

Volatile organic compounds for urinary tract infection

Clinical Policy ID: CCP.1504

Recent review date: 12/2025

Next review date: 4/2027

Policy contains: Electronic noses, mass spectroscopy, urinary tract infection, volatile organic compounds.

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Coverage policy

Volatile organic compounds for diagnosing urinary tract infection are considered experimental/investigational and not clinically proven.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Laboratory analyzed Urine culture and sensitivity.
- Urine dipstick test.

Background

There are multiple challenges associated with the diagnosis of urinary tract infections. Current methods such as gas chromatography mass spectroscopy are expensive, require trained personnel, and are time consuming. In addition, hematuria or chronic urinary catheter use for a neurogenic or anatomically impaired bladder can complicate diagnosis (Dospinescu, 2020).

Bacteria are present in the tissues around the urethral opening and often colonize the urine. Because bacteria are more likely to ascend to the female bladder, which has a shorter urethral length, rates of urinary tract infection

are higher among women. Various gram-positive and gram-negative bacteria, most commonly *Escherichia coli*, cause most urinary tract infections. Common infection diagnostic terms include cystitis, hemorrhagic cystitis, pyelonephritis, and catheter-associated urinary tract infection (Flores-Mireles, 2015; Foxman, 2014).

Risk factors for urinary tract infection include female sex; shorter urethra; prior infection; advanced age; recent sexual intercourse; use of a condom, diaphragm, or spermicide; vaginal infection; trauma/manipulation; diabetes; obesity; genetic susceptibility; or anatomic abnormalities. The estimated lifetime risk of urinary tract infection for women, based on self-reported history of diagnosis by a physician, is 60.4%. Recurrence is common. Most complicated infections are attributed to indwelling catheters (Flores-Mireles, 2015; Foxman, 2014).

Antibiotics are the standard treatment for urinary tract infections. Rising rates of antibiotic resistance, combined with high recurrent infection rates, are of concern to clinicians and emphasize the need for therapies and stewardship strategies that are less susceptible to the development of resistance (Flores-Mireles, 2015). Recent surveillance data indicate that at least one in five *Escherichia coli* isolates causing urinary tract infection shows reduced susceptibility to commonly used first-line agents such as ampicillin, co-trimoxazole, and fluoroquinolones, with higher rates reported in many regions (Mouanga-Ndzime, 2024; World Health Organization, 2023). Improved diagnosis may enhance appropriate selection of antibiotics. In clinical practice, urinary tract infection is diagnosed using a combination of symptom assessment, urinalysis, and microbiologic testing. Dipstick testing and automated urinalysis are rapid but have only moderate specificity; contemporary evaluations report sensitivities generally in the range of 80% to 90% and specificities of approximately 40% to 60% when compared with urine culture (Najeeb, 2015; Kristensen, 2025; Moragas, 2025). Urine culture remains the reference standard for pathogen identification and susceptibility testing but typically requires 24 to 72 hours for final results, during which time empiric antibiotics are often prescribed (Dospinescu, 2020). Rapid point of care tests and molecular assays for urinary tract infection pathogens are in development and limited clinical use but have not yet been adopted as standard diagnostic tools in major guidelines.

Volatile organic compounds are carbon-based compounds that can originate from microbial pathogens or from the host response to infection and inflammation, and many have been associated with common urinary tract pathogens. Urinary volatile organic compound profiles and electronic nose technologies are being investigated as potential tools to improve the diagnosis of urinary tract infections, but existing studies are heterogeneous and have not yet established sufficient accuracy or standardization for routine clinical use (Afonso, 2022; Dospinescu, 2020). Volatile organic compounds have also been studied as diagnostic or screening tools for other conditions, particularly several cancers, although none of these applications have become established in clinical practice (Brusselmans, 2018; Catino, 2019; Farraia, 2022; Oakley-Girvan, 2017; Zhou, 2020). Analytical platforms used for volatile organic compound analysis include gas chromatography, proton transfer reaction mass spectrometry, ion mobility spectrometry, selected ion flow tube mass spectrometry, field asymmetric ion mobility spectrometry, gas chromatography with flame ionization detection, and a variety of odor sensor or electronic nose devices (Dospinescu, 2020; Afonso, 2022). In 2001, the U.S. Food and Drug Administration granted 510(k) premarket notification clearance for the Osmetech Microbial Analyser Urinary Tract Infection Detector, a urine screening kit that utilizes electronic nose technology to detect volatile compounds associated with bacteriuria (U.S. Food and Drug Administration, 2001). No subsequent volatile organic compound-based device for the treatment of urinary tract infections has been incorporated into major clinical practice guidelines, and such technologies remain investigational.

Findings

The American Academy of Family Physicians practice guidelines on urinary tract infection for children/infants and adults only mentions urine microscopy and dipstick testing as diagnostic methods (Michels, 2015; Veauthier, 2020). For diagnosing recurrent urinary tract infections and asymptomatic bacteriuria, the American Urological

Association and the Infectious Diseases Society of America recommend urine culture but do not mention volatile organic compound testing (Anger, 2022; Nicolle, 2019).

A systematic review of 25 studies and meta-analysis of ten studies examined the efficacy of portable electronic noses for diagnosis or monitoring various pathologies through analysis of urine samples, including four studies (n = 211) using different electronic nose systems for diagnosis of urinary tract infections. The authors stated the heterogeneity of the diagnostic measurements and findings did not permit conclusions about their use for diagnosing urinary tract infections and called for additional research and standardization of analytical methods (Afonso, 2022).

One review concludes that of the existing models, electronic noses and ion mobility spectrometry systems are still the most suitable candidates in the diagnosis of urinary tract infection, since they are easy to use, portable, relatively low-cost, and have methods which can be automated (Dospinescu, 2020).

A study of 84 urine samples that tested for 85 volatile organic compounds identified five isolates positively associated with *Escherichia coli*-resistant strains, and two with sensitive strains of urinary tract infections. The accuracy of identifying resistant and sensitive strains was 91.1% and 79.5%, respectively (Hewett, 2020).

A study used thermal desorption-gas chromatography-mass spectrometry to 'smell' antibiotic-resistant bacteria in 18 bacterial isolates (*Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*). The isolates were grown with and without the presence of antibiotic. Nine and 22 compounds differed significantly between cephalexin and ciprofloxacin sensitive/resistant isolates, respectively ($P < .05$) (Smart, 2019).

In 2023, we added two guidelines (Anger, 2022; Nicolle, 2019) and one new systematic review (Afonso, 2022) and deleted two older individual studies and two studies that were assessed in the systematic review. No policy changes are warranted.

In 2024, no new relevant literature was found. No policy changes warranted.

In 2025, the background section was updated with some new literature. No policy changes were warranted.

References

On November 3, 2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "volatile organic compounds" (MeSH), "urinary tract infections" ([MeSH], "electronic noses," "Mass spectroscopy," "urinary tract infection," and "volatile organic compounds." We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

12/2021: initial review date and clinical policy effective date: 1/2022

12/2022: Policy references updated.

12/2023: Policy references updated.

12/2024: Policy references updated.

12/2025: Policy references updated.