

# COVID-19 Correlates of Protection Analysis Report

mock Study

USG COVID-19 Response Biostatistics Team

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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. 27
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Direct VE = VE comparing vaccine vs. placebo with marker set to distribution in placebo.  
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Prop. mediated = fraction of total risk reduction from vaccine attributed to antibody response. 27



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## Chapter 1

# 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).

### 1.1 Figures for Stochastic Interventional CoPs for Day 57

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

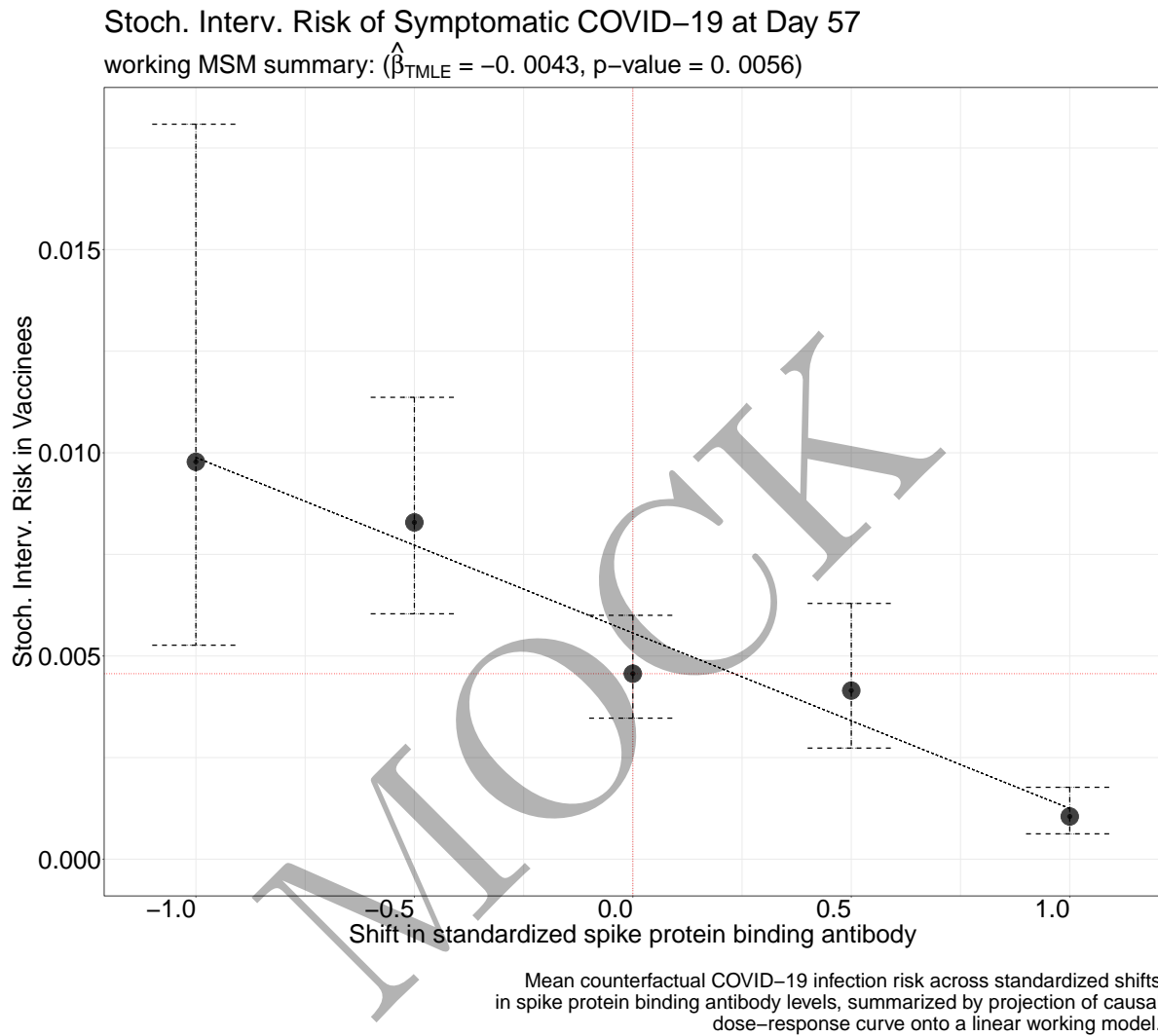


Figure 1.1: Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 57

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

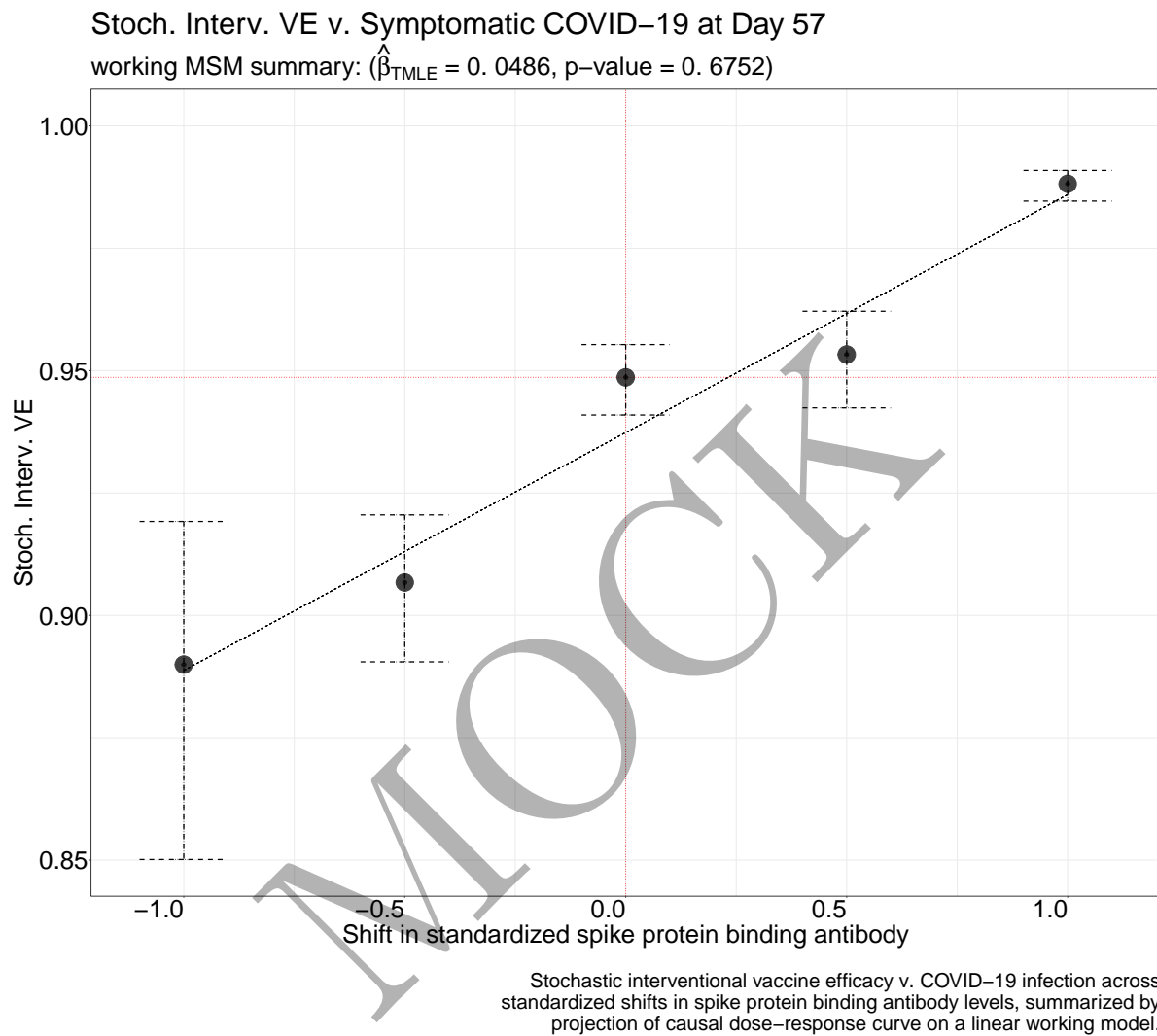


Figure 1.2: Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 57

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

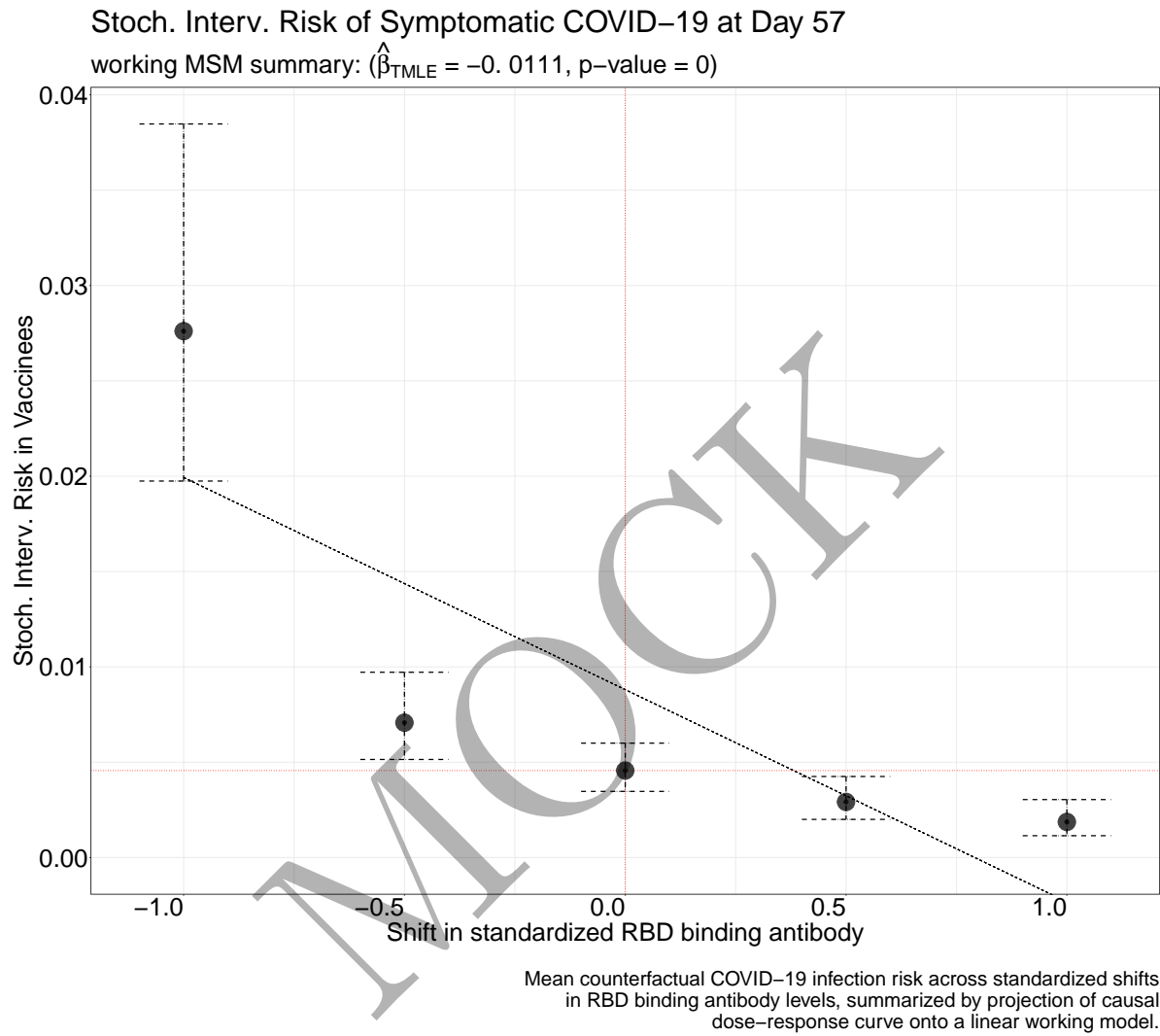


Figure 1.3: Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 57

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

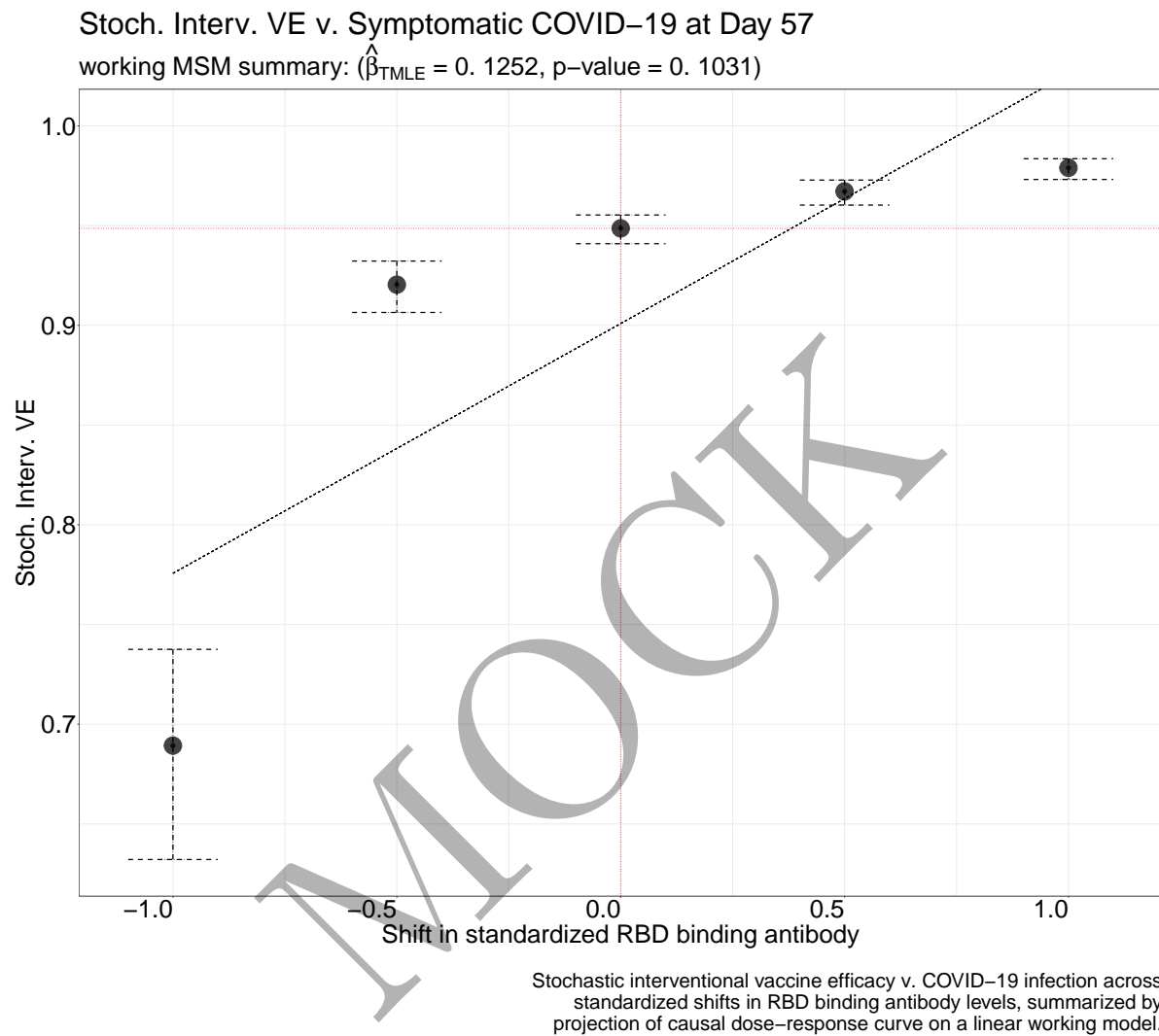


Figure 1.4: Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 57

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

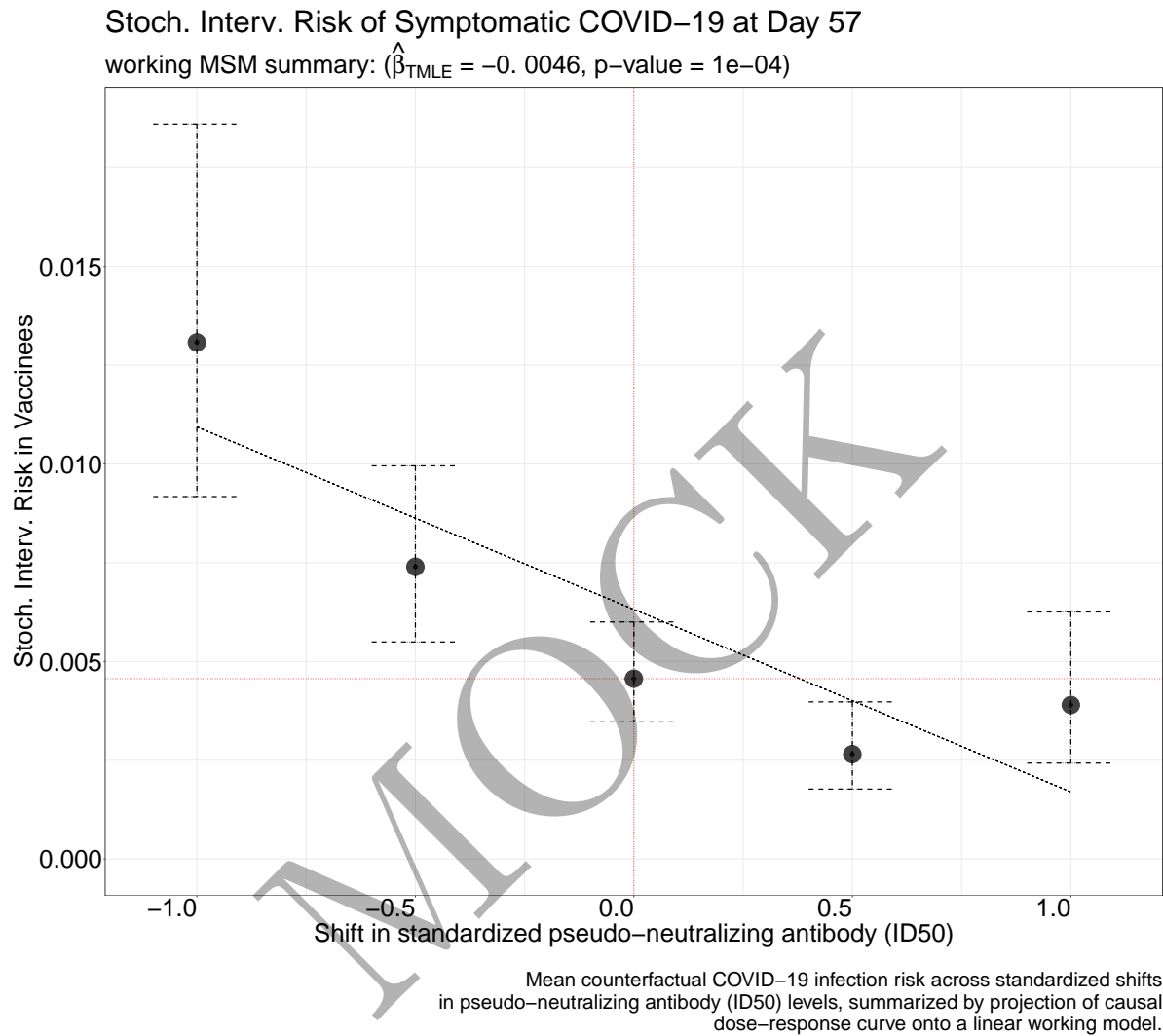


Figure 1.5: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57

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

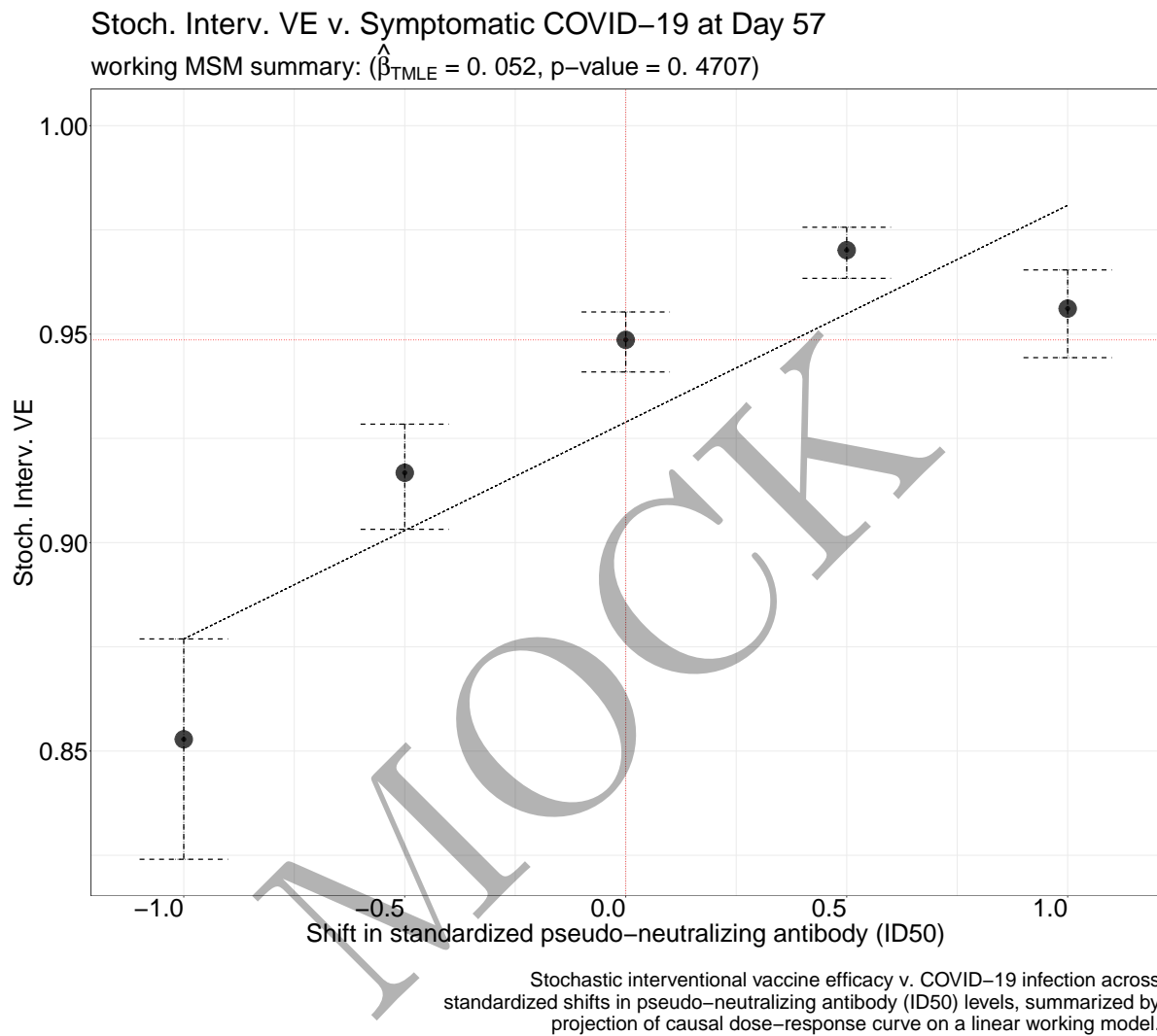


Figure 1.6: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 57

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

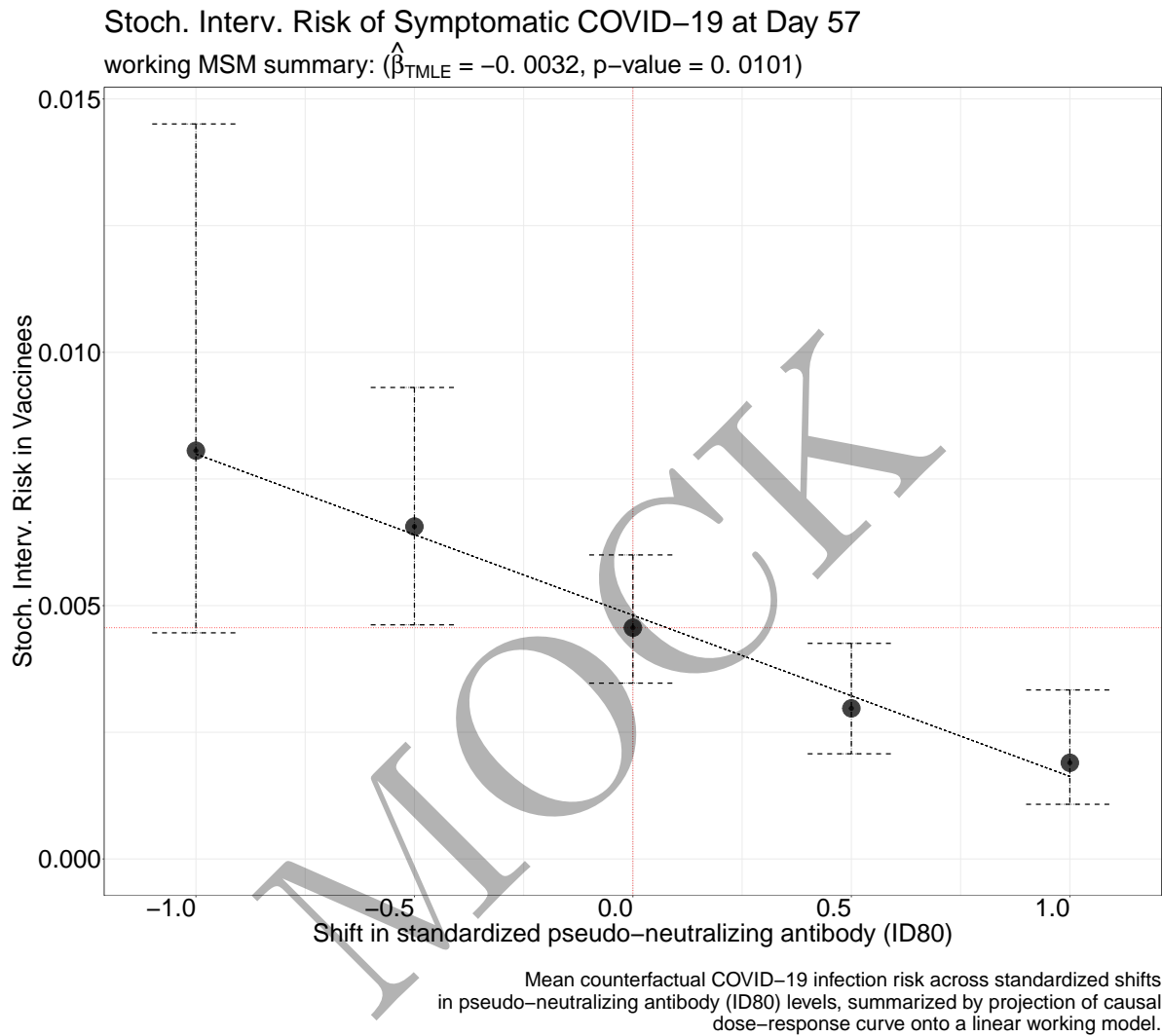


Figure 1.7: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57



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

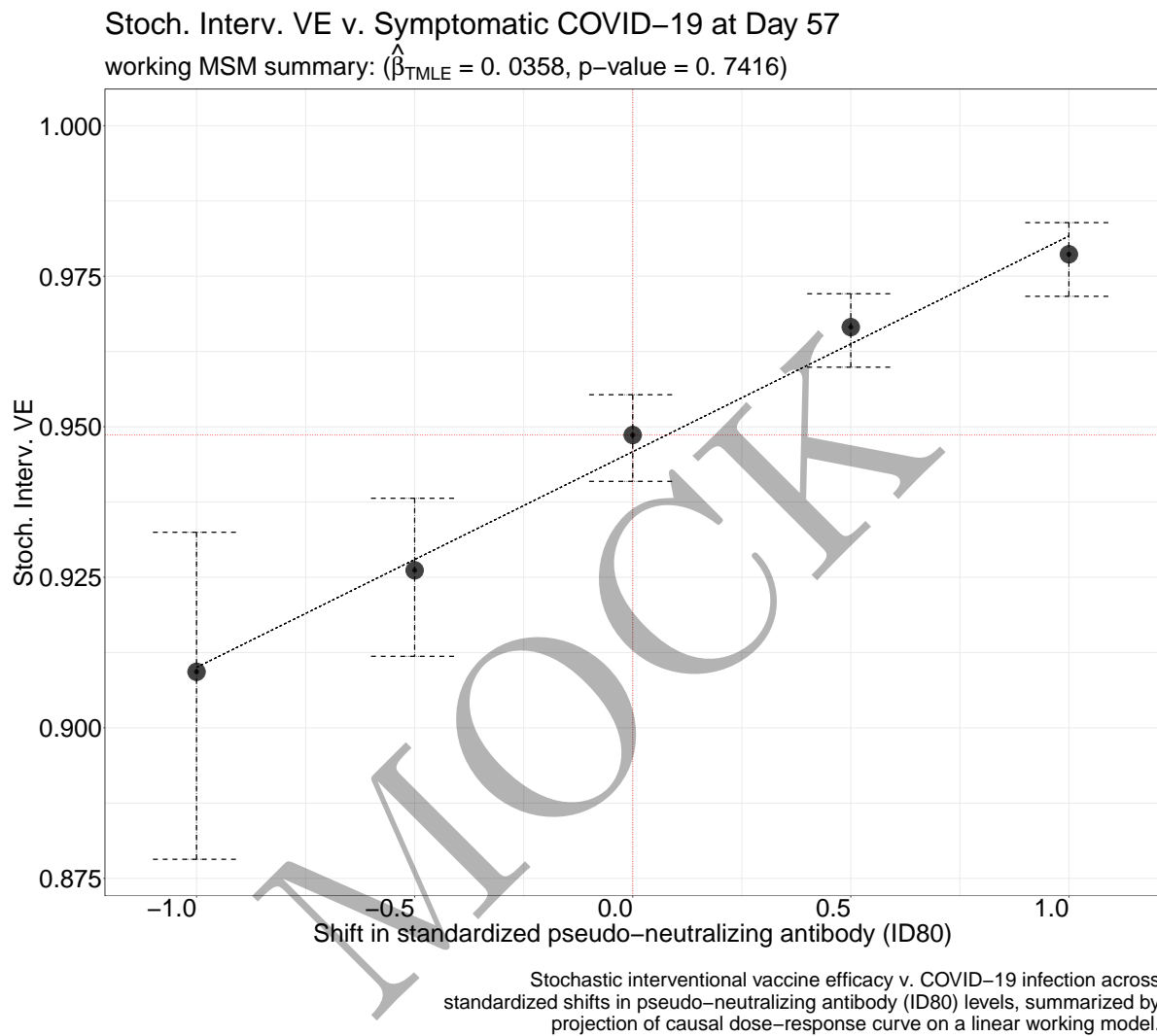


Figure 1.8: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 57

## 1.2 Figures for Stochastic Interventional CoPs for Day 29

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

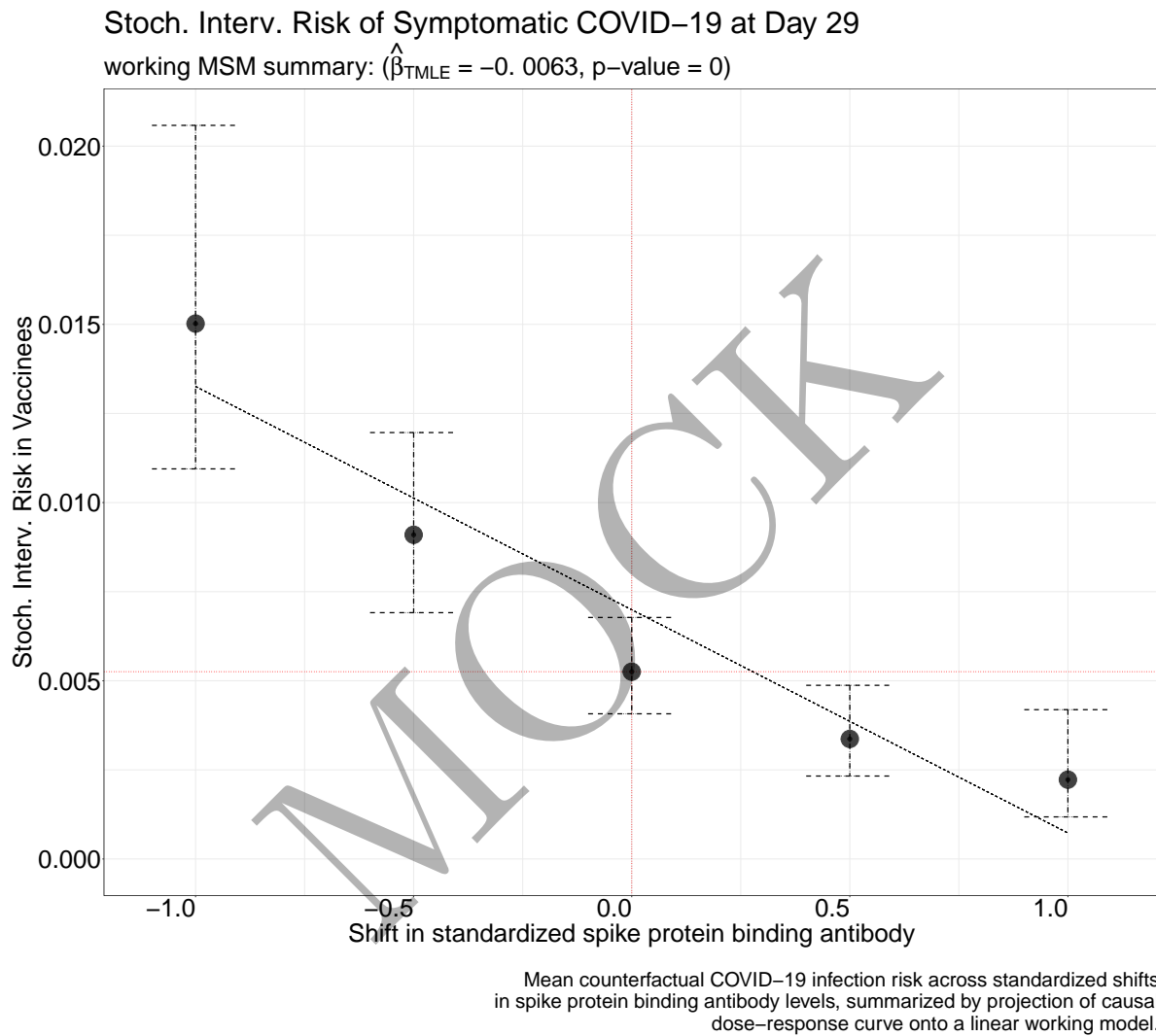


Figure 1.9: Stochastic interventional risk estimates, with confidence intervals, for spike protein binding antibody at Day 29

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

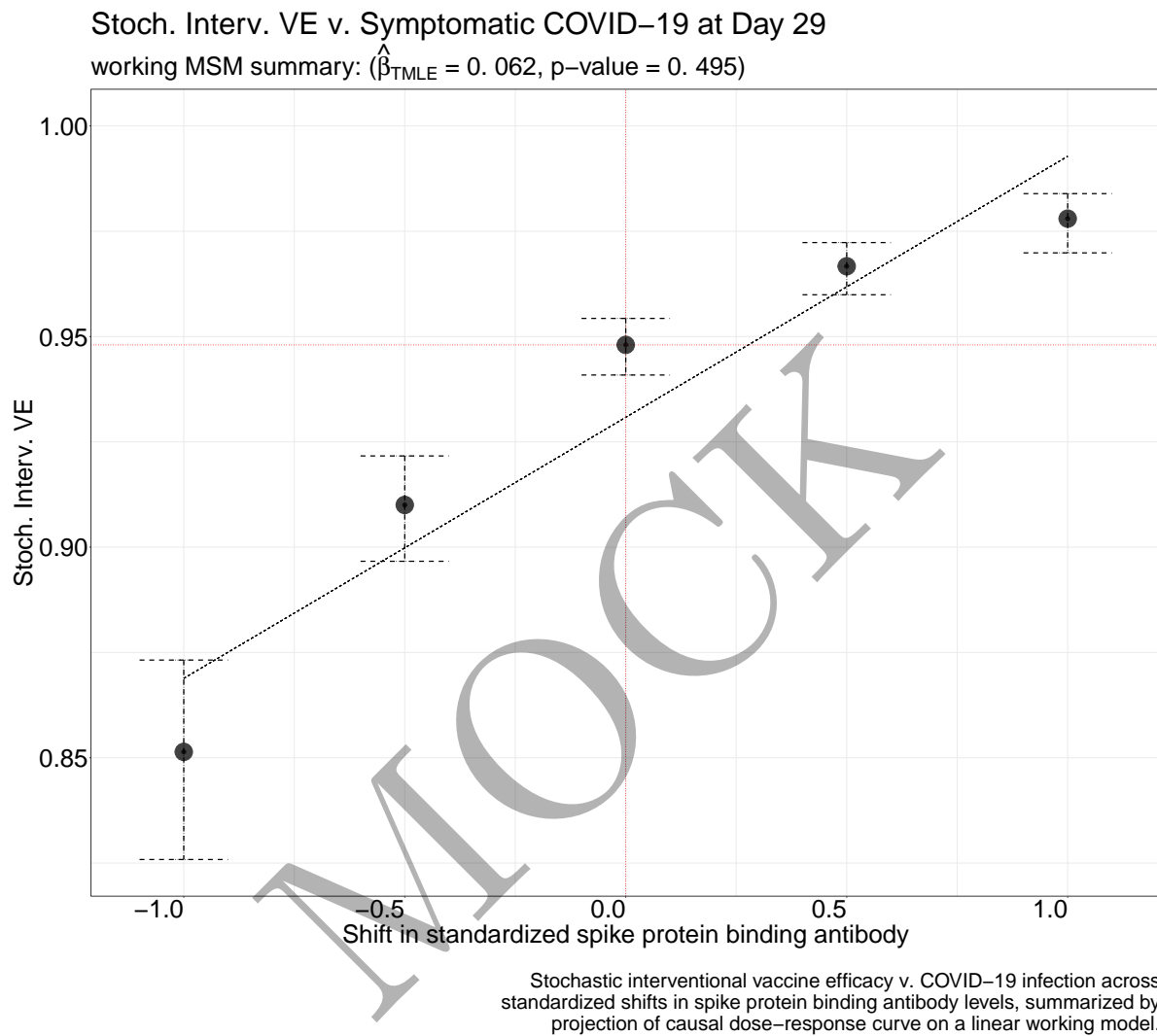


Figure 1.10: Stochastic interventional VE estimates, with confidence intervals, for spike protein binding antibody at Day 29

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

Stoch. Interv. Risk of Symptomatic COVID-19 at Day 29

working MSM summary: ( $\hat{\beta}_{\text{TMLE}} = 0.0044$ ,  $p\text{-value} = 0.0935$ )

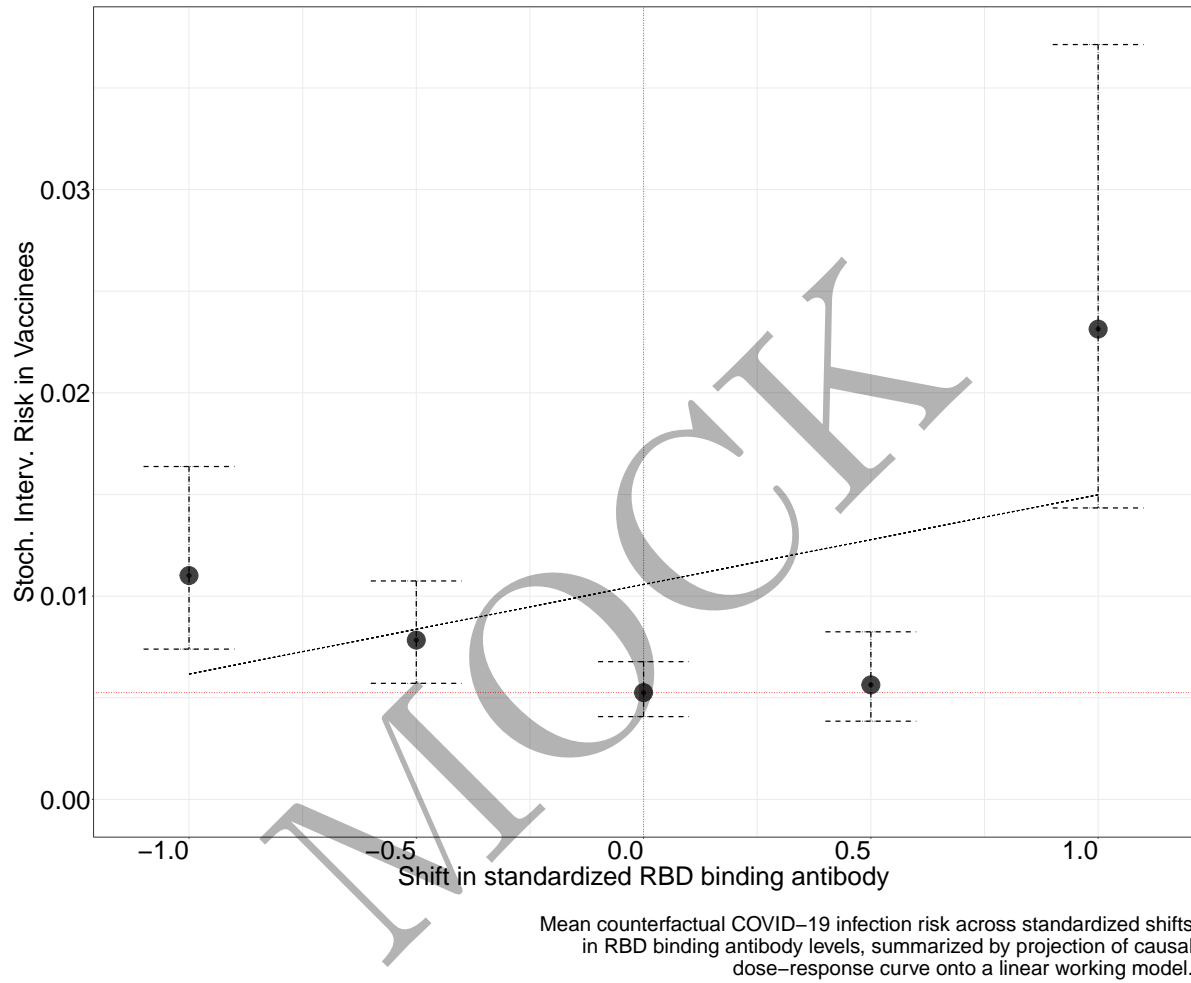


Figure 1.11: Stochastic interventional risk estimates, with confidence intervals, for RBD binding antibody at Day 29

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

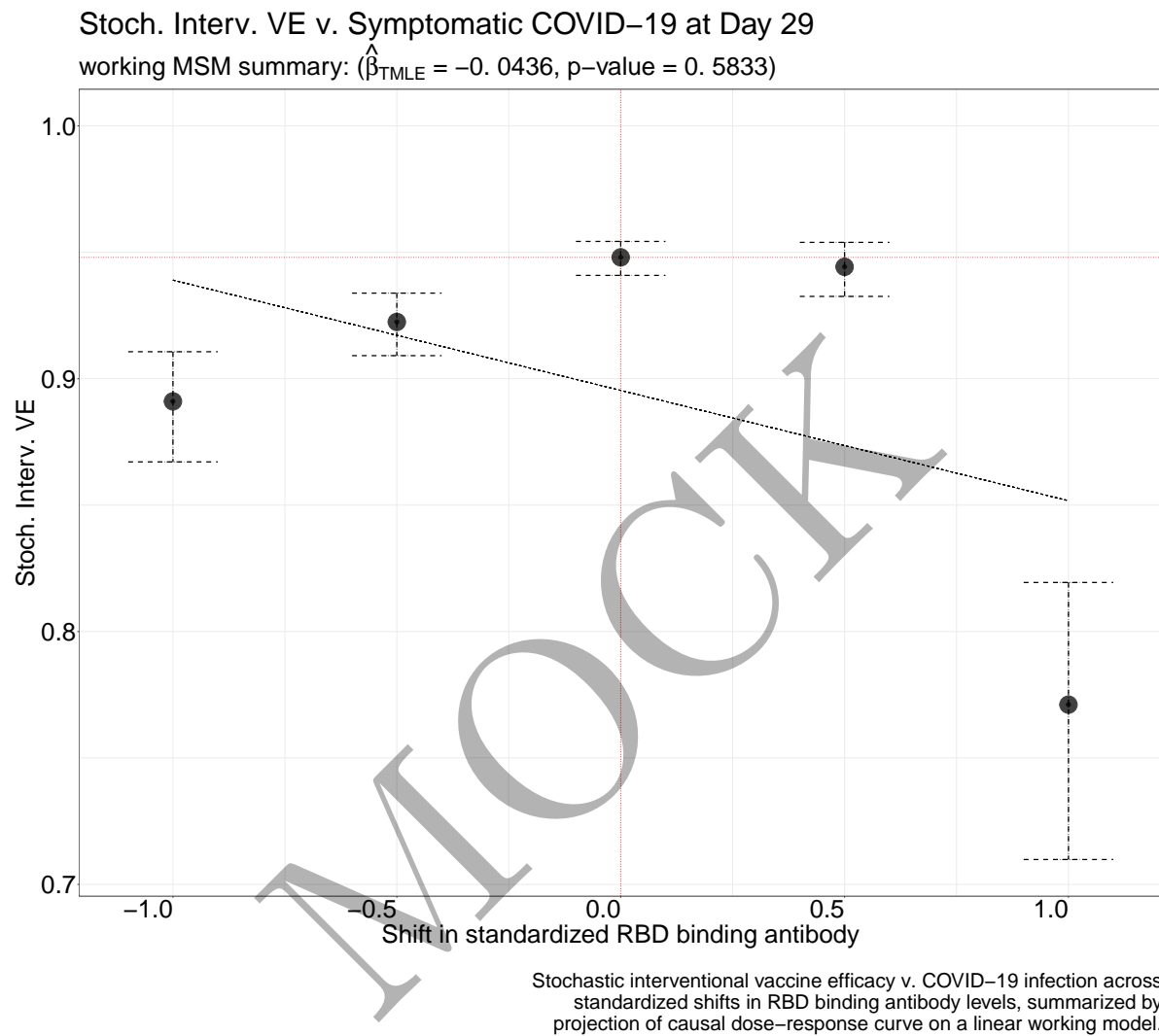


Figure 1.12: Stochastic interventional VE estimates, with confidence intervals, for RBD binding antibody at Day 29

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

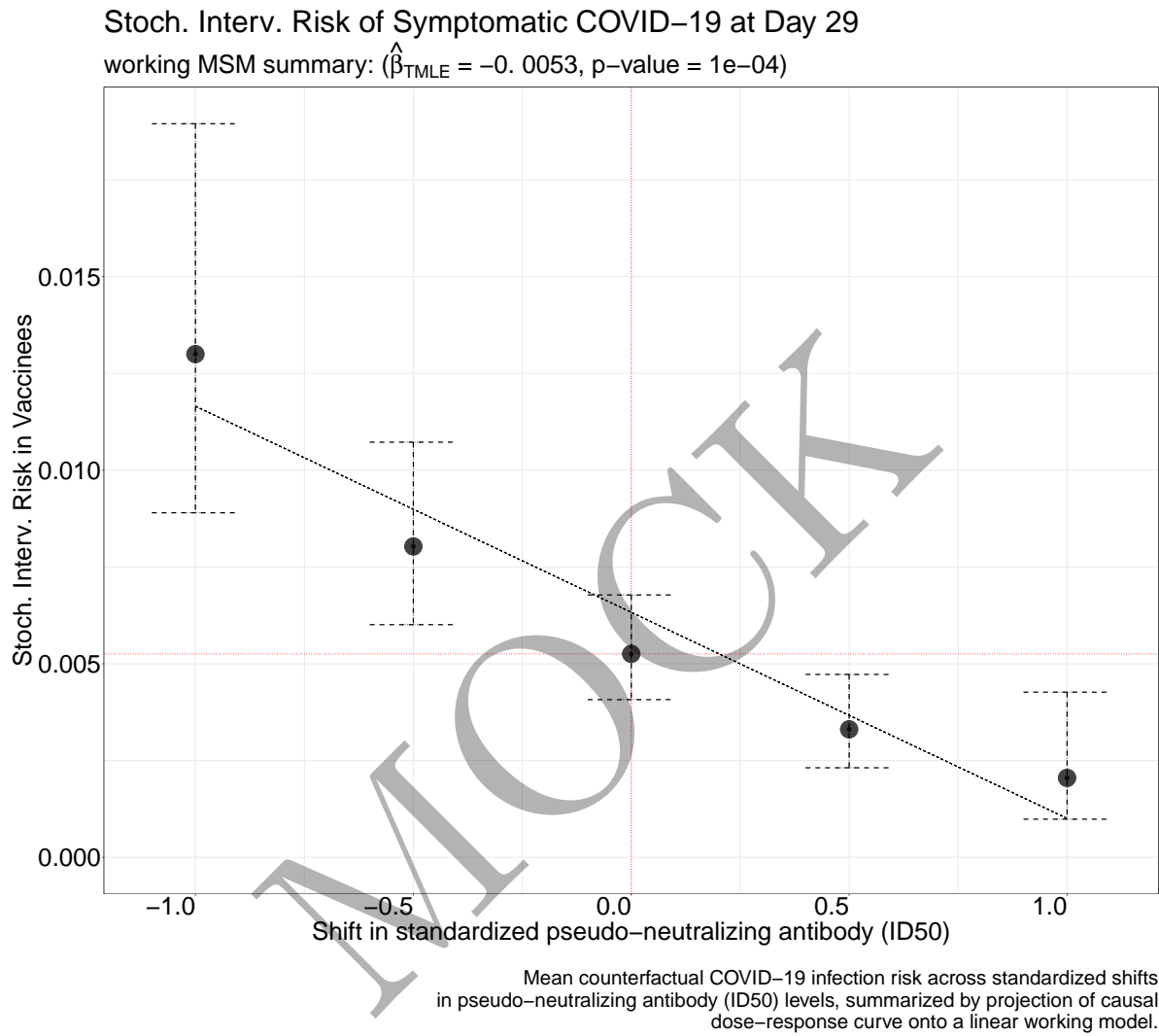


Figure 1.13: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29

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

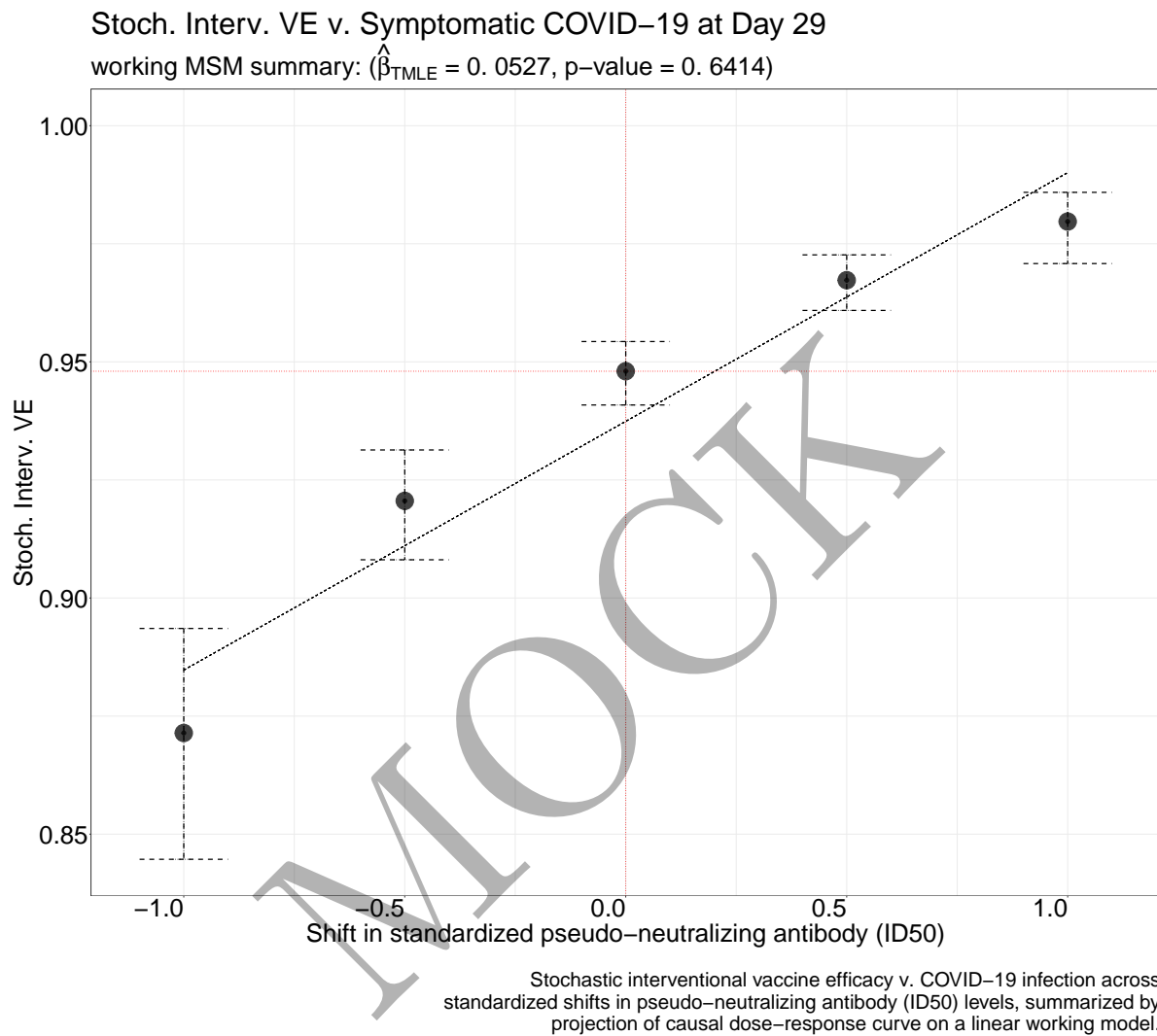


Figure 1.14: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID50) at Day 29

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

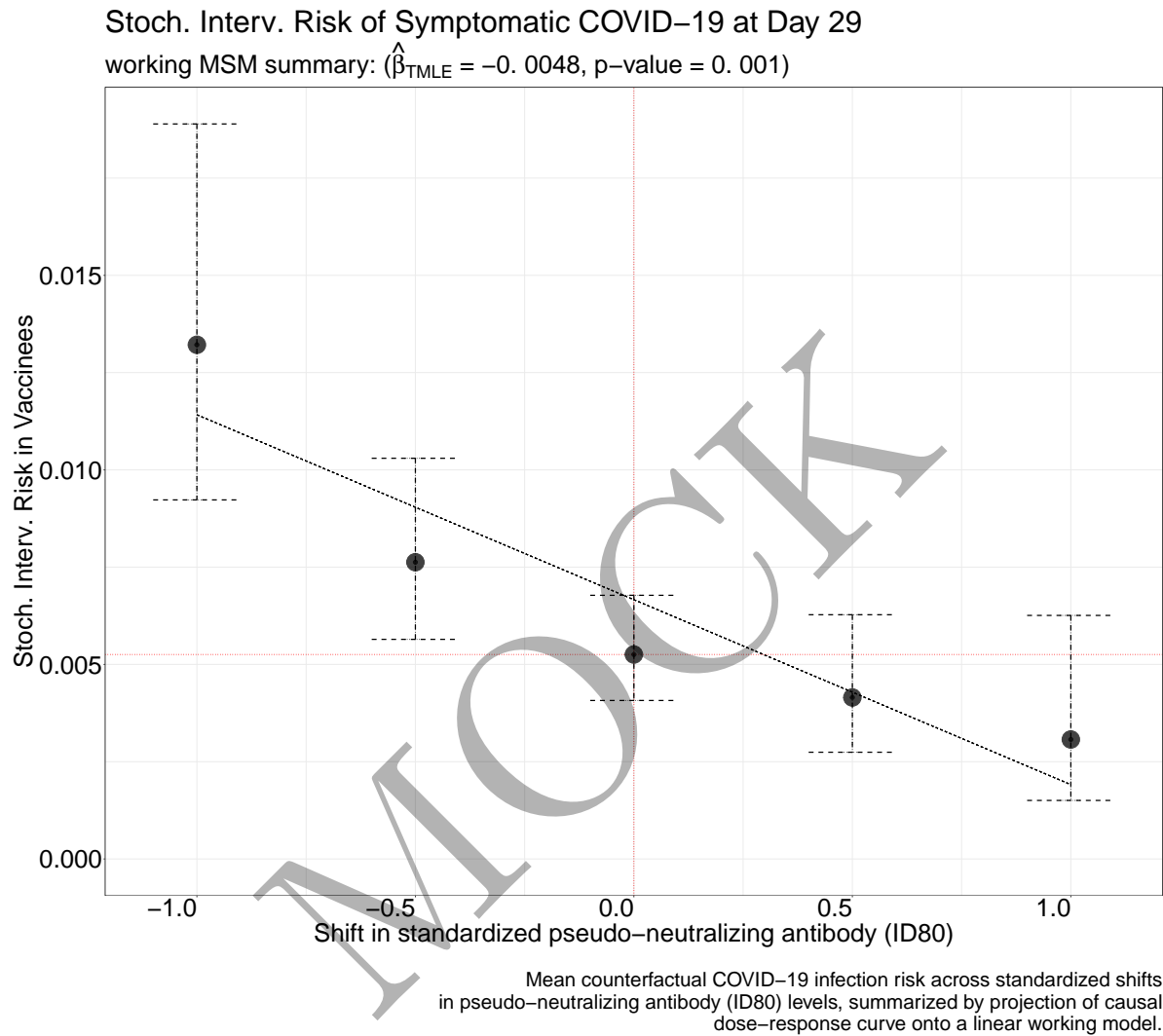


Figure 1.15: Stochastic interventional risk estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29



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

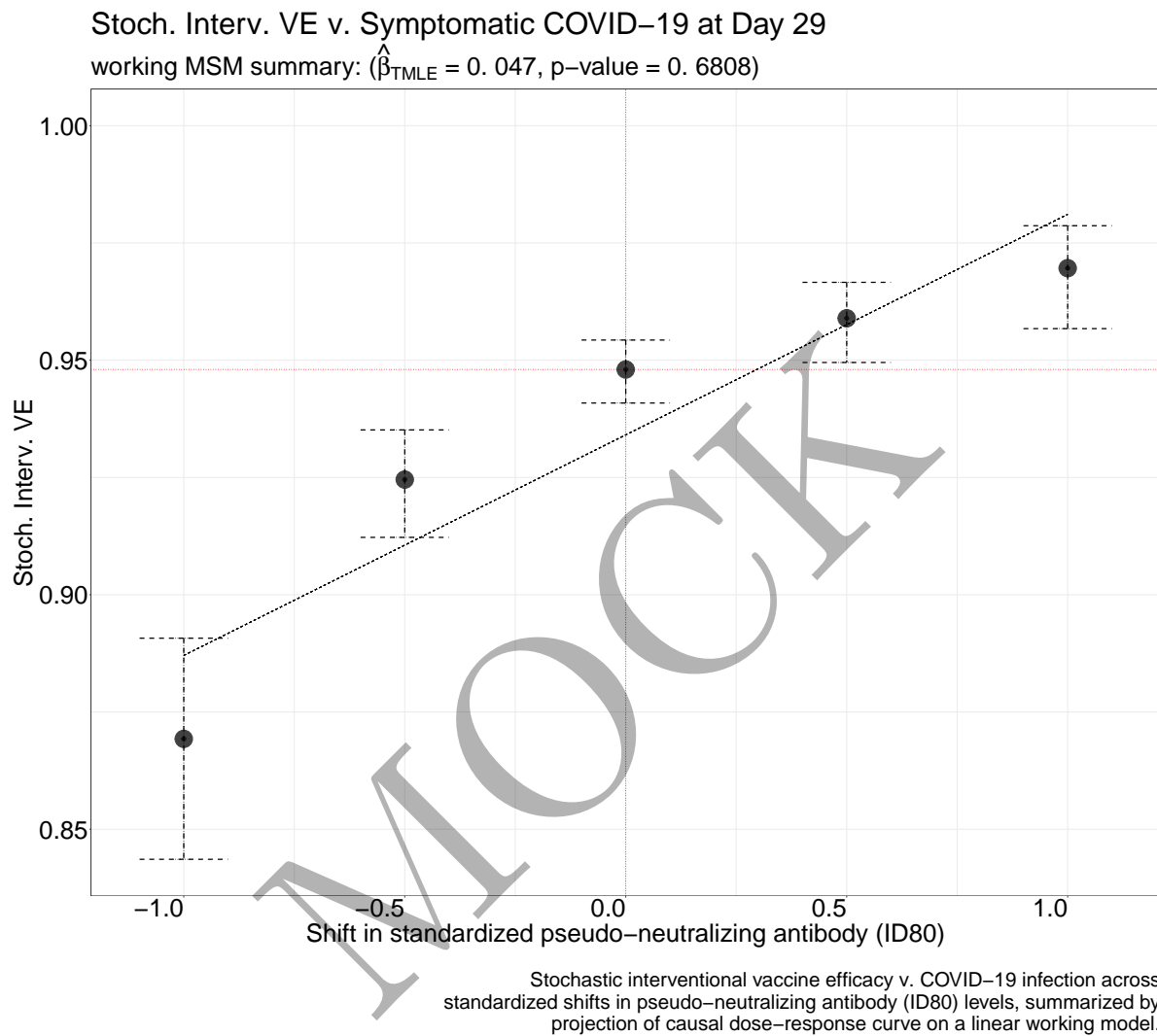


Figure 1.16: Stochastic interventional VE estimates, with confidence intervals, for pseudo-neutralizing antibody (ID80) at Day 29

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## Chapter 2

# Mediators of Vaccine Efficacy

Table 2.1: 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 | NA                                | NA                    | NA                    |
| Day 29 | Binding Antibody to Spike    | NA                                | NA                    | NA                    |
| Day 29 | Binding Antibody to RBD      | NA                                | NA                    | NA                    |
| Day 29 | PsV Neutralization 50% Titer | 0.441 (0.396, 0.482)              | 0.894 (0.865, 0.917)  | 0.794 (0.824, 0.765)  |
| Day 29 | PsV Neutralization 80% Titer | 0.915 <sup>a</sup> (0.713, 0.975) | 0.301 (-1.356, 0.793) | 0.127 (0.556, -0.303) |

<sup>a</sup> NA denotes insufficient overlap in antibody response between vaccinated and control participants.

Table 2.2: 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    | 0.900 (0.842, 0.937) | 0.403 (0.136, 0.587)   | 0.183 (0.316, 0.050)   |
| Day 57 | Binding Antibody to RBD      | 0.924 (0.867, 0.957) | 0.210 (-0.253, 0.502)  | 0.084 (0.249, -0.082)  |
| Day 57 | PsV Neutralization 50% Titer | 0.917 (0.839, 0.957) | 0.282 (-0.245, 0.585)  | 0.117 (0.315, -0.081)  |
| Day 57 | PsV Neutralization 80% Titer | 0.919 (0.871, 0.950) | 0.258 (-0.062, 0.481)  | 0.106 (0.235, -0.023)  |
| Day 29 | Binding Antibody to Spike    | 0.953 (0.882, 0.981) | -0.261 (-1.910, 0.454) | -0.082 (0.212, -0.377) |
| Day 29 | Binding Antibody to RBD      | 0.941 (0.888, 0.969) | -0.007 (-0.764, 0.425) | -0.002 (0.196, -0.201) |
| Day 29 | PsV Neutralization 50% Titer | 0.906 (0.827, 0.948) | 0.371 (-0.039, 0.619)  | 0.164 (0.346, -0.017)  |
| Day 29 | PsV Neutralization 80% Titer | 0.915 (0.864, 0.946) | 0.305 (-0.009, 0.521)  | 0.129 (0.263, -0.005)  |

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## Chapter 3

# Appendix

- This report was built from the [CoVPN/correlates\\_reporting](https://github.com/CoVPN/correlates_reporting) repository with commit hash 26a0bd0db55903868ad9d18674aa22780290feba. A diff of the changes introduced by that commit may be viewed at [https://github.com/CoVPN/correlates\\_reporting/commit/26a0bd0db55903868ad9d18674aa22780290feba](https://github.com/CoVPN/correlates_reporting/commit/26a0bd0db55903868ad9d18674aa22780290feba)
- The sha256 hash sum of the raw input file, “COVID\_VEtrial\_practicedata\_primarystage1.csv”: 45ff85033ffbc717462d678b41bc4060a12c7bc60952e2cb72297bb5500b97b9
- The sha256 hash sum of the processed file, “practice\_data.csv”: b0200c809e38148017579ee8697fc0ff5682aac2c67ced0474