

COVID correlates analysis report CoR

2021-02-07

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

All analyses for D57 markers are run on the population with EventTimePrimaryD57 \geq 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.		P-value (2-sided)	q-value	FWER
		Pt. Est.	95% CI			
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.	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.

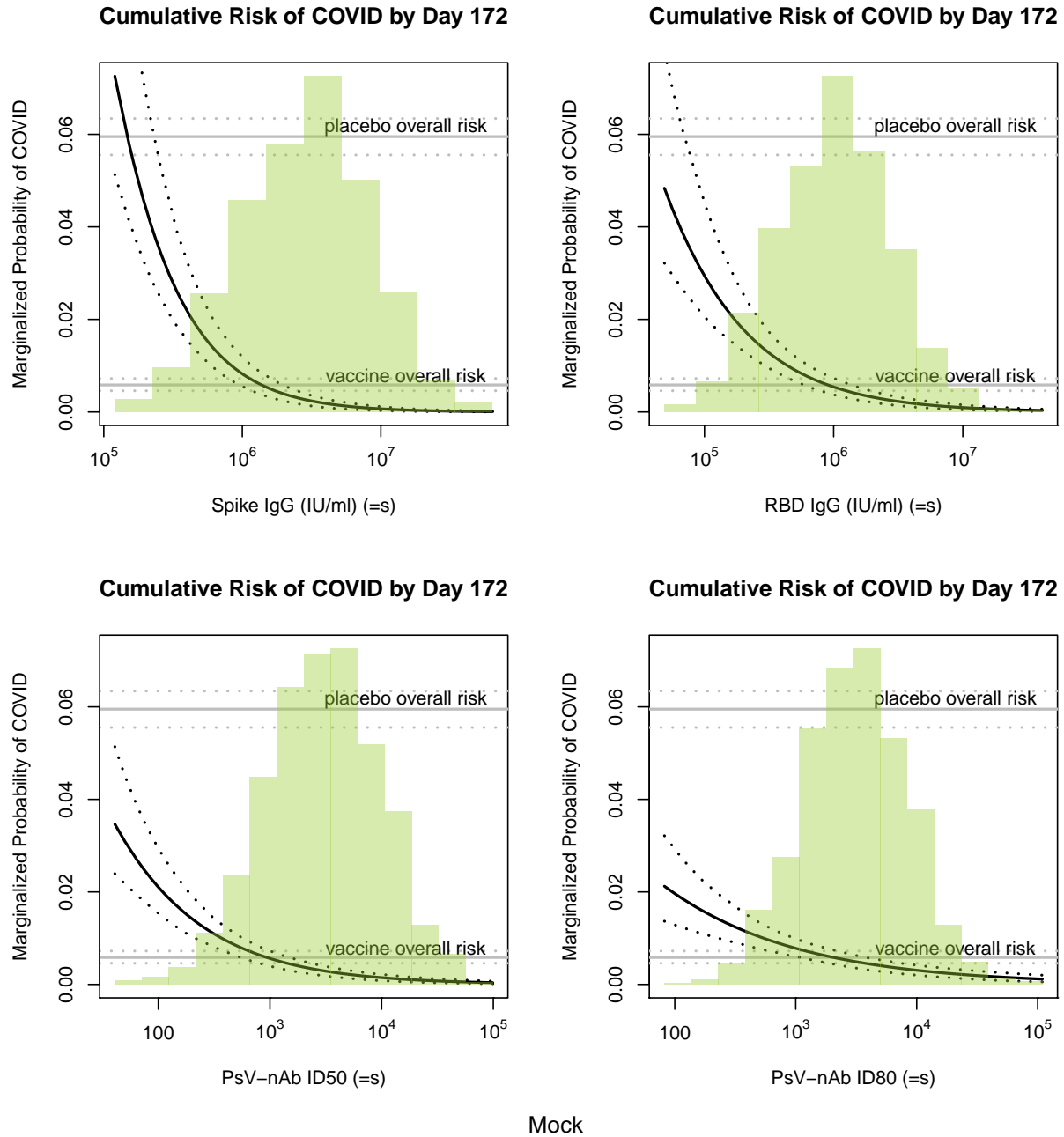


Figure 1: Marginalized cumulative risk by Day 172 as functions of Day 57 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 172 and its 95% point-wise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

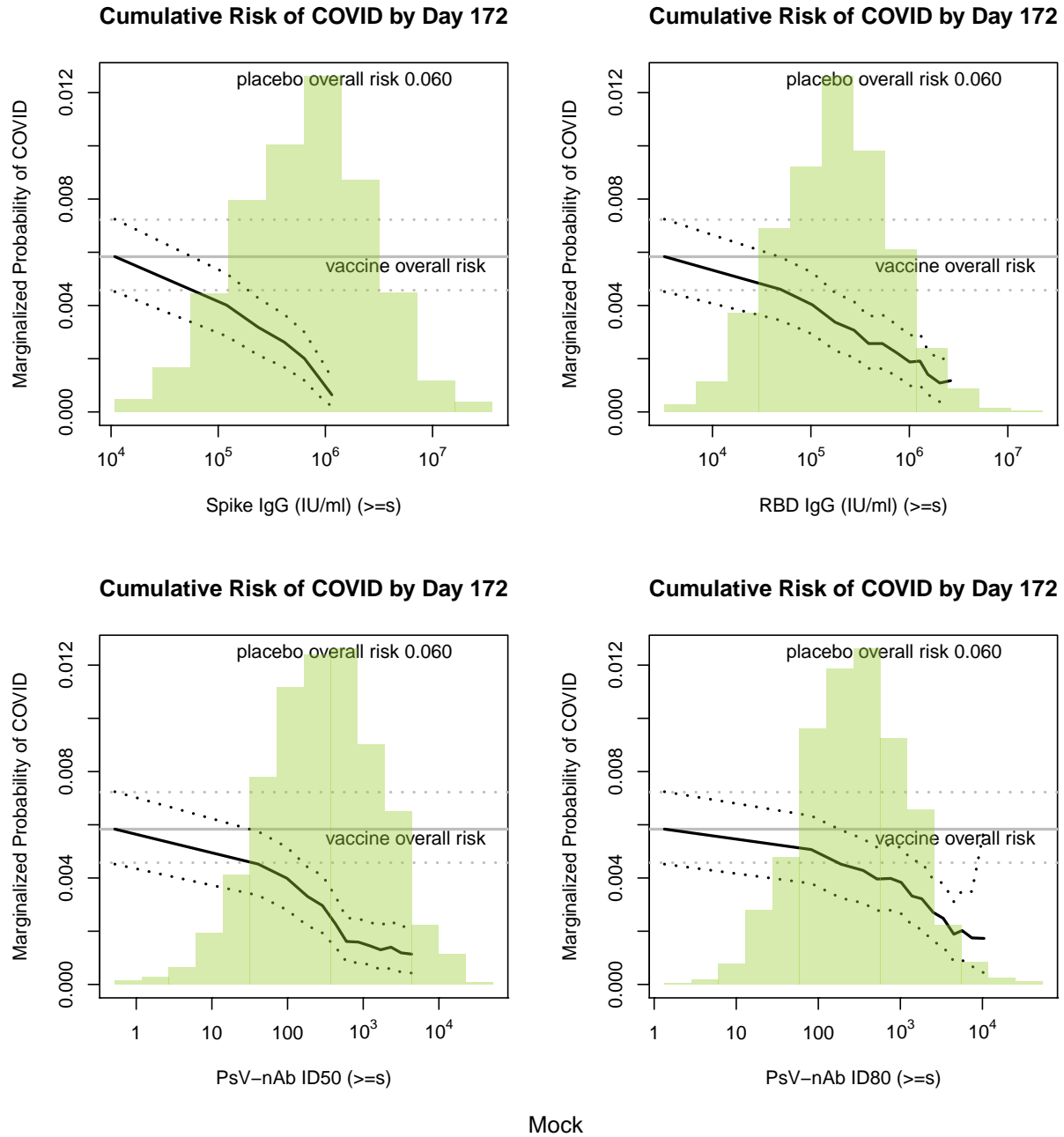


Figure 2: Marginalized cumulative risk by Day 172 as functions of Day 57 markers above a threshold ($\geq s$) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 172 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid.

Controlled Vaccine Efficacy against COVID by Antibody Titer

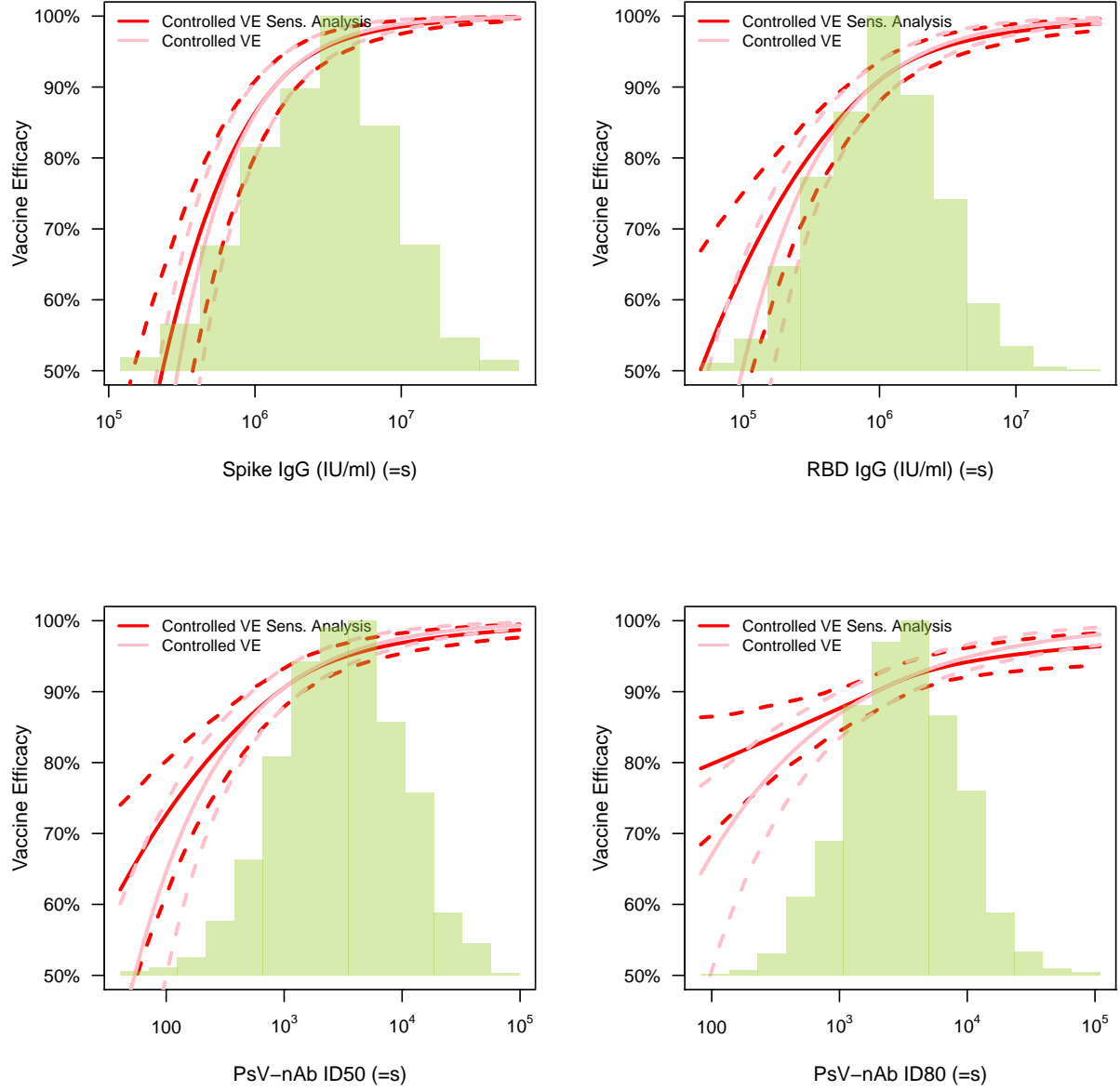


Figure 3: Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. Histograms of the immunological markers in the vaccine arm are overlaid.

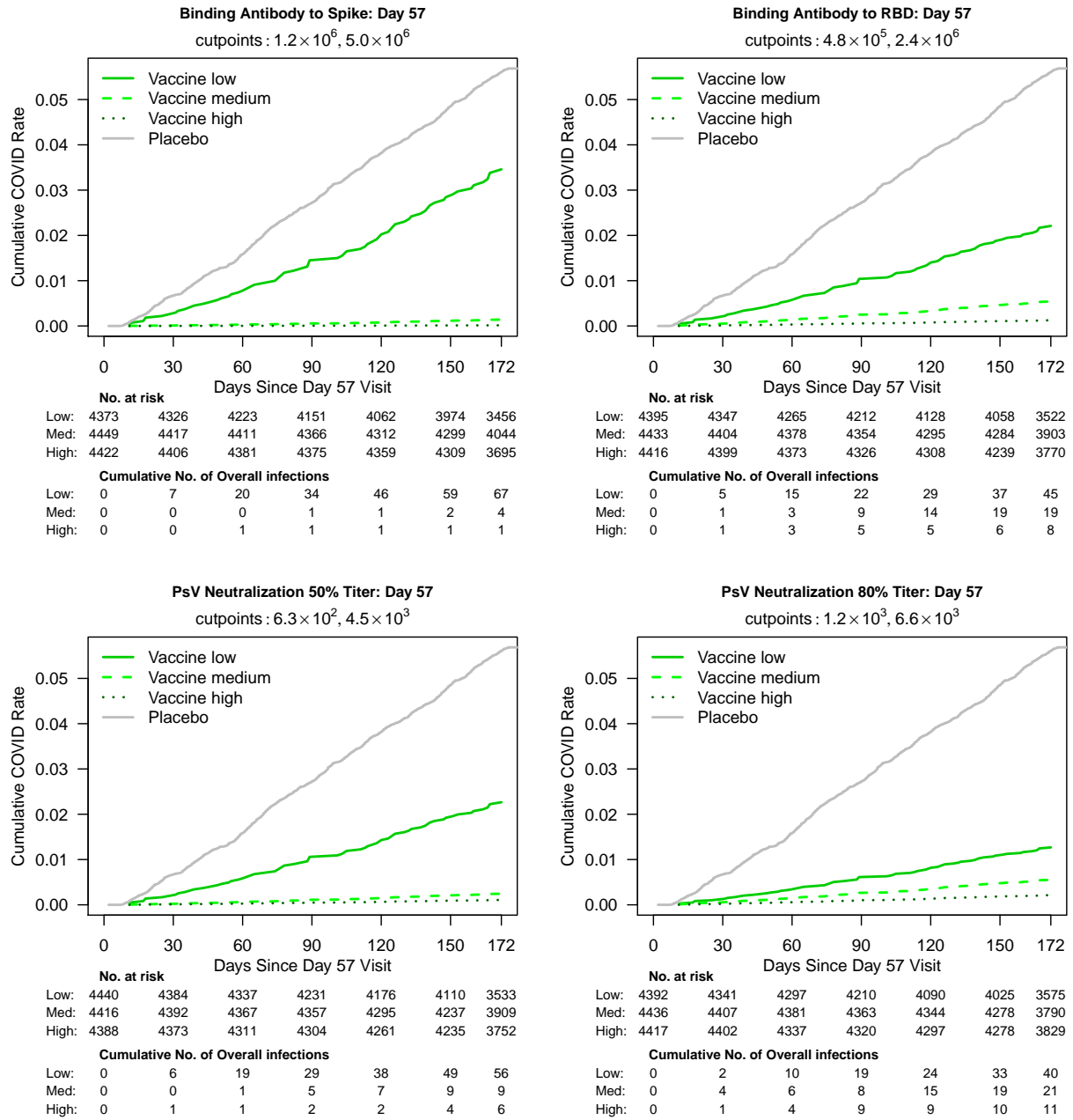


Figure 4: Marginalized cumulative incidence rate curves for trichotomized Day 57 markers among baseline seronegative vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

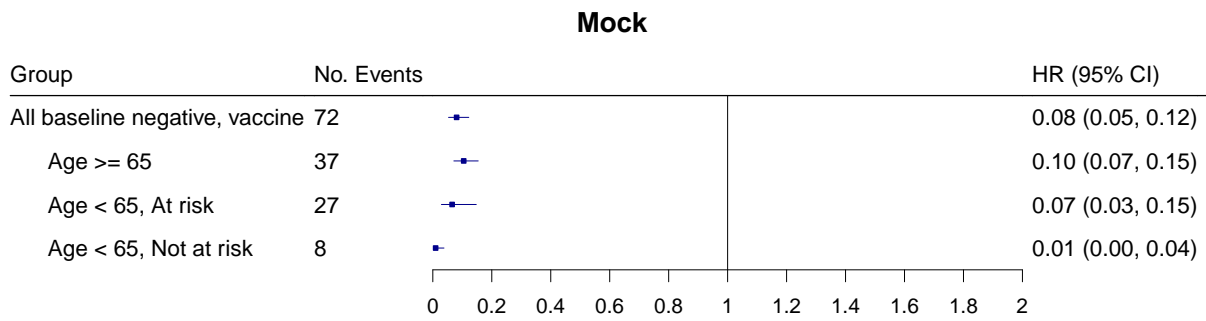


Figure 5: Forest plots of hazard ratios of Day 57 binding Ab to spike markers among baseline seronegative vaccine recipients (top row) and each of the 3 randomization strata with 95% point-wise confidence intervals.

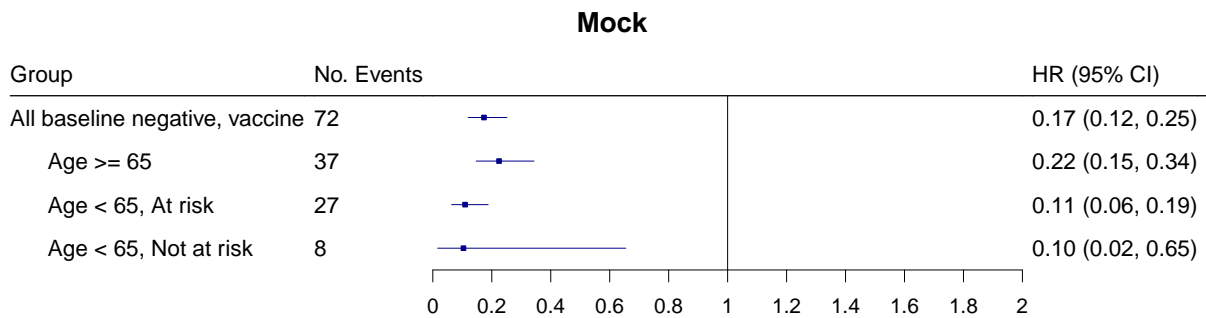


Figure 6: Forest plots of hazard ratios of Day 57 binding Ab to RBD markers among baseline seronegative vaccine recipients (top row) and each of the 3 randomization strata with 95% point-wise confidence intervals.

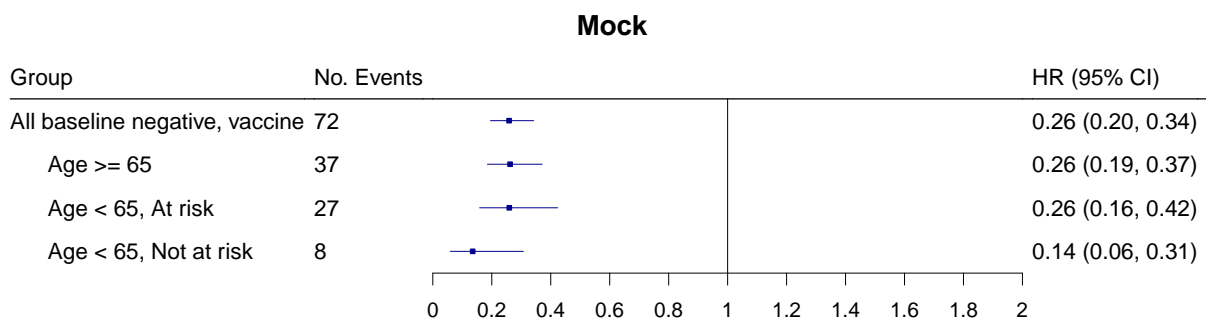


Figure 7: Forest plots of hazard ratios of Day 57 pseudo neut ID50 markers among baseline seronegative vaccine recipients (top row) and each of the 3 randomization strata with 95% point-wise confidence intervals.

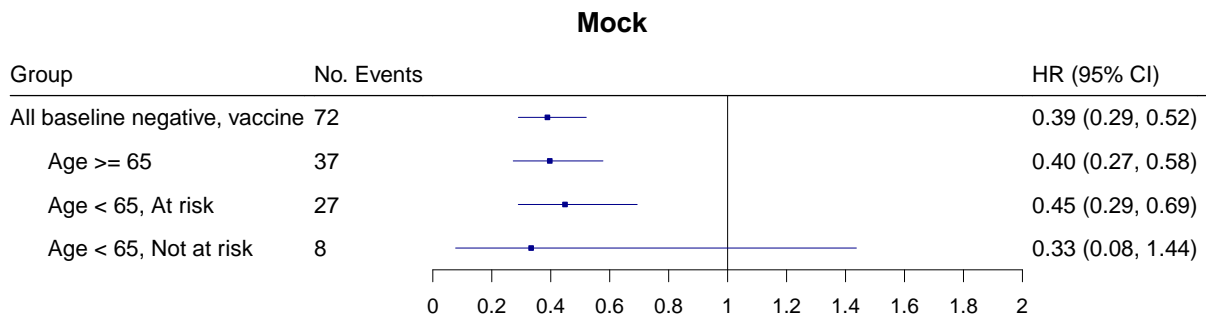


Figure 8: Forest plots of hazard ratios of Day 57 pseudo neut ID80 markers among baseline seronegative vaccine recipients (top row) and each of the 3 randomization strata with 95% point-wise confidence intervals.

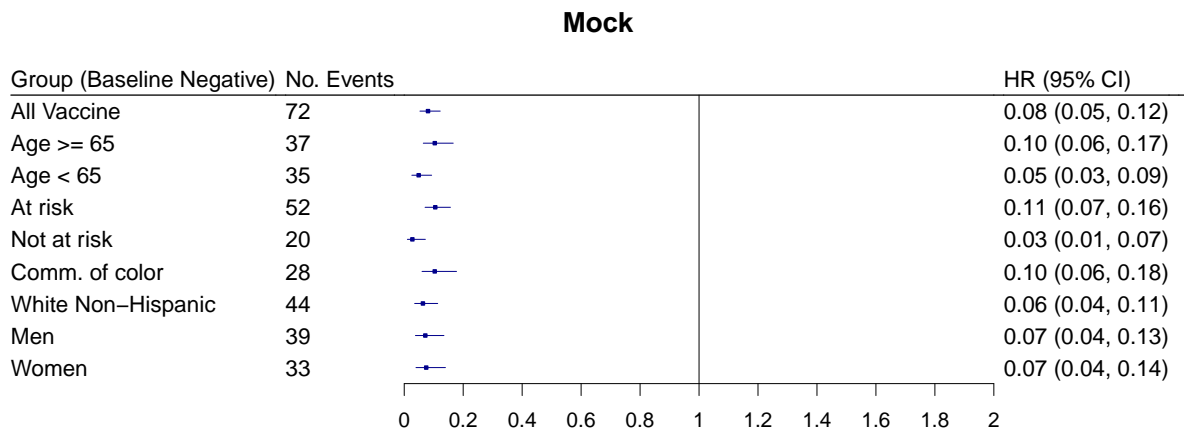


Figure 9: Forest plots of hazard ratios of Day 57 binding Ab to spike markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

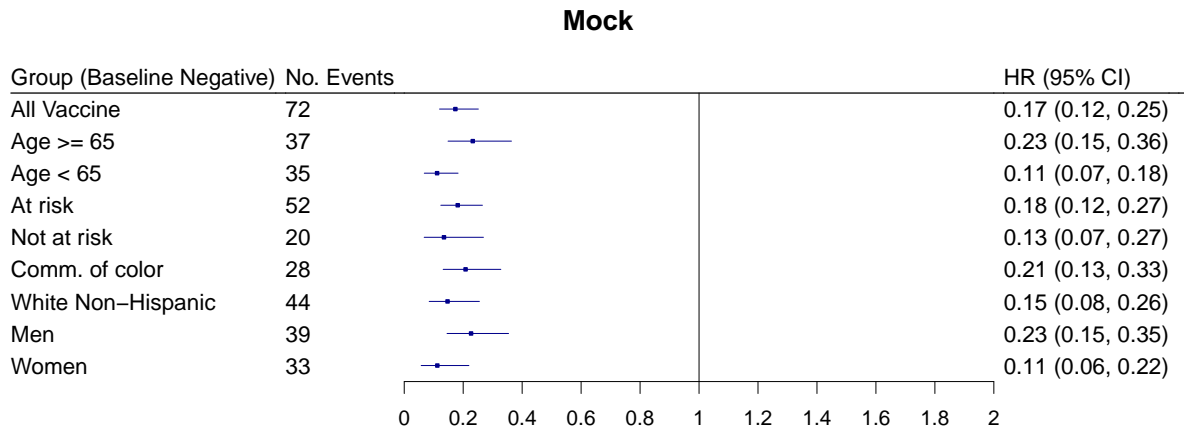


Figure 10: Forest plots of hazard ratios of Day 57 binding Ab to RBD markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

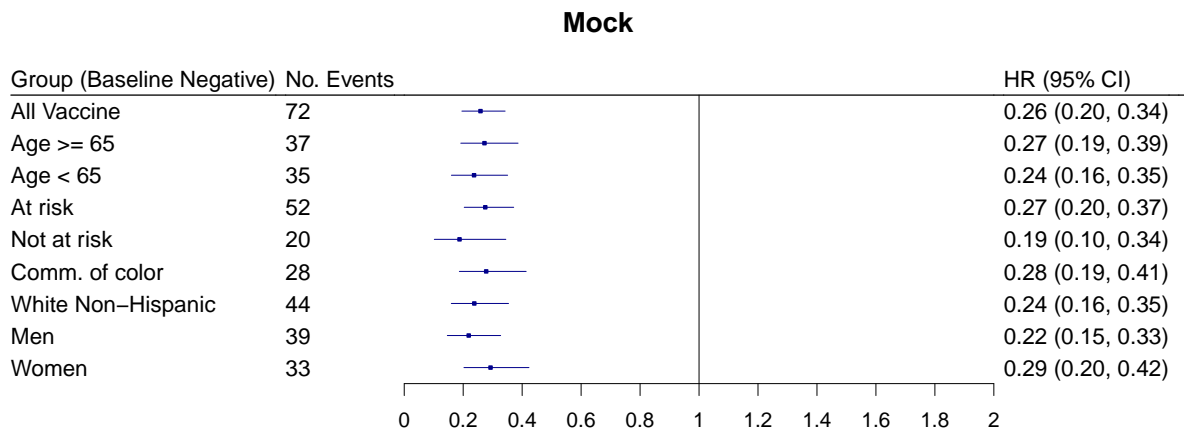


Figure 11: Forest plots of hazard ratios of Day 57 pseudo neut ID50 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

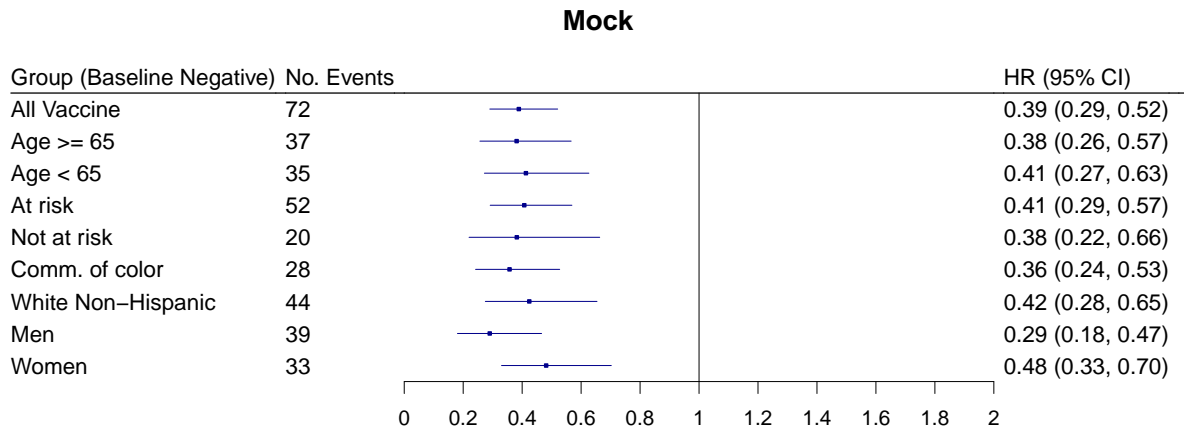


Figure 12: Forest plots of hazard ratios of Day 57 pseudo neut ID80 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.