

# Alternatives to prophylactic antibiotics for the treatment of recurrent urinary tract infection in women

<b>Submission date</b> 18/05/2016	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 31/05/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 11/05/2022	<b>Condition category</b> Urological and Genital Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Most women experience infective cystitis (otherwise known as urinary tract infection or UTI) at least once in their life and some get repeated episodes which are uncomfortable and stressful; this is known as recurrent urinary tract infection (rUTI) and affects around 300,000 women each year in the UK. Giving long term low dose antibiotics is the most frequently used prevention for rUTI and although reasonably effective at suppressing the infecting bacteria, it has side effects and sometimes causes bacteria to become resistant to antibiotics. There are some alternative preventative options for rUTI that don't involve antibiotics but doctors are unsure how well they work and so tend mostly to advise antibiotics. The ALTAR trial aims to compare one such alternative non-antibiotic prevention for rUTI, a drug called methenamine hippurate, against the current standard of daily low dose antibiotic to see if the methenamine is at least as good at preventing UTI and has fewer side effects, particularly a lower chance of resistant bacteria developing.

### Who can participate?

Women aged at least 18 with rUTI.

### What does the study involve?

The participants are randomly allocated to one of 2 groups. Those in group 1 are given a low dose antibiotic once a day for 12 months. Those in group 2 are given methenamine hippurate, a urinary antiseptic given as a tablet, twice a day for 12-months. Each participant is followed during the 12 months that they take the UTI prevention and then for 6 months afterwards to record the benefits, side effects and costs of each treatment. They are all asked to provide urine samples at the start of their time on the study and then every 3 months until the end of their participation in the study (18 months later). If a participant suffers from a UTI during the study, they are asked to provide an additional urine sample to determine the type of bug causing the infection. Blood samples are taken at the start of the study, and then at 3 months, 6 months, 9 months and 12 months. Participants may be asked provide an additional sample at 18 months depending on the results of the previous tests. Skin swabs taken from the area near the anus are also take from each participant at the start of the study and then every 6 months until the end

of their participation in the study at 18 months. Participants are also asked to complete questionnaires on the number of infections the participants have had and what effect this has had on their general health. The questionnaires also measure the impact the infection and treatment is having on the participant's life in terms of cost and benefit. They are completed at the start of the study and at 3, 6, 9, 12, 15 and 18 months during the study. Participants are given a diary to use to keep a record of any urinary infections as they happen to make completing the questionnaires easier.

What are the possible benefits and risks of participating?  
Not provided at time of registration

Where is the study run from?  
Seven NHS hospitals in the UK

When is the study starting and how long is it expected to run for?  
February 2016 to November 2019

Who is funding the study?  
National Institute for Health Research (UK)

Who is the main contact?  
Gillian Watson, [gillian.watson@newcastle.ac.uk](mailto:gillian.watson@newcastle.ac.uk)

**Study website**  
<https://research.ncl.ac.uk/altar/>

## Contact information

**Type(s)**  
Public

**Contact name**  
Ms Gillian Watson

**Contact details**  
Newcastle Clinical Trials Unit  
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[Altar.Trial@ncl.ac.uk](mailto:Altar.Trial@ncl.ac.uk)

## Additional identifiers

**EudraCT/CTIS number**  
201500348736

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

20802

## **Study information**

### **Scientific Title**

A multicentre, pragmatic patient randomised noninferiority trial comparing two drugs for the prevention of recurrent urinary tract infection in women both during a 12 month period of use and in the subsequent 6 months following completion of the prophylactic medication.

### **Acronym**

ALTAR

### **Study objectives**

1. To determine the relative clinical effectiveness and cost effectiveness for the NHS of two licensed preventative treatments for women with recurrent uncomplicated urinary tract infection (UTI).
2. The null hypothesis being tested is that the nonantibiotic treatment (methenamine hippurate) is inferior to the standard treatment of extended course prophylactic antibiotic for prevention of rUTI in women.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

North East – Tyne & Wear South Regional Ethics Committee, 23/12/2015, ref: 15/NE/0381

### **Study design**

Randomised; Both; Design type: Treatment, Prevention, Drug, Qualitative

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

### **Study setting(s)**

Not specified

### **Study type(s)**

Treatment

### **Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet

### **Health condition(s) or problem(s) studied**

Specialty: Renal disorders, Primary sub-specialty: Renal disorders; UKCRC code/ Disease: Renal/ Noninflammatory disorders of female genital tract

## **Interventions**

A multicentre, pragmatic patient randomised noninferiority trial comparing two treatments for the prevention of rUTI in women during a 12 month period of treatment and in the 6 months following treatment completion. The standard is once daily prophylactic antibiotic, using either trimethoprim 100 mg, nitrofurantoin 50 or 100 mg depending on body weight or cefalexin 250 mg once daily for 12 months which are the recommended drugs licensed for this purpose. The choice of antibiotic will be decided by considering previous bacterial sensitivities, safety, and patient or clinician preference. The alternative (experimental) treatment is a 1 g twice daily oral urinary antiseptic methenamine hippurate for 12 months. Participants in both arms would continue to receive treatment courses of antibiotic for UTI as needed. Apart from random allocation to either option, all participants will receive usual care including use of on demand discrete treatment antibiotic courses for UTI.

## **Intervention Type**

Other

## **Primary outcome measure**

1. The incidence of symptomatic antibiotic treated UTI selfreported by participants over the 12 month treatment period
2. Incremental Cost per Quality Adjusted Life Year (QALY) gained (based on responses to the Euroqol 5 dimension, 5 level (EQ5D 5L) health status questionnaire completed at baseline and 3, 6, 9 and 12 months

## **Secondary outcome measures**

1. The occurrence of symptomatic UTI in the 6 months follow up period after stopping the allocated preventative therapy. (patient reported or clinically recorded)
2. Recorded participant antibiotic use
3. Antimicrobial resistance: Ecological change in terms of type of bacteria and their resistance patterns in isolates from i) midstream urine samples and ii) faecal reservoir (via optional rectal or perineal swabs) during the 12 month treatment period and in the 6 months following completion of treatment.
4. Number of microbiological proven UTIs during treatment and follow up
5. Occurrence of asymptomatic bacteriuria (ABU) during treatment and follow up
6. Hospitalisation due to UTI during treatment and follow up
7. HRQoL: Measured using the EQ5D 5L questionnaire
8. Incremental costs to the NHS, personal social services, and the patient at the end of the 12 month treatment and 18 month follow up phases measured using a cost-utility and a cost-benefit analysis
9. Model based estimates of costs, QALYs and net benefits over the longer terms, potentially over the patients estimated lifetime

## **Overall study start date**

01/02/2016

## **Completion date**

31/01/2020

# Eligibility

## Key inclusion criteria

1. Women aged 18 years and over
2. Women with rUTI who, in consultation with a clinician, have decided that prophylaxis is an appropriate option (to include women who have suffered at least three episodes of symptomatic UTI within the preceding 12 months or two episodes in the last 6 months or a single severe infection requiring hospitalisation)
3. Able to take a once daily oral dose of at least one of nitrofurantoin, or trimethoprim, or cephalexin
4. Able to take methenamine hippurate
5. Women who agree to take part in the trial but who are already taking Methenamine or antibiotic prophylaxis will be consented for participation and will stop their preventative therapy for a 3-month washout period. They will then be reassessed and if still eligible undergo baseline assessment and randomisation
6. Able to give informed consent for participation in trial
7. Able and willing to adhere to an 18-month study period

## Participant type(s)

Patient

## Age group

Adult

## Lower age limit

18 Years

## Sex

Female

## Target number of participants

Planned Sample Size: 240; UK Sample Size: 240

## Total final enrolment

240

## Key exclusion criteria

1. Women unable to take methenamine hippurate e.g. known allergy to methenamine hippurate, severe hepatic impairment (Child–Pugh class C, score of 10 or more), gout, eGFR < 10 ml/min, Proteus sp. as consistent proven causative organism for rUTIs
2. Women who are unable to take nitrofurantoin and trimethoprim and cephalexin
3. Women with correctable urinary tract abnormalities that are considered to be contributory to the occurrence of rUTI
4. Presence of symptomatic UTI – this will be treated and symptoms resolved prior to randomisation.
5. Pregnancy or intended pregnancy in next 12 months
6. Women who are breast feeding
7. Women already taking methenamine or antibiotic prophylaxis and declining a 3-month washout period

**Date of first enrolment**

07/07/2016

**Date of final enrolment**

31/10/2017

## **Locations**

**Countries of recruitment**

England

Scotland

United Kingdom

**Study participating centre****Freeman Hospital**

Freeman Road  
High Heaton  
Newcastle upon Tyne  
United Kingdom  
NE7 7DN

**Study participating centre****Cambridge University Hospital (Addenbrooks Hospital)**

Hills Road  
Cambridge  
Cambridgeshire  
United Kingdom  
CB2 0QQ

**Study participating centre****Central Manchester University Hospital, Manchester Royal Infirmary**

Manchester Royal Infirmary  
Oxford Road  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre****St James University Hospital**

Beckett Street  
Leeds

West Yorkshire  
United Kingdom  
LS9 7TF

**Study participating centre**  
**NHS Greater Glasgow and Clyde**  
Queen Elizabeth University Hospital  
1345 Govan Road  
Glasgow  
United Kingdom  
G51 4TF

**Study participating centre**  
**Royal Liverpool & Broadgreen University Hospitals NHS Trust**  
Prescot Street  
Liverpool  
United Kingdom  
L7 8XP

**Study participating centre**  
**Mid Yorkshire Hospitals NHS Trust**  
Rowan House  
Aberford Road  
Wakefield  
West Yorkshire  
United Kingdom  
WF1 4EE

**Study participating centre**  
**Pennine Acute Hospitals NHS Trust**  
North Manchester General Hospital  
Delaunays Road  
Crumpsall  
Manchester  
United Kingdom  
M8 5RB

## **Sponsor information**

**Organisation**

The Newcastle upon Tyne Hospitals NHS Foundation Trust

**Sponsor details**

Level 1, Regent Point  
Gosforth  
Newcastle Upon Tyne  
England  
United Kingdom  
NE3 3HD

**Sponsor type**

Hospital/treatment centre

**ROR**

<https://ror.org/05p40t847>

**Funder(s)****Funder type**

Government

**Funder Name**

National Institute for Health Research

**Alternative Name(s)**

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

**Results and Publications****Publication and dissemination plan**

The results of the study will be presented at topic-specific national/international conferences and be published in a general medical, infectious diseases or urology themed peer-reviewed journals. The trial will provide high-level evidence to use in new or updates of existing systematic reviews such as those published by Cochrane or SIGN.



The results will be disseminated to members of professional groups such as BAUS and EAU through updates and presentations. Participants will be provided with a lay summary of results. They will also have access to a copy of journal articles through the trial website.

### **Intention to publish date**

30/11/2020

### **Individual participant data (IPD) sharing plan**

Not provided at time of registration

### **IPD sharing plan summary**

Available on request

### **Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	protocol	09/11/2018		Yes	No
<a href="#">Results article</a>		09/03/2022	11/03/2022	Yes	No
<a href="#">Funder report results</a>		01/05/2022	11/05/2022	Yes	No
<a href="#">HRA research summary</a>			26/07/2023	No	No