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Cranberries for urinary tract infection

Submission date 21/01/2019	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 24/01/2019	**Overall study status** Completed	
Last Edited 24/02/2021	**Condition category** Urological and Genital Diseases	

Plain English summary of protocol

Background and study aims
Urinary tract infections (UTIs) are the commonest bacterial infections affecting women and are usually treated with antibiotics. Because of frequent and sometimes inappropriate use of antibiotics, many bacteria have adapted so that they are no longer killed by antibiotics (antibiotic resistance). There has therefore been increasing interest in using non-antibiotic treatments. One such is cranberry extract. The sugars in cranberries are believed to prevent bacteria from sticking to the wall of the bladder, reducing the ability of bacteria to cause a UTI. Cranberries might also make it easier for antibiotics to surround and kill bacteria. Women with a UTI will be invited to take part in a small-scale trial; the main aim of this trial is to test whether the trial design works and is acceptable to patients (called a 'feasibility trial').

Who can participate?
Women aged 18 or above with symptoms of a UTI

What does the study involve?
Women are randomly allocated to one of three groups: treatment with antibiotics, treatment with antibiotics and cranberry capsules, or initial treatment with cranberry capsules, but also with an antibiotic prescription that they can take to the pharmacy if they don't get better with cranberry alone ('back-up antibiotics'). Participants complete a diary for up to two weeks about their symptoms (e.g. pain on passing urine), how bad the symptoms are, how long they last, and whether or not they take antibiotics. Some women (both in and outside the feasibility trial) are interviewed about how they manage UTIs and their thoughts on, or experience of, the trial. This will help in the planning of a subsequent larger trial.

What are the possible benefits and risks of participating?
Participants will receive a £10 voucher as a thank you for taking part if they complete the electronic symptom diary. Participants taking part in an interview will receive a further £10 voucher after the interview has been completed. Taking part in this study will help with the design of a similar study to this but on a much larger scale (with more participants and in different parts of the country). The results of the larger study may help to safely reduce antibiotic use in women with simple UTIs. Participants in group three will not receive immediate antibiotics and may therefore be at higher risk of developing an upper UTI. Although not anticipated, it is possible that discussions in the interview could cause emotional distress.

Where is the study run from?
GP practices in Oxfordshire (UK)

When is the study starting and how long is it expected to run for?
December 2018 to June 2020

Who is funding the study?
1. NIHR School for Primary Care Research
2. Indena SpA

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
39742

Study information

Scientific Title

Does cranberry extract reduce antibiotic use for symptoms of acute uncomplicated urinary tract infections? A feasibility study

Acronym
CUTI

Study objectives
To assess the feasibility of conducting a definitive randomised clinical trial of the use of cranberry extract in treating the symptoms of acute, uncomplicated urinary tract infection and safely reducing antibiotic use.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central – Oxford B Research Ethics Committee, Whitefriars, Level 3, Block B, Lewin's Mead, Bristol, BS1 2NT, Tel: +44 (0)207 1048033, Email: nrescommittee.southcentral-oxfordb@nhs.net, 18/01/2019, ref: 18/SC/0673

Study design
Randomised; Both; Design type: Treatment, Drug, Qualitative

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Urinary tract infection

Interventions
Electronic randomisation using REDCap electronic database in a 1:1:1 ratio into one of three treatment groups:
Arm 1 - Immediate prescription of first line recommended antibiotics alone
Arm 2 - Immediate prescription of first line recommended antibiotics with the addition of cranberry capsules for up to 7 days
Arm 3 - Delayed prescription of first line recommended antibiotics and immediate cranberry capsules for up to 7 days

Participants receiving cranberry capsules (Redicran) will be advised to take (orally) two capsules twice a day, 12 hours apart, until they are free of symptoms, but up to a maximum of seven days. Participants in arm 3 will be advised to start antibiotics if their symptoms worsen or fail to improve after 3-5 days. The cranberry capsules (Redicran) contain 60 mg of cranberry extract and 18 mg of proanthocyanidins.

Participants will be asked to complete an electronic diary and and/or telephoned to encourage its completion and to obtain a minimal data set if the diary has not been adequately completed. A review of participants' notes will take place at 1 month. Some participants will also be consented and interviewed about their UTI experience, their thoughts on taking part in the trial and their thoughts on non-antibiotic treatment for UTIs.

Intervention Type
Other

Primary outcome measure
1. Quality and completeness of data obtained through participant completed diaries assessed through audit of proportion of diaries returned and completed by the end of participant follow up.
2. Rate of participant recruitment and number of participants lost to follow up through collation of results at the end of the study period.
3. Estimate of proportion of invited GPs and eligible potential participants agreeing to participate in the trial. At the end of the study, the trialists will review the proportion of GPs approached who agree to participate. They will also review screening and enrolment logs at the end of the study to determine the proportion of eligible potential participants that participate in the study.
4. Acceptability of study to participants, including assessment of face validity and acceptability of a 50-point Likert scale to be used in the participant symptom diary. This will be assessed though review of participant responses to questions in their completed symptom diaries at the end of participant follow up. Furthermore, interviews will take place with some trial participants at least one month after they were recruited into the trial.
5. Participants' experiences of UTIs, views on self-care and self-help for UTIs and experiences of (if applicable) and thoughts on the CUTI trial will be assessed through interviews with some participants of the CUTI trial, as well as some women who were not part of the CUTI trial but have recent experience of a UTI

(added 21/09/2020)
6. Acceptability of the study to recruiters through interviews with recruiters to the trial

Secondary outcome measures
Current secondary outcome measures as of 21/09/2020:

Assessed using patient records at the end of the study period:
1.Proportion of participants consuming a course (or part thereof) of antibiotics in intervention and control groups
2. Number of antibiotic courses (or part thereof) consumed by participants in each group
3. Duration of symptoms rated moderately bad or worse in treatment and control groups
4. Symptom burden in treatment and control groups
5. Proportion of participants experiencing one or more adverse events, serious adverse events, requiring additional input from a healthcare practitioner, or taking time off usual/paid activities in each arm of the trial

6. Proportion of participants randomised to receive antibiotics only that consume cranberry products
7. Proportion of participants using additional treatments for their symptoms in each group
8. Comparison of time to feeling fully recovered between groups

Previous secondary outcome measures:

At the end of the study period, there will be preliminary statistical assessment of:
1. The number of participants consuming a course (or part thereof) of antibiotics
2. The duration of acute urinary tract symptoms rated moderately bad or worse
3. Any harms related to cranberry extract consumption. Assessment of harms will also take place through review of participant electronic medical records up to one month post randomisation to determine whether any adverse events occurred, and through interviews with some participants of the CUTI trial

Overall study start date
01/12/2018

Completion date
30/06/2020

Eligibility

Key inclusion criteria
1. Potential participant is willing and able to give informed consent for participation in the study
2. Female aged 18 years or above

CUTI Trial only:
1. Potential participant is making contact with general practice/primary care provider with urinary symptoms suggestive of acute, uncomplicated lower urinary tract infection (namely dysuria, urgency, frequency, polyuria/nocturia, haematuria and/or suprapubic pain), which the GP would normally treat with an immediate prescription of antibiotics
2. Symptom duration of under seven days (i.e. 6 days or less)
3. Potential participant is willing to receive either an immediate or delayed antibiotic prescription

CUTI Interviews only:
1. Has experienced one or more UTIs in the past 12 months

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants

Planned Sample Size: 75; UK Sample Size: 75

Total final enrolment
81

Key exclusion criteria
CUTI Trial only:
The potential participant may not enter the study if ANY of the following apply:
1. Has taken antibiotics within the past 7 days
2. Cranberry allergy
3. Already taking cranberry products regularly
4. Known or suspected pregnancy
5. Breastfeeding
6. Warfarin user (cranberries may interact with Warfarin)
7. Unable to get a clean-catch/midstream urine sample
8. In-dwelling catheter
9. Receiving end of life care/palliative care
10. Known underlying structural urological abnormalities (including polycystic kidneys)
11. Previous urological surgery
12. Immunosuppressed [e.g. active cancer (excluding localised skin cancer), receiving chemotherapy, taking regular high dose oral steroids (> 5mg/day) , HIV infection]
13. Diabetes mellitus treated with insulin
14. Signs of clinically suspected upper UTI/pyelonephritis
15. Inability to complete symptom diary accurately (e.g. dementia or psychosis)
16. Is currently involved in an interventional research study on UTI
17. Unable to access internet/email over the next two weeks
18. Is unable to decide on the same day that they contacted a primary care provider whether they would like to participate

CUTI Interviews only:
1. Potential participant was immunosuppressed at the time of their UTI (including active cancer, receiving chemotherapy, diabetes mellitus treated with insulin or taking regular high-dose oral steroids (> 5 mg/day)
2. Potential participant has underlying urological abnormalities or has had previous urological surgery
3. Potential participant is receiving end of life care or palliative care
4. Potential participant declined to participate in the CUTI trial

Date of first enrolment
01/03/2019

Date of final enrolment
02/03/2020

Locations

Countries of recruitment
United Kingdom

Study participating centre
GP practices in Oxfordshire
United Kingdom
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Sponsor information

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University of Oxford

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Sponsor type
University/education

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
NIHR School for Primary Care Research; Grant Codes: 2014-10043 - 413 and 437

Funder Name
Indena SpA; Grant Codes: 203921/Z/16/Z

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
30/06/2021

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	23/12/2019	31/12/2019	Yes	No
Results article	results	22/02/2021	24/02/2021	Yes	No
HRA research summary			28/06/2023	No	No