

# EAT-UP

**A clinical trial of extended antibiotic treatment in combination with methenamine hippurate compared to standard of care treatment.**

## Lay Summary

### INTRODUCTION

Chronic Urinary Tract Infection (UTI) is a newly recognised type of UTI where symptoms are constant and occur every day, unlike recurrent UTIs, which come and go with symptom-free breaks in between. Current treatment for chronic UTI within the NHS is based on recommended guidelines for recurrent UTI. The standard approach typically includes one of the following treatments:

- Short courses of antibiotics at treatment (higher) doses during symptom flares (where your symptoms are temporarily worse).
- Long-term, prophylactic (low) dose daily antibiotic (where medication is used at low doses to try to prevent symptoms reoccurring).
- Long-term use of a urinary antiseptic (which helps keep your urine bacteria free), called methenamine hippurate.

These often do not work for people with chronic UTI, and symptoms can persist. Moreover, standard urine tests may fail to detect infections, making diagnosis and treatment more challenging. Doctors are looking for a different treatment plan that may be more effective.

### AIMS

- The EAT-UP trial will investigate whether longer courses of treatment (higher) dose antibiotics combined with methenamine hippurate (a urinary antiseptic) are a more effective treatment at reducing levels of infection and symptoms than standard of care treatments (described above).
- The trial will also assess the safety and feasibility of this new treatment approach in women with chronic UTI.

### BRIEF EXPERIMENTAL PLAN

This trial aims to recruit 192 females aged 18 and over who have experienced chronic UTI symptoms for at least three months. Participants will be recruited from NHS hospitals across England. They will be randomly assigned to one of two groups:

**Group 1** will receive a **treatment dose** antibiotic **in combination with** the urinary antiseptic, methenamine hippurate (1 g twice daily).

The treating clinician will select one of the following antibiotics based on the individual needs of the participant, such as their medical history, concomitant medications and any known allergies:

- Cefalexin (500mg four times daily), or
- Nitrofurantoin (100mg twice daily), or
- Trimethoprim (200mg twice daily)

**Group 2** will receive a **low-dose prophylactic** antibiotic **or** the urinary antiseptic, methenamine hippurate.

The treating clinician will select one of the following treatments based on the individual needs of the participant, such as their medical history, concomitant medications and any known allergies:

- Amoxicillin (250mg once daily), or
- Cefalexin (125mg once daily), or

- Nitrofurantoin (50mg once daily), or
- Trimethoprim (100mg once daily), or
- Methenamine Hippurate (1g twice daily)

Over 12 weeks, participants will provide blood and urine samples, as well as swab samples from the area between the vagina and anus. Additionally, participants will complete symptom questionnaires.

## URINE TESTING

The NHS typically uses dipstick tests and urine cultures to check for UTIs. However, research has shown that these standard tests may sometimes miss infections in people with chronic UTI. In the EAT-UP trial, participants' urine samples will be examined using a microscope, a method called 'fresh urine microscopy'. At each visit, participants will provide a urine sample, which the local research team will examine under a microscope and photograph. These images will be sent to a central laboratory at University College London, where the number of white blood cells will be counted. Research has shown that the presence of white blood cells in urine, especially in high amounts, is a strong indicator of UTI. The results will be shared with each participant's local clinician and research team.

## POTENTIAL PATIENT BENEFIT

The goal is to find a more effective way to manage chronic UTI, reducing symptoms and improving quality of life for patients with this condition. If successful, this study may support changes to treatment guidelines and lead to better outcomes for those living with chronic UTI.