Open Forum Infectious Diseases

MAJOR ARTICLE

The Niche for *Escherichia coli* Sequence Type 131 Among Veterans: Urinary Tract Abnormalities and Long-Term Care Facilities

Dimitri M. Drekonja,[1,3] Michael A. Kuskowski,[4] Ruth Anway,[2] Brian D. Johnston,[1,3] and James R. Johnson[1,2]

[1]Infectious Diseases Section, and [2]Research Service, Minneapolis Veterans Affairs Healthcare System, Minnesota; Departments of [3]Medicine, and [4]Psychiatry, University of Minnesota Medical School, Minneapolis

Background. Antimicrobial resistance among *Escherichia coli* is increasing, driven largely by the global emergence of sequence type 131 (ST131). However, the clinical significance of ST131 status is unknown. Among veterans, we assessed whether ST131 causes more severe, persistent, or recurrence-prone infections than non-ST131 *E. coli*.

Methods. Isolates were assessed by polymerase chain reaction for membership in ST131 and relevant subclones thereof (*H*30R and *H*30Rx) and by broth microdilution for susceptibility to 11 antibiotics. Clinical and epidemiological data were systematically abstracted from the medical record. Between-group comparisons were made using *t* tests and Fisher's exact test.

Results. Of the 311 unique *E. coli* isolates, 61 (19.6%) represented ST131. Of these, most (51 of 61, 83.6%) represented the *H*30R subclone; only 5 of 51 (9.8%) represented *H*30Rx. Relative to non-ST131 and non-*H*30R isolates, neither ST131 nor *H*30R were associated with more severe disease, worse clinical outcomes, or more robust hosts. Instead, both were more likely to be isolated from patients without manifestations of infection (for ST131, 36.1% vs 21.2% [$P = .02$]; for *H*30R, 39% vs 21% [$P = .008$]) and who had prior healthcare contact or long-term care facility (LTCF) exposure (for ST131, 33% vs 14% [$P = .002$]; for *H*30R, 37% vs 14% [$P < .001$]). Despite a greater likelihood of discordant initial therapy, outcomes did not differ between ST131 and *H*30R isolates vs other *E. coli* isolates.

Conclusions. Among veterans, ST131 and its *H*30R subclone were associated with LTCF-exposed hosts but not with worse outcomes.

Keywords. antimicrobial resistance; epidemiology; *Escherichia coli*; virulence.

Extraintestinal *Escherichia coli* infections, which are common and costly, range in severity from cystitis to more serious illnesses such as pyelonephritis, urosepsis, and meningitis [1, 2]. Their management has become progressively more challenging with the rising prevalence of antimicrobial resistance in *E. coli*, a trend driven by the rapid global emergence of "high-risk" clones such as sequence type 131 (ST131) [3], as defined by multilocus sequence typing involving housekeeping genes.

Sequence type 131 combines extensive antimicrobial resistance with seemingly increased virulence—as suggested by early reports of severe disease and increased number of known virulence genes—possibly heralding an era of increasing antimicrobial resistance and disease severity [4–6]. The recent recognition that the ST131 pandemic is driven almost entirely by the *H*30R ST131 subclone (associated with fluoroquinolone resistance), with its *H*30Rx subset (associated with extended-spectrum β-lactamase production), has only added to concerns regarding a newly emerged super pathogen [7, 8]. Both of these subclones arose from the most prevalent subclone of ST131, *H*30. The emergence of the CTX-M-15-extended spectrum β-lactamase among community-dwelling (vs hospitalized) patients raises further alarms regarding the spread of antimicrobial resistance beyond populations historically considered to be at risk [3].

The evidence that ST131, and particularly its *H*30R and *H*30Rx subclones, is especially virulent is inconclusive. Animal model studies have suggested that ST131 is either demonstrably or not demonstrably more virulent than other *E. coli* [9–12]. Likewise, although 2 molecular epidemiological studies demonstrated an association between the *H*30R subclone and recurrent urinary tract infection (UTI) and sepsis [13, 14] (compared with non-*H*30R strains), or between *H*30Rx and sepsis [8], these studies did not take host characteristics into account, and others studies have associated ST131 with patient characteristics, suggesting impaired host defenses, specifically advanced age, and long-term care facility (LTCF) residence [15, 16]. Indeed, the largest and most recent such study found that, compared with other *E. coli*, ST131-*H*30 was associated with compromised hosts and, after adjustment for host factors, similar clinical presentations but persistent infection and later complications [17].

Received 18 April 2016; accepted 14 June 2016.

Correspondence: D. M. Drekonja, Minneapolis VA Medical Center, 1 Veterans Drive, Mail code 111F, Minneapolis, MN 55417 (drek0002@umn.edu).

Open Forum Infectious Diseases®
Published by Oxford University Press on behalf of the Infectious Diseases Society of America 2016.

DOI: 10.1093/ofid/ofw138

Consequently, further study that accounts for host status is needed to determine whether ST131 truly is a more aggressive pathogen than non-ST131 *E. coli*.

In this study, we sought to test the hypotheses that ST131 causes infections that are more severe, persistent, and recurrent, and that occur in less compromised hosts than those caused by non-ST131 *E. coli*. For this experiment, we (1) collected clinical information from consecutive patients at the Minneapolis Veterans Affairs Medical Center (MVAMC) from whom *E. coli* was isolated, (2) characterized the corresponding *E. coli* isolates for ST131, *H*30R, and *H*30Rx status, and (3) then compared clonal background with disease severity and underlying host characteristics.

METHODS

Patients and Isolates

Consecutive *E. coli* isolates from unique patients, as recovered by the MVAMC microbiology laboratory between December 10, 2010 and April 25, 2011 from any specimen type, were retrieved and characterized by the research laboratory for membership in ST131, *H*30R, and *H*30Rx by using established polymerase chain reaction-based assays that detect single-nucleotide polymorphisms that are specific for each of the nested clonal lineages, with fluoroquinolone-resistant *H*30-positive isolates being regarded as *H*30R [18]. Antimicrobial susceptibility results, as generated by the clinical laboratory using a Vitek-2 instrument, were recorded. Of the present study isolates and source patients, 100 were included in a recently published multicenter study that explored similar epidemiologic associations in a broader population [17]. The present study was independently conceived and designed to assess the effects of ST131 in a predominantly male veteran population; a predetermined number of the present samples (n = 100) and associated data were provided to a multicenter study that was conducted in parallel [17].

Clinical and Epidemiological Data

Study personnel reviewed each source patient's medical record in the VA Computerized Patient Record System to abstract demographic, epidemiological, and clinical information. Demographic data included age, race, and gender. Epidemiological information included hospitalization, dialysis, or LTCF residence in the previous year, both within the VA system and elsewhere. Clinical information included characteristics of the presenting illness, its management and outcome, and underlying host status, as detailed below.

Specific clinical data included the presence or absence of any signs or symptoms of infection (both systemic and localized to the site of isolation), comorbid conditions, and (for patients with a urine isolate) any complicating factors known to predispose patients to more frequent or difficult to manage UTIs (obstruction, neurogenic bladder, urinary instrumentation, recent urologic surgery, calculi, and indwelling drainage device). Urinalysis results were not used as a sign of infection. Details of antimicrobial therapy were recorded, including whether the initial therapy was active against the *E. coli* isolate. Outcomes assessed included clinical recurrence, microbiologic recurrence (ie, repeated isolation of *E. coli* from the same clinical site), *Clostridium difficile* infection, escalation in level of care (defined as transfer to a higher-acuity setting), use of advanced imaging (defined as computerized tomography, magnetic resonance imaging, or ultrasonography), and mortality, both in-hospital and overall. Source patients were followed for 30 days. The Institutional Review Board of the MVAMC approved all study procedures and granted a waiver of informed consent for this study.

Statistical Methods

Between-group comparisons were made using SPSS, *t* tests for continuous variables, and Fisher's exact test for categorical variables. The criterion for statistical significance was $P < .05$.

RESULTS

Study Isolates

Three hundred eleven unique (by patient) *E. coli* isolates were obtained from the MVAMC clinical microbiology laboratory during the study period. Of these, 61 (19.6%) were identified as ST131, most of which (51, 83.6%) represented the *H*30R subclone. Only 5 (9.8%) of the 51 *H*30R isolates represented the *H*30Rx subclone; accordingly, further analysis was limited to ST131 and *H*30R status.

Clinical Source

Among the 311 total isolates, urine was the most common source (260, 83.6%), followed by wound (36, 11.6%), blood (6, 1.9%), respiratory (5, 1.6%), peritoneal fluid (4, 1.3%), and unclassified (1, 0.3%). No differences in ST131 or *H*30R subclone status by source were identified.

Demographic and Epidemiologic Associations

Source patients were predominantly male (86.2%), as expected in a VA population, and elderly, with a mean age of 67.8 years (standard deviation, 15.1). Most patients (78.8%) were seen in the outpatient setting. Race was most commonly white (78.5%), unknown (15.4%), or African American (3.5%). Prior contact with healthcare facilities in the past year was common, with more than 30% of patients having been hospitalized and 43.1% having had 1 of the assessed exposures (Table 1). The only significant demographic or epidemiologic correlate of having an ST131 or ST131-*H*30R isolate was LTCF exposure, which was over twice as common in association with ST131 and *H*30R isolates as with other isolates (for ST131, 32.8% vs 14.4% [$P = .002$]; for *H*30R, 37.3% vs 14.2% [$P < .001$]).

Medical Comorbidities

Comorbid conditions were common in the source patients, as were known urological complicating factors (Tables 2 and 3). Diabetes was present in approximately 50% of patients, and

Table 1. Epidemiological Exposure in the Year Before Study Entry, Overall and Stratified by ST131 and *H*30R Status

Exposure	No. of Isolates (Column %)				No. of Isolates (Column %)		
	Overall (n = 311)	ST131 (n = 61)	Non-ST131 (n = 250)	*P* Value, ST131 vs Non-ST131	*H*30R (n = 51)	Non-*H*30R (n = 260)	*P* Value, *H*30R vs Non-*H*30R
Hospitalization	117 (37.6)	26 (42.6)	91 (36.4)	.38	23 (45.1)	94 (36.2)	.27
LTCF	56 (18.0)	20 (32.8)	36 (14.4)	.002	19 (37.3)	37 (14.2)	<.001
Dialysis	10 (3.2)	1 (1.6)	9 (3.6)	.69	1 (2.0)	9 (3.5)	.71
Any exposure	134 (43.1)	32 (52.5)	102 (40.8)	.11	28 (54.9)	106 (40.8)	.07

Abbreviations: *H*30R, ST131 subclone *H*30R; LTCF, long-term care facility; ST131, sequence type 131.

chronic kidney disease was present in approximately 20%. Among the 260 patients with urine-source isolates, obstruction was the most common complicating factor (28.1%), followed closely by indwelling drainage devices (25.8%). Of the patients with urine-source isolates, a numerically greater proportion of patients with an ST131 isolate had an underlying urological condition compared with those with a non-ST131 isolate (66.1% vs 51.5%; $P = .07$) (Table 3). Likewise, a significantly greater proportion of patients with an *H*30R isolate had an underlying urological condition compared with those with a non-*H*30R isolate (73.9% vs 50.5%; $P = .005$).

Clinical Manifestations

Clinical manifestations consistent with infection were documented in 236 (75.9%) of the 311 source patients. Manifestations included urinary frequency and dysuria (assessed for urine isolates), wound erythema (assessed for wound isolates), cough (assessed for respiratory isolates), and/or vital sign abnormalities and peripheral blood leukocytosis (assessed for any isolate). Sequence type 131 and *H*30R status were associated with colonization rather than symptomatic infection, with infectious manifestations present in association with only 39 (63.9%) of 61 ST131 isolates, vs 197 (78.8%) of 250 non-ST131 isolates ($P = .02$), and with only 31 (60.8%) of 51 *H*30R isolates, vs 205 (78.8%) of 260 non-*H*30R isolates ($P = .008$). Systemic manifestations were infrequent, the most common being leukocytosis (18.0%) and fever (9.3%); no differences in these were observed between ST131 or *H*30R isolates and non-ST131 or *H*30R isolates.

For specific clinical manifestations, only 2 (both, urinary tract-specific) were significantly associated with ST131 and the *H*30R subclone, both negatively so (Table 4). That is, compared with patients with non-ST131 urine isolates, patients with ST131 urine isolates had a lower likelihood of both dysuria (10.7% vs 31.4%; $P = .002$) and urinary frequency (8.9% vs 22.1%; $P = .03$). Likewise, patients with *H*30R subclone isolates, compared with patients with non-*H*30R isolates, had a lower likelihood of both dysuria (8.7% vs 30.8%; $P = .003$) and frequency (6.5% vs 22.0%; $P = .02$).

Antimicrobial Resistance

The ST131 isolates exhibited a greater prevalence of resistance to multiple antimicrobials compared with the non-ST131 isolates. In addition to the expected association with fluoroquinolone resistance (85.2% vs 8.4%; $P < .001$), ST131 isolates also were significantly more often resistant to trimethoprim/sulfamethoxazole (TMP/SMZ), ampicillin, ampicillin/sulbactam, and gentamicin. The *H*30R isolates exhibited an even stronger association with fluoroquinolone resistance (100% [by definition] vs 8.5% for non-*H*30R isolates; $P < .001$), plus significant associations

Table 2. Comorbid Medical Conditions Present in 311 Veteran Source Patients, Overall and Stratified by ST131 and *H*30R Status

Medical Condition	No. of Isolates (Column %)				No. of Isolates (Column %)		
	Overall (n = 311)	ST131 (n = 61)	Non-ST131 (n = 250)	*P* Value, ST131 vs Non-ST131	*H*30R (n = 51)	Non-*H*30R (n = 260)	*P* Value, *H*30R vs Non-*H*30R
Diabetes	142 (45.7)	24 (39.3)	118 (47.2)	.32	19 (37.3)	123 (47.3)	.22
Chronic kidney disease	53 (17.0)	7 (11.5)	46 (18.4)	.25	6 (11.8)	47 (18.1)	.32
Dementia	32 (10.3)	8 (13.1)	24 (9.6)	.48	8 (15.7)	24 (9.2)	.20
Immune suppression	31 (10.0)	4 (6.6)	27 (10.8)	.45	4 (7.8)	27 (10.4)	.63
Cirrhosis	7 (2.3)	2 (3.3)	5 (2.0)	.63	2 (3.9)	5 (1.9)	.60
Neutropenia	4 (1.3)	0 (0)	4 (1.6)	.59	0 (0)	4 (1.5)	.61
Any of above	190 (61.1)	35 (57.4)	155 (62.0)	.56	30 (58.8)	160 (61.5)	.75

Abbreviations: *H*30R, ST131 subclone *H*30R; ST131, sequence type 131.

Table 3. Urinary Tract Complicating Factors Present Among 260 Veterans With Urinary *Escherichia coli* Isolates, Overall and Stratified by ST131 and *H*30R Status

	No. of Isolates (Column %)				No. of Isolates (Column %)		
Urological condition	Overall (n = 260)	ST131 (n = 56)	Non-ST131 (n = 204)	*P* Value, ST131 vs Non-ST131	*H*30R (n = 46)	Non-*H*30R (n = 214)	*P* Value, *H*30R vs Non-*H*30R
Obstruction	73 (28.1)	17 (30.4)	56 (27.5)	.74	16 (34.8)	57 (26.6)	.28
Indwelling drainage device	67 (25.8)	17 (30.4)	50 (24.5)	.39	16 (34.8)	51 (23.8)	.14
Neurogenic bladder	47 (18.1)	14 (30.6)	33 (16.2)	.17	13 (28.3)	34 (15.9)	.06
Urinary instrumentation	19 (7.3)	6 (10.7)	13 (6.3)	.38	6 (13.0)	13 (6.1)	.12
Calculi	13 (5.0)	5 (8.9)	8 (3.9)	.16	5 (10.9)	8 (3.7)	.06
Recent surgery	10 (3.8)	4 (7.1)	6 (2.9)	.23	3 (6.5)	7 (3.3)	.39
Any abnormality	142 (54.6)	37 (66.1)	105 (51.5)	.07	34 (73.9)	108 (50.5)	.005

Abbreviations: *H*30R, ST131 subclone *H*30R; ST131, sequence type 131.

with resistance to ampicillin, ampicillin/sulbactam, and gentamicin, and a numerically greater prevalence of TMP/SMZ resistance that approached significance (29.4% vs 18.1%; $P = .08$).

Clinical Outcomes

Among patients who had documented manifestations of infection, the ST131 isolates' more extensive and prevalent antimicrobial resistance resulted in a significantly greater likelihood of discordant initial antimicrobial therapy for them, compared with non-ST131 isolates (11 of 39 [28.2%] vs 6 of 197 [3.0%]; $P < .001$). Patients with *H*30R isolates were even more likely to receive discordant initial therapy, relative to patients with non-*H*30R isolates (35.5% vs 2.9%; $P < .001$). Despite this, assessed outcomes did not differ significantly between patients with ST131 vs non-ST131 isolates or between those with *H*30R versus non-*H*30R isolates. All assessed outcomes were rare, limiting our power to detect between-group differences. Although 7 of 8 assessed outcomes were numerically less common among ST131 or *H*30R source patients, there were no statistically significant differences, and the overall rates were similar to those of non-ST131 source patients (Table 5).

DISCUSSION

This observational study of 311 consecutive *E. coli* isolates (including 61 ST131 isolates, 51 representing the *H*30R subclone) and their corresponding source patients provides an in-depth assessment of the host epidemiology, clinical presentations, disease severity, and outcomes associated with this globally disseminated clone among veterans. Contrary to our prior hypotheses, ST131 and *H*30R were not associated with more severe disease, worse clinical outcomes, or more robust hosts. On the contrary, both ST131 and *H*30R were actually more likely to be isolated from source patients who lacked manifestations of infection and who had prior healthcare contact or LTCF exposure. Moreover, despite a greater likelihood of discordant initial therapy, ST131 and *H*30R isolates were numerically less likely than other *E. coli* isolates to be associated with adverse outcomes. These findings, which largely replicate those of a recent multicenter study that included 100 of the present study isolates [17], uniquely document a lack of association of ST131 with adverse outcomes, possibly related to the present study's all-veteran, predominantly male population.

Table 4. Clinical Manifestations of Infection Documented Among 260 Veterans With Urinary *Escherichia coli* Isolates, Overall and Stratified by ST131 and *H*30R Status

	No. of Isolates (Column %)				No. of Isolates (Column %)		
Clinical Manifestation	Overall (n = 260)	ST131 (n = 56)	Non-ST131 (n = 204)	*P* Value, ST131 vs Non-ST131	*H*30R (n = 46)	Non-*H*30R (n = 214)	*P* Value, *H*30R vs Non-*H*30R
Dysuria	70 (26.9)	6 (10.7)	64 (31.4)	.002	4 (8.7)	66 (30.8)	.003
Frequency	50 (19.2)	5 (8.9)	45 (22.1)	.03	3 (6.5)	47 (22.0)	.02
Urgency	40 (15.4)	6 (10.7)	34 (16.7)	.31	4 (8.7)	36 (16.8)	.19
Hematuria	37 (14.2)	4 (7.1)	33 (16.2)	.13	3 (6.5)	34 (15.9)	.11
Flank pain	17 (6.5)	6 (10.7)	11 (5.4)	.22	4 (8.7)	13 (6.1)	.74
Suprapubic pain	12 (4.6)	4 (7.1)	8 (3.9)	.47	2 (4.3)	12 (5.6)	1.0

Abbreviations: *H*30R, ST131 subclone *H*30R; ST131, sequence type 131.

Table 5. Assessed Outcomes, Overall and Stratified by ST131 and *H*30R Status, Among the 236 Patients With Documented Manifestations of Infection

Outcome	No. of Isolates (Column %)				No. of Isolates (Column %)		
	Overall (n = 236)	ST131 (n = 39)	Non-ST131 (n = 197)	*P* Value, ST131 vs Non-ST131	*H*30R (n = 31)	Non-*H*30R (n = 205)	*P* Value, *H*30R vs Non-*H*30R
Clinical recurrence	9 (3.8)	2 (5.1)	7 (3.6)	.65	2 (6.5)	7 (3.4)	.61
Microbiological recurrence	3 (1.3)	0	3 (1.5)	1	0 (0)	3 (1.5)	1
Clostridium difficile infection	2 (0.8)	0	2 (1.0)	1	0 (0)	2 (1.0)	1
Mortality, overall	8 (3.4)	0	8 (4.1)	.36	0 (0)	8 (3.9)	.39
In-hospital mortality	8 (3.4)	0	8 (4.1)	.36	0 (0)	8 (3.9)	.39
ICU admission	15 (6.3)	2 (5.1)	13 (6.6)	1	2 (6.5)	13 (6.3)	1
Escalation in level of care	14 (5.9)	1 (2.6)	13 (6.6)	.48	1 (3.2)	13 (6.3)	.70
Use of advanced imaging[a]	56 (23.7)	8 (20.5)	48 (24.4)	.68	6 (19.4)	50 (24.4)	.65
Any of above	77 (32.6)	11 (28.2)	66 (33.5)	.58	9 (29.0)	66 (32.2)	.84

Abbreviations: *H*30R, ST131 subclone *H*30R; ICU, intensive care unit; ST131, sequence type 131.

[a] Computerized tomography, magnetic resonance imaging, or ultrasonography.

Overall, our findings suggest that, despite ST131's high prevalence and extensive virulence and resistance profiles, on a by-case basis ST131 may lead to more colonization than other *E. coli*, and it may favor hosts with urinary tract abnormalities and LTCF exposure. The *H*30R subclone accounted for the majority (51 of 61, 83.6%) of ST131 isolates; accordingly, the *H*30R isolates had largely similar associations, as did the ST131 isolates. Unfortunately, our study had too few *H*30Rx subclone isolates to meaningfully assess associations specifically with this subclone.

Source patients with a history of LTCF exposure were significantly more likely to have an ST131 isolate; this was not true for other healthcare exposures (ie, hospitalization or dialysis). Whether this association of ST131 with LTCF exposure, which has been documented previously [17, 19], is due to the underlying comorbid conditions of patients with LTCF exposure—vs selective antimicrobial exposure, infection control lapses within LTCFs, or a combination of these—is unknown. However, the resistance characteristic of ST131, combined with the high level of antimicrobial use in such facilities, seems likely to provide ideal selection for the survival of ST131 and similarly resistant pathogens [15, 17]. The finding that, when present in a urine culture, ST131 was less likely than other *E. coli* to be associated with dysuria or frequency may reflect that it is well suited to asymptomatic colonization of the urinary tract, possibly aided by the factors discussed above, ie, resistance, antimicrobial use, and a population with numerous comorbid conditions, including underlying urinary tract abnormalities.

More than one third of source patients with an ST131 isolate received discordant initial antimicrobial therapy, compared with fewer than 3 percent of other patients, a greater than 10-fold difference, as observed also in the recent multicenter study [17]. This was largely driven by the high percentage of ST131 isolates resistant to fluoroquinolones, which are still widely used for empiric therapy of UTIs, even in hospitalized patients. The lack of demonstrable harm from this discordant therapy has several possible explanations, including that few patients were critically ill, active therapy was likely initiated within 1 to 2 days (once susceptibility results became available), there was insufficient analytical power to detect such harms, and there was an omission of other possibly relevant outcome variables (eg, qualify of life).

Strengths of the study include the inclusion of consecutive *E. coli* isolates, which limits bias potentially associated with other sampling techniques, and consistent data abstraction using a standardized form. In addition, the all-veteran study population, which increases the applicability of the findings to veterans in general, was unique to this study; eg, veterans constituted <10% of patients in the recent multicenter study [17]. Weaknesses include reliance on clinician documentation, because clinical information could be abstracted only if providers documented their findings accurately and completely. In addition, although fully 61 (19.6%) of the 311 study isolates were ST131, a larger sample size for ST131, *H*30R, and especially *H*30Rx isolates would have permitted a more robust exploration of associations with these strains, including for severe disease. However, arguing against such an association was our failure to detect, among patients with an ST131 or *H*30R isolate, even a suggestive trend toward more severe disease or a greater likelihood of infection-associated clinical manifestations or persistence/recurrence.

CONCLUSIONS

Among veterans with ST131 isolated from a clinical specimen, disease severity and clinical outcomes were not appreciably worse compared with veterans with non-ST131 isolates. The ST131 and its *H*30R subclone were associated with asymptomatic

colonization and LTCF exposure. Future research should (1) further define the clinical and epidemiological correlates of this highly prevalent and extensively antimicrobial-resistant clone and (2) seek to identify opportunities for improved management and prevention.

Acknowledgments

We thank the Minneapolis Veterans Affairs Medical Center clinical microbiology laboratory for providing clinical isolates. We also thank Connie Clabots for providing technical assistance in the laboratory.

Financial support. This work was supported by the Office of Research and Development, Medical Research Service, Department of Veterans Affairs grant numbers 1I01CX000192 and I01CX000920-01A1 (to J. R. J.) and grant number 1I01CX000830-01A2 (to D. M. D.).

Potential conflicts of interest. J. R. J. has received research grants/contracts from ICET, Merck, Syntiron, Crucell/Jannsen, and Tetraphase for unrelated work, and has patent applications regarding tests to identify *Escherichia coli* strains. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Johnson JR, Russo TA. Uropathogenic *Escherichia coli* as agents of diverse non-urinary tract extraintestinal infections. J Infect Dis **2002**; 186:859–64.
2. Russo TA, Johnson JR. Medical and economic impact of extraintestinal infections due to *Escherichia coli*: focus on an increasingly important endemic problem. Microbes Infect **2003**; 5:449–56.
3. Banerjee R, Johnson JR. A new clone sweeps clean: the enigmatic emergence of *Escherichia coli* sequence type 131. Antimicrob Agents Chemother **2014**; 58:4997–5004.
4. Owens RC Jr, Johnson JR, Stogsdill P, et al. Community transmission in the United States of a CTX-M-15-producing sequence type ST131 *Escherichia coli* strain resulting in death. J Clin Microbiol **2011**; 49:3406–8.
5. Mantengoli E, Luzzaro F, Pecile P, et al. *Escherichia coli* ST131 producing extended-spectrum beta-lactamases plus VIM-1 carbapenemase: further narrowing of treatment options. Clin Infect Dis **2011**; 52:690–1.
6. Ender PT, Gajanana D, Johnston B, et al. Transmission of an extended-spectrum-beta-lactamase-producing *Escherichia coli* (sequence type ST131) strain between a father and daughter resulting in septic shock and emphysematous pyelonephritis. J Clin Microbiol **2009**; 47:3780–2.
7. Colpan A, Johnston B, Porter S, et al. *Escherichia coli* sequence type 131 (ST131) subclone H30 as an emergent multidrug-resistant pathogen among US veterans. Clin Infect Dis **2013**; 57:1256–65.
8. Price LB, Johnson JR, Aziz M, et al. The epidemic of extended-spectrum-beta-lactamase-producing *Escherichia coli* ST131 is driven by a single highly pathogenic subclone, H30-Rx. mBio **2013**; 4:e00377–13.
9. Vimont S, Boyd A, Bleibtreu A, et al. The CTX-M-15-producing *Escherichia coli* clone O25b: H4-ST131 has high intestine colonization and urinary tract infection abilities. PLoS One **2012**; 7:e46547.
10. Ciesielczuk H, Betts J, Phee L, et al. Comparative virulence of urinary and bloodstream isolates of extra-intestinal pathogenic *Escherichia coli* in a *Galleria mellonella* model. Virulence **2015**; 6:145–51.
11. Lavigne JP, Vergunst AC, Goret L, et al. Virulence potential and genomic mapping of the worldwide clone *Escherichia coli* ST131. PLoS One **2012**; 7:e34294.
12. Johnson JR, Porter SB, Zhanel G, et al. Virulence of *Escherichia coli* clinical isolates in a murine sepsis model in relation to sequence type ST131 status, fluoroquinolone resistance, and virulence genotype. Infect Immun **2012**; 80:1554–62.
13. Tchesnokova V, Billig M, Chattopadhyay S, et al. Predictive diagnostics for *Escherichia coli* infections based on the clonal association of antimicrobial resistance and clinical outcome. J Clin Microbiol **2013**; 51:2991–9.
14. Banerjee R, Johnston B, Lohse C, et al. *Escherichia coli* sequence type 131 is a dominant, antimicrobial-resistant clonal group associated with healthcare and elderly hosts. Infect Control Hosp Epidemiol **2013**; 34:361–9.
15. Burgess MJ, Johnson JR, Porter SB, et al. Long-term care facilities are reservoirs for antimicrobial-resistant sequence type 131 *Escherichia coli*. Open Forum Infect Dis **2015**; 2:ofv011.
16. Ludden C, Cormican M, Vellinga A, et al. Colonisation with ESBL-producing and carbapenemase-producing *Enterobacteriaceae*, vancomycin-resistant enterococci, and meticillin-resistant *Staphylococcus aureus* in a long-term care facility over one year. BMC Infect Dis **2015**; 15:168.
17. Johnson JR, Thuras P, Johnston BD, et al. The pandemic H30 subclone of *Escherichia coli* sequence type 131 (ST131) is associated with persistent infections and adverse outcomes independently from its multi-drug resistance and associations with compromised hosts. Clin Infect Dis **2016**; 62:1529–36.
18. Johnson JR, Clermont O, Johnston B, et al. Rapid and specific detection, molecular epidemiology, and experimental virulence of the O16 subgroup within *Escherichia coli* sequence type 131. J Clin Microbiol **2014**; 52:1358–65.
19. Lopez-Cerero L, Navarro MD, Bellido M, et al. *Escherichia coli* belonging to the worldwide emerging epidemic clonal group O25b/ST131: risk factors and clinical implications. J Antimicrob Chemother **2014**; 69:809–14.