



## PRINCIPLE Trial Newsletter 2: 17<sup>th</sup> June 2020

### *Current study numbers*

[www.principletrial.org](http://www.principletrial.org)

As of the 17th of June, we have **850** general practices open to recruitment and **534** patients have been randomised to the study! We are open to recruitment in all four UK administrations, and are a truly national study.

### *The Hydroxychloroquine arm is paused*

The regulators asked us to pause recruitment into the hydroxychloroquine arm on the 22nd of May. No further trial participants have been randomised to receive hydroxychloroquine since that time. The trial's Data Monitoring and Safety Committee has scrutinised our data for any safety signals, and we are considering our response to the Medicine and Healthcare Products Regulatory Authority. In the meantime, we are working up proposals for new potential treatments to evaluate in the trial.

### *The current comparison is between usual care and usual care plus azithromycin*

Perhaps the commonest dilemma that primary care clinicians face when treating somebody with Covid-19-like-illness is whether or not to prescribe an antibiotic. Despite an absence of evidence, clinicians often prescribe antibiotics, usually doxycycline, for COVID-19 like illness. The PRINCIPLE trial can fill this evidence-based vacuum about the benefits or otherwise of doing this. It is full steam ahead in answering the Covid-19 'antibiotic question'.

### *Why azithromycin?*

- It is anti-inflammatory
- Has anti-viral properties
- Treats bacteria causing community acquired pneumonia, which is a common cause of deterioration and deaths in people with Covid-19-like-illness.

***Don't prescribe, please RANDOMISE!***

Sadly, many patients are not eligible for the trial because they are already on an antibiotic. Unless there is a definite, urgent indication for antibiotics, we're asking clinicians to randomise patients into the trial before prescribing an antibiotic, so that we can ascertain potential benefit and harms from antibiotic treatment for COVID-19 in the community.

### ***Contraindications to hydroxychloroquine removed from eligibility assessment***

We have now removed contraindications that are specific to hydroxychloroquine, such as retinal disease, and treatment with insulin. Such patients can now be randomised into the trial, provided they don't have contraindications to azithromycin.

### ***Let us give every eligible patient the chance to contribute to PRINCIPLE***

Although, mercifully, the pandemic is waning rapidly, **yesterday there were 1015 new cases in the UK**. Giving those who are potentially eligible amongst this number the opportunity to contribute to the trial would be of great service to them, and a great service to our clinical discipline!

- Consider proactively contacting patients when your practice receives notification of a **positive result from a test centre** in someone over 50 with comorbidities, or is over 65.
- Consider asking about cases of Covid-19-like-illness and reminding staff about the study when taking calls from **care homes**

### ***The long game***

The PRINCIPLE trial has led the world in primary care trial design and delivery in many innovative ways: our infrastructure has taken a lot of hard work, creativity, commitment, and resource to set up and refine. The potential relevance of our platform study is not only for COVID-19 like illness: the platform could also be used to evaluate treatments for other viral illnesses such as influenza, respiratory syncytial virus, and any new or emerging respiratory pathogen. PRINCIPLE seeks to remain relevant over the longer term: COVID-19-like-illness will not disappear completely any time soon. Should there be a second wave, we need to be ready to implement research immediately. We therefore continue to consider new interventions, and refine our processes to keep it relevant.

One of the beauties of our flexible, platform trial design, is that interventions can be replaced or dropped, and new ones added in: use of existing control participants adds power and efficiency to the study.

This National Urgent Public-Health priority platform trial for Primary Care is thus being future-proofed, so it can continue to serve our discipline and our patients, and remain relevant as new interventions are brought forward for evaluation. We will continue to recruit even while there are low levels of COVID-19 activity, and we will be super-ready for any second wave.

### ***Thank you!***

Finally, thank you to all of the practices, LCRNs, and 111 for your amazing creativity and hard work in contributing to the PRINCIPLE trial, and for your help in finding treatments that could benefit the people we care for!

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NUFFIELD DEPARTMENT OF  
**PRIMARY CARE** Primary Care  
HEALTH SCIENCES 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.*

