

IARHPV Correlates Analyses Report

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Chapter 1

Disclaimers

Reproducibility Notice

This project integrates the virtual environments framework provided by [the `renv` package](#) for computational reproducibility. By taking this approach, all results are generated using a consistent versioning of both R and several R packages. This version of the report was built with R version 4.0.4 (2021-02-15), [pandoc](#) version 2.3.1, and the following R packages:

package	version	source
bookdown	0.21.7	Github (rstudio/bookdown@0cec2fd)
bslib	0.2.4.9002	Github (rstudio/bslib@c7835c2)
data.table	1.14.0	CRAN (R 4.0.4)
delayed	0.4.0	Github (tlverse/delayed@f415340)
devtools	2.3.2	CRAN (R 4.0.4)
dplyr	1.0.5	CRAN (R 4.0.4)
ggplot2	3.3.3	CRAN (R 4.0.4)
hal9001	0.4.0	Github (tlverse/hal9001@b41ed5d)
haldensify	0.1.5	Github (nhejazi/haldensify@16350cc)
here	1.0.1	CRAN (R 4.0.4)
kableExtra	1.3.4	CRAN (R 4.0.4)
knitr	1.31	CRAN (R 4.0.4)
latex2exp	0.5.0	CRAN (R 4.0.4)
mvtnorm	1.1-1	CRAN (R 4.0.4)
origami	1.0.3	CRAN (R 4.0.4)
readr	1.4.0	CRAN (R 4.0.4)
rmarkdown	2.7.4	Github (rstudio/rmarkdown@a11240d)
skimr	2.1.3	CRAN (R 4.0.4)
sl3	1.4.3	Github (tlverse/sl3@982fd6)
stringr	1.4.0	CRAN (R 4.0.4)
SuperLearner	2.0-28	CRAN (R 4.0.4)
svyVGAM	1.0	CRAN (R 4.0.4)
tibble	3.1.1	CRAN (R 4.0.4)
tidyr	1.1.3	CRAN (R 4.0.4)
txshift	0.3.6	Github (nhejazi/txshift@c0f572a)
VGAM	1.1-5	CRAN (R 4.0.4)
xtable	1.8-4	CRAN (R 4.0.4)

To get started with using this project and its `renv` package library, we first recommend briefly reviewing the

`renv` collaboration guide.

Chapter 2

M18 Univariate CoR: Logistic Regression Models

The main regression model is the logistic regression model fit with osDesign unless specified otherwise. One model per row.

2.1 Odds ratios

Table 2.1: Inference for M 18antibody marker covariate-adjusted correlates of risk of HPV pooled over treatment arms: Odds ratios per 10-fold increment in the marker*

IARCHPV Immunologic Marker	No. cases / No. at-risk**	OR per 10-fold incr. Pt. Est. 95% CI	P-value (2-sided)	q-value ***	FWER
Anti L1, L2 IgG HPV6 (AU/ml)	26/3,023	0.76 (0.44-1.33)	0.340	0.810	1.000
Anti L1, L2 IgG HPV11 (AU/ml)	26/3,023	0.91 (0.53-1.56)	0.724	0.810	1.000
Anti L1, L2 IgG HPV16 (IU/ml)	26/3,023	0.87 (0.51-1.50)	0.626	0.810	1.000
Anti L1, L2 IgG HPV18 (IU/ml)	26/3,023	0.62 (0.39-1.01)	0.052	0.405	0.525
Anti L1, L2 IgG HPV31 (AU/ml)	26/3,023	1.44 (0.54-3.86)	0.465	0.810	1.000
Anti L1, L2 IgG HPV33 (AU/ml)	26/3,023	4.01 (0.01-1770.99)	0.655		
Anti L1, L2 IgG HPV45 (AU/ml)	26/3,023	0.31 (0.04-2.63)	0.281		
Anti L1, L2 IgG HPV52 (AU/ml)	26/3,023	1.38 (0.27-7.06)	0.702		
Anti L1, L2 IgG HPV58 (AU/ml)	26/3,023	1.29 (0.24-7.11)	0.766		
Anti L1, L2 IgG Score	26/3,023	0.90 (0.55-1.47)	0.687		

*Baseline covariates adjusted for: Age. *No. at-risk = estimated number in the population for analysis, i.e. trial participants entering or eligible to enter the sampling cohort post the M18 visit; no. cases = number of this cohort with an observed HPV endpoint. ***q-value and FWER (family-wide error rate) are computed over the set of p-values both for quantitative markers and categorical markers using the Westfall and Young permutation method (NA replicates).

Table 2.2: Inference for Day 18antibody marker covariate-adjusted correlates of risk of HPV pooled over treatment groups: Odds ratios per SD increment in the marker*

IARCHPV Immunologic Marker	No. cases / No. at-risk**	OR per SD incr. Pt. Est. 95% CI	P-value (2-sided)	q-value ***	FWER
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Anti L1, L2 IgG HPV6 (AU/ml)	26/3,023	0.83	(0.57-1.22)	0.340	0.810	1.000
Anti L1, L2 IgG HPV11 (AU/ml)	26/3,023	0.93	(0.64-1.36)	0.724	0.810	1.000
Anti L1, L2 IgG HPV16 (IU/ml)	26/3,023	0.91	(0.61-1.34)	0.626	0.810	1.000
Anti L1, L2 IgG HPV18 (IU/ml)	26/3,023	0.70	(0.49-1.00)	0.052	0.405	0.525
Anti L1, L2 IgG HPV31 (AU/ml)	26/3,023	1.16	(0.77-1.75)	0.465	0.810	1.000
Anti L1, L2 IgG HPV33 (AU/ml)	26/3,023	1.08	(0.78-1.50)	0.655		
Anti L1, L2 IgG HPV45 (AU/ml)	26/3,023	0.74	(0.43-1.28)	0.281		
Anti L1, L2 IgG HPV52 (AU/ml)	26/3,023	1.08	(0.72-1.63)	0.702		
Anti L1, L2 IgG HPV58 (AU/ml)	26/3,023	1.05	(0.75-1.47)	0.766		
Anti L1, L2 IgG Score	26/3,023	0.92	(0.60-1.39)	0.687		

*Baseline covariates adjusted for: Age. **No. at-risk = estimated number in the population for analysis, i.e. trial participants entering or eligible to enter the sampling cohort post the M18 visit; no. cases = number of this cohort with an observed HPV endpoint. ***q-value and FWER (family-wide error rate) are computed over the set of p-values both for quantitative markers and categorical markers using the Westfall and Young permutation method (NA replicates).

Table 2.3: Inference for Day 18 antibody marker covariate-adjusted correlates of risk of HPV in the vaccine group: Hazard ratios for Middle vs. Upper tertile vs. Lower tertile*

IARCHPV 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	
Anti L1, L2 IgG HPV6 (AU/ml)	Lower	12/1,012	0.0119	1	N/A	N/A	0.327	0.810	1.000
	Middle	7/1,011	0.0069						
	Upper	6/1,000	0.0060	0.62	(0.27-1.43)	0.266			
Anti L1, L2 IgG HPV11 (AU/ml)	Lower	9/1,029	0.0087	1	N/A	N/A	0.810	0.810	1.000
	Middle	9/ 999	0.0090						
	Upper	7/ 995	0.0070	1.13	(0.45-2.83)	0.796			
Anti L1, L2 IgG HPV16 (IU/ml)	Lower	11/1,030	0.0107	1	N/A	N/A	0.675	0.810	1.000
	Middle	7/ 999	0.0070						
	Upper	7/ 994	0.0070	0.69	(0.27-1.78)	0.442			
Anti L1, L2 IgG HPV18 (IU/ml)	Lower	14/1,007	0.0139	1	N/A	N/A	0.081	0.405	0.729
	Middle	3/1,015	0.0030						
	Upper	9/1,001	0.0090	0.24	(0.07-0.83)	0.025			
Anti L1, L2 IgG HPV31 (AU/ml)	Lower	16/1,834	0.0087	1	N/A	N/A	0.798	0.810	1.000
	Middle	6/ 598	0.0100						
	Upper	4/ 591	0.0068	1.24	(0.48-3.18)	0.658			
Anti L1, L2 IgG HPV33 (AU/ml)	Lower	25/2,961	0.0084	1	N/A	N/A	0.521		
	Middle	1/ 62	0.0161						
	Upper	NA/ NA		2.14	(0.21-21.83)	0.521			
Anti L1, L2 IgG HPV45 (AU/ml)	Lower	24/2,524	0.0095	1	N/A	N/A	0.228		
	Middle	2/ 499	0.0040						
	Upper	NA/ NA		0.45	(0.12-1.65)	0.228			
Anti L1, L2 IgG HPV52 (AU/ml)	Lower	23/2,565	0.0090	1	N/A	N/A	0.620		
	Middle	3/ 458	0.0066						
	Upper	NA/ NA		0.75	(0.24-2.37)	0.620			
Anti L1, L2 IgG HPV58 (AU/ml)	Lower	22/2,633	0.0084	1	N/A	N/A	0.626		
	Middle	4/ 390	0.0103						
	Upper	NA/ NA		1.31	(0.44-3.92)	0.626			
Anti L1, L2 IgG Score	Lower	11/1,008	0.0109	1	N/A	N/A	0.142		
	Middle	4/1,020	0.0039						
	Upper	10/ 995	0.0101	0.38	(0.13-1.08)	0.069			

*Baseline covariates adjusted for: Age. Cutpoints (on the log10 scale): M18bindL1L2_HPV6 [0.48, 1.15), M18bindL1L2_HPV11 [0.57, 1.24), M18bindL1L2_HPV16 [1.13, 1.78), M18bindL1L2_HPV18 [0.45, 1.13), M18bindL1L2_HPV31 [-0.1, 0.58), M18bindL1L2_HPV33 [0.18), M18bindL1L2_HPV45 [0.06), M18bindL1L2_HPV52 [-0.1), M18bindL1L2_HPV58 [0.04), M18bindL1L2_mdw [-0.41, 0.26) **No. at-risk = estimated number in the population for analysis, i.e. trial participants entering or eligible to enter the sampling cohort post the M18 visit; no. cases = number of this cohort with an observed HPV endpoint. ***Generalized Wald-test p-value of the null hypothesis that the hazard rate is constant across the Lower, Middle, and Upper tertile groups. † q-value and FWER (family-wide error rate) are computed over the set of p-values both for quantitative markers and categorical markers using the Westfall and Young permutation method (NA replicates).

Table 2.4: Number of cases and non-cases in ph2 or not

ph2	Event Indicator	
	0	1
FALSE	2871	1
TRUE	126	25

Chapter 3

Appendix

This report was built with code from:

https://github.com/youyifong/correlates_reporting2-2/commits/c7ebff1ad87e235e0c748866b2e0d593f65f7624

and data from:

/networks/cavd/Objective 4/GH-VAP/ID27-Sankaranarayanan/analysis/correlates/adata/id27hvp_data_processed_20231120

with sha256 hash sum: 350c85a0acb389c54a80d28cef49a58340bbd731e5df78508938a9e45b2de8cb