COVID-19 Correlates of Protection Analysis Report

MockCOVE Study

USG COVID-19 Response Biostatistics Team

June 25, 2021

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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.

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

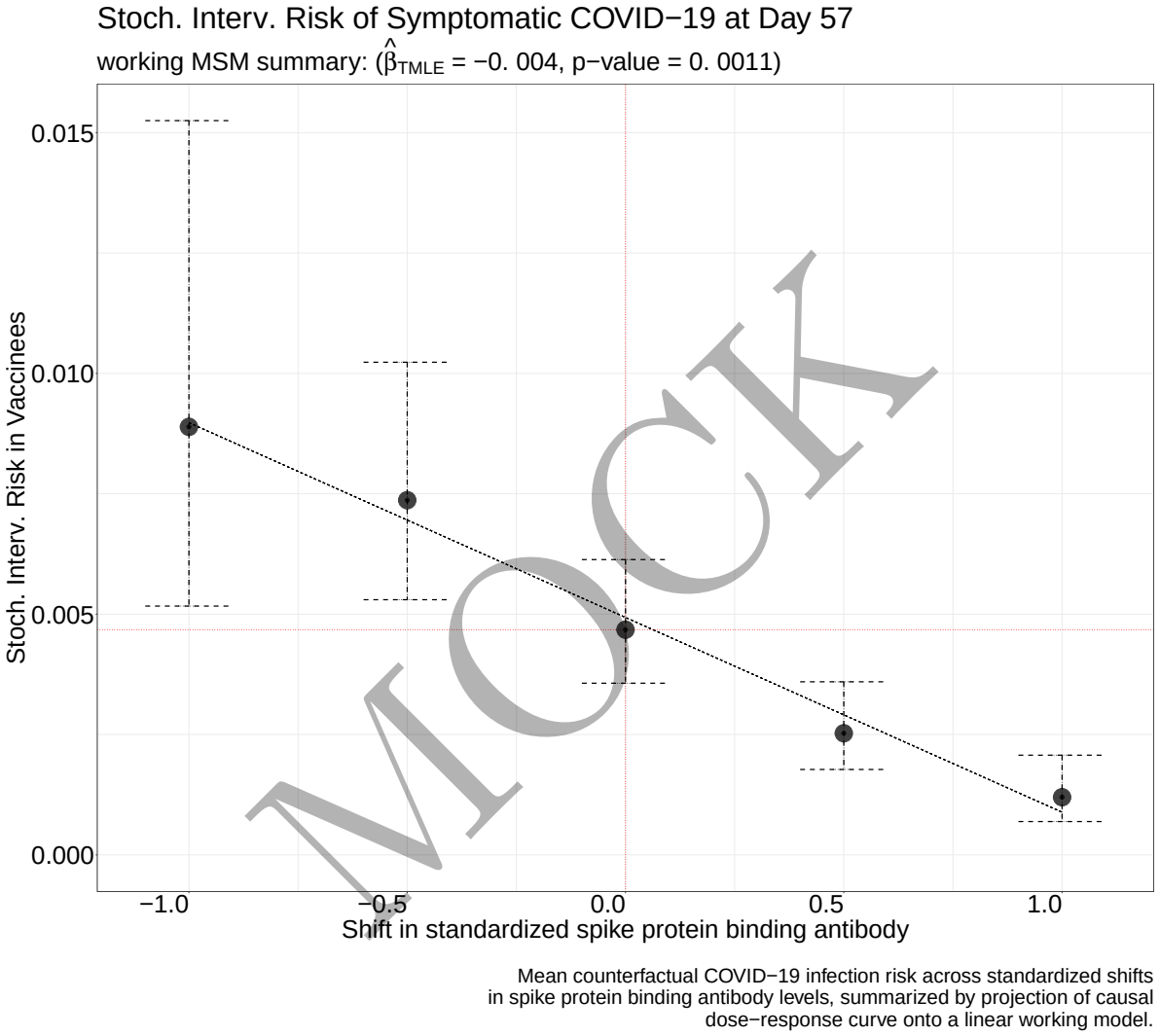

Figure 2.1: Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 57

2.1.2 Stoch. interv. VE: spike protein binding antibody

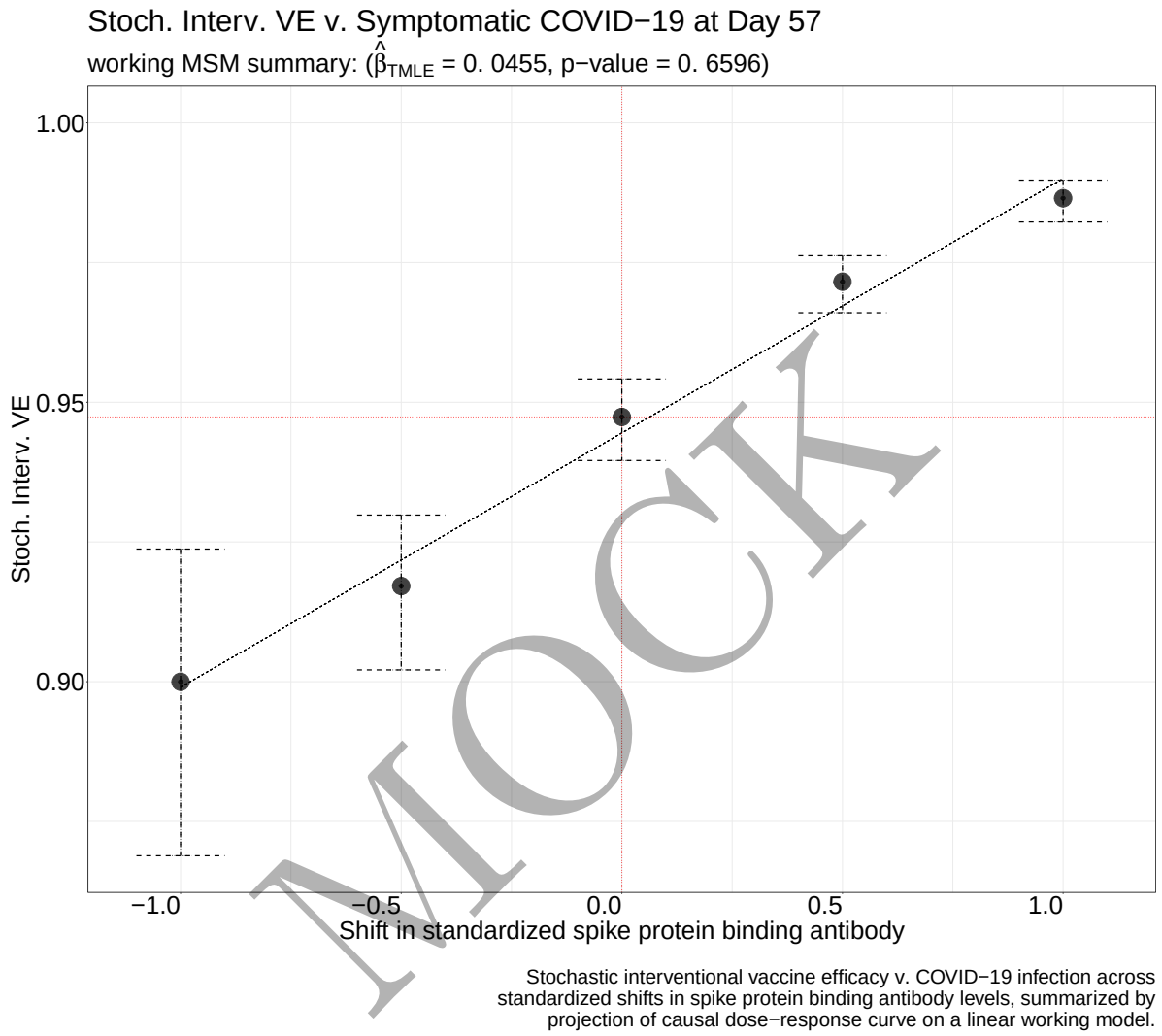

Figure 2.2: Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 57

2.1.3 Stoch. interv. risk: RBD binding antibody

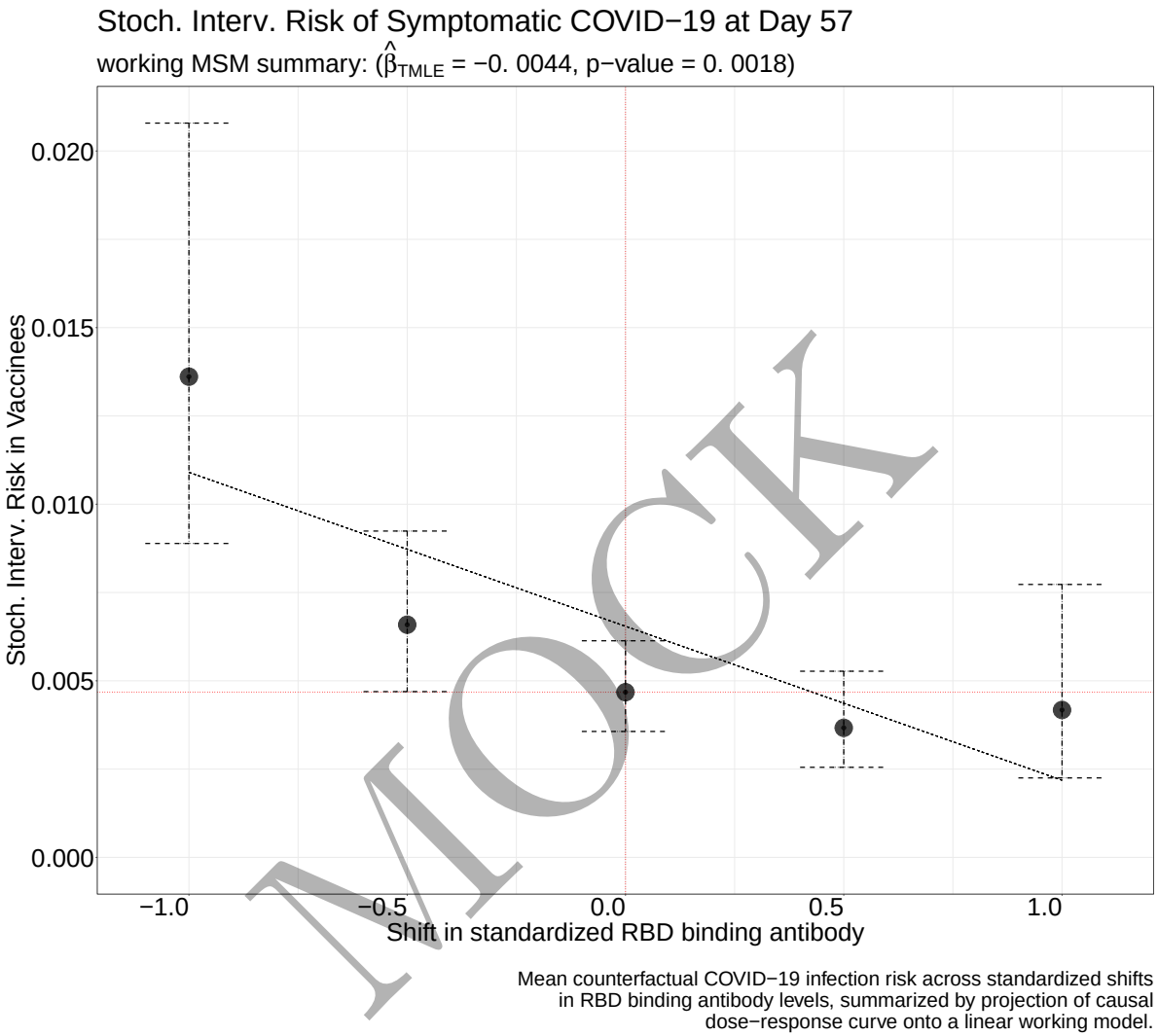

Figure 2.3: Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 57

2.1.4 Stoch. interv. VE: RBD binding antibody

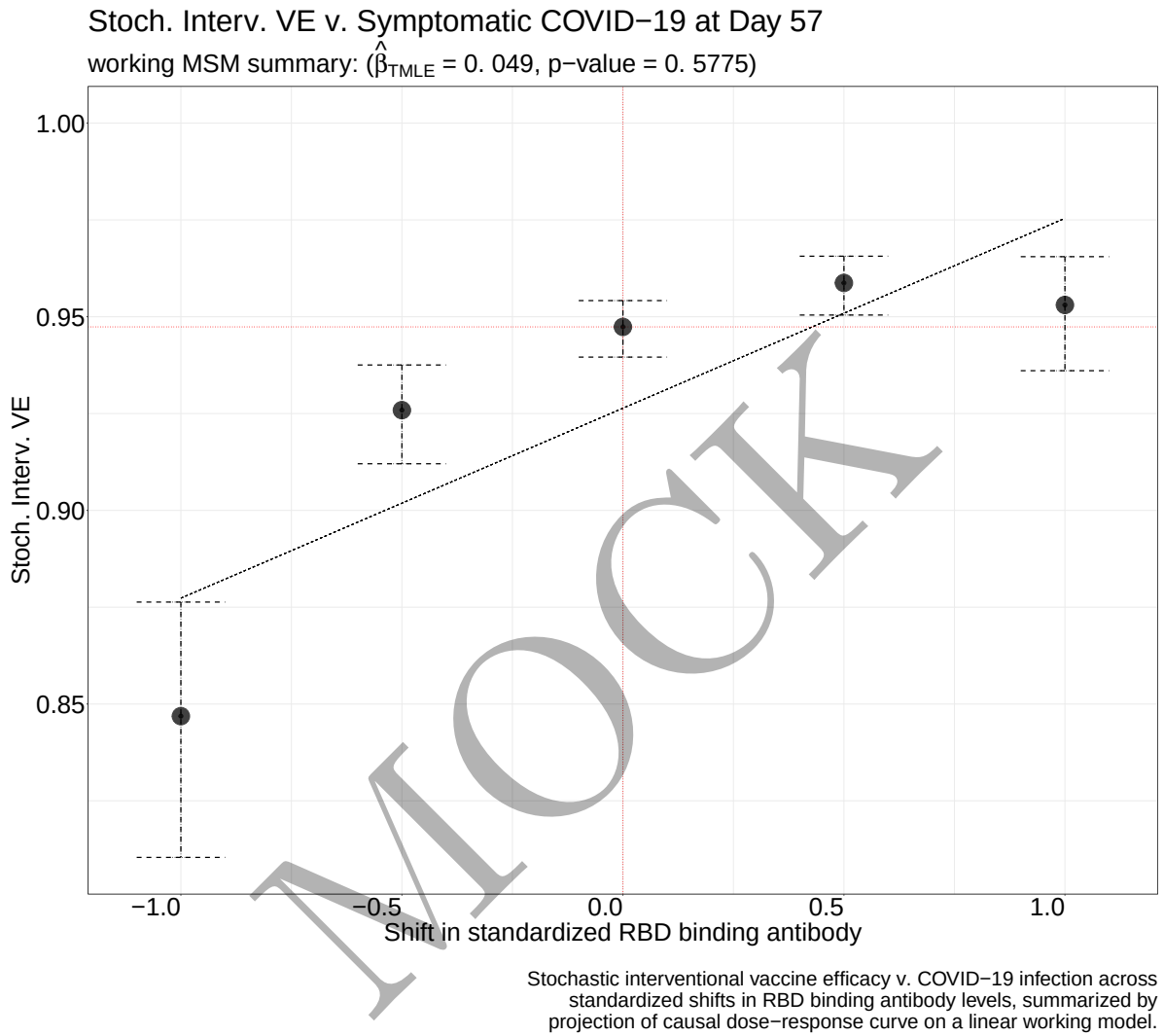

Figure 2.4: Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 57

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

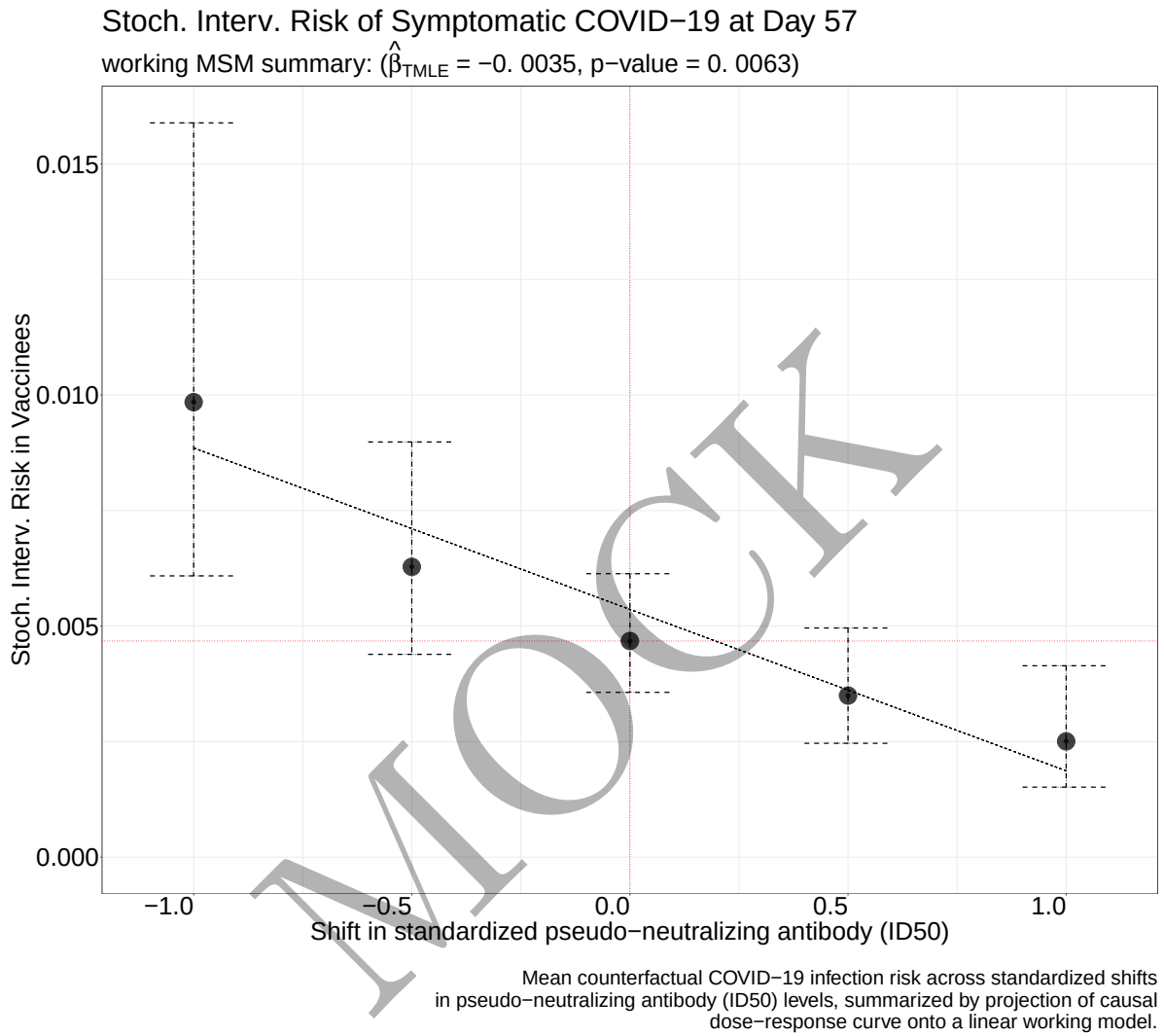

Figure 2.5: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57

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

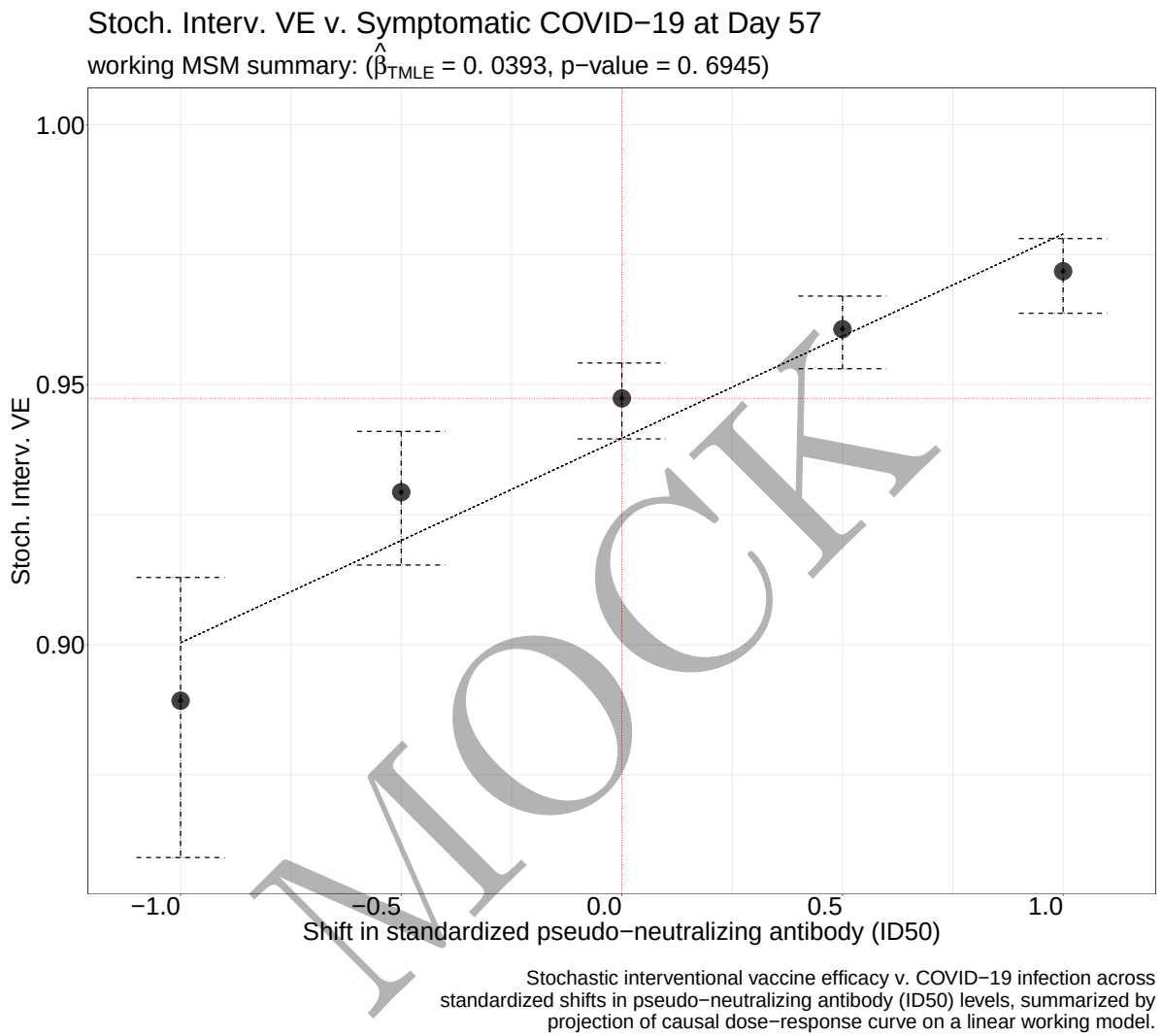

Figure 2.6: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57

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

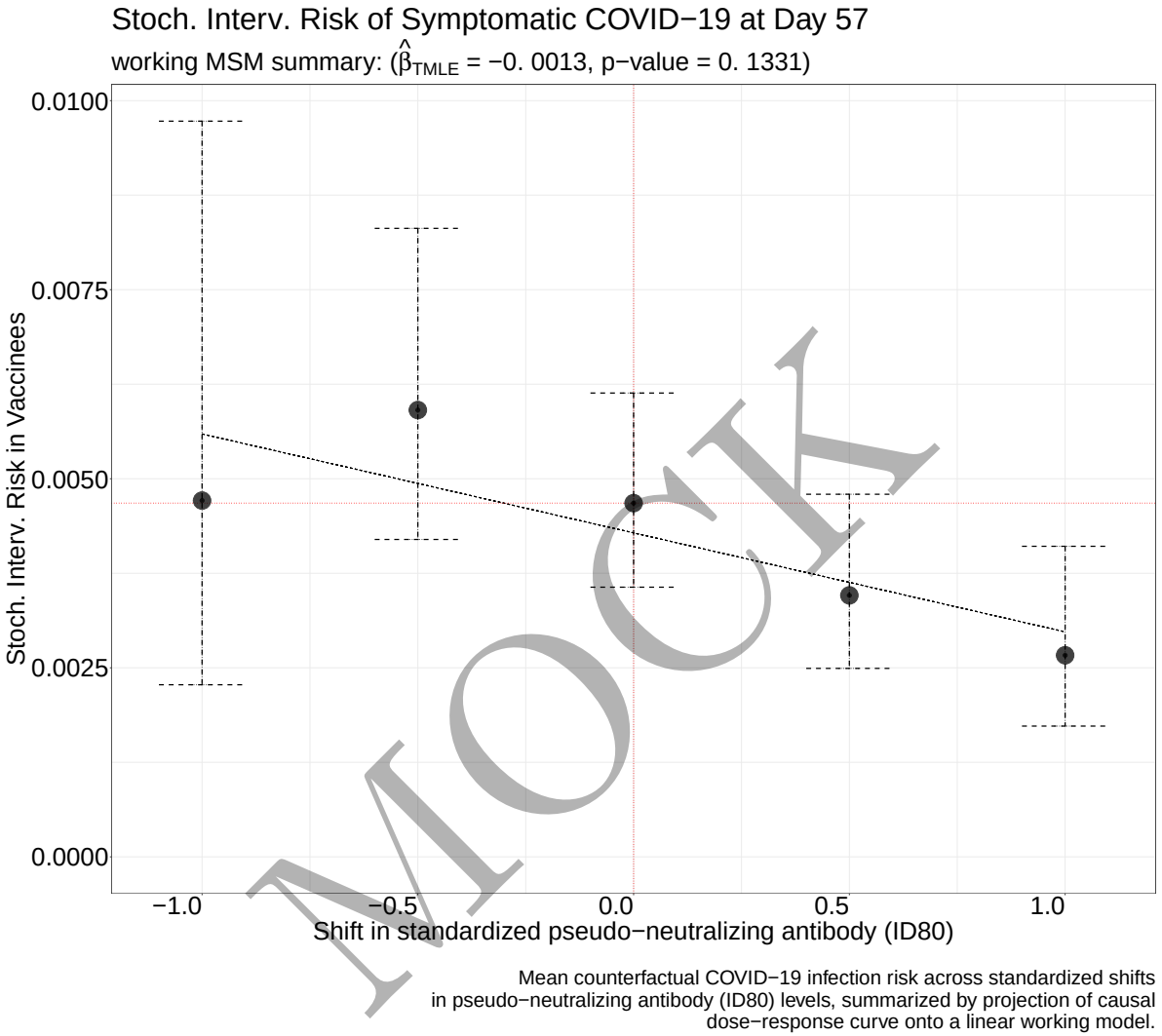

Figure 2.7: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57

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

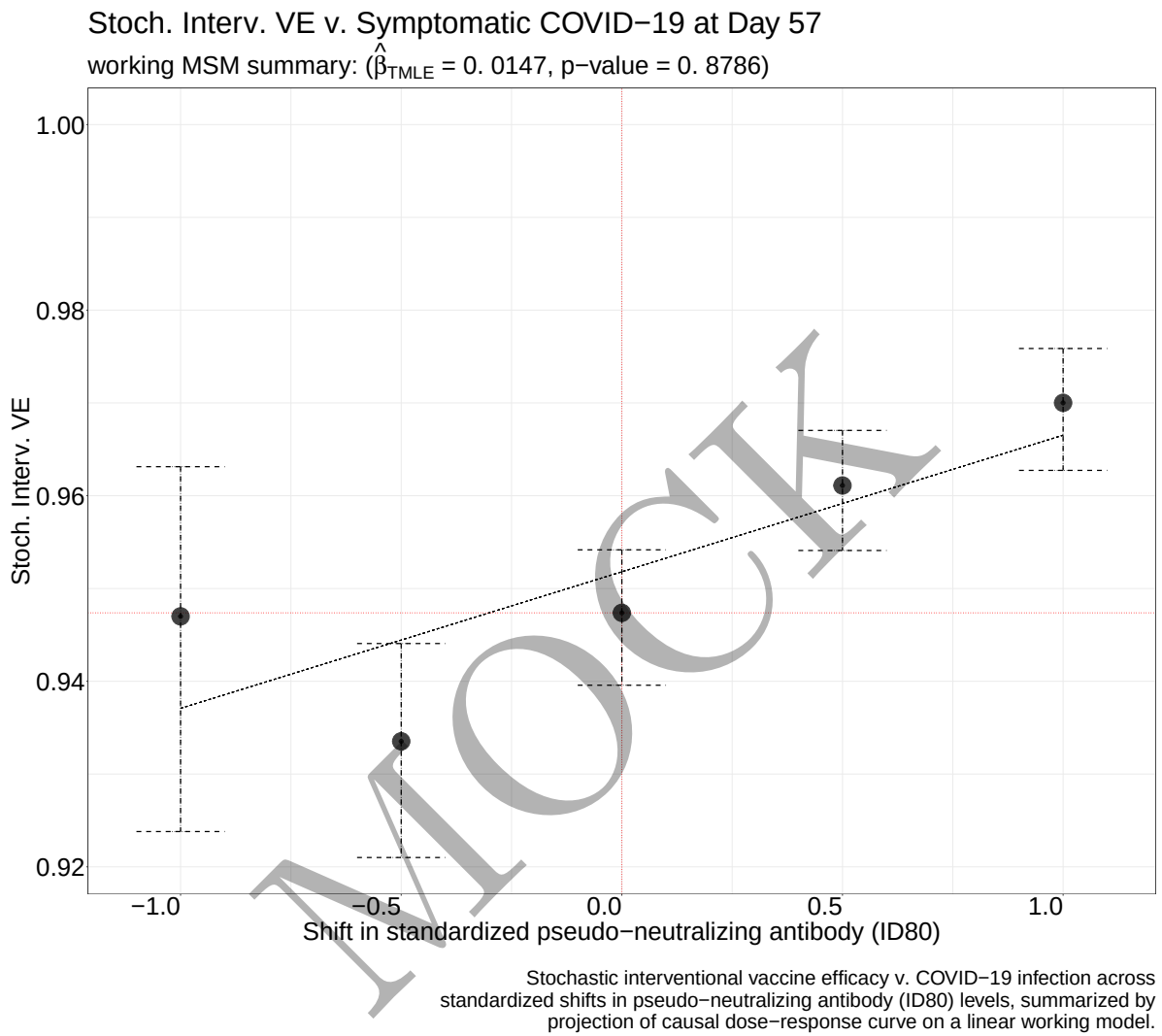

Figure 2.8: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57

2.2 Figures for Stochastic Interventional CoPs for Day 29

2.2.1 Stoch. interv. risk: spike protein binding antibody

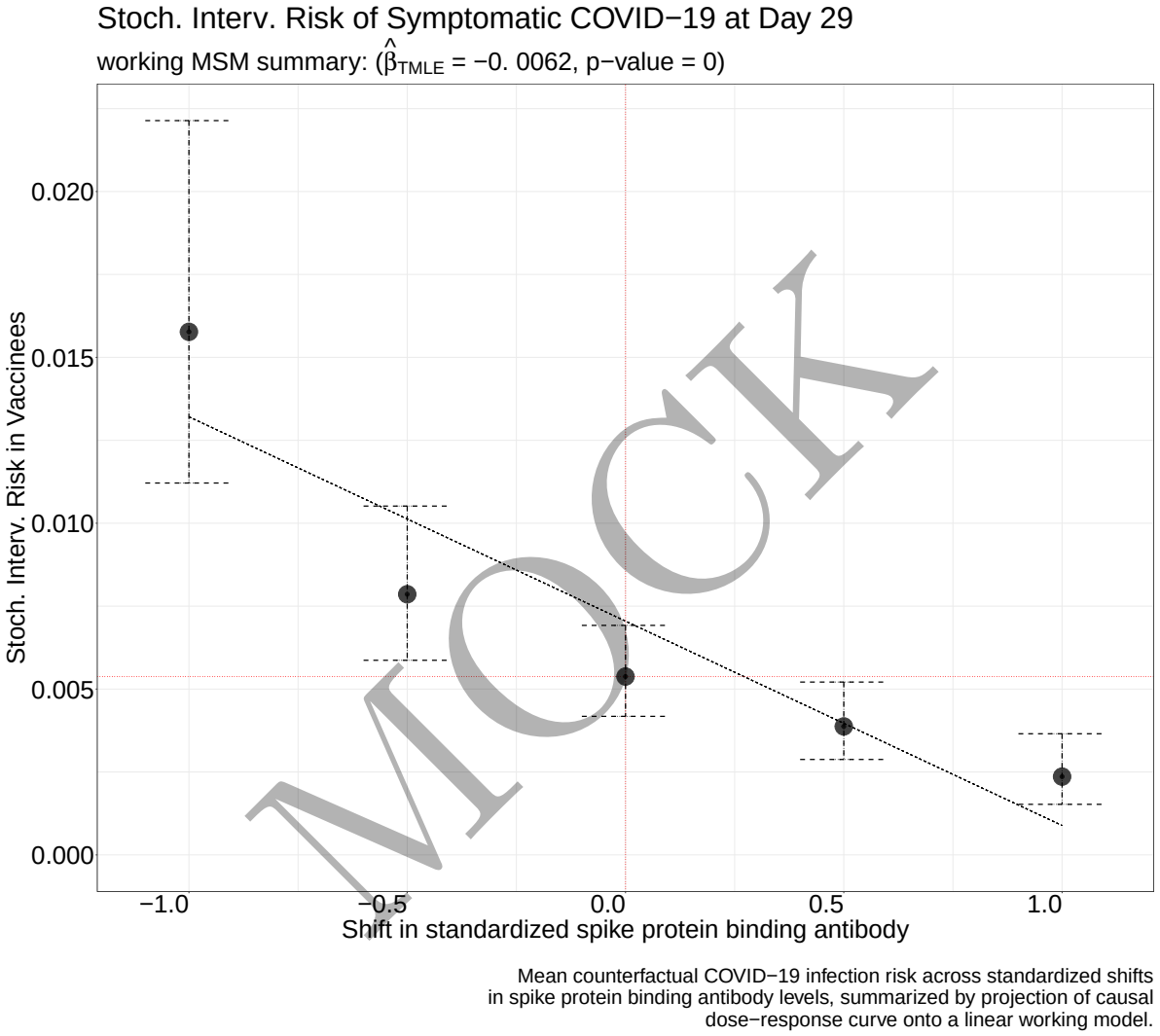

Figure 2.9: Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 29

2.2.2 Stoch. interv. VE: spike protein binding antibody

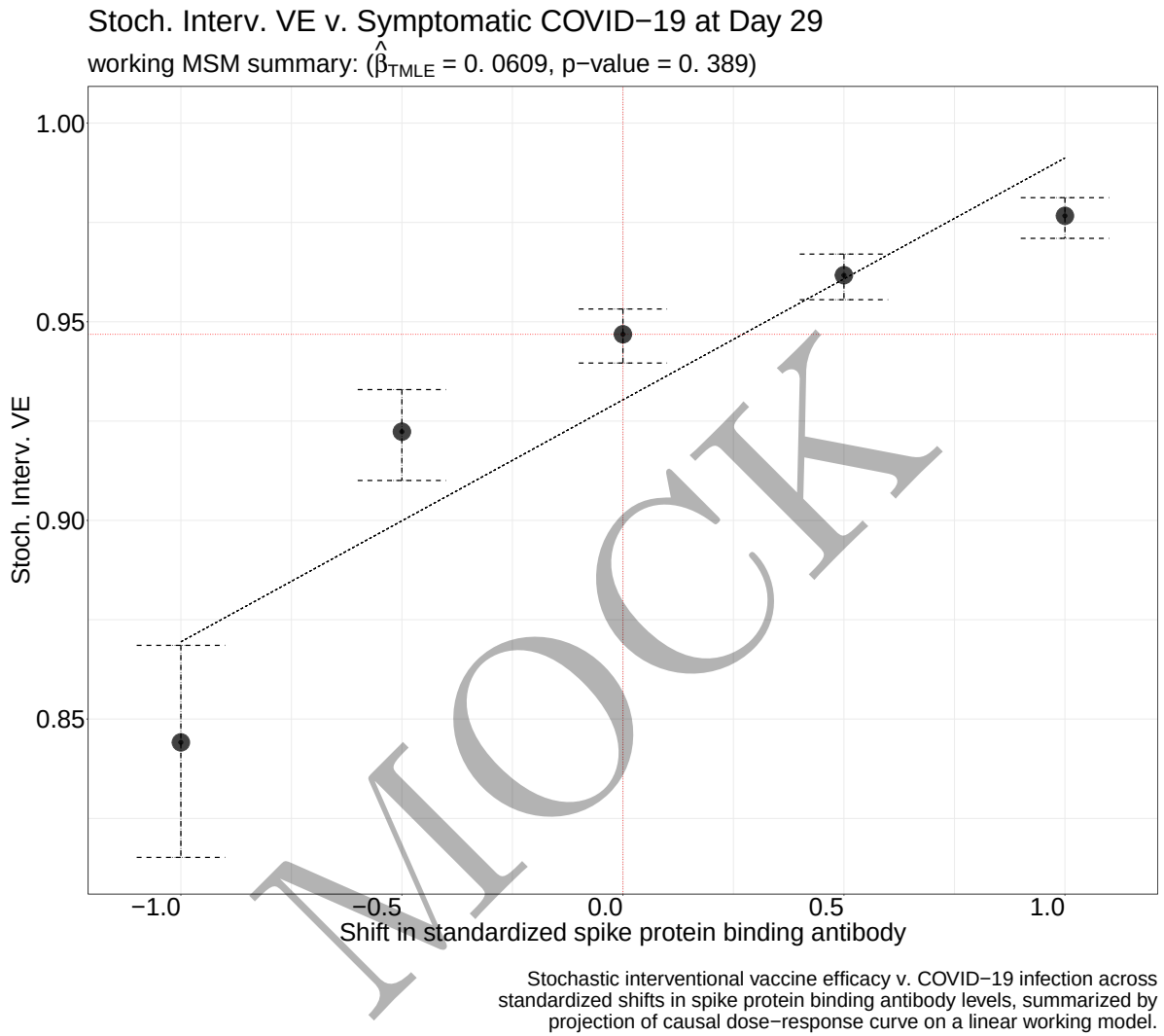

Figure 2.10: Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 29

2.2.3 Stoch. interv. risk: RBD binding antibody

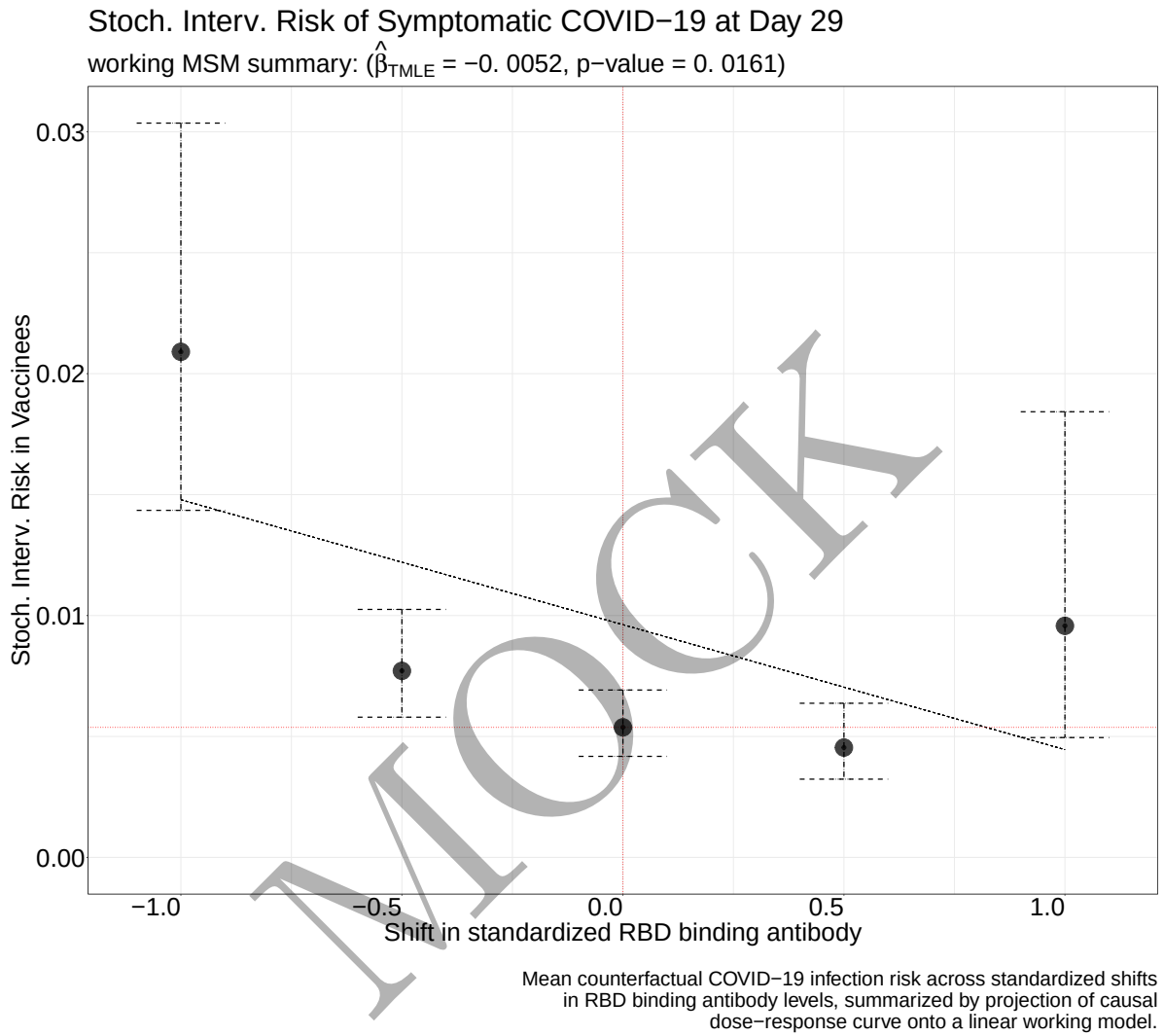

Figure 2.11: Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 29

2.2.4 Stoch. interv. VE: RBD binding antibody

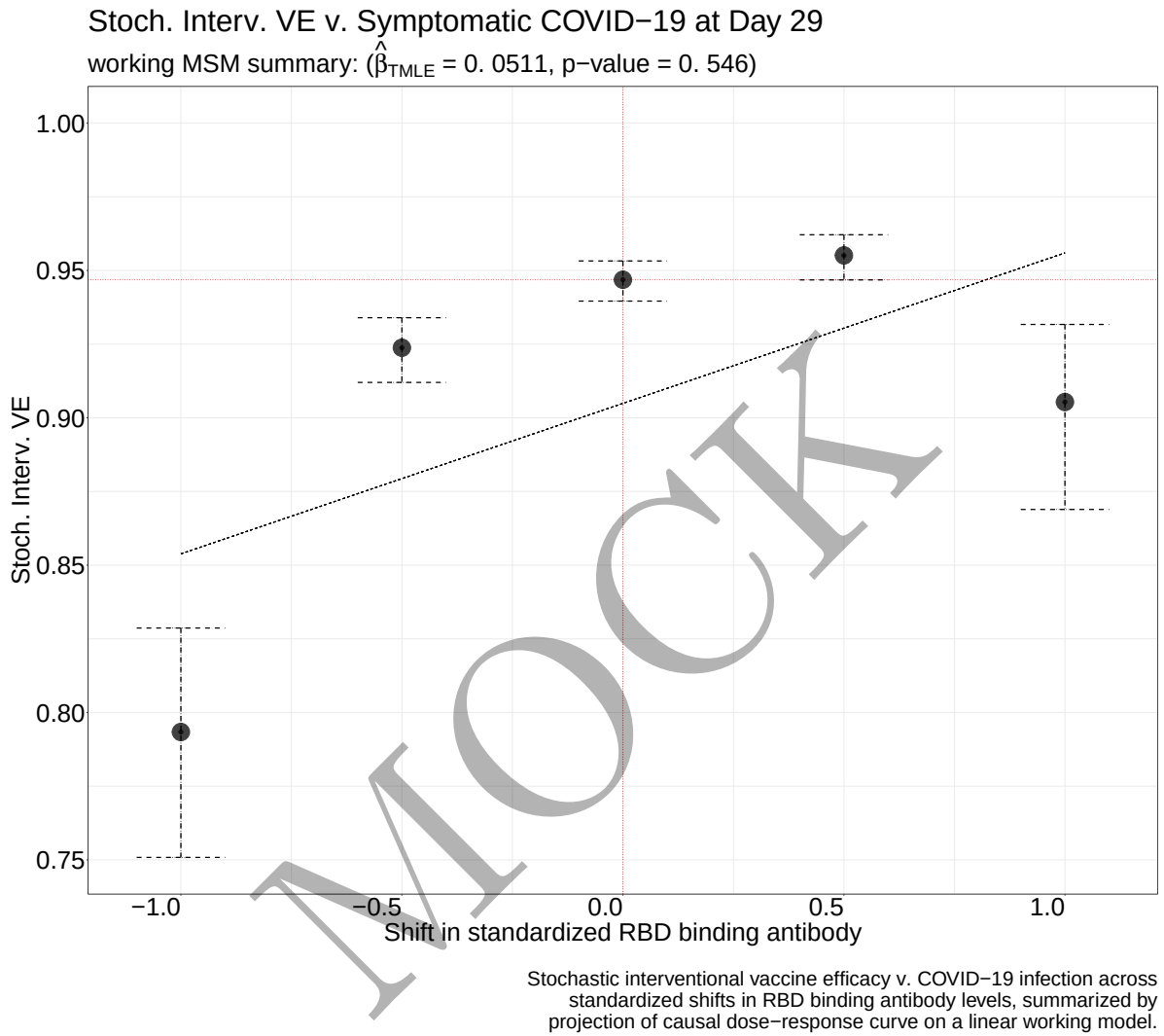

Figure 2.12: Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 29

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

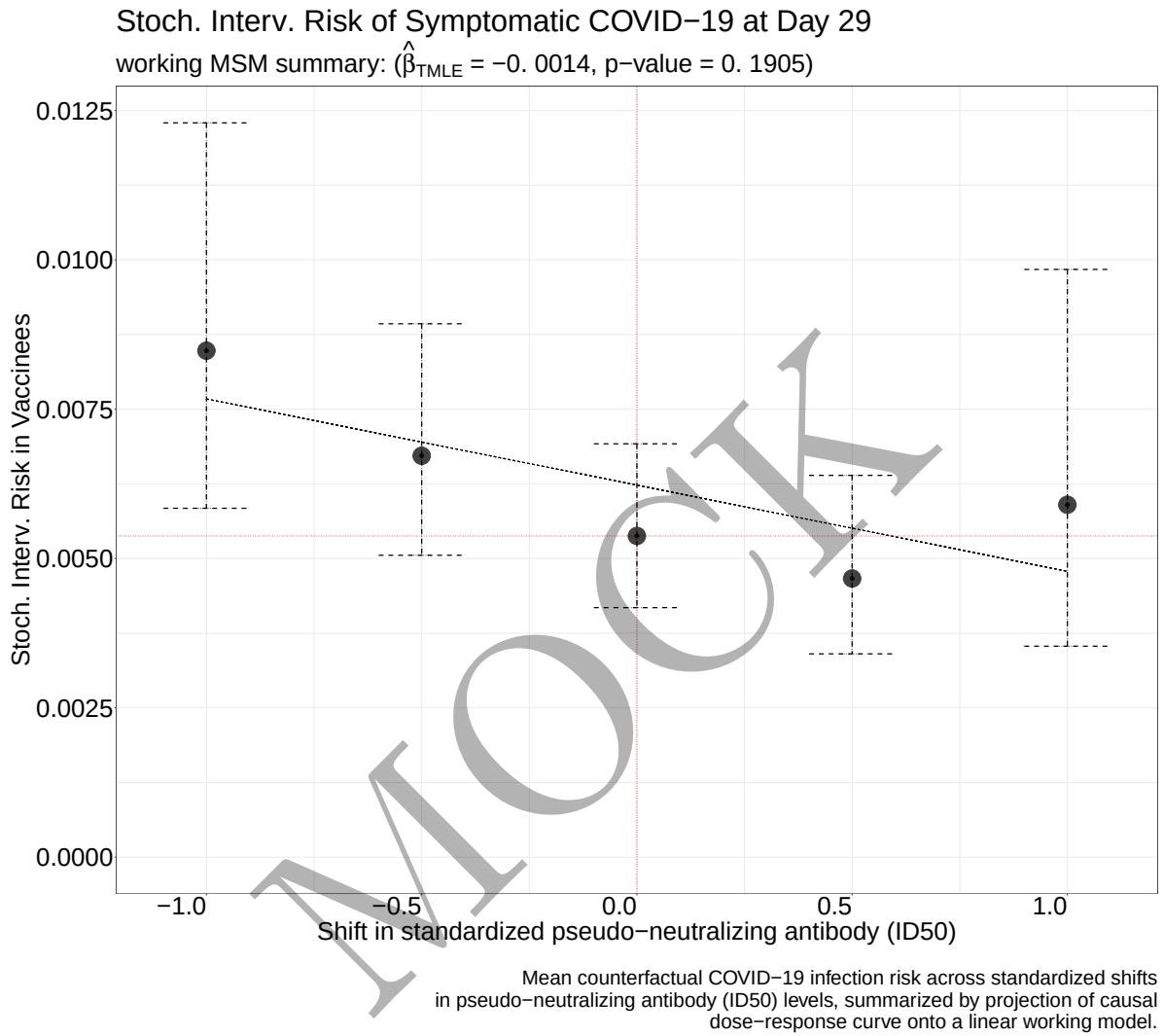

Figure 2.13: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29

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

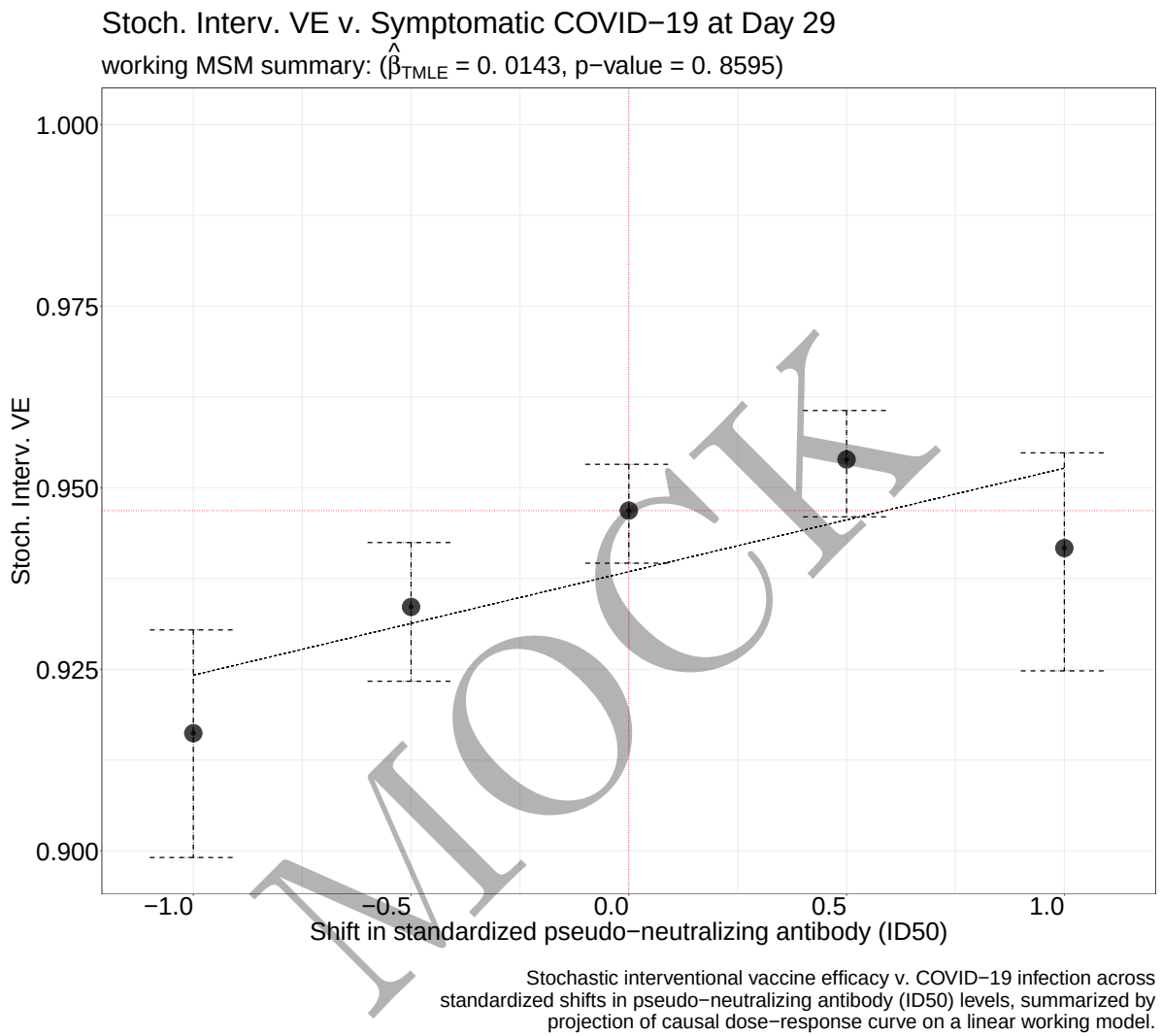

Figure 2.14: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29

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

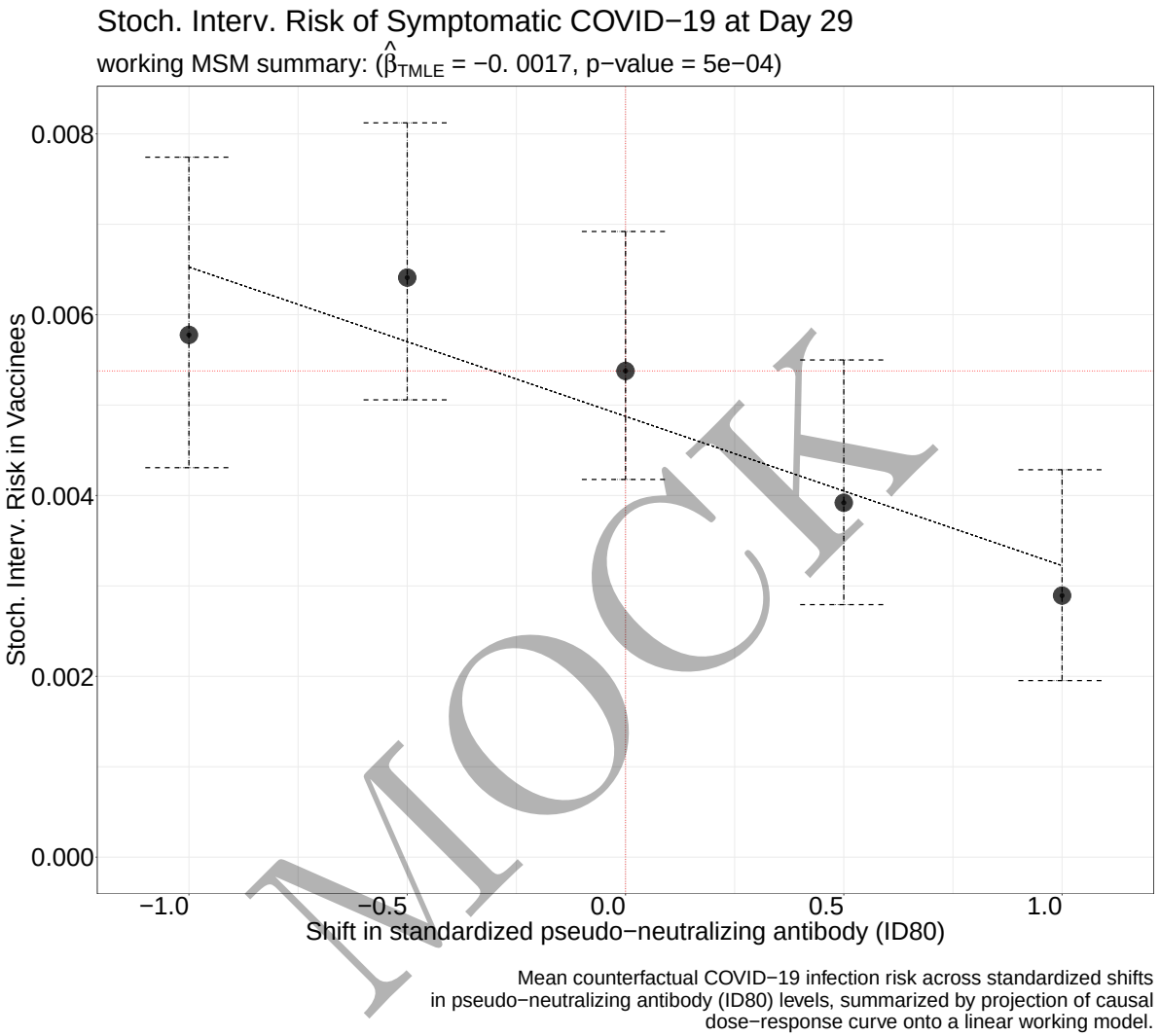

Figure 2.15: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29

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

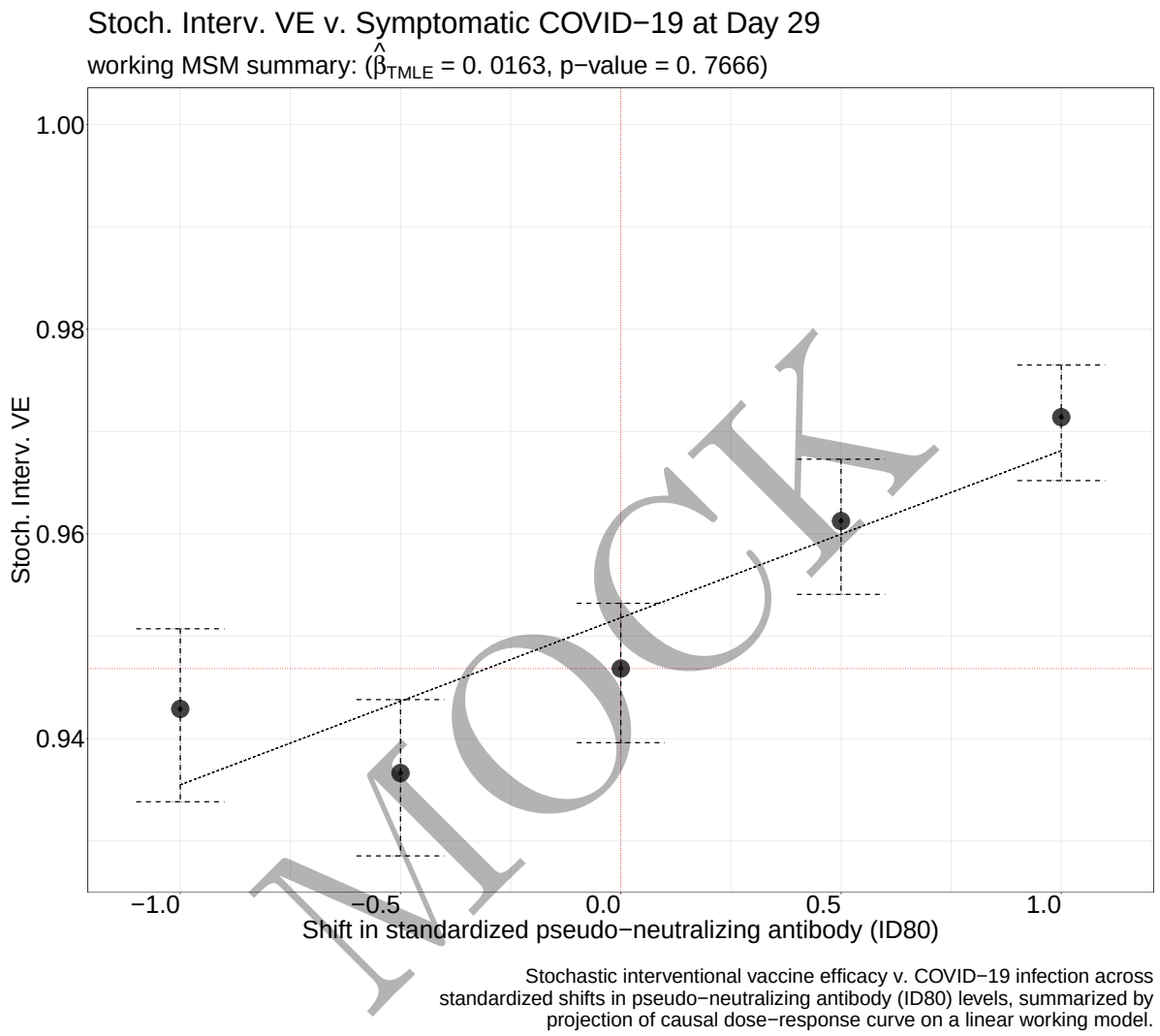

Figure 2.16: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29

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	0.953 (0.649, 0.994)	-0.135 (-7.377, 0.846)	-0.043 (0.639, -0.725)
Day 29	PsV Neutralization 80% Titer	0.933 (0.884, 0.961)	0.210 (-0.283, 0.513)	0.080 (0.246, -0.085)

[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 (-0.084, 0.438)	0.084 (0.196, -0.028)
Day 57	Binding Antibody to RBD	0.949 (0.907, 0.972)	-0.038 (-0.738, 0.380)	-0.013 (0.162, -0.188)
Day 57	PsV Neutralization 50% Titer	0.938 (0.907, 0.959)	0.146 (-0.175, 0.379)	0.053 (0.162, -0.055)
Day 57	PsV Neutralization 80% Titer	0.927 (0.891, 0.951)	0.279 (-0.014, 0.487)	0.111 (0.225, -0.003)
Day 29	Binding Antibody to Spike	0.940 (0.912, 0.960)	0.107 (-0.193, 0.332)	0.039 (0.138, -0.060)
Day 29	Binding Antibody to RBD	0.946 (0.915, 0.966)	0.008 (-0.418, 0.306)	0.003 (0.124, -0.119)
Day 29	PsV Neutralization 50% Titer	0.941 (0.912, 0.960)	0.101 (-0.249, 0.352)	0.036 (0.148, -0.075)
Day 29	PsV Neutralization 80% Titer	0.935 (0.900, 0.958)	0.182 (-0.193, 0.440)	0.069 (0.197, -0.059)

Chapter 4

Appendix

- This report was built from the `CoVPN/correlates_reporting` repository with commit hash a57fe67fa9b57a58b6fb3665cdd6b4e2183a934b. A diff of the changes introduced by that commit may be viewed at https://github.com/CoVPN/correlates_reporting/commit/a57fe67fa9b57a58b6fb3665cdd6b4e2183a934b
- 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": 28964ce20cfcd70a621aff9df412c42b11