

# Inflammatory proteins in the urine and bladder tissue of women with lower urinary tract symptoms

<b>Submission date</b> 24/11/2024	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 28/11/2024	<b>Overall study status</b> Ongoing	<input checked="" type="checkbox"/> Protocol
<b>Last Edited</b> 28/11/2024	<b>Condition category</b> Urological and Genital Diseases	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Lower urinary tract symptoms (LUTS), such as urinary urgency, urge incontinence, chronic bladder related, and recurrent urinary tract infections affect more than half of the female population worldwide. Despite their prevalence, the underlying mechanisms that cause LUTS are poorly understood, which is likely a reflection of a multifactorial aetiology. Many women will additionally experience overlapping symptoms and conditions of the bladder in their lifetime.

Various bladder conditions have been found to be linked to a pro-inflammatory state within the bladder itself. Cell signalling proteins called cytokines have been found to be elevated in the urine and in bladder tissue samples of those with LUTS compared to those without. However, how various cytokines may be related to particular LUTS remains unclear. We hypothesise that different inflammatory pathways may be responsible for causing LUTS in women with overactive bladder syndrome (OAB) and bladder pain syndrome (BPS). We also hypothesise that women with acute urinary tract infection with or without a diagnosis of OAB or BPS may leave a further additional differing cytokine profile signifying an infective process.

The purpose of this study is to build on existing research that has been carried out in the field of biomarkers, urinary cytokines, and bladder pain syndrome. In our study we aim to look not only at women with chronic bladder pain but with other chronic lower urinary tract symptoms to understand whether there is an inflammatory component and then try and better understand the pathophysiology and pathogenesis of these conditions- especially in bladder pain syndrome for which the underlying pathophysiology remains unknown. Bladder conditions in women are not only well understood but often symptoms can overlap over time. Currently treatment is often offered in a "trial" -where a treatment is tried and if it does not help then another is tried. Better than this method would be the ability to target treatment. With better understanding of the inflammatory pathways that underpin chronic lower urinary tract symptoms this could be achieved in the future. This study aims to further our understanding of these bladder symptoms and conditions.

### Who can participate?

Any women with lower urinary tract symptoms that have been ongoing for 3 months or more who has been referred to St Mary's Hospital London for the investigation and management of these symptoms. Participants will already have decided that they are willing to have their lower urinary tract symptoms investigated with a procedure called a cystoscopy, where the inside of the bladder is looked at via a camera and then small bladder tissue samples are taken. All participants for this study are undergoing rigid cystoscopy with bladder biopsies under a general anaesthetic.

### What does the study involve?

The study involves participants filling out three validated questionnaires about their bladder symptoms: 1) the King's Health Questionnaire, 2) the O'Leary/Sant interstitial cystitis index, 3) the International Consultation of Incontinence Questionnaire-female lower urinary tract symptoms- ICIQ-fluts. Participants then undergo rigid cystoscopy and bladder biopsy- at the time of cystoscopy a sterile sample of urine is collected and an extra tissue

### What are the possible benefits and risks of participating?

Participants are all already undergoing cystoscopy procedures with bladder biopsies already being taken- however extra tissue samples are taken for research which increases the risk of bleeding from the bladder and the risk of bladder perforation. These risks are very low less than 1/1000.

There are no short-term benefits to participation. Long-term benefits could include the availability of more targeted treatment for urinary symptoms based on the inflammatory profile found.

### Where is the study run from?

St Mary's Hospital, Imperial College Healthcare Trust, London (UK)

### When is the study starting and how long is it expected to run for?

April 2023 to January 2026

### Who is funding the study?

The Charm Charity and BSUG-the British Society of Urogynaecology (UK)

### Who is the main contact?

Dr Bernadette Lemmon, blemmon@nhs.net

## Contact information

### Type(s)

Public, Scientific

### Contact name

Dr Bernadette Lemmon

### ORCID ID

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### Contact details

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### **Type(s)**

Principal Investigator

### **Contact name**

Prof Vik Khullar

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## **Additional identifiers**

### **EudraCT/CTIS number**

Nil known

### **IRAS number**

351850

### **ClinicalTrials.gov number**

Nil known

### **Secondary identifying numbers**

URO\_VK\_16\_041-Uro-gynaecology collection

## **Study information**

### **Scientific Title**

Urinary and bladder cytokine expression in women with lower urinary tract symptoms

### **Acronym**

CytoLUTS

### **Study objectives**

1. Women with lower urinary tract symptom have raised inflammatory cytokines when compared with healthy controls.
2. Women with bladder pain syndrome, overactive bladder syndrome, and those with recurrent urinary tract infections display different and distinct patterns of inflammatory cytokine expression.

## **Ethics approval required**

Ethics approval required

## **Ethics approval(s)**

1. Approved 16/11/2016, Imperial College Healthcare Tissue Bank (Department of Surgery and Cancer, Charing Cross Hospital, Fulham Palace Road, London, W6 8RF, United Kingdom; +44 7711701382; geraldin.thomas@imperial.ac.uk), ref: URO\_VK\_16\_041- Uro-gynaecology collection

2. Not yet submitted 23/11/2024, Health Research Authority and Health and Care Research Wales (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom)

## **Study design**

Single centre observational cross-sectional cohort study

## **Primary study design**

Observational

## **Secondary study design**

Cohort study

## **Study setting(s)**

Hospital, Laboratory

## **Study type(s)**

Diagnostic

## **Participant information sheet**

See outputs table

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

Identifying and understanding inflammatory changes in the urine and bladder tissue of women with chronic lower urinary tract symptoms

## **Interventions**

Women recruited for this study will be asked to fill out three validated symptom questionnaires about their chronic lower urinary tract symptoms: 1) The O'Leary Sant Interstitial Cystitis Index (ICSI) 2) the King's Health Questionnaire (KHQ) 3) The international Consultation on Incontinence Questionnaire-female lower urinary tract symptom modules (ICIQ-fluts).

All women recruited will already be undergoing cystoscopy and bladder biopsies for investigation of their bladder symptoms. At the time of cystoscopy a sterile sample of urine is taken and two extra bladder biopsies. Multiplex sandwich ELISA assaying techniques are used for the detection of a panel of inflammatory cytokines in the paired urine and bladder tissue samples and compared with healthy controls without chronic urinary tract symptoms.

## **Intervention Type**

Other

## **Primary outcome measure**

Inflammatory cytokine expression in urine and bladder tissue measured at the time of cystoscopy using a sterile sample of urine and two extra bladder biopsies. Multiplex sandwich ELISA assaying techniques are used for the detection of a panel of inflammatory cytokines in the paired urine and bladder tissue samples and compared with healthy controls without chronic urinary tract symptoms.

### **Secondary outcome measures**

Chronic lower urinary tract symptoms measured at baseline

1. The O'Leary Sant Interstitial Cystitis Index (ICSI)
2. The King's Health Questionnaire (KHQ)
3. The international Consultation on Incontinence Questionnaire-female lower urinary tract symptom modules (ICIQ-fluts)

### **Overall study start date**

30/04/2023

### **Completion date**

31/01/2026

## **Eligibility**

### **Key inclusion criteria**

1. Women with significantly bothersome lower urinary tract symptoms lasting for over 3 months
2. Women who are already undergoing cystoscopy and bladder biopsy under a general anaesthetic for the investigation of lower urinary tract symptoms
3. Women aged 18 or older
4. Women with the capacity to consent to take part in research themselves
5. Women able to complete validated symptom questionnaires in English
6. Women who have signed a valid written consent form for the provision of extra samples for research under the Imperial College Healthcare Tissue Bank Ethics

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Upper age limit**

100 Years

### **Sex**

Female

### **Target number of participants**

70

## Key exclusion criteria

1. Women under the age of 18 years
2. Women who are unable to complete validated questionnaires in English
3. Women without capacity to consent themselves for research
4. Women who have undergone previous continence procedures
5. Women with a history of urological malignancy
6. Women undergoing current treatment for urological malignancy

## Date of first enrolment

01/08/2023

## Date of final enrolment

30/01/2025

## Locations

### Countries of recruitment

England

United Kingdom

### Study participating centre

St Mary's Hospital, Imperial College Healthcare NHS Trust

Praed Street

London

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W2 1NY

## Sponsor information

### Organisation

Imperial College London

### Sponsor details

St Mary's Hospital, South Wharf Road

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### Sponsor type

University/education

**Website**

<https://www.imperial.ac.uk>

**ROR**

<https://ror.org/041kmwe10>

## Funder(s)

**Funder type**

Research organisation

**Funder Name**

British Society of Urogynaecology

## Results and Publications

**Publication and dissemination plan**

Planned publication in a peer-reviewed journal

**Intention to publish date**

30/01/2026

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

The datasets generated during and/or analysed during the current study will be initially available upon request from Dr Bernadette Lemmon, email: [blemmon@nhs.net](mailto:blemmon@nhs.net). At the end of the study datasets generated will be sorted in a non-publicly available repository - the Imperial College Tissue Bank.

**IPD sharing plan summary**

Stored in non-publicly available repository, Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	version 1	27/11/2024	28/11/2024	No	Yes
<a href="#">Protocol file</a>	version 1	27/11/2024	28/11/2024	No	No