HHS Public Access

Author manuscript

Diagn Microbiol Infect Dis. Author manuscript; available in PMC 2020 December 01.

Published in final edited form as:

Diagn Microbiol Infect Dis. 2019 December ; 95(4): 114874. doi:10.1016/j.diagmicrobio.2019.114874.

Analysis of Urine-specific Antibiograms from Veterans to Guide Empiric Therapy for Suspected Urinary Tract Infection

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Abstract

Urinary tract infection (UTI) is common among patients at Veterans Affairs Medical Centers (VAMCs), many of whom are elderly men with underlying urological problems. Most UTI guidelines address uncomplicated UTI in women, and clinicians may select empiric therapy based on local hospital-wide *Escherichia coli* cumulative susceptibility (antibiogram) data. To inform selection of empiric therapy for UTI at the Minneapolis VAMC (MVAMC), we compiled antimicrobial susceptibility testing (AST) results for one year's urine isolates. We analyzed these AST results (bioMerieux VITEK®) for 2,494 microbiologically significant urine isolates at MVAMC from June 2013 through May 2014. For antimicrobial-organism combinations that were not tested we imputed results based on local or published data, and/or expert opinion. For ambiguous antimicrobial-organism combinations we analyzed susceptibility as both 0% and 100%. We calculated cumulative percent susceptible for 26 relevant antimicrobial agents, overall and stratified by Gram stain characteristic and clinical site. The study population included 1,548 Gram-negative and 946 Gram-positive urine isolates. Species distribution varied significantly by clinical site. *E. coli* represented only 27% of isolates overall (9–37%, depending on site); also prevalent were *Enterococcus* (14%) and other Gram-positive organisms (23%). Urine-specific antibiograms varied significantly by Gram stain characteristic, between *E. coli* and other Gram-negative organisms, and by clinical site. Of the oral agents, only fosfomycin provided ≥ 80% susceptibility. Ultimately, *E. coli* represented urine isolates poorly with respect to species distribution and AST results. We conclude that urine-specific antibiograms, stratified by Gram stain characteristic and clinical site, may improve empirical UTI therapy for veterans.

Keywords

Urinary Tract Infections; Antimicrobial Susceptibility; *Escherichia coli*; Fosfomycin

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Potential conflicts of interest: Authors K.J.M., L.M., and J.J.H. have no conflicts. Author J.R.J. has received grants or contracts from Achaogen, Allergan, Melinta, Merck, Shionogi, Syntiron, and Tetraphase; has consultancies with Crucell/Janssen and Syntiron; and has patent applications for tests to detect specific *E. coli* strains.

Introduction

Empirical antimicrobial therapy for urinary tract infection (UTI) ideally should provide reliable activity against the patient's urine organism. To accomplish this, therapy must be selected with attention to the likely pathogens and their anticipated antimicrobial susceptibility patterns [1].

A prominent 2010 international practice guidelines document regarding UTI management addresses empirical therapy selection but is limited to acute uncomplicated cystitis and pyelonephritis in pre-menopausal women [1]. However, UTI is a significant problem also among veterans, many of whom are elderly men, often with anatomical or functional urinary tract abnormalities. No available guidelines address empiric antimicrobial therapy for UTI in this distinctive population.

Existing guidelines and expert opinion often suggest reliance on the susceptibility patterns of local uropathogens when choosing empiric therapy for UTI [1–4]. However, such data usually are unavailable, because laboratories typically report cumulative susceptibility (antibiogram) data stratified by species, not specimen type, and for all samples combined, not stratified by clinical site. Clinicians therefore commonly rely on their local laboratory's overall antibiogram for *E. coli*, the cause of 75–95% of uncomplicated UTI episodes in women [3]. Yet, previous studies have shown that susceptibility patterns of *E. coli* at a given institution can vary according to clinical setting such as intensive care unit vs. inpatient ward vs. outpatient sites [5, 6].

Previous studies of the antibiograms of urine isolates (hereafter, urine-specific antibiograms) from children [7–9], inpatients versus outpatients [10], and Emergency Department patients [11] found important differences between these setting-specific urine antibiograms and the overall hospital antibiogram, which suggests that use of such data conceivably could improve clinical care. However, it remains unclear whether these differences were due to the isolates being urine-specific, setting-specific, or both. To our knowledge, no study has assessed urine-specific antibiograms stratified by clinical site among veterans.

Accordingly, we compiled and analyzed urine-specific antibiograms for the Minneapolis Veterans Affairs Medical Center (MVAMC), using one year's antimicrobial susceptibility testing (AST) data. Our goal was to identify appropriate empiric treatment options for UTI in our population, both overall and stratified by clinical site of origin, and to determine whether the *E. coli* antibiogram is a suitable surrogate for a urine-specific antibiogram, either overall or for individual clinical sites.

Materials and Methods

Study population.

We compiled organism identity and AST results for 2,494 (96%) of the 2,587 total urine isolates recovered and reported by the MVAMC clinical laboratory from June 2013 through May 2014, excluding only the 93 diphtheroid isolates as presumed contaminants. We were limited by the laboratory's criteria for microbiological significance, according to which

organisms are identified only if present at ≥ 100,000 colony forming units (CFU) per mL for voided urine, and ≥ 5,000 CFU/mL for catheterized urine.

Only one isolate of a given organism from the same patient within 30 days was analyzed, regardless of source. Of the 2,494 isolates, 2,109 (85%) had undergone AST by the clinical laboratory for selected agents on a bioMerieux VITEK® instrument; we used these results. For the remaining isolates, which included *Aerococcus urinae* (n = 11), *Aerococcus viridans* (n = 4), coagulase-negative *Staphylococcus* (n = 293; only one *S. saprophyticus*), viridans group *Streptococcus* (n = 86), *Streptococcus agalactiae* (n = 43), and *Streptococcus bovis* (n = 2), we imputed antimicrobial susceptibility results, as described below.

Susceptibility imputations.

Because of this study's exploratory nature, we assessed a broadly inclusive list of antimicrobial agents (n = 26) that included all agents the MVAMC clinical microbiology laboratory routinely tests against urine organisms, plus fosfomycin. The laboratory performs routine AST only for certain urine organisms (depending on organism identity), and then only for certain organism-specific antimicrobials, which are selected based largely on the organism's Gram stain characteristic. Additionally, based on clinician request the laboratory also performs AST selectively for specific organisms, agents, or combinations thereof that are not tested routinely. Consequently, for many of the antimicrobial-organism combinations relevant to the present study, few or no directly determined AST results were available. Therefore, for valid overall comparisons between agents regardless of organism identity or Gram stain characteristic, we imputed results for the antimicrobial-organism combinations that the laboratory did not test directly. Susceptibility imputations relied on published data [12–26], opinions from expert colleagues, local aggregate data from before the study period, and/or data generated during the study period for the subset of study isolates of a given organism type that underwent AST by special request.

We chose not to report AST data for tetracyclines. For Gram-negative organisms the MVAMC microbiology laboratory does not perform tetracycline AST unless requested by a clinician (which seldom occurs) and the literature contains few relevant data to support imputations. Therefore, despite the availability of tetracycline AST data for some Gram-positive organisms (from both the MVAMC laboratory and the literature), tetracycline data could not be included in a cumulative report for all urine isolates combined.

Additionally, for certain antimicrobial-organism combinations, because of (i) the absence of local data and (ii) conflicting expert opinions and published evidence, we performed imputations by assuming both extremes of the plausible range of susceptibility prevalence values. Specifically, for *Enterococcus* species with trimethoprim-sulfamethoxazole (TMP/SMX) [27], and *Staphylococcus saprophyticus* and *Proteus species* with fosfomycin [26], we imputed both 0% and 100% susceptibility. Likewise, for *Pseudomonas aeruginosa* and fosfomycin we imputed both 0% and 50% susceptibility [20]. We chose the 50% as the upper bound because few of our *Pseudomonas* isolates were extensively multi-drug resistant (e.g., 87% were susceptible to cefepime and 95% to piperacillin/tazobactam).

Overall, our reported susceptibility data (70,632 total isolate-specific antimicrobial-organism combinations) reflect 46% direct determinations, 42% imputations based on historical local data, external published data, and expert opinion, and 12% imputations based on current local data from other isolates within the same organism category.

Statistical analysis.

We calculated the cumulative percent of urine isolates susceptible to each of 26 antimicrobial agents, both overall and stratified by Gram stain characteristic and clinical site, i.e., community residential centers (CRCs), extended care center (ECC), intensive care unit (ICU), inpatient ward, or outpatient. Similar calculations were made for *E. coli* isolates only. Comparisons for percent susceptible were tested using a Chi-squared test, with $P < .05$ considered statistically significant. Because this was an exploratory analysis, we did not adjust for multiple comparisons, a decision supported by a biostatistician colleague (personal communication, Paul Thuras).

Results

Species distribution.

The 2,494 urine isolates included 1,548 Gram-negative and 946 Gram-positive organisms. *E. coli* accounted for only 27% of isolates overall (by site for 9% ICU to 37% CRC), and 44% of the Gram-negative isolates overall (by site for 13% ICU to 70% CRC). *Enterococcus* and other Gram-positive organisms were also prevalent, both overall (15% and 22%, respectively) and at each site (Table 1).

Statistical analysis showed that the five clinical sites differed significantly for the prevalence of each of the main microbial categories, both overall and for at least one site compared with the others (Table 1). By contrast, they did not differ significantly for the prevalence of Gram-positive or Gram-negative organisms collectively, or of the minor microbial subsets (i.e., < 5% of the total population: *Streptococcus* species and miscellaneous Gram-positive organisms).

Urine specific-antibiograms overall.

Urine-specific antibiograms (for 26 total agents) demonstrated overall percent susceptibility < 80% for all oral agents except fosfomycin (fluoroquinolones, 61–68%; TMP-SMX, 57% or 78% depending on *Enterococcus*; nitrofurantoin, 64%), and < 90% for all intravenous agents (ceftriaxone, 65%; ertapenem, 69%; imipenem, 89%; piperacillin/tazobactam, 86%) (Table 2). By contrast, fosfomycin exhibited 81%-95% overall imputed susceptibility. The urine-specific antibiogram based solely on directly determined data (which were available for only a subset of all antimicrobial-organism combinations) differed significantly from the comprehensive antibiogram that included imputations.

Urine specific-antibiograms by organism.

Urine-specific antibiograms differed significantly between all Gram-negative organisms combined, all Gram-positive organisms combined, and all *E. coli* (Table 2). For *E. coli*, where comparisons were possible (given the limited list of agents for which the hospital

laboratory reports results), the urine-specific antibiogram did not differ significantly from the hospital's overall (i.e., all-sites and all-specimen-types) antibiogram from the same period (data not shown). By contrast, among the present urine isolates the susceptibility results for most of the studied antimicrobials differed significantly between *E. coli* vs. all Gram-negative organisms combined (Table 2).

Urine-specific antibiograms by clinical site.

Urine-specific antibiograms differed significantly across the five clinical sites for 22 of the 28 antimicrobial susceptibility endpoints assessed. The antibiogram for all sites combined differed significantly for at least 1 antimicrobial in comparison with each clinical site's antibiogram, and for most antimicrobials in comparison with the antibiograms for CRC and inpatient ward (Table 3). Moreover, for each clinical site except the ICU (where small numbers limited statistical power) the antibiogram for all organisms differed significantly for one or more antimicrobials from the same site's *E. coli* antibiogram (data not shown).

Discussion

Our analysis of urine-specific antibiograms from the MVAMC clinical microbiology laboratory showed that the laboratory's aggregate susceptibility data for *E. coli*, on which clinicians may rely for empiric antibiotic selection for UTI, represents poorly all urine isolates (either overall or by clinical site), all Gram-negative urine isolates, or even the *E. coli* urine isolates at individual clinical sites. Moreover, *E. coli*, although the leading species, accounted for only a minority of urine isolates, both overall and by site; instead, multiple other Gram-negative species, *Enterococcus*, and other Gram-positive organisms accounted collectively for most isolates. Finally, the urine-specific antibiogram differed significantly, overall and for most clinical sites, from both the urine *E. coli* antibiogram and the contemporaneous hospital *E. coli* antibiogram. Therefore, for construction of antibiograms at our center – and, likely, at other similar centers – *E. coli* is a poor surrogate for the total urine isolate population, and variation between different clinical sites is substantial.

Our analysis failed to identify optimal agents for empiric therapy of UTI at our center. For nearly all agents the overall percent of urine isolates that were susceptible fell below the guideline-recommended threshold values of 80% for treating lower urinary tract infections and 90% for treating upper urinary tract infections [1]. Fosfomycin, the only exception, exhibited 81%-95% overall imputed susceptibility. In the United States, fosfomycin is available only as an oral formulation and is approved only for treatment of lower urinary tract infections. It may be an important empiric treatment option to consider in our veteran population, especially if the patient previously had a multidrug-resistant organism or a mix of Gram-positive and Gram-negative organisms. Among Gram-negative organisms the difference in susceptibility prevalence between cefepime (94%) and ceftriaxone (83%) was attributable almost entirely to *Pseudomonas aeruginosa*. This suggests that providers should still consider traditional risk factors for resistant organisms, such as hospital exposure, when choosing a parenteral agent for suspected UTI.

In that regard, the emerging concept of "patient-specific antibiograms" that incorporate patient characteristics such as age, length of hospital stay, co-morbid diagnoses, previous

antibiotic exposure, and prior AST results may assist with decisions regarding empirical antimicrobial therapy [28]. Additionally, studies of the clinical efficacy of TMP/SMX against *Enterococcus* and of fosfomycin against urinary organisms generally could clarify the role of these agents in empiric therapy for UTI in veterans and similar patients, reducing the current uncertainty that obliged us to perform sensitivity analyses using extreme values for percent susceptible.

Our study had several limitations. First, the susceptibility data were de-identified, precluding medical record review to determine whether isolates represented symptomatic UTI versus asymptomatic bacteriuria, and to assess clinical outcomes in relation to in vitro susceptibility. Notably, our objective was to recommend empiric antibiotic options for providers intent on treating for UTI, irrespective of clinical presentation. Many patients are treated for UTI despite not fulfilling standard criteria for symptomatic UTI. Additionally, some Gram-positive organisms (such as coagulase-negative staphylococci) that might be considered contaminants in healthy women can be important pathogens for veterans with indwelling catheters. Although sensitivity analysis showed that removal of data for coagulase-negative staphylococci significantly altered the antibiogram (not shown), we chose to retain these data, given the target patient population. By contrast, removal of data for viridans group *Streptococcus* did not meaningfully alter the antibiogram (not shown).

Second, because 22% of veterans diagnosed with UTI in the outpatient setting at our MVAMC do not have a urine culture done [29], the isolates studied likely do not represent all diagnosed UTIs in our population. Third, the clinical site recorded for each isolate was the origin of the urine specimen and may not reflect the acuity of the case, if for example the urine sample was collected in a clinic or the emergency department, but the patient ultimately was admitted to an inpatient ward or the ICU. Fourth, the findings might not be generalizable outside of the VA system. Fifth, the absence of susceptibility testing results for many antimicrobial-organism combinations obliged extensive use of imputation, which was limited by the available evidence and expert opinion, although these same limitations apply also in clinical practice.

Our study also had notable strengths. First, its focus on urine isolate-specific AST data may better reflect the susceptibility profiles of uropathogens, as opposed to diverse-source pathogens. Second, the large number of urine isolate-specific antimicrobial-organism combinations (70,632), which represented a full year of data across all clinical sites served by MVAMC, allowed an analysis that included the full spectrum of urine culture findings across our institution. Third, MVAMC serves a population mainly of elderly men, many of whom have anatomical or functional urinary tract abnormalities. Because existing UTI guidelines address empiric antibiotic selection only for uncomplicated UTI in women, our findings provide novel important information for providers caring for elderly men.

In conclusion, our findings identify serious limitations in reliance on the existing hospital laboratory antibiogram for guidance in selecting empiric UTI therapy at our institution, contradict the assumption that *E. coli* is a reliable surrogate for urine organisms generally, and show that, at our center, system-wide data apply unreliably to individual clinical sites. Use of urine-specific antibiograms that are stratified by clinical site conceivably could

improve empirical selection of UTI therapy for veterans, as could performance of urine Gram stains combined with stratification of urine antibiogram data by Gram stain characteristic.

Acknowledgements

Funding: This work was supported by the National Institute of Child Health and Human Development at the National Institutes of Health [T32 HD068229] and by the National Institute of Allergy and Infectious Diseases at the National Institutes of Health [T32 AI055433], both for K.J.M.

Prior presentations: Findings of the study were presented as posters at *IDWeek 2015* and *IDWeek 2017*. Both meetings were in San Diego, California in October 2015 and October 2017, respectively.

Appreciation: We thank Barbara Murray for her expert opinion regarding TMP/SMX and

Enterococcus. We also thank Dimitri Drekonja for reviewing the manuscript prior to submission.

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Highlights

- *E. coli* represented only 27% of all urine isolates (range per clinical site: 9–37%)
- Urine-specific antibiograms varied between *E. coli* vs. other Gram-negatives
- Urine-specific antibiograms also varied by Gram stain group and clinical site
- *E. coli* was a poor susceptibility profile surrogate for urine isolates generally
- Of the tested oral agents, only fosfomycin provided ≥ 80% susceptibility

Table 1.

Species distribution of urine isolates by clinical site.

	Prevalence of organism, column %[a]						P value[b]					
Organism	**All (n = 2494)**	**CRC (n = 90)**	**ECC (n = 98)**	**ICU (n = 33)**	**WARD (n = 541)**	**OTPT (n = 1732)**	**5 sites**	**All vs. CRC**	**All vs. ECC**	**All vs. ICU**	**All vs. WARD**	**All vs. OTPT**
Gram-positives	37	48	30	27	37	38	.08	.06	.09	.21	.80	.82
Enterococcus	15	8	17	12	20	14	**.003**	.05	.58	.61	**.01**	.29
Staphylococcus	16	34	10	15	11	18	**<.001**	**<.001**	.09	.81	**.001**	.29
Streptococcus	5	6	2	0	5	6	.38	.90	.16	.18	.97	.68
Other Gram-positive spp.	1	0	0	0	1	1	.68	.46	.44	.66	.40	.93
Gram-negatives	61	52	70	73	63	62	.08	.06	.09	.21	.80	.82
Escherichia coli	27	37	22	9	17	30	**<.001**	.05	.30	**.02**	**<.001**	**.02**
Klebsiella spp.	12	7	28	15	13	12	**<.001**	.10	**<.001**	.64	.77	.46
Pseudomonas spp.	7	0	8	15	15	4	**<.001**	**.01**	.61	.06	**<.001**	**.001**
Other Gram-negative spp	15	9	12	33	17	15	**.01**	.08	.37	**.005**	.35	.78

[a] Site definitions: CRC, community residential centers; ECC, extended care center; ICU, intensive care unit; WARD, inpatient ward; OTPT, outpatient (including Emergency Department and Urgent Care).

[b] P values < .05 (by Chi squared test) are shown in boldface.

Table 2.

Urine-specific antibiogram by organism type, including *Escherichia coli.*

	Proportion susceptible, column %				P value[a]			
Antimicrobial	**All (n = 2494)**	**Gram-positives (n = 946)**	**Gram-negatives (n = 1548)**	***E. coli* (n = 679)**	**All vs. Gram-positives**	**All vs. Gram-negatives**	**All vs. *E. coli***	**Gram-negatives vs. *E. coli***
amikacin	62	0	100	100	**<.001**	**<.001**	**<.001**	.10
ampicillin	39	54	31	56	**<.001**	**<.001**	**<.001**	**<.001**
ampicillin/sulbactam	59	73	51	65	**<.001**	**<.001**	**.006**	**<.001**
penicillin	39	53	31	56	**<.001**	**<.001**	**<.001**	**<.001**
cefazolin	55	37	65	90	**<.001**	**<.001**	**<.001**	**<.001**
cefepime	72	37	94	95	**<.001**	**<.001**	**<.001**	.48
cefoxitin	56	37	67	90	**<.001**	**<.001**	**<.001**	**<.001**
ceftazidime	62	10	93	94	**<.001**	**<.001**	**<.001**	.67
ceftriaxone	65	37	83	94	**<.001**	**<.001**	**<.001**	**<.001**
ciprofloxacin	61	37	76	72	**<.001**	**<.001**	**<.001**	**.04**
clindamycin	14	38	0	0	**<.001**	**<.001**	**<.001**	N/A[f]
ertapenem	69	37	88	100	**<.001**	**<.001**	**<.001**	**<.001**
erythromycin	12	33	0	0	**<.001**	**<.001**	**<.001**	N/A
fosfomycin 100/50[b]	95	100	92	100	**<.001**	**<.001**	**<.001**	**<.001**
fosfomycin 0[c]	81	86	79	100	**.003**	**.03**	**<.001**	**<.001**
gentamicin	74	43	93	92	**<.001**	**<.001**	**<.001**	.22
imipenem	89	75	97	100	**<.001**	**<.001**	**<.001**	**<.001**
levofloxacin	65	47	75	72	**<.001**	**<.001**	**<.001**	.11
linezolid	37	98	0	0	**<.001**	**<.001**	**<.001**	N/A
moxifloxacin	68	56	75	72	**<.001**	**<.001**	**.047**	.11
nitroflirantoin	64	82	53	91	**<.001**	**<.001**	**<.001**	**<.001**
oxacillin	13	35	0	0	**<.001**	**<.001**	**<.001**	N/A
piperacillin/tazobactam	86	73	94	98	**<.001**	**<.001**	**<.001**	**<.001**
quinupristin/dalfopristin	24	62	0	0	**<.001**	**<.001**	**<.001**	N/A

	Proportion susceptible, column %				P value[a]			
Antimicrobial	**All (n = 2494)**	**Gram-positives (n = 946)**	**Gram-negatives (n = 1548)**	***E. coli* (n = 679)**	**All vs. Gram-positives**	**All vs. Gram-negatives**	**All vs. *E. coli***	**Gram-negatives vs. *E. coli***
tobramycin	58	0	94	91	**<.001**	**<.001**	**<.001**	**.009**
trimethoprim/sulfamethoxazole 100[d]	78	88	72	77	**<.001**	**<.001**	.58	**.02**
trimethoprim/sulfamethoxazole 0[e]	57	33	72	77	**<.001**	**<.001**	**<.001**	**.02**
vancomycin	37	98	0	0	**<.001**	**<.001**	**<.001**	N/A

[a] P values < .05 (by Chi squared test) are shown in boldface.

[b] fosfomycin 100/50: *Proteus* species imputed as 100% susceptible, *Staphylococcus saprophyticus* imputed as 100% susceptible, *Pseudomonas aeruginosa* imputed as 50% susceptible.

[c] fosfomycin 0: *Proteus* species imputed as 0% susceptible, *Staphylococcus saprophyticus* imputed as 0% susceptible, *Pseudomonas aeruginosa* imputed as 0% susceptible.

[d] trimethoprim/sulfamethoxazole 100: *Enterococcus* species imputed as 100% susceptible.

[e] trimethoprim/sulfamethoxazole 0: *Enterococcus* species imputed as 0% susceptible.

[f] N/A: not applicable (0% prevalence in both groups).

Table 3:

Urine-specific antibiograms by clinical site.

	Proportion susceptible, column %[a]						P value[b]					
Antimicrobials	**All (n = 2494)**	**CRC (n = 90)**	**ECC (n = 98)**	**ICU (n = 33)**	**WARD (n = 541)**	**OTPT (n=1732)**	**5 sites**	**All vs. CRC**	**All vs. ECC**	**All vs. ICU**	**All vs. WARD**	**All vs. OTPT**
amikacin	62	52	68	73	62	62	.13	.07	.19	.20	.91	.85
ampicillin	39	34	32	28	37	41	.07	.34	.12	.15	.25	.33
ampicillin/sulbactam	59	45	50	48	54	62	**<.001**	**.01**	.07	.21	**.03**	.11
penicillin	39	34	31	28	37	41	.06	.35	.08	.16	.24	.35
cefazolin	55	53	53	36	44	58	**<.001**	.83	.78	**.04**	**<.001**	**.04**
cefepime	72	62	72	75	67	74	**.008**	**.03**	.94	.67	**.01**	.37
cefoxitin	56	54	55	42	45	59	**<.001**	.82	.92	.13	**<.001**	**.03**
ceftazidime	62	55	67	64	61	62	.57	.23	.27	.83	.72	.97
ceftriaxone	65	62	64	57	54	68	**<.001**	.56	.85	.36	**<.001**	**.04**
ciprofloxacin	61	46	71	71	55	63	**<.001**	**.002**	**.046**	.18	**.01**	.25
clindamycin	14	36	6	10	9	16	**<.001**	**<.001**	**.02**	.39	**<.001**	.22
ertapenem	69	63	69	63	57	72	**<.001**	.29	.87	.54	**<.001**	**.02**
erythromycin	12	35	6	5	10	13	**<.001**	**<.001**	**.03**	.27	.09	.42
fosfomycin 100/50[c]	95	100	96	92	90	97	**<.001**	**.03**	.75	.25	**<.001**	**.04**
fosfomycin 0[d]	81	90	84	69	72	84	**<.001**	**.04**	.55	.09	**<.001**	**.04**
gentamicin	74	82	76	88	68	75	**.002**	.09	.61	.07	**.004**	.54
imipenem	89	68	92	85	90	89	**<.001**	**<.001**	.21	.48	.40	.97
levofloxacin	65	47	71	71	56	67	**<.001**	**<.001**	.16	.33	**<.001**	.08
linezolid	37	48	29	27	37	38	.06	**.045**	.08	.23	.94	.89
moxifloxacin	68	48	74	76	58	71	**<.001**	**<.001**	.26	.34	**<.001**	.053
nitrofurantoin	64	79	51	42	52	69	**<.001**	**.004**	**.01**	**.01**	**<.001**	**.004**
oxacillin	13	12	6	9	10	14	**.03**	.79	**.04**	.49	.06	.37
piperacillin/tazobactam	86	66	85	81	87	86	**<.001**	**<.001**	.71	.49	.38	.69
quinupristin/dalfopristin	24	43	15	15	18	25	**<.001**	**<.001**	.06	.26	**.01**	.35
tobramycin	58	48	68	73	78	58	**<.001**	**.045**	**.049**	.10	**<.001**	.88

Antimicrobials	Proportion susceptible, column %[a] All (n = 2494)	CRC (n = 90)	ECC (n = 98)	ICU (n = 33)	WARD (n = 541)	OTPT (n=1732)	P value[b] 5 sites	All vs. CRC	All vs. ECC	All vs. ICU	All vs. WARD	All vs. OTPT
trimethoprim/sulfamethoxazole 100[e]	78	88	79	74	74	79	**.02**	**.03**	.90	.47	.07	.29
trimethoprim/sulfamethoxazole 0[f]	57	75	73	62	49	60	**<.001**	**0.001**	**.002**	.72	**<.001**	.16
vancomycin	37	44	27	27	36	38	.07	.15	**.04**	.26	**.77**	.59

[a] Site definitions: CRC, community residential centers; ECC, extended care center; ICU, intensive care unit; WARD, inpatient ward; OTPT, outpatient (including Emergency Department and Urgent Care).

[b] P values < .05 (by Chi squared test) are shown in boldface.

[c] fosfomycin 100/50: *Proteus* species and *Staphylococcus saprophyticus* imputed as 100% susceptible, *Pseudomonas aeruginosa* as 50% susceptible.

[d] fosfomycin 0: *Proteus* species, *Staphylococcus saprophyticus*, and *Pseudomonas aeruginosa* imputed as 0% susceptible.

[e] trimethoprim/sulfamethoxazole 100: *Enterococcus* species imputed as 100% susceptible.

[f] trimethoprim/sulfamethoxazole 0: *Enterococcus* species imputed as 0% susceptible.

Diagn Microbiol Infect Dis. Author manuscript; available in PMC 2020 December 01.