American Journal of Emergency Medicine (2012) **30**, 942–949

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The American Journal of Emergency Medicine

www.elsevier.com/locate/ajem

Brief Report

Antimicrobial resistance in uncomplicated urinary tract infections in 3 California EDs ☆

Shannon E. Moffett MD [a,*], Bradley W. Frazee MD [a], John C. Stein MD [b], Bahar Navab MPH [c], Judy Maselli MSPH [d], Sukhjit S. Takhar MD [e,f], Ralph Gonzales MD [g]

[a] *Department of Emergency Medicine, Alameda County Medical Center—Highland Campus, Oakland, CA 94602, USA*
[b] *Department of Emergency Medicine, UCSF Medical Center, San Francisco, CA 94143, USA*
[c] *Health Services and Policy Analysis Doctoral Program, University of California, Berkeley, Berkeley, CA 94720, USA*
[d] *Division of General Internal Medicine, University of California, San Francisco, San Francisco, CA 94143, USA*
[e] *Department of Emergency Medicine, Brigham and Women's Hospital, Boston, MA 02115, USA*
[f] *Division of Emergency Medicine, Harvard Medical School, Boston, MA 02115, USA*
[g] *Department of Medicine, UCSF Medical Center, San Francisco, CA 94143, USA*

Received 11 January 2011; revised 11 May 2011; accepted 11 May 2011

Abstract

Background: Increased trimethoprim/sulfamethoxazole (TMP/SMX) resistance has led to changes in empiric treatment of female urinary tract infections (UTI) in the emergency department (ED), particularly increased use of fluoroquinolones (*Acad Emerg Med*.2009;16(6):500-507). Whether prescribing changes have affected susceptibility in uropathogens is unclear. Using narrow-spectrum agents and therapy tailored to local susceptibilities remain important goals.

Objective: The primary goal of this study is to characterize the susceptibility patterns of uropathogens among ambulatory female ED patients with UTI. Its secondary goal is to identify demographic or clinical factors predictive of resistance to narrow-spectrum agents.

Methods: This was a cross-sectional study of women with suspected UTI referred to a trial of computer kiosk–aided treatment of UTI in 3 Northern California EDs. Demographic and clinical data were gathered from the kiosk and chart, and features associated with resistance were identified by bivariate and multivariable regression analysis.

Results: Two hundred eighty-three participants, aged 15 to 84 years, were diagnosed with UTI and cultured. One hundred thirty-five (48%) of cultures were positive, with full susceptibilities reported (81% *Escherichia coli*). Only 2 isolates (1.5%) were fluoroquinolone resistant. Resistance to TMP/SMX was 18%, to nitrofurantoin 5%, and to cefazolin 4%. Seventy-four percent were sensitive to all 3 narrow-spectrum agents. Resistance to narrow-spectrum agents did not vary significantly by diagnosis, age, recent UTI, or any clinical or demographic factors; but overall, there was a trend toward lower resistance rates in our population than in our hospitals' published antibiograms.

Conclusion: In our population of ambulatory female ED patients, resistance to TMP/SMX is just below the 20% threshold that the Infectious Disease Society of America recommends for continued empiric

☆ This study was sponsored by a research grant from the Innovations for the Underserved Program of the California Health Care Foundation (#09-15024 & 08-1133). It has not been published or presented elsewhere, and the authors have no conflicts of interest to report. Reprints are not available from the authors.

* Corresponding author.
E-mail address: smoffett@stanfordalumni.org (S.E. Moffett).

doi:10.1016/j.ajem.2011.05.008

use (*Clin Infect Dis*.1999;29(4):745-758, *Clin Infect Dis*.2011;52(5):e103-120), whereas resistance to other narrow-spectrum agents, such as nitrofurantoin and cephalexin, may be lower than published antibiograms for our sites. Fluoroquinolone resistance remains very low.

1. Introduction

1.1. Background

It has been estimated that symptomatic urinary tract infection (UTI) is responsible for 8 million physician visits annually [1]. In the decade between the release of the 1999 Infectious Disease Society of America (IDSA) guidelines for empiric treatment of UTI [2] and the recent release of the 2010 guidelines [3], there has been a documented increase in uropathogen resistance to trimethoprim/sulfamethoxazole (TMP/SMX), long considered the first-line narrow-spectrum antibiotic for empiric therapy [2]. Many studies of ambulatory populations now report resistance levels exceeding the 20% cutoff suggested by the IDSA as the maximum allowing empiric TMP/SMX treatment (eg, 29.6% in a Denver ambulatory female population in 2005 and 29.6% in a similar Durham, North Carolina population in 2007) [4,5].

Fluoroquinolone treatment of uncomplicated UTI has increased during this period [6-8], likely due to fear of increasing resistance to narrow-spectrum antibiotics as well as to ease of dosing. There is now concern that fluoroquinolone resistance may be on the rise in the United States [4,9-11] and abroad [12-14], along with hope that resistance to TMP/SMX might return to low levels, given less selective pressure for resistance secondary to decreased prescribing rates of TMP/SMX in favor of fluoroquinolones.

To our knowledge, there have been no studies assessing such shifts in uropathogen resistance in ambulatory female emergency department (ED) patients.

1.2. Importance

Current surveillance data such as these help elucidate distinctive features of the ambulatory ED UTI population, allowing improved tailoring of antibiotic regimens and a rigorous search for markers of resistance.

1.3. Goals

To determine susceptibility to both narrow- and broad-spectrum antimicrobials among urinary pathogens isolated from symptomatic ambulatory women presenting to the ED. A secondary goal was to identify demographic or historical factors predictive of resistance to TMP/SMX or other narrow-spectrum agents.

2. Methods

2.1. Study design

This is a cross-sectional study of consecutive women with suspected UTI presenting to the ED. Data were collected from women referred for participation in a randomized controlled trial of computer-assisted UTI management (details of which will be published separately).

2.2. Setting

The study was conducted at 3 Northern California EDs—site 1, a tertiary care university hospital with an annual ED census of 39 000 (data collected October 2008-September 2010), and sites 2 and 3, both urban public hospitals, with annual ED censuses of 85 000 (site 2, data collected November 2008-September 2010) and 60 000 (site 3, data collected October 2009-March 2010). Approval was granted by each hospital's institutional review board, and all participants consented.

2.3. Selection of participants

Emergency department triage staff were instructed to refer consecutive women to the computer module [15] (located in a kiosk near triage) if their chief complaint was dysuria, urinary urgency, or frequency, or if they had symptoms that the triage nurse considered consistent with UTI. Patients were not referred if clinically unstable, not English or Spanish speaking, or reporting an unrelated second chief complaint. The computer kiosk administered a questionnaire, after which it was determined whether the patient was eligible for randomization to computer-assisted treatment. Emergency department staff were asked to perform urine cultures and antimicrobial susceptibility testing on all women eligible for randomization in the UTI kiosk trial. The decision to perform cultures on those ineligible was left to the treating clinician. Our study population includes both groups and, thus, allows for bacteriologic surveillance of a cross-section of clinically stable women presenting to the ED with urinary complaints. For the purposes of the analysis outlined here, the computer kiosk served only as a data collection device. Patients were excluded if their final diagnosis did not include UTI or a urine culture was not performed.

2.4. Data collection and processing

Current and previous medical history was obtained using an audiovisual computer survey; vital signs, physical

examination findings, test results, and final diagnoses were obtained via chart review. Microbiologic testing was performed by the study sites' clinical laboratories. Standard semiquantitative microbiologic methods were used [16], and *positive cultures* were defined as those demonstrating 1000 colonies/mL or higher. (This threshold follows IDSA and the recommendation of Stamm et al [17] of ≥100 colonies/mL [2,17]. However, our clinical laboratories' standard methods precluded discerning values less than 1000 colonies/mL). Microbes considered uropathogens were *E coli*, *Escherichia fergesonii*, *Enterobacter aerogenes*, *Citrobacter koserii*, *Citrobacter freundi*, *enterococcus* spp, "enteric gram-negative rods," group B streptococci including *Streptococcus agalactiae*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Staphylococcus saprophyticus*. Urine specimens showing 3 or more species were considered contaminated. Microbial identification and minimum inhibitory concentrations were determined using commercial multisubstrate broth microdilution panels according to manufacturer's recommendations (MicroScan; Dade Behring, Inc, West Sacramento, CA). Minimum inhibitory concentration break points were those established by Clinical Laboratory Standards Institute [18].

Cases in which laboratories reported only "gram-negative rods," without speciation or resistance, were considered positive if associated urinalysis showed greater than trace leukocyte esterase. For group B streptococci, often a contaminant but now recognized as an occasional true urinary pathogen [19], we considered a culture positive if no other organism grew and urinalysis showed greater than trace leukocyte esterase. Two patients' urine grew more than 1 organism—both grew *E coli*: 1 also grew *Klebsiella pneumoniae*; the other, *enterococcus*. Only the *E coli* susceptibility was used in the predictor analysis.

All cases were categorized as either cystitis or pyelonephritis. "Cystitis" included the following free text diagnoses: cystitis, hemorrhagic cystitis, uncomplicated UTI, acute cystitis, simple UTI, and UTI. "Pyelonephritis" included pyelonephritis, possible early pyelonephritis, UTI vs pyelonephritis, UTI/pyelo, early pyelonephritis, uncomplicated pyelonephritis, and suspected pyelonephritis.

2.5. Outcome measures

Antimicrobial susceptibility rates were the primary outcome measure. To reflect common practice, we focused on susceptibility to 4 first-line antibiotics (TMP/SMX, cefazolin/cephalexin, nitrofurantoin, and fluoroquinolones) among all uropathogens combined. In addition, to facilitate comparisons with other studies, we examined susceptibility of *E coli* alone. We then sought predictor variables associated with resistance to any of the narrow-spectrum antibiotics (TMP/SMX, cephalexin, nitrofurantoin) and to TMP/SMX alone.

2.6. Primary data analysis

Among positive cultures, we calculated the proportion susceptible to TMP/SMX, cefazolin or cephalexin, nitrofurantoin, and fluoroquinolones, then calculated the proportion susceptible to all 3 of the narrow-spectrum agents.

To identify predictors of resistance to narrow-spectrum agents, we first performed bivariate analysis using factors hypothesized a priori to be associated with resistance (patient age ≥45 years, current antibiotic use, history of UTI within the past month, final diagnosis of pyelonephritis) as well as

Table 1 Characteristics of those cultured vs not cultured

Characteristic	Cx not performed (n = 119)	Cx performed (n = 283)	*P*
Site 1	25 (21.0%)	192 (67.8%)	<.0001
Site 2	78 (65.6%)	65 (23.0%)	
Site 3	16 (13.5%)	26 (9.2%)	
Age median (y) (interquartile range) (range)	28 (23, 41)	31 (24, 43)	.0784
Age ≥45 y	21 (17.7%)	65 (23.0%)	.2350
Spanish language	19 (16.0%)	17 (6.0%)	.0014
Flank pain	58 (48.7%)	138 (48.8%)	.9965
Reported fever	33 (27.7%)	84 (29.7%)	.6943
Vomiting	26 (21.9%)	73 (25.8%)	.4018
Vag D/C	35 (29.4%)	58 (20.5%)	.0529
UTI past month	16 (13.5%)	40 (14.1%)	.8555
Prior UTI ever (n = 158)	57 (68.7%)	141 (78.3%)	.0915
Diabetes	6 (5.0%0	23 (8.1%)	.2751
Other comorbidities	12 (10.1%)	22 (7.8%)	.4473
Currently taking antibiotics	5 (4.2%)	10 (3.5%)	.7470
Measured fever	1 (0.8%)	6 (2.1%)	.3705
HR >100 (n = 396)	16 (13.7%)	37 (13.3%)	.9122
SBP <95 (n = 396)	1 (0.9%)	7 (2.5%)	.4454
CVAT (n = 322)	13 (15.7%)	57 (23.9%)	.1193
Pelvic examination performed (n = 248)	14 (18.4%)	29 (16.9%)	.7647
Urine pregnancy test performed (n = 383)	78 (66.1%)	208 (78.5%)	.0100
LE+, nitrite+, or >10 WBC (n = 319)	87 (93.6%)	211 (93.4%)	.9516
Dx, cystitis	105 (88.2%)	226 (79.9%)	.0444
Dx, pyelo	14 (11.8%)	57 (20.1%)	
Received IV or IM medications	3 (2.5%)	46 (16.3%)	.0001

CX indicates culture, Vag D/C vaginal discharge, HR heart rate, SBP systolic blood pressure, CVAT costovertebral angle tenderness documented, LE leukocyte esterase, WBC white blood cells, Dx diagnosis, IV intravenous and IM intramuscular.

29 other demographic, historical, and clinical features derived from the computer interview and chart review (see Table 1). From the set of variables moderately associated with resistance ($P < .20$ by χ^2 or Fisher exact test when appropriate), manual backward selection was used in building the multivariate models, with sequential deletion of the least-significant variables until only those with $P < .05$ remained. This model-building approach was repeated for potential predictors of TMP/SMX resistance and, then for cases with an *E coli* isolate, again looking for predictors of resistance to any narrow-spectrum agent or to TMP/SMX alone. All statistical analyses were performed in SAS (version 9.2; SAS Institute, Cary, NC).

3. Results

Based on chart review performed after data were prospectively collected, referral rates of women who met inclusion criteria at triage were 78% (site 1), 41% (site 2), and 26% (site 3). Fig. 1 is a flow diagram demonstrating recruitment, data collection, and exclusion. Seventy percent of patients referred to the kiosk and diagnosed with UTI had a culture performed (32% of those as part of kiosk study and 68% by clinician decision). Table 1 compares these patients to those who did not undergo culture. The 2 groups were similar for most measured variables, although the cultured group was diagnosed with pyelonephritis more frequently, more likely to receive parenteral antibiotics and be tested for pregnancy (see Table 1). Cultures were positive in 158 patients or 56% of those diagnosed with UTI and cultured. One hundred thirty-five cultures had full susceptibilities reported.

Table 2 shows characteristics of the final population of women diagnosed with UTI and having a positive culture. Median age was 31 years (interquartile range, 24-43; range, 16-84); 4% used the Spanish language module. Participants commonly reported flank pain (46%), vomiting (27%), and fever (29%); and 32 (24%) were assigned a final diagnosis of

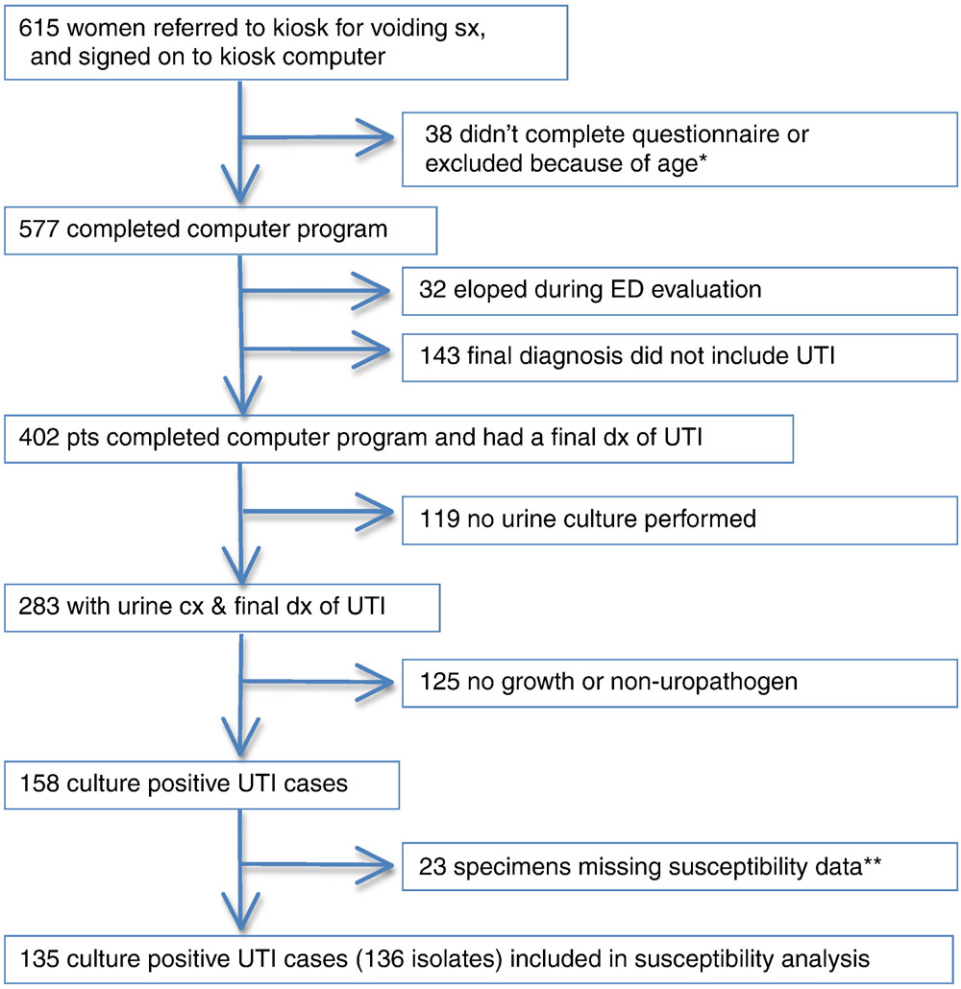

Fig. 1 Study flow. *The protocol for referral to the kiosk changed after data collection had begun. Later subjects were excluded from the questionnaire portion if older than 65 years. **Of these, 8 specimens appeared to be frankly contaminated (also growing "mixed genital flora"), 9 grew *S saprophyticus* (does not routinely undergo susceptibility testing), 3 (12.5%) grew group B *streptococcus* spp (does not routinely undergo susceptibility testing), 1 grew *E aerogenes*, 1 grew *proteus* spp.

Table 2 Characteristics of the 135 subjects included in the analysis of predictors of resistance

Variable	n (%)
Site 1	95 (70)
Site 2	33 (24)
Site 3	7 (5)
Spanish language module	6 (4)
Age ≥45 y	33 (24)
Illness features	
Dysuria	125 (93)
Urgency	129 (96)
Frequency	127 (94)
Fever (reported)	39 (29)
Flank pain	62 (46)
Vomiting	37 (27)
Vaginal discharge (reported)	28 (21)
Symptoms >7 d	23 (17)
Medical history	
Any prior UTI (n = 79)	24 (30)
UTI in the past month	10 (7)
Diabetes	9 (7)
Currently taking antibiotics	4 (3)
History of kidney surgery	5 (4)
History of kidney disease	3 (2)
HIV	0 (0)
Cancer history	2 (1)
Taking other regular medication	57 (42)
Vital signs (n = 134)	
Heart rate >100 beats per minute	18 (13)
Systolic blood pressure <95 mm Hg	5 (4)
Fever (measured)	4 (3)
Urinalysis results	
Nitrites positive (n = 95)	39 (41)
Leukocyte esterase positive (n = 98)	82 (84)
WBC >5 per high-power field (n = 99)	94 (95)
RBC >3 per high-power field (n = 100)	78 (78)
Urine pregnancy positive	1 (1)
Chlamydia positive	0 (0)
E coli isolated	125 (93)
Clinical decisions	
Final diagnosis of pyelonephritis	32 (24)
Got parenteral antibiotics in ED	18 (15)
Got PO antibiotics in ED	59 (48)
Pelvic examination performed in ED (n = 85)	11 (13)

Some variables from chart review were unavailable for all 135 subjects; in these cases, the total number for which data are available is shown.

pyelonephritis. However, fever was documented in only 4 patients (3%).

Table 3 gives microbiology results. Among uropathogens with complete data, TMP/SMX susceptibility was 82.2%; nitrofurantoin, 94.8%; cephalexin, 95.6%; and susceptibility to all narrow-spectrum agents was 74%. If pansusceptibility of *S saprophyticus* (8 isolates) is assumed, as is generally the case, susceptibility to TMP/SMX increases to 83%; and to all 3 narrow-spectrum agents, to 76%. For *E coli* alone, TMP/SMX susceptibility was 81%. Two *E coli* isolates were fluoroquinolone resistant. There were no statistically significant differences between susceptibility rates at the 3 sites. At each site, *E coli* susceptibility was higher than expected based on the site's antibiogram (see Table 4).

In univariate analysis, variables showing moderate association with resistance of any organism to any narrow-spectrum agent were as follows (unadjusted odds ratio [OR], 95% confidence interval [CI]): Spanish language module (6.3, 1.1-36.2), dysuria (3.3, 0.4-27.6), urgency (1.9, 0.2-16), reported fever (0.5, 0.2-1.3), prior UTI (2.4, 0.7-8.2), UTI in the past month (2.0, 0.5-7.6), nitrites positive (0.3, 0.1-0.8), and isolation of *E coli* (0.2, 0.1-0.8).

In multivariable regression analysis, Spanish language remained significantly associated with an increased likelihood of resistance of any organism to any narrow-spectrum agent (adjusted OR 7.5; 95% CI, 1.30-43.4); and isolation of *E coli* was associated with a decreased likelihood of resistance to any narrow-spectrum agent (adjusted OR, 0.18; 95% CI, 0.05-0.68), yielding a 2-variable model for which the C statistic was 0.63. Because there were only 6 Spanish speakers in our study sample, we did not perform additional statistical tests of interaction.

Table 3 Microbiology results

Uropathogen isolates (n = 160 from 158 patients)	n (%)	
E coli	130 (81)	
S saprophyticus	8 (5)	
Proteus mirabilis	5 (3)	
Enteric gram-negative rods [a]	5 (3)	
E aerogenes	3 (2)	
Klebsiella pneumonia	3 (2)	
Enterococcus spp	2 (1)	
Group B *Streptococcus*	2 (1)	
Citrobacter koserii	2 (1)	
Antimicrobial susceptibilities (n = 136) [b]		95% CI (%)
Narrow-spectrum susceptible (TMP/SMX + cefazolin + nitrofurantoin)	100 (74)	65-81
TMP/SMX susceptible	112 (82)	76-89
Nitrofurantoin susceptible	128 (94)	89-97
Cefazolin susceptible	130 (96)	91-98
Cipro or Levo susceptible	134 (99)	95-100
Antimicrobial susceptibility of *E coli* (n = 125)		
Narrow-spectrum susceptible (TMP/SMX + cefazolin + nitrofurantoin)	96 (77)	68-84
TMP/SMX susceptible	101 (81)	73-87
Nitrofurantoin susceptible	123 (98)	94-100
Cefazolin susceptible	120 (96)	91-98
Cipro or Levo susceptible	123 (98)	94-100

[a] Met our criteria for true UTI (see "Methods" section).
[b] Twenty-four isolates excluded that did not undergo susceptibility testing to all 4 antibiotics of interest.
Cipro represents ciprofloxacin, Levo levofloxacin.

Table 4 *E coli* susceptibility by site, compared with site-specific antibiogram data

	TMP/SMX		Nitrofurantoin		Cefazolin		Fluoroquinolones	
	Study results, n (%)	Antibiogram (%)	Study results, n (%)	Antibiogram (%)	Study results, n (%)	Antibiogram (%)	Study results, n (%)	Antibiogram (%)
Site 1	71 (80)	(75)	88 (99)	(97)	85 (96)	(82)	(98)	(79)
Site 2	25 (86)	(67)	28 (97)	(98)	28 (97)	(84)	(100)	(77)
Site 3	5 (71)	(68)	7 (100)	[a]	7 (100)	(84)	(100)	(76)
P	.61		.65		.83		.66	

Site 1, outpatient isolates only; sites 2 and 3, inpatient and outpatient isolates.
[a] Not included on site 3 antibiogram.

We could not include previous UTI in multivariable regression because of a large number of missing data. However, performing the analysis on only the subset of patients—n = 79—for whom prior UTI data were available yielded no significant changes in the 95% CIs; and prior UTI was not, in this analysis, significantly associated with resistance (*E coli* adjusted OR, 0.11; 95% CI, 0.02-0.62; Spanish language adjusted OR, 7.57; 95% CI, 1.23-46.66; previous UTI adjusted OR, 1.98; 95% CI, 0.54-7.22). No independent predictors of TMP/SMX resistance were identified, nor were any variables predictive of *E coli* resistance to any narrow-spectrum agent.

4. Limitations

These findings are limited to the geographic region represented in the study, with the 3 sites representing 3 distinct and diverse populations in Northern California (San Francisco County, Alameda County, and Fresno County). Although we collected data from 3 centers, the university hospital site where the study originated was disproportionately represented, in part, because of the longer data collection period there. The research coordinators were also based there, giving them daily contact with triage staff, both factors likely leading to increased recruitment at that site. Criteria for kiosk referral (literate, Spanish- or English-speaking, referral by busy triage nurse) might result in a select population. In addition, 30% of patients diagnosed with UTI did not have a urine culture performed; and full sensitivities were not reported on all positive cultures. This could have affected validity if the uropathogens or factors associated with resistance differed in the group in whom cultures were not ordered from the cultured group; however, most measured characteristics were similar in the noncultured and cultured groups. The proportion of women with UTIs that underwent urine culture by clinician decision (68%) is higher than expected, given that most of these women meet IDSA guidelines for empiric treatment (for comparison, the culture rate of those women ≥18 in the National Hospital Ambulatory Medical Care Survey (NHAMCS) data set with a diagnosis of UTI was 41.9%) [20], likely reflecting a shift in practice that occurred as an effect of awareness of the study—or generally increased concern over resistance—rather than severity of the cases. Only 56% of those diagnosed with UTI and cultured had a positive culture. However, the few other studies that report this value have shown a similar or higher rate of false-positive diagnoses [21,22].

Our sample size was too small to allow precise estimates of resistance by organisms other than *E coli*. Some data suggest that predictors of resistance may vary by organism [23], which, if true, would make it difficult to identify predictors of resistance in the small and varied non–*E coli* group. However, we believe that the clinically important issue for ED providers is the resistance pattern and predictors of resistance among all uropathogens combined (an all-comers population) because the causative organism is not known at the time of prescribing.

We do not have data to support our contention that there has been increased fluoroquinolone and decreased TMP/SMX use for UTI at our institutions. However, there is little reason to believe that Northern California somehow evaded increases in fluoroquinolone use for UTIs observed nationally.

Finally, the small number of resistant cases—and the missing data on prior UTI—limited our ability to perform robust model building, compare models, and test interactions. Thus, comparisons of models by goodness-of-fit tests were not performed.

5. Discussion

There are no other studies in the emergency medicine literature providing current data on uropathogen susceptibility in a relatively unselected ambulatory ED population—a group not routinely cultured or represented in hospital antibiograms. Uropathogens isolated from our ED population showed a trend toward lower rates of resistance at each site than expected based on that site's antibiogram. If validated, this finding could have important implications for empiric prescribing from the ED, given the goal—reiterated in the 2010 update to the IDSA Practice Guidelines for treatment of acute uncomplicated cystitis—of using narrow-spectrum agents when possible to minimize selective pressure toward drug resistance and other "collateral damage" [3].

Resistance to TMP/SMX is near but still less than 20% in our population, whereas resistance to the other narrow-spectrum agents remains very low. Susceptibility to fluoroquinolones appears to be preserved in our patient population, although this antibiotic class is used commonly for both urinary tract and respiratory tract infections. At all sites, susceptibility to nitrofurantoin was high, supporting the broader use of nitrofurantoin for uncomplicated cystitis, as encouraged in the new IDSA guidelines. Nitrofurantoin is preferred over cephalexin for cystitis because the macrocystal form is dosed twice daily and a 5-day course is effective [24], whereas recommended dosing of cephalexin is 4 times daily for 7 days and is less studied. Both agents are rated safe in pregnancy. Studies with patient-based outcomes are needed comparing nitrofurantoin to fluoroquinolones in cystitis. Nitrofurantoin should not be used for pyelonephritis because of poor tissue penetration.

These data do not support our hypothesis that decreased use of TMP/SMX for UTI might promote a return of susceptibility to TMP/SMX among uropathogens, as has been seen in other circumstances, such as the reversion of macrolide-resistant group A *Streptococcus* after reductions in macrolide use for sore throat [25]. In fact, we found a similar level of TMP/SMX resistance to studies from a decade ago. One possible reason for maintained resistance is the rise in TMP/SMX prescribing for skin and soft tissue infections (covering methicillin-resistant *Staphylococcus aureus*). Conversely, these data also show that uropathogen fluoroquinolone susceptibility is preserved in our population.

Our study was underpowered for conducting a robust analysis of predictors of antibiotic resistance, particularly because many of the key predictors, such as prior antibiotic use or comorbidities, were uncommon in our study population. Although our finding that Spanish language patients had increased levels of resistance is intriguing and deserves further study, it must be interpreted with extreme caution given the small sample size and the wide CIs in the regression analysis. If confirmed in a larger study, it could reflect the consequences of very short courses of "under-the-counter" antibiotics for acute illnesses that are common in selected Latino communities [26] or perhaps cross-border differences in microbial colonization persisting among recent immigrants.

6. Conclusion

In these recent data from an ambulatory Northern California ED population, TMP/SMX resistance rates in uropathogens approach the threshold at which empiric use is not recommended; but overall, susceptibility was higher in our population than expected based on hospital antibiograms, and fluoroquinolone susceptibility remains high. A high rate of nitrofurantoin susceptibility makes this an attractive narrow-spectrum alternative for cystitis. Larger studies that might reveal significant predictors of resistance to narrow-spectrum agents as well as longitudinal studies tracking actual susceptibility changes and further attempts to characterize differences between susceptibility rates in ambulatory ED populations and more general hospital populations would be helpful.

Acknowledgment

We would like to acknowledge Richard Jacobs, MD, Professor of Medicine, UCSF Medical center, for offering his infectious disease expertise and invaluable assistance during the preparation of this report.

References

[1] The National Kidney and Urologic Diseases Advisory Board 1990 long-range plan: window on the 21st century. J Urol 1991;145(3):568-93.

[2] Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America (IDSA). Clin Infect Dis 1999;29(4):745-58.

[3] Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis 2011;52(5):e103-20.

[4] Johnson L, Sabel A, Burman WJ, et al. Emergence of fluoroquinolone resistance in outpatient urinary *Escherichia coli* isolates. Am J Med 2008;121(10):876-84.

[5] Olson RP, Harrell LJ, Kaye KS. Antibiotic resistance in urinary isolates of *Escherichia coli* from college women with urinary tract infections. Antimicrob Agents Chemother 2009;53(3):1285-6.

[6] Caterino JM, Weed SG, Espinola JA, Camargo Jr CA. National trends in emergency department antibiotic prescribing for elders with urinary tract infection, 1996-2005. Acad Emerg Med 2009;16(6):500-7.

[7] Taur Y, Smith MA. Adherence to the Infectious Diseases Society of America guidelines in the treatment of uncomplicated urinary tract infection. Clin Infect Dis 2007;44(6):769-74.

[8] Kallen AJ, Welch HG, Sirovich BE. Current antibiotic therapy for isolated urinary tract infections in women. Arch Intern Med 2006;166(6):635-9.

[9] Zhanel GG, Hisanaga TL, Laing NM, et al. Antibiotic resistance in outpatient urinary isolates: final results from the North American Urinary Tract Infection Collaborative Alliance (NAUTICA). Int J Antimicrob Agents 2005;26(5):380-8.

[10] Kashanian J, Hakimian P, Blute Jr M, et al. Nitrofurantoin: the return of an old friend in the wake of growing resistance. BJU Int 2008;102(11):1634-7.

[11] Boyd LB, Atmar RL, Randall GL, Hamill RJ, Steffen D, Zechiedrich L. Increased fluoroquinolone resistance with time in *Escherichia coli* from >17,000 patients at a large county hospital as a function of culture site, age, sex, and location. BMC Infect Dis 2008;8:4.

[12] Shigemura K, Arakawa S, Miura T, Nakano Y, Tanaka K, Fujisawa M. Significance of fluoroquinolone-resistant *Escherichia coli* in urinary tract infections. Jpn J Infect Dis 2008;61(3):226-8.

[13] Fluit AC, Jones ME, Schmitz FJ, Acar J, Gupta R, Verhoef J. Antimicrobial resistance among urinary tract infection (UTI) isolates in Europe: results from the SENTRY Antimicrobial Surveillance Program 1997. Antonie Van Leeuwenhoek 2000;77(2):147-52.

[14] Kahan NR, Chinitz DP, Waitman DA, Dushnitzky D, Kahan E, Shapiro M. Empiric treatment of uncomplicated urinary tract infection with fluoroquinolones in older women in Israel: another lost treatment option? Ann Pharmacother 2006;40(12):2223-7.

[15] Aagaard EM, Nadler P, Adler J, Maselli J, Gonzales R. An interactive computer kiosk module for the treatment of recurrent uncomplicated cystitis in women. J Gen Intern Med 2006;21(11):1156-9.
[16] McCarter YS, Burd EM, Hall GS, Zervos M. Laboratory diagnosis of urinary tract infections. ASM Press; 2009.
[17] Stamm WE, Counts GW, Running KR, Fihn S, Turck M, Holmes KK. Diagnosis of coliform infection in acutely dysuric women. N Engl J Med 1982;307(8):463-8.
[18] Clinical Laboratory Standards Institute, Wayne P. Performance standards for antimicrobial susceptibility testing. 12th Informational Supplement, Document M100-S20; 2010.
[19] Munoz P, Coque T, Rodriguez Creixems M, Bernaldo de Quiros JC, Moreno S, et al. Group B *Streptococcus*: a cause of urinary tract infection in nonpregnant adults. Clin Infect Dis 1992;14(2):492-6.
[20] National Hospital Discharge Survey (NHAMCS–ER data only). Hyattsville (Md): Public Health Service; 2004. Accessed 2011.
[21] McIsaac WJ, Prakash P, Ross S. The management of acute uncomplicated cystitis in adult women by family physicians in Canada. Can J Infect Dis Med Microbiol 2008;19(4):287-93.
[22] O'Brien K, Hillier S, Simpson S, Hood K, Butler C. An observational study of empirical antibiotics for adult women with uncomplicated UTI in general practice. J Antimicrob Chemother 2007;59(6):1200-3.
[23] Gupta K, Sahm DF, Mayfield D, Stamm WE. Antimicrobial resistance among uropathogens that cause community-acquired urinary tract infections in women: a nationwide analysis. Clin Infect Dis 2001;33(1):89-94.
[24] Gupta K, Hooton TM, Roberts PL, Stamm WE. Short-course nitrofurantoin for the treatment of acute uncomplicated cystitis in women. Arch Intern Med 2007;167(20):2207-12.
[25] Seppala H, Klaukka T, Vuopio-Varkila J, et al. The effect of changes in the consumption of macrolide antibiotics on erythromycin resistance in group A streptococci in Finland. Finnish Study Group for Antimicrobial Resistance. N Engl J Med 1997;337(7):441-6.
[26] Cespedes A, Larson E. Knowledge, attitudes, and practices regarding antibiotic use among Latinos in the United States: review and recommendations. Am J Infect Control 2006;34(8):495-502.