Urine sampling techniques in symptomatic primary-care patients: a diagnostic accuracy review

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Abstract

Background: Choice of urine sampling technique in urinary tract infection may impact diagnostic accuracy and thus lead to possible over- or undertreatment. Currently no evidence-based consensus exists regarding correct sampling technique of urine from women with symptoms of urinary tract infection in primary care. The aim of this study was to determine the accuracy of urine culture from different sampling-techniques in symptomatic non-pregnant women in primary care.

Methods: A systematic review was conducted by searching Medline and Embase for clinical studies conducted in primary care using a randomized or paired design to compare the result of urine culture obtained with two or more collection techniques in adult, female, non-pregnant patients with symptoms of urinary tract infection. We evaluated quality of the studies and compared accuracy based on dichotomized outcomes.

Results: We included seven studies investigating urine sampling technique in 1062 symptomatic patients in primary care. Mid-stream-clean-catch had a positive predictive value of 0.79 to 0.95 and a negative predictive value close to 1 compared to sterile techniques. Two randomized controlled trials found no difference in infection rate between mid-stream-clean-catch, mid-stream-urine and random samples.

Conclusions: At present, no evidence suggests that sampling technique affects the accuracy of the microbiological diagnosis in non-pregnant women with symptoms of urinary tract infection in primary care. However, the evidence presented is indirect and the difference between mid-stream-clean-catch, mid-stream-urine and random samples remains to be investigated in a paired design to verify the present findings.

Keywords: "Urinary tract infections" [Mesh], "Urine" [Mesh], "Specimen handling" [Mesh], "Urine specimen collection" [Mesh], "Primary health care" [Mesh], "General practice" [Mesh]

Background

Symptomatic urinary tract infection (UTI) in women is a common condition in general practice, and every day general practitioners or their staff instruct women in delivering urine samples for examination [1]. The main concern when sampling urine is that inadequate handling may increase the risk of contamination in turn leading to overdiagnosis and overtreatment of UTI. Sterile collection of urine samples can be performed using suprapubic puncture or urethral catheterization and use of these collection techniques could possibly reduce contamination and thereby overdiagnosis and overtreatment. However, in a primary care setting these methods are considered obsolete today due to the associated discomfort for the patient and a minor risk of iatrogenic infection and other complications. Current methods include i) mid-stream-clean-catch technique (MSCC) where the patient is instructed to clean the labia before voiding using tap water, soap or disinfectants, ii) mid-stream urine (MSU) without prior cleaning, iii) random samples delivered without instruction or iv) home-voided samples with or without standardized transport media. These sampling techniques are mostly based on tradition or expert opinion and ease-of-use for patient and doctor rather than stringent evidence. A study from 2000 conducted in primary care found no evidence that...
sampling technique affected contamination rate or infection rate in urine samples [2], but new evidence within this area is often questioned and debated [3–5]. Since sampling techniques (MSCC, MSU, random samples and home voiding) differ extensively in preparation time and discomfort, ease-of-use for doctors as well as their patients, it is relevant to review their diagnostic yield. The aim of this study was to conduct a systematic review to determine the accuracy of urine culture from different sampling techniques in symptomatic patients in primary care.

Method

Literature search
We searched Medline and Embase for clinical studies conducted in primary care published before May 2015 in English, Swedish, Danish or Norwegian. Combinations of the words "urinary tract infection", cystitis, bacteriuria, urine, specimen, handling, urinalysis, collection, midstream and "clean catch" were used. To identify more studies from before 1970, a slightly different search-string was used for the older studies in Medline. The literature search and inclusion of studies was performed by AH. The full search strings can be seen in Appendix A.

Inclusion criteria
Clinical studies randomizing or using a paired design to compare the result of urine culture obtained with two or more collection techniques in adult, self-helped, non-pregnant (and not post-partum) women with symptoms of UTI in primary care (general practice, outpatients clinics or comparable settings). We did not discriminate between complicated and uncomplicated cases of UTI.

Exclusion criteria

- Studies investigating mainly patients who were not self-helped, were asymptomatic, pregnant, children or men (wrong group)
- Studies conducted in the secondary sector (wrong setting)
- Studies using other modalities than culture as reference (wrong gold standard)
- Studies where data for the selected outcome was not available (missing data)
- Studies using a different design than described in the inclusion criteria (wrong design)

The references of included studies were screened and experts in the field were contacted to provide additional literature.

Data extraction
Data from included studies were entered into a data-form with information on setting, number of patients, age, inclusion- and exclusion-criteria for the study, reference and index text, the assigned cut off for infection vs. contamination, the bacteria identified and study design. Data on absolute numbers of infected urine samples, true and false positives and negatives or predictive values of one sampling method versus another were likewise extracted from the included studies. If these measures were not directly provided in the article, we calculated them if possible. Selected outcomes were dichotomized for the planned analyses as negative/positive culture. Culture results presented as equivocal and contaminated were grouped with the negative results. Data from the relevant patients were extracted when studies also included patients covered by the exclusion criteria. Data extraction was done by both authors and discrepancies were discussed and corrected. When data was not available or incomplete we referred from contacting authors, as most studies were more than 10 years old.

Definition of reference standard
Assuming an increasing contamination rate in the order of: 1) Suprapubic puncture, 2) urethral catheterization samples, 3) MSCC, 4) MSU, 5) Random samples, 6) Home-voided urine, the least contaminated was used as reference and the most contaminated as index test. For example, if a study investigated both MSCC and random urine sampling in a paired design, MSCC was used as reference standard and random samples as index test.

Study designs
This review included both paired studies and randomized controlled trials (RCT). RCTs were analysed separately.

Quality assessment
The included studies were evaluated using QUADAS-2 for assessment of diagnostic accuracy studies [6]. No study was excluded based on low quality according to this tool. Both studies using paired samples and randomized controlled trials were assessed with QUADAS-2.

Data analysis
The specified dichotomized outcomes were used to calculate predictive values, sensitivity and specificity in paired studies. The generated sensitivity and specificity values were used to create forest plots on the diagnostic accuracy. Diagnostic accuracy plots were performed using Review Manager (RevMan) Version 5.3. Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2014.

Results

Literature search
The initial search resulted in 570 titles in Medline and 749 titles in Embase. After review of titles, abstracts and articles we included seven full text articles presenting results.
from seven studies investigating urine sampling technique in 1062 non-pregnant women with symptoms of UTI in primary care. A flow diagram of the literature search and review of titles, abstracts, and articles is shown in Fig. 1. Two of the studies were from general practice while the remaining five were from outpatient clinics or student clinics. The included studies are shown in Table 1. A list of excluded studies is provided in Appendix B.

**Quality of included studies according to Quadas-2**

The quality of the included studies is summarized in Table 2. Generally the studies were judged to be of moderate to high risk of bias. No study was considered having low risk of bias. The most common error was lack of blinding of the interpreter to the results of the index and reference tests or lack of reporting of blinding. The applicability of the studies was not regarded a general concern. The full quality assessment is described in Additional file 1.

**Data from included studies**

**Paired design studies**

Four studies used a paired design to compare MSCC urine samples to samples obtained with urethral catheterization or suprapubic puncture (n = 589) [7–10]. Urethral catheterization and suprapubic puncture are essentially sterile techniques and served as reference e.g. gold standard. Two of these studies applied ≥10 cfu/ml as the cut-off for infection in both index- and reference-test, one study used a cut-off of ≥10⁵ cfu/ml and one reported absolute counts for both index- and reference-test (Table 1). The positive predictive value (PPV) of a MSCC sample varied according to the chosen cut-off for infection: cutoff: ≥10 cfu/ml 0.79 (0.71-0.86); cutoff: ≥10⁵ cfu/ml 0.95 (0.83-

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**Table 1** Characteristics of included studies

| Study      | Setting           | Design          | Patients (n) | Incidence | Technique            | Cutoff index⁴ | Cutoff reference⁴ |
|------------|-------------------|-----------------|--------------|-----------|----------------------|---------------|-------------------|
| Hooton 2013| Outpatient clinic | Paired samples  | 202³         | 0.70      | MSCC vs. Cat         | ≥10 cfu/ml    | ≥10 cfu/ml        |
| Lifshitz 2000| University clinic | RCT             | 242          | 0.55      | Random vs. MSCC⁵     | ≥10⁵ cfu/ml   | ≥10⁵ cfu/ml       |
| Baerheim 1990| General practice  | Paired samples  | 73           | 0.74      | Home vs. MSCC        | ≥10⁴ cfu/ml   | ≥10⁴ cfu/ml       |
| Walter 1989 | Outpatient clinic | Paired samples  | 105          | 0.40      | MSCC vs. Cat         | ≥10⁵ cfu/ml   | ≥10⁵ cfu/ml       |
| Bradbury 1988| General practice  | RCT             | 158          | 0.25      | MSU vs. MSCC         | > 10⁵ cfu/ml  | > 10⁵ cfu/ml      |
| Stamm 1982  | Outpatient clinic/student clinic | Paired samples | 187          | 0.52      | MSCC vs. Cat/Sup     | Reporting absolute counts | ≥10 cfu/ml |
| Mabeck 1969 | Outpatient clinic | Paired samples  | 95           | -         | MSCC vs. Sup         | Reporting absolute counts | Reporting absolute numbers |

Detailed legend: Characteristics of included studies. ³The definition has been simplified. ⁴Reporting the number of samples not patients. ⁵MSCC and MSCC + vaginal tampon. RCT Randomized controlled trial; MSCC Mid-stream-catch; MSU Mid-stream-urine; Cat Urethral Catheterization; SUP suprapubic puncture; cfu colony-forming units
The negative predictive value of a MSCC was close to 1 in all four studies. The accuracy found in the four studies is shown in Table 3. The achieved specificity was influenced by the selected cut-off levels, with higher thresholds corresponding to increasing specificity. We did not perform a meta-analysis or calculate heterogeneity as the applied cut-offs varied considerable thus impeding a meaningful pooling of the results.

One study investigated home-voided samples against MSCC taken in general practice [11]. This study found a high PPV of home-voided samples of 0.92 (0.81-0.98), but a lower NPV of 0.71 (0.48-0.88). The results of this study are shown in Table 4.

The studies by Stamm and Mabeck reported absolute counts of colony-forming units in the voided urine samples and this allowed us to investigate the current cut-off for primary uropathogens of $10^4$ cfu/ml in voided urine samples against 10 cfu/ml in suprapubic puncture [12]. Using these current cut-offs we calculated the sensitivity of MSCC to be 0.81 (0.71-0.88) in the study by Stamm and 0.96 (0.85-0.99) in the study by Mabeck. Corresponding specificities were 0.90 (0.82-0.95) in the study by Stamm and 0.59 (0.43-0.73) in the study by Mabeck.

### Randomized controlled trials
Two randomized controlled trials were identified comparing MSU or random samples to MSCC with infection rate and contamination rate in the randomization-groups as their primary outcomes (number of patients = 400) [2, 13]. Because of the randomized design, accuracy could not be calculated from these studies. The studies are shown in Table 5. None of the studies found significant differences in infection rate or contamination rate between sampling techniques.

### Discussion
This diagnostic accuracy review is the first to assess the available evidence from different urine sampling techniques on symptomatic patients with suspected UTI in primary care. Overall, we did not find consistent evidence to suggest important differences in diagnostic accuracy among the included urine sampling techniques (MSCC, MSU or random voiding). The slightly lower specificity of voided samples compared to invasive sampling techniques (suprapubic puncture and catheter) will cause 5–10 % of healthy patients to be overdiagnosed. This does not, in our opinion, outweigh the discomfort and risk of complications associated with sterile techniques. The quality of the studies was

### Table 2 Quality of included studies assessed using Qaudas-2

| Study         | RISK OF BIAS | APPLICABILITY CONCERNS |
|---------------|--------------|------------------------|
|               | PATIENT SELECTION | INDEX TEST | REFERENCE STANDARD | FLOW AND TIMING | PATIENT SELECTION | INDEX TEST | REFERENCE STANDARD |
| Hooton 2013   | ✔️            | ✔️           | ✔️                  | ✔️             | ✔️                  | ✔️           | ✔️                  |
| Lifshitz 2000 | ✔️            | ✔️           | ✔️                  | ✔️             | ✔️                  | ✔️           | ✔️                  |
| Baehreim 1990 | ✔️            | ✔️           | ✔️                  | ✔️             | ✔️                  | ✔️           | ✔️                  |
| Walter 1989   | ✔️            | ✔️           | ✔️                  | ✔️             | ✔️                  | ✔️           | ✔️                  |
| Bradbury 1988 | ✔️            | ✔️           | ✔️                  | ✔️             | ✔️                  | ✔️           | ✔️                  |
| Stamm 1982    | ✔️            | ✔️           | ✔️                  | ✔️             | ✔️                  | ✔️           | ✔️                  |
| Mabec 1969    | ✔️            | ✔️           | ✔️                  | ✔️             | ✔️                  | ✔️           | ✔️                  |

**Detailed legend:**
- ✔️ Low Risk
- ✗ High Risk
- ? Unclear Risk

### Table 3 MSCS vs. sterile samples

| Study       | Cut-off (cfu/ml) | TP | TN | FN | FP  | PPV (95% CI) | NPV (95% CI) | SEN (95% CI) | SPE (95% CI) | Sensitivity (95% CI) | Specificity (95% CI) |
|-------------|-----------------|----|----|----|-----|--------------|--------------|--------------|--------------|----------------------|----------------------|
| Walter 1989 | $> 10^5$ cfu/ml | 103| 41 | 61 | 2   | 0.95 (0.85-0.99) | 0.58 (0.90-1.00) | 0.98 (0.88-1.00) | 0.67 (0.68-0.99) |                       |                      |
| Mabec 1969  | $> 10^3$ cfu/ml | 95 | 39 | 57 | 0   | 0.91 (0.77-0.97)  | 0.80 (0.91-1.00) | 0.90 (0.88-1.00) | 0.79 (0.64-0.84) |                       |                      |
| Hooton 2013 | $> 10$ cfu/ml   | 202| 84 | 44 | 1   | 0.90 (0.84-0.94)  | 0.88 (0.86-1.00) | 0.99 (0.96-1.00) | 0.73 (0.60-0.84) |                       |                      |
| Stamm 1982  | $> 10$ cfu/ml   | 187| 98 | 83 | 0   | 0.79 (0.71-0.86)  | 1.00 (0.93-1.00) | 1.00 (0.95-1.00) | 0.71 (0.60-0.86) |                       |                      |

**Detailed legend:** Diagnostic accuracy of mid-stream-clean-catch samples vs. urethral catheterization/suprapubic puncture. 95 % confidence intervals in brackets. A cut-off of $> 10^4$ cfu/ml has been chosen in the study by Mabec. TP True positives; TN True negatives; FN False negatives; FP False positives; PPV Positive predictive value; NPV Negative predictive value; SEN Sensitivity; SPE Specificity
moderate and substantial heterogeneity was present between study designs and applied diagnostic cut-offs. With the available evidence, each general practitioner can choose freely the sampling technique most appropriate for his or her practice and patients.

The current review included two studies from general practice and 5 from outpatient clinics or student clinics. Participants were symptomatic patients under investigation for urinary tract infection. We have no reason to suspect the included patients differ from the average UTI patient in primary care. Thus we believe the results can be considered applicable to most primary care settings including general practice.

The included methods of urine sampling included, the different cut-offs for infection applied and the time span between studies of up to 50 years does however suggest that the overall results regarding their diagnostic accuracy should be considered with caution.

The current consensus regarding a cut-off for infection (eg. 10^5 cfu/ml for primary uropathogens) was not directly assessed in any of the studies, but we calculated the sensitivity and specificity based on the two studies by Mabeck and Stamm. While the sensitivity was above 0.80 in both studies, the specificity differed between studies and was low (0.59) in the study by Mabeck. However, this could be a chance finding and caution should be excised when interpreting these results as they are based on few older studies and we do not know if this result would still apply today with current microbiological procedures. Furthermore, current cut-offs are based on microbiological assessments and have, to our knowledge, never been validated in relation to patient-relevant outcomes like cure-rate or impact on daily activities. The development of such patient-centred outcomes may be more applicable to a general practice setting.

The European urine analysis guideline recommends a MSCC without detergents [12]. However, this guideline is based on studies including pregnant, asymptomatic as well as hospitalized patients and their conclusions do not necessarily apply to the average patient in general practice. Studies based in secondary care have found varying accuracy of voided urine samples depending on their patient group, design and gold standard [14–18]. However, studies investigating symptomatic, otherwise healthy women seem to essentially reproduce our findings [19, 20].

Conclusions
The present review does not present evidence to suggest one urine sampling technique over another according to diagnostic performance; rather this should at present depend on ease of use and convenience for patients and practices. This lack of evidence is in part due to few available studies and further testing on current diagnostic cut-offs as well as new patient-centred outcomes is warranted.

Appendix A
Search Strings
SEARCH:
Search string Medline 01.01.1971 – 31.05.2015: ("Urinary Tract Infections"[Mesh] OR "Cystitis"[Mesh] OR “Urinary Tract Infection” OR Cystitis OR "Bacteriuria"[Mesh] OR Bacteriuria) AND (Urine OR "Urine"[Mesh]) AND ("Specimen Handling"[Mesh] OR "Urinalysis"[Mesh] OR "Urine Specimen Collection"[Mesh]) OR Collection OR midstream OR "clean catch") NOT ("Animals"[Mesh] NOT "Humans"[Mesh]) NOT "Pregnancy"[Mesh] NOT "Child"[Mesh] NOT "Infant"[Mesh] NOT "Male"[Mesh]
Search string Medline 01.01.1955 - 31.12.1970: ("Urinary Tract Infections"[Mesh] OR "Cystitis"[Mesh] OR “Urinary Tract Infection” OR Cystitis OR "Bacteriuria"[Mesh] OR Bacteriuria) AND (Urine OR "Urine"[Mesh]) AND ("Specimen Handling"[Mesh] OR "Urinalysis"[Mesh] OR "Urine Specimen Collection"[Mesh]) OR Collection OR midstream OR "clean catch") OR "Urine/microbiology"[Mesh]) NOT("Animals"[Mesh] NOT "Humans"[Mesh]) NOT "Pregnancy"[Mesh] NOT "Child"[Mesh] NOT "Infant"[Mesh] NOT "Male"[Mesh]
Search string Embase: (urinary tract infection/or cystitis.mp. or cystitis/or bacteriuria/or bacteriuria.mp.) AND (urine/or urine.mp.) AND (collection or specimen or midstream).af. And (woman or women or female).af.
Filter: Language = English, Swedish, Danish, Norwegian

| Study          | Technique      | Patients (n) | Incidence | Index infected (95 % CI) | Reference infected (95 % CI) |
|----------------|----------------|--------------|-----------|--------------------------|-----------------------------|
| Bradbury 1988  | MSU vs. MSCC   | 158          | 0.25      | (0.18-0.31)              | 0.25 (0.14-0.35)             |
| Lifshitz 2000  | Random vs. MSCC| 242          | 0.55      | (49-61)                  | 0.57 (0.46-0.68)             |

Detailed legend: Infection rates in randomized controlled trials included in the review. 95 % confidence intervals in brackets. MSCC mid-stream clean catch; MSU Mid-stream urine; Random random sample without instruction
### Table 6 Complete list of excluded studies

| Title                                                                 | Author                                      | Year | Identified | Excusion  | Excluded after |
|----------------------------------------------------------------------|---------------------------------------------|------|------------|------------|----------------|
| Abnormal urinalysis results are common, regardless of specimen collection technique, in women without urinary tract infections. | Frazee B.W, Enriquez K, Ng V, Alter H.      | 2015 | Embase     | Wrong group | Abstract       |
| A midstream urine collector is not a good alternative to a sterile collection method during the diagnosis of urinary tract infection. | Verliat-Guinaud J, Blanc P, Gamier F, Gajdos V, Guigonis V. | 2015 | Medline    | Wrong group  | Abstract       |
| Re: Voided midstream urine culture and acute cystitis in premenopausal women. | Schaeffer E.M.                             | 2014 | Embase     | Commentary/review | Abstract   |
| Associations between individual lower urinary tract symptoms and bacteriuria in random urine samples in women. V. | Sorrentino F, Cartwright R, Digesu GA, Tolton L, Franklin L, Singh A, Greco P, Khullar V | 2014 | Medline    | Wrong setting | Abstract       |
| Infection: Utility of midstream urine cultures questioned. | Payton S.                                  | 2014 | Medline    | Commentary/ review | Abstract   |
| Voided midstream urine culture is a good test for acute cystitis in premenopausal women. | Cox L, Clemens JQ.                         | 2014 | Medline    | Commentary/ review | Article    |
| Easy peesy: A patient satisfaction survey on an innovative device for collection of mid-stream urine (MSU) samples. | Khorsandi M, Hussain B, Chow W.            | 2013 | Embase     | Wrong design | Abstract       |
| Peezy at ease: Our initial 106 patients experience on an innovative device for collection of Mid-Stream Urine (MSU) samples. | Chow W.M, Hussain B.                      | 2013 | Embase     | Wrong design | Abstract       |
| Effect of urogenital cleaning with paper soap on bacterial contamination rate while collecting midstream urine specimens | Shrestha R, Gyawali N, Gurung R, Amatya R, Bhattacharya SK. | 2013 | Medline    | Wrong setting | Article    |
| Urine collection in the emergency department: what really happens in there? | Frazee BW, Frausto K, Cisse B, White DE, Alter H. | 2013 | Medline    | Wrong setting | Abstract       |
| Urine specimen collection: how a multidisciplinary team improved patient outcomes using best practices. | Dolan VJ, Cornish NE.                     | 2013 | Medline    | Wrong setting | Abstract       |
| *Mixed growth of doubtful significance* is extremely significant in patients with lower urinary tract symptoms. | Sathiananthamoorthy S, Swamy S, Kupelian A, Horsley H, Gill K, Collins L, Malone-Lee J. | 2012 | Embase     | Wrong design | Abstract       |
| The impact of improperly collected urine cultures on patient treatment in the emergency department. | Francis K, Lucente K.M, Kim Y.             | 2012 | Embase     | Wrong design | Abstract       |
| Managing UTI in primary care: should we be sending midstream urine samples? | Hay AD.                                    | 2010 | Medline    | Commentary/ review | Abstract   |
| A comparative study on bacterial cultures of urine samples obtained by clean-void technique versus urethral catheterization. | Lau AY, Wong SN, Yip KT, Fong KW, Li SP, Que TL. | 2007 | Medline    | Wrong group | Abstract       |
| Comparison of sampling methods for urine cultures. | UnlA¼ H, Sardan YC, Ulker S                | 2007 | Medline    | Wrong setting | Abstract       |
| Effect of perineal cleansing on contamination rate of mid-stream urine culture. | Blake DR, Doherty LF.                     | 2006 | Medline    | Wrong group | Abstract       |
| Obtaining a catheter specimen of urine. | Gilbert R.                                | 2006 | Medline    | Commentary/ review | Article    |
| Taking a midstream specimen of urine. | Gilbert R.                                | 2006 | Medline    | Commentary/ review | Abstract   |
| A novel midstream urine-collection device reduces contamination rates in urine cultures amongst women. | Jackson SR, Dryden M, Gillett P, Kearney P, Weatherall R. | 2005 | Embase     | Wrong group | Abstract       |
| Catheter specimens of urine: an audit of practice. | Gilbert R, Henderson S.                   | 2005 | Medline    | Wrong design | Abstract       |
| Contamination of urine specimens did not differ with collection technique in women with acute dysuria. | Lifshitz E, Kramer L.                     | 2001 | Medline    | Commentary/ review | Abstract   |
| Collection and transport of urine for culture. | Perera CU.                                | 2001 | Medline    | Commentary/ review | Abstract   |
Table 6  Complete list of excluded studies (Continued)

| Title                                                                 | Author(s)                                              | Year | Database | Design  | Group     | Abstract/Commentary |
|-----------------------------------------------------------------------|--------------------------------------------------------|------|----------|---------|-----------|---------------------|
| Honey jars and diagnosis of urinary tract infections–ascent quality work. | Forsum U.                                              | 2001 | Medline  | Wrong design | Article   |                     |
| A technique for collection of uncontaminated urine for culture from female patients. | Gleason D.M., Bottaccini M.R., Reilly R.J., McNeill J. | 2000 | Embase   | Wrong group | Article   |                     |
| The midstream muddle.                                                 | Bannatyne RM.                                          | 2000 | Medline  | Commentary/ review | Abstract |                     |
| Urine collection and culture in elderly people.                       | Clague J., Horan M.                                    | 1998 | Medline  | Wrong design | Article   |                     |
| A simple and efficient urine sampling method for bacteriological examination in elderly women. | Michielsen W.J., Geurs F.J., Venschraegen G.L., Claey s G.W., Afschrift M.B. | 1997 | Medline  | Wrong group | Article   |                     |
| Assessment of urine collection technique for microbial culture.        | Prandoni D., Boone M.H., Larson E., Blane C.G., Fitzpatrick H. | 1996 | Medline  | Wrong group | Article   |                     |
| Collecting clean-catch urine in the nursing home: obtaining the uncontaminated specimen. | Brazier A.M., Palmer M.H.                              | 1995 | Embase   | Commentary/ review | Abstract |                     |
| Bacteriuria–sampling methods and significance.                        | Pfau A.                                                | 1994 | Medline  | Wrong design | Article   |                     |
| Collection of urine for culture.                                       | Jaffe J.S.                                             | 1994 | Medline  | Commentary/ review | Abstract |                     |
| Does a clean-catch urine sample reduce bacterial contamination?        | Leisure M.K., Dudley S.M., Donowitz L.G.               | 1993 | Medline  | Wrong group | Article   |                     |
| Urine sampling technique.                                             | Curtis P., Kim-Foley S., Kebede M.                     | 1993 | References | Commentary/ review | Abstract |                     |
| Evaluation of urine sampling technique: bacterial contamination of samples from women students | Baerheim A. (1), Digranes A., Hunskaar S. | 1992 | References | Wrong group | Article   |                     |
| Bacteriological findings in urine specimens from women. Association with urinary tract symptoms and sampling methods. | Baerheim A., Digranes A., Hunskaar S., Laerum E. | 1991 | Medline  | Wrong design | Abstract |                     |
| Perineal cleansing and midstream urine specimens in ambulatory women.  | Holliday G., Strike P.W., Masterton R.G.                | 1991 | References | Wrong group | Article   |                     |
| Urine sampling in ambulatory women.                                   | Walter F.G.                                            | 1990 | Medline  | Duplicate   | Abstract  |                     |
| An approach to urinary tract infections in ambulatory women.           | Ronald A.R., Conway B.                                 | 1988 | References | Commentary/ review | Article   |                     |
| Laboratory diagnosis of urinary tract infection in ambulatory women.   | Latham R.H., Wong E.S., Larson A.                      | 1985 | Embase   | Wrong design | Abstract |                     |
| Clean-catch versus straight-catheter urinalysis results in women.      | Guss D.A., Dunford J.V., Griffith L.D., Neuman T.S., Baxt W.G., Winger B., Gruber S.L. | 1985 | Medline  | Wrong design | Article   |                     |
| Validity of urinary catheter specimen for diagnosis of urinary tract infection in the elderly. | Grahn D., Norman D.C., White M.L., Cantrell M., Yoshikawa T.T. | 1985 | Medline  | Wrong group | Abstract  |                     |
| Is the Clean-Catch Midstream Void Procedure Necessary for Obtaining Urine Culture Specimens from Men? | Lipsky B.A., Inui T.S., Plorde J.J., Berger R.E. | 1984 | References | Wrong group | Article   |                     |
| Comparison of mid catheter collection and suprapubic aspiration of urine for diagnosing bacteriuria due to fastidious micro-organisms. | Savige J.A., Birch D.F., Fairley K.F. | 1983 | Medline  | Wrong setting | Article   |                     |
| THE MYTH OF THE CLEAN CATCH URINE SPECIMEN                             | Immergut M.A., Gilbert E.C., Frensilll F.J., Goble M.  | 1981 | References | Wrong group | Article   |                     |
| [Diagnosis of urinary infections by the transportable agar method. Collection of urine in non-sterile containers]. | Svendsen I., Eklund A.                                | 1980 | Medline  | Wrong design | Article   |                     |
| An automatic midstream urine collector.                                | King M.R.                                              | 1980 | Medline  | Wrong setting | Article   |                     |
| Perineal cleansing before midstream urine, a necessary ritual.         | Morris R.W., Watts M.R., Reeves D.S.                   | 1979 | Medline  | Missing data | Article   |                     |
| Comparison of paired midstream voided and catheterized urine samples from female patients in a general hospital. | Barnes W.F., Albers D.D.                              | 1978 | Medline  | Wrong group | Article   |                     |
| New method for obtaining uncontaminated urine from women.              | Cade R., Raulerson J.D., Mahoney J.J., Duprey P., Privette M., Phelan M.C., Beers H., Fuller T.J., Juncos L.I., Grubb W.G. | 1978 | Medline  | Wrong group | Abstract  |                     |
Table 6 Complete list of excluded studies (Continued)

| Comparison of paired midstream voided and catheterized urine samples from female patients in a general hospital. | Barnes WF, Albers DD | 1978 | References | wrong group | Article |
| Qualitative assessment of midstream urine cultures in the detection of bacteriuria. | Gower P.E. Roberts A.P. | 1975 | Embase | wrong group | Abstract |
| Bacterial contamination of urine, collected in fractions from different phases of micturition. A study in healthy women. | Henning C, Tornvall G. | 1975 | Medline | wrong group | Abstract |
| Correlation of a new urine collection-culture tube with the standard loop technique. | Martin LP, Ahmed M. | 1974 | Medline | wrong setting | Article |
| [Examination of the urine. Collection, transport and quantitative bacteriological assessment]. | Vejlsgaard R. | 1969 | Medline | Commentary/review | Article |
| Suprapubic bladder aspiration in diagnosis of urinary tract infection. | Bailey RR, Little P.J. | 1969 | Medline | Wrong design | Article |
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Additional file

Additional file 1: Quadas-2. (PDF 427 kb)

Abbreviations
FN, false negatives; FP, false positives; MSCC, mid-stream-clean-catch technique; MSU, mid-stream urine; NPV, negative predictive value; PPV, positive predictive value; RCT, randomized controlled trials; SEN, sensitivity; SPE, specificity; TN, true negatives; TP, true positives; UTI, urinary tract infection

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Availability of data and materials
Complete list of excluded studies and full quality evaluation can be found in appendices. For additional data, please contact the corresponding author.

Authors’ contributions
The literature search and inclusion of studies was performed by AH. Both authors performed the data extraction and quality assessment. Both authors have critically revised the manuscript and approved the final version.

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Not applicable.

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The authors declare, they have followed the PRISMA Guidelines in conducting this study.

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