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RESEARCH

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Sociodemographic disparities in antibiotic-resistant outpatient urine cultures in a Boston hospital, 2015–2020: a cross-sectional analysis

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Abstract

Background Antibiotic resistance in uropathogens has rapidly escalated over time, complicating treatment and increasing morbidity and mortality. Few studies have explored how the social determinants of health may be associated with patients' risks for acquiring antibiotic-resistant (AR) uropathogens.

Methods We identified urine cultures collected from outpatients presenting to Tufts Medical Center Primary Care Practices between 2015 and 2020. Specimens were included if patients' age, sex, and residential address were recorded in the electronic medical record (EMR) and if their urine culture yielded *Enterococcus* spp. or one or more gram-negative bacterial organism(s) or for which antibiotic susceptibility profiling and species identification was conducted. We abstracted patients' sociodemographic characteristics from the EMR and used US Census Bureau data to identify characteristics about patients' census tracts of residence. We evaluated associations between individual- and neighborhood-level characteristics and patients' risk of having a urine culture resistant to (1) three or more antibiotic classes (i.e., multidrug resistant [MDR]), (2) first-line treatments, (3) fluoroquinolones, (4) aminoglycosides, or (5) ceftriaxone using logistic regression models and a Bonferroni correction to account for multiple hypothesis testing.

Results We included urine cultures from 1,306 unique outpatients, most of whom were female (89%). Patients largely self-identified as Non-Hispanic White (36%), Asian (15%), or Non-Hispanic Black (11%). Over 60% lived in an environmental justice-designated census tract. Most included isolates were *Escherichia coli* (76%) or *Klebsiella pneumoniae* (7%). Using public insurance increased patients' odds of having a uropathogen resistant to first-line antibiotics, but living in a limited-income neighborhood reduced patients' odds of having a MDR uropathogen by 47%. We noted a strong but non-significant positive trend between speaking a language other than English and having an aminoglycoside-resistant uropathogen (*p-value* = 0.02). Most notably, after controlling for other factors, we observed no statistically significant associations between race or ethnicity and AR uropathogens.

Conclusion The social determinants of health may play important and intersecting roles in determining a patient's risk of having a resistant uropathogens that is more challenging or expensive to treat. It is crucial to acknowledge

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how race is likely to be a proxy for other factors affecting health, and to consider that some groups may be disproportionately impacted by antibiotic resistance.

Keywords Uropathogen, Antimicrobial resistance, Social determinants of health, Health disparities, Urinary tract infection, Multidrug resistance

Background

Antibiotic resistance is one of the top ten threats to global health, food security, and development [1]. To date, few studies have examined whether minoritized groups in the US experience a disproportionate burden of antibiotic resistance [2, 3]. A recent systematic review of 25 international studies including 31,284 patients found that race/ethnicity [4] was one of the least commonly evaluated risk factors for acquisition of multidrug-resistant urinary tract infections (UTIs). Of studies that did assess race/ethnicity, all of them found that minority ethnicity was significantly associated with antibiotic resistance [5]. Given that race and ethnicity are social constructs and do not inherently increase an individuals' risk for antibiotic-resistant (AR) UTI, the social determinants of health (SDOH) serve as important proxies for the downstream effects of institutional and structural racism that adversely affect minority health and healthcare access. A variety of SDOH have been independently linked to increased risk of acquiring of AR pathogens, including inequities in health literacy [6, 7], barriers to healthcare access, inappropriate use of non-prescribed antibiotics, residence in crowded or multi-generational housing [8], foreign travel, or birth in regions with high burden of antibiotic resistance, among others [2]. However, the relatively limited number of studies examining AR in the context of SDOH renders it difficult to establish whether these patterns are unique to specific geographic regions, or generalizable to other areas of the US.

Urine cultures are one of the most ordered microbiological tests in the outpatient setting. Since bacteria found in urine cultures are most often of gut origin, thus reflecting a microenvironment strongly influenced by environmental factors (diet, travel, recent antibiotic use) [9–11], urine cultures are a particularly useful modality to study associations between SDOH and antibiotic resistance [10, 12]. Several recent US studies suggest that minority groups may be more likely to have community-acquired UTIs caused by AR bacteria. Specifically, Latinx/Hispanic race or ethnicity [13–15], Asian race [16], Middle Eastern ethnicity [17], low socioeconomic status (SES) [13, 18], and limited English proficiency [18] have all been identified as risk factors among US adults and children. Patterns in antibiotic resistance can differ considerably between regions; thus, awareness of both regional differences and sociodemographic risk factors for antibiotic resistance are crucial to improving patient outcomes [19].

We conducted a retrospective analysis of the association between sociodemographic characteristics of outpatients or the neighborhoods in which they lived and differences in the presence of AR bacteria in their urine. We hypothesized that both individual-level factors and characteristics of the neighborhoods in which patients lived would be associated with the prevalence of AR bacteria in their urine.

Methods

Setting

Tufts Medical Center (TMC) is a community-based full service academic medical center located in the Boston metropolitan region midway between Chinatown and the Theater District. TMC serves a diverse outpatient population and is categorized as a Massachusetts High Public Payer hospital, with 64.4% of gross patient service revenue from public payers [20].

Study Population

Urine cultures collected from August 15, 2015, through December 1, 2020, at TMC's adult primary care practices were identified through TMC's electronic medical record (Logician Enterprise Electronic Medical Record®; EMR), laboratory reporting system (Siemens Soarian Clinical Access®) and electronic surveillance program (TheraDoc®). Specimens were included if a patient's birth date, sex, and residential ZIP Code were recorded in the EMR and if their urine culture yielded one or more bacterial organisms for which antibiotic susceptibility profiling and species identification was conducted. Only cultures that yielded gram negative organisms or *Enterococcus* spp. were included. *Enterococcus* spp. was included given its role as a common opportunistic inhabitant of the gut flora and the rising prevalence of *Enterococcus* spp., and specifically *E. faecalis*, as a causative organism in both community-acquired and nosocomial UTI [21, 22]. If a patient's urine culture yielded multiple organisms of interest, antibiotic susceptibility profiling and species identification must have been conducted for at least one. If a patient had multiple urine cultures meeting the above criteria reported during the study period, only the most recent urine culture was included (Figure S1). Including the most recent isolate rather than the first isolate from patients with repeat cultures did not appear to consistently bias our findings towards more instances of antibiotic resistance (Table S1).

Laboratory methods

In the Tufts Medical Center clinical microbiology laboratory, uropathogens are cultured on standard blood and MacConkey agar. Prior to 2019, organisms were identified on the VITEK 2 microbial identification platform using standard gram positive and gram negative identification cards. Starting in 2019, organisms were identified using MALDI-TOF technology (Biomerieux Vitek MS). Susceptibility testing is performed on the VITEK 2 (GN-79 and GP-75 cards).

Outcome definition

We examined five distinct resistance profiles, including uropathogens resistant to [1] three or more antibiotic classes (classified as "multidrug-resistant" (MDR)) [2] first-line antibiotic treatments for suspected UTI (trimethoprim-sulfamethoxazole or nitrofurantoin) [3] Fluoroquinolones [4] aminoglycosides, and [5] ceftriaxone (as a proxy for Extended Spectrum Beta Lactamase [ESBL] producing organisms) (Table S2). We considered intrinsic resistance among some organisms when tabulating multidrug resistance. Specifically, resistance to sulfa-trimethoprim, ampicillin, and ampicillin-sulbactam were discounted among *Pseudomonas aeruginosa*; resistance to cefoxitin, cefazolin, ampicillin, and ampicillin-sulbactam were discounted among *Enterobacter* spp., and resistance to nitrofurantoin was discounted among *Proteus* spp. *P. aeruginosa* exhibits intrinsic resistance to additional antibiotics (e.g. ceftriaxone, nitrofurantoin) but TMC does not report susceptibility testing results for these antibiotics for *P. aeruginosa*; thus we did not consider these in our definition of MDR.

Patient-level risk factors

Patient medical record number, visit date, date of birth, sex, race, ethnicity, residential address, preferred language of communication, and insurance type on file were abstracted from the EMR for all patient encounters meeting inclusion criteria.

Neighborhood-level risk factors

Census tract variables were obtained from the 2020 US Census Bureau American Community Survey 5-year estimates (Table S3) [23]. Using criteria set by the Massachusetts Executive Office of Energy and Environmental Affairs (EEA) [23], census tracts were classified as: "low-income", meaning median household income (MHHI) was less than 65% of the state's average MHHI over the five year time period between 2015 and 2020 (i.e., $55,264), "limited-English speaking", meaning ≥ 25% of households in the census tract identified as speaking English less than "Very Well", or having a "significant minority population", meaning > 40% of the census tract consisted of individuals identifying as racial or ethnic minorities. Census tracts were additionally classified as environmental justice (EJ) populations if they met any of the above criteria or were at least 25% minority with < 150.5% MHHI [23, 24].

Patients with residential addresses outside of Massachusetts were excluded from all analyses, and patients whose residential addresses failed to geo-code to a census tract were excluded from analyses that included neighborhood-level risk factors.

Statistical analysis

Primary analysis

We used logistic regression models to evaluate the relationships between patient-level and neighborhood-level risk factors and each of the five resistance profiles of interest in patient isolates. Age and sex were included in all models. Variables which belonged to the majority sociodemographic category were used as reference variables, i.e., White, English language, and private insurance for patient-level risk factors, while MHHI >$55,264, minority < 40% of census tracts, and < 25% households speaking English less than "Very Well" served as reference variables for categorical neighborhood-level exposures. Where sample size allowed, we also explored the effects of specific non-English languages on the resistance profiles of interest. Detailed methods and results are described in the Supplementary Materials. We evaluated statistical significance using a Bonferroni-corrected p-value of 0.01 to account for multiple comparisons. All statistical analyses were conducted using R Statistical Software (v4.3.0; R Core Team 2023) [26].

Secondary analysis

We selected covariates with a p-value < 0.20 for inclusion in secondary analyses. To avoid collinearity, we excluded the EJ variable in the secondary analysis if both it and one of its individual components (i.e. low-income, limited-English speaking, or significant minority population) had a p-value of < 0.20. No other collinear variables were identified for any model using the *corr* function in R. Age and sex were forced into each secondary model.

Geospatial visualization

Methods for visualizing the prevalence of AR uropathogens in Boston-area communities are described in the Supplementary Materials.

Results

We obtained 2,384 positive cultures from 1,557 patients, 1,306 of which were from unique patient encounters meeting inclusion criteria (Figure S1). Demographic and clinical characteristics of these patients are in Table 1. Most isolates included in our final analysis were *Escherichia coli* (n = 1036), but *Klebsiella pneumionae*

Table 1 Demographic and clinical characteristics of patients with positive urine cultures meeting eligibility criteria from Tufts Medical Center, 2015–2020

	No. Isolates (%) (*N* = 1,306)
Patient Characteristics	
Sex	
Female	1,165 (89.2%)
Male	141 (10.8%)
Age	
18–34	380 (29.1%)
35–51	257 (19.7%)
52–68	351 (26.9%)
69–85	257 (19.7%)
85 or over	58 (4.4%)
Missing	3 (0.2%)
Race/Ethnicity*	
Non-Hispanic White	466 (35.7%)
Non-Hispanic Asian	189 (14.5%)
Non-Hispanic Black	141 (10.8%)
Hispanic	57 (4.4%)
Missing	453 (34.7%)
Language†	
English	1,139 (87.2%)
Chinese	80 (6.1%)
Vietnamese	31 (2.4%)
Spanish	27 (2.1%)
Other	28 (2.1%)
Insurance Status‡	
Public	647 (49.5%)
Private	638 (48.9%)
Uninsured	9 (0.7%)
Missing	12 (0.9%)
Susceptibility profile of selected organisms in urine	
Aminoglycoside-resistant	105 (8.3%)
Ceftriaxone-resistant	56 (4.4%)
Fluoroquinolone-resistant	170 (13.0%)
Resistant to First-line Treatment	366 (28.0%)
Multidrug Resistant	333 (25.56%)
Characteristics of Census Tract Where Patient Resides	
EJ-Designated Census Tract	
No	500 (38.3%)
Yes	806 (61.7%)
Pct of Households Identifying as Speaking English Less Than 'Very Well'	
< 25%	1,022 (78.3%)
≥ 25%	284 (21.7%)
Pct Total that Is a Racial/Ethnic Minority	
≤ 40%	664 (50.8%)
> 40%	642 (49.2%)
Median Household Income	
> $55,264	1,009 (77.3%)
≤ $55,264	284 (21.7%)
Missing	13 (1.0%)
Median Household Income ($10,000s) (mean, SD)	8.90 (4.02)
Pct that Did Not Complete High School (mean, SD)	11.1 (9.20)

Table 1 (continued)

	No. Isolates (%)
	(N = 1,306)
Pct Foreign-born (mean, SD)	25.9 (14.2)
Pct Living in Households with > 1 Person/Room (mean, SD)	3.11 (3.41)

*Race and/or ethnicity were categorized as non-Hispanic White, non-Hispanic Asian, non-Hispanic Black, Hispanic, or non-Hispanic Other, which included American Indian or Alaska Native and Native Hawaiian or Other Pacific Islander. Language was categorized as English, Chinese, Vietnamese, Spanish, or Other, which included Bosnian (*n*=4), Portuguese (*n*=4), and Cape Verdean (*n*=3), among others

†Patients with "NA" listed as their preferred language were assumed to be English speakers as this section of the intake form is used to indicate the need for an interpreter; we confirmed through personal communication with clinic staff that "English" or "NA" is typically used to indicate patients that do not need an interpreter

‡Insurance was categorized as public, private, or uninsured based on information provided by the Massachusetts Division of Insurance [47]

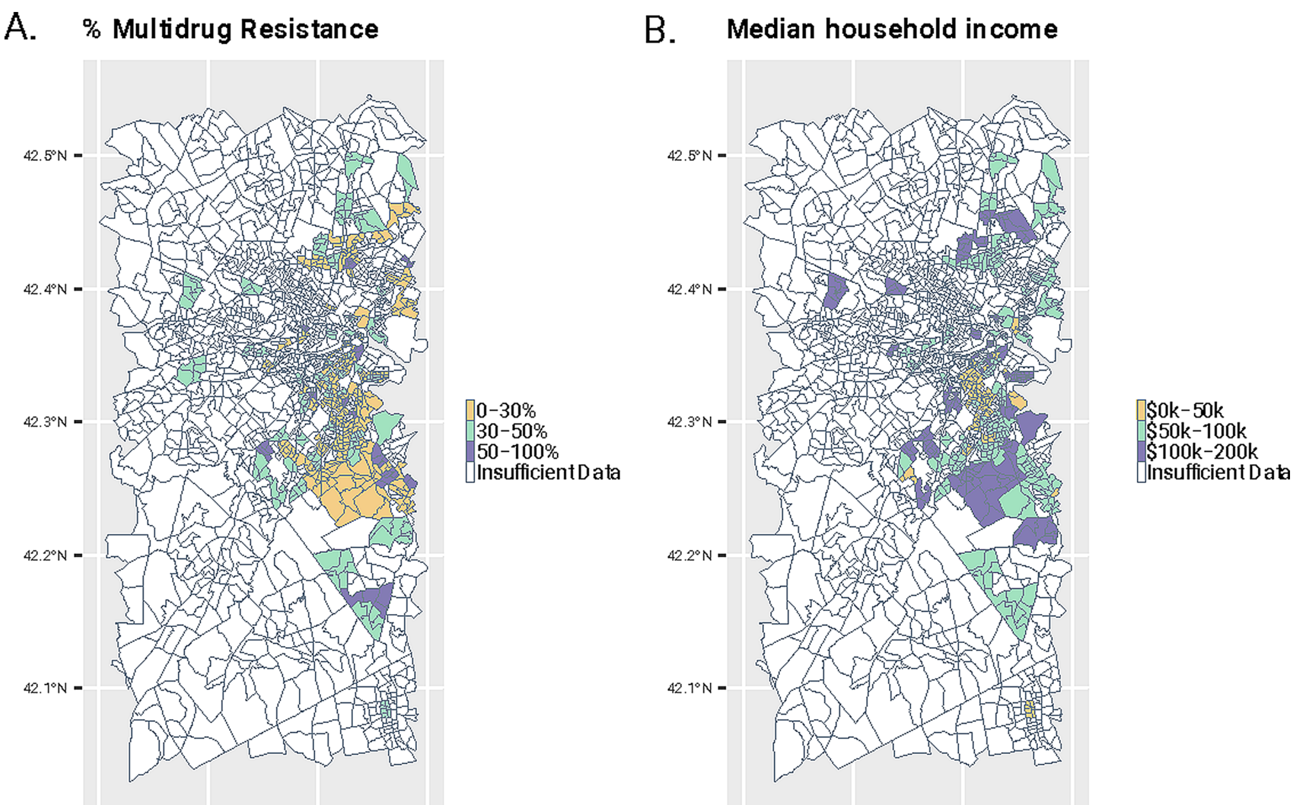

Fig. 1 Proportion of urine culture isolates expressing **(A)** multidrug resistance in census tracts with > 3 unique outpatients treated at Tufts Medical Center, Boston, MA, from 2015–2020. Census-tract level characteristics found to be significantly associated with this outcome in secondary analysis included **(B)** median household income (MHHI) in U.S. dollars. Map is zoomed into the Greater Boston area, where > 90% of patients resided (see Supplemental Materials)

(*n*=100), *Proteus mirabilis* (*n*=65), *Enterococcus faecalis* (*n*=34), *Citrobacter koseri* (*n*=24), *Enterobacter aerogenes* (*n*=13) and other minor species (< 10 isolates each) were also included (Table S4).

Most isolates were collected from women (89.2%). A total of 333 (25.56%) had multidrug resistance, 366 (28.0%) were resistant to first-line antibiotics, 170 (13.0%) were resistant to fluoroquinolones, 105 (8.3%) were resistant to aminoglycosides, and 56 (4.4%) were resistant to ceftriaxone.

Out of 1,478 land census tracts in Massachusetts [27], 559 were represented. Of the 1,306 unique patient isolates included, 806 (61.7%) were from individuals residing in an EJ-designated census tract, 284 (21.7%) were from residents of a low-income census tract, 284 (21.7%) were from residents of a limited-English speaking census tract, 642 (49.2%) were from residents of a census tract with a significant minority population. Patients with AR uropathogens tended to reside in southeast Boston (Fig. 1).

Multidrug Resistance (MDR)

Approximately 25% (*n*=333) of isolates were MDR (Table 2). MDR was not significantly associated with any

Table 2 Individual and neighborhood-level risk factors for multidrug resistant urine cultures in patients meeting eligibility criteria from Tufts Medical Center, 2015–2020

	No. Isolates (*N*, %)		Primary Analysis		Secondary Analysis	
	Not Multidrug Resistant (*N*=973)	**Multidrug Resistant (*N*=333)**	**OR (95% CI)**	***p*-val**	**OR (95% CI)**	***p*-val**
Patient Characteristics						
Age (Mean, SD)	50.8 (20.3)	54.1 (20.1)	1.00 (1.00, 1.01)	0.015	1.01 (1, 1.01)	0.075
Sex (n, %)						
Female	873 (89.7%)	292 (87.7%)	Ref		Ref	
Male	100 (10.3%)	41 (12.3%)	1.12 (0.75, 1.66)	0.582	1.17 (0.78, 1.74)	0.453
Individual-level Factors						
Race and Ethnicity* (n, %)						
Non-Hispanic White	341 (35.0%)	125 (37.5%)	Ref			
Asian	129 (13.3%)	60 (18.0%)	1.24 (0.86, 1.8)	0.25		
Black	108 (11.1%)	33 (9.9%)	0.87 (0.56, 1.36)	0.538		
Hispanic	42 (4.3%)	15 (4.5%)	0.97 (0.52, 1.82)	0.931		
Missing	353 (36.3%)	100 (30.0%)				
Language† (n, %)						
English	864 (88.8%)	275 (82.6%)	Ref		Ref	
Other Language	109 (11.2%)	58 (17.4%)	1.52 (1.06, 2.19)	0.022	1.45 (1, 2.09)	0.052
Insurance Type‡ (n, %)						
Private	497 (51.1%)	150 (45.0%)	Ref			
Public	462 (47.5%)	176 (52.9%)	1.16 (0.89, 1.51)	0.272		
Missing / Uninsured	14 (1.4%)	7 (2.1%)				
Neighborhood-level Factors						
EJ-Designated Census Tract (n, %)						
No	376 (38.6%)	124 (37.2%)	Ref			
Yes	597 (61.4%)	209 (62.8%)	1.11 (0.85, 1.43)	0.451		
Pct of Households Identifying as Speaking English Less Than 'Very Well' (n, %)						
< 25%	776 (79.8%)	246 (73.9%)	Ref		Ref	
≥ 25%	197 (20.2%)	87 (26.1%)	1.43 (1.07, 1.92)	0.016	1.26 (0.83, 1.92)	0.284
Pct Total that Is a Racial/Ethnic Minority (n, %)						
≤ 40%	502 (51.6%)	162 (48.6%)	Ref			
> 40%	471 (48.4%)	171 (51.4%)	1.17 (0.91, 1.51)	0.219		
Median Household Income (n, %)						
≥ $54,850	744 (76.5%)	265 (79.6%)	Ref		Ref	
< $54,850	221 (22.7%)	63 (18.9%)	0.81 (0.59, 1.11)	0.192	0.53 (0.36, 0.79)	0.002
Missing	8 (0.8%)	5 (1.5%)				
Median Household Income ($10,000s) (Mean, SD)	8.85 (4.04)	9.07 (3.97)	1.01 (0.98, 1.04)	0.466		
Pct that Did Not Complete High School (Mean, SD)	10.8 (8.95)	11.9 (9.85)	1.01 (0.98, 1.04)	0.04	1.02 (1, 1.04)	0.058

Table 2 (continued)

	No. Isolates (*N*, %)		Primary Analysis		Secondary Analysis	
	Not Multidrug Resistant (*N*=973)	Multidrug Resistant (*N*=333)	OR (95% CI)	*p*-val	OR (95% CI)	*p*-val
Pct Foreign-born (Mean, SD)	25.5 (14.2)	26.9 (14.5)	1.01 (1, 1.02)	0.086	1 (0.99, 1.01)	0.997
Pct Living in Households with > 1 Person/Room (Mean, SD)	3.05 (3.40)	3.31 (3.44)	1.03 (0.99, 1.07)	0.123	1.01 (0.96, 1.05)	0.786

*Race and/or ethnicity were categorized as non-Hispanic White, non-Hispanic Asian, non-Hispanic Black, Hispanic, or non-Hispanic Other, which included American Indian or Alaska Native and Native Hawaiian or Other Pacific Islander. Language was categorized as English, Chinese, Vietnamese, Spanish, or Other, which included Bosnian (*n*=4), Portuguese (*n*=4), and Cape Verdean (*n*=3), among others

†Patients with "NA" listed as their preferred language were assumed to be English speakers as this section of the intake form is used to indicate the need for an interpreter; we confirmed through personal communication with clinic staff that "English" or "NA" is typically used to indicate patients that do not need an interpreter

‡Insurance was categorized as public, private, or uninsured based on information provided by the Massachusetts Division of Insurance [47]

individual- or neighborhood-level risk factors in primary analysis. However, there was a strong trend toward a positive association with residence in a limited-English census tract (Odds Ratio [OR]: 1.43, 95% Confidence Interval [CI]: 1.07, 1.92, $p=0.016$).

Secondary analysis revealed a significant association between residing in a low-income census tract and reduced odds of acquiring an MDR uropathogen. Specifically, patients living in a low-income census tract had nearly half the odds of having an MDR uropathogen compared to the reference group (OR 0.53, 95% CI [0.36, 0.79], $p=0.002$).

First-line Antibiotic Resistance

28% ($n=366$) of isolates were resistant to at least one first-line treatment (Table 3). Of 254 isolates resistant to sulfa-trimethoprim, 90.2% were *E. coli* (Table S5). Of 132 isolates resistant to nitrofurantoin, 62.1% were *K. pneumoniae* and 17.4% were *E. coli* (Table S5). Only *K. pneumoniae* ($n=10$), *E. coli* ($n=8$), *Enterobacter clocae* ($n=1$) and *Morganella morganii* ($n=1$) isolates expressed resistance to both. Having public insurance was significantly associated with this resistance profile (OR 1.4, 95% CI [1.1, 1.79], $p=0.006$).

Having a uropathogen resistant to first-line antibiotics was significantly associated with neighborhood-level educational attainment in the primary analysis; specifically, for every 1% increase in the percent of residents older than 25 years that did not complete high school, a patient's odds of having a uropathogen resistant to first-line antibiotics increased by 2% (OR 1.02, 95% CI [1.01, 1.03], $p=0.003$). We observed strong trends towards a positive association with living in a limited-English speaking census tract (OR 1.40, 95% CI [1.05, 1.85], $p=0.023$) and the percent of foreign-born inhabitants in the primary analysis as well; for every 1% increase in foreign-born inhabitants in a neighborhood, a patient's odds of having a uropathogen resistant to first-line antibiotics was 1% higher (OR 1.01, 95% CI [1, 1.02], $p=0.035$).

In the secondary analysis, having public insurance continued to be strongly associated with increased odds of having a uropathogen resistant to first-line antibiotics (OR 1.43, 95% CI [1.10, 1.86], $p=0.007$) when controlling for the neighborhood-level exposures described above. No neighborhood-level effects were significantly associated with this outcome.

Fluoroquinolone resistance

One hundred seventy (13.0%) isolates were resistant to fluoroquinolones (Table S5). Primary analysis revealed that fluoroquinolone resistance was not significantly associated with any individual- or neighborhood-level risk factors besides age (OR 1.01, 95% CI [1.01, 1.02], $p=0.004$). We did identify some strong trends toward an association with living in a limited-English speaking census tract (OR 1.58 95% CI [1.10, 2.29], $p=0.014$, proportion of residents that did not complete high school (OR 1.02, 95% CI [1, 1.04], $p=0.024$, proportion of foreign-born residents (OR 1.01, 95% CI [1, 1.03], $p=0.015$) and overcrowding in a census tract (OR 1.05, 95% CI [1.01, 1.1], $p=0.022$). None of these exposures were significant in the secondary analysis.

Aminoglycoside Resistance

One hundred and five (8.3%) of the total isolates were resistant to aminoglycosides (Table 4). In primary analyses, we found that aminoglycoside resistance was significantly associated with having a primary language other than English. Compared to primary English speakers, patients with a different primary language had nearly twice the odds of having an aminoglycoside-resistant uropathogen (OR 1.99, 95% CI [1.2, 3.28], $p=0.007$). Of note, there was also a strong but non-significant association between having an aminoglycoside-resistant uropathogen and Asian race. Relative to White people, Asian people had nearly twice the odds of having an aminoglycoside-resistant uropathogen (OR 1.91, 95% CI [1.1, 3.3], $p=0.021$).

No neighborhood-level primary analyses were significantly associated with this resistance profile in primary analyses, but we identified a strong, non-significant association with residence in a limited-English speaking neighborhood (OR 1.75, 95% CI [1.12, 2.73], $p=0.013$).

In secondary analysis, the effect of speaking a non-English language was no longer statistically significant, although the effect size increased in magnitude (OR 2.33, 95% CI [1.13, 4.81], $p=0.022$) after accounting for other exposures.

Older age was associated with increased odds of having an aminoglycoside-resistant infection in both the primary analysis (OR 1.02, 95% CI [1.01, 1.03], $p=0.000$) and secondary analysis (OR 1.02, 95% CI [1.01, 1.03], $p=0.006$).

Ceftriaxone resistance

Few ceftriaxone-resistant isolates were identified ($n=56$). No individual or neighborhood-level risk factors were found to be associated with this resistance profile besides older age, which was significantly associated with increased odds of having a ceftriaxone-resistant infection in both the primary analysis (OR 1.03, 95% CI [1.01, 1.04], $p=0.001$) and secondary analysis (OR 1.03, 95% CI [1.01, 1.04], $p=0.004$) (Table S6).

Discussion

In this cross-sectional, single-center study of urine cultures from 1,306 outpatients, we identified several characteristics of patients and the neighborhoods they lived in that were associated with their risk of having an AR uropathogen. Strikingly, while we observed a number of individual- and neighborhood-level characteristics that were associated with patients' risk of AR uropathogens in primary analyses, in which we controlled only for patients' age and sex, nearly all of these characteristics were no longer statistically significant in secondary analyses, when other SES characteristics were controlled for. Specifically, in secondary analyses, only residence in a low-income neighborhood, having public insurance, and older age remained significantly associated with AR uropathogen risk. Unusually, we observed that lower neighborhood income levels were associated with reduced odds of having a MDR uropathogen. Our findings indicate that the SDOH, i.e., the conditions of the environments where we live, work, and play, likely play important and highly intersecting roles in determining an individual's risk of having AR uropathogens.

After controlling for additional factors, we observed no statistically significant associations between race/ethnicity and the presence of all resistant uropathogens included in the study. Given that one third of patients did not self-report their race/ethnicity, this could be attributed to insufficient sample size to detect these associations. Or, given that race is a social construct, it could be that associations between race and AR infections are driven by confounding factors. This likely explains why so many of the characteristics found to be significant in primary analysis were no longer so in secondary analysis. Supporting this theory, a 2017 study of MRSA infections found that accounting for SES, access to healthcare, and poor environmental conditions explained up to 91% of observed racial disparities [28]. It is crucial to note that while race-conscious medicine encourages investigators to consider how race is likely to be a proxy for other factors affecting health, racially minoritized groups may nevertheless be disproportionately impacted by antibiotic resistance.

We unexpectedly observed that living in a lower-income neighborhood was associated with reduced odds of having a MDR uropathogen, which differs from previous studies, while finding that having public insurance, typically considered a proxy for poverty, was positively associated with patients' risk of having a uropathogen resistant to first-line antibiotics. A 2021 study of California outpatients reported that being enrolled in Medicaid *or* living in a census tract with a low socioeconomic deprivation score were *both* independently associated with patients' risk of MDR UTI [18]. In contrast to this, we found that living in a low-income neighborhood reduced patients' odds of having a MDR uropathogen by 47% when controlling for their age, sex, primary language, and multiple neighborhood-level characteristics. Poverty is widely thought to elevate the risk for acquiring

Table 3 Individual and neighborhood-level risk factors for first-line antibiotic-resistant urine cultures in patients meeting eligibility criteria from Tufts Medical Center, 2015–2020

	No. Isolates (%)		Primary Analysis		Secondary Analysis	
	Susceptible *N* = 940	**Resistant** *N* = 366	**OR (95% CI)**	***p*-val**	**OR (95% CI)**	***p*-val**
Patient Characteristics						
Age (Mean, SD)	50.8 (20.3)	53.6 (20.2)	1.01 (1.00, 1.01)	0.052	1.00 (1, 1.01)	0.204
Sex (n, %)						
Female	842 (90.3%)	321 (87.7%)	Ref		Ref	
Male	90 (9.7%)	45 (12.3%)	1.22 (0.82, 1.80)	0.324	1.25 (0.84, 1.86)	0.270
Individual-level Factors						
Race and Ethnicity* (n, %)						
Non-Hispanic White	327 (35.1%)	137 (37.4%)	Ref			
Asian	130 (13.9%)	57 (15.6%)	1.04 (0.72, 1.5)	0.591		
Black	96 (10.3%)	44 (12.0%)	1.12 (0.74, 1.69	0.844		
Hispanic	39 (4.2%)	17 (4.6%)	1.04 (0.57, 1.91)	0.892		
Missing	340 (36.5%)	111 (30.3%)				
Language† (n, %)						
English	818 (87.8%)	314 (85.8%)	Ref			
Other Language	114 (12.2%)	52 (14.2%)	1.08 (0.75, 1.56)	0.671		
Insurance Type‡ (n, %)						
Private	490 (52.6%)	154 (42.1%)	Ref		Ref	
Public	429 (46.0%)	204 (55.7%)	1.43 (1.11, 1.86)	0.006	1.43 (1.10, 1.85)	0.007
Missing/Uninsured	13 (1.4%)	8 (2.2%)				
Neighborhood-level Factors						
EJ-Designated Census Tract (n, %)						
No	362 (38.8%)	133 (36.3%)	Ref			
Yes	570 (61.2%)	233 (63.7%)	1.15 (0.9, 1.49)	0.269		
Pct of Households Identifying as Speaking English Less Than 'Very Well' (n, %)						
< 25%	743 (79.7%)	272 (74.3%)	Ref		Ref	
≥ 25%	189 (20.3%)	94 (25.7%)	1.40 (1.05, 1.85)	0.023	1.19 (0.79, 1.79)	0.415
Pct Total that Is a Racial/Ethnic Minority (n, %)						
≤ 40%	479 (51.4%)	180 (49.2%)	Ref		Ref	
> 40%	453 (48.6%)	186 (50.8%)	1.13 (0.88, 1.44)	0.048	0.65 (0.43, 1.96)	0.032
Median Household Income (n, %)						
≥ $54,850	731 (78.4%)	272 (74.3%)	Ref		Ref	
< $54,850	8 (0.9%)	5 (1.4%)	1.26 (0.94, 1.68)	0.118	1.01 (0.69, 1.48)	0.948
Missing	8.99 (4.02)	8.65 (3.98)				
Median Household Income ($10,000s) (Mean, SD)	8 (0.9%)	5 (1.4%)	0.98 (0.95, 1.01)	0.136		
Pct that Did Not Complete High School (Mean, SD)	25.4 (13.9)	27.1 (15.0)	1.02 (1.01, 1.03)	0.003	1.02 (1.00, 1.05)	0.034

Table 3 (continued)

	No. Isolates (%)		Primary Analysis		Secondary Analysis	
	Susceptible *N* = 940	Resistant *N* = 366	OR (95% CI)	*p*-val	OR (95% CI)	*p*-val
Pct Foreign-born (Mean, SD)	10.6 (8.77)	12.3 (10.1)	1.01 (1, 1.02)	0.035	1.01 (0.99, 1.02)	0.423
Pct Living in Households with > 1 Person/Room (Mean, SD)	3.06 (3.41)	3.25 (3.40)	1.02 (0.99, 1.06)	0.248		

*Race and/or ethnicity were categorized as non-Hispanic White, non-Hispanic Asian, non-Hispanic, Hispanic, or non-Hispanic Other, which included American Indian or Alaska Native and Native Hawaiian or Other Pacific Islander. Language was categorized as English, Chinese, Vietnamese, Spanish, or Other, which included Bosnian (*n* = 4), Portuguese (*n* = 4), and Cape Verdean (*n* = 3), among others

†Patients with "NA" listed as their preferred language were assumed to be English speakers as this section of the intake form is used to indicate the need for an interpreter; we confirmed through personal communication with clinic staff that "English" or "NA" is typically used to indicate patients that do not need an interpreter

‡Insurance was categorized as public, private, or uninsured based on information provided by the Massachusetts Division of Insurance [47]

AR uropathogens as those with low incomes may be more likely to live in crowded or multigenerational housing [28, 29], which facilitates the spread of bacteria, and may be less likely to access medical care for various reasons including inability to get time off of work [30, 31]. It remains unclear why we observed an opposite trend related to poverty and AR uropathogen risk. A 2021 study of Cook County Hospital patients found that patients with ceftriaxone-resistant versus -susceptible Enterobacterales infections (including UTIs) were clustered in census tracts with higher percentages of uninsured residents [13]. We also observed that patients relying on public insurance had 43% higher odds of having a uropathogen resistant to first-line antibiotics, when controlling for patient's age, sex, and multiple neighborhood-level characteristics, which is more in line with previous studies. However, we considered Medicare and Medicaid (MassHealth) patients together in this exposure category; because Medicare is age-based, public insurance status is not necessarily correlated to decreased access to resources or lower SES.

In primary analyses, we consistently observed strong but non-significant positive trends ($p<0.025$ for all) between speaking a language other than English and/or living in a limited-English neighborhood and the risk of AR uropathogens, including MDR uropathogens and uropathogens resistant to first-line treatments, aminoglycosides, and fluoroquinolones. None of these associations were statistically significant in secondary analyses. Nevertheless, there are reasons to postulate that language might impact risk of antibiotic resistance. Inability to speak English could result in challenges in accessing healthcare or be associated with differences in including travel patterns, social contacts, or medication practices. First-generation immigrants, who often lack access to a regular healthcare provider, are more likely to have inadequate health literacy levels, lower knowledge of correct antibiotic usage, and higher likelihood of reporting injudicious antibiotic usage [33, 34]. Individuals who do not speak English as their primary language, are foreign born, or who are the children of immigrants may also frequently travel to their native countries. Travel to Asia, North Africa, and Latin America by an individual or their household contacts is a well-established risk factor for gut colonization with AR Enterobacterales [35, 36], which may subsequently be detected in urine. Individuals who travel to certain parts of the world may also purchase antibiotics (which are typically available without a prescription and for less money) to take home with them, contributing to the selection of antibiotic resistance in communities where this is common [37, 38]. Some of these factors could underlie recent findings that Latinx/Hispanic race or ethnicity [13–15], Asian race [16], and

Table 4 Individual and neighborhood-level risk factors for aminoglycoside resistant urine cultures in patients meeting eligibility criteria from Tufts Medical Center, 2015–2020

	No. Isolates (%)		Primary Analysis		Secondary Analysis	
	Susceptible (*N* = 1164)	Resistant (*N* = 105)	OR (95% CI)	*p*-val	OR (95% CI)	*p*-val
Patient Characteristics						
Age (Mean, SD)	50.7 (20.1)	59.1 (20.5)	1.02 (1.01, 1.03)	0.000	1.02 (1.01, 1.03)	0.006
Sex (n, %)						
Female	1,056 (90.7%)	94 (89.5%)	Ref	Ref	Ref	
Male	108 (9.3%)	11 (10.5%)	0.89 (0.46, 1.73)	0.728	0.83 (0.36, 1.93)	0.663
Individual-level Factors						
Race and Ethnicity* (n, %)						
Non-Hispanic White	413 (35.5%)	34 (32.4%)	Ref		Ref	
Asian	156 (13.4%)	26 (24.8%)	1.91 (1.1, 3.3)	0.372	1.17 (0.58,2.35)	0.665
Black	126 (10.8%)	12 (11.4%)	1.38 (0.68, 2.78)	0.021	1.32 (0.63, 2.79)	0.465
Hispanic	50 (4.3%)	4 (3.8%)	0.96 (0.33, 2.85)	0.949	0.68 (0.21, 2.14)	0.509
Missing	419 (36.0%)	29 (27.6%)				
Language† (n, %)						
English	1031 (88.6%)	79 (75.2%)	Ref		Ref	
Other Language	133 (11.4%)	26 (24.8%)	1.99 (1.2, 3.28)	0.007	2.33 (1.13, 4.8)	0.022
Insurance Type‡ (n, %)						
Private	593 (50.9%)	43 (41.0%)	Ref			
Public	553 (47.5%)	60 (57.1%)	1.18 (0.77, 1.82)	0.446		
Missing/Uninsured	18 (1.5%)	2 (1.9%)				
Neighborhood-level Factors						
EJ-Designated Census Tract (n, %)						
No	446 (38.3%)	40 (38.1%)	Ref			
Yes	718 (61.7%)	65 (61.9%)	1.1 (0.73, 1.67)	0.642		
Pct of Households Identifying as Speaking English Less Than 'Very Well' (n, %)						
< 25%	918 (78.9%)	73 (69.5%)	Ref		Ref	
≥ 25%	246 (21.1%)	32 (30.5%)	1.75 (1.12, 2.73)	0.013	1.4 (0.71, 2.76)	0.337
Pct Total that Is a Racial/Ethnic Minority (n, %)						
≤ 40%	597 (51.3%)	49 (46.7%)	Ref		Ref	
> 40%	567 (48.7%)	56 (53.3%)	1.33 (1.12, 2.73)	0.168	1.16 (0.56, 2.37)	0.693
Median Household Income (n, %)						
≥ $54,850	904 (77.7%)	80 (76.2%)	Ref			
< $54,850	250 (21.5%)	22 (21.0%)	1.03 (0.63, 1.69)	0.905		
Median Household Income ($10,000s) (Mean, SD)	8.95 (4.05)	8.81 (3.80)	0.99 (0.94, 1.04)	0.571		
Pct that Did Not Complete High School (Mean, SD)	10.9 (9.05)	12. (10.4)	1.01 (0.99, 1.04)	0.184	0.99 (0.95, 1.03)	0.631

Table 4 (continued)

	No. Isolates (%)		Primary Analysis		Secondary Analysis	
	Susceptible (*N*=1164)	**Resistant (*N*=105)**	**OR (95% CI)**	***p*-val**	**OR (95% CI)**	***p*-val**
Pct Foreign-born (Mean, SD)	25.8 (14.3)	26.8 (14.2)	1.01 (0.99, 1.02)	0.276		
Pct Living in Households with > 1 Person/Room (Mean, SD)	3.12 (3.41)	3.11 (3.37)	1.02 (0.96, 1.08)	0.6		

*Race and/or ethnicity were categorized as non-Hispanic White, non-Hispanic Asian, non-Hispanic Black, Hispanic, or non-Hispanic Other, which included American Indian or Alaska Native and Native Hawaiian or Other Pacific Islander. Language was categorized as English, Chinese, Vietnamese, Spanish, or Other, which included Bosnian (*n*=4), Portuguese (*n*=4), and Cape Verdean (*n*=3), among others

†Patients with "NA" listed as their preferred language were assumed to be English speakers as this section of the intake form is used to indicate the need for an interpreter; we confirmed through personal communication with clinic staff that "English" or "NA" is typically used to indicate patients that do not need an interpreter

‡Insurance was categorized as public, private, or uninsured based on information provided by the Massachusetts Division of Insurance [47]

Middle Eastern ethnicity [17] are risk factors for AR uropathogens.

Across resistance types, there were positive trends between older age and risk of AR uropathogen. This association was particularly pronounced—and significant—for aminoglycoside and ceftriaxone resistance. This aligns with previous research on this subject, some of which suggests that odds of having an antibiotic-resistance uropathogen increase as we age [13, 14].

To our knowledge, this is one of the first US studies to examine risk factors for aminoglycoside-resistant uropathogens. Aminoglycosides are used to treat MDR-gram negative complicated cystitis, including carbapenem-resistant infections, when other options are limited [39]. A recent review reported that aminoglycoside resistance genes are most frequently reported in Asian settings [40]. Thus, it is possible that travel to Asia or other world regions or close interactions with those who do increases patients' risk of aminoglycoside-resistant uropathogen. Tufts Medical Center is located in Chinatown, giving us an opportunity to include a uniquely high percentage of Asian patients (15% despite comprising 5.7% of the US population) [23]. However, while we found significant associations between speaking a non-English primary language and self-identifying as Asian and having an aminoglycoside-resistant uropathogen in our primary analyses, these associations fell short of being statistically significant in secondary analysis.

This study had several strengths. First, demographic data were self-reported rather than assumed by healthcare staff. Second, we used a highly conservative correction factor for multiple hypothesis testing. Third, creating geospatial maps allowed us to qualitatively identify census tracts with increased risk of antibiotic resistance clustered in southeast Boston, where many vulnerable populations reside [41]. This study also had some limitations. First, our findings may not be generalizable beyond TMC's catchment area. Second, because we did not conduct chart review, we could not control for known patient risk factors for AR uropathogens, including recent hospitalization, recent antibiotic use, recent travel, presence of comorbidities (i.e. diabetes, urological disorders), and differences in providers' prescribing patterns. Relatedly, because we did not conduct chart review, we report AR uropathogens but cannot confirm that patients had diagnosed UTIs. Third, study patients only included those who sought care and for whom a urine culture was ordered, but there are sociodemographic and geographic differences in who seeks and is able to access primary care [42, 43]. Structural racism, accessibility, and affordability issues may also affect for whom clinicians order laboratory tests [44]. The decision to use dipstick, culture, or clinical criteria (without a test) for UTI diagnosis differs widely between institutions and individual clinicians

[45, 46], while a culture is nearly always ordered once a patient fails to be cured with first-line antibiotics. This almost certainly inflates the prevalence of AR uropathogens in our analysis, and perhaps not equally across demographic groups. Exploration of additional patient factors affecting acquisition and appropriate usage of antibiotics, such as cultural bias, expectation of receiving antibiotics at visits, as well as examination of provider factors such as implicit bias and provider attitudes should also be examined in future studies. Lastly, while future research using machine learning and advanced GIS methods could explore spatial and temporal patterns of antibiotic resistance, i.e. elucidate patterns of *antibiotic resistance* cluster emergence and regionalization [13, 47], we were unable to explore this with our relatively limited, geographically-constrained dataset.

Conclusions

The recent COVID-19 pandemic unmasked the impact that social determinants of health have on underprivileged and minoritized communities and underscored that infectious diseases do not impact all people equally. With antibiotic resistance predicted to be the next global pandemic, it is essential that we work to understand its differential impact on our most at-risk populations. This study confirmed associations between antibiotic resistance and social determinants of health but showed that the magnitude and direction of these associations may vary by outcome. These findings highlight the pressing need to improve the social determinants of health, improve living conditions for the poor, and bolster health literacy with attention to education about antibiotic resistance, particularly in vulnerable communities.

Supplementary Information

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Supplementary Material 1

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Author contributions

CWC, SD, and MLN conceptualized the study, acquired data, and wrote the first draft of the manuscript. MLN, LKW, and KG performed statistical analyses. AR performed geospatial visualizations. All authors reviewed the manuscript and approved the final version for submission.

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Data availability

A de-identified dataset is available upon written request.

Declarations

Ethical approval and consent to participate

This study was determined to be exempt by the Tufts Health Sciences Institutional Review Board (STUDY00001311) and the University of Massachusetts T.H. Chan School of Medicine Institutional Review Board (STUDY00000435).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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