.113	$1.30 * 10^1$	0.00580	0.00245	0.00915
1.264	$1.84 * 10^1$	0.00537	0.00153	0.00920
1.491	$3.10 * 10^1$	0.00436	0.00085	0.00788
1.610	$4.07 * 10^1$	0.00436	0.00000	0.00898
1.729	$5.36 * 10^1$	0.00431	0.00000	0.00875
2.377	$2.38 * 10^2$	0.00000	NA	NA
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

7.3.2 Day 29 bindRBD (counting events after 1 day post dose)

Figure 7.6: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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.

MOCK

Table 7.6: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.099	$7.96 * 10^1$	0.00853	0.00654	0.01051
0.436	$2.73 * 10^0$	0.00826	0.00618	0.01033
0.585	$3.85 * 10^0$	0.00826	0.00607	0.01045
0.739	$5.48 * 10^0$	0.00784	0.00558	0.01010
0.998	$9.95 * 10^0$	0.00741	0.00510	0.00972
1.187	$1.54 * 10^1$	0.00671	0.00396	0.00946
1.370	$2.34 * 10^1$	0.00601	0.00291	0.00911
1.562	$3.65 * 10^1$	0.00589	0.00198	0.00980
1.852	$7.11 * 10^1$	0.00589	0.00065	0.01112
1.955	$9.02 * 10^1$	0.00450	0.00135	0.00765
2.081	$1.21 * 10^2$	0.00450	0.00000	0.01406
2.237	$1.73 * 10^2$	0.00450	0.00000	0.01406
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

7.4 Plots and Tables with estimates and pointwise confidence intervals for Day 29 (monotone-corrected) (counting events after 1 day post dose)

MOCK

7.4.1 Day 29 bindSpike (counting events after 1 day post dose)

Figure 7.7: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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.

MOCK

Table 7.7: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.813	$1.54 * 10^1$	0.00851	0.00652	0.01049
0.187	$1.54 * 10^0$	0.00793	0.00586	0.01000
0.341	$2.19 * 10^0$	0.00774	0.00569	0.00979
0.509	$3.23 * 10^0$	0.00720	0.00516	0.00923
0.789	$6.15 * 10^0$	0.00690	0.00465	0.00914
0.958	$9.08 * 10^0$	0.00650	0.00371	0.00928
1.113	$1.30 * 10^1$	0.00580	0.00245	0.00915
1.264	$1.84 * 10^1$	0.00537	0.00153	0.00920
1.491	$3.10 * 10^1$	0.00436	0.00085	0.00788
1.610	$4.07 * 10^1$	0.00436	0.00000	0.00898
1.729	$5.36 * 10^1$	0.00431	0.00000	0.00875
2.377	$2.38 * 10^2$	0.00000	NA	NA
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

7.4.2 Day 29 bindRBD (counting events after 1 day post dose)

Figure 7.8: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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.

MOCK

Table 7.8: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with pointwise 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.099	$7.96 * 10^1$	0.00853	0.00654	0.01051
0.436	$2.73 * 10^0$	0.00826	0.00618	0.01033
0.585	$3.85 * 10^0$	0.00826	0.00607	0.01045
0.739	$5.48 * 10^0$	0.00784	0.00558	0.01010
0.998	$9.95 * 10^0$	0.00741	0.00510	0.00972
1.187	$1.54 * 10^1$	0.00671	0.00396	0.00946
1.370	$2.34 * 10^1$	0.00601	0.00291	0.00911
1.562	$3.65 * 10^1$	0.00589	0.00198	0.00980
1.852	$7.11 * 10^1$	0.00589	0.00065	0.01112
1.955	$9.02 * 10^1$	0.00450	0.00135	0.00765
2.081	$1.21 * 10^2$	0.00450	0.00000	0.01406
2.237	$1.73 * 10^2$	0.00450	0.00000	0.01406
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

7.5 Plots and Tables with estimates and simultaneous confidence intervals for Day 29 (monotone-corrected)

MOCK

7.5.1 Day 29 bindSpike

Figure 7.9: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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.

MOCK

Table 7.9: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.813	$1.54 * 10^1$	0.00853	0.00569	0.01137
0.187	$1.54 * 10^0$	0.00794	0.00498	0.01090
0.341	$2.19 * 10^0$	0.00775	0.00482	0.01069
0.509	$3.23 * 10^0$	0.00720	0.00429	0.01012
0.789	$6.15 * 10^0$	0.00691	0.00368	0.01013
0.958	$9.08 * 10^0$	0.00653	0.00253	0.01053
1.113	$1.30 * 10^1$	0.00581	0.00099	0.01063
1.264	$1.84 * 10^1$	0.00539	0.00000	0.01092
1.491	$3.10 * 10^1$	0.00438	0.00000	0.00941
1.610	$4.07 * 10^1$	0.00438	0.00000	0.01099
1.729	$5.36 * 10^1$	0.00432	0.00000	0.01068
2.377	$2.38 * 10^2$	0.00000	NA	NA
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

7.5.2 Day 29 bindRBD

Figure 7.10: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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.

MOCK

Table 7.10: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.099	$7.96 * 10^1$	0.00853	0.00576	0.01129
0.436	$2.73 * 10^0$	0.00825	0.00536	0.01113
0.585	$3.85 * 10^0$	0.00825	0.00519	0.01130
0.739	$5.48 * 10^0$	0.00782	0.00467	0.01097
0.998	$9.95 * 10^0$	0.00740	0.00418	0.01062
1.187	$1.54 * 10^1$	0.00672	0.00289	0.01055
1.370	$2.34 * 10^1$	0.00599	0.00167	0.01031
1.562	$3.65 * 10^1$	0.00585	0.00039	0.01131
1.852	$7.11 * 10^1$	0.00585	0.00000	0.01315
1.955	$9.02 * 10^1$	0.00448	0.00009	0.00887
2.081	$1.21 * 10^2$	0.00448	0.00000	0.01794
2.237	$1.73 * 10^2$	0.00448	0.00000	0.01794
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

7.6 Plots and Tables with estimates and simultaneous confidence intervals for Day 29 (monotone-corrected)

MOCK

7.6.1 Day 29 bindSpike

Figure 7.11: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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.

MOCK

Table 7.11: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.813	$1.54 * 10^1$	0.00853	0.00569	0.01137
0.187	$1.54 * 10^0$	0.00794	0.00498	0.01090
0.341	$2.19 * 10^0$	0.00775	0.00482	0.01069
0.509	$3.23 * 10^0$	0.00720	0.00429	0.01012
0.789	$6.15 * 10^0$	0.00691	0.00368	0.01013
0.958	$9.08 * 10^0$	0.00653	0.00253	0.01053
1.113	$1.30 * 10^1$	0.00581	0.00099	0.01063
1.264	$1.84 * 10^1$	0.00539	0.00000	0.01092
1.491	$3.10 * 10^1$	0.00438	0.00000	0.00941
1.610	$4.07 * 10^1$	0.00438	0.00000	0.01099
1.729	$5.36 * 10^1$	0.00432	0.00000	0.01068
2.377	$2.38 * 10^2$	0.00000	NA	NA
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

7.6.2 Day 29 bindRBD

Figure 7.12: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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 7.12: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.099	$7.96 * 10^1$	0.00853	0.00576	0.01129
0.436	$2.73 * 10^0$	0.00825	0.00536	0.01113
0.585	$3.85 * 10^0$	0.00825	0.00519	0.01130
0.739	$5.48 * 10^0$	0.00782	0.00467	0.01097
0.998	$9.95 * 10^0$	0.00740	0.00418	0.01062
1.187	$1.54 * 10^1$	0.00672	0.00289	0.01055
1.370	$2.34 * 10^1$	0.00599	0.00167	0.01031
1.562	$3.65 * 10^1$	0.00585	0.00039	0.01131
1.852	$7.11 * 10^1$	0.00585	0.00000	0.01315
1.955	$9.02 * 10^1$	0.00448	0.00009	0.00887
2.081	$1.21 * 10^2$	0.00448	0.00000	0.01794
2.237	$1.73 * 10^2$	0.00448	0.00000	0.01794
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

MOCK

7.7 Plots and Tables with estimates and simultaneous confidence intervals for Day 29 (monotone-corrected) (counting events after 1 day post dose)

MOCK

7.7.1 Day 29 bindSpike (counting events after 1 day post dose)

Figure 7.13: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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.

MOCK

Table 7.13: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.813	$1.54 * 10^1$	0.00851	0.00568	0.01134
0.187	$1.54 * 10^0$	0.00793	0.00498	0.01088
0.341	$2.19 * 10^0$	0.00774	0.00482	0.01067
0.509	$3.23 * 10^0$	0.00720	0.00429	0.01010
0.789	$6.15 * 10^0$	0.00690	0.00369	0.01010
0.958	$9.08 * 10^0$	0.00650	0.00253	0.01047
1.113	$1.30 * 10^1$	0.00580	0.00102	0.01057
1.264	$1.84 * 10^1$	0.00537	0.00000	0.01084
1.491	$3.10 * 10^1$	0.00436	0.00000	0.00937
1.610	$4.07 * 10^1$	0.00436	0.00000	0.01095
1.729	$5.36 * 10^1$	0.00431	0.00000	0.01064
2.377	$2.38 * 10^2$	0.00000	NA	NA
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

7.7.2 Day 29 bindRBD (counting events after 1 day post dose)

Figure 7.14: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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 7.14: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.099	$7.96 * 10^1$	0.00853	0.00577	0.01128
0.436	$2.73 * 10^0$	0.00826	0.00538	0.01113
0.585	$3.85 * 10^0$	0.00826	0.00522	0.01130
0.739	$5.48 * 10^0$	0.00784	0.00470	0.01097
0.998	$9.95 * 10^0$	0.00741	0.00420	0.01062
1.187	$1.54 * 10^1$	0.00671	0.00290	0.01053
1.370	$2.34 * 10^1$	0.00601	0.00171	0.01031
1.562	$3.65 * 10^1$	0.00589	0.00046	0.01131
1.852	$7.11 * 10^1$	0.00589	0.00000	0.01315
1.955	$9.02 * 10^1$	0.00450	0.00013	0.00887
2.081	$1.21 * 10^2$	0.00450	0.00000	0.01777
2.237	$1.73 * 10^2$	0.00450	0.00000	0.01777
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

MOCK

7.8 Plots and Tables with estimates and simultaneous confidence intervals for Day 29 (monotone-corrected) (counting events after 1 day post dose)

MOCK

7.8.1 Day 29 bindSpike (counting events after 1 day post dose)

Figure 7.15: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindSpike 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.

MOCK

Table 7.15: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindSpike levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.813	$1.54 * 10^1$	0.00851	0.00568	0.01134
0.187	$1.54 * 10^0$	0.00793	0.00498	0.01088
0.341	$2.19 * 10^0$	0.00774	0.00482	0.01067
0.509	$3.23 * 10^0$	0.00720	0.00429	0.01010
0.789	$6.15 * 10^0$	0.00690	0.00369	0.01010
0.958	$9.08 * 10^0$	0.00650	0.00253	0.01047
1.113	$1.30 * 10^1$	0.00580	0.00102	0.01057
1.264	$1.84 * 10^1$	0.00537	0.00000	0.01084
1.491	$3.10 * 10^1$	0.00436	0.00000	0.00937
1.610	$4.07 * 10^1$	0.00436	0.00000	0.01095
1.729	$5.36 * 10^1$	0.00431	0.00000	0.01064
2.377	$2.38 * 10^2$	0.00000	NA	NA
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

7.8.2 Day 29 bindRBD (counting events after 1 day post dose)

Figure 7.16: Adjusted threshold-response function for a range of thresholds of the Day 29 Day29bindRBD 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.

MOCK

Table 7.16: Table of monotone-corrected risk estimates for a range of thresholds of Day 29 Day29bindRBD levels with simultaneous 95% confidence intervals.

$\log_{10}$-Threshold	Threshold	Risk estimate	CI left	CI right
-0.099	$7.96 * 10^1$	0.00853	0.00577	0.01128
0.436	$2.73 * 10^0$	0.00826	0.00538	0.01113
0.585	$3.85 * 10^0$	0.00826	0.00522	0.01130
0.739	$5.48 * 10^0$	0.00784	0.00470	0.01097
0.998	$9.95 * 10^0$	0.00741	0.00420	0.01062
1.187	$1.54 * 10^1$	0.00671	0.00290	0.01053
1.370	$2.34 * 10^1$	0.00601	0.00171	0.01031
1.562	$3.65 * 10^1$	0.00589	0.00046	0.01131
1.852	$7.11 * 10^1$	0.00589	0.00000	0.01315
1.955	$9.02 * 10^1$	0.00450	0.00013	0.00887
2.081	$1.21 * 10^2$	0.00450	0.00000	0.01777
2.237	$1.73 * 10^2$	0.00450	0.00000	0.01777
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

MOCK

Chapter 8

Univariate CoR: Nonparametric Threshold Modeling (<=s)

The same methodology as the previous section is apply to estimate the "below" threshold-response function $E_W E[Y = 1|A = 1, X, S \leq s]$.

MOCK

MOCK

Chapter 9

Day D29 Univariate CoR: Nonlinear modeling

MOCK

To explore nonlinear association and threshold modeling, we fit smoothing spline models with degrees of freedom selected by cross-validation using the mgcv R package.

Figure 9.1: Marginalized risk as functions of Day 29 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands (5 replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: baseline risk score, Region (US, South Africa, Latin America). The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 0.3, 1.6, 2.4, 15 for bAb Spike, bAb RBD, PsV nAb ID50, PsV nAb ID80, respectively. ‡ Count cases starting 7 days post Day 29.

MOCK

Chapter 10

Day D29start1 Univariate CoR: Nonlinear modeling

MOCK

To explore nonlinear association and threshold modeling, we fit smoothing spline models with degrees of freedom selected by cross-validation using the mgcv R package.

Figure 10.1: Marginalized risk as functions of Day 29 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands (5 replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: baseline risk score, Region (US, South Africa, Latin America). The horizontal lines indicate the overall cumulative risk of the vaccine and placebo arms by Day 149 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod = 0.3, 1.6, 2.4, 15 for bAb Spike, bAb RBD, PsV nAb ID50, PsV nAb ID80, respectively. ‡ Count cases starting 1 days post Day 29.

MOCK

Chapter 11

Appendix

- This report was built from the `CoVPN/correlates_reporting` repository with commit hash 5bd7088949f8e440fb7203aa648fae633bc03420. A diff of the changes introduced by that commit may be viewed at https://github.com/CoVPN/correlates_reporting/commit/5bd7088949f8e440fb7203aa648fae633bc03420
- The sha256 hash sum of the raw input file, "COVID_ENSEMBLE_practicedata.csv": c5c374aafab433f963f8b9a6426b1ff
- The sha256 hash sum of the processed file, "janssen_pooled_mock_data_processed.csv": 5d6af1d6b6307d64f61e32e01a297faedb5e41c17bcedbc7807f46f4f8200c75

MOCK