# COVID-19 Correlates of Protection Analysis Report

MockCOVE Study

USG COVID-19 Response Biostatistics Team

June 30, 2021

# Contents

# List of Tables

# List of Figures

# 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.

# 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

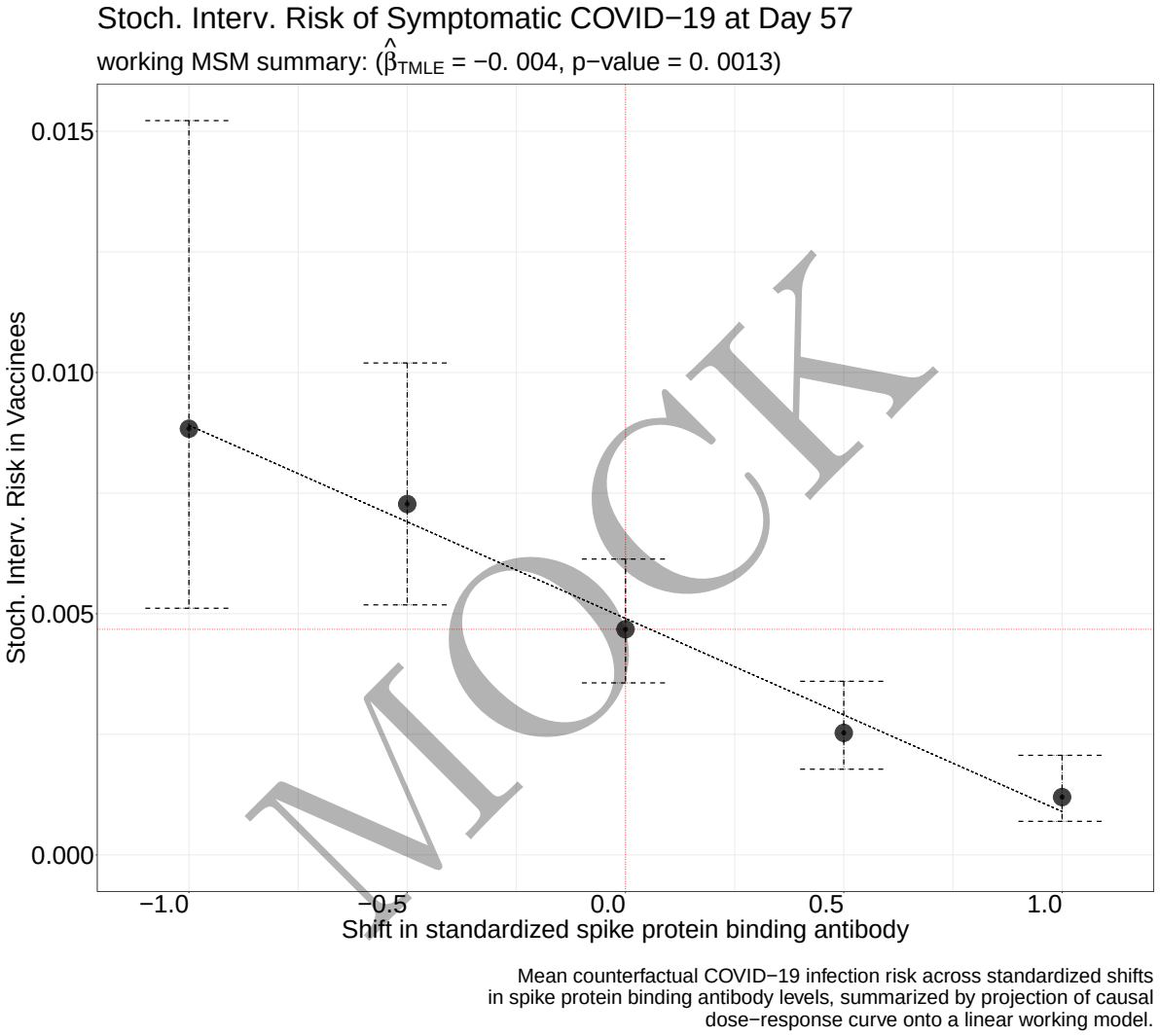


Figure 2.1: Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 57

### 2.1.2 Stoch. interv. VE: spike protein binding antibody

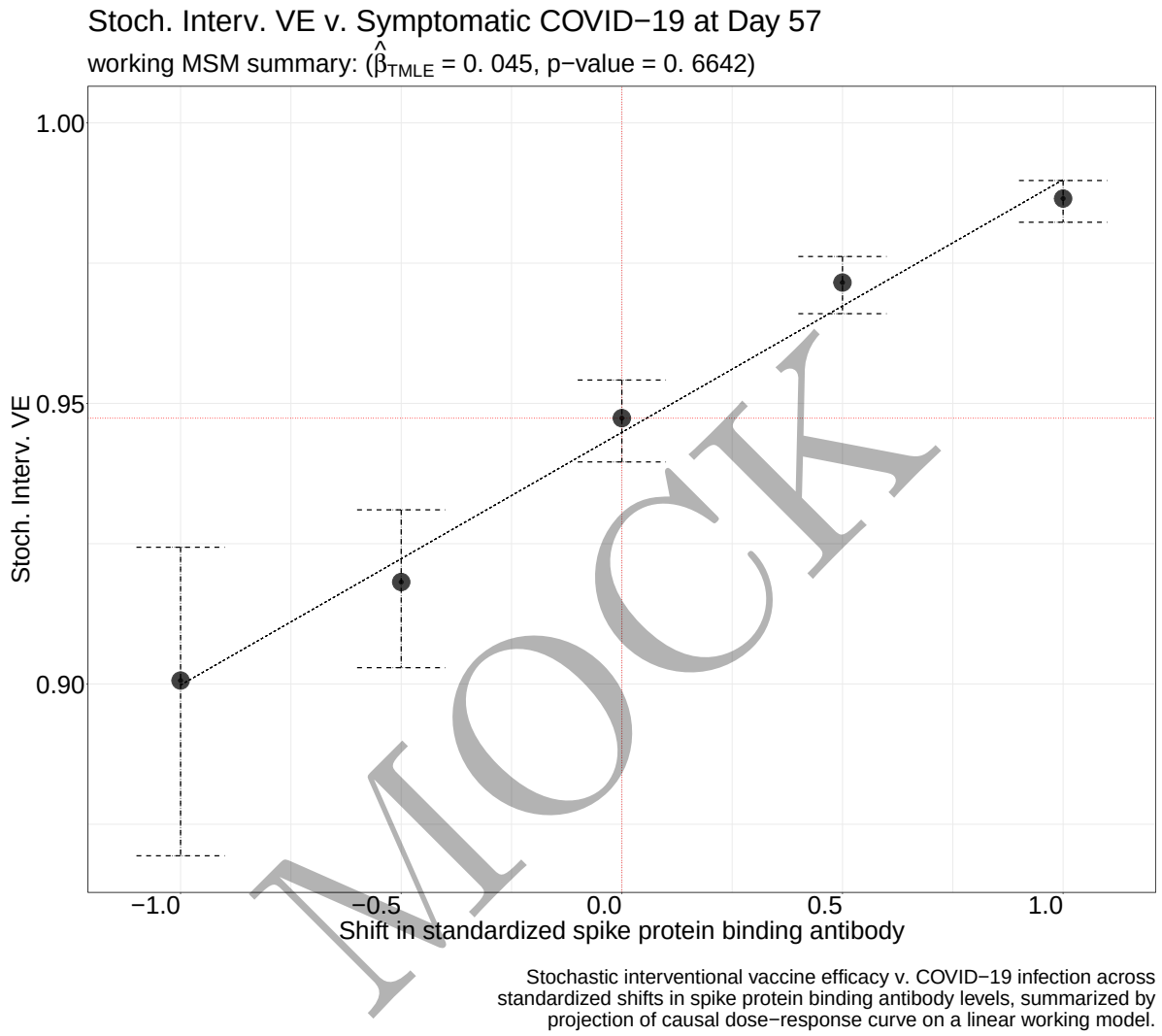




Figure 2.2: Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 57

### 2.1.3 Stoch. interv. risk: RBD binding antibody

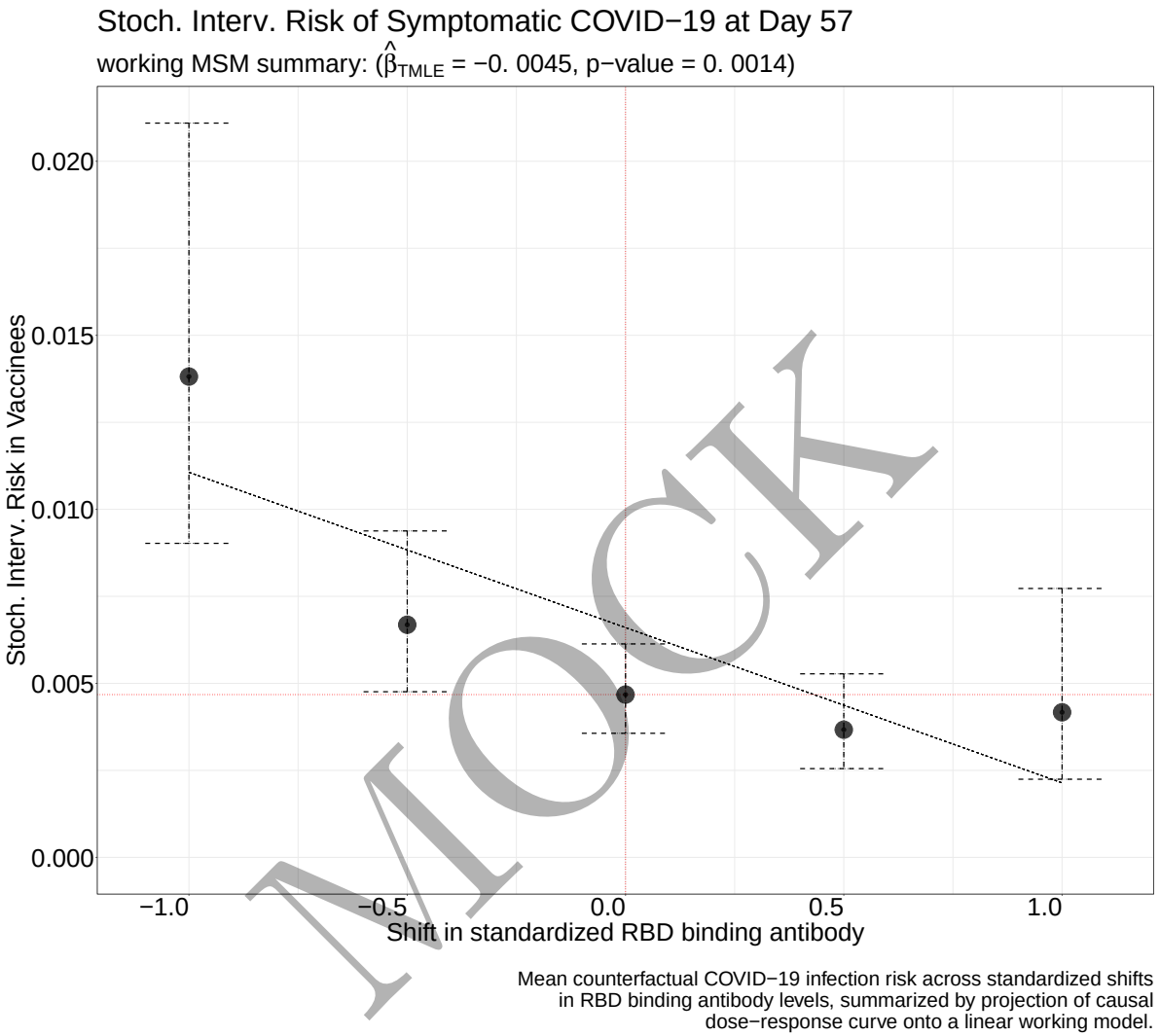




Figure 2.3: Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 57

### 2.1.4 Stoch. interv. VE: RBD binding antibody

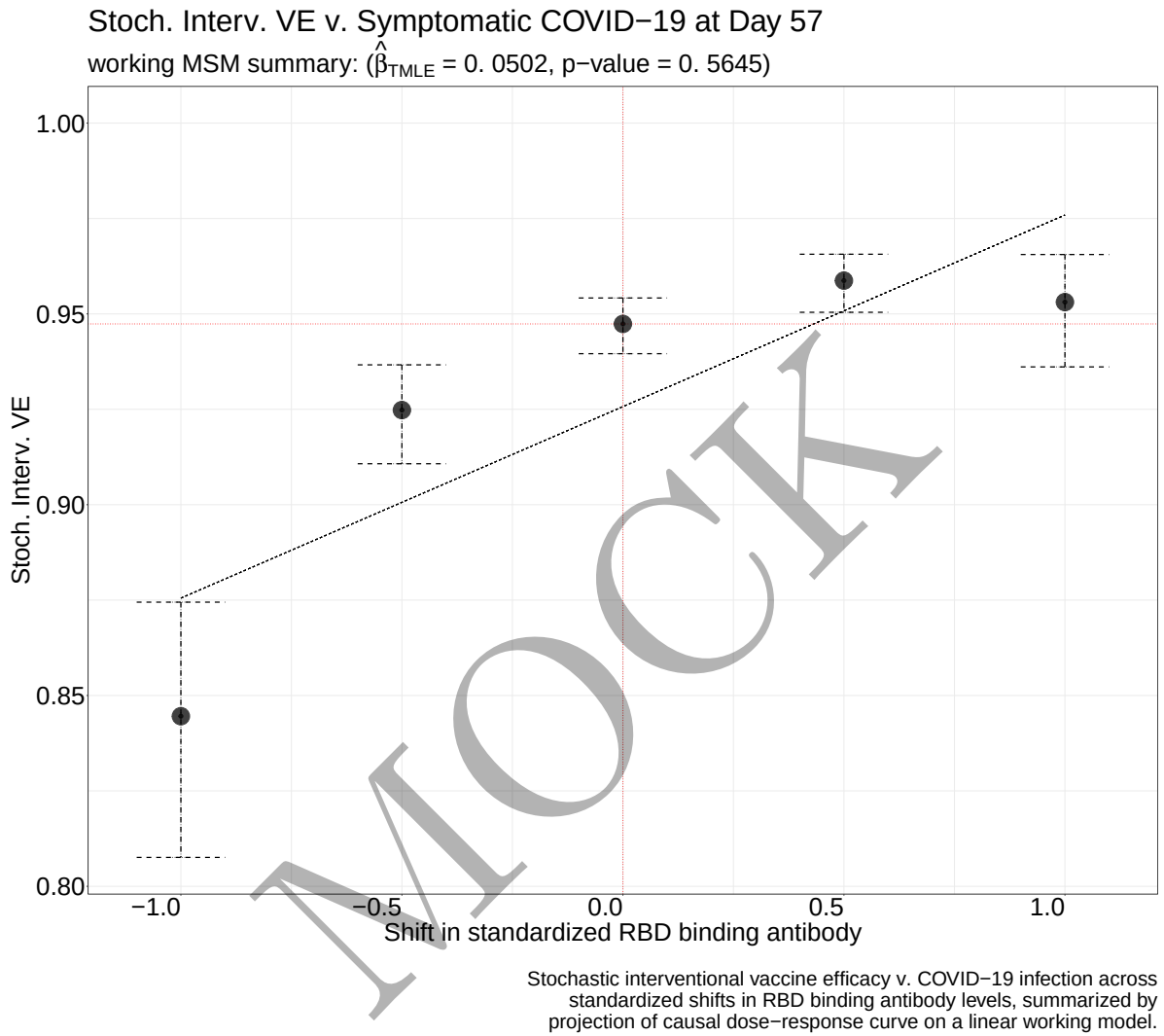



Figure 2.4: Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 57

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

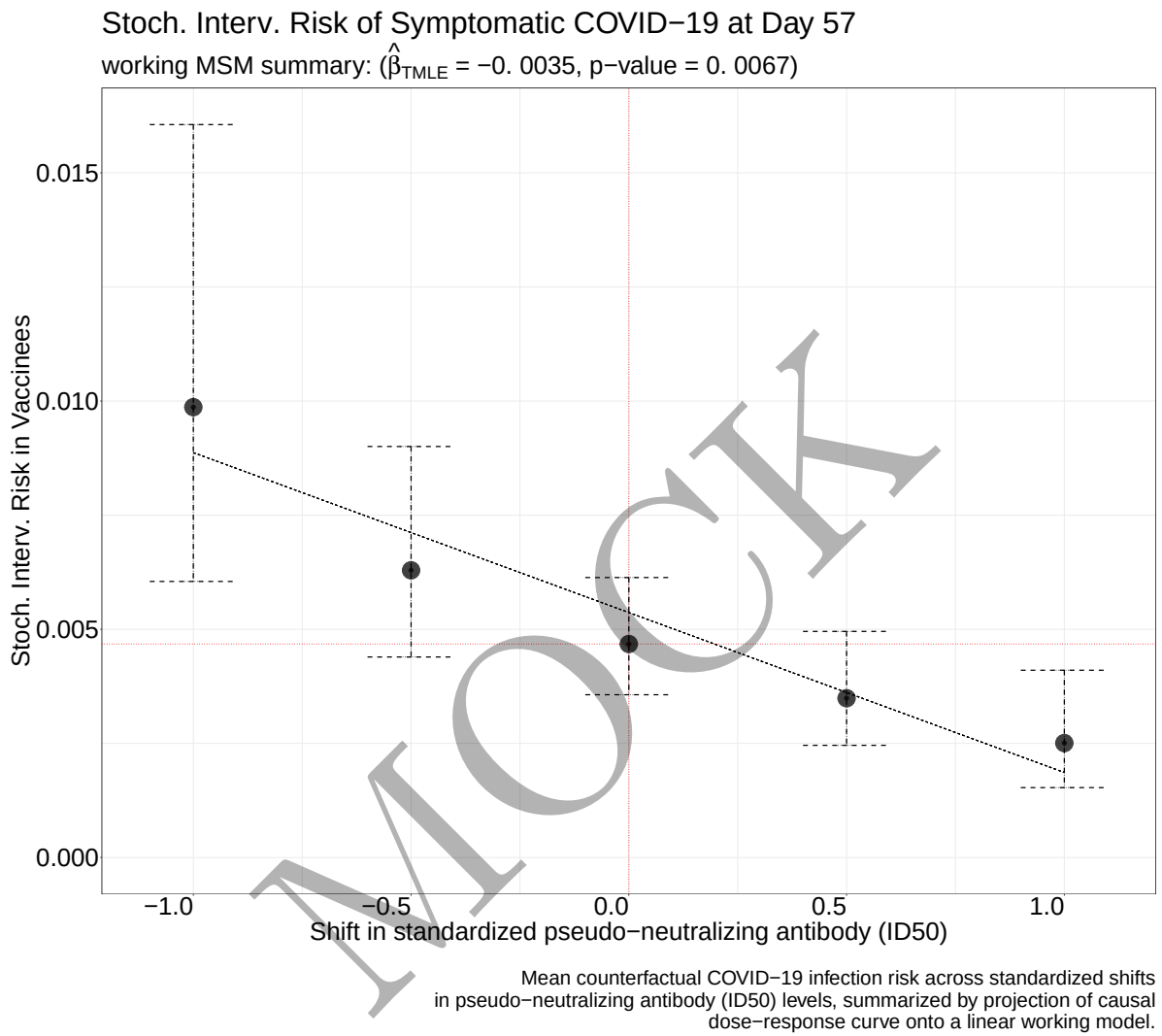


Figure 2.5: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57

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

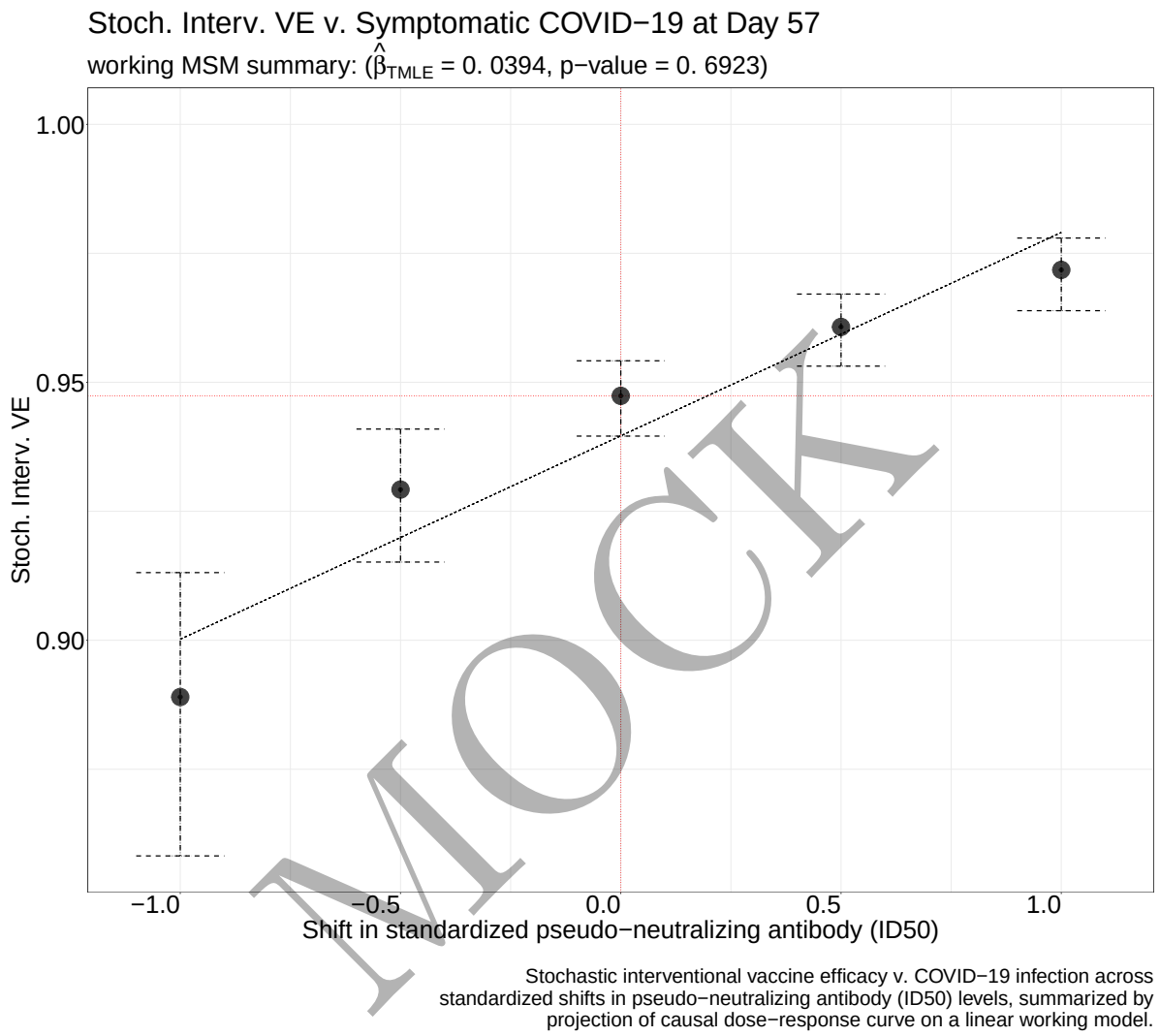


Figure 2.6: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57

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

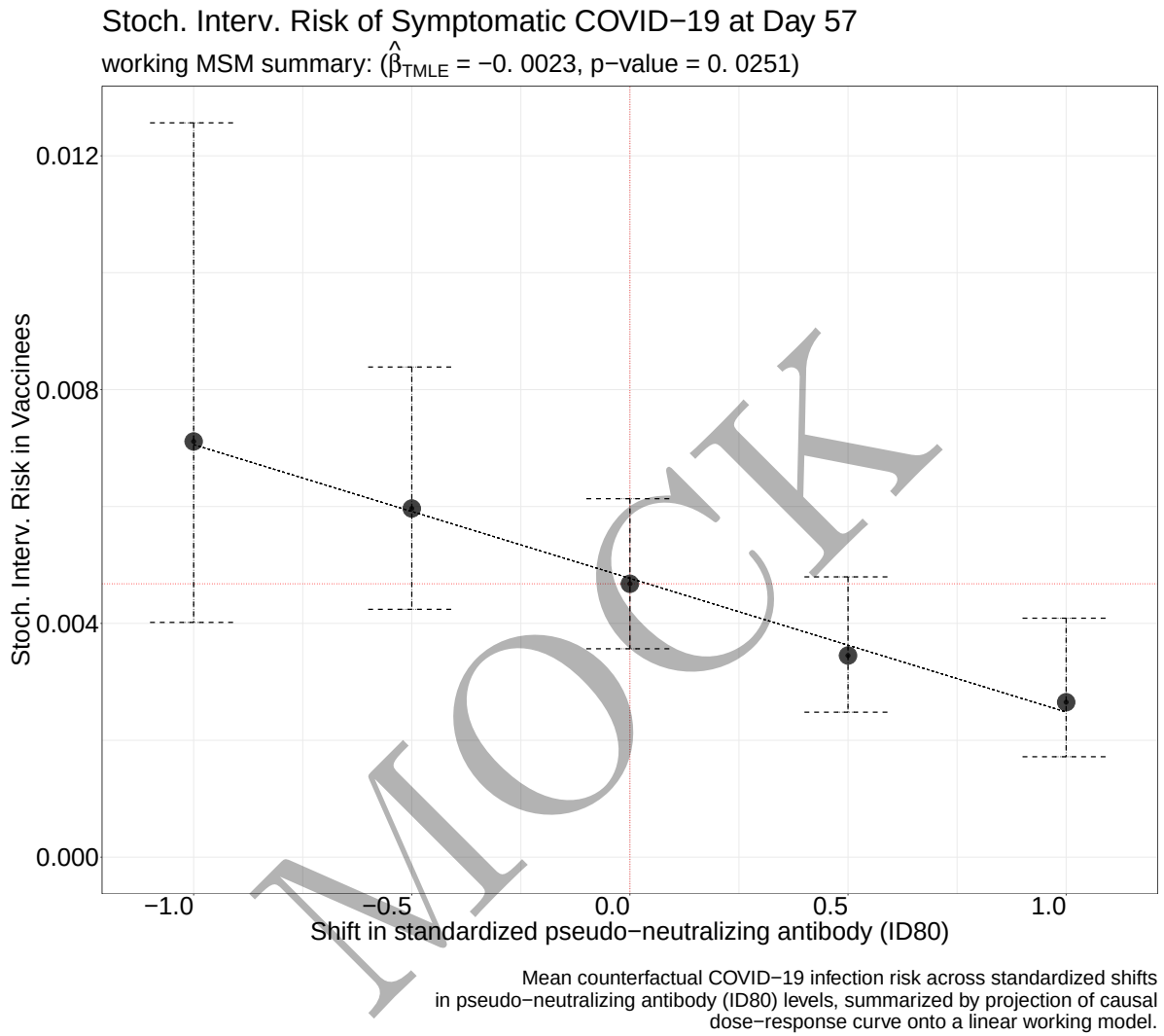




Figure 2.7: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57

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

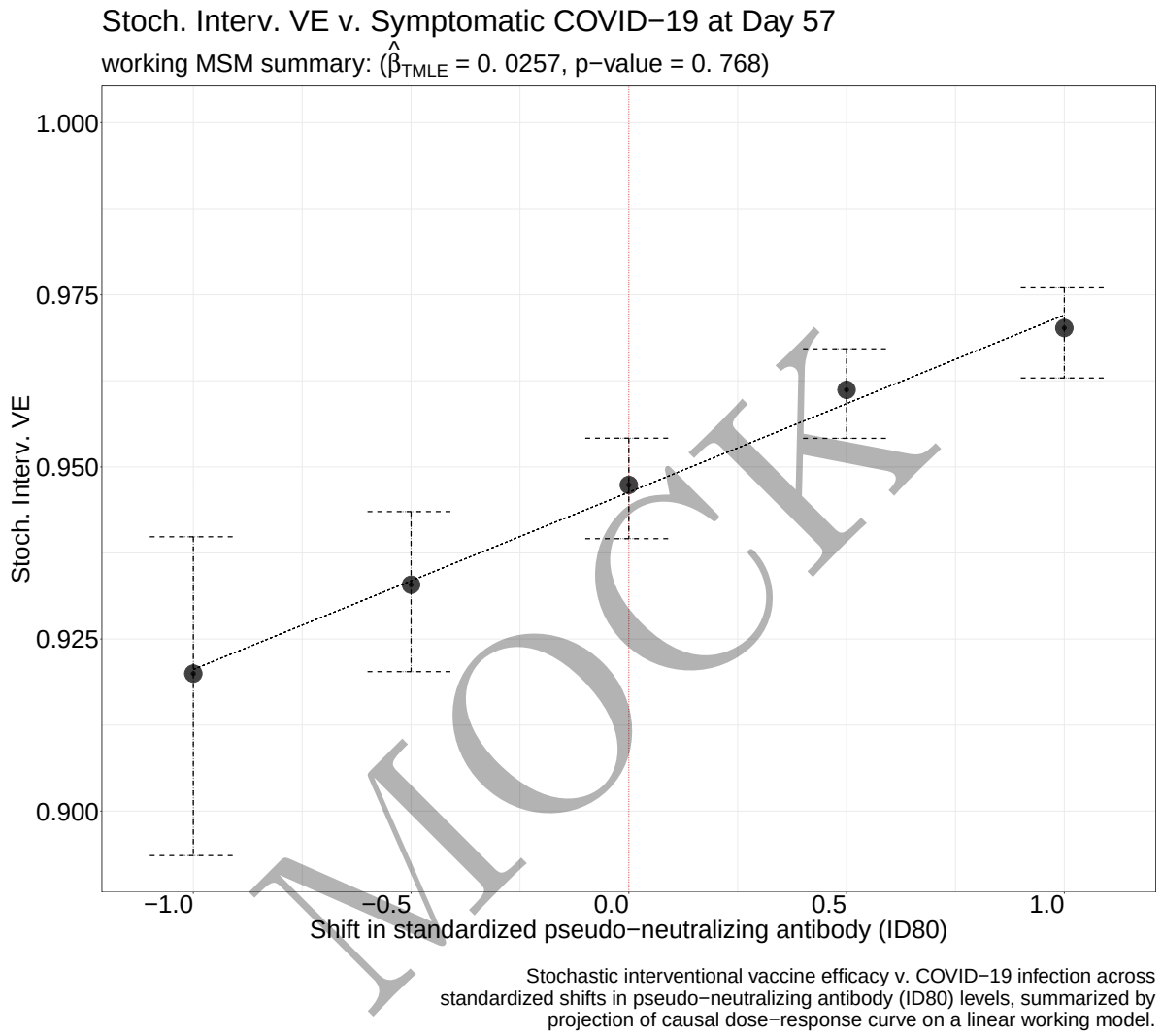




Figure 2.8: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57

## 2.2 Figures for Stochastic Interventional CoPs for Day 29

### 2.2.1 Stoch. interv. risk: spike protein binding antibody

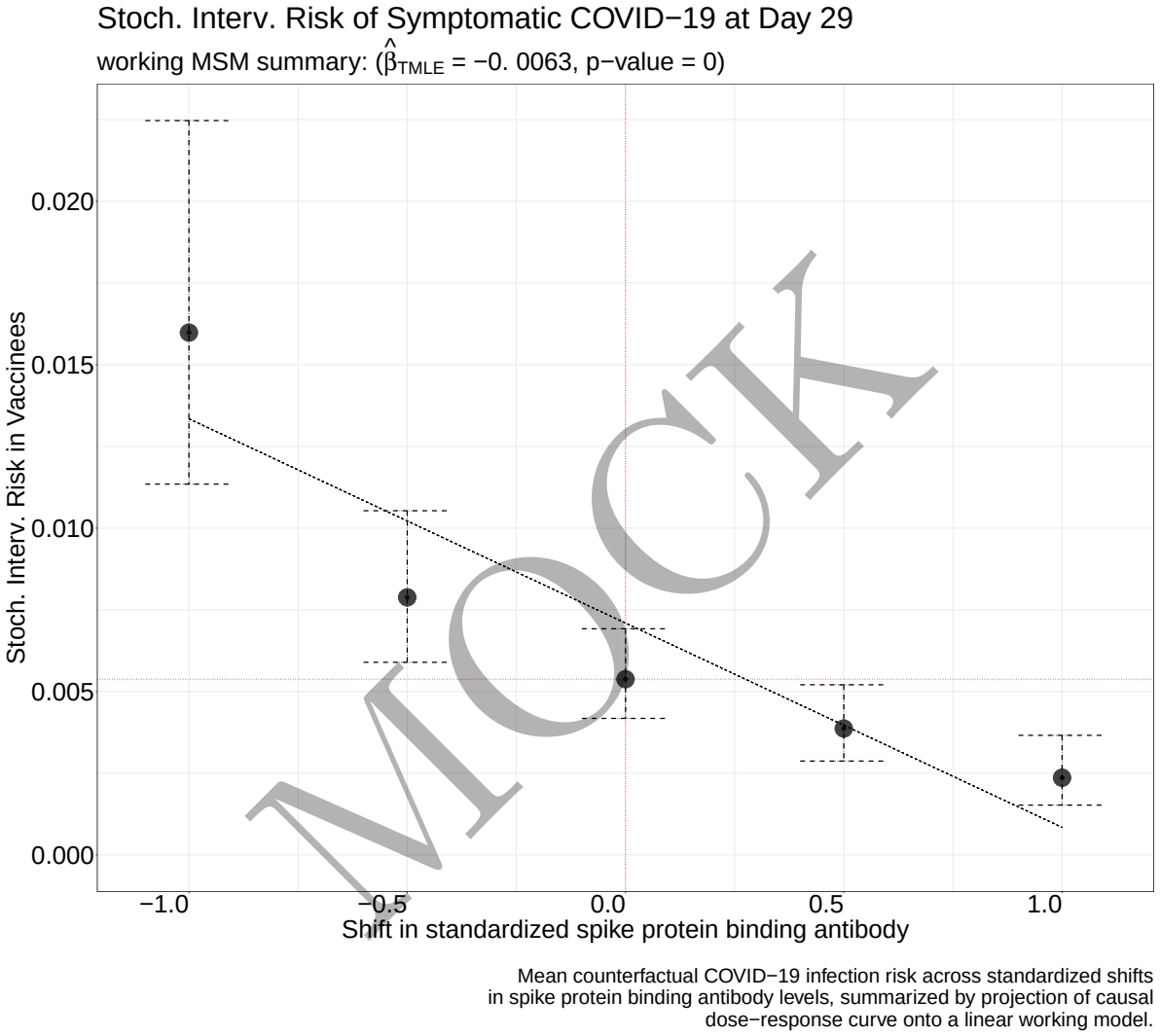


Figure 2.9: Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 29

### 2.2.2 Stoch. interv. VE: spike protein binding antibody

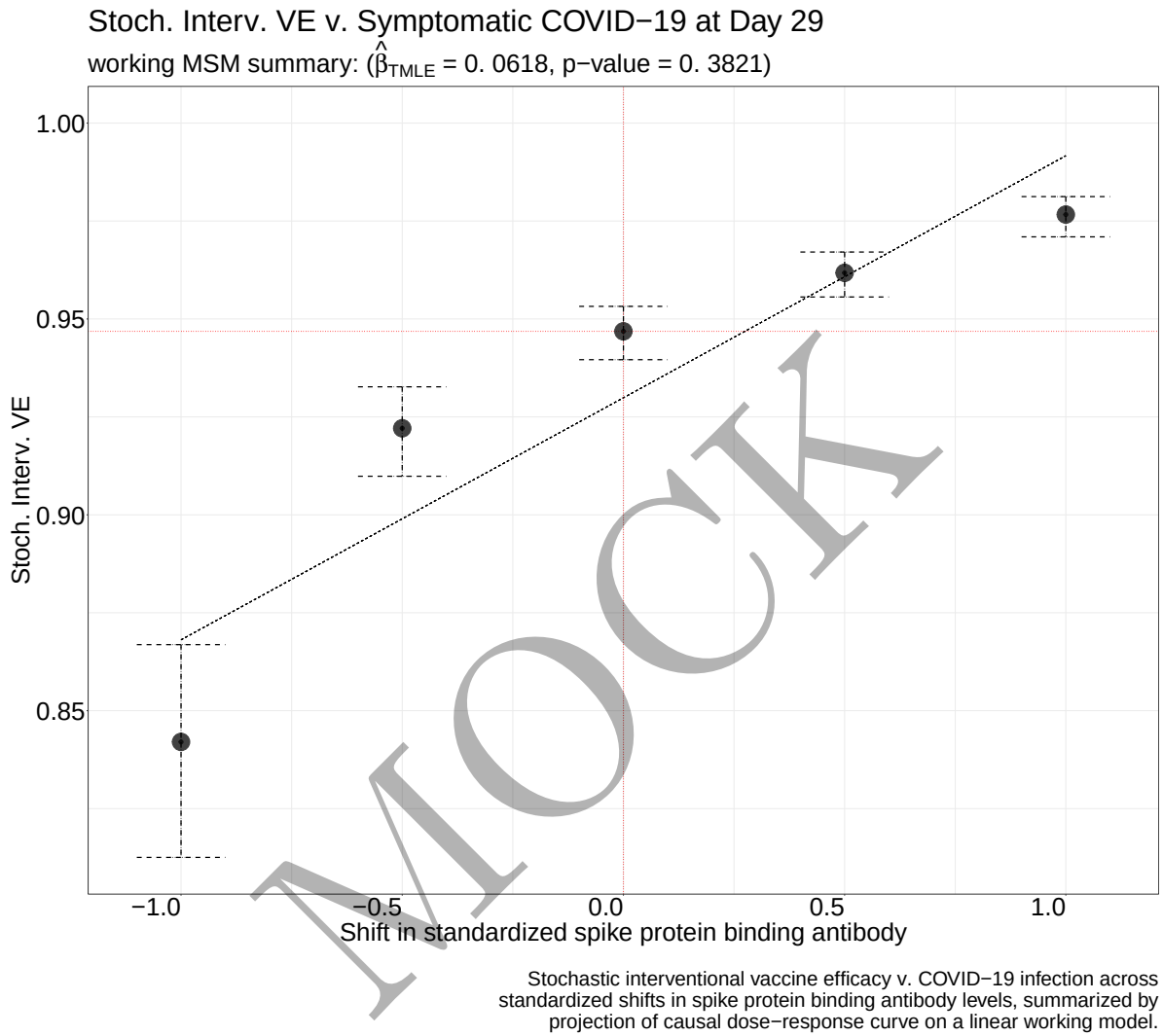



Figure 2.10: Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 29

### 2.2.3 Stoch. interv. risk: RBD binding antibody

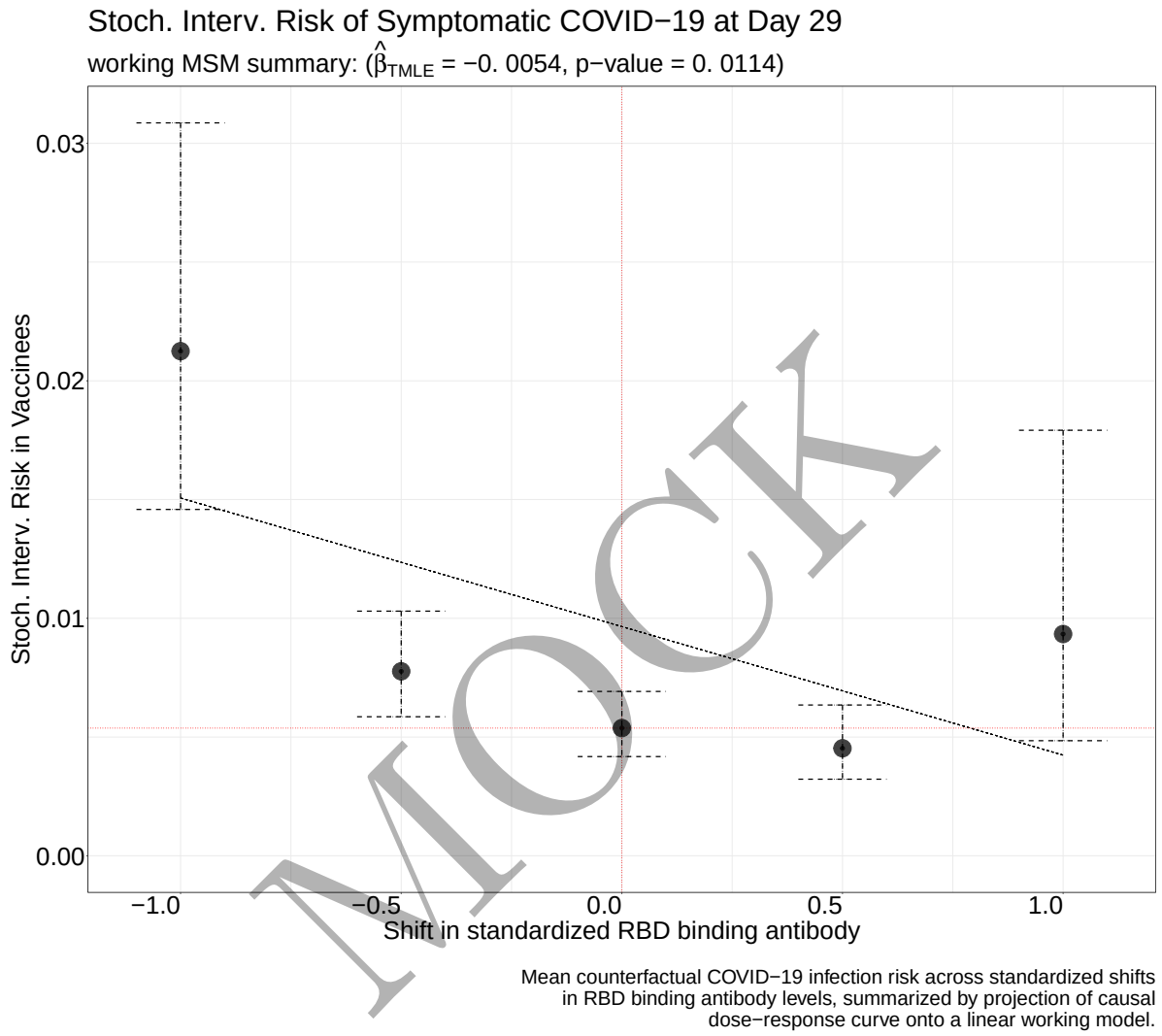




Figure 2.11: Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 29

### 2.2.4 Stoch. interv. VE: RBD binding antibody

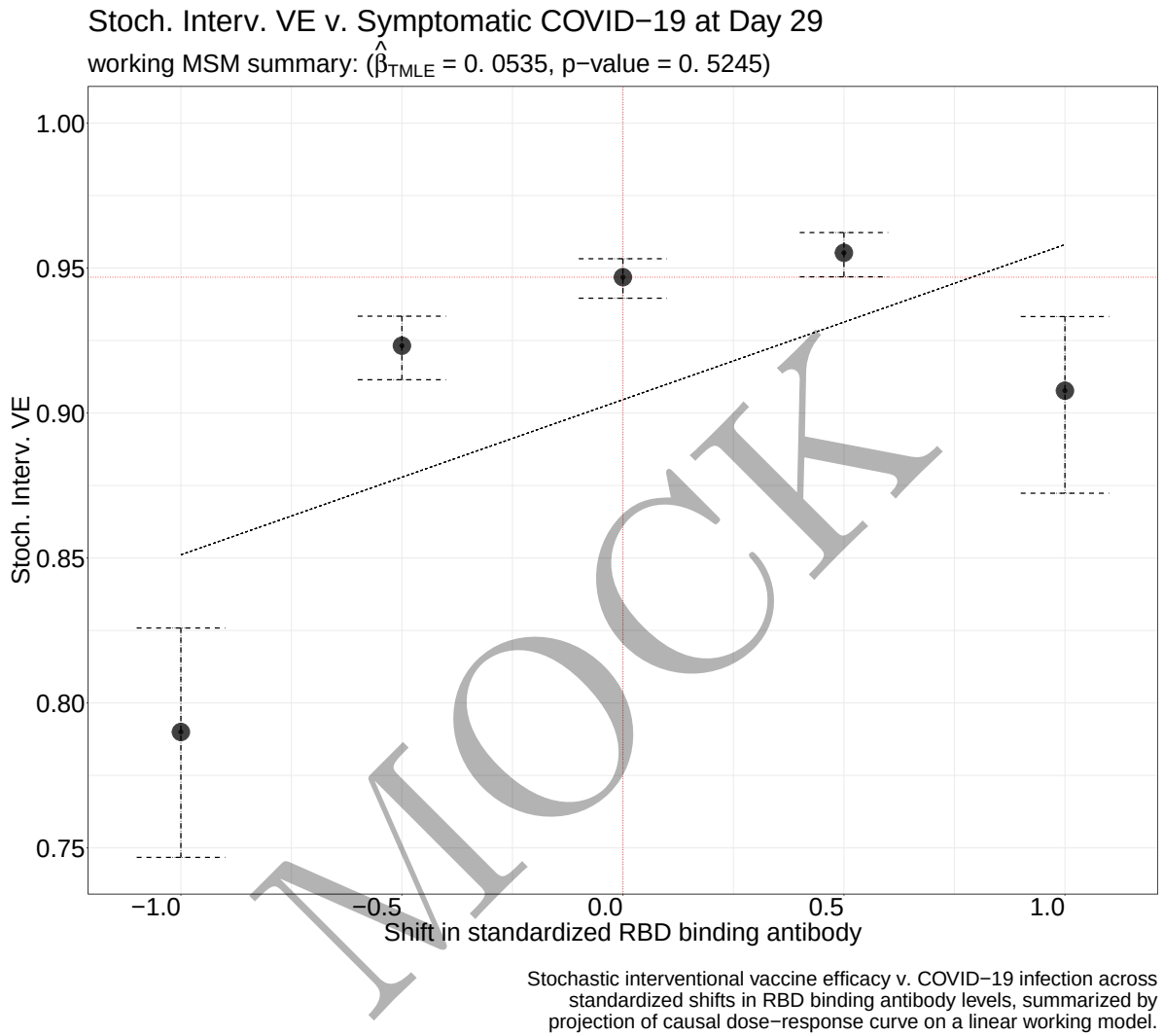


Figure 2.12: Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 29

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

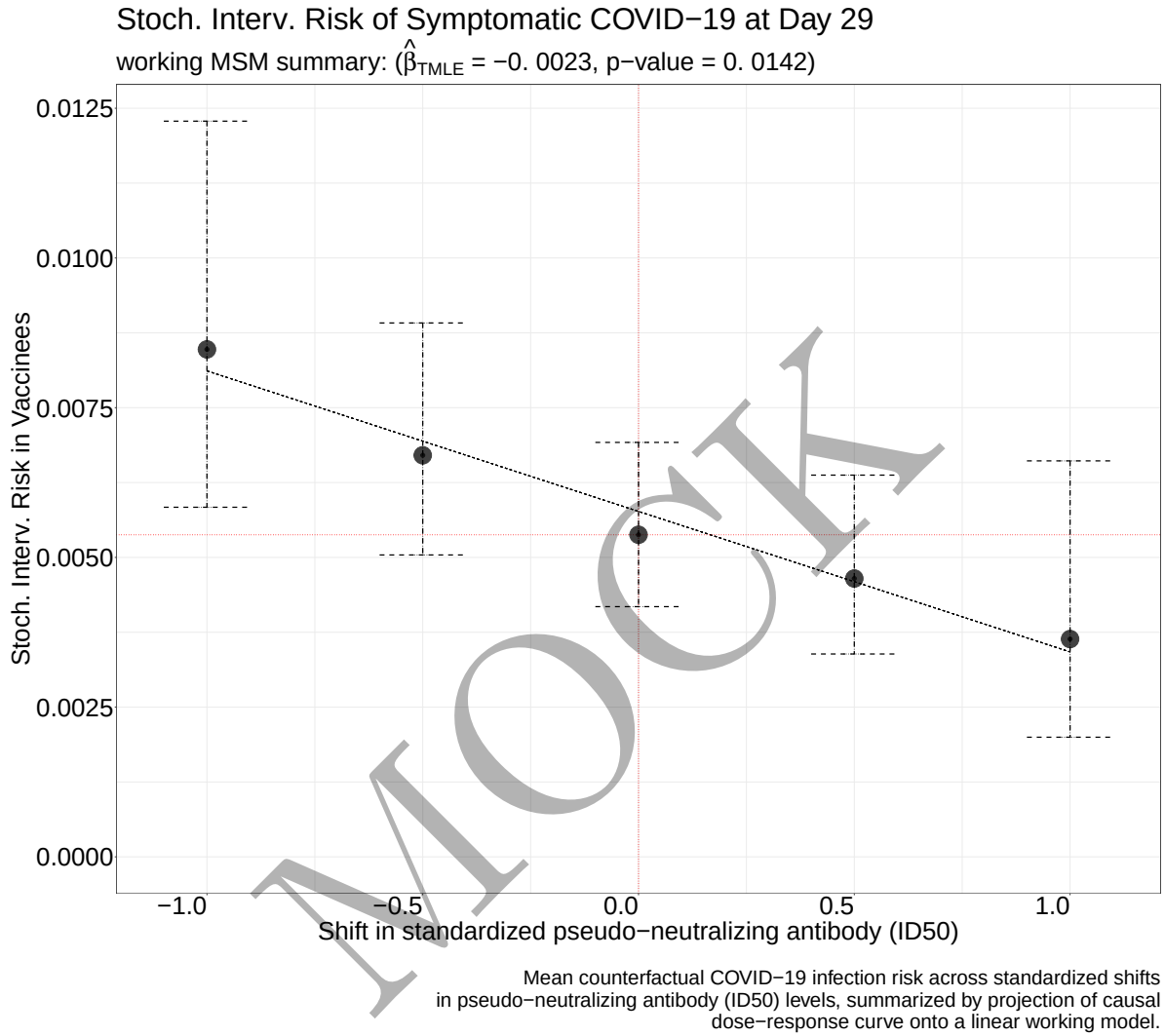




Figure 2.13: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29

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

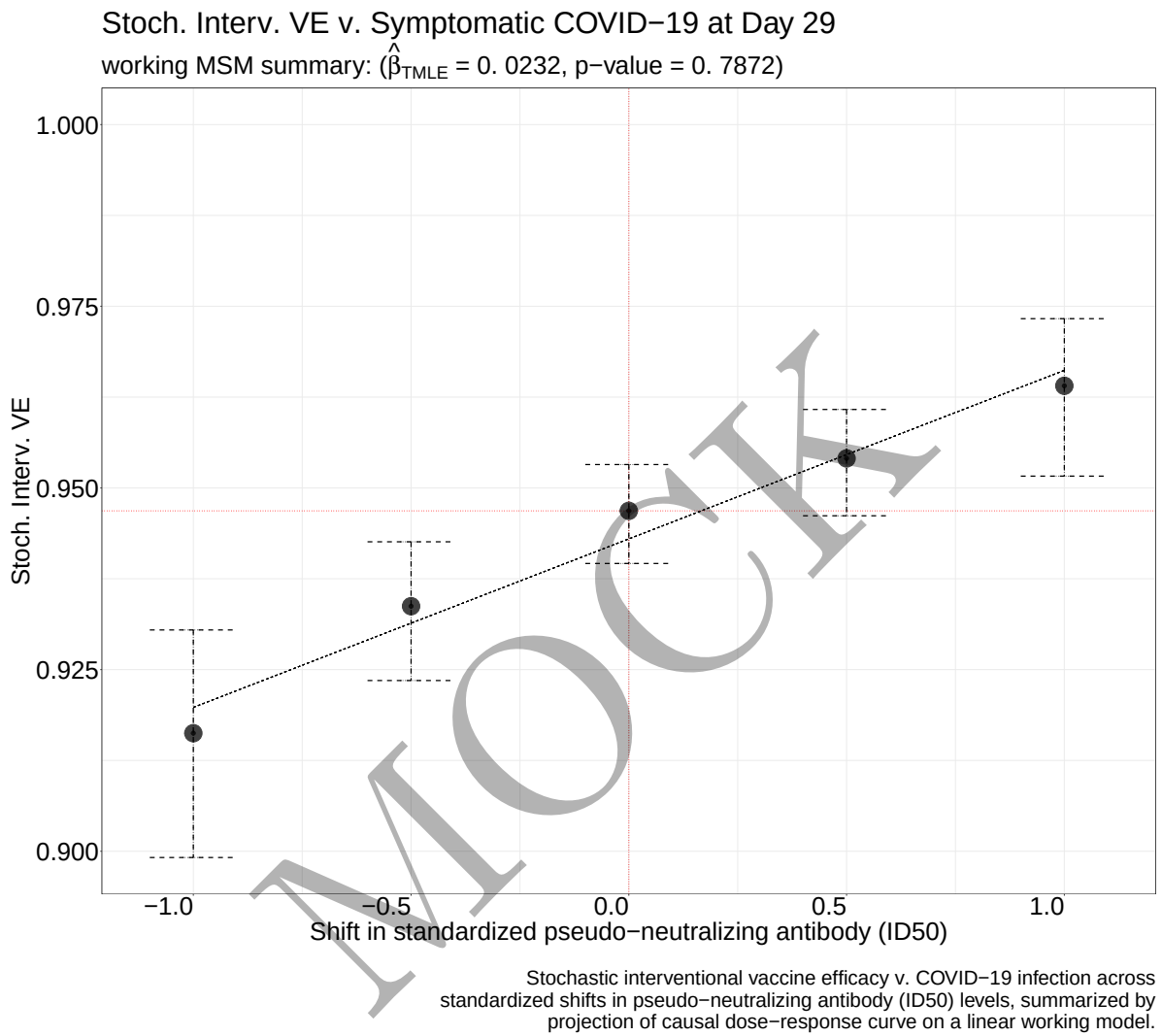


Figure 2.14: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29

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

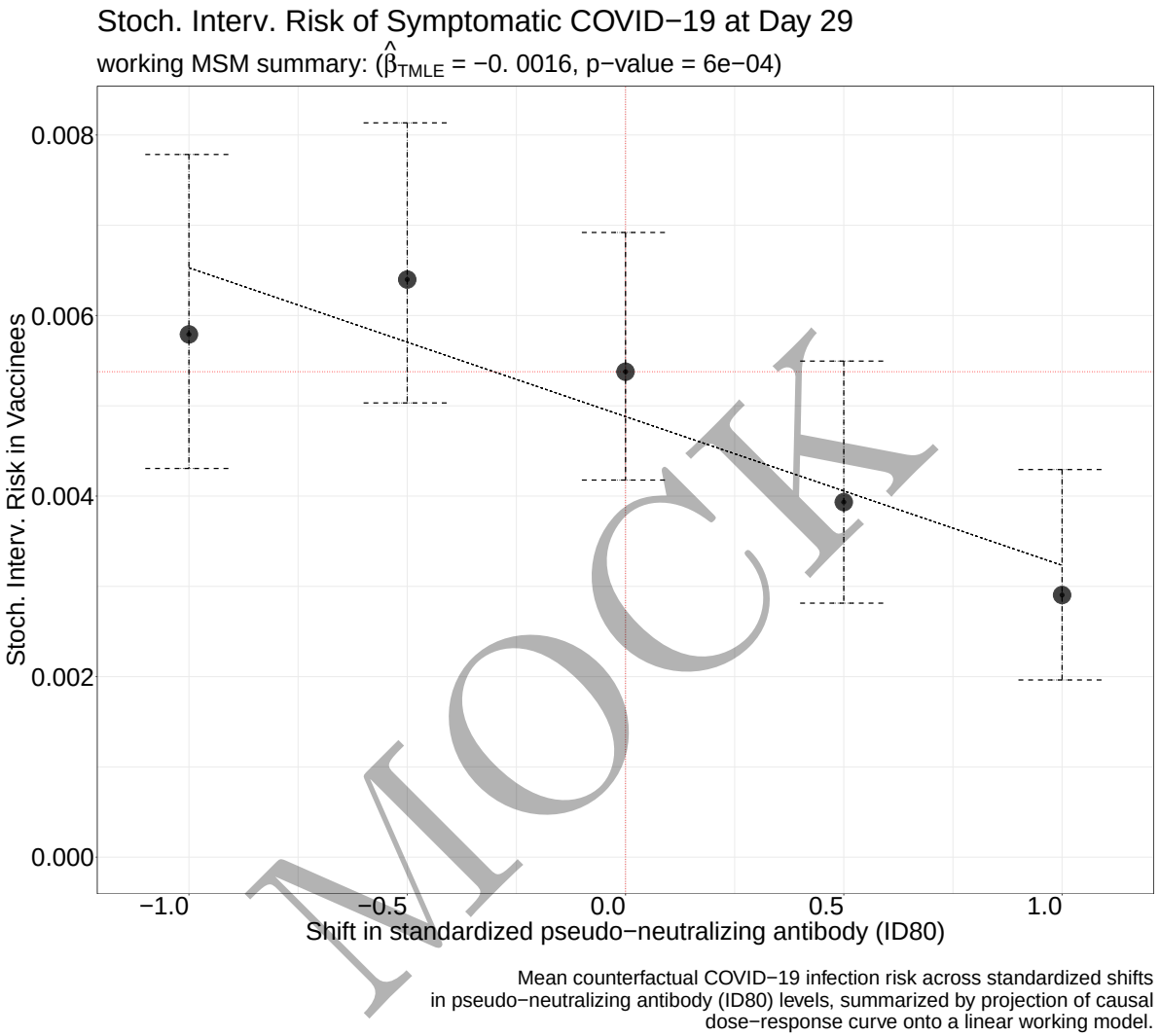


Figure 2.15: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29

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

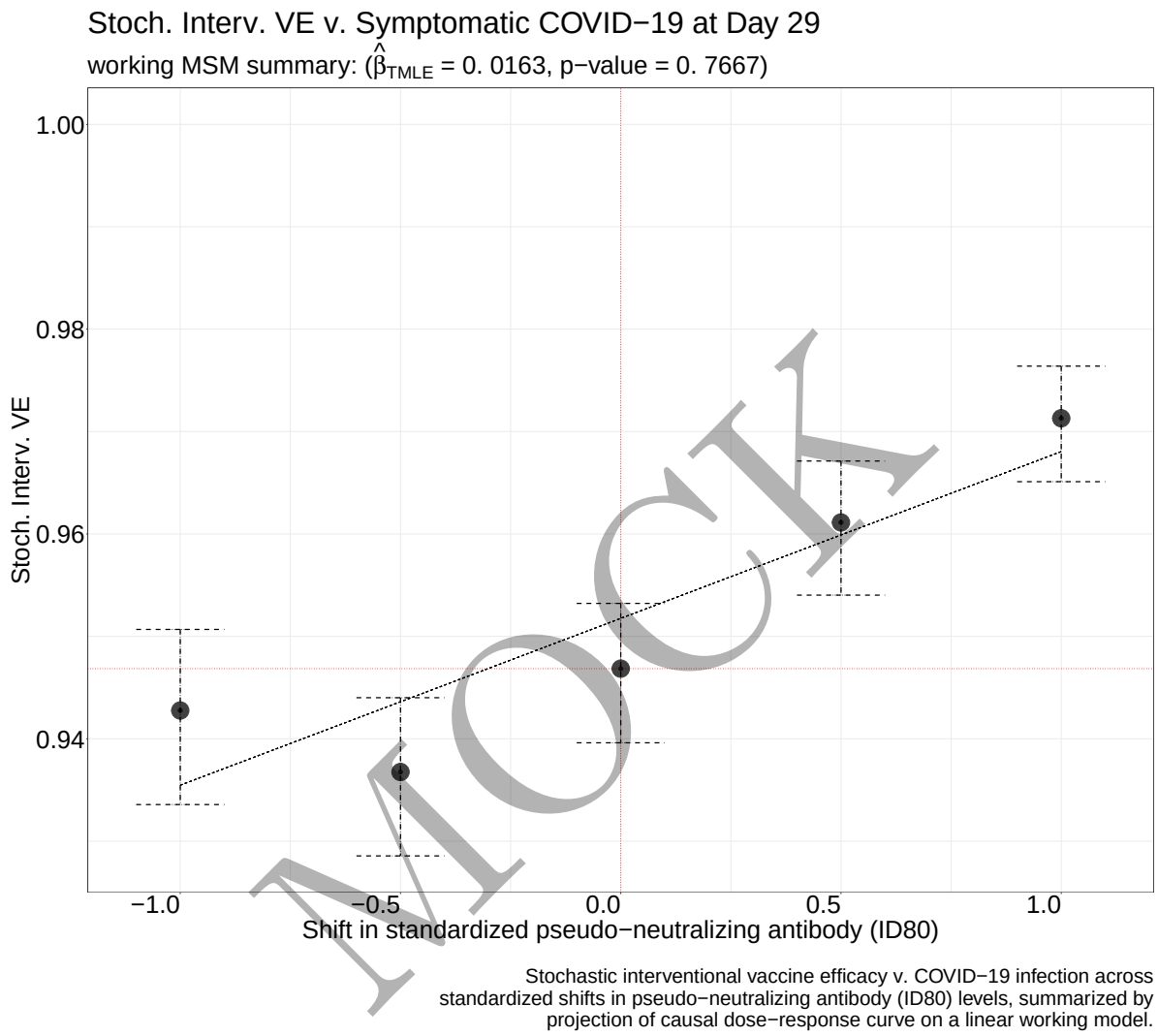


Figure 2.16: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29

# 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 04c2c73a0998adffdacfa5b49aac9b2b00dd6df3. A diff of the changes introduced by that commit may be viewed at https://github.com/CoVPN/correlates_reporting/commit/04c2c73a0998adffdacfa5b49aac9b2b00dd6df3
- 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