

# Haematuria and When to Worry

---

Ms Anna Walsh, Consultant Urologist

January 25<sup>th</sup> 2025

# Who am I?



# Case 1

52 YO



# NVH definition

BAUS/NICE:

2 out of 3 occasions, NO urine infection

2+ or 3+ on dipstick urinalysis  
PPV, does not need confirmatory microscopy

Trace or 1+, confirm on microscopy  
and 10 RBC/ microlitre is regarded as significant



the dipstick should prompt clinical evaluation.

blood cells per high-power field (RBC/HPF) on a properly obtained sample.

# Dipstick Vs Microscopy

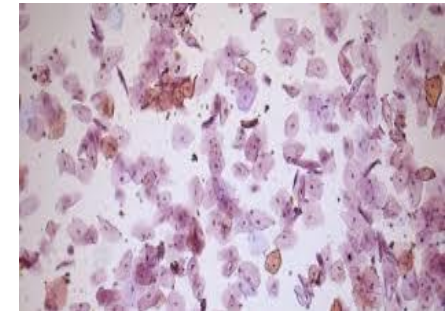
Dipstick sensitivity >90%

- Poor specificity however
- 1+ on dipstick = 10-40 RBC/hpf



Microscopy

- >3 RBC/hpf
- False negative with Delayed samples and cell lysis



# Haematuria clinic referral guidelines UK 2015

---

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for bladder cancer if they are:

- aged 45 and over and have:
  - **unexplained** visible haematuria without urinary tract infection **or**
  - visible haematuria that persists or recurs after successful treatment of urinary tract infection, **or**
- aged 60 and over and have unexplained non-visible haematuria **and** either dysuria or a raised white cell count on a blood test. **[new 2015]**

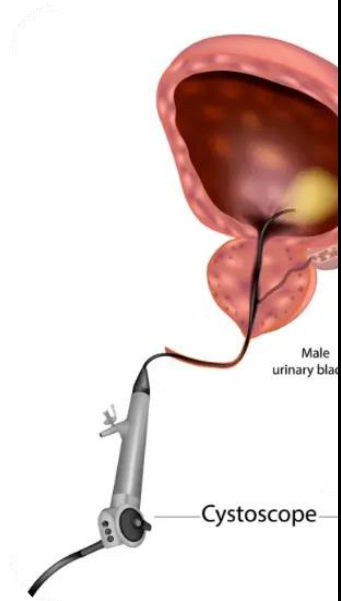
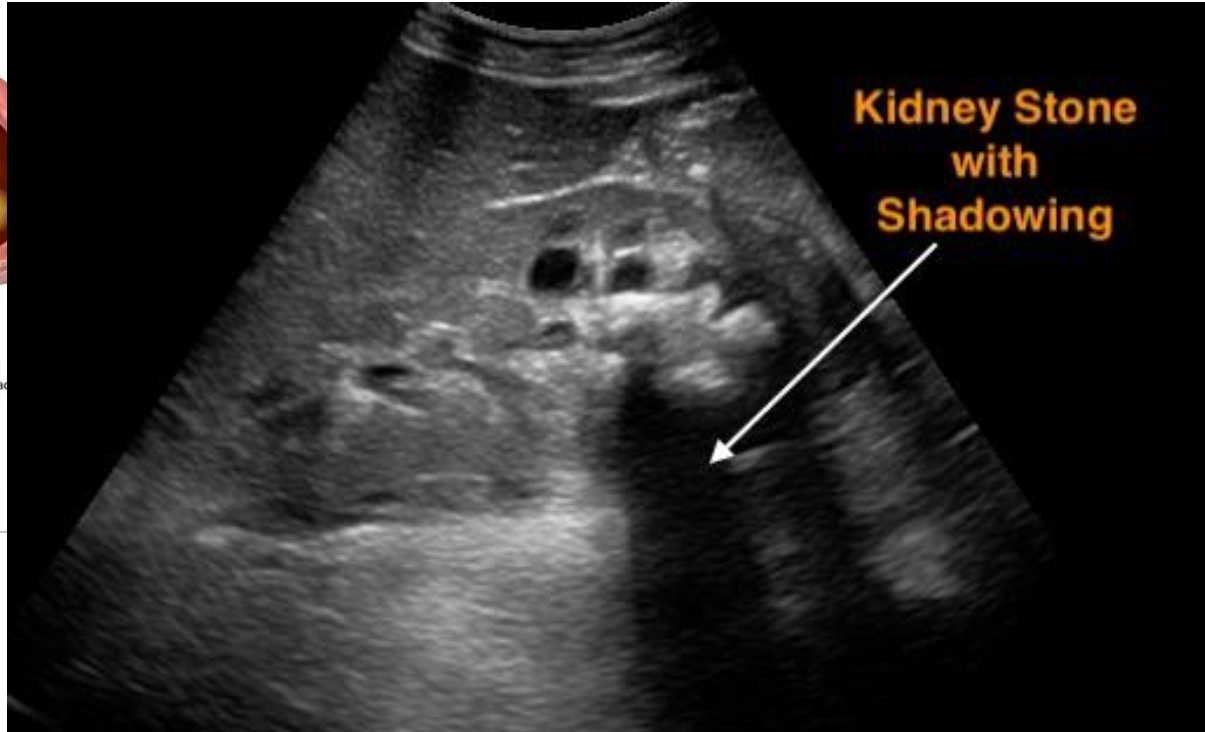
Consider **non-urgent** referral for bladder cancer in people aged 60 and over with recurrent or **persistent** unexplained urinary tract infection. **[new 2015]**

# Haematuria referral guidelines AUA 2020

Low-risk (meets all criteria)	Intermediate-risk (meets any one criteria)	High-risk (meets any one criteria)
<ul style="list-style-type: none"><li>▶ Age &lt;50 for women and &lt;40 for men</li><li>▶ Never smoker, or smoking history &lt;10 pack years</li><li>▶ 3-10 RBC/HPF on urinalysis</li><li>▶ No additional risk-factors for urothelial cancer</li></ul>	<ul style="list-style-type: none"><li>▶ Age 50-59 for women and 40-59 for men</li><li>▶ Smoking history 10-30 pack years</li><li>▶ 11-25 RBC/HPF on urinalysis</li><li>▶ Additional risk-factors for urothelial cancer</li><li>▶ Low-risk patient with persistent microscopic haematuria on repeat urinalysis</li></ul>	<ul style="list-style-type: none"><li>▶ Age &gt;60 years old</li><li>▶ Smoking history &gt;30 pack years</li><li>▶ &gt;25 RBC/HPF on urinalysis</li><li>▶ History of visible haematuria</li></ul>



# Investigation:





# Haematuria clinic referral guidelines UK

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for bladder cancer if they are:

- aged 45 and over and have:
  - **unexplained** visible haematuria without urinary tract infection **or**
  - visible haematuria that persists or recurs after successful treatment of urinary tract infection, **or**
- **aged 60 and over** and have unexplained non-visible haematuria **and** either **dysuria or a raised white cell count on a blood test. [new 2015]**

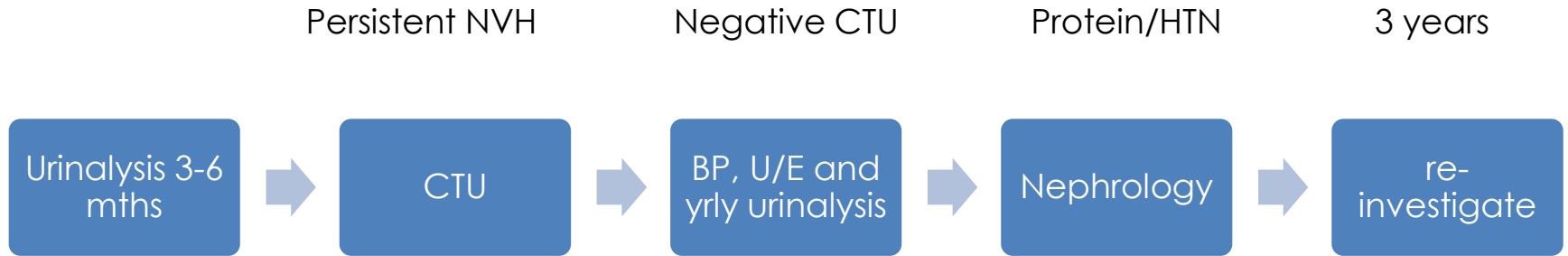
Consider **non-urgent** referral for bladder cancer in people aged 60 and over with recurrent or **persistent** unexplained urinary tract infection. **[new 2015]**

# Haematuria referral guidelines AUA

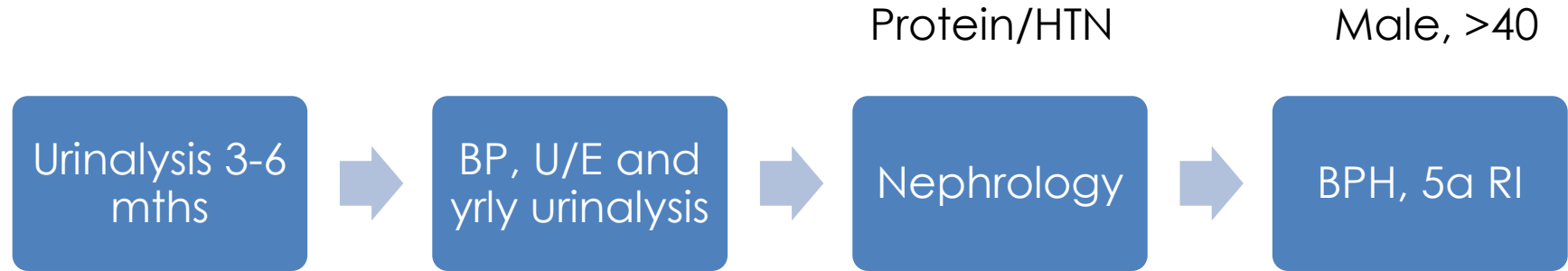
Low-risk (meets all criteria)	Intermediate-risk (meets any one criteria)	High-risk (meets any one criteria)
<ul style="list-style-type: none"><li>▶ Age &lt;50 for women and &lt;40 for men</li><li>▶ Never smoker, or smoking history &lt;10 pack years</li><li>▶ 3-10 RBC/HPF on urinalysis</li><li>▶ No additional risk-factors for urothelial cancer</li></ul>	<ul style="list-style-type: none"><li>▶ Age 50-59 for women and 40-59 for men</li><li>▶ Smoking history 10-30 pack years</li><li>▶ 11-25 RBC/HPF on urinalysis</li><li>▶ Additional risk-factors for urothelial cancer</li><li>▶ Low-risk patient with persistent microscopic haematuria on repeat urinalysis</li></ul>	<ul style="list-style-type: none"><li>▶ Age &gt;60 years old</li><li>▶ Smoking history &gt;30 pack years</li><li>▶ &gt;25 RBC/HPF on urinalysis</li><li>▶ History of visible haematuria</li></ul>

# NVH and negative flexible cystoscopy/Ultrasound

---



## Persistent VH and negative flexible cystoscopy/CT



Consider renal arteriography, retrograde ureteropyelogram,  
cystoscopy/bx

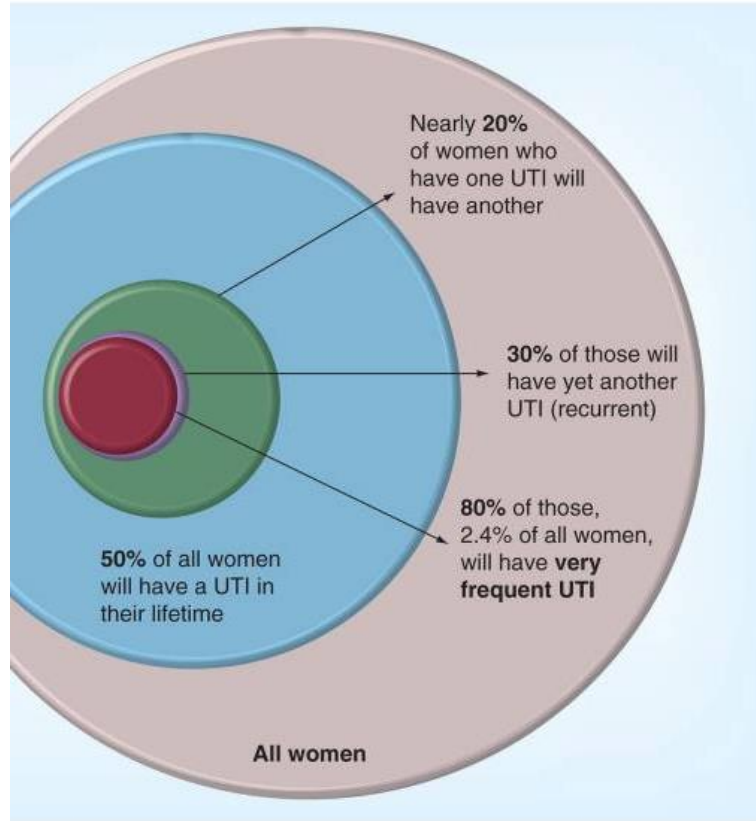
# VH and UTI case

---

45 YO



# Recurrent UTI



*Expert Rev Vaccines. 2012; 11(6): 663–676.*

## Investigation: US

---

USS is beneficial in women with persistent and relapsing infections to exclude or identify complications

Franco Best Pract Res Clin Obstet Gynaecol 2005

118 patients – 8% significant abnormalities on flexi cysto – NPV of imaging 99% = “no cystoscopy in women without risk factors and normal imaging”

Lawrentschuk Int J Urol 2006

Proteus UTI and urolithiasis:

- 44% of bacteraemic Proteus UTI have urolithiasis
- 24% of non-bacteraemic Proteus UTI have urolithiasis

Chen et al 2012



# Management



Cranberry  
D-mannose  
Methanamine Hippurate  
Topical Vaginal Oestrogen  
Oral vaccine



Prophylactic  
Self start



Cystistat  
IALuRil  
Gentamicin

In, then out, then in again...

Can Cranberries Contribute to Reduce the Incidence of Urinary Tract Infections? A Systematic Review with Meta-Analysis and Trial Sequential Analysis of Clinical Trials. *Luís, Ângelo et al, The Journal of Urology 2017, Volume 198, Issue 3, 614 - 621*

## CRANBERRY PRODUCTS REDUCE URINARY TRACT INFECTIONS

Systematic review, meta-analysis and trial sequential analysis



28 trials

**32.5%**

RR 0.675 (95% CI: 0.55-0.79)

**Significant risk reduction**



**Most helpful in pts with recurrent UTIs**

Luis, et al. *J Urol.* Sep, 2017.

THE JOURNAL  
of UROLOGY®



Copyright © 2017 American Urological Association Education and Research, Inc., Published by Elsevier



# D-Mannose

In a randomised placebo-controlled non-blinded clinical trial, it was shown that a daily dose of 2 g D-mannose was significantly superior to placebo and as effective as 50 mg nitrofurantoin in preventing UTIs.

- *D-mannose powder for prophylaxis of recurrent urinary tract infections in women: a randomized clinical trial. Kranjčec et al World Journal of Urology 2014, Volume 32(1),pp 79–84*

MINI REVIEW – INFECTIONS | [ARTICLES IN PRESS](#)

## Role of D-Mannose in the Prevention of Recurrent Urinary Tract Infections: Evidence from a Systematic Review of the Literature

[Rena Kyriakides](#) • [Patrick Jones](#) • [Bhaskar K. Somani](#)  

Published: September 21, 2020 • DOI: <https://doi.org/10.1016/j.euf.2020.09.004>

# Vaginal Oestrogen

Vaginal oestrogen cream (estriol cream 0.5mg applied topically at night for 2weeks then twice weekly) for 8months significantly reduced the risk of recurrent infection in postmenopausal women compared with placebo (16.0% versus 62.8%, NNT 3 [range 2 to 4]; high quality evidence).

- *Raz R and Stamm WE. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. N Engl J Med 1993; 329: 753–756.*



# Methanamine Hippurate

---

Compared to antibiotic prophylaxis, methenamine is

- Non inferior
- Less costly
- Considered as alternative to daily abx prophylaxis in women/female genitourinary system

Study protocol | [Open Access](#) | Published: 09 November 2018

## **ALternatives To prophylactic Antibiotics for the treatment of Recurrent urinary tract infection in women (ALTAR): study protocol for a multicentre, pragmatic, patient-randomised, non-inferiority trial**

[Rebecca Forbes](#), [Ased Ali](#), [Alaa Abouhajar](#), [Catherine Brennand](#), [Heather Brown](#), [Sonya Carnell](#), [Thomas Chadwick](#), [Ian Eardley](#), [Jan Lecouturier](#), [Helen Mossop](#), [Ian Pearce](#), [Robert Pickard](#), [Nikesh Thiruchelvam](#), [Katherine Walton](#), [Jennifer Wilkinson](#) & [Chris Harding](#) ✉

[Trials](#) **19**, Article number: 616 (2018) | [Cite this article](#)

**15k** Accesses | **6** Citations | **8** Altmetric | [Metrics](#)



Clinical Trial > Eur Urol. 1994;26(2):137-40. doi: 10.1159/000475363.

## Uro-Vaxom and the management of recurrent urinary tract infection in adults: a randomized multicenter double-blind trial

P Magasi<sup>1</sup>, J Pánovics, A Illés, M Nagy

Affiliations + expand

PMID: 7957468 DOI: [10.1159/000475363](https://doi.org/10.1159/000475363)

### Abstract

A total of 112 patients with recurrent lower urinary tract infection (UTI) completed the 6-month period of the trial. Patients were treated for 3 months, under double-blind conditions, with one capsule daily of either Uro-Vaxom (UV) or placebo, together with an antibiotic or chemotherapeutic agent when necessary, and observed for a further 3 months. During the 6 months of the trial a significant decrease in the number of recurrences ( $p < 0.0005$ ) was noted in the UV group as compared to the placebo group. A total of 67.2% of the patients had no recurrences ( $p < 0.0005$ ). The incidence of bacteriuria (germs  $> \text{or} = 10(5)/\text{ml}$ ), dysuria and leukocyturia was significantly reduced. UV was well tolerated, no side effects were recorded during the trial. The drug is a useful adjuvant for the management of UTIs and for the prevention of recurrences.

# Prophylactic antibiotics

---

Long term prophylaxis can range from 4 mths to 5 yrs

- 95% will remain UTI free but 50% relapse following cessation

*Nicolle et al. Am J Med 2002*

Cochrane review of RCT's - RR 0.21 for single recurrence (NNT 1.85) but RR after completion of prophylaxis 0.82

*Albert et al. Cochrane Database 2004*

Single randomised study found prophylactic nitrofurantoin superior to oestrogen

*Raz et al. Clin Infect Dis 2003*



## Self start antibiotics

---

85-95% of women with previous UTI can self diagnose successfully

Gupta et al. Ann Intern Med 2001

Clinical and Microbiological cure rates > 90%

Best used in motivated women with previous culture confirmed cystitis

Hooton NEJM 2012

Advantages are less antimicrobial exposure and high patient satisfaction rates

*Post coital antibiotics* reserved for group where it has been identified as the dominant risk factor.

# Intravesicle treatments

- GAG replacement therapy

CEOG Clinical and Experimental  
Obstetrics & Gynaecology

## Long-term efficacy of intravesical instillation of hyaluronic acid/chondroitin sulfate in recurrent bacterial cystitis: 36 months' follow-up

D. De Vita<sup>1\*</sup>, M. Madonia<sup>2\*</sup>, E. Coppola<sup>1</sup>, C. Sciorio<sup>3</sup>, S. Giordano<sup>3</sup>, S. Dessole<sup>4</sup>, G. Capobianco<sup>4</sup>

<sup>1</sup>Chronic Pelvic Pain Centre, Dep. of Obstetrics and Gynaecology, Ospedale S. Maria Della Speranza, Battipaglia

<sup>2</sup>Institute of Urology, University of Sassari, Sassari; <sup>3</sup>Ostetricia e Ginecologia, ASL Napoli 2 Nord, Naples

<sup>4</sup>Gynecologic and Obstetric Clinic, Dep. of Surgical, Microsurgical and Medical Sciences, University of Sassari (Italy)

<sup>5</sup>Division of Plastic Surgery, Department of Surgery, Turku University Hospital, OS Turku (Finland)

### Summary

**Purpose of Investigation:** To compare the efficacy and safety of intravesical instillation of hyaluronic acid/chondroitin sulfate with conventional long-term antibiotic prophylaxis in women with recurrent bacterial cystitis. **Materials and Methods:** In this analysis of a prospective study, where women with recurrent bacterial cystitis were randomised to intravesical hyaluronic acid 800 mg/chondroitin sulfate 1,000 mg (group 1) or long-term antibiotic prophylaxis (group 2 – control group), patients in group 1 were evaluated 36 months after treatment. Outcomes included cystitis recurrence, subjective pain symptoms based on a visual analogue scale (VAS), three-day voiding, pelvic pain and urgency/frequency symptoms (PUF scale), sexual function questionnaire, quality of life based on King's Health Questionnaire (KHQ), maximum cystometric capacity (MCC), and adverse events. **Results:** Twelve women (mean  $\pm$  standard deviation 59.3  $\pm$  13.9 years old) underwent follow-up at 36 months after treatment. There were improvements in all efficacy evaluations at 36 months' follow-up, with significantly favourable mean changes from baseline in cystitis frequency ( $-5.4$  episodes/year;  $p < 0.001$ ), three-day voiding ( $-10.7$  voids;  $p = 0.002$ ), urinary VAS ( $-6.7$  points;  $p < 0.001$ ), PUF ( $-14.2$  points;  $p < 0.001$ ), sexual function ( $-4.3$  points;  $p < 0.001$ ) and KHQ ( $-34.0$ ;  $p < 0.001$ ) scores, and MCC ( $+131.7$ ;  $p < 0.001$ ). No adverse events were reported. **Conclusions:** Intravesical hyaluronic acid/chondroitin sulfate significantly reduced cystitis recurrence and associated symptoms and was well tolerated in women with recurrent bacterial cystitis at 36 months' after treatment.

**Key words:** Chondroitin sulfate; Hyaluronic acid; Intravesical instillation; Recurrent bacterial cystitis; Recurrent urinary tract infection

## Antibiotics

Review

> Int Urogynecol J. 2022 May;33(5):1125-1143. doi: 10.1007/s00192-021-05042-z.

Epub 2022 Jan 4.

## Efficacy of antimicrobial intravesical treatment for uncomplicated recurrent urinary tract infections: a systematic review

Meghana Reddy<sup>1</sup>, Philippe E Zimmern<sup>2</sup>

Affiliations + expand

PMID: 34982189 DOI: 10.1007/s00192-021-05042-z

### Abstract

**Introduction and hypothesis:** Intravesical antimicrobials (IVA) provide a localized modality of treatment for recurrent urinary tract infections (rUTIs). Owing to the sporadic use of these treatments, we conducted a systematic review on the efficacy of IVA in the management of uncomplicated rUTIs.

**Methods:** A systematic review was conducted for all English language articles from inception to April 2021 utilizing the Cochrane and Preferred Reporting Items for Systematic Reviews and Meta-Analyses standards with the following databases: PubMed, OVID Embase, Biomed Central, and Scopus. References were cross-examined for further articles. Risk of bias was assessed in the articles included using the Cochrane and Joanna Briggs Institute tools.

**Results:** The initial search resulting in 476 titles led to 15 full-text articles. Of the 13 in the final review (2 RCTs), 3 used gentamicin and 10 used hyaluronic acid IVA. These included 764

# Haematuria clinic referral guidelines UK

Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for bladder cancer if they are:

- aged 45 and over and have:
  - **unexplained** visible haematuria without urinary tract infection **or**
  - **visible haematuria** that persists or recurs after successful treatment of urinary tract infection, **or**
- **aged 60 and over and have unexplained non-visible haematuria and either dysuria or a raised white cell count on a blood test. [new 2015]**

Consider **non-urgent** referral for bladder cancer in people aged **60 and over with recurrent or persistent** unexplained urinary tract infection. **[new 2015]**

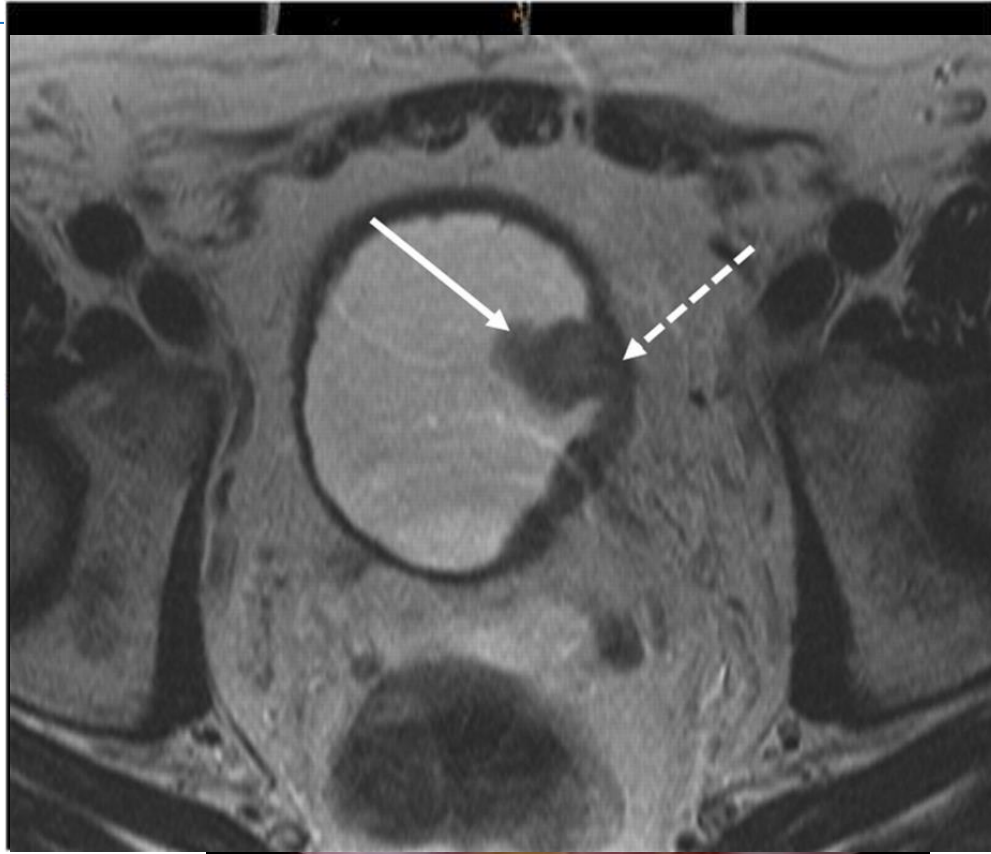
# Haematuria referral guidelines AUA

Low-risk (meets all criteria)	Intermediate-risk (meets any one criteria)	High-risk (meets any one criteria)
<ul style="list-style-type: none"><li>▶ Age &lt;50 for women and &lt;40 for men</li><li>▶ Never smoker, or smoking history &lt;10 pack years</li><li>▶ 3-10 RBC/HPF on urinalysis</li><li>▶ No additional risk-factors for urothelial cancer</li></ul>	<ul style="list-style-type: none"><li>▶ Age 50-59 for women and 40-59 for men</li><li>▶ Smoking history 10-30 pack years</li><li>▶ 11-25 RBC/HPF on urinalysis</li><li>▶ Additional risk-factors for urothelial cancer</li><li>▶ Low-risk patient with persistent microscopic haematuria on repeat urinalysis</li></ul>	<ul style="list-style-type: none"><li>▶ Age &gt;60 years old</li><li>▶ Smoking history &gt;30 pack years</li><li>▶ &gt;25 RBC/HPF on urinalysis</li><li>▶ History of visible haematuria</li></ul>

## VH case - UC

87 yo male





# Cancer and haematuria, the studies

PLATI

2018

Wh

Pro

Wei s

on be

Affili



>>

Show Outline



Original Article | Open Access |

## The IDENTIFY study: the investigation and detection of urological neoplasia in patients referred with suspected urinary tract cancer – a multicentre observational study

Sinan Khadhour , Kevin M. Gallagher, Kenneth R. MacKenzie, Taimur T. Shah, Chuanyu Gao, Sacha Moore, Eleanor F. Zimmermann, Eric Edison, Matthew Jefferies ... [See all authors](#) ▾

First published: 14 May 2021 | <https://doi.org/10.1111/bju.15483> | Citations: 25

PubMed indexed collaborators members are presented in [Appendix](#).

SECTIONS



PDF



TOOLS



SHARE



# Urothelial Cancer

---

Risk Factors for Urothelial cancer

Smoking

Strong family history of bladder cancer (2 or more relatives)

Occupational exposure to carcinogens

Pelvic irradiation

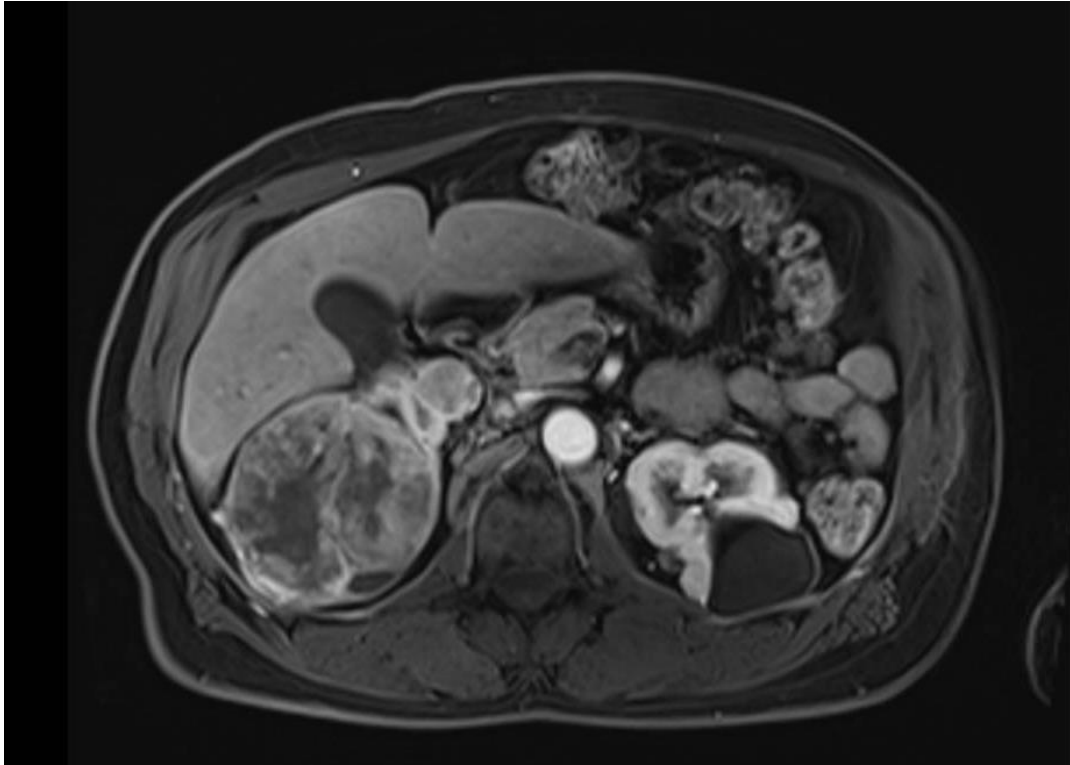
Cyclophosphamide treatment

Previous schistosomiasis infection

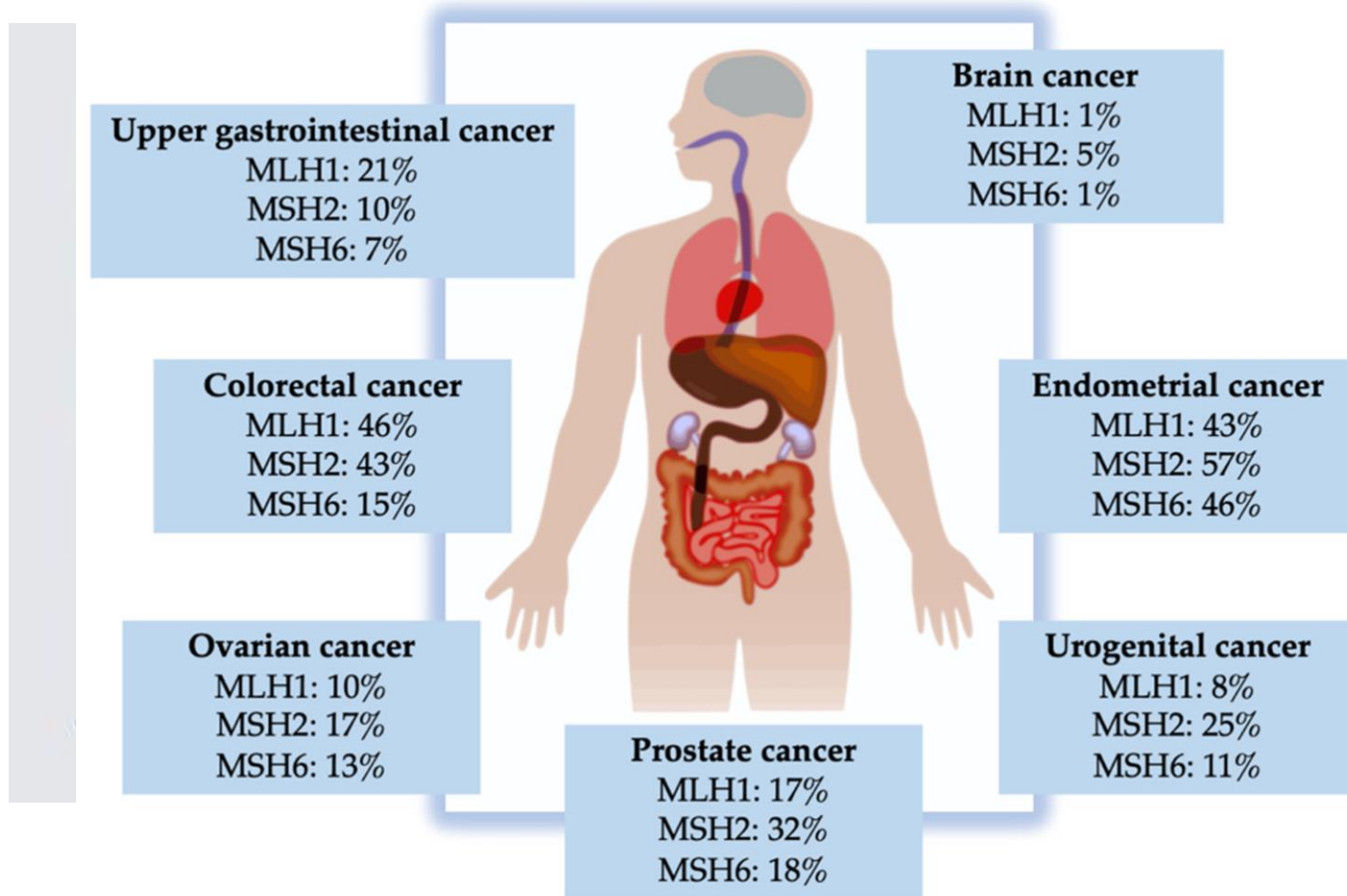
Significant filling bladder symptoms in the absence of a urinary infection (urgency, frequency, dysuria)

# Renal cancer

---



# Hereditary malignancy



# Hereditary renal cancer : screening & management strategies

---

Families with 2 or more affected with RCC

Multifocal/bilateral tumours

Non-renal manifestations

Early age of onset (<46 years)

Clinical/histopathological diagnosis

Germline mutation analysis

Multi-disciplinary approach

Appropriate surgical intervention (early with HLRCC)

Haematuria clinic

Female, menopausal LUTS, recurrent UTI

Urological malignancy

- Renal cancer
- Upper tract urothelial cancer
- Bladder cancer
- Prostate cancer

Hereditary/genetic malignancy

# Thank you