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.

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.

We will evaluate drugs that are well known and have been used for many years around the world.
Please see Appendices for drug specific information and the known side-effects.

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 these drugs outweigh any possible harms from these drugs. So, we do not know yet if these drugs do 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.

We aim to test as many people as possible included in the study for COVID-19, some will receive the trial treatment 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 new continuous cough - this 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) and/or a high temperature - this means you feel hot to touch on your chest or back (you do not need to take your temperature). You need to have had these symptoms for **fewer than 15 days.** The study is for people with ongoing symptoms. People who feel they are already well on the way to recovery should not take part.

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 or high blood pressure
- 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.**

You should continue to take your usual prescribed medicines if you join 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 do not have internet access or would like to call us instead, then you can contact us using the contact details on page 12

Informed Consent

If we think you are eligible to participate in the study, you will be asked to complete a consent form online or by telephone. 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. So a Trial Partner is someone who you know who might be able to help you with the study. A Trial Partner does not have to live with you, but you just need to be in regular contact with them.

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, we will let you know by email or phone. 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.

Randomisation

The final part of the process will tell you whether you will receive standard care (which includes a swab, if available) or standard care plus the trial treatment (includes a swab, if available). 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 or phone call to let you know which group you have been allocated to; your GP and the trial team will also receive this email.

Swab

We hope to be able to offer swab tests for the COVID-19 coronavirus to everyone who takes part in the trial. This will be a nose and/or a throat swab. If we have swabs available, we will ask you to provide a swab at the start of the trial, and then again 5 days later.

However, there is a worldwide shortage of swabs so we may not be able to offer swab tests to all who take part in the trial. If you are offered a swab, you will be given instructions on how to take your own sample at home using a swab kit. We will also tell you how to post the sample to the labs using the envelopes we provide. If you are not able to get the swab to a post box, then store it in a fridge and post it when you are able to do so.

You will be asked to send the swab to Public Health England or another central laboratory service using the packaging we provide. The swab aims to give an idea of whether you have COVID-19, and the result will be sent to your GP. The swab test for COVID-19 has a high *false negative* rate and so although the swab result may be negative, you may still have COVID-19 and we advise that you continue with the medication regardless of the result. Public Health England (PHE) may keep the specimen for up to 5 years, following their own approved processes.

Blood test

We are also asking everyone in the study for their consent to be contacted once their symptoms have passed, to have a blood test for COVID-19 coronavirus. You do not have to agree to be contacted about a blood test to take part in the trial. Even if you agree that we can ask you to have a blood test, you will be able to say no at the time if you don't want one.

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 also receive instructions on how to take it and for how long and asked to confirm receipt via text or telephone call. 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 2, 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, so that 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 will happen to me if I take part? Flowchart.

You may receive a text or letter 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 clinician 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 should receive a swab kit if available and instructions of how to take your own sample at the start of the trial and possibly on day 5. 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.

Optional Follow-up

We are planning to interview a group of participants after the main trial. This is optional and you will be able to confirm on the consent form whether you are happy to be contacted by the research team. If you agree to be contacted, the research team will contact you with details of the interview in approximately 28 days. You can then decide whether you want to take part or not.

We are planning to test all participants for COVID-19 coronavirus infection from a blood sample if a suitable test becomes available.

This is optional, and you will be able to confirm on the consent form whether you are happy to be contacted by the research team. If you agree to be contacted, the research team will contact you with details of the blood test within six months of completing the study. You can then decide whether you want to take part or not in the blood test. You can still take part in the trial even if you don't want to give a blood sample.

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.

Please see Appendices for details of the side-effects common to each drug.
You will be able to tell us if you are experiencing any of these symptoms in your daily diary.

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. We hope that all participants will receive a swab (based on worldwide availability), and be told if the swab is positive or not for COVID-19. We also hope to reduce the burden on the NHS. This may not always be possible, due to supply issues.

At the moment, we really do not know if is the trial treatments are 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 a drug we are testing, 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 one of the first drug we are evaluating, 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 12. 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.

What if there are any problems?

If you have any questions about this trial, please contact the Trial Team (See Page 12for 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, Host Organisations, Sponsor auditors, and the Medicines and Health Care Products Regulatory Authority, 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 of 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 12.

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 xxx 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 xxxxxx

Trial Email Address:

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