ISRCTN68263889 https://doi.org/10.1186/ISRCTN68263889

# Bladder treatments to prevent recurrent urinary tract Infections (the VESPER trial): a randomised study comparing different treatment options with both participants and researchers knowing which treatment is given.

**Submission date**
16/11/2024

**Recruitment status**
Recruiting

**Registration date**
08/01/2025

**Overall study status**
Ongoing

**Last Edited**
09/05/2025

**Condition category**
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

**Plain English summary of protocol**
Background and study aims
Most women experience urine infections during their lifetime, but some get repeated episodes, which considerably reduce quality of life. This is known as recurrent urinary tract infection (rUTI) and is defined as at least two episodes in six months or three in a year. rUTI is a very common reason for antibiotic prescription. Overuse and misuse of antibiotics drive increased antimicrobial resistance, which is a critical global health threat. Daily, low-dose, oral antibiotics for up to 6 months is the standard preventative treatment for rUTI; however, they do not work for some women. Patients with infections that are difficult to control may need treatment given directly into the bladder through the urethra (water pipe) using a very thin disposable single-use catheter (known as bladder instillations). Patients usually receive these treatments over 6-months. Currently, about 75% of surveyed urology specialists report regular use of instillations but the supporting evidence for these treatments is lacking, and current clinical guidelines can only recommend more (second line) daily oral antibiotics.
The VESPER randomised controlled trial compares two treatments given directly into the bladder: intravesical gentamicin and intravesical glycosaminoglycan (GAG) preparations to prevent UTI against the current recommended treatment of daily oral second-line antibiotics. Women seen in a hospital urology/urogynaecology clinic with rUTI who have not improved after first-line treatments will be invited to participate.
We will compare the number of UTI episodes occurring in each group during the 6-months of treatment to see which treatment is best at preventing UTI. We will follow up each woman during the trial and record UTI occurrence as well as the benefits, side effects and costs of treatment. We will record the types of bacteria found and their resistance to antibiotics. The trial is funded by the National Institute for Health Research Health Technology Assessment programme.

Who can participate?
Patients are informed that if they are pregnant or planning to become pregnant in the next 12 months or are currently breastfeeding, they will not be eligible to take part in the trial. Participants need to agree to use a highly effective method of contraception during the trial and for at least one month after the last dose of the trial treatment. Participants are advised of the risks of the medications to an unborn child and are given advise on what to do if they become pregnant whilst taking the medications. Participants are also informed that if they do become pregnant that the research team will ask them to complete a pregnancy reporting form and will wish to follow the participant up to at least the end of their pregnancy.

What does the study involve?
Participants are asked to complete a diary and answer questions at an initial baseline appointment and again at the months 1, 3, 6, 12, appointments and during any breakthrough UTIs that may pose an increased burden. However, the questions have been kept to the minimum possible whilst obtaining the information needed for the trial.
Some participants may agree to an interview, and there is a potential for participants to be upset at reflecting on their condition.
PPI's have been involved from the early stages of this trial design and have had input into the drafting of participant-facing documents.
Preparatory PPI exercises during trial development included a series of focus groups comprising patients with rUTI and discussion with national patient organisations such as Bladder Health UK and Live UTI-free. Patients stressed the significant impact of each UTI episode and stated that any new treatments that could reduce UTI frequency, even by 1 episode per year, would be welcome. Patients informed us that rUTI were impactful enough for them to consider invasive procedures such as the catheterisation required for intravesical instillations.

What are the possible benefits and risks of participating?
By joining us in this trial you are helping to improve the management of recurrent urinary tract infections, and this may benefit you or other women in the future.
Participants may possibly experience side effects from the three different treatment arms. The types of side effects and their likelihood of happening are explained in the participant information sheet. Participants are advised to seek medical advice should they feel unwell. All adverse reactions will be recorded. Serious adverse reactions and suspected unexpected serious adverse reactions (SUSARs) will be recorded and reported as per regulatory requirements. Monitoring of SAEs will be in place, and where triggered, sites will be contacted to discuss any concerns.

Where is the study run from?
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
November 2024 to September 2027

Who is funding the study?
National Institute for Health and Care Research Health Technology Assessment programme (UK)

Who is the main contact?
Dr Janine Bates, batesmj@cardiff.ac.uk
Prof. Chris Harding, c.harding@nhs.net

# Contact information

### Type(s)
Public

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Scientific, Principal investigator

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## Additional identifiers

### Clinical Trials Information System (CTIS)
Nil known

### Integrated Research Application System (IRAS)
1011153

### ClinicalTrials.gov (NCT)
Nil known

### Protocol serial number
10774

## Study information

### Scientific Title
Intravesical preparations for recurrent urinary tract infection prevention (the VESPER trial): a multi-arm, multi-site open label randomised superiority trial

### Acronym

VESPER

## Study objectives
The primary objective of VESPER is to evaluate the clinical and cost-effectiveness of two experimental interventions for women with refractory rUTI: intravesical gentamicin; Intravesical GAG replacement; and compare to the control arm of antibiotic prophylaxis (second-line prophylactic daily oral antibiotics [comparator arm]).
The primary clinical effectiveness outcome is the rate of symptomatic, antibiotic-treated UTI, self-reported by participants from randomisation to the 6-month treatment period (verified from medical records).
The primary economic outcome is the incremental cost per quality-adjusted life year (QALY) gained, based on responses to EQ-5D-5L, over 12 months.

Secondary objectives:
Evaluate the clinical, economic and safety outcomes:
1. Antibiotic use: number of courses of antibiotics prescribed for UTI
2. Microbiologically proven UTIs
3. AMR in E. coli isolated from urine or perineal swabs
4. Bacterial species or antibiograms
5. Asymptomatic bacteriuria defined as a positive urine culture without symptoms
6. Adherence with allocated treatment (patient reported)
7. Adverse events
8. Hospitalisation due to UTI
9. Costs to NHS and personal social services (PSS) at 12 months and modelled over participant lifetime
10. QALYs at 12 months based on completion of the EQ-5D-5L at baseline, 3, 6, & 12 months and modelled over participant lifetime
11. Incremental cost per QALY gained at 6 months
12. Incremental cost per QALY gained over a lifetime horizon
13. Willingness-to-pay
14. Treatment Satisfaction Questionnaire
15. Contextual factors influencing adherence, acceptability and implementation

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Approved 07/01/2025, Wales Research Ethics Committee 1 Cardiff. (Health and Care Research Wales Castlebridge 4 15-19 Cowbridge Road East , Cardiff, CF11 9AB, United Kingdom; 02922 940912; Wales.REC1@wales.nhs.uk), ref: 24/WA/0358

## Study design
Interventional randomized parallel group SMART controlled trial

## Primary study design
Interventional

## Study type(s)
Safety, Efficacy

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

Recurrent uncomplicated urinary tract infection.

## Interventions

Current interventions as of 09/05/2025:
Intravesical Prophylactic Treatment:
- Intravesical antibiotics – 80 mg of Gentamicin diluted to 50 ml with normal saline instilled into the bladder weekly for month 1, fortnightly for Months 2 & 3 and monthly for Months 4, 5 & 6*
- Intravesical GAG replacement compounds (Ialuril, Cystistat, Gepan, etc) – 1 vial of GAG replacement. compound instilled into the bladder weekly for month 1, fortnightly for Months 2 & 3 and monthly for Months 4, 5 & 6*
*11 instillations

Comparator:
- Second-line prophylactic daily oral antibiotics as per NICE antimicrobial prescribing guidelines - Nitrofurantoin (50/100 mg), Trimethoprim (100 mg), Amoxicillin (250 mg) or Cefalexin (125/250 mg once a day).

Randomisation:
Randomisation will be in a 1:3:3 ratio to receive: (1) Oral antibiotic prophylaxis, (2) Intravesical Gentamicin, (3) Intravesical GAG replacement for 6 months.
Computerised web-based remote randomisation (available 24 hours a day) will be used. The randomisation system will be built by the in-house CTR information Systems and Technology Solutions team (TMS2).
In the event that the online randomisation system is unavailable at site, or the site has problems accessing the online website, then the local investigator may contact the CTR (during office hours). Manual randomisation may be performed by CTR staff on request of the local investigator.
If the online system does not work, a telephone back-up managed by the CTR Trial team will be available for use during office hours Monday to Friday: 08:30-16:00.

Previous interventions:
Intravesical Prophylactic Treatment:
- Intravesical antibiotics – 80 mg of Gentamicin in 80 ml of saline instilled into the bladder weekly for month 1, fortnightly for Months 2 & 3 and monthly for Months 4, 5 & 6*
- Intravesical GAG replacement compounds (Ialuril, Cystistat, Gepan, etc) – 1 vial of GAG replacement. compound instilled into the bladder weekly for month 1, fortnightly for Months 2 & 3 and monthly for Months 4, 5 & 6*
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If the online system does not work, a telephone back-up managed by the CTR Trial team will be available for use during office hours Monday to Friday: 08:30-16:00.

### Intervention Type
Drug

### Phase
Phase IV

### Drug/device/biological/vaccine name(s)
Gentamicin, amoxicillin, cefalexin, nitrofurantoin, trimethoprim

### Primary outcome(s)
Rate of symptomatic, antibiotic-treated UTI, self-reported by participants from randomisation to the 6-month treatment period

### Key secondary outcome(s))
Incremental cost per quality-adjusted life year (QALY) gained, based on responses to EQ-5D-5L, over 12 months

### Completion date
30/09/2027

## Eligibility

### Key inclusion criteria
Current inclusion criteria as of 09/05/2025:
1. Women (assigned female at birth) with recurrent uncomplicated UTI who have failed first-line treatments (at least three episodes of symptomatic antibiotic-treated urinary infection in the previous 12 months or two episodes of UTI in the last 6 months despite the use of first-line treatments). Failed first-line treatments can include antibiotics, methenamine (antiseptic) or vaginal oestrogen.
2. Women aged >16 years
3. Women able to receive intravesical treatments and take second-line oral antibiotic prophylaxis
4. Women able to give informed consent
5. Women willing to adhere to a 12month study protocol

Previous inclusion criteria:
1. Women with recurrent uncomplicated UTI who have failed first-line treatments (at least three episodes of symptomatic antibiotic-treated urinary infection in the previous 12 months or two episodes of UTI in the last 6 months despite the use of first-line treatments). Failed first-line treatments can include antibiotics, methenamine (antiseptic) or vaginal oestrogen
2. Women aged ≥16 years
3. Women able to receive intravesical treatments and take second-line oral antibiotic prophylaxis
4. Women able to give informed consent
5. Women willing to adhere to a 12-month study protocol

### Participant type(s)

Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
16 years

### Sex
Female

### Key exclusion criteria
Current exclusion criteria as of 09/05/2025:
1. Women (assigned female at birth) unable to receive intravesical treatments or second-line oral antibiotic prophylaxis
2. Women with structural or functional urinary tract abnormalities considered contributory to rUTI
3. Pregnancy or intended pregnancy in the next 12 months
4. Women who are breastfeeding

Previous exclusion criteria:
1. Women unable to receive intravesical treatments or second-line oral antibiotic prophylaxis
2. Women with structural or functional urinary tract abnormalities considered contributory to rUTI
3. Pregnancy or intended pregnancy in the next 12 months
4. Women who are breastfeeding

### Date of first enrolment
15/04/2025

### Date of final enrolment
30/09/2026

## Locations

### Countries of recruitment
United Kingdom

### Study participating centre
-
United Kingdom
-

## Sponsor information

**Organisation**
Newcastle upon Tyne Hospitals NHS Foundation Trust

**ROR**
https://ror.org/05p40t847

# Funder(s)

**Funder type**
Government

**Funder Name**
Health Technology Assessment Programme

**Alternative Name(s)**
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
United Kingdom

# Results and Publications

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

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