

Horizon Scan Report 0028

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**Diagnostic Technology:** Alternative sampling methods for collection of urine specimens in older adults

**Clinical Question:** Which sampling methods other than in-and-out catheterization or suprapubic aspiration can be used to collect valid uncontaminated urine specimens for microbiological culture in older adults?

**Background, Current Practice and Advantages over Existing Technology:**

Urinary tract infections (UTIs) are one of the most common bacterial infections in older populations. Despite increasing research into this infectious disease, substantial uncertainty still surrounds its diagnosis. Symptoms tend to be less specific in frail elderly and difficulties with cognition or communication can further impair clinical evaluation.<sup>1,2</sup> Consequently, physicians often resort to urinary analysis to support the diagnosis.

Urine samples should be collected by a protocol that minimizes contamination from the genital mucosa and perineal skin. Guidelines recommend the collection of a mid-stream specimen in adults. However, obtaining such samples from older persons may be difficult, as they can be cognitively impaired, have physical constraints and/or suffer from incontinence.<sup>3</sup> In persons unable to control voiding or cooperate, in-and-out catheterization and suprapubic aspiration have therefore become standard methods for urine collection. These techniques can, however, cause pain or discomfort and induce a small risk of infection.<sup>4</sup> Moreover, they are also difficult to perform and more time- and resource-consuming.<sup>5</sup> To overcome these disadvantages there is a need for alternative urine collection methods in older adults.

**Details of Technology:**

Several alternative methods for collecting urine specimens have been used in elderly individuals, depending on gender.

- In men, the use of condom catheters to obtain a urine specimen for culture is most promising. They are already frequently used as continence care products for men.
- As an alternative to the external catheter in men, external urine collection devices have been developed for urine sampling in adult women. These funnel-like devices need to be held near the vulva. When the person urinates, the urine runs into a small container connected to the funnel.
- Urine culture collection from disposable nappies has been used for urine collection in children. This technique has now been applied to geriatric care where it can be used with incontinence pads and adult diapers.
- Finally, urine sampling via simple clean catch technique into a (disinfected) bed pan, disposable hat/bowel or urinal has also been explored, without midstream being required.

A literature search was conducted to determine the validity of these alternative sampling methods compared to in-and-out catheterization and suprapubic aspiration, the current reference methods (gold standards) in the elderly. The test performance results, i.e. sensitivity (Se), specificity (Sp), positive and negative likelihood ratios (LR+ and LR-) and positive and negative predictive values (PPV and NPV), are reported with their 95% confidence intervals (95% CI).<sup>6</sup>

**Patient Group and Use:**

- To collect high quality and non-contaminated urine specimens which can aid in the diagnosis of UTI in older adults (aged 65 years or above) who are unable to self-collect urine specimens and/or cooperate with the urine collection due to cognitive impairments, physical constraints, illness and/or lack of voiding control;
- To identify a feasible urine collection method that is less time consuming and thus easier to achieve in busy clinical environments (e.g. in general practice, nursing homes or other health care settings), and that can minimise patient discomfort and reduce risk of complications.

**Importance:**

More than half of the specimens analysed in UK microbiological laboratories are urine samples. The submission rate is highest in the over 64 age group (range 180-269/1000 patient population in primary care). This large amount of urine

specimen submission reflects a considerable workload in laboratories and primary care, with cost implications.<sup>7</sup> Large numbers of positive cultures occur in older people, especially in nursing homes and geriatric wards (15-50%)<sup>1</sup>, supporting the hypothesis that a proportion may result from contamination. Simple techniques are therefore needed in order to optimise collection of uncontaminated urine samples in elderly individuals and optimise clinical practice.

### Previous Research:

#### Accuracy compared to existing technology

Six studies meeting the research question criteria were identified.<sup>8-13</sup> Annex 1 gives details on the individual characteristics of these studies, together testing 328 older adults.

Three studies explored the validity of clean catch urine specimen collection, one tested urine specimens obtained from diapers and two studies used condom catheters as index method. Cleansing methods prior to sampling differed between studies. Reference methods used were in-and-out catheterisation (n=4), urethral catheterisation (clamped for 30 minutes) (n=1) and suprapubic aspiration (n=1). Three studies were conducted in a female population, two in male residents and one study in both men and women. The research was conducted in either geriatric hospital wards (n=3) or in long-term care facilities (LTCF; n=3). Table 1 shows a summary of the test performance results by study.

**Table 1. Summary of the test performance results of the included studies**

Author	Index vs. Reference	No of patients	Threshold	Bacteriuria <sup>(1)</sup>	Se (95% CI)	Sp (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
Verheggen et al. (1991) <sup>8</sup>	Clean catch vs. urethral catheter specimen	67 men (32.8%) and women	$\geq 10^5$ CFU/ml of no more than 2 different species or $10^3$ - $10^5$ CFU/ml of one species with many colonies	28.4%	0.90 (0.69-0.97)	0.98 (0.89-1.00)	0.94 (0.74-0.99)	0.96 (0.86-0.99)	42.9 (6.1-300.5)	0.1 (0.0-0.4)
Ouslander et al. (1995) <sup>9</sup>	Clean catch vs. sterile in-and-out cath	101 Women	>50,000 CFU/ml Note: Almost 95% of specimens grew $\geq 10^5$ CFU/ml	28.7%	0.90 (0.74-0.96)	0.92 (0.83-0.96)	0.81 (0.65-0.91)	0.96 (0.88-0.99)	10.8 (5.0-23.4)	0.1 (0.0-0.3)
Michielsen et al.* (1997) <sup>10</sup>	Clean catch vs. suprapubic aspiration	58 women	$\geq 10^5$ CFU/ml <sup>(2)</sup>	48.3%	0.98 (0.85-1.00)	0.86 (0.69-0.94)	0.86 (0.71-0.94)	0.98 (0.85-1.00)	6.8 (2.9-15.9)	0.0 (0.0-0.3)
Belmin et al. (1993) <sup>11</sup>	Clean diaper vs. in-and-out cath.	52 women	Infection if (1) leukocyte >10,000/ml (2) bacterial count > $10^5$ CFU/ml	57.7%	0.93 (0.78-0.98)	0.91 (0.72-0.98)	0.93 (0.79-0.98)	0.91 (0.72-0.98)	10.3 (2.7-38.6)	0.1 (0.0-0.3)
Ouslander et al.* (1987) <sup>12</sup>	Clean condom catheter vs. sterile in-and-out cath.	26 men	$\geq 10^5$ CFU/ml	38.5%	0.86 (0.57-0.97)	0.97 (0.77-1.00)	0.95 (0.66-1.00)	0.92 (0.71-0.98)	29.4 (1.9-455.1)	0.1 (0.0-0.6)
Nicolle et al.* (1988) <sup>13</sup>	Sterile & clean condom catheter <sup>(3)</sup> vs. sterile in-and-out cath.	24 men	$\geq 10^5$ CFU/ml <sup>(4)</sup>	75.0%	0.98 (0.81-1.00)	0.90 (0.46-0.99)	0.98 (0.81-1.00)	0.90 (0.46-0.99)	9.8 (0.7-135.5)	0.0 (0.0-0.4)

CFU = colony-forming units; \* Where two by two tables contained zero cells, we added 0.5 to each cell to enable calculations; <sup>(1)</sup> Prevalence of bacteriuria according to the reference test; <sup>(2)</sup> Recalculation of the results as the authors made a distinction between infection and asymptomatic bacteriuria: UTI: (1) culture  $\geq 10^5$  CFU/ml + (2)  $\geq 10$  leucocytes per high-power field and growth on culture; Bacteriuria: (1) culture  $\geq 10^5$  CFU/ml + (2) <10 leucocytes per high-power field; <sup>(3)</sup> No difference was observed in test performance results between sterile and clean condom catheters; <sup>(4)</sup> Recalculation of the results as the authors considered any organism present in any quantitative count in the reference test as an infecting strain.

Three studies explored the validity of clean catch specimens: two were conducted in a geriatric hospital ward, the other in seven nursing homes. The majority of study participants were women (90.3%; n=204/226). The reference methods were in-and-out catheterisation (n=1), urethral catheterisation (catheter clamped for 30 minutes) (n=1) and suprapubic aspiration (n=1).<sup>8-10</sup> The sensitivity and specificity varied from 90-98% and 86-98%, respectively. The authors of all three studies concluded that the clean catch collection method is valid and that it can avert the use of more invasive methods.

Urine sampling from disposable diapers for microbiological analysis was assessed in a French study in hospitalised incontinent women (n=52). Urine was extracted by pressing over a sterile flask using diapers without an ultra-absorbent gel. Given the high sensitivity of 93% and the high specificity of 91% the authors considered this urine sampling technique was a fairly reliable method for use in severely incontinent elderly women, but it was noted that the results cannot be generalized to other types of diapers, such as gel-based ones.<sup>11</sup>

However, in a non-clinical study, researchers poured 60 urine samples (age and gender of patients unknown) over gel-based diapers, bisected a sample of the diaper's material and compared microbiological results with those from the original urine specimens. A good sensitivity (100%) and specificity (97%) was found. Extraction from gel-based diapers, thus, also sounds promising, but needs further exploration.<sup>14-15</sup>

In the late 1980's the validity of condom catheters to collect urine specimens in elderly men was explored by two studies (n=50), both conducted in a LTCF and using sterile in-and-out catheterisation as the reference method.<sup>12-13</sup> Clean condom catheters were applied in both studies. However, Nicolle et al. additionally explored the validity of urine collected by a sterile condom catheter, but found no difference in test performance results, nor a difference in contamination rates between the two types of catheters.<sup>13</sup>

With a sensitivity of 86-98% and a specificity of 90-97% the condom catheter method can potentially replace catheterization for urine collection.

We found no studies exploring external urine collection devices (UCD) in elderly women. A UK clinical trial involving 2182 adult women visiting outpatient clinics (0.7% older than 65 years) found that samples collected by the UCD were significantly less likely to be contaminated and require re-testing than midstream specimens (relative reduction of 31%).<sup>16</sup> Whether or not this method can be used in the elderly in whom physical constraints and cognitive impairment may limit good technique needs to be explored.

The prevalence of bacteriuria varied between 28% and 75% in the selected studies. Similar rates are reported in the literature. It is estimated that 20-25% of all women and 10% of all men over 65 years have bacteriuria. The figures appear to be even higher in the institutionalised: 15-50% in nursing home residents and 30-50% in hospitals.<sup>17-19</sup>

Before generalisation of the results, potential influence of the inclusion criteria and applied thresholds on the prevalence rates in the six included papers should be considered. In the study of Ouslander et al. a prevalence of 29% was found. However, their subjects had participated in a study examining the effects of eradicating bacteriuria on the severity of urinary incontinence and, therefore, half of them had received a 7-day course of norfloxacin in the weeks prior to the urine collection. On the other hand, the study used a lower threshold.<sup>9</sup>

#### *Impact compared to existing technology*

The alternative sampling methods show to be promising techniques for detecting microorganisms in urine specimens from older people. The existing evidence is, however, not sufficient to make recommendations for clinical practice due to several study limitations. First of all, no recent studies were found. All included studies date from more than a decade ago and it can be assumed that the older population has changed since then. The elderly might now be even more care dependent because of an increased average age and more chronic diseases. Moreover, the urine collection methods were tested in small sample sizes which could lead to an overestimation of the test accuracy. This can certainly be the case for the condom catheter sampling method which was tested in two studies, totalling only 50 men. As a consequence of the small number of patients tested large 95% CI were also calculated, especially for LR+.

The studies were conducted in well-defined settings (e.g. hospital, nursing home) and populations (e.g. only in men or only in women). The performance results of the index test might be different in other clinical situations.

At present, there is no consensus on the minimum colony-forming units (CFU)/ml value associated with a bacteriuria, particularly in elderly populations. The standard for reporting in most research is  $10^5$  CFU/ml and is mainly associated with a midstream collection. However, different societies have recommended reporting far lower CFU counts (e.g.  $10^2$  CFU/ml in European guidelines).<sup>20-22</sup> With new molecular or spectrometric techniques for the identification and quantification of bacteria being developed and implemented, more changes to the threshold can be expected in the future.<sup>23-24</sup>

When possible, test performance results using a threshold of  $\geq 10^5$  CFU/ml were calculated and reported in order to increase comparability between papers. This was, however, not possible for all studies (see table 1).

Notwithstanding the study limitations, the test results of the urine collection methods sound promising and the techniques may take a worthy place in clinical practice as alternatives to the more invasive procedures such as suprapubic aspiration and in-and-out catheterisation. However, it is clear that more and larger diagnostic studies are needed to confirm the findings.

#### *Guidelines and Recommendations*

Guidelines on urine sampling methods for microbiological analysis mainly focus on children and adults and are lacking for use in older people as ethical concerns limit solid research in this frail population.

We have not identified a NICE guideline on this topic. The SIGN guideline on the management of suspected bacterial UTI in adults warns for the risk of false positive results in all tests for diagnosis of bacteriuria other than the gold standard, i.e. urine obtained by the needle aspiration of the bladder. They also state no bacterial count can be taken as absolute gold standard for the diagnosis of UTI. Nonetheless, the guideline did not distinguish elderly adults from younger adults.<sup>25</sup>

#### **Cost-effectiveness and economic impact:**

The cost-effectiveness of alternative urine collection methods in elderly has not yet been evaluated. However, they would be expected to be far less costly than either suprapubic aspiration or in-and-out catheterisation which often require multiple clinical staff and sometimes physicians to conduct, involving time and other resources, particularly in confused patients.

Valid methods to collect high-quality urine specimens are needed. Contaminated cultures can lead to re-collection and re-testing of specimens which, in turn, increases costs (material and health care and laboratory personnel), delays diagnosis and treatment, and induces risk for poor patient outcomes and patient dissatisfaction. If a physician does decide not to re-test, there is a risk of inappropriate antimicrobial treatment which can contribute to the increase in resistance.<sup>3,26</sup>

#### **Research Questions:**

- Can the validity of the most promising urine collection methods be confirmed by comparable but larger studies?
- How do the alternative urine collection methods and gold standards compare in terms of costs and safety and what are the patients' and healthcare workers' preferences?

#### **Suggested next step:**

Larger diagnostic studies using more standardised methodologies need to be conducted in order to confirm the validity of the alternative sampling methods. Moreover, qualitative and observational studies should provide more insight in how healthcare workers currently take urine samples in the elderly, especially in those with cognitive impairments, physical constraints and/or severe incontinence.

#### **Expected outcomes:**

Further investigation of the value of alternative urine sampling methods may provide evidence for the implementation of these methods in guidelines and clinical practice. The reduction of unnecessary invasive investigations and therapy should be an attainable target.

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### Annex 1: Characteristics of the included studies

Author (year)	Setting (n) Country	Population	Inclusion and/or exclusion criteria	No of patients	Mean age in years	Who collected samples?	Details of index			Reference test	Timing	Contamination: %, definition and included/excluded from analysis
							Method	Cleansing	Recipient			
Verheggen et al. (1991)	Geriatric ward in hospital (n=1) The Netherlands	Men and women	Patient admitted during the eight month study period  Exclusion: (1) patients with indwelling catheter at admission, (2) patients in whom no clean catch sample or catheter sample could be obtained, (3) patients with vulvovaginitis, prostatitis, pyelonephritis, genital herpes or any other sexually transmitted disease	67	81	Unclear (a nurse)	Clean catch	Water in women; no cleansing in men	Sterile recipient in women; urinal for men (sterile or disinfected ?)	Indwelling catheter specimen (clamped for 30 minutes)	Index on the first morning after admission, reference on the second morning	5.6% (4/71)  Two or more epithelial pavement cells in the preparate  Excluded
Ouslander et al. (1995)	NHs <sup>1</sup> (n=7) USA	Incontinent women	Patients enrolled in an intervention trial for urinary incontinence.  Inclusion: (1) identification as regularly incontinent of urine by nursing staff with verification by physical checks for wetness, (2) passing a behavioural screen (state name or reliably point to two objects), (3) lack of a severe behavioural disturbance that would preclude cooperation with the intervention, (4) absence of a condition that might preclude participation in the 3- to 4-month trial	101	86	Research nurse and well-trained nurse's aides	Clean catch	Povidine-iodine	Disinfected bed pan	Sterile in-and-out cath. <sup>2</sup>	Reference immediately after index	Unclear
Michielsen et al. (1997)	Geriatric ward in hospital (n=1) Belgium	Women	Patients for whom a urine examination was requested by the treating physician not only because of symptoms of a UTI but also for atypical symptoms and diabetes dysregulation	58	81	Unclear	Clean catch	Water	Sterile recipient in toilet or bed pan	Suprapubic aspiration	Reference just before voiding	25.8%  Sample showing <10 <sup>5</sup> CFU/ml or ≥10 <sup>5</sup> CFU/ml with several species of bacteria  Included

<sup>1</sup> NH = Nursing Home; <sup>2</sup>cath. = catheterization; <sup>3</sup>VA = Veteran Administration; <sup>4</sup>LTCF = Long-Term Care Facility

**Annex 1: Characteristics of the included studies (continued)**

Author (year)	Setting (n) Country	Population	Inclusion and/or exclusion criteria	No of pa- tients	Mean age in years	Who collected samples?	Details of index			Reference test	Timing	Contamination: %, definition and included/excluded from analysis
							Method	Cleansing	Recipient			
Belmin et al. (1993)	Geriatric ward in hospital (n=1) France	Incontinent women	Patients for whom a urine examination had been prescribed by the physician for several clinical or biological reasons including fever, suprapubic tenderness, dehydration etc.	52	Range: 68-98	Unclear	Urine pressed out of a clean diaper without ultra-absorbent gel	Wet glove and soap if needed	Sterile flask	In-and-out cath.	Reference just after diaper impregnation	Not stated, only 'moderate contamination'
Ouslander et al. (1987)	NH care unit in VA <sup>3</sup> centre (n=1) USA	Men continuously wearing an external catheter	Inclusion: patients who wearing external catheters continuously and for whom post void residual determinations had been ordered.  Patients had no signs or symptoms of an acute UTI	26	Not stated (mean age in centre: 72)	A study nurse	Clean condom catheter	Povidine-iodine	Sterile drainage system	Sterile in-and-out cath.	Reference +/- 15 minutes after index	3.9%  More than three organisms in the specimen  Included
Nicolle et al. (1988)	LTCF <sup>4</sup> (n=1) Canada	Incontinent men	Residents for whom consent could not be obtained were excluded	24	78	Normal nursing staff (blinded)	Sterile and clean condom catheter	Soap and water (rinsed with sterile saline)	Sterile drainage system (leg bag)	Sterile in-and-out cath.	Consecutive sampling	45.8%  Organisms isolated from index but not present in reference  Included

<sup>1</sup> NH = Nursing Home; <sup>2</sup> cath. = catheterization; <sup>3</sup> VA = Veteran Administration; <sup>4</sup> LTCF = Long-Term Care Facility