# **Supplementary Online Content**

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This supplementary material has been provided by the authors to give readers additional information about their work.

# eAppendix 1. Challenge Timeline

We launched the COVID-19 EHR DREAM challenge Question 1 (Q1) on May 6 2020 and Question 2 (Q2) on August 19 2020. When we started the challenge on May 6 2020, there were insufficient patients to split the data into training and evaluation datasets, so we initially started an open phase for Q1 where we only provided an evaluation dataset. We encouraged participants to submit models using either rule-based models or pre-trained models using data from other sources like COVID-19 Electronic Health Record (EHR) data from their own institutes' data warehouse or publicly available data. This open phase (dataset version "Week 1-8") for Q1 lasted 8 weeks until we enabled model training on July 6 2020. The data for Q2 had enough patients to start the challenge question with a training dataset provided. Q1 was run for 30 weeks and Q2 was run for 18 weeks until December 23 2020.

# eAppendix 2. Challenge Dataset

## **COVID-19 Dataset**

The challenge data was derived from the University of Washington (UW) Enterprise Data Warehouse (EDW) and contained EHR data from patients tested for COVID-19 at multiple medical sites across the UW Medicine Health system including UW Medical Center, Northwest Hospital, Harborview Medical Center, Neighborhood Clinics, and Seattle Cancer Care Alliance. The data contained visit history, laboratory results, demographic data, diagnosis codes, and procedures performed. UW Medicine Research IT converted the EHR data from the EDW to a standardized Observational Medical Outcomes Partnerships Common Data Model (OMOP CDM v5.3.1). Historical health data for patients who contracted COVID-19 during the pandemic ranged as far back as 2010.

#### **Challenge dataset**

We ran the COVID-19 EHR DREAM challenge as a continuous benchmarking exercise where the datasets were updated every 2-5 weeks to incorporate new patients and update existing patients' clinical trajectory. We curated two sub-datasets (diagnostic Q1 challenge dataset and prognostic Q2 challenge dataset) separately for the two challenge questions for the purpose of model training and evaluation. The Q1 challenge dataset involving all patients who received a COVID-19 test by the date when each data update was conducted, was split into training and evaluation datasets using a temporal ordering where the EHR data for the most recent 20% of patients tested for COVID-19 were included in the evaluation dataset and the remaining 80% of patients were included in the training dataset. The Q2 challenge dataset included only patients who tested positive for COVID-19 at an outpatient setting by the date when data update was conducted. This data was randomly split into training (70%) and evaluation datasets (30%) in order to maintain the same true positive prevalence (hospitalization within 21 days versus all patients tested positive during an outpatient visit). Gold standards for the training data were provided for model training and gold standards for evaluation dataset were hidden by the challenge organizers for scoring. For both the Q1 challenge dataset and Q2 challenge dataset, EHR data after each patient's COVID-19 test were removed. We incorporated new patients (i.e., patients who were not included in previous data update) into the evaluation datasets and made sure no patient data existing in the training dataset of previous versions was included in later evaluation dataset versions. OI challenge dataset has 6 versions over 30 weeks and Q2 challenge dataset has 4 versions over 18 weeks. See eTable 1 and eTable 2 for details about the challenge datasets.

## Synthetic data

We also curated a synthetic dataset which was adapted from the SynPuf (Synthetic OMOP dataset) to accurately reflect the distribution and size of the UW COVID-19 patient dataset. We randomly sampled clinical terms and concepts that appeared in more than 100 person's clinical records and populated the synthetic data with these terms. To better capture the record distribution, we created synthetic visit records and added them to individual patients until the synthetic record distribution resembled the real data record distribution, making sure that the number of patients with one visit, 10 visits, 100 visits was similar between the two datasets.

| Dataset version                                     | Week<br>1-8 | Week  | <u>(9-11</u> | Week  | 12-13 | Week  | 14-17 | Week  | 18-21 | Week  | 22-25 | Week  | 26-30 |
|---|-------------|-------|--------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Demograp<br>hic                                     | Eval        | Train | Eval         | Train | Eval  | Train | Eval  | Train | Eval  | Train | Eval  | Train | Eval  |
| Age (%)   |             |       |              |       |       |       |       |       |       |       |       |       |       |
| 0-17  | 1.64        | 2.09  | 3.95         | 2.50  | 5.43  | 2.86  | 5.79  | 3.26  | 4.86  | 3.50  | 4.41  | 3.68  | 3.71  |
| 18-24   | 5.85        | 6.79  | 17.88        | 9.05  | 9.21  | 9.10  | 9.44  | 9.14  | 9.24  | 9.14  | 12.47 | 9.26  | 10.97 |
| 25-49   | 41.41       | 40.71 | 36.81        | 39.88 | 40.45 | 39.93 | 39.25 | 39.96 | 35.91 | 39.65 | 35.82 | 39.45 | 35.08 |
| 50-64   | 27.27       | 26.33 | 22.10        | 25.48 | 23.69 | 25.28 | 23.64 | 25.05 | 25.89 | 25.04 | 24.34 | 24.97 | 25.17 |
| 65-99   | 23.83       | 24.08 | 19.26        | 23.08 | 21.22 | 22.82 | 21.88 | 22.58 | 24.09 | 22.67 | 22.96 | 22.64 | 25.07 |
| Gender<br>(%)                                       |             |       |              |       |       |       |       |       |       |       |       |       |       |
| Female  | 53.07       | 51.80 | 51.17        | 51.57 | 50.89 | 51.56 | 50.44 | 51.40 | 50.74 | 51.35 | 51.02 | 51.28 | 51.57 |
| Male  | 46.90       | 48.13 | 48.71        | 48.36 | 49.07 | 48.38 | 49.52 | 48.54 | 49.24 | 48.60 | 48.97 | 48.67 | 48.41 |
| Other/Nan   | 0.03        | 0.07  | 0.12         | 0.07  | 0.04  | 0.06  | 0.04  | 0.06  | 0.02  | 0.05  | 0.01  | 0.05  | 0.02  |
| Race (%)  |             |       |              |       |       |       |       |       |       |       |       |       |       |
| White   | 66.54       | 65.75 | 62.74        | 65.23 | 63.78 | 65.20 | 62.68 | 64.93 | 63.45 | 64.75 | 65.37 | 64.71 | 67.71 |
| Asian   | 9.25        | 8.88  | 9.60         | 9.07  | 8.14  | 8.99  | 8.46  | 8.91  | 9.83  | 9.02  | 10.80 | 9.18  | 13.77 |
| Black   | 9.70        | 10.01 | 8.55         | 9.73  | 9.02  | 9.70  | 8.67  | 9.56  | 10.22 | 9.57  | 8.50  | 9.56  | 10.46 |
| Other/Nan   | 14.51       | 15.36 | 19.11        | 15.97 | 19.06 | 16.10 | 20.18 | 16.61 | 16.50 | 16.66 | 15.32 | 16.55 | 8.06  |
| Covid-19<br>test (%)                                |             |       |              |       |       |       |       |       |       |       |       |       |       |
| Positive  | 8.77        | 4.78  | 3.66         | 4.67  | 4.10  | 4.67  | 3.92  | 4.61  | 3.06  | 4.60  | 1.94  | 4.50  | 1.80  |
| Negative  | 91.23       | 95.22 | 96.34        | 95.33 | 95.90 | 95.33 | 96.08 | 95.39 | 96.94 | 95.40 | 98.06 | 95.50 | 98.20 |
| population<br>(count)                               | 9134        | 35276 | 8464         | 45106 | 11186 | 49891 | 12325 | 58175 | 14054 | 64836 | 16008 | 71792 | 17841 |
| Earliest<br>COVID<br>measurem<br>ent date<br>(2020) |             |       | 06-20        |       | 07-09 |       | 07-19 |       | 08-06 |       | 08-23 |       | 09-12 |

eTable 1. Demographics Decomposition for Question 1 Challenge Datasets

| Dataset version            | Week 1-4 |       | Wee   | Week 5-8 |       | Week 9-13 |       | Week 14-18 |  |
|----------------------------|----------|-------|-------|----------|-------|-----------|-------|------------|--|
| Demographic                | Train    | Eval  | Train | Eval     | Train | Eval      | Train | Eval       |  |
| Age (%)                    |          |       |       |          |       |           |       |            |  |
| 0-17                       | 5.84     | 4.66  | 6.13  | 6.53     | 6.02  | 6.66      | 5.96  | 6.56       |  |
| 18-24                      | 17.91    | 17.54 | 16.91 | 17.99    | 17.62 | 18.15     | 17.45 | 18.18      |  |
| 25-49                      | 43.80    | 44.40 | 45.01 | 42.83    | 44.20 | 42.36     | 44.35 | 42.47      |  |
| 50-64                      | 20.54    | 23.51 | 20.82 | 23.41    | 20.82 | 23.45     | 20.69 | 23.40      |  |
| 65-99                      | 11.91    | 9.89  | 11.12 | 9.24     | 11.34 | 9.38      | 11.55 | 9.39       |  |
| Gender (%)                 |          |       |       |          |       |           |       |            |  |
| Female                     | 50.68    | 51.87 | 50.27 | 51.91    | 50.10 | 51.13     | 49.87 | 51.12      |  |
| Male                       | 49.24    | 48.13 | 49.66 | 48.09    | 49.84 | 48.87     | 50.06 | 48.88      |  |
| Other/Nan                  | 0.08     | 0.00  | 0.07  | 0.00     | 0.06  | 0.00      | 0.06  | 0.00       |  |
| Race (%)                   |          |       |       |          |       |           |       |            |  |
| White                      | 48.16    | 43.21 | 46.47 | 41.88    | 46.97 | 41.60     | 46.83 | 41.64      |  |
| Asian                      | 6.69     | 9.94  | 6.73  | 9.74     | 6.85  | 10.17     | 33.66 | 10.03      |  |
| Black                      | 11.51    | 15.49 | 12.08 | 15.10    | 12.39 | 15.25     | 12.53 | 15.50      |  |
| Other/Nan                  | 33.63    | 31.36 | 34.73 | 33.28    | 33.79 | 32.97     | 6.98  | 32.83      |  |
| 21-day hospitalization (%) |          |       |       |          |       |           |       |            |  |
| Positive                   | 5.04     | 5.04  | 4.99  | 4.94     | 5.12  | 5.14      | 5.52  | 5.37       |  |
| Negative                   | 94.96    | 94.96 | 95.01 | 95.06    | 94.88 | 94.86     | 94.48 | 94.63      |  |
| population (count)         | 1251     | 536   | 1484  | 628      | 1561  | 661       | 1576  | 671        |  |

eTable 2. Demographics Decomposition for Question 2 Challenge Datasets

**eTable 3.** Demographics Decomposition for the Cumulative Dataset, Temporal-Split Cumulative Evaluation Dataset (Evaluation 1, Evaluation 2 and Evaluation 3) and Ensemble Validation Dataset

|    | Demographic  | cumulative<br>training<br>dataset | cumulative<br>evaluation<br>dataset | Evaluation<br>1 | Evaluation<br>2 | Evaluation<br>3 | ensemble<br>validation<br>dataset |
|----|--|-----------------------------------|-------------------------------------|-----------------|-----------------|-----------------|-----------------------------------|
|    | Age (%)  |                                   |                                     |                 |                 |                 |                                   |
|    | 0-17   | 3.05                              | 4.51                                | 5.60            | 3.75            | 4.18            | 5.58                              |
|    | 18-24  | 9.06                              | 9.91                                | 9.82            | 11.50           | 8.40            | 6.93                              |
|    | 25-49  | 39.89                             | 37.73                               | 38.03           | 34.92           | 40.25           | 38.23                             |
|    | 50-64  | 25.21                             | 24.34                               | 24.27           | 25.00           | 23.76           | 23.9                              |
|    | 65-99  | 22.79                             | 23.51                               | 22.28           | 24.83           | 23.40           | 25.36                             |
|    | Gender (%)   |                                   |                                     |                 |                 |                 |                                   |
|    | Female   | 51.47                             | 51.07                               | 50.76           | 51.68           | 50.77           | 52.06                             |
|    | Male   | 48.47                             | 48.90                               | 49.21           | 48.31           | 49.17           | 47.9                              |
|    | Other/Nan  | 0.06                              | 0.03                                | 0.03            | 0.01            | 0.06            | 0.04                              |
|    | Race (%)   |                                   |                                     |                 |                 |                 |                                   |
|    | White  | 64.66                             | 65.14                               | 61.91           | 67.79           | 65.72           | 68.00                             |
|    | Asian  | 8.89                              | 10.30                               | 9.85            | 10.48           | 10.58           | 11.17                             |
|    | Black  | 9.51                              | 8.64                                | 9.15            | 8.04            | 8.73            | 8.14                              |
|    | Other/Nan  | 16.93                             | 15.92                               | 19.10           | 13.69           | 14.97           | 12.69                             |
|    | Covid-19 test (%)  |                                   |                                     |                 |                 |                 |                                   |
|    | Positive   | 5.16                              | 4.02                                | 3.93            | 2.45            | 5.68            | 2.16                              |
|    | Negative   | 94.84                             | 95.98                               | 96.07           | 97.55           | 94.32           | 97.84                             |
| Q1 | Number of patients tested for COVID  | 54600                             | 53936                               | 17932           | 18020           | 17984           | 12870                             |
|    | Patients hospitalized within 21 days (%)   |                                   |                                     |                 |                 |                 |                                   |
|    | Positive   | 5.73                              | 5.10                                |                 |                 |                 | 7.66                              |
|    | Negative   | 94.27                             | 94.90                               |                 |                 |                 | 92.34                             |
| Q2 | Number of patients<br>tested positive for<br>COVID in outpatient<br>setting(count) | 1554                              | 1552                                |                 |                 |                 | 208                               |

# eAppendix 3. Computational Resources for the Challenge

For models submitted by participants, we used a Common Workflow Language (CWL) pipeline to coordinate submission queues and automatically download and run Docker images. We provided two computation environments for participants (1) a cloud environment, with access to 32 CPU cores and 249 GB RAM, and (2) a UW on-premises server, with access to 32 CPU cores and 70 GB RAM. Participants were allowed up to 2 hours runtime at each environment.

## eAppendix 4. Model Selection Criteria

We received valid submissions (models scoring area under the receiver operating characteristic (AUROC) > 0.5) to Q1 from 18 teams. Over the course of the challenge, teams submitted multiple models that were scored against different versions of the COVID-19 patient datasets. For this analysis, we selected each team's best performing model (highest AUROC), regardless of the data version on which the model achieved its highest score. We re-trained each of the models on the cumulative training dataset and evaluated them on the cumulative evaluation datasets to select the top 10 models used for the analysis. Q1 model ranking is listed in eTable 4. We received valid submissions (models scoring AUROC > 0.5) to Q2 from 7 teams. Q2 model ranking is listed in eTable 5.

AUROC was used as the primary scoring metric for assessing model performance. The Bayes Factor, K, (bootstrapped distributions n = 1000) was computed to determine if the AUROCs between two models were consistently different. If two models were found to have a small Bayes Factor (K < 19), we used the area under the precision-recall curve (AUPRC) as a tie-breaking metric. Bayes factor was calculated using the number of times the current group won divided by the number of times the comparison group won. E.g., During the bootstrapping for Home-Sweet-Home and UWisc-Madison-BMI, Home-Sweet-Home won 1000 times, UWisc-Madison-BMI won 0 times. So, in eTable 4, the Bayes score of Home-Sweet-Home compared to UWisc-Madison-BMI is Inf.

**eTable 4.** The Performance Ranking of Models Submitted to Question 1. Bootstrapping (n = 1000, sample size 10000, sampled with replacement) to get a distribution of model performance.

|                     | Mode   | el Performance or | n cumulat | tive dataset  |
|---------------------|--------|-------------------|-----------|---------------|
| Team                | AUROC  | AUROC 95% CI      | AUPRC     | Bayes Factor* |
| Home-Sweet-Home     | 0.7757 | (0.7748, 0.7765)  | 0.2974    | Inf           |
| UWisc-Madison-BMI   | 0.6893 | (0.6884, 0.6902)  | 0.1692    | 3.07          |
| Bryson-and-Yao-Team | 0.6782 | (0.6774, 0.6791)  | 0.0805    | 499.00        |
| sucovid             | 0.6250 | (0.6240,0.6260)   | 0.0838    | 0.75          |
| Romaleks            | 0.6290 | (0.6281, 0.6299)  | 0.0682    | 3.65          |
| Gelo                | 0.6162 | (0.6153, 0.6170)  | 0.0589    | 1.06          |
| COVIDIL             | 0.6147 | (0.6138, 0.6156)  | 0.0564    | 6.52          |
| o888ca              | 0.5998 | (0.5989, 0.6006)  | 0.0540    | 19.83         |
| varikmp             | 0.5661 | (0.5652, 0.5670)  | 0.0504    | 1.61          |
| MLS                 | 0.5585 | (0.5576, 0.5593)  | 0.0444    |               |

**eTable 5.** The Performance Ranking of Models Submitted to Question 2. Bootstrapping (n = 1000, sample size 1000, sampled with replacement) to get a distribution of model performance.

|                     | Mode   | Performance on   | cumulat | tive dataset |
|---------------------|--------|------------------|---------|--------------|
| Team                | AUROC  | AUROC 95% CI     | AUPR    | Bayes Factor |
| ivanbrugere         | 0.7963 | (0.7943,0.7982)  | 0.1875  | 3.20         |
| MBakir              | 0.7759 | (0.7738,0.7780)  | 0.1783  | 6.93         |
| ArkansasAICampus20  | 0.7407 | (0.7388, 0.7426) | 0.1617  | 12.17        |
| Bryson-and-Yao-Team | 0.6701 | (0.6674, 0.6728) | 0.1593  | 0.11         |
| Gelo                | 0.7395 | (0.7376, 0.7415) | 0.1403  | 0.93         |
| varikmp             | 0.7411 | (0.7389, 0.7432) | 0.1308  | 15.95        |
| Home-Sweet-Home     | 0.6588 | (0.6563, 0.6613) | 0.0944  | -            |



eFigure 1. Weekly Best-Performing Models Submitted to Question 1

# eTable 6. Best Model Performance Reached Weekly for Question 1

| Week | AUROC | AUPRC | Dataset, version |
|------|-------|-------|------------------|
| 1    | 0.525 | 0.097 | Week 1-8         |
| 2    | 0.546 | 0.097 | Week 1-8         |
| 3    | 0.560 | 0.105 | Week 1-8         |
| 4    | 0.562 | 0.107 | Week 1-8         |
| 5    | 0.597 | 0.122 | Week 1-8         |
| 6    | 0.603 | 0.125 | Week 1-8         |
| 7    | 0.606 | 0.127 | Week 1-8         |
| 8    | 0.616 | 0.149 | Week 1-8         |
| 9    | 0.657 | 0.079 | Week 9-11        |
| 10   | 0.679 | 0.063 | Week 9-11        |
| 11   | 0.693 | 0.073 | Week 9-11        |
| 12   | 0.760 | 0.127 | Week 12-13       |
| 13   | 0.788 | 0.156 | Week 12-13       |
| 14   | 0.797 | 0.288 | Week 14-17       |
| 15   | 0.809 | 0.272 | Week 14-17       |
| 16   | 0.814 | 0.404 | Week 14-17       |
| 17   | 0.822 | 0.407 | Week 14-17       |
| 18   | 0.819 | 0.304 | Week 18-21       |
| 19   | 0.827 | 0.303 | Week 18-21       |
| 20   | 0.825 | 0.298 | Week 18-21       |
| 21   | 0.824 | 0.310 | Week 18-21       |
| 22   | 0.810 | 0.266 | Week 22-25       |
| 23   | 0.578 | 0.038 | Week 22-25       |
| 24   | 0.572 | 0.025 | Week 22-25       |
| 25   | 0.537 | 0.021 | Week 22-25       |
| 26   | 0.721 | 0.115 | Week 26-30       |
| 27   | 0.617 | 0.037 | Week 26-30       |
| 28   | 0.721 | 0.115 | Week 26-30       |
| 29   | 0.528 | 0.019 | Week 26-30       |
| 30   | 0.601 | 0.029 | Week 26-30       |



eFigure 2. Weekly Best-Performing Models Submitted to Question 2

| Week | AUROC | AUPRC | Dataset version |
|------|-------|-------|-----------------|
| 1    | 0.670 | 0.171 | Week 1-4        |
| 2    | 0.972 | 0.878 | Week 1-4        |
| 3    | 0.970 | 0.885 | Week 1-4        |
| 4    | 0.982 | 0.897 | Week 1-4        |
| 5    | 0.759 | 0.217 | Week 5-8        |
| 6    | 0.796 | 0.279 | Week 5-8        |
| 7    | 0.786 | 0.202 | Week 5-8        |
| 8    | 0.796 | 0.279 | Week 5-8        |
| 9    | 0.804 | 0.166 | Week 9-13       |
| 10   | 0.745 | 0.113 | Week 9-13       |
| 11   | 0.775 | 0.232 | Week 9-13       |
| 12   | 0.708 | 0.142 | Week 9-13       |
| 13   | 0.739 | 0.118 | Week 9-13       |
| 14   | 0.778 | 0.143 | Week 14-18      |
| 15   | 0.780 | 0.122 | Week 14-18      |
| 16   | 0.780 | 0.122 | Week 14-18      |
| 17   | 0.784 | 0.152 | Week 14-18      |
| 18   | 0.786 | 0.152 | Week 14-18      |

eTable 7. Best Model Performance Reached Weekly for Question 2

|                             | Prospective evaluation  |                         | Gene                    | der                        | Age                        |                            |                            |                            |                            |                            |
|-----------------------------|-------------------------|-------------------------|-------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|
| Team                        | Evaluation<br>1         | Evaluation<br>2         | Evaluation<br>3         | Female                     | Male                       | 0-17                       | 18-24                      | 25-49                      | 50-64                      | 65-99                      |
| Home-<br>Sweet-<br>Home     | 0.829 (0.828,<br>0.830) | 0.700 (0.699,<br>0.702) | 0.772 (0.771,<br>0.772) | 0.778<br>(0.777,<br>0.778) | 0.773<br>(0.772,<br>0.774) | 0.708<br>(0.707,<br>0.708) | 0.772<br>(0.771,<br>0.773) | 0.797<br>(0.796,<br>0.798) | 0.749<br>(0.748,<br>0.750) | 0.763<br>(0.762,<br>0.764) |
| UWisc-<br>Madison-<br>BMI   | 0.706 (0.705,<br>0.707) | 0.656 (0.655,<br>0.657) | 0.696 (0.695,<br>0.696) | 0.689<br>(0.688,<br>0.690) | 0.687<br>(0.686,<br>0.688) | 0.590<br>(0.590,<br>0.591) | 0.649<br>(0.649,<br>0.650) | 0.692<br>(0.691,<br>0.692) | 0.677<br>(0.676,<br>0.678) | 0.669<br>(0.668,<br>0.670) |
| Bryson-<br>and-Yao-<br>Team | 0.719 (0.719,<br>0.720) | 0.648 (0.647,<br>0.649) | 0.665 (0.664,<br>0.665) | 0.670<br>(0.669,<br>0.671) | 0.681<br>(0.680,<br>0.681) | 0.603<br>(0.603,<br>0.604) | 0.664<br>(0.663,<br>0.665) | 0.690<br>(0.689,<br>0.691) | 0.671<br>(0.670,<br>0.671) | 0.664<br>(0.663,<br>0.665) |
| sucovid                     | 0.679 (0.678,<br>0.680) | 0.607 (0.606,<br>0.608) | 0.595 (0.595,<br>0.596) | 0.640<br>(0.639,<br>0.641) | 0.609<br>(0.608,<br>0.610) | 0.619<br>(0.618,<br>0.620) | 0.648<br>(0.648,<br>0.649) | 0.660<br>(0.659,<br>0.661) | 0.602<br>(0.601,<br>0.603) | 0.574<br>(0.573,<br>0.575) |
| Romaleks                    | 0.657 (0.656,<br>0.657) | 0.588 (0.587,<br>0.589) | 0.629 (0.628,<br>0.630) | 0.632<br>(0.631,<br>0.633) | 0.624<br>(0.623,<br>0.625) | 0.516<br>(0.516,<br>0.517) | 0.554<br>(0.553,<br>0.555) | 0.644<br>(0.643,<br>0.644) | 0.615<br>(0.614,<br>0.615) | 0.625<br>(0.624,<br>0.626) |
| Gelo                        | 0.629 (0.628,<br>0.630) | 0.593 (0.592,<br>0.594) | 0.620 (0.619,<br>0.621) | 0.605<br>(0.604,<br>0.606) | 0.632<br>(0.631,<br>0.633) | 0.500<br>(0.499,<br>0.501) | 0.600<br>(0.600,<br>0.601) | 0.620<br>(0.619,<br>0.621) | 0.605<br>(0.604,<br>0.606) | 0.595<br>(0.594,<br>0.596) |
| COVIDIL                     | 0.640 (0.639,<br>0.641) | 0.571 (0.570,<br>0.572) | 0.618 (0.618,<br>0.619) | 0.627<br>(0.626,<br>0.628) | 0.603<br>(0.602,<br>0.603) | 0.547<br>(0.546,<br>0.547) | 0.582<br>(0.581,<br>0.582) | 0.640<br>(0.639,<br>0.640) | 0.587<br>(0.586,<br>0.588) | 0.590<br>(0.589,<br>0.591) |
| o888ca                      | 0.638 (0.637,<br>0.638) | 0.557 (0.556,<br>0.558) | 0.593 (0.592,<br>0.594) | 0.600<br>(0.599,<br>0.601) | 0.596<br>(0.595,<br>0.597) | 0.541<br>(0.541,<br>0.542) | 0.555<br>(0.554,<br>0.556) | 0.622<br>(0.621,<br>0.623) | 0.564<br>(0.563,<br>0.565) | 0.559<br>(0.558,<br>0.560) |
| varikmp                     | 0.611 (0.611,<br>0.612) | 0.555 (0.554,<br>0.556) | 0.538 (0.537,<br>0.539) | 0.567<br>(0.566,<br>0.568) | 0.565<br>(0.564,<br>0.566) | 0.530<br>(0.530,<br>0.531) | 0.605<br>(0.604,<br>0.606) | 0.575<br>(0.574,<br>0.576) | 0.558<br>(0.557,<br>0.559) | 0.508<br>(0.506,<br>0.509) |
| MLS                         | 0.590 (0.589,<br>0.591) | 0.522 (0.521,<br>0.523) | 0.552 (0.551,<br>0.553) | 0.567<br>(0.566,<br>0.568) | 0.550<br>(0.550,<br>0.551) | 0.485<br>(0.484,<br>0.486) | 0.535<br>(0.534,<br>0.536) | 0.572<br>(0.571,<br>0.572) | 0.516<br>(0.516,<br>0.517) | 0.499<br>(0.498,<br>0.500) |

**eTable 8.** Subpopulation Post-Challenge for Question 1. AUROCs and 95% CI of AUROCs on sub-evaluation groups for Question 1.

**eTable 9.** Subpopulation Post-challenge for Question 2. AUROCs and 95% CI of AUROCs on sub-evaluation groups for Question 2.

|                         | Status  |  |
|-------------------------|---|--|
| Team                    | patients tested positive during an outpatient visit | patients tested positive at any visit types' |
| ivanbrugere             | 0.794 (0.792, 0.796)                                | 0.799 (0.797, 0.801)                         |
| MBakir                  | 0.776 (0.774, 0.778)                                | 0.773 (0.770, 0.775)                         |
| ArkansasAICampus20      | 0.740 (0.738, 0.741)                                | 0.725 (0.723, 0.727)                         |
| Bryson-and-Yao-<br>Team | 0.672 (0.669, 0.674)                                | 0.695 (0.692, 0.698)                         |
| Gelo                    | 0.741 (0.739, 0.743)                                | 0.728 (0.726, 0.730)                         |
| varikmp                 | 0.740 (0.738, 0.742)                                | 0.728 (0.726, 0.731)                         |
| Home-Sweet-Home         | 0.659 (0.656, 0.662)                                | 0.652 (0.649, 0.655)                         |

| Q1 top<br>models                                | Home-Sweet-Home   | UWisc-Madison-BMI  | Bryson-and-Yao-<br>Team  |
|---|---|--|--|
| Number of<br>features used                      | 168   | 55   | 22   |
| Feature selection                               | Data driven   | pre-selected engineered<br>features                              | pre-selected<br>engineered features  |
| machine<br>learning<br>model type               | LightGBM  | LightGBM   | Logistic Regression  |
| EHR data<br>cut-off date                        | After January 1st, 2020 (for some tables)   | Only after February 1st, 2020                                    | No cut-off date  |
| OMOP table<br>used for<br>building the<br>model | measurement, condition occurrence,<br>observation, drug exposure, device<br>exposure, procedure occurrence,<br>visit occurrence, person,<br>goldstandard (for training) | person, condition<br>occurrence, measurement                     | person, condition<br>occurrence,<br>measurement                                |
| Q2 top<br>models                                | Ivanbrugere   | ArkansasAlCampus   | Bryson-and-Yao-<br>Team  |
| Number of<br>features used                      | 6209  | 15232  | 49   |
| Feature selection                               | data-driven   | data-driven + pre-selected<br>engineered features                | data-driven + pre-<br>selected engineered<br>features                          |
| Machine<br>learning<br>model type               | Boosted trees (catboost)  | Ensemble of random trees<br>(ExtraTreesClassifier)               | Logistic Regression  |
| EHR data<br>cut-off date                        | No: all dates   | No: all dates  | Condition: After<br>January 1st 2015<br>Measurement: After<br>January 1st 2019 |
| OMOP table<br>used for<br>building the<br>model | condition occurrence, observation,<br>measurement, drug exposure,<br>person, visit occurrence   | condition, drug exposure,<br>measurement, observation,<br>person | person, condition<br>occurrence,<br>measurement                                |

eTable 10. Analysis for Top Models Submitted to Challenge Question 1 and Question 2

|    | Home-Sweet-Home   | UWisc-Madison-BMI   | Bryson-and-<br>Yao-Team     |
|----|---|---|-----------------------------|
| 1  | Age   | Ethnicity   | Female                      |
| 2  | Count of Telephone call to a patient after 2020/01/01, if not existing, on or before 2020/01/01   | Most recent value of Leukocytes<br>[#/volume] in Blood by Automated<br>count after 2020-02-01 | Loss of sense<br>of smell   |
| 3  | Count of outpatient visit after 2020/01/01, if not existing, on or before 2020/01/01  | Age   | Hispanic                    |
| 4  | Mean measurement of Mean Albumin<br>[Mass/volume] in Serum or Plasma after<br>2020/01/01, if not existing, on or before<br>2020/01/01           | Most recent value of Creatinine<br>[Mass/volume] in Serum or Plasma<br>after 2020-02-01       | Not Hispanic<br>or Latino   |
| 5  | Mean measurement of diastolic blood pressure<br>after 2020/01/01, if not existing, on or before<br>2020/01/01                                   | Presence of cough after 2020-02-<br>01  | Cough                       |
| 6  | Mean measurement of carbon dioxide, total<br>[Moles/volume] in Serum or Plasma after<br>2020/01/01, if not existing, on or before<br>2020/01/01 | Presence of fever after 2020-02-01  | Race-<br>unknown            |
| 7  | Count of viral pneumonia after 2020/01/01, if not existing, on or before 2020/01/01   | Most recent value of hematocrit after 2020-02-01  | Fever                       |
| 8  | Maximum measurement of Systolic blood pressure after 2020/01/01, if not existing, on or before 2020/01/01                                       | Presence of Viral pneumonia after 2020-02-01  | Pneumonia                   |
| 9  | Minimum measurement of Systolic blood pressure after 2020/01/01, if not existing, on or before 2020/01/01                                       | Most recent value of Hemoglobin<br>[Mass/volume] in Blood after 2020-<br>02-01                | Diastolic blood<br>pressure |
| 10 | Mean measurement of Systolic blood pressure<br>after 2020/01/01, if not existing, on or before<br>2020/01/01                                    | Sex   | White-race                  |

|  | eTable | <b>11.</b> Top | 10 Features | for Question ' |
|--|--------|----------------|-------------|----------------|
|--|--------|----------------|-------------|----------------|

|    | Ivanbrugere  | ArkansasAlCampus   | Bryson and Yao<br>Team  |
|----|--|--|---|
| 1  | Peripheral oxygen saturation   | The amount of time (in days)<br>between each of the 12 most<br>recent OMOP entries for a<br>patient, and/or the number of<br>entries available if that number is<br>less than 12 | Acute severe<br>refractory<br>exacerbation of<br>asthma   |
| 2  | Emergency Room Visit   | Race   | Edema, generalized  |
| 3  | Drug test(s), presumptive, any<br>number of drug classes, any number<br>of devices or procedures; by<br>instrument chemistry analyzers (eg,<br>utilizing immunoassay [eg, EIA,<br>ELISA, EMIT, FPIA, IA, KIMS, RIA]),<br>chromatography (eg, GC, HPLC), and<br>mass spectrometry eit | Protein S actual/normal in<br>Platelet poor plasma by<br>Coagulation   | Gestation period, 28<br>weeks   |
| 4  | MCHC [Mass/volume] by Automated count  | Collection duration of Urine   | Late effect of medical<br>and surgical care<br>complication   |
| 5  | Acute renal failure syndrome   | Patient age  | The location id of the person   |
| 6  | Postoperative state  | Prostate specific Ag<br>[Mass/volume] in Serum or<br>Plasma  | Deficiency of<br>macronutrients   |
| 7  | Hematocrit [Volume Fraction] of Blood by Automated count   | Other cells/100 leukocytes in<br>Body fluid by Manual count  | Psychoactive<br>substance use<br>disorder   |
| 8  | Leukocytes [#/volume] in Blood by<br>Automated count   | Anion gap in Serum or Plasma   | Disease of the<br>respiratory system<br>complicating<br>pregnancy, childbirth<br>and/or the<br>puerperium |
| 9  | Oxygen [Partial pressure] in Venous blood  | Specific gravity of Urine by<br>Automated test strip   | Coag./bleeding tests abnormal   |
| 10 | Creatinine [Mass/volume] in Serum or<br>Plasma   | Lymphocytes/100 leukocytes in<br>Bronchial specimen  | Complication<br>occurring during<br>pregnancy   |

# eTable 12. Top 10 Features for Question 2

# eAppendix 5. Ensemble Model

Top models for each of the challenge questions (10 for Q1 and 7 for Q2) were retrained separately on cumulative training dataset. The 10 trained models were applied on cumulative evaluation dataset and ensemble validation dataset to generate prediction correspondingly - the individual model would output a confidence interval between 0 and 1 indicative of the likelihood of a patient test positive for COVID-19 (Q1) or hospitalized within 21 days after testing positive in outpatient settings (Q2). A logistic regression model with 10-fold cross validation was trained on individual predictions generated on the cumulative evaluation dataset. The trained ensemble model was then applied on the individual predictions generated on ensemble validation dataset to generate an ensemble prediction. AUROC and AUPRC were computed by comparing the ensemble prediction to the gold standard for ensemble validation dataset. (eFigure 3)

The Q1 ensemble model combining the top 10 teams reached an AUROC of 0.714 (95%CI 0.713-0.715) and AUPRC of 0.106, compared to Q1 best individual model's AUROC of 0.699 (95%CI 0.698-0.700) and AUPRC of 0.112. When stratifying the ensemble validation dataset based on demographics profile, Q1 ensemble model outperformed the best individual model in 10 of total 13 subgroups. (P<.001, eFigure4, eTable 13) The Q2 ensemble model combining the top 7 teams reached an AUROC of 0.740 (95%CI 0.739-0.742) and AUPRC of 0.286, compared to Q2 best individual model's AUROC of 0.772 (95%CI 0.771-0.774) and AUPRC of 0.193.



eFigure 3. Ensemble Model Diagram





**eTable 13.** Model Performance (AUROCs and 95% CI of AUROCs) Comparison Between Question 1 Ensemble Model and Question 1 Best Individual Model on Demographics Subgroups

|           |                        | Ensemble model      | Best individual model |
|-----------|------------------------|---------------------|-----------------------|
|           | Black                  | 0.729(0.728, 0.730) | 0.699(0.698, 0.700)   |
|           | White                  | 0.699(0.698, 0.700) | 0.676(0.675, 0.677)   |
|           | Asian                  | 0.683(0.682, 0.684) | 0.689(0.688, 0.690)   |
| Race      | Other                  | 0.682(0.681, 0.683) | 0.668(0.667, 0.669)   |
|           | Male                   | 0.666(0.665, 0.667) | 0.671(0.670, 0.672)   |
| Gender    | Female                 | 0.760(0.759, 0.761) | 0.730(0.728, 0.731)   |
|           | 0-17                   | 0.581(0.580, 0.582) | 0.614(0.613, 0.616)   |
|           | 18-24                  | 0.800(0.800, 0.801) | 0.762(0.761, 0.763)   |
|           | 25-49                  | 0.694(0.693, 0.695) | 0.687(0.686, 0.688)   |
|           | 50-64                  | 0.702(0.701, 0.703) | 0.691(0.690, 0.693)   |
| Age       | 65-99                  | 0.724(0.723, 0.726) | 0.696(0.695, 0.698)   |
|           | Hispanic or Latino     | 0.675(0.674, 0.676) | 0.673(0.672, 0.674)   |
| Ethnicity | Not Hispanic or Latino | 0.714(0.713, 0.716) | 0.696(0.695, 0.698)   |

# eAppendix 6. Top Teams' Model Description

# **Question 1 write-up**

## Home Sweet Home

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#### 1. Introduction

The methods developed by team Home Sweet Home include missing value imputation, concept id ranking, feature extraction, a two-step feature selection, feature normalization, and classification. Information contained in measurement, condition, observation, drug exposure, device exposure, procedure, and visit tables is used to derive features. In addition, age, gender, race, and ethnicity information is also included. Concept ids are ranked with respect to number of occurrences among COVID-19 patients tested as positive, which enables to sort features with respect to their importance for the pandemic. Home Sweet Home has been the best performing team so far in question 1 of the COVID-19 DREAM Challenge on the last six dataset versions. The software is available at <a href="https://aguedutr-my.sharepoint.com/:f:/g/personal/zafer aydin agu\_edu\_tr/EnA2BRYcJdpPoAk71tJcZ1EBz5Ck0KgnDhmKnocW4">https://aguedutr-my.sharepoint.com/:f:/g/personal/zafer aydin agu\_edu\_tr/EnA2BRYcJdpPoAk71tJcZ1EBz5Ck0KgnDhmKnocW4</a> UwtPA?e=UDM6Qc.

# 2. Methods

#### 2.1 Missing value imputation

We performed the following missing value imputation steps on data tables. The missing values in regular date fields or start date fields of the tables are filled with January 1st, 1900, in end date fields are filled with January 1st, 2100 and those in value\_as\_number field of the measurement table are filled with 0.0.

#### 2.2 Ranking concept ids

In each table of train data, we ranked concept ids with respect to their frequency of occurrence counts in positively labeled person\_ids. In computing the frequencies, we eliminated duplicates that are caused by multiple entries for the same person. We only considered data that could be related to covid-19 pandemic in the USA. For this purpose, we eliminated data if measurement\_date, condition\_end\_date, device\_exposure\_end\_date, drug\_exposure\_end\_date, procedure\_date, and visit\_date\_fields are equal to a date on or before January 1st, 2020.

#### 2.3 Feature extraction

In order to meet time quota restrictions of the challenge, we selected a maximum of the first 100 concept ids from each table of train set after the ranking process explained in Section 2.2. The same concept ids are also used to extract features for the test set in order to have equal number of features in both sets. Four types of features are extracted from the data tables: multi-instance learning based, count based, age, and one hot encoding based. These are explained in detail below.

#### 2.3.1 Multi-instance learning features

In this work, for each measurement\_concept\_id selected from the measurement table, minimum, maximum, and average of the value\_as\_number fields are computed as multi-instance learning (MIL) features. For a given person\_id and measurement\_concept\_id, if measurement data exists after January 1st, 2020 the MIL features are computed using data in this timeframe only. Otherwise, the MIL features are computed using data before this date if available. For the measurement\_concept\_id 3003694, which represents blood and Rh group, an ordinal encoding approach is used, which represents the feature values by integers from 0 to 7.

#### 2.3.2 Count features

Count features are computed for measurement, condition, observation, drug exposure, device exposure, procedure, and visit tables. For instance, the measurement count feature includes the number of times a given measurement is present in the measurement table for a given person\_id and measurement\_concept\_id. For drug exposure, drug quantity information is used as the count value. For the rest of the tables, a count of 1 is used for each entry. No time window constraint is applied for deriving the observation counts. For the remaining tables, count data after January 1st, 2020 is used only.

## 2.3.3 Age and one-hot encoding features

The age of each person is computed from the year of birth data available in person.csv file and is used as a single numeric feature. Gender, race, and ethnicity features are represented using a one-hot encoding approach applied to each feature separately.

## 2.4 Feature selection step 1

A wrapper-based feature selection strategy is employed on each data matrix of the train set separately (excluding age, gender, race, and ethnicity). A forward selection approach is used based on the ranking information derived as in Section 2.2. Starting from the empty set, in each iteration, a feature is included to the feature set and a 2-fold cross-validation is performed on the data matrix using lightGBM as the classifier [1] and stratified sampling to assign data samples to folds. The optimum feature set is found as the one that maximizes the AUPRC score. For MIL-based measurement features, once a feature is selected during the forward search, it is selected simultaneously from the three data matrices that contain minimum, maximum, and average values. The optimum number of features found for each table of the train set are used to select features for the tables of the test set directly using the same ranking information obtained for the train set.

#### 2.5 Feature selection step 2

Data matrices are concatenated along the feature dimension (excluding gender, race, and ethnicity matrices). A second feature selection is performed on this concatenated matrix, which uses an embedded selection strategy. For this purpose, SelectFromModel module [2] of the scikit-learn library [3] of Python is employed, in which the base learner is set to lightGBM [1] with default settings. The same features selected for the train set are also selected for the test set.

#### 2.6 Feature normalization

The data matrices excluding the matrices for gender, race, and ethnicity are normalized to the interval [0,1] using min-max scaling strategy [4].

## 2.7 Classification

The data matrix obtained at the end of the second feature selection step is concatenated with the data matrices for gender, race and ethnicity. In the training phase, a lightGBM classifier [1] with default settings is trained on this dataset and its learned parameters are used to compute predictions for the evaluation phase.

#### 3. Results

Table 1 shows the leaderboard results of the team Home Sweet Home for four dataset versions of question 1. The team has been ranked as first on these datasets.

Table 1: Results of Home Sweet Home for challenge question 1

| AUPRC   | 0.1154     | 0.2664     | 0.3102     | 0.4069     |
|---------|------------|------------|------------|------------|
| AUROC   | 0.7211     | 0.8095     | 0.8243     | 0.8222     |
| Dataset | Week 26-30 | Week 22-25 | Week 18-21 | Week 14-17 |

## 4. References

[1] lightGBM: <u>https://lightgbm.readthedocs.io/en/latest/</u>

[2] SelectFromModel: https://scikit-

learn.org/stable/modules/generated/sklearn.feature\_selection.SelectFromModel.html

[3] scikit-learn: https://scikit-learn.org/stable/

[4] Min-max scaler: https://scikit-learn.org/stable/modules/generated/sklearn.preprocessing.MinMaxScaler.html

#### UWisc-Madison-BMI

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#### Introduction

The task of Question 1 is to predict the risk that a patient's first SARS-CoV-2-test is positive given the patient's past EHR. We process diagnosis and measurement information and build a LightGBM model to make the prediction. Features are selected based on recent epidemiological studies [1,2].

## Methods

We build binary indicators to show whether the following conditions and measurement exist after February 1st, 2020. 29 condition features and 23 measurement features are selected, we include the concept id and concept name of each feature we have selected: '254761': Cough, '259153': Pain in throat, '378253': Headache, '437663': Fever, '4185711': Loss of sense of smell, '43530714': Sensory disorder of smell and/or taste, '255848': Pneumonia, '256722': Bronchopneumonia, '256723': Pneumonia and influenza, '261326': Viral pneumonia, '443410': Infective pneumonia, '437677': Abnormal findings on diagnostic imaging of lung, '4305080': Abnormal breathing, '4223659': Fatigue, '442752': Muscle pain, '4195085': Nasal congestion, '45757468': Vomiting without nausea, '27674': Nausea and vomiting, '31967': Nausea, '441408': Vomitting, '196523': Diarrhea, '80141': Functional diarrhea, '4057826': Irritable bowel syndrome with diarrhea, '4168213': Chest pain on breathing, '372448': Loss of consciousness, '380844': Prolonged loss of consciousness, '381135': Brief loss of consciousness, '435786': Disorder of sleep-wake cycle, '436522': Irregular sleep-wake pattern,'3020891': Temperature, '3027018': Heart rate, '3012888': Diastolic blood pressure, '3004249': Systolic blood pressure, '3023314': Hematocrit, '3013650': Neutrophils, '3004327': Lymphocytes, '3016502': SpO2, '4196147': Peripheral oxygen saturation, '3044938': Influenza virus A RNA [Presence] in Unspecified specimen by NAA with probe detection, '3044254': Respiratory syncytial virus RNA [Presence] in Unspecified specimen by NAA with probe detection, '3042596': Human coronavirus RNA [Presence] in Unspecified specimen by NAA with probe detection, '3042194': Human metapneumovirus RNA [Presence] in Unspecified specimen by NAA with probe detection, '3038297': Parainfluenza virus 4 RNA [Presence] in Unspecified specimen by NAA with probe detection, '3016723': Creatinine [Mass/volume] in Serum or Plasma, '3023103': Potassium [Moles/volume] in Serum or Plasma, '3025634': Parainfluenza virus 1 RNA [Presence] in Unspecified specimen by NAA with probe detection, '3000963': Hemoglobin [Mass/volume] in Blood, '3000905': Leukocytes [#/volume] in Blood by Automated count, '3008037': Lactate [Moles/volume] in Venous blood, '3005491': Lactate [Moles/volume] in Plasma venous, '3022250': Lactate dehydrogenase [Enzymatic activity/volume] in Serum or Plasma by Lactate to pyruvate reaction, '706181': SARS coronavirus 2 IgG Ab [Presence] in Serum or Plasma by Immunoassay.

Combining demographics information (gender, age, and race) and features listed above, there are 55 features in total for each patient. A LightGBM model is used to make the prediction. Missing values (if any) in the measurement data are handled by the LightGBM: the missing values are ignored when the model decides where to split and then are allocated to the branch where the loss is reduced the most [3]. Some of the hyperparameters are set as follows and others remain default values:'objective': 'binary';'metric': 'cross\_entropy';'learning\_rate': 0.01;'num\_leaves': 32;'feature\_fraction': 0.95.

#### Results

The AUROC and AUPR are 0.738 and 0.1127 respectively with the dataset version of "Week 18-21". **Reference** 

 Sun Y, Koh V, Marimuthu K, Ng OT, Young B, Vasoo S, Chan M, Lee VJ, De PP, Barkham T, Lin RT. Epidemiological and clinical predictors of COVID-19. Clinical Infectious Diseases. 2020 Jul 28;71(15):786-92.
Siordia Jr JA. Epidemiology and clinical features of COVID-19: A review of current literature. Journal of Clinical Virology. 2020 Apr 10:104357.

[3] "What Happens With Missing Values During Prediction? · Issue #2921 · Microsoft/Lightgbm". *Github*, 2021, https://github.com/microsoft/LightGBM/issues/2921.

#### **Bryson and Yao Team**

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#### Introduction

This model is based on logistic regression and developed to predict if a patient will test positive for COVID-19 using the scikit-learn package [1]. The model is developed in order to obtain high accuracy and true positive rate.

## Method

The age, ethnicity, gender and race of patients, together with nine conditions and four measurements are selected as features of our model. The conditions are dyspnea, cough, fever, sore throat, headache, pneumonia, muscle pain, loss of smell and fatigue. These are the common conditions observed on COVID-19 patients and they have a high correlation with COVID-19 [2]. The measurements are diastolic blood pressure, C-reactive protein measurement, lymphocyte count, and lactate dehydrogenase measurement [2,3]. All of these features were put into the logistic model as binary features (values 0.0 or 1.0), with the measured values binarized by comparing them with the normal standard value for that measurement.

According to Johns Hopkins Coronavirus Resource Center [4], the rate of positivity of Covid-19 tests varies between 5% and 20% over the past year, implying the database would contain a majority of negative results whose proportion may vary over time. This unbalanced data can lead to a biased model that predicts lots of positive cases negative. This problem was avoided by using a weighted logistic regression model that automatically adjusts weights inversely proportional to class frequencies in the input data.

To facilitate generalization and avoid over-fitting for what are initially fairly small datasets, we employed elastic net regularization, using a grid-search cross-validation strategy to determine optimal L1 and L2 regularization parameters, evaluated using the F1 score.

#### **Result Discussion**

The models are tested by Dream Challenge with the data set version "Week 12-13" and the AUROC and AUPRC are given as feedback.

With the simplest logistic regression model that trained with the features selected above, the AUROC is 0.6566 and AUPRC is 0.0793. With the weight logistic regression model, the AUROC increased to 0.6604 and AUPRC to 0.0817. After applying elastic net regularization and grid search, the AUROC and AUPRC increased significantly to 0.7375 and 0.0979 respectively, resulting in a significant increase in true positive rate.

# Reference

[1] https://scikit-learn.org/

[2] Feng C, Huang Z, Wang L, Chen X, Zhai Y, Zhu F, et al.A NovelTriage Tool of Artificial Intelligence Assisted Diagnosis Aid System for Suspected COVID-19 pneumonia In Fever Clinics. medRxiv. 2020.

Available from: https://www.medrxiv.org/content/early/2020/03/20/2020.03.19.20039099.

[3] Henry BM, Aggarwal G, Wong J, Benoit S, Vikse J, Plebani M, et al. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. The American journal of emergency medicine. 2020 Sep;38(9):1722–1726. 32738466[pmid].

Available from: <u>https://pubmed.ncbi.nlm.nih.gov/32738466</u>.

[4] Johns Hopkins Coronavirus Resource Center . Daily state-by-state testing trends.

Available from: https://coronavirus.jhu.edu/testing/individual-states

# Question 2 write up

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#### Introduction

Our proposed method for Question 2 of the EHR Dream Challenge - COVID-19 prediction focuses on diverse model selection with the fewest domain assumptions. We find that gradient-boosted trees are competitive against more sophisticated embedding-based methods and achieve the highest performance on Q2 without consideration of data date ranges, imputation, or other feature engineering.

## Method

Our method does hyperparameter grid search over gradient-boosted tree models AdaBoost [1] and Catboost [2]. We select the model with maximum mean AUROC over (k=3) model instantiations using random training/validation partitions (p=0.5) of input training data. All models are evaluated over the same training/validation samples (e.g. there are exactly k=3 partitions over the model selection).

#### Data

We build a binary feature vector over all concepts, over all time within the patient history. Within the "person" table, we drop "day\_of\_birth" and "time\_of\_birth" fields and otherwise create a one-hot encoding of categorical values, including "year\_of\_birth."

We apply this one-hot encoding over all concepts in all tables, yielding 6209 total binary features.

## Hyperparameters

We use the following hyperparameter grid search for each method:

| AdaBoost                                       | Catboost  |
|--|---|
| Depth: 5<br>N: 200<br>Learning rate: 0.1, 0.25 | Depth: 5<br>Objectives: "Logloss", "CrossEntropy"<br>N: 100, 200<br>Learning rate: 0.01, 0.05, 0.1, 0.5<br>L2 leaf regularization: 1, 5, 9,13<br>Features (rsm): 0.5, 0.75<br>Class weights: "Balanced", Null |

In the above 'N' denotes the number of ensemble trees, random subspace method (rsm) denotes the proportion of features to be randomly sampled per split within the tree. The final model selected is:

| Depth: 5   |  |
|--|--|
| Objective: "Logloss"<br>N: 200<br>Learning rate: 0.01<br>L2 leaf regularization: 13<br>Features (rsm): 0.50<br>Class weights: "Balanced" |  |

As expected, model selection chooses a larger ensemble (N: 200) and does class balancing. Finally, the model uses the largest weight regularization (L2 leaf regularization: 13) to avoid overfitting.

## Analysis

This methodology allows for novel competing models to be quickly added in model selection without loss of model performance (e.g. the prior best model may still be selected). For example, we included neural network embedding methods within the model selection but did not see improved performance. We had limited visibility to the model selected on real data, so we could not confirm that a gradient-boosting model was chosen. However, we found better improvements in wider gradient-boosting hyperparameter search and more robust train/validation sampling at increased k. Without compute budgeting, model selection over all of these would strictly improve performance vs. higher compute cost.

We did not consider any temporal windowing to train only on "recent" visits. We started with the simplest model and found it surprisingly competitive without these filters. It is likely that these predictive features are rare within the entirety of the patient record. The learned association may not incur Type I errors due to prior events not related to recent covid treatments.

#### Reference

[1] <u>https://scikit-learn.org/</u>

[2] https://catboost.ai/

## Arkansas AI Campus (ArkansasAICampus20)

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#### **Model Description**

An important aspect of this challenge was that participating teams were unable to see real patient data. The simulated data provided for model testing provided little information about which features might correlate to patient hospitalization risk, so we built a flexible framework for evaluating alternative models and automated feature engineering. We chose the ExtraTreesClassifier from the Scikit-Learn Python library (https://scikit-learn.org) based on empirical performance. Other models we considered included XGBoost1 and LightGBM.2

**Training:** Our model was trained by first performing the preprocessing feature extraction described below, then simple random oversampling of the existing positive examples was used to achieve an overall positive ratio of 40%. This augmented dataset was used to train ExtraTreesClassifier, with the following parameters: 'n\_estimators': 1800, 'max\_depth': 4, 'max\_features': 'sqrt', 'bootstrap': True, 'n\_jobs': -1, 'oob\_score': True, 'class\_weight': 'balanced subsample', 'random state': 0.

A secondary logistic regression model (LogisticRegression from Scikit-Learn) was fit to the predictions produced by ExtraTreesClassifier. Its presence provided a consensus model for ensembles; it was active in this version even though only one ExtraTreesClassifier was employed.

# **Data Preprocessing**

We utilized information from the person, measurement, observation, condition\_occurrence, and drug\_exposure tables, as well as dates of contact from the procedure\_occurrence, device\_exposure, and visit\_occurrence tables to determine the last recorded date of contact with each patient.

Features from the person table were race (5 features), ethnicity (2 features,), gender (2 features), and an engineered age feature derived from the difference between a patient's date of birth and last contact date. We used 38 raw features from the condition\_occurrence table, selected manually. We used 11 raw features from the drug\_exposure table, all hand selected. 207 raw features from the measurement table were used, selected by a combination of manual choice and random selection. The observation table provided four hand selected features: "Cardiac rhythm", "Blood pressure method", "Tobacco user", "History of alcohol use".

After the raw features were selected, we performed an automated feature engineering / expansion process. A Boolean feature valid\_test\_flag was added indicating whether the patient had an entry for a COVID-19 test within 21 days of the last contact date. For each raw feature, we derived and added the following: A Boolean indicating whether the value was present or missing, the standardized feature (=0, =1), the standard deviation, a numeric measurement of the

amount of missing data. We reduced the size of the dataset, retaining the most recent 12 values for each feature, a "baseline" feature storing the oldest entry for each feature, and a numeric indicator of where in the dataset the baseline value was found. After the feature expansion, our dataset contained 15,232 features, named according to the following pattern:

FEATURENAME\_tX: (X [0,11]), the raw (12-t) th newest measurement recorded for FEATURENAME.

FEATURENAME\_notna: flag indicating value of FEATURENAME was not missing

FEATURENAME\_normed\_tX: (X [0,11]), the standardized (=0, =1) (12-t) th newest measurement recorded for FEATURENAME.

FEATURENAME\_std: standard deviation for this feature

FEATURENAME\_sprc: a measure of sparsity for this feature

FEATURENAME\_bl: oldest available value for FEATURENAME

FEATURENAME\_tdelta: analog for relative age of FEATURENAME\_bl (larger value implies older)

FEATURENAME is derived from the OMOP table name and concept id, e.g., "measurement\_3000067" (measurement table, concept ID 3000067).

Engineered features not directly from the OMOP tables are:

age: an analog for patient age, calculated as the difference between last contact date and birth date.

delta: measures the time difference (in negative days) from the last known contact for that patient for each feature. valid\_test\_flag: Boolean indicating whether the patient had a record of a COVID-19 test less than 22 days from the last contact date.

We define "contact" to mean any dated entry in any OMOP table attributed to that patient ID. "Last contact" is the most recent contact for the corresponding patient.

The automated feature expansion process produces redundant features for values "age", "gender", "race",

"ethnicity", and "delta" since those values cannot re-occur, but are still expanded into "timestep" and "baseline" columns), and some are Boolean in nature, but a "normed" version and standard deviation computed and added to the dataset. For this reason, features such as race\_8552\_t8 and race\_8552\_t9 contain identical information and should be viewed as a single feature. Any of these might be selected to play a role in the underlying decision trees.

#### References

1. Chen, T. & Guestrin, C. XGBoost: A Scalable Tree Boosting System. Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining - KDD '16 785–794 (2016). doi:10.1145/2939672.2939785

2. Ke, G. et al. LightGBM: A highly efficient gradient boosting decision tree. in Proceedings of the 31st International Conference on Neural Information Processing Systems 3149–3157 (Curran Associates Inc., 2017).

#### **Bryson-and-Yao-Team**

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#### Introduction

This model was based on logistic regression and developed to predict if a patient who has tested positive for COVID-19 in out-patients will be hospitalized within 21 days of their COVID-19 test.

# Method

Logistic regression, implemented within scikit-learn [1], was used to develop the model. The features are selected from patients' information, condition occurrences and measurements. All the condition occurrences that appeared after 2015 are extracted. The four hand-selected measurements that appeared after 2019 are extracted. The measurements are diastolic blood pressure, C-reactive protein measurement, lymphocyte count, and lactate dehydrogenase measurement [1,2]. These are turned into binary features by comparing each measurement to its normal expected standard range. Besides the patients' information like gender, ethnicity, race and age, the location id which indicates the address of patients is included in the features before feature selection, because the numbers of positive cases are different among areas, and the hospitality rates are different, which may influence the prediction.

Features are selected by using the chi-square value, where the chi-square values of all the features in the training set are calculated and ranked. The calculation is fast and easy, so it is helpful to select features. The best fifty features with the best chi-square value was selected to give the features used in model training. The hospitality rate for different areas are not published, so it is hard to know if the dataset is unbalanced. Thus, we used a weighted logistic regression model so that the weight of input data is adjusted, to eliminate any bias if the data is unbalanced. Elastic net regularization with grid search on the ratio between L1 and L2 regularization is employed to achieve the best model. The F1 score acts as the evaluation of models created during the grid search using cross-validation. The model with the greatest F1 score is then finally selected.

#### Result

The models were tested by Dream Challenge with the data set version "Week 1-4", and it achieved AUROC: 0.6696 and AUPRC: 0.1714.

#### Reference

[1] https://scikit-learn.org/

[2] Feng C, Huang Z, Wang L, Chen X, Zhai Y, Zhu F, et al. A NovelTriage Tool of Artificial Intelligence Assisted Diagnosis Aid System for Suspected COVID-19 pneumonia In Fever Clinics. medRxiv. 2020.

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