Platform Randomised controlled trial of point of care Diagnostics for Enhancing the quality of aNtibiotic prescribing for Community acquired acute respiratory tract infection in ambulatory care in Europe (PRUDENCE Trial)

ADULT PARTICIPANT INFORMATION LEAFLET

We would like to invite you to take part in a study (which we are calling PRUDENCE) which will investigate whether General Practitioners (GPs) find specialised diagnostic tests helpful when deciding how to treat patients with community acquired acute respiratory tract.
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?

The Problem

The development of antibiotics (such as penicillin) was a major breakthrough in medical science. Antibiotics are used to treat illness caused by bacteria. Development of these medicines meant that illnesses, like pneumonia, which were once often fatal, could now usually be successfully treated. But the effectiveness of antibiotics is now decreasing because they are being overused. Bacteria that are being exposed to antibiotics can change genetically, making it harder for the antibiotics to work against them. As a result, "superbugs" are developing. We have no effective treatment for some of these "superbugs". The development of resistance to antibiotics is a major public health concern worldwide. Using antibiotics too often and for the wrong illness increases antibiotic resistance.

Diagnostic tests used when a patient first visits their doctor (point of care diagnostic tests), could help identify patients that will and will not benefit from antibiotic treatment, and lead to better use of the precious medicines. This is especially true for community-acquired acute respiratory tract infections (CA-ARTI), such as sore throat or cough, the commonest acute reasons for antibiotics use in community care.

The Trial

The PRUDENCE Trial will test whether having a diagnostic test result available, when health care professions make a decision about antibiotic prescribing, results fewer antibiotics being prescribed without harming to patients. The trial will run in community care, including doctor's surgeries, paediatric centres or long-term care homes, in several countries and will last for about two years. We hope the results will improve care.

Aim

The aim of PRUDENCE is to determine if having a CA-ARTI diagnostic (CA-ARTI-Dx) test result available when a clinician is considering, or intending to prescribe an antibiotic, leads to more appropriate prescribing decisions, without causing harm to patients.

Can I take part?

To take part, you need to be presenting to primary care with cough, which started less than 28 days ago, or sore throat, which started less than 14 days ago. Your GP will also be considering or planning to prescribe an antibiotics for your symptoms. We intend to recruit approximately 2500

people to the trial.

Do I have to take part?

Participation is 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 health care you receive in any way, now or in the future.

What will happen to me if I take part?

Informed Consent

You will be given time to think about whether you would like to take part in this study, you will be able to ring friends or family members if you wish to discuss taking part with them. If you would like to take part, you will then be asked to complete a consent form . A member of the research team will go through the consent form with you. You will be able to keep a copy of your consent form.

Initial Questionnaire

A member of the clinical team will complete a short questionnaire including 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 so that the trial team can contact you and ask you questions about your recovery.

COVID-19 Test

Due to the current COVID-19 pandemic we will include a test for coronavirus. This test will only be used if the test is available at the time of the study, if the COVID-19 pandemic is still ongoing and if you meet the criteria below.

If you have had symptoms for 5 days or less, we will test you to see if your illness is due to the coronavirus SARS-CoV-2 causing the COVID-19 worldwide pandemic. This test will involve taking a swab from your nose. The test will take 15 minutes. If it is positive your doctor will treat you according to the current NHS guidelines but you will not be able to continue with this study. If the test result is negative you can continue into the next step of the study.

If you have had symptoms for more than 5 days the test will not be able to accurately confirm if you have the virus so you will continue onto the next step of the study without having this test.

Randomisation

Then the clinical team member will tell you whether you will receive usual care (without a diagnostic test), or a diagnostic test. You will be randomly allocated, like rolling a dice, by our computer system to one of these groups and neither you, your GP nor the trial team can decide which group you will be in.

Usual Care

Clinicians will provide the treatment and advice for managing your illness as they would normally do i.e. as if you were not taking part in the study.

Diagnostic tests

If you are randomised to the diagnostic test group, a member of the clinical team will take a sample from you. This could be a swab (a small bit of cotton wool on a stick) from your nose or mouth, or a pinprick of blood from your finger. The clinical team member will perform the diagnostic test, which varies according to the nature of the test but is usually no more than 20 minutes. More information on the diagnostics tests that are being used in this study are given at the back of this leaflet.

Once the test result is ready, your doctor will discuss their recommended treatment and offer any additional advice for managing your illness.

Samples

Samples will only be taken from you for study purposes if you are randomised to having a diagnostic test. The samples will be handled and processed according to the diagnostic test instructions and any leftover sample will be destroyed.

Follow-Up

The clinical team will give you a paper diary or link to an online diary as you prefer. They will go through the diary with you, explain how to complete it and answer any questions. You will be asked to complete the diary for 14 days starting on the day you consulted with your doctor for this illness. It should take no more than five minutes to complete the diary each day.

The diary will include questions about your illness, recovery, healthcare use, out-

of-pocket expenditure, time off work or school, quality of life, satisfaction with the initial consultation, beliefs about the need for antimicrobials for respiratory symptoms and your

thoughts on managing symptoms in the future. If you have completed a paper diary you will be provided with a stamped addressed envelope to return it to the trial team once complete. This data will then be entered into the online database by the research team. If you complete your diary online this will automatically be entered into the online database each day.

If the trial team have not received your completed daily diary after 14 - 17 days, they will ask you a brief set of questions, similar to those asked in the diary, by telephone. You will also be called on or just after day 28, the last day of the follow up period, to ask a brief set of questions about the final two weeks of your illness/recovery. Each telephone call will last no more than five minutes. We will make up to three attempts to call you on each occasion.

The trial team may send you text reminders to complete the daily diary. However, you will have the opportunity to opt out of this if you wish.

We may access your medical records to collect information should you be hospitalized during the follow up period.

What will happen to me if I take part? Flowchart

1
- You contact your general practice/healthcare provider with symptoms of a cough or sore throat and the consulting clinician is considering or has decided to prescribe you antibiotics

2
- Your eligibility to the study is checked
- If eligible, you are told all the details of the trial and given the opportunity to ask questions
- If you are happy to take part you will provide informed consent

3
- A member of the clinical team will complete a short questionniare by asking you some questions about your illness and review your medical history
- If you have had symtpoms for 5 days or less you will have a test for the coronavirus SARS-CoV-2.
- If positive for COVID-19 you will be managed according to the current NHS guidelines but will not be able to continue with the study
- If you test negative or have had symtpoms for more than 5 days you will conitnue to randomisation

4
- You will be randomly allocated to one of the followng:
- 1) Usual care
- 2)CA-ARTI diagnsotic test

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- If you are randomised to usual care the consulting clinican will complete the questionnaire and provide any treatment and advice for managing your illness following best practice and national guidelines
- If you are randomised to a diagnostic test, a sample will be taken required for the diagnostic test and the test will be performed according to the manufactuers instructions. Once the test result is available the consulting clinician will complete the study questionnaire and provide any treatment and/or additional advice for managing your illness.
- You will be provided with a paper or online 14 day diary and explained how to complete it.

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- At home you will complete the daily diary, this should take no more than 5 minutes each day
- We will ring you on day 14 to 17 if you have not completed or returned the diary
- We will ring you on or just after day 28 to ask you questions about your illness/recovery over the past two weeks

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- Optional: You may be contacted to take part in an interview about your experience in this trial and your throughts on the use of diagnsotics tests in the management of your symptoms

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

If you are randomized to usual care plus a diagnostic test, a biological sample will be taken. Depending on what type of sample, some discomfort may be felt. The consultation may take longer than it would normally take without a diagnostic test.

What are the possible benefits of taking part?

By participating in this study you may not personally benefit but you will help doctors learn more about which diagnostic tests could help them make better decisions when treating people with cough or sore throat. You will be helping with research that may lead to a more personalised approach to antibiotic prescribing, one that better targets antibiotics to patients who are likely to benefit, and directs alternative, non-antibiotics treatments to patients who are unlikely to benefit.

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.

If you wish to withdraw from the trial, please contact the trial team using the details below. A 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

We will be unable to provide expenses or payments as part of this study. Costs for parking at the study visit may be incurred but that these will not be reimbursed.

What if there are any problems?

If you have any questions about this trial, please contact the Trial Team (See Page 9 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 valuedx@phc.ox.ac.uk or 01865 289296, 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?

General Data Protection Regulations (GDPR) require 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, authorised people within the ValueDx project and Sponsor auditors 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 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 by the University of Oxford for up to 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 personal identifiable data will be given to them during this process. De-identified data (this data will not contain any personally identifiable information) obtained from your samples may also be used for commercial purposes.

GDPR provides you with control over your personal data and how it is used. However, when you agree to your information being used in research, 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 valuedx@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 intervention 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. In addition, the information will be used to improve guidelines for medical professionals. 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 9) or go to https://value-dx.eu/.

Who is organising and funding the research?

Funding has been provided by Innovative Medicines Initiative 2 Joint Undertaking, a large funding body, jointly initiated by the EU and private companies. PRUDENCE has been set up by the Primary Care Clinical Trials Unit at the University of Oxford and is part of a larger European project called ValueDx: https://value-dx.eu/.

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.

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, you can contact the trial team here:

Trial Address:

PRUDENCE Trial

Nuffield Department of Primary Care Health Sciences

Radcliffe Primary Care

Radcliffe Observatory Quarter, Woodstock Road

Oxford

OX2 6GG

Trial Team:

Tel. 01865 289296

Trial Email Address:

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