

# COVID-19 Correlates of Protection Analysis Report

## MockCOVE Study

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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



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# 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.

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## 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

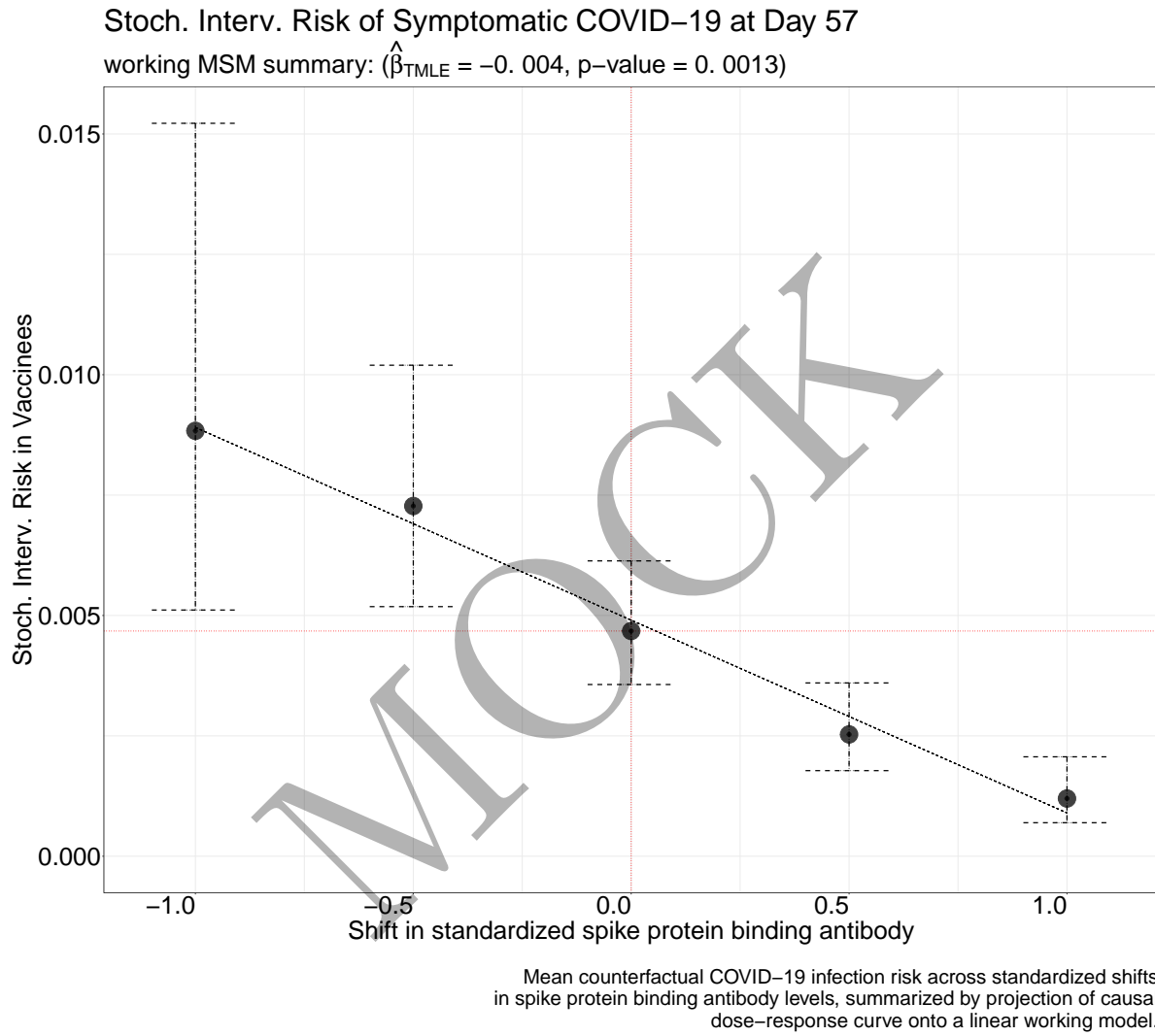


Figure 2.1: Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 57

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

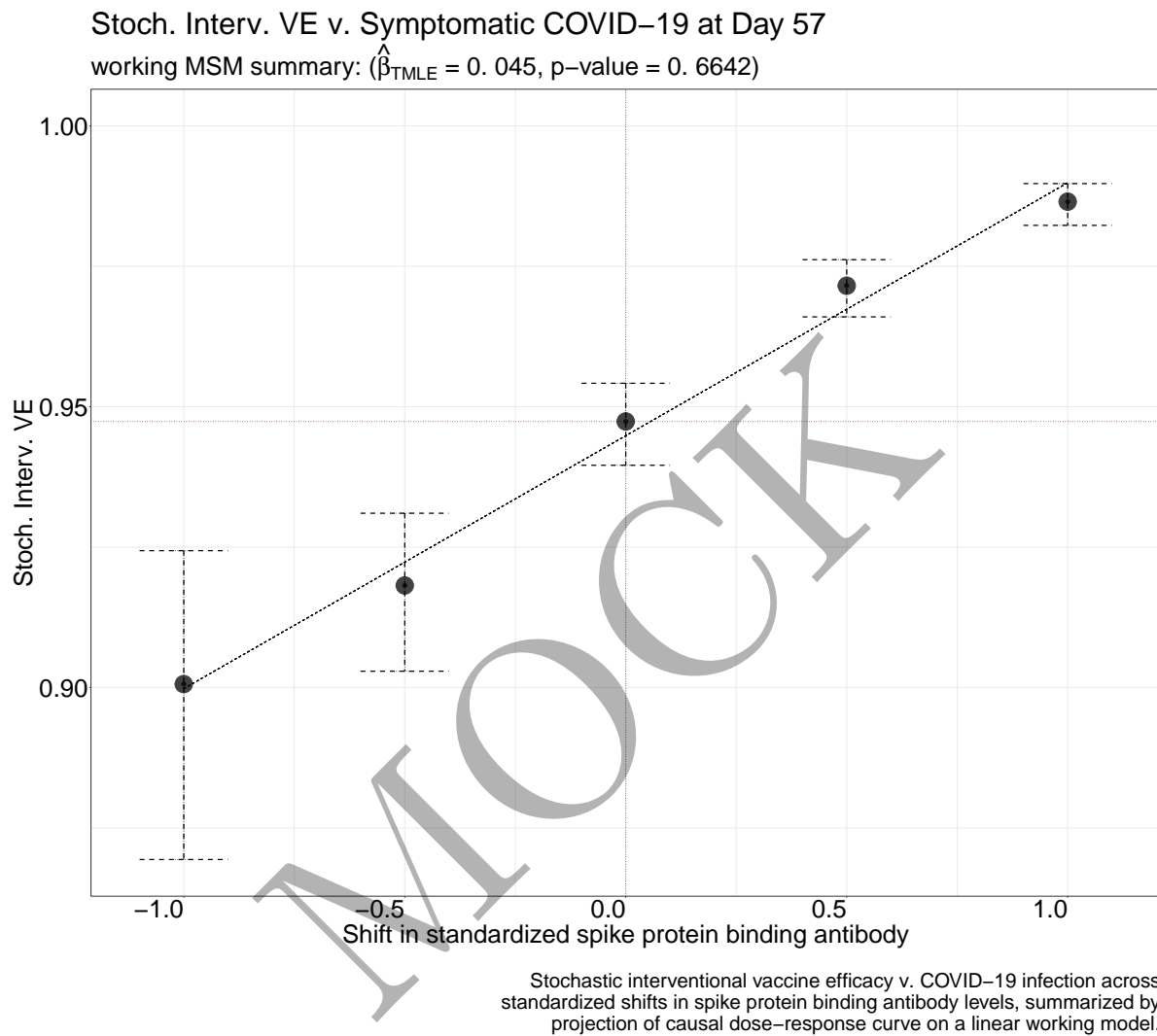


Figure 2.2: Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 57

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

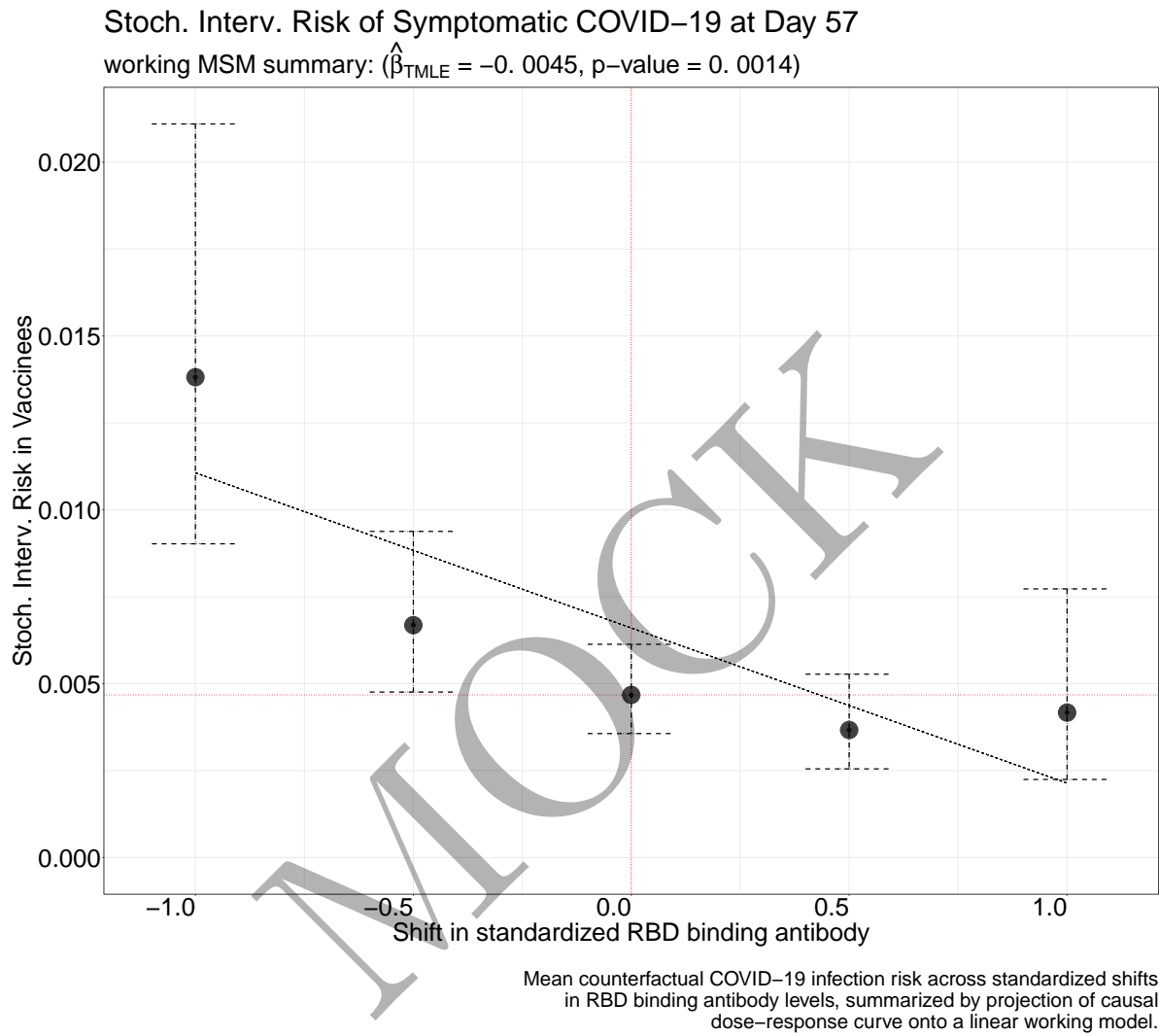


Figure 2.3: Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 57

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

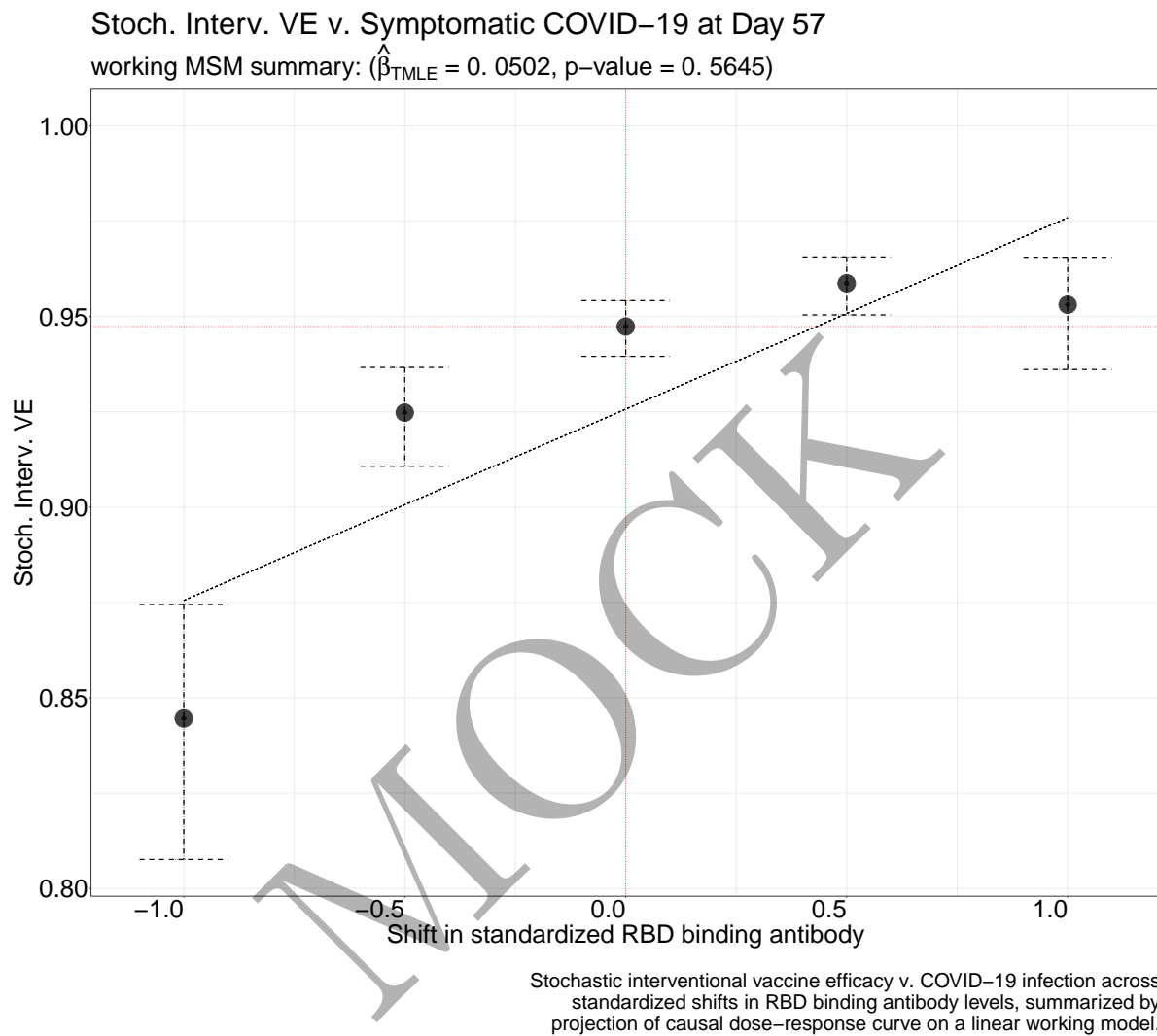


Figure 2.4: Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 57

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

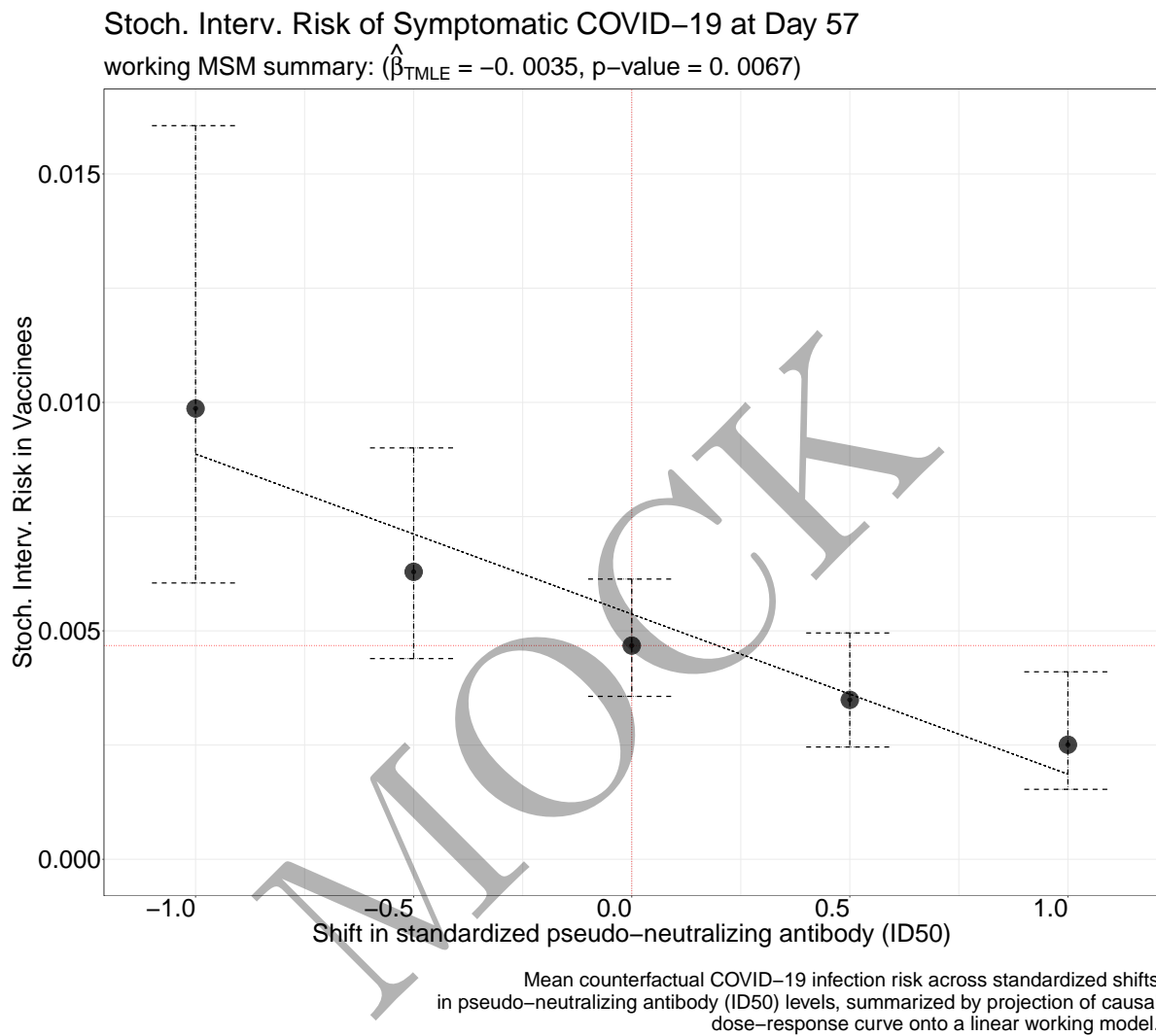


Figure 2.5: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57



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

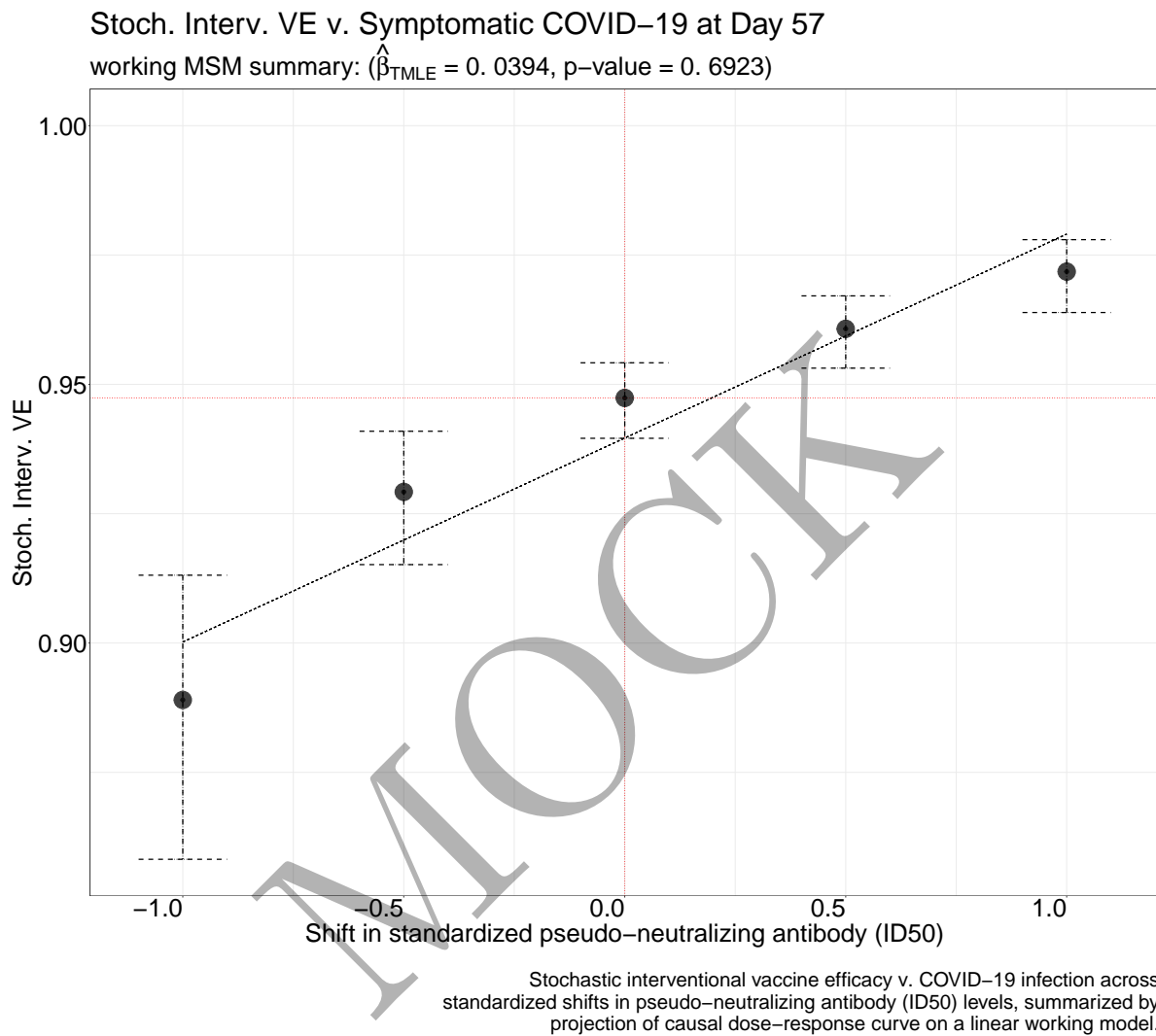


Figure 2.6: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57

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

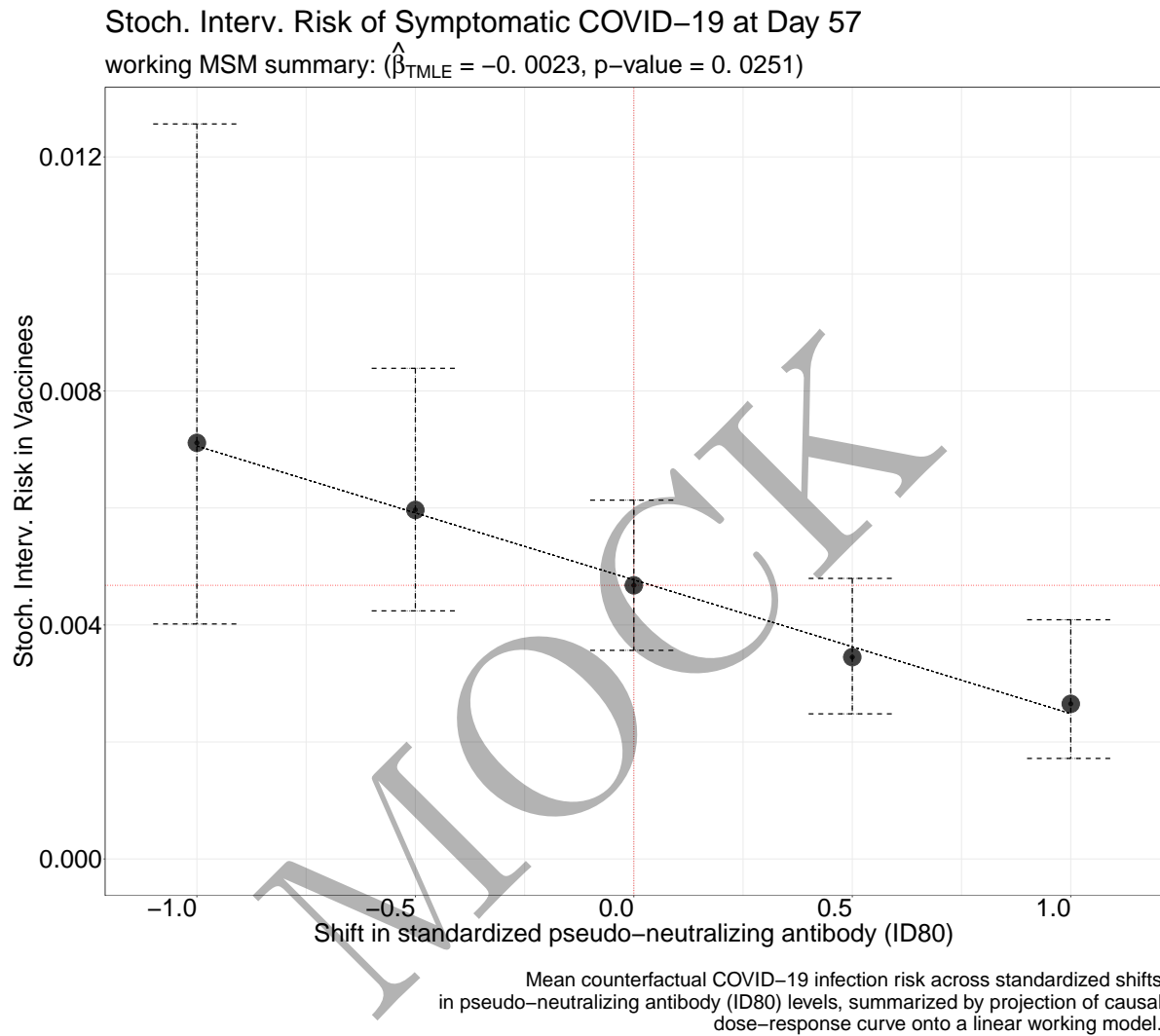


Figure 2.7: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57

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

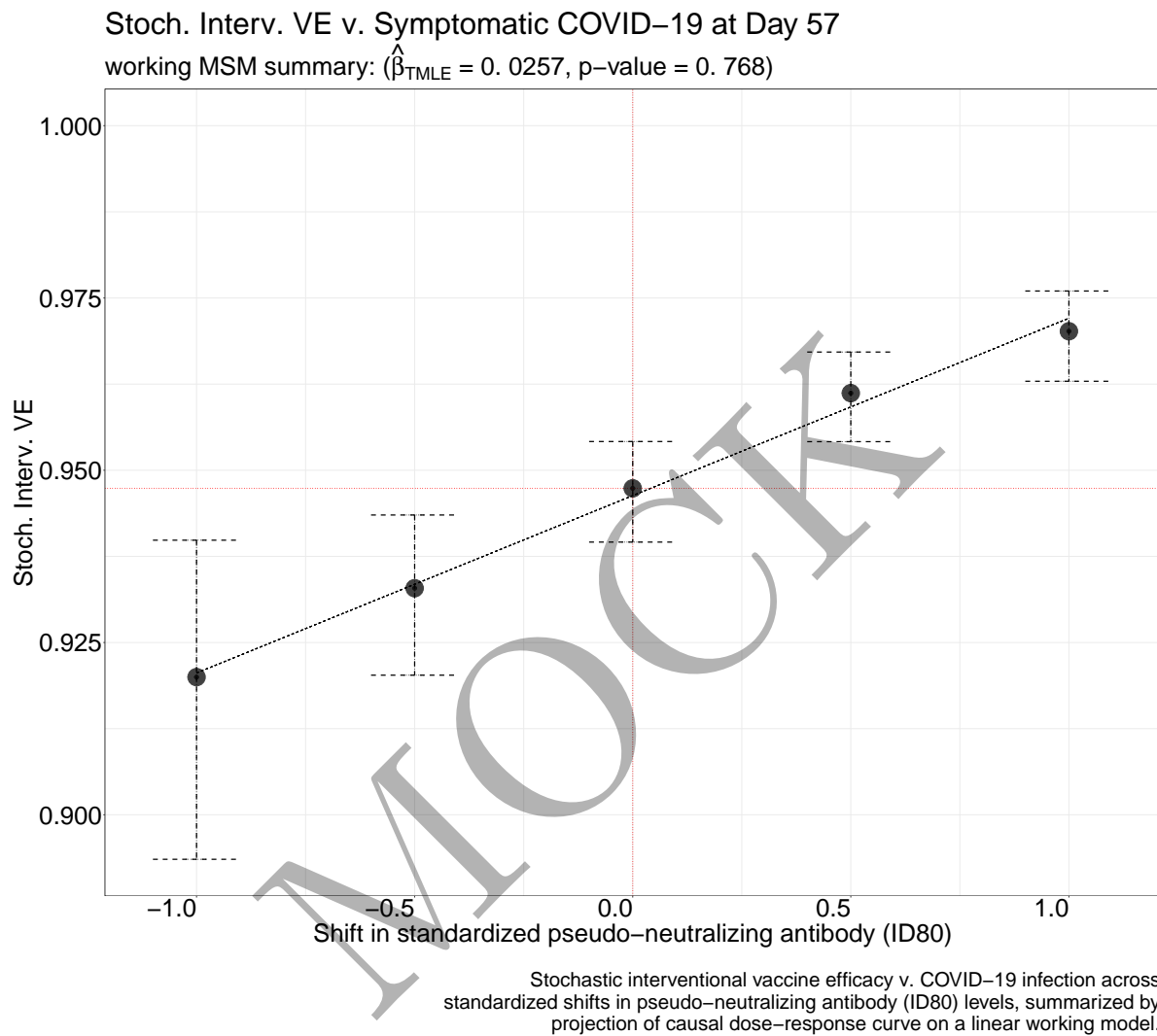


Figure 2.8: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57

## 2.2 Figures for Stochastic Interventional CoPs for Day 29

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

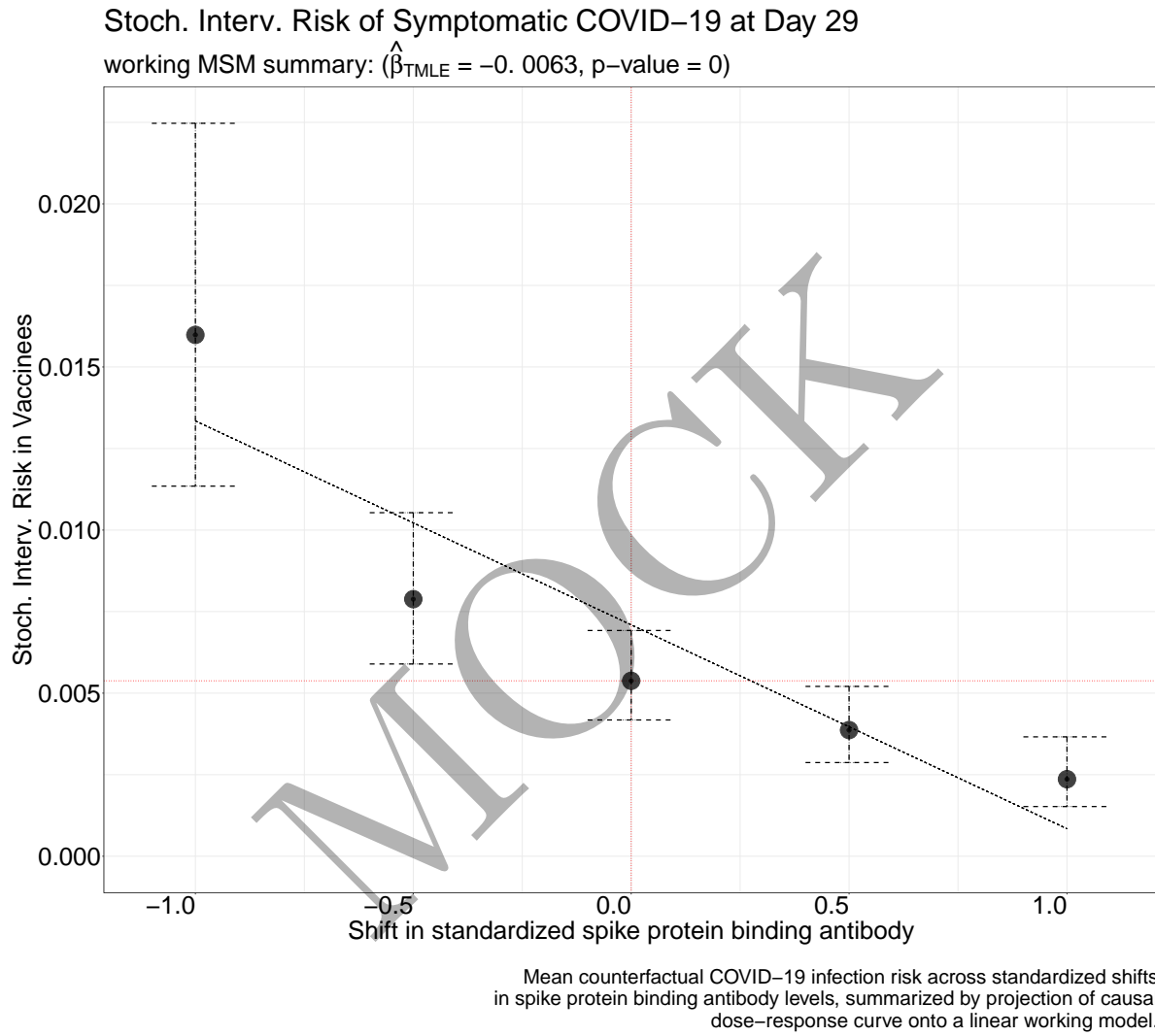


Figure 2.9: Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 29

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

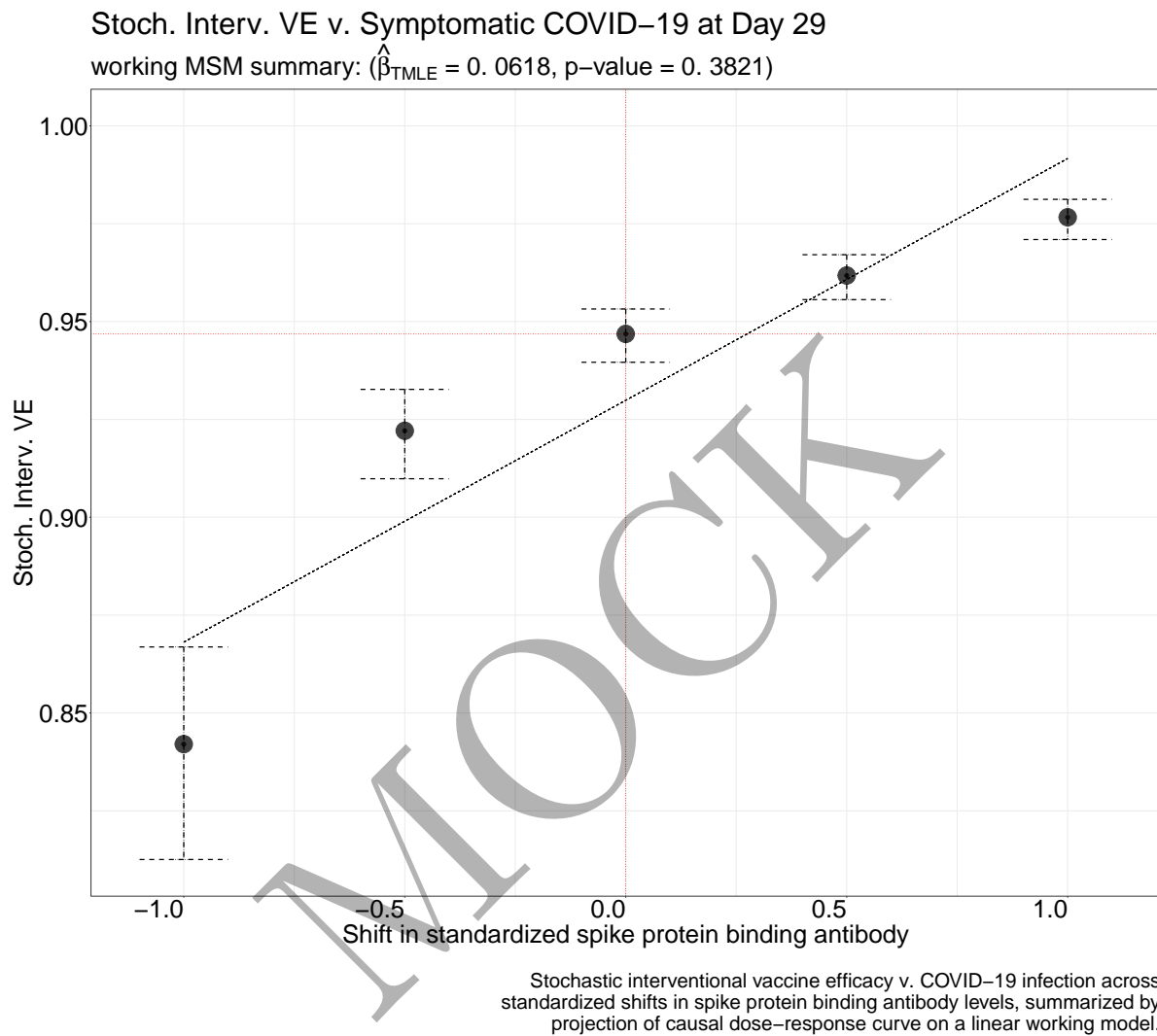


Figure 2.10: Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 29

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

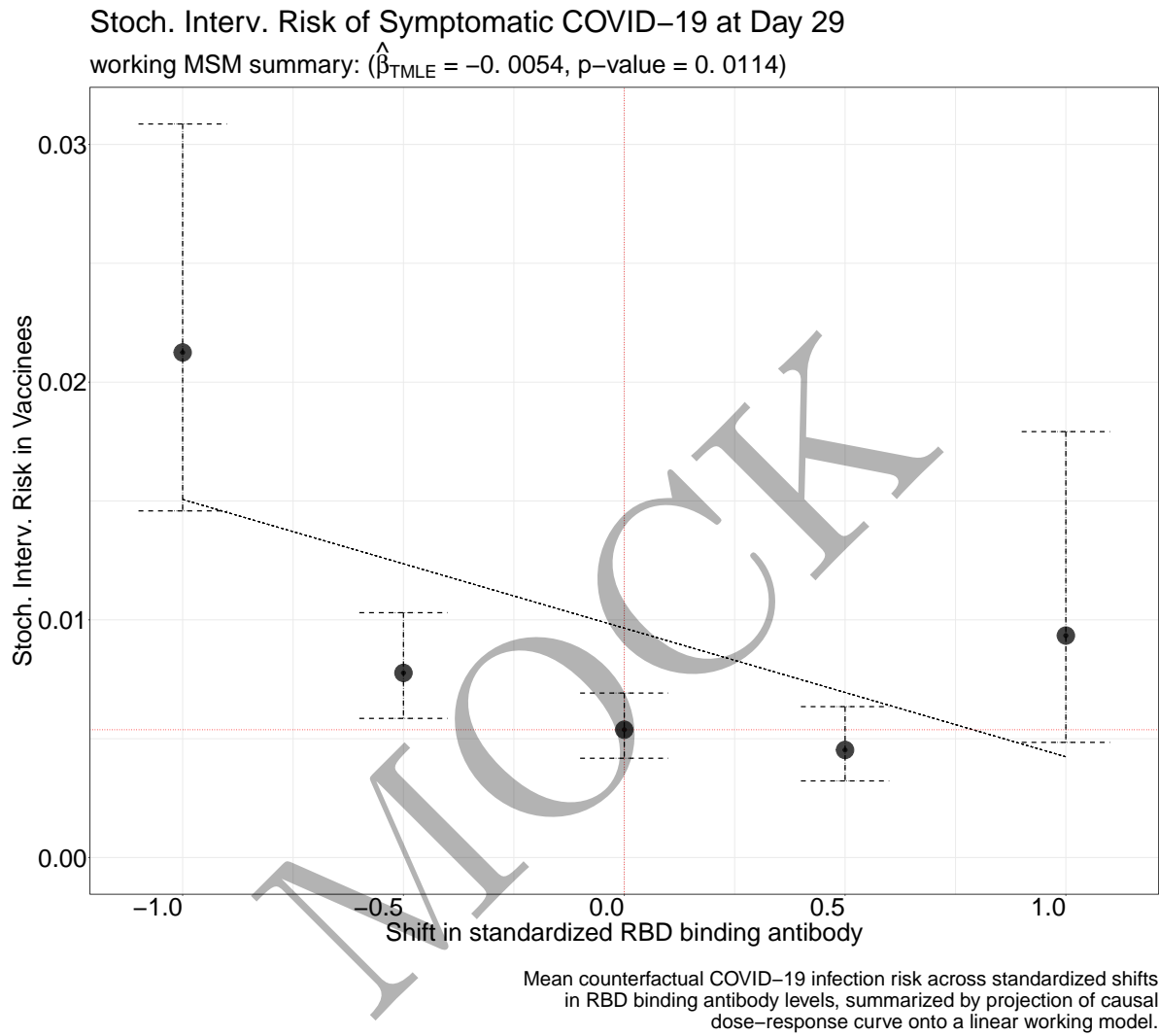


Figure 2.11: Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 29

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

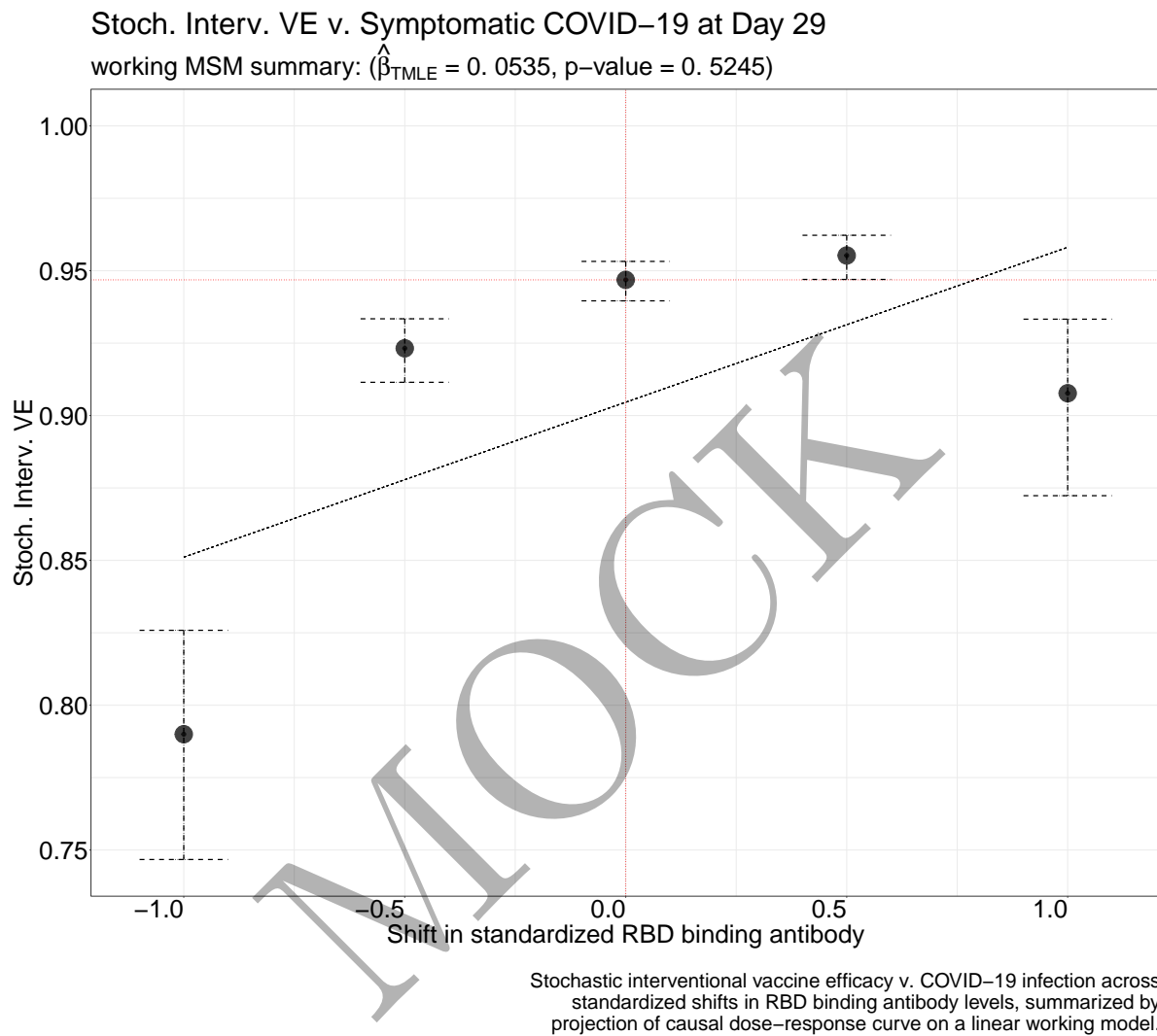


Figure 2.12: Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 29

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

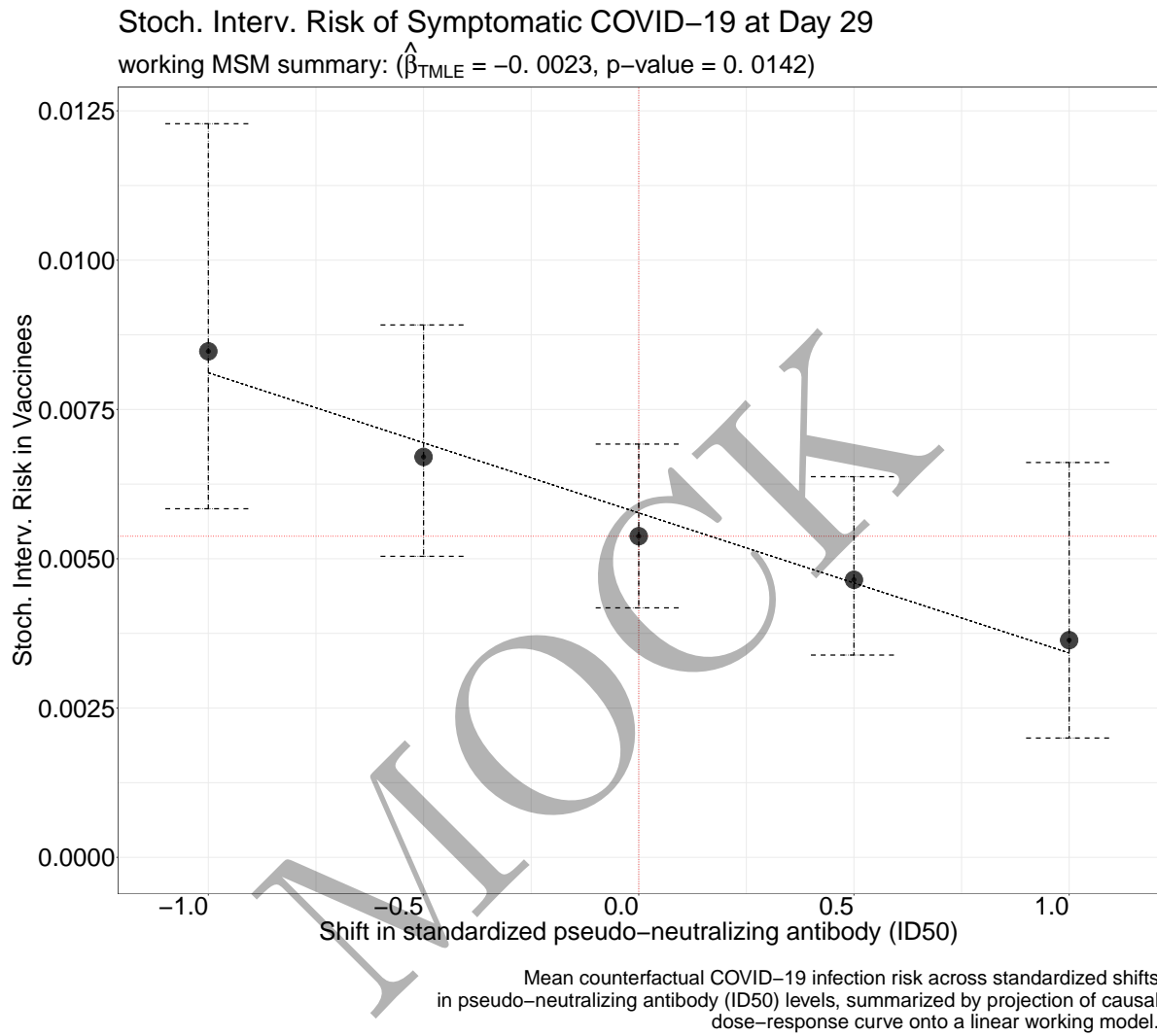


Figure 2.13: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29



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

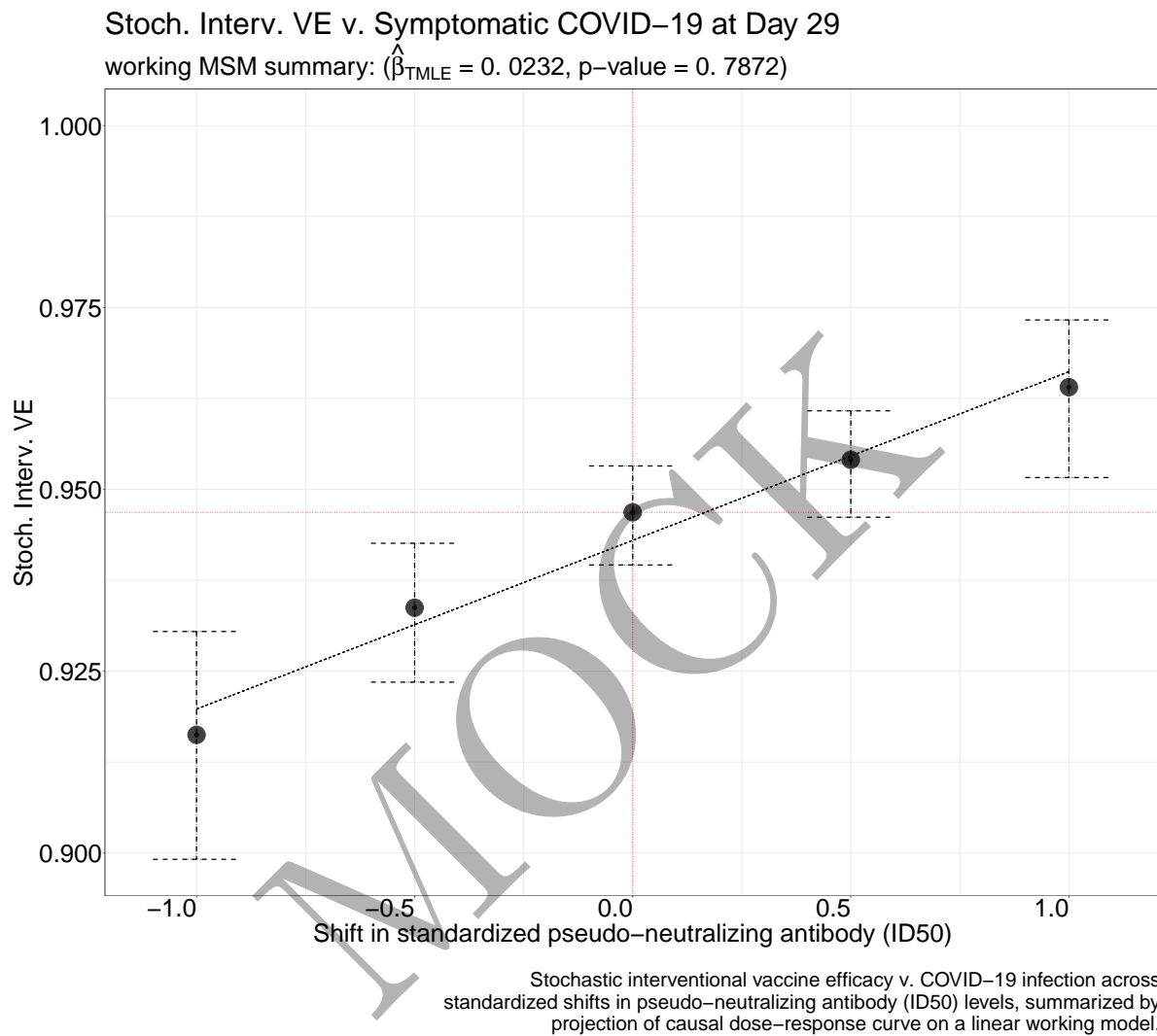


Figure 2.14: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29

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

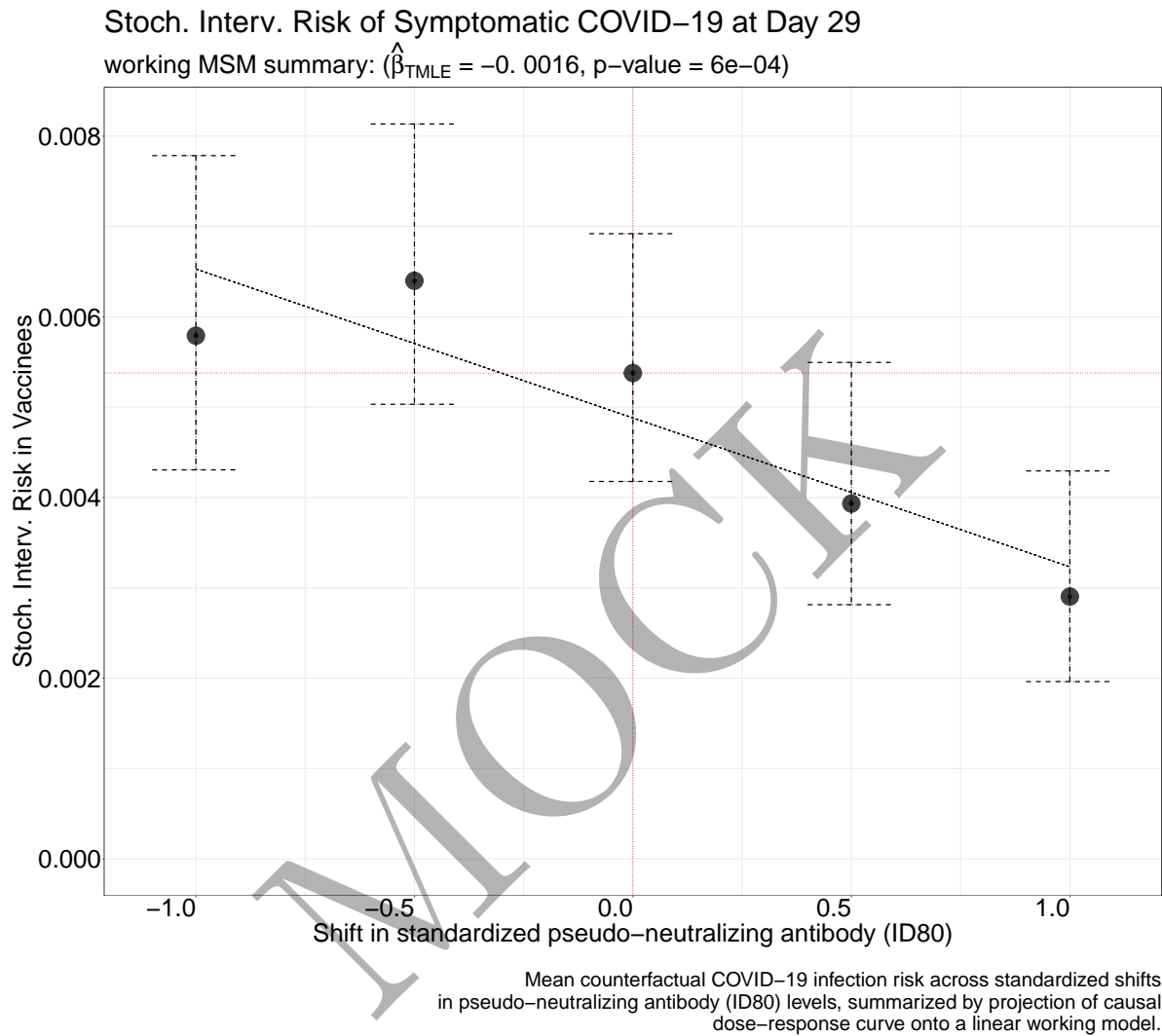


Figure 2.15: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29

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

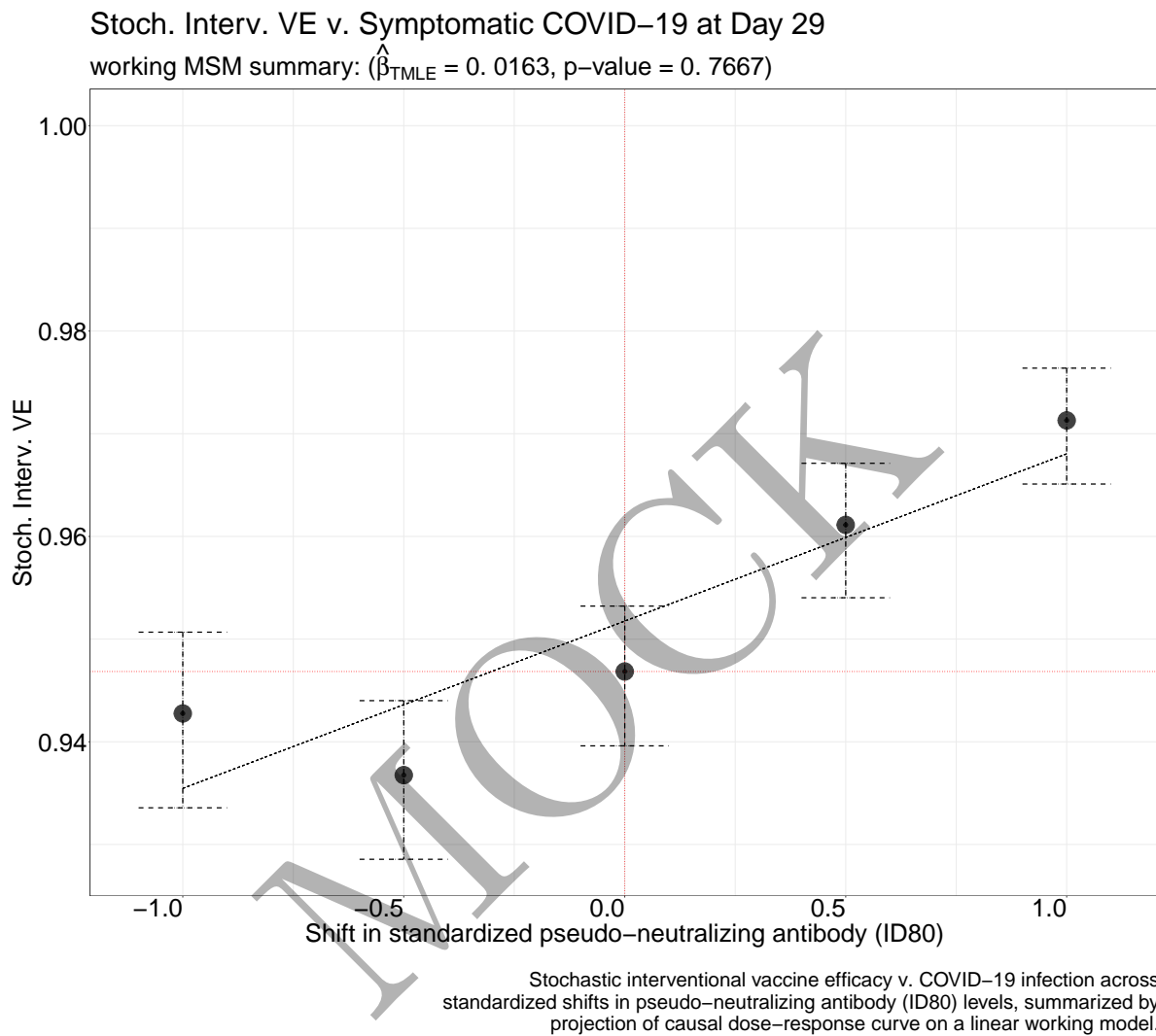


Figure 2.16: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29

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## 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 29	PsV Neutralization 80% Titer	0.906 (0.846, 0.942)	0.407 (0.079, 0.618)	0.181 (0.029, 0.333)

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 29	PsV Neutralization 80% Titer	0.914 (0.869, 0.943)	0.350 (0.050, 0.555)	0.149 (0.019, 0.279)

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## Chapter 4

# Appendix

- This report was built from the [CoVPN/correlates\\_reporting](https://github.com/CoVPN/correlates_reporting) repository with commit hash ee8258c54596789017e0e2f28a9c897cba95349d. A diff of the changes introduced by that commit may be viewed at [https://github.com/CoVPN/correlates\\_reporting/commit/ee8258c54596789017e0e2f28a9c897cba95349d](https://github.com/CoVPN/correlates_reporting/commit/ee8258c54596789017e0e2f28a9c897cba95349d)
- 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