1	
2	Received Date : 01-Mar-2016
3	Revised Date : 26-Jun-2016
4	Accepted Date : 02-Jul-2016
5	Article type : Brief Reports
6	
7	
8	How Often Do Clinically Diagnosed Catheter-associated Urinary Tract
9	INFECTIONS IN NURSING HOMES MEET STANDARDIZED CRITERIA?
10	
11	Chelsie E. Armbruster, PhD ¹ , Katherine Prenovost, PhD ² , Harry L. T. Mobley, PhD ¹ , Lona
12	Mody, MD, MSc ^{2,3}
13	¹ Department of Microbiology and Immunology, University of Michigan Medical School, Ann
14	Arbor, MI, United States; ² VA Center for Clinical Management Research, VA Ann Arbor
15	Healthcare System, Ann Arbor, MI, United States; ³ Division of Geriatric and Palliative Care
16	Medicine, University of Michigan Medical School, Ann Arbor, MI, United States
17	
18	Corresponding Author:
19	Chelsie Armbruster
20	Microbiology and Immunology
21	6613B Medical Sciences II
22	1150 W Medical Center Drive
23	Ann Arbor, MI 48109
24	Phone: (734) 763-5364
25	Fax: (734) 764-3562
26	Email: chelarmb@umich.edu
	This is the author manuscript accepted for publication and has undergone full peer review but has

not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the <u>Version of Record</u>. Please cite this article as <u>doi:</u> <u>10.1111/jgs.14533</u>

27

28 Alternate Corresponding Author:

29 Email: lonamody@umich.edu

30

31 This work and the parent study were supported by Veterans Affairs Healthcare System Geriatric

- 32 Research Education and Clinical Care Center (GRECC, Mody), the National Institute on Aging
- 33 (K24AG050685, R01 AG032298, and R01 AG041780 to Mody, and 5P30 AG024824 for the
- 34 Claude D. Pepper Older Americans Independence Center), the National Institute of Allergy and
- 35 Infectious Diseases (F32 AI102552 to Armbruster), and the National Institute of Diabetes and
- 36 Digestive and Kidney Diseases (K99 DK105205 to Armbruster).
- 37
- 38 This work was presented at IDweek2015.
- 39
- 40 **Running Head:** CAUTI Symptoms and Epidemiology in NHs
- 41 ABSTRACT
- 42 **Objectives:** Determine the relationship of clinically diagnosed catheter-associated urinary tract
- 43 infection (CAUTI) to standardized criteria and assess microorganism-level differences in
- 44 symptom burden in a cohort of catheterized nursing home (NH) residents.
- 45 **Design:** Post-hoc analysis of a prospective longitudinal study.
- 46 Setting: Twelve NHs in Southeast Michigan.
- 47 Participants: 233 NH residents with indwelling urinary catheters.
- 48 Measurements: Clinical and demographic data, including CAUTI epidemiology and symptoms,
- 49 were obtained at study enrollment, 14 days, and monthly thereafter for up to one year.
- 50 **Results:** One hundred twenty participants with an indwelling catheter (51%) were prescribed
- 51 systemic antibiotics for 182 clinically diagnosed CAUTIs. Participants were predominantly
- white (90%), male (52%), with a mean age of 73.7 years. 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
- 55 Network (NHSN) criteria, and 50% met either Loeb's minimum or NHSN criteria. CAUTIS
- 56 involving *Staphylococcus aureus* and *Enterococcus* spp. were least likely to meet criteria.
- 57 CAUTIs involving *K. pneumoniae* were most likely to meet Loeb's minimum criteria (OR=9.7

[95% CI, 2.3-40.3]), possibly due to an association with acute change in mental status (OR=5.9
[95% CI, 1.8-19.4]).

60 Conclusion: Fifty percent of clinically diagnosed CAUTIs met standardized criteria, which

61 represents an improvement in antibiotic prescribing practices. At the microorganism-level, our

62 exploratory data indicates that symptom burden may differ between microorganisms.

63 Exploration of CAUTI signs and symptoms associated with specific microorganisms may yield

64 beneficial information to refine existing tools guiding appropriate antibiotic treatment.

65

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

67 pneumoniaeINTRODUCTION

Urinary tract infection (UTI) and catheter-associated UTI (CAUTI) are the most common 68 infections in nursing homes (NHs) leading to the majority of antibiotic prescriptions,¹ though 69 70 one-third are misdiagnosed asymptomatic bacteriuria for which antimicrobial therapy is not beneficial.^{2,3} However, catheter-associated bacteriuria can progress to symptomatic cystitis, 71 pyelonephritis, and even bacteremia.⁴⁻⁷ Approximately 10-50% of individuals catheterized for ≥ 7 72 days will develop CAUTI while essentially all individuals catheterized long term will experience 73 at least one CAUTI.^{2,14} Thus, it is critical to further refine guidelines for CAUTI diagnosis and 74 initiation of antibiotics. 75

Current CAUTI diagnosis criteria include clinical signs and symptoms such as fever, 76 77 rigors, hypotension, flank pain, leukocytosis, and acute changes in mental and functional status, as well as a positive urine culture.^{8,9} Loeb's minimum criteria are standards for initiation of 78 antibiotics in long term care settings based on assessment of infection signs and symptoms,⁸ 79 while the National Healthcare Safety Network (NHSN) criteria are standards for CAUTI 80 surveillance in long term care settings.⁹ Recent estimates indicate that only 10-16% of 81 prescriptions for UTI in NHs adhere to Loeb's minimum criteria,¹⁰ and only 31% of UTIs 82 prescribed antibiotics meet the NHSN criteria.¹¹ These discrepancies could be due to several 83 factors, including prescription of antibiotics for asymptomatic bacteriuria and the challenges of 84 85 accurately identifying infections involving atypical symptoms. Prescribing practices could be 86 improved by investigation of signs and symptoms that are most (and least) common during infection with traditional CAUTI pathogens, such as Escherichia coli, compared to 87 88 microorganisms more likely to be present during asymptomatic bacteriuria, such as

Staphylococcus and *Enterococcus* species.³ For instance, if *Staphylococcus 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 concerning possible differences in clinical presentation of CAUTI caused 92 by distinct microorganisms, or whether symptom burden may be indicative of CAUTI 93 epidemiology. The innate immune response is largely responsible for the signs and symptoms of 94 UTI, particularly activation of toll-like receptors (TLRs) by pathogen-associated molecular 95 patterns (PAMPs) such as lipopolysaccharide (LPS). TLR signaling, the magnitude of the 96 resulting immune response, and infection symptoms can be modulated by specific virulence 97 factors or PAMP modifications.¹² For example, expression of different fimbrial types by Gram-98 negative bacteria can modulate LPS-induced TLR signaling cascades and infection outcome in a 99 mouse model of UTI.¹² Dysuria is linked to certain LPS decorations rather than strictly resulting 100 from LPS-induced TLR signaling.¹³ Delirium can result from systemic inflammation,¹⁴ and may 101 also be modulated by the level of innate immune activation. Flow cytometry analysis of 102 bacterial, leukocyte, and erythrocyte counts in urine was recently found to be indicative of 103 infection by broad groups of microorganisms in non-catheterized individuals.¹⁵ The value of 104 clinical signs and symptoms for predicting UTI was investigated for individuals with spinal cord 105 injuries on clean intermittent catheterization,¹⁶ but not with respect to specific microorganisms. 106 Thus, classes of microorganisms may be associated with specific patterns of infection signs and 107 108 symptoms. If so, this information could be useful for guiding appropriate antibiotic treatment in catheterized NH residents, particularly if clear differences exist between CAUTIs caused by 109 microorganisms in which distinct treatment differences exist, such as S. aureus versus E. coli. 110 Our study had three primary goals: 1) determine adherence of clinically diagnosed 111 CAUTI from a cohort of NH residents to standardized criteria, 2) determine if specific 112 microorganisms are more likely to be present in clinically diagnosed CAUTIs that meet 113 standardized criteria than others, and 3) conduct an exploratory assessment of associations 114 between CAUTI signs and symptoms and specific microorganisms. We addressed these goals 115 through post-hoc analyses of data collected from a prospective study of catheterized residents 116 from 12 NHs in southeast Michigan. 117

118 Methods

119

120 Parent Study Design and Population.

A secondary, post-hoc analysis was conducted from data collected through the Targeted 121 Infection Prevention (TIP) parent study.¹⁷ The parent study was a cluster-randomized 122 intervention trial conducted in 12 community-based NHs in Michigan from May 2010 to April 123 2013, focused on reducing prevalence of multi-drug resistant organisms. The study was approved 124 by the University of Michigan Institutional Review Board. Inclusion criteria were: a) any NH 125 resident with an indwelling urinary catheter (Foley or suprapubic) and/or a feeding tube 126 (nasogastric or percutaneous endoscopic gastrostomy tube) for more than 72 hours; and b) 127 informed consent from the resident or their power of attorney. Residents receiving end-of-life 128 129 care were excluded. This cohort was optimal for our objectives due to prolonged follow-up data (100 days, on average). Demographics, infection, and CAUTI symptoms data were obtained by 130 trained research staff through clinical chart review at monthly visits, as were urine microbiology 131 data. Four hundred eighteen NH residents were enrolled in the TIP study; 292 residents had an 132 133 indwelling urinary catheter for >72 hours. Of these, full baseline demographic and CAUTI symptom data (if applicable) were available for 233 residents. Study visits occurred at the time 134 135 of enrollment, on day 14, and monthly thereafter for a maximum of one year (or until death, discharge, or device discontinuation). 136

137

138 **Definitions.**

139 *Clinically diagnosed CAUTI*: NH residents with a UTI reported in their medical records, 140 an indwelling catheter in place for >72 hours prior to the date of the UTI, and a corresponding 141 prescription of at least a 3-day course of systemic antibiotics were considered to have a clinically 142 diagnosed CAUTI.¹⁷ In the event of catheter removal, participants were censored from our 143 analysis on the date of removal.

144

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 were present: 1) fever, defined as having a single temperature >100°F or >2°F above baseline; 2) new costovertebral tenderness; 3) rigors, or 4) acute mental status change.⁸ If there was no mention of a particular sign or symptom in the medical record, it was assumed to be absent. Rigors was reported in the records of less than 5% of clinically diagnosed CAUTIs and therefore excluded from

151 microorganism-level analysis.

152

153 National Healthcare Safety Network (NHSN) criteria: Clinically diagnosed CAUTIs were considered to meet NHSN criteria if a positive urine culture, defined as $\geq 10^5$ colony-forming 154 units (cfu) of one or two microorganisms per milliliter of urine, was reported and the following 155 signs and symptoms were present: 1) No alternative site of infection and a) fever, defined as a 156 single temperature $>100^{\circ}$ F, repeated temperatures $>99^{\circ}$ F, or $>2^{\circ}$ F above baseline, b) rigors, or c) 157 new hypotension; 2) leukocytosis, defined as >14,000 leukocytes/mm³ or a left shift (>6% bands 158 or ≥ 1.500 bands/mm³) and a) acute mental status change, or b) acute functional decline; 3) new 159 onset suprapubic or costovertebral angle pain or tenderness, or 4) purulent discharge around the 160 catheter or acute pain, swelling or tenderness of testes, epididymis, or prostate.⁹ If there was no 161 mention of a particular sign or symptom in the medical record, it was assumed to be absent. 162 Rigors, hypotension, purulent discharge around the catheter, and acute pain, swelling, or 163 tenderness of testes, epididymis, or prostate were reported in the records of less than 5% of 164 CAUTIs and therefore excluded from microorganism-level analysis. 165 166

Acute change in mental status: Fluctuation in behavior, inattention, disorganized thinking, and
 an altered level of consciousness compared to baseline.^{8,9} Data concerning mental status was
 obtained by trained research staff through clinical chart review.

170

Acute change in functional status: Reported by clinical evaluation or by a new 3-point increase
 in total activities of daily living (ADL) score.⁹ Data concerning functional status was obtained by
 trained research staff through clinical chart review.

174

175 Statistical Analysis.

Preliminary logistic models explored infection by specific microorganisms as a function of clinical CAUTI signs and symptoms followed by multivariable models that combined CAUTI signs and symptoms. All logistic regressions were adjusted for facility-level clustering to account for residents nested in NHs, and clinically diagnosed CAUTIs were grouped based on urine culture results: 1) *Proteus mirabilis, 2*) *Enterococcus* spp., 3) *Escherichia coli, 4*) *Pseudomonas aeruginosa, 5*) *Staphylococcus aureus*, or 6) *Klebsiella pneumoniae*. Groupings were not 182 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

184 13 (StataCorp LP, College Station, TX). **RESULTS**

185

186 Description of Study Population

Study participants were predominantly white (90%), male (52%), elderly (mean age 73.7 187 \pm 12.7) with 126 (54%) being \geq 75 years of age, and dependent for care (mean physical self-188 maintenance score 21.6 ± 3.9) as shown in Table 1. The most common conditions upon 189 enrollment were diabetes (99 [42%]), dementia (80 [34%]), a history of cerebrovascular 190 accidents (48 [21%]), and chronic obstructive pulmonary disease (45 [19%]). A total of 274 191 urine cultures were reported from our cohort of 233 catheterized NH residents. Eleven urine 192 cultures (4%) were reported without an accompanying prescription of antibiotics. The remaining 193 263 urine cultures came from 120 unique study participants and had an accompanying 194 195 prescription of systemic antibiotics and symptom data. For the purposes of our study, these 263 cases will be considered "clinically diagnosed" CAUTIs. There were no major discernable 196 197 differences between groups of catheterized NH residents, although dementia was approximately twice as common in residents with clinically diagnosed CAUTI compared to those without (odds 198 ratio, OR=2.0 [95% CI 1.2-3.4]; P<0.012). 199

200

201 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* (28 [22%]),

206 E. coli (23 [18%]), and P. aeruginosa (18 [14%]), and fifty-seven CAUTIs (31%) involved two

- species and were predominantly caused by *Enterococcus* spp. (23 [40% of the 57 dual-species
- 208 CAUTIs]), *P. mirabilis* (20 [35%]), and *P. aeruginosa* (16 [28%]). The most common
- 209 combinations in dual-species infection were *P. aeruginosa* with *Enterococcus* spp. (n=6), *P.*
- 210 *mirabilis* with *Enterococcus* spp. (n=5), and *P. mirabilis* with *P. aeruginosa* (n=4).
- 211

212 Adherence of Clinically Diagnosed CAUTIs to Standardized Criteria

213 The proportion of CAUTIs that met standardized criteria are shown in Table 3 and grouped by predominant microorganism. All 182 clinically diagnosed CAUTIs were prescribed 214 systemic antibiotics; 74 (40%) met Loeb's minimum criteria; 59 (32%) met NHSN criteria; 91 215 (50%) met at least one standardized definition of symptomatic CAUTI. The most common 216 findings were $\geq 10^5$ cfu of at least one microorganism (161 [90%]), an acute change in mental 217 status (51 [28%]), fever (38 [21%]), leukocytosis or neutrophilia (23 [13%]), and an acute 218 change in functional status (12 [7%]). Fourteen (8%) CAUTI cases had concurrent pneumonia 219 noted in the charts; 12 (86%) had positive urine cultures, 7 (50%) had fever, and 6 (43%) had 220 acute mental status change (data not shown). Seven of the 12 cases with positive urine cultures 221 222 met NHSN criteria, which excludes fever as a criterion if there is an alternate source of infection. In the remaining 5 cases, systemic antimicrobial use could potentially be attributed to either 223 pneumonia or CAUTI. 224

225

226 Microorganism-level Differences in CAUTI Signs and Symptoms

CAUTIS involving S. aureus had the lowest percentages that met Loeb's minimum (30%) 227 228 or NHSN (5%) criteria, followed by CAUTIs involving *Enterococcus* species (Table 3). CAUTIs involving K. pneumoniae had the highest percentage that met Loeb's minimum (86%) or NHSN 229 criteria (43%). Logistic models using Firth's bias correction were run for any microorganism that 230 had at least ten occurrences of a CAUTI criterion.¹⁸ As Firth models do not allow for clustering, 231 232 dummy coded facility variables were included. Despite small sample sizes, firthlogit models indicated that CAUTIs caused by K. pneumoniae were approximately ten times more likely to 233 234 meet Loeb's minimum criteria than CAUTIs caused by other microorganisms (OR=9.7 [95% CI, 2.3-40.3]; P<0.003). Ten of the 51 CAUTIs that reported an acute change in mental status (20%) 235 236 involved K. pneumoniae, suggesting that this criterion may contribute to an increased likelihood of K. pneumoniae CAUTIs meeting criteria. Indeed, CAUTIs involving K. pneumoniae were 237 more likely to have a reported acute change in mental status compared to CAUTIs caused by 238 other microorganisms (OR=5.9 [95% CI, 1.8-19.4]; P<0.004). The association between K. 239 pneumoniae and acute change in mental status remained robust in a multivariable model adjusted 240 241 for age, gender, dementia, and facility (adjusted odds ratio, aOR=6.2 [95% CI 1.7-22.9]; P<0.003).DISCUSSION 242

243 In this study, we assessed adherence of clinically diagnosed CAUTIs to Loeb's minimum and NHSN CAUTI criteria in a cohort of NH residents and conducted an exploratory assessment 244 of associations between CAUTI signs and symptoms and specific microorganisms. Fifty percent 245 of the catheterized NH residents participating in the study had a clinically diagnosed CAUTI, 246 and CAUTIs were often recurrent. Thirty-two percent of clinically diagnosed CAUTIs met 247 NHSN criteria, consistent with a recent report of similar CAUTI criteria in aged-care facilities in 248 Australia,¹¹ and forty percent met Loeb's minimum criteria for initiation of antibiotics, which is 249 in alignment with a recent study concerning NH residents with dementia.¹⁹ Overall, 50% of 250 clinically diagnosed CAUTIs prescribed antibiotics met standardized criteria, which is a 251 significant improvement over the 17% of all infections estimated to meet either set of criteria in 252 2012.²⁰ Taken together, these studies indicate that adherence to criteria for initiating antibiotic 253 prescription may be improving in long term care facilities. 254

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 20-50% of older adults present with fever during acute infection,^{10, 21} only 21% of clinically diagnosed CAUTIs in our study had fever meeting standardized criteria cutoffs. Twenty-eight percent of the CAUTIs in our 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 species and Enterococcus species are common in asymptomatic 261 bacteriuria, and also frequently considered to be contaminants in urine cultures.³ It is therefore 262 not surprising that the clinically diagnosed CAUTIs involving these microorganisms had the 263 lowest percentages that met standardized criteria in our cohort. Among clinically diagnosed 264 CAUTIS caused by more traditional pathogens, those involving K. pneumoniae were the most 265 266 likely to meet at least one standardized definition. Although limited by a small sample size, CAUTIs involving K. pneumoniae appeared to be associated with an acute change in mental 267 268 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 269 270 change in mental status and therefore met Loeb's minimum criteria, while only 4 of these 10 271 CAUTIS met NHSN criteria. It is important to note that three K. pneumoniae CAUTIS with acute change in mental status also had pneumonia reported in the charts at the study visit. While all 272 three cases met NHSN CAUTI criteria, pneumonia may have been the underlying cause for 273

274 fever, leukocytosis, or mental status change. Further exploration of CAUTI symptom burden at 275 the microorganism-level is necessary to confirm these exploratory findings, and to explore 276 molecular mechanisms underlying the association between K. pneumoniae and mental status 277 changes if these findings remain robust in a larger sample. If particular microorganisms are indeed associated with specific patterns in symptom burden, these associations might be of use in 278 refining existing tools for guiding initiation of antibiotic treatment. For instance, if S. aureus can 279 be differentiated from E. coli based on symptom burden, this information could aid in guiding 280 appropriate empirical treatment. 281

Strengths of this study include analysis of CAUTI at multiple NH facilities, collection of 282 data pertaining to standardized CAUTI signs and symptoms for each enrolled NH resident by 283 trained research staff at monthly follow-up visits, and alignment of standardized CAUTI 284 285 definitions and symptoms to specific microorganisms. However, the results of this study should be interpreted in the context of a few notable limitations. First, as this study represents a post-hoc 286 287 analysis of data collected for a prospective parent study, we relied on clinical record keeping, the microbiology laboratories conducting urine cultures for each NH facility, and the judgement of 288 289 the healthcare personnel caring for the enrolled participants to assess and document CAUTI symptoms and microbiological results. As such, any resident characteristics or CAUTI 290 291 symptoms not recorded in the medical records were assumed to be absent. As signs and symptoms pertaining to standardized criteria may have been present but not recorded for some 292 293 clinically diagnosed CAUTIs, we may have underestimated the percentage meeting each 294 definition. This is particularly important for mental status change as a recent study found that 295 only 2-53% of symptoms in nursing home residents with delirium were documented in the nursing notes.²² Second, signs and symptoms of infection were only recorded at study visits if 296 297 the resident had a record of a clinically diagnosed infection, so we are not able to determine the likelihood of each sign and symptom being appropriately attributed to CAUTI verses another 298 299 etiology. Finally, the total number of CAUTIs caused by each microorganism for our analysis was limited. Further exploration of these preliminary findings will require a prospective, 300 longitudinal study with systematic assessment of signs and symptoms of possible infection, 301 302 particularly mental status, as well as routine urine culturing to better distinguish between asymptomatic bacteriuria and infection. 303

304 Bacteriuria in catheterized individuals is frequently asymptomatic and inappropriately treated with antibiotics, contributing to the rise of antibiotic resistance in NHs and hospitals.²³⁻²⁷ 305 306 While our study is exploratory in nature and utilizes a limited sample of participants and CAUTIS, further investigations of this nature may uncover a core pattern of clinical signs and 307 symptoms associated with specific microorganisms. If a combination of standardized CAUTI 308 symptoms are indeed indicative of infection by specific microorganisms, this information would 309 be invaluable for refining existing tools and determining which course of action should be taken 310 to manage the infection. Predictive factors for specific microorganisms could therefore guide 311 appropriate antibiotic use for catheterized individuals and may reduce inappropriate antibiotic 312 use for asymptomatic bacteriuria, particularly for older adults in hospital and long-term care 313

314 settings.ACKNOWLEDGMENTS

We thank the leadership and healthcare personnel at all participating NHs, and the

members of the TIP Study Team. We also thank Sara McNamara, Kristen Gibson, and Julia

317 Mantey for helpful comments and critiques. All significant contributors consented to authorship.

318 CONFLICT OF INTEREST CHECKLIST

Elements of Financial/Personal		*Author 1:		Author 2:		Author 3:		Author 4:	
Conflicts	CA	CA KP			НМ		LM		
	Yes	No	Yes	No	Yes	No	Yes	No	
Employment or Affiliation		Х		Х		Х		Х	
Grants/Funds		Х		X		X		Х	
Honoraria		Х		Х		Х		Х	
Speaker Forum		Х		X		Х		Х	
Consultant		Х		X		Х		Х	
Stocks		Х		X		X		Х	
Royalties		Х		X		X		X	

Expert Testimony	X	Х	Х	Х
Board Member	X	Х	Х	Х
+				
Patents	X	Х	Х	Х
Personal Relationship	Х	Х	Х	Х

319 *Authors can be listed by abbreviations of their names

- 320 For "yes", provide a brief explanation:
- 321

322 AUTHOR CONTRIBUTIONS

323 Armbruster: concept and design, analysis, and interpretation of data, drafting and revising the

article. Prenovost: analysis and interpretation of data, critically reviewing the article for

325 important intellectual content. Mobley: interpretation of data, critically reviewing the article for

326 important intellectual content. Mody: concept and design, acquisition, analysis, and

327 interpretation of data from the parent study, critically reviewing the article for important

- intellectual content. All authors reviewed and approved the submitted version of the article.
- 329

330 SPONSOR'S ROLE

331 The sponsor was not involved in the study design, methods, subject recruitment, data collections,

analysis, or preparation of the paper. The content is solely the responsibility of the authors and

does not necessarily represent the official views of the funders.**REFERENCES**

Loeb M, Brazil K, Lohfeld L, *et al.* Optimizing antibiotics in residents of nursing homes:
protocol of a randomized trial. *BMC health services research*. 2002;2: 17.

1336 [2] Loeb M, Simor AE, Landry L, *et al.* Antibiotic use in Ontario facilities that provide

chronic care. *Journal of general internal medicine*. 2001;**16**: 376-383.

- 338 [3] Nicolle LE, Bradley S, Colgan R, *et al.* Infectious Diseases Society of America
- 339 guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis.*

340 2005;**40**: 643-654.

341 [4] Daniels KR, Lee GC, Frei CR. Trends in catheter-associated urinary tract infections

- among a national cohort of hospitalized adults, 2001-2010. American Journal of Infection
- 343 *Control.* 2014;**42**: 17-22.

344 [5] Hooton TM, Bradley SF, Cardenas DD, et al. Diagnosis, Prevention, and Treatment of

345 Catheter-Associated Urinary Tract Infection in Adults: 2009 International Clinical Practice

346 Guidelines from the Infectious Diseases Society of America. *Clinical Infectious Diseases*.

347 2010;**50**: 625-663.

348 [6] Nicolle LE. Catheter-related urinary tract infection: practical management in the elderly.
349 *Drugs Aging*. 2014;**31**: 1-10.

350 [7] Warren JW, Damron D, Tenney JH, *et al.* Fever, bacteremia, and death as complications

of bacteriuria in women with long-term urethral catheters. *J Infect Dis.* 1987;**155**: 1151-1158.

352 [8] Loeb M, Bentley DW, Bradley S, *et al.* Development of minimum criteria for the

initiation of antibiotics in residents of long-term-care facilities: results of a consensus

354 conference. *Infect Control Hosp Epidemiol*. 2001;**22**: 120-124.

Stone ND, Ashraf MS, Calder J, *et al.* Surveillance definitions of infections in long-term
care facilities: revisiting the McGeer criteria. *Infect Control Hosp Epidemiol.* 2012;**33**: 965-977.

357 [10] Olsho LE, Bertrand RM, Edwards AS, *et al.* Does adherence to the Loeb minimum

criteria reduce antibiotic prescribing rates in nursing homes? *J Am Med Dir Assoc*. 2013;14: 309
e301-307.

360 [11] Bennett NJ, Johnson SA, Richards MJ, et al. Infections in Australian Aged-Care

- 361 Facilities: Evaluating the Impact of Revised McGeer Criteria for Surveillance of Urinary Tract
- 362 Infections. *Infect Control Hosp Epidemiol*. 2016: 1-3.
- 363 [12] Fischer H, Yamamoto M, Akira S, et al. Mechanism of pathogen-specific TLR4

activation in the mucosa: Fimbriae, recognition receptors and adaptor protein selection.

- 365 *European Journal of Immunology*. 2006;**36**: 267-277.
- Rudick CN, Jiang M, Yaggie RE, *et al.* O-antigen modulates infection-induced pain
 states. *PLoS One*. 2012;7: e41273.
- 368 [14] Sankowski R, Mader S, Valdes-Ferrer SI. Systemic inflammation and the brain: novel
- 369 roles of genetic, molecular, and environmental cues as drivers of neurodegeneration. Frontiers in
- 370 *cellular neuroscience*. 2015;**9**: 28.

371 [15] Monsen T, Rydén P. Flow Cytometry Analysis Using Sysmex UF-1000i Classifies

- 372 Uropathogens Based on Bacterial, Leukocyte, and Erythrocyte Counts in Urine Specimens
- among Patients with Urinary Tract Infections. *J Clin Microbiol*. 2015;**53**: 539-545.
- 374 [16] Massa LM, Hoffman JM, Cardenas DD. Validity, Accuracy, and Predictive Value of
- 375 Urinary Tract Infection Signs and Symptoms in Individuals With Spinal Cord Injury on
- 376 Intermittent Catheterization. *The Journal of Spinal Cord Medicine*. 2009;**32**: 568-573.
- 377 [17] Mody L, Krein SL, Saint S, et al. A targeted infection prevention intervention in nursing
- home residents with indwelling devices: A randomized clinical trial. *JAMA Internal Medicine*.
 2015;175: 714-723.
- 380 [18] FIRTH D. Bias reduction of maximum likelihood estimates. *Biometrika*. 1993;80: 27-38.
- 381 [19] D'Agata E, Loeb MB, Mitchell SL. Challenges in assessing nursing home residents with
- advanced dementia for suspected urinary tract infections. *J Am Geriatr Soc.* 2013;**61**: 62-66.
- 383 [20] Wang L, Lansing B, Symons K, et al. Infection rate and colonization with antibiotic-
- resistant organisms in skilled nursing facility residents with indwelling devices. *Eur J Clin Microbiol Infect Dis.* 2012;31: 1797-1804.
- Bellmann-Weiler R, Weiss G. Pitfalls in the diagnosis and therapy of infections in elderly
 patients--a mini-review. *Gerontology*. 2009;55: 241-249.
- [22] Voyer P, McCusker J, Cole MG, *et al.* Nursing documentation in long-term care settings:
 New empirical evidence demands changes be made. *Clin Nurs Res.* 2014;23: 442-461.
- 390 [23] Tambyah PA, Maki DG. Catheter-associated urinary tract infection is rarely
- symptomatic: a prospective study of 1,497 catheterized patients. *Arch Intern Med.* 2000;160:
 678-682.
- 393 [24] Cope M, Cevallos ME, Cadle RM, *et al.* Inappropriate treatment of catheter-associated
 asymptomatic bacteriuria in a tertiary care hospital. *Clin Infect Dis.* 2009;48: 1182-1188.
- 395 [25] Dommeti PMD, Wang LBS, Flannery EL, *et al.* Patterns of Ciprofloxacin-Resistant
- 396 Gram-Negative Bacteria Colonization in Nursing Home Residents. *Infection Control and*
- 397 *Hospital Epidemiology*. 2011;**32**: 177-180.
- 398 [26] Mody L, Maheshwari S, Galecki A, *et al.* Indwelling device use and antibiotic resistance
- in nursing homes: identifying a high-risk group. *J Am Geriatr Soc*. 2007;55: 1921-1926.
- 400 [27] Rogers MA, Mody L, Chenoweth C, et al. Incidence of antibiotic-resistant infection in
- 401 long-term residents of skilled nursing facilities. *Am J Infect Control*. 2008;**36**: 472-475.
- 402

TABLES

Characteristic	Total	Clinically	No clinically	^a P value
	(n=233)	diagnosed CAUTI	diagnosed CAUTI	
$\overline{\mathbf{O}}$		(n=120)	(n=113)	
Age, mean (SD; range), years	73.7 (12.7; 35-105)	75.0 (11.9; 35-105)	72.4 (13.4; 38-97)	.257
Comorbidity score, mean (SD;	2.8 (1.9; 0-10)	2.9 (1.9; 0-10)	2.7 (1.8; 0-9)	.533
range)				
PSMS score, mean (SD; range)	21.6 (3.9; 13-30)	22.1 (3.8; 14-30)	21.0 (4.0; 13-30)	.150
Gender				
Male	121 (52)	63 (52)	58 (51)	.809
Female	112 (48)	57 (48)	55 (49)	.809
Race				
White	209 (90)	106 (88)	103 (91)	.430
Black or African American	21 (9)	12 (10)	9 (8)	.527
Other	3 (1)	2 (2)	1 (1)	.387
Underlying conditions				
Diabetes	99 (42)	47 (39)	52 (46)	.207
Dementia	80 (34)	50 (42)	30 (26)	.012
CVA	48 (21)	28 (23)	20 (18)	.255
COPD	45 (19)	24 (20)	21 (19)	.725

Table 1. Demographic Characteristics of Catheterized Nursing Home Residents.

Hemiplegia	32 (14)	21 (17)	11 (10) .190
Renal disease	29 (12)	15 (12)	14 (12) .987
Tumor (any)	23 (10)	11 (9)	12 (10) .772
Myocardial infarction	23 (10)	11 (9)	12 (10) .770

Note. Data are No. (%) of residents, unless otherwise indicated. CAUTI, catheter-associated urinary tract infection; SD, standard deviation; PSMS, physical self-maintenance score; CVA, cerebrovascular accident; COPD, chronic obstructive pulmonary disease. ^aClustered bivariate logistic regression.

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

Ţ		Single-Species	Urine Cultures	Dual-Species Urine Cultures			
Microorganism	^a Total No.	^b No. of Urine	^c Percent (%)	^d No. of Urine	^e Percent (%)		
	Urine	Cultures		Cultures			
$\overline{\mathbf{O}}$	Cultures						
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 baumanii	4	2	2	2	3		
Enterobacter spp.	5	5	4	0	0		
Serratia marscesens	1	1	1	0	0		
Corynobacterium spp.	1	1	1	0	0		
Other	8	4	3	4	7		
Total	182	125	100	57	100		

^aNumber of urine cultures containing each microorganism.

^bNumber of single-species urine cultures containing each microorganism. ^cPercent of all single-species cultures represented by each microorganism. ^dNumber of dual-species urine cultures containing each microorganism. ^ePercent of all dual-species cultures represented by each microorganism

Author Manusc

Characteristics of clinically diagnosed CAUTIs	^b Total	Pm	Ent	Ec	Pa	Sa	Кр
H	[n=182]	[n=48]	[n=38]	[n=37]	[n=34]	[n=20]	[n=14]
^a Standardized CAUTI Definitions							
Loeb's minimum criteria [n=182]	74	16	12	20	14	6	12
$\overline{\mathbf{O}}$	(40)	(33)	(32)	(54)	(41)	(30)	(86)*
NHSN criteria [n=182]	59	17	10	15	12	1	6
	(32)	(35)	(26)	(40)	(35)	(5)	(43)
Either criteria [n=182]	91	22	16	24	19	6	12
	(50)	(46)	(42)	(65)	(56)	(30)	(86)*
^b Individual criteria							
Acute mental status change [n=182]	51	10	10	13	10	5	10
	(28)	(21)	(26)	(35)	(29)	(25)	(71)*
Fever $>100^{\circ}$ F, repeated temperatures $>99^{\circ}$ F, or	38	13	6	10	7	2	4
>2°F above baseline [n=182]	(21)	(27)	(16)	(27)	(20)	(10)	(29)
Leukocytosis/ neutrophilia >14,000/mm ³ [n=182]	23	4	6	6	6	1	3
	(13)	(8)	(16)	(16)	(18)	(5)	(21)
Acute functional status change [n=179]	12	2	7	5	2	2	2
	(7)	(4)	(3)	(13)	(6)	(10)	(14)
Urine culture $\geq 10^5$ cfu/ml [n=178]	161	45	31	36	30	15	14
	(90)	(94)	(84)	(97)	(88)	(75)	(100)

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

Note. Data are No. (%) of clinically diagnosed CAUTIs, by microorganism, presenting with each criterion. See "Methods" for definition of standardized criteria. NHSN, National Healthcare Safety Network; CAUTI, catheter-associated urinary tract infection; *Pm, Proteus mirabilis; Ent, Enterococcus* species; *Ec, Escherichia coli; Pa, Pseudomonas aeruginosa; Sa, Staphylococcus aureus; Kp, Klebsiella pneumonia.*

^aNumber of clinically diagnosed CAUTIs assessed for meeting each definition is given in brackets.

^bNumber of clinically diagnosed CAUTIs assessed for each criterion is given in brackets.

^cNumber of clinically diagnosed CAUTIs attributed to each microorganism is given in brackets.

*P < .05 by logistic models with Firth's bias correction.

Author Manuer