COVID-19 Baseline Risk Score Analysis Report $_{\rm MockCOVE\ Study}$

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June 21, 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.



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, | 0/30000 (0.0%) | NA |
| EthnicityHispanic | 0=non-minority) Indicator ethnicity = Hispanic (0 = | 0/30000 (0.0%) | NA |
| EthnicityNotreported | Non-Hispanic) Indicator ethnicity = Not reported (0 = | 0/30000 (0.0%) | NA |
| EthnicityUnknown | Non-Hispanic) Indicator ethnicity = Unknown (0 = | 0/30000 (0.0%) | NA |
| Black | Non-Hispanic) Indicator race = Black $(0 = White)$ | 0/30000 (0.0%) | NA |
| Asian | Indicator race $=$ Asian (0 = White) | 0/30000 (0.0%) | NA |
| NatAmer | Indicator race = American Indian or Alaska Native (0 = White) | 0/30000 (0.0%) | NA |
| PacIsl | Indicator race = Native Hawaiian or Other Pacific Islander (0 = White) | 0/30000 (0.0%) | NA |
| Multiracial | Indicator race = Multiracial (0 = White) | 0/30000 (0.0%) | NA |
| Other | Indicator race = Other (0 = White) | 0/30000 (0.0%) | NA |
| Notreported | Indicator race = Not reported (0 = White) | 0/30000 (0.0%) | NA |
| Unknown | Indicator race = unknown (0 = White) | 0/30000 (0.0%) | NA |
| HighRiskInd | Baseline covariate high risk pre-existing condition (1=yes, 0=no) | 0/30000 (0.0%) | NA |
| Sex | Sex assigned at birth (1=female, 0=male) | 0/30000 (0.0%) | NA |
| Age | Age at enrollment in years, between 18 and 85 | 0/30000 (0.0%) | NA |
| BMI | BMI at enrollment (kg/m^2) | 0/30000 (0.0%) | NA |

Table 2.2: All learner-screen combinations (28 in total) used as input to the Superlearner.

| Learner | Screen* |
|--------------------|--|
| SL.mean | all |
| SL.glm | all glmnet univar_logistic_pval highcor_random |
| SL.glm.interaction | glmnet univar_logistic_pval highcor_random |
| SL.glmnet | all |
| SL.gam | glmnet univar_logistic_pval highcor_random |
| SL.xgboost | all |
| SL.ranger.imp | all |

Note:

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 ${\bf r}$

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

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

^{*}Screen details:



Figure 2.1: Cross-validated AUC (95% CI) of algorithms for predicting COVID-19 disease status starting 7 days after Day 57.



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 $^{\rm CI}$



Figure 2.3: ROC curves based off CV-estimated predicted probabilities for the top 2 learners, Superlearner and Discrete SL.

Table 2.3: Weights assigned by Superlearner.

| Learner | Screen | Weight |
|--------------------|---------------------------------|--------|
| SL.gam | screen_highcor_random | 0.488 |
| SL.glmnet | screen_all | 0.253 |
| SL.ranger.imp | screen_all | 0.139 |
| SL.glm.interaction | $screen_glmnet$ | 0.120 |
| SL.mean | screen_all | 0.000 |
| SL.glm | screen_all | 0.000 |
| SL.xgboost | screen_all | 0.000 |
| SL.glm | screen_glmnet | 0.000 |
| SL.glm | screen_univariate_logistic_pval | 0.000 |
| SL.glm | screen_highcor_random | 0.000 |
| SL.glm.interaction | screen_univariate_logistic_pval | 0.000 |
| SL.glm.interaction | screen_highcor_random | 0.000 |
| SL.gam | screen_glmnet | 0.000 |
| SL.gam | screen_univariate_logistic_pval | 0.000 |

Predictors Coefficient Odds.Ratio Importance Learner Screen Weight screen_highcor_random SL.gam 0.488(Intercept) -2.8730.057 NASL.gam screen_highcor_random 0.488s(Age,2) 0.8292.290 NAs(BMI,2) 0.955 NASL.gam screen_highcor_random 0.488-0.046 0.950 NΑ $_{\mathrm{SL.gam}}$ screen_highcor_random 0.488MinorityInd -0.0520.488EthnicityHispanic 0.0041.004 NASL.gam screen_highcor_random $_{\mathrm{SL.gam}}$ screen_highcor_random 0.488EthnicityNotreported 0.043 1.044 NASL.gamscreen_highcor_random 0.488EthnicityUnknown -0.073 0.930 NASL.gam0.488Black0.0041.004 NAscreen highcor random $_{\mathrm{SL.gam}}$ screen_highcor_random 0.488Asian 0.069 1.071 NASL.gamscreen_highcor_random 0.488NatAmer 0.0151.016 NAPacIsl SL.gam screen_highcor_random 0.488-0.013 0.987NΑ $_{\mathrm{SL.gam}}$ screen_highcor_random 0.488Multiracial -0.046 0.955 NASL.gam screen highcor random 0.488Other 0.0641.066 NA $_{\mathrm{SL.gam}}$ screen_highcor_random 0.488Notreported 0.003 1.003 NASL.gam screen_highcor_random 0.488Unknown 0.003 1.003 NAHighRiskInd-0.026 0.974 NASL.gam screen_highcor_random 0.488 SL.gam screen_highcor_random 0.488Sex-0.001 0.999 NA0.253 -2.665 0.070 NΑ SL.glmnet screen all (Intercept) SL.glmnetscreen_all 0.253MinorityInd 0.000 1.000 NASL.glmnet 0.253EthnicityHispanic 0.000 1.000 NΑ screen all SL.glmnet screen_all 0.253EthnicityNotreported 0.000 1.000 NA0.253 EthnicityUnknown NASL.glmnet screen_all 0.000 1.000 0.253 1.000 SL.glmnet Black 0.000 NAscreen all SL.glmnetscreen_all 0.253Asian 0.000 1.000 NA0.253NatAmer 1.000 NASL.glmnet screen all 0.000 SL.glmnetscreen_all 0.253PacIsl 0.000 1.000 NASL.glmnet 0.253Multiracial 0.000 1.000 NAscreen all SL.glmnetscreen_all 0.253Other 0.000 1.000 NASL.glmnet 0.253 Notreported 0.000 1.000 NAscreen_all 0.253 1.000 SL.glmnetscreen all Unknown 0.000 NASL.glmnetscreen_all 0.253HighRiskInd 0.000 1.000 NA0.253 0.000 1.000 NASL.glmnet screen all Sex SL.glmnetscreen all 0.253Age 0.4441.559 NASL.glmnetscreen_all 0.253 $_{\mathrm{BMI}}$ 0.000 1.000 NASL.ranger.imp screen all 0.139 MinorityInd NΑ NA9.100 SL.ranger.impscreen_all 0.139 EthnicityHispanic NANA9.685 0.139 EthnicityNotreported NΑ 9.247 SL.ranger.imp screen all NΑ SL.ranger.impscreen_all 0.139Ethnicity UnknownNANA6.908screen_all 0.139 Black NANA9.156 SL.ranger.imp 0.139NA SL.ranger.imp screen all Asian NA 7 256 SL.ranger.impscreen_all 0.139NatAmerNANA5.3810.139 PacIsl NA NA 2.553 SL.ranger.imp screen_all SL.ranger.imp0.139 Multiracial NANA5.054SL.ranger.imp0.139 Other NA NΑ 6.375 screen all

SL.ranger.imp

screen_all

0.139

Notreported

NA

NA

6.779

Table 2.4: Predictors in learners assigned weight > 0.0 by Superlearner.

Table 2.4: Predictors in learners assigned weight > 0.0 by Superlearner. (continued)

| Learner | Screen | Weight | Predictors | Coefficient | Odds.Ratio | Importance |
|--|--------------------------------|--------|---------------------------------------|-------------|------------|------------|
| SL.ranger.imp | screen_all | 0.139 | Unknown | NA | NA | 4.201 |
| SL.ranger.imp | screen_all | 0.139 | HighRiskInd | NA | NA | 17.116 |
| SL.ranger.imp | screen_all | 0.139 | Sex | NA | NA | 17.890 |
| SL.ranger.imp | screen_all | 0.139 | Age | NA | NA | 182.028 |
| SL.ranger.imp | screen_all | 0.139 | BMI | NA | NA | 231.544 |
| SL.glm.interaction | screen_glmnet | 0.12 | (Intercept) | -2.963 | 0.052 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported | -0.075 | 0.928 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityUnknown | -0.283 | 0.753 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black | -0.043 | 0.958 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Asian | 0.023 | 1.023 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Multiracial | -0.422 | 0.656 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Other | 0.074 | 1.077 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | HighRiskInd | -0.057 | 0.945 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Age | 0.849 | 2.337 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | BMI | -0.065 | 0.937 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:EthnicityUnknown | NA | NA | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:Black | 0.039 | 1.039 | NA |
| SL.glm.interaction | screen glmnet | 0.12 | EthnicityNotreported:Asian | 0.002 | 1.002 | NA |
| SL.glm.interaction | screen glmnet | 0.12 | EthnicityNotreported:Multiracial | -0.525 | 0.592 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:Other | 0.034 | 1.035 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:HighRiskInd | -0.069 | 0.934 | NA |
| SL.glm.interaction | screen glmnet | 0.12 | EthnicityNotreported:Age | 0.001 | 1.001 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:BMI | 0.043 | 1.044 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityUnknown:Black | 0.008 | 1.008 | NA |
| SL.glm.interaction | screen glmnet | 0.12 | EthnicityUnknown:Asian | -0.067 | 0.936 | NA |
| SL.glm.interaction | screen glmnet | 0.12 | EthnicityUnknown:Multiracial | -0.529 | 0.589 | NA |
| SL.glm.interaction | screen glmnet | 0.12 | EthnicityUnknown:Other | 0.066 | 1.068 | NA |
| SL.glm.interaction | screen glmnet | 0.12 | EthnicityUnknown:HighRiskInd | -0.009 | 0.991 | NA |
| SL.glm.interaction | screen glmnet | 0.12 | EthnicityUnknown:Age | 0.114 | 1.121 | NA |
| SL.glm.interaction | screen glmnet | 0.12 | EthnicityUnknown:BMI | -0.061 | 0.941 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black:Asian | NA | NA | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black:Multiracial | NA | NA | NA |
| SL.glm.interaction | screen glmnet | 0.12 | Black:Other | NA | NA | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black:HighRiskInd | -0.018 | 0.982 | NA |
| SL.glm.interaction | screen glmnet | 0.12 | Black:Age | 0.012 | 1.012 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black:BMI | -0.028 | 0.972 | NA |
| SL.glm.interaction | screen glmnet | 0.12 | Asian:Multiracial | NA | NA | NA |
| SL.glm.interaction | screen glmnet | 0.12 | Asian:Other | NA | NA | NA |
| SL.glm.interaction | screen_gimnet screen glmnet | 0.12 | Asian:Other Asian:HighRiskInd | 0.031 | 1.032 | NA NA |
| SL.glm.interaction | screen_gimnet | 0.12 | Asian:Age | 0.018 | 1.032 | NA NA |
| SL.glm.interaction | screen_glmnet screen_glmnet | 0.12 | Asian: Age Asian: BMI | -0.025 | 0.976 | NA NA |
| SL.glm.interaction | screen_gimnet | 0.12 | Multiracial:Other | NA | NA | NA |
| SL.glm.interaction | screen_gimnet screen_glmnet | 0.12 | Multiracial:HighRiskInd | -0.082 | 0.921 | NA NA |
| SL.glm.interaction SL.glm.interaction | screen_gimnet screen glmnet | 0.12 | Multiracial: Age | 0.103 | 1.108 | NA NA |
| | | | | | | |

| Learner | Screen | Weight | Predictors | Coefficient | Odds.Ratio | Importance |
|--------------------|---------------|--------|---------------------------------------|-------------|------------|------------|
| SL.glm.interaction | screen_glmnet | 0.12 | Other:HighRiskInd | 0.036 | 1.037 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Other:Age | -0.019 | 0.981 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Other:BMI | 0.036 | 1.037 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | HighRiskInd:Age | 0.025 | 1.026 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | HighRiskInd:BMI | -0.090 | 0.914 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Age:BMI | 0.012 | 1.012 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | (Intercept) | -2.963 | 0.052 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported | -0.075 | 0.928 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityUnknown | -0.283 | 0.753 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black | -0.043 | 0.958 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Asian | 0.023 | 1.023 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Multiracial | -0.422 | 0.656 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Other | 0.074 | 1.077 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | HighRiskInd | -0.057 | 0.945 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Age | 0.849 | 2.337 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | BMI | -0.065 | 0.937 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:EthnicityUnknown | NA | NA | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:Black | 0.039 | 1.039 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:Asian | 0.002 | 1.002 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:Multiracial | -0.525 | 0.592 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:Other | 0.034 | 1.035 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:HighRiskInd | -0.069 | 0.934 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:Age | 0.001 | 1.001 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityNotreported:BMI | 0.043 | 1.044 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityUnknown:Black | 0.008 | 1.008 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityUnknown:Asian | -0.067 | 0.936 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityUnknown:Multiracial | -0.529 | 0.589 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityUnknown:Other | 0.066 | 1.068 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityUnknown:HighRiskInd | -0.009 | 0.991 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityUnknown:Age | 0.114 | 1.121 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | EthnicityUnknown:BMI | -0.061 | 0.941 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black:Asian | NA | NA | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black:Multiracial | NA | NA | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black:Other | NA | NA | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black:HighRiskInd | -0.018 | 0.982 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black:Age | 0.012 | 1.012 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Black:BMI | -0.028 | 0.972 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Asian:Multiracial | NA | NA | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Asian:Other | NA | NA | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Asian:HighRiskInd | 0.031 | 1.032 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Asian:Age | 0.018 | 1.018 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Asian:BMI | -0.025 | 0.976 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Multiracial:Other | NA | NA | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Multiracial:HighRiskInd | -0.082 | 0.921 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Multiracial:Age | 0.103 | 1.108 | NA |

Table 2.4: Predictors in learners assigned weight > 0.0 by Superlearner. (continued)

Table 2.4: Predictors in learners assigned weight > 0.0 by Superlearner. (continued)

| _ | | | | | | |
|--------------------|---------------|--------|-------------------|-------------|------------|------------|
| Learner | Screen | Weight | Predictors | Coefficient | Odds.Ratio | Importance |
| SL.glm.interaction | screen_glmnet | 0.12 | Multiracial:BMI | 0.000 | 1.000 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Other:HighRiskInd | 0.036 | 1.037 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Other:Age | -0.019 | 0.981 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Other:BMI | 0.036 | 1.037 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | HighRiskInd:Age | 0.025 | 1.026 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | HighRiskInd:BMI | -0.090 | 0.914 | NA |
| SL.glm.interaction | screen_glmnet | 0.12 | Age:BMI | 0.012 | 1.012 | NA |



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.



Chapter 3

Appendix

- This report was built from the CoVPN/correlates_reporting repository with commit hash 226bc7eaf9eb64ac9661a9ae7c2793973f8d3ac6. A diff of the changes introduced by that commit may be viewed at https://github.com/CoVPN/correlates_reporting/commit/226bc7eaf9eb64ac9661a9ae7c2793973f8d3ac6
- 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": 28964ce20cfcd70a621aff9df412c42b1178d5e749e0f49ddd79fbff2dc7c90a