COVID-19 Correlates of Risk Analysis Report

MockENSEMBLE Study

USG COVID-19 Response Biostatistics Team

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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)

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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.

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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 = 905)	Placebo (N = 110)	Total (N = 1015)
Age			
Age 18 - 59	453 (50.1%)	54 (49.1%)	507 (50.0%)
Age $\geq$ 60	452 (49.9%)	56 (50.9%)	508 (50.0%)
Mean (Range)	56.2 (18.0, 85.0)	54.3 (18.0, 85.0)	56.0 (18.0, 85.0)
BMI			
Underweight BMI $<$ 18.5	9 (1.0%)	2 (1.8%)	11 (1.1%)
Normal 18.5 $\leq$ BMI $<$ 25	163 (18.0%)	21 (19.1%)	184 (18.1%)
Overweight 25 $\leq$ BMI $<$ 30	360 (39.8%)	41 (37.3%)	401 (39.5%)
Obese BMI $\geq$ 30	373 (41.2%)	46 (41.8%)	419 (41.3%)
Risk for Severe Covid-19			
At-risk	449 (49.6%)	55 (50.0%)	504 (49.7%)
Not at-risk	456 (50.4%)	55 (50.0%)	511 (50.3%)
Age, Risk for Severe Covid-19			
Age 18 - 59 At-risk	226 (25.0%)	27 (24.5%)	253 (24.9%)
Age 18 - 59 Not at-risk	227 (25.1%)	27 (24.5%)	254 (25.0%)
Age $\geq$ 60 At-risk	223 (24.6%)	28 (25.5%)	251 (24.7%)
Age $\geq$ 60 Not at-risk	229 (25.3%)	28 (25.5%)	257 (25.3%)
Sex			
Female	507 (56.0%)	59 (53.6%)	566 (55.8%)
Male	398 (44.0%)	51 (46.4%)	449 (44.2%)
Hispanic or Latino ethnicity			
Hispanic or Latino	363 (40.1%)	47 (42.7%)	410 (40.4%)
Not Hispanic or Latino	478 (52.8%)	56 (50.9%)	534 (52.6%)
Not reported and unknown	64 (7.1%)	7 (6.4%)	71 (7.0%)
Race			
White	390 (43.1%)	49 (44.5%)	439 (43.3%)

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Table 2.1: *(continued)*

Characteristics	Vaccine (N = 905)	Placebo (N = 110)	Total (N = 1015)
Black or African American	329 (36.4%)	36 (32.7%)	365 (36.0%)
Asian	21 (2.3%)	3 (2.7%)	24 (2.4%)
American Indian or Alaska Native	135 (14.9%)	15 (13.6%)	150 (14.8%)
Multiracial	19 (2.1%)	6 (5.5%)	25 (2.5%)
Not reported and unknown	11 (1.2%)	1 (0.9%)	12 (1.2%)
Underrepresented Minority Status in the U.S.			
URM	226 (25.0%)	27 (24.5%)	253 (24.9%)
Non-URM	229 (25.3%)	28 (25.5%)	257 (25.3%)
Country			
United States	455 (50.3%)	55 (50.0%)	510 (50.2%)
Argentina	47 (5.2%)	4 (3.6%)	51 (5.0%)
Brazil	86 (9.5%)	7 (6.4%)	93 (9.2%)
Chile	9 (1.0%)	1 (0.9%)	10 (1.0%)
Columbia	56 (6.2%)	8 (7.3%)	64 (6.3%)
Mexico	1 (0.1%)		1 (0.1%)
Peru	25 (2.8%)	8 (7.3%)	33 (3.3%)
South Africa	226 (25.0%)	27 (24.5%)	253 (24.9%)
HIV Infection			
Negative	833 (92.0%)	107 (97.3%)	940 (92.6%)
Positive	72 (8.0%)	3 (2.7%)	75 (7.4%)

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.

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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 = 280)	Placebo (N = 281)	Total (N = 561)
Age			
Age 18 - 59	139 (49.6%)	142 (50.5%)	281 (50.1%)
Age $\geq$ 60	141 (50.4%)	139 (49.5%)	280 (49.9%)
Mean (Range)	55.9 (18.0, 85.0)	55.5 (18.0, 85.0)	55.7 (18.0, 85.0)
BMI			
Underweight BMI $<$ 18.5	1 (0.4%)	1 (0.4%)	2 (0.4%)
Normal 18.5 $\leq$ BMI $<$ 25	61 (21.8%)	48 (17.1%)	109 (19.4%)
Overweight 25 $\leq$ BMI $<$ 30	134 (47.9%)	107 (38.1%)	241 (43.0%)
Obese BMI $\geq$ 30	84 (30.0%)	125 (44.5%)	209 (37.3%)
Risk for Severe Covid-19			
At-risk	138 (49.3%)	141 (50.2%)	279 (49.7%)
Not at-risk	142 (50.7%)	140 (49.8%)	282 (50.3%)
Age, Risk for Severe Covid-19			
Age 18 - 59 At-risk	68 (24.3%)	71 (25.3%)	139 (24.8%)
Age 18 - 59 Not at-risk	71 (25.4%)	71 (25.3%)	142 (25.3%)
Age $\geq$ 60 At-risk	70 (25.0%)	70 (24.9%)	140 (25.0%)
Age $\geq$ 60 Not at-risk	71 (25.4%)	69 (24.6%)	140 (25.0%)
Sex			
Female	174 (62.1%)	150 (53.4%)	324 (57.8%)
Male	106 (37.9%)	131 (46.6%)	237 (42.2%)
Hispanic or Latino ethnicity			
Hispanic or Latino	109 (38.9%)	107 (38.1%)	216 (38.5%)
Not Hispanic or Latino	148 (52.9%)	159 (56.6%)	307 (54.7%)
Not reported and unknown	23 (8.2%)	15 (5.3%)	38 (6.8%)
Race			
White	107 (38.2%)	116 (41.3%)	223 (39.8%)
Black or African American	110 (39.3%)	103 (36.7%)	213 (38.0%)
Asian	4 (1.4%)	6 (2.1%)	10 (1.8%)
American Indian or Alaska Native	45 (16.1%)	43 (15.3%)	88 (15.7%)
Multiracial	10 (3.6%)	10 (3.6%)	20 (3.6%)
Not reported and unknown	4 (1.4%)	3 (1.1%)	7 (1.2%)
Underrepresented Minority Status in the U.S.			
URM	69 (24.6%)	71 (25.3%)	140 (25.0%)
Non-URM	71 (25.4%)	69 (24.6%)	140 (25.0%)
Country			
United States	140 (50.0%)	140 (49.8%)	280 (49.9%)
Argentina	15 (5.4%)	9 (3.2%)	24 (4.3%)
Brazil	31 (11.1%)	29 (10.3%)	60 (10.7%)
Chile	6 (2.1%)	4 (1.4%)	10 (1.8%)
Columbia	12 (4.3%)	17 (6.0%)	29 (5.2%)
Mexico	2 (0.7%)	1 (0.4%)	3 (0.5%)
Peru	5 (1.8%)	9 (3.2%)	14 (2.5%)

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Table 2.2: *(continued)*

Characteristics	Vaccine (N = 280)	Placebo (N = 281)	Total (N = 561)
South Africa	69 (24.6%)	72 (25.6%)	141 (25.1%)
HIV Infection			
Negative	261 (93.2%)	258 (91.8%)	519 (92.5%)
Positive	19 (6.8%)	23 (8.2%)	42 (7.5%)

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.

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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=790 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	11	11	6	13	11	14	5	12	0	0	0	0	0	0	0	0
Non-Cases	55	57	58	54	58	58	57	56	0	0	0	0	0	0	0	0
Placebo																
Day 29 Cases	16	34	22	30	21	30	12	39	0	0	0	0	0	0	0	0
Non-Cases	7	5	7	6	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.

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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=786 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	16	7	13	23	5	6	2	7	0	0	0	0	0	0	0	0
Non-Cases	54	55	57	54	57	54	57	56	0	0	0	0	0	0	0	0
Placebo																
Day 29 Cases	44	60	40	69	21	24	13	22	0	0	0	0	0	0	0	0
Non-Cases	7	7	7	7	5	7	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.

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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)	156	72.2/161 = 44.9% (37.2%, 52.8%)	11.20 (8.87, 14.15)	893	10500.6/18983 = 55.3% (51.7%, 58.9%)	15.86 (14.29, 17.59)	-0.1 (-0.19, -0.02)	0.71 (0.55, 0.91)
Day 29	Anti Spike IgG (BAU/ml)	156	54.7/161 = 34.0% (26.9%, 41.8%)	5.84 (4.78, 7.14)	893	8646.6/18983 = 45.5% (42.1%, 49.1%)	9.27 (8.51, 10.10)	-0.12 (-0.19, -0.03)	0.63 (0.51, 0.78)
Day 29	Anti N IgG (BAU/ml)	156	5.2/161 = 3.2% (1.3%, 7.5%)	1.06 (0.81, 1.38)	893	1216.6/18983 = 6.4% (4.9%, 8.4%)	1.67 (1.47, 1.90)	-0.03 (-0.06, 0.01)	0.63 (0.47, 0.85)

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.

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Chapter 3

Graphical Descriptions of Antibody Marker Data

3.1 Boxplots

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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.

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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

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

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```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

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```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

MOCK

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

MOCK

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

MOCK

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

MOCK

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

MOCK

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

MOCK

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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

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```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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

MOCK

\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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)

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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)

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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)

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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)

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

\caption{

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)

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```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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)

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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)

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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)

} \end{figure}

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r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
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\begin{figure}

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\caption{

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)

} \end{figure}

```
r COR=ifelse(grepl("ENSEMBLE", study_name), "D29", "D29D57")
```

\begin{figure}

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\caption{

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)

} \end{figure}

3.6 Scatter plots

\begin{figure}[H]

\caption{

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

} \end{figure}

\begin{figure}[H]

\caption{

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

} \end{figure}

\begin{figure}[H]

\caption{

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

} \end{figure}

\begin{figure}[H]

\caption{

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

} \end{figure}

\begin{figure}[H]

\caption{

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

} \end{figure}

\begin{figure}[H]

\caption{

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

} \end{figure}

\begin{figure}[H]

\caption{

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

} \end{figure}

\begin{figure}[H]

\caption{

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

} \end{figure}

\begin{figure}[H]

\caption{

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

} \end{figure}

\begin{figure}[H]

\caption{

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

} \end{figure}

\begin{figure}[H]

\caption{

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

} \end{figure}

\begin{figure}[H]

\caption{

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

} \end{figure}

Chapter 4

Graphical Descriptions of Time to Event Data

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Chapter 5

Day D29 Univariate CoR: Cox Models of Risk

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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)	161/19,144	0.37	(0.27-0.51)	<0.001	<0.001	<0.001
Anti RBD IgG (BAU/ml)	161/19,144	0.55	(0.42-0.72)	<0.001	<0.001	<0.001

*Baseline covariates adjusted for: Age + 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 or infected 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	74/6,390	0.0116	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	53/6,399	0.0083	0.57	(0.38-0.86)	0.008			
	Upper	34/6,355	0.0054	0.30	(0.19-0.47)	<0.001			
Anti RBD IgG (BAU/ml)	Lower	65/6,383	0.0102	1	N/A	N/A	0.001	<0.001	<0.001
	Middle	58/6,387	0.0091	0.78	(0.52-1.18)	0.240			
	Upper	38/6,374	0.0060	0.44	(0.28-0.69)	<0.001			
Placebo		511/19,095	0.0268						

*Baseline covariates adjusted for: Age + as.factor(Region). Maximum failure event time 149 days. Cut-points: Anti Spike IgG (BAU/ml) [0.72, 1.21), Anti RBD IgG (BAU/ml) [0.93, 1.53), 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 or infected 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)	0.30	0.27–0.38	0.40	0.36–0.50	6.1	4.8
Anti RBD IgG (BAU/ml)	0.44	0.32–0.58	0.59	0.43–0.78	3.9	2.8

[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 Age + as.factor(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	.0472 (.0332,.0575)	1	.0197 (.0154,.0216)	7	.0092 (.0079,.0097)	40	.0044 (.0036,.0053)
0	.0458 (.0323,.0554)	1	.0191 (.0150,.0209)	8	.0089 (.0077,.0094)	43	.0043 (.0035,.0051)
0	.0444 (.0315,.0535)	1	.0185 (.0146,.0202)	8	.0087 (.0074,.0092)	47	.0042 (.0033,.0050)
0	.0430 (.0306,.0516)	2	.0179 (.0142,.0195)	9	.0085 (.0073,.0090)	50	.0040 (.0032,.0049)
0	.0417 (.0298,.0498)	2	.0174 (.0138,.0188)	9	.0084 (.0072,.0089)	53	.0039 (.0031,.0048)
0	.0405 (.0290,.0481)	2	.0169 (.0135,.0183)	10	.0081 (.0070,.0087)	54	.0039 (.0031,.0048)
0	.0392 (.0282,.0464)	2	.0168 (.0134,.0182)	11	.0079 (.0068,.0085)	58	.0038 (.0030,.0046)
0	.0380 (.0274,.0447)	2	.0163 (.0131,.0176)	11	.0076 (.0066,.0082)	63	.0037 (.0029,.0045)
0	.0369 (.0267,.0432)	2	.0158 (.0127,.0170)	12	.0074 (.0064,.0080)	67	.0035 (.0028,.0044)
0	.0357 (.0260,.0416)	2	.0153 (.0123,.0165)	12	.0073 (.0063,.0080)	73	.0034 (.0027,.0043)
0	.0346 (.0253,.0402)	2	.0148 (.0120,.0159)	13	.0071 (.0062,.0078)	78	.0033 (.0026,.0042)
0	.0336 (.0246,.0388)	3	.0145 (.0118,.0156)	14	.0069 (.0060,.0076)	84	.0032 (.0025,.0041)
0	.0325 (.0239,.0375)	3	.0144 (.0117,.0154)	15	.0067 (.0058,.0074)	91	.0031 (.0024,.0040)
0	.0315 (.0233,.0362)	3	.0139 (.0114,.0149)	16	.0065 (.0056,.0072)	98	.0030 (.0023,.0039)
0	.0306 (.0227,.0350)	3	.0135 (.0111,.0144)	17	.0064 (.0055,.0072)	105	.0029 (.0022,.0038)
0	.0296 (.0220,.0338)	3	.0131 (.0108,.0139)	18	.0063 (.0054,.0070)	113	.0028 (.0022,.0037)
1	.0287 (.0214,.0327)	3	.0128 (.0106,.0137)	19	.0061 (.0052,.0068)	122	.0027 (.0021,.0036)
1	.0278 (.0209,.0316)	3	.0127 (.0105,.0135)	21	.0059 (.0050,.0067)	132	.0027 (.0020,.0035)
1	.0270 (.0203,.0305)	4	.0123 (.0102,.0130)	22	.0057 (.0048,.0065)	142	.0026 (.0019,.0034)
1	.0261 (.0197,.0295)	4	.0119 (.0099,.0126)	24	.0055 (.0046,.0063)	153	.0025 (.0019,.0033)
1	.0253 (.0192,.0285)	4	.0115 (.0096,.0122)	26	.0054 (.0045,.0062)	164	.0024 (.0018,.0032)
1	.0246 (.0187,.0275)	5	.0112 (.0094,.0118)	28	.0052 (.0043,.0060)	177	.0023 (.0017,.0031)
1	.0238 (.0182,.0266)	5	.0108 (.0091,.0114)	30	.0050 (.0042,.0059)	191	.0023 (.0017,.0031)
1	.0231 (.0177,.0257)	5	.0105 (.0088,.0110)	30	.0050 (.0041,.0058)	205	.0022 (.0016,.0030)
1	.0223 (.0172,.0248)	6	.0102 (.0086,.0107)	32	.0049 (.0040,.0057)	221	.0021 (.0016,.0029)
1	.0217 (.0167,.0240)	6	.0101 (.0086,.0107)	35	.0047 (.0039,.0056)	238	.0021 (.0015,.0028)
1	.0210 (.0163,.0232)	6	.0098 (.0083,.0103)	37	.0046 (.0037,.0054)	500	.0015 (.0010,.0022)
1	.0203 (.0158,.0224)	7	.0095 (.0081,.0100)	39	.0045 (.0037,.0053)	1000	.0011 (.0007,.0017)

MODEL

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 68.5% (95% CI 66.9 to 74.3%).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.2	-0.7186 (-1.0275,-0.1352)	1	0.3051 (0.2777, 0.4866)	8	0.6851 (0.6681, 0.7453)	50	0.8534 (0.8228, 0.8846)
0	-0.6664 (-0.9565,-0.1053)	1	0.3267 (0.3021, 0.5006)	9	0.6916 (0.6738, 0.7500)	53	0.8570 (0.8265, 0.8879)
0	-0.6158 (-0.8880,-0.0762)	2	0.3476 (0.3250, 0.5142)	9	0.6950 (0.6768, 0.7525)	54	0.8580 (0.8274, 0.8887)
0	-0.5666 (-0.8218,-0.0478)	2	0.3678 (0.3471, 0.5275)	10	0.7045 (0.6852, 0.7596)	58	0.8624 (0.8318, 0.8927)
0	-0.5188 (-0.7578,-0.0201)	2	0.3841 (0.3649, 0.5382)	11	0.7138 (0.6935, 0.7664)	63	0.8667 (0.8362, 0.8965)
0	-0.4725 (-0.6960, 0.0070)	2	0.3875 (0.3685, 0.5404)	11	0.7227 (0.7015, 0.7730)	67	0.8709 (0.8404, 0.9002)
0	-0.4275 (-0.6363, 0.0338)	2	0.4065 (0.3892, 0.5529)	12	0.7314 (0.7093, 0.7797)	73	0.8750 (0.8445, 0.9038)
0	-0.3839 (-0.5786, 0.0598)	2	0.4250 (0.4092, 0.5651)	12	0.7334 (0.7111, 0.7813)	78	0.8789 (0.8485, 0.9072)
0	-0.3416 (-0.5229, 0.0852)	2	0.4429 (0.4286, 0.5770)	13	0.7398 (0.7169, 0.7863)	84	0.8827 (0.8524, 0.9105)
0	-0.3005 (-0.4692, 0.1099)	2	0.4602 (0.4474, 0.5885)	14	0.7480 (0.7242, 0.7926)	91	0.8864 (0.8562, 0.9137)
0	-0.2606 (-0.4172, 0.1340)	3	0.4722 (0.4604, 0.5966)	15	0.7559 (0.7313, 0.7987)	98	0.8900 (0.8599, 0.9168)
0	-0.2220 (-0.3671, 0.1574)	3	0.4770 (0.4655, 0.5998)	16	0.7635 (0.7382, 0.8047)	105	0.8934 (0.8635, 0.9198)
0	-0.1845 (-0.3187, 0.1802)	3	0.4933 (0.4831, 0.6107)	17	0.7657 (0.7402, 0.8064)	113	0.8968 (0.8670, 0.9226)
0	-0.1481 (-0.2719, 0.2023)	3	0.5091 (0.5001, 0.6214)	18	0.7709 (0.7449, 0.8105)	122	0.9000 (0.8704, 0.9254)
0	-0.1128 (-0.2268, 0.2239)	3	0.5244 (0.5162, 0.6317)	19	0.7781 (0.7514, 0.8164)	132	0.9031 (0.8738, 0.9280)
0	-0.0786 (-0.1832, 0.2450)	3	0.5327 (0.5247, 0.6373)	21	0.7850 (0.7578, 0.8228)	142	0.9062 (0.8770, 0.9306)
1	-0.0453 (-0.1412, 0.2654)	3	0.5392 (0.5314, 0.6418)	22	0.7918 (0.7641, 0.8290)	153	0.9091 (0.8802, 0.9331)
1	-0.0131 (-0.1006, 0.2853)	4	0.5536 (0.5461, 0.6516)	24	0.7983 (0.7701, 0.8349)	164	0.9120 (0.8833, 0.9355)
1	0.0181 (-0.0614, 0.3047)	4	0.5675 (0.5603, 0.6611)	26	0.8046 (0.7760, 0.8407)	177	0.9148 (0.8863, 0.9378)
1	0.0484 (-0.0236, 0.3236)	4	0.5810 (0.5739, 0.6704)	28	0.8108 (0.7818, 0.8462)	191	0.9174 (0.8892, 0.9400)
1	0.0778 (0.0129, 0.3420)	5	0.5941 (0.5866, 0.6794)	30	0.8167 (0.7874, 0.8515)	205	0.9200 (0.8920, 0.9421)
1	0.1063 (0.0476, 0.3598)	5	0.6068 (0.5989, 0.6884)	30	0.8177 (0.7884, 0.8525)	221	0.9225 (0.8948, 0.9442)
1	0.1339 (0.0799, 0.3772)	5	0.6190 (0.6103, 0.6972)	32	0.8224 (0.7929, 0.8567)	238	0.9250 (0.8975, 0.9462)
1	0.1607 (0.1111, 0.3942)	6	0.6283 (0.6186, 0.7040)	35	0.8280 (0.7982, 0.8617)	500	0.9455 (0.9210, 0.9625)
1	0.1866 (0.1413, 0.4106)	6	0.6309 (0.6209, 0.7058)	37	0.8334 (0.8034, 0.8666)	1000	0.9596 (0.9380, 0.9733)
1	0.2118 (0.1704, 0.4267)	6	0.6425 (0.6310, 0.7142)	39	0.8367 (0.8065, 0.8695)	6.8	.6536 (.6407,.7223)
1	0.2362 (0.1986, 0.4423)	7	0.6536 (0.6407, 0.7223)	40	0.8386 (0.8084, 0.8713)	122	.9000 (.8704,.9254)
1	0.2599 (0.2259, 0.4575)	7	0.6645 (0.6501, 0.7302)	43	0.8437 (0.8134, 0.8759)	500	.9455 (.9210,.9625)
1	0.2828 (0.2522, 0.4722)	8	0.6750 (0.6592, 0.7378)	47	0.8486 (0.8182, 0.8804)		

MODEL

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	-0.0057 (-0.1864,.3357)	1	0.4088 (0.3855,.5633)	8	0.6852 (0.6682,.7454)	50	0.8328 (0.7980,.8684)
0	0.0105 (-0.1618,.3437)	1	0.4212 (0.4001,.5707)	9	0.6916 (0.6738,.7500)	53	0.8357 (0.8006,.8712)
0	0.0265 (-0.1376,.3516)	2	0.4335 (0.4139,.5782)	9	0.6950 (0.6768,.7525)	54	0.8364 (0.8012,.8719)
0	0.0423 (-0.1137,.3595)	2	0.4456 (0.4274,.5856)	10	0.7044 (0.6851,.7595)	58	0.8399 (0.8044,.8752)
0	0.0581 (-0.0901,.3674)	2	0.4556 (0.4386,.5918)	11	0.7134 (0.6930,.7661)	63	0.8434 (0.8074,.8784)
0	0.0737 (-0.0669,.3753)	2	0.4577 (0.4408,.5930)	11	0.7219 (0.7006,.7723)	67	0.8467 (0.8104,.8815)
0	0.0892 (-0.0440,.3835)	2	0.4696 (0.4541,.6004)	12	0.7300 (0.7078,.7786)	73	0.8499 (0.8132,.8845)
0	0.1045 (-0.0215,.3916)	2	0.4814 (0.4672,.6078)	12	0.7319 (0.7094,.7800)	78	0.8530 (0.8160,.8873)
0	0.1197 (0.0007,.3997)	2	0.4931 (0.4801,.6151)	13	0.7377 (0.7146,.7845)	84	0.8560 (0.8187,.8901)
0	0.1348 (0.0226,.4078)	2	0.5046 (0.4929,.6224)	14	0.7451 (0.7210,.7902)	91	0.8589 (0.8214,.8928)
0	0.1497 (0.0441,.4159)	3	0.5128 (0.5019,.6276)	15	0.7521 (0.7271,.7956)	98	0.8617 (0.8239,.8955)
0	0.1645 (0.0653,.4239)	3	0.5161 (0.5055,.6297)	16	0.7588 (0.7330,.8008)	105	0.8645 (0.8264,.8980)
0	0.1792 (0.0862,.4319)	3	0.5274 (0.5179,.6369)	17	0.7607 (0.7346,.8023)	113	0.8672 (0.8289,.9004)
0	0.1937 (0.1068,.4398)	3	0.5387 (0.5302,.6442)	18	0.7652 (0.7386,.8058)	122	0.8698 (0.8312,.9028)
0	0.2081 (0.1270,.4478)	3	0.5498 (0.5421,.6514)	19	0.7714 (0.7439,.8109)	132	0.8723 (0.8336,.9051)
0	0.2224 (0.1470,.4557)	3	0.5559 (0.5483,.6554)	21	0.7773 (0.7491,.8164)	142	0.8748 (0.8358,.9073)
1	0.2366 (0.1666,.4635)	3	0.5608 (0.5534,.6586)	22	0.7829 (0.7540,.8217)	153	0.8772 (0.8380,.9095)
1	0.2506 (0.1859,.4714)	4	0.5718 (0.5646,.6658)	24	0.7884 (0.7588,.8268)	164	0.8795 (0.8402,.9116)
1	0.2645 (0.2049,.4792)	4	0.5826 (0.5756,.6729)	26	0.7936 (0.7634,.8317)	177	0.8818 (0.8422,.9137)
1	0.2782 (0.2236,.4870)	4	0.5933 (0.5864,.6800)	28	0.7986 (0.7678,.8363)	191	0.8840 (0.8443,.9156)
1	0.2918 (0.2420,.4947)	5	0.6039 (0.5966,.6872)	30	0.8035 (0.7720,.8408)	205	0.8861 (0.8463,.9176)
1	0.3053 (0.2597,.5024)	5	0.6144 (0.6067,.6945)	30	0.8043 (0.7728,.8416)	221	0.8882 (0.8482,.9194)
1	0.3187 (0.2762,.5101)	5	0.6248 (0.6162,.7018)	32	0.8081 (0.7761,.8451)	238	0.8903 (0.8501,.9212)
1	0.3320 (0.2925,.5178)	6	0.6329 (0.6232,.7076)	35	0.8126 (0.7801,.8493)	500	0.9082 (0.8670,.9369)
1	0.3451 (0.3086,.5255)	6	0.6351 (0.6252,.7092)	37	0.8169 (0.7839,.8534)	1000	0.9216 (0.8798,.9483)
1	0.3581 (0.3244,.5331)	6	0.6453 (0.6340,.7165)	39	0.8195 (0.7862,.8558)	6.8	.6536 (.6407,.7223)
1	0.3709 (0.3400,.5407)	7	0.6555 (0.6425,.7238)	40	0.8211 (0.7876,.8574)	122	.9000 (.8704,.9254)
1	0.3837 (0.3554,.5482)	7	0.6655 (0.6511,.7310)	43	0.8251 (0.7912,.8612)	500	.9455 (.9210,.9625)
1	0.3963 (0.3705,.5558)	8	0.6754 (0.6597,.7382)	47	0.8290 (0.7946,.8649)		

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 =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	.0183 (.0142,.0210)	3	.0126 (.0105,.0138)	13	.0089 (.0077,.0094)	52	.0063 (.0053,.0070)
1	.0181 (.0141,.0207)	4	.0125 (.0105,.0138)	14	.0088 (.0076,.0093)	55	.0062 (.0052,.0069)
1	.0178 (.0139,.0203)	4	.0124 (.0104,.0136)	15	.0086 (.0075,.0092)	58	.0061 (.0051,.0068)
1	.0176 (.0138,.0200)	4	.0122 (.0103,.0134)	15	.0086 (.0074,.0091)	61	.0060 (.0050,.0067)
1	.0173 (.0136,.0197)	4	.0121 (.0102,.0132)	16	.0085 (.0074,.0090)	65	.0059 (.0050,.0067)
1	.0171 (.0135,.0194)	4	.0119 (.0101,.0130)	17	.0084 (.0073,.0089)	69	.0058 (.0049,.0066)
1	.0169 (.0133,.0191)	5	.0117 (.0099,.0128)	18	.0083 (.0071,.0088)	69	.0058 (.0049,.0066)
1	.0166 (.0132,.0188)	5	.0116 (.0098,.0126)	19	.0082 (.0070,.0087)	72	.0058 (.0048,.0065)
1	.0164 (.0131,.0185)	5	.0115 (.0098,.0126)	20	.0081 (.0069,.0086)	76	.0057 (.0047,.0064)
1	.0162 (.0129,.0182)	5	.0114 (.0097,.0124)	21	.0079 (.0068,.0085)	81	.0056 (.0046,.0064)
1	.0159 (.0128,.0180)	5	.0113 (.0096,.0122)	22	.0078 (.0068,.0084)	85	.0055 (.0046,.0063)
1	.0157 (.0126,.0177)	6	.0111 (.0095,.0121)	22	.0078 (.0068,.0084)	90	.0054 (.0045,.0062)
2	.0155 (.0125,.0174)	6	.0110 (.0094,.0119)	23	.0077 (.0067,.0083)	95	.0054 (.0044,.0062)
2	.0153 (.0124,.0172)	6	.0108 (.0093,.0117)	24	.0076 (.0066,.0082)	100	.0053 (.0043,.0061)
2	.0151 (.0122,.0169)	7	.0107 (.0092,.0115)	26	.0075 (.0065,.0081)	100	.0053 (.0043,.0061)
2	.0149 (.0121,.0166)	7	.0105 (.0091,.0113)	27	.0074 (.0064,.0080)	106	.0052 (.0043,.0060)
2	.0147 (.0120,.0164)	7	.0104 (.0089,.0112)	29	.0073 (.0063,.0079)	112	.0051 (.0042,.0060)
2	.0145 (.0118,.0161)	8	.0102 (.0088,.0110)	30	.0072 (.0062,.0078)	118	.0051 (.0041,.0059)
2	.0143 (.0117,.0159)	8	.0101 (.0087,.0108)	32	.0071 (.0061,.0077)	125	.0050 (.0040,.0058)
2	.0141 (.0116,.0157)	9	.0099 (.0086,.0107)	34	.0070 (.0060,.0076)	132	.0049 (.0040,.0058)
2	.0141 (.0116,.0156)	9	.0098 (.0085,.0105)	36	.0069 (.0059,.0075)	134	.0049 (.0039,.0057)
2	.0139 (.0114,.0154)	10	.0097 (.0084,.0104)	36	.0069 (.0059,.0075)	139	.0049 (.0039,.0057)
2	.0137 (.0113,.0152)	10	.0097 (.0084,.0103)	38	.0068 (.0058,.0074)	147	.0048 (.0038,.0056)
3	.0135 (.0112,.0149)	10	.0095 (.0082,.0102)	40	.0067 (.0058,.0074)	155	.0047 (.0038,.0056)
3	.0133 (.0110,.0147)	11	.0094 (.0081,.0100)	42	.0066 (.0057,.0073)	163	.0047 (.0037,.0055)
3	.0131 (.0109,.0145)	11	.0093 (.0080,.0099)	44	.0065 (.0056,.0072)	173	.0046 (.0037,.0054)
3	.0129 (.0108,.0143)	12	.0091 (.0079,.0097)	47	.0064 (.0055,.0071)	500	.0035 (.0026,.0044)
3	.0128 (.0107,.0141)	13	.0090 (.0078,.0096)	49	.0064 (.0054,.0070)	1000	.0029 (.0021,.0038)

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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 68.5% (95% CI 66.9 to 74.3%).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.8	.3330 (.2463,.4883)	4	.5435 (.5152,.6324)	15	.6856 (.6701,.7444)	61	.7814 (.7512,.8258)
1	.3422 (.2586,.4942)	4	.5481 (.5208,.6359)	15	.6864 (.6708,.7451)	65	.7845 (.7538,.8284)
1	.3512 (.2707,.5000)	4	.5543 (.5284,.6407)	16	.6899 (.6738,.7480)	69	.7875 (.7565,.8309)
1	.3602 (.2826,.5058)	4	.5605 (.5358,.6455)	17	.6942 (.6774,.7516)	69	.7878 (.7568,.8312)
1	.3690 (.2943,.5114)	4	.5666 (.5432,.6502)	18	.6985 (.6810,.7551)	72	.7904 (.7591,.8335)
1	.3777 (.3059,.5170)	5	.5726 (.5505,.6549)	19	.7027 (.6845,.7586)	76	.7933 (.7617,.8359)
1	.3863 (.3172,.5226)	5	.5785 (.5576,.6594)	20	.7068 (.6881,.7620)	81	.7962 (.7642,.8384)
1	.3948 (.3284,.5281)	5	.5806 (.5601,.6611)	21	.7109 (.6915,.7653)	85	.7990 (.7667,.8408)
1	.4031 (.3393,.5335)	5	.5843 (.5646,.6640)	22	.7149 (.6948,.7686)	90	.8018 (.7692,.8432)
1	.4113 (.3501,.5389)	5	.5901 (.5716,.6684)	22	.7149 (.6948,.7687)	95	.8046 (.7717,.8455)
1	.4195 (.3605,.5442)	6	.5958 (.5784,.6728)	23	.7188 (.6981,.7719)	100	.8071 (.7739,.8479)
1	.4275 (.3707,.5494)	6	.6014 (.5851,.6772)	24	.7227 (.7013,.7751)	100	.8073 (.7741,.8481)
2	.4354 (.3807,.5546)	6	.6069 (.5917,.6814)	26	.7266 (.7045,.7784)	106	.8100 (.7765,.8507)
2	.4432 (.3906,.5597)	7	.6123 (.5981,.6857)	27	.7304 (.7077,.7817)	112	.8126 (.7789,.8532)
2	.4509 (.4003,.5647)	7	.6177 (.6045,.6898)	29	.7341 (.7108,.7849)	118	.8152 (.7813,.8557)
2	.4584 (.4098,.5697)	7	.6230 (.6108,.6940)	30	.7378 (.7139,.7881)	125	.8178 (.7836,.8581)
2	.4659 (.4192,.5747)	8	.6282 (.6170,.6980)	32	.7415 (.7169,.7913)	132	.8203 (.7860,.8605)
2	.4733 (.4285,.5796)	8	.6334 (.6228,.7020)	34	.7451 (.7200,.7944)	134	.8213 (.7868,.8614)
2	.4806 (.4376,.5844)	9	.6385 (.6284,.7060)	36	.7486 (.7229,.7975)	139	.8228 (.7882,.8628)
2	.4859 (.4442,.5879)	9	.6435 (.6340,.7099)	36	.7486 (.7230,.7975)	147	.8253 (.7905,.8651)
2	.4878 (.4465,.5894)	10	.6475 (.6377,.7130)	38	.7521 (.7259,.8005)	155	.8277 (.7928,.8674)
2	.4948 (.4553,.5948)	10	.6484 (.6386,.7137)	40	.7555 (.7288,.8035)	163	.8301 (.7950,.8697)
2	.5018 (.4640,.6002)	10	.6533 (.6431,.7177)	42	.7589 (.7317,.8064)	173	.8325 (.7972,.8719)
3	.5087 (.4725,.6055)	11	.6581 (.6471,.7216)	44	.7623 (.7346,.8093)	500	.8727 (.8357,.9081)
3	.5155 (.4808,.6107)	11	.6628 (.6511,.7256)	47	.7656 (.7374,.8122)	1000	.8936 (.8568,.9260)
3	.5222 (.4891,.6159)	12	.6675 (.6550,.7294)	49	.7688 (.7402,.8150)	9.7	.6484 (.6386,.7137)
3	.5288 (.4972,.6210)	13	.6721 (.6588,.7333)	52	.7721 (.7430,.8177)	1000	.8936 (.8568,.9260)
3	.5353 (.5052,.6260)	13	.6767 (.6626,.7370)	55	.7752 (.7458,.8205)		(,)
3	.5418 (.5130,.6310)	14	.6812 (.6664,.7407)	58	.7783 (.7485,.8231)		

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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	.4786 (.4109,.6000)	4	.5783 (.5521,.6604)	15	.6857 (.6702,.7445)	61	.7685 (.7364,.8154)
1	.4821 (.4163,.6018)	4	.5811 (.5557,.6625)	15	.6865 (.6709,.7452)	65	.7707 (.7381,.8174)
1	.4856 (.4218,.6036)	4	.5849 (.5607,.6654)	16	.6900 (.6738,.7481)	69	.7729 (.7397,.8193)
1	.4892 (.4272,.6054)	4	.5888 (.5657,.6683)	17	.6942 (.6774,.7516)	69	.7731 (.7399,.8196)
1	.4927 (.4327,.6072)	4	.5926 (.5707,.6712)	18	.6985 (.6809,.7551)	72	.7750 (.7413,.8212)
1	.4963 (.4381,.6091)	5	.5965 (.5756,.6742)	19	.7025 (.6844,.7584)	76	.7771 (.7429,.8230)
1	.4998 (.4435,.6109)	5	.6004 (.5806,.6771)	20	.7065 (.6877,.7617)	81	.7791 (.7444,.8248)
1	.5034 (.4489,.6128)	5	.6018 (.5824,.6782)	21	.7103 (.6909,.7649)	85	.7811 (.7459,.8266)
1	.5070 (.4543,.6147)	5	.6043 (.5856,.6801)	22	.7140 (.6939,.7680)	90	.7830 (.7473,.8283)
1	.5106 (.4597,.6166)	5	.6082 (.5905,.6831)	22	.7141 (.6939,.7680)	95	.7849 (.7487,.8300)
1	.5142 (.4648,.6185)	6	.6122 (.5955,.6861)	23	.7176 (.6968,.7709)	100	.7866 (.7500,.8318)
1	.5178 (.4700,.6205)	6	.6161 (.6004,.6891)	24	.7211 (.6996,.7738)	100	.7868 (.7501,.8319)
2	.5214 (.4751,.6224)	6	.6201 (.6054,.6921)	26	.7246 (.7023,.7767)	106	.7886 (.7515,.8339)
2	.5250 (.4802,.6244)	7	.6241 (.6103,.6952)	27	.7279 (.7049,.7796)	112	.7904 (.7528,.8358)
2	.5287 (.4853,.6264)	7	.6281 (.6153,.6983)	29	.7311 (.7075,.7825)	118	.7922 (.7540,.8377)
2	.5323 (.4903,.6284)	7	.6321 (.6202,.7013)	30	.7342 (.7099,.7852)	125	.7939 (.7553,.8395)
2	.5360 (.4954,.6305)	8	.6361 (.6251,.7044)	32	.7373 (.7123,.7879)	132	.7956 (.7565,.8413)
2	.5397 (.5005,.6326)	8	.6402 (.6297,.7075)	34	.7403 (.7147,.7906)	134	.7962 (.7570,.8419)
2	.5434 (.5056,.6346)	9	.6442 (.6343,.7107)	36	.7431 (.7169,.7931)	139	.7973 (.7577,.8431)
2	.5461 (.5093,.6362)	9	.6483 (.6390,.7138)	36	.7432 (.7170,.7931)	147	.7989 (.7589,.8448)
2	.5471 (.5106,.6369)	10	.6516 (.6419,.7163)	38	.7460 (.7191,.7956)	155	.8005 (.7600,.8465)
2	.5508 (.5157,.6397)	10	.6524 (.6427,.7170)	40	.7487 (.7213,.7980)	163	.8021 (.7611,.8481)
2	.5546 (.5207,.6425)	10	.6565 (.6464,.7203)	42	.7514 (.7234,.8004)	173	.8036 (.7622,.8498)
3	.5583 (.5257,.6453)	11	.6606 (.6498,.7237)	44	.7540 (.7254,.8027)	500	.8290 (.7794,.8766)
3	.5621 (.5307,.6482)	11	.6648 (.6531,.7271)	47	.7566 (.7274,.8049)	1000	.8419 (.7873,.8901)
3	.5658 (.5358,.6510)	12	.6689 (.6564,.7306)	49	.7591 (.7293,.8071)	9.7	.6484 (.6386,.7137)
3	.5696 (.5407,.6538)	13	.6731 (.6598,.7341)	52	.7615 (.7311,.8093)	1000	.8936 (.8568,.9260)
3	.5734 (.5457,.6567)	13	.6773 (.6633,.7375)	55	.7639 (.7329,.8114)		(,)
3	.5772 (.5507,.6596)	14	.6815 (.6667,.7410)	58	.7662 (.7347,.8134)		

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5.3 Multivariate Cox Models of Risk

Table 5.10: 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*

	HR per 10 fold incr.	P value
Anti Spike IgG (BAU/ml)	0.39 (0.26-0.58)	<0.001
Anti RBD IgG (BAU/ml)	0.93 (0.66-1.33)	0.698
Generalized Wald Test		0.000

*Baseline covariates adjusted for: Age + as.factor(Region). Maximum failure event time 149 days.
‡ Count cases starting 7 days post Day 29.

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Chapter 6

Day D29start1 Univariate CoR: Cox Models of Risk

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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)	171/19,180	0.38	(0.28-0.53)	<0.001	<0.001	<0.001
Anti RBD IgG (BAU/ml)	171/19,180	0.55	(0.42-0.72)	<0.001	<0.001	<0.001

*Baseline covariates adjusted for: Age + 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 or infected 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	77/6,401	0.0120	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	55/6,403	0.0086	0.57	(0.38-0.86)	0.007			
	Upper	39/6,377	0.0061	0.34	(0.22-0.52)	<0.001			
Anti RBD IgG (BAU/ml)	Lower	70/6,397	0.0109	1	N/A	N/A	0.001	<0.001	<0.001
	Middle	60/6,408	0.0094	0.75	(0.50-1.11)	0.153			
	Upper	41/6,376	0.0064	0.44	(0.29-0.68)	<0.001			
Placebo		534/19,180	0.0278						

*Baseline covariates adjusted for: Age + as.factor(Region). Maximum failure event time 149 days. Cut-points: Anti Spike IgG (BAU/ml) [0.72, 1.21), Anti RBD IgG (BAU/ml) [0.92, 1.53), 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 or infected 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.

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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.

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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.

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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)	0.34	0.33–0.43	0.45	0.44–0.58	5.4	4.1
Anti RBD IgG (BAU/ml)	0.44	0.32–0.63	0.59	0.43–0.84	3.9	2.6

[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 Age + as.factor(Region); UL = upper limit.
‡ Count cases starting 1 days post Day 29.

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(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.

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(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.

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(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.

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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	.0472 (.0304,.0523)	1	.0203 (.0155,.0212)	7	.0098 (.0086,.0103)	40	.0048 (.0043,.0059)
0	.0458 (.0297,.0507)	1	.0197 (.0152,.0205)	8	.0095 (.0084,.0101)	43	.0047 (.0041,.0058)
0	.0444 (.0290,.0491)	1	.0191 (.0148,.0199)	8	.0092 (.0082,.0098)	47	.0046 (.0040,.0057)
0	.0431 (.0283,.0476)	2	.0186 (.0144,.0192)	9	.0090 (.0080,.0096)	50	.0044 (.0039,.0055)
0	.0419 (.0276,.0461)	2	.0180 (.0141,.0186)	9	.0089 (.0080,.0096)	53	.0043 (.0038,.0054)
0	.0406 (.0270,.0446)	2	.0176 (.0139,.0183)	10	.0087 (.0078,.0093)	54	.0043 (.0037,.0054)
0	.0394 (.0263,.0432)	2	.0175 (.0138,.0181)	11	.0084 (.0075,.0091)	58	.0042 (.0036,.0053)
0	.0383 (.0257,.0418)	2	.0169 (.0134,.0175)	11	.0082 (.0073,.0089)	63	.0040 (.0035,.0052)
0	.0371 (.0251,.0405)	2	.0164 (.0131,.0170)	12	.0079 (.0071,.0087)	67	.0039 (.0034,.0050)
0	.0361 (.0245,.0392)	2	.0159 (.0128,.0164)	13	.0078 (.0071,.0086)	73	.0038 (.0033,.0049)
0	.0350 (.0239,.0380)	2	.0155 (.0125,.0159)	13	.0077 (.0069,.0085)	78	.0037 (.0032,.0048)
0	.0340 (.0234,.0368)	3	.0152 (.0123,.0156)	14	.0074 (.0067,.0083)	84	.0036 (.0031,.0047)
0	.0330 (.0228,.0356)	3	.0150 (.0122,.0154)	15	.0072 (.0065,.0081)	91	.0035 (.0030,.0046)
0	.0320 (.0223,.0345)	3	.0146 (.0119,.0150)	16	.0070 (.0063,.0079)	98	.0034 (.0029,.0045)
0	.0310 (.0217,.0334)	3	.0141 (.0116,.0145)	17	.0069 (.0062,.0078)	105	.0032 (.0028,.0044)
0	.0301 (.0212,.0323)	3	.0137 (.0113,.0140)	18	.0068 (.0061,.0077)	113	.0032 (.0027,.0043)
1	.0292 (.0207,.0313)	3	.0135 (.0112,.0139)	19	.0066 (.0059,.0075)	122	.0031 (.0026,.0042)
1	.0284 (.0202,.0303)	3	.0133 (.0111,.0136)	21	.0064 (.0057,.0073)	132	.0030 (.0025,.0041)
1	.0275 (.0198,.0294)	4	.0129 (.0108,.0132)	22	.0062 (.0055,.0072)	142	.0029 (.0024,.0040)
1	.0267 (.0193,.0284)	4	.0125 (.0106,.0128)	24	.0060 (.0053,.0070)	153	.0028 (.0023,.0039)
1	.0259 (.0188,.0275)	4	.0121 (.0103,.0125)	26	.0058 (.0052,.0068)	164	.0027 (.0023,.0038)
1	.0251 (.0184,.0266)	5	.0118 (.0101,.0121)	28	.0056 (.0050,.0067)	177	.0026 (.0022,.0037)
1	.0244 (.0179,.0258)	5	.0114 (.0098,.0118)	30	.0055 (.0049,.0065)	191	.0025 (.0021,.0036)
1	.0237 (.0175,.0250)	5	.0111 (.0096,.0115)	30	.0054 (.0048,.0065)	205	.0025 (.0020,.0036)
1	.0230 (.0171,.0242)	6	.0108 (.0094,.0112)	32	.0053 (.0047,.0064)	221	.0024 (.0020,.0035)
1	.0223 (.0167,.0234)	6	.0107 (.0094,.0112)	35	.0051 (.0045,.0062)	238	.0023 (.0019,.0034)
1	.0216 (.0163,.0226)	6	.0104 (.0091,.0109)	37	.0050 (.0044,.0061)	500	.0017 (.0014,.0027)
1	.0210 (.0159,.0219)	7	.0101 (.0089,.0106)	39	.0049 (.0043,.0060)	1000	.0013 (.0010,.0022)

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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 0.029 in placebo recipients, with cumulative vaccine efficacy 68.0% (95% CI 66.3 to 73.0%).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.2	-0.6468 (-0.7526,-0.0543)	1	0.3111 (0.3131, 0.4785)	8	0.6783 (0.6603, 0.7296)	50	0.8458 (0.8070, 0.8680)
0	-0.5986 (-0.6968,-0.0294)	1	0.3316 (0.3351, 0.4911)	9	0.6855 (0.6662, 0.7350)	53	0.8498 (0.8109, 0.8715)
0	-0.5518 (-0.6432,-0.0052)	2	0.3516 (0.3559, 0.5035)	9	0.6880 (0.6682, 0.7368)	54	0.8504 (0.8115, 0.8721)
0	-0.5063 (-0.5916, 0.0186)	2	0.3710 (0.3760, 0.5163)	10	0.6974 (0.6759, 0.7438)	58	0.8550 (0.8159, 0.8763)
0	-0.4620 (-0.5416, 0.0418)	2	0.3836 (0.3890, 0.5248)	11	0.7065 (0.6834, 0.7507)	63	0.8593 (0.8202, 0.8804)
0	-0.4191 (-0.4930, 0.0648)	2	0.3898 (0.3954, 0.5289)	11	0.7153 (0.6908, 0.7577)	67	0.8636 (0.8244, 0.8843)
0	-0.3774 (-0.4460, 0.0872)	2	0.4081 (0.4143, 0.5411)	12	0.7239 (0.6980, 0.7646)	73	0.8677 (0.8285, 0.8881)
0	-0.3368 (-0.4003, 0.1090)	2	0.4258 (0.4326, 0.5530)	13	0.7263 (0.7000, 0.7665)	78	0.8717 (0.8325, 0.8918)
0	-0.2974 (-0.3561, 0.1304)	2	0.4430 (0.4503, 0.5647)	13	0.7322 (0.7050, 0.7713)	84	0.8756 (0.8364, 0.8954)
0	-0.2592 (-0.3132, 0.1512)	2	0.4597 (0.4675, 0.5760)	14	0.7403 (0.7119, 0.7777)	91	0.8793 (0.8402, 0.8988)
0	-0.2220 (-0.2717, 0.1716)	3	0.4707 (0.4786, 0.5835)	15	0.7481 (0.7186, 0.7840)	98	0.8830 (0.8439, 0.9021)
0	-0.1859 (-0.2314, 0.1915)	3	0.4759 (0.4836, 0.5870)	16	0.7557 (0.7252, 0.7901)	105	0.8865 (0.8475, 0.9054)
0	-0.1509 (-0.1923, 0.2109)	3	0.4916 (0.4987, 0.5977)	17	0.7585 (0.7276, 0.7924)	113	0.8900 (0.8511, 0.9085)
0	-0.1168 (-0.1545, 0.2298)	3	0.5068 (0.5127, 0.6082)	18	0.7631 (0.7316, 0.7961)	122	0.8933 (0.8546, 0.9115)
0	-0.0838 (-0.1178, 0.2483)	3	0.5216 (0.5262, 0.6184)	19	0.7703 (0.7378, 0.8019)	132	0.8965 (0.8580, 0.9144)
0	-0.0517 (-0.0823, 0.2664)	3	0.5278 (0.5315, 0.6226)	21	0.7772 (0.7439, 0.8075)	142	0.8997 (0.8613, 0.9172)
1	-0.0205 (-0.0479, 0.2840)	3	0.5360 (0.5387, 0.6283)	22	0.7839 (0.7499, 0.8129)	153	0.9027 (0.8644, 0.9200)
1	0.0098 (-0.0145, 0.3012)	4	0.5499 (0.5509, 0.6379)	24	0.7904 (0.7557, 0.8182)	164	0.9056 (0.8676, 0.9226)
1	0.0392 (0.0178, 0.3181)	4	0.5634 (0.5628, 0.6474)	26	0.7968 (0.7614, 0.8236)	177	0.9085 (0.8706, 0.9252)
1	0.0677 (0.0492, 0.3345)	4	0.5765 (0.5744, 0.6565)	28	0.8029 (0.7670, 0.8292)	191	0.9113 (0.8736, 0.9276)
1	0.0954 (0.0795, 0.3505)	5	0.5893 (0.5856, 0.6655)	30	0.8088 (0.7724, 0.8346)	205	0.9139 (0.8764, 0.9300)
1	0.1223 (0.1089, 0.3661)	5	0.6016 (0.5963, 0.6742)	30	0.8098 (0.7733, 0.8355)	221	0.9165 (0.8793, 0.9323)
1	0.1484 (0.1373, 0.3814)	5	0.6136 (0.6064, 0.6827)	32	0.8146 (0.7777, 0.8398)	238	0.9191 (0.8820, 0.9345)
1	0.1738 (0.1649, 0.3963)	6	0.6225 (0.6140, 0.6890)	35	0.8202 (0.7829, 0.8449)	500	0.9405 (0.9065, 0.9532)
1	0.1984 (0.1916, 0.4108)	6	0.6252 (0.6163, 0.6909)	37	0.8256 (0.7879, 0.8498)	1000	0.9553 (0.9247, 0.9658)
1	0.2223 (0.2175, 0.4250)	6	0.6365 (0.6259, 0.6990)	39	0.8291 (0.7912, 0.8529)	6.8	.6474 (.6353,.7069)
1	0.2455 (0.2426, 0.4389)	7	0.6474 (0.6353, 0.7069)	40	0.8309 (0.7929, 0.8546)	142	.8997 (.8613,.9172)
1	0.2680 (0.2668, 0.4524)	7	0.6580 (0.6439, 0.7147)	43	0.8360 (0.7977, 0.8592)	1000	.9553 (.9247,.9658)
1	0.2898 (0.2903, 0.4656)	8	0.6683 (0.6522, 0.7223)	47	0.8410 (0.8024, 0.8636)		

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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	.0349 (-0.0271,.3821)	1	.4136 (0.4153,.5561)	8	.6784 (0.6604,.7297)	50	.8242 (0.7800,.8495)
0	.0493 (-0.0091,.3878)	1	.4252 (0.4282,.5623)	9	.6855 (0.6662,.7350)	53	.8273 (0.7826,.8523)
0	.0637 (0.0085,.3935)	2	.4367 (0.4404,.5686)	9	.6880 (0.6682,.7368)	54	.8278 (0.7830,.8528)
0	.0779 (0.0257,.3992)	2	.4482 (0.4525,.5757)	10	.6973 (0.6758,.7437)	58	.8313 (0.7859,.8562)
0	.0920 (0.0427,.4050)	2	.4558 (0.4605,.5804)	11	.7061 (0.6830,.7503)	63	.8347 (0.7887,.8595)
0	.1061 (0.0595,.4109)	2	.4595 (0.4645,.5827)	11	.7145 (0.6899,.7570)	67	.8380 (0.7915,.8626)
0	.1200 (0.0762,.4168)	2	.4708 (0.4763,.5897)	12	.7225 (0.6964,.7633)	73	.8412 (0.7941,.8657)
0	.1339 (0.0927,.4227)	2	.4819 (0.4881,.5967)	13	.7246 (0.6982,.7651)	78	.8443 (0.7967,.8687)
0	.1476 (0.1091,.4287)	2	.4930 (0.4997,.6037)	13	.7301 (0.7027,.7694)	84	.8473 (0.7992,.8716)
0	.1613 (0.1253,.4346)	2	.5040 (0.5112,.6107)	14	.7373 (0.7086,.7752)	91	.8503 (0.8017,.8744)
0	.1748 (0.1413,.4406)	3	.5114 (0.5187,.6155)	15	.7443 (0.7143,.7807)	98	.8531 (0.8040,.8771)
0	.1883 (0.1572,.4466)	3	.5149 (0.5220,.6177)	16	.7509 (0.7197,.7860)	105	.8559 (0.8063,.8798)
0	.2016 (0.1729,.4526)	3	.5257 (0.5324,.6247)	17	.7533 (0.7217,.7879)	113	.8585 (0.8086,.8824)
0	.2149 (0.1884,.4586)	3	.5365 (0.5420,.6317)	18	.7573 (0.7249,.7910)	122	.8611 (0.8108,.8848)
0	.2280 (0.2038,.4646)	3	.5471 (0.5514,.6387)	19	.7633 (0.7299,.7959)	132	.8637 (0.8129,.8873)
0	.2411 (0.2190,.4706)	3	.5516 (0.5552,.6417)	21	.7692 (0.7347,.8005)	142	.8662 (0.8150,.8896)
1	.2540 (0.2340,.4766)	3	.5577 (0.5603,.6457)	22	.7748 (0.7393,.8050)	153	.8686 (0.8169,.8919)
1	.2669 (0.2489,.4827)	4	.5682 (0.5691,.6526)	24	.7801 (0.7437,.8093)	164	.8709 (0.8188,.8941)
1	.2796 (0.2636,.4887)	4	.5786 (0.5780,.6596)	26	.7853 (0.7480,.8137)	177	.8732 (0.8207,.8963)
1	.2923 (0.2782,.4948)	4	.5889 (0.5868,.6666)	28	.7903 (0.7521,.8183)	191	.8754 (0.8225,.8984)
1	.3048 (0.2926,.5009)	5	.5992 (0.5956,.6735)	30	.7951 (0.7560,.8227)	205	.8776 (0.8243,.9004)
1	.3173 (0.3069,.5069)	5	.6093 (0.6041,.6805)	30	.7959 (0.7567,.8234)	221	.8797 (0.8260,.9024)
1	.3297 (0.3209,.5130)	5	.6194 (0.6123,.6875)	32	.7997 (0.7598,.8269)	238	.8818 (0.8277,.9044)
1	.3420 (0.3349,.5192)	6	.6271 (0.6187,.6928)	35	.8041 (0.7635,.8311)	500	.8999 (0.8427,.9213)
1	.3541 (0.3487,.5253)	6	.6295 (0.6206,.6944)	37	.8084 (0.7670,.8350)	1000	.9136 (0.8543,.9338)
1	.3662 (0.3623,.5314)	6	.6394 (0.6289,.7014)	39	.8112 (0.7693,.8375)	6.8	.6474 (.6353,.7069)
1	.3782 (0.3758,.5376)	7	.6493 (0.6372,.7085)	40	.8126 (0.7704,.8388)	142	.8997 (.8613,.9172)
1	.3901 (0.3891,.5437)	7	.6590 (0.6450,.7156)	43	.8166 (0.7737,.8425)	1000	.9553 (.9247,.9658)
1	.4019 (0.4023,.5499)	8	.6688 (0.6526,.7227)	47	.8205 (0.7769,.8461)		

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.

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(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	.0194 (.0148,.0227)	3	.0134 (.0113,.0146)	13	.0094 (.0084,.0100)	52	.0066 (.0059,.0076)
1	.0192 (.0147,.0224)	3	.0133 (.0113,.0146)	14	.0093 (.0083,.0099)	55	.0065 (.0058,.0076)
1	.0189 (.0145,.0220)	4	.0132 (.0112,.0144)	15	.0092 (.0082,.0098)	58	.0065 (.0057,.0075)
1	.0187 (.0144,.0216)	4	.0130 (.0111,.0141)	15	.0091 (.0082,.0097)	61	.0064 (.0056,.0074)
1	.0184 (.0142,.0213)	4	.0128 (.0109,.0139)	16	.0090 (.0081,.0096)	65	.0063 (.0055,.0073)
1	.0181 (.0141,.0209)	4	.0126 (.0108,.0137)	17	.0089 (.0079,.0095)	69	.0062 (.0054,.0073)
1	.0179 (.0140,.0206)	5	.0125 (.0107,.0134)	18	.0088 (.0078,.0094)	69	.0062 (.0054,.0073)
1	.0176 (.0138,.0203)	5	.0123 (.0106,.0132)	19	.0087 (.0077,.0093)	72	.0061 (.0054,.0072)
1	.0174 (.0137,.0199)	5	.0122 (.0105,.0132)	20	.0085 (.0076,.0092)	76	.0060 (.0053,.0071)
1	.0172 (.0135,.0196)	5	.0121 (.0105,.0130)	21	.0084 (.0075,.0091)	81	.0059 (.0052,.0070)
1	.0169 (.0134,.0193)	5	.0119 (.0103,.0128)	22	.0083 (.0074,.0090)	85	.0059 (.0051,.0070)
1	.0167 (.0133,.0190)	6	.0118 (.0102,.0126)	22	.0083 (.0074,.0090)	90	.0058 (.0051,.0069)
2	.0165 (.0131,.0187)	6	.0116 (.0101,.0124)	23	.0082 (.0073,.0089)	95	.0057 (.0050,.0068)
2	.0162 (.0130,.0184)	6	.0115 (.0100,.0122)	24	.0081 (.0072,.0088)	99	.0056 (.0049,.0068)
2	.0160 (.0129,.0181)	7	.0113 (.0099,.0120)	26	.0080 (.0071,.0087)	100	.0056 (.0049,.0068)
2	.0158 (.0127,.0178)	7	.0111 (.0097,.0118)	27	.0079 (.0070,.0086)	106	.0055 (.0048,.0067)
2	.0156 (.0126,.0175)	7	.0110 (.0096,.0117)	29	.0077 (.0069,.0085)	112	.0055 (.0048,.0066)
2	.0154 (.0125,.0172)	8	.0108 (.0095,.0115)	30	.0076 (.0068,.0085)	118	.0054 (.0047,.0066)
2	.0151 (.0124,.0169)	8	.0107 (.0094,.0113)	32	.0075 (.0067,.0084)	125	.0053 (.0046,.0065)
2	.0150 (.0123,.0168)	9	.0105 (.0093,.0111)	34	.0074 (.0066,.0083)	132	.0052 (.0046,.0064)
2	.0149 (.0122,.0166)	9	.0104 (.0091,.0110)	36	.0073 (.0065,.0082)	134	.0052 (.0045,.0064)
2	.0147 (.0121,.0164)	10	.0103 (.0091,.0109)	36	.0073 (.0065,.0082)	139	.0052 (.0045,.0064)
2	.0145 (.0120,.0161)	10	.0102 (.0090,.0108)	38	.0072 (.0064,.0081)	147	.0051 (.0044,.0063)
3	.0143 (.0119,.0158)	10	.0101 (.0089,.0107)	40	.0071 (.0063,.0080)	155	.0050 (.0044,.0063)
3	.0141 (.0118,.0156)	11	.0100 (.0088,.0105)	42	.0070 (.0062,.0080)	163	.0049 (.0043,.0062)
3	.0139 (.0116,.0153)	11	.0098 (.0087,.0104)	44	.0069 (.0061,.0079)	173	.0049 (.0042,.0061)
3	.0137 (.0115,.0151)	12	.0097 (.0086,.0102)	47	.0068 (.0060,.0078)	500	.0037 (.0031,.0051)
3	.0135 (.0114,.0148)	13	.0096 (.0085,.0101)	49	.0067 (.0059,.0077)	1000	.0031 (.0026,.0045)

MOCK

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 0.029 in placebo recipients, with cumulative vaccine efficacy 68.0% (95% CI 66.3 to 73.0%).

s	Estimate	s	Estimate	s	Estimate	s	Estimate
0.8	.3208 (.2456,.4610)	3	.5340 (.5145,.6061)	15	.6801 (.6632,.7301)	61	.7778 (.7390,.8148)
1	.3302 (.2578,.4664)	4	.5401 (.5217,.6108)	15	.6807 (.6636,.7305)	65	.7809 (.7414,.8175)
1	.3394 (.2699,.4718)	4	.5464 (.5292,.6157)	16	.6846 (.6666,.7339)	69	.7839 (.7439,.8202)
1	.3486 (.2817,.4770)	4	.5527 (.5367,.6210)	17	.6890 (.6700,.7378)	69	.7841 (.7441,.8204)
1	.3576 (.2934,.4822)	4	.5589 (.5440,.6263)	18	.6933 (.6733,.7415)	72	.7869 (.7463,.8229)
1	.3664 (.3049,.4874)	5	.5650 (.5511,.6316)	19	.6976 (.6766,.7452)	76	.7899 (.7487,.8255)
1	.3752 (.3162,.4925)	5	.5711 (.5582,.6367)	20	.7018 (.6799,.7489)	81	.7928 (.7511,.8281)
1	.3838 (.3273,.4982)	5	.5726 (.5600,.6381)	21	.7059 (.6831,.7525)	85	.7957 (.7534,.8307)
1	.3923 (.3383,.5039)	5	.5770 (.5652,.6418)	22	.7099 (.6863,.7560)	90	.7985 (.7558,.8333)
1	.4007 (.3490,.5096)	5	.5829 (.5720,.6469)	22	.7100 (.6864,.7561)	95	.8013 (.7581,.8358)
1	.4090 (.3596,.5152)	6	.5887 (.5788,.6518)	23	.7140 (.6895,.7596)	99	.8037 (.7600,.8379)
1	.4171 (.3700,.5207)	6	.5944 (.5848,.6567)	24	.7180 (.6927,.7630)	100	.8041 (.7603,.8383)
2	.4252 (.3803,.5262)	6	.6000 (.5904,.6615)	26	.7219 (.6958,.7664)	106	.8068 (.7626,.8407)
2	.4331 (.3904,.5316)	7	.6055 (.5960,.6663)	27	.7258 (.6989,.7698)	112	.8095 (.7649,.8432)
2	.4410 (.4003,.5370)	7	.6110 (.6014,.6709)	29	.7296 (.7019,.7731)	118	.8122 (.7671,.8455)
2	.4487 (.4101,.5423)	7	.6164 (.6068,.6756)	30	.7334 (.7047,.7763)	125	.8148 (.7693,.8479)
2	.4563 (.4197,.5475)	8	.6217 (.6121,.6801)	32	.7371 (.7075,.7796)	132	.8174 (.7715,.8502)
2	.4638 (.4291,.5527)	8	.6270 (.6173,.6846)	34	.7407 (.7103,.7827)	134	.8182 (.7722,.8509)
2	.4713 (.4384,.5581)	9	.6321 (.6219,.6890)	36	.7443 (.7130,.7858)	139	.8199 (.7736,.8525)
2	.4757 (.4440,.5615)	9	.6373 (.6264,.6934)	36	.7443 (.7130,.7858)	147	.8224 (.7758,.8547)
2	.4786 (.4476,.5636)	10	.6407 (.6294,.6963)	38	.7479 (.7157,.7889)	155	.8249 (.7779,.8569)
2	.4858 (.4566,.5691)	10	.6423 (.6308,.6977)	40	.7514 (.7184,.7920)	163	.8273 (.7800,.8591)
2	.4929 (.4654,.5746)	10	.6473 (.6352,.7019)	42	.7549 (.7211,.7949)	173	.8297 (.7821,.8612)
3	.4999 (.4739,.5799)	11	.6521 (.6396,.7061)	44	.7583 (.7237,.7979)	500	.8707 (.8190,.8971)
3	.5068 (.4821,.5852)	11	.6570 (.6438,.7102)	47	.7616 (.7263,.8008)	1000	.8919 (.8397,.9158)
3	.5137 (.4903,.5905)	12	.6617 (.6481,.7143)	49	.7649 (.7289,.8037)	10.8	.6521 (.6396,.7061)
3	.5204 (.4983,.5956)	13	.6664 (.6522,.7183)	52	.7682 (.7314,.8065)	1000	.8919 (.8397,.9158)
3	.5271 (.5063,.6007)	13	.6711 (.6562,.7223)	55	.7714 (.7340,.8093)		(,)
3	.5336 (.5140,.6058)	14	.6756 (.6597,.7262)	58	.7746 (.7365,.8120)		

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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	.4686 (.4098,.5783)	3	.5698 (.5518,.6364)	15	.6803 (.6633,.7302)	61	.7646 (.7236,.8039)
1	.4722 (.4152,.5796)	4	.5735 (.5565,.6391)	15	.6808 (.6637,.7306)	65	.7669 (.7250,.8059)
1	.4758 (.4206,.5808)	4	.5774 (.5614,.6419)	16	.6846 (.6666,.7340)	69	.7691 (.7264,.8079)
1	.4794 (.4261,.5821)	4	.5814 (.5663,.6453)	17	.6890 (.6700,.7378)	69	.7693 (.7265,.8081)
1	.4831 (.4315,.5834)	4	.5853 (.5712,.6487)	18	.6933 (.6733,.7415)	72	.7713 (.7277,.8099)
1	.4867 (.4369,.5847)	5	.5893 (.5762,.6521)	19	.6974 (.6765,.7451)	76	.7734 (.7290,.8118)
1	.4903 (.4423,.5861)	5	.5932 (.5811,.6555)	20	.7014 (.6795,.7486)	81	.7755 (.7303,.8137)
1	.4940 (.4476,.5879)	5	.5943 (.5823,.6564)	21	.7053 (.6825,.7520)	85	.7775 (.7315,.8156)
1	.4977 (.4530,.5899)	5	.5972 (.5860,.6590)	22	.7090 (.6854,.7553)	90	.7795 (.7327,.8175)
1	.5013 (.4584,.5919)	5	.6012 (.5909,.6624)	22	.7091 (.6854,.7553)	95	.7815 (.7338,.8194)
1	.5050 (.4637,.5940)	6	.6053 (.5958,.6659)	23	.7128 (.6882,.7585)	99	.7831 (.7348,.8209)
1	.5087 (.4690,.5960)	6	.6093 (.6001,.6693)	24	.7164 (.6909,.7617)	100	.7834 (.7350,.8212)
2	.5125 (.4744,.5981)	6	.6134 (.6041,.6728)	26	.7199 (.6935,.7647)	106	.7852 (.7361,.8229)
2	.5162 (.4797,.6002)	7	.6174 (.6082,.6763)	27	.7232 (.6961,.7676)	112	.7871 (.7371,.8247)
2	.5199 (.4850,.6023)	7	.6215 (.6122,.6798)	29	.7265 (.6985,.7705)	118	.7889 (.7382,.8264)
2	.5237 (.4903,.6045)	7	.6256 (.6162,.6833)	30	.7297 (.7007,.7733)	125	.7906 (.7392,.8280)
2	.5274 (.4956,.6067)	8	.6297 (.6203,.6869)	32	.7328 (.7028,.7760)	132	.7924 (.7401,.8297)
2	.5312 (.5008,.6088)	8	.6338 (.6244,.6904)	34	.7359 (.7048,.7786)	134	.7929 (.7405,.8302)
2	.5350 (.5061,.6113)	9	.6380 (.6279,.6940)	36	.7388 (.7068,.7812)	139	.7940 (.7411,.8313)
2	.5373 (.5093,.6129)	9	.6421 (.6314,.6975)	36	.7388 (.7068,.7812)	147	.7957 (.7420,.8328)
2	.5388 (.5114,.6140)	10	.6450 (.6338,.6999)	38	.7417 (.7087,.7837)	155	.7973 (.7429,.8344)
2	.5426 (.5166,.6167)	10	.6463 (.6350,.7011)	40	.7445 (.7106,.7862)	163	.7990 (.7438,.8359)
2	.5464 (.5218,.6194)	10	.6505 (.6386,.7047)	42	.7472 (.7124,.7886)	173	.8005 (.7446,.8374)
3	.5502 (.5268,.6222)	11	.6547 (.6422,.7083)	44	.7499 (.7141,.7909)	500	.8265 (.7573,.8620)
3	.5541 (.5317,.6250)	11	.6589 (.6459,.7119)	47	.7525 (.7158,.7932)	1000	.8397 (.7623,.8751)
3	.5579 (.5367,.6277)	12	.6632 (.6496,.7155)	49	.7550 (.7175,.7954)	10.8	.6521 (.6396,.7061)
3	.5618 (.5416,.6305)	13	.6674 (.6533,.7191)	52	.7575 (.7191,.7976)	1000	.8919 (.8397,.9158)
3	.5657 (.5466,.6334)	13	.6717 (.6569,.7228)	55	.7600 (.7206,.7997)		(,)
3	.5696 (.5515,.6362)	14	.6760 (.6601,.7265)	58	.7623 (.7221,.8018)		

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6.3 Multivariate Cox Models of Risk

Table 6.10: 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*

	HR per 10 fold incr.	P value
Anti Spike IgG (BAU/ml)	0.42 (0.28-0.62)	<0.001
Anti RBD IgG (BAU/ml)	0.90 (0.64-1.26)	0.534
Generalized Wald Test		0.000

*Baseline covariates adjusted for: Age + as.factor(Region). Maximum failure event time 149 days.
‡ Count cases starting 1 days post Day 29.

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Chapter 7

Univariate CoR: Nonparametric Threshold Modeling (>=s)

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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

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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.

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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	$1.54 * 10^1$	0.00804	0.00609	0.00999
0.240	$1.74 * 10^0$	0.00721	0.00521	0.00921
0.401	$2.52 * 10^0$	0.00687	0.00493	0.00881
0.522	$3.33 * 10^0$	0.00666	0.00468	0.00864
0.758	$5.73 * 10^0$	0.00681	0.00462	0.00900
0.951	$8.93 * 10^0$	0.00680	0.00408	0.00953
1.097	$1.25 * 10^1$	0.00580	0.00279	0.00880
1.229	$1.69 * 10^1$	0.00529	0.00178	0.00881
1.480	$3.02 * 10^1$	0.00472	0.00083	0.00860
1.592	$3.91 * 10^1$	0.00501	0.00095	0.00907
1.728	$5.35 * 10^1$	0.00463	0.00066	0.00860
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.

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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	$7.96 * 10^1$	0.00808	0.00613	0.01003
0.340	$2.19 * 10^0$	0.00774	0.00574	0.00975
0.540	$3.47 * 10^0$	0.00784	0.00569	0.00999
0.686	$4.85 * 10^0$	0.00752	0.00532	0.00973
0.979	$9.53 * 10^0$	0.00707	0.00479	0.00936
1.178	$1.51 * 10^1$	0.00689	0.00428	0.00949
1.340	$2.19 * 10^1$	0.00673	0.00346	0.00999
1.553	$3.57 * 10^1$	0.00612	0.00251	0.00973
1.838	$6.89 * 10^1$	0.00601	0.00212	0.00989
1.997	$9.93 * 10^1$	0.00466	0.00144	0.00788
2.127	$1.34 * 10^2$	0.00406	0.00000	0.01233
2.237	$1.73 * 10^2$	0.00406	0.00000	0.01233
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

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.

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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	$1.54 * 10^1$	0.00804	0.00609	0.00999
0.240	$1.74 * 10^0$	0.00721	0.00521	0.00921
0.401	$2.52 * 10^0$	0.00687	0.00493	0.00881
0.522	$3.33 * 10^0$	0.00671	0.00473	0.00869
0.758	$5.73 * 10^0$	0.00671	0.00452	0.00890
0.951	$8.93 * 10^0$	0.00671	0.00398	0.00944
1.097	$1.25 * 10^1$	0.00580	0.00279	0.00880
1.229	$1.69 * 10^1$	0.00533	0.00182	0.00885
1.480	$3.02 * 10^1$	0.00481	0.00093	0.00869
1.592	$3.91 * 10^1$	0.00481	0.00075	0.00887
1.728	$5.35 * 10^1$	0.00463	0.00066	0.00860
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.

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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	$7.96 * 10^1$	0.00808	0.00613	0.01003
0.340	$2.19 * 10^0$	0.00780	0.00579	0.00981
0.540	$3.47 * 10^0$	0.00780	0.00565	0.00995
0.686	$4.85 * 10^0$	0.00752	0.00532	0.00973
0.979	$9.53 * 10^0$	0.00707	0.00479	0.00936
1.178	$1.51 * 10^1$	0.00689	0.00428	0.00949
1.340	$2.19 * 10^1$	0.00655	0.00328	0.00982
1.553	$3.57 * 10^1$	0.00640	0.00279	0.01002
1.838	$6.89 * 10^1$	0.00601	0.00212	0.00989
1.997	$9.93 * 10^1$	0.00466	0.00144	0.00788
2.127	$1.34 * 10^2$	0.00406	0.00000	0.01233
2.237	$1.73 * 10^2$	0.00406	0.00000	0.01233
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

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

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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.

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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	$1.54 * 10^1$	0.00859	0.00660	0.01058
0.240	$1.74 * 10^0$	0.00771	0.00567	0.00975
0.401	$2.52 * 10^0$	0.00739	0.00541	0.00937
0.522	$3.33 * 10^0$	0.00725	0.00523	0.00927
0.758	$5.73 * 10^0$	0.00725	0.00501	0.00949
0.951	$8.93 * 10^0$	0.00725	0.00444	0.01006
1.097	$1.25 * 10^1$	0.00649	0.00335	0.00963
1.229	$1.69 * 10^1$	0.00604	0.00264	0.00945
1.480	$3.02 * 10^1$	0.00571	0.00166	0.00976
1.592	$3.91 * 10^1$	0.00571	0.00141	0.01001
1.728	$5.35 * 10^1$	0.00571	0.00145	0.00997
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.

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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	$7.96 * 10^1$	0.00863	0.00664	0.01062
0.340	$2.19 * 10^0$	0.00830	0.00625	0.01035
0.540	$3.47 * 10^0$	0.00830	0.00612	0.01049
0.686	$4.85 * 10^0$	0.00803	0.00578	0.01027
0.979	$9.53 * 10^0$	0.00748	0.00517	0.00980
1.178	$1.51 * 10^1$	0.00730	0.00464	0.00996
1.340	$2.19 * 10^1$	0.00691	0.00357	0.01025
1.553	$3.57 * 10^1$	0.00675	0.00305	0.01044
1.838	$6.89 * 10^1$	0.00648	0.00249	0.01047
1.997	$9.93 * 10^1$	0.00504	0.00173	0.00835
2.127	$1.34 * 10^2$	0.00458	0.00000	0.01338
2.237	$1.73 * 10^2$	0.00458	0.00000	0.01338
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.

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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	$1.54 * 10^1$	0.00859	0.00660	0.01058
0.240	$1.74 * 10^0$	0.00771	0.00567	0.00975
0.401	$2.52 * 10^0$	0.00739	0.00541	0.00937
0.522	$3.33 * 10^0$	0.00725	0.00523	0.00927
0.758	$5.73 * 10^0$	0.00725	0.00501	0.00949
0.951	$8.93 * 10^0$	0.00725	0.00444	0.01006
1.097	$1.25 * 10^1$	0.00649	0.00335	0.00963
1.229	$1.69 * 10^1$	0.00604	0.00264	0.00945
1.480	$3.02 * 10^1$	0.00571	0.00166	0.00976
1.592	$3.91 * 10^1$	0.00571	0.00141	0.01001
1.728	$5.35 * 10^1$	0.00571	0.00145	0.00997
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.

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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	$7.96 * 10^1$	0.00863	0.00664	0.01062
0.340	$2.19 * 10^0$	0.00830	0.00625	0.01035
0.540	$3.47 * 10^0$	0.00830	0.00612	0.01049
0.686	$4.85 * 10^0$	0.00803	0.00578	0.01027
0.979	$9.53 * 10^0$	0.00748	0.00517	0.00980
1.178	$1.51 * 10^1$	0.00730	0.00464	0.00996
1.340	$2.19 * 10^1$	0.00691	0.00357	0.01025
1.553	$3.57 * 10^1$	0.00675	0.00305	0.01044
1.838	$6.89 * 10^1$	0.00648	0.00249	0.01047
1.997	$9.93 * 10^1$	0.00504	0.00173	0.00835
2.127	$1.34 * 10^2$	0.00458	0.00000	0.01338
2.237	$1.73 * 10^2$	0.00458	0.00000	0.01338
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.

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	$1.54 * 10^1$	0.00804	0.00531	0.01077
0.240	$1.74 * 10^0$	0.00721	0.00441	0.01000
0.401	$2.52 * 10^0$	0.00687	0.00416	0.00959
0.522	$3.33 * 10^0$	0.00671	0.00393	0.00949
0.758	$5.73 * 10^0$	0.00671	0.00365	0.00977
0.951	$8.93 * 10^0$	0.00671	0.00289	0.01053
1.097	$1.25 * 10^1$	0.00580	0.00159	0.01000
1.229	$1.69 * 10^1$	0.00533	0.00041	0.01025
1.480	$3.02 * 10^1$	0.00481	0.00000	0.01025
1.592	$3.91 * 10^1$	0.00481	0.00000	0.01050
1.728	$5.35 * 10^1$	0.00463	0.00000	0.01019
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

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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.

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	$7.96 * 10^1$	0.00808	0.00536	0.01080
0.340	$2.19 * 10^0$	0.00780	0.00500	0.01060
0.540	$3.47 * 10^0$	0.00780	0.00481	0.01079
0.686	$4.85 * 10^0$	0.00752	0.00445	0.01060
0.979	$9.53 * 10^0$	0.00707	0.00390	0.01025
1.178	$1.51 * 10^1$	0.00689	0.00326	0.01052
1.340	$2.19 * 10^1$	0.00655	0.00199	0.01110
1.553	$3.57 * 10^1$	0.00640	0.00137	0.01144
1.838	$6.89 * 10^1$	0.00601	0.00059	0.01142
1.997	$9.93 * 10^1$	0.00466	0.00018	0.00915
2.127	$1.34 * 10^2$	0.00406	0.00000	0.01559
2.237	$1.73 * 10^2$	0.00406	0.00000	0.01559
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

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

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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.

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	$1.54 * 10^1$	0.00804	0.00531	0.01077
0.240	$1.74 * 10^0$	0.00721	0.00441	0.01000
0.401	$2.52 * 10^0$	0.00687	0.00416	0.00959
0.522	$3.33 * 10^0$	0.00671	0.00393	0.00949
0.758	$5.73 * 10^0$	0.00671	0.00365	0.00977
0.951	$8.93 * 10^0$	0.00671	0.00289	0.01053
1.097	$1.25 * 10^1$	0.00580	0.00159	0.01000
1.229	$1.69 * 10^1$	0.00533	0.00041	0.01025
1.480	$3.02 * 10^1$	0.00481	0.00000	0.01025
1.592	$3.91 * 10^1$	0.00481	0.00000	0.01050
1.728	$5.35 * 10^1$	0.00463	0.00000	0.01019
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

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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.

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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	$7.96 * 10^1$	0.00808	0.00536	0.01080
0.340	$2.19 * 10^0$	0.00780	0.00500	0.01060
0.540	$3.47 * 10^0$	0.00780	0.00481	0.01079
0.686	$4.85 * 10^0$	0.00752	0.00445	0.01060
0.979	$9.53 * 10^0$	0.00707	0.00390	0.01025
1.178	$1.51 * 10^1$	0.00689	0.00326	0.01052
1.340	$2.19 * 10^1$	0.00655	0.00199	0.01110
1.553	$3.57 * 10^1$	0.00640	0.00137	0.01144
1.838	$6.89 * 10^1$	0.00601	0.00059	0.01142
1.997	$9.93 * 10^1$	0.00466	0.00018	0.00915
2.127	$1.34 * 10^2$	0.00406	0.00000	0.01559
2.237	$1.73 * 10^2$	0.00406	0.00000	0.01559
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

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

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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.

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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	$1.54 * 10^1$	0.00859	0.00581	0.01137
0.240	$1.74 * 10^0$	0.00771	0.00486	0.01055
0.401	$2.52 * 10^0$	0.00739	0.00462	0.01016
0.522	$3.33 * 10^0$	0.00725	0.00442	0.01008
0.758	$5.73 * 10^0$	0.00725	0.00412	0.01038
0.951	$8.93 * 10^0$	0.00725	0.00332	0.01118
1.097	$1.25 * 10^1$	0.00649	0.00210	0.01088
1.229	$1.69 * 10^1$	0.00604	0.00128	0.01080
1.480	$3.02 * 10^1$	0.00571	0.00005	0.01136
1.592	$3.91 * 10^1$	0.00571	0.00000	0.01172
1.728	$5.35 * 10^1$	0.00571	0.00000	0.01166
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	$7.96 * 10^1$	0.00863	0.00586	0.01140
0.340	$2.19 * 10^0$	0.00830	0.00545	0.01115
0.540	$3.47 * 10^0$	0.00830	0.00526	0.01134
0.686	$4.85 * 10^0$	0.00803	0.00490	0.01115
0.979	$9.53 * 10^0$	0.00748	0.00426	0.01070
1.178	$1.51 * 10^1$	0.00730	0.00360	0.01100
1.340	$2.19 * 10^1$	0.00691	0.00227	0.01155
1.553	$3.57 * 10^1$	0.00675	0.00161	0.01188
1.838	$6.89 * 10^1$	0.00648	0.00093	0.01203
1.997	$9.93 * 10^1$	0.00504	0.00043	0.00964
2.127	$1.34 * 10^2$	0.00458	0.00000	0.01682
2.237	$1.73 * 10^2$	0.00458	0.00000	0.01682
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

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

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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.

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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	$1.54 * 10^1$	0.00859	0.00581	0.01137
0.240	$1.74 * 10^0$	0.00771	0.00486	0.01055
0.401	$2.52 * 10^0$	0.00739	0.00462	0.01016
0.522	$3.33 * 10^0$	0.00725	0.00442	0.01008
0.758	$5.73 * 10^0$	0.00725	0.00412	0.01038
0.951	$8.93 * 10^0$	0.00725	0.00332	0.01118
1.097	$1.25 * 10^1$	0.00649	0.00210	0.01088
1.229	$1.69 * 10^1$	0.00604	0.00128	0.01080
1.480	$3.02 * 10^1$	0.00571	0.00005	0.01136
1.592	$3.91 * 10^1$	0.00571	0.00000	0.01172
1.728	$5.35 * 10^1$	0.00571	0.00000	0.01166
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.

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	$7.96 * 10^1$	0.00863	0.00586	0.01140
0.340	$2.19 * 10^0$	0.00830	0.00545	0.01115
0.540	$3.47 * 10^0$	0.00830	0.00526	0.01134
0.686	$4.85 * 10^0$	0.00803	0.00490	0.01115
0.979	$9.53 * 10^0$	0.00748	0.00426	0.01070
1.178	$1.51 * 10^1$	0.00730	0.00360	0.01100
1.340	$2.19 * 10^1$	0.00691	0.00227	0.01155
1.553	$3.57 * 10^1$	0.00675	0.00161	0.01188
1.838	$6.89 * 10^1$	0.00648	0.00093	0.01203
1.997	$9.93 * 10^1$	0.00504	0.00043	0.00964
2.127	$1.34 * 10^2$	0.00458	0.00000	0.01682
2.237	$1.73 * 10^2$	0.00458	0.00000	0.01682
2.699	$5.00 * 10^2$	0.00000	NA	NA
3.000	$1.00 * 10^3$	0.00000	NA	NA

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Chapter 8

Univariate CoR: Nonparametric Threshold Modeling (<=s)

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

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Chapter 9

Day D29 Univariate CoR: Nonlinear modeling

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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 vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: Age + as.factor(Region). 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. ‡ Count cases starting 7 days post Day 29.

Figure 9.2: Marginalized risk as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: Age + as.factor(Region). 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 = 1.6. ‡ Count cases starting 7 days post Day 29.

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Chapter 10

Day D29start1 Univariate CoR: Nonlinear modeling

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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 vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: Age + as.factor(Region). 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. ‡ Count cases starting 1 days post Day 29.

Figure 10.2: Marginalized risk as functions of Day 29 markers (=s) among vaccine recipients with 95% bootstrap point-wise confidence bands (10 replicates) as modeled by GAM with automatic smoothness estimation. Baseline covariates adjusted for: Age + as.factor(Region). 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 = 1.6. ‡ Count cases starting 1 days post Day 29.

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Chapter 11

Appendix

```
#> [1] "reading data from janssen_pooled_mock_data_processed_with_riskscore.csv"
```

- This report was built from the `CoVPN/correlates_reporting` repository with commit hash af6c6467b70d77c258c3d408a0413b6f9f890a1d. A diff of the changes introduced by that commit may be viewed at https://github.com/CoVPN/correlates_reporting/commit/af6c6467b70d77c258c3d408a0413b6f9f890a1d
- The sha256 hash sum of the processed file, "janssen_pooled_mock_data_processed_with_riskscore.csv": bd7abb0d9b05615aaa493d5804bcff3b5ad51654e359b6c3a18fba701d094627

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