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1

CLINICAL GUIDELINE

British Association of Sexual Health and HIV national guideline on the management of non-gonococcal urethritis (NGU)

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2

1. CONTENTS

2. ABSTRACT

The British Association for Sexual Health and HIV United Kingdom guideline on the management of non-gonococcal urethritis (NGU) 2025 provides details on the aetiology and clinical features of NGU, with recommendations on diagnosis and treatment of acute and persistent/recurrent NGU.

Non-gonococcal urethritis is characterised by urethral inflammation, and it can be infectious or non-infectious. The most common organisms causing NGU are *Chlamydia trachomatis* and *Mycoplasma genitalium*. Diagnosis of NGU is based on clinical history and evidence of an excess of polymorphonuclear leucocytes in the anterior urethra of symptomatic men. Nucleic acid amplification tests to determine the specific aetiology are used to guide treatment and reduce complications. Recommendations include advising patients to abstain from sexual intercourse until they and their partner(s) have completed treatment and follow-up to prevent re-infection.

Keywords: Non-gonococcal urethritis, urethritis, *Chlamydia trachomatis*, *Mycoplasma genitalium*

3. ABBREVIATIONS

Abbreviation	Definition
AGREE	Appraisal of Guidelines, Research and Evaluation
AUFC	Automated Urine Flow Cytometry
BASHH	British Association for Sexual Health and HIV
bd	Twice Daily
BV	Bacterial Vaginosis
CEG	Clinical Effectiveness Group
CP	Chronic Abacterial Prostatitis
CPPS	Chronic Pelvic Pain Syndrome
FVU	First Voided Urine
GRADE	Grading of Recommendations, Assessment, Development, and Evaluations
hpf	High Power Field
HSV	Herpes Simplex Virus
LE	Leucocyte esterase
MB	Methylene Blue
MIC	Minimum Inhibitory Concentration
MSM	Men Who Have Sex With Men
NAAT	Nucleic Acid Amplification Test
NGU	Non-gonococcal Urethritis
od	Once Daily
PCR	Polymerase Chain Reaction
PID	Pelvic Inflammatory Disease
PMNLs	Polymorphonuclear Leucocytes
stat	Immediately
STI	Sexually Transmitted Infections
UK	United Kingdom

Abbreviation	Definition
UTI	Urinary Tract Infection
vs.	*versus*

4. WHAT IS NEW IN THE 2025 GUIDELINE?

- *Haemophilus influenzae, Haemophilus parainfluenzae* and *Neisseria meningitidis* are included as probable causative pathogens of non-gonococcal urethritis (NGU).
- Automated urinary flow cytometry (AUFC) analysis of a first voided urine (FVU) specimen is included as a diagnostic test for NGU, in addition to a Gram-stained urethral smear.
- Leucocyte esterase (LE) dipstick test on a FVU specimen is no longer recommended for the diagnosis of urethritis.
- Nucleic acid amplification test (NAAT) for *M. genitalium* on a FVU specimen is recommended for all symptomatic men with a diagnosis of NGU.
- NAATs for herpes simplex virus (HSV) should be considered when the aetiology of NGU is suspected to be viral.
- Azithromycin 1 g stat is no longer recommended for the treatment of NGU.
- Azithromycin 1 g orally single dose, then 250 mg for four days or azithromycin 1 g orally single dose, then 500 mg once daily for two days are included as alternative regimens for the treatment of acute NGU.

5. INTRODUCTION AND METHODOLOGY

5.1. Objectives

The objective of this guideline is to effectively manage symptomatic urethritis in people with a penis, and to prevent complications that can arise.

This guideline offers recommendations on the diagnostic tests, treatment regimens and health promotion principles needed for the effective management of NGU, covering the management of the initial presentation, as well as how to prevent transmission and future infection.

The guideline is aimed primarily at health care professionals seeing patients aged 16 years or older (see specific guidelines for those under 16) in departments offering specialist level 3 care in sexually transmitted infection (STI) management within the United Kingdom (UK). However, the principles of the recommendations are applicable across all levels. The diagnosis of NGU pertains to penile symptoms; therefore this guideline is directed to the management of penile symptoms only except where it addresses the management of partners of those with NGU.

The recommendation of this guideline may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgement of the clinician and consideration of individual patient circumstances and available resources.

5.2. Search Strategy and Methods

This guideline was produced according to specifications set out in the Clinical Effectiveness Group (CEG) document 'framework for guideline development and assessment' (2015, updated 2019) accessed at:
https://www.bashh.org/_userfiles/pages/files/resources/2020_guidelines_framework.pdf

This guideline has been updated by reviewing the previous UK national guideline on the management of NGU (2015[1] and 2018 update[2]) and conducting a comprehensive literature search of publications from January 2014 to January 2023. Medline, Embase and Cochrane library databases were used to identify published articles including the search terms 'nongonococcal urethritis', 'non-gonococcal urethritis', 'nonspecific urethritis', or 'non-specific urethritis' (and broadened the search to include 'urethritis' and urethritis combined with '*Chlamydia trachomatis*' or '*Mycoplasma genitalium*'). Reviews, case reports,

editorials, comments, letters, and research pertaining to the development of laboratory assays and the study of genomics were excluded. Additional articles, not retrieved from the initial comprehensive literature search, and book chapters were considered when appropriate. Due to the paucity of clinical trials, all entries in the English language were reviewed, and if relevant the full text obtained.

To structure the analysis of the evidence, the authors formulated six "PICO" questions (Appendix 1) addressing the patient problem or population (P), intervention (I) (or aetiology/diagnosis/frequency/prognosis), comparison (C) and outcome(s) (O). The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) system was used to assess the evidence and make recommendations (Appendix 2).

Direct comparison of published studies is hindered by the majority lacking a clear microscopic definition of NGU or using an alternative definition to 'five or more polymorphonuclear leucocytes (PMNLs) per high powered field (hpf) averaged over five fields with the greatest concentration of polymorphs' and varying urethral specimen collection techniques. Generally, only those studies which had objective evidence of urethral inflammation were included. If such studies were included this is commented in the text.

5.3. Equality Impact Assessment

An assessment of the guideline and its recommendations was undertaken to ensure the principles of equality and diversity were adhered to and is available in Appendix 3.

The British Association for Sexual Health and HIV (BASHH) has adopted an anatomical approach without assuming gender in the majority of guidelines and uses gender terminology in line with BASHH 'Sexual health standards for trans, including non-binary, people'.

5.4. Stakeholder Involvement, Piloting and Feedback

The writing group consisted of genitourinary medicine physicians with experience in managing NGU (CT, KB, MC, MR and PJH) and a sexual health adviser (CE). The first draft was produced by the writing group and then circulated to the BASHH Clinical Effectiveness Group (CEG) for review using the Appraisal of Guidelines, Research and Evaluation (AGREE) tool (Appendix 4). The second draft of the guideline was posted on the BASHH website for wider consultation (2 months) and any comments received during the consultation period were reviewed by the authors and acted on appropriately. The document was also reviewed by a

patient representative, target users and the public panel of BASHH, and their feedback was considered by the authors and used to inform the guideline. The final draft was presented to the CEG for review and piloting in sexual health clinics (Appendix 5).

Once the guideline is published, the CEG will keep it under review should critical new evidence become available that affects the current recommendations. The guideline will be formally reviewed and updated, if necessary, every five years.

5.5. Introduction

Urethritis, or inflammation of the urethra, is a multifactorial condition which is sexually acquired in the majority of cases. It is characterised by urethral discharge, dysuria and/or urethral discomfort but may be asymptomatic. The diagnosis of urethritis is confirmed by demonstrating an excess of PMNLs in the anterior penile urethra without the presence of intracellular Gram-negative diplococci. This is usually assessed by microscopy analysis of a Gram- or methylene blue-stained urethral smear. Automated urine flow cytometry of a FVU specimen can also be used for the diagnosis of urethritis if *N. gonorrhoeae* is excluded. Urethritis is described as either gonococcal, when *Neisseria gonorrhoeae* is detected, or non-gonococcal (NGU) when it is not. The most common organisms causing NGU are *Chlamydia trachomatis* and *Mycoplasma genitalium*.[3-13]

There are a number of uncertainties with NGU. There is significant inter-observer and intra-observer error in performing and reading urethral slides and counting PMNLs, especially in samples with low-grade inflammation.[14, 15] In 10 to 45% of NGU cases, a pathogenic microorganism is not detected.[3, 6, 7, 16] The cause of organism-negative or idiopathic NGU is unclear.

6. AETIOLOGY

6.1. Causative Pathogens

The prevalence of the common microorganisms associated with NGU is listed in Table 1.

There is conflicting evidence on whether the sex of the patient's partner affects the most likely cause of NGU.[3, 23]

6.1.1. *Chlamydia trachomatis* and *Mycoplasma genitalium*

The most common organisms causing NGU are *C. trachomatis* and *M. genitalium*.[3-13]

- The prevalence of *C. trachomatis* and *M. genitalium* in men with NGU probably varies by age group, with some studies suggesting a higher proportion of infections identified among younger men with NGU.[5, 8, 17]
- No symptom and/or sign can be reliably used to distinguish NGU caused by C. *trachomatis* and *M. genitalium* from men with idiopathic NGU. [6, 8, 17-19]
- *M. genitalium*, but not *C. trachomatis*, has been associated with balano-posthitis in a single study.[20]
- Co-infection with *C. trachomatis* and *M. genitalium* is uncommon, occurring in < 5% of men with NGU.[3, 6, 17, 21, 22]

6.1.2. Ureaplasma urealyticum and *Ureaplasma parvum*

Ureaplasmas spp. have been inconsistently associated with NGU. The majority of men with *Ureaplasma* spp. infections are asymptomatic and NGU may only develop in the presence of a high organism load (>1000 copies/mL of FVU).[3, 7, 22, 24-26]

- A meta-analysis including seven studies and 1,507 NGU patients demonstrated an association of *U. urealyticum* infection with NGU[27], yet no association has been observed in two more recent studies with one study only observing an association in men with >30 PMNLs per hpf.[3, 22, 28]
- One study indicated association of *U. urealyticum* infection with NGU in men with fewer lifetime sexual partners but no association in men with more lifetime sexual

partners.[9] This result suggests that previous exposure to *U. urealyticum* and adaptive immunity may reduce the bacterial load and the likelihood of NGU.[7, 9]

- *U. parvum* is unlikely to cause NGU.[27] It is usually detected more often in controls (men without NGU) than cases (men with NGU).[27, 29]
- Earlier studies did not differentiate between the two species *U. urealyticum* (biovar 2) and *U. parvum* (biovar 1) which continues to be the case if culture alone is used and with some NAATs. Clinicians should be aware of this when interpreting test results with no biovar differentiation.[7, 24, 25, 27]

6.1.3. Haemophilus influenzae and *Haemophilus parainfluenzae*

Haemophilus influenzae, which colonises the respiratory tract, has recently been associated with NGU and may be transmitted by unprotected oral sex.[3, 6, 7, 30] It is possible that *Haemophilus parainfluenzae* may also cause NGU.[31, 32]

6.1.4. *Trichomonas vaginalis*

Trichomonas vaginalis can cause NGU in men who have sex with women (MSW). In the UK, the prevalence of *T. vaginalis* is relatively low, affecting < 2% of men with NGU.[4, 13, 33] In women, risk factors for *T. vaginalis infection* include older age, black ethnicity and socio-economic deprivation.[34, 35]

6.1.5. *Mycoplasma penetrans*

Mycoplasma penetrans in a recent study was associated with NGU in men who have sex with men (MSM) but not in MSW.[3] This requires confirmation and further study.

6.1.6. *Neisseria meningitidis*

Neisseria meningitidis sequence type 11 has been linked to clusters of NGU in the United States and may represent a urethrotropic clade.[36, 37]

6.1.7. Bacterial vaginosis-associated bacteria

There is some evidence that bacterial vaginosis (BV)-associated bacteria may cause NGU.[38-40] However, despite a number of case-control studies using species specific polymerase chain reactions (PCRs) or 16S rRNA microbiome sequencing, no single microorganism has been consistently associated with NGU.[3, 16, 39-41]

6.1.8. Adenovirus

Adenovirus can cause NGU and transmission occurs by oral and ano-genital sex and possibly also by auto-inoculation.[6, 42-44] Clinical features include dysuria, meatitis and conjunctivitis with urethral discharge often being either scanty or absent.[6, 42] Symptoms and signs are self-limiting and usually resolve within three weeks.[43] The urethral smear may not demonstrate ≥ 5 PMNLs per hpf and the leukocytes observed may be predominantly mononuclear.[6, 42, 45].

6.1.9. Herpes simplex virus

Herpes simplex virus types 1 and 2 can cause NGU and clinical features include dysuria, meatitis (with or without genital ulceration) and inguinal lymphadenopathy.[44, 46, 47] In most cases shedding of HSV from the urethra stops spontaneously and signs and symptoms resolve within 7 to 19 days.[46] Microscopy analysis of urethral smear or FVU from men with HSV-NGU may reveal a high proportion of mononuclear leukocytes and/or not demonstrate ≥5 PMNLs per hpf.. [6, 44, 46, 47]

6.1.10. Other pathogens

Candida spp., urethral stricture and foreign bodies probably account for a small proportion of NGU, whilst the role of Epstein-Barr virus is questionable.[48, 49]

6.2. Urinary tract infection

A urinary tract infection (UTI) was found in 6% of men with acute NGU in a single study.[50]

6.3. Organism-negative or idiopathic NGU

In 10-45% of men with NGU, no pathogens are identified after screening for common infections.[3, 6-8, 17, 22] Idiopathic NGU seems to be more prevalent in older men and is associated with a less marked inflammatory response. [6, 17, 51, 52] The cause of organism-negative or idiopathic NGU is unclear. Some cases are almost certainly non-infective.[3, 7, 13, 16, 30, 53]

6.3.1. Asymptomatic NGU

Asymptomatic NGU, without an observable discharge, probably has a different aetiology from symptomatic NGU, with *C. trachomatis* and *M. genitalium* being detected less frequently.[5, 18,

[51, 52, 54] It is not recommended to test asymptomatic men for NGU by microscopy of a urethral smear.[55] (**Grade 2B**)

7. CLINICAL FEATURES

7.1. Symptoms and Signs

Symptoms:

- Urethral discharge;
- Dysuria;
- Penile tip irritation;
- Urethral discomfort and/or itch;
- Nil.

Signs:

- Urethral discharge;
- Penile tip erythema;
- Normal examination.

7.2. Complications

- Epididymo-orchitis;
- Sexually acquired reactive arthritis – acute or chronic.

8. DIAGNOSIS OF URETHRITIS AND INVESTIGATIONS

8.1. Diagnosis of urethritis

Men with symptoms compatible with urethritis and those with a visible discharge should be assessed for the presence of urethritis.

Urethritis is diagnosed by demonstrating an excess of PMNLs in the anterior urethra without the presence of intracellular Gram-negative diplococci.

We recommend the diagnosis of NGU should be confirmed by microscopy analysis of a Gram- or methylene blue (MB)-stained urethral smear showing no Gram-negative intracellular diplococci and ≥5 PMNLs per hpf (averaged over 5 fields with greatest concentration of PMNLs). [52, 54, 56-58] (**Grade 1B**)

- The sensitivity of the smear test for diagnosing urethritis, is affected by the period since last passing urine. We recommend the optimum time to ensure a definite diagnosis in a symptomatic men is a minimum of 2 hours since voiding urine. (**Grade 1D**).
- The quality of the urethral smear is dependent on sample collection and the interpretation of the microscopy results is subject to inter- and intra-observer variation.[14, 15]
- Urethral smears should be prepared by collecting urethral secretions using a 5-mm plastic loop or a cotton tipped swab introduced about 1 cm into the urethra. We recommend the use of a 5-mm plastic loop as this is less painful than a Dacron swab, which is less painful than a Rayon swab.[61] (**Grade 1C**)
- There is no evidence regarding the acceptability or the level of pain experienced using these methods of urethral secretion collection in the UK. Other devices can be used to collect the urethral secretion for the urethral smear, including a sterile blunt curette or spatula. These sampling methods may have better recovery of PMNLs to the slide and therefore it has been proposed to use ≥10 PMNLs per hpf for diagnosis of NGU, with 5-9 PMNLs per hpf regarded as a "grey zone". Syndromic management for patients in the "grey zone" should be reserved in those who have severe symptoms or other risk factors.[28, 62] **(Grade 2D)**

- If a visible discharge is present, we recommend the urethral smear can be prepared by collecting a small sample of the discharge without introducing the device into the urethra. (**Grade 1D**)

- If the leukocytes observed by microscopy are predominantly mononuclear and the patient reports dysuria, conjunctivitis, meatitis or inguinal lymphadenopathy, consider the investigation of a viral aetiology.[45-47] (**Grade 2C**)

Automated urine flow cytometry of a FVU specimen (having not voided for 2 hours) can be used for the diagnosis of urethritis if *N. gonorrhoeae* is excluded. Therefore, AUFC should not be seen as a replacement for microscopy as the presence or absence of Gram-negative intracellular diplococci cannot be assessed.

- We recommend urethritis can be confirmed by AUFC analysis of a FVU specimen (FVU-AUFC) if ≥ 30 leucocytes per µL of urine are demonstrated.[63] (**Grade 1C**)

Leucocyte esterase dipstick test on a FVU specimen is not recommended for the diagnosis of urethritis.[64, 65] Use of an LE dipstick test should only be considered in settings with no access to microscopy or AUFC (see Section 8.4).

8.2. Investigations in symptomatic men with confirmed diagnosis of urethritis

- We recommend testing for the following pathogens if NGU is confirmed:
    - *C. trachomatis* (**Grade 1B**)
    - *N. gonorrhoeae* (**Grade 1B**)
    - *M. genitalium* (**Grade 1B**)
- We recommend a NAAT on a FVU as the specimen of choice. (**Grade 1B)**

Implementing *M. genitalium* NAAT (in addition to *C. trachomatis*/*N. gonorrhoeae* NAATs) at first presentation of NGU correlates with a reduction in clinical visits for persistent NGU. [72]

- If patients have severe dysuria, constitutional symptoms, lymphadenopathy, meatitis or genital ulceration, particularly with a mononuclear cell response on urethral smear, consider testing for HSV using a NAAT. (**Grade 2C**)

- Symptoms of UTI may overlap with those of urethritis. A urinary dipstick analysis on a mid-stream urine specimen should be considered in men with symptoms of UTI (including dysuria, macroscopic haematuria, nocturia, urinary frequency or urgency) or at low risk for a STI. If urinalysis is positive for nitrites and leucocytes, a urine culture and antibiotic sensitivity we recommend testing.[50, 66] (**Grade 1D**) If a UTI is confirmed consider further urological assessment in line with National Institute for Health and Care Excellence Clinical Knowledge Summary on management of lower UTI in men. [73]

8.3. Investigations in symptomatic men without confirmed diagnosis of urethritis

- In approximately one third of the men with symptoms of urethritis, the result of urethral smear microscopy is normal (< 5 PMNLs per hpf).[28]
- To prevent perpetuating symptoms of urethritis, it is not recommended to treat men with symptoms without a confirmed diagnosis of urethritis. Empirical treatment should only be given in exceptional circumstances.
- If the result of urethral smear microscopy is normal and/or FVU-AUFC analysis is negative we recommend awaiting for the results of NAATs. **(Grade 1D**)
- If the result of urethral smear microscopy is normal (and/or FVU-AUFC analysis is negative) and *C. trachomatis*/*N. gonorrhoeae* NAATs are negative, we recommend the patient can be reassured, and advised to reattend for an early morning urethral smear if symptoms persist (**Grade 1D**).
- Men attending for an early morning smear should be advised to hold the urine overnight and to re-attend not having voided urine. We recommend to advise the patient to take their last drink at about 8 p.m. and to void about 3 hours later to avoid waking with a full bladder. (**Grade 1D**)
- If the result of the early morning urethral smear microscopy is normal, consider performing FVU-AUFC analysis (and vice-versa). (**Grade 2D**)
- If the result of microscopy of the early morning urethral smear is negative, and on FVU-AUFC analysis (if available), microscopy analysis of Gram- or MB-stained thread from a FVU specimen thread can be considered. Urethritis can be diagnosed if

the specimen has ≥ 10 PMNLs per hpf (averaged over five fields with greatest concentration of PMNLs).[10] (**Grade 2D**)

8.4. Investigations in settings without access to microscopy or AUFC analyses

Symptomatic patients should be strongly encouraged to attend a centre that has microscopy available.

9. MANAGEMENT OF ACUTE NGU

9.1. General Advice

Patients should be given a detailed explanation of their condition including: short- and long-term implications for the health of themselves and their partner(s); infective and non-infective causes of NGU; and available treatments and side-effects. This should be reinforced by providing clear written information (see www.bashh.org/guidelines for a patient information leaflet on NGU[79]).

Patients should be advised to abstain from sexual intercourse until they and their partner(s) have completed treatment and follow-up. Safer sexual practices[80] should be discussed and the importance of adhering to treatment and testing/treating sexual partner(s) should be emphasised.

9.2. Treatment of acute NGU

We recommend treatment of men with severe symptoms be initiated as soon as the diagnosis of urethritis is made and without waiting for the results of *C. trachomatis*/*N. gonorrhoeae*/*M. genitalium* NAATs and *N. gonorrhoeae* culture. (**Grade 1C**)

We recommend men with mild symptoms and/or low-grade urethritis (i.e. 5 to 15 PMNLs per hpf on urethral smear), can be reviewed when the results of NAATs are available. In some cases, this allows for resolution of inflammation/urethritis without treatment.[81] (**Grade 1D**)

Alternatively, point-of-care *C. trachomatis*/*N. gonorrhoeae* NAATs of symptomatic men at first presentation may allow for early antimicrobial treatment without requirement for microscopy and culture (when the results are positive).[82-85] This approach may improve antimicrobial stewardship and partner management.

Ideally, treatment should be effective (cure rate > 95%), easy to take (twice daily or less), with a low side-effect profile, and cause minimal interference with daily lifestyle**.** However, assessing treatment efficacy is difficult as persistence of inflammation may not indicate persistent infection.[10, 86-88] Detectable inflammation may persist for an unknown length of time, even when the putative organism has been eliminated.[89] Two randomised controlled trials

including men with NGU treated with doxycycline 100 mg twice daily (bd) 7 days or azithromycin 1 g orally stat showed clinical cure rates <80%.[12]

9.2.1. Recommended regimen

Doxycycline 100 mg orally bd for seven days (Grade 1B)

- Doxycycline 100 mg orally bd for seven days with overall efficacy of 97% in men who are *C. trachomatis*-positive.[90]
- Doxycycline 100 mg orally bd for seven days is only effective in 25 to 45% of men who are *M. genitalium*-positive yet there is no evidence that it confers antimicrobial resistance.[11, 12, 91, 92]
- The majority of other potential bacterial pathogens remain susceptible to doxycycline including *Haemophilus* spp and *U. urealyticum.*[88, 93]
- Switching from azithromycin 1 g stat to doxycycline as first-line NGU treatment correlates with a reduction of persistent NGU.[72, 94]
- There is no evidence that treatment with doxycycline induces antimicrobial resistance in *C. trachomatis* or *M. genitalium*. Clinicians should refer to the most recent UK national guideline on the management of *C. trachomatis* and *M. genitalium* for further details.

9.2.2. Alternative Regimens

Azithromycin 1 g orally single dose, then 500 mg od for two days (three days total treatment) (Grade 1C)

- Azithromycin 1 g stat is no longer recommended for the treatment of *C. trachomatis* and *M. genitalium*.[71, 95, 96]Azithromycin 1 g is associated with development of macrolide resistance in *M. genitalium* [11, 12, 59, 90, 97, 98], is likely to increase macrolide-resistant strains in the population [99-101] and has a reduced efficacy in *C. trachomatis*-positive men with urethritis.[90, 102, 103]
- Men should be advised to abstain from sexual intercourse until 14 days after the start of the treatment, and until symptoms have resolved. Where azithromycin has been used this is likely to reduce the risk of selecting/inducing macrolide resistance if the patient is (re)exposed to *M. genitalium.*[71]

- Azithromycin for three or four days (1 g stat then 500 mg od for two or three days) is at least as effective as azithromycin for five days (500 mg orally single dose, then 250 mg od for four days), resulting in high concentrations for a prolonged duration in all tissue sites and similar cure rates.[104, 105]
- Azithromycin for five days is about 95% effective in eradicating macrolide-susceptible *M. genitalium* and maybe more effective at eradicating *C. trachomatis* in men with urethritis.[101, 106-108] It appears to induce lower rates of macrolide antimicrobial resistance than the three day regimen, although there is limited literature evaluating this.[100, 106]
- Azithromycin has a long half life (68 hours) with sub inhibitory concentrations (MIC) levels for *N. gonorrhoeae* and *M. genitalium* persisting for 2 to 4 weeks extracellularly and probably longer intracellularly.[104] Increasing the total dose to 2.5 g is likely to be effective [71, 105] but should be accompanied by recommending no sexual intercourse with a new partner for 2 weeks after commencing therapy. [71, 109, 110]
- The majority of other bacterial pathogens remain susceptible to azithromycin including *U. urealyticum*, *Haemophilus* spp. and *M. penetrans* [88, 93, 111, 112]

10. FOLLOW-UP

We recommend patients who remain symptomatic (at least two weeks after initiating treatment) should be asked to return to the clinic and re-evaluated for urethritis with an appropriate treatment regimen provided if indicated (see below) and the possibility of re-infection explored. (**Grade 1C**)

11. PERSISTENT/RECURRENT NGU

Persistent or recurrent NGU, when symptoms do not resolve or recur within 90 days following initial treatment of acute NGU, occurs in 5-25% of men.[10-12, 87, 113, 114]

The aetiology of persistent/recurrent NGU is probably multifactorial, with an infectious agent being identified in <50% of cases.[7, 8, 10, 11]

M. genitalium has been identified in 20 to 70% and *C. trachomatis* in 5 to 10% of men treated with doxycycline 100 mg bd for seven days. [8, 12, 114, 115]

U. urealyticum and *U. parvum* may also play a role in some men with persistent NGU, but urethritis appears to resolve despite persistent infection.[10, 111, 116]

Trichomonas vaginalis can be identified in up to 10% of men in populations where it is endemic, but it is an uncommon cause of NGU in the UK (<5%).[8, 114]

11.1. Investigations in men with symptoms of persistent/recurrent NGU

We recommend testing only for persistent/recurrent NGU at least two weeks after initial treatment of acute NGU.[11, 12, 117] (**Grade 1C**)

NAATs for *C. trachomatis*/*N. gonorrhoeae* on a FVU specimen is recommended for all men with persistent/recurrent symptoms of NGU if at risk of new infection or if not performed an initial assessment. (**Grade 1A**)

- If ongoing evidence of urethritis, perform NAAT for *M. genitalium* on a FVU specimen (if not undertaken at first presentation).[71] (**Grade 1A**)
    - If *M. genitalium* NAAT result is positive, AMR should be considered. Clinicians should refer to the most recent UK national guideline on the management of *M. genitalium* for further details.
- If ongoing evidence of urethritis, consider NAATs for *T. vaginalis* on a FVU specimen. (**Grade 2D**)
    - NAAT for *T. vaginalis* should be considered if it is prevalent (≥2% in symptomatic women) in the local population. [95]
    - If *T. vaginalis* NAAT result is positive, clinicians should refer to the most recent UK national guideline on the management of *T. vaginalis* for further details.

1

12. MANAGEMENT OF PERSISTENT/RECURRENT NGU

- Assess treatment adherence. (**Grade 1D**)
- Re-assess sexual history and evaluate for possible reinfection. (**Grade 1D**)
- Only treat men with symptoms of urethritis and confirmed diagnosis of urethritis (see above). (**Grade 2C**)
- Reassure symptomatic men without evidence of ongoing inflammation with information on why they might be experiencing pain. Guide them on how to relax their pelvic floor and advise to re-attend for an early morning smear if symptoms persist. (**Grade 2C**)

12.1. Treatment of persistent or recurrent NGU

Treatment of persistent/recurrent NGU should cover *M. genitalium*, *C. trachomatis*, *Ureaplasmas* spp., *T. vaginalis* and possibly BV-associated bacteria. The only randomised controlled trial for persistent/recurrent NGU was undertaken before *M. genitalium* had been identified as an important pathogen (but before macrolide resistance was common) and used erythromycin, a first-generation macrolide.[119] Although a 3-week erythromycin regimen was more efficient than placebo, it is not clear how relevant this regimen is today, given that better macrolides are available with fewer side-effects.[120]

12.1.1. Recommended regimens (second attendance or first follow-up visit)

12.1.1.1. If doxycycline 100 mg bd for seven days used as first line treatment

Azithromycin 1 g orally single dose, then 500 mg od for 3 days (4 days total treatment)
PLUS **Metronidazole 400 to 500 mg orally bd for 7 days** (**Grade 2B**)

12.1.1.2. If azithromycin used as first line treatment

Doxycycline 100 mg orally bd for seven days

PLUS **metronidazole 400 to 500mg orally bd for seven days** (**Grade 1A**)

12.1.2. Continuing symptoms

There is growing evidence on how best to manage patients who either remain symptomatic following second-line treatment, or who have frequent recurrences after treatment. After excluding persistent infection, management should focus on improving symptoms.

The management of men with persistent/recurrent NGU who fail second-line treatment is a condition known as CPPS.[74, 123, 124] Guidance on the management of CPPS in people with a penis in UK sexual health clinic settings has been published.[118]

There is evidence that increased pelvic floor tone, of which the patient is usually unaware, is likely to be the underlying cause of continuation of symptoms in many patients, in the absence of persistent/recurrent infection.[74, 75, 123-126] A holistic bio-psychosocial approach has been demonstrated to be effective in managing men with chronic abacterial prostatitis (CP)/CPPS and persistent/recurrent NGU in whom infection has been excluded.[74, 75, 118, 123, 125-127] This involves incorporating a detailed explanation of: [74, 75, 124, 127, 128]

1. How increased pelvic floor tone can cause their symptoms - this can result in referred pain elsewhere in the pelvis, difficulty in urination including dysuria and pain on ejaculation secondary to constriction of external urethral sphincter with intra-prostatic reflux of urine;
2. Identification of stressors and working with the patient to look at how these could be reduced;
3. Pelvic floor relaxation exercises with or without use of alpha blockers and antibiotics.

13. TRACING AND TREATMENT OF CONTACTS

Contact tracing should be performed according to BASHH guidelines (www.bashh.org/guidelines), with reference to look back periods. Patients should be informed of the importance of partner notification and supported to do this by appropriately trained professionals.

Current partner(s) with whom there is likely to be further sexual contact should be tested, and treated if positive.[129, 130] Partners should be given the same antibiotic as the index patient unless there is available resistance information to suggest otherwise.

Patient and current partner(s) should be advised not to be sexually active until all have completed treatment.

Any specific diagnosis made should have partner notification managed in line with the infection-specific BASHH guidance.

Details of all contacts should be obtained at the first visit. This will aid facilitating partner notification in the event of a positive test result.

There is evidence suggesting that men with idiopathic NGU may be more likely to have *C. trachomatis*-positive partner(s) (see aetiology). However, in a study conducted before NAATs for *C. trachomatis* and *M. genitalium* were available, there was no evidence of treatment benefit of partners of men with *C. trachomatis*-negative NGU.[130]

14. AUDITABLE OUTCOME MEASURES

- Proportion of patients with diagnosis of NGU tested at first presentation for *C. trachomatis, N. gonorrhoeae* ad *M. genitalium.*
- Proportion of partners of NGU patients notified according to published BASHH standards.
- Proportion of patients treated with recommended regimen for confirmed NGU or not treated due to documented reasons.
- Proportion of patients offered information (written or digital) about their diagnosis and management.
- Proportion of symptomatic patients who had a Gram- or MB- stained urethral smear or FVU-AUFC.

15. RECOMMENDATIONS FOR FURTHER RESEARCH

What are the causes of pathogen-negative NGU?

How might we best manage the partners of people with NGU?

Can NGU be managed remotely or in centres without access to microscopy without evidence of harm?

16. QUALIFYING STATEMENT

The recommendations in this guideline may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on professional clinical judgement, consideration of individual patient circumstances and available resources.

All possible care has been undertaken to ensure specification of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing clinician to ensure the accuracy and appropriateness of the medication they prescribe.

17. REVIEW ARRANGEMENTS

An author group will be invited by the BASHH CEG to review and revise the guideline in 2030 using the BASHH framework for guideline development. However, addenda may be issued sooner than 2030, particularly if relevant new data are available relating to testing or treatment options.

18. DISCLOSURES

18.1. Acknowledgements

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18.2. Declaration of Conflicting Interests

All members of the guideline writing committee completed the BASHH conflict of interest declaration and submitted it to the CEG. No authors had any relevant conflicts of interest to declare, and the content of the guideline is not attributed to any organisation they are associated with.

18.3. Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

18.4. Editorial Independence

This guideline was commissioned, edited, and endorsed by the BASHH CEG without external funding being sought or obtained. All members of the guideline writing committee completed the BASHH conflicts of interest declaration detailed below at the time the guideline's final draft was submitted to the CEG.

18.5. Membership of the Clinical Effectiveness Group

Current membership of the BASHH Clinical Effectiveness Group is available at https://www.bashh.org/bashh-groups/clinical-effectiveness-group/

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19. TABLE

Table 1 Prevalence of microorganisms associated with NGU in case control studies.

Microorganism	Prevalence in cases vs controls (%)	References
C. trachomatis	22-48 vs. 0-3	3, 6, 7, 11-13, 22, 51, 132, 133
M. genitalium	9-33 vs. 3-5	3, 6, 7, 11-13, 22, 51, 132-134
U. urealyticum	15-26 vs. 11-21	3, 6, 7, 11, 22, 132
U. parvum	8-16 vs. 18-31	6, 7, 88, 132
***Haemophilus* spp**	5-14 vs. 0-2	3, 6, 7
T. vaginalis	1-13 vs. 0-2	3, 6, 7, 11, 12, 22
M. penetrans	1-8 vs. 0-1	3, 41
N. meningitidis	0-2 vs. 0	6, 7
Adenovirus	3-8 vs. 0	6, 7
Herpes simplex virus type 1 and type 2	1-5 vs. <1-1	3, 6, 7
Idiopathic*	10-45	3, 6, 11, 22, 41

*At least four microorganisms tested for. All studies except Srinivasan et al[3] assumed *U. urealyticum* was causual.

v.s.: versus.

20. REFERENCES

1. Horner P, Blee K, O'Mahony C, et al. 2015 UK National Guideline on the management of non-gonococcal urethritis. *Int J STD AIDS* 2016; 27: 85-96.
2. British Association for Sexual Health and HIV (BASHH). Update to the 2015 BASHH UK National Guideline on the management of non-gonococcal urethritis, www.bashhguidelines.org/media/1199/ngu-bashh-update-2018.pdf (2018, accessed 08/02/2024).
3. Srinivasan S, Chambers LC, Tapia KA, et al. Urethral Microbiota in Men: Association of Haemophilus influenzae and Mycoplasma penetrans With Nongonococcal Urethritis. *Clin Infect Dis* 2020; 73: e1684-e1693.
4. Pond MJ, Nori AV, Witney AA, et al. High prevalence of antibiotic-resistant Mycoplasma genitalium in nongonococcal urethritis: the need for routine testing and the inadequacy of current treatment options. *Clin Infect Dis* 2014; 58: 631-637.
5. Leung A, Eastick K, Haddon LE, et al. Mycoplasma genitalium is associated with symptomatic urethritis. *Int J STD AIDS* 2006; 17: 285-288.
6. Ito S, Hanaoka N, Shimuta K, et al. Male non-gonococcal urethritis: From microbiological etiologies to demographic and clinical features. *Int J Urol* 2016; 23: 325-331.
7. Frølund M, Lidbrink P, Wikström A, et al. Urethritis-associated Pathogens in Urine from Men with Non-gonococcal Urethritis: A Case-control Study. *Acta Derm Venereol* 2016; 96: 689-694.
8. Sena AC, Lensing S, Rompalo A, et al. Chlamydia trachomatis, Mycoplasma genitalium, and Trichomonas vaginalis infections in men with nongonococcal urethritis: predictors and persistence after therapy. *J Infect Dis* 2012; 206: 357-365.
9. Wetmore CM, Manhart LE, Lowens MS, et al. Ureaplasma urealyticum is associated with nongonococcal urethritis among men with fewer lifetime sexual partners: a case-control study. *J Infect Dis* 2011; 204: 1274-1282.
10. Horner P, Thomas B, Gilroy CB, et al. Role of Mycoplasma genitalium and Ureaplasma urealyticum in acute and chronic nongonococcal urethritis. *Clin Infect Dis* 2001; 32: 995-1003.
11. Manhart LE, Gillespie CW, Lowens MS, et al. Standard treatment regimens for nongonococcal urethritis have similar but declining cure rates: a randomized controlled trial. *Clin Infect Dis* 2013; 56: 934-942.
12. Schwebke JR, Rompalo A, Taylor S, et al. Re-evaluating the treatment of nongonococcal urethritis: emphasizing emerging pathogens--a randomized clinical trial. *Clin Infect Dis* 2011; 52: 163-170.
13. Khatib N, Bradbury C, Chalker V, et al. Prevalence of Trichomonas vaginalis, Mycoplasma genitalium and Ureaplasma urealyticum in men with urethritis attending an urban sexual health clinic. *Int J STD AIDS* 2015; 26: 388-392.
14. Smith R, Copas AJ, Prince M, et al. Poor sensitivity and consistency of microscopy in the diagnosis of low grade non-gonococcal urethritis. *Sex Transm Infect* 2003; 79: 487-490.
15. Willcox JR, Adler MW and Belsey EM. Observer variation in the interpretation of Gram-stained urethral smears: implications for the diagnosis of non-specific urethritis. *Br J Vener Dis* 1981; 57: 134-136.
16. Frolund M, Falk L, Ahrens P, et al. Detection of ureaplasmas and bacterial vaginosis associated bacteria and their association with non-gonococcal urethritis in men. *PloS one* 2019; 14: e0214425.
17. Wetmore CM, Manhart LE, Lowens MS, et al. Demographic, behavioral, and clinical characteristics of men with nongonococcal urethritis differ by etiology: a case-comparison study. *Sex Transm Dis* 2011; 38: 180-186.
18. Horner PJ, Thomas B, Gilroy CB, et al. Do all men attending departments of genitourinary medicine need to be screened for non-gonococcal urethritis? *Int J STD AIDS* 2002; 13: 667-673.
19. Jordan SJ, Toh E, Williams JA, et al. No Pathogen-Specific Sign or Symptom Predicts the Etiology of Monomicrobial Nongonococcal Urethritis in Men. *Sex Transm Dis* 2020; 47: 329-331.
20. Horner PJ and Taylor-Robinson D. Association of Mycoplasma genitalium with balanoposthitis in men with non-gonococcal urethritis. *Sex Transm Infect* 2010; 87: 38-40.
21. Horner PJ, Gilroy CB, Thomas BJ, et al. Association of Mycoplasma genitalium with acute non-gonococcal urethritis. *Lancet* 1993; 342: 582-585.
22. Jordan SJ, Toh E, Williams JA, et al. Aetiology and prevalence of mixed-infections and mono-infections in non-gonococcal urethritis in men: a case-control study. *Sex Transm Infect* 2020; 96: 306-311.
23. Rane VS, Fairley CK, Weerakoon A, et al. Characteristics of acute nongonococcal urethritis in men differ by sexual preference. *J Clin Microbiol* 2014; 52: 2971-2976.
24. Shimada Y, Ito S, Mizutani K, et al. Bacterial loads of Ureaplasma urealyticum contribute to development of urethritis in men. *Int J STD AIDS* 2014; 25: 294-298.

25. Horner P, Donders G, Cusini M, et al. Should we be testing for urogenital Mycoplasma hominis, Ureaplasma parvum and Ureaplasma urealyticum in men and women? - a position statement from the European STI Guidelines Editorial Board. *J Eur Acad Dermatol Venereol* 2018; 32: 1845-1851.
26. Deguchi T, Shimada Y, Horie K, et al. Bacterial loads of Ureaplasma parvum contribute to the development of inflammatory responses in the male urethra. *Int J STD AIDS* 2015; 26: 1035-1039.
27. Zhang N, Wang R, Li X, et al. Are Ureaplasma spp. a cause of nongonococcal urethritis? A systematic review and meta-analysis. *PloS one* 2014; 9: e113771.
28. Moi H, Hartgill U, Skullerud KH, et al. Microscopy of Stained Urethral Smear in Male Urethritis; Which Cutoff Should be Used? *Sex Transm Dis* 2017; 44: 189-194.
29. Cox C, McKenna JP, Watt AP, et al. Ureaplasma parvum and Mycoplasma genitalium are found to be significantly associated with microscopy-confirmed urethritis in a routine genitourinary medicine setting. *Int J STD AIDS* 2016; 27: 861-867.
30. Plummer EL, Ratten LK, Vodstrcil LA, et al. The Urethral Microbiota of Men with and without Idiopathic Urethritis. *mBio* 2022; 13: e0221322.
31. Magdaleno-Tapial J, Valenzuela-Onate C, Giacaman-von der Weth MM, et al. Haemophilus Species Isolated in Urethral Exudates as a Possible Causative Agent in Acute Urethritis: A Study of 38 Cases. *Actas dermo-sifiliograficas* 2019; 110: 38-42.
32. Deza G, Martin-Ezquerra G, Gomez J, et al. Isolation of Haemophilus influenzae and Haemophilus parainfluenzae in urethral exudates from men with acute urethritis: a descriptive study of 52 cases. *Sex Transm Infect* 2016; 92: 29-31.
33. Carne CA, Gibbs J, Delaney A, et al. Prevalence, clinical features and quantification of genital non-viral infections. *Int J STD AIDS* 2013; 24: 273-277.
34. Nicholls JE, Turner KME, North P, et al. Cross-sectional study to evaluate Trichomonas vaginalis positivity in women tested for Neisseria gonorrhoeae and Chlamydia trachomatis, attending genitourinary medicine and primary care clinics in Bristol, South West England. *Sex Transm Infect* 2018; 94: 93-99.
35. Mitchell HD, Lewis DA, Marsh K, et al. Distribution and risk factors of Trichomonas vaginalis infection in England: an epidemiological study using electronic health records from sexually transmitted infection clinics, 2009–2011. *Epidemiol Infect* 2014; 142: 1678-1687.
36. Toh E, Gangaiah D, Batteiger BE, et al. Neisseria meningitidis ST11 Complex Isolates Associated with Nongonococcal Urethritis, Indiana, USA, 2015-2016. *Emerg Infect Dis* 2017; 23: 336-339.
37. Bazan JA, Peterson AS, Kirkcaldy RD, et al. Notes from the Field: Increase in Neisseria meningitidis-Associated Urethritis Among Men at Two Sentinel Clinics - Columbus, Ohio, and Oakland County, Michigan, 2015. *MMWR Morb Mortal Wkly Rep* 2016; 65: 550-552.
38. Keane FE, Thomas BJ, Whitaker L, et al. An association between non-gonococcal urethritis and bacterial vaginosis and the implications for patients and their sexual partners. *Genitourin Med* 1997; 73: 373-377.
39. Manhart LE, Khosropour CM, Liu C, et al. Bacterial vaginosis-associated bacteria in men: association of Leptotrichia/Sneathia spp. with nongonococcal urethritis. *Sex Transm Dis* 2013; 40: 944-949.
40. Hawkins DA, Fontaine EA, Thomas BJ, et al. The enigma of non-gonococcal urethritis: role for Bacteroides ureolyticus. *Genitourin Med* 1988; 64: 10-13.
41. Frolund M, Wikstrom A, Lidbrink P, et al. The bacterial microbiota in first-void urine from men with and without idiopathic urethritis. *PloS one* 2018; 13: e0201380.
42. Samaraweera GR, Garcia K, Druce J, et al. Characteristics of adenovirus urethritis among heterosexual men and men who have sex with men: a review of clinical cases. *Sex Transm Infect* 2016; 92: 172-174.
43. Hanaoka N, Ito S, Konagaya M, et al. Infectious human adenoviruses are shed in urine even after disappearance of urethral symptoms. *PloS one* 2019; 14: e0212434.
44. Bradshaw CS, Tabrizi SN, Read TRH, et al. Etiologies of Nongonococcal Urethritis: Bacteria, Viruses, and the Association with Orogenital Exposure. *J Infect Dis* 2006; 193: 336-345.
45. Tonsberg E and Hartgill U. The urethral smear as a tool in diagnosing adenovirus-induced urethritis. *Int J STD AIDS* 2014; 25: 1047-1049.
46. Ito S, Yasuda M, Kondo H, et al. Clinical courses of herpes simplex virus-induced urethritis in men. *J Infect Chemother* 2017; 23: 717-719.
47. Ong JJ, Morton AN, Henzell HR, et al. Clinical Characteristics of Herpes Simplex Virus Urethritis Compared With Chlamydial Urethritis Among Men. *Sex Transm Dis* 2017; 44: 121-125.
48. Shahmanesh M. Problems with non-gonococcal urethritis. *Int J STD AIDS* 1994; 5: 390-399.
49. Berntsson M, Lowhagen GB, Bergstrom T, et al. Viral and bacterial aetiologies of male urethritis: findings of a high prevalence of Epstein-Barr virus. *Int J STD AIDS* 2010; 21: 191-194.

50. Leung A, Taylor S, Smith A, et al. Urinary tract infection in patients with acute non-gonococcal urethritis. *Int J STD AIDS* 2002; 13: 801-804.
51. Moi H, Reinton N, Randjelovic I, et al. Urethral inflammatory response to ureaplasma is significantly lower than to Mycoplasma genitalium and Chlamydia trachomatis. *Int J STD AIDS* 2017; 28: 773-780.
52. Horner PJ and Martin DH. Mycoplasma genitalium Infection in Men. *J Infect Dis* 2017; 216: S396-S405.
53. Horner P. The Etiology of Acute Nongonococcal Urethritis-The Enigma of Idiopathic Urethritis? *Sex Transm Dis* 2011; 38: 187-189.
54. Falk L, Fredlund H and Jensen JS. Symptomatic urethritis is more prevalent in men infected with *Mycoplasma genitalium* than with *Chlamydia trachomatis*. *Sex Transm Infect* 2004; 80: 289-293.
55. Sutton AJ, Roberts TE, Jackson L, et al. Cost-effectiveness of microscopy of urethral smears for asymptomatic Mycoplasma genitalium urethritis in men in England. *Int J STD AIDS* 2018; 29: 72-79.
56. Swartz SL, Kraus SJ, Herrmann KL, et al. Diagnosis and etiology of nongonococcal urethritis. *J Infect Dis* 1978; 138: 445-454.
57. Jordan SJ, Schwebke JR, Aaron KJ, et al. Meatal Swabs Contain Less Cellular Material and Are Associated with a Decrease in Gram Stain Smear Quality Compared to Urethral Swabs in Men. *J Clin Microbiol* 2017; 55: 2249-2254.
58. Leipertz G, Chambers L, Lowens S, et al. P796 Reassessing the gram stain smear (GSS) polymorphonuclear leukocyte (PMN) cutoff for diagnosing non-gonococcal urethritis (NGU). *Sex Transm Infect* 2019; 95: A339.
59. Chernesky M, Jang D, Chong S, et al. Impact of urine collection order on the ability of assays to identify Chlamydia trachomatis infections in men. *Sex Transm Dis* 2003; 30: 345-347.
60. Mathew T, O'Mahony C and Mallinson H. Shortening the voiding interval for men having chlamydia nucleic acid amplification tests. *Int J STD AIDS* 2009; 20: 752-753.
61. Apoola A, Herrero-Diaz M, FitzHugh E, et al. A randomised controlled trial to assess pain with urethral swabs. *Sex Transm Infect* 2011; 87: 110-113.
62. Moi H, Reinton N and Moghaddam A. Mycoplasma genitalium is associated with symptomatic and asymptomatic non-gonococcal urethritis in men. *Sex Transm Infect* 2009; 85: 15-18.
63. Pond MJ, Nori AV, Patel S, et al. Performance evaluation of automated urine microscopy as a rapid, non-invasive approach for the diagnosis of non-gonococcal urethritis. *Sex Transm Infect* 2015; 91: 165-170.
64. Fraser PA, Teasdale J, Gan KS, et al. Neutrophil enzymes in urine for the detection of urethral infection in men. *Genitourin Med* 1995; 71: 176-179.
65. Patrick DM, Rekart ML and Knowles L. Unsatisfactory performance of the leukocyte esterase test of first voided urine for rapid diagnosis of urethritis. *Genitourin Med* 1994; 70: 187-190.
66. British Association for Sexual Health and HIV (BASHH). BASHH Summary Guidance on Testing for Sexually Transmitted Infections, 2023 https://www.bashh.org/_userfiles/pages/files/resources/bashh_summary_guidance_on_stis_testing_2023.pdf (2023, accessed 17/05/2024).
67. Reinton N, Moi H, Olsen AO, et al. Anatomic distribution of Neisseria gonorrhoeae, Chlamydia trachomatis and Mycoplasma genitalium infections in men who have sex with men. *Sex Health* 2013; 10: 199-203.
68. Fifer H, Saunders J, Soni S, et al. 2018 UK national guideline for the management of infection with Neisseria gonorrhoeae. *Int J STD AIDS* 2020; 31: 4-15.
69. Clutterbuck D, Asboe D, Barber T, et al. 2016 United Kingdom national guideline on the sexual health care of men who have sex with men. *Int J STD AIDS* 2018: 956462417746897.
70. Nwokolo NC, Dragovic B, Patel S, et al. 2015 UK national guideline for the management of infection with Chlamydia trachomatis. *Int J STD AIDS* 2016; 27: 251-267.
71. Soni S, Horner P, Rayment M, et al. British Association for Sexual Health and HIV national guideline for the management of infection with Mycoplasma genitalium (2018). *Int J STD AIDS* 2019; 30: 938-950.
72. Johnson KA, Sankaran M, Kohn RP, et al. Testing for Mycoplasma genitalium and Using Doxycycline as First-Line Therapy at Initial Presentations for Non-Gonococcal Urethritis (NGU) Correlate With Reductions in Persistent NGU. *Clin Infect Dis* 2023; 76: 1674-1677.
73. NICE - National Institute for Health and Care Excellence. Clinical Knowledge Summary - Urinary tract infection (lower) - men, https:// cks.nice.org.uk/topics/urinary-tract-infection-lower-men/ (2023).
74. Crofts M, Mead K, Persad R, et al. How to manage the chronic pelvic pain syndrome in men presenting to sexual health services. *Sex Transm Infect* 2014; 90: 370-373.

75. Horner P, Crofts M and Luzzi G. 03_09 Prostatitis and male pelvic pain., https://www.e-lfh.org.uk/ (2019).
76. Horner PJ, Connor E, Williams S, et al. A holistic biopsychosocial management approach for cis-gender males with chronic pelvic pain syndrome attending sexual health services: a retrospective case review. *Sex Transm Infect* 2024; 100: 113-115.
77. Coble BI, Nordahl-Akesson E, Vinnerberg A, et al. Urine-based testing for Chlamydia trachomatis using polymerase chain reaction, leucocyte esterase and urethral and cervical smears. *Scand J Clin Lab Invest* 2006; 66: 269-277.
78. Marrazzo JM, Whittington WL, Celum CL, et al. Urine-based screening for *Chlamydia trachomatis* in men attending sexually transmitted disease clinics. *Sex Transm Dis* 2001; 28: 219-225.
79. Clinical Effectiveness Group of the British Association for Sexual Health and HIV (BASHH). Patient Information Leaflet - Non-gonococcal Urethritis, https://www.bashhguidelines.org/patient-information-leaflets (2015).
80. Clutterbuck DJ, Flowers P, Barber T, et al. UK national guideline on safer sex advice. *Int J STD AIDS* 2012; 23: 381-388.
81. Swartz SL and Kraus SJ. Persistent urethral leukocytosis and asymptomatic chlamydial urethritis. *J Infect Dis* 1979; 140: 614-617.
82. Boylan J, Sundar S, Gardiner R, et al. P289 A cost-neutral rapid STI service implementation providing the right treatment at the right time to improve patient experience and outcomes. *Sex Transm Infect* 2021; 97: A134-A134.
83. Adams EJ, Ehrlich A, Turner KME, et al. Mapping patient pathways and estimating resource use for point of care versus standard testing and treatment of chlamydia and gonorrhoea in genitourinary medicine clinics in the UK. *BMJ Open* 2014; 4: e005322.
84. Courtenay M, Castro-Sanchez E, Fitzpatrick M, et al. Tackling antimicrobial resistance 2019-2024 - The UK's five-year national action plan. *J Hosp Infect* 2019; 101: 426-427.
85. Walter SR, Jackson J, Myring G, et al. Impact of rapid near-patient STI testing on service delivery outcomes in an integrated sexual health service in the United Kingdom: a controlled interrupted time series study. *BMJ Open* 2023; 13: e064664.
86. Horner PJ, Cain D, McClure M, et al. Association of antibodies to *Chlamydia trachomatis* heat-shock protein 60 kD with chronic nongonococcal urethritis. *Clin Infect Dis* 1997; 24: 653-660.
87. Horner P, Thomas B, Gilroy C, et al. Antibodies to Chlamydia trachomatis heat-shock protein 60 kDa and detection of *Mycoplasma genitalium* and *Ureaplasma urealyticum* are associated independently with chronic nongonococcal urethritis. *Sex Transm Dis* 2003; 30: 129-133.
88. Khosropour CM, Manhart LE, Gillespie CW, et al. Efficacy of standard therapies against Ureaplasma species and persistence among men with non-gonococcal urethritis enrolled in a randomised controlled trial. *Sex Transm Infect* 2015; 91: 308-313.
89. Lomas DA, Natin D, Stockley RA, et al. Chemotactic activity of urethral secretions in men with urethritis and the effect of treatment. *J Infect Dis* 1993; 167: 233-236.
90. Kong FYS, Tabrizi SN, Law M, et al. Azithromycin versus doxycycline for the treatment of genital chlamydia infection – a meta-analysis of randomised controlled trials. *Clin Infect Dis* 2014; 59: 193-205.
91. Khosropour CM, Manhart LE, Colombara DV, et al. Suboptimal adherence to doxycycline and treatment outcomes among men with non-gonococcal urethritis: a prospective cohort study. *Sex Transm Infect* 2014; 90: 3-7.
92. Mena LA, Mroczkowski TF, Nsuami M, et al. A randomized comparison of azithromycin and doxycycline for the treatment of Mycoplasma genitalium-positive urethritis in men. *Clin Infect Dis* 2009; 48: 1649-1654.
93. Deguchi T, Ito S, Hatazaki K, et al. Antimicrobial susceptibility of Haemophilus influenzae strains isolated from the urethra of men with acute urethritis and/or epididymitis. *J Infect Chemother* 2017; 23: 804-807.
94. Cohen S, Sankaran M, Kohn RP, et al. Decline in Persistent Urethritis after Change in Clinical Protocols for the Diagnosis and Management of Non-gonococcal Urethritis (NGU). *Sex Transm Dis* 2022; 49: S32-S33.
95. Horner PJ, Blee K, Falk L, et al. 2016 European guideline on the management of non-gonococcal urethritis. *Int J STD AIDS* 2016; 27: 928-937.
96. Nwokolo NC, Dragovic B, Patel S, et al. Update on the treatment of Chlamydia trachomatis (CT) infection, https://www.bashhguidelines.org/media/1191/update-on-the-treatment-of-chlamydia-trachomatis-infection-final-16-9-18.pdf (2018).

97. Horner PJ. Editorial Commentary: Mycoplasma genitalium and Declining Treatment Efficacy of Azithromycin 1 g: What Can We Do? *Clin Infect Dis* 2015; 61: 1400-1402.
98. Lau A, Bradshaw CS, Lewis D, et al. The Efficacy of Azithromycin for the Treatment of Genital Mycoplasma genitalium: A Systematic Review and Meta-analysis. *Clin Infect Dis* 2015; 61: 1389-1399.
99. Couldwell DL and Lewis DA. Mycoplasma genitalium infection: current treatment options, therapeutic failure, and resistance-associated mutations. *Infect Drug Resist* 2015; 8: 147-161.
100. Horner P. P09.03 Treatment of mycoplasma genitalium with azithromycin 1 g is less efficacious and associated with induction of macrolide resistance compared to a 5-day regimen. *Sex Transm Infect* 2015; 91: A148.
101. Horner P, Blee K and Adams E. Time to manage Mycoplasma genitalium as an STI: but not with azithromycin 1 g! *Curr Opin Infect Dis* 2014; 27: 68-74.
102. Handsfield H. Management of Herpetic Urethritis and Female Partners of Men With Nongonococcal Urethritis. *Sex Transm Dis* 2017; 44: 131-133.
103. Kissinger PJ, White S, Manhart LE, et al. Azithromycin Treatment Failure for Chlamydia trachomatis Among Heterosexual Men With Nongonococcal Urethritis. *Sex Transm Dis* 2016; 43: 599-602.
104. Kong FYS, Horner P, Unemo M, et al. Pharmacokinetic considerations regarding the treatment of bacterial sexually transmitted infections with azithromycin: a review. *J Antimicrob Chemother* 2019; 74: 1157-1166.
105. Read TRH, Fairley CK, Murray GL, et al. Outcomes of resistance-guided sequential treatment of Mycoplasma genitalium Infections: a prospective evaluation. *Clin Infect Dis* 2019; 68: 554-560.
106. Anagrius C, Loré B and Jensen JS. Treatment of *Mycoplasma genitalium*. Observations from a Swedish STD Clinic. *PloS one* 2013; 8: e61481.
107. Falk L, Enger M and Jensen JS. Time to eradication of Mycoplasma genitalium after antibiotic treatment in men and women. *J Antimicrob Chemother* 2015; 70: 3134-3140.
108. Horner P. Azithromycin antimicrobial resistance and genital Chlamydia trachomatis infection: duration of therapy may be the key to improving efficacy. *Sex Transm Infect* 2012; 88: 154-156.
109. Unemo M, Ross J, Serwin AB, et al. 2020 European guideline for the diagnosis and treatment of gonorrhoea in adults. *Int J STD AIDS* 2020: 956462420949126.
110. Unemo M, Ross J, Serwin AB, et al. Background review for the '2020 European guideline for the diagnosis and treatment of gonorrhoea in adults'. *Int J STD AIDS* 2021; 32: 108-126.
111. Stamm WE, Batteiger BE, McCormack WM, et al. A randomized, double-blind study comparing single-dose rifalazil with single-dose azithromycin for the empirical treatment of nongonococcal urethritis in men. *Sex Transm Dis* 2007; 34: 545-552.
112. Ito S, Hatazaki K, Shimuta K, et al. Haemophilus influenzae Isolated From Men With Acute Urethritis: Its Pathogenic Roles, Responses to Antimicrobial Chemotherapies, and Antimicrobial Susceptibilities. *Sex Transm Dis* 2017; 44: 205-210.
113. Jordan S, Toh E, Batteiger T, et al. Prevalence and etiology of post-azithromycin persistent non-gonococcal urethritis (NGU) symptoms in men. *Sex Transm Infect* 2019; 95: A338-A339.
114. Ng A and Ross JD. Trichomonas vaginalis infection: How significant is it in men presenting with recurrent or persistent symptoms of urethritis? *Int J STD AIDS* 2016; 27: 63-65.
115. Taylor-Robinson D, Gilroy CB, Thomas BJ, et al. Mycoplasma genitalium in chronic non-gonococcal urethritis. *Int J STD AIDS* 2004; 15: 21-25.
116. Bowie WR, Alexander ER, Stimson JB, et al. Therapy for nongonococcal urethritis: double-blind randomized comparison of two doses and two durations of minocycline. *Ann Intern Med* 1981; 95: 306-311.
117. Chambers LC, Hughes JP, Glick SN, et al. Resolution of Symptoms and Resumption of Sex After Diagnosis of Nongonococcal Urethritis Among Men Who Have Sex With Men. *Sex Transm Dis* 2019; 46: 676-682.
118. Horner PJ, Crofts M and Butterly J. How to effectively manage chronic pelvic pain syndrome in cis-gender men presenting to sexual health services using a holistic biopsychosocial approach. *Sex Transm Infect* 2023.
119. Hooton TM, Wong ES, Barnes RC, et al. Erythromycin for persistent or recurrent nongonococcal urethritis. A randomized, placebo-controlled trial. *Ann Intern Med* 1990; 113: 21-26.
120. Amsden GW. Erythromycin, clarithromycin, and azithromycin: are the differences real? *Clin Ther* 1996; 18: 56-72.
121. Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. *MMWR Recomm Rep* 2021; 70: 1-187.

122. Durukan D, Read TRH, Murray G, et al. Resistance-Guided Antimicrobial Therapy Using Doxycycline-Moxifloxacin and Doxycycline-2.5 g Azithromycin for the Treatment of Mycoplasma genitalium Infection: Efficacy and Tolerability. *Clin Infect Dis* 2020; 71: 1461-1468.
123. Ramsden S, Isotta-Day H and Horner P. Chronic pelvic pain in men. *Medicine* 2018; 46: 337-341.
124. Rees J, Abrahams M, Doble A, et al. Diagnosis and treatment of chronic bacterial prostatitis and chronic prostatitis/chronic pelvic pain syndrome: a consensus guideline. *BJU Int* 2015; 116: 509-525.
125. Crofts M, Mead K, Persad R, et al. An evaluation of a dedicated chronic pelvic pain syndrome clinic in genitourinary medicine. *Sex Transm Infect* 2014; 90: 373.
126. Kenyon S, Crofts M and Horner P. An extended evaluation of a dedicated male chronic pelvic pain clinic within a sexual health service. *Sex Transm Infect* 2014; 90: 572.
127. Nickel JC, Baranowski AP, Pontari M, et al. Management of men diagnosed with chronic prostatitis/chronic pelvic pain syndrome who have failed traditional management. *Rev Urol* 2007; 9: 63-72.
128. Schneider H, Wilbrandt K, Ludwig M, et al. Prostate-related pain in patients with chronic prostatitis/chronic pelvic pain syndrome. *BJU Int* 2005; 95: 238-243.
129. Ong JJ, Sarumpaet A, Chow EPF, et al. Should Female Partners of Men With Non-Gonococcal Urethritis, Negative for Chlamydia trachomatis and Mycoplasma genitalium, Be Informed and Treated? Clinical Outcomes From a Partner Study of Heterosexual Men With NGU. *Sex Transm Dis* 2017; 44: 126-130.
130. Fitzgerald MR. Effect of epidemiological treatment of contacts in preventing recurrences of non-gonococcal urethritis. *Br J Vener Dis* 1984; 60: 312-315.
131. Price MJ, Ades AE, Soldan K, et al. The natural history of Chlamydia trachomatis infection in women: a multi-parameter evidence synthesis. *Health Technol Assess* 2016; 20: 1-250.
132. Ondondo RO, Whittington WL, Astete SG, et al. Differential association of ureaplasma species with non-gonococcal urethritis in heterosexual men. *Sex Transm Infect* 2010; 86: 271-275.
133. McIver R, Jalocon D, McNulty A, et al. Men Who Have Sex With Men With Mycoplasma genitalium-Positive Nongonococcal Urethritis Are More Likely to Have Macrolide-Resistant Strains Than Men With Only Female Partners: A Prospective Study. *Sex Transm Dis* 2019; 46: 513-517.
134. Ovens KJ, Reynolds-Wright JJ, Cross ELA, et al. High rates of treatment failure for Mycoplasma genitalium among men and women attending a sexual health clinic. *BMJ Sex Reprod Health* 2020; 46: 132-138.

APPENDIX 1: LIST OF PICO QUESTIONS

PICO QUESTION 1. In people attending health services in the UK with penile signs and symptoms suggestive of urethritis, what laboratory test(s) should be used to diagnose penile NGU?

- **Population:** People attending health services in the UK with signs and symptoms suggestive of penile urethritis;
- **Intervention**: Clinical assessment for NGU or laboratory testing to confirm condition;
- **Comparison:** No risk assessment or testing or alternative methods of diagnosis;
- **Outcome:** Detection of NGU.

PICO QUESTION 2. In people attending sexual health services in the UK who have had urethritis confirmed, what further laboratory test(s) should be deployed to diagnose an infective aetiology?

- **Population:** People attending health services in the UK with confirmed penile NGU;
- **Intervention:** Laboratory testing to confirm aetiology;
- **Comparison:** No further laboratory testing;
- **Outcome:** Detection of pathogens.

PICO QUESTION 3. In people attending sexual health services in the UK with confirmed penile NGU, what antibiotic management should be used if pathogen-specific diagnostic test results are not yet available?

- **Population:** People attending health services in the UK with confirmed penile NGU;
- **Intervention:** Treatment with antibiotics;
- **Comparison:** No antibiotic treatment;
- **Outcome:** Relief of symptoms; treat any infective aetiology(ies); reduce risk reinfection and onward transmission.

PICO QUESTION 4. In people attending sexual health services in the UK with ongoing symptoms and/or signs of penile NGU, what further diagnostic tools should be used to identify the most likely aetiology and inform management strategies

- **Population:** People attending sexual health services, previously treated for penile NGU (< 3 months) with ongoing symptoms and/or signs of urethritis;
- **Intervention:** Further testing and management;
- **Comparison:** No follow up;
- **Outcome:** Patient satisfaction; reduction in index patient morbidity; reduction of onward transmission if identified infectious aetiology.

PICO QUESTION 5. In people attending sexual health services in the UK meeting diagnostic criteria for penile NGU despite initial antibiotic treatment and who have tested negative for initial investigations, what antibiotic management should be used?

- **Population:** People attending sexual health services, previously treated for penile NGU (< 3 months) with ongoing symptoms and/or signs of urethritis;
- **Intervention:** Further testing and management;
- **Comparison:** No follow-up;
- **Outcome:** Patient satisfaction; reduction in index patient morbidity; reduction of onward transmission if identified infectious aetiology.

PICO QUESTION 6. In people attending sexual health services treated for penile NGU what management of former and current sexual partners will maximise benefits and cause least harm for index patient and their partner(s)?

- **Population:** People attending sexual health services treated for penile NGU where pathogen-specific results are not yet available or are negative;
- **Intervention**: Immediate partner notification;
- **Comparison**: Deferred or no partner notification;

- **Outcome:** Reduction of reinfection in the index case; reduction of harm to the partner; reduction in onward transmission of pathogen if subsequently identified in index case.

APPENDIX 2: GRADE SYSTEM FOR ASSESSING EVIDENCE

Introduction:

There has been a general move to using the GRADE system by many guideline producing bodies in recent years and the BMJ published a series of papers about the method in 2008 [1,2,3,4,5,6].

The GRADE system applied in its purest form requires scientific analyses of evidence to produce "tables" from a series of "PICO" questions: Questions that identify the patient problem or population (P), intervention (I) (or aetiology/diagnosis/frequency/prognosis), comparison (C) and outcome(s) (O). Practically this is very labour intensive and requires someone very experienced in this area, and many large guideline writing bodies employ a scientist to do this for them. However, some bodies adapt the GRADE system according to their own needs, assess the evidence in the way they have done in the past, and then make strengths of recommendations according to the GRADE system, which when applied in this way is quite simple to do and understand. BASHH have adopted GRADE to use in this manner.

The principles of GRADE:

1. Assessment of the evidence

GRADE offers four levels of evidence quality: high, moderate, low, and very low, with randomised trials classed as high-quality evidence and observational studies as low-quality evidence. Quality may be downgraded because of limitations in study design or implementation, imprecision of estimates (wide confidence intervals), variability in results, indirectness of evidence, or publication bias. Quality may be upgraded because of a very large

[1] Guyatt GH, Oxman AD, Vist G, et al; GRADE Working Group. BMJ 2008; 336:924-926.

[2] Guyatt GH, Oxman AD, Kunz R, et al; GRADE Working Group. BMJ 2008; 336(7651):995-8.

[3] Schünemann HJ, Oxman AD, Brozek J, et al; GRADE Working Group. BMJ 2008; 336(7653):1106-10.

[4] Guyatt GH, Oxman AD, Kunz R, et al; GRADE Working Group. BMJ 2008; 336(7654):1170-3.

[5] Guyatt GH, Oxman AD, Kunz R, et al; GRADE Working Group. BMJ 2008; 336(7652):1049-51.

[6] Jaeschke R, Guyatt GH, Dellinger P, et al; GRADE working group. BMJ 2008; 337:a744.

magnitude of effect, a dose-response gradient, and if all plausible biases would reduce an apparent treatment effect.

Summary of factors affecting quality of evidence:

Study limitations	Imprecision	Large magnitude of effect
Inconsistency of results	Publication bias	Dose-response gradient
Indirectness of evidence	Factors that might increase quality of evidence	Plausible confounding, which would reduce a demonstrated effect

Based on the analysis of the evidence with these factors borne in mind the evidence should be graded as follows:

A	A body of evidence of high-quality meta-analyses, systematic reviews of and RCTs directly applicable to the target population
B	As above but relating to high quality case control or cohort studies with low risk of bias or confounding and high probability that a relationship is causal
C	As B but trials may have some flaws
D	Non-analytic evidence (e.g., case reports or series or expert opinion)

However, when reviewing evidence graded A-D as above the grading can be altered follows:

- The strength of recommendation should be higher if the following apply:
    - A large effect of an intervention is demonstrated.
    - Dose response/evidence of gradient.
    - All plausible confounding would reduce a demonstrated effect or would suggest a spurious effect when results show no effect.
- Lower if there is evidence of:
    - Serious/very serious study limitations
    - Inconsistency
    - Indirectness
    - Imprecision

- Publication bias
- Study limitations
- Inconsistency of results
- Indirectness of evidence
- Imprecision
- Publication bias

2. Formulating recommendations

There are only two strengths of recommendation, which may be either for or against an intervention: 1 = strong or 2 = weak. Pragmatically, this means the following:

- Strong recommendation for intervention:

For patients — Most people in this situation would want the recommended course of action and only a small proportion would not.

For clinicians — Most people should receive the intervention.

For quality monitors — Adherence to this recommendation could be used as a quality criterion or performance indicator. If clinicians choose not to follow such a recommendation, they should document their rationale.

- Weak recommendation for intervention:

For patients — Most people in this situation would want the suggested course of action, but many would not.

For clinicians — Examine the evidence or a summary of the evidence yourself and be prepared to discuss that evidence with patients, as well as their values and preferences.

For quality monitors — Clinicians' discussion or consideration of the pros and cons of the intervention, and their documentation of the discussion, could be used as a quality criterion.

- No specific recommendation:
  - The advantages and disadvantages are equivalent.
  - The target population has not been identified.

- Insufficient evidence on which to formulate a recommendation.

3. Consideration of using PICO

This may be helpful if guideline writing committee wish to utilise this method, this is explained in the NICE guideline manual; chapter 4:6.

Patients/population	Which patients or population of patients are we interested in? How can they be best described? Are there subgroups that need to be considered?
Intervention	Which intervention, treatment or approach should be used?
Comparison	What is/are the main alternative/s to compare with the intervention?
Outcome	What is really important for the patient? Which outcomes should be considered, such as intermediate or short-term measures; mortality; morbidity and treatment complications; rates of relapse; late morbidity and readmission; return to work, physical and social functioning? Should other measures such as quality of life, general health status and costs be considered?

4. Consideration of costs

These may or may not legitimately be included in the GRADE system, but it would be sensible in the current climate to always consider these, and if they are not considered this should be stated and why – for example, there is no significant difference in cost between the recommended treatments.

Generally speaking, GRADE suggests a balance sheet should inform judgments about whether the net benefits are worth the incremental costs. Evidence profiles should always present resource use, not just monetary values.

5. Using the GRADE grid to resolve differences:

This supports the Delphi technique we already adopt, i.e., to develop a consensus within the group.

6. GRADE training for BASHH guideline authors

Authors need to be familiar and confident in using the GRADE system, and training for this is available as follows:

- The papers from the BMJ series in 2008, as listed in the introduction to this appendix. The articles can be accessed through the grade working group web site at: http://www.gradeworkinggroup.org/publications/index.htm
- McMaster GRADE online modules: these have been recommended by the GRADE working group and take about 20 minutes each to complete. The web address is: http://cebgrade.mcmaster.ca/
- Journal of Clinical Epidemiology 2011: published a 20-part series that is available through the GRADE working group website (link above).

Summary:

BASHH have now moved to the GRADE system for evaluating evidence and making recommendations by asking guideline authors and reviewers to apply the principles outlined in sections 1-3 above. Authors should consider structuring their analysis of evidence into PICO questions addressing Population / Intervention / Comparison / Outcome as stated in section 4. Costs should be included in the evaluation and formulation of recommendations as stated in section 5. When resolution of conflicting opinions is required, the GRADE grid should be used. This appendix is a brief summary of the GRADE system how it is to be adopted by BASHH guideline authors.

APPENDIX 3: EQUALITY IMPACT ASSESSMENT TABLE

BASHH Guideline Equality Impact Assessment (based on NICE documentation shared with BASHH August 2019)				
Guidance title: BASHH Guidelines for the Management of NGU		Completed by: CERI EVANS		Date: 17/12/24
How relevant is the topic to equality?	Inequalities in health impact of the condition or public health issue	Potential of guidance to add value	Priority for NHS or other government department	Topic relevance; conclusions and outcomes
	• Prevalence and impact of condition or public health problem; • Prevalence of risk factors.	• Inequalities in access, uptake or impact; • Timeliness; • Equality issues identified by proposers of the topic; • Equality issues identified by patient or lay organisations.	• Department of Health or other centralised NHS bodies such as NHS England; • Local authorities; • Home Office; • Other agencies.	• If equality issues had impact on the guidance summarise these impacts.
Sex/gender	NGU only affects those with a penis (the guidelines have adopted a gender-neutral, anatomical approach in line with BASHH best practice)	NA	NA	NA
Race	Some aetiological agents of NGU may be more or less common in certain ethnicities	NA		The guideline does suggest consideration of ethnicity in patients with persistent NGU when considering aetiological agents in light of published data; this does not inform recommended

BASHH Guideline Equality Impact Assessment (based on NICE documentation shared with BASHH August 2019)				
Guidance title: BASHH Guidelines for the Management of NGU		Completed by: CERI EVANS		Date: 17/12/24
				treatments for syndromic management
Disability	NGU can affect all those with a penis who are sexually active although there are no specific data that determine the prevalence in those living with disability	There are potential issues regarding access to care for those with physical disability given that the guideline has stressed that where possible, symptomatic patients should be strongly encouraged to attend a centre that has microscopy available.	Increased funding for sexual health services to be able to deliver outreach care where needed, is essential.	The guideline itself is not impacted directly by this issue.
Age	NGU can affect all those with a penis who are sexually active	NA	NA	NA
Sexual orientation	NGU can affect all those with a penis who are sexually active. There are very limited data regarding differences in aetiological agent when stratified by sexual orientation. These data are insufficient to merit changes in recommendation for investigations or treatments.	NA	NA	The guideline does not stipulate different treatment pathways for those of different sexual orientations

Title: BASHH national guideline on the management of NGU	
Version No.: Draft 1 version 4.0	**Date:** June 2025

BASHH Guideline Equality Impact Assessment (based on NICE documentation shared with BASHH August 2019)				
Guidance title: BASHH Guidelines for the Management of NGU		Completed by: CERI EVANS		Date: 17/12/24
Gender reassignment	NGU affects cis-men / transwomen who have a penis	NA	NA	The guideline does not stipulate different treatment pathways for those who have had gender reassignment
Religion/belief	Surveillance data does not tell us about any association between NGU and religion/ belief.	NA	NA	NA
Pregnancy & maternity	N/A	N/A	NA	NA
Other definable characteristics & socioeconomic factors that may affected by protected characteristics, including: • Prisoners and young offenders; • Refugees and asylum seekers; • Migrant workers; • Looked after children; • Homeless people; • Deprivation; • Disadvantage associated with geographical distinctions.	Some people in this inclusion health populations may be vulnerable to additional adverse determinants of health including sexual coercion and violence. Departmental safeguarding procedures should be in place to identify and respond to any issues.	The guidelines are primarily for those working in level 3 specialist sexual health services and safeguarding concerns should be addressed by departmental policies. Genitourinary physicians receive level 3 safeguarding training.	Safeguarding concerns should be addressed.	Consideration of patients in these groups being at risk of sexual exploitation/abuse should be made as part of Genitourinary Medicine department's safeguarding training.

Title: BASHH national guideline on the management of NGU	
Version No.: Draft 1 version 4.0	**Date:** June 2025

APPENDIX 4: AGREE II USER MANUAL

The AGREE II consists of 23 key items organized within 6 domains followed by 2 global rating items ("Overall Assessment"). Each domain captures a unique dimension of guideline quality [7].

DOMAIN 1. SCOPE AND PURPOSE

1. The overall objective(s) of the guideline is (are) specifically described.

2. The health question(s) covered by the guideline is (are) specifically described.

3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.

DOMAIN 2. STAKEHOLDER INVOLVEMENT

4. The guideline development group includes individuals from all relevant professional groups.

5. The views and preferences of the target population (patients, public, etc.) have been sought.

6. The target users of the guideline are clearly defined.

DOMAIN 3. RIGOUR OF DEVELOPMENT

7. Systematic methods were used to search for evidence.

8. The criteria for selecting the evidence are clearly described.

9. The strengths and limitations of the body of evidence are clearly described.

10. The methods for formulating the recommendations are clearly described.

11. The health benefits, side effects, and risks have been considered in formulating the recommendations.

12. There is an explicit link between the recommendations and the supporting evidence.

13. The guideline has been externally reviewed by experts prior to its publication.

[7] Appraisal of Guidelines for Research & Evaluation (AGREE) II User Manual, update from December 2017. Access: https://www.agreetrust.org/wp-content/uploads/2017/12/AGREE-II-Users-Manual-and-23-item-Instrument-2009-Update-2017.pdf

14. A procedure for updating the guideline is provided.

DOMAIN 4. CLARITY OF PRESENTATION

15. The recommendations are specific and unambiguous.

16. The different options for management of the condition or health issue are clearly presented.

17. Key recommendations are easily identifiable.

DOMAIN 5. APPLICABILITY

18. The guideline describes facilitators and barriers to its application.

19. The guideline provides advice and/or tools on how the recommendations can be put into practice.

20. The potential resource implications of applying the recommendations have been considered.

21. The guideline presents monitoring and/or auditing criteria.

DOMAIN 6. EDITORIAL INDEPENDENCE

22. The views of the funding body have not influenced the content of the guideline.

23. Competing interests of guideline development group members have been recorded and addressed.

APPENDIX 5: PILOT FEEDBACK FORM

Guideline	
Dates for the period of guideline piloting	
Name	
Affiliation	
Date	
Good points about the guideline	
Points for improvement	
Any other general comments	