Participant Information Sheet

In this information sheet, we will give you information about the study to help you decide whether or not you will agree for you to take part. If you have any questions or concerns, you will have a chance to discuss them with the study staff.

**Study Title**  
Chloroquine/ hydroxychloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting; a randomised, placebo-controlled prophylaxis study (COPCOV)

**Short Title**  
Study of chloroquine/ hydroxychloroquine and coronavirus disease (COVID-19) in the healthcare setting

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**Sponsor**  
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Introduction

We are conducting a study to find out whether a drug called chloroquine/ hydroxychloroquine (Note: remove chloroquine or hydroxychloroquine as appropriate. Chloroquine will be used in Asia and Hydroxychloroquine will be used in Europe, Africa and elsewhere), may prevent you getting coronavirus illness. This drug has been used for over 50 years mainly to prevent malaria (in travelers or in pregnant women) or to treat malaria, or to treat rheumatoid arthritis. People have taken it for many years at a time. It is considered very safe, and it may have effects against the virus. We would like to find out if this drug can prevent you from getting coronavirus disease.

In total, approximately 40,000 participants working in facilities involved in COVID-19 case management or with other risk of COVID-19 infection are expected to be recruited into this study. The study team plan to recruit an average of 400-800 participants per site in 50-100 sites globally.

What is the main purpose of this research?

We are conducting a study to find out if chloroquine/ hydroxychloroquine can prevent coronavirus illness in those working in healthcare facilities or with other risk of COVID-19 infection.

What is this study about?

Currently there is no widely-available vaccine in all countries in which the study is being conducted, no drug that prevents coronavirus disease (COVID-19), and the only proven effective treatment is for patients who are already hospitalized and require oxygen (dexamethasone, a steroid anti-inflammatory). Therefore there remains an urgent need to identify drugs which can prevent the spread of infection and may prevent those working in healthcare facilities or
other persons at risk of contracting COVID-19 from getting infected, so they can continue to care for patients and protect themselves and their families.

Although chloroquine/ hydroxychloroquine has antiviral effects in the laboratory, we really do not know if it will be beneficial in preventing infection in people. A recent trial has shown it is not an effective treatment of COVID-19 infection, but this trial will find out if chloroquine/ hydroxychloroquine can prevent disease. Like all drugs, chloroquine/ hydroxychloroquine has side effects; in most people it is a safe and well-tolerated drug at the doses and duration used in this study. Some of you may already have taken chloroquine previously to prevent malaria when you travelled to a malaria endemic area. In order find out if chloroquine/ hydroxychloroquine prevents COVID-19, we will need to compare it to something. As there is no other prevention, we will compare it to a placebo, which is an identical tablet, but contains no chloroquine/ hydroxychloroquine or other active ingredient.

Vaccine

The study will NOT change your chance to be vaccinated against COVID-19 during the study or in the future. The study remains important as hydroxychloroquine and chloroquine are available now and could help prevent COVID-19 while we wait for the world’s population to be vaccinated. If chloroquine/ hydroxychloroquine is shown to be beneficial, this knowledge and these drugs could still be of benefit to people for this and future pandemics. If you are offered the vaccine, please let the study team know so we can plan accordingly.

What will happen to you if you participate in the study?

In this study we invite adults who work in a healthcare facility or other persons at risk of contracting COVID-19 to participate.

If you agree to participate we will assess you to see if you can take part in this study. If yes, and if you agree to participate in the study and adhere to the protocol, you will be asked to give some information about yourself including some questions about medical conditions, whether you are taking any other medications, your weight and height, and will have some blood taken. Then, you will be randomised (like a flip of a coin) to receive either chloroquine/ hydroxychloroquine or placebo (a pill that looks the same as the chloroquine/ hydroxychloroquine but does not have any active drug). Half of participants will be given chloroquine/ hydroxychloroquine and half of participants will be given placebo, and neither you, nor the study team will know if you are getting chloroquine/ hydroxychloroquine or placebo.

The first dose will normally be 3-5 tablets, this is a “loading dose” to ensure adequate blood levels are reached immediately. The dose will be calculated based on your weight and the study team will watch you take the first pills, depending on the total number of pills in your loading dose the study team may tell you to finish the rest of the pills later that day at home (to reduce chance of side effects).

After the loading dose you will take 1 tablet a day for 3 months with breakfast (or in the evening if you work in a healthcare facility at night). It is very important for you to continue to take
these tablets every day, but you will be able to contact a member of the study team at any
time if you experience any side-effects or you feel unwell.

We will ask you about your place of residence, place of work and contact details (including
mobile phone number).

We will also take a sample of your blood once a month during the study period. The first and
the last sample will be from the arm, and the other two samples will be taken from a finger
prick. We will use this blood for special tests, to measure chloroquine/ hydroxychloroquine
levels in the blood to check that you are taking the medication, to see if you get any viral
infections during the study, as well as looking at parts of the blood which help you to under-
stand how you respond to infections (vitamin levels and genetic tests).

If you do get coronavirus infection, we will ask that your doctor gives us information about
your illness, such as results of tests, what treatment you received and what happened to you.

We will ask you to go about your life as normal, including going to work. We will give you a
thermometer to check your temperature twice a day, and record how you are feeling. We will
help you download a special mobile application (app) in which you record how you are feeling
twice a day and your temperature. The study team will make sure the application is working
on your phone, that you know how to use it, and you know how to check your temperature
before you leave. If you do not register data into the app at least once a day the study team
will contact you.

If you report feeling unwell you will be asked some extra questions on the application. If you
feel unwell and report it in the application, or contact the study team, a study team member
will contact you and arrange to collect a swab. The swab will be a nose and throat swab, which
is used to wipe the back of mouth and each nostril, and can test for the presence of corona-

virus as well as other viruses. In some instances a sputum sample or additional blood samples
may be collected. These samples will be tested later. If feasible we will update you with results
from your swabs and blood tests for COVID-19 at a later date, but this will likely be many
months later and may not be possible. You will be asked to comply with local regulations,
including self-isolation if you are unwell and further testing for the coronavirus if this is re-
quired.

You must not self-medicate with chloroquine/ hydroxychloroquine during the study.

Summary of first visit. If you can take part in the study and agree to do so, you will:

- Sign two copies of the Informed Consent Form (one will be kept with us and you will
  keep the other)
- Give information about yourself, your contact details and place of residence
- Give information about your health (present and in the past)
- Give information about how you are feeling
- Be weighed and have your height measured
- Have a blood test
- Take your first dose of tablets
- Have the application downloaded on your smartphone and be shown how and when to
  use it
• Be given your own thermometer and shown how to use it
• Be given 30 tablets (1 to be taken each day) before your shift (in the morning if you work days, and in the evening if you work nights)
• Be given your unique study ID and a number to contact the study team at any time
• Be told to inform the study team if you become unwell or have any issues
• Be given an appointment to come back in 30 days for more tablets. If you feel unwell you will be asked to NOT come back to the study site and instead phone the study team. They will advise.

On the day you come back for your monthly follow up visits (30 days and 60 days after the first visit), we will ask you NOT to take your medication on that day, as this can interfere with the finger prick test. You will be asked to bring your medication blister packs (even if finished) and confirm your study ID. We will ask you some questions about the tablets, whether you took them every day and if you had any side-effects, and how you’ve been since we last saw you. We will then perform a finger prick test, where a few drops of blood will be taken from your finger and this will be tested for chloroquine/ hydroxychloroquine levels. At the end of this visit, you will be given another 30 tablets and an appointment to come back in 30 days. You should take your daily study tablet after your visit is completed.

At the final study visit (90 days after the first visit), you will also be asked to bring your medication blister packs (even if finished) and confirm your study ID. On that day we will also ask you some questions about the tablets, whether you took them every day and if you had any side-effects. We will then take some blood from your arm using a needle and we will not give you any further tablets.

If you had been unwell during the study, we may ask you to continue to record in the mobile application how you feel and contact you up to 60 days after your illness starts. In these cases we may contact you and receive information up to 150 days after your first visit.

You are expected to participate in the study for up to a total of 5 months.

Summary of following visits:
• Do not take the study tablet on the day of the visit as this can interfere with the finger prick test
• Bring medication blister packs to visit, confirm your study ID
• Questions about medication and side-effects, and how you are feeling
• Blood test: finger prick at 2 visits, on the last visit we will again take blood from a vein in your arm.
• Appointment in 30 days and 30 more tablets. If last visit (Day 90), you will not be given another appointment or more tablets

What do I do if I don’t feel well or if I have any problems?

Remember that if you feel unwell at any time during the study:
• Seek medical advice as you normally would, especially if you have a medical condition such as diabetes, renal (kidney) disease, cardiovascular (heart) disease, hypertension
(high blood pressure), hyperlipidemia (high cholesterol) or if you smoke, because any of these conditions may mean your symptoms become more severe

- Please do NOT attend study site
- Use your application to say you do not feel well and the study team will contact you
- You can contact the study team any time if you have worries, questions or feel unwell on the number provided to you
- Continue to take your tablets everyday unless you are told by the study team or your healthcare professional to stop them
- Follow local guidelines (for example, from your employer) about COVID-19 testing and isolation
- If you are unable to attend a follow up visit as a result of symptoms or isolation contact the study team for advice

What do I do if I see a Doctor or go to hospital?

- If you feel unwell at any time during the study, please contact the study team by phone
- If you see a doctor or go to hospital, please let them know you are in this study and taking study medication. Your doctor or the hospital can contact a member of the study team for more information at any time
- Please let the study team know if you have visited a doctor or hospital. This will give us a chance to check you are well and we will know where you are and can help answer any questions they may have
- Please let the study team know if you are offered a vaccine against COVID-19, or have been vaccinated against COVID-19. This will give the study team an opportunity to discuss stopping the study medication and further study assessments.
- If you are diagnosed with COVID-19 and need to be hospitalized you should stop taking your study medication

What happens if I get coronavirus?

If a test confirms you have been infected with coronavirus, you should contact the study team as soon as possible to inform them that you have been diagnosed with coronavirus.

You should still continue taking your study medication for up to 90 days unless one of the following happens:

1. You are hospitalized as a result of COVID-19 illness
2. You are told by the study team or your healthcare professional to stop them

You should NOT attend the study site, unless asked to do so by the study team. As we want to know if the tablets you have been taking will make the disease less severe, we may contact your doctor and ask for information about your illness, including any tests or treatments that are performed, especially if you went to hospital. If you’re at home, to check how you are doing, we will ask you to continue to report how you are feeling on the application and contact
us if any change. We will continue to be in contact with you until Day 90, up until 60 days after the start of your illness, whichever is longer.

**Are there any risks or disadvantages to me of taking part?**

**Risk of chloroquine/ hydroxychloroquine**

Chloroquine/ hydroxychloroquine is registered and commonly used for the treatment of malaria and rheumatoid arthritis. In most people it is usually very well-tolerated, unless the drug is taken in overdose. Headache and gastrointestinal symptoms, such as nausea and diarrhoea, are the most common side effects reported with chloroquine/ hydroxychloroquine use. Another common side effect in certain groups of people is itching. Hydroxychloroquine may cause less itching than chloroquine.

Other adverse reactions relating to the heart and blood system, the central nervous system, the skin, low blood sugar and hypersensitivity, have all been described though usually after high doses or long duration of treatment. Chloroquine/ hydroxychloroquine taken over a period of years can cause problems with the eyes which may affect vision.

Although chloroquine/ hydroxychloroquine is generally safe and well-tolerated, it is not known whether it protects against COVID-19. Other trials evaluating chloroquine/ hydroxychloroquine treatment in COVID 19 showed that it was not effective in the later stages of the disease. For these reasons you should continue to protect yourself against COVID-19 as advised by local guidelines (for example from your employer).

Although chloroquine/ hydroxychloroquine has antimalarial effects, there are many areas of the world where malaria is endemic and there is substantial chloroquine resistance. In case you require antimalarial prophylaxis, you should not assume that you are protected by the drug and should discuss this with your doctor.

Occasionally people experience mild side effects for a few hours after taking a loading dose of chloroquine/ hydroxychloroquine, including blurred vision. If this happens to you, you should avoid driving or operating machinery until your vision returns to normal. If this happens following subsequent doses or you experience other side effects, please contact the site study team.

**Risk of blood withdrawal from the arm or the finger prick**

The risks of blood withdrawal from the arm or the finger prick include discomfort, occasional bleeding or bruising of the skin at the site of needle puncture, and very rarely infection.

If an infection of the skin occurs, it will usually go away quickly.

**Risk of nose and throat swab**

The nose and throat swab can be slightly uncomfortable but only takes a few seconds.

**Risk for pregnant or breastfeeding women**

Chloroquine/ hydroxychloroquine is the recommended treatment for malaria which is sensitive to this drug.
Chloroquine/ hydroxychloroquine is considered safe in pregnancy, but as a precaution, women who are known to be pregnant and women who are planning to become pregnant are excluded from the trial. This is standard practice in trials such as this study where the benefit of taking a drug is not yet known so there is no benefit to set against even a tiny risk to a pregnancy. If you do become pregnant during your participation in the trial, you should discontinue the study medication and let the study staff know. There is no contraindication to breast feeding.

If any new information about the safety of the chloroquine/ hydroxychloroquine becomes available during the course of this study, we will tell you as soon as possible.

**What should you do if you have side effects?**

Although these drugs have been well-studied, there may be mild side effects that will occur that have not been noticed before. You should inform the study staff right away if you have any problems. If you have any side-effects or any unexpected problems during participation in the study, we will treat these problems fully and with no charge to you.

**What are the advantages of taking part/not taking part?**

There is no proven benefit to you of joining the study. The potential benefit is that those taking chloroquine/ hydroxychloroquine may be less likely to get coronavirus infection and also that they may be less likely to become unwell with it. If chloroquine/ hydroxychloroquine prevents coronavirus, there is a potential benefit to those taking the placebo, that they are less likely to be given coronavirus by another participant of the study taking chloroquine/ hydroxychloroquine. There is a benefit to society by helping us find out as quickly as possible whether this drug works.

The results of the study will improve our understanding and inform us if chloroquine/ hydroxychloroquine is effective in preventing coronavirus infection and other viruses, which will be useful in future pandemics. The results of this study may provide the first effective drug at preventing infection.

Those enrolled in the study will also be given a thermometer which they can keep.

**What will happen if you choose not to take part in the study, or if you change your mind after you agree?**

Your participation in this study is entirely voluntary. You are free to withdraw from the study at any time and it will not affect your care.

The study doctor and the study sponsor have rights to withdraw you from this study if it’s considered that it is in your best interest.

If you become infected with coronavirus while participating in the study or choose not to participate, you will receive standard care per local standards.
What will happen if a COVID-19 vaccine becomes available in my country and I wish to receive this?

The study will not interfere with you being vaccinated as part public health policy. If you are offered a COVID-19 vaccine and wish to receive this then you should inform the study team as soon as possible.

The study team will then arrange with you to stop the study medication and how to complete study visits and procedures i.e. blood tests, prior to you receiving the vaccine.

The team will ask you to arrange a visit where they will collect a blood sample before your first dose of vaccine, and also have an additional blood test 28 days later. These samples may be used to determine if the study medication has been effective, or had any effect on your body’s response to the vaccine. This information will be analysed after the end of study and you will not receive the information.

What will the blood sample be used for?

The blood volume that will be taken for the study is approximately 16 milliliters (approximately 1 tablespoon). The blood samples will be used to determine if the chloroquine/hydroxychloroquine prevents you from getting coronavirus and other infections, how coronavirus is affected by other infections and be used to understand risks of infection (including genetic risks). They will also tell us about whether people are taking the medication and how different people have different levels of the drug in their bodies.

If you are vaccinated while in the study you will be asked for one additional blood sample, which means you will give approximately 21 milliliters (approximately 1 and a half tablespoons).

Your blood sample will be stored for genetic tests related to the risk of coronavirus infection. All testing will be anonymised so there it cannot be traced to your personal details.

Some of your blood/specimen may be shipped abroad for further investigations.

Some of your leftover blood samples will be stored and may be used for further studies in the future.

Will there be any financial cost or compensation to you?

In case, you are experiencing any side effects or harms which are directly caused by the study, we will treat you according to the standard treatment free of charge.

Study-associated costs will be reimbursed as allowed per local rules.

List of Study Member Contacts

If you have any questions or concerns after reading this information sheet, you will have a chance to discuss them fully with a member of our team before you decide whether or not
to take part. We will also be available throughout the study to answer any questions or address any concerns that you may have later on.

If you have any questions while you are at home, you can contact the study staff by telephone as below.

Name:

Telephone number:

or

Name:

Telephone number:

If you haven’t been treated as specified in this information sheet or you wish to know the participant’s rights, contact the secretariat office of the Ethics Committee. *(Ethics committee contact information will be added per site).*

**Confidentiality**

Your name will not be in any report or on any sample being shipped away from the hospital. We repeat that the information we collect from you and from analysing of your blood samples will be kept confidential by the study team. We will not share personal information with anyone outside the study.

No one other than the study team, authorised personnel from the study sponsor, monitor, ethics committee and regulatory authorities such as Food and Drug Administration are allowed direct access to personally identified medical records.

When the study is completed, we will combine the test results with those of the other participants, and the overall results will be analysed.

The clinical data, genetic information and results from blood analyses that is stored in our database may be shared with other researchers to use in the future. The other researchers will not be given any information that could identify you.

**Data protection**

The University of Oxford is responsible for ensuring the safe and proper use of any personal information you provide, solely for research purposes.
Informed Consent Form

I would like to take part in a study, titled: “Chloroquine/ hydroxychloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting; a randomised, placebo-controlled prophylaxis study (COPCOV)

I have read the participant information sheet and have had the opportunity to ask questions about the study and any questions I have asked have been answered to my satisfaction.

I understand that I can withdraw or stop taking part in the research at any time without affecting further services and hospital care to which I am entitled to in the future. To consent to take part in this study, I allow the investigators to use my personal information obtained from this research. My information will be presented as part of research results without revealing my name or identity.

If I have doubts about the study procedures or I experience adverse side-effect from the research, I will be able to contact study doctors or study staff at any time.

I fully understand the statements in the participant information sheet and this informed consent form.

I consent to participate in this study.
I agree to adhere to the study protocol.
I will not self-medicate with chloroquine or hydroxychloroquine outside the study.
I will inform any medical professional prescribing medications during the trial period that I am taking study medication.
I understand I should seek medical advice if I become unwell during the study, particularly if I have diabetes, renal (kidney) disease, cardiovascular (heart) disease, hypertension (high blood pressure), hyperlipidemia (high cholesterol), or am a smoker.
I understand that I must stop study medication if I am diagnosed with COVID-19 and need to be hospitalized due to my symptoms.
I understand that I should inform the study team if I am offered a COVID-19 vaccine and that I must stop study medication if I receive a COVID-19 vaccine during participation.
I allow my blood to be tested for genetic tests related to susceptibility or response to the COVID-19 infection.
I allow my blood to be stored for future studies related to susceptibility or response to the COVID-19 infection.
I allow my blood/specimen to be shipped abroad.
I allow my anonymised clinical data, genetic information and results from blood analyses that is stored in the database to be shared with other researchers for use in the future. These data will be carefully and securely anonymised so it will not be possible to identify the individual.
Signature of Participant ..............................................
Print name of Participant ...........................................
Date .................................................................

Signature of person conducting the informed consent ..............................................
Print name of person conducting the informed consent ...........................................
Date .................................................................

To sign 2 originals: 1 copy for participant, 1 copy for site file
For the participants who cannot read or sign in the consent form, the participant can thumb print in the following box.

I cannot read but investigator/study staffs have read information in this informed consent form to me and explain until I fully understand the given information. Therefore I provide my thumbprint to voluntary consent for myself taking part in this research study in the following aspects:

I consent to participate in this study.
I agree to adhere to the study protocol.
I will not self-medicate with chloroquine or hydroxychloroquine outside the study
I will inform any medical professional prescribing medications that I am taking study medication
I understand I should seek medical advice if I become unwell during the study, particularly if I have diabetes, renal (kidney) disease, cardiovascular (heart) disease, hypertension (high blood pressure), hyperlipidemia (high cholesterol), or am a smoker.
I understand that I must stop study medication if I am diagnosed with COVID-19 and need to be hospitalized due to my symptoms.
I understand that I should inform the study team if I am offered a COVID-19 vaccine and that I must stop study medication if I receive a COVID-19 vaccine during participation.
I allow my blood to be tested for genetic tests related to susceptibility or response to the COVID-19 infection.
I allow my blood to be stored for future studies related to susceptibility or response to the COVID-19 infection.
I allow my blood/specimen to be shipped abroad.
I allow my anonymised clinical data, genetic information and results from blood analyses that is stored in the database to be shared with other researchers for use in the future. These data will be carefully and securely anonymised so it will not be possible to identify the individual.

Right thumb print of the Participant

Signature of person conducting the informed consent......................................................

Print name of person conducting the informed consent......................................................

Date ........................
Signature of witness..............................................................................................................................................

Print name of witness...........................................................................................................................................

Date ..............................................

To sign 2 originals: 1 copy for participant, 1 copy for site file