

PRINCIPLE Trial Newsletter: April 2020

A warm welcome to the PRINCIPLE Trial of treatments for COVID-19 in the community.

PRINCIPLE is one of only three national priority trials, and is the only one that is being done in primary care.

Together, we have an incredible opportunity for general practice to make a unique and hugely important contribution to the evidence-base that supports care in the community for this terrible condition. Our goal is to identify treatments that are effective in helping people at higher risk of complications recover quicker, and reduce the need for hospital admission. PRINCIPLE is a 'platform trial', which means that the master protocol allows treatments to be replaced or added in as the trial goes on, and we certainly plan to test more than one intervention. The first drug we are evaluating is hydroxychloroquine.

Our first newsletter outlines some important changes we are making to the trial.

With best wishes,

Professor Christopher Butler and the PRINCIPLE Trial Team – University of Oxford

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About hydroxychloroquine

A quick word about this drug: hydroxychloroquine is considered to stand the best chance, based on current evidence, of making a difference early on in the disease course.

Therefore we urgently need to know whether it improves outcomes for patients treated in primary care, before they require hospitalisation.

It has a long history for treating acute malaria, for malaria prophylaxis, and treatment of connective tissue disorders. It has a generally benign side-effect profile, and very few problems have been reported from many hospital-based clinical trials of COVID-19.

However, there has been publicity about trial withdrawals and reports of adverse effects from the drug chloroquine, which although related to hydroxychloroquine, has a very different side-effect profile.

A group of researchers from across the University of Oxford have recently reviewed data from the medical records of 950,000 patients who had previously taken hydroxychloroquine and have concluded that it is safe for short-term use.

You can read more about that research here:
<https://www.ndorms.ox.ac.uk/news/oxford-led-international-research-finds-hydroxychloroquine-safe-in-over-130-000-patients>

Patient eligibility update

We have recently just randomised our 150th patient, congratulations to all involved. This is a good start, and below are suggestions as to how we can include as many eligible patients as possible!

Template letter

We have provided a template letter which practices can now send to potentially eligible patients, in addition to the SMS/text message that is currently being used. Practices can choose to use either, or both, to alert eligible patients to get in touch if they develop symptoms of COVID-19.

NHS 111 and COVID-19 Hubs

Practices can also check for suitable patients from NHS 111 or COVID-19 Hub notifications, if patients with COVID-19 symptoms have used these services.

Nursing and care homes

Lastly, we hope to recruit residents of nursing and care homes who have capacity to provide consent for themselves. So do let care home staff know about the study when in contact with them, and when taking calls from care homes, please consider whether any residents that are discussed could be randomised.



Duration of symptoms extended to 2 weeks

Until now, we have required patients to have been sick for no longer than seven days prior to inclusion. However, our Trial Steering Committee felt that people who have been sick for longer might well benefit from treatment in primary care, so we need to know if the treatment works in people who have been sicker for longer as well.

We have therefore extended the permissible duration of symptoms prior to the eligibility check to be two weeks.



Swab availability

There is a worldwide shortage of swabs, and in some cases, we are not able to provide our study participants with the opportunity to have a diagnostic swab.

We have made this clearer in the Patient Information Leaflet. Some people prefer not to be swabbed, while others might not wish to participate unless they are swabbed. If there are no swabs available, then we should make this clear to patients before they finally agree to participate.



Blood test

We are now asking patients on the consent form to give us permission to approach them about providing a blood test within six months of their time in the study.

We are hoping that soon we will have a reliable test that will tell us who really was, and was not, positive for COVID-19. At the moment, our primary analysis will include everybody randomised with 'COVID-Like-Illness'.

Given that people are currently being treated in primary care on the basis of symptoms alone, this approach will provide very useful information. However, we will also do an "intent to treat infected analysis," including just those patients who we know for sure had COVID-19 illness.



Supplementary summary pictorial Patient Information Sheet

We are also launching a summary pictorial Patient Information Sheet that we hope will make it easier for people who might be ill and frail to understand the study, and therefore provide even better informed consent.



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Clinical Trials Unit

You have received this update because you are a registered practice with the PRINCIPLE Trial, which is managed by the Oxford University Primary Care Clinical Trials Unit.

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