PRINCIPLE
Platform Randomised trial of INterventions against COVID-19 In older peoPLE

Platform Randomised trial of INterventions against COVID-19 In older people

PARTICIPANT INFORMATION LEAFLET

We would like to invite you to take part in a study about treatments for COVID-19 infection called PRINCIPLE.
Before you decide if you would like to take part it is important that you understand why we are doing this research and what it would involve for you.

Please take time to read the following information carefully and decide if you wish to take part.

You may like to talk to others, friends or family members about the trial. Please ask if there is anything that is not clear or if you would like more information.

University of Oxford
Nuffield Department of Primary Care Health Sciences
Primary Care Clinical Trials Unit
RCGP Royal College of General Practitioners Research & Surveillance Centre
UKRI Medical Research Council

EudraCT number:2020-001209-22

NHS

What is the purpose of the trial?

COVID-19

The risk of complications from COVID-19 is generally greater in people aged 50 years and older with underlying health conditions and in those aged 65 years and older. This new viral infection can lead to significant medical problems, hospitalisation, and sometimes death.

So far, there are no treatments that have been proven in clinical trials to be effective in treating COVID-19 infection. Most of the infections are being managed in the community and it is essential that we identify treatments that help to reduce the progression of the disease and therefore the need for hospital admission. An ideal treatment would be one that is safe, with few side-effects, helps prevent disease progression, and can be administered in the community.

The Trial

As yet, there are currently no known treatments for COVID-19 that have been proven to be effective. Our trial aims to evaluate potential treatments as they are identified. To be able to do this, we aim to test one or more suitable, potential treatments for COVID-19, as soon as they become available.

In the first instance, we will evaluate a drug called hydroxychloroquine. This is a drug that is well known and has been used for many years around the world for conditions such as Malaria and Rheumatoid Arthritis, but is not currently used to treat this kind of infection.

We want to make treatments that are proven to be effective as widely and as rapidly available as possible. However, we do not want to give people medication that does not work, and may simply put them at unnecessary risk of side effects.

At the moment we really do not have enough information about whether any benefits from taking this drug outweigh any possible harms from the drug. So we do not know yet if this drug does work for COVID-19, and that is why we urgently need to do a proper trial so we have the information we need to guide the provision of best care for all.

Aim

We aim to find out whether selected treatments given to those at higher risk of becoming more ill when they are infected with COVID-19 helps reduce the need for hospitalisation and the length of stay required, helps people recover quicker and get fewer complications.

All people included in the study will be provided with a test for COVID-19, some will receive the medication we are testing and some will be allocated to current usual care without the medication we are testing.

Can I take part?

We intend to recruit at least 3000 people to the trial.

To take part, you need to be experiencing symptoms that are likely to be caused by a COVID-19 infection - a continuous cough and/or a high temperature. A high temperature means you feel hot to touch on your chest or back (you do not need to measure your temperature). A new, continuous cough means coughing a lot for more than an hour, or 3 or more coughing episodes in 24 hours (if you usually have a cough, it may be worse than usual) You need to have had these symptoms for **fewer than eight days.**

You also need to be **aged 50 to 64, with at least one of the following conditions:**

∗ • weakened immune system due to a serious illness or medication (e.g. chemotherapy)

• heart disease

• asthma or lung disease

• Diabetes not treated with insulin

• liver disease

• stroke or neurological problem

Or you can take part if you have symptoms of COVID-19 and are **aged 65 and over.**

Participants should not be taking any other medications other than their usual prescribed medication and medications prescribed in the study.

Do I have to take part?

Participation is entirely voluntary. It is up to you to decide whether to take part in the trial or not. A decision not to take part will not affect the standard of care you receive from the NHS in any way, now or in the future.

What will happen to me if I take part?

You will visit our website if you experience symptoms of COVID-19. The information on the website is the same as the information in this leaflet. Once you have read it, if you are interested in taking part, we will ask you to complete a short online form to see if you are eligible. If you would like to call us to discuss the trial before agreeing to take part, then you can contact us using the contact details on page 15.

Informed Consent

If we think you are eligible to participate in the study, you will be asked to complete an online consent form. Instructions on how to fill out the form will be provided, so you will know what to do. You will be able to download and keep a copy of your informed consent form.

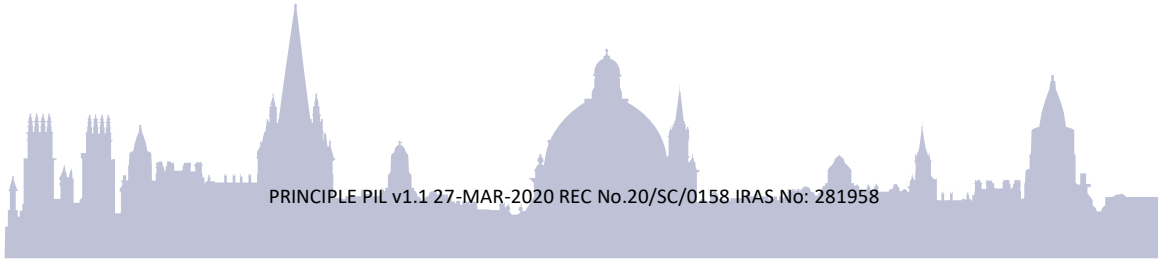
Initial Questionnaire

Then, you will be asked to complete a short questionnaire giving some details about you and the symptoms you have been experiencing. We will also collect some contact details such as your name, email address and telephone number. We will also ask you to provide details of a Trial Partner. This could be a relative, spouse, friend or carer, if such a person is available, who we will contact for information about you if we are unable to get hold of you for whatever reason

Letting Your GP Know

Once you have completed the informed consent and additional questions the website will notify the trial team and your GP with this information. A qualified medical practitioner will then check that there are no other medical reasons why you cannot participate.

If we find that you cannot participate, you will be sent an email to let you know. If you are able to take part in the trial, our computer system will randomise you to let us know which group you will be in. There is more information on this in the next section.



What will happen to me if I take part? Flowchart.

You may receive a text from your practice with a link to this participant information sheet, be told about the study by another health care provider, by the trial team or you may be made aware via national media coverage. You then let us know you are interested in taking part by completing the online form you are directed to. The form will ask you some questions about your health and your symptoms. You will also complete a consent form to say that you want to take part.

We will then ask a qualified medical practitioner to confirm that there are no medical issues to stop you from taking part.

After this, our computer system will allocate you at random (like rolling a dice) to receive either:

- Standard Care as advised by the NHS plus Trial Treatment or
- Standard Care as advised by the NHS

Neither you, your GP or the trial team can choose which group you will be allocated.

Follow-up

You will receive a swab kit and instructions of how to take your own sample. We will also tell you how to post the sample to the labs. If randomised to the trial treatment group, you will be provided with the drug which you will be asked to take for the required number of days.

You will also be asked to answer some questions each day online for up to 28 days telling us about any symptoms you might be experiencing and how well you are feeling. We will ask you to complete this diary online, if we don't receive the information from you, we will call you to remind you to answer the questions.

During the follow up period we will also ask that you, or someone close to you notifies us if you are admitted to hospital.

Randomisation

The final part of the process will tell you whether you will receive standard care (which includes a swab) or standard care plus the trial treatment (includes a swab). You will be randomly allocated (like rolling a dice) by our computer system to one of these groups and neither you, your GP or the trial team can decide which group you will be in.

You will receive an email to let you know which group you have been allocated to; your GP and the trial team will also receive this email.

Swab

Everyone who takes part in the trial will be asked to take two swabs, one from their nose and one from their throat. You will instructions on how to take your own sample at home using the swab kit. We will also tell you how to post the sample to the labs using the envelopes we provide.

You will be asked to send the swab to Public Health England using the packaging we provide. The swab will confirm whether or not you have COVID-19 and the result will be sent to your GP.

Public Health England (PHE) may keep the specimen for up to 5 years, following their own approved processes.

Trial Treatment

If you are randomised to the standard care plus trial treatment group, arrangements will be made for the drug to be delivered to you or you may collect/nominate an individual to collect the drug from a local pharmacy, or local GP. You will be told exactly how you will receive the medication. You will also receive instructions on how to take it and for how long.

Should your condition worsen at any time during the trial, you should not contact the study team but contact your GP or other usual services that are open to you.

Follow-Up

You will receive a text message from us to ask you to complete questions relating to your symptoms and how well you feel every day for up to 28 days after you start the trial. This will be an online daily diary. If the trial team don't receive your daily diary answers online, they will text or telephone you on day 7, day 14 and day 28 of the follow up period and ask you a brief set of questions over the phone.

What happens if I am admitted to Hospital?

It is important that we know if you are admitted to hospital at any point during the 28 day follow up period. We need to know this whether or not you are taking the trial medication. We will give you a card that you can carry to let other healthcare professionals know that you are taking part in this trial, it is also really important that someone close to you knows that you are taking part in the trial, then if you are admitted to hospital, they can use the details on the card to let us know.

We may also access your medical records and data held about you in central NHS registries and databases (including NHS Digital, Public Health England, other equivalent bodies, and genetic or other research databases if you have provided samples to them) to collect information on any hospital admission that you may have during the follow up period

What are the possible disadvantages or side effects of taking part?

With any medicine, including ones that are already used within the NHS, there is a risk of side effects. For the treatment we are using in this trial, the common side effects (experienced by less than 10% of people who take the medication) are:

Hydroxychloroquine

* abdominal pain;
* decreased appetite;
* diarrhoea;
* headache;
* nausea;
* skin reactions;
* vomiting.

You will be able to tell us if you are experiencing any of these symptoms in your daily diary.

This medication occasionally causes blurred vision, which typically resolves once the medication is stopped. If you develop **any** problems with your vision, please stop taking the medication immediately, seek clinical advice, and do not drive or operate any heavy machinery.

This medication might lower blood sugar levels in some people. If this happens, you might feel hungry, sweaty, dizzy, have a faster or pounding heartbeat. If you develop these symptoms, please eat something sweet and seek clinical advice if the symptoms persist.

What are the possible benefits of taking part?

By taking part in this trial, you will be contributing towards the understanding of how we can treat COVID-19 and how the symptoms progress. This may or may not help to reduce the duration and severity of symptoms when people fall ill. All participants will also receive a swab, and be told if the swab is positive or not for COVID-19. We also hope to reduce the burden on the NHS.

At the moment, we really do not know if hydroxychloroquine is effective against COVID-19. The trial has been designed so that the results will be analysed not just at the end of the trial, but as the trial goes along. So as soon as we have an answer about the effectiveness of the first drug we are testing, hydroxychloroquine, we can make recommendations about best care.

Because we have designed the trial in such a way that the results will be analysed as it goes along, as soon as we get evidence that one arm is more effective, we will be able to allocate more people to the most effective arm of the study. In this way more people in the trial will have a greater chance of getting the most effective trial treatment. If it turns out that the first drug we are evaluating, hydroxychloroquine, is more effective than usual care, then this will become the standard of care in the trial, and any new drug added into the trial will be compared against it.

What will happen if I do not want to continue with the trial?

If you decide to take part, you can still withdraw at any time without giving a reason. Information collected up to that point will still be used.

The swab sample that you provide and send to Public Health England will still be processed and stored for up to five years, according to their standard processes.

If you wish to withdraw from the trial, please contact the trial team using the contact details on page 15. The decision to withdraw will not affect the standard of care you receive from the NHS in any way, now or in the future.

Expenses and Payments

You will be reimbursed for your participation through gift vouchers worth a total of £20. You will receive the voucher at the end of your follow up period, once we have received your completed symptom diary. If you would normally pay for your prescriptions, we will increase the calue of the voucher to £30, in order to offset the cost of the prescription charge.

What if there are any problems?

If you have any questions about this trial, please contact the Trial Manager (See Page 15 for contact details).

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 trial.

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 trial, you should contact the trial team on principle@phc.ox.ac.uk or 0800 138 0880 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 to my data?

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. Responsible members of the University of Oxford may be given access to the trial data for monitoring and/or audit of the trial to ensure that the research is complying with applicable regulations.

We will be using information from you and your medical records and data held about you in central NHS registries and databases (including NHS Digital, Public Health England, other equivalent bodies, and genetic or other research databases if you have provided samples to them) in order to undertake this trial and will use the minimum personally-identifiable information possible. We will keep identifiable information about you for up to six months after the trial has finished. This excludes any research documents with personal information, such as consent forms, which will be held securely at the University of Oxford for 20 years after the end of the study.

Berry Consultants may assist with the statistical analysis for this trial and we will have to share the trial data with them in order for them to do this. The company is based in the USA, however no identifiable data will be given to them during this process.

The Royal College of General Practitioners Research Surveillance Centre may be used in order to gather data you haven't completed in your daily diaries. Data collected will include participant identifiable information and will be accessed at the University of Oxford according to PC-CTU Information Governance policies and GDPR. Data will only be held for the duration for which its required, this will be reviewed annually.
If we use a courier or home delivery service to provide you with trial materials, we will provide them with your name and address. These companies will use and store your data in accordance with GDPR.
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 principle@phc.ox.ac.uk

What if relevant new information becomes available during the trial?

Sometimes during the course of a research project, new information becomes available about the treatment that is studied.

If this happens, the trial team will tell you about it and discuss with you whether you want to continue in the trial or not.

If you decide to continue you may be asked to sign an updated consent form.

What will happen to the results of the trial?

Results will be published in scientific journals, presented at scientific conferences, and published on the Oxford University departmental website. It will not be possible to identify you in any report, publication or presentation. If you would like to receive copies of any publications arising from this trial, please contact the trial team (details are on page 15).

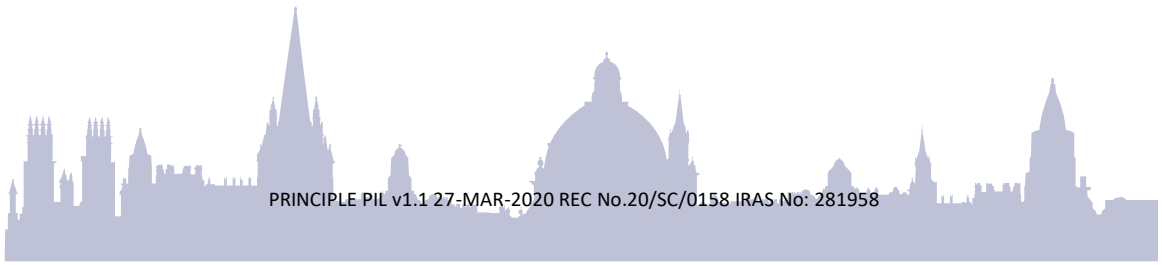
Who is organising and funding the research?

Funding has been provided by UK Research and Innovation/Medical Research Council. PRINCIPLE has been set up by the Primary Care Clinical Trials Unit at the University of Oxford.

Who has reviewed the trial?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee (REC). The REC is there to protect your safety, rights, wellbeing and dignity. This trial has been ethically reviewed and was approved by the South Central - Berkshire Research Ethics Committee.

This trial has also received approval from the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA regulates the use of all medicines in the UK.



Thank you for taking the time to read this information leaflet and considering taking part in this trial.

If you would like any further information about this trial, you can contact the trial team here:

Trial Address:
PRINCIPLE Trial
Nuffield Department of Primary Care Health Sciences
Radcliffe Primary Care
Radcliffe Observatory Quarter, Woodstock Road
Oxford
OX2 6GG

Trial Team:
Tel. 0800 138 0880

Trial Email Address:
principle@phc.ox.ac.uk