Scripps Research
Translational Institute

ImmunoCARE: Rapid, Accurate COVID Testing to Reduce Hospitalization of Immunocompromised Individuals

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Study Protocol

Submitted to IRB: May 14, 2024

IRB Approved: August 20, 2024

Version 1.8

NCT05655546

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Background

Immunocompromised individuals around the world are at significantly higher risk of adverse outcomes and death from COVID-19 infection (Baek, Lee, Kim, Choi, & Jung, 2021). People over the age of 65 also face higher risk of adverse outcomes and hospitalization (Vo, La, Wu, 2022). Even with vaccination, these populations remain at significantly higher risk of hospitalization and severe disease (Ryan, 2021; Sun et al., 2022). These factors impact quality of life (Amonoo et al., 2021) and pose a threat of significant financial burden when standard of care is indicated (Stephenson, 2021).

The pandemic illuminated already existing gaps in our healthcare system and limitations in our ability to track and mitigate community transmission (Kliff & Sanger-Katz, 2020). To address this, in part, the FDA has granted emergency use authorization for dozens of home devices that can be used to diagnose COVID-19 (Rizk et al., 2021). Easy to access testing and diagnosis, combined with measures such as isolation and social distancing, are some of our strongest tools that positively mitigate community transmission (Manabe, Sharfstein, & Armstrong, 2020). Additionally, we know that early detection through frequent testing has a positive correlation with people at high risk getting the medication they need, like Paxlovid, within the short window at disease onset when it is most effective. (Petty & Malani, 2022; Smith et al., 2021)

Cue Health is a San Diego, California based healthcare technology company that develops portable diagnostic tests for at-home use. Cue developed the first FDA-authorized COVID-19 diagnostic test that was used at home and available over the counter, without a prescription. Cue's COVID-19 tests amplify and detect the genomic RNA of SARS-CoV-2. The testing system consists of a swab and cartridge that reads the user's specimen, and an application that produces the results. The app also provides access to a mobile health dashboard to connect with on-demand telemedicine, proctoring, and prescription services (CueHealth, 2022).

The Digital Trials Center (DTC) at the Scripps Research Translational Institute (Scripps Research) is a leader in large-scale decentralized research studies, which harnesses digital health technologies to address pressing health problems. The DTC portfolio includes the direct-to-participant experience of the All of Us Research Program, which has engaged over 100,000 individuals across the United States.

The DTC is also home to advanced data analytics that incorporate machine learning and other artificial intelligence approaches. DTC has launched several IRB-approved digital studies that address diabetes (PROGRESS), maternal health (PowerMOM) and sleep (Refresh).

In March 2020, Scripps launched the Digital Engagement & Tracking for Early Control, & Treatment (DETECT) study, an app-based research platform that allows for consented

participants to share their wearable device data, self-reported symptoms, test results, vaccine information, and to optionally connect electronic health record (EHR) data. DETECT builds from our team's prior work utilizing wearable device data to monitor influenza-like-illnesses at a state level (Radin, Wineinger, Topol, & Steinhubl, 2020). DETECT aims to provide a deeper understanding of physiological and behavioral changes associated with viral illness, including COVID-19 with the goal of ultimately improving real-time digital disease detection. DETECT has enrolled over 40,000 participants from across the country. The observational data collected has led to several findings including the ability to discriminate between COVID-19 and other illnesses among symptomatic individuals (Quer, Radin, et al., 2021; Gadaleta et. al., 2021) and a prolonged deviation of daily resting heart rate (RHR) for SARS-CoV-2 positive individuals (Radin et al., 2021). Another analysis showed deviation in resting heart rate post-vaccination with observed differences between doses as well as between types of mRNA vaccines (Quer, Gadaleta, et al., 2022). Most recently, the DETECT team published and confirmed the utility of wearable device data in the early detection of COVID-19 and other acute respiratory infections (Radin et al., 2022).

Scripps DTC and Cue Health, in a new collaborative partnership, will combine their expertise in portable COVID-19 testing and direct to participant research to address the needs of the immunocompromised community.

Purpose

To examine whether a combination of at-home nucleic acid amplification tests, on-demand telemedicine, and delivery of Paxlovid within hours of testing positive for COVID-19, can reduce severe outcomes and hospitalization of immunocompromised patients. We will also analyze whether these efforts lower the cost of care compared to standard of care.

Study Design

We plan to conduct a randomized control trial with 10,000 participants. Participation will last for a minimum of 4months and maximum of 8 months, depending upon COVID-19 case rates. Half of participants will be randomized to the control group and continue their existing testing and healthcare practices. The remaining participants will be randomized into the intervention arm. Participants in the intervention will receive one Cue Cartridge Reader for the duration of the study and up to 10 Cue COVID Molecular tests per month for their own

use and to share with others who could expose them to COVID-19 (e.g. close contacts). In the case that a Cue Flu+COVID Molecular Test is available through FDA EUA or other authorization, participants may be provided this multiplex test in lieu of the Cue COVID Molecular Test.

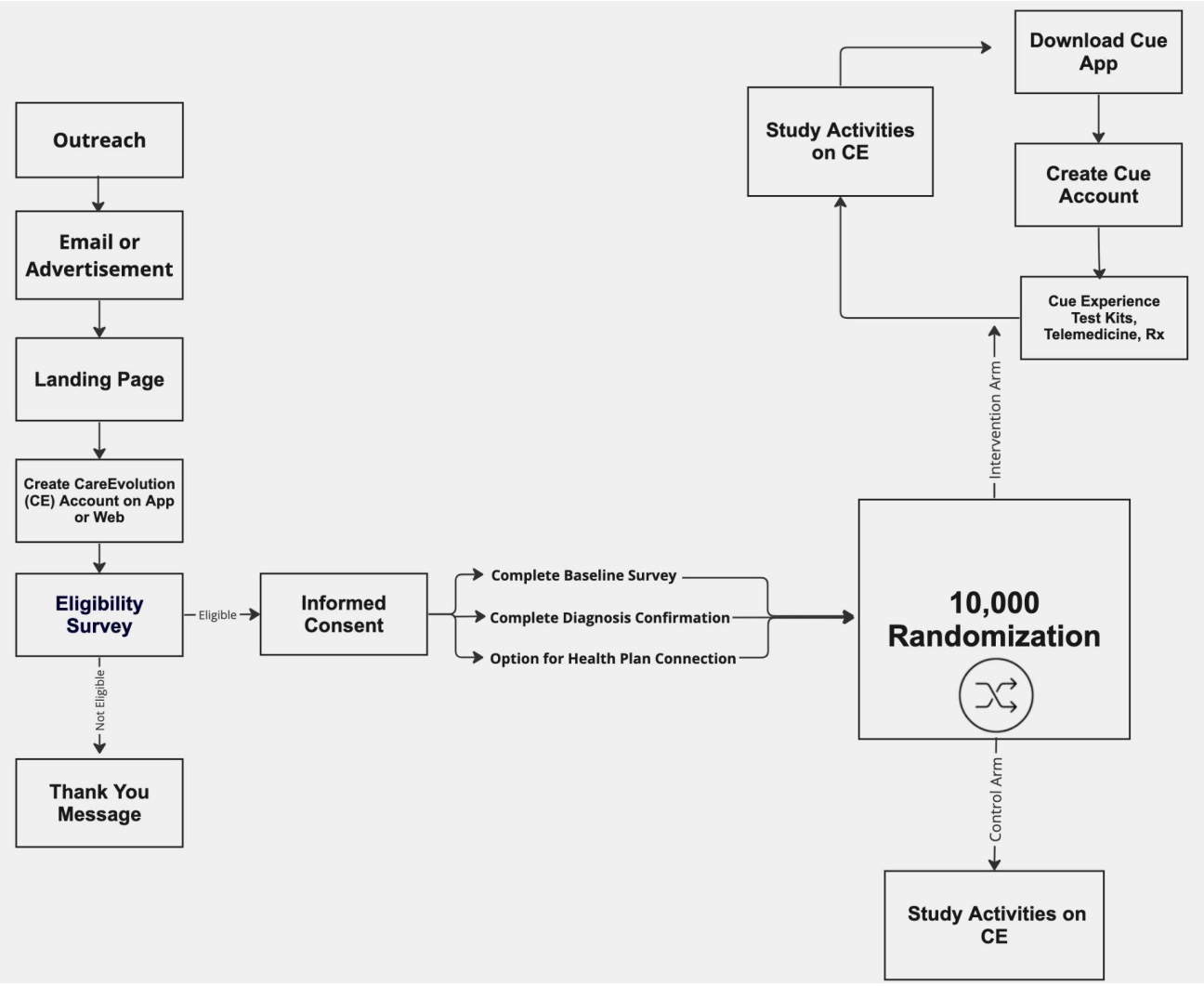
Table 1. Summary of Study Arms

Study Arm	Number of participants	COVID-testing practice
Control	5,000	None within this study
Intervention Arm	5,000	10 Cue tests per month to participants' for self and close contact use. Option to utilize Cue's telehealth and Rx delivery.

All intervention participants will be asked to test themselves if they are exposed or when symptoms arise. The primary outcome will be the number of hospitalizations that will be assessed from survey and claims data. We will also compare infection rates, ICU admissions, ED visits, deaths and cost of care between the control and intervention group. Our hypothesis is that access to high sensitivity portable molecular testing and subsequent antiviral treatment will significantly decrease hospitalization and thereby the cost of care.

Interested individuals will access the study via the MyDataHelps platform by web or app to complete the eligibility and informed consent process. Within the MyDataHelps experience, participants will complete study activities such as surveys and optional sharing of claims data. Participants who are randomized to the intervention group will have the option to use Cue Care should they test positive for COVID-19. In the case that the COVID Flu+COVID test is available, the intervention group will also have the option to use Cue Care should they test positive for Influenza. Cue Care contracts licensed Healthcare providers to deliver telemedicine and treatment for COVID-19.

Figure 1: Participant Flow



Study Population

To meet our study objectives, participants who enroll will be considered moderately to severely immunocompromised, this can be due to several types of conditions and treatments. Participants will provide documentation from a medical provider confirming their diagnosis. We will also enroll those who are 65 years or older, with no immunosuppressive diagnosis, due to the risk of severe outcomes and hospitalization within this age group. Additionally, because Medicare is widely used in this population, connecting Medicare claims for those enrolling by age will be required. This portion of participants will make up no more than 25% of the study population.

Inclusion Criteria

- Living in the United States
- 18 years or older
- Can read and understand English
- Use of compatible device (as described in Appendix B)
- Vaccinated against COVID-19 (completed at least the initial course, e.g. at least 2 doses of Moderna or Pfizer, one dose of J&J)
- Willing and able to participate in study interventions including:
    - Use of smartphone, including camera and bluetooth
    - Upload verification of diagnosis, if needed
    - Completing Surveys
    - Use of Cue Health App
    - Use of MyDataHelps Web or App
- Belonging to one of these two groups:
    - Immunocompromised due to disease or therapy, including:
        - Symptomatic HIV
        - Graft versus host disease
        - Immunoglobulin deficiency/Immunodeficiency
        - Immunosuppressive therapy
        - Leukemia
        - Lymphoma (Hodgkin or non-Hodgkin)
        - Metastatic Cancer
        - Multiple Myeloma
        - Solid organ malignancy
        - Transplant, hematopoietic stem cell
        - Transplant, solid organ
    - 65 years of age or older

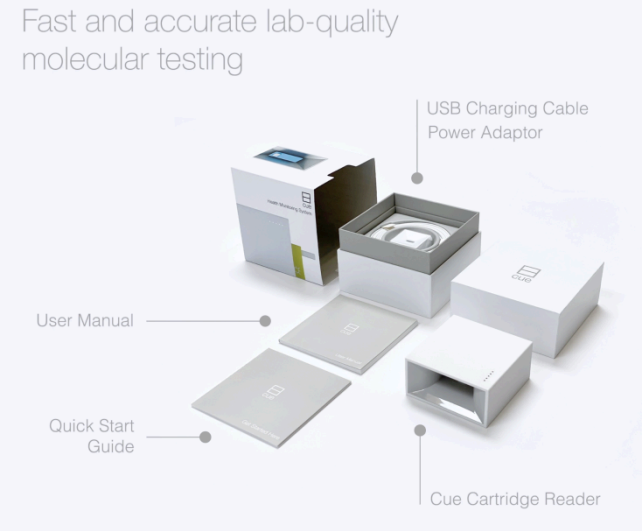
Confirmation of immunocompromised status or age will be performed in one of three ways. Participants will be able to 1) upload a document directly into the MyDataHelps app, 2) email it to a study coordinator, or 3) have their eligibility automatically verified via claims data, if connected. Methods 1 and 2 will require the study team to review and confirm diagnosis prior to prompting the participant to complete the next study activity. Participants

will be notified by push notification, email and/or SMS (depending on their notification preferences) that their diagnosis has been verified and they are eligible to move forward to participation. Method 3 will be automated back end verification of diagnosis and/or immunosuppressive medication history in MyDataHelps using the participants connected claims data for identification of qualifying ICD-10 diagnosis codes.

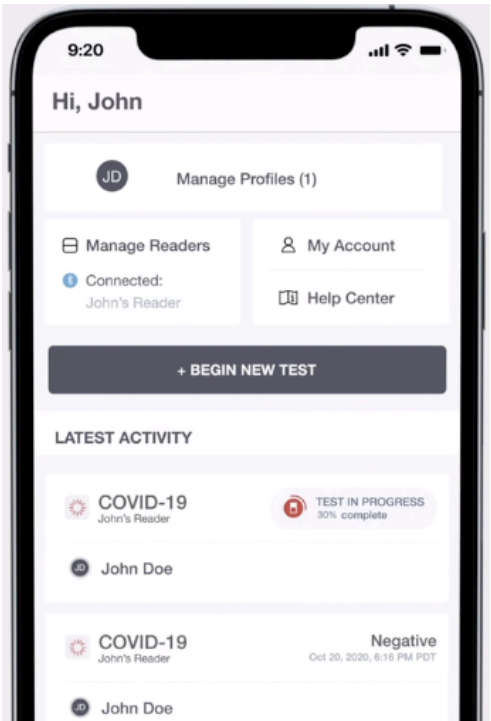
Study Interventions

All Groups (n=10,000)
Baseline study activities for all groups include: verification of immunocompromised status, downloading MyDataHelps or using the web version, completion of digital informed consent, baseline survey completion, optional connection to claims data source, monthly survey completion and reimbursement for participation.

Control Group (n=5,000)
Participants in the control group will complete the baseline study activities, as described above. If symptoms arise or COVID-19 infection occurs, participants will test and seek care as they normally would.



Intervention Arm (n=5,000)
Participants in this group will complete the baseline study activities, as described above. Additionally, participants will be instructed to create a Cue Health account and download the Cue Health App. Using the app and the 10 Cue Health COVID-19 molecular tests that are provided (or Cue Health Flu+COVID molecular tests if available and FDA authorized), the participant will perform tests after exposure or if symptoms arise. Participants can also use the test for close contacts who are exposed to COVID-19 and/or have symptoms. If COVID-19 infection occurs, participants will have access to telemedicine to discuss further with a healthcare professional. When clinically indicated, medication for the treatment of COVID-19 (and/or Influenza in case of Cue Health Flu+COVID test availability) will be prescribed and delivered to the participants' delivery address. Participants can also seek care through other healthcare providers or not seek care, at their discretion.



Device Use and Procedures

CareEvolution MyDataHelps Web or App

MyDataHelps by CareEvolution is the app or website that participants will use for digital consent, surveys, optional connection of claims data and reimbursement. In-app content can be reviewed in the appendices.

The Cue Health Monitoring System

The Cue Health Monitoring System is a complete diagnostic tool for COVID-19 that uses Nucleic Acid Amplification and provides actionable results within 20 minutes. Within each system there is a USB Charging Cable Power Adaptor, The Cue Cartridge Reader, Quick Start Guide, User Manual, and the COVID-19 Cartridge Pack consisting of the collection wand and test cartridge. Participants will receive these items in the mail after ordering their Monitoring System within the Cue Health App. The Cue Health Monitoring System works with The Cue Health App to deliver results to the participant.

The Cue Health App

The Cue Health App will be downloaded by participants in the intervention arm. Once participants download the app they will set up their account using their email and a unique password. Participants will need to view and accept the End User License Agreement as well as the Cue Privacy Policy to complete account creation. Once the participants Cue account is created, users will verify their registration email. At this time participants will set up their profile within the Cue Health app. Not all information is required to be filled in to complete this process. Participants will also have the option to enable alerts and location services (location services data will not be used for research). Neither are required for use of the app. Next, participants will pair the Cue Cartridge Reader to their mobile device.

Pairing the Cue Cartridge Reader to the Mobile Smart Device

First, participants will connect their cartridge to the power source to allow the device to charge. Once charged, the user will scan the QR code on the bottom of the cartridge to connect the two. Once connected the device is ready to use for testing.

Running the Cue COVID-19 Molecular Test

On the home screen in the Cue Health App participants will click +Begin New Test. Next, participants will read the use and precautions statement to proceed. Next, participants will open the single use test cartridge and sample wand provided in their Cue Health Monitoring System. Participants will remove the test cartridge from the tray and insert it into the cartridge reader. At this point, the cartridge is preheating for use and users should not insert the sample swab or remove the cartridge from the reader. When the cartridge is ready, the app will prompt the participant to collect the nasal sample. Instructions are provided in the app. Once collected, the sample wand is inserted into the test cartridge and sample analysis begins. When the test is complete the app screen will automatically advance to the test results. Test results can also be viewed on the home screen or in the test center within the participants Cue Health profile.

If the Cue Flu+COVID molecular test is available and FDA authorized, the above instructions are the same except that on the results screen where both COVID and Influenza results will be shown.

Cue Care

Within the Cue Health App, Cue Care allows individuals to access telehealth services from third party medical groups. Medical Groups provide telehealth or other healthcare services, like prescriptions, through licensed providers who practice medicine and nursing. Participants who enroll in this study and are randomized to the treatment arm will have access to Cue Care. Using Cue Care is not a requirement of this study and participants always have the option to act on their test results with their own providers, or to not seek care at all.

Reimbursement

Participants will be reimbursed for their participation. Total reimbursement will be up to $2 00 in Amazon gift cards. When the onboarding, informed consent, diagnosis verification, optional claims data sharing process, and baseline survey are complete, participants will be provided with a $20 Amazon gift card. Participants who do not share claims data will receive $10 after completing consent and the baseline survey, then $20 after completing the final survey. Throughout the study, participants will be provided with $10 Amazon gift cards on a monthly basis for up to 8 months. If the study period runs shorter than 8 months, participants will receive the remaining gift card balance, to total up to $100, at study closure. Participants who do not share claims data and do not complete all monthly surveys may be offered half of the compensation they missed from monthly surveys upon completion of the final survey. For example, if a participant does not complete three monthly surveys (which would have earned them $30 of compensation), they may be offered an additional $15 for completing their final survey. This is to incentivize participants to provide an account of their COVID experiences over the course of the study in the final survey, a crucial data point to achieve study objectives.

Interim analysis for ImmunoCARE has that claims data is more balanced between the two arms than survey data. To collect more claims data , an additional $100 Amazon gift card will be offered to enrollees for connection of available insurance claims data.

Surveys

Participants will take surveys throughout the course of this study. To determine eligibility, prospective participants will complete the eligibility survey. Once enrolled, participants will complete the baseline survey where we will collect demographic and health information, including comorbidities. Each month, participants will be asked to report on their COVID exposures, diagnoses, and/or hospitalizations. The ability to report the positive diagnosis of a close contact will be available on the participant dashboard at all times. Surveys can be reviewed in the appendices. In an effort toward complete data collection we will collect

phone numbers, secondary contacts, and birth dates from participants who cannot share their claims data. Participants and their secondary contacts will only be called at the end of the study, by a research coordinator, to ask participants to complete surveys and remind them about reimbursement opportunities. Participants will be considered lost to follow up after three phone calls. Birth dates will be used to search the national death index.

Outreach

Center for Equitable and Diverse Research (CEDR), a division of the Institute for Public Health at SDSU. CEDR will be involved in conducting in-person outreach and education, study recruitment, and technical assistance as needed to help participants in San Diego County complete study requirements including the 1) eligibility survey, 2) using and navigating the MyDataHelps Web or App including assistance in completing monthly questionnaires, 3) creating the CUE Health App account, 4) completion of the informed consent process, 5) confirmation of immunocompromised status or age and 5) navigation of the CUE Health app.

CEDR will utilize a multi-strategy approach to study recruitment that will use the Community Health Worker/Promotores (CHW/P) model to conduct individual and group outreach and education activities with community members, community clinics, senior centers, and community organizations. Example activities include outreach at health fairs, community clinic waiting rooms, patient groups and senior centers; provider education to generate patient referrals; and partnerships with community-based organizations and advocacy groups to raise awareness with the community members they serve. During all outreach and education activities, prospective study participants will be asked for consent to voluntarily provide their contact information for follow-up calls and text messages to support enrollment and study retention. CEDR will share the IRB-approved outreach one-pager found in Appendix 4 with interested participants which will include the CEDR email address and phone number for those who have questions about the study. Talking points for use by outreach staff while speaking with participants about the study can be found in Appendix 25.

Risks and Benefits of Participation

The risks of participating in this study are minimal.

There may be a small risk for emotional or mental discomfort from concern about whether they may have an infectious illness or not. It is also possible, despite guidance otherwise, that participants may avoid seeking routine care due to the availability of home testing. Participants who are randomized to the control group may be disappointed that they are not

receiving the Cue product. For those who use the Cue tests, there may be slight discomfort when the nasal swab is performed for sample collection, though this will be minimal.

In spite of all the safety measures that will be used, we cannot guarantee that a participant's identity will never become known. Consequently, it may be possible, in the unlikely setting of a data breach, that collected study information could be used to help identify the participant.

If participants have any concerns, they will be able to contact a study team member by email.

The benefits of this study include the opportunity to contribute to research that could benefit the immunocompromised population. For some, there is the added benefit of access to frequent and reliable COVID-19 testing with the option to seek treatment if they test positive.

Sample Size and Data Analysis

This study has been adapted to a maximum number of 10,000 participants. Participants will be divided into 2 groups, a Control Arm and an Intervention Arm. Sample sizes have been calculated for detecting a difference in number of hospitalizations in Control Arm versus Intervention Arm. The main assumptions used are:

- The percentage of COVID-19 positive cases over 4 months in this group is 5.9% (based on historical reported case data).
- We expect a reduction of 5% in number of COVID-19 infections for the Intervention Arm with respect to the Control Arm.
- 28% of COVID-19 cases among immunocompromised will require hospitalization (Singson et.al, 2022) and 10% among >65 years old non-immunocompromised. Given that the percentage of 65+ non-immunocompromised will be limited to 25%, we expect that 23.5% of participants with COVID-19 infection will be hospitalized.
- We expect a relative reduction in the fraction of hospitalizations per positive case by at least 30% for the Intervention arm with respect to the Control arm.
- Of the participants hospitalized, 38% will be admitted to the ICU.
- The number of hospitalizations will be assessed based on survey data. We expect that at least 80% of participants will complete the FINAL SURVEY even if they have been hospitalized.
- The experiment will be run for 4 to 8 months (depending on number of COVID cases), and we expect to have a similar number of COVID-19 cases per month.
- Interim analyses on the number of events and progress towards achieving enough events for a well-powered statistical test significance may be run start at month 1 or later. Determination of ending the study timeline may be based on having sufficient number of COVID cases and/or hospitalization events to achieve statistical power. Importantly, we will utilize data on the total number of events to determine when to

end the experiment; we will not use information on the difference in the number of events between study arms.

Table 2: Sample size (target)

Sample size estimation	Control Arm N=5000	Intervention Arm N=5000
Loss to follow-up / drop-out / failure	5%	5%
Expected total number of COVID-19 positives	540	513
Loss to report: expected ratio of individuals not reporting in survey	20%	20%
Expected total number of COVID-19 positives correctly reported	432	410
Expected total number of reported hospitalizations	102	68
Expected total number reported in ICU	39	26

Given the assumptions of above, we should reach a target of 900 confirmed COVID positive cases reported in the survey or claims (approximately 450 per arm), that we expect to reach in 8 months if the rate of infection remains stable. The statistical power of the test (alpha=0.05) is equal to 0.76, meaning that if all assumptions hold, we have a 76% chance of observing a statistically significant difference in the number of hospitalizations between Control and Intervention arms.

The minimum target is to reach 800 confirmed COVID positive cases (approximately 400 per arm). The corresponding statistical power of the test (alpha=0.05) in this case is less than 0.7, meaning that if all assumptions hold, we have less than a 70% chance of observing a statistically significant difference in the number of hospitalizations between Control and Intervention arms.

The experiment will proceed for between 4 and 8 months. We will aim to meet the target number of COVID cases (900) before 8 months, however we may decide to end once the minimum number of cases is reached (800) if the national COVID case trends suggest that we will not reach the target number of cases within 8 months. The study length will be re-evaluated if the minimum number of cases is not met within 8 months.

As a secondary output, we will also consider the total cost for the individuals in the two study arms, based on claims data if available.

Risk Management Procedures

Loss of privacy

Participants will be identified by a 10-digit, randomly assigned alphanumeric study ID. Only the investigators and research staff will have access to the patient's fully identified medical information. The information that matches the code to the identifying information will be kept in a safeguarded database that is password protected.

Adverse Events

We do not expect any adverse events to occur. However, unless otherwise required by local regulations, the sponsor (Scripps Research Translational Institute) is responsible for complying with required timelines for any safety reporting obligation to Health Authority (HA), IRB and to any participating (co or sub) investigators, as defined in applicable laws and regulations. The safety reporting responsibilities to HA and IRB are defined in the collaborative research support agreement.

Data Acquisition, Storage and Analysis

All study data will be integrated by CareEvolution via the study app and the Cue Health app and securely transferred to Scripps Research where it will be stored on servers secured with two-factor authentication.

Future research

Participant information will be kept for up to 6 years after completion of this study for future research that has not yet been planned. Individual information after the removal of identifiers such as names, emails or zip codes will be kept indefinitely for future research studies at Scripps Research Translational Institute.

Subject Payment/Costs

There is no cost to the subject for study participation. Reimbursement of up to $200 will be redeemable through Amazon gift cards.

Estimated Duration of Study

We had initially planned for each participant to be part of the study for up to 8 months. However, due to the FDA issuing a warning letter regarding Cue Health's COVID-19 test accuracy and calling for discontinuing use of the device in May 2024, we have decided to end the study early. We plan to analyze the data primarily to characterize the effect of the COVID-19 pandemic on the study population. If connected, claims data collection will persist for about three months after participation ends, and data analysis will continue for one to two years following the completion of data collection.

Consent Procedures

Study purpose, methods, materials, risks, benefits, and alternatives will be provided in a detailed onboarding process as well as in the long form consent, both within the MyDataHelps app. Participants will have the ability to reach the study team by phone or email with anything they may need. Those individuals who were recruited by CDER can reach out to the CDER team for technical assistance as needed. Informed consent will be obtained in the app with a digital signature. Participants will be given a copy of their signed consent form.

Data Security

The collection and processing of personal data from participants enrolled in this study will be limited to the data needed to investigate this study's hypothesis and the clinical data typically used as covariates in the analysis of clinical studies. Access to data will be limited to those authorized by Principal Investigators, including CareEvolution and CueHealth. Privacy policies and user agreements

Scripps Research Translational Institute affirms the participant's right to protection against invasion of privacy. Data files are stored on a password-protected computer/database and will be accessible only to the above-listed investigators and research staff. Only the research staff will have the link that can match the code to traditional identifying information. The data sets used for analysis will be coded and not contain information that could be used to identify the patient.

Participant Withdrawal

Participation is voluntary and the participant can discontinue participation at any time without loss of benefits or penalty. A participant who wishes to withdraw consent can make a request through the app during the study period. Any data that has been entered in the database will be included in the analysis of the study. All study activities and data collection will stop at the time of withdrawal.

Monitoring

Scripps Research Translational Institute will monitor the study and study investigators will be responsible for notifying the IRB with any deviations or adverse events as required by the local laws and regulations. Source documents will be reviewed to ensure all subjects have properly signed and dated the informed consent and any HIPAA-related documentation required for data sharing.

Record Retention

Research records with participant identification will be kept for 6 years after study completion. The collected data and related health information, after removal of identifiers like name, email or zip codes, will be kept indefinitely. Record retention will comply with the specific requirements of the IRB.

Publication

The results of this research will be presented at conferences, shared publicly, and/or in publications. Scripps will provide a report or update to the CHWs, partner organizations and other interested parties (i.e. government and public officials, community leaders, etc.)

Study Funding

Funding for this study is provided by Cue Health, who is also a scientific collaborator on the study.

References

Amonoo, H. L., Topping, C. E. W., Clay, M. A., Reynolds, M. J., Rice, J., Harnedy, L. E., . . . El-Jawahri, A. (2021). Distress in a Pandemic: Association of the Coronavirus Disease-2019 Pandemic with Distress and Quality of Life in Hematopoietic Stem Cell Transplantation. *Transplant Cell Ther, 27*(12), 1015 e1011-1015 e1017. doi:10.1016/j.jtct.2021.09.001

Baek, M. S., Lee, M. T., Kim, W. Y., Choi, J. C., & Jung, S. Y. (2021). COVID-19-related outcomes in immunocompromised patients: A nationwide study in Korea. *PLoS One, 16*(10), e0257641. doi:10.1371/journal.pone.0257641

Ryan, L. (2021). Vaccinated but Not Protected—Living Immunocompromised During the Pandemic. *JAMA, 325*(24), 2443-2444. doi:10.1001/jama.2021.9321

Stephenson, J. (2021). As COVID-19 Hospitalizations of Unvaccinated Patients Soar, Private Insurers No Longer Waiving Out-of-Pocket Costs. *JAMA Health Forum, 2*(8), e213263-e213263. doi:10.1001/jamahealthforum.2021.3263

Sun, J., Zheng, Q., Madhira, V., Olex, A. L., Anzalone, A. J., Vinson, A., . . . National, C. C. C. C. (2022). Association Between Immune Dysfunction and COVID-19 Breakthrough Infection After SARS-CoV-2 Vaccination in the US. *JAMA Intern Med, 182*(2), 153-162. doi:10.1001/jamainternmed.2021.7024

Kliff, S., & Sanger-Katz, M. (2020). Bottleneck for US coronavirus response: the fax machine. *New York Times*.

Manabe, Y. C., Sharfstein, J. S., & Armstrong, K. (2020). The Need for More and Better Testing for COVID-19. *JAMA, 324*(21), 2153-2154. doi:10.1001/jama.2020.21694

Petty, L. A., & Malani, P. N. (2022). Oral Antiviral Medications for COVID-19. *JAMA, 327*(24), 2464-2464. doi:10.1001/jama.2022.6876

Rizk, J. G., Forthal, D. N., Kalantar-Zadeh, K., Mehra, M. R., Lavie, C. J., Rizk, Y., . . . Lewin, J. C. (2021). Expanded Access Programs, compassionate drug use, and Emergency Use Authorizations during the COVID-19 pandemic. *Drug Discov Today, 26*(2), 593-603. doi:10.1016/j.drudis.2020.11.025

Smith, R. L., Gibson, L. L., Martinez, P. P., Ke, R., Mirza, A., Conte, M., . . . Brooke, C. B. (2021). Longitudinal Assessment of Diagnostic Test Performance Over the Course of Acute SARS-CoV-2 Infection. *The Journal of Infectious Diseases, 224*(6), 976-982. doi:10.1093/infdis/jiab337

CueHealth. (2022). Retrieved from cuehealth.com

Quer, G., Gadaleta, M., Radin, J. M., Andersen, K. G., Baca-Motes, K., Ramos, E., . . . Steinhubl, S. R. (2021). The Physiologic Response to COVID-19 Vaccination. *medRxiv*. doi:10.1101/2021.05.03.21256482

Quer, G., Radin, J. M., Gadaleta, M., Baca-Motes, K., Ariniello, L., Ramos, E., . . . Steinhubl, S. R. (2021). Wearable sensor data and self-reported symptoms for COVID-19 detection. *Nat Med, 27*(1), 73-77. doi:10.1038/s41591-020-1123-x

Radin, J. M., Quer, G., Pandit, J. A., Gadaleta, M., Baca-Motes, K., Ramos, E., . . . Topol, E. J. (2022). Sensor-based surveillance for digitising real-time COVID-19 tracking in the USA (DETECT): a multivariable, population-based, modelling study. *Lancet Digit Health*. doi:10.1016/S2589-7500(22)00156-X

Radin, J. M., Quer, G., Ramos, E., Baca-Motes, K., Gadaleta, M., Topol, E. J., & Steinhubl, S. R. (2021). Assessment of Prolonged Physiological and Behavioral Changes Associated With COVID-19 Infection. *JAMA Netw Open, 4*(7), e2115959. doi:10.1001/jamanetworkopen.2021.15959

Radin, J. M., Wineinger, N. E., Topol, E. J., & Steinhubl, S. R. (2020). Harnessing wearable device data to improve state-level real-time surveillance of influenza-like illness in the USA: a population-based study. *Lancet Digit Health, 2*(2), e85-e93. doi:10.1016/S2589-7500(19)30222-5

Singson JR, Kirley PD, Pham H, et al. Factors Associated with Severe Outcomes Among Immunocompromised Adults Hospitalized for COVID-19 — COVID-NET, 10 States, March 2020–February 2022. MMWR Morb Mortal Wkly Rep 2022;71:878–884. DOI: http://dx.doi.org/10.15585/mmwr.mm7127a3

Gadaleta, M., Radin, J.M., Baca-Motes, K. *et al.* Passive detection of COVID-19 with wearable sensors and explainable machine learning algorithms. *npj Digit. Med.* 4, 166 (2021). https://doi.org/10.1038/s41746-021-00533-1

Vo AD, La J, Wu JT, et al. Factors Associated With Severe COVID-19 Among Vaccinated Adults Treated in US Veterans Affairs Hospitals. JAMA Netw Open. 2022;5(10):e2240037. doi:10.1001/jamanetworkopen.2022.40037

Appendix 1: Documentation

Cue Health Privacy Policy
Cue Health Terms of Use and End User License Agreement
FDA Emergency Use Authorization Letter
Cue COVID-19 Test Instructions for Use
Cue Health Monitoring System Quick Start Guide
Cue Health Monitoring System User Manual
CareEvolution MyDataHelps Privacy and Use Policy
Cue Care Terms of Use

Appendix 2: Compatible Devices

- Apple®
  - Apple® iPhone® 8 Plus or later with iOS® 13 or higher
  - Apple® iPad® models with iPadOS® version 13.0 or higher with Bluetooth® Standard 4.2 or later (Bluetooth® 5.0 preferred)
    - iPad 6th generation or later
    - iPad Air® 3rd generation or later
    - iPad mini® 5th generation or later
    - iPad Pro® 2nd generation or later
- Android™
  - Smartphone models with OS 9.0 (API level 28) or higher; display size 5.5" or higher; Bluetooth® Standard 4.2 or later (Bluetooth 5.0 preferred); Wi-Fi® dual-band 2.4GHz and 5 GHz (5 GHz preferred).
  - Any Android™ smartphone device which meets the above minimum requirements may be used. The following are recommended devices that meet these requirements:
    - Google Pixel™ 4, 4a, 5, 6
    - Samsung Galaxy® A21, A71 5G unlocked, S8/S8+/S8 Note and later
    - Motorola® Moto G fast

Appendix 3: Participant Surveys

Note: Email is being collected at the time of screening and will be used to contact participants if there are changes in their eligibility status.

Eligibility Survey

Please complete the following survey to determine your eligibility for participation in this study.

1. Can you read and understand English? (Yes/No)
2. Are you over the age of 18? (Yes/No)
3. Are you 65 years or older? (Yes/No)
4. Do you live in the United States? (Yes/No)
5. Do you have a smartphone with a recent operating system installed (Android: OS 9.0 or higher, Apple: iOS 13.0 or higher)? (Yes/No)
6. Are you willing to connect your health insurance claims to the study app? (Yes/No)
   Tap the info icon for a list of health plan providers.
   a. List that appears if the info icon is tapped:
   b. Medicare
   c. Medicaid
   d. Anthem BlueCross and BlueShield
   e. Anthem BlueCross
   f. Empire BlueCross BlueShield
   g. Empire BlueCross
   h. Wellpoint
   i. Carelon
   j. Unicare
   k. Simply Healthcare Plans
   l. National Government Services, Inc.
   m. MMM
   n. Health Sun
   o. HealthLink
   p. Amerigroup
   q. None of these
7. Are you immunocompromised? (Yes/No)

   7a. If Yes → Please classify your diagnosis. (Select all that apply.)
   - Symptomatic HIV
   - Graft versus host disease
   - Immunoglobulin deficiency/Immunodeficiency
   - Immunosuppressive therapy
   - Leukemia
   - Lymphoma (Hodgkin or non-Hodgkin)

- Metastatic Cancer
- Multiple Myeloma
- Solid organ malignancy, with immunosuppression
- Transplant, hematopoietic stem cell
- Transplant, solid organ
- None of these

8. Are you able to upload verification of your immunocompromised status, if necessary? This can be a screenshot of an EMR (electronic medical record), diagnosis list, or a doctor's note. (Yes/No)
9. Have you completed a COVID-19 vaccine primary series? (Yes/No)
    a. If you have a medical exemption for COVID-19 vaccination, please email the study team at ImmunoCARE@scripps.edu
10. One more thing, will you share your email or phone number? We will contact you if there is a change to your eligibility status. This is optional at this point.
    a. What is your phone number or email address?

If 1, 2, 4, and 5 are YES and either

1. 3 is yes, 6 is yes, and 6a is not "None of these"
2. 7 is yes and 7a is not "None of these"

then:

If 1 through 8 are YES and 6a is not "None of these": Thank you! You are **eligible** to participate. Please continue to learn more about our study.

Otherwise: Thank you for your interest in participating in the ImmunoCARE Study. Unfortunately, you did not meet the study's eligibility requirements at this time.

Baseline Survey

Thank you for consenting to participate in this study. Please complete this baseline survey.

1. What is your date of birth?
2. What is your phone number?
3. In case we cannot contact you, please provide the telephone number of a relative or friend who would know where you can be reached. This is optional.
4. What terms best express how you describe your gender identity? (Check all that apply)
    - Man
    - Woman
    - Transgender
    - Non Binary
    - Other (please specify)
    - Prefer not to answer
5. Which categories describe you? Select all that apply. Note, you may select more than one group
    - American Indian or Alaskan Native
    - Asian
    - Black, African American, African
    - Hispanic, Latino, or Spanish
    - Middle Eastern or Northern African
    - Native Hawaiian or other Pacific Islander
    - White
    - None of these fully describe me (please specify)
    - Prefer not to answer
6. What is your annual household income from all sources?
    - $25,000 or less
    - More than $25,000
7. What is your zip code?
8. Please indicate if you have any of the following chronic conditions
    - Diabetes
    - High blood pressure
    - Asthma
    - COPD
    - Emphysema
    - Chronic Bronchitis
    - Heart Failure
    - Chronic Kidney Disease
    - Other (please specify)
9. How many doses of the COVID-19 vaccine have you received?

If none: please confirm your medical exemption from COVID-19 vaccination was reviewed by the study team.

10. For your *[nth]* dose, please indicate:
    - Date
    - Type: [ ] Full dose [ ] Booster
    - Manufacturer:
      [ ] Pfizer
      [ ] Moderna
      [ ] Janssen (Johnson & Johnson)
      [ ] Novavax
      [ ] Other (if you received it abroad)
      [Repeats for the number of doses reported in 7.]
11. Over the last month have you:
    - Been exposed to a close contact with COVID-19? [ ] Yes [ ] No
    - Contracted COVID-19? [ ] Yes [ ] No
    - Been prescribed medication for COVID-19? [ ] Yes [ ] No
    - Been to Urgent Care due to COVID-19? [ ] Yes [ ] No
    - Been to the Emergency Room due to COVID-19? [ ] Yes [ ] No
    - Been admitted to the hospital for COVID-19? [ ] Yes [ ] No
    - Been in the Intensive Care Unit due to COVID-19? [ ] Yes [ ] No
    - Needed additional health care (e.g. dialysis, CT scan, MRI) as a result of COVID-19?
      [ ] Yes [ ] No

      Is there any context you would like to share about the responses above? (open text box)

<u>Monthly Survey</u>

Thank you for your continued participation in the ImmunoCARE study. This survey is intended to capture information about how you have been feeling and any COVID-19 exposures and infections you have had since we last checked in. Once you complete this survey you will earn a $10 Amazon gift card to thank you for your time.

1. Since we last checked in, have you:
    - Been exposed to a close contact with COVID-19? [ ] Yes [ ] No
    - Contracted COVID-19? [ ] Yes [ ] No
    - Been prescribed medication for COVID-19? [ ] Yes [ ] No
    - Been to Urgent Care due to COVID-19? [ ] Yes [ ] No
    - Been to the Emergency Room due to COVID-19? [ ] Yes [ ] No
    - Been admitted to the hospital for COVID-19? [ ] Yes [ ] No

- Been in the Intensive Care Unit due to COVID-19? [ ] Yes [ ] No
- Needed additional health care (e.g. dialysis, CT scan, MRI) as a result of COVID-19?

  [ ] Yes [ ] No
-

Is there any context you would like to share about your previous responses? (open text box)

Thank you for sharing this information with the study team. Your Amazon gift card is now available.

If No → Thank you for confirming you have not had COVID-19 since we last checked in. Your Amazon gift card is now available.

End of Study Survey

Thank you for your participation in the ImmunoCARE study. This survey is intended to capture information about how you have been feeling and any COVID-19 exposures and infections you have had since enrolling in ImmunoCARE. Once you complete this survey you will earn an Amazon gift card to thank you for your time.

Since you enrolled in ImmunoCARE, have you:

- Been exposed to a close contact with COVID-19? [ ] Yes [ ] No
- Contracted COVID-19? [ ] Yes [ ] No
- Been prescribed medication for COVID-19? [ ] Yes [ ] No
- Been to Urgent Care due to COVID-19? [ ] Yes [ ] No
- Been to the Emergency Room due to COVID-19? [ ] Yes [ ] No
- Been admitted to the hospital for COVID-19? [ ] Yes [ ] No
- Been in the Intensive Care Unit due to COVID-19? [ ] Yes [ ] No
- Needed additional health care (e.g. dialysis, CT scan, MRI) as a result of COVID-19?

  [ ] Yes [ ] No

Is there any context you would like to share about your previous responses? (open text box)

Thank you for sharing this information with the study team. Your Amazon gift card is now available.

If No → Thank you for confirming you have not had COVID-19 since we last checked in. Your Amazon gift card is now available.

Appendix 4: Outreach One Pager

HEADING

ImmunoCARE: Rapid, Accurate COVID Testing to Reduce Hospitalization of Immunocompromised Individuals

INTRO

Are you at high risk of hospitalization from COVID-19 infection due to age or a compromised immune system? The ImmunoCare study aims to reduce that risk. Scripps Research – a renowned biomedical research institute – and Cue Health, a leading health care technology company that develops portable diagnostic tests for at-home use, are launching the ImmunoCARE Study.

SUBHEADING

More on The ImmunoCARE Study

ImmunoCARE is an innovative research project to study whether repeated at-home tests, on-demand telemedicine, and quick delivery of medication for those who test positive for COVID-19 can reduce COVID-19 severity in immunocompromised people and those over 65.

ImmunoCARE will enroll 10,000 participants. Half of participants will test for COVID-19 and seek care as they normally would; the other half will receive 10 at-home COVID-19 tests per month from Cue Health for themselves and others in their household. All participants will be asked to complete monthly surveys about COVID-19 exposure, infection, and hospitalization.

Who can enroll

ImmunoCARE is available to individuals who are moderately to severely immunocompromised or are 65 and older. Participants will provide documentation from health claims data confirming their diagnosis and age. Additional criteria for enrollment can be found at immunocare.scripps.edu or scan the QR code. the link below.

Our thanks to you

As our thanks for your participation, all eligible participants will receive a series of Amazon gift cards as compensation throughout the study.

Questions?

If you have any questions about the study, feel free to reach out to the study team at immunocare@scripps.edu.CEDR@sdsu.edu or leave a message at 619-594-2922.

Appendix 5: Invitation Email

SUBJECT LINE:

Immunocompromised and concerned about COVID-19?

PREHEADER:

Join The ImmunoCARE study which aims to reduce hospitalizations

BODY:

Dear [FIRST NAME],

Are you at high risk of hospitalization from COVID-19 infection due to a compromised immune system or age? The ImmunoCare study aims to reduce that risk. Scripps Research – a renowned biomedical research institute – and Cue Health, a leading health care technology company that develops portable diagnostic tests for at-home use, are launching the ImmunoCARE Study.

ImmunoCARE is an innovative research project designed to examine whether a combination of repeated at-home tests, on-demand telemedicine, and quick delivery of Paxlovid after testing positive for COVID-19 can reduce severe outcomes and hospitalization of people just like you.

We can only succeed in this research with your help. Eligible participants will take part in a 4- to 8-month study and may receive at-home diagnostic tests free of charge.

Learn more and take our eligibility survey today.

CTA

LEARN MORE

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 6: You're Eligible Email

SUBJECT LINE:

Welcome to the ImmunoCARE

PREHEADER:

Download the study app today!

BODY COPY:

Dear [FIRST NAME],

Thank you for your interest in participating in the ImmunoCARE Study. We are pleased to inform you that you've met all of the eligibility criteria!

The first step is to download the study app, MyDataHelps. Once you do, you will create a new account and provide your consent to participate. After that, you will be on your way to helping researchers learn more about how to keep people safe from severe COVID-19 infection.

Get started today!

CTA:

DOWNLOAD APP

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 7: You're Not Eligible Email

SUBJECT LINE:

Thank you for your interest in ImmunoCARE

PREHEADER:

We appreciate your willingness to join our study

BODY COPY:

Dear [FIRST NAME],

Thank you for your interest in participating in the ImmunoCARE Study. Unfortunately, you did not meet the study's eligibility requirements at this time.

We greatly appreciate your time and commitment to advancing research to improve COVID-19 outcomes.

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 8: Consent Reminder Email

SUBJECT LINE:

Your ImmunoCARE registration is incomplete

PREHEADER:

Please complete your ImmunoCARE consent

BODY COPY:

Dear [FIRST NAME],

Thank you for your interest in the ImmunoCARE Study. We appreciate your willingness to help advance research on reducing COVID-19 hospitalizations for immunocompromised individuals. You are still eligible to participate!

Your consent is required to proceed with participation in this research study. To access the ImmunoCARE consent, open your MyDataHelps app.

If you have any questions about the consent process, you may contact us at Immunocare@scripps.edu.

Thank you again for your participation in this critical research study to reduce COVID-19 hospitalizations.

Take Care,

The ImmunoCARE Study Team

If you have any questions, please reach out to the study team at Immunocare@scripps.edu

Appendix 9: Baseline Survey Reminder Email

SUBJECT LINE:

Reminder: Your ImmunoCARE survey is waiting!

Alternate subject line: Don’t forget to complete your first survey

PREHEADER:

Take the survey today!

BODY COPY:

Dear [FIRST NAME],

Thank you for joining the ImmunoCARE Study. The next step is to complete the Baseline Survey, which asks questions about your demographic information and health conditions. This survey will help researchers understand where you are starting the study from and how the study progresses.

This survey should only take a few minutes. Once you complete this survey, you will earn a $20 Amazon gift card to thank you for your time.

Thank you again for your participation.

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 10: Monthly Survey Reminder Email 1

SUBJECT LINE:

It’s time for your monthly ImmunoCARE survey

PREHEADER:

Take the survey today!

BODY COPY:

Dear [FIRST NAME],

As a valued participant in the ImmunoCARE Study, your survey responses are of critical importance to researchers.

It’s time to take this month’s survey to share whether you have had any COVID-19 exposures or infections since we last heard from you.

The survey should only take a few minutes of your time, and you will receive an Amazon gift card for answering.

Thank you again for your time and participation in ImmunoCARE.

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 11: Monthly Survey Reminder Email 2

SUBJECT LINE:

Do you have a minute for ImmunoCARE?

PREHEADER:

Your monthly survey only takes a few minutes

BODY COPY:

Dear [FIRST NAME],

Do you have a minute? A minute or two is all it takes to complete this month's ImmunoCARE survey.

By letting us know if you've been exposed to, infected with, or hospitalized from COVID-19 in the past month, you're helping advance research on reducing hospitalizations and improving outcomes for immunocompromised individuals.

Once you complete your survey, you will receive a code for your Amazon gift card as our thanks to you.

Thank you again for your time and participation in ImmunoCARE.

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 12: Your Gift Card is Ready To Claim Email

SUBJECT LINE:

Our gift to you for participating in ImmunoCARE

PREHEADER:

Your Amazon gift card code is ready

BODY COPY:

Dear [FIRST NAME],

We are grateful for your participation in the ImmunoCARE Study. To thank you, we are pleased to give you an Amazon gift card for completing a series of steps throughout the study.

Your gift card for [INSERT AMOUNT] is ready to use. Login to your My Data Helps account to access your Amazon gift card code.

Thank you again for your valued participation in ImmunoCARE.

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 13: ImmunoCARE Landing Page

The ImmunoCARE Study:
Rapid, Accurate COVID Testing to Reduce Hospitalization of Immunocompromised Individuals

About the study

The risks associated with COVID-19 infection is higher for immunocompromised individuals and people over 65 than the general public. ImmunoCARE is an innovative research project to study whether repeated at-home tests, on-demand telemedicine, and quick delivery of medication for those who test positive for COVID-19 can reduce COVID-19 severity in immunocompromised people.

ImmunoCARE is a joint research project from Scripps Research – a renowned biomedical research organization – and Cue Health, a leading health care technology company that develops portable diagnostic tests for at-home use.

Who can enroll

ImmunoCARE is available to individuals who are moderately to severely immunocompromised. Participants will provide documentation from a medical provider confirming their diagnosis.

Additional inclusion criteria includes:

- Living in the United States
- 18 years or older
- Vaccinated against COVID-19
- Willing and able to participate in study interventions including:
    - Use of a compatible smartphone, including camera and bluetooth
    - Willing and able to share health insurance claims data from Medicaid, Medicare, or an Anthem plan if over 65 and not otherwise immunocompromised
    - Completing Surveys
    - Use of Cue Health App and tests
    - Use of MyDataHelps by Web or App
- Immunocompromised, including
    - Symptomatic HIV
    - Graft versus host disease
    - Immunoglobulin deficiency/Immunodeficiency
    - Immunosuppressive therapy
    - Leukemia
    - Lymphoma (Hodgkin or non-Hodgkin)
    - Metastatic Cancer
    - Multiple Myeloma
    - Solid organ malignancy
    - Transplant, hematopoietic stem cell
    - Transplant, solid organ
    - 65 years or older

What we will ask you to do

ImmunoCARE will enroll 10,000 participants. Half of participants will test for COVID-19 and seek care as they normally would; the other half will receive at-home COVID-19 tests from Cue Health for themselves and others in their household. All participants will be asked to complete monthly surveys about COVID-19 exposure, infection, and hospitalization.

Our thanks to you

As our thanks for your participation, all eligible participants will receive a series of Amazon gift cards as compensation for time throughout the study.

Join today

Interested in helping advance research on COVID-19 outcomes for immunocompromised individuals? Click below to see if you are eligible to participate!

CTA: Let's Go

Questions? Reach out to us at ImmunoCARE@scripps.edu

[LINK TO MDH web and app stores]

Appendix 14: MyDataHelps In-app Copy

Heading:
Welcome to the ImmunoCARE Study

Body:
ImmunoCARE is an innovative research project to study whether repeated at-home tests, on-demand telemedicine, and quick delivery of medication for those who test positive for COVID-19 can reduce COVID-19 severity in immunocompromised people and those over 65.

Please complete the following survey to determine whether you are eligible for this study. If eligible, you will learn more about our study and decide whether you would like to enroll.

Button Text:
Next

[Eligibility Survey questions here; see Appendix 3]

Heading:
What is the ImmunoCARE study?

Body:
You are being invited to participate in the ImmunoCARE. This is a cohort study, meaning you will be randomized into one of two groups.
Half of the participants will receive Cue Health products to see if they decrease COVID-19 cases and hospitalizations. The other half will continue their normal behaviors, without Cue products. This helps us measure if having access to Cue products decreases the number of COVID-19 infections and severity.

Participants have no obligation to use all the features of the Cue Care product. Consent for this study and all study activities is completely voluntary. You do not have to participate if you do not want to. If you join and change your mind, you can drop out at any time.

To thank you for your time, you may be eligible to receive electronic Amazon gift cards for your time throughout the study.

If you have questions about the study, please ask us by emailing ImmunoCARE@scripps.edu.

Button Text:
Next

Heading:
The ImmunoCARE Study

Body:
Our commitment

- Keeping your information private is our top priority.
- You will be guided throughout the study.
- We deeply respect your time.
- We will let you know what we are learning.

Your rights

- You can leave the study whenever you want.
- You can choose which tasks to complete.
- There is no cost to participate.

This study is led by Scripps Research Translational Institute, a non-profit academic institution in La Jolla, California and funded by Cue Health.

Button Text:
Next

Heading:
The ImmunoCARE Study

Body:
Expectations & Requirements

- Share your health insurance claims data
- Take surveys each month
- If needed, upload confirmation of your immunocompromised status
- If randomized to a treatment group, use Cue Health tests

The next couple screens ask you about the State you live in and provide comprehensive information to help you make an informed decision about joining ImmunoCARE.

If you have any questions, email us at ImmunoCARE@scripps.edu

Button Text:
Next

Heading:
State of Residence

Body:
What state do you live in? [Dropdown with list of states]

Button Text:
Next

Pre-conditions:
California residency indicated

Heading:
California Experimental Subject's Bill of Rights

Body:
[Contents of the California Bill of Rights]

Button Text:
Next

Heading:
Consent to Participate in Research

Body:
[Contents of Long Form Consent]

Button Text:
Next

Heading:
Participant Agreement

Body:
I have read and understood the explanation of the study. I have had a chance to ask questions and have them answered to my satisfaction. I agree to take part in this study. I have not been forced or made to feel obligated to take part. I am free to withdraw my consent at any time.

If I want to participate, I must sign this consent form. If I would like a copy of this document, I am able to save it and keep it for my records.

By providing my name below and continuing to the next screen, I am authorizing this document and agreeing to participate in this study.

First Name: [input field]
Last Name: [input field]

Button Text:
Yes/No

Heading:
Signature

Body:
Please sign using your finger on the line below.

[Touch area for signature]

Button Text:
Next

Heading:
Thank you

Body:
Thank you for joining the ImmunoCARE study! Your signed consent form is available in the Settings tab under Documents.

Continue to the following screen to connect your health plan and share your claims data with us or upload an image to confirm your eligibility We will verify your diagnosis and monitor your health outcomes at the conclusion of the study.

If you decide to share your claims data, please share access to your data for 1 year when prompted.

Button Text:
Next

Heading (claims):
Diagnosis Confirmation

Body:
The claims data from your health plan indicate a previously diagnosed condition that we need to learn more about for the purposes of this study.

Please upload a document confirming your diagnosis on the next screen. This can be a doctor's note, a screenshot of your EHR diagnosis list, lab work, test results or medication list.

Accepted file types are [list of file types]. If your document is another type, please email it to the study team at ImmunoCARE@scripps.edu

Button Text:
Next

Heading (no claims):
Diagnosis Confirmation

Body:
Thank you for your participation!

Please upload a document confirming your diagnosis or age on the next screen. This can be a doctor's note, a screenshot of your EHR diagnosis list, lab work, test results or medication list.

Accepted file types are [list of file types]. If your document is another type, please email it to the study team at ImmunoCARE@scripps.edu

Button Text:
Next

Heading:
[None]

Body:
[None]

Button Text:
Capture or Upload Image

Heading:
Thank you

Body:
Thank you for confirming your medical information. We will be reviewing the document you uploaded and will notify you when we are ready for you to continue with the study.

Button Text:
Done

Heading:
Document Review

Body:
Our research coordinator iscurrently reviewing the document you uploaded confirming your diagnosis or age. This process can take a few business days, we appreciate your patience.

No further action is required on your part. We will notify you once we complete our review so you can continue with the study.

Button Text:
Done

Heading:
Baseline survey

Body:
Help us learn about other diagnoses and understand any differences between demographic groups, such as income, race, ethnicity, and age.

Button Text:
Next

[Baseline survey questions here; see Appendix 3]

Pre-conditions:
Participant randomized into treatment arm

Heading:
Thank you

Body:
Thank you for sharing this information with the study team.

You have been randomized to the treatment group.

As such, the next step is to register an account with Cue Health and download their app on your smartphone. You will also order your testing kit through the mobile app.

Continue to the next task for additional instructions.

Button Text:
Done

Pre-conditions:
Participant randomized into control arm

Heading:
Thank you

Body:
Thank you for completing all of the onboarding activities.

You have been randomized to the control group.

This means you will come back to this app monthly to tell us how things are going and answer a few questions. Your $20 Amazon gift card for completing onboarding will be available shortly. In the future, you will receive a $10 Amazon gift card for each monthly survey you complete.

Button Text:
Done

Pre-conditions:
Participant randomized into intervention arm

Heading:
Cue+ Membership

Body:
To begin, you must create an account with Cue Health using the link we will give you next. This link is unique to you and must not be shared with anyone else.

As a participant in our study, you have access to 10 Cue Health tests per month for free.

When creating your Cue account, you must use the email address you previously gave us to ensure you receive your testing kit at no cost. Make sure it appears below correctly. If you need to change it, exit this survey and go to the Account tab.

Email: [read-only, pre populated input field]

Button Text:
Next

Heading:
Create Cue Health account

Body:
Create an account with Cue Health using the link below.

You will be placing the order for $0.

Cue Health [link to Cue+ order page on Cue Health website]

Remember to use the email address we have on file.

Button Text:
Next

Heading:
[None]

Body:
Now that you have created an account with Cue Health, you may download the app on your smartphone.

Search for Cue Health on your smartphone's app store. It should look like one of the two screenshots below depending on your device.

Once you've found it, proceed to installing it and sign in.

[Two cropped screenshots showing Cue Health logo and app name]

Button Text:
Next

Heading:
[None]

Body:
Have you successfully installed the Cue Health app and signed in?

[ ] Yes
[ ] No

Button Text:
Next

Heading:
Order a Cue test kit

Body:
Great! You may now order your testing kit.

In the Cue Health app, order the 10 COVID-19 Tests & Cue Reader. Since you are a study participant, you should see $0 as the price for the package.

Button Text:
Next

Heading:
[None]

Body:
Have you successfully placed an order for the testing kit?

[ ] Yes
[ ] No

Button Text:
Next

Heading:
Thank you

Body:
Thank you for completing this task.

Once you receive the testing kit, return to the app and let us know. You'll get familiarized with the kit at that point and take your first test.

Button Text:
Done

Heading:
Take test

Body:
Open your testing kit package and get familiarized with its contents. Proceed to take a baseline COVID-19 test with this device.

Button Text:
Next

Heading:
[None]

Body:
Have you taken your first test with the Cue Health kit?

[ ] Yes
[ ] No

Button Text:
Next

Heading:
Thank you

Body:
Thank you for completing this task.

Please remember to take a Cue COVID-19 test when you may have been exposed or are experiencing symptoms. If someone in your household may have been exposed to COVID-19 or is symptomatic, give them a test to use. Please set up profiles in the Cue App for each person who uses Cue tests.

We'll also notify you next month when it's time for your check-in.

Button Text:
Done

Heading:
Monthly check-in

Body:
Thank you for your continued participation in this study.

This survey is intended to capture information about how you have been feeling and any COVID-19 exposures and infections you have had since we last checked in.

Once you complete this survey, you will earn a $10 Amazon gift card to thank you for your time.

Button Text:
Done

[Monthly check-in survey questions here; see Appendix 3]

Heading:
Thank you

Body:
Thank you for sharing this information with the study team. Your Amazon gift card is now available.

Please remember to take a Cue COVID-19 test when you may have been exposed or are experiencing symptoms. If someone in your household may have been exposed to COVID-19 or is symptomatic, give them one test to use. You can set up a profile for them in your Cue App.

Button Text:
Done

Heading:
Amazon Gift Card

Body:
You are now eligible for a [$20 | $10] Amazon gift card.

[Gift card code]

In order to use your gift card, add it to your Amazon.com account.

Button Text:
Done

Heading:
[None]

Body:
Have you taken your first test with the Cue Health kit?

[ ] Yes
[ ] No

Button Text:
Done

Heading:
When to test

Body:
You should use your Cue Health Molecular COVID-19 test if you may have been exposed to COVID-19 or notice any of the following symptoms, or think you might be getting sick:

- Fever
- Chills
- Congested or runny nose
- Cough
- Sore throat
- Congestion
- Stomachache
- Headaches
- Body aches
- Fatigue
- Neck pain
- Shortness of breath
- Chest tightness
- Sneezing
- Wheezing
- Weakness

If someone in your household may have been exposed to COVID-19 or is experiencing any of these symptoms, you can set up a Cue profile for them in your Cue account and provide them with a test.

Button Text:
Done

Appendix 15: Notifications

Theme	Trigger	Title	**Push and SMS copy** Note: All SMS copy will include a link to log in to the participant portal.
Consent completion	5 hours after account creation, if consent has not been completed	Are you ready to join?	To take part in the ImmunoCARE study, please complete consent.
Reminder 1: Consent completion	3 days after account creation, if consent has not been completed	Next step: complete consent	To learn how you can help the study of COVID-19 outcomes in immunocompromised individuals, review consent materials.
Reminder 2: Consent completion	7 days after account creation, if consent has not been completed	Questions about ImmunoCARE?	If you have any questions before you join, feel free to email us at ImmunoCARE@scripps.edu
Share diagnosis info	5 hours consent completion (for conditions that cannot be verified by claims or for those who did not connect their claims data.)	Verify your diagnosis	Please upload confirmation of your immunocompromised status
Reminder 1: Share diagnosis info	3 days after consent completion (for conditions that cannot be verified by claims or for those who did not connect their claims data.); requested information will vary by diagnosis	Next step: share diagnosis info	To verify your eligibility, please upload a document showing your diagnosis [alternate: medication list, lab results, test results].

Reminder 2: Share diagnosis info	7 days after consent completion (for conditions that cannot be verified by claims or for those who did not connect their claims data.)	Last reminder: confirm diagnosis	To move forward, please share a document showing your diagnosis. [alternate: medication list, lab results, test results].
Connect health plan claims data (post consent)	5 hours consent completion	Connect your health claims data	Please search for your health insurance provider to share.
Reminder 1: Connect health plan claim (post consent)	3 days after consent completion	Ready to share your claims data?	You need to share claims data to move forward.
Reminder 2: Connect health plan claim (post consent)	7 days after consent completion	Last reminder: share your claims data	Please search for your health insurance provider to share and continue participating.
Baseline survey	5 hours after eligible for baseline survey	Next step: baseline survey	Please share information to help us learn about you.
Reminder 1: Baseline survey	3 days after eligible for baseline survey	Do you have time for a 5 min survey?	Click to complete baseline survey
Reminder 2: Baseline survey	7 days after eligible for baseline survey	Last reminder: Baseline survey	Your baseline survey is waiting.
Ready to order first kit	Upon being assigned to test arm and Cue verifying their email address for account creation	You are eligible for free COVID tests	Download the Cue Health app to create your account and order
Reminder 1: Ready to order first kit	3 days after first invitation to order tests, if Cue confirms they have not ordered	Time to order a test kit	Click here to get instructions

Reminder 2: Ready to order first kit	7 days after first invitation to order tests, if Cue confirms they have not ordered	You've been selected!	Download an app to order a testing kit
Take first test	7 days after eligible for ordering or 5 days after Cue confirmed participant placed first order and has not taken test	Take your first Cue test	When you receive your Cue tests, please take one to try it out.
Reminder 1: Take first test	10 days after eligible for ordering or 8 days after Cue confirmed participant placed first order and has not take test	Did you take your first Cue test?	If you have your Cue tests, please try it out.
Reminder 2: Take first test	14 days after eligible for ordering or 12 days after Cue confirmed participant placed first order and has note taken test	Final reminder: take first Cue test	Get to know Cue tests before you need them.
Test reorder reminder	30 days after last tests received or presumed order date	Order more Cue tests	If you have fewer than 6 tests, we recommend you reorder in the Cue app.
Alt 1: Test reorder reminder	30 days after last tests received or presumed order date	Time to reorder Cue tests	Don't run out - order more Cue tests in the Cue app today.
Alt 2: Test reorder reminder	30 days after last tests received or presumed order date	You are eligible to order more Cue tests	Open the Cue app to order more tests when you're ready.
Monthly survey is ready v1	30 days have passed since previous survey was completed	Your monthly survey is ready	Complete this 1-2 minute survey and earn a $10 Amazon gift card.
Monthly survey is ready v2	30 days have passed since previous survey was completed	Your monthly Survey is waiting for you	Complete this 1-2 minute survey and earn a $10 Amazon gift card.

Monthly survey is ready v3	30 days have passed since previous survey was completed	Don’t forget!	Complete this 1-2 minute survey and earn a $10 Amazon gift card.
Monthly survey is ready v4	30 days have passed since previous survey was completed	Do you have time for a 5 min survey?	Complete this 1-2 minute survey and earn a $10 Amazon gift card.
Reminder: monthly survey v1	30 days have passed since previous survey was completed	Survey time!	Let us know about any COVID exposures and infections and earn a $10 Amazon gift card.
Reminder: monthly survey v2	30 days have passed since previous survey was completed	Reminder: monthly survey	Let us know about any COVID exposures and infections and earn a $10 Amazon gift card.
Reminder: monthly survey v3	30 days have passed since previous survey was completed	How are you?	Let us know about any COVID exposures and infections and earn a $10 Amazon gift card.
Reminder: monthly survey v4	30 days have passed since previous survey was completed	Keep us updated on how you are feeling!	Let us know about any COVID exposures and infections and earn a $10 Amazon gift card.
Gift card is ready	5 hours after gift card becomes available, if they haven’t viewed the gift card screen	Your gift card is ready	Log in to claim your $10 Amazon gift card.
Study conclusion	After completion of final survey or 1 month after sending the end of study survey.	The ImmunoCARE study is over	Thank you for everything you’ve done in the past [number of months] months. We’ll share study results when they’re ready.
EOS Survey	At the end of the data collection period (between 4 and 8 months)	Most important survey to date	Thank you for everything you’ve done. Take your last survey to finish out your participation and earn your gift card.

EOS Survey	At the end of the data collection period (between 4 and 8 months) + 5 days	Earn gift cards for Surveys you missed!	Take the end of study survey.

Appendix 16: Calls to Action (prompts for each study task)

These calls to action and descriptive text may be used in the app to launch tasks.

Connect your health plan
We'll receive claims data to learn more about your health. If you cannot or do not want to share your claims, please let us know by opting out.

Confirm your diagnosis
We need additional documentation regarding your diagnosis

Diagnosis verified
Complete your next survey

Baseline survey
Tell us more about yourself

Create your Cue Health account
You'll be able to register and order your testing kit at no cost

Take the COVID-19 test
Complete this task once you have received the Cue testing kit

Monthly check-in
Let us know if you've been exposed to or treated for COVID-19

alt: Let us know whether you've been exposed to or treated for COVID-19

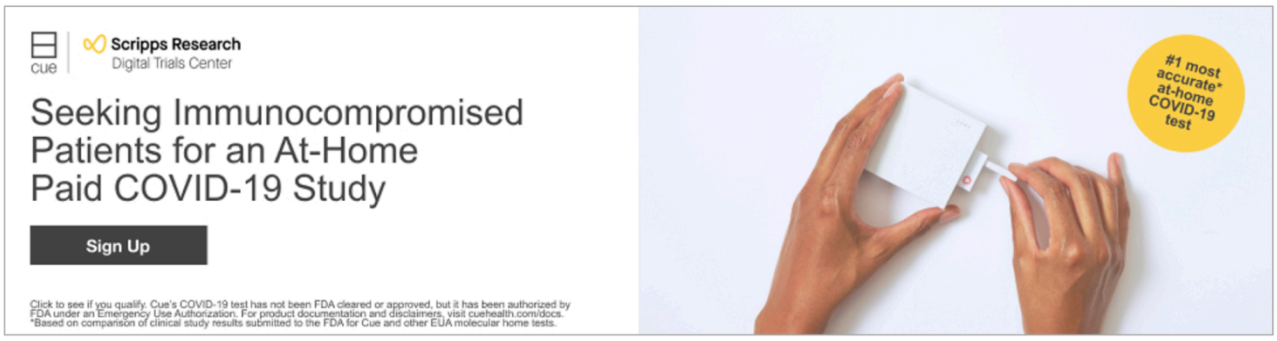
Report symptoms or exposure
Let us know if you're having symptoms or have been exposed to COVID-19

Claim your gift card
You have received a gift card for completing a task

When to use a Cue test
See the list of symptoms to look out for

Appendix 17: Marketing Materials

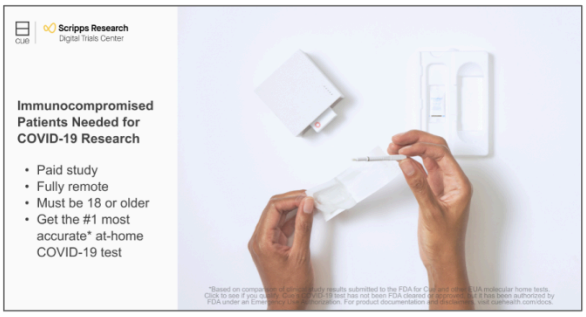
Below are example designs of marketing materials. Images may vary.



Post Copy (~125 chars):
Seeking immunocompromised patients for a COVID-19 study. Eligible, qualified participants may get free Cue Health products.

Link Headline (35):
See If You're Qualified

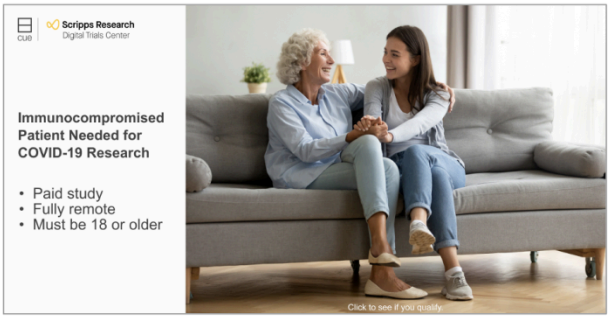
CTA Button: Sign Up



Post Copy (125 chars):
We're looking for immunocompromised patients for a COVID-19 study. Click to see if you qualify.

Link Headline (35):
Paid COVID-19 Testing Study

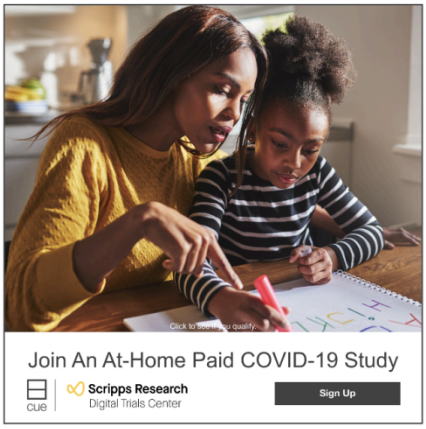
CTA Button: Sign Up



Post Copy (125 chars):
If you're an immunocompromised patient, join this paid study about the benefits of early COVID-19 testing.

Link Headline (35):
Paid COVID-19 Test Study

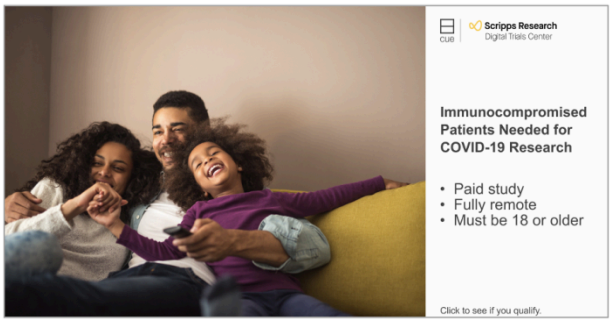
CTA Button: Sign Up



Post Copy (125 chars):
We're looking for immunocompromised patients for a paid COVID-19 study. Click to see if you qualify.

Link Headline (35):
Paid COVID-19 Testing Study

CTA Button: Sign Up



Post Copy (125 chars):
If you're an immunocompromised patient, you could join a paid study aimed at reducing COVID-19 infections.

Link Headline (35):
Paid COVID-19 Test Study

CTA Button: Sign Up

Appendix 18: Research Match

Background:

ResearchMatch.org will be utilized as a recruitment tool for this protocol. ResearchMatch.org is a national electronic, web-based recruitment tool that was created through the Clinical & Translational Science Awards Consortium in 2009 and is maintained at Vanderbilt University as an IRB-approved data repository.

Preface: ResearchMatch aims to serve as an effective, relevant, and complementary recruitment tool that will help connect willing volunteers with researchers who are searching for appropriate volunteers to be placed in their clinical and other health related research studies. For more information visitwww.researchmatch.org

Email copy to use via researchmatch.org:

A research team with The Scripps Research Institute in La Jolla, CA, believes you might be a good match for the following study:

The ImmunoCARE Study

Are you at high risk of hospitalization from COVID-19 infection due to a compromised immune system or age? The ImmunoCare study aims to reduce that risk. Scripps Research – a renowned biomedical research institute – and Cue Health, a leading health care technology company that develops portable diagnostic tests for at-home use, are launching the ImmunoCARE Study.

ImmunoCARE is an innovative research project designed to examine whether a combination of repeated at-home tests, on-demand telemedicine, and quick delivery of Paxlovid after testing positive for COVID-19 can reduce severe outcomes and hospitalization in immunocompromised people and those over 65.

We can only succeed in this research with your help. Eligible participants will take part in a 4- to 8-month study and may receive at-home diagnostic tests free of charge.

Additional inclusion criteria includes:

- Living in the United States
- 18 years or older
- Vaccinated against COVID-19
- Willing and able to participate in study interventions including:
    - Use of a compatible smartphone, including camera and bluetooth
    - Willing and able to share health insurance claims data from Medicaid, Medicare, or an Anthem plan if over 65 and not otherwise immunocompromised
    - Completing Surveys
    - Use of Cue Health App and tests
    - Use of MyDataHelps by Web or App
- Immunocompromised, including
    - Symptomatic HIV
    - Graft versus host disease
    - Immunoglobulin deficiency/Immunodeficiency
    - Immunosuppressive therapy
    - Leukemia
    - Lymphoma (Hodgkin or non-Hodgkin)
    - Metastatic Cancer
    - Multiple Myeloma
    - Solid organ malignancy
    - Transplant, hematopoietic stem cell
    - Transplant, solid organ
    - 65 years or older

Participation in the study is voluntary and does include compensation.

Yes, I'm interested! No, thanks.

Note: Potential participants who click Yes, I am interested will show up within the researcher's ResearchMatch portal. The message below will be sent to interested participants. Potential Participants who click No, thanks are directed back to researchmatch.org and the following link:https://www.researchmatch.org/recruitmentresponse?cn=2&id=5401753265359&guid=4464672 1865.921&gid=18598032.0513

Response Email:

Dear XXX,

Thank you for your interest in participating in The ImmunoCARE Study. To learn more about the study, please visit Immunocare.scripps.edu for more information and next steps.

If you have any questions, please let us know.

Best,

The ImmunoCARE Study Team

Appendix 19: Optum Specific Outreach One Pager

Optum Option One

HEADING

ImmunoCARE: Rapid, Accurate COVID Testing to Reduce Hospitalization of Immunocompromised Individuals

INTRO

Are you at high risk of hospitalization from COVID-19 infection due to age or a compromised immune system? The ImmunoCare study aims to reduce that risk. Scripps Research – a renowned biomedical research institute – and Cue Health, a leading health care technology company that develops portable diagnostic tests for at-home use, are partnering with your Optum Physician to launch the ImmunoCARE Study.

SUBHEADING

More on The ImmunoCARE Study

ImmunoCARE is an innovative research project to study whether repeated at-home tests, on-demand telemedicine, and quick delivery of medication for those who test positive for COVID-19 can reduce COVID-19 severity in immunocompromised people and those over 65.

ImmunoCARE will enroll 10,000 participants. Half of participants will test for COVID-19 and seek care as they normally would; the other half will receive 10 at-home COVID-19 tests per month from Cue Health for themselves and others in their household. All participants will be asked to complete monthly surveys about COVID-19 exposure, infection, and hospitalization.

Who can enroll

ImmunoCARE is available to individuals who are moderately to severely immunocompromised or are 65 and older. Participants will have the option to provide documentation from health claims data confirming their diagnosis and age. Additional criteria for enrollment can be found at immunocare.scripps.edu or scan the QR code. the link below.

Our thanks to you

As our thanks for your participation, all eligible participants will receive a series of Amazon gift cards as compensation throughout the study.

Questions?

If you have any questions about the study, feel free to reach out to the study team at immunocare@scripps.edu.

Optum Option two:

[Optum logo]

[Participant address]

[QR Code] Find out if you qualify and learn more.

Optum.com/ImmunoCARE

Join the ImmunoCARE study

What is the ImmunoCARE study?
This study will look at COVID-19 and people with weak (compromised) immune systems. People with weak immune systems can't fight germs well. They can become sick more often. COVID-19 can be especially dangerous for them. This study will look to find better ways to protect them from COVID-19.

Will I be paid for participating in the study?
If you qualify, you'll receive an Amazon gift card when you sign up and complete some information. After that, you'll receive an Amazon gift card each month for up to 8 months. There's no cost for you to take part in the study.

Who is running the ImmunoCARE study?
For the study, your Optum doctor will partner with:
• Scripps Research, a renowned biomedical research institute
• Cue Health, a leading health care technology company that makes home C0VID-19 tests

What will I need to do in the study?
People who join the study will be assigned to one of two groups. (You will be put into a group randomly. You won't be able to choose your group.) The first group will test for COVID-19 and seek care as they normally would.

The other group will get tools and services to find, and care for, COVID-19 quickly at home. This will include:
• Special COVID-19 test kits. The kits are designed to find COVID-19 early.
• Virtual care, on demand. If a test shows you have COVID-19, you can see a doctor by video right away.
• Quick delivery of a COVID-19 medicine, PaxlovidTM. If your doctor orders Paxlovid for you as part of your regular medical care, you'll get it delivered the same day as long as it is ordered early enough in the day.

They will also be asked to:
• Use the CUE Health app. It's needed to use the test kit and get virtual care.
• Complete a survey once a month.

The goal of the study is to learn if fast testing and care can:
• Stop COVID-19 early or keep it from getting so severe that you need hospital care
• Lower the cost of care compared to standard care

How long will the study last?
The study will last 4 to 8 months.

Who can join the study?
You may qualify for this study if you have:
• HIV with or without symptoms (like fever, chills, rash)
• Graft versus host disease (when a bone marrow transplant attacks the body)
• Immunoglobulin deficiency or immunodeficiency (when the immune system is missing a key part for fighting germs)
• Immunosuppressive drugs (medicine that keeps the body from rejecting a bone marrow or organ transplant); exception: steroids
• Cancers of the immune system, like leukemia, multiple myeloma or lymphoma (Hodgkin or non-Hodgkin)

• Metastatic cancer (any cancer that has spread)
• Solid organ cancer (examples: breast, lung, colon)
• Bone marrow transplant
• Solid organ transplant (examples: heart, lung, kidney)

Will my medical information be shared?
If you join the study, you will be given a random study ID number to identify you. We will not share your personal health information with anyone outside of this study.

Any person depicted in the stock image is a model.

Appendix 20: Optum Specific Invitation Email

SUBJECT LINE:

Immunocompromised and concerned about COVID-19?

PREHEADER:

Join The ImmunoCARE study which aims to reduce hospitalizations

BODY:

Dear [FIRST NAME],

Are you at high risk of hospitalization from COVID-19 infection due to a compromised immune system or age? The ImmunoCare study aims to reduce that risk. Scripps Research – a renowned biomedical research institute – and Cue Health, a leading health care technology company that develops portable diagnostic tests for at-home use, are partnering with your Optum Physician to launch the ImmunoCARE Study.

ImmunoCARE is an innovative research project designed to examine whether a combination of repeated at-home tests, on-demand telemedicine, and quick delivery of Paxlovid after testing positive for COVID-19 can reduce severe outcomes and hospitalization of people just like you.

We can only succeed in this research with your help. Eligible participants will take part in a 4- to 8-month study and may receive at-home diagnostic tests free of charge.

Learn more and take our eligibility survey today.

CTA

LEARN MORE

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 21: ImmunoCARE Animated Explainer Video | Script

INTRO & INCENTIVE

- People who are immunocompromised or over the age of 65 are still at high risk of developing severe disease from COVID-19, but a new study could help reduce that risk.

- The ImmunoCARE study is enrolling 10,000 participants nationwide and is providing some participants with free highly sensitive at-home COVID tests, access to telemedicine and delivery of antiviral medications. All participants will get Amazon gift cards as a thank you for taking part.

- Interested? Keep watching to learn more, or head to immunocare.scripps.edu to get started.

- Scientists at the Scripps Research Digital Trials Center are investigating if early detection and rapid treatment can reduce COVID-19 hospitalizations among immunocompromised people and those over 65.

- The study is fully remote, meaning you won't need to visit a clinic or have in-person consultations.

ELIGIBILITY & ACCOUNT SET UP

- To find out if you are eligible to participate, you'll need to visit the study website and complete a brief survey.
    - TEXT ON SCREEN (NOT PART OF SCRIPT):
        - Live in the United States
        - 18 years or older

- § Access to smartphone
- § Vaccinated against COVID-19
- § Diagnosed as moderately to severely immunocompromised, or be 65 years or older
- § Willing to participate in all study activities

· If you are eligible to participate, you will be prompted to create an account on the study web app, complete the informed consent process and fill out a short baseline survey.

SYNCING HEALTH PLAN

· Next, you will also be asked to connect to your health plan. This allows scientists to verify your immunocompromised status or age and study any medical care you received through your plan related to COVID-19. We use strict privacy practices.

· If it cannot be verified through your health plan data, you will need to provide proof of your immunocompromised status or age by sharing a document directly with the study team.

INTERVENTION

· Once your status is verified, you will be randomly assigned to either the control arm or the intervention arm. It is important to have participants in both of these groups so scientists can accurately determine whether the intervention is working.

· Those assigned to the control arm will complete a monthly survey about any COVID-19 exposures and diagnosis. If they develop symptoms, they will test and seek care as they normally would.

· Those assigned to the intervention arm will also complete a monthly survey and create an account on the Cue Health mobile app. These participants will receive 10 Cue Health COVID-19 molecular at-home tests each month. Participants will perform tests after exposure or if symptoms arise. The tests can also be used for members of the same household, who have been exposed to COVID-19 or have symptoms.

· These nucleic acid amplification tests detect the genomic RNA of SARS-CoV-2, the virus that causes COVID-19, and are much more sensitive than more common rapid antigen tests.

· If a test is positive, participants can consult with a healthcare professional through the Cue Health app. When clinically indicated, medication for the treatment of COVID-19 will be prescribed and delivered to the participant's home. Participants can also seek care through their own healthcare provider, or not seek care at their discretion.

OUTRO

· The scientists expect the study to run for up to 8 months. Participation is voluntary and you can withdraw at any time.

· Help us support those who are still at high risk of severe outcomes from COVID-19.

· For more information, visit immunocare.scripps.edu

Appendix 22: End of Study Survey Reminder

SUBJECT LINE:

End of Study Survey

PREHEADER:

Your end of study survey only takes a few minutes

BODY COPY:

Dear [FIRST NAME],

Do you have a minute? A minute or two is all it takes to complete this end of study survey, it's the most important survey yet!

By letting us know if you've been exposed to, infected with, or hospitalized from COVID-19 in the past month, you're helping advance research on reducing hospitalizations and improving outcomes for immunocompromised individuals.

Once you complete your survey, you will receive a code for your Amazon gift card as our thanks to you.

Thank you again for your time and participation in ImmunoCARE.

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 23: Upload your diagnosis confirmation

SUBJECT LINE:

Confirm your diagnosis

PREHEADER:

Upload confirmation of your diagnosis

BODY COPY:

Dear [FIRST NAME],

Please take a moment to upload confirmation of your diagnosis.

Once you complete this step, you can move forward with your participation in ImmunoCARE.

Thank you again for your time and participation in ImmunoCARE.

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 24: Claims reimbursement email

SUBJECT LINE:

Share your data and receive an Amazon Gift Card

PREHEADER:

Connect your health claims data and receive a $30 Amazon Gift Card

BODY COPY:

Dear [FIRST NAME],

We are grateful for your participation in the ImmunoCARE Study. Preliminary analysis of the ImmunoCARE data is revealing the research value of claims data. Would you consider connecting yours? This will help ImmunoCARE get a more complete data set prior to study close out. Participants who agree to connect their health claims data will receive a $30 Amazon gift card as a thank you, while supplies last.

Login to your My Data Helps account to connect to your insurance claims. If you have any questions or trouble connecting your claims data, feel free to reach out to us at ImmunoCARE@scripps.edu.

[Optional: button with text “Log in to share”]

Thank you again for your valued participation in ImmunoCARE.

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 25: Outreach Talking Points

Introduction:

- Briefly introduce yourself and express gratitude for the person's time.
- Mention that you'd like to share information about a valuable opportunity called the ImmunoCARE Study, which does not involve any treatment.

Study Purpose:

- Explain that the ImmunoCARE Study is a collaboration between Scripps Research and Cue Health.
- Explain that the study aims to understand and improve COVID-19 outcomes specifically for immunocompromised individuals and those aged 65 and above.

- Emphasize the study does not involve treatment.

Target Population:

- Highlight the increased risk for severe outcomes from COVID-19 in individuals with compromised immune systems or over the age of 65.
- Mention the specific conditions that make someone eligible, such as Symptomatic HIV, Graft versus host disease, Immunoglobulin deficiency, etc.

Study Activities:

- Explain the two groups within the study: one group continues normal testing and care-seeking, while the other receives at-home COVID-19 tests and additional support.
- Emphasize that all participants, regardless of group, will be asked to complete monthly surveys about COVID-19 exposure, infection, and hospitalization.

Innovative Approaches:

- Discuss the innovative aspects of the study, including at-home testing, telemedicine consultations, and rapid medication delivery.
- Stress the importance of finding practical and effective ways to support individuals in managing COVID-19.

Participant Appreciation:

- Express gratitude for the participant's potential contribution to the research.
- Mention that eligible participants will receive compensation in the form of Amazon gift cards as a token of appreciation for their time throughout the study.

Joining the Study:

- Share the official study website link: https://immunocare.scripps.edu/
- Provide information on how individuals can check their eligibility and sign up for the study.

Impact of Participation:

- Stress the potential impact of their involvement, highlighting that their contribution could significantly influence our understanding and management of COVID-19 in vulnerable populations.

Questions and Concerns:

- Encourage participants to ask any questions they may have about the study.
- Provide referrals for health and social services when participants describe barriers to participation related to social determinants of health.
- Provide your contact information (email or phone number) or direct them to the study website or email address (ImmunoCARE@scripps.edu) for more detailed information.

Closing:

- Thank them for considering participation in the ImmunoCARE Study.
- Reiterate the importance of their potential role in advancing crucial research efforts.

Appendix 26: FDA Alert Email

SUBJECT LINE:

Do Not Use Cue Health Device

PREHEADER:

Cue Health's COVID-19 Tests Have a Risk of False Results

BODY COPY:

Dear [FIRST NAME],

This is an alert regarding the ImmunoCARE Study. The U.S. Food and Drug Administration (FDA) issued a communication to recommend that patients, caregivers, and health care providers do not use Cue Health's COVID-19 Tests due to an increased risk of false results.

We are determining next steps for the ImmunoCARE Study. In the meantime, please discontinue use of your Cue Health tests. We thank you for your participation and apologize for any inconvenience this may cause.

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu

Appendix 27: FDA Alert Push Notification/SMS

Theme: FDA Alert Push/SMS

Trigger: Push once IRB approved

Title: Don't Use Cue Health Device

Push or SMS copy: Cue Health's COVID-19 Tests Have a Risk of False Results, please discontinue use

Appendix 28: ImmunoCARE Study Closure

SUBJECT LINE:

The ImmunoCARE Study is Ending

PREHEADER:

Please take your End of Study Survey

BODY COPY:

Dear [FIRST NAME],

We are writing you as a valued participant in the ImmunoCARE study to share important news. We are stopping the ImmunoCARE study early in response to the FDA warning calling for discontinuing use of Cue COVID-19 tests.

The ImmunoCARE study team appreciates your participation and understanding. If you have not done so already, please take your end of study survey and share your claims data. Participants who agree to connect their health claims data will receive a $30 Amazon gift card as a thank you, while supplies last.

Take Care,

The ImmunoCARE Study Team

Questions? Reach out to us at Immunocare@scripps.edu