

COVID-19 Baseline Risk Score Analysis Report

MockCOVE Study

USG COVID-19 Response Biostatistics Team

September 23, 2021

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Chapter 1

Disclaimers

- The data presented in the analysis originated from the Moderna Sponsored mRNA-1273-P301 clinical study and are provided to NIAID in accordance with Clinical Trial Agreement between the parties. The study was funded in part by BARDA under Government Contract No. 75A50120C00034
- The preliminary immunogenicity data presented here do not reflect the Sponsors statistical analysis plan and therefore should not be interpreted as a protocol defined read-out of the clinical study.
- These data are not to be disclosed without written permission of Moderna.

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Chapter 2

Baseline Risk Score (Proxy for SARS-CoV-2 Exposure)

Table 2.1: Variables considered for risk score analysis.

| Variable.Name | Definition | Total.missing.values | Comments |
|----------------------|--|----------------------|----------|
| MinorityInd | Baseline covariate underrepresented minority status (1=minority, 0=non-minority) | 0/13294 (0.0%) | NA |
| EthnicityHispanic | Indicator ethnicity = Hispanic (0 = Non-Hispanic) | 0/13294 (0.0%) | NA |
| EthnicityNotreported | Indicator ethnicity = Not reported (0 = Non-Hispanic) | 0/13294 (0.0%) | NA |
| EthnicityUnknown | Indicator ethnicity = Unknown (0 = Non-Hispanic) | 0/13294 (0.0%) | NA |
| Black | Indicator race = Black (0 = White) | 0/13294 (0.0%) | NA |
| Asian | Indicator race = Asian (0 = White) | 0/13294 (0.0%) | NA |
| NatAmer | Indicator race = American Indian or Alaska Native (0 = White) | 0/13294 (0.0%) | NA |
| PacIsl | Indicator race = Native Hawaiian or Other Pacific Islander (0 = White) | 0/13294 (0.0%) | NA |
| Multiracial | Indicator race = Multiracial (0 = White) | 0/13294 (0.0%) | NA |
| Other | Indicator race = Other (0 = White) | 0/13294 (0.0%) | NA |
| Notreported | Indicator race = Not reported (0 = White) | 0/13294 (0.0%) | NA |
| Unknown | Indicator race = unknown (0 = White) | 0/13294 (0.0%) | NA |
| HighRiskInd | Baseline covariate high risk pre-existing condition (1=yes, 0=no) | 0/13294 (0.0%) | NA |
| Sex | Sex assigned at birth (1=female, 0=male) | 0/13294 (0.0%) | NA |
| Age | Age at enrollment in years, between 18 and 85 | 0/13294 (0.0%) | NA |
| BMI | BMI at enrollment (kg/m^2) | 0/13294 (0.0%) | NA |

Table 2.2: All learner-screen combinations (14 in total) used as input to the Superlearner.

| Learner | Screen* |
|---------|---|
| SL.mean | all |
| SL.glm | all glmnet univar_logistic_pval highcor_random |

Note:

*Screen details:

all: includes all variables

glmnet: includes variables with non-zero coefficients in the standard implementation of SL.glmnet that optimizes the lasso tuning parameter via cross-validation

univar_logistic_pval: Wald test 2-sided p-value in a logistic regression model < 0.10

highcor_random: if pairs of quantitative variables with Spearman rank correlation > 0.90 , select one of the variables at random

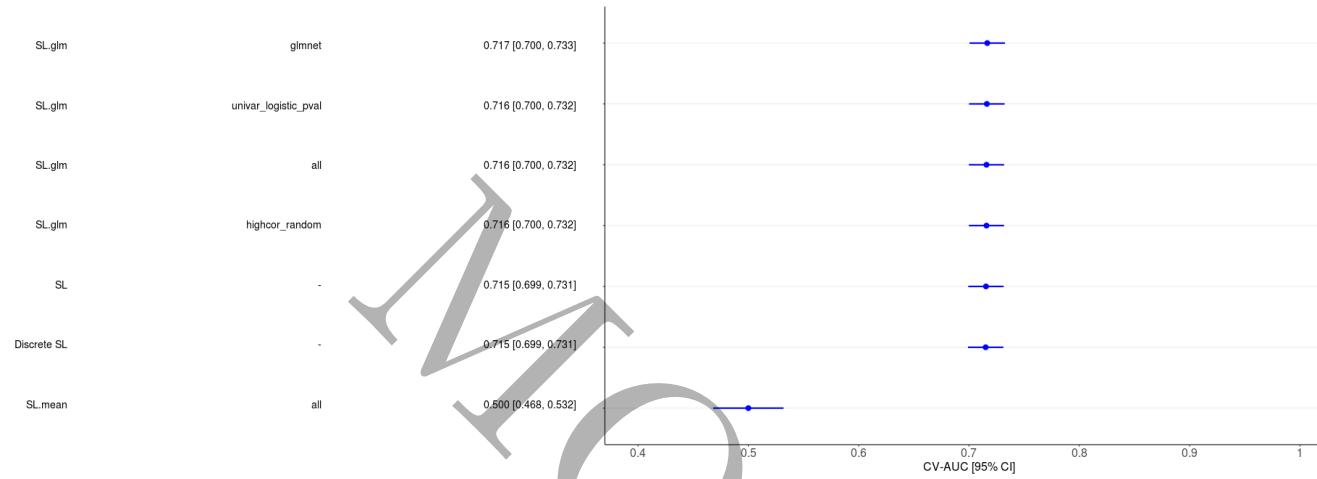


Figure 2.1: Cross-validated AUC (95% CI) of algorithms for predicting COVID-19 disease status starting 7 days after Day 57. CV-AUCs were computed using only data from the placebo arm.

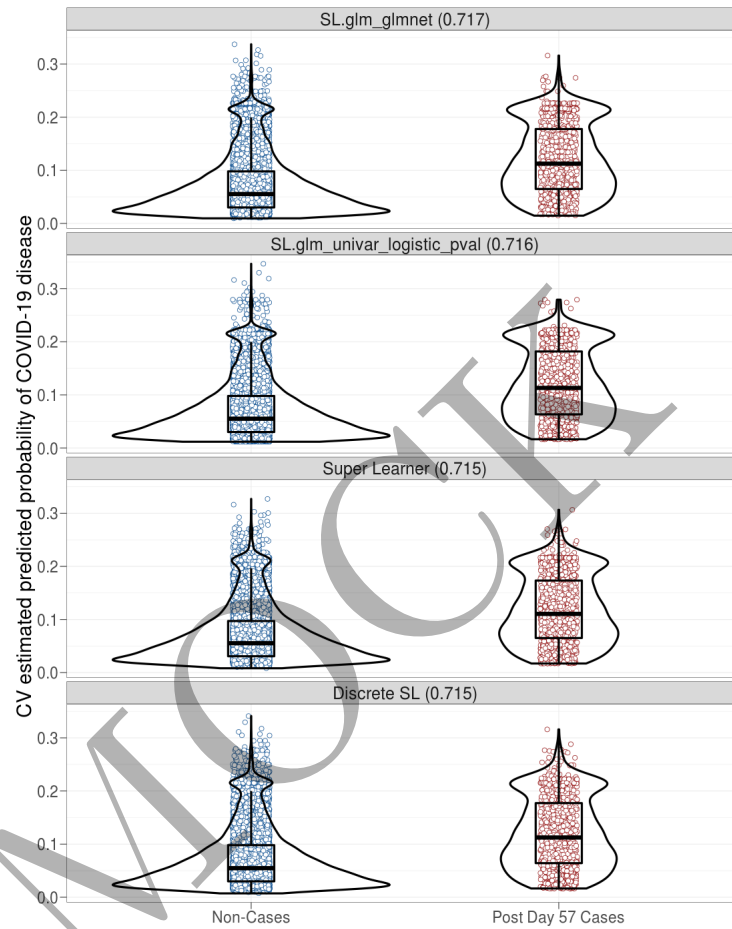


Figure 2.2: CV-estimated predicted probabilities of COVID-19 disease 7 days after Day 57 by case/control status for top 2 learners, SuperLearner and Discrete SL. CV-estimated predicted probabilities were computed using only data from the placebo arm.

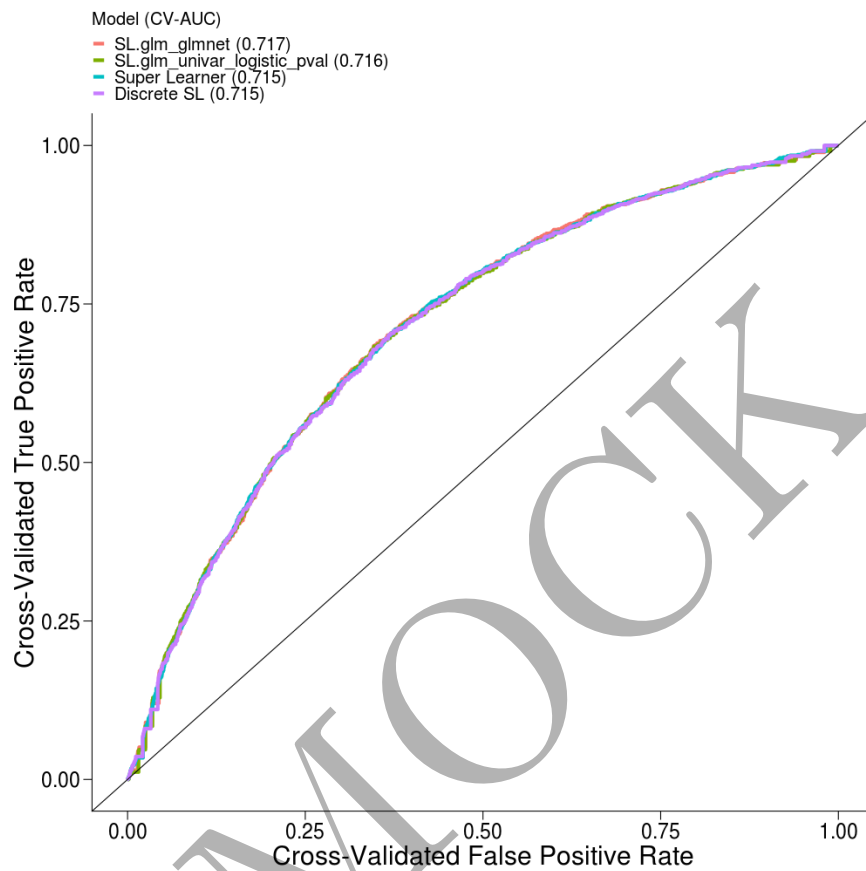


Figure 2.3: ROC curves based off CV-estimated predicted probabilities for the top 2 learners, Superlearner and Discrete SL. CV-estimated predicted probabilities were computed using only data from the placebo arm.

Table 2.3: Weights assigned by Superlearner.

| Learner | Screen | Weight |
|----------------|---------------------------------|---------------|
| SL.glm | screen_glmnet | 0.397 |
| SL.glm | screen_univariate_logistic_pval | 0.366 |
| SL.glm | screen_all | 0.215 |
| SL.mean | screen_all | 0.022 |
| SL.glm | screen_highcor_random | 0.000 |

Table 2.4: Learners assigned weight > 0.0 by Superlearner sorted by weight. Predictors within each learner are sorted by variable importance which is the absolute value in Coefficient (in case of learners like SL.glm, SL.gam, SL.glm.interaction), or Gain (in case of SL.xgboost) or Importance (in case of SL.ranger.imp).

| Learner | Screen | Weight | Predictors | Coefficient | Odds.Ratio |
|---------|---------------------------------|--------|----------------------|-------------|------------|
| SL.glm | screen_glmnet | 0.397 | (Intercept) | -2.771 | 0.063 |
| SL.glm | screen_glmnet | 0.397 | Age | 0.825 | 2.281 |
| SL.glm | screen_glmnet | 0.397 | EthnicityUnknown | -0.071 | 0.931 |
| SL.glm | screen_glmnet | 0.397 | Multiracial | -0.054 | 0.948 |
| SL.glm | screen_glmnet | 0.397 | Asian | 0.049 | 1.05 |
| SL.glm | screen_glmnet | 0.397 | EthnicityNotreported | 0.048 | 1.049 |
| SL.glm | screen_glmnet | 0.397 | Other | 0.048 | 1.05 |
| SL.glm | screen_glmnet | 0.397 | BMI | -0.046 | 0.955 |
| SL.glm | screen_glmnet | 0.397 | Black | -0.04 | 0.96 |
| SL.glm | screen_glmnet | 0.397 | PacIsl | -0.027 | 0.973 |
| SL.glm | screen_glmnet | 0.397 | EthnicityHispanic | -0.023 | 0.977 |
| SL.glm | screen_univariate_logistic_pval | 0.366 | (Intercept) | -2.766 | 0.063 |
| SL.glm | screen_univariate_logistic_pval | 0.366 | Age | 0.823 | 2.278 |
| SL.glm | screen_univariate_logistic_pval | 0.366 | EthnicityUnknown | -0.072 | 0.931 |
| SL.glm | screen_univariate_logistic_pval | 0.366 | Asian | 0.055 | 1.056 |
| SL.glm | screen_all | 0.215 | (Intercept) | -2.771 | 0.063 |
| SL.glm | screen_all | 0.215 | Age | 0.825 | 2.281 |
| SL.glm | screen_all | 0.215 | EthnicityUnknown | -0.071 | 0.931 |
| SL.glm | screen_all | 0.215 | Asian | 0.061 | 1.062 |
| SL.glm | screen_all | 0.215 | Other | 0.052 | 1.054 |
| SL.glm | screen_all | 0.215 | EthnicityNotreported | 0.049 | 1.05 |
| SL.glm | screen_all | 0.215 | Multiracial | -0.048 | 0.954 |
| SL.glm | screen_all | 0.215 | BMI | -0.046 | 0.955 |
| SL.glm | screen_all | 0.215 | MinorityInd | -0.024 | 0.976 |
| SL.glm | screen_all | 0.215 | Black | -0.023 | 0.978 |
| SL.glm | screen_all | 0.215 | PacIsl | -0.022 | 0.979 |
| SL.glm | screen_all | 0.215 | HighRiskInd | -0.019 | 0.981 |
| SL.glm | screen_all | 0.215 | EthnicityHispanic | -0.014 | 0.987 |
| SL.glm | screen_all | 0.215 | Unknown | 0.01 | 1.01 |
| SL.glm | screen_all | 0.215 | NatAmer | 0.009 | 1.009 |
| SL.glm | screen_all | 0.215 | Notreported | 0.006 | 1.006 |
| SL.glm | screen_all | 0.215 | Sex | -0.004 | 0.996 |

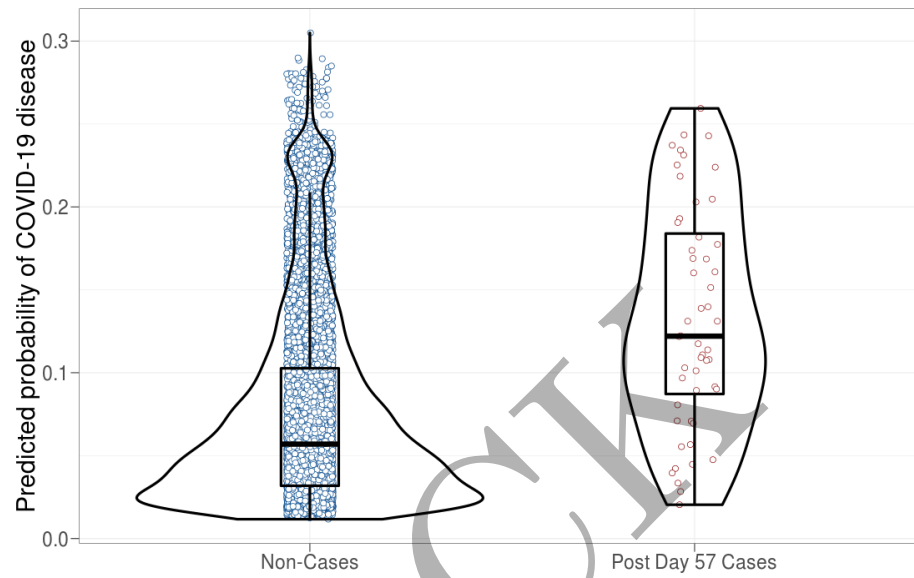


Figure 2.4: Superlearner predicted probabilities of COVID-19 disease in vaccinees 7 days after Day 57 by case/control status.

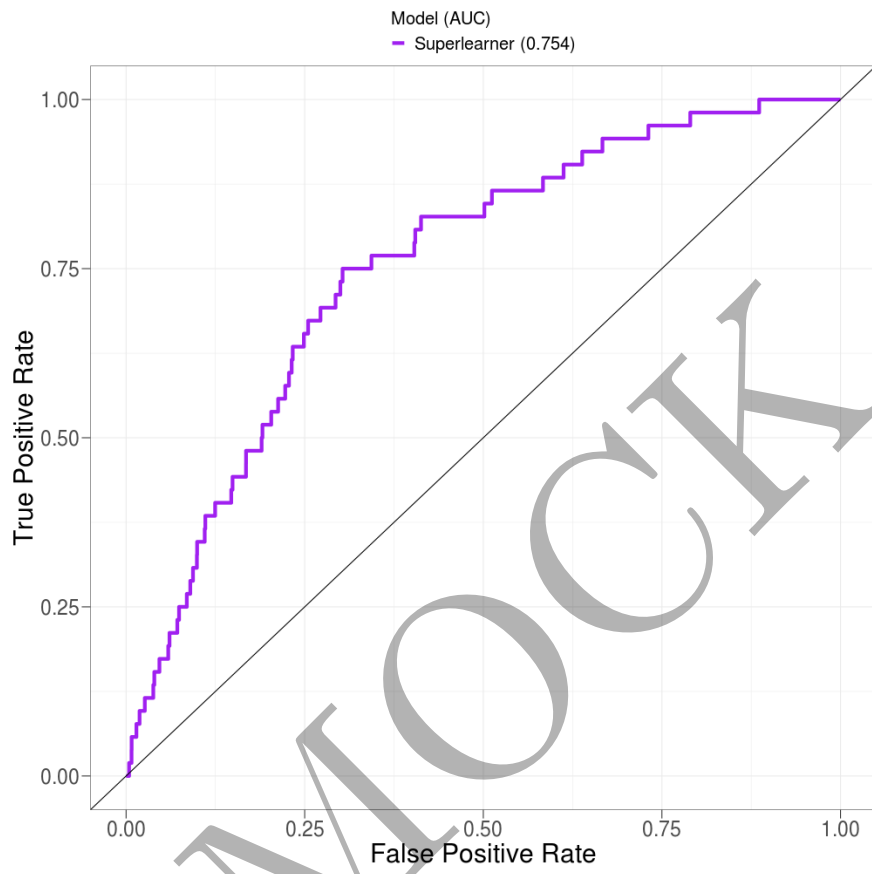


Figure 2.5: ROC curve based off Superlearner predicted probabilities in vaccinees.

Table 2.5: Cases per treatment arm prior to risk score analysis.

| Study-Arm | Non-Cases | Post-Day 57-Cases |
|-----------|-----------|-------------------|
| Placebo | 12271 | 1023 |
| Vaccine | 13168 | 52 |

Table 2.6: Cases per treatment arm post risk score analysis.

| Study-Arm | Non-Cases | Post-Day 57-Cases |
|-----------|-----------|-------------------|
| Placebo | 12271 | 1023 |
| Vaccine | 13168 | 52 |

Chapter 3

Appendix

- This report was built from the [CoVPN/correlates_reporting](https://github.com/CoVPN/correlates_reporting) repository with commit hash 6d7148a7abef866982a36689526c7581d51587e9. A diff of the changes introduced by that commit may be viewed at https://github.com/CoVPN/correlates_reporting/commit/6d7148a7abef866982a36689526c7581d51587e9
- The sha256 hash sum of the raw input file, “COVID_VEtrial_practicedata_primarystage1.csv”: 83d0f55d1745ffd42be124d8f9ec9a9903abcc13cd22f95e537542a08b41300a
- The sha256 hash sum of the processed file, “moderna_mock_data_processed.csv”: d806a7fb38690eff7ecb69f0bd6f74afc54fd2cab78067e383459bdcfa41cf32