COVID correlates analysis report CoR

2021-02-03

1 Univariate CoR: Cox Proportional Hazards Modeling of Relative and Absolute Risk

All analyses for D57 markers are run on the population with EventTimePrimaryD57>=7. The main regression model is the Cox proportional hazards model. All plots are made with Cox models fit unless specified otherwise. The trichotomized variables in Table 1 are defined with respect to inverse probability weighted quantiles computed using the Hmisc::wtd.quantile function.

Table 1: Inference for Day 57 antibody marker covariate-adjusted correlates of risk of COVID in the vaccine group: Hazard ratios per 10-fold increment in the marker*

Mock Immunologic Marker	No. cases / No. at-risk**	HR per 10-fold incr. Pt. Est.	95% CI	P-value (2-sided)	q-value	FWER
Spike IgG (IU/ml)	72/13,254	0.08	(0.05-0.12)	<0.001	<0.001	<0.001
RBD IgG (IU/ml)	72/13,254	0.17	(0.12-0.25)	<0.001	<0.001	<0.001
PsV-nAb ID50	72/13,254	0.26	(0.20-0.34)	<0.001	<0.001	<0.001
PsV-nAb ID80	72/13,254	0.39	(0.29-0.52)	<0.001	<0.001	<0.001

*Baseline covariates adjusted for: age in years, at risk or not, community of color or not, baseline risk score. Average follow-up time 175 days, maximum follow-up time 185 days.
**No. at-risk = number of per-protocol baseline negative vaccine recipients at-risk for COVID at Day 57; no. cases = number of this cohort with an observed COVID endpoints.

Table 2: Inference for Day 57 antibody marker covariate-adjusted correlates of risk of COVID in the vaccine group: Hazard ratios for Middle vs. Upper tertile vs. Lower tertile*

Mock Immunologic Marker	Tertile	No. cases / No. at-risk**	Attack rate	Haz. Ratio Pt. Est.	Haz. Ratio 95% CI	P-value (2-sided)	Overall P-value***	Overall q-value	Overall FWER
Spike IgG (IU/ml)	Lower	67/4,373	0.0153	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	4/4,449	0.0009	0.04	(0.01-0.11)	<0.001			
	Upper	1/4,422	0.0002	0.00	(0.00-0.03)	<0.001			
RBD IgG (IU/ml)	Lower	45/4,395	0.0102	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	19/4,433	0.0043	0.24	(0.13-0.43)	<0.001			
	Upper	8/4,416	0.0018	0.05	(0.02-0.12)	<0.001			
PsV-nAb ID50	Lower	56/4,440	0.0126	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	9/4,416	0.0020	0.10	(0.05-0.22)	<0.001			
	Upper	6/4,388	0.0014	0.05	(0.02-0.11)	<0.001			
PsV-nAb ID80	Lower	40/4,392	0.0091	1	N/A	N/A	<0.001	<0.001	<0.001
	Middle	21/4,436	0.0047	0.43	(0.24-0.78)	0.005			
	Upper	11/4,417	0.0025	0.16	(0.08-0.34)	<0.001			
Placebo		713/13,299	0.0536						

*Baseline covariates adjusted for: age in years, at risk or not, community of color or not, baseline risk score. Average follow-up time 175 days, maximum follow-up time 185 days. Cutpoints: Spike IgG (IU/ml) [6.09, 6.7), RBD IgG (IU/ml) [5.68, 6.38), PsV-nAb ID50 [2.8, 3.66), PsV-nAb ID80 [3.08, 3.82).
**No. at-risk = number of per-protocol baseline negative vaccine recipients at-risk for COVID at Day 57; no. cases = number of this cohort with an observed COVID endpoints.
***Generalized Wald-test p-value of the null hypothesis that the hazard rate is constant across the Lower, Middle, and Upper tertile groups.

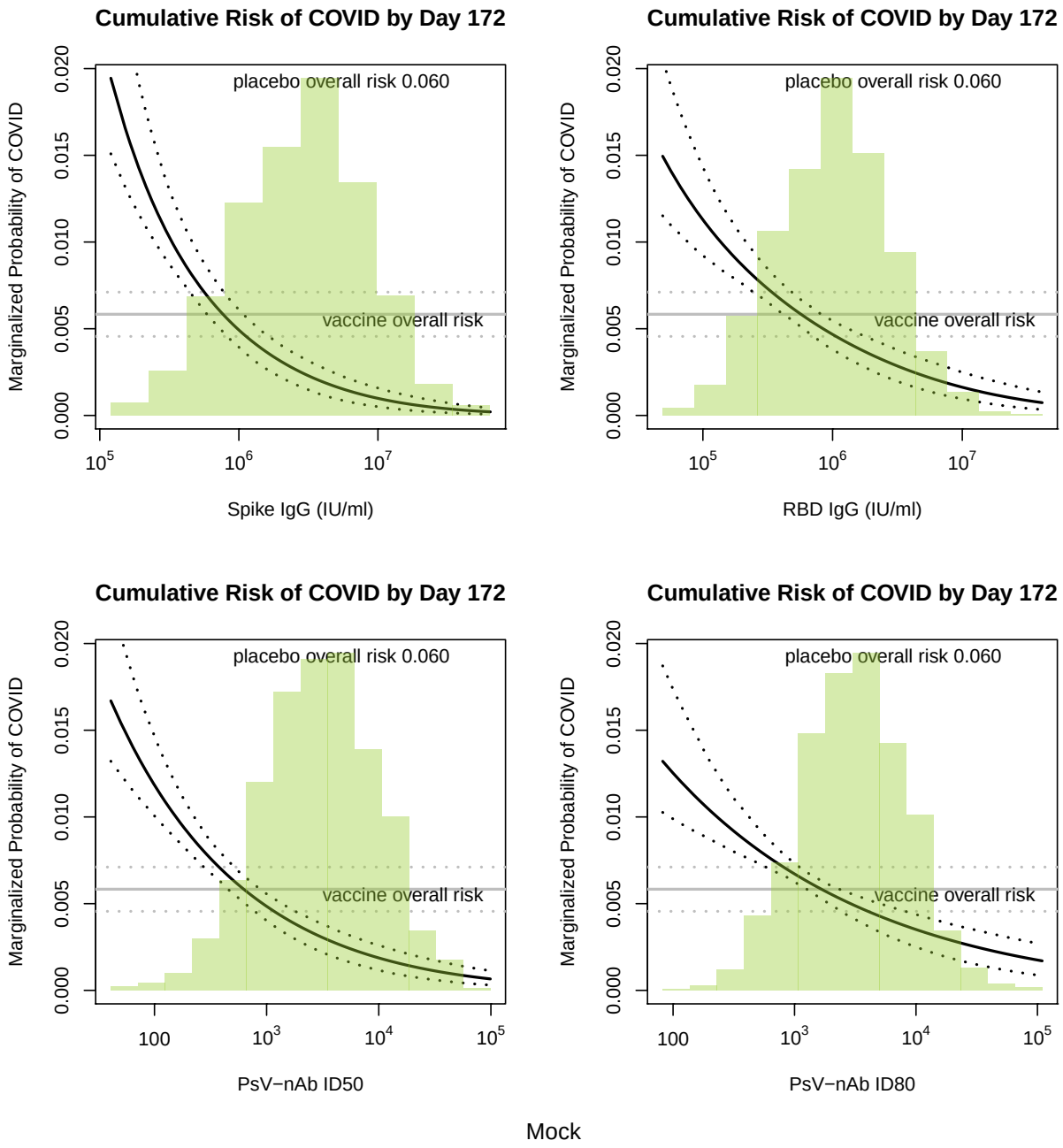

Figure 1: Marginalized cumulative risk by Day 172 as functions of Day 57 markers among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 172 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid.

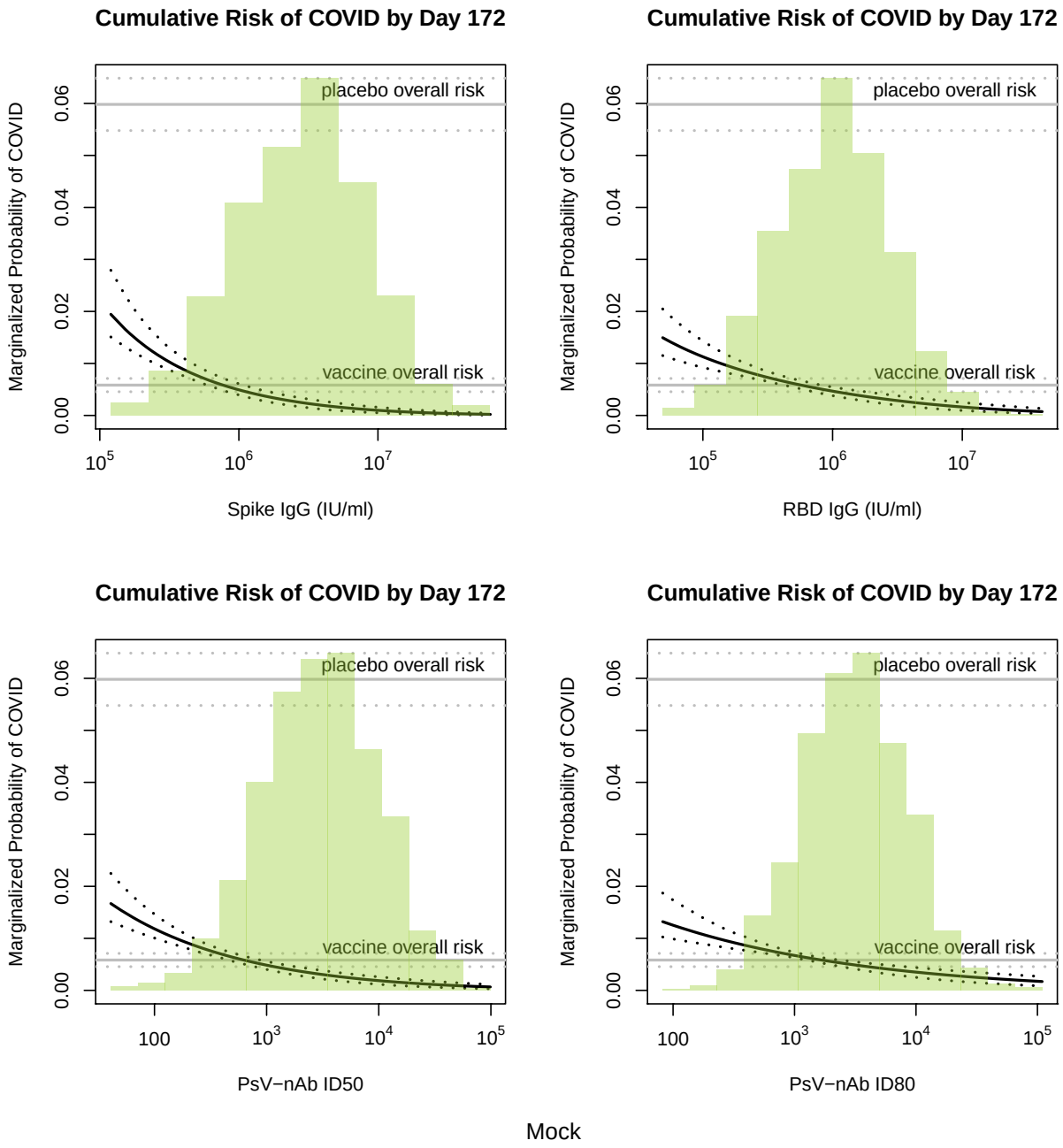

Figure 2: Marginalized cumulative risk by Day 172 as functions of Day 57 markers among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 172 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid.

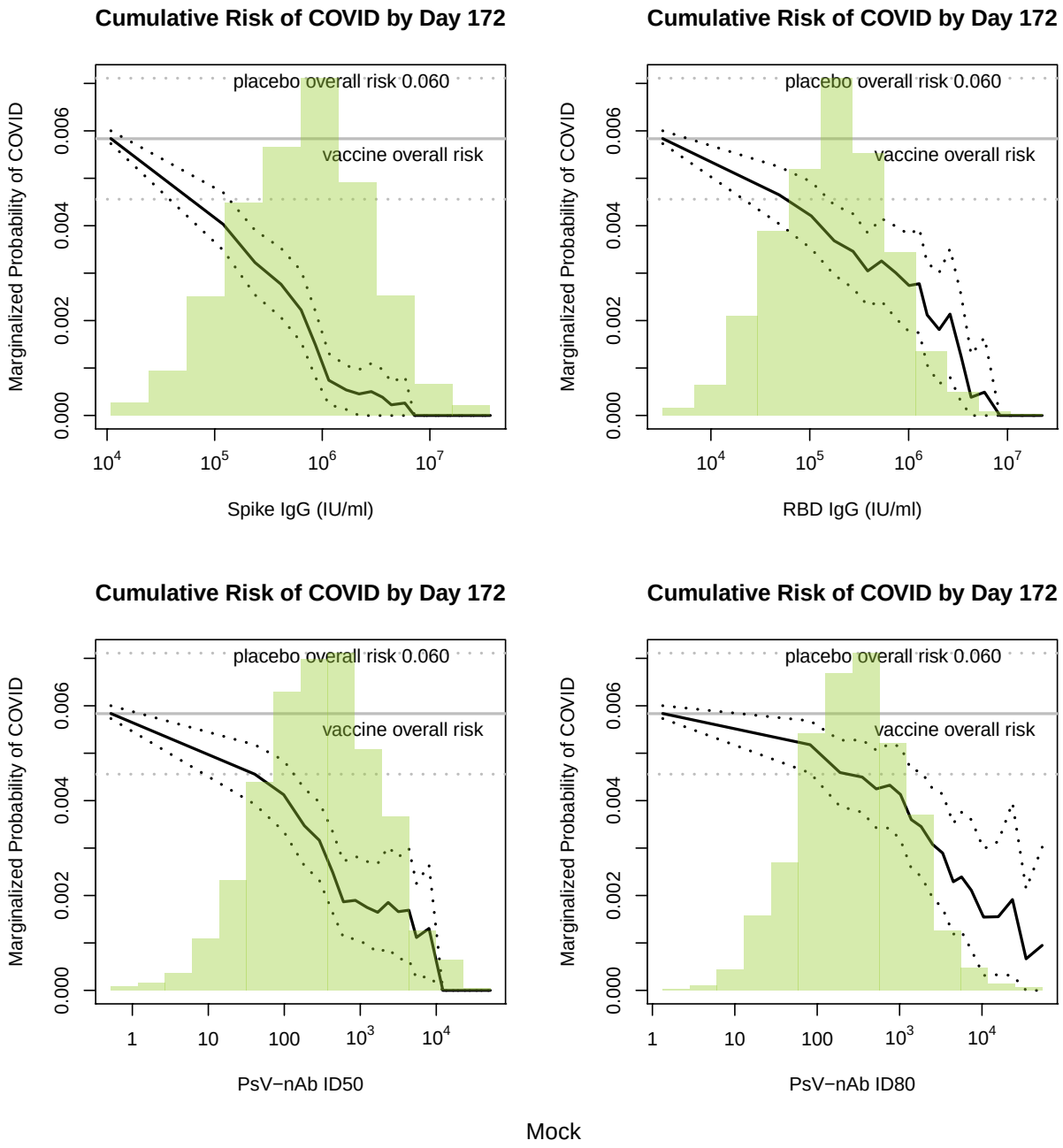

Figure 3: Marginalized cumulative risk by Day 172 as functions of Day 57 markers above a threshold among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 172 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid.

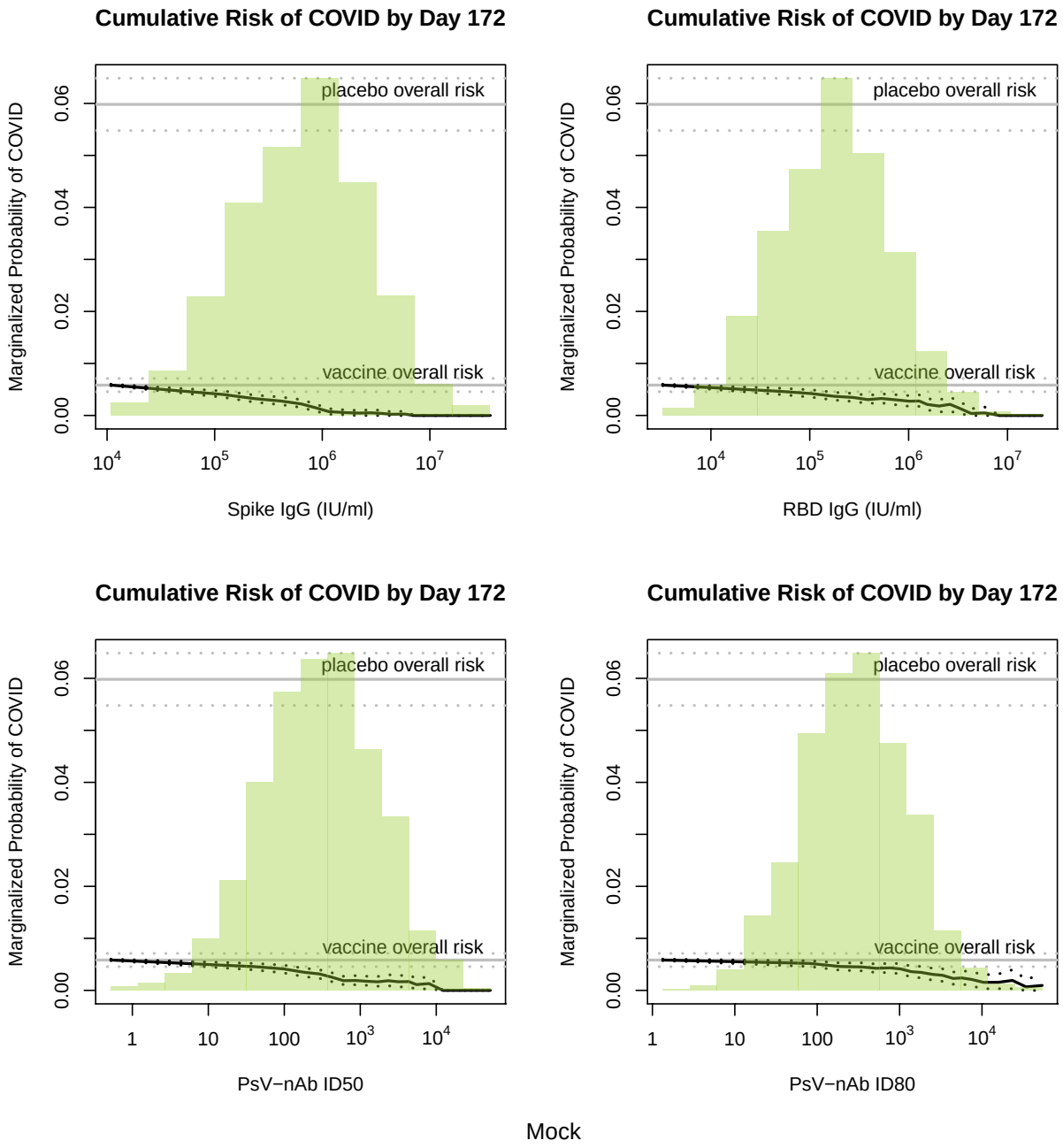

Figure 4: Marginalized cumulative risk by Day 172 as functions of Day 57 markers above a threshold among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 172 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid.

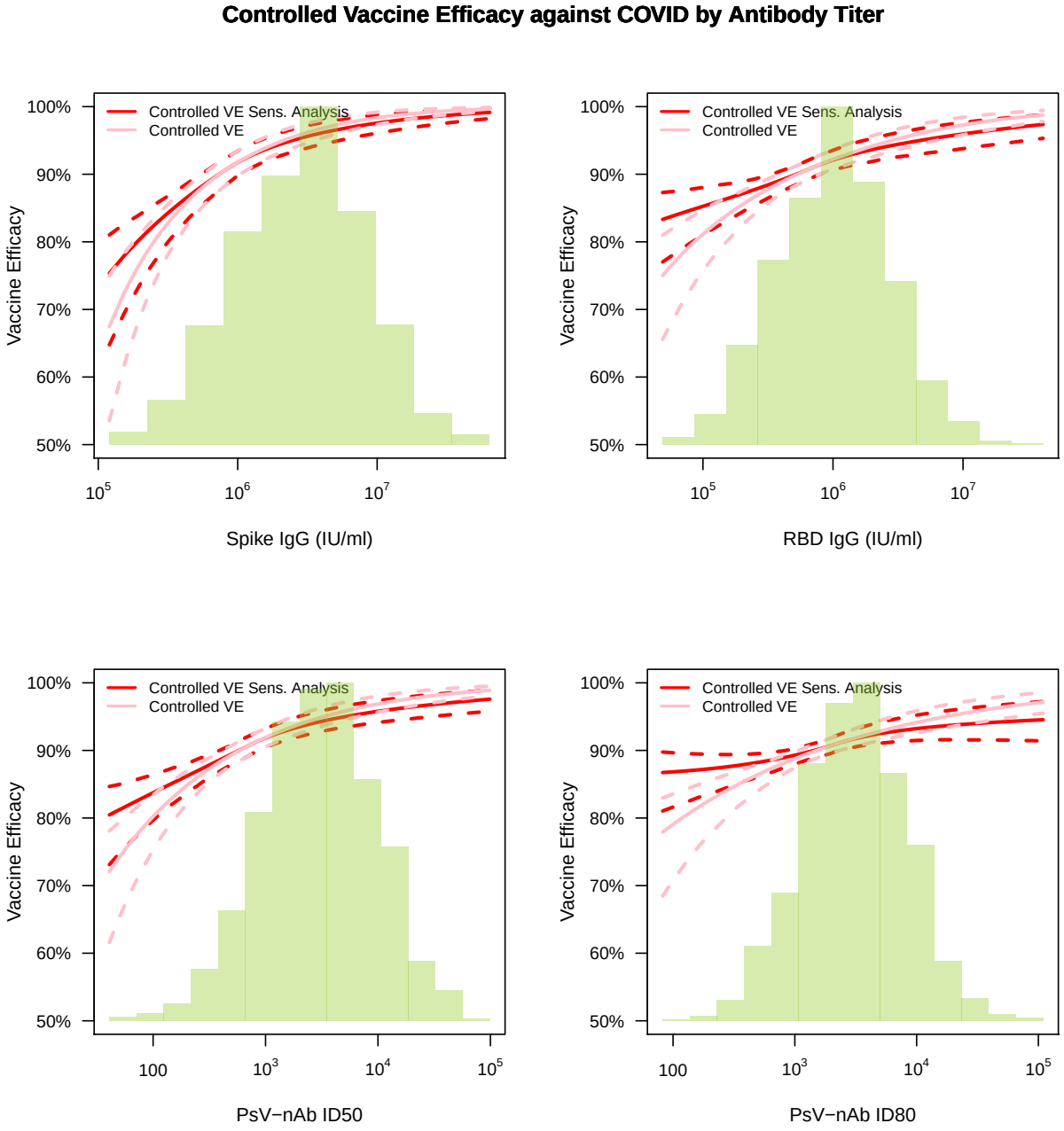

Figure 5: Controlled VE with sensitivity analysis as functions of Day 57 markers among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. Histograms of the immunological markers in the vaccine arm are overlaid.

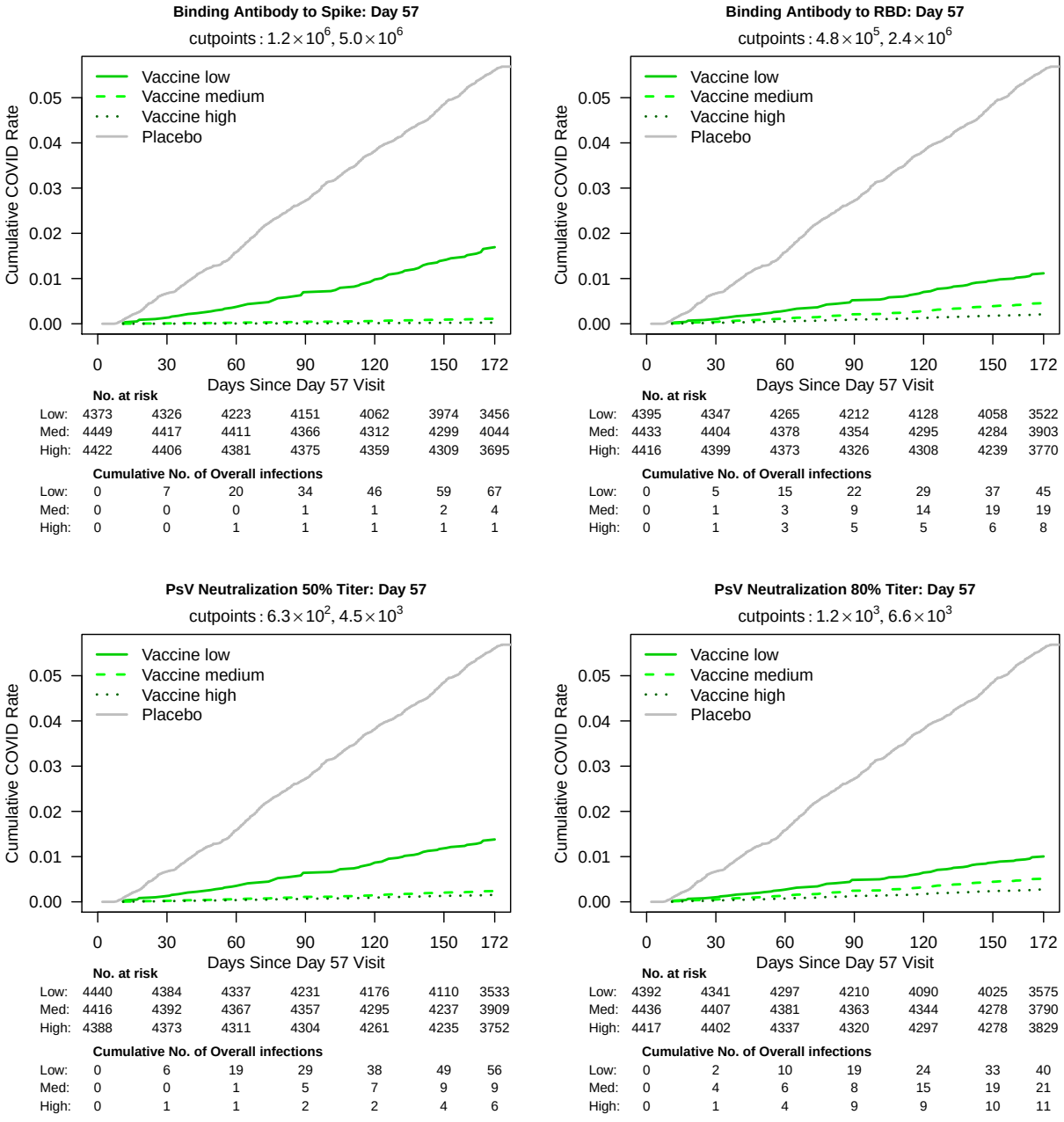

Figure 6: Marginalized cumulative incidence rate curves for trichotomized Day 57 markers among baseline seronegative vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

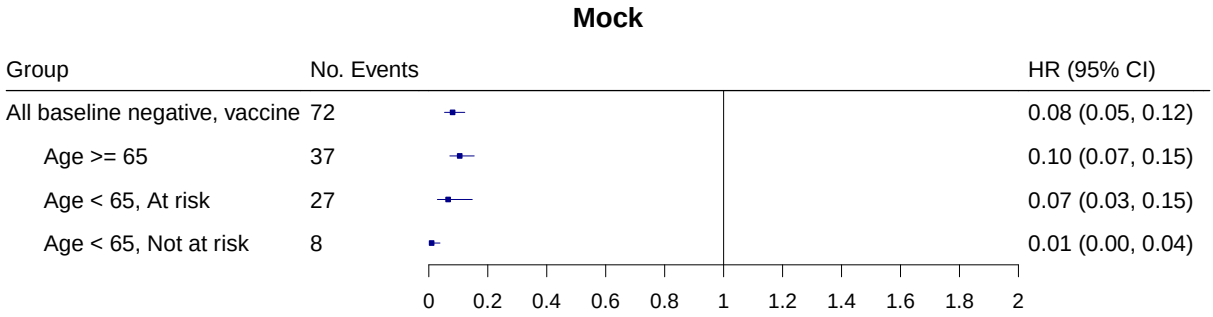

Figure 7: Forest plots of hazard ratios of Day 57 binding Ab to spike markers among baseline seronegative vaccine recipients (top row) and each of the 3 randomization strata with 95% point-wise confidence intervals.

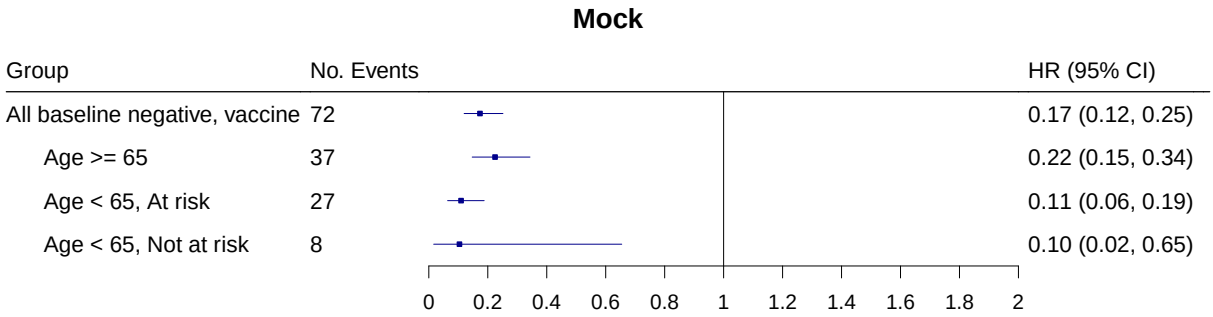

Figure 8: Forest plots of hazard ratios of Day 57 binding Ab to RBD markers among baseline seronegative vaccine recipients (top row) and each of the 3 randomization strata with 95% point-wise confidence intervals.

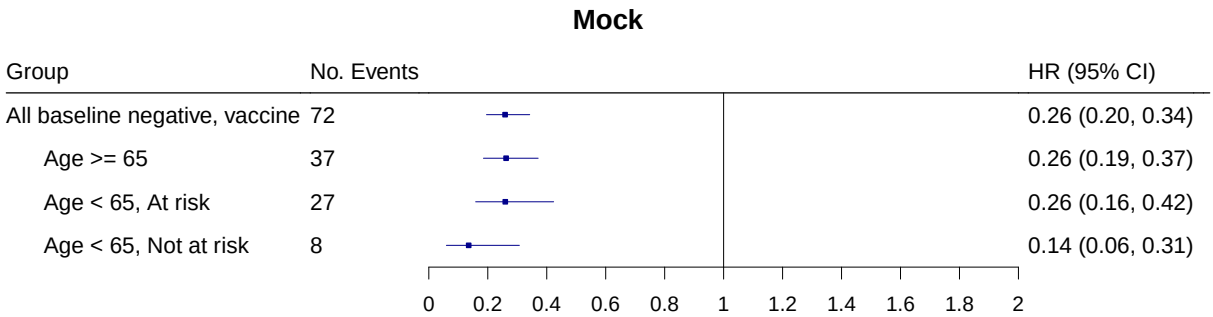

Figure 9: Forest plots of hazard ratios of Day 57 pseudo neut ID50 markers among baseline seronegative vaccine recipients (top row) and each of the 3 randomization strata with 95% point-wise confidence intervals.

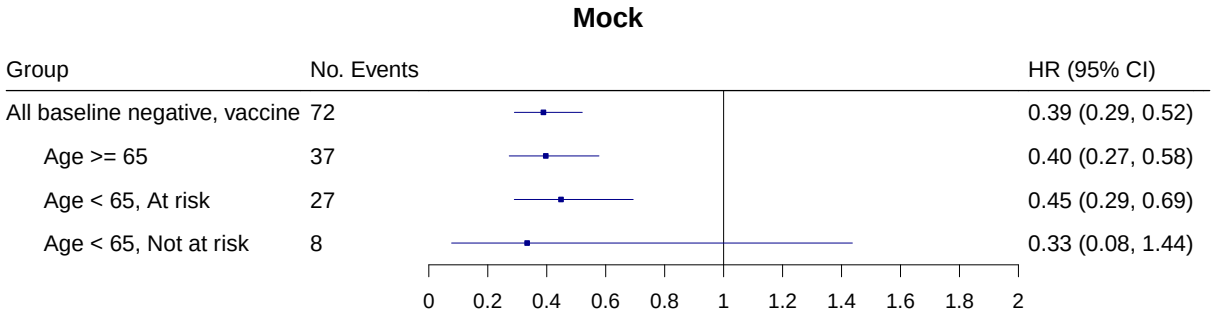

Figure 10: Forest plots of hazard ratios of Day 57 pseudo neut ID80 markers among baseline seronegative vaccine recipients (top row) and each of the 3 randomization strata with 95% point-wise confidence intervals.

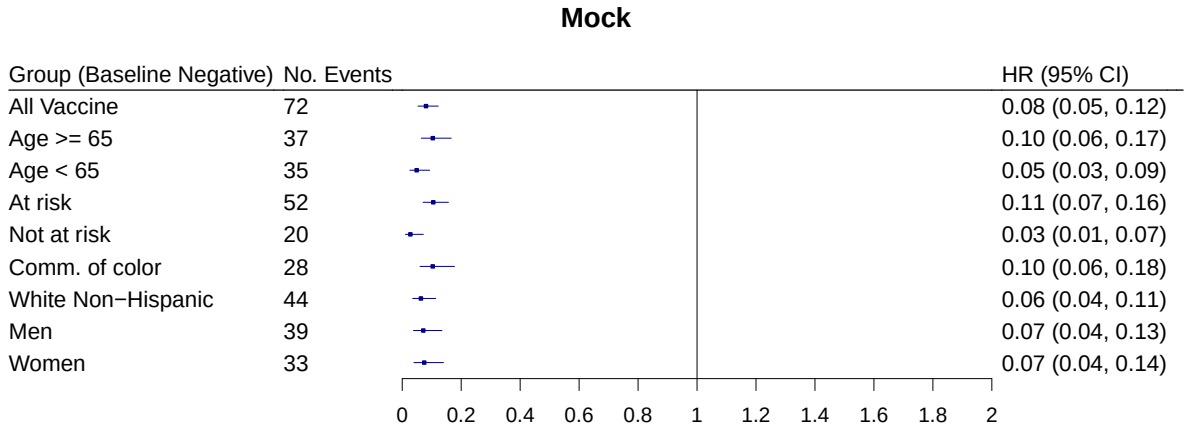

Figure 11: Forest plots of hazard ratios of Day 57 binding Ab to spike markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

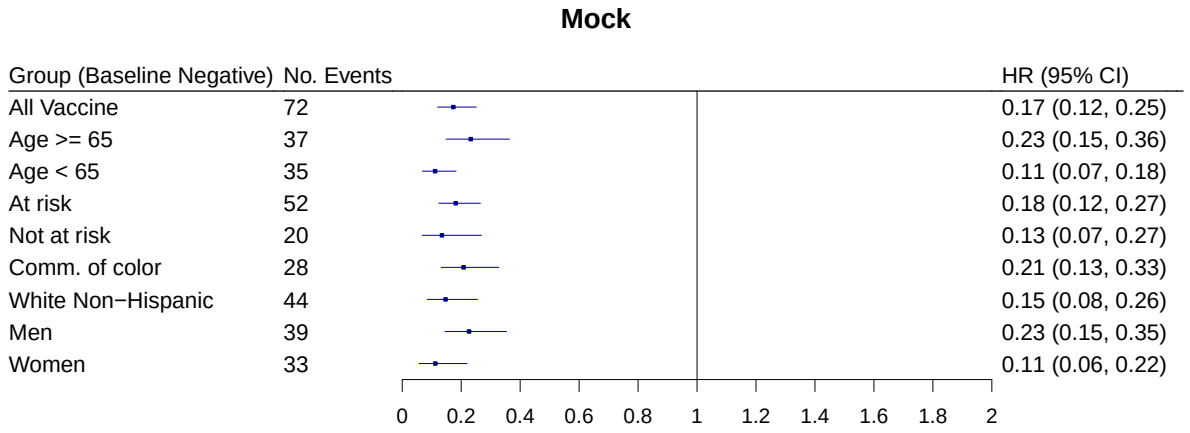

Figure 12: Forest plots of hazard ratios of Day 57 binding Ab to RBD markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

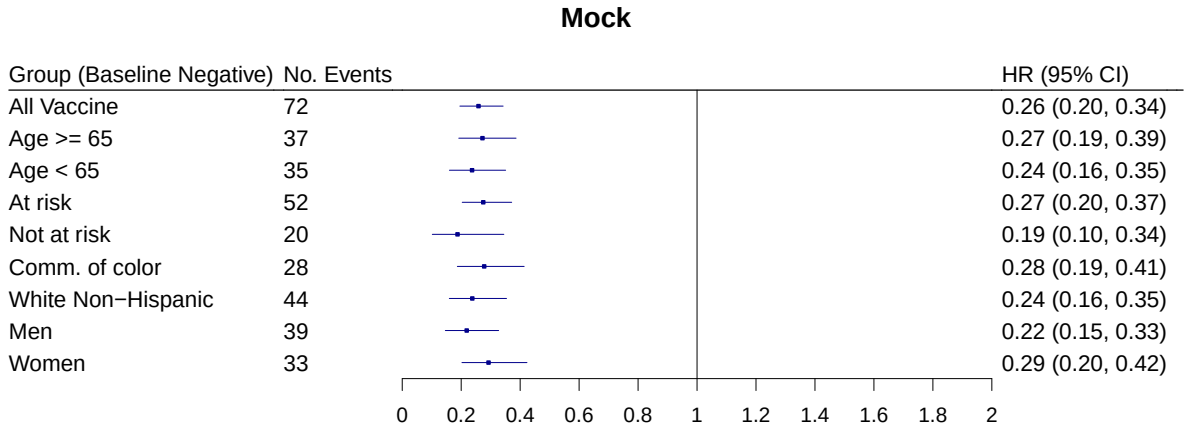

Figure 13: Forest plots of hazard ratios of Day 57 pseudo neut ID50 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

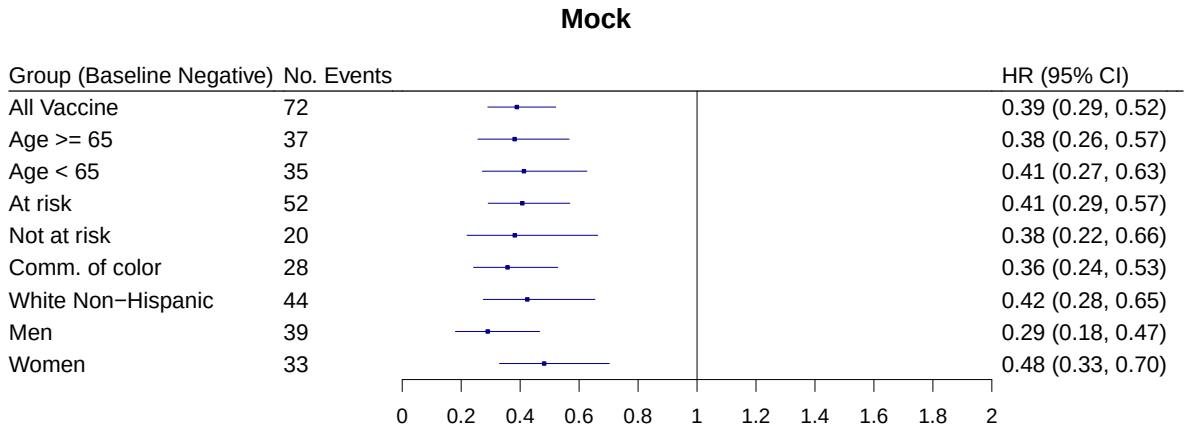

Figure 14: Forest plots of hazard ratios of Day 57 pseudo neut ID80 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.