BMJ Best Practice

Urinary tract infections in men

Straight to the point of care

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Summary

Urinary tract infection (UTI) in men rarely occurs before 50 years of age.

Often associated with abnormal structure or function of the urinary tract (complicated UTI).

Catheter-associated UTI is the most common cause of nosocomial infection.

Imaging of the urinary tract is recommended for men with persistent haematuria, voiding dysfunction without a clearly identifiable cause such as benign prostatic hyperplasia (BPH), failure of initial therapy, or signs of upper tract infection.

Treatment with a fluoroquinolone antibiotic is generally appropriate in men as they are likely to have a UTI classified as complicated. Asymptomatic bacteriuria does not require treatment except before urological procedures.

Definition

UTI is an inflammatory reaction of the urinary tract epithelium in response to pathogenic microorganisms, most commonly bacteria.

Epidemiology

Combined data for men and women from all patient-care settings identify urinary tract infection (UTI) as the most common infection overall, and the second most common infection among non-institutionalised patients.[7] Forty percent of all nosocomial infections in men and women are UTIs; 80% of these develop secondary to indwelling catheters.[8] Men account for 20% of the overall occurrences of UTI, with an estimated lifetime prevalence of 13,689 per 100,000.[9] Ageing contributes to UTI occurrence in men.[10] UTIs rarely develop in men before 50 years of age.[9] Also, residence in a long-term care facility correlates with the likelihood of men developing bacteriuria and UTI.[10] The ratio of UTI occurrence between institutionalised women and men is almost equal (2 to 3:1), unlike the ratio for younger women and men (25:1).[11] In addition, up to 40% of institutionalised men have asymptomatic bacteriuria.[4] [9] [11]

Aetiology

Urinary tract infection (UTI) results from pathogenic organisms gaining access to the urinary tract and not being effectively eliminated. The bacteria ascend the urethra and generally have an intestinal origin; therefore, *Escherichia coli* causes most UTIs in men and women.[5] [12] [13] [14]

Men, however, more frequently have UTI that is classified as complicated and associated with a varied group of causative organisms. Other gram-negative bacteria that cause UTI in men include *Klebsiella* , *Proteus* , and *Providencia* .[3] [6] [12] [13] [14] Gram-positive infections also occur in complicated UTI patients. A 5-year study involving male veterans demonstrated that 40% of community-acquired infections and 55% of inpatient infections resulted from organisms such as *Enterococcus* and *Staphylococcus* .[15] When UTI develops in patients in hospitals or long-term care facilities or as the result of indwelling catheters, *Pseudomonas* , *Candida* , and resistant organisms must be considered.[16] [17]

Pathophysiology

UTI develops when the balance between host defence mechanisms and the virulence of the invading organism is distorted.[18] For example, men with immunodeficiency from HIV infection more often acquire UTI.[3] [19] Another important defence mechanism is urine flow. Disruption of this defence often contributes to the development of UTI in men and results in a classification of complicated UTI. In general, complicated UTI occurs as a result of structural or functional abnormalities of the urinary tract that impair urine flow, such as:[1]

- Prostate disorders
- Calculi within the collecting system or the kidney
- External drainage devices or internal devices such as stents
- Urinary diversion surgeries
- Vesicoureteral reflux
- Neurogenic bladder disorders, including diabetes mellitus.

Available studies in men frequently identify impaired urine flow due to prostate hyperplasia, urinary calculi, or urethral stricture as a factor related to UTI.[16] [20] [21] [22] Also, reviewing the epidemiology of UTI in men corroborates the hypothesis that altered urine flow is significant to the pathophysiology.

With ageing, the incidence of problems causing complicated UTI increases, and this corresponds to the increased incidence of UTI in older men. Structural or functional abnormalities of the urinary tract occur more

frequently in older men.[13] The incidence of UTI in men is highest among those residing in long-term care facilities.[9]

Other risk factors include a history of anal intercourse, which is associated with urological symptoms and infection in both men and women.[23] In one study, UTI was more common amongst men who have sex with men, compared to men who have sex with women alone.[24]

Vaginal intercourse also may result in UTI if the vagina is colonised by pathogenic organisms.[19]

In summary, factors contributing to UTI development in men include alteration of the host defences, with altered urine flow contributing significantly.

Classification

Healthcare-associated versus community-acquired

Healthcare-associated (nosocomial) UTI implies acquisition of the pathogenic organism from within a healthcare facility, whereas community-acquired infection occurs without exposure to such a facility.

Complicated

Complicated UTI implies the presence of other factors that hinder the efficacy of therapy, such as:[1] [2] [3]

- Structural or functional abnormalities of the urinary tract
- Immunodeficiency (e.g., HIV infection)
- Indwelling catheter
- Infection due to resistant organisms.

UTIs in men are often complicated.

Recurrent

Recurrent UTI results from either persistence of an infection that is inadequately treated or the acquisition of a new infection.

Asymptomatic bacteriuria

Patients with ≥10^5 CFU/mL in culture from a single specimen, but without dysuria, frequency, urgency, or suprapubic or costovertebral angle (CVA) pain, are classified as having asymptomatic bacteriuria.[4]

Case history

Case history #1

A 59-year-old man describes urinary frequency, urgency, and dysuria for several days. He denies the presence of haematuria or penile discharge, but does have 3 episodes of nocturia most nights. His past medical history includes benign prostatic hyperplasia (BPH). The patient is in a monogamous relationship with his wife.

THEORY

Case history #2

A 70-year-old man, who has been an inpatient for 4 days with an exacerbation of congestive heart failure, is now complaining of unilateral back pain. He has had an indwelling urinary catheter to strictly monitor urine output since admission. He also relates a history of increasing suprapubic discomfort for the last 24 hours. Examination confirms fever, suprapubic tenderness, and costovertebral angle tenderness.

Other presentations

Symptoms specifically related to urinary tract infection (UTI) include dysuria, frequency, urgency, suprapubic pain, or costovertebral angle pain. In men, however, fever and urethral discharge may also occur.[5] [6] Some patients may have symptoms related to BPH or urethral stricture, such as hesitancy, incomplete emptying, or nocturia. In addition, there may be symptoms of prostatitis, such as rectal or perineal pain. Older patients may present with altered mental status secondary to UTI. However, with the high prevalence of asymptomatic bacteriuria in this group, it is important to search for other causes of altered mental status despite the presence of abnormal urine testing or culture.

Approach

There is debate over the exact number of bacteria in a urine culture that is needed to define urinary tract infection (UTI) in men. The standardised threshold in symptomatic patients is >100,000 CFU/mL for organisms identified as common pathogens; however, many sites now use either 10,000 CFU/mL or 1000 CFU/mL threshold, based on the method of collection or patient population as a baseline for culture work-up and clinical significance.[43]

Urine from a man with urinary tract symptoms (dysuria, frequency, urgency, suprapubic pain, costovertebral angle pain) that grows ≥10^3 colony-forming units (CFU)/mL of one, or predominantly one, organism in culture suggests the presence of UTI.[25] [44]

History

Most UTIs in men occur after 50 years of age, and the incidence is highest among those residing in long-term care facilities.

Dysuria most often results from infection.[6] Also, frequency, urgency, and suprapubic pain signal UTI. Costovertebral angle pain suggests extension of UTI to the kidney (pyelonephritis). Rectal or perineal pain can indicate UTI associated with prostatitis. Men may present with urethral discharge or have symptoms related to impaired urine flow, such as hesitancy or nocturia.[25] Finally, the history includes identification of systemic signs (e.g., fever, rigors) and possible immunocompromised states (e.g., diabetes mellitus) that may indicate a more severely ill patient requiring hospitalisation.

The past medical history can reveal the following risks contributing to UTI:[25]

- Previous UTI
- Benign prostatic hyperplasia (BPH)
- Urinary tract stones
- Previous urological surgery or instrumentation
- Recent hospitalisation

The social history will identify sexual practices and preferences; anal sex in particular increases risk of UTI.

Physical examination

The physical examination is useful in excluding other possible causes for the patient's symptoms. It should at least include the abdomen, genitalia, rectum, and palpation of the costovertebral angle.

A tender boggy prostate, firm enlarged prostate, or nodularity suggests prostatitis, prostate hyperplasia, and prostate cancer, respectively.

Penile lesions or discharge suggest sexually transmitted infection.

Tenderness or swelling of the epididymis or testes implies the presence of epididymitis or orchitis, respectively.

Fever may occur in patients with complicated UTI.

Laboratory

A dipstick or microscopic urinalysis (U/A) is the initial test for men with suspected UTI. If dipstick is negative for nitrites and leukocyte esterase, or microscopic U/A is negative for bacteria and leukocytes, this excludes infection, but the presence of these markers does not rule in UTI.[2] [45] Negative results should prompt a search for another cause of the patient's symptoms. A positive U/A in a man with typical UTI symptoms should be followed by a urine culture and empirical antibiotic therapy while awaiting the culture result. In the absence of signs and symptoms of a UTI, a urine culture is typically not recommended.[43] In men with a positive U/A, obtaining a Gram stain of the urine can guide the initial antibiotic choice; however, it is not required, because empirical therapy can be chosen based on the anticipated pathogenic bacteria. Gram stain, like U/A, does not confirm the presence of UTI.[15] Culture is essential to confirm the diagnosis of UTI and because of the potential for non-traditional organisms in men.[5] [19] The presence of $\geq 10^2$ CFU/mL of one, or predominantly one, organism in culture confirms UTI in symptomatic men. A midstream clean-catch urine sample used for culture compares favourably with suprapubic aspiration or catheter specimens.[46]

No difference exists in the approach to patients in the outpatient and long-term care settings. However, in long-term care, U/A is even less predictive of the presence of UTI because a high proportion of these patients have pyuria related to asymptomatic bacteriuria.[11] [4] But a negative U/A does exclude the presence of UTI.[4] [11]

Biological markers of bacterial infection, such as the myeloid cell soluble trigger receptor expression (sTREM-1), have not been a reliable method for detecting infection of the male urinary tract as a result of their low sensitivity.[42] [47] [48]

Imaging

Imaging of the kidneys, ureters, and bladder by computed tomography (CT), ultrasound, or intravenous urogram, should be reserved for:[1] [3]

- Those who have voiding dysfunction without a clearly identifiable cause such as BPH
- Cases of treatment failure
- Those with persistent haematuria
- Those with signs of upper tract infection.

Although imaging of men with UTI frequently results in abnormal findings, it usually does not alter treatment. Therefore, it is not indicated in all cases.[1] [3] [12] [13] [19] [26]

The healthcare provider must choose an imaging technique based on availability of local resources and the underlying pathology that is suspected. CT scan offers the best overall detail but is expensive. A plain x-ray of kidneys, ureters, and bladder can be helpful if stones are suspected, but CT scan is more reliable. If an obstructive process is suspected, ultrasound can rule this out. The intravenous urogram (IVU) has only limited usefulness compared with the other modes of imaging, but the clinician may consider obtaining an IVU if continued suspicion exists after a negative CT or ultrasound, or in cases where a less expensive test is desired.

History and exam

Key diagnostic factors

presence of risk factors (common)

- Key risk factors include renal tract obstruction (e.g., benign prostatic hyperplasia [BPH], stones, stricture), previous urinary tract infection (UTI), age >50 years, and instrumentation of renal tract.

dysuria (common)

- Denotes inflammation of the urinary tract epithelium and most commonly results from infection.[6]

urgency (common)

- Presence of this symptom significantly increases the probability of UTI.

frequency (common)

- Presence of this symptom significantly increases the probability of UTI.

suprapubic pain (common)

- Presence of this symptom significantly increases the probability of UTI.

costovertebral angle pain (uncommon)

- Suggests extension of UTI to the kidney (pyelonephritis), but UTI without direct renal involvement occurs more often.

Other diagnostic factors

hesitancy (common)

- Occurs with obstruction of urine flow (e.g., BPH).

nocturia (common)

- Occurs with obstruction of urine flow (e.g., BPH).

enlarged prostate (common)

- Suggests the presence of BPH.

tender prostate (uncommon)

- Suggests the presence of prostatitis.

rectal/perineal pain (uncommon)

- May occur in patients with UTI associated with prostatitis.

fever/rigors (uncommon)

- May occur with underlying prostatitis or with complicated UTI, which can result in spread of the infection to the upper tract.[1] [49]

urethral discharge (uncommon)

- Occasional discharge has been reported.[6]

Risk factors

Strong

benign prostatic hypertrophy

- Benign prostatic hypertrophy (BPH) and other causes of urine-flow obstruction are often identified as risk factors in trials relating to urinary tract infection (UTI) in men.[3] [6] [22]
- Up to 30% of young men with UTI have anatomical or functional abnormalities of the urinary tract, and this is higher in older men.[10] [13] [25] In one study of UTI in men with an average age of 54, 53% had abnormal findings on urinary tract imaging.[26]

urinary tract stones

- Urinary calculi and other causes of urine-flow obstruction are often identified as risk factors in trials relating to UTI in men.[3] [6] [22]

urological surgery, instrumentation

- Urinary surgery, instrumentation, and other causes of urine-flow obstruction are often identified as risk factors in trials relating to UTI in men.[3] [6] [22]
- Up to 30% of young men with UTI have anatomical or functional abnormalities of the urinary tract, and this is higher in older men.[10] [13] [25] In one study of UTI in men with an average age of 54, 53% had abnormal findings on urinary tract imaging.[26]

urethral strictures

- Urethral strictures and other causes of urine-flow obstruction are often identified as risk factors in trials relating to UTI in men.[3] [6] [22]

age >50

- Up to 30% of young men with UTI have anatomical or functional abnormalities of the urinary tract, and this is higher in older men.[10] [13] [25] In one study of UTI in men with an average age of 54, 53% had abnormal findings on urinary tract imaging.[26]
- The majority of UTIs in men occur after 50 years of age.[6] [9] [26]
- Asymptomatice bacteriuria is present in up to 10% of community-dwelling men who are older than 80 years of age.[10]

previous UTI

- Epidemiological data suggest that the risk of acquiring another UTI increases with each subsequent infection.[5]

catheterisation

- UTI is the most common nosocomial infection, and the majority of cases result from indwelling catheters.[8]
- Removal of a catheter within 5 days of placement decreases the rate of occurrence.[27]
- Changing chronic indwelling catheters before initiating antimicrobial therapy has also been shown to improve microbiological cure.[28][29]

Weak

anal sex

- It is commonly accepted that vaginal sex increases the risk in women, but this seems to be less of a risk factor in men. Anal intercourse has been associated with UTI in women, and in men who have sex with men.[23] [24]

vaginal sex

- It is commonly accepted that vaginal sex increases the risk in women, but this seems to be less of a risk factor in men. If, however, vaginal colonisation with enteric pathogens has occurred, the risk increases.[19] [30]

recent hospitalisation

- Most UTIs are not nosocomial in origin.

uncircumcised

- Circumcision reduces the risk of UTI development in boys.[31] However, the mechanism by which the prepuce increases risk and whether it contributes to UTI in adult men remains unclear.

Investigations

1st test to order

Test	Result
dipstick urinalysis • Either pyuria or nitrites may correspond to infection, but the presence of both improves the sensitivity to an overall range of 68% to 88%.[45] [46] • Conversely, if both are negative, the test accurately predicts the absence of infection, with specificity ranging between 77% and 100% in all populations.[45] [46] • In the nursing home setting, urinalysis is less reliable in predicting the presence of infection, because a high proportion of these patients have pyuria related to asymptomatic bacteriuria.[4] [11] Also, urinalysis is not reliable in determining the presence of catheter-associated UTI.[16]	**positive leukocyte esterase and/or nitrite**
urine microscopy • Will help confirm the finding of leukocytes and can identify the presence of bacteria. One trial identified 10 WBC/mm^3 as having 71% sensitivity and 76% specificity.[46]	**leukocytes and/or bacteria**
urine culture • A value of ≥10^2 colony-forming units (CFU)/mL of one, or predominantly one, organism provides a sensitivity of 95% and specificity of 85% for UTI in symptomatic men.[50] • Midstream clean-catch urine used for culture is appropriate, with a sensitivity and specificity similar to bladder urine obtained by suprapubic aspiration and urethral catheterisation.[46] • As many as 40% of men in long-term care facilities will have ≥10^5 CFU/mL growth of bacteria without symptoms related to the urinary tract (asymptomatic bacteriuria).[4]	**≥10^2 CFU/mL**
Gram stain • May help in determining initial empirical antibiotic therapy; however, the accuracy is limited. • Like urinalysis, Gram stain better predicts the absence of infection. • One trial analysing 4900 specimens identified the sensitivities for gram-positive cocci and gram-negative rods as 63% and 45%, respectively; and specificities as 91% and 94%, respectively.[15]	**bacteria**

Other tests to consider

Test	Result
CT renal tract • Provides excellent anatomical detail and is the best test for identifying perirenal abscess. • Should be reserved for those who have voiding dysfunction without a clearly identifiable cause such as benign prostatic hyperplasia (BPH), in cases of treatment failure, in men with persistent haematuria, or in those with signs of upper tract infection.[1] [3]	**perirenal abscess, urinary calculi, or tumours**
ultrasound • Should be reserved for those suspected of having a structural abnormality without a clearly identifiable cause such as BPH, in cases of treatment failure, in men with persistent haematuria, or in those with signs of upper tract infection.[1] [3] • Compared with intravenous urogram, ultrasound offers a better choice because it is non-invasive and does not require use of contrast agents.	**rules out obstruction**
plain x-ray kidneys, ureters, and bladder (KUB) • Not consistently reliable. • Should be reserved for those suspected of having a structural abnormality without a clearly identifiable cause such as BPH, in cases of treatment failure, in men with persistent haematuria, or in those with signs of upper tract infection.[1] [3] • One study involving 114 men (average age 54) found that plain x-ray KUB combined with ultrasound compared favourably with intravenous urogram in identifying structural abnormalities of the urinary tract.[26]	**urinary tract stone, abscess**
intravenous urogram (IVU) • Should be reserved for those who have voiding dysfunction without a clearly identifiable cause such as BPH, in cases of treatment failure, in men with persistent haematuria, or in those with signs of upper tract infection.[1] [3] • Plain x-ray KUB combined with ultrasound may perform as well as IVU.[26]	**rules out obstruction**

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Benign prostatic hypertrophy (BPH)	• Symptoms of obstructed urine flow may occur. • UTI symptoms are uncommon unless obstruction leads to UTI development.	• Elevated prostate specific antigen (PSA) may suggest presence of hyperplasia. • An enlarged and firm prostate identified on digital rectal examination helps to confirm the diagnosis.
Prostatitis	• Most commonly presents with rectal pain and symptoms of obstructed urine flow. • Dysuria and urinary frequency may occur.	• A tender and boggy prostate on digital rectal examination suggests prostatitis.
Pyelonephritis	• Often a complication of UTI, but can occur without history of UTI. • May be indicated by costovertebral angle pain with tenderness on examination.	• Presence of WBC casts on urinalysis indicates pyelonephritis.
Urinary tract stones	• Urinary tract stones may result in damage of the urinary epithelium and consequently dysuria; however, they also typically cause pain. • A past medical history of stone formation can help to identify risk.	• Both intravenous urogram and CT scan will identify the presence of a urinary tract stone, but CT scan is more accurate and does not require use of intravenous contrast.
Gonococcal urethritis	• New or multiple sexual partners implies risk. • Frequency and urgency of urination as well as fever are often absent. • The presence of purulent urethral discharge is more suggestive of gonorrhoea than UTI.[5] • Occurs more commonly in young men.	• A gonococcal DNA intra-urethral probe accurately identifies the presence of gonorrhoea.
Chlamydia urethritis	• New or multiple sexual partners implies risk. • Frequency and urgency of urination as well as fever are often absent. • Occurs more commonly in young men.	• Urine culture will be sterile. • A chlamydia DNA intra-urethral probe accurately identifies the presence of chlamydia.

Condition	Differentiating signs / symptoms	Differentiating tests
Bladder cancer	• Patients may present with symptoms resembling UTI but often have haematuria.[5] [6]	• Cystoscopy with confirmatory tissue biopsy determines the presence of bladder cancer.
Prostate cancer	• Symptoms of obstructed urine flow may occur. • UTI symptoms are uncommon unless obstruction leads to UTI development.	• Elevated PSA suggests presence of malignancy. • Tissue biopsy confirms the diagnosis.
Renal cancer	• Patients may present with symptoms resembling UTI but often have haematuria.[5] [6]	• CT scan will identify the presence of a renal mass. • Pathological analysis, typically at the time of surgical removal, confirms the diagnosis.
Epididymitis	• Most often presents with scrotal pain and is not associated with dysuria, urgency, or frequency. • Tender, swollen epididymis.	• Urinalysis and culture are negative in isolated epididymitis, but UTI may be present additionally.
Reactive arthritis	• Symptoms unrelated to the urinary tract may be present, such as arthralgia, back pain, or ocular symptoms.	• Urine culture will be sterile. • Blood testing may reveal hypergammaglobulinaemia and a positive HLA-B27 tissue antigen.
Behcet's syndrome	• Symptoms unrelated to the urinary tract may be present, such as arthralgia, back pain, ocular symptoms, and oral ulcers.	• Urine culture will be sterile. • Seems to have relationship to HLA-B5 antigen. • A positive pathergy test and the presence of serum immune complexes may aid in diagnosis.

Criteria

Urinary tract infection

Urine culture demonstrates ≥10^2 colony-forming units (CFU)/mL of a single or predominant organism in a patient with symptoms specific to the urinary tract.[25] [50]

Asymptomatic bacteriuria

Urine culture demonstrates ≥10^5 CFU/mL of a single organism obtained by clean catch on one occasion from a man without specific urinary tract symptoms.[4]

Screening

Screening for the presence of bacteriuria in patients with chronic indwelling catheters is not recommended.[4] [51]

Screening and treatment for the presence of asymptomatic bacteriuria in adult men, except before planned urological procedures that disrupt the mucosa, are not recommended, because elimination of asymptomatic bacteriuria does not alter morbidity or mortality.[4] [51] However, before urological procedures that may disrupt the urinary tract lining, an attempt should be made to sterilise the urine, thereby decreasing the risk of bacteraemia and sepsis.[52]

Approach

The goal of treatment is the eradication of bacteria; antimicrobial agents are the primary means of therapy.

Symptomatic men with culture-proven urinary tract infection (UTI) should be treated with antimicrobial agents.[44]

Men with a positive urinalysis by dipstick or microscopic examination and specific symptoms (dysuria, frequency, urgency, suprapubic pain, or costovertebral angle pain) should receive empirical therapy until the culture results demonstrate absence of significant bacteriuria or suggest need for a different antimicrobial based on the sensitivities provided.

Catheter-associated UTI (a complicated UTI) must be treated with diligence because of the risk of developing bacteraemia, but screening for or treatment of asymptomatic bacteriuria in catheterised patients is not recommended.[4] [Evidence A] [Evidence C] If therapy is initiated, then the catheter should be changed before starting antibiotics.[29]

Intravenous therapy and hospitalisation are indicated for patients who are severely ill, such as in cases of suspected bacteraemia.[44] Intravenous therapy is continued until the patient is stabilised and afebrile. Oral antibiotic therapy using fluoroquinolones may be considered as an alternative to intravenous because of excellent bioavailability. Illness severity is judged by the presence of a generally toxic-appearing patient, with fever, tachycardia, tachypnoea, hypotension, or an elevated white blood cell count. The decision to hospitalise can also be based on the patient's inability to take medications orally (e.g., in cases of protracted vomiting). For patients with UTI who are otherwise immunocompromised, the clinician should maintain a lower threshold for hospitalisation.

Choice of antibiotics

Treating UTI in men differs from female UTI therapy. Most recommendations derive from data regarding women, but men more often have UTI classified as complicated. Treatment options include beta-lactam antibiotics (often in combination with other antibiotics [e.g., aminoglycosides]), trimethoprim/sulfamethoxazole (TMP/SMX), nitrofurantoin, and fluoroquinolones.[10] [44]

The choice of initial empirical therapy should be guided by local resistance patterns.[44] All men should have a urine culture to assure that the initial empirical antibiotic choice is appropriate.

The goal of therapy (eradication of bacteria) and the primary means of therapy (oral antibiotics) remain the same for both men and women. The basic principles of choosing an antibiotic include:

- Identifying the probable organism causing the infection
- Identifying the patient's prior hypersensitivities
- Weighing the potential adverse effects
- Considering the presence of renal or liver disease
- Considering the cost of therapy.

Overall, *Escherichia coli* causes the majority of UTIs. However, *E coli* is identified as the causative organism in less than 50% of men with UTI, so a more variable group of bacterial species must be considered.[3] [6] [11] [12] [13] [14] [21] [25] [54] Additional microorganisms causing UTI in men include *Klebsiella* , *Proteus* , *Providencia* , *Enterococcus* , and *Staphylococcus* . Catheter-related UTI may also be associated with *Pseudomonas* and resistant organisms.

Using trimethoprim/sulfamethoxazole (TMP/SMX) as first-line empirical therapy for UTI in women may not apply to men.[55] Furthermore, using TMP/SMX first-line is only recommended if local *E coli* resistance patterns are less than 20%, and US data suggest that TMP/SMX resistance ranges between 18% and 22%.[54] A trial involving men in German outpatient settings noted 34% resistance to TMP/SMX.[14] Risk factors identified for having an infection resistant to TMP/SMX include recent use of TMP/SMX or any antibiotic and recent hospitalisation.[56]

Trials to determine antibiotic choice for treating UTI in men are sparse. The few available trials involving use of TMP/SMX in men suggest poor success. A small study of men with recurrent UTI compared 10 days of TMP/SMX with 12 weeks of therapy; microbiological cure occurred in 3 out of 15 and 9 out of 15, respectively.[57]

In contrast, the fluoroquinolones perform better in head-to-head comparison and in length of therapy required for microbiological cure.

- One study involving both men and women with complicated UTI resulted in cure rates of 95% and 43% for lomefloxacin and TMP/SMX, respectively.[58]
- In another study, 2 weeks of ciprofloxacin in men with febrile UTI compared favourably with 4 weeks of therapy.[21]

However, fluoroquinolones have been associated with serious, disabling, and potentially irreversible adverse effects, including tendonitis, tendon rupture, arthralgia, neuropathies, and other musculoskeletal or nervous system effects.[59] Warnings have also been issued about the increased risk of aortic dissection, significant hypoglycaemia, and mental health adverse effects in patients taking fluoroquinolones.[60] [61]

Depending on patient characteristics and local resistance patterns, fluoroquinolone antibiotics remain a reasonable first-line treatment of UTI in men due to the higher risk of a complicated course in this patient group.[44]

Due to high levels of resistance, the European Association of Urology recommends against the use of fluoroquinolones for the empirical treatment of complicated UTI in patients from urology departments or when patients have used fluoroquinolones in the last 6 months.[44]

TMP/SMX may be considered first-line in younger men without evidence of complicated UTI and with consideration to local resistance patterns.

Of note, oral antibiotic therapy, and specifically ciprofloxacin, compared favourably with intravenous ciprofloxacin in a trial of 141 patients with pyelonephritis, community-acquired UTI, or hospital-acquired UTI.[62] [63]

In the setting of increasing drug resistance in uropathogens, the following treatments are approved in some countries for use in adults with complicated UTI caused by susceptible organisms who have limited or no alternative options: meropenem/vaborbactam, plazomicin, cefiderocol, and imipenem/cilastatin/relebactam.[64] [65] [66] [67] [68]

Length of therapy

Complicated infections require longer therapy. Most authorities recommend a minimum of 14 days in patients with complicated UTI, and men often have complicated UTI.[11] [44] [69] Furthermore, the incidence of UTI in men is related to ageing, and a minimum of 14 days of therapy corresponds to recommendations for geriatric patients.[11] Data suggest a shorter course option specifically for higher

dose levofloxacin in complicated UTI; however, only approximately one third of the study subjects were male.[70]

In younger men, complicated infections occur less frequently. They may also have a clearly identifiable risk for UTI, such as sexual activity. In such cases, 7 days of therapy may be adequate.

Treatment failure and recurrence

When treatment fails, as evidenced by incomplete resolution of urinary tract symptoms or development of complications secondary to UTI, then a comprehensive evaluation of the urinary tract with imaging should be pursued to identify possible underlying structural or functional abnormalities. Identifying and correcting such abnormalities may be required for successful clearance of UTI.

In addition, poor response to therapy in the short term may indicate the presence of upper tract infection (pyelonephritis) and a need for intravenous therapy, or it may signal the presence of peri-renal abscess requiring surgical drainage. Urology consultation should be considered for men with treatment failure.

After completing acute UTI treatment, men should have clinical follow-up within 2 to 4 weeks. During this visit, further testing is not required, but the physician should ensure resolution of symptoms and completion of antibiotic therapy, and seek to identify factors that may indicate complicated UTI. The patient should be informed that recurrence of UTI necessitates detailed evaluation of the urinary tract with imaging.

Asymptomatic bacteriuria

Treatment of asymptomatic bacteriuria is not recommended in most cases, because it does not alter morbidity or mortality.[4] However, before a urological procedure that may disrupt the urinary tract lining, an attempt should be made to sterilise the urine to decrease the risk of bacteraemia and sepsis. The optimal choice of antibiotics, and timing and duration of therapy, have not been well defined by clinical trials. However, treatment should occur before urological procedures.

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Initial		(summary)
asymptomatic bacteriuria before urological procedure		
	1st	**oral antibiotic therapy**

Acute		(summary)
not severe and tolerating oral therapy		
	1st	**oral antibiotic therapy**
severe or not tolerating oral therapy		
	1st	**hospitalisation plus intravenous antibiotic therapy**

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Initial

asymptomatic bacteriuria before urological procedure

1st **oral antibiotic therapy**

Primary options

» trimethoprim/sulfamethoxazole: 160/800 mg orally twice daily for 1-2 days

OR

» nitrofurantoin: 100 mg orally 4 times daily for 1-2 days

OR

» amoxicillin/clavulanate: 500 mg orally 3 times daily for 1-2 days
Dose refers to amoxicillin component.

OR

» cefalexin: 500 mg orally 4 times daily for 1-2 days

OR

» levofloxacin: 500 mg orally once daily for 1-2 days

OR

» ciprofloxacin: 500 mg orally twice daily for 1-2 days

» The purpose of therapy is to temporarily eliminate bacteriuria, because the presence of non-sterile urine during urological procedures increases the risk of bacteraemia and sepsis.

» The optimal choice of antibiotics and timing and duration of therapy have not been well defined by clinical trials. However, treatment should occur before urological procedures that may disrupt the mucosal lining of the urinary tract.[4] A urine culture with antibiotic sensitivities obtained several days before the procedure will help to guide antibiotic choices.

Initial

» Fluoroquinolones have been associated with serious, disabling, and potentially irreversible adverse effects, including tendonitis, tendon rupture, arthralgia, neuropathies, and other musculoskeletal or nervous system effects.[59] Warnings have also been issued about the increased risk of aortic dissection, significant hypoglycaemia, and mental health adverse effects in patients taking fluoroquinolones.[60] [61] Depending on patient characteristics and local resistance patterns, fluoroquinolone antibiotics nevertheless remain a reasonable first-line choice for treatment of UTI in men due to the higher risk of a complicated course in this patient group.[44]

» After the procedure, the antibiotic can be discontinued unless a catheter remains in place.

» Risks relate to the specific adverse effects of the antibiotic chosen and general antibiotic complications, such as pseudomembranous colitis or induction of resistance.

Acute

not severe and tolerating oral therapy

1st **oral antibiotic therapy**

Primary options

» trimethoprim/sulfamethoxazole: 160/800 mg orally twice daily for 7-14 days

OR

» nitrofurantoin: 100 mg orally 4 times daily for 7-14 days

OR

» amoxicillin/clavulanate: 500 mg orally 3 times daily for 7-14 days; or 875 mg orally twice daily for 7-14 days
Dose refers to amoxicillin component.

OR

» cefalexin: 500 mg orally 4 times daily for 7-14 days

OR

» levofloxacin: 750 mg orally once daily for 7-14 days

OR

» ciprofloxacin: 500 mg orally twice daily for 7-14 days

» The choice of initial empirical therapy should be guided by local resistance patterns.[44]
All men should have a urine culture to assure that the initial empirical antibiotic choice is appropriate.

» Treatment options include beta-lactams, trimethoprim/sulfamethoxazole (TMP/SMX), nitrofurantoin, and fluoroquinolones.[10] [44]

» Risks relate to the specific adverse effects of the antibiotic chosen and general antibiotic complications such as pseudomembranous colitis or induction of resistance.

» Fluoroquinolones have been associated with serious, disabling, and potentially irreversible adverse effects, including tendonitis, tendon rupture, arthralgia, neuropathies, and other musculoskeletal or nervous system effects.[59]

Acute

Warnings have also been issued about the increased risk of aortic dissection, significant hypoglycaemia, and mental health adverse effects in patients taking fluoroquinolones.[60] [61] Depending on patient characteristics and local resistance patterns, fluoroquinolone antibiotics remain a reasonable first-line choice for treatment of UTI in men due to the higher risk of a complicated course in this patient group.[44] Due to high levels of resistance, the European Association of Urology recommends against the use of fluoroquinolones for the empirical treatment of complicated UTI in patients from urology departments or when patients have used fluoroquinolones in the last 6 months.[44] TMP/SMX may be used first-line in younger men without evidence of complicated UTI and with consideration to local resistance patterns.

» Antibiotic dosing may need to be altered based on the patient's renal status.

» Catheter-associated UTI (a complicated UTI) must be treated with diligence because of the risk of developing bacteraemia, but screening for or treatment of asymptomatic bacteriuria in catheterised patients is not recommended.[4] [Evidence A] [Evidence C] If therapy is initiated, then the catheter should be changed before starting antibiotics.[29] [44]

» Treatment for 7 to 14 days is generally recommended.[44]

severe or not tolerating oral therapy

1st **hospitalisation plus intravenous antibiotic therapy**

Primary options

» ceftriaxone: 1-2 g intravenously every 24 hours

OR

» ampicillin: 2 g intravenously every 6 hours
-and-
» gentamicin: 1.5 mg/kg intravenously every 8 hours

OR

» gentamicin: 1.5 mg/kg intravenously every 8 hours

OR

MANAGEMENT

Acute

» ticarcillin/clavulanic acid: 3.2 g intravenously every 8 hours
Dose consists of 3 g of ticarcillin plus 0.2 g of clavulanic acid.

OR

» imipenem/cilastatin: 500 mg intravenously every 6-8 hours
Dose refers to imipenem component.

OR

» aztreonam: 1 g intravenously every 8 hours

OR

» piperacillin/tazobactam: 2.25 to 4.5 g intravenously every 6 hours
Dose consists of 2, 3 or 4 g of piperacillin plus 0.25, 0.375 or 0.5 g of tazobactam.

OR

» meropenem/vaborbactam: 4 g intravenously every 8 hours
Dose consists of 2 g of meropenem plus 2 g of vaborbactam.

OR

» plazomicin: 15 mg/kg intravenously every 24 hours, maximum 7 days treatment

OR

» cefiderocol: 2 g intravenously every 8 hours

OR

» imipenem/cilastatin/relebactam: 1.25 g intravenously every 6 hours
Dose consists of 500 mg of imipenem plus 500 mg of cilastatin plus 250 mg of relebactam.

OR

» levofloxacin: 750 mg intravenously every 24 hours

OR

Acute

» ciprofloxacin: 400 mg intravenously every 12 hours

» The choice of initial empirical therapy should be guided by local resistance patterns.[44] All men should have a urine culture to assure that the initial empirical antibiotic choice is appropriate.

» Treatment options include beta-lactam antibiotics (often in combination with other antibiotics [e.g., aminoglycosides]), and fluoroquinolones.[10] [44]

» In the setting of increasing drug resistance in uropathogens, the following treatments are also approved in some countries for use in adults with complicated UTI caused by susceptible organisms who have limited or no alternative options: meropenem/vaborbactam, plazomicin, cefiderocol, and imipenem/cilastatin/relebactam.[64] [65] [66] [67] [68]

» Intravenous antibiotics are continued until the patient is stabilised and can tolerate oral therapy.

» Risks relate to the specific adverse effects of the antibiotic chosen and general antibiotic complications, such as pseudomembranous colitis or induction of resistance.

» Fluoroquinolones have been associated with serious, disabling, and potentially irreversible adverse effects, including tendonitis, tendon rupture, arthralgia, neuropathies, and other musculoskeletal or nervous system effects.[59] Warnings have also been issued about the increased risk of aortic dissection, significant hypoglycaemia, and mental health adverse effects in patients taking fluoroquinolones.[60] [61] Depending on patient characteristics and local resistance patterns, fluoroquinolone antibiotics nevertheless remain a reasonable first-line choice for treatment of UTI in men due to the higher risk of a complicated course in this patient group.[44]

» Due to high levels of resistance, the European Association of Urology recommends against the use of fluoroquinolones for the empirical treatment of complicated UTI in patients from urology departments or when patients have used fluoroquinolones in the last 6 months.[44]

» Dosing may need to be altered based on the patient's renal status, and consideration should

Acute

be given to the possibility of *Pseudomonas* infection in catheterised patients.

» Catheter-associated UTI (a complicated UTI) must be treated with diligence because of the risk of developing bacteraemia, but screening for or treatment of asymptomatic bacteriuria in catheterised patients is not recommended.[4] [Evidence A] [Evidence C] If therapy is initiated, then the catheter should be changed before starting antibiotics.[29][44]

» Treatment for 7-14 days is generally recommended.[44]

Emerging

Escherichia coli fractions

Oral immunostimulation with *E coli* extracts is a safe and effective method for preventing recurrent UTIs compared with placebo at short-term follow up.[28] Studies have been initiated to gather more data on the long-term efficacy, the treatment regimen, and the mechanism of action of immunostimulants and to find broader indications for this therapy.[41] [42] [71]

Primary prevention

Trials involving boys suggest that circumcision is preventative.[31] However, no clear recommendations exist for adult males. Silver- or antibiotic-coated catheters decrease catheter-associated bacteriuria but have not conclusively been shown to prevent urinary tract infection (UTI); therefore, removal or avoidance of the catheter offers the best prevention.[27] [32] [33] [34] [35] [36] [37] The quality and applicability of evidence regarding prophylaxis for use of several pharmacological (e.g., methenamine hippurate) and non-pharmaceutical treatment strategies (e.g., encouraging cranberry juice intake) in clinical practice for different patient groups is debatable, as there are significant gaps in understanding for particular subgroups of men with UTI. Trial of these therapies should never preclude investigation for structural abnormality in the male urinary tract.[38] [39] [40] [41] [42]

Secondary prevention

Secondary prevention of UTI in men is possible when a correctable or treatable cause of the UTI exists. For example, treatment of benign prostatic hyperplasia (BPH) and restoration of appropriate urine flow may decrease the risk of future UTI development.

Underlying conditions contributing to UTI should be sought using imaging of the urinary tract in men with:

- Voiding dysfunction without a clearly identifiable cause such as BPH
- Treatment failure
- Persistent haematuria
- Signs of upper tract infection.

Urological consultation may be necessary to correct an underlying structural or functional abnormality.

Patient discussions

Patients should be instructed that recurrence of UTI symptoms requires follow-up, because this may indicate underlying functional or anatomical abnormalities of the urinary tract and a need for further diagnostic evaluation.

Men with symptoms of obstructed urinary flow such as hesitancy or nocturia should seek care to identify a potentially correctable disorder (e.g., benign prostatic hyperplasia [BPH]) before UTI re-occurs.

Little and inconclusive evidence exists for preventing UTI in men using cranberry products.[38] This may be offered as a trial but should not be a substitute for detailed urinary tract evaluation when indicated.

Alteration of sexual practices may be needed, such as abstinence from anal sex in those who acquired UTI in this manner. Also, use of condoms may prevent introduction of bacteria into the urethra.

Monitoring

Monitoring

After completing acute UTI treatment, men should have clinical follow-up within 2 to 4 weeks. During this visit, further testing is not required, but the physician should ensure resolution of symptoms and completion of antibiotic therapy, and seek to identify factors that may indicate complicated UTI. The patient should be informed that recurrence of UTI necessitates detailed evaluation of the urinary tract with imaging.

Patients hospitalised for UTI should have similar clinical follow-up, with imaging indicated if hospitalisation occurred because of treatment failure or pyelonephritis.

Ongoing clinical monitoring should occur in patients with indwelling catheters; prophylactic antibiotics are not indicated.[32] [75] Catheters should be removed as soon as possible. Screening for asymptomatic bacteriuria after catheter removal is not indicated.[4]

Patients with asymptomatic bacteriuria do not require follow-up unless they plan to undergo a urinary tract procedure.

FOLLOW UP

Complications

Complications	Timeframe	Likelihood
renal function impairment	**long term**	**low**
Risk factors appropriate to adult men for developing renal damage include prostatitis, obstruction, the presence of stones, and the presence of indwelling catheters.[5] These patients are likely to have recurrent infections warranting imaging of the urinary tract. Urology consultation should be obtained.		
prostatitis	**variable**	**medium**
Some men with UTI may harbour bacteria within the prostate. In one study, over 40% with a febrile UTI had evidence of prostate involvement.[74] If prostatitis occurs, a longer course of antibiotic therapy may be indicated.[49]		
pyelonephritis	**variable**	**medium**
Upper tract infection or pyelonephritis may occur in patients with UTI. Seventy-five percent of patients with pyelonephritis will have had UTI previously.[5] These patients may require hospitalisation for intravenous antibiotics unless otherwise systemically stable. If unresponsive to initial antibiotic therapy, then peri-renal abscess must be ruled out with computed tomography (CT). Urology consultation is necessary for surgical drainage if an abscess is present.		
sepsis	**variable**	**low**
Bacteraemia occurs infrequently with UTI; however, instrumentation of the urinary tract or the presence of indwelling urinary catheters increases the risk.[5] Early recognition and prompt, tailored management is indicated, in line with local guidelines.		

Prognosis

Urinary tract infection (UTI) in younger men

Younger men with UTI less often have complicated infection.[12] [13] [25] In the absence of a complicated UTI, antibiotic therapy is more effective and results in fewer failures. Younger men have a good prognosis.

UTI in older men

Older men more often have complicated UTI. Eradication of bacteria from the urinary tract may be more difficult, but resolution can be achieved with longer courses of antibiotic therapy.[72] There is also higher likelihood of recurrent infection. This risk exists in all patients who have had UTI, but greater risk of recurrence exists in patients with complicated UTI because of the possibility of underlying structural or functional abnormalities of the urinary tract.[7] [10] In addition, drug-resistant and even multidrug-resistant infections occur more often in these patients.[1] [54]

Catheter-associated UTI

Indwelling catheters are associated with high risk of developing UTI. The risk exists as long as the catheter is in place.[27] [73] Catheters also increase the risk of bacteraemia. The prognosis remains poor, and recurrent infections are likely with chronic indwelling catheters.

Asymptomatic bacteriuria

The presence of asymptomatic bacteriuria does not alter patients' morbidity or mortality except in men requiring procedures that disrupt the urinary tract lining.[4] [51] This latter group of patients may be at risk for developing bacteraemia or sepsis.

Diagnostic guidelines

United Kingdom

Urinary tract infection: diagnosis guide for primary care (https://www.gov.uk/government/publications/urinary-tract-infection-diagnosis)

Published by: Public Health England **Last published:** 2020

Europe

Guidelines on urological infections (https://uroweb.org/individual-guidelines/non-oncology-guidelines)

Published by: European Association of Urology **Last published:** 2024

North America

Guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2024 update (https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciae104/7619499#447252888)

Published by: Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM) **Last published:** 2024

Clinical practice guideline for the management of asymptomatic bacteriuria (https://www.idsociety.org/practice-guideline/practice-guidelines)

Published by: Infectious Diseases Society of America **Last published:** 2019

Treatment guidelines

United Kingdom

Urinary tract infection (recurrent): antimicrobial prescribing (https://www.nice.org.uk/guidance/ng112)

Published by: National Institute for Health and Care Excellence **Last published:** 2024

Urinary tract infection (lower): antimicrobial prescribing (https://www.nice.org.uk/guidance/NG109)

Published by: National Institute for Health and Care Excellence **Last published:** 2018

Urinary tract infection (catheter-associated): antimicrobial prescribing (https://www.nice.org.uk/guidance/ng113)

Published by: National Institute for Health and Care Excellence **Last published:** 2018

Pyelonephritis (acute): antimicrobial prescribing (https://www.nice.org.uk/guidance/ng111)

Published by: National Institute for Health and Care Excellence **Last published:** 2018

Urinary tract infection (catheter-associated): antimicrobial prescribing (https://www.nice.org.uk/guidance/ng113)

Published by: National Institute for Health and Care Excellence **Last published:** 2018

Urinary tract infection (lower): antimicrobial prescribing (https://www.nice.org.uk/guidance/NG109)

Published by: National Institute for Health and Care Excellence **Last published:** 2018

Pyelonephritis (acute): antimicrobial prescribing (https://www.nice.org.uk/guidance/ng111)

Published by: National Institute for Health and Care Excellence **Last published:** 2018

Management of suspected bacterial urinary tract infection in adults: a national clinical guideline (https://www.sign.ac.uk/our-guidelines)

Published by: Scottish Intercollegiate Guidelines Network **Last published:** 2012

Europe

Guidelines on urological infections (https://uroweb.org/individual-guidelines/non-oncology-guidelines)

Published by: European Association of Urology **Last published:** 2024

North America

Urologic procedures and antimicrobial prophylaxis (https://www.auanet.org/guidelines/urologic-procedures-and-antimicrobial-prophylaxis-(2019))

Published by: American Urological Association **Last published:** 2019

Asia

Guideline for the prevention of health care-associated infection in urological practice in Japan (https://www.jsn.or.jp/en/guideline/guideline.php)

Published by: Japanese Urological Association **Last published:** 2011

Evidence tables

Should patients with a long-term indwelling urethral catheter be screened or treated for asymptomatic bacteriuria (ASB)?[53]

This table is a summary of the analysis reported in a guideline (underpinned by a systematic review) that focuses on the above important clinical question.

View the full source guideline (https://academic.oup.com/cid/article/68/10/e83/5407612)

Evidence A * — Confidence in the evidence is high or moderate to high where GRADE has been performed and the intervention is less effective or likely to be more harmful than the comparison for key outcomes.

Population: People with a long-term indwelling urinary catheter
Intervention: Antibiotics
Comparison: No treatment

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
Adults with long-term indwelling urinary catheters and ASB		
Sepsis/bacteraemia	Favours intervention	Very Low
Antibiotic resistant bacteraemia	Favours comparison	High
Clostridium difficile infection	Favours comparison	Moderate
Mortality	No statistically significant difference [a]	Very Low

Recommendations as stated in the source guideline
In patients with long-term indwelling catheters, the Infectious Diseases Society of America recommend against screening for or treating ASB.

Note
The guideline committee noted that while very low-quality evidence demonstrated a beneficial effect of antibiotic treatment in people with long-term indwelling catheters, there is high-quality evidence of harms with increased antimicrobial resistance. The overall evidence rating in this table reflects this.

[a] One observational study did not find a significant association between antibiotics and mortality after controlling for key confounders.

EVIDENCE TABLES

Should patients with an indwelling urethral catheter for <30 days be screened or treated for asymptomatic bacteriuria (ASB)?[53]

This table is a summary of the analysis reported in a guideline (underpinned by a systematic review) that focuses on the above important clinical question.

View the full source guideline (https://academic.oup.com/cid/article/68/10/e83/5407612)

Evidence C *	Confidence in the evidence is very low or low where GRADE has been performed and there may be no difference in effectiveness between the intervention and comparison for key outcomes. However, this is uncertain and new evidence could change this in the future.

Population: People with a short-term indwelling urinary catheter of < 30 days and ASB
Intervention: Antibiotics
Comparison: No antibiotics

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
People with short-term indwelling urinary catheter (<30 days) and ASB		
Sepsis	No statistically significant difference	Very Low
Death	No statistically significant difference	Very Low

Recommendations as stated in the source guideline
In patients with a short-term indwelling urethral catheter (<30 days), the Infectious Diseases Society of America recommend against screening for or treating ASB.

Note
The guideline committee noted that many people with a short-term urethral catheter (<30 days) do not develop bacteriuria. They suggest this is due to the removal of the catheter before its onset. The committee also comment that this patient group has a high risk of hospital-acquired infection with antimicrobial-resistant organisms.

* Evidence levels

The Evidence level is an internal rating applied by BMJ Best Practice. See the EBM Toolkit (https://bestpractice.bmj.com/info/evidence-tables/) for details.

Confidence in evidence

A - High or moderate to high
B - Moderate or low to moderate
C - Very low or low

† Effectiveness (BMJ rating)

Based on statistical significance, which demonstrates that the results are unlikely to be due to chance, but which does not necessarily translate to a clinical significance.

‡ Grade certainty ratings

High	The authors are very confident that the true effect is similar to the estimated effect.
Moderate	The authors are moderately confident that the true effect is likely to be close to the estimated effect.
Low	The authors have limited confidence in the effect estimate and the true effect may be substantially different.
Very Low	The authors have very little confidence in the effect estimate and the true effect is likely to be substantially different.

BMJ Best Practice EBM Toolkit: What is GRADE? (https://bestpractice.bmj.com/info/toolkit/learn-ebm/what-is-grade/)

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Figure 1 – BMJ Best Practice Numeral Style

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