Executive Summary

CovidX triage software is built for remote screening, surveillance, and management of COVID-19. The application uses prescribed guidelines from the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) in tandem with personalized machine-learning (ML) triage algorithms to: 1) Pre-screen concerned people for COVID-19 testing, 2) assess progression of disease by identifying when new symptoms/signs are clinically significant, 3) provide efficient continuous home monitoring to improve health outcomes, and 4) provide real-time decision support for early intervention and reduction of unnecessary healthcare utilization. The ML disease severity algorithms were validated in out-of-sample tests using patient characteristic data derived from patients in Wuhan, China and the EU. Lung disease exacerbation detection and decision support algorithms were validated by comparison to pulmonary specialist opinion panels to show superior performance at identifying respiratory flare-ups and recommending the appropriate care. Prior clinical studies of mobile apps integrated with asthma and COPD algorithms have yielded clinically significant health improvement with as little as 4-5 minutes of weekly use. This product is available today and could dramatically improve COVID-19 containment and self-management through pre-screening for virus testing, at-home triage, home-monitoring, and long-term therapeutic benefit!
Why have we developed this software and how can we help the battle against COVID-19?

COVID-19 (widely refer to as novel coronavirus) has been declared a Global Pandemic by the world Health Organization with early data indicating a mortality rate of 10-20 times that of conventional influenza [1]. The virus’s doubling rate based on data through April 4th, 2020 has been estimated in a variety of studies to be in a range of 2.4 – 7.4 days with a basic reproductive number, Ro, in the range of 2.2-6.6.[2-4] (note that these numbers evolve everyday as social containment measures, travel restrictions, anti-viral and symptom control treatments, seasonality effects, herding immunity effects, and other factors influence the virus’s trajectory). This number ranges make this virus ripe for rapid proliferation without strong control measures. Containment of this illness is a paramount priority for governments and institutions around the world. One of the primary concerns regarding COVID-19 is a rapid spread that could overwhelm global healthcare systems [5], resulting in preventable mortality and substantial economic burden. While timely development of vaccines and therapies is ongoing and a potential longer-term solution, the ongoing frontline of the battle against this pandemic will be in peoples’ homes and daily activities.

Testing and inpatient care of COVID-19 has been particularly challenging in the USA due to low testing inventories and insufficient hospital personnel/space/medical supplies [5,6]. In this climate, patients who are uncertain about their diagnosis are flooding medical facilities, intermingling with people who are indeed sick, and blunting the scope for timely disease evaluation. At the moment, there are no accurate or personalized solutions for combating COVID-19 at home. If effective remote screening, monitoring, and triage tools were widely available, resources could be allocated where needed while avoiding virus transmission. From a health systems perspective, CovidX could help to reduce staff exposure to potentially infected individuals and conserve PPE.

One emerging approach to addressing unnecessary at-home health deterioration is early detection and triage using mobile/web apps, telehealth systems, and remote patient monitoring devices. These systems have the benefit of providing immediate and economical feedback to patients while reducing the need for inpatient care. Many of these apps, however, utilize rule-based decision

![Image](https://covidx.vironix.ai/)
frameworks which struggle to capture the complexity and breadth of potential patient scenarios inherent in accurate and personalized triage/diagnosis. In developing triage algorithms, we crafted a machine learning strategy that would track patient baseline health and dynamically improve in detecting and triaging deteriorations of lung health at home. CovidX API predictions include: 1) severity assessments of a person’s presenting symptoms, signs, and normal health, and 2) recommendations on the most appropriate level of care to seek when responding to flare-ups.

Patients, healthcare providers, and health systems can benefit from this kind of application in a variety of ways. A chief benefit is in decision support and early action. Users can take mitigating steps to either test early, or perhaps even more importantly, avoid placing burden on the healthcare system when they, in fact, do not need testing. Also, patients experiencing an exacerbation could call their physician, undergo outpatient testing, and take at-home mitigating, therapeutic steps before symptoms deteriorate to a point that necessitates emergency care. The continuous oximetry technologies linked to the app provide added remote monitoring capabilities and potential for early diagnosis of COVID-19 infection or deterioration. Finally, many patients who frequently experience anxiety or concern about their health may gain some comfort from having additional council nearby. A depiction of the full application features and sample screen shots of patient outputs are depicted in figure 2 below.

![CovidX app screenshots](https://covidx.vironix.ai/)

**Figure 2:** CovidX app screenshots: Figure (a) shows user outputs describing the severity of a patient’s COVID-19 profile, respiratory symptoms, and overall condition. Figure (b) shows the comprehensive suite of CovidX features.
How did we develop, test, and evaluate our COVID-19 products?

COVID-19 Screening

COVID-19 virus testing in healthcare facilities is primarily being conducted subsequent to a screening process. While the CDC has indicated to clinicians to “use their judgement ... to determine whether a patient should be tested,” the CDC has laid out guidance for clinicians that suggests screening of major symptoms and circumstantial events prior to full testing to avoid unnecessary utilization of widely needed testing kits [7,8]. The primary and emergency symptoms associated with COVID-19 screening are included in table 1.

<table>
<thead>
<tr>
<th>Primary Symptoms</th>
<th>Emergency Warning Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>Shortness of Breath at Rest</td>
</tr>
<tr>
<td>Shortness of Breath</td>
<td>Persistent Pain or Pressure in the Chest</td>
</tr>
<tr>
<td>Fever</td>
<td>New Confusion or Inability to Arouse</td>
</tr>
<tr>
<td></td>
<td>Bluish Lips or Face</td>
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</table>

Table 1: List of CDC indicated primary and emergency symptoms to consider when pre-screening for COVID-19 [8] (https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/testing.html).

In addition to the symptom considerations given in table 1, priority for COVID-19 testing in clinics is given to people who fit into the following categories [7]:

1) Patients who have been hospitalized and are displaying symptoms of COVID-19.
2) Symptomatic patients such as older adults and individuals with chronic medical conditions and/or an immunocompromised state that may put them at higher risk for poor outcomes (e.g., diabetes, heart disease, receiving immunosuppressive medications, chronic lung disease, chronic kidney disease).
3) Elderly patients above the age of 65.
4) Healthcare personnel and other essential workers (policemen, firemen, etc)
5) Any persons including healthcare personnel, who within 14 days of symptom onset, had close contact with a suspect or laboratory-confirmed COVID-19 patient, or who have a history of travel from affected geographic areas within 14 days of their symptom onset.

Using the exhaustive set of CDC and WHO guidelines in tandem with comprehensive guidelines drawn from a recent Zeijang University handbook on Covid-19 prevention [9], CovidX rapidly carries out instant remote screening and provides a recommendation to concerned people on https://covidx.vironix.ai/
how healthcare institutions would prioritize their inputted health data for COVID-19 testing and what best practices to maintain in the interim to prevent infection or other adverse health events.

Figure 2: Sample Screen shots of the CovidX pre-screening process with associated modules for preventative best practices.

Real-Time Triage of COVID-19

Understanding the clinical characteristics of people diagnosed with COVID-19 is of critical importance to managing the condition both at-home and in-clinic. As the virus has taken hold in recent months, there are only a few regions with sufficient case data to characterize the spectrum of potential patient experiences. The government in Wuhan, China confirmed that health authorities were treating dozens of COVID-19 cases on December 31st, 2019 and subsequently reported the first death on January 11, 2020 [10]. On February 28, 2020, Guan et al. published a paper entitled Clinical Characteristics of Coronavirus Disease 2019 in China in the New England Journal of Medicine [11]. This paper extracted data from both hospital medical records and the National Health Commission of China regarding 1,099 patients with laboratory-confirmed COVID-19 who were treated (hospitalized and outpatient) between December 11, 2019 and January 29, 2020. The data provides strong foundational grounding for building predictive models to identify and take the appropriate early medical action on a broad range of COVID-19 patient experiences.

We extracted the data in [11] that showed the association of patient health variables with disease severity in order to train a machine learning classifier that can indicate the disease severity of a diverse set of patient profiles, symptoms, and signs. The health demographic and clinical characteristics listed in [10] were further augmented with European Union data cataloged in [11] to yield the final feature list for algorithm training, which is given in table 2.

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Table 2: List of patient profile, vital signs, comorbidities, risk factors, and symptoms used in triaging and assessing the severity of COVID-19 patients.

The training of the CovidX triage model was done in 3 phases:

1) Data Extraction and Transformation Using Bayesian Inference
2) ML Algorithm training, cross-validation, and out-of-sample validation
3) Optimization and Deployment in web/mobile apps.

Phase 1

CovidX severity algorithms are designed to take an input of readily available patient data at home (signs, symptoms, and basic profile information) and return a real-time assessment of the severity of reported health data. In order to build an ML prediction model that is effective and applicable to the broad and diverse number of potential patient profiles, one must acquire training data that is both statistically comprehensive and clinically representative of COVID-19 cases. Given both the lack of availability of such data in practice as well as the sheer magnitude of potential patient scenarios, we used the case data from the Wuhan and EU patient sets to generate clinically comprehensive cases via a Monte Carlo Simulation. A partial snapshot of the Wuhan dataset is given in figure 3

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Figure 3: Data table showing patient demographics and clinical characteristics of 1099 hospitalized and outpatient COVID-19 patients in Wuhan China between December 11, 2019 and January 29, 2020 [11].

The dataset provides prevalence data for a particular health characteristic associated with a binary class (severe or nonsevere). This data can be interpreted as a probability of a patient being severe given a particular health characteristic. In order to generate patient scenarios for training a prediction model, however, we need the inverse information, which is the probability of a health characteristic being present given a severity diagnosis, which can be expressed as \( P(\text{feature}|\text{severity}) \). This can be determined through Bayesian inference using the Wuhan and EU datasets:

\[
P(\text{feature}|\text{severity}) = \frac{P(\text{severity}|\text{feature})}{P(\text{severity})} \cdot P(\text{feature})
\]

Note that “feature’ in this paper refers to a demographic or health variable that is used in training machine learning algorithms. We determined the aforementioned probability for all variables in table 2 and then coupled those probabilities with known clinical correlations from the literature to generate a 50,000 patient case training/testing set that is statistically and clinically representative of COVID-19 patients treated in Wuhan and the EU. We subsequently used that data to train a machine-learning classifier.

Phase 2

A variety of supervised classifiers were explored using stacking, soft/hard voting rules, and gradient boosting techniques to get an optimized model that classifies disease severity. Standard

Table 3: CovidX model performance when classifying characteristics of COVID-19 patients who are likely to need significant care.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Accuracy</td>
<td>87.4%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>85.5%</td>
</tr>
<tr>
<td>Specificity</td>
<td>87.8%</td>
</tr>
<tr>
<td>PPV</td>
<td>41.2%</td>
</tr>
<tr>
<td>NPV</td>
<td>98.4%</td>
</tr>
</tbody>
</table>
machine-learning practices were employed including train/test split of 90/10, 5-folds cross validation, and diagnostic test optimizations. Table 2 shows the algorithm performance in classifying patient health characteristics that suggested a need for extensive medical care. Note the positive predictive value (PPV) is low mostly because the population requiring emergency healthcare was 5-7% of the total population documented in the underlying datasets. For this reason, the total number of true and false positives was low relative to the number of algorithm predictions made in the test set.

![Confusion Matrix](image)

**Figure 4:** Performance studies of CovidX disease severity algorithm. The confusion matrix in figure (a) shows the overall classification accuracy (87.4%) and missed classifications in each of the nonsevere and emergency medical event classes. The feature importance figure (b) indicates that the CovidX algorithm weights shortness of breath, age, and comorbidities among the top considerations for discerning illness severity. Finally, the distribution of algorithm severity probabilities in figure (c) yields a profile of severities that is consistent with globally diagnosed patients.

The feature importance list is encouraging in that it shows that the top variables of importance to the model when distinguishing severe from non-severe patients included age>65, shortness of breath, and comorbidities such as cancer, COPD, and Diabetes. These considerations have been qualitatively noted in patient studies in both Wuhan [12] and Washington, USA [13].

**Phase 3**

The final ML model was deployed in the cloud and can be invoked via API calls from a variety of applications and software. The CovidX software takes patient data (either through device capture or through human entry) and, in real time, triages a patient’s signs and in order to detect health deterioration early and guide the right decision making. The data and app can also be used for remote surveillance for monitoring the status of patients who are discharged from a medical facility.

**How are Respiratory Triage Algorithms Developed & Tested?**

Exacerbation detection and symptom/sign severity assessments are machine-learned prediction models that were augmented and modified based on the COPD triage methodology of [14]. Given their robustness in identifying significant changes in respiratory health and alerting patients when to seek medical care, these tools are ideal for application to COVID-19,
and they provide an enhanced at-home triage benefit to anxious and sick people.

There is an inherent challenge in showing that a triage algorithm performs well given the lack of gold standard on what constitutes a “correct” assessment of health severity and the most appropriate responsive medical help. Many contemporary symptom trackers base their decision criteria on textbook materials or panels of doctors who come to an agreement on what factors are important for triage. With our approach, we followed the approach of Swaminathan et. al, and paid special attention to show that the algorithm predictions performed well against individual specialists in recommending the consensus opinion of expert panels of pulmonary specialists.

The algorithm was developed in five major phases:

1) Determination of clinically relevant variables that are relevant to assessing the severity of respiratory flare-ups.
2) Generation of patient cases and collection of physician triage data.
3) Training and optimization of a machine learning prediction.
4) Validation of algorithm through panel consensus and deployment into an API.
5) Deployment into consumer applications for patient studies.

Phase 1

A panel of pulmonologists, internists, and data scientists gathered to determine the most relevant variables for assessing respiratory flare-ups in patients with chronic lung disease. The team narrowed and refined the selections based on panel consensus, the ability to collect the select data through consumer devices/applications, and the ability of a patient, physician, or adaptable device to accurately report the data. The panel’s assessment was appended and validated through considerable literature review [15-25] to create a candidate list of variables. That candidate list was used to generate sample practice cases (vignettes) to issue to a larger group of physicians to assess whether the candidate variables were significant in case scoring. Statistical analysis of individual physician assessments was used to further down select and render a final feature set which is shown in table 4 below.

<table>
<thead>
<tr>
<th>Profile Variables</th>
<th>Comorbidities</th>
<th>Vital Signs</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Asthma</td>
<td>Normal Heart Rate</td>
<td>Shortness of Breath</td>
</tr>
<tr>
<td>Weight</td>
<td>Heart Failure</td>
<td>Heart Rate at time of</td>
<td>Cough</td>
</tr>
<tr>
<td>Height</td>
<td>Coronary Artery Disease</td>
<td>Normal SpO₂</td>
<td>Increased Phlegm</td>
</tr>
<tr>
<td>COPD Gold Stage</td>
<td>Chronic Kidney Disease</td>
<td>SpO₂ at time of patient</td>
<td>Running Nose, Sore</td>
</tr>
<tr>
<td></td>
<td></td>
<td>triage assessment</td>
<td>Throat, or Infection</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Normal Dyspnea</th>
<th>Diabetes</th>
<th>Normal Body Temperature</th>
<th>Waking at night</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent Exacerbations or Hospitalizations</td>
<td>Immunocompromised</td>
<td>Temperature at time of patient triage assessment</td>
<td>Phlegm Discoloration</td>
</tr>
<tr>
<td>Living Condition</td>
<td>High Blood Pressure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 4:** List of patient profile, comorbidity, vital sign, and symptom factors used in triage and exacerbation assessments of lung health.

**Phase 2**

An algorithm training data set was gathered from 10 physicians each triaging 500 simulated patient cases similar to a medical vignette. Cases were generated using statistical design of experiment followed by Monte Carlo Simulation to layout a comprehensive set of clinically diverse patient scenarios. These scenarios were labelled by physicians with severity assessments of patient symptoms, signs, baseline health, and potential exacerbation. A final recommendation was made by all labelers as to the level of medical care each patient should seek. After appending data with appropriate exacerbation and triage labels, the data were used to train a machine learning prediction.

**Phase 3**

A variety of machine-learning classifiers were tested with different feature selection strategies to generate the most accurate prediction model. Standard cross validation and out-of-sample validation techniques were employed. The most effective models ended up requiring the stacking of ensemble decision tree classifiers with hard voting classifiers such as a logistic regression.

**Phase 4**

The final algorithms were selected based on their overall accuracy as well as their safety in under or over triaging patient cases. These metrics were validated by comparing the algorithm’s triage classifications to the consensus decision of 9 physicians (plus algorithm) triaging 101 out-of-sample patient cases. Figure 5 below shows the performance of the optimized models in identifying the panel majority decision relative to the other physicians. The data shows that the algorithm outcompeted all case scorers in both identifying the level of medical needed in the validation set patient population, and identifying which patients needed emergency care. Further reading on the methodologies employed in developing these types of algorithms can be found in [14,26].

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Figure 5: Data comparing individual pulmonary specialist performance with respiratory triage algorithm performance in a 101-patient, out-of-sample validation test that assessed (a) agreement with panel consensus on the severity of medical care needed and (b) the accuracy, sensitivity, specificity, positive predictive value, and negative predictive value in identifying cases that require emergency room care.

Phase 5:

After validating algorithm performance in simulated patient cases in comparison to consensus specialist opinion, a consumer-ready technology must be created in which prediction models can be deployed. Given that we developed and deployed these algorithms during the recent onset of the Covid-19 crisis, the CovidX app has not been evaluated in trials to determine its health impact. However, a mobile application equipped with asthma triage algorithms trained using comparable methodologies was evaluated in observational trials at The Vancouver Clinic, Vancouver Washington in 2017 [26]. In this 22-subject pre/post study of persistent asthmatics, patients were asked to activate the symptom assessment feature of the mobile app every other day. In total, this required approximately 4-5 minutes of usage per week. Remarkably, patients showed clinically significant improvement in asthma symptom control, anxiety, and quality-of-life in as little as 2 months of using the app, and these benefits persisted for the remainder of the trial. Exhausting details of the study design, patient demographics, and trial methods can be found in [26].

Figure 6: Health outcome measures emerging from a 6-month pre-post observation trial of 22 persistent asthmatics using an asthma triage app that was developed in [26]. Health

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assessments included widely used clinical endpoints: The Asthma Control Test (ACT), the Anxiety Inventory for Respiratory Disease (AIR), and the Euroquol EQ-5D-5L. Test results indicate monotonically increasing, clinically significant health improvement in symptom control, anxiety, and quality-of-life

**Deploying Algorithms in CovidX**

Algorithms for triaging and monitoring flare-ups of both CovidX and general respiratory illness have been customized for at-home management and surveillance of COVID-19 and are available via API for deployment behind a variety of software systems, remote monitoring devices, and mobile/web apps. A depiction of the triage features is included in Fig. 5 below along with a novel BodiMetrics continuous oximetry monitoring ring.

![CovidX Algorithms](https://covidx.vironix.ai/

**Figure 7:** Screenshots of CovidX functions & features alongside continuous monitoring Circul Ring by BodiMetrics.

**Utilizing Remote Monitoring for Diagnosis and Triage**

Coupling CovidX algorithms with continuous and remote monitoring devices provides another path to instantaneous, personalized diagnosis of escalating medical events. A premier institution in the vital sign monitoring space, BodiMetrics, has established a path for deploying CovidX underneath a novel, non-invasive, FDA approved home oximetry device called the CIRCUL Ring. This device, which is a 2020 Red Dot International Design Award Winner [27], has already been tested on COVID-19 patients in Wuhan China and has been shown to be highly effective in accurately identifying changes in oxygen saturation that are indicative of COVID-19. In particular, current testing in China has shown that a sustained drop in SpO2 below 93% coupled with dyspnea symptoms and rapid breathing is a strong basis for COVID-19 diagnosis [28]. Thus, the combination of ML predictions and validated data from The CIRCUL Ring is an invaluable tool for remote monitoring and early/prolonged disease intervention.

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Defeating Uncontained Spread of COVID-19

Our strategy to reduce the spread of COVID-19 and improve quality of life around the globe rests on an understanding that population-level decision making outside of the doctor’s office will be the major driver of health outcomes and containment. CovidX is an easy-to-use, personalized, accessible application for early screening of COVID-19, early assessment of symptom flare-ups, and continuous monitoring of population health during times in which containment is paramount and traditional healthcare options are overburdened. Release and distribution of this application for global patient use will play an important role in diminishing the damage of this deadly pandemic.

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https://covidx.vironix.ai/
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