

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

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.

large 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.

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Version No.: Draft 1 version 2.0	Date: October 2024

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 • Prevalence and impact of condition or public health problem; • Prevalence of risk factors.	Potential of guidance to add value • Inequalities in access, uptake or impact; • Timeliness; • Equality issues identified by proposers of the topic; • Equality issues identified by patient or lay organisations.	Priority for NHS or other government department • Department of Health or other centralised NHS bodies such as NHS England; • Local authorities; • Home Office; • Other agencies.	Topic relevance; conclusions and outcomes • 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	NA	NA	NA

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
	practice)			
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 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	There are potential issues regarding access to care for those with physical disability given that the guideline has stressed that where possible,	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.

BASHH Guideline Equality Impact Assessment				
(based on NICE documentation shared with BASHH August 2019)				
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	with disability	symptomatic patients should be strongly encouraged to attend a centre that has microscopy available.		
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	NA	NA	The guideline does not stipulate different treatment pathways for those of different sexual orientations

BASHH Guideline Equality Impact Assessment				
(based on NICE documentation shared with BASHH August 2019)				
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	investigations or treatments.			
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 be affected by protected characteristics, including:	Some people in this inclusion health populations may be vulnerable to additional	The guidelines are primarily for those working in level 3 specialist sexual health	Safeguarding concerns should be addressed.	Consideration of patients in these groups being at risk of sexual exploitation/abuse
Prisoners and young offenders;				

BASHH Guideline Equality Impact Assessment				
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• Refugees and asylum seekers; • Migrant workers; • Looked after children; • Homeless people; • Deprivation; • Disadvantage associated with geographical distinctions.	adverse determinants of health including sexual coercion and violence. Departmental safeguarding procedures should be in place to identify and respond to any issues.	services and safeguarding concerns should be addressed by departmental policies. Genitourinary physicians receive level 3 safeguarding training.		should be made as part of Genitourinary Medicine department's safeguarding training.

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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 quality⁷.

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.

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>

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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.

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.

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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	