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Optimal Urine Culture Diagnostic Stewardship Practice—Results from an Expert Modified-Delphi Procedure

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Background. Urine cultures are nonspecific and often lead to misdiagnosis of urinary tract infection and unnecessary antibiotics. Diagnostic stewardship is a set of procedures that modifies test ordering, processing, and reporting in order to optimize diagnosis and downstream treatment. In this study, we aimed to develop expert guidance on best practices for urine culture diagnostic stewardship.

Methods. A RAND-modified Delphi approach with a multidisciplinary expert panel was used to ascertain diagnostic stewardship best practices. Clinical questions to guide recommendations were grouped into three thematic areas (ordering, processing, reporting) in practice settings of emergency department, inpatient, ambulatory, and long-term care. Fifteen experts ranked recommendations on a 9-point Likert scale. Recommendations on which the panel did not reach agreement were discussed during a virtual meeting, then a second round of ranking by email was completed. After secondary review of results and panel discussion, a series of guidance statements was developed.

Results. One hundred and sixty-five questions were reviewed. The panel reaching agreement on 104, leading to 18 overarching guidance statements. The following strategies were recommended to optimize ordering urine cultures: requiring documentation of symptoms, sending alerts to discourage ordering in the absence of symptoms, and cancelling repeat cultures. For urine culture processing, conditional urine cultures and urine white blood cell count as criteria were supported. For urine culture reporting, appropriate practices included nudges to discourage treatment under specific conditions and selective reporting of antibiotics to guide therapy decisions.

Conclusions. These 18 guidance statements can optimize use of urine cultures for better patient outcomes.

Keywords. diagnostic stewardship; expert consensus; modified Delphi; urine cultures; urinary tract infection.

Urinary tract infections (UTIs) affect more than 10 million people annually in the United States and are among the most common infections encountered in both outpatient and inpatient settings [1–5]. Despite being common, appropriate diagnosis and management of UTIs remain challenging. Frequently, patients with positive urine cultures but without urinary symptoms, known as asymptomatic bacteriuria (ASB), are prescribed unnecessary antibiotic therapy [6]. In particular, patients are often started on antibiotics in direct response to results of urine culture. Even in lieu of compelling clinical signs and symptoms of infection, clinicians often feel compelled to prescribe antibiotics when urine cultures are positive [7–9]. This occurs across all patient care settings, from the emergency department to long-term care [10–12]. Additionally, antibiotics prescribed for UTIs are often suboptimal with respect to agent or duration [13]. Antimicrobial stewardship teams generally perform retrospective review of antibiotics after a diagnosis has been made, which limits their impact on prescribing practices and overall antimicrobial use.

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Diagnostic stewardship aims to improve patient outcomes by optimizing the ordering, processing, and reporting of diagnostic tests, which can work synergistically with, and often upstream of, antimicrobial stewardship efforts [14, 15]. The best practices for diagnostic stewardship have not been defined for the management of UTIs. We used a RAND-modified Delphi approach to develop expert agreed-upon criteria on the appropriateness of diagnostic stewardship interventions for the diagnosis and management of UTIs.

METHODS

We used a modified Delphi approach associated with the RAND/UCLA Appropriateness Methodology (Figure 1) [16]. The RAND/UCLA Method assists in assessment of expert opinion when clinical trial data are insufficient to draw strong, evidence-based conclusions. A modified version of the RAND/UCLA Appropriateness Method was used to assess the appropriateness of predefined intervention strategies; in this case, strategies related to the diagnosis and management of suspected UTIs in adult patients. We excluded patients who were pregnant, had a history of renal transplantation, or were severely immunocompromised. Expert panel members reviewed strategies and weighed the relative probability of clinical benefit vs clinical harm based on available literature in order to determine areas of agreement vs disagreement or uncertainty. The VA Central Institutional Review Board reviewed this study and determined it to be exempt from review as nonhuman subjects research.

Literature Review and Development of Thematic Areas

The main thematic areas of urine culture ordering, processing, and reporting were developed by the Steering Committee (K. C. C., D. J. M., S. L., and B. W. T.) based on previously defined diagnostic stewardship intervention phases [14, 15, 17]. A literature review was performed to identify studies noted as "diagnostic stewardship" interventions or interventions to improve the use of urine cultures and subsequent diagnosis and management of UTIs. Electronic databases including PubMed, Cochrane Database, and Google Scholar were reviewed for English-language articles from 2000 to 2020. Articles described interventions related to the diagnosis and treatment of suspected UTIs in adult patient populations. A final list of clinical questions to guide the development of the survey questions was based on this review of published evidence, adjudicated, and combined with the Steering Committee's expert opinion (Supplementary Table 1). A summary of the included available literature and all articles were provided to the expert panel. Of note, the thematic areas did not focus on stewardship of urinalysis outside of its association with urine culturing, for example, optimal use of screening urinalysis.

Selection of Expert Panel

An interdisciplinary group of 15 clinicians who specialize in healthcare epidemiology and quality improvement, infectious diseases, clinical microbiology, antimicrobial stewardship, and urology were invited to participate. These 15 experts were drawn from a variety of geographically diverse practice settings, including ambulatory care, acute care, emergency medicine, and long-term care. Participants were chosen based on expertise in management of UTIs, diagnostic stewardship, clinical microbiology, and infection prevention (Supplementary Table 2). Participation was voluntary, and no financial compensation was provided.

Delphi Process

The final survey was composed of 165 questions, grouped into the 3 thematic areas of urine culture ordering, processing, and reporting (Supplementary Materials 2). Given the diversity of

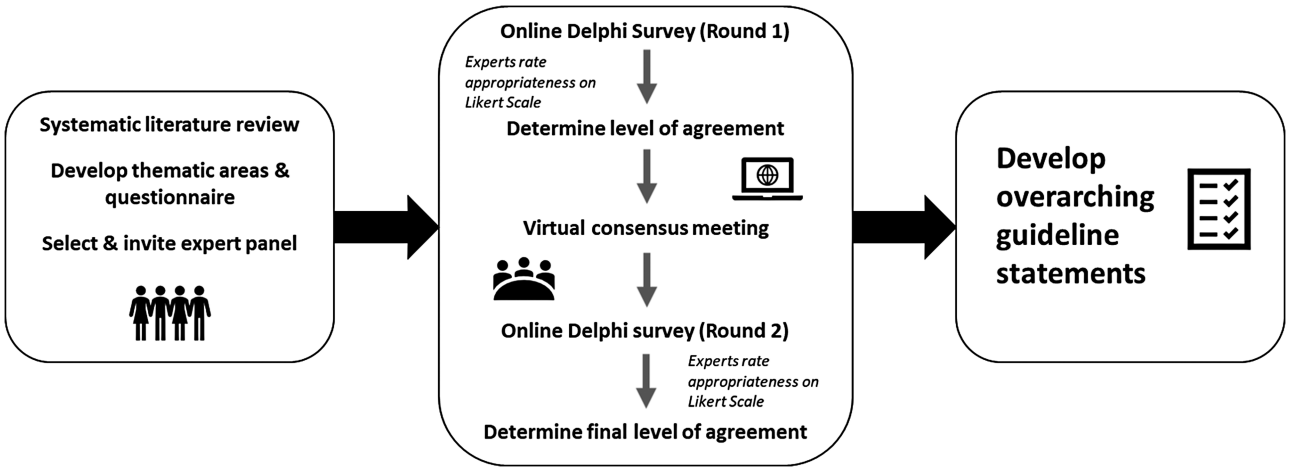

Figure 1. Key steps in the modified Delphi RAND/UCLA appropriateness method, including initial literature review and panel selection, survey distribution and initial meeting, and final agreement determination.

practitioners and practice environments involved in the management of suspected UTIs, the same questions were asked in reference to 4 care settings (ambulatory, emergency department, inpatient, and long-term care). These questions were shared with the panel via an online REDCap survey [18]. The expert panel ranked the appropriateness of diagnostic stewardship interventions on a Likert scale from 1 (highly inappropriate) to 9 (highly appropriate), with 5 denoting neutral. To summarize the results, expert panel rankings were first computed to medians for each question. If medians were between whole values (eg, 3.5), the value was rounded up to the nearest whole. The medians were further grouped into 3-point regions: 1–3, inappropriate; 4–6, neutral or uncertain; and 7–9, appropriate. Agreement was then defined as <4 respondents ranking outside of the majority 3-point region [16].

The survey was distributed electronically to the expert panel members and completed between 18 February 2021 and 13 April 2021. The Steering Committee reviewed the results of the first round to determine areas of agreement, as defined above. Items that did not meet agreement were open for discussion during the expert panel meeting, which was held on 13 April 2021. During this meeting, steering committee members shared the results of the first round and facilitated discussion among experts to clarify questions and gain further agreement. Participants on the expert panel were then allowed to reevaluate those questions and alter their ratings based on the meeting through email follow-up. Questions agreed on by the expert panel were used to form diagnostic stewardship recommendations, which then formed the overall final guidance statements.

RESULTS

All 15 experts participated in round 1; 73 (44.2%) of the 165 questions met criteria for agreement. During a 3-hour expert panel meeting on 13 April 2021, the 92 questions that did not reach agreement were further discussed; 30 questions were reworded for clarity and 4 were removed. A second round of surveys was distributed by email; all members completed the second round; and an additional 31 questions were agreed to. The questions that were agreed to be appropriate or inappropriate were condensed to remove redundancy (ie, removing practice setting if agreement was reached across all settings) into final guidance statements and approved by all participating members of the Steering Committee and expert panel.

Urine Culture Ordering

Of the 165 survey questions, 60 were relevant to urine culture ordering considered by the expert panel. Forty (66.7%) reached agreement; 28 were deemed appropriate and 12 were deemed inappropriate. These resulted in 6 guidance statements (Table 1).

There was agreement to require documentation of signs and symptoms of infection in order to order a culture, which applied to all healthcare settings. There was, however, uncertainty regarding which signs and symptoms were sufficient documentation, particularly whether documentation of fever or systemic leukocytosis with no known cause would qualify (Figure 2). Additionally, the symptoms that were appropriate differed based on the presence of urinary catheterization. There was widespread support for removing urine cultures from most standard clinical order sets, except for inpatients in septic shock. Advising clinicians not to order cultures for absence of symptoms and symptoms of UTI and not allowing repeat cultures within 5 days of a positive culture among inpatients and long-term care residents were also appropriate. Experts also agreed that it was appropriate to replace stand-alone urine culture orders with conditional urine culture orders that would be processed by the laboratory only if a urinalysis performed on the same sample yielded

Table 1. Ordering Urine Cultures: Best Practices for Diagnostic Stewardship of Urine Culture Ordering Included These Recommendations

Appropriate practices
• Require documentation of signs or symptoms of UTI to obtain a urine culture, which includes dysuria or flank pain
• Replace stand-alone urine culture orders with conditional reflex urine cultures[a,b]
• Implement best practice alerts to discourage ordering urine cultures in the absence of signs or symptoms of UTI[a]
• Automatically cancel repeat urine cultures within 5 days of a positive culture (during the same hospital admission and 7 days for long-term care residents)
Inappropriate practices
• Include urine cultures in standard order sets for:
○ Emergency department evaluation
○ Hospital admission
○ Inpatient pre-op
○ Assessment of altered mental status
○ Assessment of falls in long-term care
• Order urine cultures in response to change in urine characteristics

Guidance is for all healthcare settings unless noted specifically. Conditional reflex urine cultures are defined as cultures, although ordered by the clinician, that are only performed after specific criteria are met on urinalysis (ie, white blood cells >10 per high-power field).

Abbreviation: UTI, urinary tract infection.

[a]Except for patients undergoing urological procedures.

[b]Disagreement around use of urinary catheters and the emergency room setting.

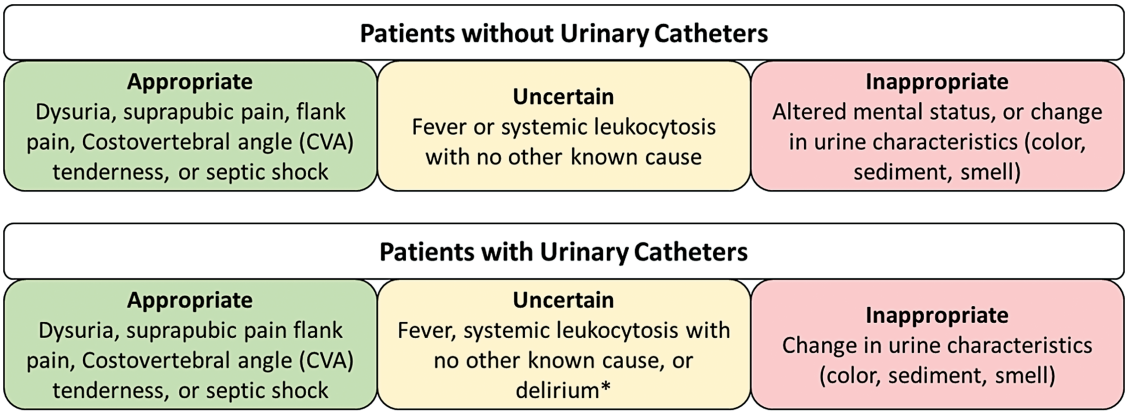

Figure 2. Appropriate urinary tract infection signs and symptoms to document when ordering urine cultures for patients with and without urinary catheters. *Delirium as defined by validated tool such as the Confusion Assessment Method [19]. Urinary catheter broadly defined to include both internal and external catheter use.

abnormal results. Note, this differs from ordering a urinalysis that would automatically reflex to performing a urine culture without a separate request for a urine culture. It was noted that stand-alone urine cultures should still be available for specialized services such as urology or obstetrics. The panel noted that changes in how cultures can be ordered can reduce the volume of testing and have a substantial positive impact on laboratory workflow [20]. From the patient and provider perspectives, decreased urine culturing can result in fewer inappropriate diagnoses of UTI and unnecessary antibiotic exposures.

Urine Culture Processing

Of the 165 survey questions, 33 relevant to urine culture processing were considered by the expert panel. Fourteen (42.4%) reached agreement; 8 were deemed appropriate, 5 were deemed inappropriate, and 1 was uncertain. These resulted in 3 guidance statements (Table 2).

Replacing stand-alone urine culture orders with conditional reflex urine cultures (urine cultures performed only after specific urinalysis criteria are met) was deemed appropriate. The counterpart to this, automatically ordering urine cultures based on abnormal results of routine urinalysis when urine culture was not specifically ordered by the clinician, was deemed highly inappropriate. After 2 rounds of surveys, there remained significant uncertainty and disagreement surrounding appropriate urinalysis criteria to reflex to culture. Overall, there was disagreement on the appropriateness of using either urine leukocyte esterase or urine nitrate as criteria; only urine white blood cell (WBC) count was agreed on as appropriate. Based on currently available evidence, there was uncertainty regarding the optimal urine WBC cutoff value. All agreed a urinalysis WBC count of ≥10 was appropriate, but some experts believed higher levels were better up to >50. Likewise, there was discussion around whether WBC cutoff should differ in patients with and without urinary catheters.

Urine Culture Reporting

Of the 165 survey questions, there were 68 relevant to urine culture reporting considered by the expert panel. Fifty (73.5%) reached agreement; 42 were deemed appropriate and 8 were deemed inappropriate. These resulted in 9 guidance statements (Table 3).

There was agreement regarding the practice of using report nudges or framing, which are behavioral interventions to guide decision-making through choice architecture by highlighting positive or negative aspects of decisions [21]. These behavioral interventions were favored by the panel as they retain provider autonomy. The panel felt that urine culture reports should include language to discourage clinicians from treating ASB. On the other hand, the panel recommended against altering reporting to advise treatment based on quantitative data from the urine culture (ie, >100 000 colony-forming units [CFU]/mL) to deemphasize colony count as a critical component of

Table 2. Processing Urine Culture: Best Practices for Diagnostic Stewardship of Urine Culture Processing Included These Recommendations

Appropriate practices
• Use elevated urine white blood cell count as a criterion to reflex to urine culture when a clinician orders a urine culture (all settings)
• Require documentation of collection site method (eg, clean catch) prior to processing urine cultures
Inappropriate practice
• Automatically reflex routine urinalyses to urine cultures for abnormal findings when a urine culture was not specifically requested by the ordering clinician

Guidance is for all healthcare settings unless noted specifically. These recommendations apply to symptomatic patients only. Patients who do not have symptoms of urinary tract infection should not be cultured.

Table 3. Reporting Urine Culture: Best Practices for Diagnostic Stewardship of Urine Culture Reporting Included These Recommendations

Appropriate practices
• For urine culture reports, to:
○ Inform clinicians that even high colony counts (ie, >100 000 CFU/mL) may not represent true infection in the absence of symptoms or signs[a]
○ Nudge clinicians to not treat asymptomatic bacteriuria[a]
○ Nudge clinicians to not treat mixed flora[a]
○ Differentiate typical uropathogens vs contaminants[a]
• Withhold urine culture results (including organism identification and antibiotic susceptibilities) when there are more than 2 unique bacterial strains identified in culture
• Preferentially report only Infectious Disease Society of America–recommended antibiotics if organism is susceptible
• Withhold fluoroquinolone susceptibilities unless there is resistance to preferred oral antibiotics
Inappropriate practices
• Nudge clinicians to not treat if there are <100 000 CFU/mL of bacteria
• Withhold information about urine culture organism identification or antibiotic susceptibilities unless the clinician contacts the clinical microbiology laboratory

Guidance is for all healthcare settings unless noted specifically. These recommendations apply to symptomatic patients only. Avoid unnecessary urine culturing in patients who do not have symptoms of true urinary tract infection.

Abbreviation: CFU, colony forming units/mL..

[a]Due to expert disagreement, this recommendation does not extend to those undergoing a urological procedure.

UTI diagnosis and instead to shift the focus toward clinical symptoms. Selective or cascade reporting was appropriate in terms of the suppression of fluoroquinolones and preferential reporting of Infectious Diseases Society of America (IDSA)–recommended agents. Withholding all urine culture results was deemed inappropriate because of potential logistical limitations and provider satisfaction as opposed to concerns regarding patient safety.

DISCUSSION

Using a rigorous RAND-modified Delphi approach with a diverse expert panel, we identified the best practices for diagnostic stewardship for urine culturing. These included requiring the presence and documentation of signs or symptoms of UTI, including dysuria or flank pain, when ordering urine cultures. Replacing stand-alone urine culture with reflex urine culture was deemed appropriate as was requiring documentation of collection method. Appropriate methods to report urine culture results included informing clinicians that positive results alone do not indicate UTI and to not treat mixed flora. Selective or cascade reporting of antibiotic susceptibilities, prioritizing IDSA-recommended agents, and suppressing fluoroquinolone antibiotics were also supported.

Including urine culture orders in standard clinical order sets was considered inappropriate as was ordering urine cultures in response to a change in urine characteristics (ie, smell or color). Automatically reflexing all abnormal urinalysis to urine culture without a specific order for culture was deemed highly inappropriate. Suppressing urine culture results without a request from a clinician was considered inappropriate by the expert panel.

A crucial consideration for expert discussion in all 3 thematic areas was clinician understanding of the pretest probability of having a UTI. It is known that clinicians generally overestimate the probability of disease prior to ordering a test [22]. Although a diagnosis of UTI can and should be based on clinical symptoms, practically, UTIs are often erroneously diagnosed based on a positive urine culture alone [23, 24]. Urine culture results must always be considered within the clinical context of patient symptoms and risk. Diagnostic stewardship can be helpful in reducing some, but not all, errors of clinical probability in diagnosing UTI.

Experts agreed that ordering urine cultures without consideration of the signs and symptoms of UTI leads to excessive culturing that misdiagnoses patients with ASB, triggering unnecessary antibiotics. This happens across all healthcare settings [25–29]. There was agreement that for symptoms such as dysuria it is appropriate to require ordering of cultures. Other symptoms, such as fever or systemic leukocytosis, were more controversial. Fever or systemic leukocytosis are often present in patients who are catheterized, critically ill, or otherwise not able to reliably report symptoms directly related to the urinary tract. Among catheterized patients in the intensive care unit, positive urine cultures are rarely the cause of fever or systemic leukocytosis but can drive inappropriate treatment of ASB [29–31]. Because the extent of the association of these systemic symptoms with true UTI, especially across patient populations and practice settings, remains poorly defined, the panel could not reach agreement regarding the appropriateness or inappropriateness of these symptoms as being sufficient for urine culture ordering.

Experts supported replacing stand-alone urine cultures with conditional urine reflex cultures. This support was based on studies across patient populations that demonstrated a decrease in inappropriate urine cultures after implementation [32–40]. Conditional urine reflex culturing cannot completely correct for inappropriate diagnosis of UTI and must be combined with other efforts. The panel noted that it was important to differentiate conditional urine reflex cultures from the practice of automatically ordering cultures on any urinalysis that shows abnormalities, a process that leads to excessive testing

[41–45]. There are numerous clinical indications for urinalysis that do not involve an infectious process. Urinalysis that is automatically linked to urine cultures can lead to indiscriminate culturing and treatment of UTI without consideration of symptoms or probability of infection [23, 46–48]. The additive effect of these efforts remains to be thoroughly investigated.

Uncertainty remained among the experts on which criteria from urinalysis are optimal for reflex to culture [49–51]. Pyuria is common in many patient populations, even without UTI; however, its absence has a strong negative predictive value [20, 52]. The absence of pyuria is an evidence-based criterion for cancelling an unnecessary urine culture. The exact urine WBC cutoff for reflexing urinalysis to urine culture was debated because currently used values are not based on strong clinical evidence [43, 53]. Thresholds for the minimum urine WBC cutoff have included >5 to >50 WBC per high-power field (HPF) [43, 50, 53]. A cutoff of >5 WBC per HPF has a high negative predictive value but can also lead to excessive testing [9, 20, 51]. A 1985 cohort study proposed the minimum cutoff of >10 WBC in ambulatory women [54]. This has become the most frequently used cutoff; as such, a minimum of 10 WBC per HPF was the lowest recommended number by the expert panel [17, 55]. Additionally, the optimal WBC cutoff value may be different in different patient populations [53, 56]. Future research should focus on the optimal criteria for conditional urine reflex cultures in different patient populations.

The expert panel agreed that tailoring reports of urine culture results is a common and appropriate practice [57]. Use of nudges was an appropriate diagnostic stewardship intervention that decreases unnecessary treatment after culturing has already been performed [58–60]. The expert group did not, however, support focusing on the microbiological cutoff of 100 000 CFUs, as this value could lead to nontreatment of symptomatic patients below this value and inappropriate treatment of asymptomatic patients above this value. The consideration of 100 000 CFUs as clinically important has dated back to the 1950s. However, studies since then have demonstrated that an overreliance on this laboratory value leads to excessive antimicrobial use [61, 62].

The role of selective reporting of antibiotic susceptibilities was seen as a common strategy to steer providers from unnecessarily broad therapy [63–68]. The panel agreed that, when feasible, prioritizing preferential agents while suppressing potentially harmful ones (ie, fluoroquinolones) was appropriate. However, evidence for the benefit of these strategies across all settings is still needed. For example, the need for frequent empiric prescribing in the emergency department and reliance on contract laboratories for certain ambulatory or long-term care sites may limit feasibility or benefit of this intervention in those areas. Last, the panel agreed that suppression of all culture results unless the provider specifically called to request them would be impractical and impede workflow for both providers and the laboratory [69]. It was also mentioned that this practice was likely infeasible with contract laboratories.

This research has several notable strengths. The clinical thematic areas and questions of interest were developed through an extensive literature review combined with the Steering Committee's collective expertise. The use of a RAND-modified Delphi method allowed for a systematic and iterative approach to determining best practices for urine culture diagnostic stewardship. Additionally, this method allows experts to clarify areas of clinical disagreement or uncertainty. Practices where clinical agreement is lacking can be the focus of future research to further advance diagnostic stewardship. There are also several limitations. Determining agreement, although providing guidance when high-quality data are lacking, on the strength of expert opinion. Also, several potential interventions were not reviewed, such as those focused solely on urinalysis or best practices for proper urine collection and transportation, as these were beyond the scope of the current work or have been addressed previously [70].

Based on a RAND-modified Delphi approach, 18 statements were developed to guide diagnostic stewardship best practices for urine culture ordering, processing, and reporting. While guidelines for diagnosis and management of UTIs and ASB are available, they address when individual clinicians should order diagnostic tests; they do not orient on how to best implement these tests within different healthcare settings. Urine cultures are widely used, but their limitations as a diagnostic test are not fully understood by all. Diagnostic stewardship provides a mechanism to improve care with the goal of the right test for the right patient, prompting the right action. There was a high level of agreement on appropriateness and feasibility for many diagnostic stewardship interventions across three thematic areas. Despite this, application of these strategies remains limited. Next steps should focus on implementation of these interventions. Diagnostic stewardship is, however, new, and experts were unable to reach agreement in several areas, underscoring the importance of continued focused research on this topic. These recommendations are the first expert-based guidance to formally examine these interventions with the aim of standardizing diagnostic stewardship practices to improve testing and treatment of UTIs. These recommendations can optimize use of this nonspecific test for better patient outcomes.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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