How Often Do Clinically Diagnosed Catheter-Associated Urinary Tract Infections in Nursing Homes Meet Standardized Criteria?

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OBJECTIVES: To determine the relationship between clinically diagnosed catheter-associated urinary tract infection (CAUTI) and standardized criteria and to assess microorganism-level differences in symptom burden in a cohort of catheterized nursing home (NH) residents.

DESIGN: Post hoc analysis of a prospective longitudinal study.

SETTING: Twelve NHs in southeast Michigan.

PARTICIPANTS: NH residents with indwelling urinary catheters (n = 233; 90% white, 52% male, mean age 73.7).

MEASUREMENTS: Clinical and demographic data, including CAUTI epidemiology and symptoms, were obtained at study enrollment, 14 days, and monthly thereafter for up to 1 year.

RESULTS: One hundred twenty participants with an indwelling catheter (51%) were prescribed systemic antibiotics for 182 clinically diagnosed CAUTIs. Common signs and symptoms were acute change in mental status (28%), fever (21%), and leukocytosis (13%). Forty percent of clinically diagnosed CAUTIs met Loeb's minimum criteria, 32% met National Health Safety Network (NHSN) criteria, and 50% met Loeb's minimum or NHSN criteria. CAUTIs involving *Staphylococcus aureus* and *Enterococcus* spp. were least likely to meet criteria. CAUTIs involving *Klebsiella pneumoniae* were most likely to meet Loeb's minimum criteria (odds ratio (OR) = 9.7, 95% confidence interval (CI) = 2.3–40.3), possibly because of an association with acute change in mental status (OR = 5.9, 95% CI = 1.8–19.4).

CONCLUSION: Fifty percent of clinically diagnosed CAUTIs met standardized criteria, which represents an improvement in antibiotic prescribing practices. At the microorganism level, exploratory data indicate that symptom burden may differ between microorganisms. Exploration of CAUTI signs and symptoms associated with specific microorganisms may yield beneficial information to refine existing tools to guide appropriate antibiotic treatment. **J Am Geriatr Soc 65:395–401, 2017.**

Key words: CAUTI; nursing homes; delirium; infection criteria; *Klebsiella pneumoniae*

Urinary tract infections (UTIs) and catheter-associated UTIs (CAUTIs) are the most common infections in nursing homes (NHs), leading to the majority of antibiotic prescriptions,[1] although one-third are misdiagnosed asymptomatic bacteriuria for which antimicrobial therapy is not beneficial.[2,3] Nevertheless, catheter-associated bacteriuria can progress to symptomatic cystitis, pyelonephritis, and even bacteremia.[4–7] Approximately 10% to 50% of individuals catheterized for 7 or more days will develop CAUTI, and almost all individuals catheterized long term will experience at least one CAUTI.[2] Thus, it is critical to further refine guidelines for CAUTI diagnosis and initiation of antibiotics.

Current CAUTI diagnostic criteria include clinical signs and symptoms such as fever, rigors, hypotension, flank pain, leukocytosis, and acute changes in mental and functional status, as well as a positive urine culture.[9,10] Loeb's minimum criteria are standards for initiation of antibiotics in long-term care settings based on assessment of infection signs and symptoms,[9] whereas the National Healthcare Safety Network (NHSN) criteria are standards for CAUTI surveillance in long-term care settings.[10] Recent estimates indicate that only 10% to 16% of prescriptions for UTIs in NHs adhere to Loeb's minimum criteria[11] and that only 31% of UTIs prescribed antibiotics meet the

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NHSN criteria.[12] These discrepancies could be due to several factors, including prescription of antibiotics for asymptomatic bacteriuria and the challenges of accurately identifying infections with atypical symptoms. Prescribing practices could be improved by comparing signs and symptoms that are most (and least) common during infection with traditional CAUTI pathogens such as *Escherichia coli* with those associated with microorganisms more likely to be present during asymptomatic bacteriuria, such as *Staphylococcus* and *Enterococcus* species.[3] For instance, if *S. aureus* could be clearly differentiated from *E. coli* based on colonization density and symptom burden, this information could aid in guiding appropriate empirical treatment.

Little is known about possible differences in clinical presentation of CAUTIs caused by distinct microorganisms or whether symptom burden may be indicative of CAUTI epidemiology. The innate immune response is largely responsible for the signs and symptoms of UTI, particularly activation of toll-like receptors (TLRs) by pathogen-associated molecular patterns such as lipopolysaccharide (LPS). Specific virulence factors or pathogen-associated molecular pattern modifications can modulate TLR signaling, the magnitude of the resulting immune response, and infection symptoms.[13] For example, expression of different fimbrial types by Gram-negative bacteria modulated LPS-induced TLR signaling cascades and infection outcome in a mouse model of UTI.[13] Dysuria is linked to certain LPS decorations rather than strictly resulting from LPS-induced TLR signaling.[14] Delirium can result from systemic inflammation[8] and may be modulated by the level of innate immune activation. Flow cytometry analysis of bacterial, leukocyte, and erythrocyte counts in urine was recently found to be indicative of infection by broad groups of microorganisms in noncatheterized individuals.[15] The value of clinical signs and symptoms for predicting UTI was investigated for individuals with spinal cord injuries undergoing clean intermittent catheterization[16] but not with respect to specific microorganisms. Thus, classes of microorganisms may be associated with specific patterns of infection signs and symptoms. If so, this information could be useful in guiding appropriate antibiotic treatment in catheterized NH residents, particularly if there are clear differences between CAUTIs caused by microorganisms in which distinct treatment differences exist, such as *S. aureus* and *E. coli*.

The current study had three primary goals: determine adherence of clinically diagnosed CAUTIs from a cohort of NH residents to standardized criteria, determine whether specific microorganisms are more likely to be present in clinically diagnosed CAUTIs that meet standardized criteria than others, and conduct an exploratory assessment of associations between CAUTI signs and symptoms and specific microorganisms. These goals were addressed using post hoc analyses of data collected from a prospective study of catheterized residents from 12 NHs in southeast Michigan.

METHODS

Parent Study Design and Population

This study was secondary post hoc analysis of data collected through the Targeted Infection Prevention parent study.[17] The parent study was a cluster-randomized intervention trial conducted in 12 community-based NHs in Michigan from May 2010 to April 2013 focused on reducing prevalence of multi-drug-resistant organisms. The University of Michigan Institutional Review Board approved the study. Inclusion criteria were indwelling urinary catheter (Foley or suprapubic) or feeding tube (nasogastric or percutaneous endoscopic gastrostomy tube) for longer than 72 hours and informed consent from the resident or the person with their power of attorney. Residents receiving end-of-life care were excluded. This cohort was optimal for the study objectives because prolonged follow-up data were available (100 days, on average). Trained research staff obtained information on demographic characteristics, infection, CAUTI symptoms, and urine microbiology through clinical chart review at monthly visits. Four hundred eighteen NH residents were enrolled in the Targeted Infection Prevention study. Full baseline demographic and CAUTI symptom data (if applicable) were available for 233 of 292 residents with an indwelling urinary catheter for longer than 72 hours. Study visits occurred at the time of enrollment, on Day 14, and monthly thereafter for a maximum of 1 year (or until death, discharge, or device discontinuation).

Definitions

Clinically Diagnosed CAUTI

NH residents with a UTI reported in their medical records, an indwelling catheter in place for longer than 72 hours before the date of the UTI, and a corresponding prescription of at least a 3-day course of systemic antibiotics were considered to have a clinically diagnosed CAUTI.[17] In the event of catheter removal, participants were censored from the analysis on the date of removal.

Loeb's Minimum Criteria

Clinically diagnosed CAUTIs were considered to meet Loeb's minimum criteria if at least one of the following signs and symptoms was present: fever (defined as having a single temperature >100°F or more than 2°F above baseline), new costovertebral tenderness, rigors, or acute mental status change.[9] If there was no mention of a particular sign or symptom in the medical record, it was assumed to be absent. Rigors were reported in the records of fewer than 5% of clinically diagnosed CAUTIs and were therefore excluded from microorganism-level analysis.

NHSN Criteria

Clinically diagnosed CAUTIs were considered to meet NHSN criteria if a positive urine culture (defined as $\geq 10^5$ colony-forming units (cfu) of one or two microorganisms per milliliter of urine) was reported and the following signs and symptoms were present: fever (a single temperature >100°F, repeated temperatures >99°F, or temperature >2°F above baseline), rigors, or new hypotension with no alternative site of infection; leukocytosis (defined as >14,000 leukocytes/μL or a left shift (>6% bands or $\geq$1,500 bands/μL) with concurrent acute mental status change or acute functional decline; new-onset suprapubic

or costovertebral angle pain or tenderness; purulent discharge around the catheter or acute pain, swelling, or tenderness of testes, epididymis, or prostate.[10] If there was no mention of a particular sign or symptom in the medical record, it was assumed to be absent. Rigors; hypotension; purulent discharge around the catheter; and acute pain, swelling, or tenderness of testes, epididymis, or prostate were reported in the records of fewer than 5% of CAUTIs and were therefore excluded from microorganism-level analysis.

Acute Change in Mental Status

Acute change in mental status consisted of fluctuation in behavior, inattention, disorganized thinking, and an altered level of consciousness from baseline.[9,10] Trained research staff obtained information on mental status through clinical chart review.

Acute Change in Functional Status

Acute change in functional status was assessed in clinical evaluation or as indicated by a new 3-point increase in total activity of daily living (ADL) score.[10] Trained research staff obtained data regarding functional status through clinical chart review.

Statistical Analysis

Preliminary logistic models were used to explore infection according to distinct microorganisms as a function of individual clinical CAUTI signs and symptoms. Multivariable models incorporating demographic characteristics were then used to confirm preliminary findings. All logistic regression analyses were adjusted for facility-level clustering to account for residents nested in NHs, and clinically diagnosed CAUTIs were grouped based on urine culture results: *Proteus mirabilis*, *Enterococcus* spp., *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Klebsiella pneumoniae*. Groupings were not mutually exclusive in that the 57 dual-species CAUTIs were each included in two groups, but separate models were run for each microorganism. Data were analyzed using Stata/MP version 13 (StataCorp LP, College Station, TX).

RESULTS

Description of Study Population

Study participants were predominantly white (90%), male (52%), elderly (mean age 73.7 ± 12.7, n = 126 (54%) aged ≥75), and dependent in care (mean physical self-maintenance score 21.6 ± 3.9) (Table 1). The most common conditions upon enrollment were diabetes mellitus (n = 99, 42%), dementia (n = 80, 34%), a history of cerebrovascular accidents (n = 48, 21%), and chronic obstructive pulmonary disease (n = 45, 19%). Two hundred seventy-four urine cultures were reported from 233 catheterized NH residents. Eleven urine cultures (4%) were reported without an accompanying prescription of antibiotics. The remaining 263 urine cultures came from 120 unique study participants and had an accompanying prescription of systemic antibiotics and symptom data. For the purposes of this study, these 263 cases were considered clinically diagnosed CAUTIs. There were no major discernable differences between groups of catheterized NH residents, although dementia was approximately twice as common in residents with clinically diagnosed CAUTI as in those without (odds ratio (OR) = 2.0, 95% confidence interval (CI) = 1.2–3.4, $P = .01$).

Table 1. Demographic Characteristics of Catheterized Nursing Home Residents

Characteristic	Total, n = 233	Clinically Diagnosed CAUTI, n = 120	No Clinically Diagnosed CAUTI, n = 113	*P*-Value[a]
Age, mean ± SD (range)	73.7 ± 12.7 (35–105)	75.0 ± 11.9 (35–105)	72.4 ± 13.4 (38–97)	.26
Comorbidity score, mean ± SD (range)	2.8 ± 1.9 (0–10)	2.9 ± 1.9 (0–10)	2.7 ± 1.8 (0–9)	.53
Physical self-maintenance score, mean ± SD (range)	21.6 ± 3.9 (13–30)	22.1 ± 3.8 (14–30)	21.0 ± 4.0 (13–30)	.15
Sex, n (%)				
Male	121 (52)	63 (52)	58 (51)	.81
Female	112 (48)	57 (48)	55 (49)	
Race, n (%)				
White	209 (90)	106 (88)	103 (91)	.43
Black	21 (9)	12 (10)	9 (8)	.53
Other	3 (1)	2 (2)	1 (1)	.39
Underlying conditions, n (%)				
Diabetes mellitus	99 (42)	47 (39)	52 (46)	.21
Dementia	80 (34)	50 (42)	30 (26)	.01
Cerebrovascular accident	48 (21)	28 (23)	20 (18)	.25
Chronic obstructive pulmonary disease	45 (19)	24 (20)	21 (19)	.72
Hemiplegia	32 (14)	21 (17)	11 (10)	.19
Renal disease	29 (12)	15 (12)	14 (12)	.99
Tumor (any)	23 (10)	11 (9)	12 (10)	.77
Myocardial infarction	23 (10)	11 (9)	12 (10)	.77

[a]Clustered bivariate logistic regression.

CAUTI = catheter-associated urinary tract infection; SD = standard deviation.

Epidemiology of Clinically Diagnosed CAUTI in NH Residents

Full identification of microorganisms was available in the records for 182 of the 263 urine cultures (69%) (Table 2). The most common microorganisms overall were *P. mirabilis*, *Enterococcus* spp., *E. coli*, *P. aeruginosa*, *S. aureus*, and *K. pneumoniae*. One hundred twenty-five CAUTIs (69%) were single species and predominantly caused by *P. mirabilis* (n = 28, 22%), *E. coli* (n = 23, 18%), and *P. aeruginosa* (n = 18, 14%), and fifty-seven CAUTIs (31%) involved two species and were predominantly caused by *Enterococcus* spp. (n = 23, 40% of the 57 dual-species CAUTIs), *P. mirabilis* (n = 20, 35%), and *P. aeruginosa* (n = 16, 28%). The most common combinations in dual-species infection were *P. aeruginosa* with *Enterococcus* spp. (n = 6), *P. mirabilis* with *Enterococcus* spp. (n = 5), and *P. mirabilis* with *P. aeruginosa* (n = 4).

Adherence of Clinically Diagnosed CAUTIs to Standardized Criteria

The proportion of CAUTIs that met standardized criteria are shown in Table 3 grouped according to predominant microorganism. All 182 clinically diagnosed CAUTIs were prescribed systemic antibiotics; 74 (40%) met Loeb's minimum criteria, 59 (32%) met NHSN criteria, and 91 (50%) met at least one standardized definition of symptomatic CAUTI. The most common findings were 10^5 cfu or more of at least one microorganism (n = 161, 90%), acute change in mental status (n = 51, 28%), fever (n = 38, 21%), leukocytosis or neutrophilia (n = 23, 13%), and acute change in functional status (n = 12, 7%). Fourteen (8%) CAUTI cases had concurrent pneumonia noted in the charts, 12 (86%) had positive urine cultures, seven (50%) had fever, and six (43%) had acute mental status change (data not shown). Seven of these 12 cases with positive urine cultures met NHSN criteria, which excludes fever as a criterion if there is an alternate source of infection. In the remaining five cases, systemic antimicrobial use could be attributed to pneumonia or CAUTI.

Table 2. Epidemiology of Single- and Dual-Species Clinically Diagnosed Catheter-Associated Urinary Tract Infection in Nursing Home Residents

Microorganism	Urine Cultures, n[a]	Single-Species Urine Cultures[b]	Dual-Species Urine Cultures[c]
		n (%)	
Proteus mirabilis	48	28 (22)	20 (35)
Enterococcus spp.	38	15 (12)	23 (40)
Escherichia coli	37	23 (18)	14 (25)
Pseudomonas aeruginosa	34	18 (14)	16 (28)
Staphylococcus aureus	20	11 (9)	9 (16)
Klebsiella pneumoniae	14	6 (5)	8 (14)
Citrobacter spp.	9	3 (2)	6 (11)
Morganella morganii	7	2 (2)	5 (9)
Providencia stuartii	7	3 (2)	4 (7)
Yeast	6	3 (2)	3 (5)
Acinetobacter baumannii	4	2 (2)	2 (3)
Enterobacter spp.	5	5 (4)	0 (0)
Serratia marcescens	1	1 (1)	0 (0)
Corynebacterium spp.	1	1 (1)	0 (0)
Other	8	4 (3)	4 (7)
Total	182	125 (100)	57 (100)

[a]Number of urine cultures containing each microorganism.
[b]Number of single-species urine cultures containing each microorganism and percentage represented by each microorganism.
[c]Number of dual-species urine cultures containing each microorganism and percentage represented by each microorganism.

Microorganism-Level Differences in CAUTI Signs and Symptoms

CAUTIs involving *S. aureus* were the least likely to meet Loeb's minimum (30%) or NHSN (5%) criteria, followed by CAUTIs involving *Enterococcus* species (Table 3). CAUTIs involving *K. pneumoniae* were most likely to meet Loeb's minimum (86%) or NHSN criteria (43%). Logistic models using Firth's bias correction were run for any microorganism that had at least 10 occurrences of a CAUTI criterion.[18] Because Firth models do not allow for clustering, dummy coded facility variables were included. Despite small sample sizes, firthlogit models indicated that CAUTIs caused by *K. pneumoniae* were approximately 10 times as likely to meet Loeb's minimum criteria as those caused by other microorganisms (OR = 9.7, 95% CI = 2.3–40.3, $P = .003$). Ten of the 51 CAUTIs in which an acute change in mental status was reported (20%) involved *K. pneumoniae*, suggesting that this criterion may contribute to greater likelihood of *K. pneumoniae* CAUTIs meeting criteria. CAUTIs involving *K. pneumoniae* were more likely to have a reported acute change in mental status than those caused by other microorganisms (OR = 5.9, 95% CI = 1.8–19.4, $P = .004$). The association between *K. pneumoniae* and acute change in mental status remained robust in a multivariable model adjusted for age, sex, dementia, and facility (adjusted OR (aOR) = 6.2, 95% CI = 1.7–22.9, $P = .003$).

DISCUSSION

This study assessed adherence of clinically diagnosed CAUTIs to Loeb's minimum and NHSN criteria in a cohort of NH residents and conducted an exploratory assessment of associations between CAUTI signs and symptoms and specific microorganisms. Fifty percent of the catheterized NH residents participating in the study had a clinically diagnosed CAUTI, and CAUTIs were often recurrent. Thirty-two percent of clinically diagnosed CAUTIs met NHSN criteria, consistent with a recent report of similar CAUTI criteria in aged-care facilities in Australia,[12] and 40% met Loeb's minimum criteria for initiation of antibiotics, which is in alignment with a recent study of NH residents with dementia.[19] Overall, 50% of clinically diagnosed CAUTIs for which antibiotics were prescribed met standardized criteria, which is a significant improvement over the 17% of all infections estimated to meet either set of criteria in 2012.[20] Taken together, these

Table 3. Characteristics of Clinically Diagnosed Catheter-Associated Urinary Tract Infections (CAUTIs) Caused by Specific Microorganisms

Characteristic	Total, N = 182	*Proteus mirabilis*, n = 48	*Enterococcus* species, n = 38	*Escherichia coli*, n = 37	*Pseudomonas aeruginosa*, n = 34	*Staphylococcus aureus*, n = 20	*Klebsiella pneumoniae*, n = 14
	n (%)						
Standardized CAUTI definitions							
Loeb's minimum criteria, n = 182	74 (40)	16 (33)	12 (32)	20 (54)	14 (41)	6 (30)	12 (86)[a]
National Healthcare Safety Network criteria, n = 182	59 (32)	17 (35)	10 (26)	15 (40)	12 (35)	1 (5)	6 (43)
Either set of criteria, n = 182	91 (50)	22 (46)	16 (42)	24 (65)	19 (56)	6 (30)	12 (86)[a]
Individual criteria							
Acute mental status change, n = 182	51 (28)	10 (21)	10 (26)	13 (35)	10 (29)	5 (25)	10 (71)[a]
Temperature >100°F, repeated temperatures >99°F, or temperature >2°F above baseline, n = 182	38 (21)	13 (27)	6 (16)	10 (27)	7 (20)	2 (10)	4 (29)
Leukocytosis, neutrophilia >14,000/μL, n = 182	23 (13)	4 (8)	6 (16)	6 (16)	6 (18)	1 (5)	3 (21)
Acute functional status change, n = 179	12 (7)	2 (4)	7 (3)	5 (13)	2 (6)	2 (10)	2 (14)
Urine culture $\geq 10^5$ colony-forming units/mL, n = 178	161 (90)	45 (94)	31 (84)	36 (97)	30 (88)	15 (75)	14 (100)

See Methods section for definition of standardized criteria.
[a]$P<.05$ by logistic models with Firth's bias correction.

studies indicate that adherence to criteria for initiating antibiotic prescription may be improving in nursing homes.

The most common signs and symptoms of CAUTI were a positive urine culture, acute change in mental status, and fever. Consistent with data indicating that only 20% to 50% of older adults present with fever during acute infection,[11,21] only 21% of clinically diagnosed CAUTIs in the current study had fever meeting standardized criteria cutoffs. Twenty-eight percent of the CAUTIs in this study had an acute change in mental status as a symptom of infection, which is higher than other recent studies and may reflect epidemiological differences discussed below.[19]

Staphylococcus spp. and *Enterococcus* spp. are common in asymptomatic bacteriuria and are frequently considered to be contaminants in urine cultures.[3] It is therefore not surprising that the clinically diagnosed CAUTIs involving these microorganisms had the lowest percentages that met standardized criteria. Among clinically diagnosed CAUTIs caused by more-traditional pathogens, those involving *K. pneumoniae* were the most likely to meet at least one standardized definition. Although limited by a small sample size, CAUTIs involving *K. pneumoniae* appeared to be associated with acute change in mental status, causing these CAUTIs to meet Loeb's minimum criteria without necessarily meeting NHSN criteria. For example, 10 of the 14 CAUTIs involving *K. pneumoniae* had an acute change in mental status and therefore met Loeb's minimum criteria, whereas only four of these 10 CAUTIs met NHSN criteria. Three individuals with *K. pneumoniae* CAUTIs with acute change in mental status also had pneumonia reported in the charts at the study visit. Although all three cases met NHSN CAUTI criteria, pneumonia may have been the underlying cause of fever, leukocytosis, or mental status change. Further exploration of CAUTI symptom burden at the microorganism level is necessary to confirm these exploratory findings and to explore molecular mechanisms underlying the association between *K. pneumoniae* and mental status changes if these findings remain robust in a larger sample. If particular microorganisms are associated with specific patterns in symptom burden, these associations might be of use in refining existing tools for guiding initiation of antibiotic treatment. For instance, if *S. aureus* can be differentiated from *E. coli* based on symptom burden, this information could aid in guiding appropriate empirical treatment.

Strengths of this study include analysis of CAUTI at multiple NHs, collection of data pertaining to standardized CAUTI signs and symptoms for each enrolled NH resident by trained research staff at monthly follow-up visits, and alignment of standardized CAUTI definitions and symptoms to specific microorganisms. However, the results of this study should be interpreted in the context of a few notable limitations. First, because the study represents a post hoc analysis of data collected for a prospective parent study, clinical record keeping, the microbiology laboratories conducting urine cultures for each NH facility, and the judgement of the healthcare personnel caring for the enrolled participants to assess and document CAUTI symptoms and microbiological results were relied on. As such, any resident characteristics or CAUTI symptoms not recorded in the medical records were assumed to be absent. Because signs and symptoms included in standardized criteria may have been present but not recorded for some clinically diagnosed CAUTIs, the percentage meeting each definition may have been underestimated. This is particularly important for mental status change because a

recent study found that 2% to 53% of symptoms in NH residents with delirium were documented in the nursing notes.[22] Second, signs and symptoms of infection were recorded at study visits only if the resident had a record of a clinically diagnosed infection, so it was not possible to determine the likelihood of each sign and symptom being appropriately attributed to CAUTI versus another etiology. Finally, each distinct microorganism caused only a small number of CAUTIs. Further exploration of these preliminary findings will require a prospective longitudinal study with systematic assessment of signs and symptoms of possible infection, particularly mental status, and routine urine culturing to distinguish better between asymptomatic bacteriuria and infection.

Bacteriuria in catheterized individuals is frequently asymptomatic and inappropriately treated with antibiotics, contributing to the rise of antibiotic resistance in NHs and hospitals.[23–27] Although the current study was exploratory in nature and used a limited sample of participants and CAUTIs, further investigations of this nature may uncover a core pattern of clinical signs and symptoms associated with specific microorganisms. If a combination of standardized CAUTI symptoms is indicative of infection with specific microorganisms, this information would be invaluable for refining existing tools and determining which course of action should be taken to manage the infection. Predictive factors for specific microorganisms could therefore guide appropriate antibiotic use for catheterized individuals and may reduce inappropriate antibiotic use for asymptomatic bacteriuria, particularly for older adults in hospital and long-term care settings.

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