Local Trust Logo

Participant Information Sheet - UK

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

International Chief Investigators	Professor Sir Nicholas White, Dr. William Schilling
UK Chief Investigator	Professor Martin Llewelyn
Sponsor	University of Oxford

Thank you for your interest in our trial. We want to find out if hydroxychloroquine and chloroquine (HCQ/CQ) can help prevent COVID infection. At the moment we don't know. The first page of this information sets out why we are doing the study. The rest of the document provides detail about what's involved. Please ask us for more information at any point.

What we're asking you to do

- We'll ask you some questions about how you are feeling and your quality of life and measure your weight and height and take a blood sample of around 10ml (half a tablespoon) from a vein in your arm and two spots of blood from a finger-prick.
- Then we'll randomise you (like a flip of a coin) to take either hydroxychloroquine or placebo tablets for three months.
- We will help you download a smart-phone app onto your phone. We ask you to use this twice a day while participating in the study to report how you are feeling and record your temperature.
- We'll give you a letter to show to your GP or any other healthcare professional you see in the event that you need to seek medical care at any point during your involvement in the study.

Recent events

The use of HCQ/CQ in COVID-19 has been in the media a lot recently, and you may be aware of some of these discussions. Just after our trial started, the regulator that authorises trials in the UK, (the Medicines and Healthcare Regulatory Agency (MHRA)), temporarily paused all trials using HCQ/CQ in COVID-19, while it reviewed new evidence. The MHRA has now authorised this trial to continue. We want to make you aware of some of the evidence to help you decide whether to take part.

There are laboratory studies that have found HCQ/CQ to be active against COVID-19 and other viruses but a recent large trial found they have no benefit as treatment in hospitalised patients with COVID-19. This may be because virus multiplication has largely stopped by the time people reach hospital and, in those who are most ill, that it is inflammation that causes harm (which is why dexamethasone, an anti-inflammatory corticosteroid, is effective). The time when an antiviral could work best is therefore likely to be very early in infection.

However it may help in prevention. Another trial which studied healthcare workers given HCQ/CQ **after** they had been exposed to COVID-19 suggested there could be a small protective effect taken in this way but they couldn't tell if the difference was just due to chance or not. In that study most people started the drug around 3 days after presumed exposure. If the effect they saw was real then, if given **before** exposure, HCQ/CQ may work well enough to provide useful protection against COVID-19. **This is what the COPCOV trial aims to find out**.

HCQ/CQ taken in the doses and for the duration used in COPCOV have an excellent safety record. A study published on May 22nd 2020 questioned their safety in patients hospitalised with COVID-19 but very unusually, this paper had to be retracted because the authors found their own data to be unreliable. The two clinical trials mentioned above did not find any significant harms. Even so, as a precaution, COPCOV will stop the study drug in participants who do get COVID-19 and are unwell enough to be admitted to hospital.

HCQ/CQ are easily manufactured, inexpensive and well tolerated drugs. If they are effective at preventing COVID-19 this would be a huge benefit for healthcare workers and many other groups of people across the world.

Please read the following full information leaflet and discuss with the study team if you would like to before deciding.

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

Introduction

We are conducting a study to find out whether chloroquine/hydroxychloroquine may prevent COVID-19 infection. These closely related drugs have been used for over 50 years to prevent and treat malaria, and to treat rheumatoid arthritis and other rheumatological conditions. People have taken them for many years at a time. They are considered safe taken at recommended doses, and may have effects against the virus. In the UK the trial is using hydroxychloroquine.

Globally, approximately 40,000 participants are expected to be recruited into this study. The study team plans to recruit an average of 400-800 participants per site in 50-100 globally, including the United Kingdom.

What is the main purpose of this research?

To find out if hydroxychloroquine can prevent, reduce or delay symptoms of COVID-19 infection in healthcare workers.

Why have I been invited?

You have been invited because you work in a healthcare facility where patients with either proven or suspected COVID-19 receive healthcare.

What are other purposes of this research?

The study will also collect information on participants' health-related quality of life and their use of health care resources during the study via linkage to medical records to test the cost effectiveness of hydroxychloroquine as a preventative treatment for COVID-19 in the UK.

What is this study about?

Currently there is no vaccine, and no drug that we know prevents coronavirus disease (COVID-19). There is an urgent need to identify drugs that can prevent the spread of infection, but also protect healthcare workers from getting the infection so they can continue to care for patients and protect their families.

Although hydroxychloroquine has antiviral effects in the laboratory, we do not know if it will be beneficial against acquiring the 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 hydroxychloroquine can **prevent** disease. Like all drugs, hydroxychloroquine has side-effects; in most people it is a safe and well tolerated drug at the doses and duration used in the COPCOV trial. To find out if hydroxychloroquine prevents COVID-19, and in the absence of any known effective prevention treatment, we will compare it to a placebo, which is an identical tablet, but contains no hydroxychloroquine or other active ingredient.

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

At an enrolment visit, the site study team will confirm that you are eligible to participate. If you have previously been tested and the result was positive for COVID-19, you will not be eligible to participate. If you have previously had symptoms of COVID-19, or been self-isolating, you will be able to participate. Then, having read this information and had your questions answered, if you do wish to participate, we will ask you to sign two copies of a consent form: one for you to keep, and one for study records.

You will then be enrolled in the study.

We will ask you to answer some questions about how you are feeling and your quality of life.

We will measure your weight and height.

We will take a blood sample of around 10ml (half a tablespoon) from a vein in your arm and two spots of blood from a finger-prick.

We will help you download a smart-phone app onto your phone. You will use this twice a day while participating in the study to report how you are feeling and record your temperature. We will give you a thermometer to do this; if you have a suitable thermometer at home, we may ask you to use that. The site study team will make sure the app is working on your phone, that you know how to use it, and you know how to check your temperature before you leave.

We will give you a letter to show to your GP or any other healthcare professional you see in the event that you need to seek medical care at any point during your involvement in the study. You can print or download additional copies of this letter and the information sheet from the UK trial website www.copcov.org.

You will be randomised (like a flip of a coin) to receive either hydroxychloroquine or placebo. Your chances of getting the hydroxychloroquine or placebo are 50:50. Neither you, nor the site study team will know if you are getting hydroxychloroquine or placebo.

The first dose will be 3-5 tablets (dependent upon your weight) and will be calculated by and taken in front of the site study team. This “loading dose” is to ensure adequate blood levels are reached immediately. Occasionally people experience mild side-effects for a few hours after taking a loading dose, 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.

Taking the study drug after enrolment

After the loading dose, you will take one tablet a day for three months with breakfast (or in the evening if you work nights). The tablets should be stored at room temperature, up to 30°C and away from moisture (do not store in the bathroom) and light. It is important to keep this and all medications out of the reach of children and pets. 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 site study team if you experience side-effects or feel unwell. We will give you details of how to do this.

If you forget to take a dose you can take this dose later, up until the time of your next daily dose. If you do not take the dose within this period of time, you should not take it and should

report the missed dose to the site study team via the mobile app and at your next follow up visit.

You must not self-medicate with Chloroquine or Hydroxychloroquine during the study.

Follow-up during the study via the mobile app

During the study, you should record your temperature and whether you feel "well or "unwell" in the study app twice per day. If you feel "unwell", the app will ask you about some specific symptoms. The site study team may contact you by telephone for more information.

If your symptoms suggest COVID-19 infection in line with NHS criteria at the time (as of April 2020, this was a new continuous cough and / or a new fever), the site study team will arrange to collect a swab to test for COVID-19 and other viral infections. This procedure may be performed at your hospital, at an occupational health department, or by you at home (following the instructions provided). You may find this video helpful:

https://www.gov.uk/government/publications/covid-19-guidance-for-taking-swab-samples/how-to-use-the-self-swabbing-kit-for-a-combined-throat-and-nose-swab-video

The swab will be a nose and throat swab, which is used to wipe the back of the mouth and each nostril. In some instances, a sputum sample may be collected. These samples will be tested later.

Results from these research samples will not be made available to you.

You must also follow any instructions regarding workplace testing if you develop symptoms suggestive of COVID-19 infection.

If you report further symptoms of respiratory tract infection through the app or have more than one episode of symptoms during the study period, the nose and throat swab will be repeated.

If you do not enter the information twice per day, you will get a reminder via the app on your phone and the site study team will contact you by telephone within 24 hours to check you are ok. If you have a problem entering the information via the app for any reason, you can contact the site study team who will be able to enter the data on your behalf.

Follow-up visits at the study site

After the enrolment visit, we will arrange three further visits with the site study team at around 30 day intervals. If you have possible symptoms of COVID-19, you will be asked not to attend the appointment and instead phone the site study team who will advise you.

At these visits, we will take a sample of your blood (a tiny finger-prick sample onto filter paper).

On the day you come back for each of your follow-up visits, 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. You will be asked some questions about the tablets, whether you took them every day, and how you've been since we last saw you. You will be asked to complete a quality of life questionnaire. At the end of each visit, you will be given an appointment to come back in around 30 days.

At the last visit, approximately 90 days after the first, we will take a blood sample from a vein in your arm. We will use these blood samples for special tests, to measure hydroxychloroquine levels, to see if you get any viral infections during the study, and to look at components of the

blood which helps us to understand how people respond to infections, for example, vitamin levels; we will also carry out genetic tests.

At the final visit, you will also be asked to bring your medication blister packs, even if finished, and confirm your study ID. You will be asked to complete a quality of life questionnaire. On that day, we will ask you questions about whether you took the tablets every day, and how you've been. We will not give you any further tablets.

If you are unwell during the study, we may ask you to continue to record in the app how you feel, and may contact you for up to 150 days after your first visit.

You should expect that you may participate in the study for up to 5 months.

What do I do if I don't feel well?

Please remember, if you feel unwell during the study:

- Do **NOT** attend study site for study appointments without being invited to do so
- Use the app to say you do not feel well and the site study team will be in contact by telephone
- **Seek medical advice as you would normally would, particularly if you have diabetes, renal disease, cardiovascular disease, hypertension, hyperlipidaemia or if you smoke, as this may mean your symptoms become more severe.**
- **Comply with guidance from your employer (for example, the hospital) and NHS England about staff testing and isolation**
- Contact the site study team if you have worries, questions or feel unwell on the number provided to you
- Continue to take your tablets everyday unless you are diagnosed with COVID-19 and need to be hospitalised, or told by the site study team or your healthcare professional to stop them
- If you are unable to attend a follow up visit as a result of symptoms or isolation, contact the site study team for advice.

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

- Please let the site study team know by phone
- Let the doctor or hospital team looking after you know you are in this study and taking study medication.
- Give the GP/Medical Information letter and your copy of this information sheet to any doctor or healthcare professional looking after you
- Your doctor or the hospital can contact a member of the site study team for more information at any time.
- **If you are diagnosed with COVID-19 AND need to be hospitalised you should stop taking the study tablets.**

What happens if I get COVID-19?

If a test performed outside of the study confirms you have or have had COVID-19, you should still continue taking your study medication unless

- you are hospitalized as a result of COVID-19 symptoms in which case you should stop the study medication
- you are told by the site study team or your healthcare professional to stop the medication, or 90 days ends, whichever is sooner.

You should contact the site study team to inform them that you have been diagnosed with COVID-19.

You should NOT attend the study site, unless asked to do so by the site study team.

As we want to know if the tablets you have been taking will make the disease less severe, we may contact your GP and ask for information about your illness, including any tests or treatments that are performed, especially if you went to hospital. If you are hospitalised during the trial, your consent form may be shared with your treating NHS Trust and medical notes may be reviewed by members of the site study team in order to collect information about your illness.

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 app and contact us if there is any change. We will continue to be in contact with you until Day 90, or up until 60 days after the start of your illness, whichever is longer.

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

Risks of hydroxychloroquine

Hydroxychloroquine is closely related to chloroquine and generally considered to have fewer side-effects. These drugs are registered and commonly used for the treatment of malaria and rheumatological diseases. In most people they are very well-tolerated, unless taken in overdose. At the dose and duration used in this study side-effects are expected to be rare.

Adverse reactions relating to the heart and blood system, the central nervous system, the skin, low blood sugar, hypersensitivity, stomach, and eyes have all been described although usually after high doses or longer duration of treatment than you will be receiving in this trial. Some people may experience itching. If you are on insulin, you should monitor closely for lower blood sugars. If you want to take new over-the-counter medications, tell the dispensing pharmacist you are involved in the trial and may be on hydroxychloroquine. You should show them the GP/Medical Information letter and your copy of this Participant Information Sheet.

If your GP or other health professionals prescribes you certain medications during the trial, they may perform an electrocardiogram (ECG, to check your hearts rhythm and electrical activity) to ensure that combining medications does not cause any adverse effect. You should show them the GP/Medical Information letter and your copy of this Participant Information Sheet.

Although hydroxychloroquine is generally safe and well-tolerated, it is not known whether it protects against COVID-19. Other trials are evaluating hydroxychloroquine treatment in COVID 19 and have shown it to be safe. For these reasons **you should continue to protect yourself against COVID-19 as advised by your employer.**

Although 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.

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 be self-limiting.

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 breast-feeding women

Hydroxychloroquine is considered safe in pregnancy, but as a precaution, women who are known to be pregnant and women who are trying for a baby are excluded from the trial. This is standard practice in trials such as COPCOV 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 research team at your site know. There is no contraindication to breast-feeding.

If any new information about the safety of 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 hydroxychloroquine has been well studied, there may be mild side-effects that will occur that have not been noticed before. You should inform the study staff straight away if you have any problems.

What are the benefits of taking part?

There is no proven benefit to you of joining the study. The potential benefit is that those taking hydroxychloroquine may be less likely to get COVID-19 and also that they may be less likely to become unwell with it. 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 hydroxychloroquine is effective in preventing COVID-19 infection. The results of this study may contribute towards identifying an effective drug at preventing infection.

What if there is a problem?

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study.

NHS indemnity operates in respect of the clinical treatment which is provided.

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, you should contact the Chief Investigator Professor Martin Llewelyn on 01273 876671 or you may contact the

University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480, or the head of CTRG, email ctrg@admin.ox.ac.uk.

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

Your participation in this study is entirely voluntary. You are free not to participate or 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 is considered that it is in your best interest.

If you withdraw because of a side-effect of the study medication, or because you are unwell, we would invite you to attend a final visit and provide appropriate clinical care until your symptoms stop, or the condition becomes stable to ensure your safety.

If you withdraw or are withdrawn from the study you can refuse the use of your data or samples at any time up until the completion of the study (final follow-up of the final participant).

What will the blood samples be used for?

The blood volume that will be taken over the whole study is a bit less than 20 milliliters (approximately 1 tablespoon). The blood samples will be used to determine if the hydroxychloroquine prevents you from getting COVID-19 and other infections, how COVID-19 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 drug levels vary between people.

Your blood sample will be stored for genetic tests related to the risk of COVID-19. All genetic testing will be anonymized so it cannot be traced to your personal details, however, your DNA is unique so can never be truly anonymous.

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

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

Will there be any financial cost or compensation to me?

There will be no payments for your participation.

Who is organising and funding the research?

The trial is sponsored by the University of Oxford and funded by a grant from the Wellcome Trust. Researchers will pay the participating hospitals for conducting the trial.

Who has reviewed the research?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by Oxford A Research Ethics Committee.

List of Site Study Team 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 the site study 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 site study staff by telephone as below.

Name: *<<INSERT SITE STUDY TEAM CONTACT>>* *Name:*

Telephone number: *Telephone number:*

Confidentiality

Your name will not be in any report or on any sample being shipped away from the hospital. We will not share identifiable personal information with anyone outside the study.

No one other than the site study team, authorised personnel from the study sponsor, monitor, and regulatory authorities such as the Medicines and Healthcare products Regulatory Agency (MHRA) are allowed direct access to personally identified medical records.

Your personal data will be stored in Oxford by Oxford University to permit data collection from your medical and other health-related records including, for example, via linkage with NHS Digital, the Office of National Statistics, and GP records for up to 15 years after your enrolment. This will permit us to understand consequences and costs of treatment in the longer term.

When the study is completed, we will combine the de-identified test results with those of the other participants in other countries, 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

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford is the data controller and is responsible for looking after your information and using it properly.

We will collect and use your personal data submitted to us online, by email, on paper or face-to-face, in accordance with the General Data Protection Regulation (GDPR) and associated data protection legislation.

We will be using information from you and your medical records, NHS Digital and other central NHS registries in order to undertake this study and will use the minimum personally-

identifiable information possible. We will keep identifiable information about you for 6-12 months after the study has finished.

The site study team will use your name and contact details, to contact you about the trial, and will use your personal details to obtain your health records in order to determine whether the trial medication reduces the severity of COVID-19 symptoms. They will keep identifiable information or research documents with personal information, such as consent forms, securely for five years after the study has finished.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at:
https://compliance.web.ox.ac.uk/individual-rights

You can find out more about how we use your information by contacting the UK Chief Investigator, Professor Martin Llewelyn on 01273 876671.

Thank you for reading

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Informed Consent Form - UK
Study of chloroquine/ hydroxychloroquine and coronavirus disease (COVID-19) in the healthcare setting

Site Code: |__|__|__|__|__| Participant ID. Number: |__|__|__|__|-|__|__|__|

Name of Researcher:	**If you agree, please initial box**
1. I have read the participant information sheet (dated..... version.....) and have had the opportunity to ask questions, and any questions I have asked have been answered to my satisfaction;	
2. I understand that I can withdraw or stop taking part in the research at any time without affecting further healthcare to which I am entitled;	
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by members of the site study team and individuals from University of Oxford, the host NHS Trust, from regulatory authorities and Monitors where it is relevant to my taking part in this research and that this activity may take place outside of the NHS setting. I give permission for these individuals to have access to my records;	
4. I understand that I should seek medical advice if I become unwell during the study, particularly if I have diabetes, renal disease, cardiovascular disease, hypertension, hyperlipidaemia or smoke;	
5. I understand that I must stop the study medication if I am diagnosed with COVID-19 and need to be hospitalised;	
6. I give permission for the site study team to contact my GP if I become unwell, informing them of my participation and requesting information about any illnesses, including any tests or treatments that are performed during my participation in the trial;	
7. I allow the investigators to use my personal information as described in this patient information sheet for the purposes of this research;	
8. I give permission for linkage to my medical and other health-related records, and for long-term storage and use of this and other information about me, for health-related research purposes;	
9. I understand that I should not self-medicate with chloroquine or hydroxychloroquine during the study;	

10. I understand I should inform any medical professional prescribing medications to me during the trial period that I am taking study medication;	
11. I agree to provide samples as described in the information sheet and give permission for long-term storage and use of my blood samples for health-related research purposes, and consider these samples a gift to University of Oxford and I understand I will not gain any direct personal or financial benefit from them;	
12. I agree to my blood undergoing genetic tests related to susceptibility or response to the COVID-19 infection and that the results of these investigations are unlikely to have any implications for me personally;	
13. I understand my samples may be shipped abroad for tests related to this trial;	
14. I understand that none of the results of my blood tests and viral swabs will be given to me;	
15. I consent to participate in this study	

_____	_____	_____
Name of Participant	*Date*	*Signature*
_____	_____	_____
Name of Person taking Consent	*Date*	*Signature*

**1 original for participant; 1 original for researcher site file; (If hospitalised) 1 copy for medical notes*