# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Diagnostics Assessment Programme

# Early value assessment: Point of care tests for urinary tract infections to reduce antimicrobial resistance

## Final scope

December 2022

## *1 Introduction*

The topic selection oversight panel identified point of care tests for urinary tract infections to reduce antimicrobial resistance as potentially suitable for early value assessment (EVA) by the Diagnostics Assessment Programme after clinical experts highlighted system interest in the topic.

The purpose of this early value assessment is to identify evidence that is available on the technologies; assess the potential clinical and cost-effectiveness of the point of care tests for urinary tract infections; and identify evidence gaps to help direct data collection and further research. This evaluation will inform committee recommendations on the conditional use of these technologies in the NHS while further evidence is generated.

The final scope was informed by discussions at the scoping workshop and assessment subgroup meeting held on 28 November 2022. A glossary of terms is provided in appendix A.

## *2 Description of the technologies*

This section describes the properties of the technologies based on information provided to NICE by the companies, clinical experts and on information available in the public domain. NICE has not carried out an independent evaluation of these descriptions.

### 2.1 Purpose of the medical technologies

Urinary tract infections (UTIs) are currently diagnosed using a combination of clinical symptoms, dipstick tests (if appropriate) and laboratory-based tests. Tests that can be done by a healthcare professional outside a laboratory setting (often called point of care tests) that can establish if pathogenic

bacteria are present before antibiotics are prescribed may reduce the use of antibiotics by people that do not need them. Point of care tests that can also perform antibiotic susceptibility testing (AST) may allow for more rapid use of targeted antibiotics than current standard care. These technologies have the potential to reduce antibiotic use and the risk of future antibiotic resistance. Improvements in detecting UTIs and quicker information on antimicrobial susceptibility could also lead to a reduced impact of UTIs on patients, reduced laboratory workloads and associated costs, and reduced healthcare resource use associated with mismanaged UTIs.

Dipstick tests are sometimes used as an initial test, but they may not be accurate, are not recommended for use in certain populations and do not identify the type of pathogen causing an infection. Follow up laboratory tests are used to confirm a UTI diagnosis. Laboratory-based tests, such as microbiological culture and AST, are typically done to find out which (if any) bacteria are present and which antibiotic is most likely to kill them. This process can take 24 to 72 hours depending on geographical location, local available facilities and day of sample collection. In some cases, antibiotics may be delayed until culture and susceptibility results are available. But a suspected UTI is often initially treated with broad spectrum (empiric) antibiotics. Empiric antibiotics may have side effects, can be less effective than targeted antibiotics and increase the risk of antibiotic resistance developing. Prescribing antibiotics to people without a bacterial infection also adds to the risk of antibiotic resistance. Misdiagnosing a UTI or prescribing an ineffective antibiotic can also have a severe impact on a person's physical and mental health and may result in a chronic UTI or in some cases, sepsis.

## 2.2 Potential product properties

This scope focuses on technologies that can be done by a healthcare professional outside of a conventional laboratory setting (a point of care test, as defined by the MHRA's guidance on the management and use of IVD point of care test devices). Public Health England's guidance 'Health matters: antimicrobial resistance' says that there is a need for rapid diagnostic tools to help GPs identify within minutes the strain of bacterial infection present and the antibiotics to which it is resistant or susceptible.

Technologies included in the scope of this assessment may identify if bacteria are present, the type of bacteria present or perform AST.

During scoping, several technologies were identified that while looking to meet criteria for inclusion in this assessment, did not have regulatory approval for use in the UK. Such technologies are included in the scope if the company has indicated that they expect regulatory approval within 12 months but will

only be included in draft or final guidance if they have regulatory approval by the planned draft or final guidance publication date.

### Point of care tests that perform antimicrobial susceptibility testing

#### *2.2.1 Astrego PA-100 analyser and PA-AST panel U-0501 (Sysmex Astrego)*

The Astrego system is a point of care diagnostic test that uses microfluidics to diagnose UTI and provide susceptibility information. The PA-100 analyser is CE-IVDR marked and the PA-AST panel U-0501 is CE-IVDD marked. The company states that the technology identifies the presence of bacteria in a urine sample in less than 30 minutes. If the sample is positive for bacteria, the test automatically performs AST with 5 antibiotics (amoxicillin-clavulanic acid, ciprofloxacin, fosfomycin, nitrofurantoin and trimethoprim). Qualitative results identifying if a pathogen is present and if it is resistant to a particular antibiotic are presented on a built-in touch screen. The company states that the PA-100 system provides full results in a total turnaround time of 30 to 45 minutes.

#### *2.2.2 Flexicult Human (SSI Diagnostica)*

Flexicult Human is a CE-IVD marked point of care culture test that diagnoses UTI and provides susceptibility information. Flexicult uses an agar plate that is divided into 6 compartments. The company says that Flexicult identifies the species and number of bacteria present in a urine sample and assesses the susceptibility of the bacteria against 5 commonly used antibiotics (mecillinam, nitrofurantoin, ampicillin, sulfamethizol and trimethoprim). Flexicult must be incubated overnight at 35 degrees and results are visible within 16 to 24 hours. Results are interpreted by visually assessing the number and type of growths on the Flexicult agar plate.

### Point of care tests without functionality to do antimicrobial susceptibility testing

Technologies that can identify whether bacteria are present in a urine sample, and potentially identify the bacteria, may still require a sample to be sent to a laboratory for AST. But they could improve the accuracy of UTI diagnosis and inform decisions about whether to prescribe antibiotics if used in place of current initial assessments: dipstick testing or no testing (for people for whom dipstick testing should not be done; see section 3.2).

#### *2.2.3 Lodestar DX (Llusern Scientific)*

The Lodestar UTI test consists of an assay panel for 6 UTI causing bacteria (*Escherichia coli, Klebsiella spp, Proteus mirabilis, Staphylococcus saprophyticus, Enterococcus spp, Pseudomonas aeruginosa*) and an

electronic reader designed to interpret assay results. Qualitative results identifying if a urine sample is positive or negative for clinically relevant concentrations of each type of bacteria are shown on an LED display. The company claims that the technology is portable, requires no sample processing and produces results in approximately 40 minutes. The Lodestar UTI test does not currently have regulatory approval, but the company states that this is expected within the next 12 months.

### *2.2.4 TriVerity (Inflammatix)*

TriVerity is a point of care diagnostic test that can be used to inform the presence, type (bacterial or viral) and severity of an infection. The TriVerity test measures the mRNA expression of 29 immune system genes and combines this with a fixed algorithm to predict the likelihood of a bacterial infection. The test needs 2.5ml of whole blood and the benchtop Myrna (Inflammatix) device to be completed. The company states that the test is still in development and final time to results has not been established. But the estimated time to result is 30 minutes. The TriVerity test does not currently have regulatory approval, but the company states that this is expected within the next 12 months.

### *2.2.5 Uriscreen (Savyon Diagnostics Ltd)*

Uriscreen is a CE-IVD marked enzyme-based test that detects the presence of catalase activity, an enzyme that may indicate the presence of bacteria and somatic cells in a urine sample. The test is done by adding a urine sample and hydrogen peroxide solution to a test tube containing Uriscreen reagent powder. Tests are considered positive for bacteria or somatic cells if foam is generated and forms a continuous ring or layer on the surface of the solution. The company states that Uriscreen provides results in 2 minutes.

### *2.2.6 Uricult, Uricult Plus and Uricult Trio (Aidian)*

The Uricult tests are 3 separate CE marked culture-based tests that detect and identify specific UTI causing bacteria in a urine sample. The Uricult test consists of a plastic slide containing 2 types of agar media that is dipped into a urine sample. Cystine-lactose-electrolyte-deficient (CLED) agar determines the total bacterial count and MacConkey agar supports growth of gram-negative bacteria. The Uricult Plus test consists of a plastic slide containing 3 types of agar media. As well as CLED and MacConkey agar media, Uricult Plus has a selective *Enterococcus* medium. The Uricult Trio test also consists of 3 types of agar media, that includes CLED, MacConkey and a selective *Escherichia coli* medium. The Uricult tests must be incubated at 36°C (plus or

minus 2 degrees) and results are visible within 16 to 24 hours. Results are interpreted by visually assessing the growths on the agar slides.

#### *2.2.7 Dipstreak, Chromostreak and Diaslide (Novamed)*

Dipstreak, Chromostreak and Diaslide are CE marked culture-based tests that detect and identify specific UTI causing bacteria in a urine sample. Dipstreak consists of a plastic slide with CLED and MacConkey agar medium and movable plastic prongs attached to the slide. The prongs are dipped into a urine sample and move across the agar media to create a 'streak'. Chromostreak contains MacConkey agar and chromogenic (Uri*Select*) agar for identification of common UTI causing bacteria (for example *Escherichia coli*, *Proteus*, and *enterococci).* Diaslide contains CLED and MacConkey agar and consists of a hinged plastic case with prongs located between the media. Dipstreak must be incubated in a vertical position at 35°C (plus or minus 2 degrees) for 18 to 24 hours. Chromostreak and Diaslide must be incubated in a vertical position at 37 °C (plus or minus 1 degree) for 18 to 24 hours. All 3 tests use the 'streaking' mechanism that the company claims isolates single bacterial colonies on the agar media. Results for all 3 tests are interpreted by visually assessing the growths on the agar slides.

#### *2.2.8 UTRiPLEX (Global Access Diagnostics)*

UTRiPLEX is a diagnostic test strip that uses chromatography to identify matrix metalloproteinase-8 (MMP8) and 4-hydroxynonenal (HNE) in a urine sample. The company states that MMP8 and HNE are biomarkers for inflammation that can be used to aid the diagnosis of a UTI. The UTRiPLEX strip is dipped into a urine sample for 10 seconds and the results can be visually read after 6 minutes. The company states that 1 or 2 lines on the UTRiPLEX strip indicates the presence of a UTI. The UTRiPLEX test does not currently have regulatory approval, but the company states that this is expected within the next 12 months.

# *3 Target conditions*

## 3.1 Urinary tract infections

UTIs are 1 of the most common conditions found in primary care and are defined as an infection of the urethra, bladder, ureters or kidneys. The most commonly identified causative pathogenic bacteria is *Escherichia coli*. NICE's clinical knowledge summary for lower UTI in women says that UTI is more common in women than men, with acute UTI occurring in up to 50% of women in their lifetime. Pujades-Rodriguez et al. (2019) reported that

approximately 83% of recorded lower UTIs in primary care between 2011 and 2015 in England were in women.

UTIs often present with urinary symptoms such as dysuria, new nocturia and cloudy urine and can be categorised as uncomplicated or complicated. Uncomplicated infections can be further classified as cystitis (infection of the lower urinary tract) or pyelonephritis (infection of the upper urinary tract). Clinical experts stated that there are no clinical features or routine investigations that conclusively distinguish an upper UTI (pyelonephritis) from a lower UTI (cystitis). But pain in the abdomen or back, fever and nausea and vomiting are more common in people with pyelonephritis. Children, older people, people who are frail and people with a urinary catheter often present with atypical symptoms which can make UTI diagnosis and treatment more complex. Most infections in adult men are complicated and relate to abnormalities of the urinary tract.

Many UTIs, particularly acute uncomplicated UTIs with no risk factors, resolve within a few days. But UTIs often recur over time and can require several courses of antibiotics to treat them. In some cases, UTIs may not respond to treatment and can become chronic, where a person may experience prolonged periods without remission from symptoms. Recurrent infection in adults is defined as at least 3 UTIs per year or 2 UTIs in the last 6 months (Diagnosis of urinary tract infections, published by Public Health England, 2020). Failure to detect the underlying cause of symptoms and successfully treat UTIs can lead to more serious consequences such as kidney failure and sepsis, as well as adversely affecting a person's quality of life.

UTIs contribute to a large proportion of antibiotic use in primary care. The 'English Surveillance Programme for Antimicrobial Utilisation and Resistance' (ESPAUR) report from 2017 says more than 1 million UTI samples were analysed in NHS laboratories across England in 2016, and that resistance was a "common" observation. One in 3 (34%) of the samples analysed were found to be resistant to an antibiotic called trimethoprim, compared to 29.1% in 2015. The NHS Business Services Authority's RightCare UTI Focus Pack from 2021 reports that 31.4 million antibiotic items were prescribed in primary care in 2019/20, and that 22% (7 million) of these items were for antibiotics commonly prescribed to treat lower UTI. Pujades-Rodriguez et al. (2019) reported that empiric antibiotics were prescribed on the same date of diagnosis for 85.7% of UTIs and only 17% of those who received antibiotics had a recorded urine test within 10 days of suspected diagnosis in England. The authors commented that laboratory culture was done infrequently and there are opportunities to reduce empiric antibiotic use when treating UTI.

## 3.2 Diagnostic and care pathway

### *3.2.1 Diagnostic tests*

#### Dipstick testing

Dipstick tests involve dipping a specially treated paper or plastic strip into a urine sample to identify the likelihood of a UTI. Bacteria in the urinary tract can produce nitrites, and blood or leukocyte esterase (from white blood cells) in the urine can indicate a possible infection. A dipstick test will change colour if these substances are present. A dipstick test can be done during an appointment and results are available within a few minutes.

Dipstick testing is quick, but there are concerns about how accurate it is to detect a UTI. For some groups (for example, adults who are catheterised or over 65) dipstick testing is considered too unreliable for use (described in sections below).

#### Laboratory based testing

Urine samples are sent to microbiology laboratories for pathogen isolation, identification and AST. Techniques based on growing, or culturing, bacteria can take up to 72 hours to produce results. Clinical experts highlighted that this varies widely across the NHS and can influenced by factors like the time-of-day a sample is taken (for example if just missing a sample pick up) and day of the week. They also commented that the exact tests done differs between laboratories. Quicker tests for identification and AST are now available, for example molecular and mass spectrometry-based techniques (see Gajic et al. [2022] and Santos et al. [2022] for reviews).

The European Committee on Antimicrobial Susceptibility Testing (EUCAST) provides guidance on AST which includes definitions of susceptibility testing categories. A microorganism is categorised as ‘resistant’ when there is a high likelihood of therapeutic failure even at increased exposure. Each susceptibility category is defined for an antibiotic by specified breakpoints that are minimum inhibitory concentrations that inhibits growth.

### *3.2.2 Diagnostic care pathway*

Public Health England’s document on the diagnosis of urinary tract infections sets out several flowcharts to guide testing for people with suspected acute UTIs. Full details of testing pathways can be found in this document. Separate pathways are presented for:

- women under 65 years with suspected UTI
- men under 65 years with suspected UTI
- adults who are catheterised or over 65 years with suspected UTI

- infants/children under 16 years with suspected UTI.

The pathways differ in terms of whether an initial dipstick test is done, deciding if a urine sample should be sent for further testing in a laboratory and deciding when or if to prescribe antibiotics.

Adults with suspected pyelonephritis or sepsis should always have a urine sample sent for culture. Antibiotic treatment should be started immediately following NICE's guideline on antimicrobial prescribing for acute pyelonephritis or local and national guidelines for sepsis. Public Health England's document on the diagnosis of urinary tract infections recommends seeking specialist advice on further investigation or management for recurrent UTIs in pregnant women, men over 16, adults with recurrent upper UTI, adults with recurrent lower UTI with an unknown underlying cause and children under 16.

**Women under 65 with suspected UTI**

The Public Health England quick reference tool on the diagnosis of UTIs recommends using dipstick tests to aid diagnosis only if 1 key diagnostic urinary symptom (dysuria, new nocturia or cloudy urine), or other severe urinary symptoms, are present. If 2 or more key symptoms are present, a UTI is likely, and a dipstick test is not recommended. The SIGN guideline for management of suspected bacterial lower urinary tract infection in adult women recommends using dipstick testing to confirm a UTI diagnosis in women under 65 only if 2 or more symptoms are present.

The Public Health England quick reference tool on the diagnosis of UTIs says that urine should be sent for culture if:

- a person has 2 or more key symptoms or a dipstick test indicates UTI is likely (positive for nitrite or leukocyte and red blood cells), and there is risk of antibiotic resistance
- a dipstick test indicates UTI is equally likely as other diagnoses (negative for nitrite and positive for leukocyte)
- there is recurrent UTI
- antibiotic treatment has failed, or a person has persistent symptoms
- the person is pregnant.

If a person is not pregnant and has mild symptoms, healthcare professionals should consider back up (delayed) prescribing. This encourages self-management as a first step but allows the person to access antibiotics without another appointment if their symptoms get worse. If a person has more severe symptoms, immediate empiric antibiotics should be considered.

### Men under 65 with suspected UTI

The Public Health England quick reference tool on the diagnosis of UTIs says that dipstick tests should not be used to rule out infection as they are unreliable for this. To confirm a UTI diagnosis, urine should always be sent for culture, and collected before antibiotics are given. Immediate treatment should be offered, and choice of antibiotic should be reviewed based on pre-treatment culture results.

### Adults who are catheterised or over 65 with suspected UTI

The Public Health England quick reference tool on the diagnosis of UTIs says that dipstick tests should not be performed in adults who are catheterised or over 65 as these groups often have asymptomatic bacteriuria that is not harmful, can give a positive dipstick result and antibiotics are not beneficial and may cause harm. Urine should always be sent for culture and collected before antibiotics are given, if feasible.

If a UTI is considered likely, antibiotics should be offered immediately. Back up antibiotics may be considered in women without catheters and low risk of complications. Choice of antibiotic should be reviewed based on culture results.

### Babies, children and young people under 16 with suspected UTI

NICE's guideline on diagnosis and management of urinary tract infections in under 16s and The Public Health England quick reference tool on the diagnosis of UTIs says that dipstick testing for leukocyte esterase and nitrites can safely be used in children over 3 months and young people under 16. NICE's guideline on diagnosis and management of urinary tract infections in under 16s recommends sending urine samples for culture and antibiotic susceptibility testing if a baby or child:

- is thought to have acute pyelonephritis
- has a high to intermediate risk of serious illness
- has a positive result for leukocyte esterase or nitrite
- has recurrent UTI
- has an infection that does not respond to treatment within 24 to 48 hours, if no sample has already been sent
- has clinical symptoms and signs but dipstick tests do not correlate.

Babies under 3 months with a suspected UTI should be referred to paediatric specialist care, with a urine sample sent for urgent microscopy and culture.

NICE's guideline on diagnosis and management of urinary tract infections in under 16s includes recommendations on when to give antibiotics based on

dipstick test results, which differ for children between 3 months and 3 years, and for those over 3 years. See recommendations 1.1.19 and 1.1.20 for details.

### *3.2.3 Treatment*

NICE's guideline on antimicrobial stewardship includes recommendations for prescribers of antimicrobials, including for patients who have non-severe infections, to consider taking microbiological samples before making a decision about prescribing an antimicrobial, providing it is safe to withhold treatment until the results are available. Clinicians may also offer self-care advice which includes using paracetamol for pain, or if preferred and suitable ibuprofen and drinking enough fluids to avoid dehydration.

Clinical experts explained that when a person presents with UTI symptoms, or a positive urine dipstick test, they are often prescribed antibiotics empirically (for broad-spectrum coverage of the most common pathogenic bacteria) before culture and susceptibility results are available. NICE's guideline on antimicrobial prescribing for lower urinary tract infections recommends reviewing the choice of antibiotic when microbiological results are available and changing the antibiotic according to the susceptibility results if bacteria are resistant and symptoms are not already improving, using a narrow-spectrum antibiotic where possible.

NICE guidelines provide recommendations on which antibiotics to use for people with UTIs. Recommendations can be found in the following guidance:

- NICE's guideline on diagnosing and management of urinary tract infection in under 16s
- NICE's guideline on assessment and initial management of fever in under 5s
- NICE's guideline on antimicrobial prescribing for catheter-associated urinary tract infections
- NICE's guideline on antimicrobial prescribing for recurrent urinary tract infections
- NICE's guideline on antimicrobial prescribing for lower urinary tract infections
- NICE's guideline on antimicrobial prescribing for acute pyelonephritis
- NICE's guideline on antimicrobial prescribing for acute prostatitis

## 3.3 Proposed position of the technology in the testing pathway

The proposed position of the technologies in this assessment is as an initial test for people with a suspected UTI. This may be in place of laboratory-based

testing (with or without a prior dipstick test) for bacterial detection, identification and AST for people with a suspected UTI, or used before any necessary laboratory-based testing. The assessment focuses on the use of the tests in primary or community care settings. Primary care services include GP practices and pharmacies, and community care services include care homes.

Tests that can more accurately identify if bacteria are present in urine before the initial antibiotic prescription decision is made (compared to dipstick tests or no tests) could reduce unnecessary use of antibiotics. This could reduce side effects from unnecessary treatment and reduce the risk of antimicrobial resistance development. Improved detection of people who would benefit from antibiotics would reduce pain from symptoms and the consequences of a worsening condition (such as hospitalisation). Correctly identifying if a person has a UTI will also reduce further unnecessary assessments, use of treatments for a condition they do not have and ongoing uncertainty that would occur if this had been missed. Correctly ruling out a UTI means that further assessment to identify the true cause of symptoms can be done quicker. Quicker identification and AST results (than laboratory-based testing) could improve choice of antibiotic, potentially reducing use of broad-spectrum antibiotics (a large contributor to antimicrobial resistance) and making it more likely treatment will be successful.

The extent to which these point of care tests can improve antibiotic prescribing will likely depend on how quickly results are available and how they can be implemented into clinical decision making in primary and community care settings. For example, in the POETIC study (Butler et al., 2018) of a UTI test (which could take up to 24 hours for results) it was left to clinicians to decide how to use the test result. Suggestions about how to reduce empirical prescribing based on this were to:

- prescribe the following day
- initially prescribe empirically, but review this decision the following day
- provide an initial delayed antibiotic prescription and use the test to guide use of this.

The authors commented that clinicians using the test (including in the UK) generally prescribed initial antibiotics empirically without waiting for the result. Very few stopped antibiotic treatment that had already been started when the test indicated no UTI. Clinical experts commented that empiric antibiotics may still be prescribed if test results are not available on the same day that a person presents to primary care. Clinical experts also noted that few empirical antibiotics are changed once sensitivities are known. This may be because

resistance patterns are generally well known in their area, so the empirical antibiotic selected is proven to be effective, or because the person reports they are improving at follow up therefore a new prescription is considered unnecessary.

### 3.4 Patient issues and preferences

UTIs often cause distress and may have a large impact on a person's daily life. The symptoms of UTI, particularly painful and frequent urination, can severely impact a person's mental wellbeing, ability to perform everyday activities and may lead to people missing work. Adults with recurrent or chronic UTIs may also experience loss of earnings and opportunities for promotion. Children with UTIs, particularly if they are recurrent or chronic, often miss school which may have a negative impact on their education. It may also mean parents or carers have to take time off work to do home schooling. Experts also highlighted the strain on relationships that a long-term UTI can have. Any changes to the extent that people have to drop off urine samples for testing, travel to attend in person appointments, or pick up multiple prescriptions could have social and financial implications for people with UTIs.

Ineffective diagnosis of UTI in primary or community care settings can lead to people receiving inappropriate treatment that may have little impact on, or prolong, their symptoms. There is also often a stigma that is associated with UTIs that may make people less likely to seek help from a healthcare professional, which may also delay treatment. Urine culture and AST can take up to 72 hours which can delay targeted treatment prescription even further. Untreated UTIs can lead to prolonged and more severe health-related complications, as well as severely impacting a person's quality of life.

Empiric antibiotics are often prescribed based on a person's symptoms, or a positive dipstick test. If the results of point of care tests take longer than the length of an average primary care appointment, there may be a delay in starting treatment compared to current practice. It may also impact the time needed to be taken off work or school. This could lead to increased discomfort for people with suspected UTIs, especially those with more severe symptoms. It could also have financial and educational implications.

Improvements in access to testing, for example in terms of when and where tests can be done, could have substantial patient benefits.

# 4 Comparator

The comparators for this assessment are:

- urine dipstick test, potentially followed by laboratory-based testing **or**
- laboratory based testing alone.

The comparator varies depending on whether, in current practice, a person would have a dipstick done as an initial test (see section 3.2.2).

# 5 Scope of the assessment

**Table 3 Scope of the assessment**

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|---|---|
| **Decision question** | • Do point-of-care tests for people with suspected UTIs have the potential to be clinically and cost-effective to the NHS?<br>• What evidence is available to support the value proposition outlined in the scope and where are the evidence gaps? |
| **Populations** | People with suspected UTI who:<br>• would have an initial dipstick test in current practice (population 1)<br>• would not have an initial dipstick test in current practice (population 2)<br><br>The populations exclude people with suspected sepsis.<br><br>Where data permits, the following subgroups may be considered:<br>• People with suspected acute UTI<br>• People with suspected recurrent UTI<br>• People with suspected chronic UTI<br>• Women under 65<br>• Women over 65<br>• Men under 65<br>• Men under 65<br>• Adults with indwelling urinary catheters<br>• Babies, children and young people under 16<br>• Children under 3 months<br>• Pregnant women<br>• People who are frail or have dementia<br>• People who are pre-, peri- or post-menopausal<br>• People on prophylactic antibiotics for treatment of UTI<br>• People of different ethnicities |

| | |
|---|---|
| | • People with a higher risk of complicated UTIs (for example people with neurogenic bladder, diabetes, polycystic kidney disease or people who are immunocompromised)<br>• People with suspected pyelonephritis |
| **Interventions** | Point-of-care UTI tests that perform antibiotic susceptibility testing:<br>• Astrego PA-100 system<br>• Flexicult Human<br><br>Point-of-care UTI tests (without functionality to do antibiotic susceptibility testing):<br>• Lodestar DX, followed by laboratory-based testing if necessary<br>• TriVerity, followed by laboratory-based testing if necessary<br>• Uriscreen, followed by laboratory-based testing if necessary<br>• Uricult, Uricult Plus and Uricult Trio, followed by laboratory-based testing if necessary<br>• Dipstreak, Chromostreak and Diaslide, followed by laboratory-based testing if necessary<br>• UTRiPLEX, followed by laboratory-based testing if necessary |
| **Comparators** | • Dipstick testing, followed by laboratory-based testing (if necessary; population 1) **or**<br>• Laboratory-based testing alone (population 2) |
| **Healthcare setting** | Primary or community care |
| **Outcomes** | Intermediate measures for consideration may include:<br>• Test performance to detect bacteria, identify bacteria, or assess susceptibility to antimicrobials<br>• Test failure rate<br>• Ease of use/acceptability by clinicians<br>• Time to test results<br>• Time to antibiotic prescription<br>• Measures of antibiotic use (for example, use of broad or narrow spectrum antibiotics, based on World Health Organisation AWaRe classification, changes to prescriptions, rate, dose, duration)<br>• Measures of antibiotic resistance<br>• UTI-associated healthcare resource use (for example, GP visits and hospitalisation) |
| | Clinical outcomes for consideration may include: |

| | |
|---|---|
| | • Morbidity (such as recurrence, pyelonephritis, sepsis, adverse effects of antibiotics)<br>• Mortality |
| | Patient-reported outcomes for consideration may include:<br>• Health-related quality of life |
| | Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include:<br>• Costs of the technologies<br>• Costs of staff time to perform and interpret the tests<br>• Costs of staff training<br>• Costs of antibiotics<br>• Costs of other resource use (for example, associated with managing UTIs, for further assessments done to investigate condition, disposing of materials, adverse events or complications, GP appointments, hospitalisation) |
| **Time horizon** | The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. |

# *6 Other issues for consideration*

## 6.1 Diversity in the technologies included

Although included technologies are capable of bacterial detection, identification or AST, there may be differences in the type and concentration of bacteria they can detect, the number of antibiotics tested for susceptibility, the time it takes to produce a result and type of urine sample that can be used. Clinical experts emphasised that it is important that AST assesses response to antibiotics that are currently available to prescribers in the NHS. Clinical experts also highlighted that number of samples that a test can run at once could impact on time to results if multiple people need assessing in the same time period.

## 6.2 Antimicrobial resistance

A major potential impact of point of care diagnostic tests is on antimicrobial resistance. The UK's 5 year national action plan Tackling antimicrobial resistance 2019–2024 includes a target to reduce UK antimicrobial use in humans by 15% by 2024. Technologies that can more accurately diagnose UTIs at the point of care may reduce the number of people receiving antibiotics that do not need them. Technologies that identify bacteria or provide antimicrobial susceptibility results faster than current culture techniques may also reduce the use of empiric antibiotics in clinical practice.

The assessment should strongly consider any potential impact of the test on factors likely to affect antimicrobial resistance, for example use of antibiotics overall and use of broad-spectrum antibiotics.

### 6.3 Sustainability

The NHS has made a commitment to achieve net zero carbon emissions by 2040 for direct emissions and 2045 for indirect emissions. If implemented, new point of care tests may impact the amount of plastic used and waste created in primary or community care settings. Increases in waste production may also increase costs if disposing of materials needs extra equipment or time compared to standard care.

## *7 Potential equality issues*

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Women, pregnant women, older people, and people who are catheterised are more likely to develop a UTI. In adults, people with neurogenic bladder, diabetes, polycystic kidney disease or people who are immunocompromised have a higher risk of complicated UTIs. Comorbidities such as neurogenic bladder, diabetes, and multiple sclerosis are also related to an increased risk of catheter associated UTI. Sex, pregnancy, age and disability are protected characteristics under the Equality Act (2010).

Dipstick tests that can be used to rule out UTIs are not recommended for men, adults older than 65 and adults who are catheterised. Tests that can more accurately rule out a UTI diagnosis for these groups could have a particular benefit in reducing unnecessary use of antibiotics and side effects resulting from these.

Autistic people, people with neurological disorders (for example dementia) and people who are frail may present with atypical symptoms or struggle to communicate their symptoms with healthcare professionals. Tests that can more accurately assess for UTIs may particularly benefit these groups.

People from minority ethnic family backgrounds may experience cultural barriers that may stop them accessing healthcare for UTIs. Non-English speakers may also have trouble communicating their symptoms which may lead to delays in diagnosis and receiving effective treatment. Tests that can more accurately assess for UTIs may particularly benefit these groups.

Tests that are more accurate may reduce the need for people to provide repeat urine samples, which may benefit groups who find this difficult, such as people who are pregnant, older people, people who are incontinent or people with dementia. Any reduction in the need to travel to see a doctor, drop off samples and pick up prescriptions may benefit people with a lower socioeconomic status or people with a disability.

## *8 Potential implementation issues*

Changes may be needed to implement technologies into the current care pathway, in which assessment of symptoms with or without a dipstick test can be done quickly. The practicalities of who conducts the test, where the test is conducted, if there is space, and how results are communicated should be considered. If test results take longer than current GP appointments the practicalities of how and when prescriptions are issued and collected should also be considered. Clinical experts noted that electronic prescribing makes this process easier, but this would still be an additional step with risks that people may be lost to follow up.

Clinical experts commented that if the test takes longer to run than a consultation appointment with a prescriber, testing may need to be done in advance of this appointment so results can inform initial prescribing decisions.

Clinical experts also noted that national guidance may need to be updated if new technologies are adopted to ensure clarity on where they fit in the pathway and the impact on empirical prescribing.

## *9 Authors*

**Amy Barr**

Topic lead

**Emma McCarthy**

Associate technical analyst

**Thomas Walker**

Technical adviser

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## Appendix A Glossary of terms

### Agar plate

A petri dish filled with a thin layer of nutrient gel that is used to grow bacteria in a microbiology laboratory.

### Antibiotic susceptibility testing

A test performed to determine which antibiotics most effectively treat a urinary tract infection.

### Antimicrobial resistance

The loss of effectiveness of any anti-infective medicine, including antiviral, antifungal, antibacterial and antiparasitic medicines.

### Back up (delayed) prescribing

A back-up (delayed) prescription is a prescription (which can be post-dated) given to a patient or carer, with the assumption that it will not be dispensed immediately, but in a few days if symptoms worsen.

### Biomarker

A naturally occurring molecule, gene or characteristics that can be used to identify an infection or disease.

### Complicated UTI

A urinary tract infection with an increased likelihood of complications such as persistent infection, treatment failure and recurrent infection.

### Chromatography

The process of separating a mixture into its different components.

### Cystitis

A urinary tract infection that affects the bladder.

### Dipstick test

A diagnostic test that is dipped into a urine sample and can detect nitrites, leukocytes and red blood cells to inform the likelihood of a urinary tract infection.

### Dysuria

A pain or burning sensation when urinating.

### Empiric antibiotics

Broad spectrum antibiotics given to treat a suspected urinary tract infection.

**Gram negative bacteria**

Bacteria that do not retain the stain that is used in the Gram staining laboratory test used to detect and identify bacteria.

**Microbiological culture**

A method of multiplying bacteria to establish the type and concentration of bacteria in a urine sample. It is typically done in a laboratory.

**Microfluidics**

The technology of devices that process or manipulate very small amounts of fluids.

**mRNA**

A type of single stranded RNA found in cells that carry the genetic information needed to make proteins.

**Nocturia**

Increased urine production during the night.

**Pathogenic bacteria**

Bacteria that can cause a urinary tract infection.

**Pyelonephritis**

A urinary tract infection that affects the kidneys.

**Sepsis**

A potentially life-threatening condition that occurs when the body's response to an infection damages its own tissues.

**Somatic cells**

Any cell in the body, excluding reproductive (germ) cells.

**Uncomplicated UTI**

A urinary tract infection caused by typical pathogens in people with a normal urinary tract and kidney function, and no predisposing co-morbidities.

**Urethra**

The tube that carries urine from the bladder out of the body.

**Ureter**

The tubes that run from the kidney to the bladder.