COVID-19 Correlates of Protection Analysis Report

mock Study

USG COVID-19 Response Biostatistics Team

May 15, 2021

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Chapter 1

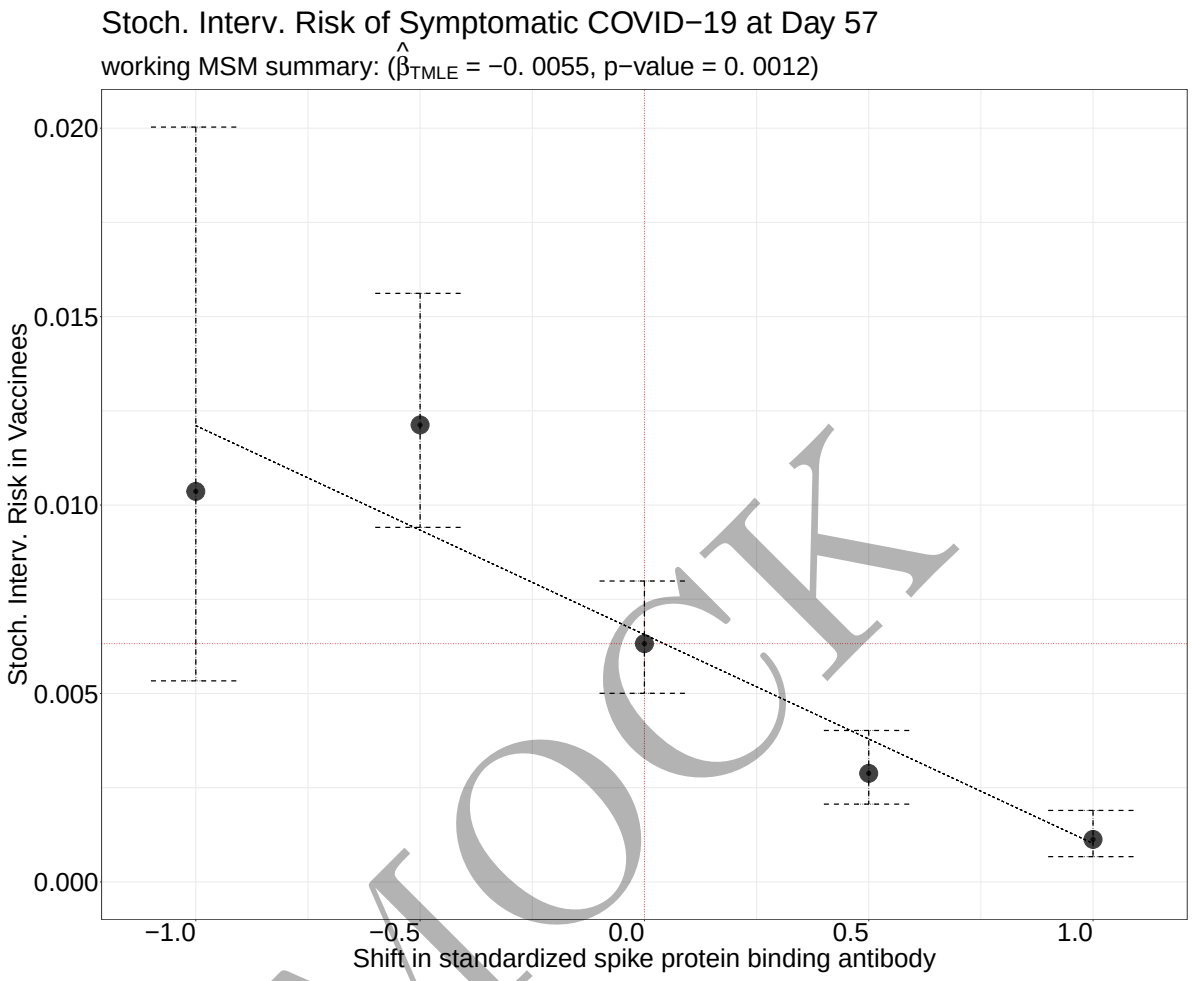
Stochastic Interventional Vaccine Efficacy Effects

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 Stoch. Interv. mCoP Figures for Day 57

1.1.1 Stoch interv. risk: spike protein binding antibody

\begin{figure}[H]



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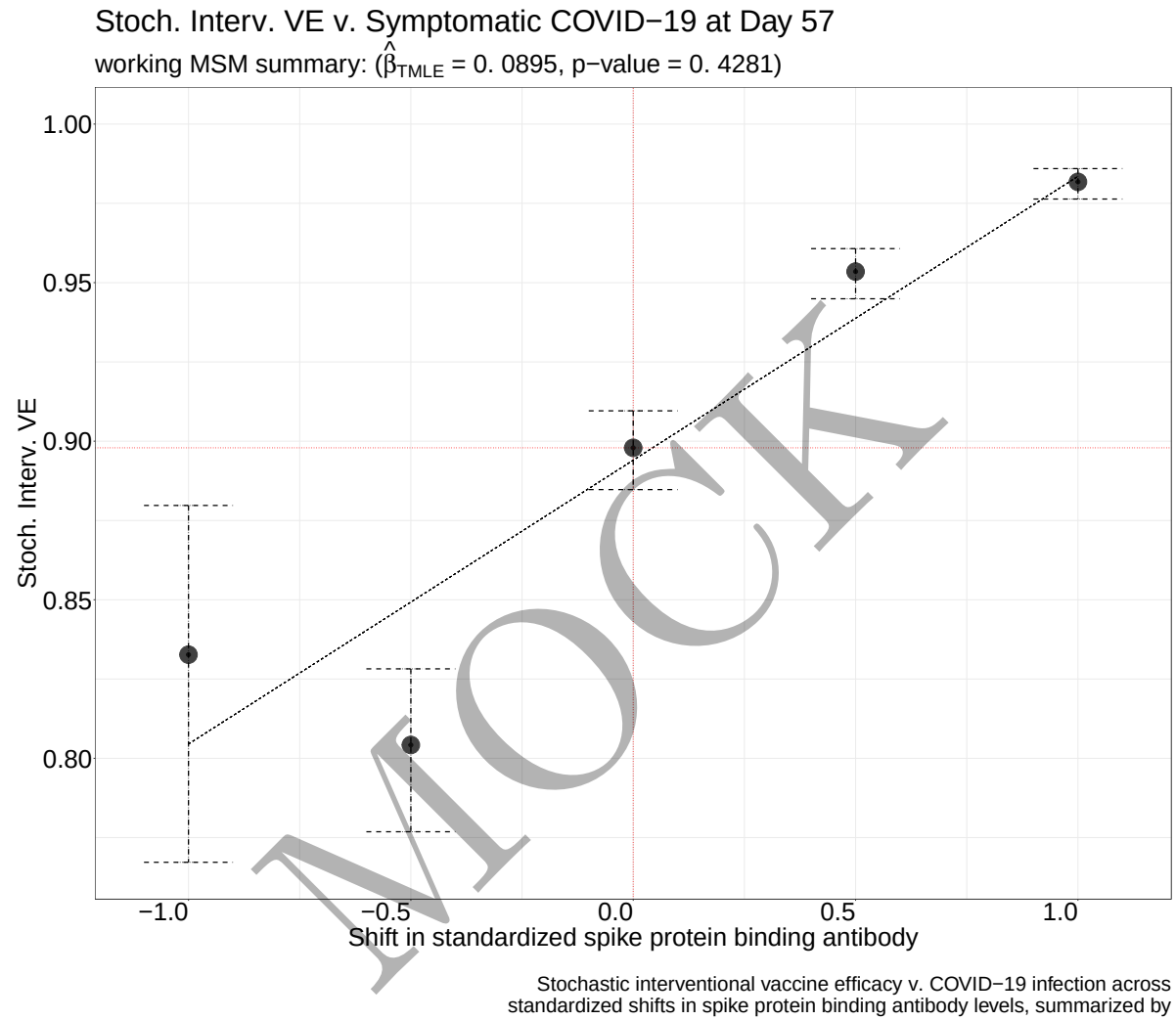
\caption{Stochastic interventional risk estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[1]]]` at `r this_time_print`} \end{figure}

1.1.2 Stoch. interv. VE: spike protein binding antibody

\begin{figure}[H]



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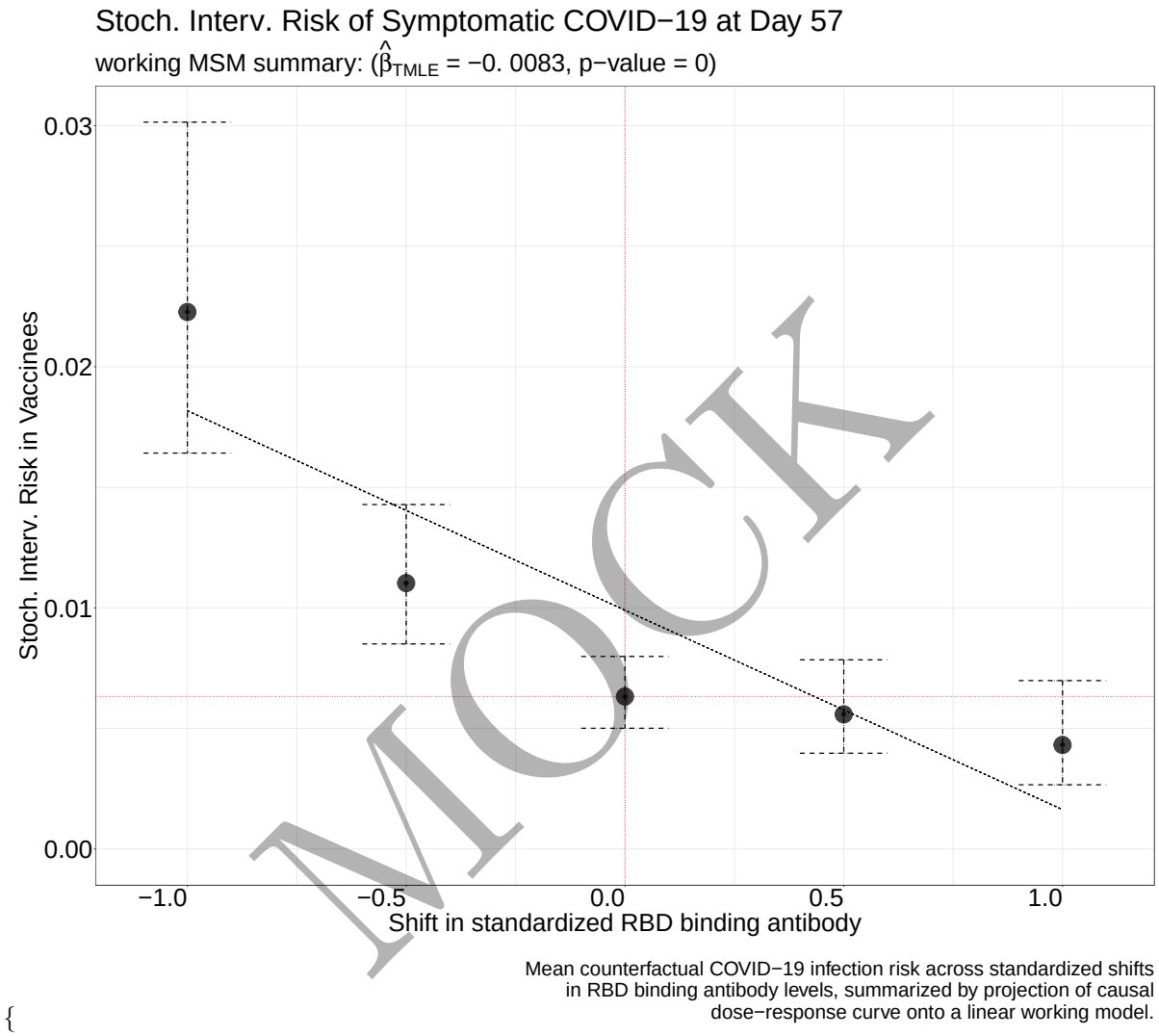
\caption{Stochastic interventional VE estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[1]]]` at `r this_time_print`} \end{figure}

1.1.3 Stoch. interv. risk: RBD binding antibody

\begin{figure}[H]



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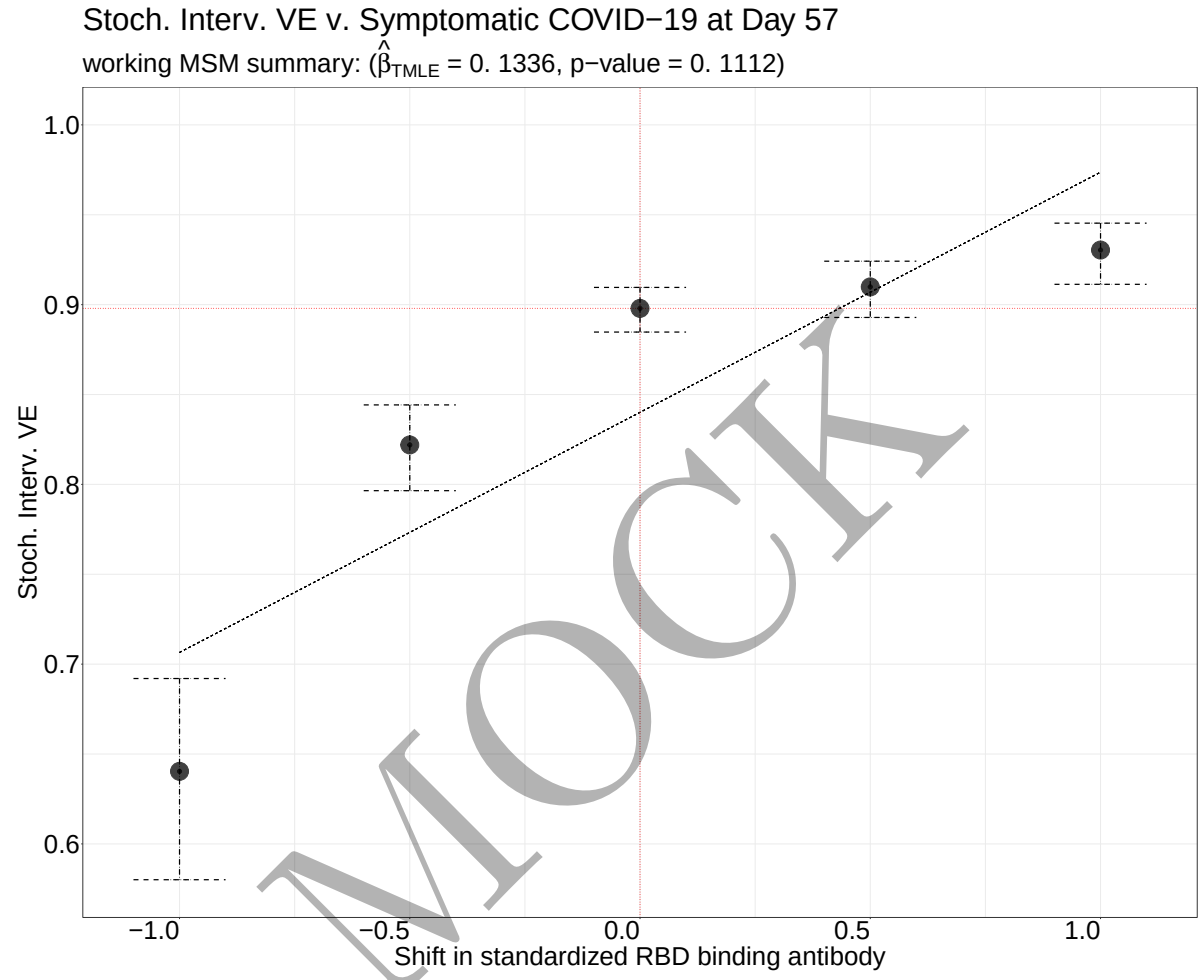
\caption{Stochastic interventional risk estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[2]]]` at `r this_time_print`} \end{figure}

1.1.4 Stoch. interv. VE: RBD binding antibody

\begin{figure}[H]



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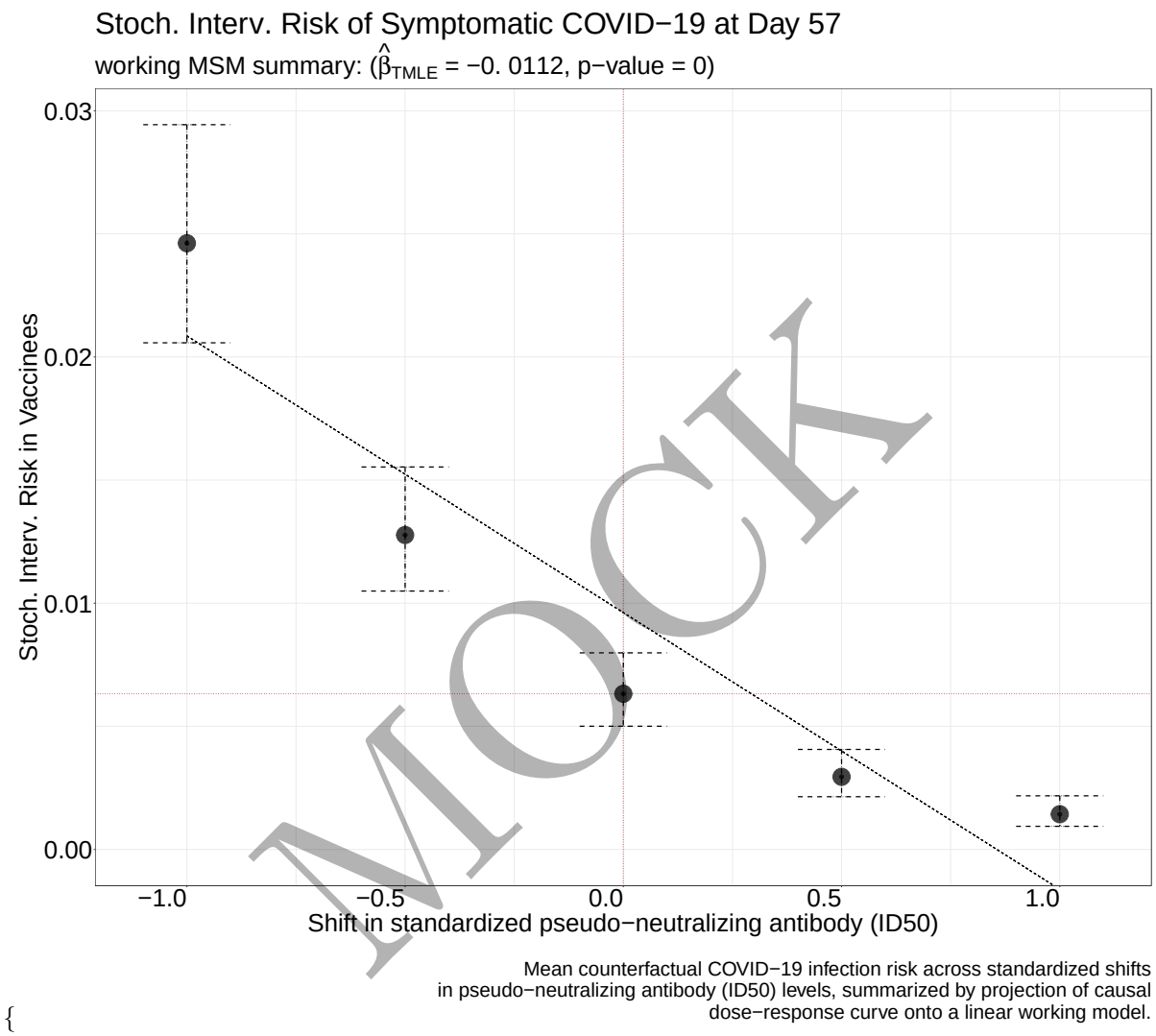
\caption{Stochastic interventional VE estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[2]]]` at `r this_time_print`} \end{figure}

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

\begin{figure}[H]



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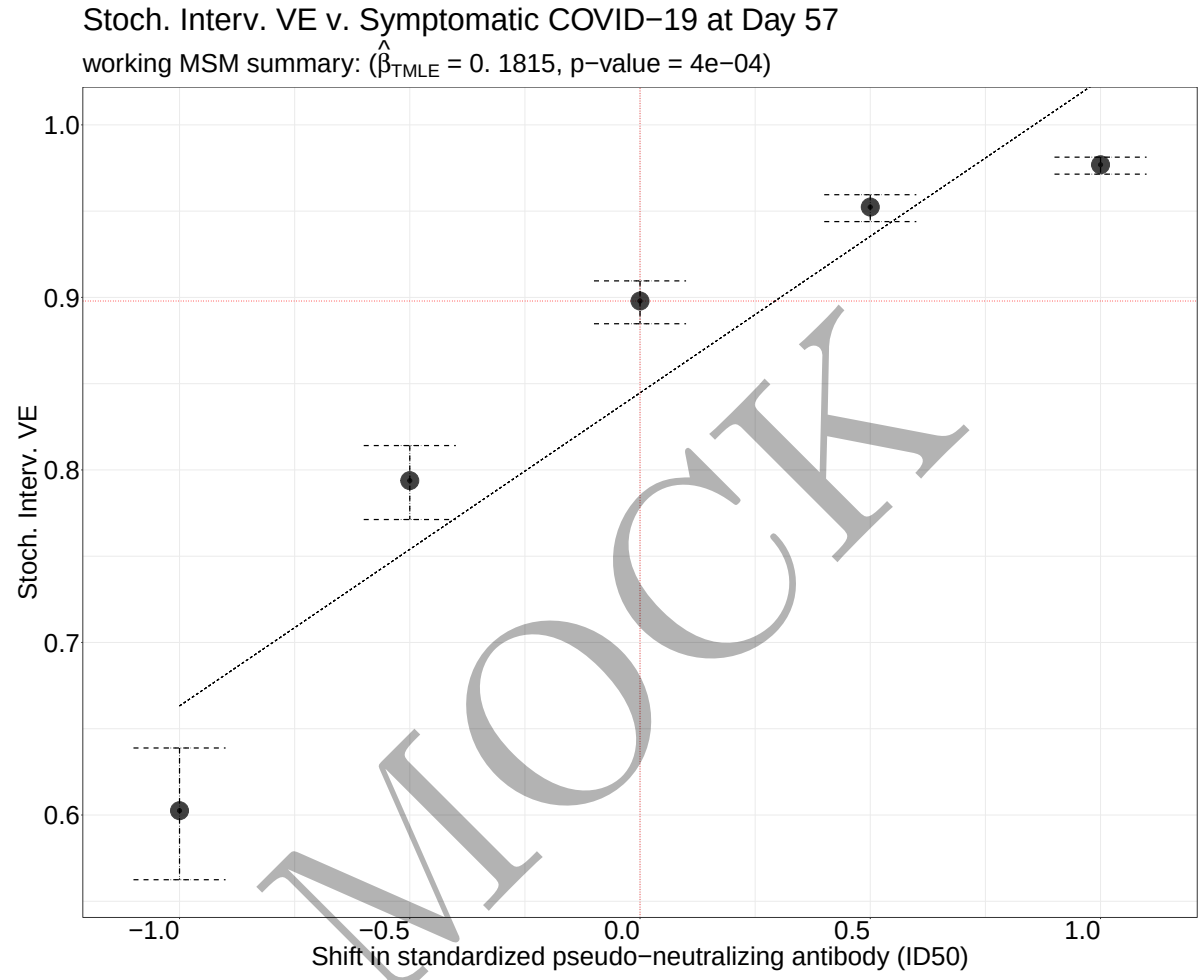
\caption{Stochastic interventional risk estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[3]]]` at `r this_time_print`} \end{figure}

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

\begin{figure}[H]



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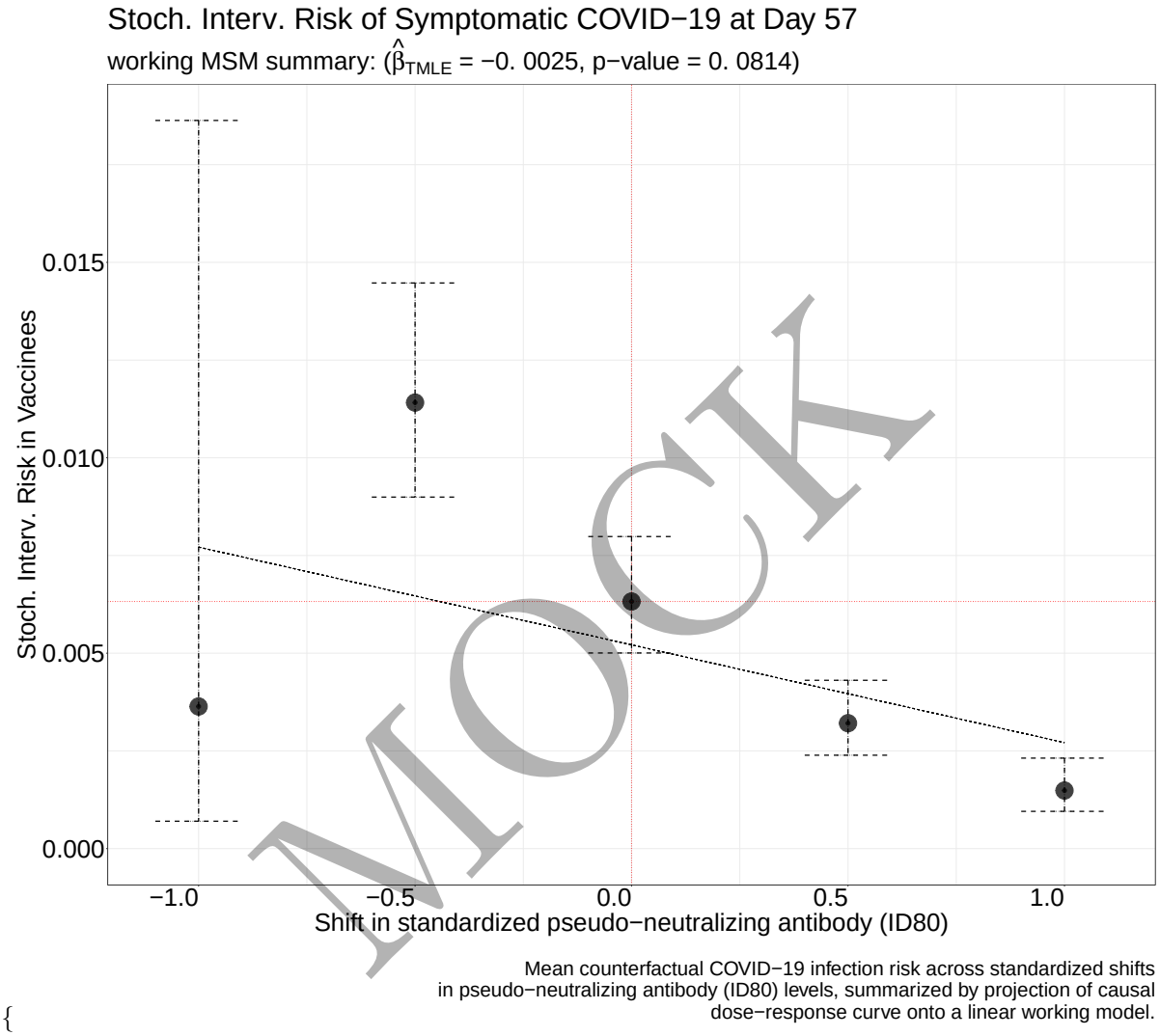
\caption{Stochastic interventional VE estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[3]]]` at `r this_time_print`} \end{figure}

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

\begin{figure}[H]



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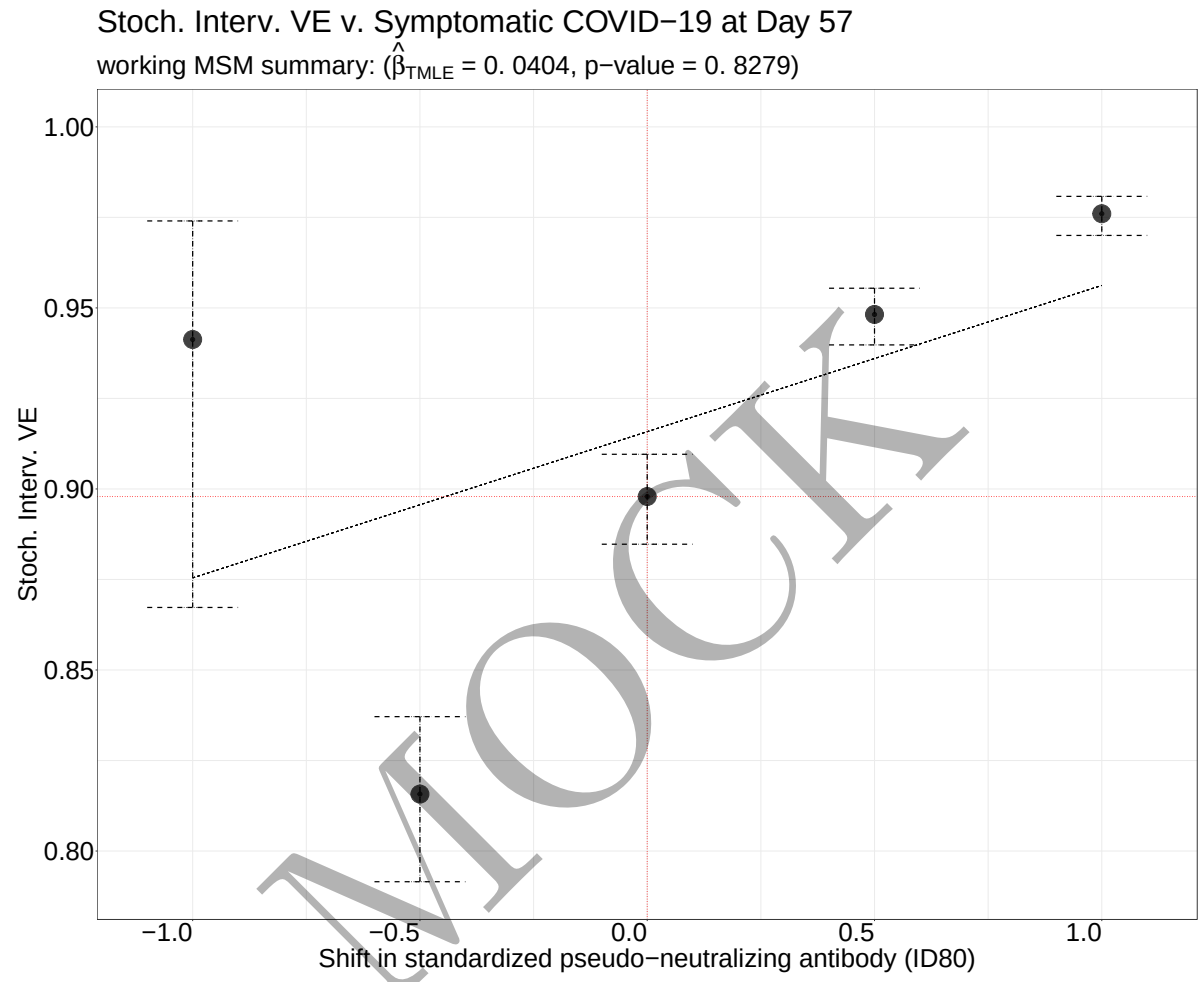
\caption{Stochastic interventional risk estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[4]]]` at `r this_time_print`} \end{figure}

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

\begin{figure}[H]



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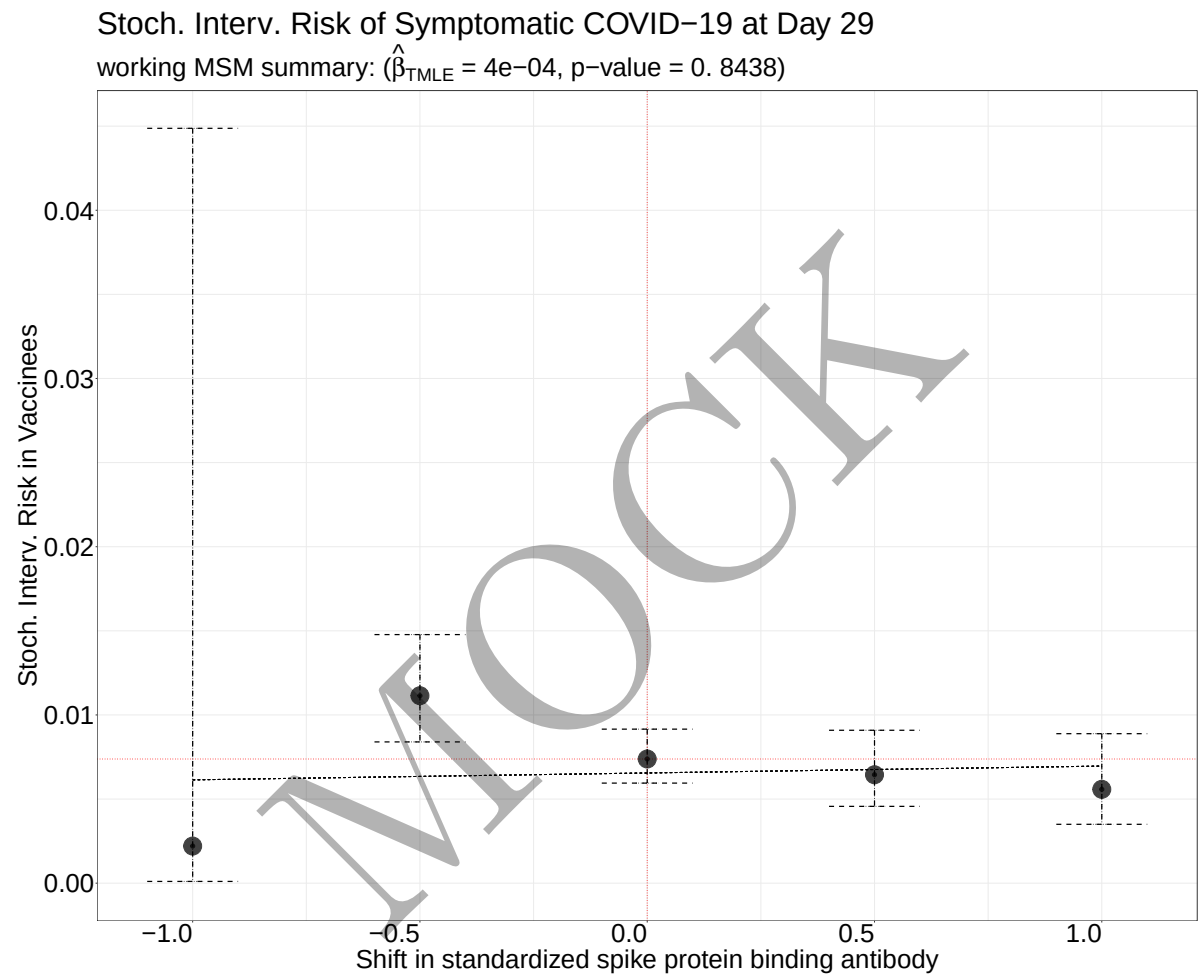
\caption{Stochastic interventional VE estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[4]]]` at `r this_time_print`} \end{figure}

1.2 Stoch. Interv. mCoP Figures for Day 29

1.2.1 Stoch. interv. risk: spike protein binding antibody

\begin{figure}[H]



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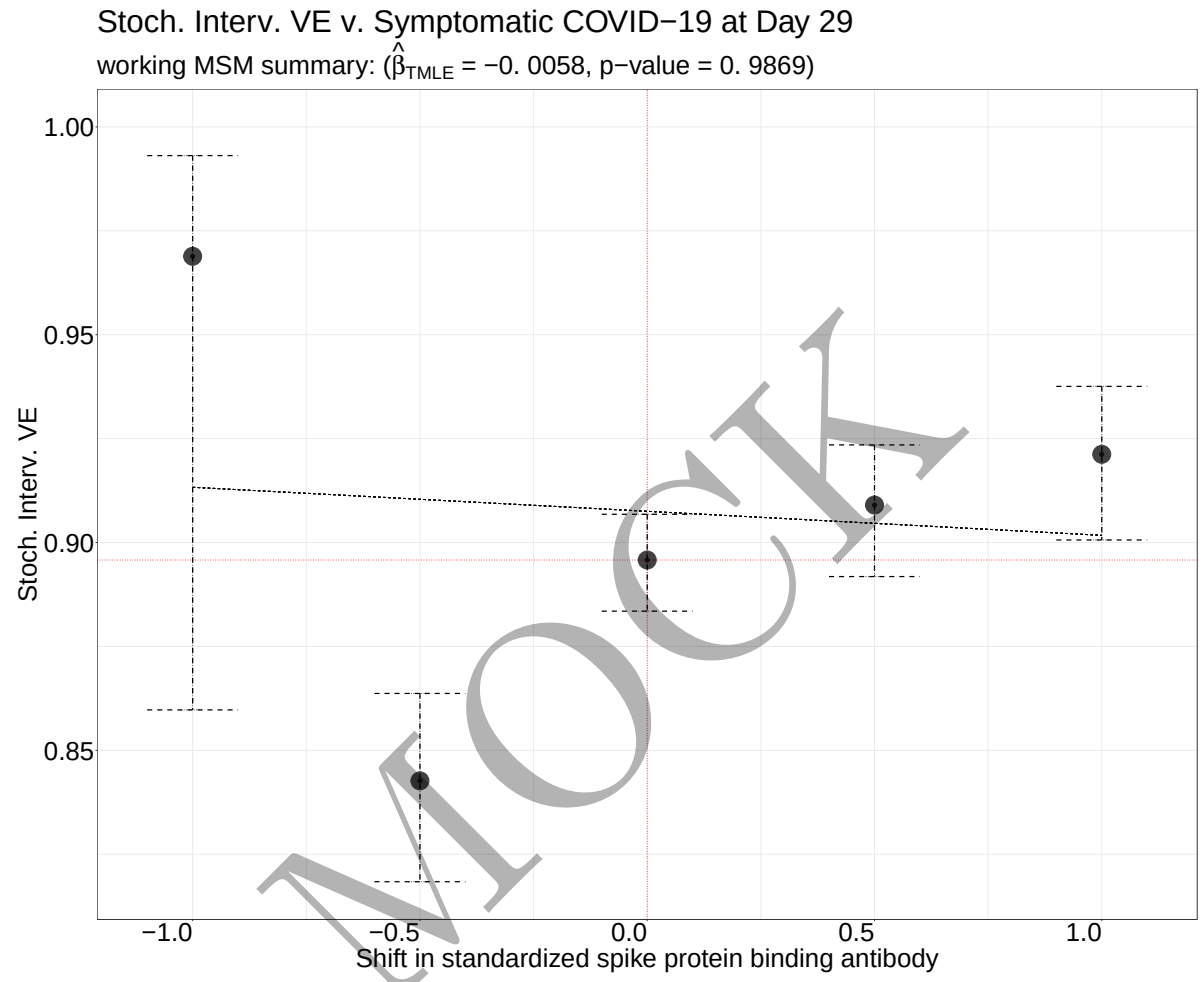
\caption{Stochastic interventional risk estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[1]]]` at `r this_time_print`} \end{figure}

1.2.2 Stoch. interv. VE: spike protein binding antibody

\begin{figure}[H]



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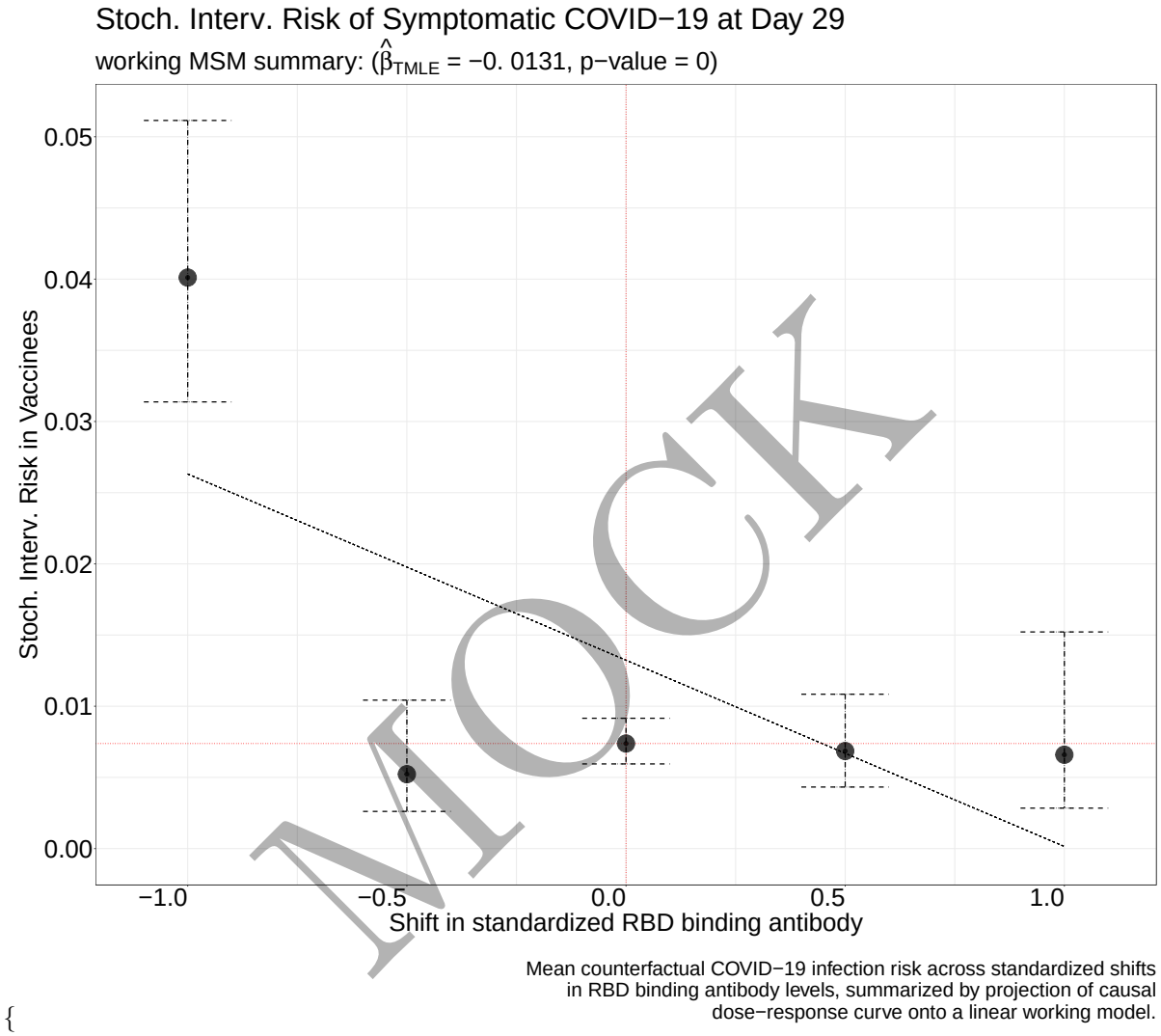
\caption{Stochastic interventional VE estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[1]]]` at `r this_time_print`} \end{figure}

1.2.3 Stoch. interv. risk: RBD binding antibody

\begin{figure}[H]



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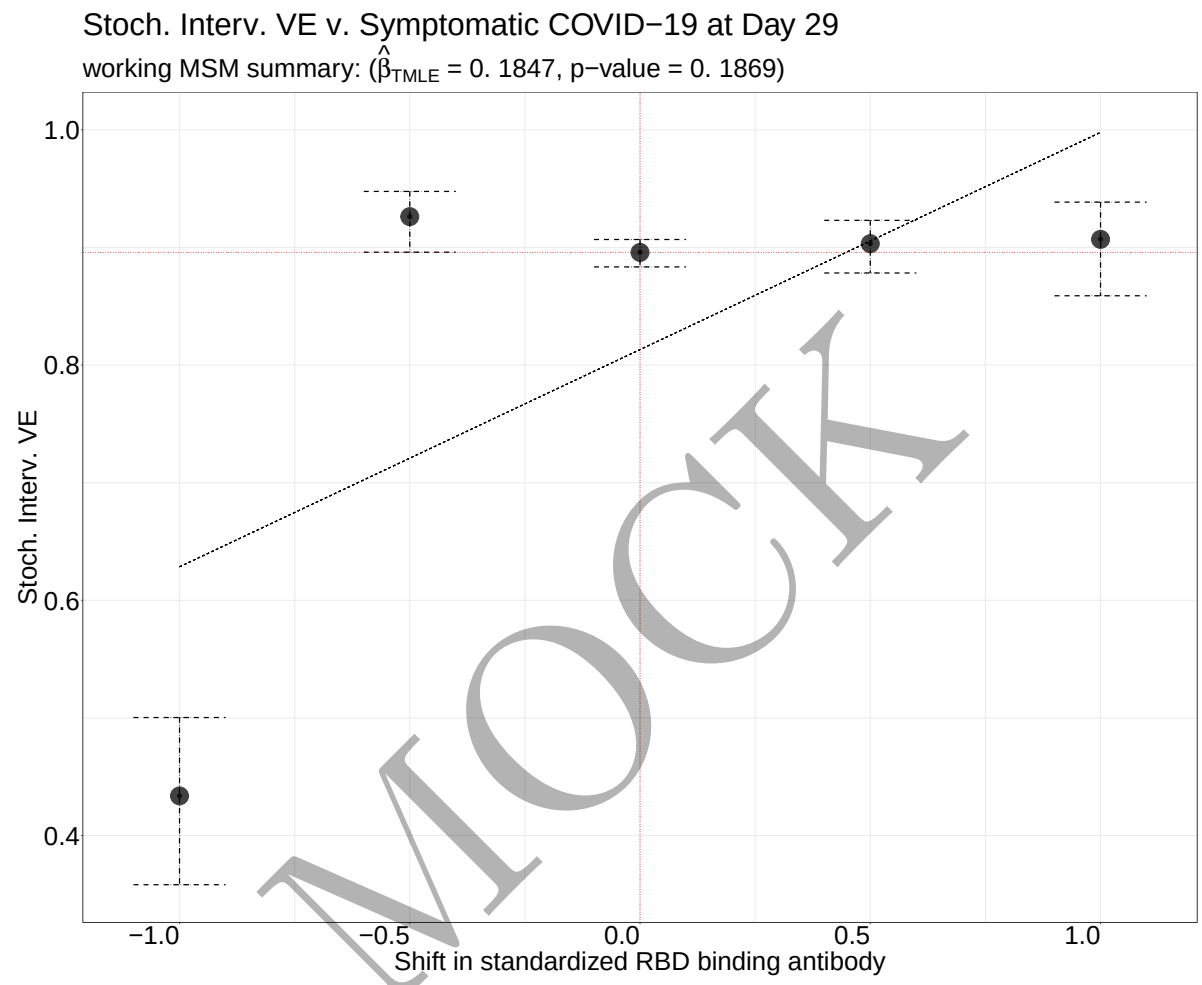
\caption{Stochastic interventional risk estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[2]]]` at `r this_time_print`} \end{figure}

1.2.4 Stoch. interv. VE: RBD binding antibody

\begin{figure}[H]



Stochastic interventional vaccine efficacy v. COVID−19 infection across standardized shifts in RBD binding antibody levels, summarized by projection of causal dose−response curve on a linear working model.

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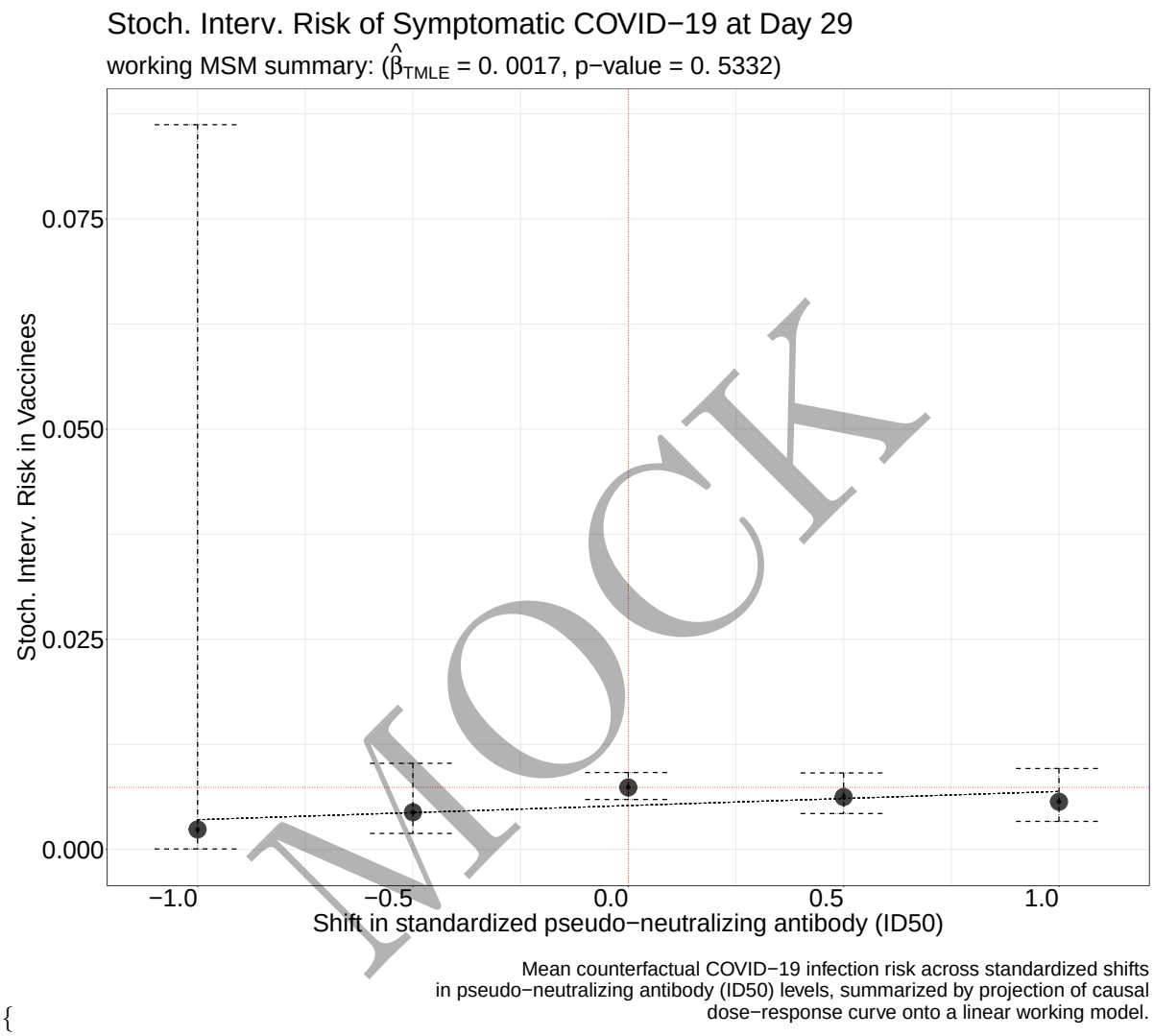
\caption{Stochastic interventional VE estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[2]]]` at `r this_time_print`} \end{figure}

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

\begin{figure}[H]



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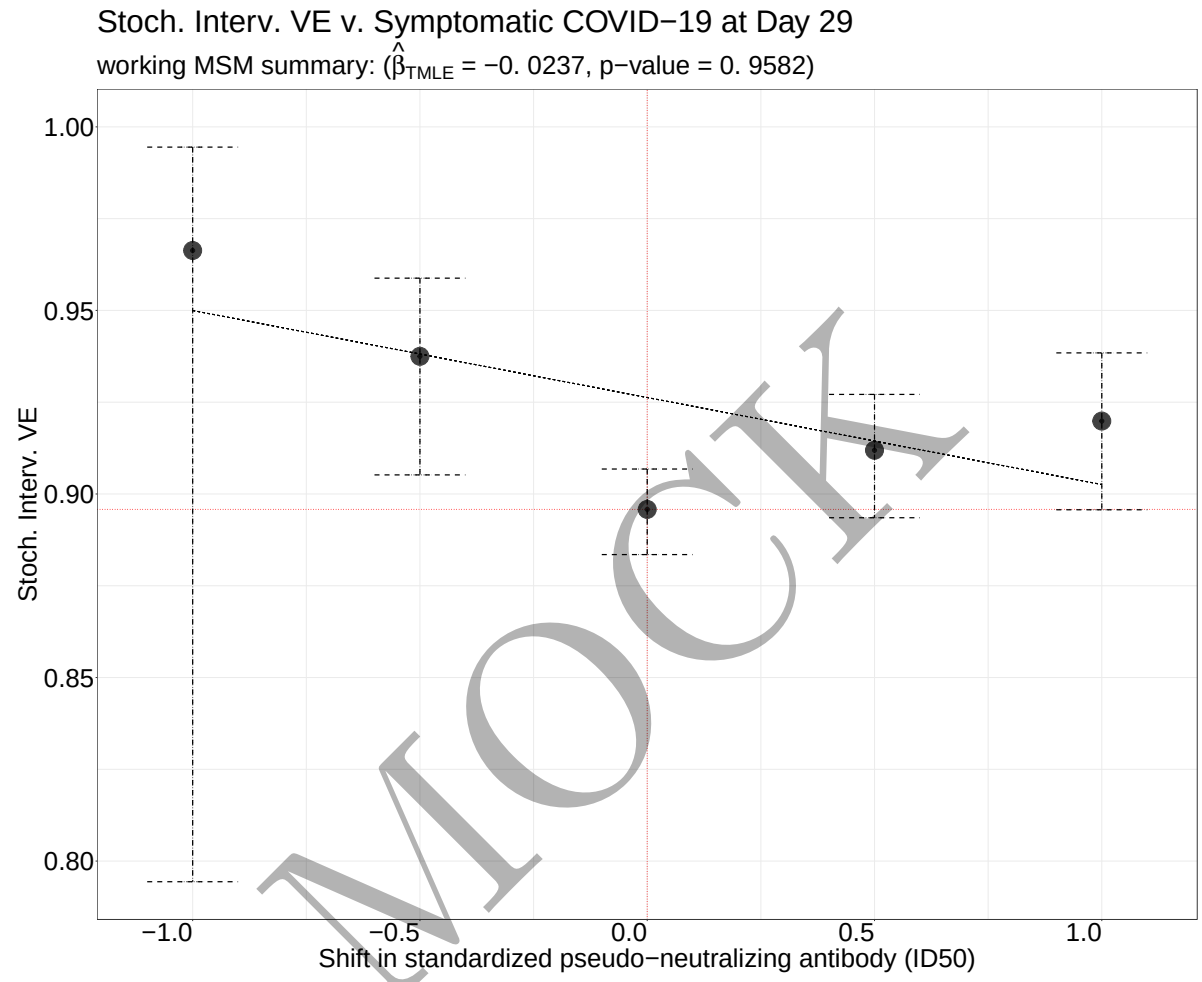
\caption{Stochastic interventional risk estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[3]]]` at `r this_time_print`} \end{figure}

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

\begin{figure}[H]

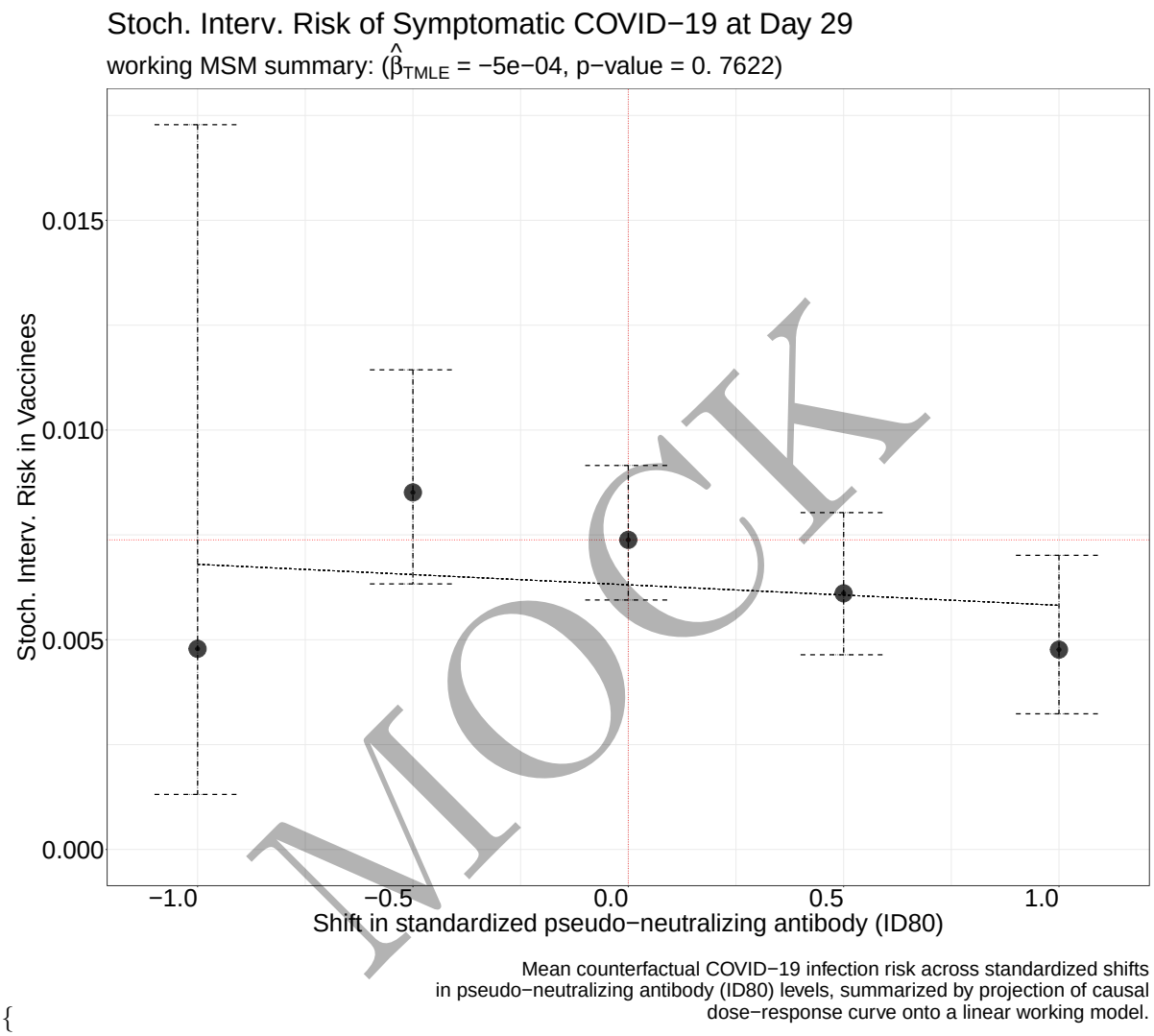


{Stochastic interventional vaccine efficacy v. COVID−19 infection across standardized shifts in pseudo−neutralizing antibody (ID50) levels, summarized by projection of causal dose−response curve on a linear working model.}

\caption{Stochastic interventional VE estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[3]]]` at `r this_time_print`} \end{figure}

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

\begin{figure}[H]



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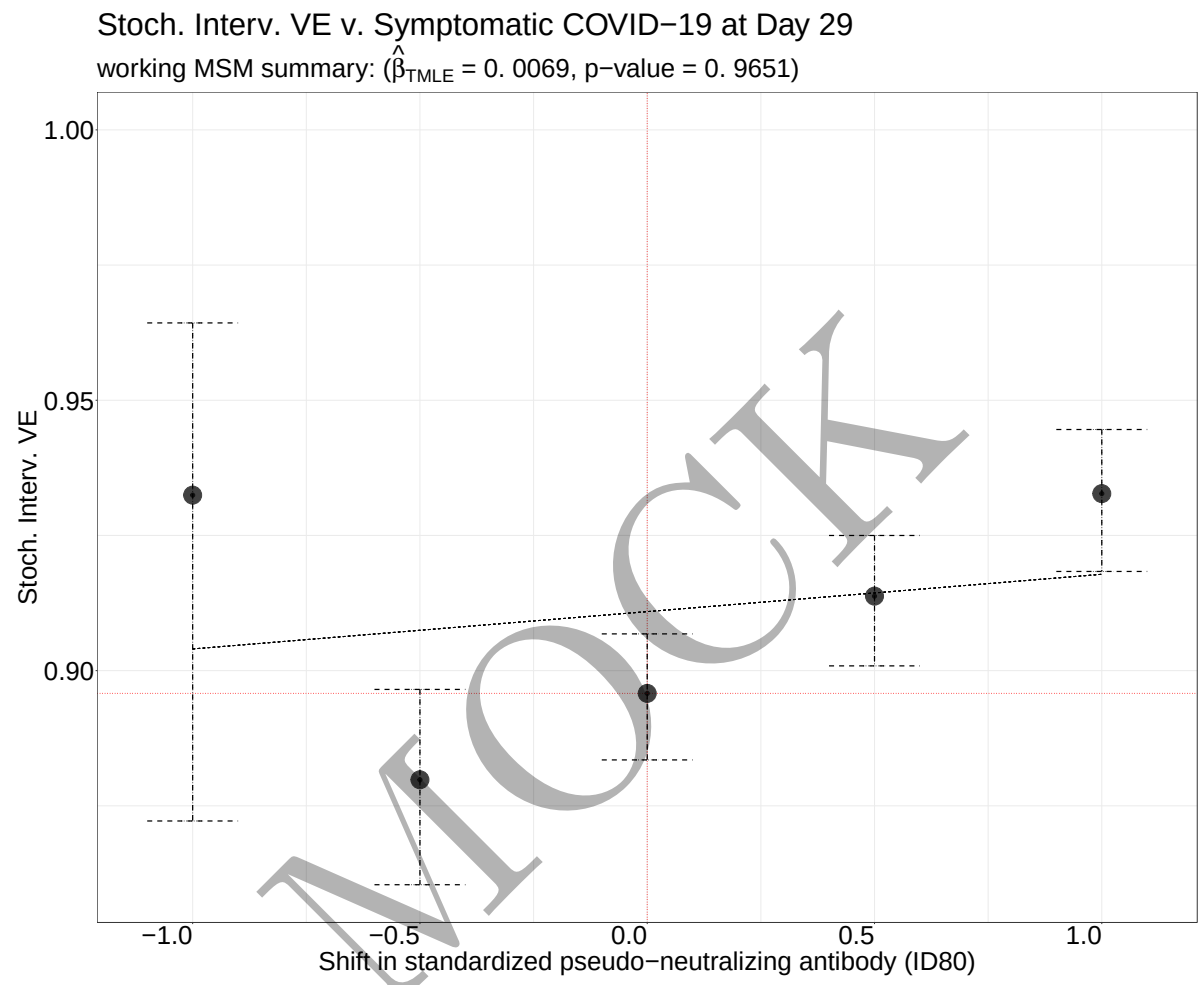
\caption{Stochastic interventional risk estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[4]]]` at `r this_time_print`} \end{figure}

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

\begin{figure}[H]



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\caption{Stochastic interventional VE estimates, with confidence intervals, for `r marker_to_name[[markers_name_short[4]]]` at `r this_time_print`} \end{figure}

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	0.205 (0.142, 0.262)	0.856 (0.823, 0.883)	0.894 (0.927, 0.861)
Day 29	PsV Neutralization 80% Titer	0.823 (0.729, 0.884)	0.352 (-0.032, 0.593)	0.200 (0.408, -0.007)

[a] 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	0.865 (0.723, 0.934)	0.157 (-0.577, 0.549)	0.078 (0.369, -0.212)
Day 57	Binding Antibody to RBD	0.777 (0.677, 0.846)	0.487 (0.305, 0.622)	0.308 (0.450, 0.166)
Day 57	PsV Neutralization 50% Titer	0.736 (0.643, 0.805)	0.568 (0.485, 0.637)	0.386 (0.480, 0.293)
Day 57	PsV Neutralization 80% Titer	0.742 (0.646, 0.812)	0.557 (0.460, 0.637)	0.375 (0.479, 0.272)
Day 29	Binding Antibody to Spike	0.890 (0.784, 0.944)	-0.047 (-0.927, 0.431)	-0.021 (0.260, -0.303)
Day 29	Binding Antibody to RBD	0.940 (0.701, 0.988)	-0.909 (-7.917, 0.591)	-0.299 (0.407, -1.004)
Day 29	PsV Neutralization 50% Titer	0.917 (0.700, 0.977)	-0.388 (-3.702, 0.590)	-0.151 (0.409, -0.712)
Day 29	PsV Neutralization 80% Titer	0.905 (0.809, 0.953)	-0.208 (-1.262, 0.355)	-0.087 (0.201, -0.376)

Chapter 3

Appendix

- This report was built from the `CoVPN/correlates_reporting` repository with commit hash cf9049a5babc4b9ceba7d58cf61697c5a28b64bb. A diff of the changes introduced by that commit may be viewed at https://github.com/CoVPN/correlates_reporting/commit/cf9049a5babc4b9ceba7d58cf61697c5a28b64bb
- The sha256 hash sum of the raw input file, "COVID_VEtrial_practicedata_primarystage1.csv": 2353971c2e14399ede55ef6ba0d4e624626433dc15ec507c2482bb886210019a
- The sha256 hash sum of the processed file, "practice_data.csv": 6250066f886245b78f7aa29fefc615ba5d10118448f298c39e