Participant Information Sheet

DURATION UTI: Impact of duration of antibiotic treatment on symptoms, recovery and antibiotic resistance in adult women with urinary tract infections (UTIs): a randomised controlled trial

Can you help?

We would like to invite you to take part in our research study.

Before you decide, it is important that you understand why the research is being done and what it would involve for you. Please take time to read this information, and discuss it with others if you wish. If there is anything that is not clear, or if you would like more information, please ask us.

Why are we doing this study?

We aim to find the shortest length of time we can give someone an antibiotic when they have a urinary tract infection (UTI) and still be able to treat that infection effectively.

UTIs, which are infections of the bladder or the kidney, are among the most common infections treated with antibiotics and are far more common in women than men. Over four million prescriptions for UTIs are given to women in the UK every year. However, there is little evidence to help doctors decide how many days of antibiotic treatment are necessary. We think that one way to keep antibiotics working for patients and for the future is to reduce the amount we prescribe, so we need to use the shortest treatment duration which still ensures that the infection is properly treated.

Bacteria can develop ways to avoid being killed by antibiotics, this is called resistance. We want to find out whether taking less days of antibiotics reduces the chances of the bacteria becoming resistant. We will do this by looking at the impact of the length of treatment on the bacteria in the bowels and also by looking at the bacteria causing any UTIs which occur after starting in the trial. We will also be looking at the cost effectiveness of the different treatment durations and the impact on your quality of life. Your involvement in the study will last for 6 weeks initially with a final follow-up 6 months after you join the study, and we will access your medical record at the 6-month point.

It is important that we have data for the full 6 weeks and at the final 6-month point, **even if you are feeling better.** This helps us understand when you started to feel better and whether you are staying well or might need more treatment.

Why am I being asked to take part?

You have been invited to take part because you are aged over 18, and the healthcare professional you have come to see with your symptoms thinks you have a bladder or kidney infection, which should be treated with antibiotics.

Taking part in this research project will not stop you from taking part in other research if you would like to do so.

More information about taking part.

Do I have to take part?

No, taking part is entirely voluntary and will not affect your current or future NHS treatment.

What happens if I change my mind?

You will continue to receive follow-up care for your UTI as part of standard care.

You are free to change your mind at any time during the study, but any data or samples which have been collected whilst you have been in the study will be used for research as detailed in this participant information sheet.

If you were to lose your capacity (ability to give permission) during the study we would use information and samples you have already provided but not collect further information or samples. Once your data has been pseudo-anonymised and combined with other data, it will not be possible to withdraw it from the study.

What are the antibiotics I might be given?

These will be the normal antibiotics that are prescribed for bladder or kidney infection. For bladder infection you will either receive nitrofurantoin or pivmecillinam. If you are allergic to either of these you are still able to take part so long as you are able to take one of the two options. For kidney infection the options include but are not limited to: cefalexin, co-amoxiclav, cefadroxil, cefaclor or amoxicillin.

What will happen if I decide to take part?

You will complete an eligibility and consent form with your doctor or an appropriately trained researcher. We will not include patients who are pregnant in the trial, therefore your clinician will assess the risk of pregnancy before including you in the trial. As per standard care procedures, a pregnancy test may be performed if your doctor suspects that there is a possibility that you might be pregnant but unaware of it. If you have a kidney infection the doctor will decide on which antibiotic to prescribe according to local policies. If you have a bladder infection, a computer will allocate you to one of two different antibiotics called nitrofurantoin and pivmecillinam (If you are allergic to one of the antibiotics you will be allocated to the other).

All participants will be allocated by computer to one of the different antibiotic durations. You will have an equal chance of being allocated to any one of the different antibiotic durations. This process is called “randomisation” and allows us to study comparable groups and understand which antibiotic durations work best.

After randomisation you will receive an email with a link to a questionnaire, to answer a few questions about yourself and your infection. This provides important information for the trial on current symptoms and how you are feeling.

These different treatment lengths will range from 2 days through to 14 days, (where a day is a 24-hour period and may cover two calendar days). The number of days you take the antibiotics for might vary from the number of days of antibiotics your doctor might have chosen to give

you, but these are based on their own judgement and guidelines that are not based on good evidence, so aim of this study is to see which of these lengths of treatment is most beneficial. Your doctor will give you a prescription for this treatment in the normal way and you will either collect this from a pharmacy, or you will be provided treatment by your doctor depending on your type of infection.

All participants recruited in a GP surgery need to provide a urine sample for the research before starting their antibiotic. You will need to provide the surgery with this sample which they will send to our research laboratory.

If you are in hospital, your doctor may have already requested a urine sample. If so, we will access the results of this from your medical record and may collect a sample of any bacteria that were found.

You will be provided with a urine sample kit to take home with you by your GP or the team looking after you at hospital.

Optional Interview Sub-study

You can choose if you would like to take part in this additional sub-study. It involves being contacted by one of the researchers for an interview about your experience of being part of the research trial. This will give an overview of individual experiences and also be valuable when considering the design of future studies. You can still take part in the main trial if you do not opt in to this sub-study.

Optional Rectal/Faecal Swab Sub-study

You can choose if you would like to take part in this additional sub-study. The purpose of the study is to increase knowledge of the impact that over-prescribing antibiotics has on antibiotic resistance; in other words, the risk of bacteria becoming resistant to antibiotic treatments., In order to do this, we need to study the bacteria that live harmlessly in the intestine.

If you agree to participate in this sub-study we will ask you to take swabs (similar to a cotton bud) from either just inside your back-passage, (rectum), or from a sample of your poo (a faecal swab). This will be before you start your antibiotics, at 2 days after you finish your antibiotic treatment, at 6 weeks after you joined the study and finally at the 6-month point after you joined the study. These swabs are straightforward to collect and should cause only minor discomfort we will provide you with sample collection instructions, sample collection kits and pre-paid postage packs for sending the samples to our Oxford lab for analysis. The swabs will not be analysed immediately and the results are not given to your doctor, because they are for research only. In addition to the self-taken swabs, we will ask you some questions when you join the study, at 6 weeks after joining and finally at the 6-month point. Questions will include details on medications, diet, smoking status and recent travel. We may use your NHS number to access data held by the UK Health Security Agency to find out details of health care attendances and urine samples you have had sent for testing in the

year prior to and year after joining the study. Participation in this sub-study is optional and you can still take part in the main trial if you do not opt in to this sub-study.

Follow up

We will keep in regular contact with you for 6 weeks after you join the trial and then contact you once more at 6 months. We will:

- **Contact you daily for 14 days** with a link to a web-based symptom diary to see if you are managing to take your antibiotics, to see how your UTI symptoms are, to see if you have had to contact the doctor, hospital or pharmacist again or take any extra medication for your UTI. If your UTI symptoms are not improving, or are getting worse, you should seek further healthcare advice as you usually would and as you have been advised by your local doctor or nurse.
- **Contact you weekly after 14 days** with a link to the symptom diary. This will be up to and including the final diary at Day 42 (6 weeks after you join the trial). If you do not have any UTI symptoms, you will only need to complete a shorter questionnaire.
- **Contact you at Day 16** with a link to a short questionnaire about your current health status (for pyelonephritis participants only).
- **Ask you to collect a urine sample** two days after you have finished your antibiotic and post it to our Cardiff lab for analysis. We will send you a link to a short video that will guide you on how to use the urine sample kit and pre-paid postage pack provided to you by your recruiting site.
- **If you experience new or recurring UTI symptoms** which you contact a healthcare professional or a pharmacist about again, we will ask you to send the research team **another urine sample**. We ask that you send a urine sample each time this happens up to and including Day 42. Your urine sample pack includes two additional kits for this purpose.
- **At the end of 6 weeks and then also at 6 months** we will ask you to fill in a questionnaire about your symptoms and whether you have needed to re-contact a healthcare professional or needed further antibiotics. Your GP or research team will be asked to complete a review of your medical records at these time points as well. We will collect your NHS number in order to help with this.
- **Rectal/Faecal Swab sub-study** If you are taking part in the swab sub-study we will ask for samples before you start treatment, when you finish your treatment, at 6 weeks and at 6 months, and ask you to fill in a short questionnaire before you start treatment, at 6 weeks and at 6 months. We will use data held by the UK Health Security Agency to find out details of any health care attendances and urine samples you have had sent for testing for a year before and for the year after you joined the study.
- **Interview sub-study** If you choose to take part in this sub-study one of the researchers will contact you with more information, take your consent to be interviewed and arrange the interview.

What happens to my samples?

Your urine samples will be frozen and stored for further analyses relating to the study.

Study analyses will involve assessing the antibiotic sensitivity of the bacteria we identify in the urine samples in more detailed ways than are done in the routine microbiology laboratory.

In some instances, we will use a technique called DNA sequencing to read all the genetic code in the bacteria we identify. This is the same technique that is sometimes used to read human genetic code. Sometimes patients worry that this means we can read their genetic code. We use a computer system which automatically removes any human genetic code from our analyses to make sure this can't happen.

If you take part in the optional rectal/faecal swab sub-study, we will use DNA sequencing and similar techniques to look at all the bacterial DNA in the swabs you provide. The DNA sequencing may be performed by a commercial provider. Again, our computer systems make sure we only analyse bacterial DNA and not human genetic code. We will also ask for your permission to store these samples in a biobank at the end of the study. You do not have to consent to this.

We won't inform you of the results of these tests as they will not affect your care and are for research purposes only.

Optional consent for the use of your urine samples in other studies. If you consent to us keeping your samples after they have been processed for the DURATION UTI trial, we may use your samples in other ethically approved research projects, which may take place in hospitals, universities, non-profit institutions or commercial laboratories worldwide.

If you do not consent to the use of your urine samples in other studies, the samples will be destroyed within 12 months from the end of the trial. Please note that ongoing sample retention will require retention of your consent form until depletion, or destruction, of samples.

Who is paying for and running the study?

The study is funded by the National Institute for Health Research. The sponsor of the study is the University of Oxford and Dr Gail Hayward is the Chief Investigator.

Has anyone reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. The study has been approved by North East - Tyne & Wear South Research Ethics Committee.

Pros and cons of taking part

You will receive treatment for your UTI as per your randomisation allocation. As we do not know the best length of treatment for a UTI, we cannot say whether the number of days you are assigned to take an antibiotic is better or worse than any other. There is a risk that too short an antibiotic prescription might mean the infection is not fully treated; in this case, symptoms might get worse again and you should seek medical advice as you would normally. On the other hand, treatment for too long might increase the risk of bacteria becoming resistant to that particular antibiotic meaning the bacteria might not respond to treatment in the future. Having a longer course of treatment might also increase the side-effects you experience because of taking the antibiotics. We need to run this study to work out how many days of taking antibiotics is best when considering all these different risks and benefits together. This will benefit future patients who experience UTIs if we can show how many days of treatment is best.

If you normally pay the prescription charge then you will pay this as usual for the treatment you are randomised to in the trial and would need to pay again if you required further antibiotics at any stage. We will give you a £20 gift voucher to reimburse you for your input into the study, and to help cover these costs.

If you agree to participate in the rectal/faecal swab sub-study, you may experience some mild discomfort taking a back-passage (rectum) swab., However, this should not be painful and you have the option to take a swab from a sample of poo instead (faecal swab). We will provide you with instructions, which will guide you on how to use the sample collection kit provided correctly, thus reducing the risk of any discomfort. As part of study procedure, we will request you to complete an online questionnaire at each sample collection time point. The questionnaires include questions on anxiety/depression and self-care, which are sensitive and potentially embarrassing, though the risk of this is small. No identifiable personal data will be published, and staff will ensure that your anonymity and confidentiality is maintained.

The requests we make when you agree to take part in the trial are:

- **To take your antibiotics for as often and as long as you are asked to.** This is important so we can understand the impact of the different lengths of treatments.
- **To be in regular contact with us** as described in the 'Follow up' section of this information booklet.

Will my taking part be kept confidential?

Yes. You will be given a study number. Any information and samples you provide will be recorded against that number, not your name. Therefore, all information is pseudo-anonymised, as is any data we collect from your medical records.

All the study data is owned by the University of Oxford. It will be kept locked away or on secure computer servers in locked rooms with restricted access. Pseudo-anonymised data may be shared with other researchers for research purposes.

Responsible members of the University of Oxford, Brighton and Sussex Clinical Trials Unit (CTU), regulatory bodies such as Medicines and Healthcare products Regulatory Agency (MHRA) and the relevant GP surgeries, Pharmacies or NHS trusts may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

We, the University of Oxford, along with the laboratories at Oxford and in Cardiff, and the team at the Brighton and Sussex CTU will be using information from you and your medical records in order to undertake this study. Research is a task that we perform in the public interest. The University of Oxford, as the sponsor, is the data controller. This means that we, as University of Oxford researchers, are responsible for looking after your information and using it properly. We will be using information that you have given us and from your General Practice (GP) and Hospital medical records in order to undertake this study and will use the minimum personally-identifiable information possible. The Brighton and Sussex CTU will have access to the data of those participants recruited in secondary care to aid in their management of these participants.

The Specialist Antimicrobial Chemotherapy Unit (SACU), Microbiology Cardiff, Public Health Wales, University Hospital of Wales, Cardiff will have access to pseudo-anonymised data in order to process and analyse your urine samples.

For those who take part in the rectal/faecal swab sub-study, the Modernising Medical Microbiology research laboratory at the John Radcliffe Hospital, Oxford will have access to your pseudo-anonymised data in order to process and analyse rectal/faecal swab samples. These samples may be shared with a commercial company to perform the analysis. To label all participant samples, we will use a unique participant identifier assigned to each individual during enrolment into the study. This will mean the people performing the tests on the samples will not be able to identify who provided them.

For those who take part in the interview sub-study, a transcribing company will be given the audio-recording of your interview in order to fully transcribe this for the research team. Once the transcription company has returned the transcript, the researcher will anonymise it.

We at the University of Oxford and the Brighton and Sussex CTU will keep contact information about you for three months after the study has finished, unless you consent to be contacted for future research. In this case, we at the University of Oxford will keep your contact details for five years, stored separately from the study data on a secure university computer in the Department of Primary Care, University of Oxford. Even if you agree to us storing your contact details you do not have to take part in any of the future research projects, you are free to choose what projects to take part in. You can also request that these details are deleted at any time by contacting the study team.

We will also keep your electronic consent forms, these will be held securely at the University of Oxford separately from the main study database. We will store the pseudo-anonymised research data and research documents with personal information, such as consent forms, securely at the University of Oxford for 25 years.

If you have not been recruited by your GP Practice then your GP will be informed that you are taking part in this study by post or email, and provided with a copy of your signed consent form. A copy of the consent form from this study will be kept in your medical records for as long as those records are retained.

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

What will happen to the results of the study?

We will combine data from all the study participants, including your data, and publish the findings in journals and at conferences. You would not be identified from any report or publication placed in the public domain. You will be able to access a summary copy of the results after they have been published via the trial website: https://www.phctrials.ox.ac.uk/studies/duration-uti-trial

What if there are any problems?

If there is a problem or you have any concerns, you can contact the study coordinator (details on last page). 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 study. NHS indemnity operates in respect of the clinical treatment with which you are provided.

If you want to make a complaint

If you wish to complain about any aspect of the way in which you have been approached or treated in this study, or how your information is handled during the course of this study, you should contact the study team on duration@phc.ox.ac.uk, or you may contact the University of Oxford Research Governance, Ethics and Assurance (RGEA) team office on 01865 616480 or the head of RGEA on RGEA.complaints@admin.ox.ac.uk

The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study. If you wish to

contact the PALS team please contact <insert relevant NHS site phone number and email from the PALS website http://www.ouh.nhs.uk/patient-guide/pals.aspx>.

What will happen to my data?

Data protection legislation requires that we, the University of Oxford (whose legal name is The Chancellor Masters and Scholars of the University of Oxford), 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 sponsor for this study and is responsible for looking after your information and using it properly.

We will need to use information from your medical records, your GP, your hospital records and national datasets for this research project. We will share your information related to this research project with the following types of organisations: University of Oxford, Brighton and Sussex Clinical Trials Unit (CTU), regulatory bodies such as Medicines and Healthcare products Regulatory Agency (MHRA) and Research Ethics Committees, relevant GP surgeries, pharmacies or NHS trusts, UK Health Security Agency, central NHS records, and the laboratories taking part in the analysis of the samples.

This information will include your:

- NHS number
- GP details
- Date of Birth
- Trial ID number

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure by:

- Using secure storage systems
- Following strict data protection policies
- Complying with legal and ethical requirements

Your personal data will not be shared outside the UK.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study. We will keep your study data for the minimum period of time according to PC-CTU SOPs and as defined in the trial protocol.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. You have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records, your hospital and your GP. If you do not want this to happen, tell us and we will stop.

You can find out more aboutwe use your information by:

- asking one of the research team xxxxx
- sending an email to xxxx
- calling us on xxxx
- contacting the University's' Data protection officer data.protection@admin.ox.ac.uk
- looking at University's privacy notice available at **https://compliance.admin.ox.ac.uk/research-data**

If you would like to find out more about the use of confidential data in research, the HRA has developed a general information leaflet which is available at https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/templates/template-wording-for-generic-information-document/

Contact details

If you want to discuss the study, please contact the DURATION UTI team at: <duration@phc.ox.ac.uk > for PC participants or <insert local site details> for SC participants.

You can also visit the study website https://www.phctrials.ox.ac.uk/studies/duration-uti-trial for details about this study.