Risk Stratification and Early Alerting Regarding COVID-19 Hospitalization

NCT04709068

11-March-2021

Protocol

January 2021

Risk Stratification and Early Alerting Regarding COVID-19 Hospitalization (Risk SEARCH)

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Funder: Biomedical Advanced Research and Development Authority
U.S. Department of Health and Human Services

Short title: Risk SEARCH

Overview: In the proposed research, we will use Current Health's remote monitoring wearable device to create novel algorithms to help us predict the progression and severity of COVID-19 in individuals that have recently become infected in the community. Risk scores based on demographics, or for patients in hospital, already exist. However, by using continuous remote patient monitoring, in combination with machine learning and data analysis, we hope to both predict and detected changes in the risk of an individual infected with COVID-19 requiring hospitalization, intensive care unit (ICU) treatment, or death based on their vital signs while still in the community.

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Overview

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We plan to use a pilot and two-stage approach, including an observational stage to 'train' a predictive algorithm and a validation stage to test its efficacy. In the pilot stage, we will recruit up to 50 participants to test the recruitment pathway, trial logistics, and to begin model building. In stage one, the training stage, we plan to recruit 1000 study participants, who will contribute information from the remote monitoring device, demographic data, and daily questionnaires on symptoms they experience. This information will help our data scientists train a dataset using machine learning and algorithm development techniques. In the second stage, we will validate or test that algorithm on a different sample of up to 1000 study participants. Based on current epidemiological data, the recruitment of this number of participants in each stage should provide us with 100 events/hospitalizations in each cohort (see Graph 2, below).

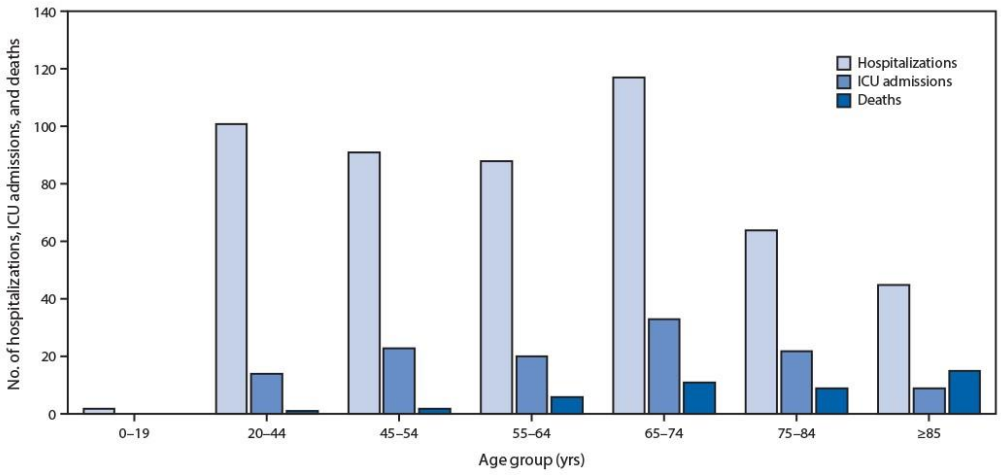
Using a hospital-grade home-based, remote monitoring wearable gives us the opportunity to create a unique and extremely useful tool in predicting and managing the clinical effects of the COVID-19 pandemic. Our algorithm might bridge the gap between demographic models and in-hospital models of disease progression by providing real-time data from the community. If we are successful, this tool could be made available immediately to enable better resource allocation for patients after diagnosis. In addition, it enables patient-centered management, increasing confidence for low and high risk patients, and those managing their care. The results of this research will provide a database that can be used in future trials to assess treatment efficacy and offer the potential for rapid algorithm iteration in the event of a future pandemic.

Background

Landscape of SARS-CoV-2/COVID-19

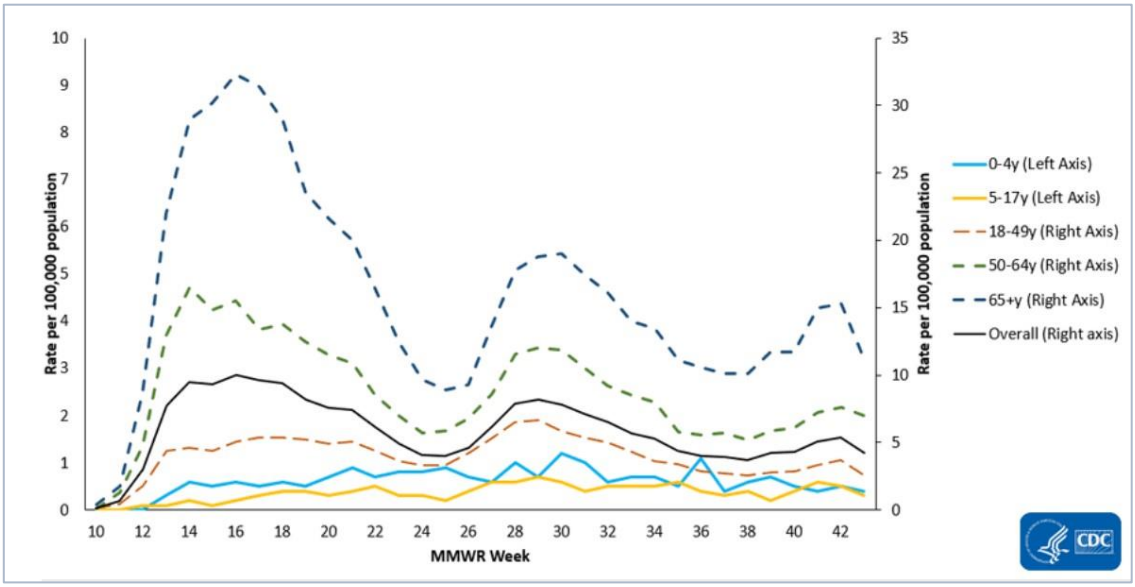
SARS-CoV-2/COVID-19 is a highly contagious virus that has rapidly spread across the globe, with the United States among the countries consistently reporting the highest number of cases.[1] Emerging reports of risk factors for hospitalization and death in patients infected with SARS-CoV-2/COVID-19 include increasing age, BMI > 40, being male, and having diabetes, among others.[2,3] CDC data from the first month of the SARS-CoV-2/COVID-19 outbreak in the United States showed that the absolute number of hospitalizations per age group is similar between the ages of 20 and 75. However, deaths and ICU admissions tend to increase with age.[4] (Graph 1).

Graph 1. Absolute number of hospitalizations, ICU admissions, and deaths in the United States as of March 16, 2020, CDC MMWR



Cases and hospitalizations were on the decline at the end of summer 2020.[5] However, the overall weekly hospitalization rates in the United States have increased since the end of September (MMWR week 39, see Graph 2), driven mostly by adults over 18 years of age.[5]

Graph 2. Weekly COVID-19-associated hospitalization rates by age group – COVID-NET, March 1 – October 24, 2020



Time from symptom onset to death

Data assessing the time course from onset of symptoms to death or time to recovery remain limited and generally do not include vital sign measures in the community.[6] After onset of symptoms, the highest probability of death occurs just under 12 days, so there may be time after symptom onset to predict the likelihood of clinical decline and guide clinical intervention in many patients.[6]

Currently, predictors of hospitalization across the lifespan remain general, demographic and largely intuitive.[7] For example, individuals with advanced disease or multi-morbidity are at increased risk for poor outcomes when infected with COVID-19. A major goal of this work is to identify novel digital biomarkers that will enable early identification of patients who are likely to have severe disease while still in the community. This early identification could allow for more timely and aggressive supportive care, potentially reducing more severe disease and poor outcomes.

Digital biomarkers and algorithm development using large databases

There is a body of research utilizing commercially available wearable devices (e.g., Fitbit) that seeks to identify biomarkers that could predict infection ahead of noticeable symptoms.[8,9] There is another avenue of research utilizing large, extensive preexisting databases to find and validate risk prediction algorithms that can estimate hospital admissions and death in COVID-19 infected adults.[3,7] We plan to utilize already existing population-based algorithms and combine these with continuously collected vital signs from our medical-grade, remote monitoring wearable device. Unlike Fitbit or other commercially available wearables, the quality of observations from Current Health's remote monitoring device is much higher than so it can be used like a hospital monitor in the community. The Current Health device also stores the raw waveforms, allowing for retrospective audit of observation quality.

To our knowledge, this will be the first effort to apply these advanced models utilizing continuously collected, high-quality vital signs in the community, for the prediction of COVID19 disease progression.

Research Objective and Outcomes

The overall objective of this contract is to train, develop, validate and release a digital biomarker-based algorithm that, in COVID-19 PCR or antigen positive patients, within 30 days of a positive test:

1. **Primary Outcome**: predicts likelihood of requiring a stay in hospital of 24 hours or longer

2. **Secondary Outcomes**:
    a. Predicts likelihood of being admitted to ICU for either non-invasive (CPAP, BiPAP, high flow nasal oxygen), invasive ventilation or vasopressor support.
    b. Predicts likelihood of death.

3. **Tertiary Outcomes**: Provides successful delivery, setup, daily interface engagement, and compliance with wearing of the device

Methods

Study Design

This study will be broken down into a pilot phase, followed by two stages of data collection. We will recruit, consent, and enroll approximately 2050 participants with a COVID-19 positive test over the course of the study. In the pilot phase and stages one and two, the following methods will apply.

Participants will be asked to wear the Current Health remote patient monitoring device for up to 30 days. Participants will also be provided with a Current Health tablet with an application installed. The tablet is not password protected, but no responses are stored locally, and they are associated with vital signs via the Current Health dashboard. The participant will be asked to complete a welcome survey on the first day of participation. The tablet will remind the participant each day to answer a brief series of questions about their symptoms and decisions on the tablet. The welcome and daily surveys include the content below:

Welcome Survey: Welcome! Today is your first day in Community by Current Health's COVID-19 Study. We need to collect some information about you. We will only ask these questions **one time**. This survey should take **less than 5 minutes to complete**.

Thank you again for taking part in this study. With your help our researchers will gain a better understanding of COVID-19 and be able to predict recovery and progression.

1) What is your date of birth?
2) What is your sex? Male/Female/other or prefer not to specify

   If Female
   1) To your own knowledge are you currently pregnant?
   2) Do you have menstrual periods?
   3) Are you:
      - Pregnant or breastfeeding
      - Taking hormonal birth control
      - Undergoing menopause or post-menopausal - Highly active (working out, training, fitness, etc.) 4) When was your last period?
3) What is your occupational category? Healthcare (doctor, nurse, dentist, etc.)
   Service industry (food service, grocery, mechanic, plumber, etc.)
   Retail
   Office – able to work from home
   Office – unable to work from home
   Currently unemployed
   Student – remote
   Student – attending class in person 4)

What is your household make-up?
   Living alone
   Living with people

5) Do other members of your household currently have COVID-19? Y/N
6) Are any other members of your household enrolled in Community by Current Health's COVID-10 Study? Y/N
7) What is your self-identified race/ethnicity?
   White Hispanic

White Non-Hispanic
Black or African American
Asian
American Indian or Alaska Native
Native Hawaiian and Pacific Islander 8) What is your height?

9) What is your weight (in pounds)?
10) Do you have **asthma**? Y/N
11) Do you have **cancer**? Y/N
12) Do you have **chronic obstructive pulmonary disease (COPD)**? Y/N
13) Do you have **diabetes**? Y/N
14) Do you have a **heart condition**? Y/N
15) Do you have **high blood pressure**? Y/N
16) Do you have **kidney disease** or **reduced kidney function**? Y/N
17) Have you ever had an **organ transplant**? Y/N
18) Do you have **sickle cell disease**? Y/N
19) Are you a **smoker**? Y/N
20) Do you take **beta blockers**? Beta blockers are medicines designed to reduce heart rate, which can affect vital sign readings. For example: Tenormin, Cardiacor, Emcor, Betaloc, Inderal, or Angilol. Y/N
21) Please enter any feedback about this survey:

Thank you for filling out your welcome survey! Your responses have been recorded.

Daily Survey:

Each day Current Health will ask you a **brief series of questions** about symptoms and decisions that may be related to COVID-19. Your daily response and information collected from the wearable device will create the most accurate picture of your health. This survey should take **less than 5 minutes** to complete.

1) In the **past 24 hours,** did you have (or continue to have) any of the following symptoms:

- loss of smell or taste
- dry cough
- sore throat
- fever or feeling feverish
- chills
- muscle aches
- diarrhea
- nausea
- other, please specify (free text)

[FOR EACH YES] Is your <symptom> better or worse than yesterday?

- Categorical scale: Much worse, Worse, The same, Better, Much better

2) Due to how you are feeling **today,** do you plan to speak to a health care provider?

3) Due to how you are feeling **today,** do you plan to go to the hospital?

4) Do you feel as though you have completely recovered from COVID-19 as of today?

Thank you for completing your daily survey! Your responses have been recorded.

For our study participants, data will be collected "blind". The participant will not be able to see their data in real time, and no data will be reviewed or acted upon by the study team unless there is a clinically indicated trigger elicited by the system. These triggers exist to prompt the capture of study-specific information, not to direct patient care.

1. Reduction in SpO_2 below 88% for 60 minutes
2. Increase in pulse rate to more than 90 beats per minute for 60 minutes with minimal body movement (Current Health motion score < 2)
3. Increase in respiratory rate to more than 25 breaths per minute with minimal body movement (Current Health motion score < 2)

In these instances, participants will be contacted and asked the following two to three questions:

We cannot provide you with any medical advice but would like to ask you a few questions. First, have you experienced any new signs or symptoms including:

Shortness of breath
Chest pain or pressure
New or worsening cough
Fever or feeling feverish
Chills
Headache
Sore throat
Muscle aches or joint pain
Abdominal pain
Diarrhea
Nausea
Other, please specify

If yes, to any symptom:

- Do you consider the symptom to be mild, moderate, or severe (worst ever)?

- Do you intend to seek medical care at an emergency room, urgent care, or hospital in the near future?

If no:

- Has your device been working properly, or has it been damaged in any way?

Throughout the study, if a participant believes they have recovered from COVID-19 for any of the reasons listed below and tells the study team they will be resuming normal life and would like to exit the study, we will consider these participants fully compliant. COVID-19 recovery would be considered in any of the following situations:

1. Participant receives a follow-up COVID-19 PCR test that is negative
2. Participant was asymptomatic and isolated for 14 days without symptoms
3. Participant was symptomatic and onset of symptoms was at least 14 days prior with the last three days symptom free

Conversely, if a participant feels that they are experiencing severe symptoms related to SARS-CoV-2/COVID-19 that warrant a visit to the hospital or urgent care facility (which will be also evident by our questionnaire), the participant will be instructed to contact their healthcare provider, contact a nearby hospital to arrange for appropriate assessment, or call 911 if an emergency. We will not provide medical advice, or a real-time monitoring service, as this will likely bias the outcomes of the trial. This will be made explicitly clear to participants in the Informed Consent Form and process of consent. The outcome of that visit will be captured by a study team member.

A study participant will be considered fully adherent to study protocol if they:

- Wear the device for at least 20 hours a day, at least 6 days a week up to 30 days
- Answer the questions on the tablet at least 6 days a week up to 30 days
- Return the wearable device kit and tablet

Inclusion and Exclusion Criteria

Table 1. Criteria for study participants

Inclusion	Exclusion
1) Living in the United States (contiguous states) 2) Aged 21 years or older	1) Under the age of 21 2) Received a positive test result more than 48 hours prior to contacting study staff or has a pending test for COVID19
3) Able to provide documentation of +PCR or +antigen test for COVID-19 within the past 48 hours 4) Self-reports that comfortable and willing to wear the wearable device and interact with a tablet-based interface daily	5) Able to provide a next of kin/designated person who can be contacted in the event of hospitalization for follow up. 3) Cannot confirm a PCR or antigen positive test for COVID-19 4) Is unable to read English

5) Is unwilling to wear the device 24 hours/day except for showering/bathing or interact with a tablet-based interface for daily questionnaire
6) Is unwilling or unable to provide baseline data required for entry into the study
7) Is unable to provide a next of kin/designated person who can be contacted in the event of hospitalization for follow-up
8) Heavy tattooing on both upper arms
9) Known atrial fibrillation (permanent or paroxysmal)
10) Has taken/is taking part in a COVID-19 vaccine or treatment trial

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Pilot Phase

The pilot phase study with a goal of 50 participants will test the feasibility of recruitment, trial logistics, observed patient events, timeline to deterioration, and environmental test settings. The primary aim is to make any revisions to recruitment strategy and to the final number of "critical events" (e.g., hospitalization) required. The secondary aim is to produce descriptive statistics on pilot data and understand user issues that could affect study data. Descriptive statistics will include univariate analysis such as frequency, box plots, or histograms, and where appropriate, bivariate analysis on covariates using methods such as regression, Fisher's exact tests, or chi-squared analyses.

Algorithmic Approach – Bayesian Network

The proposed methodical approach will use a Bayesian network to predict risk/probability of the study outcomes. There are four levers to consider in model development that will be elaborated on separately: 1) variables in the model 2) characterization of variables 3) distribution of variables and 4) provided prior direction of effect. The latter two levers lend themselves more to Bayesian methods. Variables that will be collected in the study are outlined below, however each variable will need to be analyzed to determine statistical significance and interaction effects to determine if it belongs in the final model.

The characterization of variables refers to how they will be categorized, binned, or otherwise transformed, such as using multiple variables to make an aggregated score variable that acts as input to the risk model. For example, a continuous BMI variable may be taken and grouped it into clinical categories (e.g., normal, overweight, obese, etc.), then further combine the variable with a patient's self-reported health to generate a "wellness score". These variable transformations will be done iteratively in the training stage. The distribution of the variable is the percent in each category/bin. Traditional machine learning methods require that the distribution of a variable comes only from study data. However, in Bayesian methods if a value of interest is unknown or will not be able to be explicitly measured in the study, a *prior* can be provided to make inference; this is especially helpful in smaller sample sizes. For reference, a *prior*, of an uncertain quantity is the probability distribution that would express one's beliefs about this quantity before some evidence is taken into account. An example of how prior probabilities from literature maybe incorporated in the study is to state the probabilities of false positives and false negative rates in positive COVID-19 nasal swab PCR testing. Direction of effect refers to the causal flow of Bayesian networks. These are prespecified by existing literature, clinical knowledge, and subject matter knowledge to

consider how one event precedes another. In this study design, such causal flow is able to explicitly state that infection precedes the onset of symptoms.

Finally, Bayesian networks are more transparent than other models, as they rely on traditional conditional probabilities, that is, how the likelihood of having a characteristic affects the likelihood of having another characteristic or the probability experiencing an event. Model transparency will likely help with clinical adoption and utility.

Stage 1

Training Stage – Model Creation & Training Algorithm

The overall aim of Stage 1 is to collect enough data to perform machine learning analytics on data from the Current Health device to create a Bayesian network algorithm that successfully predicts the risk/probability of no severe disease, hospitalization, ICU admission, and death following SARS-CoV-2/COVID-19 infection. The outcomes are *not* mutually exclusive categories, and can be hierarchical, i.e., when a patient first goes to hospital and then is admitted to the ICU. Conversely, a patient at risk could experience death without ever being hospitalized. This will be accounted for by calculating probabilities of each outcome and compare the conditional probabilities analyzing the risk of ICU admission, given that hospitalization has already occurred. One thousand participants will be recruited for the training stage.

A Bayesian network will first be developed using all 1000 participants in the training set. A Bayesian network illustrated (Appendix A, Fig1) has “nodes” which represent the variables and “arc” or “edge” which is the directional arrow drawn connecting the nodes. The probability of a “base model” is where no participant observations have been made, so each variable is the marginal (independent) probability. When information is input for each participant, I.e., in base model probability of sex is 50% male, 50% female, but once it is known a participant is male, the probability will be updated to 100% male. This in turn updates the risk probability of no severe disease, hospitalization, ICU, and death, now knowing the participant is male.[10]

Once the Bayesian network model is constructed, to account for model variation, that is a model’s parameters change depending on the data the model is being given, nested crossvalidation will be performed to ensure model stability and reduce issues with overfitting.[10] Sensitivity analysis will be conducted to determine variables that have most effect and are statistically significant to outcome variable also called a “target node". If necessary, to further check data stability bootstrapping resampling will be explored.

Not all readings from the wearable are perfect, meaning some data from the wearable can be considered noise from factors such as wearing device in the wrong orientation (upsidedown) or large amounts of movement inhibiting reading. The study team will instruct participant on correct use of the wearable during onboarding then check the signal robustness to ensure noisy data is either transformed to be used or filtered out.

Stage 2

Testing Stage – Expansion for Model Creation or Validation

To assess the algorithm performance, algorithm testing on a total of 1,000 participants will be conducted. This cohort of 1,000 testing participants will be held entirely separate from the

training participants to minimize data snooping bias in the study. In machine learning, it is typical to obtain initial testing cohort results to determine if the model created from the training data is performing well. After the first 100 participants in the testing cohort are monitored for 30 days, the algorithm will be tested for understanding initial performance. As more participants are recruited into the study, follow-up algorithm testing will occur for each 100 participants that are added to the testing cohort.

Although the outcome of the participants in the validation set is known, the outcomes will be initially ignored, as if researchers did not know participant outcome. This simulates what researchers know about a participant, preceding the participant's outcome. The testing participants' collected variables (demographic, medical history, continuous data from wearable, and symptom data) will be run through the developed Bayes network algorithm and comparison models. The algorithm will return probabilities of the study outcomes. The algorithm's probabilities will then be compared with the true outcome of the participant recorded by the study team.

The differences between the algorithm prediction and participant's true outcome will be used to calculate performance metrics such as positive predictive value (PPV), area under the curve/receiver operating characteristic (AUC/ROC), and Brier scores. The final part of algorithm validation will be calibration analysis, sensitivity analysis, and determining any subpopulations that may have had poor predictive performance.

The benchmarks of model performance will be as follows: area under curve between 0.50 and 0.55 is poor, 0.55 to 0.65 is moderate, 0.65 to 0.75 is acceptable, and >0.75 is excellent.[11] Brier scores will be used to verify the accuracy of the event prediction during calibration, where a perfect score is 0 and imperfect score is 1. Different specificity and sensitivity levels will need to be considered when creating a feature that automatically triggers notification of study staff that a participant is likely (probability of hospitalization >50%) to reduce alarm and alarm fatigue. In addition, the duration of time a patient spends in a high-risk state needs to be considered. For example, if a participant's oxygen saturation levels (SpO_2) levels decrease for a brief period, then regain to normal levels, we will evaluate this to determine if it is an indicative of patient deterioration or not.

We hypothesize that our model will achieve an accuracy of 75% or higher.

Table 2. Variables collected for analysis	
Continuously acquired variables 1. Respiration rate 2. Pulse rate 3. Oxygen saturation 4. Skin temperature 5. Step count 6. Activity levels *Categorical variables* 7. Symptoms 8. Days when reporting for employment 9. Outcomes of any SARS-CoV-2/COVID-19 testing 10. Admission to hospital, ICU, death	*Categorical variables (continued)* 13. Age 14. Sex 15. Occupation 16. Household make-up (living alone or with people) 17. Other household members with COVID19 18. Other household members enrolled in this study 19. Menopausal state and time since last menstrual cycle / Pregnancy status 20. Race/Ethnicity 21. Zip code 22. BMI (height & weight) 23. Comorbidities 24. Acute and Chronic Medication

Recruitment Strategies

The primary recruitment tactics will involve digital marketing through social media (Facebook Advertising), and Google Advertising. We will use CDC data to target areas experiencing outbreaks of SARS-CoV-2/COVID-19. Additional recruitment tactics include email content and circulation of physical materials such as flyers, posters, or bulletin boards and direct mailers. All marketing material will direct to the website, including study team contact information, for initial screening. Throughout the enrollment process, Current Health will communicate updates on the clinical trial and/or enrolment process via phone calls, text messages, or emails. All materials will be developed by Current Health, reviewed by BARDA funders, and approved by the Advarra Institutional Review Board before becoming patientfacing. No communications via email or text message will contain protected health information.

We plan to create a website to serve as the primary communication method with participants prior to enrollment in the clinical trial. This website (https://community.currenthealth.com) sits as a subdomain on the Current Health corporate website, which is secure and HIPAA compliant. We have included the website wording, and sample screenshots as appendices.

On the website, we articulate:

- The goals of the clinical trials
- Qualification criteria for participants
- What is expected of participants as part of the clinical trial
- What compensation the participant can expect to receive
- Support contact information for participants enrolled in the clinical trial

- Information regarding Current Health

Once participants have progressed through the website, their details will be passed to a study team member. The study team member will contact the participant via email or text message and send a copy of the Informed Consent Form. The study team member and participant will arrange a mutually convenient time to speak via telephone or Zoom. Together, they will review the Informed Consent Form and engage with the process of consent. Once consent has been obtained via secure electronic means, the participant will be shipped a Current Health device by a logistics partner (Seko).

Data Analysis

By recruiting participants that have already been identified as being SARS-CoV-2/COVID-19 positive, we expect that approximately of 10% of individuals from each age group will eventually develop severe or critical COVID-19 symptoms and require hospitalization or treatment in an intensive care unit. Currently there are not sufficiently rigorous statistical models for predicting statistical power for machine learning studies. Some of the issues related to sample size for machine learning models have been recently reviewed in the scientific literature. Machine learning models can be trained to find an effect, but it is not clear if the effect is the result of over-fitting and/or poor sample selection. Nested crossvalidation and calibration have been proposed to mitigate these issues. Based on extensive prior experience of our group, we expect that 100 events in continuously monitored participants will be sufficient to assess the training performance of the model for early identification of novel digital biomarkers indicative of disease severity as well future trajectory of the severity of disease. Using the 100 events and approximate 10% event rate, testing and training cohorts of 1,000 participants (2,000 participants total) were determined.

Although not required in observational clinical trials due to no directly measured effect size, sample size calculations were conducted under different circumstances to ensure sample is sufficiently large for a clinical prediction model.[12]

Substudy

Objectives

The overall objective of this RiskSEARCH sub-study is to understand the participant experience of joining the study and participating, by wearing the Current Health wearable device 24 hours/day and answering daily surveys on the tablet. Research Objectives

1. To explore recruitment and retention for the RiskSEARCH (COVID-19) study
2. To explore feasibility, acceptability, and usability of the intervention, i.e., the Current Health wearable device and tablet
3. To explore barriers and facilitators of study compliance

Interviews with participants and data analysis

We will interview up to 20 participants (depending on data saturation) and ask them to take a modified Telehealth Usability Questionnaire that assesses usability of telehealth implementation and service.[13] (see Appendix C) Participants will be purposively sampled for a range of characteristics (e.g., level of device use, age, gender, socioeconomic status by zip code). We will also specifically seek to interview those who did not take up the intervention to explore the reasons for this. A semi-structured interview guide (Appendix D) will be used to explore participant insights related to acceptability and usability of the website and Current Health device/tablet, patterns of usage, and barriers to use.

Interviews will be completed by trained study team members via telephone or internet-based call. Interviews will be audio recorded and transcribed verbatim with the help of HIPAAcompliant software (e.g., Trint). Participants will have the opportunity to request sole interviewers and handwritten note taking of responses. A separate informed consent process will take place for the qualitative interviews.

Qualitative data analysis will explore the acceptability of the intervention, the extent to which participants engaged with it, and contextual factors that may have influenced engagement. The study team will analyse data using qualitative and quantitative methodologies. Qualitative methods using software (e.g., NVivo) will include analysis to identify emergent themes that could provide direction for future design improvements to make the device more comfortable or engaging. Quantitative methods will include the use of descriptive statistics to report frequencies of responses.

Research governance

Ethical issues

As this study involves human subjects, we will submit an application to the Advarra Institutional Review Board. Participation in this study has a low risk of harms and discomforts: the Current Health device is a widely deployed wearable that has been subjected to rigorous usability testing. Potential participants will be made aware of potential harms and discomforts in the Informed Consent Form. During the consenting process one of our study team members will be available to answer any concerns or questions. Participants will be compensated for their time during the study, contingent on their wearing the device for the duration of the study and completing the daily survey and returning the device at the end. Participants may leave the study at any time. If a participant does experience any adverse event, this will be investigated using the Current Health Post Market Surveillance process.

As with many studies, there is a chance that confidentiality could be compromised; however, we are taking precautions to minimize this risk. All our participant data will be de-identified for analysis.

FDA Clearance

Current Health has 510k FDA regulatory clearance for use in the USA. The clearance covers both the physical wearable and relevant cloud-based software components of the platform for wearable vital signs monitoring and alarming of patients both in the hospital and at home.

The 510k clearance was obtained for Generation 1 (G1) of the wearable device. Participants in the study will be using the newer iteration, Generation 2 (G2). G2 uses the same sensing optics and has an identical technical specification to G1, but is smaller and lighter, improving patient comfort. G2 is being released under the FDA's Enforcement Policy for Non-Invasive Remote Monitoring Devices Used to Support Patient Monitoring During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (Revised), while formal 510k is concurrently sought. Further information is available in the Current Health Outline Regulatory Strategy (200911) if required.

Data Management & Security

After participants are identified as being eligible for this protocol, they will be assigned a randomized and unique identifier under which all subsequent data will be stored. The only mechanism for linking this number to the participant will be through a key that is stored within the Current Health Firewall. Only study team members will have access to the key. Consequently, all participant data collected by the Current Health Device will be stored under this anonymized number, and any information linking to participant data collected by Current Health study team members will also be anonymized under this number. The key will be destroyed at the end of the data analysis portion of this study. For the qualitative substudy, all de-identified interviews will be recorded and stored on a HIPAA compliant platform until transcribed. Once the data are analyzed, audio recordings will be destroyed.

Participant data (including daily survey data) are sent to the Current Health cloud-based system when participants are near the transmitter located within their homes. De-identified welcome survey data are collected and stored in Jotform's HIPAA compliant database. No Protected Health Information (PHI) data is transmitted via the wearable, only anonymized raw waveform data. The device will not attempt to transmit data under unregistered/free access wifi systems and will store data for up to ten hours in the absence of the home-based hotspot. The servers (SOC-2 certified AWS data centers) and solutions housed by Current Health meet stringent guidelines for HIPAA security. The Current Health Information Security Management System is ISO 27001 certified, and also 21 CFR Part 11 and HIPAA Compliant.

Current Health has robust security standards that meet HIPAA compliance standards and no identified, identifying data, or key will be shared or transferred.

Internally, all data collected, stored or analyzed at Current Health will be done behind the Current Health firewall. As noted above, no data used for analyses will be identifiable other than by the unique, random participant number assigned at the time eligibility is determined. All computing systems and servers at Current Health used for these study data are HIPAA compliant. Shared drives are password protected, backed up daily on secure servers, and ensure version control.

Device Decontamination

Current Health has stringent post-use device reprocessing and decontamination methods for medical facilities using methods that meet or exceed both ISO and FDA guidelines for the decontamination of reusable medical devices. Their pre-existing decontamination strategies have already been shown to be effective at eliminating SARS-CoV-2/COVID-19.

Current Health works with chosen medical logistics partners who are experienced in handling, decontaminating and recycling medical equipment. Each kit is shipped back to Current Health in specific medical bags to ensure safety of courier staff as well as staff employed by their medical logistics partners.

Timeframe

The award was granted 30 September 2020. Enrollment for the pilot study will begin in January 2021 will be conducted over eight months with a final report submitted in August 2021.

Dissemination

The primary dissemination method will be the preparation of a report for the Biomedical Advanced Research and Development Authority (BARDA) of the U.S. Department of Health and Human Services. A draft final report will be prepared for BARDA for review and comment and the study team will revise as required for the final report. The final report for this project will provide a comprehensive overview of the work undertaken and results obtained. This will then be prepared for publication in an academic journal.

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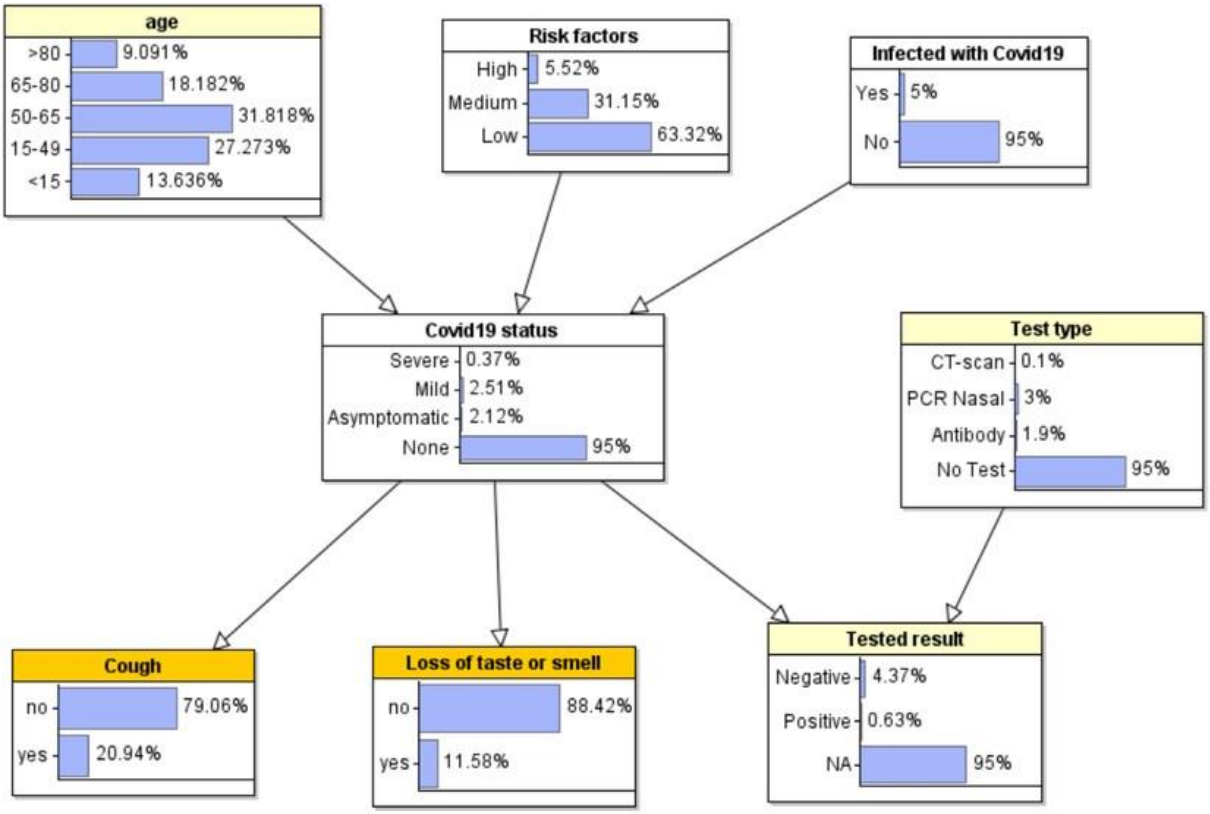
Appendix A. Simplified Bayesian Network[10]

A simplified Bayesian network. This is an example of a “base model”, where no observations specific to a patient have been specified.



Appendix B. Sample Size Calculations with Multiple Considerations[12]

Calculation 1: Sample size required for precise estimation of the overall outcome probability in the target population. In this study a 10% event rate has been estimated. The number of participants required under the assumption this is a true event rate:

Binary outcomes: For a binary outcome, an approximate 95% confidence interval for the overall outcome proportion (ϕ) is,

$$\hat{\phi} \pm 1.96\sqrt{\frac{\hat{\phi}(1-\hat{\phi})}{n}}$$

and so the absolute margin of error (δ) is $1.96\sqrt{\frac{\hat{\phi}(1-\hat{\phi})}{n}}$. Thus, to aim for precise estimation of the overall outcome probability in the target population, based on the anticipated outcome proportion ($\hat{\phi}$) and the desired margin of error, the required sample size is calculated as:

$$n = \left(\frac{1.96}{\delta}\right)^2 \hat{\phi}(1-\hat{\phi})$$

To estimate the required number of participants to properly observe 10% event rate at margin error of ≤0.05:

$$n = \left(\frac{1.96}{0.05}\right)^2 0.1(1-0.1) = 139\ participants$$

This calculation does not represent the main goal of the study, rather is the lowest bar for number of participants for the state event observation rate.

Calculation 2: Sample size required to help ensure a developed prediction model of a binary outcome will have a small mean absolute error in predicted probabilities when applied in other targeted individuals.

Given that we do not know the predictive power of a model, this estimate is conservative to apply a model to new individuals. The calculation below is given with an event rate of 0.1 (10%) (ϕ) and approximately 30 model parameters (P) based upon our 21 variables listed in the study.

For a binary outcome van Smeden et al[14] use simulation, across a range of scenarios, to derive an approximation (on the natural log scale, denoted by ln) of the expected average error in the outcome probabilities when a derived model is applied to new individuals from the target population. Their derived formula was originally developed based on 12 or fewer predictor parameters, but we have since updated the simulations to allow for 30 or fewer predictor parameters. The derived formula is:

$$\ln(MAPE) = -0.508 - 0.544\ln(n) + 0.259\ln(\Phi) + 0.504\ln(P)$$

Here, n is the sample size of the development dataset, Φ is the anticipated outcome proportion (≤0.5), and P is the number of candidate predictor parameters (≤30). MAPE denotes the Mean Absolute Prediction Error (ie, the average error in the model's estimated outcome probability one would allow for in the intended setting of application of the model). Rearranging this equation, and choosing a target value for MAPE, the required sample size is:

$$n = \exp\left(\frac{-0.508 + 0.259\ln(\phi) + 0.504\ln(P) - \ln(MAPE)}{0.544}\right)$$

$$n = exp\left(\frac{-0.508 + 0.259\ln(0.1) + 0.504\ln(30) - \ln(0.05)}{0.050.544}\right) = 756\ participants$$

Appendix C. Telehealth Usability Questionnaire[13]

Telehealth Usability Questionnaire								
Components	**Question**	**7**	**6**	**5**	**4**	**3**	**2**	**1**
Usefulness								
1	Current Health improves my access to healthcare services							
2	Current Health saves me time traveling to a hospital or specialist clinic							
3	Current Health provides for my healthcare needs							
Ease of Use & Learnability								
1	It was simple to use the Current Health kit							
2	It was easy to learn to use the Current Health kit							
3	I believe I could become productive quickly using the Current Health kit							
Interface Quality								
1	The way I interact with the Current Health kit is pleasant							
2	I like using the Current Health kit							
3	The Current Health kit is simple and easy to understand							
4	This Current Health kit is able to do everything I would want it to be able to do							
Interaction Quality								
1	I could easily talk to the clinician using the Current Health tablet							
2	I could hear the clinician clearly using the Current Health tablet							
3	I felt I was able to express myself effectively							
4	Using the Current Health tablet, I could see the clinician as well as if we met in person							
Reliability								
1	I think the visits provided through Current Health are the same as in-person visits							
2	Whenever I made a mistake using Current Health, I could recover easily and quickly							
3	The Current Health tablet gave error messages that clearly told me how to fix problems							
Satisfaction and Future Use								
1	I feel comfortable communicating with the clinician using the Current Health tablet							
2	Current Health is an acceptable way to receive healthcare services							

3	I would use Current Health services again							
4	Overall, I am satisfied with Current Health							

7: Strongly Agree; 6: Agree; 5: Somewhat Agree; 4: Neutral; 3: Somewhat Disagree; 2: Disagree; 1: Strongly Disagree

*Adapted from the Telehealth Usability Questionnaire[13]

Appendix D. RiskSEARCH Interview Schedule

Thank you for agreeing to speak to me today about your experience in the study. In this interview I would like to discuss your views of the COVID-19 study which you have been taking part in, how you found the experience, and what impact it had on you.

The interview should take about 40 minutes, but if you want to take a break or stop at any time just tell me and we can stop immediately. You don't have to answer any question you don't want to, so if that is the case, just say so and we can move on to something else. There are no right or wrong answers.

I'd like to reassure you, again, of confidentiality. Any information you give us will be used anonymously - your name will not be attached to the transcripts of this interview or included in any reports of our findings from these interviews.

Please feel free to add anything that you think is important but which I may not ask you about. It is only by talking to people in this way, can we develop a monitor that is really useful to you and other people who are in a similar situation to you in the future.

I'd like to make sure you have had an opportunity to read the Informed Consent Form which we sent you by email. Do you have any question about the Informed Consent Form? Have you read it and do you have questions about it? Do you consent to being interviewed? In particular, are you happy that your anonymous data can be stored and shared with other genuine researchers (this is not necessary for interview to take place)? Are you happy to proceed with the interview?

Context

1. What led you to sign up for the study?

Study

2. We are interested in hearing about your views on the enrollment process, for example, navigating the website, completing the online eligibility questionnaire, talking to a study team member to give consent, getting the device and setting it up, etc. How was this process for you? (Prompt: barriers)

3. Are you still involved with/participating in the COVID-19 study? If not, why?

4. Have there been any negative effects of taking part in the study?

5. What did you think about the following COVID-19 study stuff?
    a. Website
    b. Emails from the study team
    c. Calls with the study team
    d. $100 for participating
    e. Other?
6. What was the best and the worst thing about taking part in the study?

Community by Current Health website

7. When you used the Community by Current Health website, could you tell me more about when and how often?
    a. How long did you use it for?
    b. If you stopped, why?
    c. What ideas do you have for encouraging people to keep using it?
8. Tell me about your experience using the website.
    a. Was the information helpful?
    b. Was the layout usable?
    c. What would you like to have seen?
    d. What were your patterns of use?
    e. Were there issues with the design?
9. Aside from this study, can you tell us about anything else you've used or done to contribute to COVID-19 research?

Wearable Device

10. Have you had any challenges in receiving, setting up the device or wearing it?
11. Have you had any technical issues?
    a. If so, have you received the support you needed to resolve the issues?
12. If you have had periods of time you have not worn the device, could you tell me why that is? (prompt: times of days or activities that led to removing the device)
13. What have you liked about wearing the device?
14. What have you disliked about wearing the device?
15. What could make using and wearing the device easier or more engaging?

Tablet

16. Have you had any challenges in using the tablet?
17. Have you had days you missed answering the survey and if so, what contributed to these?
18. What have you liked about the tablet?
19. What could make using the tablet easier to use or more engaging?
20. When setting up the kit, did you follow the printed guide, the on-tablet guide, or both?
21. Were the instructions on the tablet to fill in the questionnaire clear? Are there any improvements that we should consider?
22. Are there any other features you would like to see added to the tablet device?
23. We're about to finish up. Now is your opportunity to share any other feedback or thoughts you have about the study.

Thank you for your time today. We will send payment to you through PayPal.

Risk SEARCH Statistical Analysis Plan

TRIAL FULL TITLE	Risk Stratification and Early Alerting Regarding COVID-19 Hospitalization (Risk SEARCH)
Document Number	900002
SAP VERSION	3
SAP VERSION DATE	February 10th, 2021
TRIAL STATISTICIAN	Hope Watson
Protocol Version (SAP associated with)	3
TRIAL PRINCIPAL INVESTIGATORS	Juliana Pugmire Matt Wilkes
SAP AUTHOR(s)	Hope Watson, Juliana Pugmire

1.Administrative Information

1.1. SAP Version

SAP Version	Date
1	December 14th, 2020
2	January 11th 2021
3	February 10th, 2021

1.2. Protocol Version

Protocol Version	Date
1	November 23rd, 2020
2	December 18th, 2020
3	January 21st, 2021

1.3. SAP Revisions

The revisions in this draft SAP have been redlined with track changes and dates in addition to previous versions kept in a version controlled cloud environment.

1.4. Roles and Responsibilities

Names	Affiliations	Role
Hope Watson	Current Health	Data Scientist
Juliana Pugmire	Current Health	Principal Investigator
Matt Wilkes	Current Health	Principal Investigator
James Zhou	BARDA	Statistical Reviewer

1.5. SAP Signatures

I give my approval for the attached SAP entitled Risk Stratification and Early Alerting Regarding COVID-19 Hospitalization (Risk SEARCH) dated February 9th, 2021.

Names	Role	Signature	Date
Hope Watson	Data Scientist/ Statistician (Author)	DocuSigned by: Hope Watson Signer Name: Hope Watson Signing Reason: I am the author of this document Signing Time: 10/2/2021 | 2:04:03 PM PST 1424C36812904295AB5B355F8947CA21	10/2/2021
Juliana Pugmire	Principal Investigator	DocuSigned by: Juliana Pugmire Signer Name: Juliana Pugmire Signing Reason: I have reviewed this document Signing Time: 11/2/2021 | 8:27:37 AM PST 02ABAD0F985845319549B3AF08940F78	11/2/2021
Matt Wilkes	Principal Investigator	DocuSigned by: Signer Name: Matt Wilkes Signing Reason: I have reviewed this document Signing Time: 11/2/2021 | 1:19:09 AM PST 76EE3D55AE6B45DB85043E56915C534C	11/2/2021
James Zhou	Statistical Reviewer	DocuSigned by: James Zhou Signer Name: James Zhou Signing Reason: I approve this document Signing Time: 10/2/2021 | 9:04:36 AM PST 3D966BADAA4745AE84C82D3C9AB543AF	10/2/2021

2.Table of Contents

3. Abbreviations and Definitions

BMI	Body Mass Index
BN	Bayesian Network
CH	Current Health
CRA	Clinical Research Associate
CRF	Case Report Form
DP	Designated Person
IMP	Investigational Medical Product
NOK	Next of Kin
Risk SEARCH	Risk Stratification and Early Alerting Regarding COVID-19 Hospitalization
SAP	Statistical Analysis Plan

4. Introduction

4.1. Preface

In the proposed research, we will use Current Health's remote monitoring wearable device to create novel algorithms to help us predict the progression and severity of COVID-19 in individuals that have recently become infected in the community. Risk scores based on demographics, or for patients in hospital, already exist. However, by using continuous remote patient monitoring, in combination with machine learning and data analysis, we hope to predict the risk of an individual infected with COVID-19 requiring hospitalization, intensive care unit (ICU) treatment, or death based on their vital signs while still in the community.

Using a hospital-grade home-based, remote monitoring wearable gives us the opportunity to create a unique and extremely useful tool in predicting and managing the clinical effects of the COVID-19 pandemic. Our algorithm might bridge the gap between demographic models and in-hospital models of disease progression by providing real-time data from the community. If we are successful, this tool could be made available immediately to enable better resource allocation for patients after diagnosis. In addition, it enables patient-centered management, increasing confidence for low and high-risk patients, and those managing their care. The results of this research will provide a database that can be used in future trials to assess treatment efficacy and offer the potential for rapid algorithm iteration in the event of a future pandemic.

4.2. Scope of the analyses

These analyses will assess the model robustness and predictive performance for primary and secondary outcomes (5.1) in COVID-19 PCR or antigen positive participants.

5. Study Objectives and Endpoints and Hypotheses

5.1. Study Objectives, Endpoints, and Outcomes

The overall objective of this study is to train, develop, validate and release a digital biomarker-based algorithm that, in COVID-19 PCR or antigen positive participants, within 30 days of a positive test:

1. Primary Outcomes:
    a. Predicts likelihood of requiring a stay in hospital of at least 24 hours
    b. Predicts likelihood of recovery from COVID-19 defined as:
        i. For asymptomatic participants: 14 days without symptoms following positive test
        ii. For symptomatic: at least 14 days since onset of symptoms, with the last three days symptom free
2. Secondary Outcomes:
    a. Predicts likelihood of being admitted to ICU for either non-invasive (CPAP, BiPAP, high flow nasal oxygen), invasive ventilation or vasopressor support.
    b. Predicts likelihood of death.
3. Tertiary Outcomes: Successful delivery, setup, daily interface engagement, and compliance with wearing of the device

5.2. Statistical Hypotheses

These study methods are designed to create an algorithm, specifically a Bayesian Network (BN), and then test the statistical accuracy of the developed Bayesian Network and comparison models on the primary and secondary outcomes. The model acceptance criteria and stated hypothesis is the model's ability to predict the primary outcome of hospitalization of study participants with 75% accuracy. The secondary outcomes will be more exploratory with less strict acceptance criteria. The ability to successfully predict secondary outcomes will largely depend on the number of secondary outcomes observed and if it warrants adequate power.

The benchmarks of model performance will be as follows: AUC between 0.50 and 0.55 is poor, 0.55 to 0.65 is moderate, 0.65 to 0.75 is acceptable, and >0.75 is excellent. Brier scores will be used to verify the accuracy of the event prediction during calibration, where a perfect score is 0 and imperfect score is 1. Brier scores will be calculated for each individual prediction, representing one study participant, and an aggregate Brier score for the sequence of predictions of the participant set.

Different specificity and sensitivity levels will need to be considered when creating a feature that automatically triggers notification of study staff to reduce number of unnecessary alarms and alarm fatigue. In addition, the duration of time a patient spends in a high-risk state needs to be considered. For example, if a participant's oxygen saturation levels (SpO_2) levels decrease for a brief period, then regain to normal levels, we will evaluate this to determine if it is an indicative of

patient deterioration or not. This will likely be undertaken by generating a rolling average or median of a certain number of time periods, t, to ascertain a confident deterioration event.

If the model performs statistically significantly better than 75% (AUC >0.75) with reasonable specificity, sensitivity, and calibration the model will be finalized and deployed.

6. Study Methods

6.1. General Trial Design and Plan

General study design characteristics:

- Longitudinal observational cohort trial
- Virtual trial (in contrast to a single or multicenter design)
- Level and method of blinding: Participants will be aware of wearing the medical device, therefore there is no blinding to actual device wearing. However, participants will be blinded from seeing their own data being captured by the device.
- Sequence and duration of all study periods: screening, baseline, active treatment, follow-up.

6.2. Randomization and Blinding

No randomization will be conducted in this experiment, as it is a longitudinal observational cohort trial.

For our study participants, data will be collected “blind”. The participant will not be able to see their data in real time, and no data will be reviewed or acted upon by the study team unless there is a clinically indicated trigger elicited by the system. These triggers exist to prompt the capture of studyspecific information, not to direct participant care.

6.3. Sample Size

By recruiting participants that have already been identified as SARS-CoV-2/COVID-19 positive, we expect that approximately 10% of individuals from each age group will eventually develop severe or critical COVID-19 symptoms and require hospitalization or treatment in an intensive care unit. Currently there are not sufficiently rigorous statistical models for predicting statistical power for machine learning studies. Some of the issues related to sample size for machine learning models have been recently reviewed in the scientific literature. Machine learning models can be trained to find an effect, but it is not clear if the effect is the result of over-fitting and/or poor sample selection. Nested cross-validation and calibration have been proposed to mitigate these issues. Based on extensive prior experience of our group, we expect that 100 events in continuously monitored participants will be sufficient to assess the training performance of the model for early identification of novel digital biomarkers indicative of disease severity as well as future trajectory of the severity of disease. Using the 100 events and approximate 10% event

rate, we determined that testing and training cohorts of 1,000 participants each (2,000 participants total) will be sufficient.

Although not required in observational clinical trials due to no directly measured effect size, sample size calculations were conducted under different circumstances to ensure sample is sufficiently large for a clinical prediction model. [1]

Calculation 1[1]: Sample size required for precise estimation of the overall outcome probability in the target population. In this study a 10% event rate has been estimated. The number of participants required under the assumption this is a true event rate where *n* is the required sample size, ϕ is the anticipated outcome proportion, and δ is the absolute margin of error.

$$n = \left(\frac{1.96}{\delta}\right)^2 \phi(1-\phi)$$

To estimate the required number of participants to properly observe 10% event rate at margin error of ≤0.05:

$$n = \left(\frac{1.96}{0.05}\right)^2 0.1(1-0.1) = 139\ participants$$

This calculation does not represent the main goal of the study, rather is the lowest bar for number of participants for the stated event observation rate.

Calculation 2[1]: Sample size required to help ensure a developed prediction model of a binary outcome will have a small mean absolute error in predicted probabilities when applied in other targeted individuals. MAPE is the mean absolute prediction error, P is the number of candidate predictor parameters, and the constants are derived from simulations in Smeden et al.[2] The goal of using this formula is to avoid the reductionistic "rule of 10" that would indicate the sample size required needs to be 10 times the number of parameters (in this study parameters are variables). However, using only the rule of thumb fails to account for number of categories and frequency of the category within the parameters.

$$n = exp\left(\frac{-0.508 + 0.259\ln(\phi) + 0.504\ln(P) - \ln(MAPE)}{0.544}\right)$$

Given that we do not know the predictive power of a model, this estimate is conservative to apply a model to new individuals. The calculation below is given with an event rate of 0.1 (10%) (ϕ) and approximately 30 model parameters (P) based upon our 21 variables listed in the study.

$$n = exp\left(\frac{-0.508 + 0.259\ln(0.1) + 0.504\ln(30) - \ln(0.05)}{0.544}\right) = 756\ participants$$

6.4. Statistical Analyses and Stopping Guidance

Analyses will be conducted in three distinct parts of the trial. Analysis following the pilot study of 50 participants including feasibility, adherence rates, univariate and bivariate statistics, and informing structural design of the Bayesian Network. Descriptive statistics will include univariate analysis such as frequency, box plots, or histograms, and where appropriate, bivariate analysis on covariates using methods such as regression, Fisher's exact tests, or chi-squared analyses.

Stages 1 and 2 are covered in more depth (9.1) but generally following a training and testing machine learning design, respectively. Stopping guidance is determined by both recruitment feasibility and model performance. After a total of 2050 participants are reported, the recruitment will stop. If the model performs statistically significantly better than 75% (AUC >0.75) with reasonable specificity, sensitivity, and calibration, the model will be finalized and deployed. Benchmarks were established as reasonable for similar outcomes in literature.[3,4] If the model does not meet this standard, we will conduct further analysis into where performance failures were most pervasive to decide how performance could best be improved. Adjustments to significance levels due to analysis stages are not relevant to Bayesian methods.

6.5. Timing of Final Analysis

We will perform the final analysis after 1000 participants in the validation phase have been observed. Final analysis will include machine learning validation and reporting. The current timeline aims to have this completed by July 30th, 2021 but is subject to changes due to study recruitment delays.

6.6. Timing of Outcome Assessments

The frequency and timing of all the relevant study assessments is considered from the time the participant CH kit arrives to 30 days of observation or a met outcome.

Study Task	**Timeline**
Kit Setup	Day 1
Participant Intake Survey	Day 1 to Day 3
*Daily Survey	Daily
CRA Adherence Checks	Day 1 to Day 30 ongoing
Vital signs captured by CH wearable	Day 1 to Day 30 ongoing
Outcome Verification	Day 1 to Day 30 ongoing *and 30 days after observation period ends*

*Daily symptom questionnaire will close if not completed within a given number of hours. Participant will still be able to fill out the following day's daily symptom questionnaire.

Variables collected from study assessments will be generally as follows:

- Demographic – Categorical
- Medical history and medication – Boolean
- Symptom presence – Boolean ("Much better" to "Much worse")
- Symptom severity – Ordinal categorical

7. Statistical Principles

7.1. Consideration for Bayesian Methods

Both Bayesian and frequentist statistics will be used in this analysis. In the Bayesian view, a probability is assigned to a hypothesis, while with the frequentist view, a hypothesis is tested without being assigned a probability. The reporting interpretation and semantics of the different methods will be explicitly stated in comparing confidence versus credible intervals.

7.2. Confidence Intervals and P values

The level of statistical significance will be set at α=0.05 threshold.

As this study is primarily Bayesian focused, 95% credible intervals will be used for single parameters, and credible regions will be used for multivariate parameters.[5]

Where confidence intervals are appropriate, 95% confidence will be used.

7.3. Adherence and Protocol Deviations

A study participant will be considered fully adherent to study protocol if they:

- Wear the CH device for at least 20 hours a day, at least 6 days a week;
- Answer the questions on the tablet at least 6 days a week;
- Return wearable kit and device.

Adherence metrics will be presented in absolute and percentage terms. Both measures will account for how long a participant is in the study. For example, a participant that is observed the entire 30 days will have a possible total of 720 hours (30 days x 24 hours) and 30 answered tablet symptom surveys. This participant's minimum adherence level would be 600 hours of device wear and at least 26 completed symptom surveys. A participant that meets an outcome much earlier due to hospitalization after 7 days would still be considered adherent if prior to hospitalization they wore the device 140 hours and completed 6 symptom surveys.

A summary table will generally be presented with the following variables per participant:

Participant ID
Time in trial (hours)
Hours of CH device observation
Wearable adherence percentage
Time in trial (days)
Number of surveys completed
Survey adherence percentage
Overall study adherence (Y/N)

Following collection all participants this information will be aggregated to the CONSORT flow chart metrics.

7.3.1. Full Analysis Population

- All subjects who receive CH kit
- The participants will be represented in flow diagram and analyzed for where participants systematically dropped out or did not adhere to study protocol. Participant feedback will also be captured and analyzed on this population.

7.3.2. Per Protocol Population

- All subjects who adhere to the major criteria in the protocol as defined by adherence of wearing the CH device for 20 hours a day, 6 days a week, answer tablet surveys at least 6 days a week, and return the CH wearable device kit and tablet.
- The adherent per protocol population will be used for BN training and testing.

8. Trial Population

8.1. Recruitment and Screening

Participant recruitment will primarily use social media (Facebook) and internet advertisements. The study population may contain biases such as a younger audience and those “tech savy” enough to wear a medical device for the duration of the study compared to the general population. These potential limitations will be considered in the study’s scope of generalizability. For screening, participants who are more likely to fit inclusion criteria could be correlated with other social determinants of health, which will also be in the study’s scope of generalizability. Where population demographic information deviates far from the general population expected this will be highlighted.

8.2. Eligibility

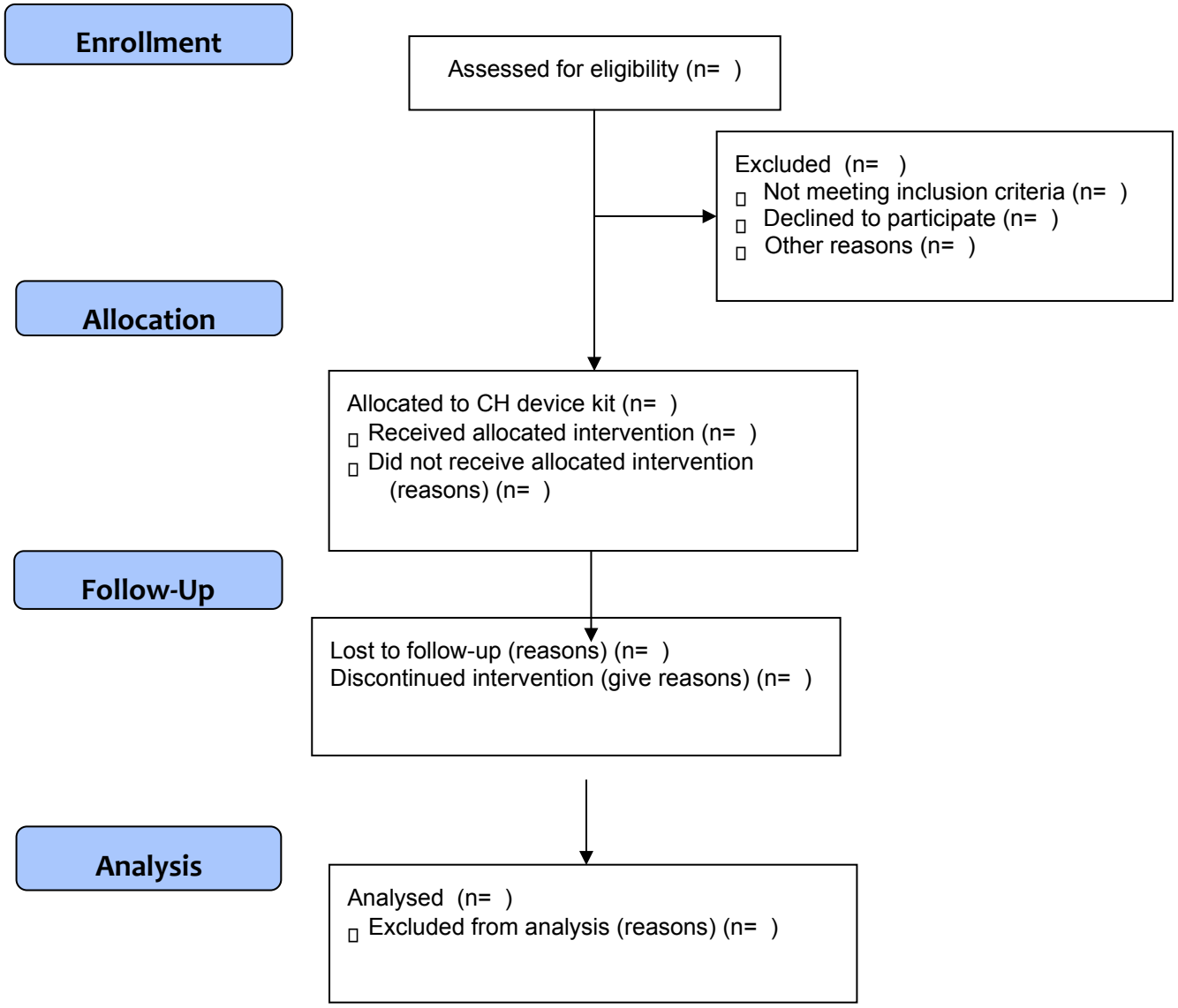
Inclusion and Exclusion Criteria

Table 1. Criteria for study participants

Inclusion	Exclusion
1. Living in the United States 2. Aged 21 years or older 3. Able to provide documentation of +PCR or +antigen test for COVID-19 within the past 48 hours 4. Self-reports that comfortable and willing to wear the wearable device and interact with a tablet-based interface daily 5. Able to provide a next of kin/designated person who can be contacted in the event of hospitalization for follow up.	1. Under the age of 21 2. Received a positive test result more than 48 hours prior to contacting study staff or has a pending test for COVID-19 3. Cannot confirm a PCR or antigen positive test for COVID-19. 4. Is unable to read English 5. Is unwilling to wear the device 24 hours/day except for showering/bathing or interact with a tablet-based interface for daily questionnaire 6. Is unwilling or unable to provide baseline data required for entry into the study 7. Is unable to provide a next of kin/designated person who can be contacted in the event of hospitalization for follow-up 8. Heavy tattooing on both upper arms 9. Known atrial fibrillation (permanent or paroxysmal) 10. Has taken/is taking part in a COVID19 vaccine or treatment study

8.3. CONSORT flow diagram

A CONSORT diagram modified for the observational design of the trial will be outlined as follows. Upon study completion each n= will be provided and reasons for ineligibility and loss of follow-up will be noted.



8.4. Withdrawal and Follow-up

Participants may withdrawal at any time from the study if they no longer wish to wear the CH device and not respond to tablet based questions. The level of withdrawal, non-adherence, and loss of follow-up will be analyzed separately from modeling (7.3). Where possible CRA will capture reasons for withdrawal such as discomfort of continuous wear of device on upper arm. Withdrawal and loss of follow-up will be presented in the modified CONSORT flow diagram.

8.5. Baseline Participant Characteristics

Characteristics will be presented in a descriptive summary table — continuous variables as mean and standard deviation or median and quartiles, and categorical and binary variables as absolute and relative frequencies. The analysis population will be produced for those who complete the trial to a study outcome including recovery. Surveys will be administered via tablet, which is part of the CH device kit a participant receives. The list of baseline participant characteristics and description of how they will be recorded are captured in the following table. The variables planned to be captured represent the most recent literature findings of COVID-19 risk factors.[6]

Description	Variable	Variable Type
*Participant Intake Survey		
Date of birth	dob	Date (MMDDYYY)
Sex	sex	Categorical: Male, Female, Other or prefer not to specify
Pregnant	pregnant	Binary: Yes, No
Presence of menstrual periods	menstrual_periods	Binary: Yes, No
Absence of menstrual periods reason	no_periods_reason	Categorical: Pregnant or breastfeeding, Taking hormonal birth control, Undergoing menopause or post-menopausal, High active, Other
Date of last period	last_period	Date (MMDDYYY)
Occupational category	occupational_cat	Categorical: Healthcare, Service industry, Retail, Office - able to work from home, Office - unable to work from home, Currently unemployed, Student - remote, Student - attending class in person
Household make-up	household_makeup	Binary: Living alone, Living with people
Do other members of your household currently have COVID-19?	household_covid	Binary: Yes, No

Are any other members of your household enrolled in Current Health's COVID-19 study?	household_study	Binary: Yes, No
What is your self-identified race/ethnicity?	race_ethnicity	Categorical: White Hispanic, White Non-Hispanic, Black or African American, Asian, American Indian or Alaska Native, Native Hawaiian and Pacific Islander
Height	height	Discrete (user input)
Weight (in pounds)	weight	Continuous: (pounds or kg user input)
Asthma	asthma	Binary: Yes, No
Cancer	cancer	Binary: Yes, No
Chronic obstructive pulmonary disease (COPD)	copd	Binary: Yes, No
Diabetes	diabetes	Binary: Yes, No
Heart condition	heart_condition	Binary: Yes, No
High blood pressure	hbp	Binary: Yes, No
Kidney disease or reduced kidney function	kidney_disease	Binary: Yes, No
Organ transplant	organ_transplant	Binary: Yes, No
Sickle cell disease	sickle_cell_disease	Binary: Yes, No
Smoker	smoker	Binary: Yes, No
Intake survey feedback	intake_survey_feedbacbk	Long free text
†Daily Survey		
Loss of smell or taste	loss_smell_taste	Binary: Yes, No
Is your loss of smell or taste better or worse than yesterday?	loss_smell_taste_likert	Categorical: Much worse, Worse, The same, Better, Much better
Dry cough	dry_cough	Binary: Yes, No
Is your dry cough better or worse than yesterday?	dry_cough_likert	Categorical: Much worse, Worse, The same, Better, Much better
Sore throat	sore_throat	Binary: Yes, No
Is your **sore throat** better or worse than yesterday?	sore_throat_likert	Categorical: Much worse, Worse, The same, Better, Much better
Fever or feeling feverish	fever	Binary: Yes, No
Is your **fever** better or worse than yesterday?	fever_likert	Categorical: Much worse, Worse, The same, Better, Much better
Chills	chills	Binary: Yes, No

Are your chills better or worse than yesterday?	chills_likert	Categorical: Much worse, Worse, The same, Better, Much better
Muscle aches	muscle_aches	Binary: Yes, No
Are your **muscle aches** better or worse than yesterday?	muscle_aches_likert	Categorical: Much worse, Worse, The same, Better, Much better
Diarrhea	diarrhea	Binary: Yes, No
Is your **diarrhea** better or worse than yesterday?	diarrhea_likert	Categorical: Much worse, Worse, The same, Better, Much better
Nausea	nausea	Binary: Yes, No
Is your **nausea** better or worse than yesterday?	nausea_likert	Categorical: Much worse, Worse, The same, Better, Much better
Are there any other symptoms or differences in health you would like to report?	daily_survey_feedback	Long free text
Will you speak to a healthcare provider due to worsening symptoms today?	self_reported_provider_care	Categorical: Yes, No, Maybe
Will you go to the hospital due to worsening symptoms today?	self_reported_hospital	Categorical: Yes, No, Maybe
Do you feel as though you have completely recovered from COVID-19 as of today?	self_reported_recovery	Categorical: Yes, No, Maybe

*Participant Intake Survey questions are to be completed by participant one time.
†Daily Survey questions are asked once a day at the same time each day.

8.6. Continuous Vital Signs

Continuous vital signs are as follows and are reported as continuous and discrete data:

Variable	Variable Type
Respiration rate	Continuous numeric
Respiration rate	Continuous numeric
Pulse rate	Continuous numeric
Oxygen saturation	Continuous numeric
Skin temperature	Continuous numeric
Step count	Discrete numeric
Activity levels	Discrete numeric

8.7. Derived Variables

In order for CH to ship a kit to a participant zip code will be collected. Zip code may be used during analysis to determine potential social determinants of health such as median household

income in an area. BMI will be derived from height and weight measurements. Date of birth will be used to calculate age and age may be used to derive age groups.

9. Analysis

9.1. Outcome definitions

Study outcomes will be ascertained by the CRA within the study observational period of 30 days or the following 30 days if the participant has not definitively experienced other outcomes of recovery or death.

Primary and secondary outcomes are presented in (5.1) and will be presented as follows.

Description	Variable	Variable Type
Recovery from COVID-19	recovered	Binary: Yes, No
Hospital stay of 24 hours or longer	hospitalized	Binary: Yes, No
ICU admission	icu_admission	Binary: Yes, No
Death	death	Binary: Yes, No

No calculations are necessary to derive primary or secondary outcomes, they all will be directly stated in binary terms.

9.2. Study Stages

Study stages will be broken into three sections: pilot, stage 1 training, and stage 2 testing and validation.

Pilot

The pilot phase study with 50 participants will test the feasibility of recruitment, trial logistics, observed participant events, timeline to deterioration, and environmental test settings. The primary aim is to make any revisions to recruitment strategy and to the final number of “critical events” (e.g., hospitalization) required. The secondary aims are to produce descriptive statistics on pilot data, understand user issues that could affect study data, and begin formulating the structure of the Bayesian network. Descriptive statistics will include univariate analysis such as frequency, box plots, or histograms, and where appropriate, bivariate analysis on covariates using methods such as regression, Fisher’s exact tests, or chi-squared analyses.

Stage 1

The overall aim of Stage 1 is to collect enough data to perform machine learning analytics on data from the Current Health device to create a Bayesian network algorithm that successfully predicts the risk/probability of no severe disease, hospitalization, ICU admission, and death following SARS-CoV2/COVID-19 infection. The outcomes are *not* mutually exclusive categories, and can be hierarchical, i.e., when a participant first goes to hospital and then is admitted to the ICU. Conversely, a participant at risk could experience death without ever being hospitalized. This will be accounted for by calculating probabilities of each outcome and compare the conditional probabilities analyzing the risk of ICU admission, given that hospitalization has already occurred. One thousand participants will be recruited for the training stage.

Once the Bayesian network model is constructed, to account for model variation, that is a model's parameters change depending on the data the model is being given, cross-validation will be performed to ensure model stability and reduce issues with overfitting. Cross validation will only be conducted in the training data, as any cross validation with testing data has been shown in instances not to aid overfitting issues.[7]

Stage 2

To assess the algorithm performance, algorithm testing on a total of 1,000 participants will be conducted. This cohort of 1,000 testing participants will be held entirely separate from the training participants to avoid any possible data snooping or data mining bias in the study. In machine learning it is typical to obtain initial testing cohort results to determine if the model created from the training data is performing well. After the first 100 participants in the testing cohort are monitored for 30 days, the algorithm will be tested for understanding initial performance. As more participants are recruited into the study, follow up algorithm testing will occur for each 100 participants that are added to the testing cohort. To avoid any potential issues with multiple testing, only the most recent testing metrics (AUC/ROC, PPV, Brier Scores, etc.) will be reported. Therefore, the unique full test set will only be run *once*.

Although the outcome of the participants in the validation set is known, the outcomes will be initially ignored, as if researchers did not know participant outcome. This simulates what researchers know about a participant preceding the participant's outcome. The testing participants' collected variables (demographic, medical history, continuous data from wearable, and symptom data) will be run through the developed algorithm. The algorithm will return probabilities of the study outcomes. The algorithm's probabilities will then be compared with the true outcome of the participant recorded by the CRA.

10. Summary of Study Data

All continuous variables will be summarized using the following descriptive statistics: n (non missing sample size), mean, standard deviation, median, maximum and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures.

Major reporting aspects of the study will be the CONSORT diagram to understand participant recruiting funnel, baseline participant characteristics tables, the Bayesian network model and its performance features, and participant predict risk scores and probabilities as outputs from the model.

11. Reporting Conventions

Describe reporting conventions, for example the precision used for reporting p-values and other numeric values. Example:

P-values ≥0.001 will be reported to 3 decimal places; p-values less than 0.001 will be reported as "<0.001". The mean, standard deviation, and any other statistics other than quantiles, will be reported to one decimal place greater than the original data. Quantiles, such as median, or minimum and maximum will use the same number of decimal places as the original data. Estimated parameters, not on the same scale as raw observations (i.e. regression coefficients) will be reported to 3 significant figures.

12. Summary of Changes to the SAP

In version 2, the hypothesis was more explicitly stated with specific target metrics that need to be met for model standards and deployment. Additional information regarding structural and parameter learning were added for further context. Information about incorporation of temporal data was added. In Version 3 information about how to randomize the for data modeling if study recruitment is not met is considered in section (9.5)

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INFORMED CONSENT FORM AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**Current Health / "Risk Stratification and Early Alerting Regarding COVID-19 Hospitalization (Risk SEARCH)"**
Protocol Number:	**2002**
Principal Investigator: (Study Doctor)	**Adam Wolfberg, MD, MPH**
Telephone:	**(415) 941-5734 (24 Hours)**
Address:	**Current Health** **500 5th Ave** **New York, NY 10017**

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide whether or not to take part. **Please take the time to read the entire information sheet carefully and talk to a study team member before making your decision.** You should not sign and date the consent if you have any questions that have not been answered.

It's Your Choice	This is a research study. Being in this research study is your choice and voluntary; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research is to study ways to remotely monitor participants who have tested positive for COVID-19 to learn more about progression and recovery from the disease. You have been asked to take part in this research because you have received a positive test for COVID19.

What's Involved	Study participation involves wearing the Current Health Wearable Health Monitoring System each day for up to 30 days. You will also be provided with a Current Health tablet with an application installed. The tablet will remind you to answer a brief series of questions each day.
	Steps for taking part in this study: You will be asked to 1. Review, sign and date Informed Consent Form 2. Review, sign and date the Authorization to Use and Disclose Protected Health Information form 3. Set up your Current Health wearable study device when you receive it in the mail 4. Wear the study device every day except when you shower or bathe 5. Answer the tablet questions daily 6. Return the wearable study device kit and tablet when the study is over (you will not have to pay for shipping)
Risks	There are minimal risks related to participation in this research study. As always, there is a chance that wearing a device could cause irritation or discomfort. There is also a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.
Benefits	This study is being done for research and to advance our understanding of COVID-19 disease. There is no direct benefit to you from your participation in the study. Information learned from the study may help other people in the future. You will be paid up to $100 for your time and effort for taking part in this study.
Healthcare	This study will not provide you with healthcare or replace your standard healthcare. The study results will not be shared with your healthcare provider.
Learn More	If you are interested in learning more about this study, please read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A study team member will talk with you about taking part in this study before you sign and date the consent form to take part. If you have questions at any time, please ask us.

Please read this form carefully. Take your time to ask the study team as many questions about the study as you would like. The study team can explain words or information that you do not understand. Reading this form and talking to the study team may help you decide whether to

take part or not. If you decide to take part in this study, you must sign your name at the end of this form and date it.

BACKGROUND AND PURPOSE

The purpose of this research is to study ways to remotely monitor participants who have tested positive for COVID-19, to learn more about progression and recovery from the disease.

You have been asked to take part in this research because **you have received a positive test for COVID-19 in the last 48 hours.**

About 2050 participants will participate in this study.

WHAT WILL HAPPEN DURING THE STUDY?

If you decide to participate, after reading the Informed Consent Form and providing a digital signature, the study team will send you a Current Health wearable study device and kit within 24 hours with instructions about how to set up and use the study device. Then you will wear the study device each day you are in the study up to 30 days. The study device tracks your pulse rate, respiratory (breathing) rate, skin temperature, oxygen saturation, step count, and activity levels. Each day, you will be reminded to answer a brief series of questions on a tablet provided with the study device.

The study team will contact you about every two weeks to ask how you are feeling and how the equipment is working.

Additionally, the Current Health system can send the study team notifications if it is not receiving data. Study team members may call you on occasion to make sure your devices are functioning properly and to remind you to answer the daily questionnaire on your tablet.

Participation in this study does not provide you access to medical care for COVID-19. Instead, it allows us to learn what body functions change with the disease and once we learn that we may be able to help future patients with these devices. If you have new or worsening symptoms, you should contact your primary care provider or go to the local emergency department for evaluation and management.

If at any time you feel your health is rapidly declining, do not hesitate to seek care from your health care provider or call 911 if it is an emergency.

At the end of participation, the study team will call you to agree on a collection time for the device. You will also be reminded to answer a brief series of questions before mailing the system back.

EXPECTATIONS

If you participate in this study, you will be expected to:

- Provide some basic information about yourself when signing up for the study, including contact details.
- Talk to a study team member and sign and date an electronic consent form.
- Receive and set up the Current Health wearable study device – the study device is straightforward to set up and full instructions are provided.
- Wear the Current Health study device on either upper arm for up to 30 consecutive days. As a participant, you will not be able to see your vital sign data collected by the study device. These go directly to the study team.
- Answer a series of brief questions on the tablet provided every day.
- Return the study device kit when the study is over or when you have stopped participating.

RISKS, SIDE EFFECTS, AND/OR DISCOMFORTS

The study will take up some of your time to wear the study device, charge it occasionally and answer questions on the study device tablet.

The study device may cause some irritation and/or discomfort when worn for prolonged periods of time. If experiencing any irritation and/or discomfort when wearing the device, you may remove the study device to give your skin a rest, swap arms and/or change the fit of the study device strap. If the irritation and/or discomfort persist, you should stop wearing the study device and contact the study team.

As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk. All your data will be de-identified for analysis. Your equipment for the study will be mailed via a separate external vendor from Current Health. You may be emailed an electronic copy of this signed and dated consent form. There may be risks of loss of privacy and confidentiality if the electronic copy of this consent form is viewed and/or stored on a personal electronic device (PED), especially if that PED is shared with other users or is lost, hacked, or subject to a search warrant or subpoena. Also, the electronic copy of the consent may not be able to be permanently removed from a PED.

ALTERNATIVES TO PARTICIPATION

This research study is for research purposes only. The only alternative is to not participate in this study.

NEW FINDINGS

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you by email notification and a call from the study team.

BENEFITS

This study is being undertaken to find out if this study device can help predict the progression and severity of COVID-19 progression in individuals so the people that need it can receive earlier intervention and better care in the future. **This study is being done for research and to advance our understanding of COVID-19 disease.** There is no direct benefit to you from your participation in the study. Information learned from the study may help other people in the future.

COMPENSATION FOR PARTICIPATION

You will be paid up to a total of $100.00 if you complete this study. We would like to emphasize that wearing the study device every day is essential for the best study results. However, you will be paid for the weeks you wear the study device and answer the tablet questions according to the following schedule:

- $25.00 for week 1, wearing the study device at least 6 days for at least 20 hours of each day and answering the tablet questions at least 6 days.
- $25.00 for week 2, wearing the study device at least 6 days for at least 20 hours of each day and answering the tablet questions at least 6 days.
- $25.00 for week 3, wearing the study device at least 6 days for at least 20 hours of each day and answering the tablet questions at least 6 days.
- $25.00 for week 4, wearing the study device at least 6 days for at least 20 hours of each day and answering the tablet questions at least 6 days.

If you do not complete the study, for any reason, you will be paid for each study week you do complete.

You will be paid at the end of the 30-day study period **once the Current Health wearable study device kit and tablet have been returned**.

If you have any questions regarding your compensation for participation, please contact the study team.

FINANCIAL DISCLOSURE

Investigators on this study have an ownership interest, and some of the investigators hold executive positions, in Current Health, the company sponsoring this research study. As a result,

the investigators may benefit financially from a successful study. Please speak with your study doctor if you have questions about this.

CONFIDENTIALITY

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The study doctor, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

COMPENSATION FOR INJURY

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study team that you think you have been injured as a result of this study, then they will help you get the care you need.

If you are injured as a result from procedures done for the purpose of this study, the sponsor will pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third-party coverage. By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

COSTS

There will be no charge to you for your participation in this study. The Current Health wearable study device and study-related procedures, like shipping the study device to you and back, will be provided at no charge to you or your insurance company.

FUTURE RESEARCH STUDIES

Identifiers might be removed from your identifiable private information collected during this study and **could then be used for future research studies or distributed to another investigator for future research studies** without additional informed consent.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: **Pro00047371**.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to participate in this study is voluntary. You may choose to not participate, or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

The study doctor or the sponsor can stop your participation at any time without your consent for any of the following reasons:

- If it is in your best interest
- If you don't follow the study procedures
- If it is discovered that you do not meet the study requirement
- If the study is canceled

We will tell you about any new information that may affect your willingness to stay in the research study.

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing and dating this consent document. I will receive a copy of this signed and dated consent document.

_____

Participant's Printed Name

_____ _____

Participant's Signature Date

_____

Printed Name of the Person Conducting the Consent Discussion

_____ _____

Signature of the Person Conducting the Consent Discussion Date

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study team will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical, medication and family history.
- Information from the Current Health wearable device
- Information from your study questionnaires.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the study team may share health data about you with authorized users. Authorized users may include:

- Representatives of Current Health.
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this study, if applicable.
- The Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- Current Health, the sponsor of this study, and the people or groups it hires to help perform this research.

Your health data will be used to conduct and oversee the research, including for instance:

- For research activities related to the Current Health wearable device.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study team at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study team to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____

Printed Name of Participant

_____ _____

Signature of Participant Date