

# CoVPN COVID-19 Correlates Analysis

the CoVPN Biostatistics Team

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# Chapter 1

## Day 57 Univariate CoR: Cox Models of Risk

The main regression model is the Cox proportional hazards model. All plots are made with Cox models fit unless specified otherwise.

### 1.1 Hazard ratios

Table 1.1: 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	0.24	(0.18-0.31)	<0.001	<0.001	<0.001
PsV-nAb ID80	72/13,254	0.38	(0.28-0.51)	<0.001	<0.001	<0.001

\*Baseline covariates adjusted for: age in years, at risk or not, community of color or not \*\*No. at-risk = number of per-protocol baseline negative vaccine recipients at-risk for COVID at 7 days post Day 57 visit; no. cases = number of this cohort with an observed COVID endpoints.

Table 1.2: 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	67/4,425	0.0151	1	N/A	N/A	<0.001	<0.001
	Middle	4/4,403	0.0009	0.04	(0.01-0.11)	<0.001		
	Upper	1/4,426	0.0002	0.00	(0.00-0.03)	<0.001		
RBD IgG (IU/ml)	Lower	45/4,437	0.0101	1	N/A	N/A	<0.001	<0.001
	Middle	19/4,398	0.0043	0.24	(0.13-0.43)	<0.001		
	Upper	8/4,420	0.0018	0.05	(0.02-0.12)	<0.001		
PsV-nAb ID50	Lower	56/4,443	0.0126	1	N/A	N/A	<0.001	<0.001
	Middle	9/4,382	0.0021	0.10	(0.05-0.22)	<0.001		
	Upper	6/4,429	0.0014	0.05	(0.02-0.11)	<0.001		
PsV-nAb ID80	Lower	40/4,434	0.0090	1	N/A	N/A	<0.001	<0.001
	Middle	21/4,400	0.0048	0.43	(0.24-0.79)	0.006		
	Upper	11/4,420	0.0025	0.17	(0.08-0.34)	<0.001		
Placebo		713/13,271	0.0537					

\*Baseline covariates adjusted for: age in years, at risk or not, community of color or not . Average follow-up time 172 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 7 days post Day 57 visit; 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.

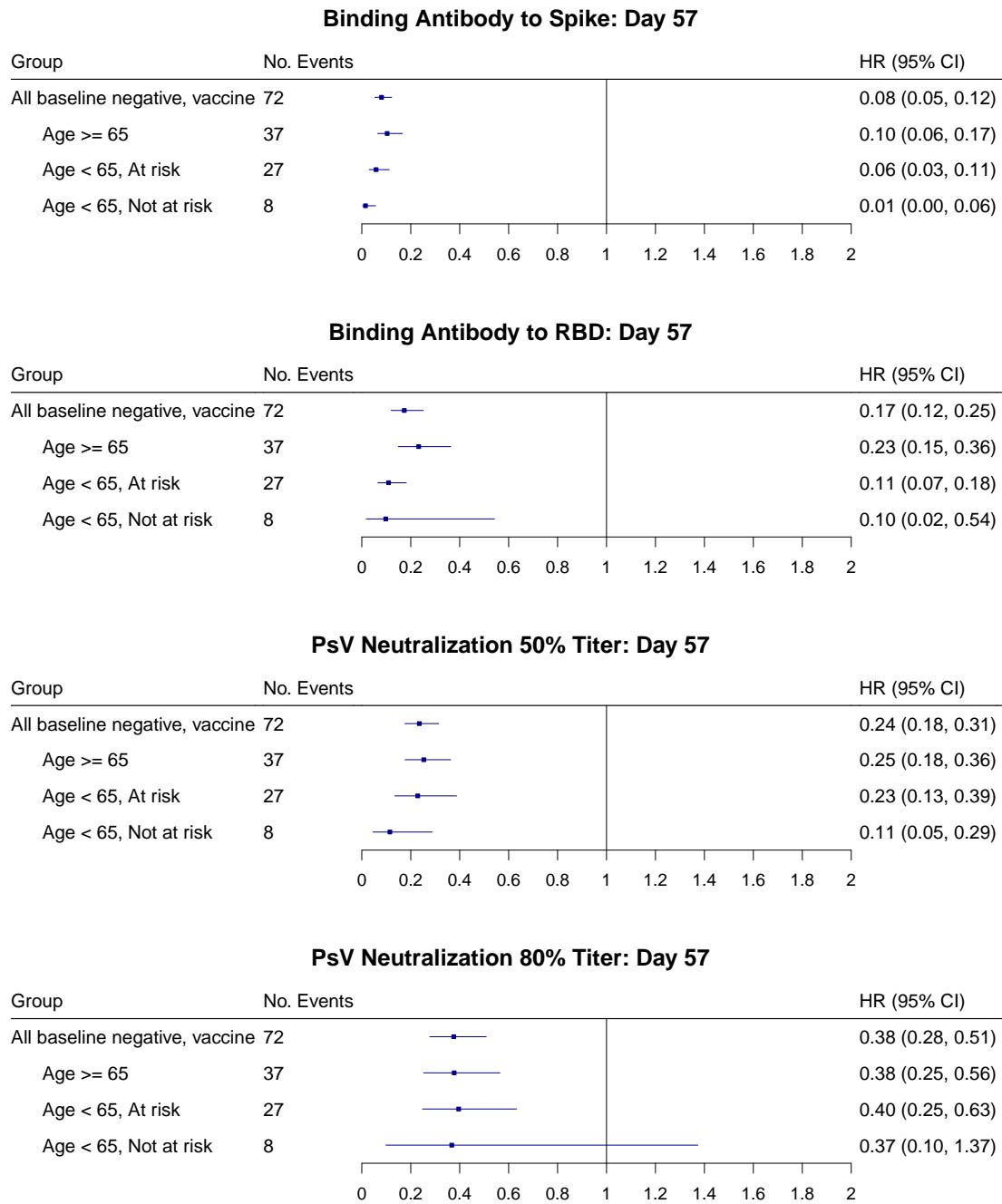


Figure 1.1: Forest plots of hazard ratios among baseline seronegative vaccine recipients and subgroups with 95% point-wise confidence intervals.

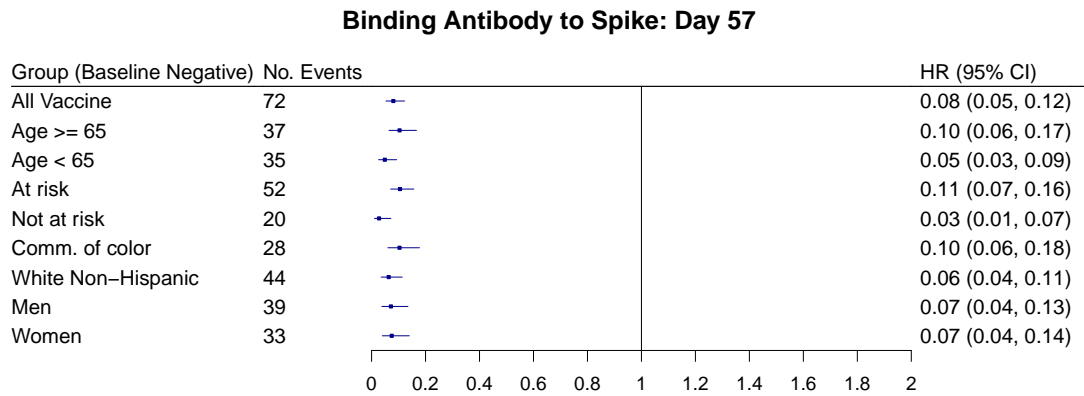


Figure 1.2: Forest plots of hazard ratios of Day 57 binding Ab to spike markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

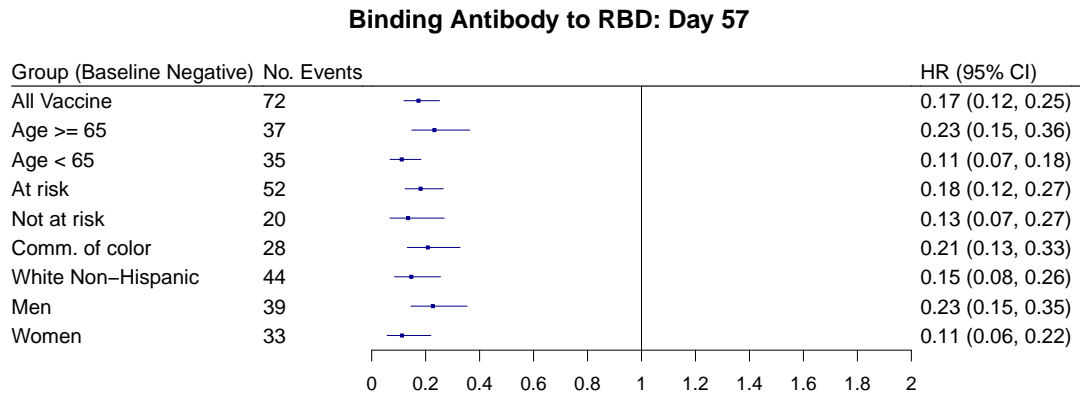


Figure 1.3: Forest plots of hazard ratios of Day57binding Ab to RBD markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

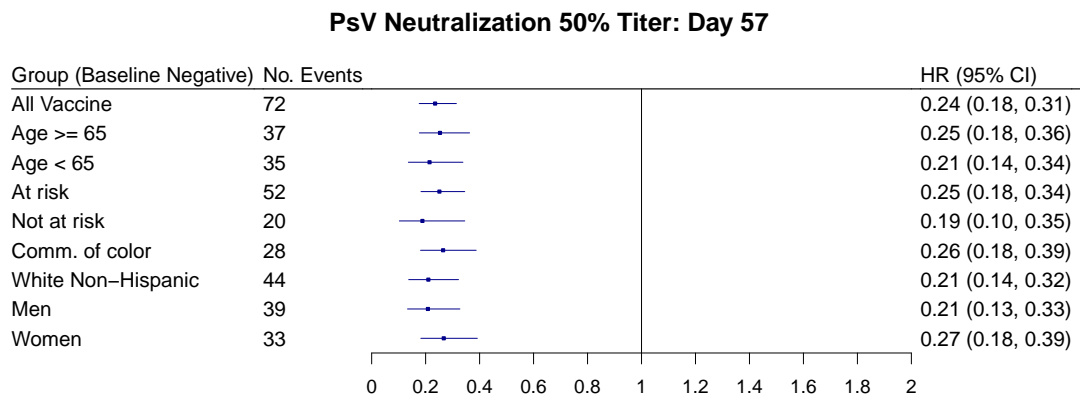


Figure 1.4: Forest plots of hazard ratios of Day 57 pseudo neut ID50 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

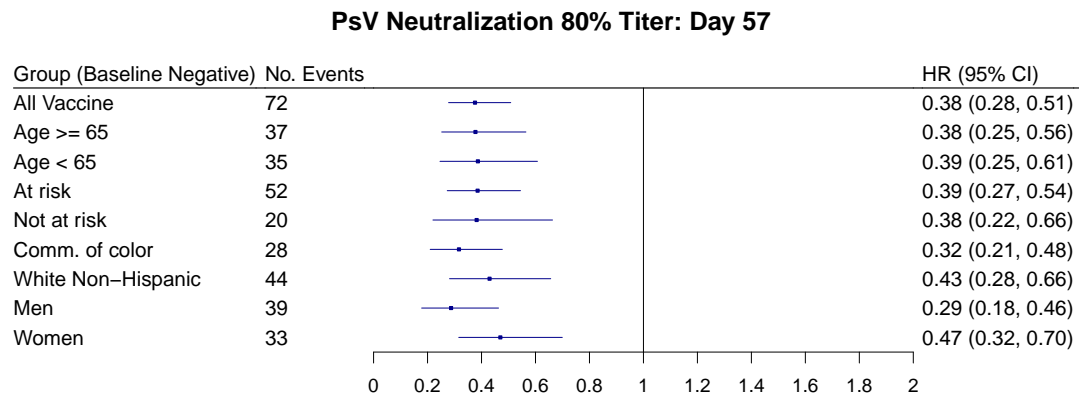


Figure 1.5: Forest plots of hazard ratios of Day 57 pseudo neut ID80 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

1.2 Marginalized risk and controlled vaccine efficacy plots

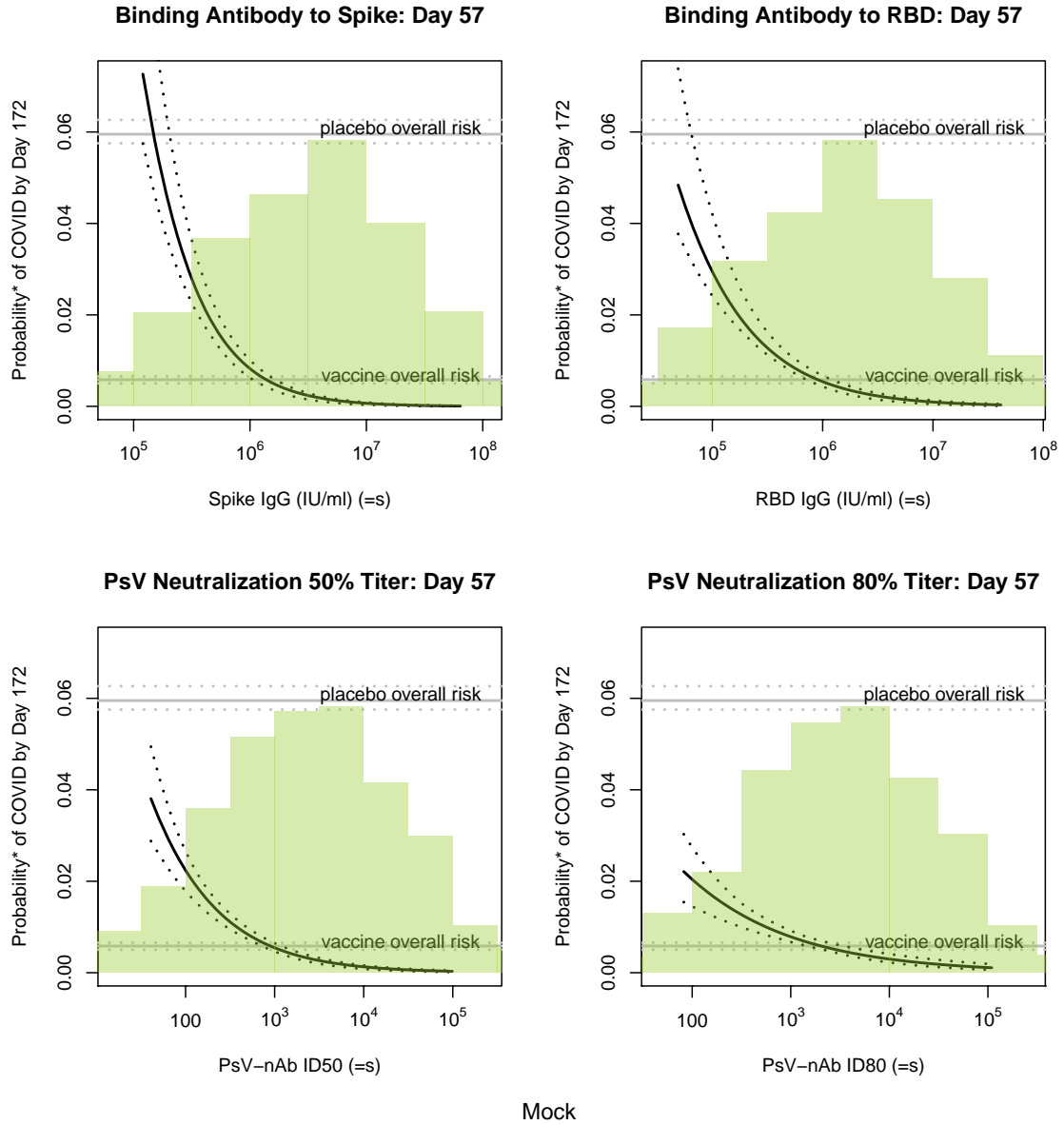


Figure 1.6: Marginalized cumulative risk by Day 'r tp' as functions of Day 57 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 172 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.



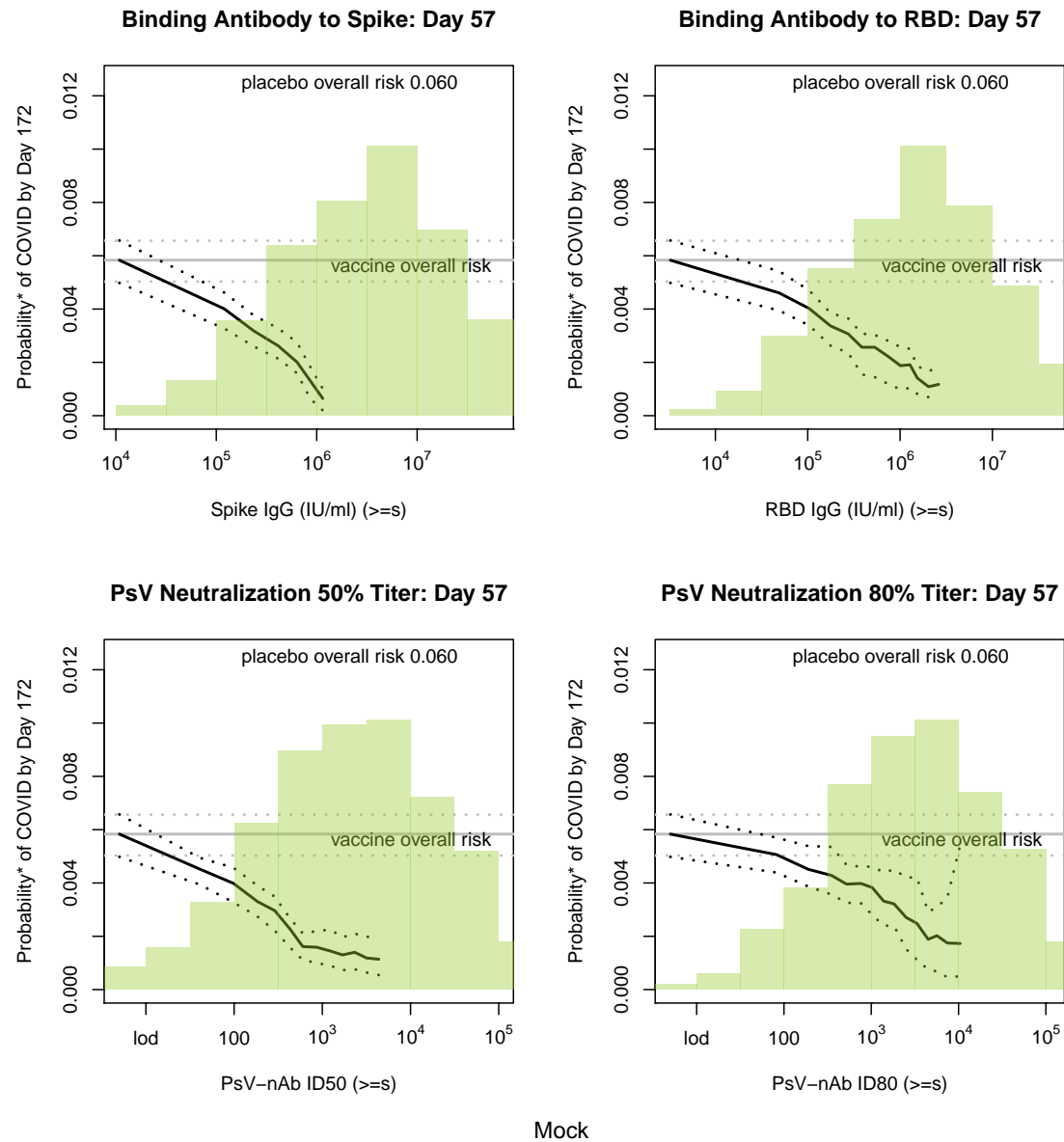


Figure 1.7: Marginalized cumulative risk by Day 172 as functions of Day 57 markers above a threshold ( $\geq s$ ) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 172 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

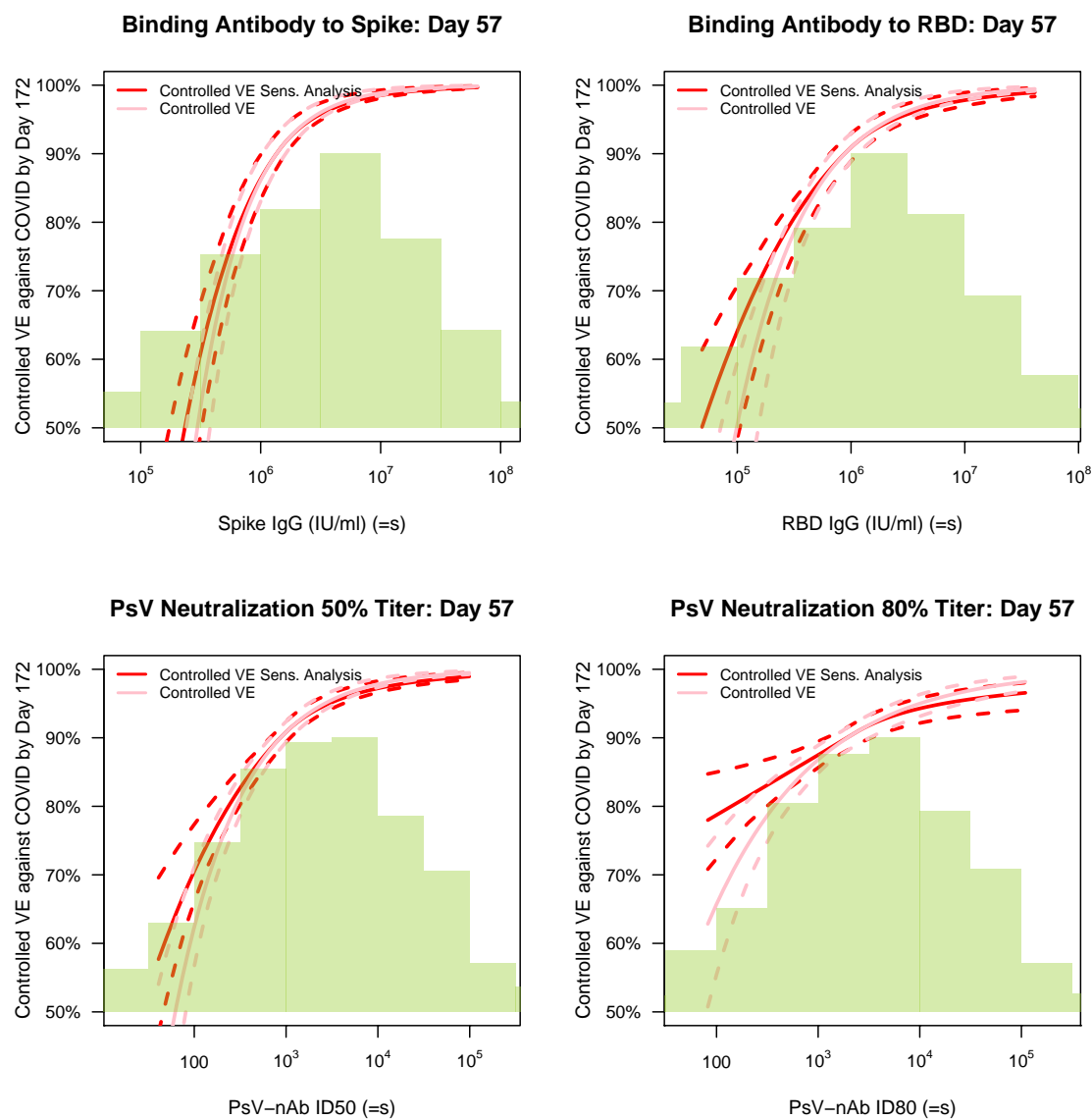


Figure 1.8: Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

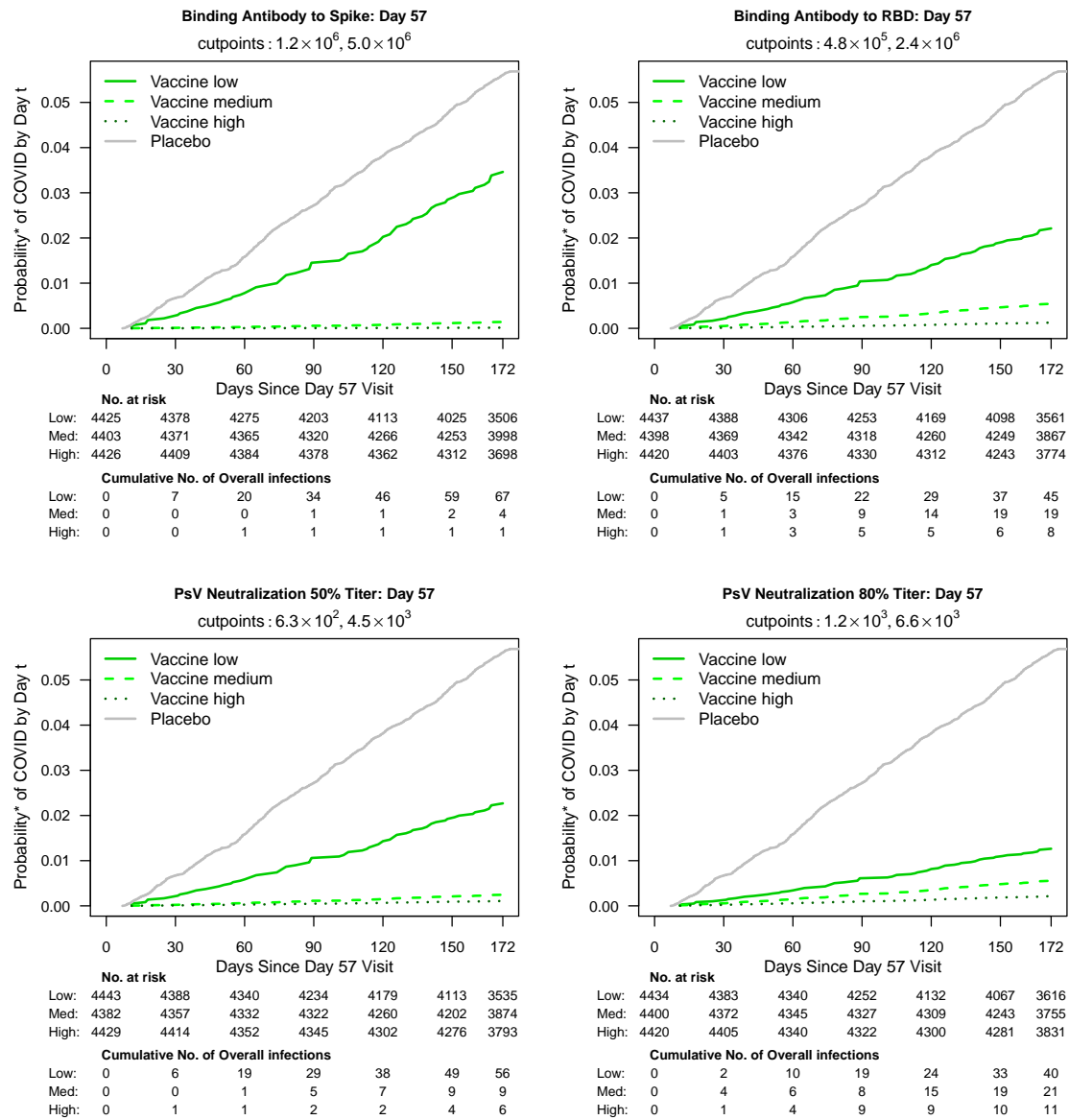


Figure 1.9: Marginalized cumulative incidence rate curves for trichotomized Day 57 markers among baseline seronegative vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.



## Chapter 2

# Day 29 Univariate CoR: Cox Models of Risk

The main regression model is the Cox proportional hazards model. All plots are made with Cox models fit unless specified otherwise.

### 2.1 Hazard ratios

Table 2.1: Inference for Day 29 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)	83/13,271	0.09	(0.05-0.16)	<0.001	<0.001	<0.001
RBD IgG (IU/ml)	83/13,271	0.25	(0.16-0.38)	<0.001	<0.001	<0.001
PsV-nAb ID50	83/13,271	0.32	(0.23-0.46)	<0.001	<0.001	<0.001
PsV-nAb ID80	83/13,271	0.57	(0.43-0.75)	<0.001	<0.001	<0.001

\*Baseline covariates adjusted for: age in years, at risk or not, community of color or not \*\*No. at-risk = number of per-protocol baseline negative vaccine recipients at-risk for COVID at 7 days post Day 29 visit; no. cases = number of this cohort with an observed COVID endpoints.

Table 2.2: Inference for Day 29 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	54/4,422	0.0122	1	N/A	N/A	<0.001	<0.001
	Middle	24/4,423	0.0054	0.20	(0.11-0.37)	<0.001		
	Upper	5/4,427	0.0011	0.02	(0.01-0.06)	<0.001		
RBD IgG (IU/ml)	Lower	46/4,419	0.0104	1	N/A	N/A	<0.001	<0.001
	Middle	25/4,428	0.0056	0.30	(0.17-0.55)	<0.001		
	Upper	12/4,424	0.0027	0.08	(0.04-0.17)	<0.001		
PsV-nAb ID50	Lower	47/4,403	0.0107	1	N/A	N/A	<0.001	<0.001
	Middle	24/4,420	0.0054	0.33	(0.19-0.59)	<0.001		
	Upper	12/4,448	0.0027	0.12	(0.06-0.25)	<0.001		
PsV-nAb ID80	Lower	30/4,416	0.0068	1	N/A	N/A	0.001	<0.001
	Middle	36/4,429	0.0081	0.94	(0.55-1.62)	0.834		
	Upper	17/4,426	0.0038	0.33	(0.17-0.64)	0.001		
Placebo		821/13,299	0.0617					

\*Baseline covariates adjusted for: age in years, at risk or not, community of color or not . Average follow-up time 200 days, maximum follow-up time 213 days. Cutpoints: Spike IgG (IU/ml) [4.38, 4.94), RBD IgG (IU/ml) [4.11, 4.66), PsV-nAb ID50 [1.67, 2.38), PsV-nAb ID80 [1.97, 2.64) \*\*No. at-risk = number of per-protocol baseline negative vaccine recipients at-risk for COVID at 7 days post Day 29 visit; 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.

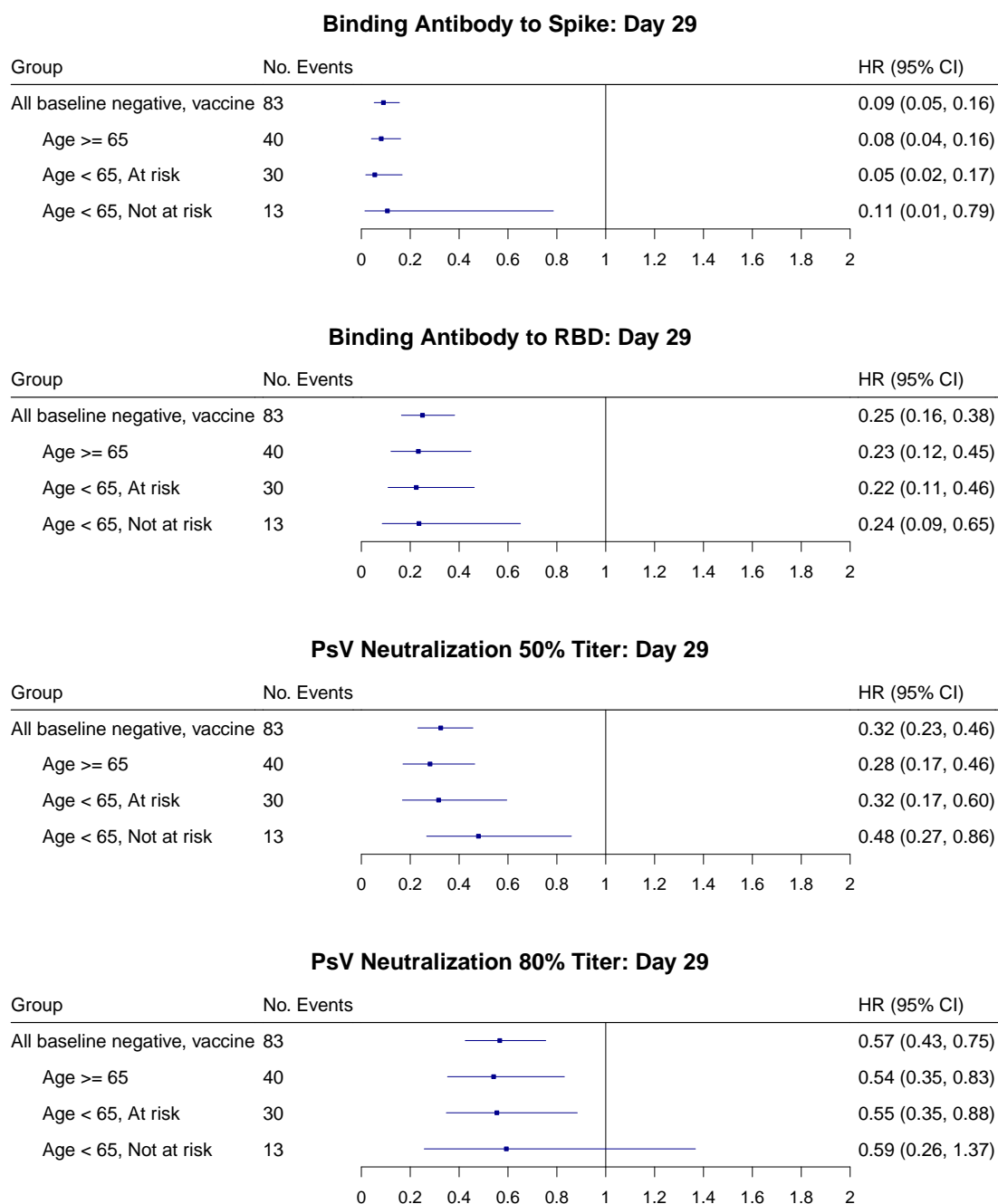


Figure 2.1: Forest plots of hazard ratios among baseline seronegative vaccine recipients and subgroups with 95% point-wise confidence intervals.

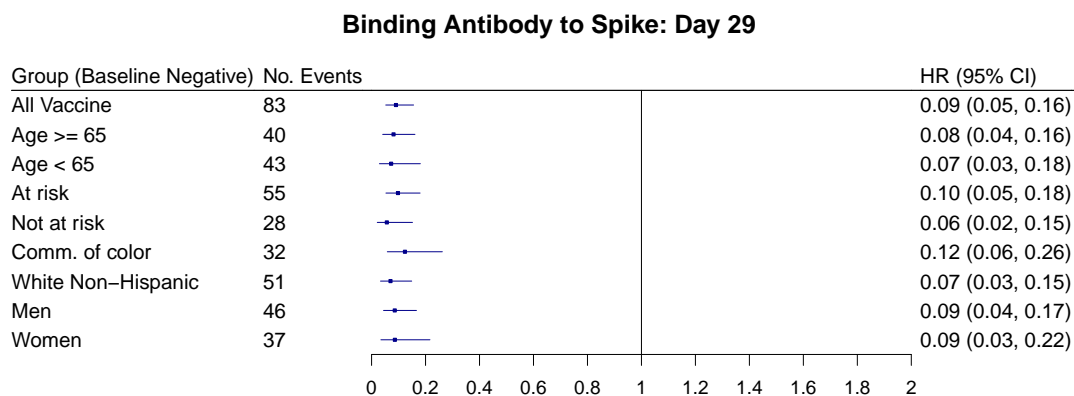


Figure 2.2: Forest plots of hazard ratios of Day 29 binding Ab to spike markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.



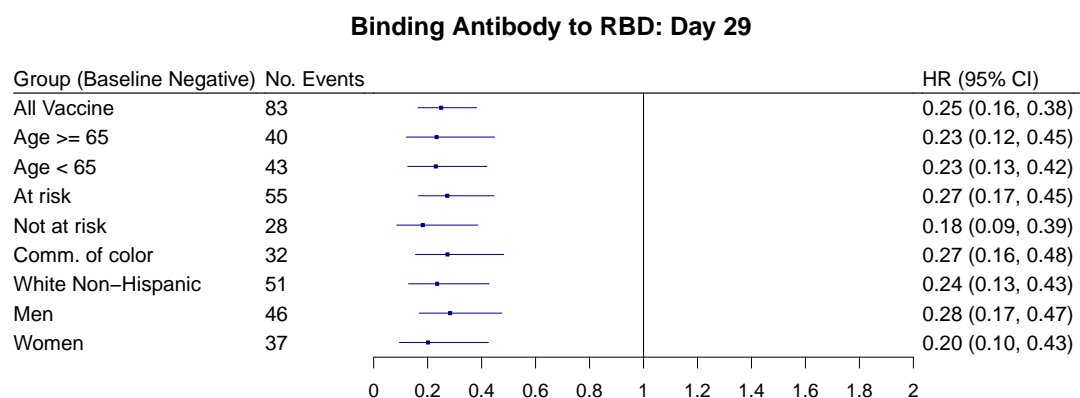


Figure 2.3: Forest plots of hazard ratios of Day29binding Ab to RBD markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

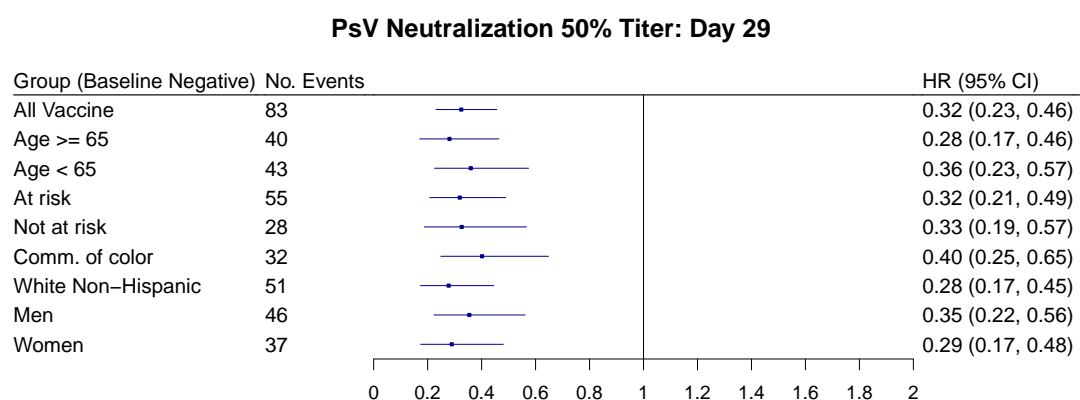


Figure 2.4: Forest plots of hazard ratios of Day 29 pseudo neut ID50 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

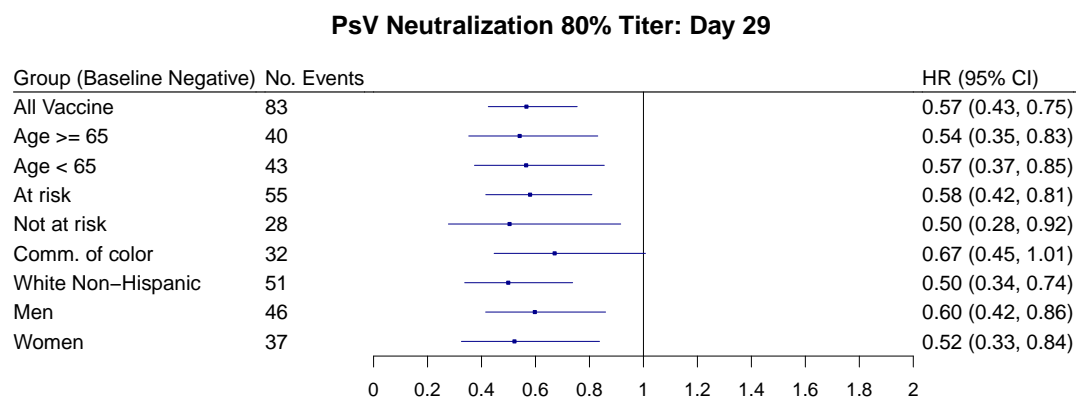


Figure 2.5: Forest plots of hazard ratios of Day 29 pseudo neut ID80 markers among baseline seronegative vaccine recipients (top row) and eight subpopulations (row 2-9) with 95% point-wise confidence intervals.

## 2.2 Marginalized risk and controlled vaccine efficacy plots

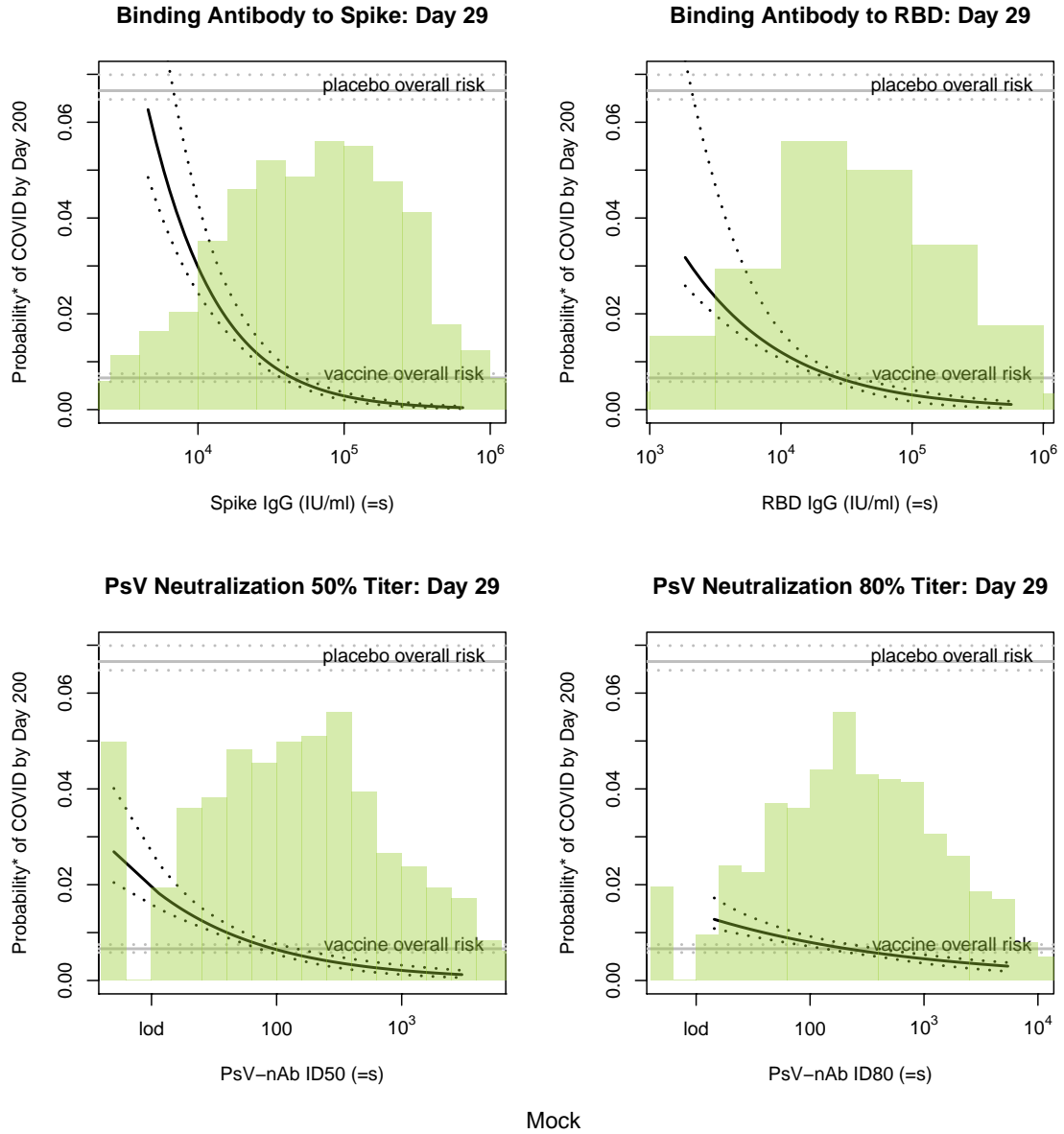


Figure 2.6: Marginalized cumulative risk by Day 'r tp' as functions of Day 29 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 200 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

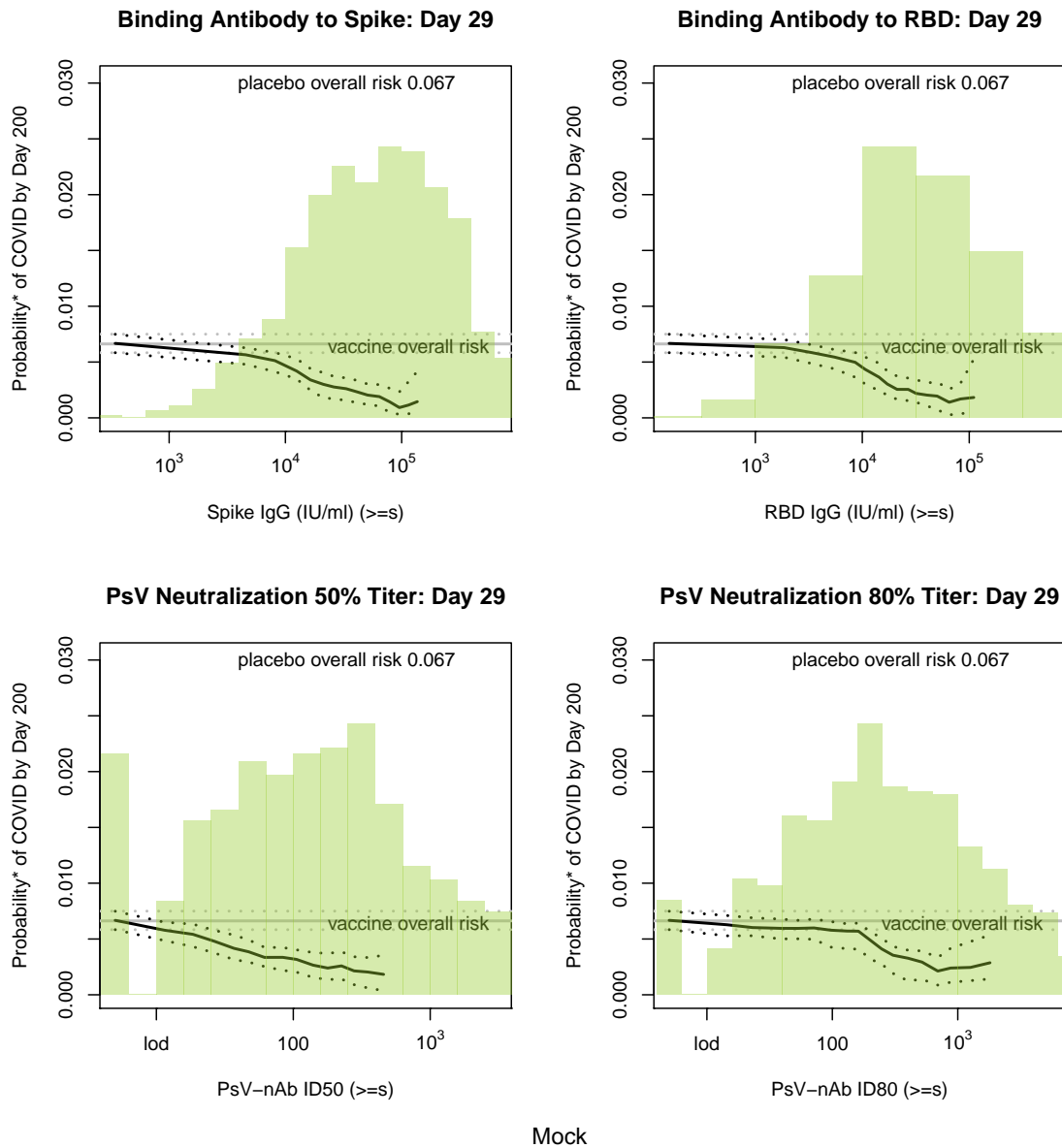


Figure 2.7: Marginalized cumulative risk by Day 'r tp' as functions of Day 29 markers above a threshold ( $\geq s$ ) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required). The horizontal lines indicate the overall cumulative risk of the vaccine arm by Day 200 and its 95% point-wise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

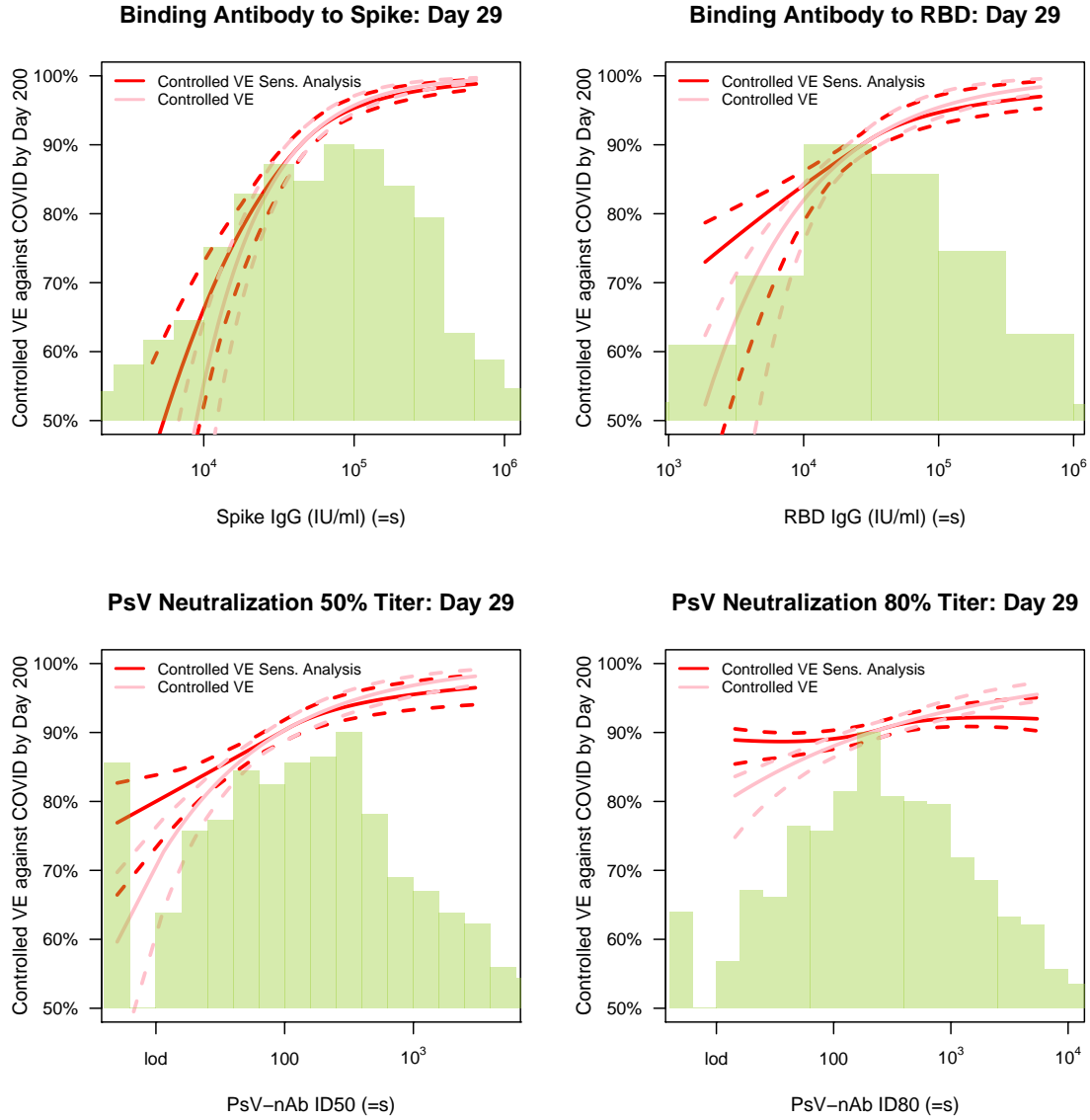


Figure 2.8: Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

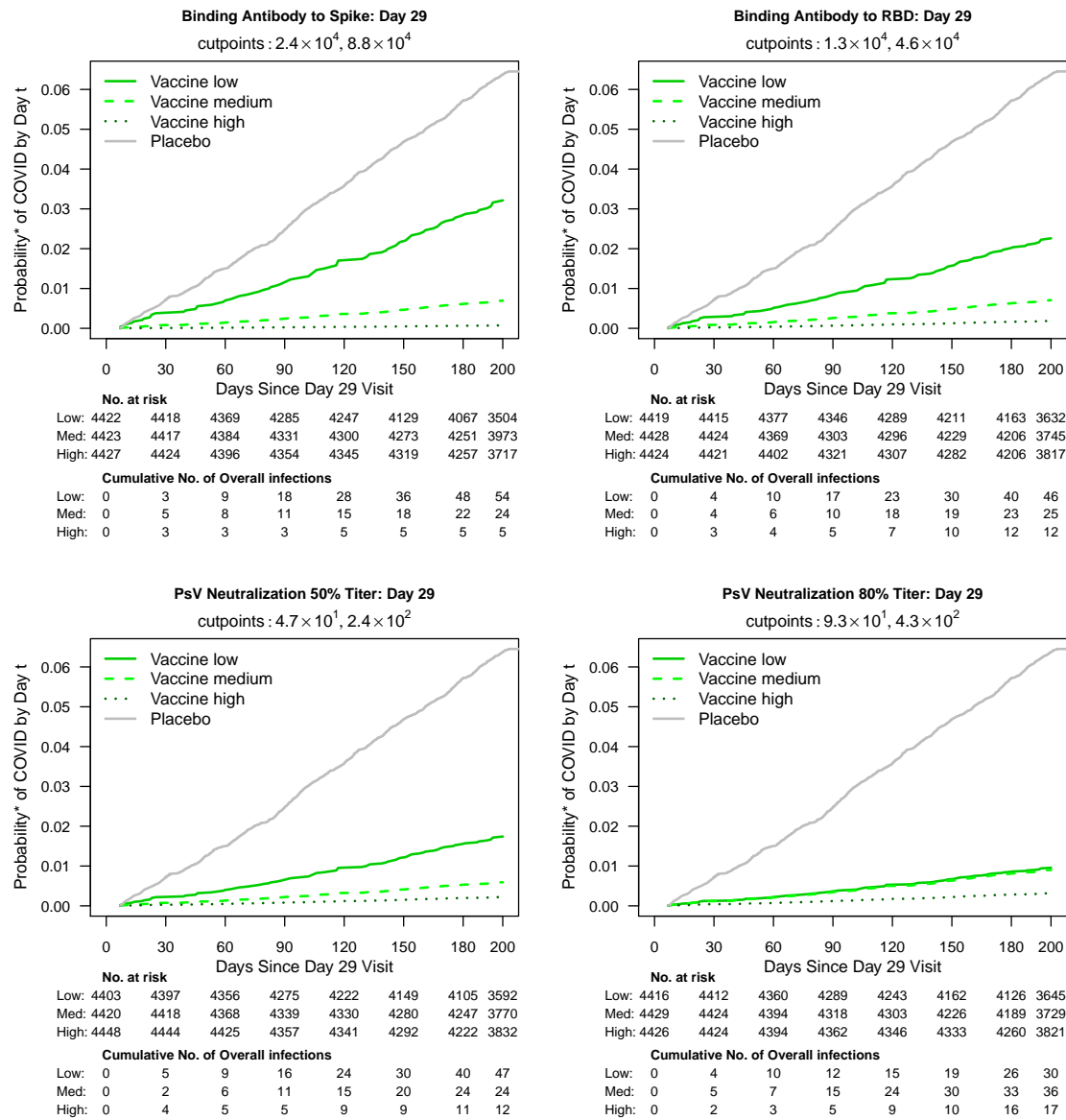


Figure 2.9: Marginalized cumulative incidence rate curves for trichotomized Day 29 markers among baseline seronegative vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.