CoR_COXPH Specifications

1 Specifications for CoR_COXPH

There are two main sets of results in the CoR_COXPH section of the report: (i) Cox regression model coefficients, and (ii) marginalized risk curves based on Cox models.

The population of interest for the D57 CoR study is defined as baseline negative, per-protocol, at risk at 7 days post the Day 57 visit. We are for the most part interested in the vaccine arm, but the placebo arm is sometimes also of interest as a comparison.

1.1 Cox regression model coefficients

Due to the two-phase sampling design, the survey package svycoxph function (using twophase function to create the design object) will be used for fitting Cox models and getting confidence intervals and P values.

Four biomarkers will be studied:

- Day57bindSpike
- Day57bindRBD
- Day57pseudoneutid50
- Day57pseudoneutid80.

Their trichotomized version adds cat at the end, e.g. Day57bindSpikecat.

Cox regression models are fit to both the baseline negative, vaccinee population (defined in more details above) and subgroups therein. All models adjust for the following baseline covariates:

- at risk or not
- community of color or not

The following two tables contain results to be verified, one for the continuous markers and the other for the trichotomized markers.

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

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						

Average follow-up time 172 days, maximum follow-up time 185 days.

** 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. The No. at-risk in the trichotomized table are weighted estimates based on the phase 2 samples.

*** Generalized Wald-test p-value of the null hypothesis that the hazard rate is constant across the Lower, Middle, and Upper tertile groups.

The q-values and FWER are computed using Sue Li's implementation of the Westfall and Young permutation-based method (kyotil::p.adj.perm) for the continuous and trichotomized markers together. We verify Sue's implementation through a Monte Carlo study that is outside of this verification plan.

For each of the continuous markers, we also fit the Cox model for subgroups defined by

- age >= 65
- age<65 and at risk
- age<65 and not at risk
- t risk
- Not at risk
- Comm of color
- White non-Hispanic
- Men
- Women