CoVPN COVID-19 Correlates Analysis

the CoVPN Biostatistics Team

 $March\ 05,\ 2021$

Contents

1	Day	57 Univariate CoR: Cox Models of Risk	9
	1.1	Hazard ratios	9
	1.2	Marginalized risk and controlled vaccine efficacy plots	1
2	Day	29 Univariate CoR: Cox Models of Risk	2
	2.1	Hazard ratios	2
	2.2	Marginalized risk and controlled vaccine efficacy plots	2'

4 CONTENTS

List of Tables

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*	9
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 * .	10
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*	21
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*	22

6 LIST OF TABLES

List of Figures

1.1	Forest plots of hazard ratios among baseline seronegative vaccine recipients and subgroups with 95% point-wise confidence intervals	11
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.	12
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.	13
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.	13
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.	14
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.	16
1.7	Marginalized cumulative risk by Day 'r tp' 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 172and its 95% pointwise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.	17
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	18

8 LIST OF FIGURES

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.	19
2.1	Forest plots of hazard ratios among baseline seronegative vaccine recipients and subgroups with 95% point-wise confidence intervals	23
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.	24
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.	25
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.	25
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.	26
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.	28
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 200and its 95% pointwise confidence interval. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.	29
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	30
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.	31
	tive incidence rate curve in the placebo arm.	٥l

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	No. cases /	HR per 1	10-fold incr.	P-value	q-value	FWER
Immunologic Marker	No. at-risk**	Pt. Est.	95% CI	(2-sided)		
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	Tertile	No. cases /	Attack	Haz	. Ratio	P-value	Overall P-	Overall q-	Overall
Immunologic Marker		No. at-risk**	rate	Pt. Est.	95% CI	(2-sided)	value***	value	FWER
Spike IgG (IU/ml)	Lower	67/4,425	0.0151	1	N/A	N/A	< 0.001	< 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	< 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	< 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	< 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.

1.1. HAZARD RATIOS

Binding Antibody to Spike: Day 57

Group	No. E	vents											HR (95% CI)
All baseline negative, vaccine	72		-										0.08 (0.05, 0.12)
Age >= 65	37	-	-										0.10 (0.06, 0.17)
Age < 65, At risk	27	-	-										0.06 (0.03, 0.11)
Age < 65, Not at risk	8	•-											0.01 (0.00, 0.06)
				١.								1	
		0	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2	

Binding Antibody to RBD: Day 57

Group	No. Ev	vents	HR (95% CI)
All baseline negative, vacci	ne 72		0.17 (0.12, 0.25)
Age >= 65	37		0.23 (0.15, 0.36)
Age < 65, At risk	27	-	0.11 (0.07, 0.18)
Age < 65, Not at risk	8	_	0.10 (0.02, 0.54)
		0 0.2 0.4 0.6 0.8 1 1.2	1.4 1.6 1.8 2

PsV Neutralization 50% Titer: Day 57

Group	No. Ev	No. Events											
All baseline negative, vaccin	ne 72		-	_								0.24 (0.18, 0.31)	
Age >= 65	37		-	_								0.25 (0.18, 0.36)	
Age < 65, At risk	27		-									0.23 (0.13, 0.39)	
Age < 65, Not at risk	8	_	•									0.11 (0.05, 0.29)	
		0	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2	

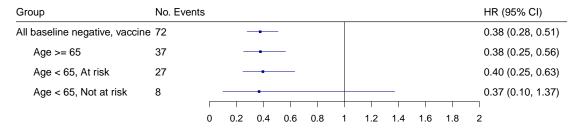


Figure 1.1: Forest plots of hazard ratios among baseline seronegative vaccine recipients and subgroups with 95% point-wise confidence intervals.

1.2 1.4

1.6 1.8

Group (Baseline Negative) No. Events HR (95% CI) All Vaccine 72 0.08 (0.05, 0.12) Age >= 65 37 0.10 (0.06, 0.17) 35 Age < 65 0.05 (0.03, 0.09) At risk 52 0.11 (0.07, 0.16) Not at risk 20 0.03 (0.01, 0.07) Comm. of color 28 0.10 (0.06, 0.18) 44 0.06 (0.04, 0.11) White Non-Hispanic 39 0.07 (0.04, 0.13) Men Women 33 0.07 (0.04, 0.14)

Binding Antibody to Spike: Day 57

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.

0.6 0.8

0.2 0.4

Group (Baseline Negative) No. Events HR (95% CI) All Vaccine 72 0.17 (0.12, 0.25) Age >= 65 37 0.23 (0.15, 0.36) 35 0.11 (0.07, 0.18) Age < 65 52 At risk 0.18 (0.12, 0.27) 0.13 (0.07, 0.27) Not at risk 20 Comm. of color 28 0.21 (0.13, 0.33) White Non-Hispanic 44 0.15 (0.08, 0.26) 39 0.23 (0.15, 0.35) Men Women 33 0.11 (0.06, 0.22)

Binding Antibody to RBD: Day 57

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.

0.6

0.8

1.2 1.4

1.6

1.8 2

0.2 0.4

Group (Baseline Negativ	HR (95% CI)		
All Vaccine	72		0.24 (0.18, 0.31)
Age >= 65	37		0.25 (0.18, 0.36)
Age < 65	35	-	0.21 (0.14, 0.34)
At risk	52		0.25 (0.18, 0.34)
Not at risk	20		0.19 (0.10, 0.35)
Comm. of color	28		0.26 (0.18, 0.39)
White Non-Hispanic	44		0.21 (0.14, 0.32)
Men	39		0.21 (0.13, 0.33)
Women	33		0.27 (0.18, 0.39)
		0 0.2 0.4 0.6 0.8 1 1.2 1.4 1.6 1.8	2

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.

Group (Baseline Negativ	nts									HR (95% CI)			
All Vaccine	72											0.38 (0.28, 0.51)	
Age >= 65	37		_		_							0.38 (0.25, 0.56)	
Age < 65	35		_	-								0.39 (0.25, 0.61)	
At risk	52		-	-	_							0.39 (0.27, 0.54)	
Not at risk	20										0.38 (0.22, 0.66)		
Comm. of color	28											0.32 (0.21, 0.48)	
White Non-Hispanic	44			-								0.43 (0.28, 0.66)	
Men	39											0.29 (0.18, 0.46)	
Women	33					-						0.47 (0.32, 0.70)	
			1										
		0	0.2	0.4	0.6	8.0	1	1.2	1.4	1.6	1.8	2	

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

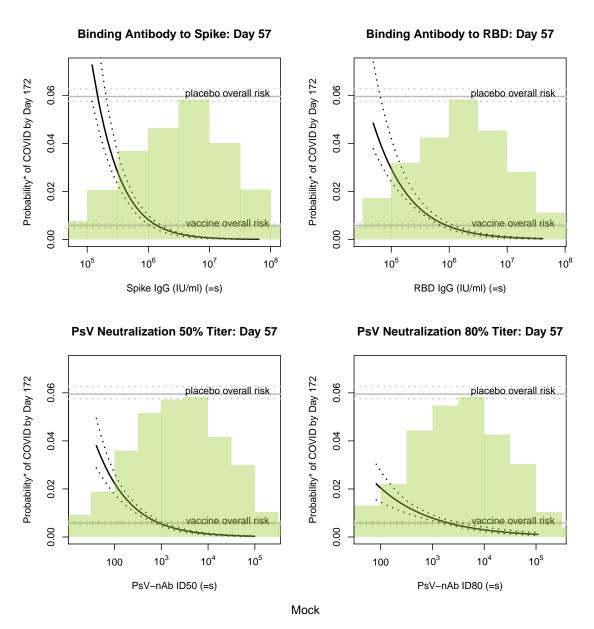


Figure 1.6: Marginalized cumulative risk by Day 'r tp' as functions of Day 57 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 172 and its 95% point-wise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

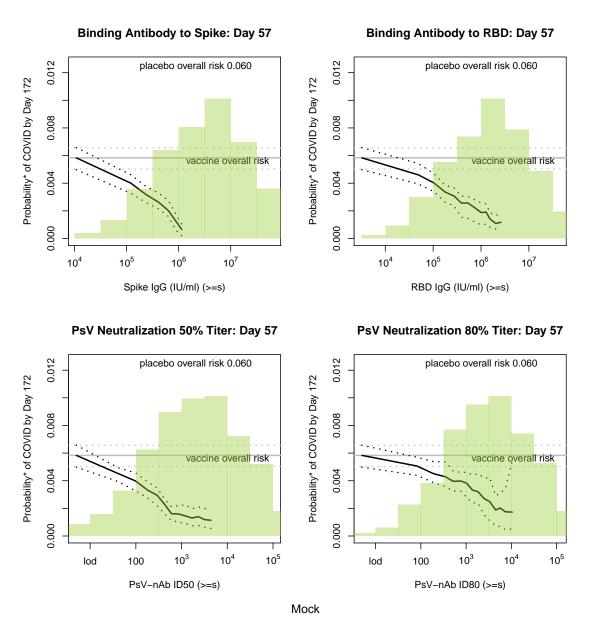


Figure 1.7: Marginalized cumulative risk by Day 'r tp' as functions of Day 57 markers above a threshold $(\geq s)$ among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required). The horizontal lines indicate the overall cumulative risk of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

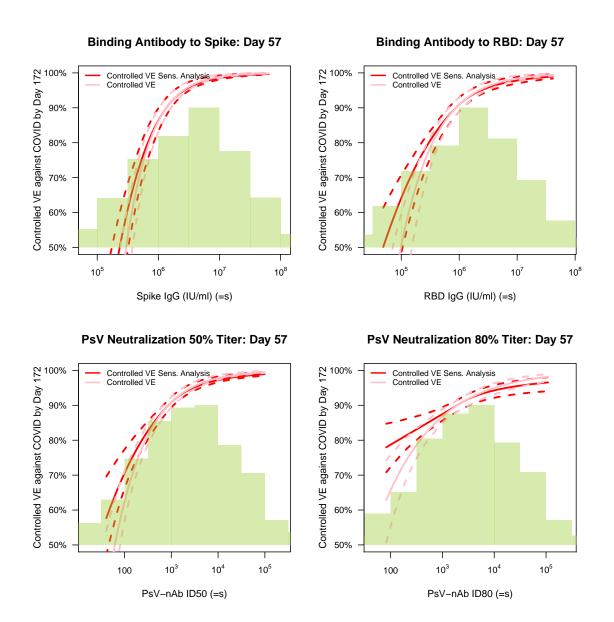


Figure 1.8: Controlled VE with sensitivity analysis as functions of Day 57 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

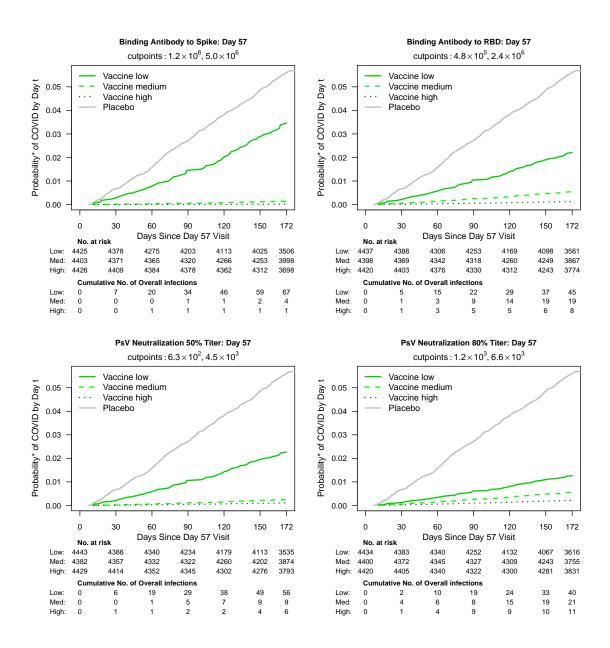


Figure 1.9: Marginalized cumulative incidence rate curves for trichotomized Day 57 markers among baseline seronegative vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.

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	No. cases /	HR per 1	10-fold incr.	P-value	q-value	FWER
Immunologic Marker	No. at-risk**	Pt. Est.	95% CI	(2-sided)		
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	Tertile	No. cases /	Attack	Haz	. Ratio	P-value	Overall P-	Overall q-	Overall
Immunologic Marker		No. at-risk**	rate	Pt. Est.	95% CI	(2-sided)	value***	value	FWER
Spike IgG (IU/ml)	Lower	54/4,422	0.0122	1	N/A	N/A	< 0.001	< 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	< 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	< 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	< 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.

2.1. HAZARD RATIOS

Binding Antibody to Spike: Day 29

23

Group	No. Eve	ents										HR (9	5% CI)
All baseline negative, vacci	ne 83	-	_									0.09 (0	0.05, 0.16)
Age >= 65	40	-	-									0.08 (0	0.04, 0.16)
Age < 65, At risk	30	-										0.05 (0	0.02, 0.17)
Age < 65, Not at risk	13											0.11 (0	0.01, 0.79)
		0	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.0		

Binding Antibody to RBD: Day 29

Group	No. Ev	No. Events										HR (95% CI)
All baseline negative, vacci	ne 83		-									0.25 (0.16, 0.38)
Age >= 65	40		-									0.23 (0.12, 0.45)
Age < 65, At risk	30											0.22 (0.11, 0.46)
Age < 65, Not at risk	13				_							0.24 (0.09, 0.65)
		0	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2

PsV Neutralization 50% Titer: Day 29

Group	No. Ever	No. Events										HR (95% CI)
All baseline negative, vacci	ne 83		_	•								0.32 (0.23, 0.46)
Age >= 65	40		_									0.28 (0.17, 0.46)
Age < 65, At risk	30			•								0.32 (0.17, 0.60)
Age < 65, Not at risk	13		-									0.48 (0.27, 0.86)
		0	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2

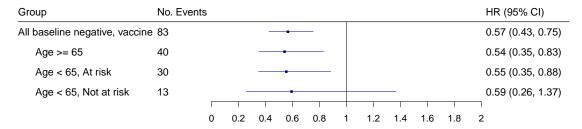


Figure 2.1: Forest plots of hazard ratios among baseline seronegative vaccine recipients and subgroups with 95% point-wise confidence intervals.

1.2 1.4

1.6 1.8

Group (Baseline Negative) No. Events HR (95% CI) All Vaccine 83 0.09 (0.05, 0.16) Age >= 65 40 0.08 (0.04, 0.16) Age < 65 43 0.07 (0.03, 0.18) At risk 55 0.10 (0.05, 0.18) Not at risk 28 0.06 (0.02, 0.15) Comm. of color 32 0.12 (0.06, 0.26) White Non-Hispanic 51 0.07 (0.03, 0.15) 0.09 (0.04, 0.17) Men 46 Women 37 0.09 (0.03, 0.22)

Binding Antibody to Spike: Day 29

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.

0.6 0.8

0.2 0.4

Binding Antibody to RBD: Day 29

Group (Baseline Negativ	e) No. Eve	ents	HR (95% CI)
All Vaccine	83		0.25 (0.16, 0.38)
Age >= 65	40		0.23 (0.12, 0.45)
Age < 65	43		0.23 (0.13, 0.42)
At risk	55		0.27 (0.17, 0.45)
Not at risk	28		0.18 (0.09, 0.39)
Comm. of color	32		0.27 (0.16, 0.48)
White Non-Hispanic	51		0.24 (0.13, 0.43)
Men	46		0.28 (0.17, 0.47)
Women	37		0.20 (0.10, 0.43)
		0 0.2 0.4 0.6 0.8 1 1.2 1.4 1.6 1.8	2

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.

Group (Baseline Negativ	e) No. Events		HR (95% CI)
All Vaccine	83		0.32 (0.23, 0.46)
Age >= 65	40		0.28 (0.17, 0.46)
Age < 65	43		0.36 (0.23, 0.57)
At risk	55		0.32 (0.21, 0.49)
Not at risk	28		0.33 (0.19, 0.57)
Comm. of color	32		0.40 (0.25, 0.65)
White Non-Hispanic	51		0.28 (0.17, 0.45)
Men	46		0.35 (0.22, 0.56)
Women	37		0.29 (0.17, 0.48)
			٦
		0 0.2 0.4 0.6 0.8 1 1.2 1.4 1.6 1.8	2

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.

Group (Baseline Negative	e) No. Events	S										HR (95% CI)
All Vaccine	83			-	-	_						0.57 (0.43, 0.75)
Age >= 65	40				•							0.54 (0.35, 0.83)
Age < 65	43				•							0.57 (0.37, 0.85)
At risk	55			_	-							0.58 (0.42, 0.81)
Not at risk	28				•		-					0.50 (0.28, 0.92)
Comm. of color	32			_	-							0.67 (0.45, 1.01)
White Non-Hispanic	51				•	_						0.50 (0.34, 0.74)
Men	46			_	-							0.60 (0.42, 0.86)
Women	37			-	•							0.52 (0.33, 0.84)
					- 1	- 1			- 1			
		0	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2

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

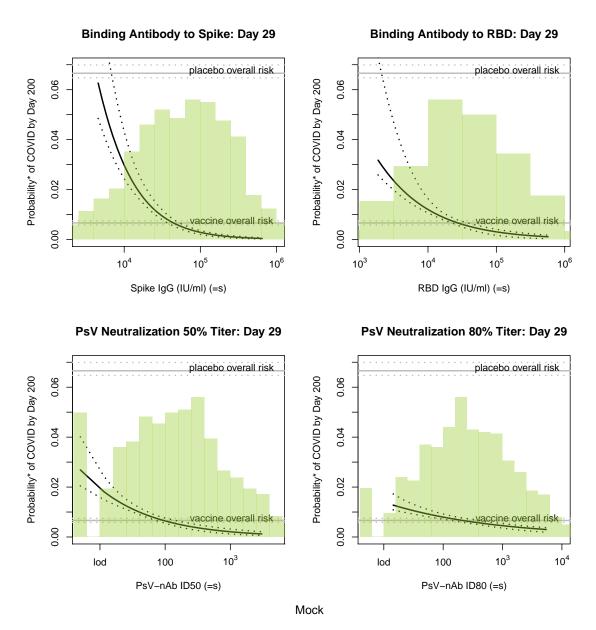


Figure 2.6: Marginalized cumulative risk by Day 'r tp' as functions of Day 29 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. The horizontal lines indicate the overall cumulative risk of the placebo and vaccine arms by Day 200 and its 95% point-wise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

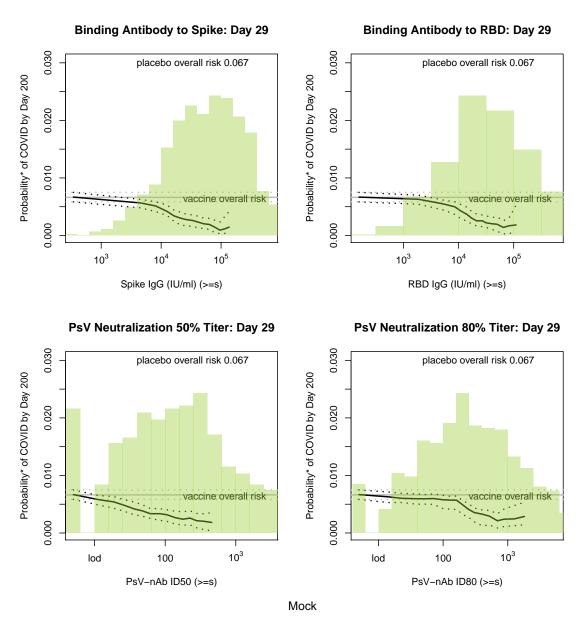


Figure 2.7: Marginalized cumulative risk by Day 'r tp' as functions of Day 29 markers above a threshold ($\geq s$) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands (at least 5 cases are required). The horizontal lines indicate the overall cumulative risk of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

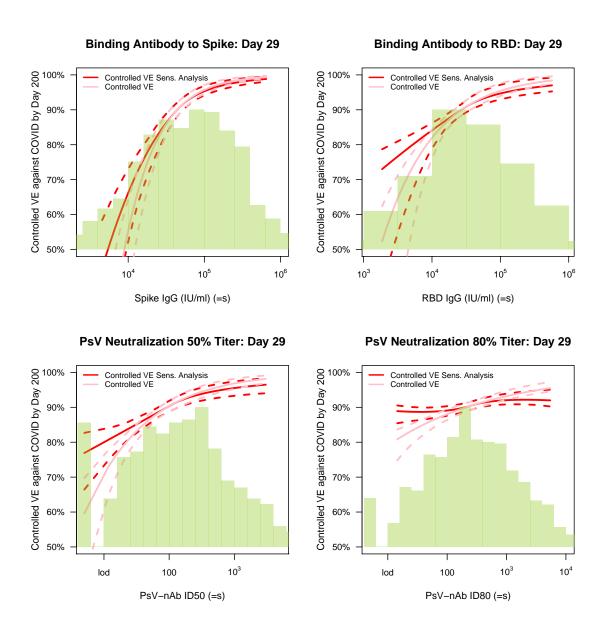


Figure 2.8: Controlled VE with sensitivity analysis as functions of Day 29 markers (=s) among baseline seronegative vaccine recipients with 95% bootstrap point-wise confidence bands. Histograms of the immunological markers in the vaccine arm are overlaid. lod: lower limit of detection.

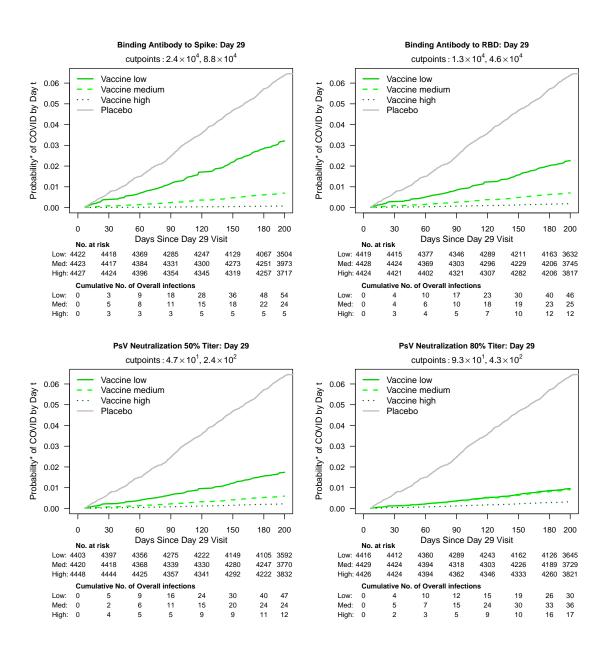


Figure 2.9: Marginalized cumulative incidence rate curves for trichotomized Day 29 markers among baseline seronegative vaccine recipients. The gray line is the overall cumulative incidence rate curve in the placebo arm.