Effectiveness of Preanalytic Practices on Contamination and Diagnostic Accuracy of Urine Cultures: a Laboratory Medicine Best Practices Systematic Review and Meta-analysis

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SUMMARY

Background. Urinary tract infection (UTI) in the United States is the most common bacterial infection, and urine cultures often make up the largest portion of workload for a hospital-based microbiology laboratory. Appropriately managing the factors affecting the preanalytic phase of urine culture contributes significantly to the generation of meaningful culture results that ultimately affect patient diagnosis and management. Urine culture contamination can be reduced with proper techniques for urine collection, preservation, storage, and transport, the major factors affecting the preanalytic phase of urine culture.

Objectives. The purposes of this review were to identify and evaluate preanalytic practices associated with urine specimens and to assess their impact on the accuracy of urine culture microbiology. Specific practices included collection methods for men, women, and children; preservation of urine samples in boric acid solutions; and the effect of refrigeration on stored urine. Practice efficacy and effectiveness were measured by two parameters: reduction of urine culture contamination and increased accuracy of patient diagnosis. The CDC Laboratory Medicine Best Practices (LMBP) initiative's systematic review method for assessment of quality improvement (QI) practices was employed. Results were then translated into evidence-based practice guidelines.

Search strategy. A search of three electronic bibliographic databases (PubMed, SCOPUS, and CINAHL), as well as hand searching of bibliographies from relevant information sources, for English-language articles published between 1965 and 2014 was conducted.

Selection criteria. The search contained the following medical subject headings and key text words: urinary tract infections, UTI, urine/analysis, urine/microbiology, urinalysis, specimen handling, preservation, biological, preservation, boric acid, boric acid/borate, refrigeration, storage, time factors, transportation, transport time, time delay, time factor, timing, urine specimen collection, catheters, indwelling, urinary reservoirs, continent, urinary catheterization, intermittent urethral catheterization, clean voided, midstream, Foley, suprapubic, bacteriological techniques, and microbiological techniques.

Main results. Both boric acid and refrigeration adequately preserved urine specimens prior to their processing for up to 24 h. Urine held at room temperature for more than 4 h showed overgrowth of both clinically significant and contaminating microorganisms. The overall strength of this body of evidence, however, was rated as low. For urine specimens collected from women, there was no difference in rates of contamination for midstream urine specimens collected with or without cleansing. The overall strength of this evidence was rated as high. The levels of diagnostic accuracy of midstream urine collection with or without cleansing were similar, although the overall strength of this evidence was rated as low. For urine specimens collected from men, there was a reduction in contamination in favor of midstream clean-catch over first-void specimen collection. The strength of this evidence was rated as high. Only one study compared midstream collection with cleansing to midstream collection without cleansing. Results showed no difference in contamination between the two methods of collection. However, imprecision was due largely to the small event size. The diagnostic accuracy of midstream urine collection from men compared to straight catheterization or suprapubic aspiration was high. However, the overall strength of this body of evidence was rated as low. For urine specimens collected from children and infants, the evidence comparing contamination rates for midstream urine collection with cleansing, midstream collection without cleansing, sterile urine bag collection, and diaper collection pointed to larger reductions in the odds of contamination in favor of midstream collection with cleansing over the other methods of collection. This body of evidence was rated as high. The accuracy of diagnosis of urinary tract infection from midstream clean-catch urine specimens, sterile urine bag specimens, or diaper specimens compared to straight catheterization or suprapubic aspiration was varied.

Authors' conclusions. No recommendation for or against is made for delayed processing of urine stored at room temperature, refrigerated, or preserved in boric acid. This does not preclude the use of refrigeration or chemical preservatives in clinical practice. It does indicate, however, that more systematic studies evaluating the utility of these measures are needed. If noninvasive collection is being considered for women, midstream collection with cleansing is recommended, but no recommendation for or against is made for midstream collection without cleansing. If noninvasive collection is being considered for men, midstream collection with cleansing is recommended and collection of first-void urine is not recommended. No recommendation for or against is made for collection of midstream urine without cleansing. If noninvasive collection is being considered for children, midstream collection with cleansing is recommended and collection in sterile urine bags, from diapers, or midstream without cleansing is not recommended. Whether midstream collection with cleansing can be routinely used in place of catheterization or suprapubic aspiration is unclear. The data suggest that midstream collection with cleansing is accurate for the diagnosis of urinary tract infections in infants and children and has higher average accuracy than sterile urine bag collection (data for diaper collection were lacking); however, the overall strength of evidence was low, as multivariate modeling could not be performed, and thus no recommendation for or against can be made.

INTRODUCTION

The most common infection occurring in the United States is urinary tract infection (UTI), accounting for nearly 7 million office visits, 1 million emergency room visits, and 100,000 hospitalizations per year (1, 2). Significantly more women than men are likely to experience UTIs, with 1 in 3 women having at least 1 episode of UTI necessitating treatment with antibiotics by the age of 24 (3). Nearly half of all women will experience at least one UTI during their lifetime (3–6). An increased risk of UTI occurs in certain population subgroups, including infants (7), pregnant women (8), the elderly (9), patients with spinal cord injuries and/or catheters (10), patients with diabetes (11) or multiple sclerosis (12), and patients with AIDS/human immunodeficiency virus (13, 14). The most common nosocomial infection is catheter-associated UTI, with over a million cases in hospital and nursing home patients every year (15). Increasing duration of catheterization increases the risk of infection (16). Urinary tract infections are the second-most-common infection in noninstitutionalized elderly populations and account for nearly 25% of all infections (9). The financial impact of UTIs is significant, with costs of up to $2 billion per year (17).

While many uncomplicated UTIs in outpatients are diagnosed clinically, the diagnosis of recurrent or complicated UTI is commonly achieved by testing urine specimens for the presence of microorganisms. As a result, urine cultures often make up the largest portion of the workloads of clinical microbiology laboratories (18). The appropriate management of components of the preanalytic phase of urine culture, namely, collection, preservation, and storage of urine specimens, has an important influence

on the generation of meaningful culture results, which ultimately affects patient diagnosis and management (19).

Quality Gap: Factors Associated with the Preanalytic Phase of Urine Culture

The major goal of proper specimen management is to ensure that specimen quality is maintained during collection and transport (20). Urine specimens can easily become contaminated with periurethral, epidermal, perianal, and vaginal flora. This contamination can be reduced with proper attention to techniques for urine collection, transport, preservation, and storage, the major components of the preanalytic phase of urine culture. A Q-Probe study conducted by the College of American Pathologists in 1998 (21) and again in 2008 (22) examined the frequency of urine culture contamination (defined as more than two isolates in quantities greater than 10,000 CFU/ml) and associated facility practices of urine collection and specimen management. Contamination rates of 41.7% (low-performance facilities), 15% (median performers), and 0.8% (high performers) correspond to the 10th, 50th, and 90th percentiles of facilities, respectively (22). Contamination rates had no correlation to collection site, use of collection kits, preservatives, or thermally insulated transport containers. However, contamination rates were substantially affected by postcollection processing, especially refrigeration of the specimen. Also, collection instructions given in the outpatient setting had a statistically significant impact on contamination rates in some cases. Based on the similarities of overall contamination rates between the two Q-Probe studies, the authors concluded that no significant progress in reducing urine culture contamination during the intervening years had been made (22). This may be a reflection of the inherent limitations of the Q-Probe methodology, which is based on one-time quality assessments dependent on the gathering of current data from large numbers of laboratories in order to establish provisional benchmarks for systematic quality improvement efforts. Many of these indicators are based primarily on self-reported surveys rather than on evidence-based scientific study designs and/or adequately specified, standardized, and consistently implemented data collection methods. Nonetheless, it is not cost-effective for laboratories to continue to waste valuable resources on the work-up of contaminated urine cultures (23). Furthermore, inappropriate reporting of contaminated urine cultures by the laboratory can result in patients receiving suboptimal or unnecessary therapy, producing poor patient outcomes and higher cost (18).

To address this important quality gap and its consequences, this research identified and evaluated practices associated with the collection, preservation, and storage of urine specimens for culture and their impact on the accuracy of urine culture microbiology. Rating criteria were used for evaluating these practices. Specific practices examined included collection methods for men, women, children, and infants; preservation of urine samples in boric acid solutions; and the effect of refrigeration on urine storage. The evidence supporting these practices for minimizing contaminated urine cultures and the impact on the accuracy of patient diagnosis were evaluated by applying the LMBP initiative's systematic review methods for quality improvement practices and by translating the results into evidence-based guidance (24). The methodology has recently been used to evaluate preanalytical practices for reducing blood culture contamination (25) and blood sample hemolysis (26).

A-6 CYCLE FOR SYSTEMATIC REVIEW

The CDC's LMBP "A-6 Cycle" systematic review methods for evaluating quality improvement practices was used for conducting this review. The methodology, reported in detail elsewhere (24), is derived from previously validated methods. It is designed to assess the results of studies of practice effectiveness that lead to best-practice recommendations that are evidence based. Using this method, a review coordinator (author Mark T. LaRocco) and individuals trained to apply the LMBP methods (authors Alice S. Weissfeld and Elizabeth K. Leibach) conducted the systematic review with guidance from an expert panel. The expert panelists (authors Nancy E. Cornish, Colleen S. Kraft, Vickie Baselski, Robert L. Sautter, Edward J. Peterson, and Debra Rodahl) were chosen based on their breath of experience and perspective in clinical microbiology and laboratory management. A description of their scientific credentials and professional affiliations can be found in the author biography section. Lastly, the team was supported by a statistician with expertise in evidence review methodologies and meta-analysis (author Jacob Franek). The expert panel reviewed the results of the evidence review and drafted the evidence-based best-practice recommendations. The recommendations were then approved by the LMBP Workgroup, consisting of 13 invited members with broad expertise in laboratory medicine, clinical practice, health services research, and health policy, as well as one *ex officio* representative from the Centers for Medicare and Medicaid Services. A list of the members of the LMBP Workgroup is provided in Appendix 1.

Review Question, Analytical Framework, and Search Strategy

The review question addressed by this analytical review was as follows: "Are there preanalytic practices related to the collection, preservation, transport, and storage of urine for microbiological culture that improve the diagnosis and management of patients with urinary tract infection?" Components of the preanalytic phase of urine culture were studied in the context of an analytical framework for factors affecting specimen contamination and diagnostic accuracy, depicted in Fig. 1. The population, intervention, comparison, and outcome (PICO) elements are as follows.

- "Population" is any patients who have urine cultures collected.
- "Intervention" is clinical practice.
- "Comparison" is made of
  ○ immediate versus delayed processing of urine held at room temperature,
  ○ immediate versus delayed processing of refrigerated urine or urine preserved in boric acid,
  ○ midstream clean-catch collection of urine without cleansing versus with cleansing (men and women),
  ○ midstream clean-catch collection of urine without cleansing versus with cleansing versus collection with a sterile urine bag versus diaper collection for infants and children.
- "Outcomes" are the results of determining the contamination rate and the diagnostic accuracy of urine culture.
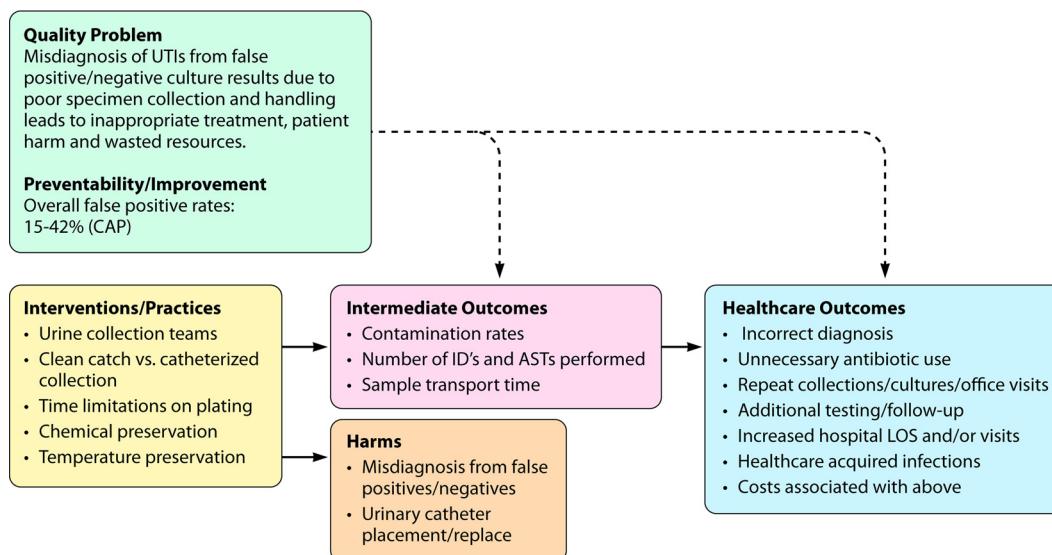
FIG 1 LMBP QI review question and analytic framework. Are there preanalytic practices related to the collection, storage, preservation, and transport of urine for microbiological culture that improve the diagnosis and management of patients with urinary tract infection? CAP, College of American Pathologists; ID's, identifications; ASTs, antimicrobial sensitivity tests; LOS, length of stay.

Specific practices involving the preanalytic phase of urine culture covered in this evidence-based review were addressed by asking the following eight clinical questions.

1. What is the difference in colony counts when comparing immediate versus delayed processing of fresh urine stored at room temperature after collection?

2. What is the difference in colony counts when comparing immediate versus delayed processing of urine kept refrigerated or preserved in boric acid?

3. What is the difference in contamination rates between midstream urine collected with cleansing versus without cleansing in women being tested for a UTI?

4. What is the diagnostic accuracy of midstream urine collected with or without cleansing compared to bladder catheterization for the diagnosis of UTI in women?

5. What is the difference in contamination rates between midstream urine collection, with or without cleansing, and first-void collection in men?

6. What is the diagnostic accuracy of midstream urine collected, with or without cleansing, compared to that of bladder catheterization or suprapubic aspiration for the diagnosis of UTI in men?

7. What are the differences in contamination rates between midstream collection with cleansing, midstream collection without cleansing, and sterile urine bag or diaper collection in children?

8. What is the diagnostic accuracy of midstream clean-catch, sterile urine bag, or diaper collection compared with that of suprapubic aspiration or catheterization for the diagnosis of UTI in children?

The search for studies of practice effectiveness was conducted to identify those with measurable outcomes collected to the rigor of review requirements. With input from the expert panel and assistance of a research librarian at the Jesse Jones Library at the Texas Medical Center in Houston, TX, a literature search strategy and set of terms were developed. A search of three electronic bibliographic databases (PubMed, SCOPUS, and CINAHL) for English-language articles published between 1965 and 2014 was conducted. In addition, hand searching of bibliographies from relevant information sources was performed. All search results were catalogued and maintained using a Web-based, commercial reference software package (RefWorks; ProQuest LLC, Ann Arbor, MI). Finally, solicitation of unpublished quality improvement studies was attempted by posting requests for data on both the Laboratory Medicine Best Practices website (https://wwwn.cdc.gov/futurelabmedicine/) and two listservs supported by the American Society for Microbiology: clinmicronet (http://www.asm.org/index.php/online-community-groups/listservs) and DivCNet (http://www.asm.org/division/c/divcnet.htm).

The search contained the following medical subject headings (MESH) and key text words: "urinary tract infections" (MESH) OR UTI (text word) OR urinary tract infect* (text word); "urine/analysis" (major) OR "urine/microbiology" (major) OR "urinalysis" (MESH); "specimen handling" (major); "preservation, biological" (MESH) OR preservation, biological (text word) OR "boric acids" (MESH) OR boric acid (text word) OR boric acid/borate (text word) OR boric acids (text word) OR "refrigeration" (MESH) OR refrigeration (text word) OR preserv* (text word); storage (text word); "time factors" (MESH) OR "transportation" (MESH) OR transport time (text word) OR delay (text word) OR time delay (text word) OR time factor (text word) OR timing (text word); "urine specimen collection" (MESH) OR urine specimen collection (text word) OR "catheters, indwelling" (MESH) OR catheters, indwelling (text word) OR "urinary reservoirs, continent" (MESH) OR urinary reservoirs, continent (text word) OR "urinary catheterization" (MESH) OR urinary catheterization (text word) OR "intermittent urethral catheterization" (MESH)

OR intermittent urethral catheterization (text word) OR clean voided (text word) OR midstream (text word) OR midstream (text word) OR midstream (text word) OR foley (text word) OR suprapubic (text word); and "bacteriological techniques" (MESH) OR bacteriological technique (text word) OR bacteriological techniques (text word) OR "microbiological techniques" (MESH) OR microbiological technique (text word) OR microbiological techniques (text word).

Titles and abstracts were initially screened by the review coordinator, with assistance from the expert panel when necessary, to select studies for a full review. A study was included if it was considered likely to provide valid and useful information and met the PICO criteria previously discussed. Specifically, these inclusion criteria required that a study (i) address a defined population/definable group of patients, (ii) evaluate a specific intervention/practice included in this review, (iii) describe at least one finding for a relevant outcome measure (percent contamination, diagnostic accuracy) reproducible in comparable settings, and (iv) present results in a format which was useful for statistical analysis. Studies failing to meet the inclusion criteria (not considered to report a relevant practice, did not include a practice of interest, or did not present an outcome measure of interest) were excluded from further review.

Studies that cleared this initial screening were then abstracted and evaluated by the expert panel. For eligible studies, information on study characteristics, interventions, outcome measures, and findings of the study was extracted using a standardized form and assigned a quality rating derived from points awarded for meeting quality criteria. Individual quality ratings were based on four dimensions: study quality, practice effectiveness, defined outcome measure(s), and findings/results. The objective for rating individual study quality was to judge whether sufficient evidence of practice effectiveness was available to support inclusion in an overall body of evidence for evaluation of a best-practice recommendation (that is, a practice likely to be effective in improving one or more outcomes of interest in comparison to other commonly used practices).

The four study quality dimensions were rated separately, with a rating score assigned up to the maximum for a given dimension. The rating scores for all four dimensions were added to reach a single summary score reflecting overall study quality. A total of 10 points were available for each study. Reviewers assigned one of three quality ratings to each study: good (8 to 10 points), fair (5 to 7 points), or poor (4 points or less). Each study was reviewed and rated by two expert panel members to minimize subjectivity and bias. Any study ranked as poor by one reviewer but good by the second reviewer was assigned to a third expert panel member for resolution. More detail on the rating process of individual studies can be found elsewhere (24–26). Studies that did not meet a study quality rating of fair or good were excluded from further consideration. Data from published studies that passed a full review were transformed to a standardized, common metric according to LMBP methods (24). Summary data and quality scores for each publication included in this evidence-based review can be found in Appendix 3 below.

The study quality ratings and results from the individual studies for each clinical question were aggregated into bodies of evidence. The consistency of effects and patterns of effects across studies and the rating of overall strength of the body of evidence (high, moderate, low, suggestive, and insufficient) were based on both qualitative and quantitative analyses. Estimates of effect and the strength of the body of evidence were then used to translate results into one of three evidence-based recommendations (recommend, no recommendation for or against, recommend against). The ratings criteria are described in greater detail elsewhere (24).

While recommendations are based on the entire body of evidence, meta-analyses to generate summary estimates of effect were undertaken for outcomes that provided sufficient data for measurements of diagnostic accuracy and contamination, i.e., proportions of specimens containing periurethral, perianal, epidermal, or vaginal flora. For the outcome of contamination proportion, summary odds ratios were calculated using Mantel-Haenszel methods in a random-effects model performed using Review Manager (RevMan) software version 5.0 (2008; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, DK). A contamination event was defined according to how individual studies defined contamination because definitions varied between studies. Wherever possible, contamination proportions were determined for the entire test population rather than a subset population (such as only among those individuals that tested negative for urinary tract infection). The I^2 statistic, which describes the percentage of variability in effects estimates due to statistical heterogeneity rather than sampling error, was used to assess between-study heterogeneity. For the outcomes of diagnostic accuracy, it was planned that point estimates of sensitivity and specificity would be summarized using the bivariate model when similar cutoff points were used; however, all models failed to converge due to a too-small number of study or sample sizes. Similarly, hierarchical summary receiver operator characteristic curves (HSROC) could not be generated because these models too failed to converge. Solutions for failure of convergence, including removing individual studies, were explored but did not improve convergence. Meta-analysis of diagnostic accuracy outcomes and curve fitting were not pursued further given the limitations of univariate methods. All work on summarizing diagnostic accuracy outcomes was performed using SAS software version 9.2 (2008; SAS Institute Inc., Cary, NC, USA) and the MetaDAS macro, version 1.3 (27). Significant growth (i.e., a positive sample) was defined according to how each individual study defined significant growth because cutoff points tended to vary among studies. All other growth, including contamination and no growth, were considered nonsignificant growth (i.e., a negative sample), as this most closely reflects actual clinical practice. Two-by-two tables were used to determine sensitivity and specificity, and exact 95% confidence intervals were calculated.

Search Results

Search results produced 5,092 unique documents that were initially screened for eligibility to contribute to evidence of effectiveness for practices defined by the eight clinical questions posed (storage and preservation of urine, collection of urine from women, collection of urine from men, and collection of urine from infants and children). There was no response to requests for unpublished data. The reduction of studies through the screening process is detailed in Fig. 2. Initial screening for topic relevance eliminated 4,917 studies. From the remaining 171 studies, 124 were eliminated for not meeting
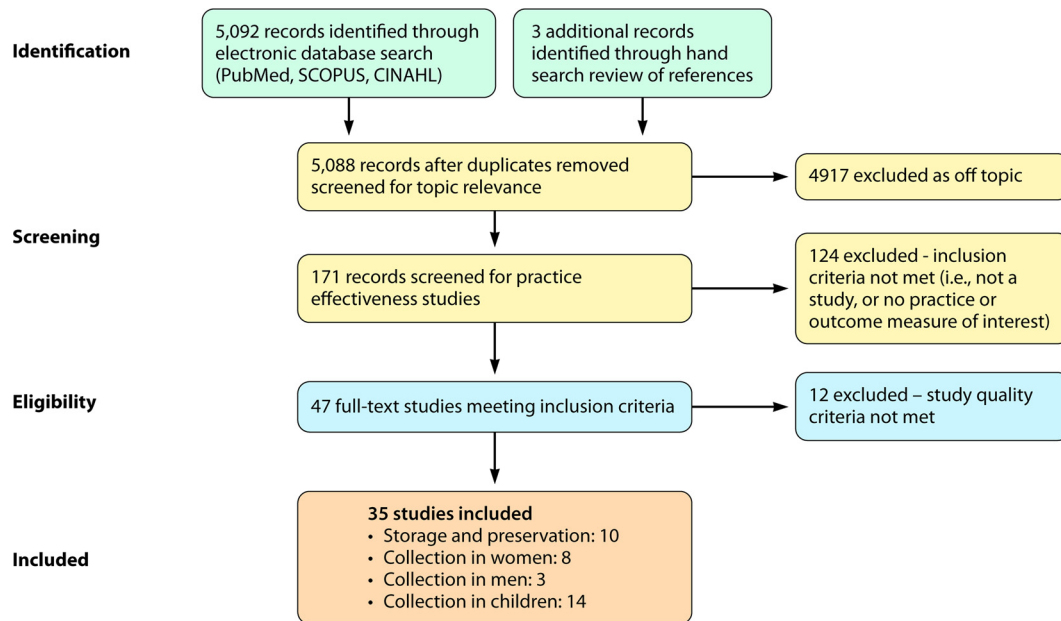
FIG 2 Systematic review flow diagram.

the inclusion criteria (i.e., having elements potentially relevant to at least one topic area review question, reporting practices that are in use and available for adoption, reporting practices reproducible in other comparable settings, and addressing a defined population/definable group of patients). Forty-seven studies met the criteria for inclusion and were subjected to full abstraction and quality scoring. After an additional 12 studies were excluded because of insufficient quality scores, the remaining 35 were included in the statistical analysis: 10 studies on storage and preservation, 8 studies on collection from

women, 3 studies on collection from men, and 14 studies on collection from infants and children.

STORAGE AND PRESERVATION OF URINE

Summary information on the 10 published studies comprising the body of evidence for the clinical questions on the storage and preservation of urine is presented in Tables 1 and 2. The publication dates for these studies range from 1969 (28) to 1999 (29). All studies were given a "fair" quality rating. Three studies examined the effect of prolonged storage of clean-catch

TABLE 1 Body-of-evidence table for clinical question 1, namely, "what is the difference in colony counts when comparing immediate and delayed (≥4 h) processing of fresh urine stored at room temperature after collection?"[a]

Study (reference), quality rating	Samples	Setting	Time period	Results
Hindman et al. (30), fair	100 random samples of urine were cultured within 2 h of collection and then again after 2 h and 4 h of storage at room temp.	Clinical Microbiology Laboratory, Hartford Hospital, Hartford, CT	Not given	SG was defined as any growth of $>10^5$ CFU/ml. All other growth was considered NSG. Upon receipt, there were 47 SG and 53 NSG specimens. After 4 h, there were 51 SG and 49 NSG specimens.
Lum and Meers (31), fair	175 clean-catch urine samples were divided, and one portion was treated with boric acid at a concn of 20 g/liter and the other held in a sterile tube. All samples were cultured upon receipt in the laboratory and again after 4 h, 24 h, and 48 h of storage at room temp.	Microbiology Department, University of Singapore, Kent Ridge, Singapore	6 mo	SG was defined as $\geq 10^5$ CFU/ml of 1 or 2 species. All other growth was considered NSG. Upon receipt, there were 38 SG and 137 NSG specimens. At 4 h, there were 42 SG and 133 NSG specimens. At 24 h, there were 90 SG and 82 NSG specimens. At 48 h, there were 109 SG and 66 NSG specimens.
Porter and Brodie (28), fair	130 midstream urine specimens that had been collected in sterile tubes and kept at room temp or preserved with 0.5 g of boric acid were mailed to a laboratory and cultured immediately upon receipt (avg delay of 24 h before receipt) and again at 72 h after receipt.	Laboratory, City Hospital, Aberdeen, Scotland	Not given	SG was defined as any growth of $>10^5$ CFU/ml. All other growth was considered NSG. Upon receipt, there were 40 SG and 90 NSG specimens. After 72 h, there were 93 SG and 37 NSG specimens.

[a] SG, significant growth; NSG, nonsignificant growth.

TABLE 2 Body-of-evidence table for clinical question 2, namely, "what is the difference in colony counts when comparing immediate and delayed (≥24 h) processing of urine kept refrigerated or preserved in boric acid?"[a]

Study (reference), quality rating	Samples	Setting	Time period	Results
Gillespie et al. (29), fair	792 midstream specimens of urine from 792 general practice patients were received preserved in 18 g/liter BA. Samples were cultured within 8 h of laboratory receipt (immediate) and again after overnight storage at room temp (delayed).	Clinical Microbiology Laboratory, Western General Hospital, Edinburgh, United Kingdom	Not given	SG was defined as >10^5 CFU/ml of a single species. All other growth was considered NSG. Positive agreement (sensitivity) was 76.1% between immediate and delayed specimens. Negative agreement (specificity) was 95.9%.
Guenther and Washington (33), fair	Midstream clean-catch or catheterized urine was collected from patients suspected of having UTIs. Split samples were transported to the laboratory in either refrigerated sterile tubes or in Becton, Dickinson urine culture kit tubes containing GBF. Sterile urine was cultured immediately upon arrival (immediate), and preserved specimens were cultured again after storage for 24 and 48 h at room temp (delayed).	Clinical Microbiology Laboratory, Mayo Clinic, Rochester, MN	Not given	SG was defined as any growth of >10^5 CFU/ml. All other growth was considered NSG. For phase 1 of the trial, positive agreement (sensitivity) between immediate and delayed cultures was 87.3%. Negative agreement (specificity) was not reported.
Hubbard et al. (34), fair	A total of 100 random clinical urine specimens were divided and tested to compare urine preserved in Becton, Dickinson urine culture kit tubes containing GBF with refrigerated urine. Each pair was cultured at 0, 5, and 24 h.	Clinical Microbiology Laboratory, University of Michigan Medical Center, Ann Arbor, MI	Not given	SG was defined as >10^5 CFU/ml of a single pathogenic species. All other growth was considered NSG. Phase 1 study data were used. With immediate culture in GBF, there were 25 specimens showing SG and 75 showing NSG. After a delay of 24 h, there were 22 specimens showing SG and 78 showing NSG. With refrigeration and immediate culture of fresh urine, there were 26 specimens showing SG and 74 specimens showing NSG. After a delay of 24 h with refrigeration, results had not changed.
Lauer et al. (35), fair	1,000 urine specimens from children and adults suspected of having UTIs were received by the laboratory. Upon receipt, specimens were refrigerated until they could be cultured. Specimens were then cultured immediately (immediate) or split into 2 samples: 1 refrigerated for 18–24 h (delayed) and 1 preserved with Becton, Dickinson urine culture kit tubes of GBF for 18–24 h (delayed) and stored at room temp.	Clinical Microbiology Laboratory, Colorado General Hospital, Denver, CO	Not given	SG was defined as >10^5 CFU/ml of a single pathogenic species. All other growth was considered NSG. Positive agreement between the results of immediate and delayed culture in GBF was 93.2%; negative agreement was 99.9%. Positive agreement between immediate and delayed culture while samples were refrigerated was 93.2%; negative agreement was 100.0%.
Lum and Meers (31), fair	175 clean-catch urine samples obtained from various hospital wards and clinics were divided; 1 portion was treated with BA at a concn of 20 g/liter and the other held in a sterile tube. All samples were cultured upon receipt in the laboratory (immediate) and again after 4 h, 24 h, and 48 h of storage at room temp (delayed).	Microbiology Department, University of Singapore, Kent Ridge, Singapore	6 mo	SG was defined as ≥10^5 CFU/ml of 1 or 2 species. All other growth was defined as NSG. With immediate culture, there were 29 specimens showing SG and 146 showing NSG. After 24 h, there were 32 specimens showing SG and 143 showing NSG.
Porter and Brodie (28), fair	130 midstream urine specimens were collected in sterile tubes kept at room temp or preserved with 0.5 g of boric acid, mailed to the laboratory, and cultured immediately upon receipt, with an avg delay of 24 h before receipt (immediate). They were cultured again after 72 h of storage at room temp (delay).	Laboratory, City Hospital, Aberdeen, Scotland	Not given	SG was defined as any growth of >10^5 CFU/ml. All other growth was defined as NSG. With immediate culture in BA, there were 18 specimens showing SG and 112 showing NSG. After a delay of 72 h, results of specimens in BA had not changed.
Southern and Luttrell (36), fair	312 midstream urine specimens were transported to the laboratory in either sterile tubes or Becton, Dickinson urine culture kit tubes containing GBF. All specimens were tested immediately upon receipt. If not tested within 20 min, specimens were refrigerated. Preserved specimens were retested after being held for 24 h at room temp.	Parkland Memorial Hospital, Dallas, TX	Not given	SG was defined as >5×10^4 CFU/ml of any growth. All other growth was defined as NSG. With immediate culture of specimens preserved in GBF, there were 8 specimens showing SG and 180 showing NSG. After a delay of 24 h, there were 40 specimens showing SG and 148 showing NSG.
Weinstein (37), fair	869 urine specimens obtained from inpatients in 3 medical units were split and transported to the laboratory in either sterile tubes, Becton, Dickinson urine culture kit tubes containing GBF, or Becton, Dickinson Vacutainer tubes containing SBF. All specimens were cultured immediately upon receipt (immediate) and then again after being held for 24 h at either room temp (BA tubes) or under refrigeration (sterile tubes).	Middlesex General University Hospital, New Brunswick, NJ	6 mo	SG was defined as ≥10^5 CFU/ml of a single species. All other growth was defined as NSG. Only results of GBF preservation are reported here since only the latter half of patients had samples also stored in SBF. With immediate culture in GBF, there were 106 specimens showing SG and 763 showing NSG. After 24 h, there were 97 specimens showing SG and 765 showing NSG (7 fewer patient specimens were available for analysis). For refrigeration, with immediate culture of fresh urine, there were 111 specimens showing SG and 758 showing NSG. After a delay of 24 h, there were 104 specimens showing SG and 758 showing NSG (7 fewer patient specimens were available for analysis).
Wright et al. (32), fair	Fresh urine specimens received by the laboratory were preserved in 3 formulations of BA: 5.5% pure BA, BA in Becton, Dickinson urine culture kit tubes containing GBF, and BA in Becton, Dickinson Vacutainer tubes containing SBF. They were tested for the presence of bacteria by culture and by various screening methods for assessing bacteriuria. Samples of fresh urine were tested upon receipt by the laboratory (immediate), and preserved samples were tested after being held for 24 h at room temp (delay).	Department of Pathology, University of Utah Medical Center, Salt Lake City, UT	Not given	SG was defined as any growth of >10^5 CFU/ml. Results of a BacT screen (culture results were not reported) were used to assess positivity. For samples preserved in BA, there were 48 showing SG with immediate culture and 41 showing SG after a delay of 24 h. For GBF samples, there were 49 showing SG with immediate culture and 46 showing SG with delayed culture. For SBF samples, there were 96 showing SG with immediate culture and 92 showing SG with delayed culture. Results of the 3 BA groups were combined for analysis.

[a] BA, boric acid; GBF, glycerol-boric acid-sodium formate; SBF, sorbitol-boric acid-sodium formate; SG, significant growth; NSG, nonsignificant growth.

TABLE 3 Difference in colony counts when results of immediate and delayed plating of fresh urine stored at room temperature were compared[a]

Study (reference)	No. of organisms at 0 h (CFU/ml)	Increase in significant growth (%) at:			
		4 h	24 h	48 h	72 h
Lum and Meers (31)	38	11	137	187	ND
Hindman et al. (30)	47	9	ND	ND	ND
Porter and Brodie (28)	40	ND	ND	ND	233

[a] The quality rating of each study was fair. ND, not determined.

urine at room temperature by culturing samples of urine immediately upon receipt and then again after 2 h and 4 h (30), after 4 h, 24 h, and 48 h (31), or after 24 h and 72 h (28) of storage at room temperature. Nine studies tested the effect of preserving urine in boric acid for 24 h on colony counts and compared the results with the results of immediate culture. Several different boric acid formulations were used, including boric acid alone (29, 31, 32), glycerol-boric acid-sodium formate (32–37), and sorbitol-boric acid-sodium formate (32, 37). The length of delay of culture while samples were preserved in boric acid was assessed at various time points across studies, but 24 h was chosen for analysis as it was the most common endpoint. Three studies examined the effect of 24-h refrigeration of urine samples on changes in colony counts from those of immediate culture (33, 35, 37). The majority of studies used clean-catch midstream urine samples, although collection methods were undefined in five studies (30, 32, 34, 35, 37). Growth was defined as either "significant" or "nonsignificant." The definitions of significant growth varied among studies, but in general, a threshold of $>10^5$ CFU/ml of one or two species of bacteria was used.

Body-of-Evidence Qualitative Analysis

The difference in colony counts when immediate and delayed processing of urine specimens stored at room temperature were compared is shown in Table 3. Data from three observational studies (28, 30, 31) found a moderate increase (approximately 10%) in colony counts after 4 h of storage at room temperature and a large increase ($>135\%$) in colony counts after storage for 24 h or more. The effect of delayed culture on urine specimens kept refrigerated or preserved in solutions of boric acid is shown in Tables 4, 5, and 6. Data from three observational studies (29, 33, 35) found 73 to 93% positive agreement (sensitivity) and 96 to 100% negative agreement (specificity) between the results of immediate culture and after a 24-h delay with specimens preserved in boric acid. Data from one study (35) found 93% positive agreement and 100% negative agreement between specimens cultured immediately

upon receipt versus after a 24-h delay with refrigeration (Table 4). Colony counts in urine samples either refrigerated or chemically preserved showed similar results. Five studies (31, 32, 34, 37, 38) showed that urine samples preserved in boric acid solutions for 24 h (Table 5) or refrigerated for 24 h (Table 6) had only minor changes in the numbers of cultures with either significant or nonsignificant growth.

These data suggest that both boric acid and refrigeration adequately preserve urine specimens prior to their processing for up to 24 h. Furthermore, the results suggest that urine held at room temperature for more than 4 h should not be processed due to overgrowth of both clinically significant and contaminating microorganisms. Based on statistical analysis of the data, however, the overall strength of this body of evidence was rated as low.

COLLECTION OF URINE FROM WOMEN

Summary information on the eight published studies comprising the body of evidence for the clinical questions on contamination rates and the diagnostic accuracy of midstream urine collection from adult females is presented in Tables 7 and 8. Three studies (39–41) were given a quality rating of "good," and five studies (38, 42–45) were rated as "fair." Five studies (38–40, 42, 43) examined the impact of perineal cleansing on contamination and are summarized in Table 7. Patient settings included a clinic for adolescents (38), a general practice (38), an antenatal ambulatory-care clinic (39, 43), and a health center for teenagers (40). Definitions of contamination varied among studies and included any growth of normal vaginal flora and/or small quantities ($<2,000$ CFU/ml) of pathogenic bacteria (38), the presence of epithelial cells (42), mixed growth in quantities of $>10^5$ CFU/ml (39) or at any quantity (43), and growth of any nonpathogen or pathogen in quantities of $<10^4$ CFU/ml (43) or $<10^5$ CFU/ml (40).

Three studies (41, 44, 45) examined the diagnostic accuracy of midstream urine collection with or without cleansing, with straight urinary catheterization as the reference standard (Table 8). Patient populations in these studies included women presenting to an emergency department (41) or ambulatory clinic (44) or admitted to a general medical ward (45). In two studies (43, 44), each patient had urine collected by midstream collection with cleansing, followed by a second collection by urinary catheterization. In the third study (46), no cleansing was performed prior to midstream collection.

Body-of-Evidence Qualitative Analysis

The evidence examining the impact of perineal cleansing on contamination of midstream urine specimens collected from females is depicted in Fig. 3. Data from four observational studies (38, 40, 42, 43) and one randomized control trial (39) found no difference

TABLE 4 Results of immediate versus delayed culture of urine preserved in boric acid or refrigerated[a]

Study (reference)	Preservative	Time zero storage conditions	Storage conditions for delayed culture	Positivity threshold (CFU/ml)	% sensitivity (95% CI)	% specificity (95% CI)
Lauer et al. (35)	GBF	Refrigeration	18–24 h in GBF	$>10^5$	93 (86–97)	100 (99–100)
Gillespie et al. (29)	BA	<8 h in BA	Overnight in BA	$>10^5$	76 (68–82)	96 (94–97)
Guenther and Washington (33)	GBF	Refrigeration	24 h in GBF	$\geq10^5$	87 (78–93)	ND
Lauer et al. (35)		Refrigeration	18–24 h of refrigeration	$>10^5$	93 (86–97)	100 (100–100)

[a] The quality rating of each study was fair. GBF, glycerol-boric acid-sodium formate; BA, boric acid; 95% CI, 95% confidence interval; ND, not determined.

TABLE 5 Effect of delayed plating of urine specimens preserved in boric acid solutions[a]

Study (reference)[b]	Preservative(s)	Preservative used for immediate culture	No. of h that culture was delayed (preservative[s])	Threshold (no. of CFU/ml)	NSG present		SG present	
					No. of specimens subjected to immediate culture	% change from no. after delay	No. of specimens subjected to immediate culture	% change from no. after delay
Southern and Luttrell (36)	GBF	GBF	24 (GBF)	$>5 \times 10^4$	180	−17.8	8	+500.0
Lum and Meers (31)	BA	GBF	24 (GBF)	$>10^5$	146	−2.1	29	+10.3
Wright et al. (32)	BA, GBF, SBF	None (fresh specimens were used)	24 (BA, GBF, SBF)	$>10^5$			193	−7.3
Weinstein (37)	GBF, SBF	GBF	24 (GBF)	$\geq 10^5$	763	+1.2[b]	106	−8.5[b]
Hubbard et al. (34)	GBF	GBF	24 (GBF)	$>10^5$	75	+4.0	25	−12.0
Porter and Brodie (28)	BA	BA	72 (BA)	$>10^5$	112	0	18	0

[a] GBF, glycerol-boric acid-formate; BA, boric acid; SBF, sorbitol-boric acid-formate; NSG, nonsignificant growth; SG, significant growth. All studies were given a quality rating of fair.

[b] There were 7 fewer patient samples available for analysis with delayed culture (862 patient pairs versus 869); the percent increase was calculated assuming 869 pairs.

in the odds of contamination between midstream urine specimens collected with or without cleansing. The overall strength of this evidence was rated as high. The diagnostic accuracy of midstream urine collection with or without cleansing is shown in Table 9. Using catheterization as the reference standard, midstream collection had a sensitivity of 98 to 100% and a specificity of 95 to 100%. However, the overall strength of this body of evidence was rated as low.

COLLECTION OF URINE FROM MEN

Summary information on the three published studies comprising the body of evidence for the clinical questions on contamination and diagnostic accuracy of midstream urine collection from adult males is presented in Tables 10 and 11. One study (46) was given a quality rating of "good," and two studies (47, 48) were rated as "fair." Two studies (46, 47) examined contamination in midstream clean-catch specimens compared to that in first-void collection specimens (Table 10). Patients in both studies were either ambulatory or hospitalized men with symptoms of urinary tract infection being seen at a VA Medical Center. In the first study (46), men had a first-void and/or midstream urine sample collected, but only half of the patients were asked to wash their glans penis prior to collection. In the second study (47), urine specimens from men were obtained by midstream clean-catch collection, first-void collection, straight catheterization, and suprapubic bladder aspiration, with 7 men being sampled more than once. Contamination was defined as either the growth of $>10^3$ CFU/ml of two or more colony types (46) or any growth of three or more microbial species (47). For the meta-analysis, only those samples obtained via midstream clean-catch collection and first-void collection without cleansing were compared.

Two studies (47, 48) examined the diagnostic accuracy of midstream urine collection from men using either straight catheterization or suprapubic aspiration as the reference standard (Table 11). One study (47) compared midstream clean-catch specimens to those collected by suprapubic aspiration or straight catheterization in a group of hospitalized or ambulatory men, while the second study (48) compared midstream clean-catch specimens to specimens collected by suprapubic aspiration in a group of patients with spinal cord injury without indwelling catheters. Significant growth in one study (47) was defined as $\geq 10^4$ CFU/ml of a single or predominant species for midstream clean-catch specimens or $\geq 10^3$ CFU/ml for specimens collected by straight catheterization or suprapubic aspiration. Significant growth in the second study (48) was defined as any growth of $\geq 10^4$ CFU/ml for either collection method.

Body-of-Evidence Qualitative Analysis

The evidence comparing levels of contamination after midstream urine collection and uncleansed first-void collection is shown in Fig. 4A. Summary data from both studies (46, 47) found a large (77%) reduction in the odds of contamination in favor of midstream clean-catch over first-void specimens. The strength of this evidence was rated as high. Only one study (46) compared midstream collection with cleansing to midstream collection without cleansing (Fig. 4B). Results showed no difference in contamination between the two methods of collection. However, imprecision was largely due to the small event size. The diagnostic accuracy of midstream urine collection from men, with straight catheterization or suprapubic aspiration used as the reference standard, is shown in Table 12. Data for both studies found high diagnostic sensitivity (82 to 100%)

TABLE 6 Effect of delayed plating of urine specimens kept refrigerated[a]

Study (reference)	Threshold (no. of CFU/ml)	NSG present		SG present	
		No. of specimens subjected to immediate culture	% change from no. after delay	No. of specimens subjected to immediate culture	% change from no. after delay
Weinstein (37)	$\geq 10^5$	758	+0.9[b]	111	−6.3[b]
Hubbard et al. (34)	$>10^5$	74	0	26	0

[a] Both studies were given a quality rating of fair. NSG, nonsignificant growth; SG, significant growth. Both studies immediately cultured fresh specimens and specimens that had been kept under refrigeration for 24 h.

[b] There were 7 fewer patient samples available for analysis with delayed culture (862 patient pairs versus 869); percentages of increase were calculated assuming 869 pairs.

TABLE 7 Body-of-evidence table for clinical question 3, namely, "what is the difference in percentages of contamination between midstream urine collection with cleansing versus without cleansing in women being tested for a UTI?"[a]

Study (reference), quality rating	Population and/or samples	Setting	Time period	Results
Blake and Doherty (38), fair	50 asymptomatic females aged 14–23 yr nonrandomly assigned to the MSCC group ($n = 25$) or the MS group ($n = 25$)	Adolescent Clinic, University of Massachusetts Medical School, Worcester, MA	2 mo	Contamination was defined as growth of bacteria found in normal vaginal or skin flora that does not cause UTI. 8 samples showed no growth in the MSCC group, and 5 showed no growth in the MS group. 1 sample in the MS group grew pathogenic bacteria (<2,000 CFU/ml). The remaining 36 samples were contaminated. Of the remaining 36, 33 grew mixed Gram-positive colonies, 2 grew mixed Gram-positive and -negative colonies, and 1 grew staphylococcal species.
Bradbury (42), fair	158 female patients suspected of having UTIs and 158 controls, all aged 16–75 yr. 316 urine specimens were collected via MSCC or MS. The control group comprised the next nonpregnant female attending with no urinary tract symptoms. Urine was collected into a sterile boric acid container. Specimens were transported to the laboratory after morning surgery. Those collected in the evening were stored in the refrigerator. All specimens were collected at surgery.	General practice, United Kingdom	Not given	Contamination was defined by the presence of epithelial cells. There were 11 contaminated specimens among the 176 in the MSCC group and 17 contaminated specimens among the 138 in the MS group.
Holliday et al. (39), good	192 asymptomatic antenatal ambulatory women randomly allocated into the MSCC or MS group for urine specimens. No preservatives were used, and samples were processed within 2 h of collection.	Royal Air Force Institute of Pathology and Tropical Medicine, United Kingdom	Not given	Contamination was defined as mixed growth of $>10^5$ CFU. There were 14 contaminated samples from the 96 women in the MSCC group and 12 contaminated specimens from the 96 women in the MS group.
Schlager et al. (40), good	100 pregnant asymptomatic adolescents aged 10–19 yr in all stages of pregnancy who enrolled during a routine prenatal visit. Each patient provided 2 urine samples collected during consecutive urinations (MSCC or MS). No preservatives were used. Urinalysis and bacterial culture were performed within 5 h of collection.	Teen Health Center, University of Virginia Health Sciences Center, VA	Not given	Contamination was defined as $<10^5$ CFU/ml of a pathogen or any no. of nonpathogens. There were 62 contaminated samples from the 100 women in the MSCC group and 55 from the 100 women in the MS group ($P = 0.38$).
Schneeberger et al. (43), fair	113 pregnant women. 3 urine samples were self-obtained from each woman by UFV, MS, and MSCC. Oral and written instructions were provided. Urine samples were refrigerated and analyzed within 48 h of collection	Obstetric clinic (Vida) in Amsterdam, Netherlands	1 yr	Contamination was defined as growth of at least 2 or more organisms. 336 urine samples were analyzed (113 UFV, 112 MS, and 111 MSCC specimens). There was 1 contaminated specimen out of 112 MS specimens and 3 contaminated specimens out of 113 MSCC specimens. If contamination was defined as growth of $\geq 10^4$ CFU of skin flora/ml by culture, there were 47 contaminated specimens out of 112 MS and 42 contaminated specimens out of 111 MSCC specimens.

[a] MSCC, midstream collection with perineal cleansing; MS, midstream collection; UFV, first-void urine collection (morning).

TABLE 8 Body-of-evidence table for clinical question 4, namely, "what is the accuracy of midstream urine collection, with or without cleansing, compared to catheterization for the diagnosis of UTI in women?"[a]

Study (reference), quality rating	Population and samples[a]	Setting	Time period	Results
Walter and Knopp (41), good	105 women suspected of having a UTIs and presenting to the emergency department triage nurse. An MSCC specimen and then a CATH specimen were collected.	Department of Emergency Medicine, Valley Medical Center, Fresno, CA	7 mo	SG was defined as >10^4 CFU/ml of a single species by either CATH or MSCC. All other growth was considered NSG. MSCC had a sensitivity of 98% and a specificity of 97%.
Lemieux and St.-Martin (45), fair	The study was separated into 3 groups. In group 1, 53 healthy student nurses volunteered for MSCC with no CATH. Group 2 consisted of 29 women, asymptomatic for UTI, admitted to a general medical ward. Both MSCC and CATH specimens were collected. Group 3 consisted of 27 patients suspected of having a UTI who were admitted to a semiprivate or general medical ward. Both MSCC and CATH specimens were collected.	Hotel-Dieu Hospital, Montreal, Canada, and Department of Medicine, University of Montreal School of Medicine, Montreal, Canada	Not given	SG was defined as >10^4 CFU/ml of a single pathogenic species by either CATH or MSCC. All other growth was considered NSG. Combining groups 2 and 3 yielded a sensitivity of 100% and a specificity of 100%.
Immergut et al. (44), fair	95 ambulatory females. Urine was obtained via MS or CATH. Specimens were immediately cultured on Uricult medium by dipping the slides into plastic cups.	Private practice, Bethesda, MD	Not given	SG was defined as any growth of >5×10^4 CFU/ml by either CATH or MS. All other growth was considered NSG. MS had a sensitivity of 100% and a specificity of 95%.

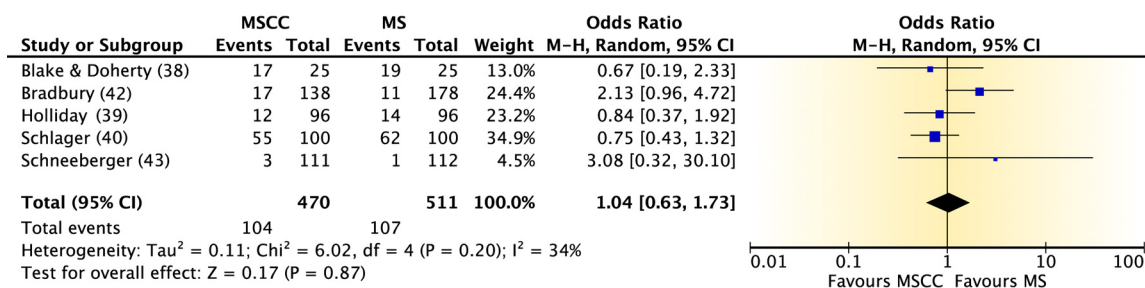[a] MSCC, midstream collection with perineal cleansing; MS, midstream collection; CATH, catheterization.

and specificity (92 to 100%) for midstream clean-catch collection. However, the overall strength of this body of evidence was rated as low.

COLLECTION OF URINE FROM CHILDREN

Summary information on the 14 published studies comprising the body of evidence for the clinical questions on contamination rates and the diagnostic accuracy of midstream urine collection from children is presented in Tables 13 and 14. Four studies (49–52) were given a quality rating of "good," and 10 studies (53–62) were rated as "fair." Six studies (49, 50, 53–56) compared differences in contamination rates in urine collected by midstream collection (with or without cleansing), collected with a sterile urine bag, or collected from diapers (Table 13). Patients studied ranged in age from 1 month to 18 years. Definitions of contamination varied among studies and included mixed growth in any concentration (54), mixed growth in any concentration or any growth of <10^5 CFU/ml (49–51), and mixed growth at a concentration of >10^5 CFU/ml (56); any specimen interpreted as contaminated by the clinical microbiology laboratory was also included (53).

Eight studies (51, 52, 57–62) examined the accuracy of midstream clean-catch, sterile urine bag, or diaper collection, with suprapubic aspiration or straight catheterization used as the reference standard for diagnosing urinary tract infections in children (Table 14). Patient age ranged from 0 to 10 years. Definitions of significant growth varied across studies, particularly for the reference standards. All studies except one defined significant growth for midstream clean-catch, sterile urine bag, or diaper collection as ≥10^5 CFU/ml. The remaining study (52) defined significant growth by sterile urine bag collection as "pure growth." Significant growth for suprapubic aspiration or straight catheterization

Study or Subgroup	MSCC Events	Total	MS Events	Total	Weight	Odds Ratio M–H, Random, 95% CI	Odds Ratio M–H, Random, 95% CI
Blake & Doherty (38)	17	25	19	25	13.0%	0.67 [0.19, 2.33]	
Bradbury (42)	17	138	11	178	24.4%	2.13 [0.96, 4.72]	
Holliday (39)	12	96	14	96	23.2%	0.84 [0.37, 1.92]	
Schlager (40)	55	100	62	100	34.9%	0.75 [0.43, 1.32]	
Schneeberger (43)	3	111	1	112	4.5%	3.08 [0.32, 30.10]	
Total (95% CI)		470		511	100.0%	1.04 [0.63, 1.73]	
Total events	104		107				

Heterogeneity: Tau^2 = 0.11; Chi^2 = 6.02, df = 4 (P = 0.20); I^2 = 34%
Test for overall effect: Z = 0.17 (P = 0.87)

FIG 3 Difference in contamination levels between midstream urine collected with cleansing (MSCC) versus without cleansing (MS) in women being tested for urinary tract infection. M-H, Mantel-Haenszel statistic; 95% CI, 95% confidence interval.

TABLE 9 Accuracy of midstream clean-catch or midstream urine collection compared to catheterization for the diagnosis of UTI in women[a]

Study (reference)	Quality rating	Subpopulation	Index test	Positive threshold for reference standard (CFU/ml)	Positive threshold for index test (CFU/ml)	% sensitivity (95% CI)	% specificity (95% CI)
Walter and Knopp (41)	Good	ND	MSCC	$>10^4$	$>10^4$	98 (88–100)	97 (89–99)
Lemieux and St.-Martin (45)	Fair	Combined	MSCC	$>10^4$	$>10^4$	100 (87–100)	100 (89–100)
		Asymptomatic	MSCC	$>10^4$	$>10^4$	ND	100 (88–100)
		Symptomatic	MSCC	$>10^4$	$>10^4$	100 (44–100)	95 (88–98)
Immergut et al. (44)	Fair	ND	MS	$>5 \times 10^4$	$>5 \times 10^4$	100 (44–100)	95 (88–98)

[a] MSCC, midstream clean-catch collection; MS, midstream urine collection; ND, not determined. The reference standard for all tests was catheterization.

was defined as any growth in one study (51), growth of $\geq10^2$ CFU in one study (59), growth of $\geq10^3$ CFU/ml in one study (62), growth of $\geq10^5$ CFU/ml in three studies (57, 60, 61), and "pure growth" in one study (52). In one study (58), the definition of significant growth was unclear.

Body-of-Evidence Qualitative Analysis

The evidence comparing contamination rates for midstream urine collection with cleansing, midstream collection without cleansing, sterile urine bag collection, and diaper collection is shown in Fig. 5. Data obtained from five observational studies (49, 53–56) and one cluster-randomized controlled trial (50) found larger reductions (68 to 73%) in the odds of contamination for specimens obtained by midstream collection with cleansing than for specimens obtained by the other methods of collection. Data from three observational studies (49, 54, 55) found no significant differences in the odds of contamination between specimens collected with sterile urine bags and specimens taken from diapers. This body of evidence was rated as high.

The accuracy of results for midstream clean-catch urine specimens, sterile urine bag specimens, or diaper specimens, with straight catheterization or suprapubic aspiration used as the reference standard for the diagnosis of urinary tract infection in children, is shown in Fig. 6. Data from eight observational studies showed varied results. The inability to meta-analyze the point estimates of sensitivity and specificity due to small sample and study sizes, together with heterogeneity in positivity thresholds, made

interpretation difficult. Similarly, HSROC curves could not be generated, and thus it is unclear which method of noninvasive urine collection is most accurate for the diagnosis of urinary tract infection in children.

ADDITIONAL CONSIDERATIONS

This section addresses additional considerations for evaluating preanalytical practices associated with urine cultures and the impact of these practices on contamination and diagnostic accuracy.

Clinical Applicability

The studies included in this review reported collection, storage, and preservation of urine samples through commonly used methods for both children and adults in both inpatient and outpatient settings; results are therefore likely to apply to other health care environments. Many of the methods for collection, storage, and preservation are widely recommended (18, 63) and are typically used in most hospitals, outpatient clinics, and clinical microbiology laboratories today (21, 22). The focus of this review, however, is largely on clean-catch midstream urine collection because this method remains the most commonly used in most patient populations and settings (18). This is primarily due to its noninvasiveness; i.e., it has no risk of producing iatrogenic infection, despite the paucity of data supporting its use as a standard (63).

Controversy remains among clinical microbiologists and infectious disease physicians about the most accurate means for diag-

TABLE 10 Body-of-evidence table for clinical question 5, namely, "what is the difference in contamination between midstream urine collection, with or without cleansing, from first-void collection from men?"[a]

Study (reference), quality rating	Population and samples	Time period	Results
Lipsky et al. (46), good	254 men attending a urology clinic. 308 specimens were obtained by UFV and MS. Half of the men (those with even Social Security numbers) cleansed their glans penis, creating 4 distinct groups of specimens: UFV, CFV, MS, and MSCC. All specimens were immediately refrigerated and delivered to a laboratory within 4 h of collection.	7 mo	Contamination was defined as $\geq10^3$ CFU/ml of 2 or more colonial types with no predominant organism. 10 (6.4%) of the 157 MSCC specimens were contaminated. 23 (15.2%) of the 151 UFV specimens were contaminated. 16 (10.6%) of the 151 MS specimens were contaminated.
Lipsky et al. (47), fair	66 ambulatory or hospitalized men who had acute dysuria or other irritative genitourinary symptoms, were known to have bacteriuria, or were scheduled for urologic procedure. 76 specimens in total from the 66 men (7 patients were restudied [5 twice and 2 four times]) obtained by SPA, UFV, MSCC, and CATH. The specimens were delivered to the laboratory within 30 min of collection and immediately inoculated.	Not given	Contamination was defined as specimens containing more than 2 microbial species. None (0%) of the 75 specimens in the MSCC group were contaminated. 5 (6.9%) specimens of the 72 in the UFV group were contaminated.

[a] MS, unclean midstream urine collection; MSCC, midstream clean-catch collection; UFV, first-void urine collection without cleansing; CFV, first-void collection with cleansing; SPA, suprapubic aspiration; CATH, urethral catheterization. The setting for these studies was the VA Medical Center, Seattle, WA.

TABLE 11 Body-of-evidence table for clinical question 6, namely, "what is the accuracy of midstream urine collection compared to straight catheterization or suprapubic aspiration for the diagnosis of UTI in men?"[a]

| Study (reference), quality rating	Population and samples	Setting(s)	Time period	Results
Lipsky et al. (47), fair	66 ambulatory or hospitalized men who had acute dysuria or other irritative genitourinary symptoms, were known to have bacteriuria, or were scheduled for a urologic procedure. 76 specimens in total were obtained from the 66 men (7 patients were restudied [5 twice and 2 four times]) obtained by SPA, UFV, MSCC, and CATH. Specimens were delivered to the laboratory within 30 min of collection and immediately inoculated.	VA Medical Center, Seattle, WA	Not given	SG was defined as $\geq 10^4$ CFU/ml of a single or predominant species ($\geq 90\%$ of the plate's growth) for MSCC and $\geq 10^3$ for SPA/CATH. All other growth was considered NSG. MSCC had a sensitivity of 82.4% and a specificity of 100.0%.
Deresinski and Perkash (48), fair	53 male spinal cord injury patients who were free of indwelling catheters. 71 samples of urine were obtained, 1 by MSCC and 1 by SPA. Note that many of the MSCC specimens were collected on first void. Urine specimens were processed for culture immediately.	Spinal Cord Injury Service, VA, and Stanford University Medical Centers, Palo Alto, CA	Not given	SG was defined as any growth of $>10^4$ CFU/ml for MSCC and SPA. All other growth was considered NSG. MSCC had a sensitivity of 100% and a specificity of 100%.

[a] MSCC, midstream clean-catch collection; UFV, first-void urine collection without cleansing; SPA, suprapubic aspiration; CATH, urethral catheterization; SG, significant growth; NSG, nonsignificant growth.

nosing urinary tract infections, including the best methods of specimen collection for women, men, children, and infants (19, 63). A recent collaboration between the American Society for Microbiology (ASM) and the Infectious Disease Societies of America (IDSA), designed to assist physicians in the appropriate use of laboratory tests for infectious diseases, addressed methods of specimen collection, as well as guidelines for testing patients for urinary tract infections (64). A recommendation was made for collection of urine in a manner to minimize contamination and included midstream collection with cleansing and immediate refrigeration of samples upon collection, although the lack of supporting data was cited (64).

In applying the findings of this review, a strength assessment of the overall body of evidence should be weighted by the quality of findings from individual reports most closely resembling populations and settings of particular interest. For instance, an overall body-of-evidence quality rating may decrease because of the aggregate number of included studies omitting study parameters of little applicability to a particular clinical setting. Researchers may take guidance, with a higher degree of confidence than the overall quality rating might indicate, from individual included studies of high or moderate strength which address specific clinical populations or settings directly comparable to their research interests. The conduct of evidence-based practice would guide clinicians to assess both the quality and the "goodness of fit" of studies relevant to their own particular questions before applying findings in support of their decisions.

This review has directed attention to the need for reexamination of preanalytic factors affecting urine culture. A great number
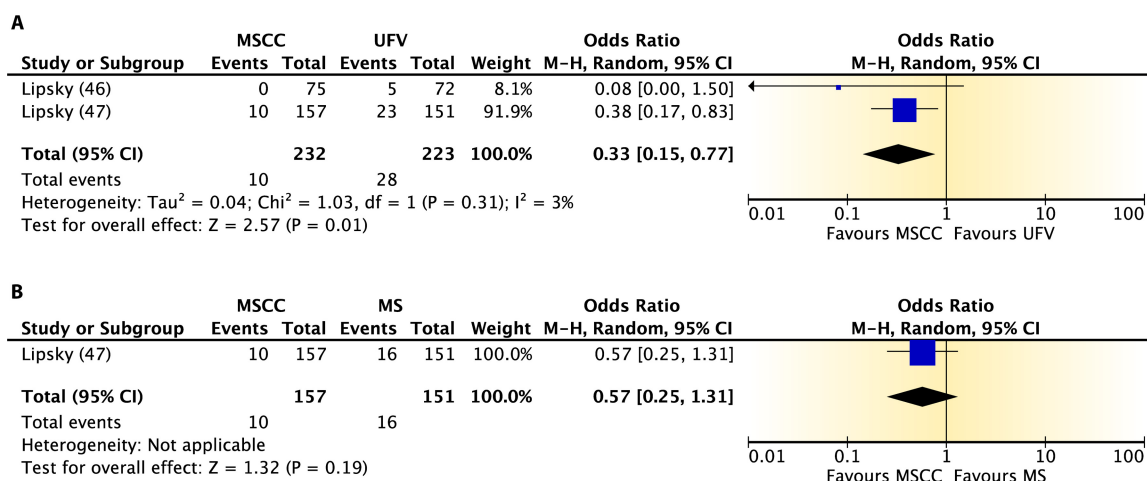
FIG 4 Difference in contamination levels between midstream collection with cleansing (MSCC) and first-void urine collection without cleansing (UFV) (A) or midstream collection without cleansing (MS) (B) for men.

TABLE 12 Diagnostic accuracy of MSCC compared to SPA or CATH for the diagnosis of UTI in men[a]

Study (reference)	Reference standard(s)	Positivity threshold for reference test (no. of CFU/ml)	Positivity threshold for index test (no. of CFU/ml)	% sensitivity (95% CI)	% specificity (95% CI)
Lipsky et al. (46)	SPA/CATH	≥10^4	≥10^4	82 (67–92)	100 (92–100)
Deresinski and Perkash (48)	SPA	>10^4	>10^4	100 (92–100)	100 (87–100)

[a] MSCC, midstream clean-catch collection; SPA, suprapubic aspiration; CATH, straight catheterization. The quality rating of both studies was fair, and the index text for both was MSCC.

of the studies covered in the review predate the regionalization and other significant restructuring of the delivery of microbiological services in the United States, which portend increased variation in collection, storage, and preservation methods. More studies are needed to support recommendations for specific populations, e.g., nursing facility residents needing skilled care. Important also is the growing need for documentation of health outcomes and cost-effectiveness of current practices through the implementation of well-designed, system-wide quality improvement studies. Of equal importance is the need to expand (and

TABLE 13 Body-of-evidence table for clinical question 7, namely, "what is the difference in contamination between MSCC, MS, SUB, and diaper collection from children?"[a]

Study (reference), quality rating	Population and samples	Setting	Time period	Results
Karacan et al. (53), fair	1,067 children aged 0–16 yr suspected of having UTIs. Urine was collected by either SUB ($n = 517$), MSCC ($n = 532$), CATH ($n = 7$), or SPA ($n = 11$). Some SUB and MSCC samples were collected by parents. Within 30 min of collection, all specimens were sent to the laboratory for culture.	Dr. Sami Ulus Children's Hospital, Ankara, Turkey	2 mo	Contamination was defined as those specimens interpreted as "contaminated" by the laboratory. 76 (14.3%) of 532 MSCC samples were contaminated, compared with 227 (43.9%) of 517 SUB samples.
Alam et al. (49), good	191 children ≤3 yr without known UTIs. Urine specimens were obtained by 3 different methods: MSCC, DIAPER, and SUB. 534 urine samples were obtained from the 191 children. Urine was cultured within 2 h of arriving at the laboratory.	Institute of Maternal and Child Health of Pernambuco, Recife, Brazil	2 mo	Contamination was defined as mixed growth or any growth of <10^5 CFU/ml. All specimens with SG of a single species of >10^5 CFU/ml were excluded. 23 (14.7%) of 156 MSCC specimens were contaminated. 45 (26.6%) of 169 SUB specimens were contaminated. 49 (29.0%) of 169 DIAPER specimens were contaminated.
Macfarlane et al. (54), fair	88 children of <2 yr with various febrile illnesses had 56 reliable urine samples collected by DIAPER. 34 children of the same age and from the same ward had SUB samples collected. 240 MSCC samples were also included in the study (no. of children not reported).	Departments of Child Health and Microbiology, Rotherham General Hospital, Rotherham, United Kingdom	3 mo	Contamination was defined as mixed growth at any concn. 34 (60.7%) of 56 DIAPER specimens were contaminated. 23 (67.6%) of 34 SUB specimens were contaminated. 64 (26.7%) of 240 MSCC specimens were contaminated.
Ahmad et al. (55), fair	45 infants aged 1–23 mo. Urine specimens were collected by DIAPER or SUB.	Departments of Child Health and Microbiology, Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom	Not given	Contamination was defined as mixed growth or any growth of <10^5 CFU/ml. 17 (37.8%) of 45 SUB specimens were contaminated. 10 (22.2%) of 45 DIAPER specimens were contaminated.
Vaillancourt et al. (50), good	350 toilet-trained children aged 2–18 yr cluster-randomized by week to urine collection groups. 350 urine specimens were obtained by either MSCC or MS with cleansing of the perineum with soap before midstream collection.	Montreal Children's Hospital, Montreal, Canada	11 mo	Contamination was defined as mixed growth of 2 or more organisms or any growth of <10^5 CFU/ml. 14 (7.8%) of 179 MSCC specimens were contaminated. 41 (23.9%) of 171 MS specimens were contaminated.
Tosif et al. (56), fair	599 children of <2 yr of age (retrospective observational study of urine culture results). Urine specimens were obtained by MSCC, SPA, CATH, or SUB. Contamination rates were stratified according to the method of collection.	Royal Children's Hospital, Melbourne, Australia	1 mo	Contamination was defined as growth of 2 or more organisms with colony counts of ≥10^5 CFU/ml. 52 of 202 MSCC specimens were contaminated, and 6 of 13 SUB specimens were contaminated.

[a] SUB, sterile urine bag collection; MSCC, midstream clean-catch collection; CATH, catheterization; SPA, suprapubic aspiration; DIAPER, diaper collection; SG, significant growth.

TABLE 14 Body-of-evidence table for clinical question 8, namely, "what is the accuracy of midstream clean-catch, sterile urine bag or diaper collection compared with suprapubic aspiration or catheterization for the diagnosis of UTI in children?"[a]

Study (reference), quality rating	Population and samples	Setting(s)	Time period	Results
Morton and Lawande (57), fair	Children aged <10 yr of age suspected of having UTIs. 287 urine specimens were obtained by SPA, and 175 were obtained by MSCC. For only 51 children, MSCC results were compared with SPA results. All samples were refrigerated after collection for a maximum of 12 h until transfer to a laboratory and culture.	Pediatric Department of Ahmadu Bello University Teaching Hospital, Zaria, northern Nigeria	Not given	SG was defined as any growth in SPA specimens and any growth of $>10^5$ CFU/ml in MSCC specimens. All other growth was considered NSG. MSCC had a sensitivity of 100% and a specificity of 100% if one assumes that the 5 specimens of SG collected by MSCC were the same 5 specimens of SG collected by SPA.
Pylkkanen et al. (58), fair	477 patients (164 infants and 313 children) suspected of having UTIs Urine specimens were obtained by SPA and SUB from infants ($n = 164$) or by MSCC from children ($n = 313$). Culture was performed immediately after collection.	Outpatient clinic at the Children's Hospital, University of Helsinki, Finland	Not given	SG was defined as consistent growth on both blood agar and Uricult dipslides for SPA specimens and any growth of $\geq10^5$ CFU/ml for MSCC specimens. Combining symptomatic and asymptomatic patients, MSCC had a sensitivity of 83.9% and a specificity of 67.7%.
Aronson et al. (59), fair	120 patients. Cleanly voided urine samples were collected simultaneously with or immediately after SPA. Samples were collected by SUB from infants of <18 mo ($n = 86$) and by MSCC from children 3–12 yr of age ($n = 34$). Immediately after collection, samples were chilled and transported to a laboratory for culture.	Department of Pediatrics, University Hospital, Lund, Sweden	Not given	SG was defined as any growth of $\geq10^2$ CFU/ml for SPA specimens and any growth of $>10^5$ for MSCC specimens. All other growth was considered NSG. MSCC had a sensitivity of 71.4% and a specificity of 80.0%. SUB had a sensitivity of 83.3% and a specificity of 56.5%.
Hardy et al. (60), fair	30 patients aged 0 to 3 yr of age. Urine was obtained by SUB, MSCC, and SPA. The 3 specimens were collected within 1 to 6 h of each other and not always in the same order. Specimens were collected in sterile plastic bottles and transported immediately for culture or refrigerated until transport later that day.	Department of Pediatrics and Department of Medical Microbiology, The Royal Free Hospital, London	Not given	SG was defined as $\geq10^5$ CFU/ml of a single species for MSCC, SUB, and SPA specimens. MSCC had a sensitivity of 25.0% and a specificity of 96.2%. SUB had a sensitivity of 50.0% and a specificity of 92.3%.
Ramage et al. (51), good	49 infants of <24 mo of age suspected of having UTIs. 58 paired urine cultures were obtained by MSCC and SPA.	Royal Hospital for Sick Children, Glasgow, Scotland	Not given	SG was defined as any growth in SPA specimens and $>10^5$ CFU/ml of a single species in MSCC specimens. MSCC had a sensitivity of 88.9% and a specificity of 95.0%.
Cohen et al. (61), fair	38 infants of <2 yr of age who presented with fever with no obvious cause. Urine was collected either by SPA/CATH or by DIAPER. All urine was sent within 1 h for culture.	Department of Pediatrics, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel	Not given	SG was defined as all growth of $>10^5$ CFU/ml of a single species in DIAPER or SPA/CATH specimens. All other growth was considered NSG. DIAPER had a sensitivity of 100% and a specificity of 94%.
Grisaru-Soen et al. (52), good	50 infants 0–18 mo of age suspected of having UTIs or neonatal fever indicating urine culture. Urine was collected by SPA and by SUB.	The Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel	Not given	SG was defined as "pure growth" in SPA or SUB specimens. All other growth was considered NSG. SUB had a sensitivity of 100% and a specificity of 83.7%.
Etoubleau et al. (62), fair	192 non-toilet-trained children of <3 yr of age from 2 emergency departments. Urine was obtained by SUB. All children had a positive microscopic examination that prompted collection by CATH.	Department of Pediatrics, Limoges University Hospital, Limoges, France, and Hospital Intercommunal, Poissy, France	Not given	SG was defined as $\geq10^3$ CFU/ml of a single species in CATH specimens and $\geq10^5$ CFU/ml of a single species in SUB specimens. All other growth was considered NSG. SUB had a sensitivity of 83.3% and a specificity of 91.1%.

[a] SUB, sterile urine bag collection; MSCC, midstream clean-catch collection; CATH, catheterization; SPA, suprapubic aspiration; DIAPER, collection from disposable diapers; SG, significant growth; NSG, nonsignificant growth.
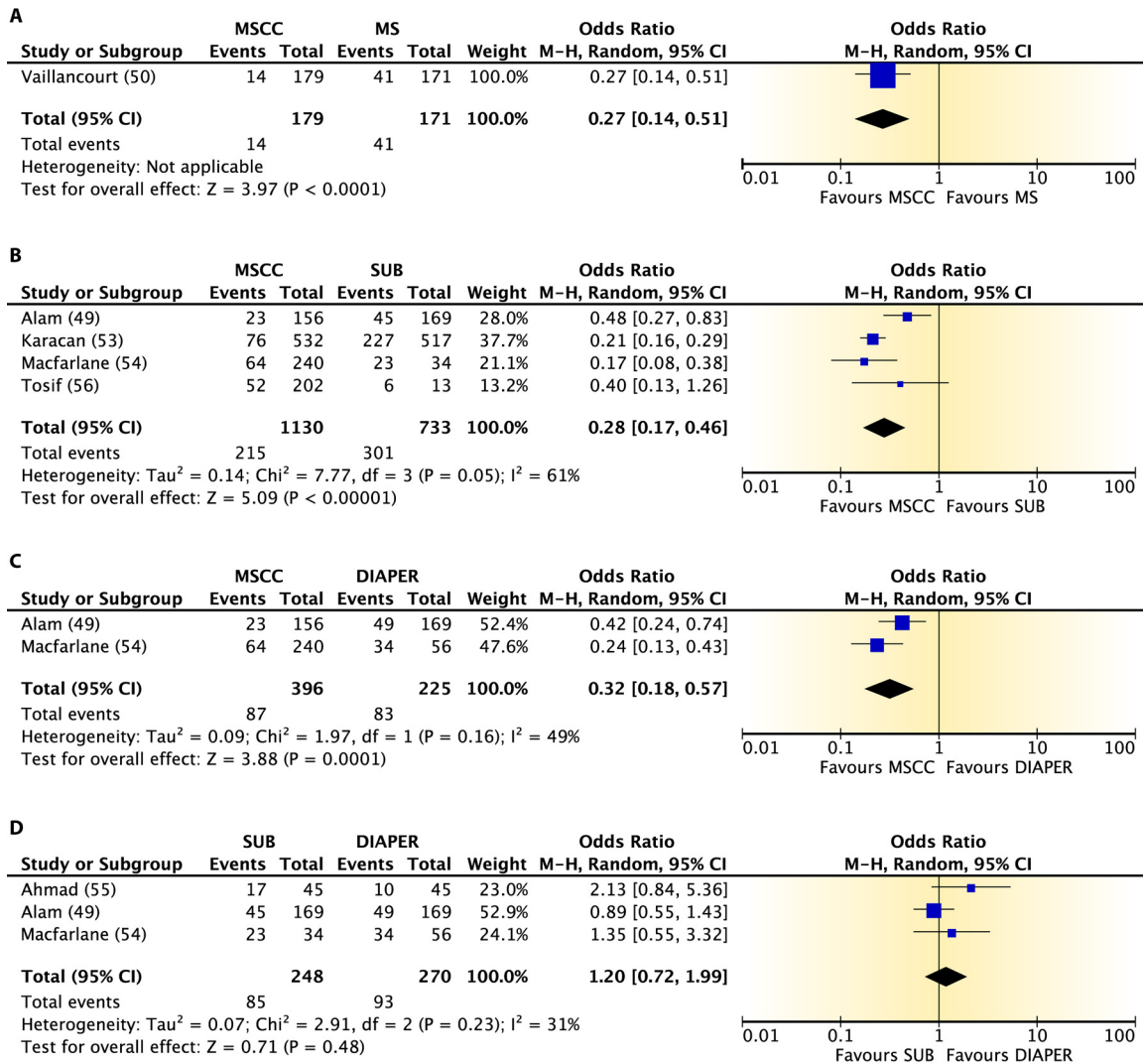
FIG 5 Comparative differences in contamination levels between midstream collection with cleansing (MSCC) and midstream collection without cleansing (MS) (A), midstream collection with cleansing and sterile urine bag collection (SUB) (B), midstream collection with cleansing and diaper collection (C), and sterile urine bag collection and diaper collection (D) for infants and children.

communicate) the literature on diagnostic testing algorithms to include nonanalytic variables, such as those measured in the included studies reported here. This systematic review provides a current and substantial literature base from which to begin investigations not only to address these gaps in current knowledge related to the effects of preanalytic factors on urine culture but also to validate these best-practice recommendations in additional settings and populations.

Associated Harms

Methods of collecting, storing, and preserving urine specimens for the diagnosis of urinary tract infections have a critical influence on culture results. Poorly collected or preserved specimens can become easily contaminated with perineal, vaginal, and periurethral flora, which can inhibit or obscure the presence of true urinary tract pathogens. Conversely, the use of high concentrations of boric acid as a preservative has been known to inhibit urinary pathogens such as *Escherichia coli* and *Klebsiella pneumoniae* (65).

Midstream urine collection may be the preferred choice for collection for most patients; however, there are patient populations and clinical scenarios where a more invasive method of collection is preferred (63). All of these issues can produce incorrect culture results, misdiagnosis, especially in asymptomatic patients, poor patient management, including the use of inappropriate or ineffective antibiotics, and potentially more complicated urinary tract infection in the long term (2, 3).

Additional Benefits

Urine specimens that are appropriately collected, transported, stored, and preserved benefit patients by producing more-accurate culture results. In addition, such practices can provide benefit to the laboratory by allowing technologists to focus on the work-up of clinically significant pathogens rather than the growth of contaminants. Urine cultures are often a major component of the typical clinical microbiology workload (18); therefore, minimizing the processing of poor-quality urine specimens can allow

MSCC vs. SPA in children

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Hardy (60)	1	1	3	25	0.25 [0.01, 0.81]	0.96 [0.80, 1.00]
Aronson (59)	10	4	4	16	0.71 [0.42, 0.92]	0.80 [0.56, 0.94]
Pylkkanen (58)	161	9	38	64	0.81 [0.75, 0.86]	0.88 [0.78, 0.94]
Ramage (51)	16	2	2	38	0.89 [0.65, 0.99]	0.95 [0.83, 0.99]
Morton (57)	5	0	0	46	1.00 [0.48, 1.00]	1.00 [0.92, 1.00]
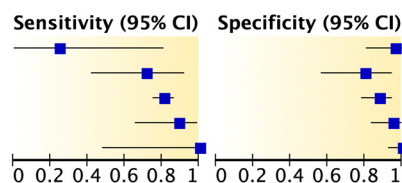
DIAPER vs. SPA/CATH in children

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Cohen (61)	5	2	0	29	1.00 [0.48, 1.00]	0.94 [0.79, 0.99]
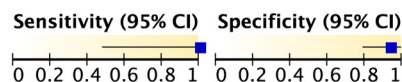
SUB vs. SPA/CATH in children

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Hardy (60)	2	2	2	24	0.50 [0.07, 0.93]	0.92 [0.75, 0.99]
Aronson (59)	20	27	4	35	0.83 [0.63, 0.95]	0.56 [0.43, 0.69]
Etoubleau (62)	85	8	17	82	0.83 [0.75, 0.90]	0.91 [0.83, 0.96]
Grisaru–Soen (52)	6	8	1	35	0.86 [0.42, 1.00]	0.81 [0.67, 0.92]
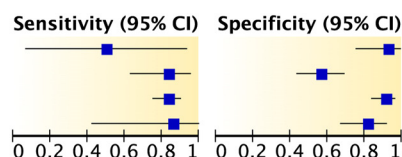
FIG 6 Accuracy of midstream clean-catch (MSCC), sterile urine bag (SUB), or diaper collection compared with that of suprapubic aspiration (SPA) or catheterization (CATH) for the diagnosis of urinary tract infection in children. TP, true positives; FP, false positives; FN, false negatives; TN, true negatives.

the laboratory to focus its resources in a more cost-effective manner (22).

Economic Evaluation

Proper attention to the preanalytic phase of urine cultures should decrease the number of contaminated urine specimens processed by the laboratory. It may also decrease the time it takes for microorganism identification and susceptibility testing of pathogens in infected patients by reducing the number of recollected specimens. Both of these scenarios would likely reduce health care costs for both patients and institutions by reducing the time to appropriate targeted therapy and by making more-effective use of laboratory and hospital resources. However, no economic evaluation analyses were found for the studies covered in this review.

Feasibility of Implementation

The methods of specimen collection and handling covered in this review are feasible in all settings and patient populations and are, in fact, commonly used in most medical environments today. There are data showing the benefit of either refrigerating or chemically preserving urine samples that are not immediately processed (28–37). Furthermore, midstream urine collection, with or without cleansing, is common practice for most clinical settings and patient populations (38–62). For facilities that have historically paid little attention to the preanalytic aspects of urine culture, there may be some resistance on the part of patients and staff that is typically associated with quality improvement initiatives. Appropriate education regarding the proper collection of urine specimens may be needed for both patients and health care workers. The additional costs associated with chemical preservatives, such as boric acid, would also need to be budgeted and justified.

Future Research Needs

The findings of this systematic review highlight the lack of recent high-quality studies that evaluate components of the preanalytical phase of urine culture. For example, the relative paucity of rigorous studies evaluating methods of storage and chemical preservation of urine specimens is troublesome considering the widespread use of these practices in many laboratories and a general consensus among microbiologists as to their benefit. A large number of the studies suffered from small sample sizes, limiting the precision of the results and reducing the likelihood that findings are applicable across a larger population. Studies also used various or unclear definitions of contamination or positivity thresholds, making meta-analysis or qualitative summary analysis problematic. Studies further suffered from missing data. For example, most studies were cross-sectional or otherwise observational (without randomization) in design, but many, particularly those retrospective in nature, did not obtain or report the results of samples from all patients obtained by all collection methods under study. These inconsistencies lead to significantly uneven comparison groups in some cases.

Future studies should strive for statistically sufficient sample sizes, use common and clearly defined definitions of contamination and thresholds for positivity, and report accuracy results across several common positivity thresholds to aid subsequent meta-analysis. An example is the number of positive/negative samples calculated if reviewers use a threshold of $>10^4$ versus $>10^5$ CFU per ml of urine. Studies should also be more rigorous in design, include more randomized controlled trials, and ensure paired sampling when possible in prospective or cross-sectional studies. Moreover, for all methods under evaluation, patients should have urine collected within a reasonable time frame, and the time delay between collection and culture should be clearly reported.

Finally, future studies should strive to obtain data on down-

TABLE 15 Summary of findings of our evidence-based review of urine culture preanalytics

Quality issue	Body of evidence quality	Body of evidence strength	Recommended	Not recommended	No recommendation for or against due to insufficient evidence
Delayed processing of urine stored at room temp vs refrigeration vs boric acid	Fair	Low			×
Midstream urine collection from women with cleansing	Good/fair	High	×		
Midstream urine collection from women without cleansing	Fair	Low			×
Midstream urine collection from women vs collection by straight catheterization	Fair/good	Low			×
Midstream urine collection from men with cleansing	Good/fair	High	×		
Midstream urine collection from men without cleansing	Fair	Low			×
First-void urine collection from men	Good/fair	High		×	
Midstream urine collection from men vs collection by straight catheterization or suprapubic aspiration	Fair	Low			×
Midstream urine collection from children with cleansing	Fair/good	High	×		
Midstream urine collection from children without cleansing	Fair/good	High		×	
Urine collection from children with sterile urine bags and/or from diapers	Fair/good	High		×	
Midstream urine collection from children vs collection by straight catheterization or suprapubic aspiration	Fair/good	Low			×

stream patient-centered outcomes as influenced by different methods of collection, preservation, or storage of urine that are under evaluation. This broader measurement pool includes system-oriented outcomes, such as time to targeted therapy, cost of antibiotic use, number of UTI discharge diagnoses, or number of *Clostridium difficile* cases avoided, such that the direct or indirect impact of implementing a particular preanalytic practice can be measured at the patient and organizational level. Information provided in Appendix 2 can be used as a guide to organize and plan studies as well as collect data for any quality improvement project that examines preanalytical practices associated with urine cultures.

Limitations

The LMBP systematic review method is compatible with other standards of practice for systematic reviews (24) but includes some unique elements, such as the rating of study quality. Rating study quality is based on attributes such as facility description, study setting and design, practice description, outcome measures, and results. How studies are ultimately considered for inclusion in the review depends on consensus assessments that may be influenced by such things as a rater's professional background and experience. Indeed, several on-topic studies were excluded because of limitations identified during quality evaluation, mostly related to poor reporting of important study, practice, or outcome details. This is likely somewhat explained by the publication dates of many of the studies, with several of both the excluded and included studies having been published in the late 1960s. As is the case with most systematic reviews, attempts were made to limit publication bias by soliciting unpublished data; however, no unpublished data were submitted. Moreover, restricting the review to English-language studies may also introduce bias.

Outside the limitations of the review process, there were a number of limitations in this review that affected the ability to draw firm conclusions and make recommendations. Most of these limitations were addressed above in the context of future research, but additional limitations will be discussed here. The study settings varied across included studies. Both inpatient and outpatient settings were included, and the specific setting examined in each study— emergency department, adolescent clinic, obstetric clinic, etc.—may not be generalizable to other settings. Some settings may be better equipped to perform certain collection methods or to educate patients or parents on how to perform certain collection methods. Similarly, the patient populations under study varied. Some studies included healthy asymptomatic patients, while others included patients with more-severe conditions, such as spinal cord injury patients. This too might affect the generalizability of results. Within the body of evidence for children, studies often included patients ranging in age from 0 to 16 years. Unfortunately, there were not enough data available to properly stratify children, such as infants, into smaller age groups, and because of this, results may not be generalizable to patients of a specific age. Finally, as discussed above, an important limitation was the variability in positivity thresholds and definitions of contamination used across studies. Although several guidelines have been developed to address definitions of significant bacteriuria for culture (18, 63, 66–68), these guidelines are not always consistent, and this lack of consistency is reflected in the studies and results reported in this review.

CONCLUSIONS AND RECOMMENDATIONS

A summary of the findings of this evidence-based review of urine culture preanalytics can be found in Table 15. Conclusions are categorized as "recommended," "not recommended," or "no recommendation for or against" and refer to studies of urine collected by noninvasive methods:

1. No recommendation for or against is made for delayed processing of urine that is stored at room temperature, refrig-

erated, or preserved in boric acid due to insufficient evidence. Data from nine studies receiving a "fair" quality rating suggest that both refrigeration and boric acid adequately preserve urine specimens for up to 24 h prior to their being processed. Furthermore, data from three studies receiving a "fair" quality rating suggest that urine held at room temperature for more than 4 h should not be processed due to overgrowth of both clinically significant and contaminating flora. However, because the overall strength of the body of evidence was rated as low, no recommendation for or against can be made due to insufficient evidence. This does not preclude the use of refrigeration or chemical preservatives in clinical practice. It does indicate, however, that more systematic studies evaluating the utility of these measures are needed.

2. If noninvasive collection is being considered for women, midstream collection with cleansing is recommended, but no recommendation for or against is made for midstream collection without cleansing due to insufficient evidence. Data from two studies, including one randomized controlled trial receiving a "good" quality rating and three studies receiving a "fair" quality rating, show that contamination rates are similar between specimens obtained by midstream collection with and without cleansing. The overall strength of this body of evidence was rated as high. However, whether midstream collection can be routinely used in place of straight catheterization is unclear. Data from three studies, two with a quality rating of "fair" and one with a rating of "good," suggest that clean-catch midstream urine collection is highly accurate for diagnosing urinary tract infections in women; however, because the overall strength of this body of evidence was rated as low, no recommendation for or against can be made.

3. If noninvasive collection is being considered for men, midstream collection with cleansing is recommended and collection of first-void urine is not recommended. No recommendation for or against is made for collection of midstream urine without cleansing due to insufficient evidence. Data from two studies, one with a quality rating of "good" and one with a rating of "fair," found a large reduction in the level of contamination in specimens obtained by midstream collection with cleansing compared to the level of contamination after collection of first-void urine. This body of evidence was rated as high. Although data from one study rated as "good" quality found no difference in contamination between midstream urine collected with and that collected without cleansing, imprecision was large due to the small event size, and no recommendation can be made as to which method is superior. Whether midstream collection can be used routinely in place of straight catheterization or suprapubic aspiration is unclear. Data from two studies receiving a "fair" quality rating suggest that midstream collection with cleansing is highly accurate for the diagnosis of urinary tract infections in men; however, because the overall strength of the body of evidence was rated as low, no recommendation for or against can be made.

4. If noninvasive collection is being considered for children,

midstream collection with cleansing is recommended and collection with sterile urine bags, from diapers, or midstream without cleansing is not recommended. Data from six studies, two with a quality rating of "good" and four rated as "fair," found large reductions in contamination in midstream clean-catch urine specimens compared to contamination after other noninvasive methods of collection. This body of evidence was rated as high. Whether midstream collection with cleansing can be routinely used in place of catheterization or suprapubic aspiration is unclear. Data from eight studies, two with a quality rating of "good" and six rated as "fair," suggest that midstream collection with cleansing is accurate for the diagnosis of urinary tract infections in infants and children and that midstream collection with cleansing has higher average accuracy than sterile urine bag collection (data for diaper collection was lacking). However, the overall strength of evidence was low, as multivariate modeling could not be performed; thus, no recommendation for or against can be made due to insufficient evidence.

APPENDIX 1

The members of the Laboratory Medicine Best Practices Workgroup from 2012 to 2014 were as follows: Robert H. Christenson, University of Maryland Medical Center, Baltimore, MD; John Fontanesi, UC—San Diego Medical School, La Jolla, CA; Julie Gayken, Regions Hospital, St. Paul, MN; James Nichols, Vanderbilt University Medical Center, Nashville, TN; Mary Nix, Agency for Healthcare Research and Quality, Rockville, MD; Milenko Tanasijevic, Brigham and Women's Hospital, Boston, MA; Sharon Geaghan, Stanford, University School of Medicine, Stanford, CA; Christine Litwin, Georgia Health Sciences University, Augusta, GA; Thomas Lorey, Permanente Medical Group Regional Laboratory, Richmond, CA; Bernadette Mazurek Melnyk, The Ohio State University, Columbus, OH; Anton Piskac, Methodist Health System, Omaha, NE; Jennifer Rhamy, St. Mary's Hospital, Oakbrook Terrace, IL; Christopher Lee Roy, Brigham and Women's Hospital, Boston, MA; and Melissa Singer (*ex officio*), Centers for Medicare and Medicaid Services, Baltimore, MD.

APPENDIX 2

LMBP Evaluation of Preanalytic Practices for the Contamination and Diagnostic Accuracy of Urine Cultures

Suggested guidance for future studies. This review identified and rated practices associated with the collection, preservation, and storage of urine specimens for culture and assessed the impact of these preanalytic practices on the diagnostic accuracy of urine culture microbiology. In theory, the design, description, methods, data collection, and analysis for any study should be written and documented so that other investigators can reproduce exactly the same study in their laboratory, with their results validating or verifying those of the original study. The following organizational plan with instructions can be used as a guide for quality improvement project design, implementation, and evaluation of preanalytic practices associated with urine cultures. Figure A1 shows a form for use in collecting data for any QI project that examines preanalytical practices associated with urine cultures.

Background Information	QI Project/Study	QI Practice	Outcome Measures	Results/Findings

LMBP Topic: **Pre-analytic Practices for Urine Cultures**
 	
1. Problem/quality issue description
A. Practices
i. Collection
☐ Midstream clean catch vs. midstream w/o cleansing
☐ Midstream clean catch vs. straight catheter/suprapubic aspiration
☐ Midstream w/o cleansing vs. straight catheter/suprapubic aspiration
☐ Midstream w or w/o cleansing vs. first void
☐ Midstream w or w/o cleansing vs. diaper collection/sterile urine bag
☐ Other _____
ii. Storage and Preservation
☐Refrigeration
☐Boric acid
☐Glycerol boric acid
☐Sorbitol boric acid
☐Room temperature
☐Other _____
iii. Transport Time _____
iv. In lab processing time _____
 	
B. Population and age range
☐Male
☐Female
☐Children
☐Infants/neonates
☐Other _____
 	
C. Collection personnel
☐ Nurse
☐ Nurse aide
☐ Physician
☐ Specialized urine collection team
☐ Lab technologist/technician
☐ Other _____
 	
2. Submitter(s) and org. affiliations
Name (s)_____
Organization_____
Phone/email_____
 	
3. Funding sources
☐ In-house
☐ Manufacturer
☐ Grant/Contract
☐ None
☐ Other _____
	4. QI project study design/type
	☐ Pre-post implementation
	☐ Split implementation (multiple sites)
	☐ Case - control
	☐ Cross-sectional
	☐ Cohort
	☐ Randomized assignment
	☐ Other
	
	Please describe checked design:
	_____
	_____
	
	5. Facility description
	☐ Hospital (# Beds_____)
	  ☐ Community
	  ☐ University based
	  ☐ Children's hospital
	  ☐ VA hospital
	  ☐ For-profit healthcare group
	  ☐ Other _____
	☐ Outpatient clinic
	☐ Pediatric clinic
	☐ Other _____
	
	6. QI project/study setting
	  ☐ Inpatient
	  ☐ Outpatient
	  ☐ Emergency Department
	☐ Pediatrics Unit
	☐ NICU
	☐ Other _____
	_____
	
	7. Overall project/study time frame (include pilot projects)
	_____ Start: _____ / End: _____
	Describe:
	_____
	_____
	
	8. Study sample/population (size and description) describe if different between compared practices.
	_____
	_____
	_____
	_____
		9. Describe usual practice
		_____
		_____
		_____
		_____
		_____
		_____
		_____
		
		10. Describe alternate/intervention practice
		_____
		_____
		_____
		_____
		_____
		_____
		
		11. Intervention duration dates (pilot, pre/post, etc.)
		Phase _____ Start: _____ / End: _____
		Phase _____ Start: _____ / End: _____
		Phase _____ Start: _____ / End: _____
		Describe:
		_____
		_____
		_____
		
		12. Resource requirements/costs:
		A. Staff / Training
		_____
		_____
		_____
		_____
		
		B. Equipment/Supplies
		_____
		_____
		_____
		
		C. Other
		_____
		_____
		_____
		_____
			13. Outcome measure(s)
			☐ Changes in urine culture colony counts
			☐ Contamination – How measured?
			_____
			_____
			☐ Diagnostic accuracy
			☐ Number of organism IDs and ASTs
			☐ Other additional laboratory tests
			☐ Antibiotic use
			☐ Repeat urine collection
			☐ Number of UTI discharge diagnoses
			☐ Length of stay
			☐ Other _____
			
			14. Recording method (how data was collected / note any differences between standard and test practices)
			☐ Logs of occurrence
			☐ Incident / adverse events reports
			☐ Audit – direct observation
			☐ Electronic information system monitoring
			☐ Other
			Describe each checked method and which practice it refers to
			_____
			_____
			_____
			_____
			
			15. Potential sources of bias
			☐ Selection bias
			☐ Performance bias
			☐ Detection bias
			☐ Confounding
			☐ Reporting bias
			☐ Other _____
			_____
			_____
			_____
				16. Results/findings as (related to study design/outcome measure)
				_____
				_____
				_____
				
				17. Data analysis – statistics
				☐ Odds ratios
				☐ Relative risk
				☐ Accuracy or agreement related statistics (sensitivity, specificity, PPV, NPV, dOR kappa etc.)
				☐ ROCs (AUC)
				☐ Other
				Describe each checked method:
				_____
				_____
				_____
				
				18. Data analysis-significance
				☐ F-Test
				☐ T-Test
				☐ Fischer Exact
				☐ Chi-square
				☐ Other
				Describe each checked method
				_____
				_____
				_____
				
				19. Barriers to implementation (an event outside of study that impacts study results)
				_____
				_____
				_____
				
				20. Study dates completed/submitted
				Completed: _____
				
				Reported on Web? (Where? Date?)

FIG A1 Form for use in collecting data for any QI project that examines preanalytical practices associated with urine cultures.

Background Information

1. Problem/quality issue description.
   A. Practices and equipment. Describe what preanalytic practices associated with the collection and preservation of urine for culture were studied and exactly how specimens were collected. Include examples of educational material handed to patients or displayed on walls in areas where patients were seen.
      i. Collection. Indicate whether specimens were obtained by midstream clean-catch collection versus midstream collection without cleansing, midstream clean-catch collection versus straight catheter collection and/or suprapubic aspiration, midstream collection without cleansing versus straight catheter collection and/or suprapubic aspiration, midstream collection with or without cleansing versus first-void urine collection, midstream collection with or without cleansing versus diaper collection and/or sterile urine bag collection, or other means.
      ii. Preservation/storage/transport. Include the time from collection of the specimen to the addition of preservative and how long it took the specimen to reach the lab after collection, as well as how long it took from receipt in the lab to setup of culture. Indicate whether boric acid, glycerol boric acid, or sorbitol boric acid was used as a preservative, whether the specimen was stored in a refrigerator or at room temperature, and any other relevant preservation or storage information.
   B. Population under study and age ranges. Include physical differences which may affect the collection of the specimen, such as physical disability, the presence of a foreskin in males, the presence of diapers, etc. With infants and neonates, consider tighter age ranges, such as 0 to 2, 2 to 4, etc.
   C. Collection personnel. Indicate whether the specimen was collected by a nurse, nurse's aide, physician, specialized urine collection team, lab technologist or technician, or other staff member.

2. Submitter(s) and organization affiliation. For additional

questions concerning the quality improvement (QI) study, contact information is required.

3. Funding source(s). Refer to the chart in Fig. A1. Check all boxes that apply.

QI Project/Study

4. QI project study design/type. With similar patient populations, describe the methods/approaches used for your project with regard to age, sex, ethnicity, and/or diagnosis to limit bias.
   A. Pre- and postimplementation. Observations are made before and after the implementation of an intervention.
   B. Split implementation design. Indicate whether multiple sites were used to conduct the QI study.
   C. Case-control study. Indicate whether the study compared subjects with a specific outcome of interest (cases) with subjects from the same source population but without that outcome (controls) to examine the association between the outcome and prior exposure (for which there was an intervention).
   D. Cross-sectional associations. Collect information on interventions (past or present) and current health outcomes, i.e., those that are restricted to health states, for a group of people at a particular point in time, to examine associations between the outcomes and exposure to interventions.
   E. Cohort. A defined group of people (the cohort) is followed over time to examine associations between different interventions received and subsequent outcomes.
   F. Randomized assignment. Patients are randomly selected to receive the intervention practice or the comparator practice.
   G. Other study design used in this QI project. Describe the study design selected.

5. Facility description. Provide a complete description of the facility type and the number of beds (or patients if the facility is an outpatient facility).

6. Study setting. Select the unit(s) within the facility where the practice was implemented, e.g., inpatient, outpatient, emergency department, pediatric unit, neonatal intensive-care unit, or other.

7. Overall project/study time frame. Record the start and end dates for the new and usual practices; if pilot testing was conducted, include start/end dates for pilot testing of the new practice. Note that this is not the same as the QI study period but rather the dates during which these practices were being used in the unit(s) in which the study was done. Put "NA" If some dates are not available.

8. Sampling strategy. The sample size is the number of patients/observations used for the usual (current) practice and the alternate practice. Use the largest available sample size at each time of measurement. For results to be reliable, the implemented practice should be the only thing affecting the results. It is the largest sample size available that represents only the results of the usual practice and the largest sample size that represents only the results of the alternate practice. Describe your sample set (tests, patient specimens, patients, or type of patient specimens) and the sample size (example: prior to [usual] practice [15,000 patient speci-

mens tested] and after [alternate] practice [13,200 patient specimens tested]).

Optimally, a power analysis should be performed prior to confirmation of sample size. Statistical power is the probability of concluding that there is a difference when there is, in fact, a difference between your standard method and your new method (i.e., the probability that your study will detect a difference, given that one truly exists). An example of a nomogram for sample size calculation can be found in reference 69.

Statistical power is the probability of concluding that there is a true and significant difference between your comparator and intervention, thus minimizing type I and type II errors (sensitivity and specificity).

For sample description, refer to the following list.

A. Random sampling. Subjects (patients) are selected for study inclusion using a formal random selection process applied to the census.

B. Convenience sampling. Some subset of the census is selected since it is easy to access. For example, using only data from records of patients whom you can easily reach would be a convenience sample.

C. Census sampling. All participants within a specified time period or location are used in census sampling.

D. Other. Describe whether you are using a different sampling method. If you are using anything other than random sampling, convenience sampling, or census sampling, you need a statistician to identify sampling strategy.

QI Practice

9. Describe the original (usual) practice. Describe the original (usual) practice(s) that will be compared to the new practice/policy/technology implemented.

10. Describe the alternate/intervention (new) practice. Describe the new practice/policy/technology, including the characteristics and components for ongoing day-to-day operations.

11. Intervention duration dates (pilot, pre/postintervention, etc.). Record the start and end dates for the pilot testing, usual practice, and new practice. This is the date on which the particular QI project was implemented and the date on which it ended. Note that a pilot test may not have been used in this study. There should be no gaps in the QI project data collection once it begins.

12. Resource requirements/costs. Describe the requirements and costs for starting and sustaining the new practice during the study. If this information is not available, list "not known." Do not list the cost of the practice that is currently being used to do patient testing.

Outcome Measures

13. Outcome measure(s). Describe how the impact of the practice was measured. Provide the specific outcome(s) and corresponding specifications/definitions used to assess or track the impact of the practices implemented. An example is a description of how urine culture contamination rates were affected or how they had an impact on the diagnostic accuracy of urine culture.

14. Recording method. Describe each method used to collect data and to which practice (usual or new) it refers.

15. Potential sources of bias. Bias is the tendency to produce results that depart systematically from the "true" results. Bias is any nonrandom factor in the conduct of a study that can influence the results of a study.

   A. Selection bias. Selection bias occurs when studies are conditioned on (that is, they differentially select for) common effects of the exposure and the outcome. Selection bias occurs after exposure and arises when the associations between exposure and outcome are different for those who participate and those who do not participate in a study (i.e., all those who are theoretically eligible). This bias includes inappropriate selection of controls in a case-control study, different losses to follow-up for groups being compared (attrition bias), incidence/prevalence bias, nonresponse bias, and inclusion or exclusion of specific groups for study.

   B. Performance bias. Performance bias includes systematic differences in the types of care provided to participants and protocol deviations. Examples include contamination of the control group with the exposure or intervention, unbalanced provision of additional interventions or cointerventions, a difference in cointerventions, and providers and participants not being adequately blind to the study results.

   C. Detection bias. Detection bias includes systematic differences in outcome assessments among groups being compared. Reasons for this bias include misclassification of the exposure, intervention, covariates, or outcomes because of varying definitions, timings, diagnostic thresholds, and memories of an event; assessors not being adequately blind to the study results; and faulty measurement techniques. Erroneous statistical analysis might also affect the validity of effect estimates.

   D. Confounding bias. Confounding bias is the presence of systematic differences between baseline characteristics of the groups that arise when patient prognostic characteristics, such as disease severity or comorbidity, influence both treatment source and outcomes. Confounders are the common cause for intervention and exposure; they occur before exposure. Confounding by indication can occur from self-selection of treatments or physician-directed selection of treatments.

   E. Reporting bias. Reporting bias is the presence of systematic differences between reported and unreported findings (e.g., differential reporting of outcomes or harms, incomplete reporting of study findings, and potential for bias in reporting through source of funding).

Results/Findings

16. Results/findings as related to study design/outcome measure. For each outcome provided, summarize the results/findings of the study/project related to the practice. Provide the total number of observations (samples) on which the results are based and statistical tests results, if a statistical analysis was performed. Include findings related to cost savings or shortened length of stay, if applicable.

17. Data analysis with regard to statistics. Describe the statistic used to measure the strength of association or the statistical measures of the performance of classification tests (e.g., sensitivity, specificity). Examples are as follows.

   A. With first-void urine collection, 10 urine samples are contaminated per 100 urine cultures performed (10% contamination rate).

   B. With midstream clean-catch urine collection, 3 urine samples are contaminated per 100 urine cultures performed (3% contamination rate).

   C. The odds ratio is 0.28 (3/10/97/90).

18. Data analysis with regard to significance. Describe the tests of significance. Include calculations of the statistical significance of a difference between the usual practice and the alternate practice on the measured outcomes listed in item 14.

19. Barriers to implementation. Describe any outside activities occurring at the same time as the project, such as staff changes or new policy, that may have influenced the results of the project. Describe any barriers that directly impacted the project.

20. Study dates completed or report submitted. Dates should include the date that the study was completed, the date it was reported (and where it was reported), and the date it was submitted to the LMBP initiative.

APPENDIX 3

Refer to Tables A1 to A4 for evidence summaries of results for storage (refrigeration versus room temperature) and boric acid preservation of urine, contamination and diagnostic accuracy of urine collected from women, contamination and diagnostic accuracy of urine collected from men, and contamination and diagnostic accuracy of urine collected from children.

TABLE A1 Evidence summary table for storage (refrigeration versus room temperature) and boric acid preservation of urine[a]

Bibliographic information	Study	Practice	Outcome measures	Results/findings
Authors: Hindman et al. (30) Title: Effect of Delay on the Culture of Urine Yr: 1976 Publication: J Clin Microbiol Affiliation: Hartford Hospital, Hartford, CT Funding: not reported	Design: nonrandomized comparison study Facility/setting: 300-bed teaching hospital Time period: not given Population/sample: 100 random specimens of urine submitted for culture and received by the laboratory within 2 h of the stated time of collection Comparator: not reported Study bias: sample size	Description: evaluation of the impact of time delay between collection and culture of urine samples Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: to determine the impact of delay in culturing urine specimens at 2 h, 4 h, and at 6 h postcollection Recording method: comparison of culture colony counts, and IDs between the different time periods	Type of findings: comparison Findings/effect size: No growth was observed in 53 of the specimens; 47 cultures were positive. Changes in counts exceeding 1 $\log_{10}$ or greater were observed in 15 of the specimens. Statistical significance/tests: Results/conclusion bias: delays of greater than 2 h in processing specimens may produce results which may cause errors in diagnosis
Total quality rating (10-pt. maximum): 6, fair	Total for study (3-pt. maximum): 2 (1 point subtracted due to small sample size)	Total for practice (2-pt. maximum): 1 (1 point was subtracted, as practice was not sufficiently described)	Total for outcome measures (2-pt. maximum): 2	Total for results/findings (3-pt. maximum): 1 (not powered to make large-scale recommendations)
Authors: Lum and Meers (31) Title: Boric Acid Converts Urine into an Effective Bacteriostatic Transport Medium Yr: 1989 Publication: J Infect Affiliations: National University of Singapore, Singapore, China Funding: not reported	Design: nonrandomized comparison study Facility/setting: academic medical center Time period: not reported Population/sample: 175 urine specimens collected from patients <2 yr old Comparator: nonpreserved urine samples Study bias: criteria for patient selection not given	Description: Samples were collected by midstream void and divided into an unpreserved portion and a portion placed in BA. Duration: 6 mo Training: nurses trained on how to split and preserve samples Staff/other resources: not reported Cost: not reported	Description: determination of the ability of boric acid to preserve the quantity and quality of microbial organisms in urine specimens Recording method: comparison of colony counts and organism significance in the 2 portions over 0, 4, 24, and 48 h	Type of findings: comparison Findings/effect size: Preserved samples showed fewer positive cultures over time than unpreserved samples; organism IDs were similar in both preserved and unpreserved samples. Statistical significance/tests: not reported Results/conclusion biases: limited patients enrolled and only those that were considered to have infections were enrolled
Total quality rating (10-pt. maximum): 6, fair	Total for study (3-pt. maximum): 1 (patient selection criteria not well defined)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 2	Total for results/findings (3-pt. maximum): 1 (no statistical analysis, trending data only; no discussion of inhibitory effect of borate at time zero)
Authors: Porter and Brodie (28) Title: Boric Acid Preservation of Urine Samples Yr: 1969 Publication: Br Med J Affiliations: City Hospital, Aberdeen, United Kingdom Funding: not reported	Design: cross-sectional Facility/setting: nonteaching hospital Time period: not reported Population/sample: 130 midstream urine samples collected in sterile tubes Comparator: unpreserved urine Study bias: no selection criteria indicated	Description: comparison of urine transport using midstream samples shipped without preservative at room temp, on ice, and with boric acid preservative Duration: not reported Training: not reported Staff/other resources: not reported Cost: 0.07 pence/specimen	Description: comparison of results of bacteriological culture and microscopic examination of urine samples transported over a distance either in a dip inoculum transport medium, an ice box, or BA preservative Recording method: results recorded as SG, DS, or NSG	Type of findings: comparison Findings/effect size: BA preserved the ice box-transported urine samples. Findings were similar. Increased numbers of bacteria were found in unpreserved urine compared to numbers in BA-preserved urine. Statistical significance/tests: not reported Results/conclusion bias: Specimens preserved in BA for >3 days gave misleading results
Total quality rating (10-pt. maximum): 6, fair	Total for study (3-pt. maximum): 2 (selection criteria not reported)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (measurements do not fully address goals of study)	Total for results/findings (3-pt. maximum): 1 (small sample size, lack of statistical analysis)
Authors: Gillespie et al. (29) Title: The Effect of Specimen Processing Delay on Borate Urine Preservation Yr: 1999 Publication: J Clin Pathol Affiliations: Western General Hospital, Edinburgh, United Kingdom Funding: not reported	Design: nonrandomized comparison Facility/setting: nonteaching hospital Time period: not reported Population/sample: consecutive samples of urine ($n = 1,175$) from 643 females and 149 males. 408 were excluded for 1 of the following reasons: the time of collection was unknown, they were catheter specimens, the vol was <10 ml, the age of the patient was <16 yr, or the reason was unstated. Comparator: not reported Study bias: none noted	Description: All samples were cultured within 8 h of specimen collection. Thereafter, every sample was kept at room temp overnight and then recultured the following morning. The specimens were processed by a semiquantitative method for the detection of bacteria. After overnight incubation, the no. of colonies growing was counted and the concn of organisms in the original sample was calculated. The culture plates resulting from immediate processing and those which had been cultured after overnight storage were read independently of each other. Duration: not reported Training: not reported. Staff/other resources: clinical microbiologist to document clinical indications for specimen referral. All samples were processed by the same Medical Laboratory Scientific Officer. Cost: not reported	Description: Bacterial culture results were recorded according to the colony counts observed. No growth, growth of <10^4 organisms/ml, and mixed growth at any concn were not regarded as significant. Growth of between 10^4 and 10^5 CFU/ml in pure culture was regarded as equivocal. A result of ≥10^5 CFU/ml in pure culture was assessed as being significant and indicating bacterial infection. All organisms from growth assessed as significant or equivocal were identified to the species level using standard microbiological methods. Recording method: The computer software package EPI-INFO (version 5; Centers for Disease Control and Prevention, Epidemiology Program Office, Atlanta, GA, USA) was used to analyze the results. The odds ratio was used to determine the statistical significance of the results.	Type of findings: comparison Findings/effect size: After overnight delayed culture, the results were altered in 16% of samples and the clinical interpretations of these findings differed in 8% of specimens. In 28 samples (3.5%), the bacterium isolated upon initial culture was not the same as that obtained by culture after overnight storage. Statistical significance/tests: The difference in the no. of samples for which the interpretation changed from a significant to a nonsignificant culture result after overnight storage and the no. of samples for which the interpretation was altered from a nonsignificant to a significant culture result was clinically significant (odds ratio = 73.89; 95% CI, 41.28 to 133.01). A slight increase from 106 to 117 in the no. of samples recorded as contaminated was also observed; this does not achieve statistical significance (odds ratio = 0.89; 95% CI, 0.66 to 1.20). Results/conclusion biases: none noted

(Continued on following page)

TABLE A1 (Continued)

Bibliographic information	Study	Practice	Outcome measures	Results/findings
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 2 (no control group)	Total for practice (2-pt. maximum): 1 (initial plating delay)	Total for outcome measures (2-pt. maximum): 2	Total for results/findings (3-pt. maximum): 3
Authors: Guenther and Washington (33) Title: Evaluation of the BD Urine Culture Kit Yr: 1981 Publication: J Clin Microbiol Affiliations: Mayo Clinic, Rochester, MN Funding: not reported	Design: observational study Facility/setting: academic medical center Time period: not reported Population/sample: The study was conducted in 2 phases. In both phases, cleanly voided midstream or catheterized urine specimens were collected from patients (no. not specified) suspected of having bacteriuria by a urine collection team. Comparator: refrigerated urine Study bias: none noted	Description: In the first phase, a sample of the specimen was drawn into the BD urine culture kit for transport at room temp, and a sample of the remaining specimen was stored and transported to the laboratory in a sterile tube at 5°C. The samples in both tubes were processed for semiquantitative culture. The BD kit (preserved urine) was stored at room temp and recultured quantitatively after 24 and 48 h. In the second phase, urine was collected into a sterile tube and transported to the laboratory, where it was cultured and then stored under refrigeration. Cultures were examined after incubation for 18 to 24 h. Urine specimens yielding >10,000 CFU of bacteria other than *Escherichia coli*/ml were selected for study by drawing ~5 ml of the refrigerated specimen from a nonsterile paper cup into the BD kit. Cultures of both the original refrigerated specimen and that just drawn into the BD kit were then made within the hour. The BD kit (preserved urine) was then stored at room temp and recultured after 24 and 48 h. Duration: not reported Training: not reported Staff/other resources: urine collection team utilized Cost: not reported	Description: comparison of colony counts in refrigerated specimens vs specimens stored in BD urine culture kit Recording method: routine lab reports	Type of findings: comparison Findings/effect size: 1. There was 98% agreement between the results for initial cultures of original urine yielding >10^5 CFU/ml and results for preserved urine. 2. Agreement between the results for initial cultures of original urine yielding 10^4 to 10^5 CFU/ml and those for preserved urine was 79.3% in phase 1 and 100% in phase 2. The no. of specimens yielding 10^4 to 10^5 CFU/ml was too small to determine whether the apparent difference in agreement between the results for the 2 phases of study was significant or simply due to random sampling error. 3. Agreement between the results for initial cultures of original urine yielding >10^5 CFU/ml and the results for urine preserved for 24 h was 87.3 and 82.6% in phases 1 and 2, respectively; however, the agreement between results for initial cultures of original urine yielding 10^4 to 10^5 CFU/ml and urine preserved for 24 h was only 55.2 and 45.8% in phases 1 and 2, respectively. By 48 h, there were substantial discrepancies between the no. of CFU/ml of the original specimen and the no. of CFU/ml of the preserved specimen. Statistical significance/tests: not reported Results/conclusion biases: none noted
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 2 (no. of patients not reported)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not well described)	Total for results/findings (3-pt. maximum): 2 (no statistical analysis performed)
Authors: Hubbard et al. (34) Title: Comparison B-D Urine Method with a Standard Culture Method and the MS-2 Method Yr: 1983 Publication: J Clin Microbiol Affiliations: University of Michigan Medical Center, Ann Arbor, MI Funding: not reported	Design: nonrandomized comparison Facility/setting: academic medical center Time period: not reported Population/sample: phase 1, 100 samples routinely submitted to the laboratory; phase 2, 158 previously positive samples Comparator: refrigerated samples Study bias: samples weighted toward positive specimens	Description: In phase 1, 100 samples routinely submitted to the microbiology lab were divided into a refrigeration group and a BD tube group. Colony counts were compared at 0, 5, and 24 h. Samples were also tested using the MS-2 urine screening system. In phase 2, 158 samples known to be positive by routine culture and MS-2 were retested by routine culture and MS-2 at 0 and 24 h. In additional experiments, MS-2 growth curves are shown for positive samples without and with BD tubes. Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: 1. Comparison of growth levels by determining colony counts in refrigerated specimens and BD tube urine samples at 0, 5, and 24 h. 2. Comparison of percentages of positivity in known positive samples among refrigerated specimens vs BD tube urine samples at 0 and 24 h. 3. Growth rates were determined for a limited sample of known-positive specimens. Recording method: routine lab reports	Type of findings: comparison Findings/effect size: In phase 1, negative cultures and those that had either contaminants or <10^5 CFU/ml exhibited no change. However, there were several discrepancies between refrigerated specimens and BD tube specimens for the 26 positive urine specimens containing >10^5 CFU/ml. The refrigerated specimens showed no change in colony counts when cultured at 0, 5, and 24 h. The BD tube specimens showed decreases in colony counts below 10^5 CFU/ml for 96% (0 h), 88% (5 h), and 85% (24 h) of cultures. In phase 2, MS-2 detected about the same no. of refrigerated specimens (91.1%) at 24 h as did the standard culture method (93.0%). In contrast, 17.1% of the BD tube specimens were not detected by the MS-2 at 0 h, and 36.7% were missed by MS-2 after being held 24 h in the BD urine transport tube. Statistical significance/tests: not reported Results/conclusion bias: BD tubes were inoculated in the laboratory and not at the bedside
Total quality rating (10-pt. maximum): 6, fair	Total for study (3-pt. maximum): 1 (BD tube not used as intended; strong bias by using known positive samples)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (no head-to-head comparison of sensitivity/specificity for routine and BD samples)	Total for results/findings (3-pt. maximum): 2 (no statistical analysis performed)

TABLE A1 (Continued)

Bibliographic information	Study	Practice	Outcome measures	Results/findings
Authors: Lauer et al. ([35](#)) Title: Evaluation of Preservative Fluid for Urine Collected for Culture Yr: 1979 Publication: J Clin Microbiol Affiliations: Division of Infectious Diseases and Clinical Microbiology Laboratory, Departments of Pediatrics and Medicine, University of Colorado Medical Center, Denver, CO Funding: supported by a grant from Becton, Dickinson	Design: observational study Facility/setting: academic medical center Time period: not reported Population/sample: 1,000 urine specimens collected from children and adults with symptoms suggesting UTIs and from pregnant women being screened for asymptomatic bacteriuria Comparator: specimens plated immediately upon receipt in the laboratory Study bias: all specimens manipulated by trained microbiologists under laboratory conditions	Description: 1. Each specimen was cultured four times on 5% sheep blood agar and MacConkey agar biplates by the surface streak technique with a calibrated 0.001-ml platinum loop at the intervals described below. 2. Well-mixed urine plated directly from the sterile container according to routine laboratory procedures served as the initial reference culture (plate 1) for all subsequent comparisons. 3. A portion of urine then was poured into a nonsterile, plastic-lined paper cup, drawn into a BD urine culture kit, mixed briefly in a vortex mixer, and recultured (plate 2). 4. The original specimen was refrigerated (4 to 100°C) for 18 to 24 h, and the urine transport tube was left on the laboratory bench at room temp (25 ± 20°C) before repeat cultures (plates 3 and 4, respectively). Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: Urine specimens that grew >10^5 CFU/ml of a potential urinary tract pathogen/ml in pure culture were considered positive. Cultures growing <10^5 CFU/ml or a mixture of organisms were considered negative. Colony counts were recorded as >10^5, 10^4–10^5, or 10^3–10^4 CFU or no growth. A single colony was classified as no growth. Recording method: not reported	Type of findings: observational Findings/effect size: 1. 88 reference cultures grew >10^5 CFU/ml of a single potential urinary tract pathogen. Culture results were comparable after refrigeration or chemical preservation for 24 h; both methods detected 82 of the 88 positive reference cultures (93.2%). The discrepancies mostly consisted of growth of the pathogen in addition to growth of a few Gram-positive urogenital tract contaminants on comparison plates but not in the reference cultures. 2. A total of 912 reference cultures, including 349 plates that showed no growth, were negative. Of the 912 specimens, only 1 was falsely positive after 24 h of refrigeration, and none was falsely positive after chemical preservation. Bacterial counts of the predominant microorganisms in the urine specimens were preserved by either refrigeration or the boric acid-glycerol-sodium formate solution and agreed within 1 log CFU/ml with the reference culture 98% of the time. Statistical significance/tests: not reported Results/conclusion biases: none reported
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 1 (specimens were not preserved at the point of collection)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 2	Total for results/findings (3-pt. maximum): 2 (no statistical analysis performed)
Authors: Southern and Luttrell ([36](#)) Title: Use of the Becton, Dickinson Urine Culture Tube with the Abbott MS-2 Urine Screening System Yr: 1984 Publication: Diagn Microbiol Infect Dis Affiliations: Department of Pathology, The University of Texas Health Science Center at Dallas, and Clinical Microbiology Laboratory, Parkland Memorial Hospital, Dallas, TX Funding: Support provided by Becton, Dickinson	Design: nonrandomized comparison Facility/setting: teaching hospital Time period: not reported Population/sample: 312 urine specimens were obtained from patients attending an obstetrical outpatient clinic for prenatal care. Many patients had symptoms referable to the urinary tract, but others were asymptomatic. Comparator: urine submitted in sterile container Study bias: restricted sample selection	Description: Patients voided urine that was collected in midstream clean-catch fashion in a sterile container. Immediately, a sample of urine was drawn into a Becton, Dickinson urine culture kit tube and another into a sterile screw-cap tube. Both tubes were sent to the laboratory as soon as possible. If transport could not be accomplished within 20 min, the sterile conventional tube was refrigerated. In the laboratory, both tubes were streaked with a calibrated quantitative loop onto eosin-methylene blue agar, Columbia nalidixic acid blood agar, and blood agar. Each tube was also inoculated into an Ampvette of the Abbott MS-2 apparatus for purposes of screening for bacteriuria. Duration: not reported Training: not reported Staff/other resources: urine collection supervised by nursing personnel Cost: not reported	Description: All specimens not determined to be positive by the MS-2 within 6 h were reported as negative. The numbers and types of organisms isolated on each plate for each specimen were recorded. If the colony count exceeded 50,000/ml for Gram-positive cocci or 100,000/ml for Gram-negative bacilli (unmixed cultures), then all isolates were identified and antimicrobial susceptibility testing was performed. The Becton, Dickinson tubes were held an additional 24 h at room temp, and a delayed quantitative culture was done for comparison with the original. Recording method: not reported	Type of findings: comparison Findings/effect size: 1. 124 urine specimens were positive in both conventional and Becton, Dickinson tubes. *Escherichia coli* (n = 72), *Klebsiella pneumoniae* (n = 20), *Enterobacter cloacae* (n = 8), *Proteus mirabilis* (n = 4), group B streptococcus (n = 12), and enterococcus (n = 8) were isolated. 2. Times for detection of positive urine samples were similar for both preserved and unpreserved samples. Delayed cultures had significant numbers of false-positive results. Antimicrobial susceptibility results did not appear to be influenced by Becton, Dickinson tube transport. MS-2 cannot adequately discriminate cultures containing <50,000 CFU/ml of urine. Statistical significance/tests: not reported Results/conclusion bias: MS-2 system could not detect colony counts below 10^2 CFU/ml
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 2 (sample selection bias)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not described)	Total for results/findings (3-pt. maximum): 2 (no statistical analysis performed)

TABLE A1 (Continued)

Bibliographic information	Study	Practice	Outcome measures	Results/findings
Author: Weinstein ([37]) Title: Evaluation of Liquid and Lyophilized Preservatives for Urine Culture Yr: 1983 Publication: J Clin Microbiol Affiliations: Departments of Medicine and Pathology, University of Medicine and Dentistry of New Jersey-Rutgers Medical School, and Microbiology Laboratory, Middlesex General University Hospital, New Brunswick, NJ Funding: supported in part by a grant from Becton, Dickinson	Design: paired comparative analysis Facility/setting: teaching hospital Time period: not reported Population/sample: A total of 869 midstream clean-catch or catheterized urine specimens were obtained in a sterile cup. 7 specimens were inadvertently discarded after initial plating in the laboratory; thus, there were 862 paired comparisons at 24 h. All urine specimens obtained from inpatients from 3 medical units were processed according to the study protocol. Comparator: unpreserved urine samples Study bias: not reported	Description: Immediately after a specimen was collected, the responsible nurse obtained 2 samples with a disposable plastic transfer device (BD urine culture kit; Becton, Dickinson Vacutainer Systems). Throughout the study period, 1 sample was obtained in the commercially available Vacutainer tube containing an LQ solution consisting of boric acid, glycerol, and sodium formate. During the latter half of the study period, a second sample was obtained in a Vacutainer tube that contained an LY similar in content to the LQ, except that sorbitol was substituted for glycerin to facilitate lyophilization. The sterile cup and preserved samples were transported to the laboratory by hospital courier, and an attempt was made in each case to determine the elapsed time between obtaining the specimen and plating it for culture. Duration: 6 mo Training: nurses instructed on urine collection Staff/other resources: not reported Cost: not reported	Description: Samples preserved in either LQ or LY were cultured only if they contained ≥0.4 ml of urine. After initial plating (time zero), the sample in the sterile cup was refrigerated (4 to 10°C) for 18 to 24 h; samples preserved in either LQ or LY were kept at room temp in the laboratory (21 to 24°C) for the same period of time. The following morning, all samples were recultured. All isolates obtained from urine cultures growing >10^4 CFU of a single microorganism/ml in pure culture were identified by standard biochemical methods at least to the genus level. Any culture which grew ≥10^5 CFU/ml of a single microorganism in pure culture was considered to be positive for the purpose of data analysis. Recording method: not reported	Type of findings: comparison Findings/effect size: 1. At the time of initial plating, 106 of 111 (95.5%) specimens that were positive after conventional transport were also positive in liquid preservative. After a 24-h holding period, agreement was 91.4% (96 of 105). At the time of initial plating, agreement between results obtained by the conventional method and those obtained by using lyophilized preservative was 96.9% (63 of 65); after 24 h, agreement was 92.4% (61 of 67). 2. The proportions of urine cultures showing no change in quantitative growth between the time of initial plating and repeat plating at 24 h were virtually identical for all 3 processing methods (83.6 ± 0.9%). 3. After the 24-h holding period, specimens processed in lyophilized preservative were less likely to show diminished quantitative growth than were specimens processed conventionally or in liquid preservative but were more likely to show an increase in growth of −1 log. Nonetheless, the apparent lack of toxicity of lyophilized preservative may make it preferable to the currently available liquid preservative. Statistical significance/tests: not performed Results/conclusion bias: impact of a >24-h delay in specimen processing was not assessed
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 3	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 1 (no statistical analysis was performed; a specimen preserved for longer than 24 h was not assessed)
Authors: Wright et al. ([32]) Title: Effect of Urine Preservation on Urine Screening and Organism Identification Yr: 1985 Publication: Arch Pathol Lab Med Affiliations: Department of Microbiology, Brigham Young University Department of Pathology, University of Utah Medical Center, Salt Lake City, UT Funding: not reported	Design: nonrandomized comparison Facility/setting: academic medical center Time period: not reported Population/sample: Fresh urine and urine preserved in 3 transport systems were tested with 6 separate urine screen systems; specimens were collected from both inpatients and outpatients. Comparator: unpreserved urine Study bias: none noted	Description: Preserved urine was screened with 6 urine screen systems: Chemstrip LN, Autobac IDX, BacT Screen, bioluminescence, and the AMS. Fresh specimens received by the laboratory were first quantitatively cultured and screened with the BacT Screen. Screen-positive samples were then added to 3 urine preservation systems, held for 24 h at room temp, and then recultured and retested in each of the 6 urine screens. Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: 3 commercially available urine transport systems were tested for their effect on rapid urine-screening procedures and organism identifications: a GBF system, a lyophilized SBF system, and a 5.5% BA system. Recording method: not reported	Type of findings: comparison Findings/effect size: 1. Quantitative cultures of urine specimens preserved for 24 h showed little or no change in the no. of viable organisms recovered. 2. Quantitative discrepancies ranged from 0% for urine preserved with GBF and tested by AMS or leukocyte esterase to 21% for urine samples in the same preservative tested by bioluminescence or nitrate. 3. Up to 62% of the organism identifications made from preserved urine specimens tested by the AMS urine card were in error. Statistical significance/tests: not performed Results/conclusion biases: impact of a >24-h delay in specimen processing was not assessed
Total quality rating (10-pt. maximum): 6, fair	Total for study (3-pt. maximum): 3	Total for practice (2-pt. maximum): 1 (practice poorly described)	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 1 (no statistical analysis performed)

[a] For scoring information, see Christenson et al. ([24]). IDs, identifications; pt., point; 95% CI, 95% confidence interval; SG, significant growth; DSG, doubtful significant growth; NSG, nonsignificant growth; LQ, liquid preservative; LY, lyophilized preservative; AMS, Automicrobic system; GBF, glycerin-boric acid-sodium formate; SBF, sorbitol-boric acid-sodium formate; BA, boric acid.

TABLE A2 Evidence summary tables for contamination and diagnostic accuracy of urine collected from women[a]

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Authors: Blake and Doherty (38) Title: Effect of Perineal Cleansing on Contamination Rate of Midstream Urine Culture Yr: 2006 Publication: J Pediatr Adolesc Gynecol Affiliations: Department of Pediatrics, University of Massachusetts Medical School, Worcester, MA Funding: supported by grant 5 K23 AI01750 from the National Institute of Allergy and Infectious Diseases	Design: randomized controlled study Facility/setting: academic medical center Time period: 6 June–1 August 2003 Population/sample: Participants selected from an adolescent clinic were assigned to either the standard collection group ($n = 25$) or the sequential collection group ($n = 25$). Participant ages ranged from 14 yr to 23 yr (mean, 18.5 yr; SD, 2.3 yr). 56% were Caucasian. Comparator: standard clean-catch collection Study bias: none noted	Description: Participants were assigned to either the standard collection group or the sequential collection group. Standard collection group ($n = 25$) participants were instructed on the collection of an MSCC urine sample. They were told to cleanse their perineum with a towelette, pass the first part of their urine into the toilet, and collect the next part of their urine in a sterile container. Sequential-collection group ($n = 25$) participants were instructed not to cleanse their perineum and to collect 2 sequential urine samples by voiding 10 to 20 ml into the first container and the remainder into a second sterile container. Midstream urine specimens from both groups were transported to the laboratory for culture. Duration: 2 mo Training: patient instructions given Staff/other resources: not reported Cost: not reported	Description: perineal flora contamination rate of midstream urine cultures collected with and without perineal cleansing Recording method: questionnaire given to patients	Type of findings: comparison of colony counts Findings/effect size: 1. No culture grew >10,000 colonies of a pathogenic bacterium. 11 (44%) of the exptl group samples and 9 (36%) of the control samples grew >10,000 colonies of perineal bacterial flora (chi square = 0.33; $P = 0.56$). Participants' previous experience collecting midstream urine was not associated with less bacterial contamination. 2. While the mean rating for comfort with the collection method was higher in the standard collection group than in the sequential-collection group, the mean ratings for ease of collection were not significantly different between groups. 3. A relatively large proportion of cultures showed perineal-flora growth in both the sequential-collection and standard-collection groups, suggesting that perineal cleansing does little to reduce contamination. Statistical significance/tests: chi-square, Fisher's exact test, and Spearman correlation were used to compare the groups. Data analyses were performed using SPSS for Windows version 12.0 (SPSS Inc. Chicago, IL). Results/conclusion biases: small sample size, use of asymptomatic patients only
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 2 (small sample size, study setting)	Total for practice (2-pt. maximum): 1 (missing elements in practice description)	Total for outcome measures (2-pt. maximum): 2	Total for results/findings (3-pt. maximum): 2 (small measurement period and no. of patient samples in analysis)
Author: Bradbury (42) Title: Collection of Urine Specimens in General Practice: To Clean or Not To Clean? Yr: 1988 Publication: J R Coll Gen Pract Affiliations: General Practitioner, Stoke-on-Trent and Research Fellow, Department of Postgraduate Medicine, University of Keele, United Kingdom Funding: funded by a grant from the Research Advisory Committee of the North Staffordshire Medical Institute	Design: individual randomized control study Facility/setting: 5-physician private-practice setting Time period: not reported Population/sample: A total of 316 urine specimens were collected from 158 female patients suspected of having UTIs and from 158 controls. The study group comprised any female aged 16–75 yr who presented with symptoms of frequency and dysuria. The control group comprised the next nonpregnant female attending the surgery with no urinary tract symptoms. The women were randomly allocated to 1 of the 2 methods of urine collection. Comparator: clean-catch collections Study bias: control group without symptoms of UTI	Description: Those using the cleaning method were instructed to wash their hands and then use the 3 cotton wool swabs provided to cleanse the genital area with soap and water. They were told to part the labia and wipe from front to back 3 times using a clean swab each time. Keeping the labia parted they passed some urine into the toilet and then caught some urine in a sterile container containing 0.4 g of boric acid as a preservative. Participants not using the cleaning method were instructed simply to pass some urine into the toilet, stop and then catch the next urine in a sterile BA container Duration: 16 mo Training: each patient was given written collection instructions Staff/other resources: not reported Cost: not reported	Description: Samples were evaluated by standard microbiological techniques and classified as definite or equivocal infection based on the quantity of microorganisms. Recording method: routine laboratory reports	Type of findings: comparison of culture results, calculation of contamination rates Findings/effect size: A total of 316 specimens, 158 from women with symptoms of cystitis and 158 from asymptomatic controls, were examined. No significant differences were found in the numbers of contaminated or unreliable results between the specimens collected with and those collected without preparatory cleansing. Statistical significance/tests: not reported Results/conclusion biases: none reported
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 1 (selection of control group, generalizability)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 2	Total for results/findings (3-pt. maximum): 2 (no statistical analysis performed)

(Continued on following page)

TABLE A2 (Continued)

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Authors: Holliday et al. (39) Title: Perineal Cleansing and Midstream Urine Specimens in Ambulatory Women Yr: 1991 Publication: J Hosp Infect Affiliations: Royal Air Force Institute of Pathology and Tropical Medicine, Halton, Aylesbury, Bucks, United Kingdom Funding: not reported	Design: randomized comparison study Facility/setting: general teaching hospital Time period: not reported Population/sample: asymptomatic antenatal patients, randomized to 2 groups of 96 each Comparator: midstream urine collection after cleansing with sterile saline and sterile gauze Study bias: lower-than-expected rate of significant bacteriuria	Description: Sterile packs were used for all specimens. Noncleansing patients were instructed in the use of the pack only. Cleansing patients received the same information but additionally were asked to clean the genital area with sterile gauze swabs soaked in sterile normal saline and used with a single backwards stroke before finally drying the area with another sterile gauze swab. Duration: not reported Training: infection control nurse provided training to antenatal nurses; nurses provided detailed instructions to patients Staff/other resources: nurses and laboratory staff Cost: not reported	Description: comparison of urine microscopy and culture results stratified by colony count in each group Recording method: routine laboratory reports	Type of findings: comparison of culture results Findings/effect size: 1. No significant difference in distributions of colony count results ($P > 0.1$ by χ^2) was found. 2. The only significant difference in microscopic findings (>50 epithelial cells) was found with 12 individuals in the noncleansing group and 4 in the cleansing group ($P = 0.017$); no other differences for WBC or RBC were found. Statistical significance/tests: chi-square test, Fisher's exact test Results/conclusion biases: results may apply only to ambulatory antenatal patients
Total quality rating (10-pt. maximum): 8, good	Total for study (3-pt. maximum): 2 (small sample size)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 2	Total for results/findings (3-pt. maximum): 2 (restricted patient population)
Authors: Schlager et al. (40) Title: Perineal Cleansing Does Not Reduce Contamination of Urine Samples from Pregnant Adolescents Yr: 1995 Publication: Pediatr Infect Dis J Affiliations: Department of Pediatrics, University of Virginia Health Sciences Center, Charlottesville, VA Funding: not reported	Design: nonrandomized comparison study Facility/setting: teen health center/academic medical center Time period: not reported Population/sample: convenience sample of 100 pregnant, low-income teens 10–19 yr; exclusions were patients with UTI or a UT abnormality and patients who had taken antibiotics within 7 days Comparator: clean-catch urine collection Study bias: potential selection bias	Description: Each subject gave 2 urine samples during consecutive urinations in 1 routine prenatal visit; the first was by midstream collection, the second by clean-catch collection. Urine samples were refrigerated immediately after collection, plated within 5 h of collection, and cultured by routine microbiological techniques. Duration: not reported Training: patients were given verbal instructions by nurses. Staff/other resources: nursing Cost: a potential cost savings of $97,560/yr if clean-catch practices were stopped	Description: Significant bacteriuria was defined as $>10^5$ CFU/ml of urine. Lower counts were considered contaminants. Results were analyzed for mean differences in colony counts between the 2 methods of collection Recording method: routine laboratory reports	Type of findings: comparative differences in the numbers and types of microorganisms Findings/effect size: Bacteriologic results were similar for urine specimens obtained by the clean-catch method and non-clean-catch (midstream) method. Statistical significance/tests: chi-square test Results/conclusion biases: results may not be applicable to other patient populations
Total quality rating (10-pt. maximum): 8, good	Total for study (3-pt. maximum): 2 (selection bias)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 2	Total for results/findings (3-pt. maximum): 2 (restricted definition of significant growth)
Authors: Schneeberger et al. (43) Title: Contamination Rates of Three Urine-Sampling Methods To Assess Bacteriuria in Pregnant Women Yr: 2013 Publication: Obstet Gynecol Affiliations: Departments of Epidemiology and Obstetrics and Gynecology, University Medical Center, Gronigen, Amsterdam, Netherlands Funding: not reported	Design: cross-sectional Facility/setting: outpatient obstetrics clinic Time period: April 2010–April 2011 Population/sample: convenience sample of 113 pregnant women who had had 3 different midstream urine samples collected consecutively: first void, midstream without cleansing, and midstream clean-catch. Comparator: midstream sample used as reference test. Study bias: sample size too small to detect some differences in collection technique	Description: 3 methods of collection were compared for differences in Gram stain, leukocyte, esterase and nitrate dip stick, and culture results. Duration: 12 mo Training: oral and written sampling instructions were provided to each patient. Staff/other resources: not reported Cost: not reported	Description: Urine culture was interpreted as follows: negative (defined as no growth or the growth of only skin flora), undefined (growth of $<10^4$ CFU/ml of 1 uropathogen), or positive (the presence of 1 uropathogen with a growth of at least 10^4 CFU/ml or more). Contaminants and uropathogens were identified by routine methods. Recording method: not reported	Type of findings: comparison Findings/effect size: Mainly low numbers of Gram-positive rods were more likely to be present in Gram stains of midstream samples than in clean-catch samples (77.7% compared with 66.7%; $P = 0.022$). Morning samples showed more mixed growth than midstream samples (6.2% compared with 0.9%; $P = 0.050$). No consistency in quantity of contaminants was found in midstream samples compared with morning and clean-catch samples. No differences were found between the other endpoints in all 3 urine samples ($P > 0.05$). The study could detect an odds ratio of 2.0 for differences in urine-sampling methods with 80% power and 5% significance for most endpoints. Statistical significance/tests: Fleiss-Cohen's weighted K statistic, odds ratios, generalized score test Results/conclusion biases: study not appropriately powered for all measures, nearly all samples were contaminated

TABLE A2 (Continued)

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 2 (sample size)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 2 (nearly 100% of samples yielded contaminants)
Authors: Walter and Knopp (41) Title: Urine Sampling in Ambulatory Women: Midstream Clean-Catch versus Catheterization Yr: 1989 Publication: Ann Emerg Med Affiliations: Department of Emergency Medicine, Valley Medical Center, Fresno, CA, and Departments of Medicine and Family and Community Medicine, University of California, San Francisco, CA Funding: supported by a grant from the Medical Research Committee of Valley Medical Center, Fresno, CA	Design: nonrandomized comparison study Facility/setting: teaching hospital Time period: May–November 1986 Population/sample: 105 consecutive women. Selection criteria included any ambulatory adult woman or legally emancipated female minor who presented to the Emergency Department triage nurse with 1 or more symptoms that could be attributed to a UTI. Comparator: catheterized urine sample Study bias: ED patients only	Description: Each patient spread her labia, prepped her periurethral area by wiping 3 povidone-iodine-soaked 4-by 4-in. gauzes in an anterior-to-posterior direction, and spontaneously voided an midstream clean-catch urine sample. Then, the patient was immediately sterilely prepped with povidone-iodine and catheterized by a nurse using a Davol single-use female catheterization kit. Duration: 7 mo Training: Patients received standardized verbal instructions from a nurse on the method for MSCC urine collection. Staff/other resources: not reported Cost: not reported	Description: Urine samples were compared by microscopic urinalysis, dipstick urinalysis, and urine culture. Leukocyte esterase and nitrites were reported as positive or negative. WBC were reported as the actual no. per HPF. Microscopic bacteriuria was reported as 0 if absent, 1+ for 1 to 10 bacteria/HPF, 2+ for 10 to 100 bacteria/HPF, 3+ for bacteria that were innumerable but loosely packed in each HPF, and 4+ for bacteria that were innumerable and tightly packed in each HPF. A culture-proven UTI was defined as more than 10,000 colonies of at least a single species/ml of catheterized urine. Recording method: not reported	Type of findings: comparison Findings/effect size: Of the 105 patients, 42 (40%) had a culture-proven UTIs. The concordance rates between MSCC and CATH urine cultures, nitrites, leukocyte esterase, significant microscopic bacteriuria, and pyuria were 96%, 94%, 93%, 90%, and 90%, respectively. There were no statistically significant differences between MSCC and catheterized specimens for sensitivities, specificities, or positive or negative predictive values for any urinalysis variable (leukocyte esterase, nitrites, significant microscopic bacteriuria, or pyuria). Statistical significance/tests: McNemar's test, Fischer's exact test, and power analysis. Two-tailed statistical tests were performed. Results/conclusion biases: Findings were limited to ambulatory women who have 1 or more symptoms compatible with a UTI and were specifically instructed in the proper technique of MSCC urine sampling.
Total quality rating (10-pt. maximum): 8, good	Total for study (3-pt. maximum): 2 (ED patients only)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 3
Authors: Lemieux and St.-Martin (45) Title: Reliability of Clean-Voided Midstream Urine Specimens for the Diagnosis of Significant Bacteriuria in the Female Patient Yr: 1968 Publication: Can Med Assoc J Affiliations: Renal Laboratory and Renal Clinic Montreal School of Medicine; Department of Bacteriology, Hotel-Dieu Hospital, Montreal, Canada Funding: supported in part by a grant from Hoffman La Roche Limited	Design: cross-sectional Facility/setting: teaching hospital Time period: not reported Population/sample: 3 groups of patients were studied. Group 1 consisted of 53 healthy student nurses (aged 18 to 23 yr; mean, 19 yr) having a first morning cleanly voided midstream specimen collected. Group 2 consisted of 29 female patients admitted to a general medical ward service (aged 21 to 53 yr; mean, 42 yr) with both clean-void and catheterized urine specimens collected at the same time. Group 3 consisted of 27 female patients (aged 24 to 54 yr; mean, 43 yr) admitted to either a semiprivate or general medical ward. Both cleanly voided and catheterized specimens were collected at the same time. Comparator: not reported Study bias: none noted	Description: All specimens were collected in the same room by the same 2 nurses. Both the nurses and patients wore sterile rubber gloves during the entire procedure of urine collection. The perineum was carefully scrubbed with green soap for 2 to 3 min. The labia majora were then separated, and the vulva was washed with green soap, with a fresh cotton swab used after each downward stroke. The same maneuver was repeated with an aqueous solution of Zephiran (benzalkonium; 1:1,000). The subjects were then instructed to void after separating the labia majora. After the stream was well started, a sterile screw-cap jar was placed into the path of the stream and a small sample of urine collected. Subjects from whom paired specimens were obtained were told to stop voiding as soon as the cleanly voided specimen was obtained. A sterile rubber French no. 8 catheter lubricated with a small amt of sterile lubricant was then inserted into the urethra, and a final specimen was collected in another screw-cap jar. The specimens were taken immediately to the laboratory, where they were processed for bacterial counts, routine bacterial identification, and Gram staining. Duration: not reported Training: 2 graduate nurses were trained to collect both cleanly voided and catheter specimens. Staff/other resources: not reported Cost: not reported	Description: Specimens were processed in the laboratory for quantitative culture with identification of uropathogens. Recording method: not reported	Type of findings: comparative colony counts Findings/effect size: In group 1, the cleanly voided urine samples contained no bacteria after 48 h in 46 (87%) of the 53 subjects. In group 2, the incidence of sterile cleanly voided urine samples was also quite high (69%), while not a single catheterized specimen showed bacterial growth after 48 h. In group 3, a very high degree of correlation was found between cleanly voided and catheter specimens with regard to both the type of organism and the bacterial counts Statistical significance/tests: not reported Results/conclusion biases: not reported

TABLE A2 (Continued)

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Total quality rating (10-pt. maximum): 6, fair	Total for study (3-pt. maximum): 1 (limited sample size; selection criteria not reported)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 2 (no statistical analysis)
Authors: Immergut et al. (44) Title: The Myth of the Clean-Catch Urine Specimen Yr: 1981 Publication: Urology Affiliations: not reported Funding: not reported	Design: nonrandomized comparison Facility/setting: physician office practice Time period: not reported Population/sample: 95 ambulatory female patients Comparator: cystoscopic specimen collection Study bias: none noted	Description: Patients were asked to urinate in private without any prepn. They collected the urine at any time during voiding in an unsterile disposable plastic cup. The specimens were immediately cultured on Uricult media by dipping the slides into the plastic cups. Routine chemical and microscopic analysis of the urine was performed on each specimen. A cystoscopic examination was performed with an instrument which had been soaked for at least 10 min in Cidex solution and then rinsed in sterile water. Urine specimens obtained through the cystoscope were similarly cultured on Uricult slides. Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: comparison of Uricult culture results between unprepped-void samples and specimens obtained during cystoscopy Recording method: not reported	Type of findings: comparison Findings/effect size: 91.5% of the cultures were negative by either method of collection. 3.2% of the voided specimens showed Gram-negative rods, which were identical to results of specimens obtained during cystoscopy. 5.3% of patients had cultures with >50,000 CFU/ml of a Gram-negative rod in their voided specimens; their specimens obtained during cystoscopy were negative. Statistical significance/tests: not reported Results/conclusion biases: not reported
Total quality rating (10-pt. maximum): 6, fair	Total for study (3-pt. maximum): 2 (no description of patient selection criteria)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not described)	Total for results/findings (3-pt. maximum): 1 (no description of types of organisms recovered. No statistical analysis performed)

[a] MSCC, midstream clean-catch collection; CATH, catheterization; HPF, high-power field.

TABLE A3 Evidence summary table for contamination and diagnostic accuracy of urine collected from men[a]

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Authors: Lipsky et al. (46) Title: Is the Clean-Catch Midstream Void Procedure Necessary for Obtaining Urine Culture Specimens from Men? Yr: 1984 Publication: Am J Med Affiliations: Departments of Medicine, Laboratory Medicine, and Urology, University of Washington School of Medicine, and Medical and Surgical Services, Seattle Veterans Administration Medical Center, Seattle, WA Funding: supported in part by the Health Services Research and Development Affiliation Program, Seattle VA Medical Center	Design: group randomized control study Facility/setting: urology clinic, VA medical center Time period: August 1981–February 1982 Population/sample: total of 308 paired specimens collected from 254 male patients. Comparator: midstream urine without cleansing Study bias: patient selection restricted to urology clinic patients	Description: Subjects were directed to collect paired voided urine specimens for culture. Those whose Social Security numbers ended in an even digit were instructed to cleanse their glans penis with a povidone-iodine pad prior to voiding. Persons with odd Social Security numbers served as noncleansed control subjects. Patients in both groups collected 10 to 20 ml of "initial" and "midstream" specimens by passing the first part of the voided urine into a sterile cup, discarding the next 100 to 200 ml of urine into the urinal, and then collecting a second aliquot of urine in another sterile container. All specimens were immediately refrigerated at 4°C and delivered within 4 h to the clinical microbiology laboratory for Gram staining and semiquantitative culture. Organisms were identified using standardized techniques. Nonhemolytic streptococci were characterized as viridans streptococci or enterococci. All other organisms were identified to the species level. Duration: 7 mo Training: A graphic instructional sign displaying the clean-void procedure was posted in the bathroom where the samples were collected. Staff/other resources: A technician was available to patients needing assistance. Cost: not reported	Description: A "positive" culture was defined as one with growth of 10,000 or more CFU/ml of a single or predominant organism. Specimens growing 1,000 CFU/ml of a single or predominant organism were called "indeterminate." Those with 1,000 or more CFU/ml with 2 or more colonial types and with no predominant organism were defined as "contaminated." Specimens growing less than 1,000 CFU/ml were considered "negative." Recording method: routine laboratory reports	Type of findings: comparison Findings/effect size: The rates of true bacteriuria and contamination were compared in the various collection technique subgroups. Neither the bacteriuria nor contamination rates were significantly different ($P > 0.05$) in circumcised and uncircumcised patients, or in those who cleansed their meatus and those who did not. Contamination but not bacteriuria rates were higher in initial than in midstream specimens. Statistical significance/tests: Statistical analysis for evaluating meatal cleansing and circumcision status was by the standard chi-square technique and by McNemar's test for paired data for evaluating collection timing. A P value of <0.05 was considered significant. Results/conclusion biases: none noted
Total quality rating (10-pt. maximum): 9, good	Total for study (3-pt. maximum): 2 (only urology clinic patients included)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 2	Total for results/findings (3-pt. maximum): 3
Authors: Lipsky et al. (47) Title: Diagnosis of Bacteriuria in Men: Specimen Collection and Culture Interpretation Yr: 1987 Publication: J Infect Dis Affiliations: Departments of Medicine and Urology, University of Washington School of Medicine, and Medical and Surgical Services, Seattle VA Medical Center, Seattle, WA Funding: not reported	Design: observational study Facility/setting: VA medical center Time period: not reported Population/sample: 66 ambulatory or hospitalized male patients who had acute dysuria or other irritative genitourinary symptoms, were known to have bacteriuria, or were scheduled for a urologic procedure. Individuals were excluded because of an inability to void at will, use of any type of internal or external device for urine collection, massive obesity, previous lower abdominal surgery or radiation therapy, known or suspected bladder neoplasm, or any coagulation disorder. Comparator: urine collected by suprapubic aspiration Study bias: subjects were not randomly selected.	Description: Specimens were collected in the following order: suprapubic aspiration (10 ml), uncleansed first void (the first 10 ml was voided without prior cleansing of the urethral meatus), clean-catch midstream void (10 ml was voided after cleansing the urethral meatus with povidone-iodine and voiding ~100 ml), and urethral catheterization (10 ml). At least 1 bladder (suprapubic aspiration or urethral catheterization) and 1 voided (uncleansed first void or clean-catch midstream void) specimen were collected from every subject. Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: Specimens were cultured by standard microbiological techniques; urine leukocytes were quantitated with a hemacytometer. Plates were examined after incubation for 18–24 h. Isolates from plates with fewer than 3 different colonial types were identified to the species level. Urine leukocytes were quantitated (in cells/mm³ of uncentrifuged urine) in a hemacytometer. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for results of culture of the uncleansed first-void and clean-catch midstream-void specimens, with bladder specimens used as the reference standard. Recording method: not reported	Type of findings: comparison Findings/effect size: Bladder bacteriuria was found in 36 of 76 sets of specimens from 66 individuals. Culture results of bladder specimens showed excellent agreement with those of clean-catch midstream-void and unclean first-void specimens. The criterion for clean-catch midstream-void specimens that best differentiated sterile from infected bladder urine was the growth of >1,000 CFU/ml of 1 predominant species. Uncleansed first-void specimens were equally sensitive (0.97) but less specific (0.91–0.92) in detection of bacteriuria. Pyuria (>1,000 leukocytes/mm³) and irritative genitourinary symptoms showed modest correlations with bladder bacteriuria.

TABLE A3 (Continued)

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
				Statistical significance/tests: Agreement between bladder and voided specimens was tested with use of a weighted k statistic with 95% CIs. Results/conclusion biases: Study participants were not consecutively or randomly selected but were a heterogeneous group of mostly elderly ambulatory men with various genitourinary disorders. When a positive culture is used for screening or in populations with a low incidence of bacteriuria, the predictive value of a positive culture will be less than in this study.
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 2 (selection bias)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 2 (higher pretest probability than found in general patient population)
Authors: Deresinski and Perkash (48) Title: Urinary Tract Infections in Male Spinal Cord Injured Patients. Part One: Bacteriologic Diagnosis Yr: 1985 Publication: J. Am. Paraplegia Soc. Affiliations: Spinal Cord Injury Service VA and Stanford University Medical Centers Palo Alto, CA Funding: not reported	Design: nonrandomized comparison study Facility/setting: teaching hospital Time period: not reported Population/sample: 71 paired samples were obtained from 53 male spinal cord injury patients, 28 paraplegics (22 complete), and 25 quadriplegics (16 complete). Comparator: suprapubic urine specimen Study bias: none noted	Description: 71 paired samples of urine, obtained by collection of a cleanly voided specimen and by SPA of the bladder, were obtained from 53 male spinal cord injury patients who were free of indwelling catheters. A direct comparison of the no. of CFU of bacteria within the paired specimens was made. Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: Quantitative urine cultures were performed on all collected samples. Bacteria were identified by routine biochemical methods. Recording method: not reported.	Type of findings: comparative Findings/effect size: 1. A direct comparison of the no. of CFU of bacteria within the paired specimens indicated that a single voided specimen was adequate in 63 of 71 (88.7 %) samples. With a threshold of 10,000 CFU/ml of urine obtained by SPA, the presence of at least 10,000 CFU/ml of voided urine provided a sensitivity and specificity of 100%. 2. In patients with colony counts of 100 to 10,000 CFU/ml in which the voided urine contains mixed flora or staphylococci, bladder urine is most likely to be sterile, and an accurate assessment may require SPA. Statistical significance/tests: not reported Results/conclusion biases: none reported
Total quality rating (10-pt. maximum): 5, fair	Total for study (3-pt. maximum): 2 (the total for the study population is not sufficiently described)	Total for practice (2-pt. maximum): 1 (poor description of practice)	Total for outcome measures (2-pt. maximum): 1 (recording method not described)	Total for results/findings (3-pt. maximum): 1 (small no. of patients studied. Data do not permit effect size calculation)

[a] SPA, suprapubic aspiration.

TABLE A4 Evidence summary table for contamination and diagnostic accuracy of urine collected from children[a]

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Authors: Karacan et al. (53) Title: Evaluation of Urine Collection Methods for the Diagnosis of Urinary Tract Infection in Children Yr: 2010 Publication: Med Princ Pract Affiliations: Department of Pediatrics, Dr. Sami Ulus Children's Hospital, Ankara, Turkey Funding: not reported	Design: cross-sectional Facility/setting: teaching hospital Time period: not reported Population/sample: 1,067 children, 88 younger than 1 mo, 126 between 1 and 6 mo, 318 between 7 and 24 mo, and 535 older than 24 mo of age. There were 521 (48.9%) girls. Of these 1,067 children, 951 (89.1%) were admitted to the outpatient clinic and 116 (10.9%) were admitted to the inpatient clinic. Comparator: none Study bias: none noted	Description: 4 methods of urine collection were studied: SPA, CCU, CATH, and UB. Duration: 2 mo Training: Nurses trained parents on UB collection. Hospital personnel were trained on proper collection of SPA and CATH specimens. Staff/other resources: not reported Cost: not reported	Description: The specimens collected by type were divided according to age group. The no. of specimens yielding significant pathogens and the no. of contaminated specimens were calculated. Semiquantitative cultures were performed by routine laboratory methods. A positive urine culture was defined as the growth of a single pathogen of more than 10^5 CFU/ml in UB and CCU specimens, $>10^4$ CFU/ml in urine specimens obtained by CATH, and any no. of colonies in a sample obtained by SPA. Urine cultures interpreted as "contaminated" by the laboratory were considered to be contaminated. Recording method: not reported	Type of findings: observational Findings/effect size: 617 subjects (57.8%) had negative culture results, 145 (13.6%) had positive culture results, and 305 (28.6%) had evidence of bacterial contamination. CCU and CATH specimens showed a contamination rate of 14.3%. However, urethral catheterization was performed in only a small no. of subjects ($n = 7$). SPA was also used in a small no. of subjects ($n = 11$), and the contamination rate for SPA was 9.1% (1/11). The contamination rate for sterile UB was 43.9%, significantly higher than rates for the other methods ($P < 0.001$). Statistical significance/tests: The data were analyzed using the Statistical Package of Social Sciences for Windows, version 10.0 (SPSS Inc., Chicago, IL, USA) program. Pearson's 2 and Fisher's exact tests were used to compare differences between groups. A P of <0.05 was considered significant. Results/conclusion biases: Parental collection of UB specimens may have contributed to a high contamination rate.
Total quality rating (10-pt. maximum): 6, fair	Total for study (3-pt. maximum): 2 (not a controlled study)	Total for practice (2-pt. maximum): 1 (poor description of practice as relates to no. of different specimen types collected)	Total for outcome measures (2-pt. maximum): 1 (recording method not described)	Total for results/findings (3-pt. maximum): 2 (insufficient no. of SPA and CATH specimens included in data analysis)
Authors: Alam et al. (49) Title: Comparison of Urine Contamination Rates Using Three Different Methods of Collection: Clean-catch, Cotton Wool Pad, and Urine Bag Yr: 2005 Publication: Ann Trop Pediatr Affiliations: Liverpool School of Tropical Medicine, Liverpool United Kingdom; Instituto Materno Infantil de Pernambuco, Recofe, Brazil Funding: not reported	Design: prospective cross-sectional Facility/setting: teaching hospital Time period: not reported Population/sample: Children aged up to 3 yr without known UTI had urine collected by 3 different methods used consecutively, namely, clean-catch, cotton wool sanitary pad, and urine bag. 534 urine samples were obtained from 191 children. There were 124 boys (65%). The median age was 2 mo (1 day–36 mo). Comparator: intersubject Study bias: order of specimen collection not defined	Description: 3 urine samples collected after perineal cleaning with soap and water (all 3 collected on same day or next day if required, with the order of collection at the nurses' discretion). The 1st was a clean-catch specimen, the 2nd was collected in a cotton pad (either sterile Newcastle or commercial sanitary pads) and aspiration with a syringe. The 3rd was collected in a Hollister urine bag taped to the infant. Samples were held in a refrigerator, transferred to sterile coded tubes, and plated within 20 min of receipt by the laboratory. Cultures were interpreted as $>10^5$ or $<10^5$ CFU/ml. Also, microscopy was performed on uncentrifuged urine. Duration: 2 mo Training: parents instructed by nursing on proper urine collection. Staff/other resources: not reported Cost: cost of pads described	Description: The percentage of urine samples contaminated by each collection method was based on a quantity of $>10^5$ or $<10^5$ CFU/ml, organism type, and agreement between sample types. Phase-contrast urine microscopy results were correlated with culture results. Recording method: not reported	Type of findings: descriptive, comparative Findings/effect size: Results from 175 patients showed similar contamination rates for pads and bags but lower rates for clean-catch specimens ($P < 0.01$). Kappa analyses showed fair agreement between clean-catch specimens and those collected in pads/bags. The difference between sterile pads and sanitary pads was not significant. No significant differences were based on gender. Microscopy showed reasonable correlation with culture positivity. Statistical significance/tests: agreement between the tests calculated using kappa statistics. More than 40% agreement was regarded as a good level of agreement. The chi-square test was used to analyze differences in proportions. Results/conclusion biases: results limited to nonsymptomatic pediatric inpatients

(Continued on following page)

TABLE A4 (Continued)

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Total quality rating (10-pt. maximum): 8, good	Total for study (3-pt. maximum): 3	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not described)	Total for results/findings (3-pt. maximum): 2 (limited patient population)
Authors: Macfarlane et al. (54) Title: Pad Urine Collection for Early Childhood Urinary Tract Infection Yr: 1999 Publication: Lancet Affiliations: Departments of Child Health and Microbiology, Rotherham General Hospital, Rotherham, United Kingdom Funding: not reported	Design: observational Facility/setting: teaching hospital Time period: not reported Population/sample: 1. 88 inpatients, all below 2 yr of age, were included. 56 UCP samples were reliably obtained; the remaining 32 samples failed for a variety of reasons and were excluded. 2. 34 children in the same age range had urine bag collection done over the preceding 9 mo. 3. 240 clean-catch samples were analyzed (no. of children not reported). Comparator: between-patient populations Study bias: nonrandom, unequal sample sizes, no standard reference method	Description: 1. The UCP was placed inside the front of the child's nappy; the child's nurse checked the pad every 15–20 min, removed it when wet, and aspirated urine from it using a 20-ml syringe. Fecally soiled pads were discarded. 2. Urine from 34 children in the same age range and ward setting that had bag urine collection done over the preceding 9 mo was similarly tested. Duration: 3 mo Training: not reported Staff/other resources: not reported Cost: not reported	Description: colony counts (CFU/ml) across all sample types. Recording method: not reported	Type of findings: observational/comparative Findings/effect size: UCPs resulted in an unhelpfully high rate of contamination (65%) similar to that for bag samples (68%). Only 27% of clean-catch urine samples were contaminated. Sterile urine or urine with a low ($<10^5$ CFU/ml) mixed bacterial count is probably sufficient in most cases to rule out UTI, whereas a sample contaminated by a heavy mixed growth may hide infection. Such samples may need to be repeated. Applying this principle to our series, the authors found that 14 (27%) of 52 pad samples, 11 (32%) of 34 bag samples, but only 29 (12%) of 240 clean-catch samples would have been repeated. Statistical significance/tests: Results/conclusion biases: not reported
Total quality rating (10-pt. maximum): 5, fair	Total for study (3-pt. maximum): 1 (different patient populations and sizes, no reference standard)	Total for practice (2-pt. maximum): 1 (limited practice description)	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 2 (no statistical analysis)
Authors: Ahmad et al. (55) Title: Urine Collection from Disposable Nappies Yr: 1991 Publication: Lancet Affiliations: Department of Child Health and Department of Microbiology, Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom Funding: not reported	Design: prospective cross-sectional Facility/setting: hospital Time period: not reported Population/sample: 2 urine samples, collected from 45 infants aged 1–23 mo, 1 with a sterile bag and 1 from a nongel diaper Comparator: bag vs diaper Study bias: only inpatients included in study, small sample size	Description: 2 consecutive urine samples were collected from 45 infants who were 1–23 mo old: 1 from a sterile urine bag and 1 from a nongel diaper. Diapers older than 4 h and containing feces were excluded. WBC and RBC evaluations were performed using microscopy. All specimens were processed for routine culture by the microbiology laboratory. Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: semiquantitative culture with standard definitions for contamination and significance ($>10^5$ CFU/ml) Recording method: not reported	Type of findings: comparative Findings/effect size: 37 of 45 urine cultures showed complete agreement between the 2 collection techniques (22 sterile urine samples, 9 mixed cultures, 6 with significant growth). 7 infants had mixed growth from bag specimens but sterile culture results from diaper specimens. 1 infant had $>10^5$ CFU/ml of different organisms in the bag specimen vs the diaper specimen. Statistical significance/tests: not reported Results/conclusion biases: none noted
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 2 (small sample size)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 2 (no statistical analysis)

TABLE A4 (Continued)

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Authors: Vaillancourt et al. (50) Title: To Clean or Not To Clean: Effect on Contamination Rates in Midstream Urine Collections in Toilet-Trained Children Yr: 2005 Publication: Pediatrics Affiliations: Division of Pediatric Emergency Medicine and Departments of Pediatrics and Epidemiology and Biostatistics, Montreal Children's Hospital, and Montreal Children's Hospital Research Institute, McGill University, Montreal, Quebec, Canada Funding: not reported	Design: randomized control study Facility/setting: teaching hospital/ED Time period: 1 November 2004–1 October 2005 Population/sample: All toilet-trained children who were between the ages of 2 and 18 yr and had a midstream urine sample requested were eligible. Comparator: those whose parents consented were cluster randomized by week to either cleaning or not cleaning the perineum with soap Study bias: only patients with a positive urinalysis were cultured	Description: At the beginning of each wk throughout the study period, the method for collecting a urine specimen for all children who presented to the ED during that wk was randomly assigned by the study investigators. During the cleaning wk, the child was given liquid soap, several gauze pads, a sterile urine collection container, and an instruction sheet. The child and/or the parent was instructed to spread the labia (for girls) or retract the foreskin (for noncircumcised boys) and to clean the urethral meatus and perineum with gauze and liquid soap twice (wiping from front to rear in girls). The child was then to urinate into the toilet and, midway through urination, to collect the urine into the sterile container. During the noncleansing wk, the child was given neither a sterile urine collection container nor an instruction sheet. Urine specimens were sent to the microbiology laboratory in sterile containers. Standard quantitative culture was performed by a laboratory technologist. Duration: 1 yr Training: Multiple posters were then displayed to inform the ED staff as to whether it was a cleansing or noncleansing wk. Verbal and written instructions for obtaining the urine specimen were given to the child and parent(s). Staff/other resources: not reported Cost: not reported	Description: The risk for a contaminated urine culture (defined as growth of $<10^5$ CFU/ml of a single organism or a mix of >2 organisms) and the risk for a positive urinalysis result (defined as a positive leukocyte esterase and/or nitrites on a dipstick or >5 WBC/HPF upon standard microscopic examination) were analyzed by intention to treat. The authors estimated the no. of children needed to detect a clinically important difference of 20%, based on an alpha value of 0.05 and a power of 80%. Recording method: A questionnaire was administered with the urine collection instructions to the parent of each participating child to document the age, gender, circumcision status (for boys), antibiotic use in the previous 2 wk, and previous renal problems (other than a previous UTI).	Type of findings: comparative Findings/effect size: A total of 350 children were enrolled. The overall prevalence of UTIs was 7%. The rate of contamination in the cleaning group was 14 (7.8%) of 179 vs 41 (23.9%) of 171 in the noncleansing group. Children who were randomly assigned to cleansing were less likely to have a positive urinalysis (37 of 179 [20.6%]) than those in the noncleansing group (63 of 171 [36.8%]). Statistical significance/tests: RR and their 95% CI for contamination and for a positive urinalysis were calculated using SPSS 11.0 (SPSS, Chicago, IL). The chi-square test was used to test for a difference in the culture results between the cleansing and noncleansing groups among samples with a positive urinalysis result. Because the intervention was randomized by wk rather than by individual patient, a GLIMMIX was also used to account for potential within-wk clustering of outcome results and to adjust for potential baseline imbalances in gender, age, and history of renal problems. The interaction terms for treatment by gender and age were also included in the GLIMMIX. Results/conclusion biases: The lack of a reference method makes assignation of true positives (infected) difficult.
Total quality rating (10-pt. maximum): 9, good	Total for study (3-pt. maximum): 3	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 2	Total for results/findings (3-pt. maximum): 2 (lack of a reference standard)
Authors: Tosif et al. (56) Title: Contamination Rates of Different Urine Collection Methods for the Diagnosis of Urinary Tract Infections in Young Children: an Observational Cohort Studyjpc_2449 Yr: 2012 Publication: J Pediatr Child Health Affiliations: Emergency Department, Murdoch Children's Research Institute, Clinical Epidemiology and Biostatistics Unit (CEBU), Royal Children's Hospital Melbourne, Emergency Department, Monash Medical Centre, Faculty of Medicine, Nursing and Health Science, Monash University, and Department of Pediatrics, The University of Melbourne, Melbourne, Australia	Design: observational Facility/setting: tertiary-care children's hospital Time period: 1 February–30 April 2008 Population/sample: urine samples from 599 patients under 24 mo of age submitted to the clinical microbiology laboratory for culture Comparator: clean-catch urine specimens Study bias: retrospective study (precise clinical indications for why/how urine was collected were not available)	Description: Microscopy and culture results from all urine specimens were retrieved from the hospital's microbiology database. The first urine specimen collected from each child in this time period was included for analysis. Urine culture results from CCU, SPA, CATH, and SUB collection were analyzed. Patient age, gender, location, and method of collection were gathered from the microbiology database. For specimens for which the method of collection was by SPA, CCU, or CATH, the medical history was reviewed for documentation of a past history of UTI, urogenital abnormality, and antibiotic use at time of urine specimen collection. Contamination rates were defined by the laboratory as growth of 2 or more organisms at a concn of $\geq 10^1$ CFU/ml for SPA and CCU samples and $\geq 10^3$ CFU/ml in CCU and SUB samples. Duration: 3 mo Training: Histories were reviewed by 2 primary investigators using a standardized form that was piloted on 10 histories, for which there was no disagreements in data extraction. Staff/other resources: not reported	Description: The primary outcome measure was the contamination rate for each urine specimen collection method. Authors also sought to adjust for possible confounding factors by investigating the effect of age, gender, location, history of UTIs and urogenital abnormality, and antibiotic use at time of urine specimen collection. Recording method: lab database, standardized form for patient histories	Type of findings: observational Findings/effect size: 1. The age range of children was 0–23 mo, with a mean age of 7 mo. Overall, most urine specimens were obtained by CCU collection (34%), followed by CATH and SPA. ED collections were by CCU collection (39%), CATH (15%), SPA (16%), SUB collection (0%), and unknown means of collection (30%), whereas inpatient collections were by CCU collection (19%), CATH (23%), SPA (11%), SUB (4%), and unknown means of collection (42%). 2. Contamination rates were 26% in CCU vs 12% in CATH specimens (OR, 0.4; 95% CI, 0.2–0.8) and 1% in SPA specimens (OR 0.03; 95% CI, 0.0–0.3). The few bag specimen samples showed a high rate of contamination (46%), and urine collected by an unspecified method had a contamination rate of 20%.

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TABLE A4 (Continued)

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Funding: not reported		Cost: not reported		3. 369 medical records were available for review. 5% of patients had had prior UTIs, 14% were receiving antibiotics when the specimen had been obtained, and 11% had a known urogenital abnormality. Only antibiotic use at the time of urine collection was associated with a lower contamination rate (OR, 0.18; 95% CI, 0.04–0.75). Results by multivariable logistic regression when adjusted for age, gender, patient location, and antibiotic use were similar. Statistical significance/tests: Logistic regression was used to compare contamination rates between collection methods, using CCU as the comparator for ORs. Statistical calculations were performed using Stata 11.0 (Stata Corp., College Station, TX). Results/conclusion biases: The use of urine dipstick tests as a method of prescreening specimens by the treating clinician prior to being sent for culture may have introduced bias.
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 1 (retrospective study of laboratory data)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 2	Total for results/findings (3-pt. maximum): 2 (prescreening of specimens by urine dipstick)
Authors: Morton and Lawande (57) Title: The Diagnosis of Urinary Tract Infection: Comparison of Urine Culture from Suprapubic Aspiration and Midstream Collection in a Children's Outpatient Department in Nigeria Yr: 1982 Publication: Ann Trop Pediatr Affiliations: Registrar in Pediatrics, Hospital for Sick Children, London United Kingdom, Registrar in Microbiology at Ahmadu Bello University Teaching Hospital, Zaria, northern Nigeria Funding: not reported	Design: observational/nonrandomized comparison study Facility/setting: outpatient clinic in a pediatric children's teaching hospital Time period: not reported Population/sample: SPA urine was collected from 287 children; 51 of these also had an MSU specimen collected. An additional 124 children had only MSU collected. Comparator: SPA urine Study bias: all SPA collections performed by a single individual	Description: SPA sample collection was by using a 19-gauge needle; the skin was cleaned with iodophor, and a 2nd attempt was made if the 1st aspiration failed. MSU collection was performed under supervision after cleansing of the external genitalia. All specimens were refrigerated prior to being processed for semiquantitative culture. Samples were also processed for urine microscopy. Duration: not reported Training: SPA was performed by a trained physician; mothers were instructed on collection of MSU. Staff/other resources: not reported Cost: not reported	Description: 1. No. of bacteria in SPA vs MSU samples were counted. 2. No. of contaminated MSU specimens from patients with sterile SPA specimens were counted. 3. Culture and microscopy results were compared for all specimens. Recording method: not reported	Type of findings: observational/comparative Findings/effect size: 1. The initial attempt at SPA was successful in 260/287 patients without complication and was easy to perform. 2. MSU collection was often difficult to perform and took up to 2 h. 3. In 51 patients with paired SPA and MSU specimens, there were no false-positive or false-negative diagnoses made with the MSU samples. 4. A high no. of contaminated specimens was found among MSU samples collected by mothers and from boys with a nonretractable prepuce. Statistical significance/tests: not reported Results/conclusion biases: none reported
Total quality rating (10-pt. maximum): 6, fair	Total for study (3-pt. maximum): 1 (total for study setting may not be generalizable; SPA collection by single individual)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 2 (no statistical analysis)

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TABLE A4 (Continued)

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Authors: Pylkkanen et al. (58) Title: Diagnostic Value of Symptoms and Clean-Voided Urine Specimen in Childhood Urinary Tract Infection Yr: 1979 Publication: Acta Paediatr Scand Affiliations: The Children's Hospital, University of Finland, Helinski, Finland Funding: Foundation of Pediatric Research; Sigrid Juselius Foundation; Orion Pharmaceutical Co.	Design: observational Facility/setting: academic medical center Time period: not reported Population/sample: 477 patients seen at an outpatient clinic were included in the study. Comparator: patients on whom SPA was performed Study bias: outpatients only	Description: 1. Urine was collected by SPA. 2. CVU was collected from infants with urine collection bags. 3. Midstream CVU was collected from children after cleansing of genitalia with 0.05% chlorhexidine solution. All specimens were examined by microscopy. All specimens were processed on Uricult dipslides. SPA specimens were also plated on blood agar Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: Cell counts were classified as ≤ 10, 11–199, or $\geq 200/mm^3$. Bacterial counts were classified as nil, scanty, or numerous by microscopy and as $<10^3$, 10^4, or $>10^5$ by quantitative culture. Urine collected by SPA was cultured on both Uricult and blood agar plates. A patient was considered infected when both cultures showed growth. Recording method: not reported	Type of findings: observational Findings/effect size: CVU specimens demonstrated significant leukocyte counts, bacterial cell counts, or $>10^5$ CFU/ml in culture for 59%, 42%, and 81% of infected (as diagnosed by SPA) symptomatic patients. Diagnostic accuracies of these indices were 88%, 94%, and 95%, respectively. In asymptomatic patients, the accuracies were considerably lower. None of the indices gave sufficient sensitivity or accuracy when used alone. Statistical significance/tests: chi-square test Results/conclusion biases: none reported
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 2 (may not be generalizable to inpatient patient populations)	Total for practice (2-pt. maximum): 1 (use of Uricult medium may impact quality of culture results)	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 3
Authors: Aronson et al. (59) Title: Combined Suprapubic Aspiration and Clean-Voided Urine Examination in Infants and Children Yr: 1973 Publication: Acta Paediatr Scand Affiliations: Department of Pediatrics, University Hospital, Lund, Sweden Funding: not reported	Design: prospective cross-sectional Facility/setting: teaching hospital Time period: not reported Population/sample: 120 specimens from infants (0–12 mo) and children (3–12 yr) Comparator: SPA urine vs cleanly voided urine Study bias: small sample size	Description: Percutaneous SPA was carried out after the suprapubic area was cleansed with alcohol and iodine. The urine was gently aspirated in a 5- or 10-ml sterile syringe and the needle withdrawn. Cleanly voided urine from infants was collected in a sterile polyethylene urine bag after previous proper cleansing of the vulva, preputial folds, and perineum. Irrigation of the vulva and prepuce was performed twice with 5 to 10 ml tepid physiologic saline. A cleanly voided midstream specimen was obtained from children after a thorough cleansing as described above. Specimens were transported to the laboratory immediately for routine culture. Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: Urinary infection was considered to be present if the bacterial count was 10^2 CFU/ml in SPA urine (true bacteriuria) and was suspected if the bacterial count in cleanly voided urine was $>10^5$ CFU/ml. Shortly after collection, the uncentrifuged urine was also examined for pyuria, expressed as the leukocyte count/mm^3. Leukocyte counts of >10 cells/mm^3 in SPA urine was considered pathological. Recording method: not reported	Type of findings: observational Findings/effect size: In infants, the suspicion of infection from cleanly voided counts of $>10^5$ CFU/ml could be excluded by a finding of normal SPA urine for 27 babies. 4 babies had infection in their SPA urine despite having only slight or moderate bacteriuria in their cleanly voided urine. 4 patients suspected of having an infection from their cleanly voided urine proved to be free of infection by examination of the SPA urine, whereas 4 patients with true bacteriuria had a low bacterial count in voided urine. Misleading information about bladder urine bacteriuria was thus obtained from bacterial culture of cleanly voided specimens in 39 of 120 examined patients. Statistical significance/tests: not reported Results/conclusion biases: Results may have been influenced by a small sample size.
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 2 (small sample size)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 2 (no statistical analysis)

TABLE A4 (Continued)

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Authors: Hardy et al. (60) Title: Comparison of Sterile Bag, Clean-Catch and Suprapubic Aspiration in the Diagnosis of Urinary Infection in Early Childhood Yr: 1976 Publication: Brit J Urol Affiliations: Department of Pediatrics and Microbiology, Royal Free Hospital, London, United Kingdom Funding: not reported	Design: cross-sectional Facility/setting: inpatient ward at a tertiary hospital Time period: not reported Population/sample: 30 inpatients; age range, 1 day to 3 yr. All were screened for urinary infections, with the bag technique being used for those without bladder control. If bacterial growth was obtained from the first bag specimen, the child was entered into the formal study. Also entered were patients whose condition demanded immediate antimicrobial therapy, for whom a delay caused by screening could not be justified. In the latter group, all 3 specimens were taken without screening. Comparator: SPA Study bias: small sample size	Description: SUB, CCU, and SPA specimens were obtained. The perineum and suprapubic regions were cleansed with sterile swabs moistened with distilled water before the specimens were collected. Specimens were sent to the laboratory for semiquantitative culture and microscopy. Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: Bacteria were quantitated on CLED culture medium and read after 18 h of incubation. The white cells were counted in unstained, uncentrifuged urine. Recording method: not reported	Type of findings: observational Findings/effect size: 1. In SPA specimens, there was no growth from 26 specimens and a pure growth of 10^5 CFU/ml or more organisms from the remaining 4 specimens. It was assumed that only these 4 had significant bacteriuria. 2. Bag and CCU specimens exhibited a high incidence (73%) of mixed growth. The mixed growth occurred from specimens that were sterile when taken by SPA. 3. There was agreement between bag, CCU, and SPA specimens in only 3 cases of no growth, and there was 1 case with significant bacteriuria. Statistical significance/tests: not reported Results/conclusion biases: Results may be impacted by small sample size.
Total quality rating (10-pt. maximum): 5, fair	Total for study (3-pt. maximum): 1 (small sample size, study population not well described)	Total for practice (2-pt. maximum): 1 (significant bacteriuria vs contamination not defined)	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 2 (no statistical analysis)
Authors: Ramage et al. (51) Title: Accuracy of Clean-Catch Urine Collection in Infancy Yr: 1999 Publication: J Pediatr Affiliations: Renal Unit and Department of Diagnostic Imaging, Royal Hospital for Sick Children, and Department of Statistics, University of Glasgow, Glasgow, United Kingdom Funding: not reported	Design: cross-sectional Facility/setting: inpatients, pediatric teaching hospital Time period: not reported Population/sample: 49 pediatric inpatients of <24 mo for whom urine culture was indicated Comparator: SPA Study bias: parents were involved in specimen collection process	Description: 58 paired urine cultures obtained by CCU collection and SPA were taken from 49 infants, 0–24 mo old (22/49 male, 45%). Comparison SPA and CCU collections occurred during a 48-h period. The urine obtained was inoculated onto a dipslide culture plate. The plates were allowed to drain and then replaced securely into the container. The specimen was cultured at 37°C and was interpreted after a minimum of 16 h. Urine cultures were defined as positive in the presence of a pure growth of >10^5 CFU/ml in those specimens obtained by CCU collection and as the growth of any quantity of organism in those obtained by SPA. Duration: not reported Training: Parents were given instruction by nurses on collection of CCU specimens. Staff/other resources: not reported Cost: not reported	Description: The primary outcome measure was the presence or absence of significant bacteriuria after both CCU collection and SPA; secondary outcome measures were the success of SPA with ultrasound guidance compared with aspiration without ultrasound guidance. Recording method: not reported	Type of findings: comparison Findings/effect size: 1. Compared to SPA specimens, CCU specimens showed a false-positive rate of 5% and a false-negative rate of 12%, with a sensitivity of 88.9% (95% CI, 65.3–98.6) and a specificity of 95.0% (95% CI, 83.1–99.4). 2. Of 16 cultures in which SPA and CCU specimens were positive, the 2 specimens that were negative by SPA but positive by CCU collection (false-positive results) demonstrated a mixed growth of >10^5 CFU/ml. In 2 SPA specimens demonstrating significant growth, a pure growth of 10^3 CFU/ml was seen in one CCU culture and a mixed growth of 10^3 CFU/ml was observed in the other (false-negative results). Statistical significance/test: chi-square test Results/conclusion biases: not reported
Total quality rating (10-pt. maximum): 8, good	Total for study (3-pt. maximum): 2 (small sample size)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 3

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TABLE A4 (Continued)

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Authors: Cohen et al. (61) Title: Urine Samples from Disposable Diapers: an Accurate Method for Urine Cultures Yr: 1997 Publication: J Fam Pract Affiliations: Pediatric Ambulatory Center and the Department of Pediatrics, Sackler School of Medicine, Tel Aviv University, Petach Tikvah, and Departments of Neonatology and Pediatrics Infectious Disease Unit, Chaim Sheba, Tel-Hashomer, Israel Funding: not reported	Design: prospective cross-sectional Facility/setting: outpatient clinic, pediatric teaching hospital Time period: not reported Population/sample: 38 infants aged 1 to 24 mo who presented to a pediatric ambulatory community clinic with fever Comparator: SPA or bladder CATH urine samples Study bias: potential subject selection bias; small sample size with inability to consider CATH and SPA separately (possible practice confounder)	Description: all infants had urine collected either by CATH or SPA and by extraction from a disposable diaper. The urine was extracted from the diapers by removing the lining layer of the diaper under aseptic conditions using sterile tweezers, and then pushing the damp fibers into the barrel of a standard 20-ml disposable syringe from which the plunger had been removed. By replacing the plunger and compressing the fibers, urine was easily obtained from the diapers. Ultra-absorbent diapers that contain a gel-like material were excluded from the study because extracting urine from them is difficult and time-consuming. In addition, diapers contaminated with feces or those that had been on the infant for longer than 3 h were excluded. The urine samples were sent to the laboratory and were cultured using standard bacteriologic techniques. Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: Laboratory technicians interpreting the urinalysis and urine cultures were blind to the patient's clinical information and to other laboratory information. Recording method: not reported	Type of findings: comparative Findings/effect size: Urinary tract infection was demonstrated by SPA or CATH specimen collection from 5 (13.2%) infants (4 female and 1 male). For all 5 children, urine cultures showed more than 10^5 CFU/ml of the same single organism from urine that had been collected from both the diapers and the SPA or CATH specimens (sensitivity of 100% [5/5] and specificity of 94% ([31/33]). A statistical analysis revealed a wide CI and estimated the low end to be 55% for sensitivity and 82% for specificity. These results were derived using the binomial distribution. Statistical significance/test: A statistical analysis (method not reported) revealed a wide CI and estimated the low end to be 55% for sensitivity and 82% for specificity. These results were derived using the binomial distribution. Results/conclusion biases: The small sample size, particularly for infants with positive results, explains why the confidence limits are much lower than the estimated values.
Total quality rating (10-pt. maximum): 5, fair	Total for study (3-pt. maximum): 1 (SPA and CATH samples not separated)	Total for practice (2-pt. maximum): 1 ("significant bacteriuria" not defined vs "contamination")	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 2 (results include very few infants with significant bacteriuria)
Authors: Grisaru-Soen et al. (52) Title: False-Positive Urine Cultures Using Bag Collection Yr: 2000 Publication: Clin Pediatr Affiliations: Pediatric Infectious Disease, Pediatrics, Pediatric Nephrology, Microbiology, Chaim Sheeba Medical Center, and Sackler Faculty of Medicine, Tel Aviv University, Israel Funding: not reported	Design: prospective cross-sectional Facility/setting: academic medical center Time period: not reported Population/sample: 50 infants aged 0 to 18 mo (mean age, 2.8 mo; median age, 1.4 mo); inclusion criteria were a suspicion of UTI or the presence of neonatal fever, no antibiotics during preceding week, and no anatomic abnormalities or systemic disease preventing urine collection by SPA or bag collection Comparator: SPA sample Study bias: none noted	Description: SPA was done first, followed by bagged urine collection. Specifics and instructions were not reported for how procedures were performed; urine transport was not described, and urine workup was not described or defined. Duration: not reported Training: not reported Staff/other resources: not reported Cost: not reported	Description: culture results reported as pure growth, mixed growth, or no growth Recording method:	Type of findings: comparison Findings/effect size: 7 SPA specimens exhibited pure growth of organisms, for a true UTI rate of 14%. 14 bagged urine specimens exhibited pure growth (13 of which were falsely positive, as SPA was negative), 23 exhibited mixed growth, and 1 that exhibited mixed growth also had a positive SPA result; the remaining mixed-growth specimens were negative by SPA. The bagged-urine contamination rate was 62%. 30/50 bagged urine samples gave a false-positive result as either pure or mixed growth. Negative bagged urine samples were suitable to exclude a diagnosis of UTI. Statistical significance/tests: not reported Results/conclusion biases: none noted
Total quality rating (10-pt. maximum): 8, good	Total for study (3-pt. maximum): 3	Total for practice (2-pt. maximum): 1 (microbiological methods not described)	Total for outcome measures (2-pt. maximum): 1 (recording method not described)	Total for results/findings (3-pt. maximum): 3

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TABLE A4 (Continued)

Bibliographic information	Total for study	Practice	Outcome measures	Results/findings
Authors: Etoubleau et al. (62) Title: Moving from Bag to Catheter for Urine Collection in Non-Toilet-Trained Children Suspected of Having Urinary Tract Infection: a Paired Comparison of Urine Cultures Yr: 2009 Publication: J Pediatr Affiliations: Department of Pediatrics, Limoges University Hospital, Hopital de la Mere et de l'Enfant, Limoges, France Funding: not reported	Design: prospective cross-sectional Facility/setting: academic medical center/emergency departments Time period: October 2004–June 2007 Population/sample: 192 non-toilet-trained children of <3 yr of age from 2 emergency departments (all had fever of unknown origin on presentation) Comparator: urine obtained by CATH Study bias: The indication for CATH was left up to the physician, depending on bag urinalysis results and the patient's clinical and biological data.	Description: An adhesive urine bag was placed on the child by a nurse. Urinalysis was performed, and then depending on this information, CATH was performed. Urine culture results from bag vs catheter-obtained specimens were assessed, with catheter culture as the reference. Duration: 44 mo Training: nurses trained on catheterization procedure Staff/other resources: not reported Cost: not reported	Description: comparison of bag cultures and catheter cultures for making a clinical diagnosis of UTI. Definitions were as follows: positive urine culture for bag specimens, $\geq 10^5$ CFU/ml; positive urine culture for CATH specimens, $\geq 10^3$ CFU/ml (1 species only); polybacterial urine culture (considered a contaminated sample), $\geq 10^5$ or $\geq 10^3$ CFU/ml (depending on collection method) and >2 species present upon culture; negative urine culture, all the other specimens. Recording method: not reported	Type of findings: comparison Findings/effect size: A total of 7.5% and 29% of bag-obtained specimens had false-positive and false-negative results, respectively, compared to CATH specimens. Bag-obtained specimens led to either a misdiagnosis or an impossible diagnosis in 40% of cases vs 5.7% when urethral catheterization was used. Statistical significance/test: percentage comparisons performed using the chi-square test Results/conclusion biases: Failure to perform a successful catheterization was common. The contamination rate for CATH specimens was also higher than expected.
Total quality rating (10-pt. maximum): 7, fair	Total for study (3-pt. maximum): 2 (selective catheterization)	Total for practice (2-pt. maximum): 2	Total for outcome measures (2-pt. maximum): 1 (recording method not reported)	Total for results/findings (3-pt. maximum): 2 (high contamination rate for catheter specimens)

[a] SPA, suprapubic aspiration; CCU, clean-catch urine; CVU, cleanly voided urine; CATH, straight catheterization; SUB, sterile urine bag; UCP, urine collection pad; MSU, midstream urine; ED, emergency department; HPF, high-power field; RR, relative risks; 95% CI, 95% confidence interval; GLIMMEX, generalized linear mixed model; OR, odds ratio; CLED, cystine lactose electrolyte-deficient.

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Alice Schauer Weissfeld, Ph.D., is the president, chief executive officer, and laboratory director of Microbiology Specialists Incorporated, a reference laboratory that she cofounded in 1984. She earned her doctoral degree in microbiology at Rutgers University, New Brunswick, NJ, and completed a postdoctoral fellowship in Public Health and Medical Laboratory Microbiology at Baylor College of Medicine, Houston, TX. Dr. Weissfeld is a diplomate of the American Board of Medical Microbiology of the American Academy of Microbiology and was elected to fellowship in the American Academy of Microbiology in 1986. She is currently a member of ASM's new Professional Practice Committee and chair of its Subcommittee on Evidence-Based Medicine. The Subcommittee oversees the development of laboratory medicine best-practice guidelines using a robust, methodical, and transparent method developed by the CDC and is participating in a cooperative agreement with the CDC to evaluate metrics to encourage the dissemination of ASM's guidelines.

Colleen S. Kraft earned her M.D. from Indiana University in 2002 and her M.Sc. from Emory University in 2013. She completed a residency in internal medicine and a fellowship in infectious diseases in the Department of Medicine, Emory University. She concluded her postgraduate clinical training in an Accreditation Council for Graduate Medical Education (ACGME) fellowship in medical microbiology in the Department of Pathology and Laboratory Medicine, Emory University. She has a joint faculty appointment at Emory University in the Department of Pathology and Laboratory Medicine and the Division of Infectious Diseases. She is the medical director of the microbiology section at Emory Healthcare and program director of the medical microbiology fellowship, and she performs rounds for the inpatient infectious diseases service. Her interests are in microbiology questions that have direct clinical implication and in the support of these practices with evidence-based methods. She has been on the faculty at Emory since 2010.

Robert L. Sautter completed his B.S. and M.S. degrees at Eastern Michigan University and received his Ph.D. in microbiology from Wayne State University in 1982. He is director of microbiology and point of care for the Carolinas Pathology Group. He has held positions that include director of the Mecklenburg County Health Laboratory and of the School of Medical Technology for Harrisburg Hospital and adjunct professor for Penn State Hershey Medical Center, as well as technologist and supervisory positions at various institutions over 43 years. Dr. Sautter serves on the North Carolina Response Advisory Group's Hospital Acquired Infection (HAI) Advisory Committee, and he chairs the North Carolina subcommittee of the HAI committee concerning multidrug-resistant organisms. He serves on many hospital and university committees. He has been chair of the clinical microbiology division of the American Society for Microbiology. He also served the Clinical Laboratory Improvement Advisory Committee and the Board of Scientific Counselors of the Office of Infectious Diseases at the CDC.

Vickie Baselski received her doctoral degree in microbiology from the University of Texas at Austin in 1978 and completed a postdoctoral fellowship in medical and public health laboratory microbiology at the Centers for Disease Control. She is a diplomate of the American Board of Medical Microbiology and a fellow in the American Academy of Microbiology. Her professional service activities have included technical direction of microbiology at The University of Tennessee Bowld Hospital, The Regional Medical Center at Memphis, and Memphis Pathology Laboratory/American Esoteric Laboratory. She currently provides technical direction for microbiology at the Shelby County Health Department and at Methodist University Hospital. She is a professor of pathology and laboratory medicine at the University of Tennessee Health Science Center. As chair of the Professional Affairs Committee of ASM, she has presented to federal, state, and private professional groups in areas relating to reimbursement, including issues related to emerging technologies.

Deb Rodahl is the group director for clinical support services at the HealthEast Care System in St. Paul, MN. The HealthEast Care System is a nonprofit healthcare organization which includes 4 acute-care hospitals, 15 physician clinics, and other free-standing business entities. Deb received her B.S. degree from the University of Minnesota in 1980 and her M.B.A. from Cardinal Stritch University in 2006. Deb has been with HealthEast since 1980, where she started out as a "generalist." In 1985, she was promoted to Operations Manager for the St. John's Laboratory. In 1992, Deb was promoted to administrative director of operations with the HealthEast Laboratories and promoted to system director of laboratory services in 1997. As a laboratory manager with responsibility for acute-care labs as well as outreach laboratory services, she has a great interest in ensuring optimal preanalytical handling of all specimens.

Edward J. Peterson, Jr., M.B.A., M.T. (American Society for Clinical Pathology), earned his bachelor's degree in medical technology and biology from the State University of New York at Fredonia in 1983, and he completed his medical technology internship at Lenox Hill Hospital, New York, NY, in 1984 and his M.B.A. from St. Joseph's University, Philadelphia, PA, in 1999. He is currently the director of laboratories for Barnes-Jewish Hospital in St. Louis, MO, which is affiliated with the Washington University School of Medicine. He is an assistant professor for Rutgers University and teaches a course in health care regulations and laboratory management. During his 31-year career, he has held positions as the director of regulatory affairs, facility planning, and diagnostic services (which included supervision of laboratories, radiology, and radiation oncology), as a general lab supervisor overseeing a hematology laboratory and a blood bank, and as a hematology supervisor for hospitals in New Jersey and New York. Proper collection of specimens is an area of interest to him because it will lead to improved patient outcomes.

Nancy E. Cornish received her B.A. in philosophy and M.D. from the University of Vermont, Burlington, VT; then she completed her pathology residency at the Vermont Medical Center Hospital. She completed a microbiology fellowship at the Cleveland Clinic Foundation before serving 13 years as a pathologist and the director of microbiology at the Methodist Health Care Systems & Children's Hospital in Omaha, NE. Dr. Cornish has been active in laboratory professional organizations as a faculty member, speaker, and presenter; this includes over 20 years with the College of American Pathologists and the American Society of Clinical Pathologists and nearly 20 years with the American Society for Microbiology and the Infectious Disease Society of America. She holds certification with the American Board of Pathologists in anatomic and clinical pathology, with a special qualification in medical microbiology. Dr. Cornish is currently medical officer for the Division of Laboratory Systems at the Centers for Disease Control and Prevention.