NCT04328467

Title of Research Study: Post-exposure Prophylaxis for SARS-Coronavirus-2: A Pragmatic Randomized Clinical Trial

Investigator Team Contact Information:

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

Investigator Name: **Radha Rajasingham, MD** Investigator Affiliation: Division of Infectious Diseases and International Medicine, Department of Medicine, University of Minnesota	To Contact the Research Study Personnel with Questions or concerns, please email: FAQ.covid19prep@gmail.com

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Key Information about This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Research and clinical care are often combined. One purpose of this informed consent document is to provide you clear information about the specific research activities of this study.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you are a healthcare worker at risk of being exposed to someone with SARS coronavirus 2 who has COVID-19 disease.

What should I know about a research study?

- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The primary purpose of this research is to determine whether a medication can be given to prevent COVID-19 disease in healthcare workers at high risk of being exposed to the virus. The concept is called “pre-exposure prophylaxis” — a method where medication is given to prevent an infectious disease before contact with another infected person. This strategy has proven useful for diseases like HIV.

COVID-19 disease is caused by a virus called severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2 for short. Currently COVID-19 is infecting people across the US but no FDA-approved treatments are yet available. There are trials starting to test experimental treatments for ill, hospitalized patients; however, our study is the first proposed to try to *prevent* disease in healthcare workers at high risk for exposure to COVID-19.

It is unknown whether you will receive any direct benefit by participating in the study, as we do not know if the study medication successfully prevents disease yet. However, the data collected will be helpful in knowing how to manage COVID-19 disease moving forward.

The drug being investigated is called hydroxychloroquine (hi-drox-ee-klor-o-kwin), which is typically used to treat malaria and sometimes autoimmune diseases. It is not a new drug, having been first approved in 1955. Laboratory tests have demonstrated that it has activity against the SARS-CoV-2 virus.

How long will the research last?

We expect that you will be followed for at least 4 weeks after you enroll, and up to 12 weeks. If you develop symptoms of COVID-19, we will follow you until your symptoms resolve.

What will I need to do to participate?

You will be asked to fill out an online form. We will send you the investigational drug by priority mail to be received tomorrow. You will need to take the drug as prescribed, for up to 12 weeks. We will send you a brief weekly internet-based survey about any COVID-19 symptoms or hospitalizations that you experienced. These weekly surveys will take approximately two minutes to complete. No blood sample collections or visits to the doctor’s office are required. You will need to:

- Take the study medicine for up to 12 weeks.
    - The first day you will take 2 tablets by mouth, then 6-8 hours later take 2 tablets, then

    - Take 2 tablets once or twice weekly depending on your treatment assignment for up to 12 weeks

The hydroxychloroquine dose is similar to what is given for malaria treatment.

- We will have a short follow up email survey for you to complete on:
    - Day 1 (to confirm you have received the medicines)
    - Weekly (to ask if you have become ill or been hospitalized)

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

Hydroxychloroquine is a relatively safe drug which has been used for the prevention of malaria for over 50 years. However, like all drugs, side effects and adverse reactions are possible. Specific details are described later in the document. Some pre-existing medical conditions will prevent you from entering the study. The short duration of hydroxychloroquine use in our study should also reduce the chance of an adverse event.

Aside from possible medication side effects, there are no direct harms of this internet based study. As there is no known way to prevent COVID-19 disease, there are no standard medicines that other people are receiving. Any personal medical information collected will be kept confidential.

More detailed information about the risks of this study can be found under ***"What are the risks of this study? Is there any way being in this study could be bad for me? (Detailed Risks)" and in the "What happens to the information collected for the research?" section***

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits from study participation include preventing COVID-19 disease or reducing the severity of COVID-19 disease. However, after you complete the trial, the medication will be stopped, so any benefit it was providing will be lost. There is also an important benefit to others and the medical community at large, as a medication that proves effective in preventing or reducing the severity of COVID-19 could have worldwide importance.

More detailed information about the benefits of this study can be found under ***"Will being in this study help me in any way? (Detailed Benefits)"***

What happens if I do not want to be in this research?

As there are currently no FDA-approved medications for the treatment or prevention of COVID-19 disease, there are no known alternatives other than deciding not to participate in this research study. Deciding not to participate in the trial will otherwise not affect your ability to receive supportive medical care from a doctor or hospital if you were to become sick. If you did develop COVID-19 disease, you would likely remain eligible for any

treatment trial that was ongoing at a hospital.

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

We expect up to 3500 people may be in this research study.

What happens if I say "*Yes, I want to be in this research*"?

You will first answer an online questionnaire about your health history to determine if you can participate in this study. If you are deemed eligible and consent for study participation, then you will be randomly assigned to receive either hydroxychloroquine or a vitamin, which you will take once or twice weekly. Once assigned, the medication will be sent by priority mail overnight to you. You are to start the medication as soon as you receive it. Then you will fill out a survey every week collecting any symptoms, diagnoses, or hospitalization events that have occurred.

The experimental treatment you get will be chosen by chance, like flipping a coin. Neither you nor the research study doctor will choose what experimental treatment you get. You will have a 67% chance (2/3) of being given either treatment, and 33% chance (1/3) of receiving placebo. Neither you nor the study doctor will know which experimental treatment you are getting.

No in-person visits or blood draws are required. All data will be collected by you reporting information in online questionnaires. We will send you a brief questionnaire on:

- Tomorrow (Day 1)
- Every week until the study ends
- If you get sick or have side effects, you may complete the questionnaire additionally as needed

If you do become ill with COVID-19 symptoms, you will go through routine health procedures (i.e., contact your doctor or local Department of Health). Please call your doctors for medical care. If you become sick, we would recommend continuing the study medication, unless directed by your doctor.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for:

1. Check tomorrow to make sure you receive the shipped medication
2. Take your medication as prescribed
3. Fill out online questionnaires

What happens if I say "Yes", but I change my mind later?

If you take part in this research study, and want to leave, you should tell us. Your choice not to be in this study will not negatively affect your right to any present or future medical care.

We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

If you stop participating in the research study, information about you that has already been collected may not be removed from the study database.

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

- The main side effects of hydroxychloroquine include nausea (and upset stomach), decreased appetite, headache, rash, and blurred vision. All these symptoms should resolve once the drug is stopped.
- More serious reactions are rare but possible; typically these occur in people taking the drug for much longer periods of time than as directed in this study. These include vision damage, heart rhythm problems, low blood sugar, and muscle weakness. Persons with psoriasis may experience temporary skin worsening while taking the medication.
- Persons with a previous allergy to chloroquine or hydroxychloroquine should avoid the drug.
- Persons with Glucose-6-phosphate deficiency (G6PD) may have increased risk of hemolytic anemia when taking hydroxychloroquine.
- Persons with existing eye disease of the retina should not take hydroxychloroquine. Long-term use >1 year can be associated with rare retinal eye problems. Eye problems have not been reported with short term use.
- Persons taking medications for abnormal heart rhythms may be ineligible for the study (more information below).
- Persons taking medications for significant heart rhythm problems are ineligible for the study due to increased risk for heart rhythm abnormalities. The most common medications include:
    - Flecainide (Tambocor)
    - Procainimide (Procan)
    - Propafenone (Rythmol)
    - Amiodarone (Cordarone, Pacerone)
    - Quinidine
    - Digoxin (Lanoxin)

- Some persons will receive a vitamin instead of hydroxychloroquine. Oral vitamins are considered safe, though can occasionally cause upset stomach.

- There is a risk that you may have a bad outcome if you contract COVID-19 disease. This risk exists whether you are in the trial or not. We cannot predict for sure who will have mild or severe disease after infection from the virus. However, we do have evidence that persons >65 years old may be at higher risk for more severe disease. It is unlikely that this trial will worsen that risk in any way.
- There is some risk of a data breach involving the information we have about you. We comply with the University's security standards to secure your information and minimize risks.

What do I need to know about reproductive health and/or sexual activity if I am in this study?

Pregnant women may participate in the trial.

Hydroxychloroquine is Pregnancy Category: C – Use with caution if benefits outweigh risks. Hydroxychloroquine crosses the placenta. Animal studies show evidence of fetal harm when used in high doses and for prolonged durations with associated neurological disturbances and interference with hearing, balance, and vision in the fetus. There is no data in animals that short term use, such as for the treatment of malaria (or as in this study), causes fetal toxicity.

In humans, a 2009 comprehensive review of the published literature reported that hydroxychloroquine is not associated with any increased risk of congenital defect, spontaneous abortion, fetal death, pre-maturity, or decreased numbers of live births in pregnant women with autoimmune diseases.

The effect of SARS-CoV-2 on pregnancy is not known.

If you are or become pregnant while participating in this research study, we ask to be able to send you a short survey ~1 month after your delivery to collect information on the outcomes of your pregnancy.

Breastfeeding: Small amounts of hydroxychloroquine enter into breast milk. Small studies have reported no harmful effects in infants whose mothers' breastfed while taking hydroxychloroquine with no evidence of vision, hearing, or growth problems in infants who were followed up to one year of age.

Will it cost me anything to participate in this research study?

Taking part in this research study will not lead to any costs to you. You will not be charged for the study medications or the cost to ship them to you.

What happens to the information collected for the research, including my health information?

We try to limit the use and sharing of your information, including research study records, any medical records and any other information about you, to people who have a need for this information. But we cannot promise complete confidentiality.

If you participate in this study, your information, including your health information, will be used and shared for purposes of conducting this research. As described later in this Consent Form, your information may also be used and shared for publishing and presenting the research results. If you sign this Consent Form, you are giving us permission to use and share your health information for these purposes. We ask for access to your medical records to verify test results and review hospitalizations, you are giving permission to any health care providers who are treating you to share your medical

records with us.

What health information will be made available?

Health information about you to be used and shared for the research includes those items checked by the research team below:

☒ Your medical records, which may include records from hospital and clinic visits, emergency room visits, medical history and physical exams, medications, progress notes, lab and pathology reports. These records may be used and shared for as long as this research continues. We will limit any request to 90 days from study entry.

☒ Information collected as part of this research study, including research procedures, research visits, and any optional elements of the research you agree to, all as described in this Consent Form. This information might not be part of your medical record, and may include things like responses to surveys and questionnaires, and information collected during research visits described in this Consent Form.

Who will access and use my health information?

If you agree to participate in this study, your information will be shared with:

- The University of Minnesota research team and any institutions or individuals collaborating on the research with us;

- Others at the University of Minnesota and M Health/Fairview who provide support for the research or who oversee research (such as the Institutional Review Board or IRB which is the committee that provides ethical and regulatory oversight of research at the University, systems administrators and other technical and/or administrative support personnel, compliance and audit professionals (Such as the Quality Assurance Program of the Human Research Protection Program (HRPP)) , individuals involved in processing any compensation you may receive for your participation, and others);

- The research sponsor(s), any affiliates, partners or agents of the sponsor(s) involved in the research, organizations funding the research, and any affiliates, partners or agents of the funding organization(s) involved in the research, including state health departments;

- Organizations who provide accreditation and oversight for research and the research team, and others authorized by law to review the quality and safety of the research (such as U.S. government agencies like the Food and Drug Administration, the Office of Human Research Protections, the Office of Research Integrity, or government agencies in other countries); and

Additional sharing of your information for mandatory reporting

If we learn about any of the following, we may be required or permitted by law or policy to

report this information to authorities:

- Current or ongoing child or vulnerable adult abuse or neglect;
- Communicable, infectious or other diseases required to be reported under Minnesota's Reportable Disease Rule;
- Certain wounds or conditions required to be reported under other state or federal law; or
- Excessive use of alcohol or use of controlled substances for non-medical reasons during pregnancy.

How will my information be used in publications and presentations?

We may publish the results of this research in scientific, medical, academic or other journals or reports, or present the results at conferences. Information that makes it easy to identify you (such as your name and contact information, and medical records number) will not be part of any publication or presentation. If you have an extremely unique or rare condition that is not shared by many others, it is possible that some people may be able to determine your identity even without these identifiers.

What will be done with my data and specimens when this study is over?

Your data will not be used for any future research after this study is complete.

Do I have to sign this Consent Form and give my permission to make my information, including my health information, available for use and sharing?

No, you do not have to sign this Consent Form. But if you do not sign, you will not be able to participate in this research study. Treatment available outside of the study, payment for such treatment, enrollment in health insurance plans and eligibility for benefits will not be impacted by your decision about signing this Consent Form.

Does my permission for making my health information available for use and sharing ever expire?

Yes, we will limit collection of data to 90 days from entering the study.

May I cancel my permission for making my health information available for use and sharing?

Yes. You may cancel your permission at any time by writing to the researcher at the email address on the first page of this Consent Form. If you cancel your permission, you will no longer be in the research study. If you cancel your permission, any health information about you that was already used and shared may continue to be used and shared for the research study and any optional elements of the study to which you agree in this Consent Form.

What happens to my health information after it is shared with others?

When we share your information with others as described in this Consent Form, privacy laws may no longer protect your information and there may be further sharing of your

information.

Will I be able to look at my records?

The research team will allow you to see the information collected for this study. .

A description of this clinical trial is available at https://clinicaltrials.gov/ct2/show/NCT04328467, as required by U.S. Law. This Web site will not include your name or any other direct identifiers such as your contact information. The Web site may include a summary of the results of this research. You can search this Web site at any time.

Will I receive research test results?

When the study is complete, we will email a summary of results to all participants' email addresses. You will not know if you got the hydroxychloroquine or the vitamin.

Will I be compensated for my participation?

There is no compensation for study participation. The study medication will be provided free of charge.

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
  The research team can be reached by email at: FAQ.covid19prep@gmail.com
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, you should seek first aid and emergency treatment from your healthcare provider, as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

If you develop symptoms concerning for COVID-19 disease (such as fever, cough, shortness of breath, sore throat, muscle aches, or fatigue) you should call your healthcare provider or local health department for testing and further instructions.

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____

Signature of Participant Date

_____

Printed Name of Participant