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Diagnostic accuracy of dipsticks for urinary tract infections in acutely hospitalised patients: a prospective population-based observational cohort study

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Abstract

Objective To determine the added diagnostic value of dipsticks for urinary tract infections (UTI) in acutely hospitalised individuals.

Design Prospective population-based cohort study.

Setting North Denmark.

Participants All adults (≥18 years) examined with dipsticks at emergency departments in North Denmark Region from September 20 through 23 October 2021.

Main outcome measures UTI was defined as ≥1 symptom of new-onset frequency, dysuria or suprapubic tenderness combined with a positive urine culture. Positive dipsticks were defined as any reaction for leucocyte esterase and/or nitrite.

Results Dipsticks were used in 1052/2495 (42%) of acutely hospitalised patients with a median age of 73 years (IQR 57–82) and 540 (51%) were female. Overall, 89/1052 (8%) fulfilled the UTI criteria and urine cultures were done in 607/1052 (58%) patients. Among patients examined with both dipstick and urine culture, sensitivity and specificity for UTI were 87% (95% CI 78% to 93%) and 45% (95% CI 41% to 50%). Positive and negative predictive values were 21% (95% CI 17% to 26%) and 95% (95% CI 92% to 98%), whereas positive and negative likelihood ratios were 1.58 (95% CI 1.41 to 1.77) and 0.30 (95% CI 0.18 to 0.51). Pretest probabilities of UTI ranged from 29% to 60% in participants with specific UTI symptoms with corresponding post-test probabilities of 35–69% if dipsticks were positive and 12–27% if dipsticks were negative. Results remained comparable if final clinical diagnosis was used as outcome among all patients examined with dipsticks. Modified Poisson regression yielded an adjusted relative risk of 4.41 (95% CI 2.40 to 8.11) for empirical antibiotics for UTI in participants without specific UTI symptoms and a positive dipstick.

Conclusions Dipsticks yielded limited clinical decision support compared with a symptom-driven approach in this study and were independently associated with excess antibiotics for UTI.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Previous studies and guidelines suggest that use of urinary dipsticks for diagnosis of urinary tract infections (UTI) should be restricted to females aged under 65 years with mild to moderate symptoms of UTI. Nonetheless, urinary dipsticks are frequently used for decisions on diagnostic work-up and empirical antibiotics in hospitalised elderly or otherwise frail patients with suspected UTIs, other severe infections or unclear clinical presentations.

WHAT THIS STUDY ADDS

⇒ In this prospective population-based cohort study, urinary dipsticks were used in almost half of acutely hospitalised patients and yielded limited added clinical decision support for diagnosis of UTI using a symptom-driven approach.

⇒ Use of urinary dipsticks was associated with excess urine cultures as well as antibiotic treatment for UTI in patients without specific symptoms of UTI.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Urinary dipsticks may be a suitable target for diagnostic and antibiotic stewardship interventions at hospitals.

Introduction

Urinary dipsticks are often used for guidance on need for urine cultures and empirical antibiotics in patients with suspected urinary tract infections (UTIs), which are a leading cause for antibiotic treatment.[1–7] Current guidelines by Public Health England and the National Institute for Health and Care Excellence do not recommend dipsticks for diagnosis of UTI, except in females below 65 years

of age with mild to moderate symptoms.[8 9] This is consistent with previous studies that found dipsticks to be moderately effective for ruling out UTI using clean midstream urine samples in premenopausal women outside a hospital setting, whereas their diagnostic accuracy among inpatients remains uncertain.[10–13]

Nonetheless, clinical use of dipsticks has expanded to rule in UTI in other patient groups including elderly and hospitalised individuals with suspected UTI, severe infection or an unclear clinical presentation. Importantly, urine is rarely obtained as clean midstream samples in these patient populations and the prevalence of asymptomatic bacteriuria is high ranging from 15% to 50%.[4 14–17] This may lead to incorrect antibiotic treatment with associated risks of side effects and toxicity, *Clostridioides difficile* enterocolitis and antibiotic resistance. Equally important is the potential delay in time to correct diagnosis attributable to fixation on an erroneous assumption of UTI, especially in elderly frail patients.[18–20]

This study aimed to examine the added diagnostic accuracy of dipsticks to a symptom-driven approach at admission and associated management among acute inpatients at all emergency departments in North Denmark Region.

Methods

Study design and setting

This prospective, population-based, observational cohort study was carried out among all three hospitals providing acute care for all residents in North Denmark Region (catchment population 590 403 on 1 September 2021).[21] These hospitals belong to the same regional healthcare administrative unit with shared treatment guidelines and considerable exchange of physicians between hospitals before and after specialisation ensuring a uniform approach to patient management. Clinicians were unaware of all aspects of the study throughout the observation period in order not to influence management decisions on use of dipsticks, urine cultures, treatment and final clinical diagnosis (ie, mitigation of a potential Hawthorne effect). In Denmark, healthcare is tax financed and free of charge at the point of delivery for all residents.[22] A unique 10-digit civil registration number is assigned to all residents at birth or immigration, which allows unambiguous identification of all healthcare contacts on an individual level.

Study population and patient data

The study included all adults (≥18 years of age) examined with a dipstick within 24 hours after acute admission at emergency, internal medicine, abdominal surgery or urological departments in North Denmark Region from 20 September 2021 through 23 October 2021. Lists of all hospitalisations in North Denmark Region during the previous 24 hours were provided by the regional administrative unit and screened daily for inclusion by manual chart review. Readmissions within 7 days of discharge were excluded, but otherwise patients with several acute hospitalisations could be included multiple times during the study period. A supplementary analysis was done at Odense University Hospital in the Region of South Denmark to examine the generalisability of the results. At Odense University Hospital, patients examined by a dipstick at time of acute hospitalisation were identified retrospectively by reviewing the medical records of 150 randomly selected non-surgical patients admitted through the emergency department in November 2019.

Data on patient demographics, comorbidities, presenting symptoms and signs, biochemical and radiological analyses, microbiological investigations, treatment, final diagnosis and outcome were obtained by manual chart review of electronic medical records by two specially trained staff members (LHK, RW). If patients were treated with antibiotics, the indication and interpretation of results were registered as reported in the medical records by the treating physician.

Missing data

Data were presented as n/N (%) to account for missing data. Absence of organ-specific symptoms was sometimes summarised generically by attending physicians as 'systematically asked, no complaints'. In such cases, it was assumed that the clinician had confirmed the absence of dysuria, frequency and gross haematuria, whereas other symptoms and findings such as cloudy urine, urine retention and abnormal urine colour were categorised as 'not reported'.

To further clarify missing data in the medical records and for validation purposes, all eligible patients during the last week of the study period were also prospectively interviewed the day after admission by the main authors (LHK, RW) for presence or absence of key symptoms and findings associated with diagnosis of UTI. The interviews were carried out without involving the attending physicians and they were not informed about the study.

Index test

Urinary dipsticks were carried out as clinically indicated assessed by the attending staff who remained unaware of the study throughout the observation period. Dipsticks comprised Siemens Multistix 7 that were automatically analysed at point of care using Siemens Clinitek Status+ or Siemens Clinitek Advantus throughout the study period. A positive dipstick was defined as trace or greater reaction to leucocyte esterase (LE), reaction to nitrite or both. Ketoacidosis was primarily diagnosed using point-of-care measurement of ketones in blood, and urine microscopy for diagnosis of UTI was not available nor part of clinical practice in North Denmark Region.

Definitions of UTI (reference standard)

A definition of UTI by the Centers for Disease Control and Prevention (CDC) requires a positive urine culture combined with ≥1 of the following: fever (>38°C), urgency, frequency, dysuria or suprapubic tenderness.[23] However, we noticed that urgency was uncommonly registered in medical records in North Denmark Region during a pilot of the current study and fever is a frequent and unspecific finding among hospitalised patients. Thus, a modified CDC (mCDC) version compatible with textbook definitions of UTI in Denmark was chosen as gold standard comprising a positive urine culture combined with classic UTI symptoms, that is, ≥1 new-onset frequency, dysuria or suprapubic tenderness.[24] Urine samples were sent for culture as clinically indicated assessed by the attending staff who remained unaware of the study throughout the observation period. Only urine cultures sent within 24 hours of admission were included. Thresholds of colony-forming units per millilitre for a positive urine culture varied according to bacterial species and type of urine sample as defined by the Department of Clinical Microbiology at Aalborg University Hospital (online supplemental material). Urine cultures with microorganisms considered to be contaminants according to these standards were categorised as negative.

Final clinical diagnosis of UTI by the attending physician at discharge was used as an alternative primary outcome measure to account for antibiotic treatment before admission or if urine cultures had not been obtained. In addition, this definition may accommodate more atypical clinical presentations of UTI.

Statistical analyses

Diagnostic accuracy of dipsticks was assessed in the following two study populations:

1. All patients examined with both a dipstick and urine culture using microbiologically confirmed UTI in symptomatic patients as reference (mCDC).
2. All patients examined with a dipstick, with or without urine culture, using final clinical diagnosis as reference.

Diagnostic test metrics were computed in terms of sensitivity, specificity and positive and negative predictive values (PPV and NPV) with 95% CIs. Next, positive and negative likelihood ratios (LRs) were calculated to assess post-test probability of UTI according to dipstick results. A positive LR>10 or a negative LR<0.1 is usually considered strong evidence to rule in or rule out diagnoses in most circumstances.[25] The added value of dipsticks for diagnosis of UTI and associated management was explored in patients with and without symptoms of UTI using Bayesian statistics for assessment of post-test probabilities.

Associations between a positive dipstick and obtainment of urine cultures and empiric antibiotics for UTI in patients without specific symptoms of UTI were also examined *post hoc* using modified Poisson regression with a robust variance sandwich estimator to allow for recurrent events (ie, each patient could be included several times during the study period).[26] These analyses were adjusted for age group (0–59, 60–69, 70–79, 80–89 and 90 years or older), sex, previous hospitalisation with UTI, comorbidities (arterial hypertension, atrial fibrillation, cancer, chronic obstructive pulmonary disease, congestive heart failure, dementia, diabetes mellitus, genitourinary malformations, ischaemic heart disease, liver cirrhosis, neurogenic bladder, permanent urinary catheter, previous urological procedures, previous hospitalisation with sepsis, renal impairment or stroke), confusion at admission, antibiotic treatment within 1 week before hospitalisation, C reactive protein level levels (0–49, 50–99, 100–199 and 200 mg/L or higher) and fever at admission (≥38.0°C). Due to a limited number of events in analyses of empirical antibiotics according to dipstick results in patients without specific symptoms of UTI (n=62), adjustments for this analysis were restricted to age, sex, previous hospitalisation for UTI, comorbidities (same as above), confusion at admission, C reactive protein level and antibiotic treatment within 1 week before hospitalisation. Potential interaction between a positive dipstick and empirical antibiotic treatment for UTI according to age group was also explored in modified Poisson regression analysis.

Inter-rater variability between the two specially trained data collectors (LHK, RW) was examined in 50 patients using Cohen's kappa statistic and was interpreted using the principles outlined by Landis and Koch.[27]

Stata/MP V.17 (StataCorp, College Station, Texas, USA) was used for all statistical analyses. The study is reported according to the Standards for Reporting of Diagnostic Accuracy Studies (STARD) guideline.[28]

Patient and public involvement

Patient representatives were not included in the design or conduct of this study.

Results

A total of 3110 acute hospitalisations were identified during the 5-week study period of which 615 were transfers between departments and therefore excluded (online supplemental figure 1). Among the remaining 2495 patients, a urinary dipstick was carried out in 1052 (42%) and this group comprised the study population. The median age was 73 years (IQR 57–82), 540/1052 (51%) were female and 750/1052 (71%) were admitted at internal medicine departments (table 1). For comparison, excluded patients had a median age of 68 years (IQR 53–79), 722/1443 (50%) were female and 1169/1443 (81%) were admitted at departments of internal medicine.

Clinical characteristics

In the study population of 1052 patients examined by a dipstick, a classic UTI symptom was present at admission among 184/1052 (17%) patients. The type of urine sample was not reported in 860/1052 (81%), from a newly placed urinary catheter in 111/1052 (11%), from a permanent urinary catheter in 79/1052 (8%) and 'other' in 2/1052 (0.2%). The indication for dipstick analysis was not reported in the electronic medical records in 632/1052 (60%) of patients. In the remaining patients, the attending physician explicitly listed suspected UTI or unknown infection as indications in 393/1052 (37%), suspected gross haematuria or kidney stones in 13/1052 (1%), proteinuria in 7/1052 (0.7%) and ketoacidosis in 3/1052 (0.3%). Overall, dipsticks were interpreted as 'probable UTI' in about half of patients with strong reaction for LE, nitrite or both (online supplemental table 1).

Urine cultures were carried out in 609/1052 (58%) of which 272/609 (45%) were positive. *Escherichia coli* was the most commonly identified bacterium and was found in 139/272 (51%) of cultured urine samples (online supplemental table 2). The proportions with significant bacteriuria did not differ noticeably between patients with or without specific symptoms of UTI, dementia, confusion, a history of fever and in those with symptoms from other organ systems than the genitourinary tract (online supplemental table 3).

The mCDC criteria of UTI were fulfilled by 89/1052 (8%) of patients. In contrast, a final clinical diagnosis of UTI was assigned by the attending physician in 155/1052 (15%) patients of which 43/155 (28%) were confirmed according to the mCDC criteria. The in-hospital mortality was 4%.

Diagnostic test metrics and post-test probabilities using a symptom-driven approach

Study population 1: all patients examined with both dipstick and urine culture (n=607)

Using the mCDC definition as reference, the sensitivity and specificity of a positive dipstick were 87% (95% CI 78% to 93%) and 45% (95% CI 41% to 50%), respectively, for dipsticks positive for either LE, nitrite or both (online supplemental tables 4 and 5). The corresponding PPV and NPV were 21% (95% CI 17% to 26%) and 95% (95% CI 92% to 98%), whereas the positive and negative LRs were 1.58 (95% CI 1.41 to 1.77) and 0.30 (95% CI 0.18 to 0.51). In comparison, sensitivities and specificities were 34% (95% CI 24% to 45%) and 86% (95% CI 83% to 89%) in analyses restricted to those positive for both LE and nitrite yielding a PPV of 29% (95% CI 21% to 39%) and an NPV of 88% (95% CI 85% to 91%). The corresponding positive and negative LRs were 2.38 (95% CI 1.66 to 3.41) and 0.77 (95% CI 0.66 to 0.90), respectively.

Using the mCDC definition as reference, the pretest probabilities of UTI in patients with specific symptoms of UTI ranged from 29% (95% CI 18% to 41%) in those with costovertebral tenderness to 60% (95% CI 48% to 71%) in patients with dysuria (table 2). The corresponding post-test probabilities increased to 35% (95% CI 21% to 50%) and 68% (95% CI 55% to 80%), respectively, in those with a dipstick positive for LE, nitrite or both, and decreased

Table 1 Baseline data on hospitalised patients examined with dipsticks within 24 hours of admission at emergency departments in North Denmark Region from 20 September through 23 October 2021

n (%) or median (IQR), N=1052			
Demographics		**Other symptoms and signs**	
Gender, female (%)	540 (51)	History of fever	318/859 (37)
Age (years)	73 (57–82)	Fever at admission (≥38.0°C)	218 (21)
Internal medicine patients	750 (71)	Change of mental status	104/1002 (10)
Surgical patients	302 (29)	Urinary retention	65/147 (44)
Residence		Abnormal urine colour	43/182 (24)
Private homes, community to dwelling	927 (88)	Cloudy urine	19/94 (20)
Nursing homes or senior care housing	98 (9)	**Indication for dipstick**	
Other	27 (3)	Not reported	632 (60)
Comorbidity		UTI or unknown source of infection	393 (37)
Chronic obstructive pulmonary disease	264 (25)	Gross haematuria or kidney stones	13 (1)
Cardiac arrhythmias	235 (22)	Proteinuria	7 (0.7)
Diabetes mellitus	199 (19)	Ketoacidosis	3 (0.3)
Ischaemic heart disease	174 (17)	**Type of urine sample**	
Cerebrovascular disease	148 (14)	Not reported	860 (81)
Cancer	113 (11)	Newly placed urinary catheter	111 (11)
Heart failure	81 (8)	Permanent urinary catheter	79 (8)
Liver cirrhosis	12 (1)	Other	2 (0.2)
Predisposing conditions for UTI		**Cultures**	
Previous hospitalisation with another infection	454 (43)	Blood cultures preformed	617 (59)
Previous hospitalisation with UTI/urosepsis	247 (24)	Blood culture positive	62 (10)
Pre-existing to existing urinary catheter	113 (11)	Urine cultures preformed	609 (58)
Renal impairment	100 (10)	Urine culture positive	272 (45)
Dementia	62 (6)	**Antibiotics**	
Neurogenic bladder	17 (2)	Antibiotics within 1 week before admission	193 (18)
Recent urological surgery	27 (3)	Antibiotics at hospital	649 (62)
Anatomical malformations of the urinary tract	22 (2)	Indication suspected UTI	160 (25)
Classic UTI signs and symptoms		Indication suspected sepsis	64 (10)
Frequency	99/653 (15)	**Modified CDC criteria***	89 (9)
Dysuria	101/891 (11)	**Final clinical diagnoses**	
Costovertebral tenderness	86/856 (10)	UTI	181 (17)
Suprapubic tenderness	82/922 (9)	UTI+other diagnoses	26 (2)
Gross haematuria	36/731 (5)	Other infection	425 (40)
		Other diagnoses	446 (42)
		Outcomes	
		Intensive care unit admission	33 (3)
		In-hospital mortality	43 (4)

*mCDC: ≥1 of new-onset frequency, dysuria or suprapubic tenderness combined with a positive urine culture.
CDC, Centers for Disease Control and Prevention; UTI, urinary tract infection.

to 12% (95% CI 1% to 36%) and 27% (95% CI 8% to 55%) in those with a negative dipstick.

Study population 2: all patients examined with a dipstick regardless of urine culture or not (n=1052)

Using final clinical diagnosis as reference, the overall results of diagnostic test metrics were comparable with the above analyses except that PPVs increased and ranged from 34% (95% CI 30% to 39%) for individuals with dipsticks positive for LE, nitrite or both to 53% (95% CI 43% to 62%) in those positive for both LE and nitrite (online supplemental tables 4 and 5).

Associations between dipsticks and management (study population 2)

Patients with a positive dipstick but without specific symptoms of UTI had urine cultures obtained in 220/289 (76%) and empirical antibiotics for UTI were initiated in 48/188 (26%) compared with 189/487 (39%, p<0.001) and 14/262 (5%, p<0.001), respectively, in asymptomatic patients with negative dipsticks (table 3). Of note, culture-confirmed UTI according to mCDC was documented in 12/120 (10%) of patients with specific symptoms of UTI and a negative dipstick.

Adjusted modified Poisson analyses showed that a dipstick positive for LE, nitrite or both in patients without specific symptoms of UTI was independently associated with obtainment of urine cultures with a relative risk (RR) of 1.74 (95% CI 1.52 to 1.98) and empirical antibiotic treatment for UTI with an RR of 4.41 (95% CI 2.40 to 8.11) (figures 1 and 2). There was no statistically significant interaction between a positive dipstick and empirical antibiotic treatment for UTI according to age group (data not shown).

Table 2 Pretest and post-test probabilities of dipsticks for diagnosis of urinary tract infection according to clinical presentation at admission among acutely hospitalised adults in North Denmark Region from 20 September through 23 October 2021

Study population: all adults examined with both dipstick and urine culture n=607	Pretest probability	LR+	LR−	Post-test probability (positive dipstick)	Post-test probability (negative dipstick)
UTI reference standard: mCDC	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Overall	15 (12 to 18)	1.58 (1.41 to 1.77)	0.30 (0.18 to 0.51)	21 (17 to 26)	5 (3 to 8)
Presence of symptoms or signs of UTI					
Dysuria	60 (48 to 71)	1.44 (1.08 to 1.92)	0.24 (0.09 to 0.69)	68 (55 to 80)	27 (8 to 55)
Frequency	55 (43 to 66)	1.77 (1.23 to 2.54)	0.27 (0.12 to 0.61)	69 (55 to 80)	25 (10 to 47)
Suprapubic pain	55 (42 to 68)	1.57 (1.11 to 2.22)	0.22 (0.07 to 0.71)	66 (50 to 80)	21 (5 to 51)
Costovertebral tenderness	29 (18 to 41)	1.33 (1.02 to 1.74)	0.33 (0.08 to 1.31)	35 (21 to 50)	12 (1 to 36)
≥2 UTI symptoms	58 (46 to 69)	1.42 (1.09 to 1.85)	0.20 (0.06 to 0.65)	66 (53 to 78)	21 (5 to 51)
Study population: all adults examined with dipsticks n=1052					
UTI reference standard: final clinical diagnosis					
Overall	17 (15 to 20)	2.52 (2.25 to 2.82)	0.23 (0.17 to 0.33)	34 (30 to 39)	5 (3 to 7)
Presence of symptoms or signs of UTI					
Dysuria	41 (31 to 51)	1.82 (1.37 to 2.42)	0.24 (0.10 to 0.56)	55 (43 to 68)	14 (5 to 29)
Frequency	43 (33 to 54)	2.01 (1.40 to 2.89)	0.35 (0.19 to 0.64)	61 (47 to 74)	21 (10 to 36)
Suprapubic pain	39 (28 to 50)	1.90 (1.37 to 2.64)	0.23 (0.09 to 0.60)	55 (40 to 69)	13 (4 to 30)
Costovertebral tenderness	34 (24 to 45)	1.97 (1.42 to 2.73)	0.25 (0.10 to 0.63)	50 (36 to 65)	11 (3 to 26)
<2 UTI symptoms	50 (39 to 61)	1.64 (1.24 to 2.18)	0.24 (0.10 to 0.58)	62 (49 to 74)	19 (6 to 39)

A positive dipstick was defined as trace or stronger reaction of leucocyte esterase and/or nitrite.

LR+, positive likelihood ratio; LR−, negative likelihood ratio; mCDC, modified definition of UTI according to Centers for Disease Control and Prevention comprising ≥1 of new-onset frequency, dysuria or suprapubic tenderness combined with a positive urine culture; UTI, urinary tract infection.

Inter-rater variability and clinical interviews

Inter-rater agreement on key variables ranged from good to excellent (0.64–0.91) (online supplemental table 6). To account for missing values, a total of 71 consecutive patients were interviewed for selected symptoms and signs associated with UTI during the final week of study inclusion (online supplemental table 7). In general, symptoms missing in the medical records were confirmed as truly absent, which would lower the reported prevalences of symptoms and signs of UTI with missing values even further.

Generalisability

Dipsticks were used in 85/150 (57%) randomly selected acute medical inpatients at the emergency department at Odense University Hospital in the Region of Southern Denmark during November 2019. Associations between dipsticks and management were similar to those of North Denmark Region although a limited number of observations precluded firm conclusions (online supplemental tables 8 and 9).

Discussion

Principal findings

This prospective, population-based cohort study found that dipsticks were frequently used among acutely hospitalised patients (42%) in North Denmark Region. However, classic UTI symptoms were rarely present, and the type of urine sample was only anecdotally described as clean midstream. The positive and negative LRs and associated pretest and post-test probabilities demonstrated limited clinical decision support of dipsticks since UTI could not be effectively ruled in or out in symptomatic patients. Finally, a positive dipstick was independently associated with excess urine samples and empirical antibiotic treatment for UTI in patients without specific symptoms of UTI.

Limitations and strengths

This study has several limitations inherent of observational studies including missing data for some variables, for example, urgency. However, symptoms not reported in the medical records were generally found to be truly absent in a sample of consecutive prospective clinical interviews the day after admission. Moreover, the inter-rater validity of data extraction was found to range from good to excellent. There is no established cut-off for a positive urinary dipstick, whereas absence of both pyuria and nitrites is often considered a negative test (online supplemental table 1). Yet, 12/120 (10%) of patients with specific symptoms of UTI had a microbiologically confirmed UTI despite a negative dipstick. Misclassification of UTI according to the mCDC definition may be present since data on urgency were unavailable, urine cultures were not obtained in all symptomatic patients and some urine cultures may have been negative due to prehospital antibiotic treatment in patients with specific UTI symptoms. The mCDC

Table 3 Management and outcome according to symptoms and signs of urinary tract infection and dipstick analyses among acutely hospitalised patients admitted at emergency departments in North Denmark Region from 20 September through 23 October 2021

	Symptomatic* patients, N=276			Asymptomatic* patients, N=776		
	Positive dipstick, n/N (%)	**Negative dipstick, n/N (%)**		**Positive dipstick, n/N (%)**	**Negative dipstick, n/N (%)**	
Overall number of observations	N=156	N=120	P value	N=289	N=487	P value
Antibiotic treatment before admission	38/156 (24)	35/120 (29)	0.37	39/289 (13)	81/487 (17)	0.24
Urine culture	141/156 (90)	57/120 (48)	<0.001	220/289 (76)	189/487 (39)	<0.001
Positive	92/141 (65)	13/57 (23)	<0.001	132/220 (60)	35/189 (19)	<0.001
Blood culture	110/156 (71)	63/120 (53)	0.002	169/289 (58)	275/487 (56)	0.58
Positive	11/110 (10)	3/63 (5)	0.22	26/169 (15)	22/275 (8)	0.01
Empirical antibiotics at hospital	125/156 (80)	74/120 (62)	0.001	188/289 (65)	262/487 (54)	0.002
For UTI	76/125 (61)	22/74 (30)	<0.001	48/188 (26)	14/262 (5)	<0.001
Before obtainment of urine sample	18/125 (14)	12/74 (16)	0.73	39/188 (21)	40/262 (15)	0.13
After obtainment of urine sample	100/125 (80)	34/74 (46)	<0.001	121/188 (64)	111/262 (42)	<0.001
Urine culture not obtained	6/125 (5)	27/74 (36)	<0.001	26/188 (14)	110/262 (42)	<0.001
UTI according to mCDC	77/156 (49)	12/120 (10)	<0.001	–	–	
In-hospital mortality	4/155 (3)	1/118 (1)	0.29	13/288 (5)	25/485 (5)	0.69

*Dysuria, frequency, suprapubic pain, haematuria or costovertebral tenderness.

mCDC, modified definition of UTI according to Centers for Disease Control and Prevention comprising ≥1 of new-onset frequency, dysuria or suprapubic tenderness combined with a positive urine culture; Positive dipstick:, Trace or stronger reaction of leucocyte esterase and/or nitrite; UTI, urinary tract infection.

definition may also have reduced representativeness of more atypical clinical presentations of UTI in hospitalised patients.[29] In contrast, using final clinical diagnosis as reference may lead to an overestimation of UTI since diagnosis was sometimes based solely on dipstick results (incorporation bias). Still, analyses for each reference standard yielded comparable results, that is, the potential impact of a positive urinary dipstick on clinical decision-making remained limited. Despite lack of information on frequency and clinical characteristics among patients with UTI in those not examined with dipsticks, the generalisability of the current study is considered to be high due to the population-based

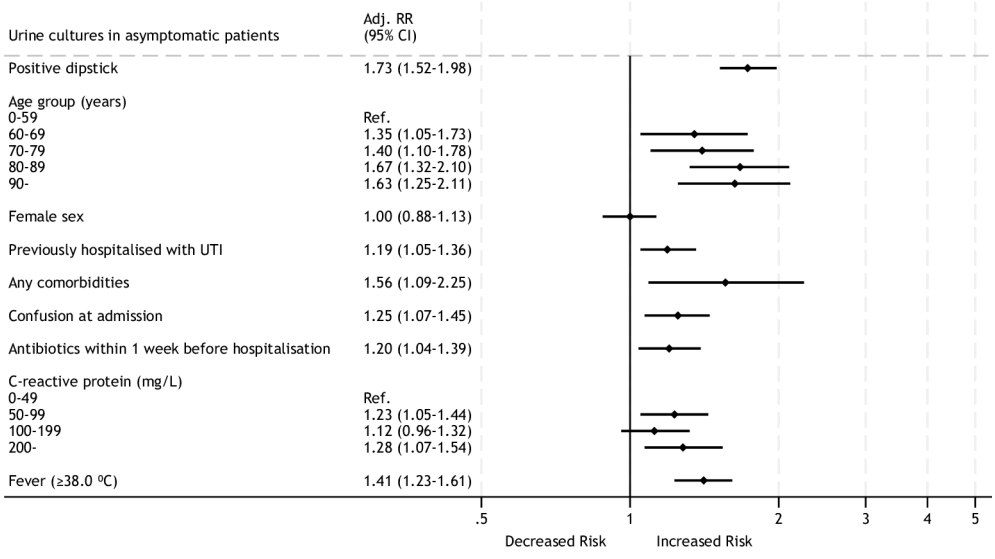

Figure 1 Association between positive dipstick and obtainment of urine cultures in acutely hospitalised asymptomatic patients in North Denmark Region from 20 September through 23 October 2021. Comorbidities included known arterial hypertension, atrial fibrillation, cancer, chronic obstructive pulmonary disease, congestive heart failure, dementia, diabetes mellitus, genitourinary malformations, ischaemic heart disease, liver cirrhosis, neurogenic bladder, permanent urinary catheter, previous urological procedures, previous hospitalisation with sepsis, renal impairment or stroke. Adj RR, adjusted relative risk; UTI, urinary tract infection.

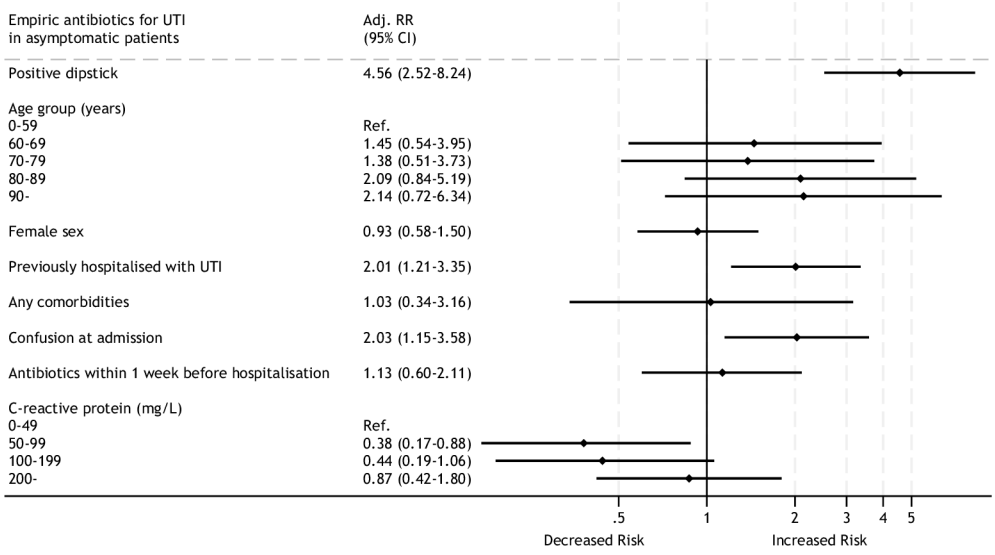

Figure 2 Association between positive dipstick and empirical antibiotic treatment for urinary tract infection in acutely hospitalised asymptomatic patients in North Denmark Region from 20 September through 23 October 2021. Comorbidities included known arterial hypertension, atrial fibrillation, cancer, chronic obstructive pulmonary disease, congestive heart failure, dementia, diabetes mellitus, genitourinary malformations, ischaemic heart disease, liver cirrhosis, neurogenic bladder, permanent urinary catheter, previous urological procedures, previous hospitalisation with sepsis, renal impairment or stroke. Adj RR, adjusted relative risk; UTI, urinary tract infection.

design and replication of the results at a university hospital in another Danish region.

Comparisons with other studies

Almost half of patients with an acute hospitalisation in this study had urine samples examined by a dipstick despite only about one-fourth of these presented with classic symptoms or findings of UTI. This suggests that dipsticks were used as a screening tool for UTI, which is in line with results from a previous meta-analysis and other studies.[13 18 19 30–33] Moreover, the type of urine sample obtained for analysis was not described in 81% of cases. Similar to another study,[18] these predominantly elderly, comorbid and acutely ill patients were usually not able to comply with the manufacturer's specifications for obtainment of clean midstream samples, and in-and-out catheterisation may not always be indicated or feasible.[18] Incorrect urine sampling likely increased risks of contamination by inclusion of debris and bacteria from the urethra.

Asymptomatic bacteriuria is present in 15–50% of elderly community dwellers or residents at long-term care facilities and is equally common among elderly patients hospitalised for non-infectious complaints or unspecific symptoms such as confusion, weakness or loss of autonomy.[4 5 17 19 33 34] This was also observed in the current study with comparable prevalences of bacteriuria regardless of presence or absence of dementia, confusion, a history of fever or hospitalisation for medical conditions not related to the genitourinary tract (online supplemental table 3).

Consistent with other studies, the combination of absence-specific UTI symptoms, likely invalid urine sample and high prevalence of asymptomatic bacteriuria in hospitalised and predominantly elderly patients may have contributed to the observed poor performance of dipsticks for improving patient management in the current study.[18 19 25 35] Despite a relatively high overall NPV of 95%, the post-test probabilities for UTI in symptomatic patients with negative dipsticks (12–27%) were unacceptably high and did not exclude UTI with reasonable certainty. Other studies found a higher diagnostic accuracy of dipsticks for UTI, which may be due to differences in study populations (eg, restriction to young female adults presenting with specific UTI symptoms at the emergency department) or use of positive urine culture as gold standard (ie, bacteriuria) without specifically incorporating symptoms of UTI.[10 17–19 29 31 35–37]

Clinical implications

Dipsticks are cheap and of convenience for point-of-care management of young females with suspected UTI in primary care. However, downstream adverse effects outside this setting with poorer performance of dipstick analyses, and a propensity of hospital physicians to initiate empirical antibiotics for UTI based on the results, seem to outweigh potential reductions in unnecessary urine cultures and treatment in those with negative tests.[18 33] Inappropriate antibiotic treatment is an important modifiable driver of antibiotic resistance and a substantial proportion of hospitalised patients with a positive dipstick were indeed treated with potentially unnecessary antibiotics in the current (up to 19%) and other studies.[13 19 32 33 35–44] According to these results, all hospitalised patients with symptoms of UTI should have a urine sample sent for culture since UTI cannot effectively be reliably ruled in or out by dipsticks and decisions of empirical antibiotics should rely on an overall assessment of the clinical condition. Of note, urine cultures may also remain relevant in patients without classic symptoms of UTI, regardless of dipstick analyses, if empirical antibiotic treatment is considered and the focus of suspected infection is unclear.

Although diagnosis and treatment of UTIs in hospitalised elderly patients remains challenging,[17 29 43] the current literature does not suggest improved patient management by dipsticks and their use is discouraged by guidelines and numerous specialist societies in the Choosing Wisely campaign.[5 8–10 14 45] The current study lends further support to this approach and highlights that dipsticks may constitute a relevant target for diagnostic and antibiotic stewardship programmes. Future studies should explore whether dipsticks can be safely omitted from the diagnostic work-up of suspected UTI at hospitals without harm to patients.

In conclusion, dipsticks were frequently used in acutely hospitalised patients in North Denmark Region regardless of the

absence of classic UTI symptoms and invalid urine samples. The associated diagnostic performance and clinical decision support was poor in this study. Use of dipsticks may be associated with unnecessary antibiotic treatment and seems to be a suitable target for antibiotic and diagnostic stewardship interventions.

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