

COVID-19 Correlates of Protection Analysis Report

MockCOVE Study

USG COVID-19 Response Biostatistics Team

June 25, 2021

Contents

1	Disclaimers	9
2	Stochastic Interventional Vaccine Efficacy	11
2.1	Figures for Stochastic Interventional CoPs for Day 57	12
2.2	Figures for Stochastic Interventional CoPs for Day 29	20
3	Mediators of Vaccine Efficacy	29
4	Appendix	31

List of Tables

- 3.1 Table of mediation effect estimates for quantitative markers with 95% confidence intervals.
Direct VE = VE comparing vaccine vs. placebo with marker set to distribution in placebo.
Indirect VE = VE in vaccinated comparing observed marker vs. hypothetical marker under placebo.
Prop. mediated = fraction of total risk reduction from vaccine attributed to antibody response. 29
- 3.2 Table of mediation effect estimates for tertile markers with 95% confidence intervals.
Direct VE = VE comparing vaccine vs. placebo with marker set to distribution in placebo.
Indirect VE = VE in vaccinated comparing observed marker vs. hypothetical marker under placebo.
Prop. mediated = fraction of total risk reduction from vaccine attributed to antibody response. 29

List of Figures

2.1	Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 57	12
2.2	Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 57	13
2.3	Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 57	14
2.4	Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 57	15
2.5	Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57	16
2.6	Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57	17
2.7	Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57	18
2.8	Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57	19
2.9	Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 29	20
2.10	Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 29	21
2.11	Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 29	22
2.12	Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 29	23
2.13	Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29	24
2.14	Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29	25
2.15	Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29	26
2.16	Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29	27

MOCK

Chapter 1

Disclaimers

- The data presented in the analysis originated from the Moderna Sponsored mRNA-1273-P301 clinical study and 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
- The preliminary immunogenicity data presented here do not reflect the Sponsors statistical analysis plan and therefore should not be interpreted as a protocol defined read-out of the clinical study.
- These data are not to be disclosed without written permission of Moderna.

MOCK

Chapter 2

Stochastic Interventional Vaccine Efficacy

We estimate the counterfactual mean of symptomatic COVID-19 infection under posited shifts in the measured activity levels of each of 4 *candidate* mechanistic correlates of protection (mCoP) biomarkers. By shifting the *standardized* biomarker activity levels by standard unit shifts along the grid $\{-1, -0.5, 0, 0.5, 1\}$, we can assess the degree to which vaccines that modulate mCoP biomarker activity to these levels could mitigate symptomatic COVID-19 infection in terms of counterfactual stochastic interventional risk and vaccine efficacy (VE).

2.1 Figures for Stochastic Interventional CoPs for Day 57

2.1.1 Stoch interv. risk: spike protein binding antibody



Figure 2.1: Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 57

2.1.2 Stoch. interv. VE: spike protein binding antibody



Figure 2.2: Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 57

2.1.3 Stoch. interv. risk: RBD binding antibody



Figure 2.3: Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 57

2.1.4 Stoch. interv. VE: RBD binding antibody

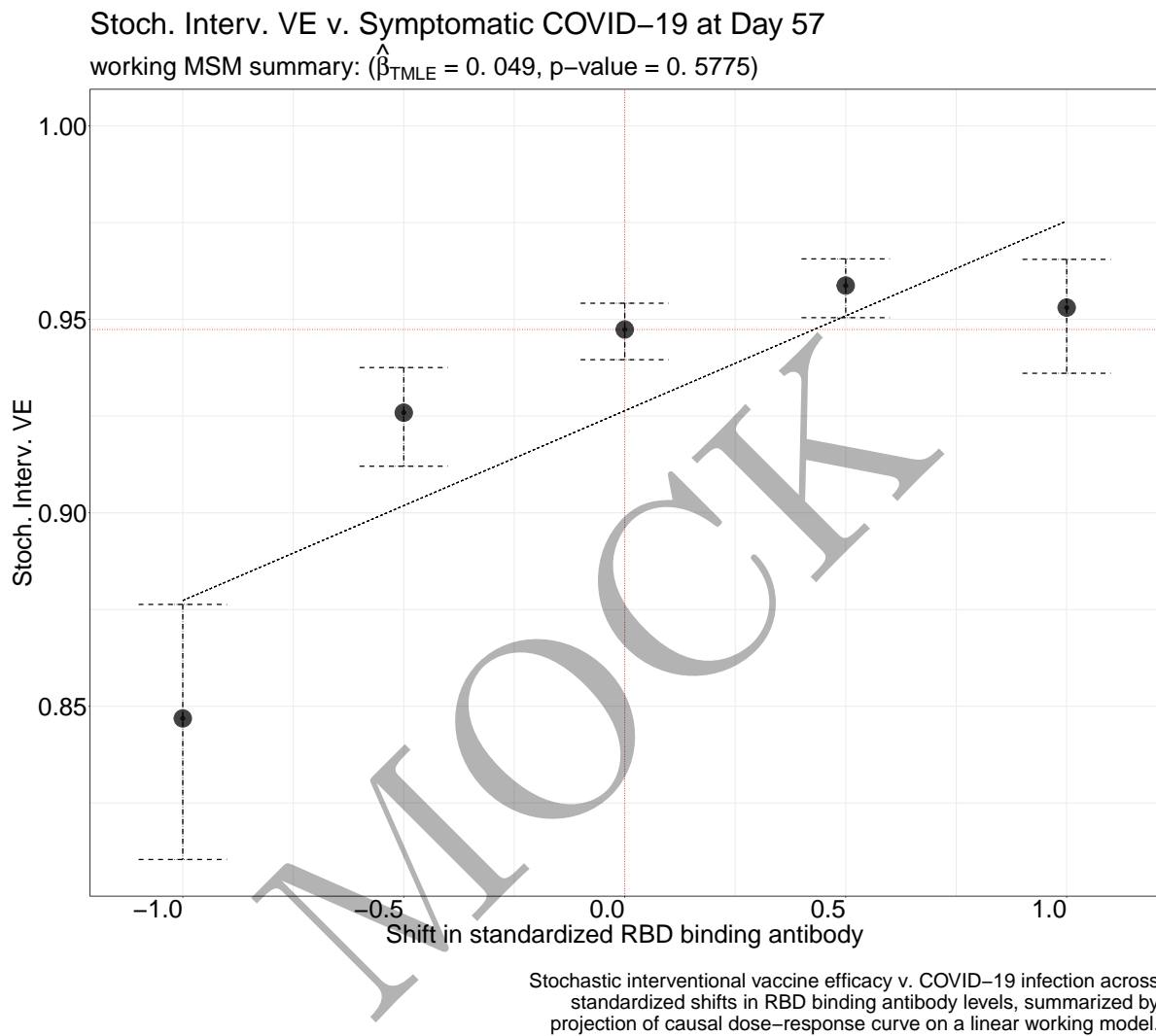


Figure 2.4: Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 57

2.1.5 Stoch. interv. risk: pseudo-neutralizing antibody (ID50)

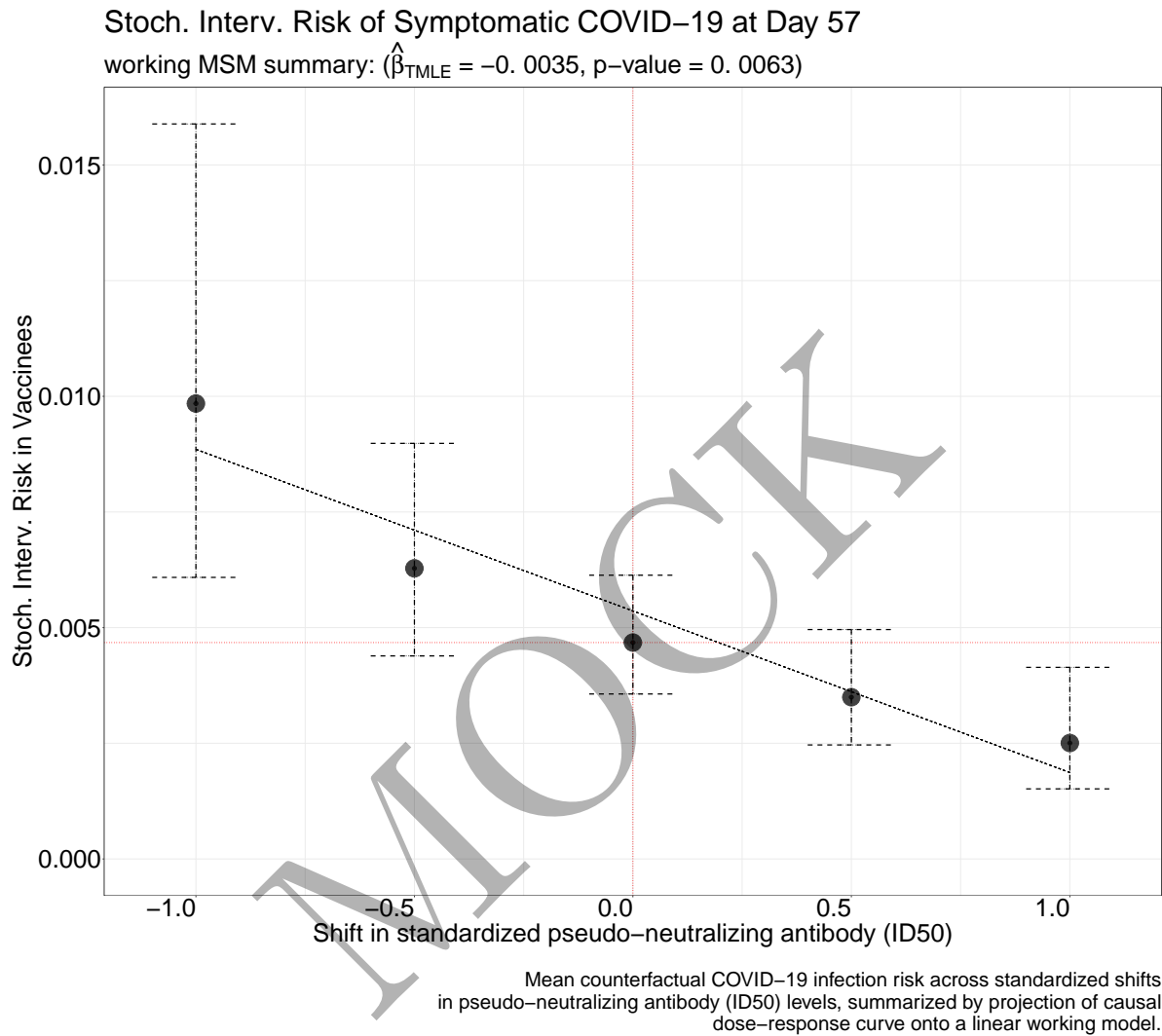


Figure 2.5: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57

2.1.6 Stoch. interv. VE: pseudo-neutralizing antibody (ID50)



Figure 2.6: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57

2.1.7 Stoch. interv. risk: pseudo-neutralizing antibody (ID80)

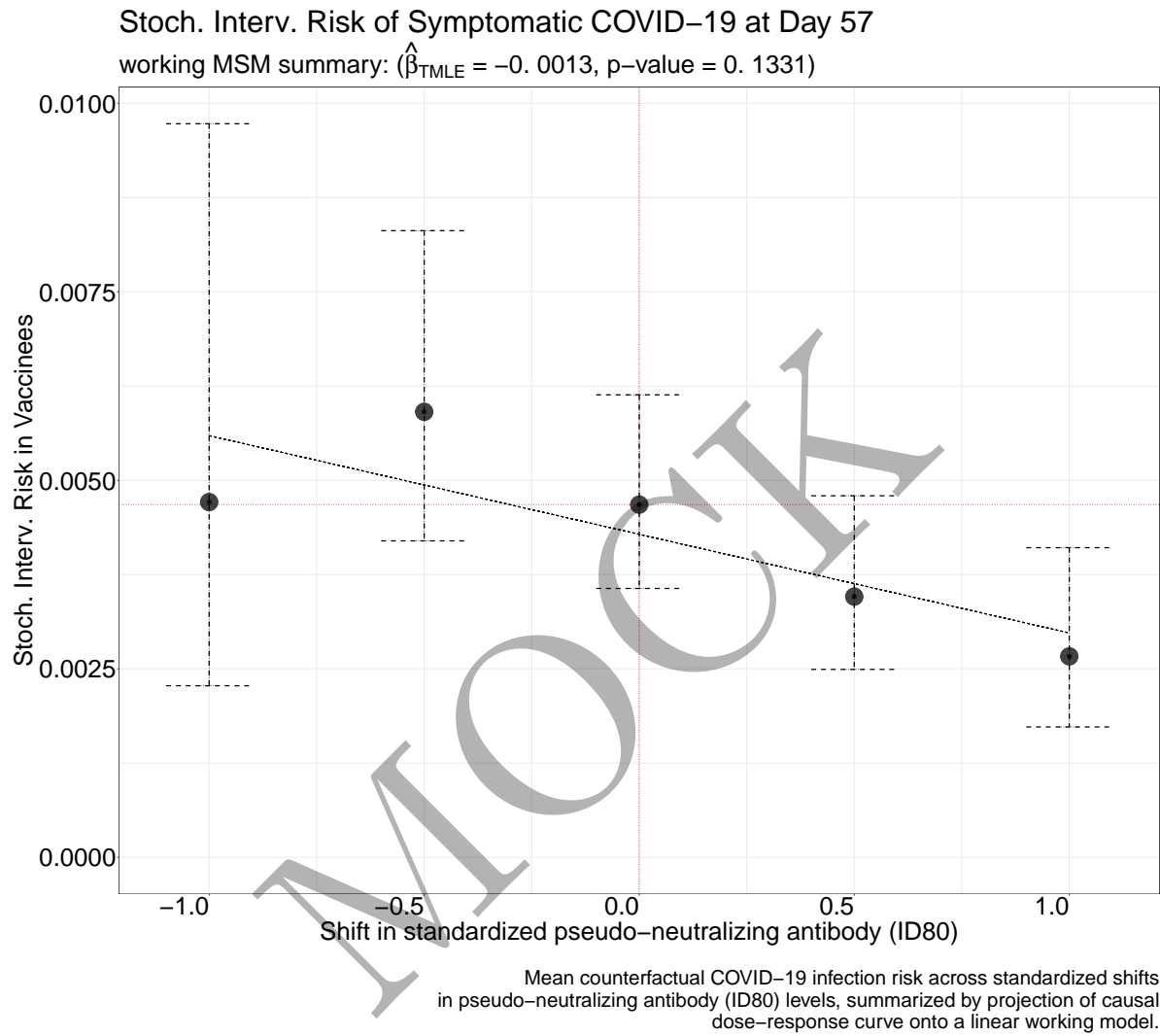


Figure 2.7: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57

2.1.8 Stoch. interv. VE: pseudo-neutralizing antibody (ID80)



Figure 2.8: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57

2.2 Figures for Stochastic Interventional CoPs for Day 29

2.2.1 Stoch. interv. risk: spike protein binding antibody

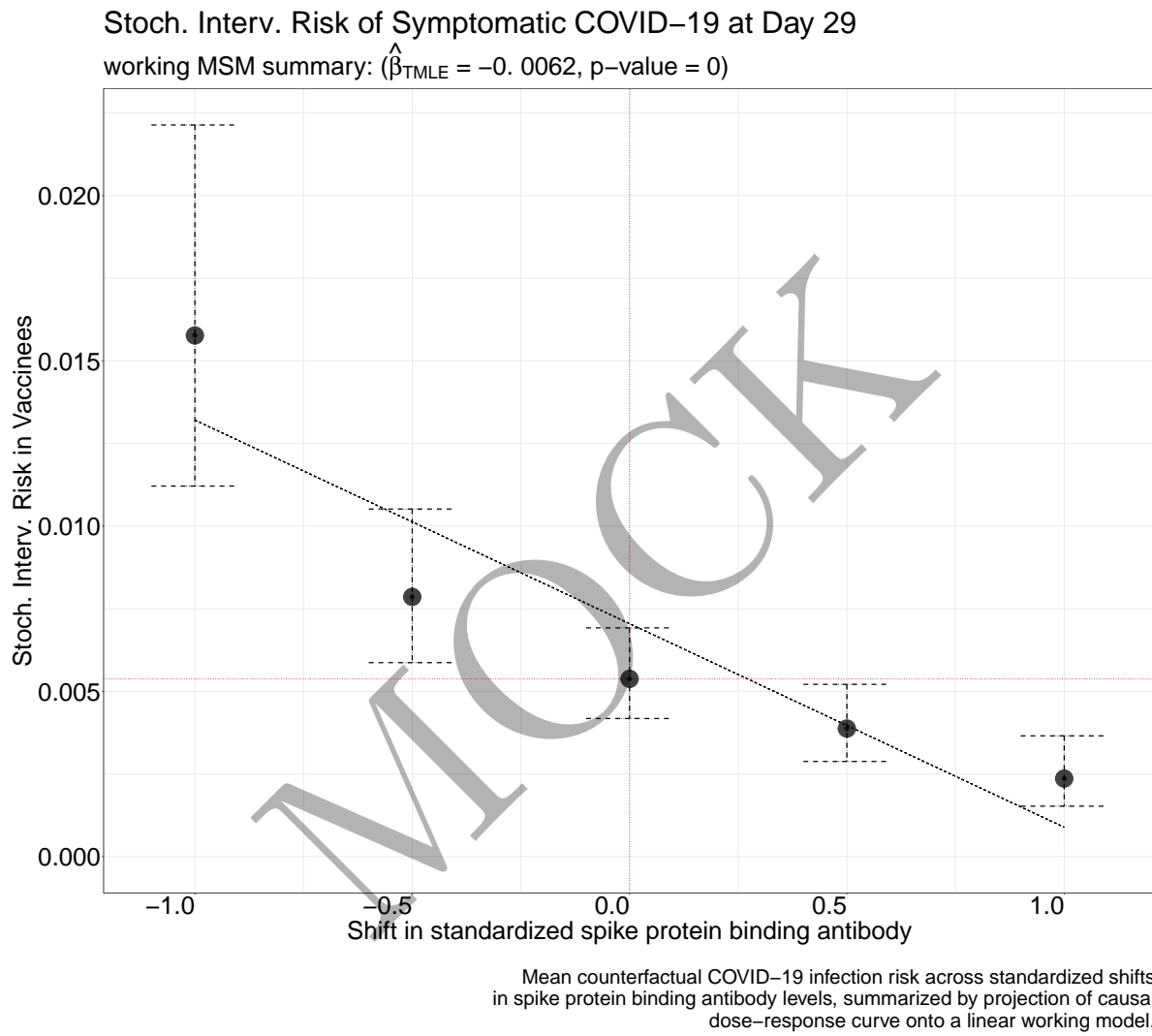


Figure 2.9: Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 29

2.2.2 Stoch. interv. VE: spike protein binding antibody



Figure 2.10: Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 29

2.2.3 Stoch. interv. risk: RBD binding antibody



Figure 2.11: Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 29

2.2.4 Stoch. interv. VE: RBD binding antibody



Figure 2.12: Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 29

2.2.5 Stoch. interv. risk: pseudo-neutralizing antibody (ID50)



Figure 2.13: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29

2.2.6 Stoch. interv. VE: pseudo-neutralizing antibody (ID50)



Figure 2.14: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29

2.2.7 Stoch. interv. risk: pseudo-neutralizing antibody (ID80)



Figure 2.15: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29

2.2.8 Stoch. interv. VE: pseudo-neutralizing antibody (ID80)



Figure 2.16: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29

MOCK

Chapter 3

Mediators of Vaccine Efficacy

Table 3.1: Table of mediation effect estimates for quantitative markers with 95% confidence intervals. Direct VE = VE comparing vaccine vs. placebo with marker set to distribution in placebo. Indirect VE = VE in vaccinated comparing observed marker vs. hypothetical marker under placebo. Prop. mediated = fraction of total risk reduction from vaccine attributed to antibody response.

Time	Assay	Direct VE	Indirect VE	Prop. mediated
Day 57	Binding Antibody to Spike	NA	NA	NA
Day 57	Binding Antibody to RBD	NA	NA	NA
Day 57	PsV Neutralization 50% Titer	NA	NA	NA
Day 57	PsV Neutralization 80% Titer	0.909 (0.903, 0.914)	0.422 (0.244, 0.557)	0.186 (0.260, 0.112)
Day 29	Binding Antibody to Spike	NA	NA	NA
Day 29	Binding Antibody to RBD	NA	NA	NA
Day 29	PsV Neutralization 50% Titer	0.952 (0.644, 0.993)	-0.102 (-7.038, 0.849)	-0.033 (0.644, -0.711)
Day 29	PsV Neutralization 80% Titer	0.932 (0.883, 0.961)	0.213 (-0.292, 0.520)	0.081 (0.250, -0.087)

^a NA denotes insufficient overlap in antibody response between vaccinated and control participants.

Table 3.2: Table of mediation effect estimates for tertile markers with 95% confidence intervals. Direct VE = VE comparing vaccine vs. placebo with marker set to distribution in placebo. Indirect VE = VE in vaccinated comparing observed marker vs. hypothetical marker under placebo. Prop. mediated = fraction of total risk reduction from vaccine attributed to antibody response.

Time	Assay	Direct VE	Indirect VE	Prop. mediated
Day 57	Binding Antibody to Spike	0.933 (0.895, 0.957)	0.219 (-0.085, 0.438)	0.084 (0.196, -0.028)
Day 57	Binding Antibody to RBD	0.949 (0.907, 0.972)	-0.039 (-0.743, 0.381)	-0.013 (0.163, -0.189)
Day 57	PsV Neutralization 50% Titer	0.938 (0.907, 0.959)	0.146 (-0.175, 0.379)	0.054 (0.162, -0.055)
Day 57	PsV Neutralization 80% Titer	0.927 (0.891, 0.950)	0.282 (-0.002, 0.486)	0.113 (0.224, 0.001)
Day 29	Binding Antibody to Spike	0.940 (0.912, 0.960)	0.106 (-0.195, 0.332)	0.038 (0.138, -0.061)
Day 29	Binding Antibody to RBD	0.946 (0.915, 0.966)	0.006 (-0.429, 0.308)	0.002 (0.126, -0.122)
Day 29	PsV Neutralization 50% Titer	0.941 (0.912, 0.960)	0.102 (-0.243, 0.351)	0.037 (0.147, -0.074)
Day 29	PsV Neutralization 80% Titer	0.934 (0.900, 0.957)	0.188 (-0.182, 0.442)	0.071 (0.198, -0.056)

MOCK

Chapter 4

Appendix

- This report was built from the [CoVPN/correlates_reporting](https://github.com/CoVPN/correlates_reporting) repository with commit hash b45e0771a8193fd6a45b77b9f21700a107beffba. A diff of the changes introduced by that commit may be viewed at https://github.com/CoVPN/correlates_reporting/commit/b45e0771a8193fd6a45b77b9f21700a107beffba
- The sha256 hash sum of the raw input file, “COVID_VEtrial_practicedata_primarystage1.csv”: 83d0f55d1745ffd42be124d8f9ec9a9903abcc13cd22f95e537542a08b41300a
- The sha256 hash sum of the processed file, “moderna_mock_data_processed.csv”: 28964ce20cfd70a621aff9df412c42b11