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MAJOR ARTICLE

Sociodemographic Inequalities in Urinary Tract Infection in 2 Large California Health Systems

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Background. Urinary tract infection (UTI) accounts for a substantial portion of outpatient visits and antibiotic prescriptions in the United States. Few studies have considered sociodemographic factors including low socioeconomic status (SES)—which may increase residential crowding, inappropriate antibiotic prescribing, or comorbidities—as UTI or multidrug-resistant (MDR) UTI risk factors.

Methods. We used 2015–2017 electronic health record data from 2 California health care systems to assess whether 3 sociodemographic factors—use of Medicaid, use of an interpreter, and census tract–level deprivation—were associated with overall UTI or MDR UTI. UTIs resistant to ≥3 antibiotic classes were considered MDR.

Results. Analyses included 601 352 UTI cases, 1 303 455 controls, and 424 977 urinary *Escherichia coli* isolates from Kaiser Permanente Southern California (KPSC) and Sutter Health in Northern California. The MDR prevalence was 10.4% at KPSC and 12.8% at Sutter Health. All 3 sociodemographic factors (ie, use of Medicaid, using an interpreter, and community deprivation) were associated increased risk of MDR UTI. For example, using an interpreter was associated with a 36% (relative risk [RR], 1.36; 95% CI, 1.31 to 1.40) and 28% (RR, 1.28; 95% CI, 1.22 to 1.34) increased risk of MDR UTI at KPSC and Sutter Health, respectively, adjusted for SES and other potential confounding variables. The 3 sociodemographic factors were only weakly associated with UTI overall.

Conclusions. We found low SES and use of an interpreter to be novel risk factors for MDR UTI in the United States.

Keywords. epidemiology; multidrug resistance (MDR); socioeconomic disparities; urinary tract infection (UTI).

Urinary tract infections (UTIs) are common in the United States, resulting in 10.5 million ambulatory visits [1] and 15% of outpatient-prescribed antibiotics [2] annually. *Escherichia coli* causes the majority of UTIs [3], and the prevalence of infections caused by drug-resistant *E. coli* has grown worldwide [4]. Between 2001 and 2010, the prevalence of uropathogenic multidrug-resistant (MDR) *E. coli* from outpatients increased from 9.1% to 17.0% [5]. Antibiotic use drives drug resistance by selecting for strains with gene mutations or acquired mobile genetic elements [6]. While risk factors for MDR UTI such as male sex, older age, and type 2 diabetes [7] may indicate differential antibiotic use, recent studies have identified novel risk factors for MDR *E. coli*, including food, travel, and social circumstances [8–10].

A broad literature on the social determinants of health has found low individual- and community-level socioeconomic status (SES), as well as being foreign born in a high-income country, to be associated with increased risk of general infection [11–14] and antibiotic-resistant infection [15–19]. Multiple pathways—health and health care, living and working conditions, travel, antibiotic use practices, or environmental factors—may account for these relationships [14, 15, 20].

Few studies have evaluated the role of SES as a risk factor for UTI or MDR UTI [8, 13, 17, 18, 21], and none in the United States, where a steep socioeconomic gradient in health exists [22]. We examined whether individual- or community-level sociodemographic factors were related to (1) risk of UTI or (2) risk of MDR UTI among UTI cases. Our goal was to identify sociodemographic disparities in these outcomes, if they existed, to reduce disparities in UTI and MDR UTI.

METHODS

We conducted a case–control and case–case study using electronic health record (EHR) data from 2015–2017 from Kaiser

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Permanente Southern California (KPSC) and Sutter Health in Northern California. KPSC, an integrated health care organization, serves >4.7 million individuals representative of the population in the region, except for slight under-representation of individuals living in the highest- and lowest-SES communities [23]. Sutter Health is a mixed-payer system that delivers care to 3.5 million patients annually and is representative of the population in the region. Both KPSC and Sutter use Epic EHR (Epic Systems Corporation, Verona, WI, USA) systems that catalogue health information: sociodemographics, diagnoses, laboratory tests, and medication orders from all care settings.

Patient Consent

This study did not require patient consent. The data set was limited and de-identified, exempted from patient consent, and approved by the institutional review boards at KPSC, Sutter Health, and Columbia University.

Study Population

KPSC uses a closed membership system, with integration of the health plan, hospitals, and physician medical groups, such that members are incentivized to receive health care within the system. As Sutter is an open system (no membership), we emulated membership by constructing a primary care cohort, identifying all individuals who visited a primary care clinic between 2008 and 2017 (n = 2 608 458). Our study included adult (≥18 years) KPSC members and Sutter primary care cohort members who received care for a UTI at an outpatient encounter (ie, in-person clinic, emergency department, and virtual care visits) between January 1, 2015, and December 31, 2017. We excluded individuals with addresses that did not geocode to a census tract, who lived outside their respective health care system catchment area, or who were missing census data (2.4% at KPSC and 3.4% at Sutter Health) (Supplementary Figure 1).

To identify UTI, we used *International Classification of Diseases, Ninth Revision* (*ICD-9*), codes 595.0, 595.9, 599.0, and 590.1x and *ICD-10* codes N30.0x, N30.9, N39.0, and N10, as well as antibiotic prescription information and positive urine culture results for *E. coli,* as in our prior work [24]. We used KPSC and Sutter laboratory guidelines to identify a positive urine culture: ≥1000 colony-forming units (CFUs)/mL for sterile samples and ≥10 000 CFU/mL for clean-catch samples. We excluded laboratory-identified contaminated cultures. We categorized patients as having a UTI if they met either of the following criteria: (1) UTI diagnosis + antibiotic order on the same day or (2) a positive *E. coli* urine culture. We grouped occurrences of UTI within 30 days of one another into a single UTI event and assigned the first health care visit in the 30-day window as the UTI event date, as multiple health care encounters may occur for the same UTI event. Both KPSC and Sutter routinely screen *E. coli* for resistance to ampicillin, trimethoprim/sulfamethoxazole (TMP-SMZ), cefazolin, ciprofloxacin, gentamicin, nitrofurantoin, and piperacillin/tazobactam using Clinical and Laboratory Standards Institute breakpoints [25]. Intermediate results were counted as resistant. We defined MDR as nonsusceptibility to at least 1 drug in at least 3 classes (of the 7 tested) based on the Centers for Disease Control and Prevention Antibiotic Resistance Patient Safety Atlas definition [26].

Our case–control study was designed to test the hypothesis that lower SES and linguistic isolation, measured by use of an interpreter, are associated with increased risk of UTI. For the case–control study, we randomly selected 1 UTI event per year per patient. We then randomly selected and 1:2 frequency-matched KPSC and Sutter patients without a UTI event (ie, controls) during that year based on age category (0–14, 15–24, 25–44, 45–64, 65–84, ≥85), sex, and year. UTI cases were eligible to serve as controls during years they had no UTI.

Our case–case study tested the hypothesis that lower SES and linguistic isolation are associated with increased risk of MDR UTI. The case–case study, therefore, consisted of all positive *E. coli* urine culture events. If multiple cultures occurred within a single UTI event, we analyzed just the first positive culture.

Sociodemographic Risk Factors

We used 2 variables to capture different facets of SES [27]: (1) Medicaid use for the UTI (cases) or health care (controls) encounter and (2) census tract–level socioeconomic deprivation [28]. We also assessed requiring an interpreter, a marker of linguistic isolation or immigration status. We assembled the deprivation index using the 2011–2015 American Community Survey [29]; a higher score indicated lower deprivation (see the Supplementary Methods for details). Medicaid use had minimal missingness (≤0.2%), and we assumed that an absence of information on requiring an interpreter meant that the individual did not require one.

Covariates

EHR data provided additional patient sociodemographics: age at time of health care encounter, sex, race/ethnicity (Non-Hispanic Asian or Pacific Islander, Black, White, Hispanic, and other or unknown), smoking status (yes, no, missing), marital status (married, domestic partner, common law; single; divorced, separated, widowed; and other or unknown), season (winter, Dec–Feb; spring, Mar–May; summer, June–Aug; fall; Sept–Nov) and year of encounter, average number of health care visits annually (combined frequency of outpatient [including virtual], inpatient, and emergency), average number of antibiotic orders annually, Charlson Comorbidity Index (CCI) [30], diagnosis of type 2 diabetes, and county of residence. For smoking status (at time of encounter), we treated missing values (9%) as informative, which we included in regression modeling as its own category. Census tract–level covariates were obtained from the 2011–2015 American Community Survey based on geocoded patient addresses and included population density [16] and percent agricultural workers (risk of antibiotic-resistant infection has previously been associated with residential proximity to livestock [8, 31]).

Statistical Analyses

First, we estimated the relative risk of having a UTI associated with each sociodemographic variable (Medicaid status [0/1], whether needed an interpreter [0/1], and area-level deprivation [first quartile vs all others]) using targeted minimum loss–based estimation [32]. This estimation approach fits both an exposure model conditional on covariates and an outcome model conditional on the exposure and covariates (described above), solves the efficient influence function such that it is doubly robust (meaning either model can be incorrect and still result in a consistent estimator), and involves a debiasing step that optimizes the bias–variance tradeoff for the particular effect of interest. We used an ensemble of machine learning algorithms in model fitting, where the weights of each algorithm optimize prediction [33]. We used generalized linear models, Bayesian generalized linear models, multivariate additive regression splines, extreme gradient boosting, and generalized additive models. Consistent with prior recommendations [34], we used observation-level weights to correct for bias induced by the case–control-matched design. Cases were given a weight equal to the overall probability of case status (ie, having a UTI, P(UTI = 1)). Controls were given a weight equal to: [P(UTI = 1)*P(UTI = 0 | matching variables)]/[2*P(UTI = 1 | matching variables)]. We also accounted for clustering of multiple observations within an individual in our efficient influence function–based variance estimation.

Second, we estimated the relative risk of having an MDR UTI as compared with a susceptible UTI that was associated with each sociodemographic variable (as operationalized above). We used targeted minimum loss–based estimation to estimate each relative risk using the sample ensemble of machine learning algorithms in model fitting and accounting for multiple observations within unique individual-in-variance estimation, but this time without observation-level weights.

Models for the main effects of Medicaid use, requiring an interpreter, and census tract–level socioeconomic deprivation each controlled for the other 2 factors. All analyses were stratified by health care system due to potentially significant differences in care provision, covariate measurement, and geography that might modify overall relationships. We performed analyses using R Statistical Software, version 3.5.1 (R Core Team; https://www.R-project.org/) and the following R packages: ltmle [35] and SuperLearner [33].

We conducted 2 secondary analyses. First, from our overall UTI sample, we identified cases of pyelonephritis (kidney infection) using the *ICD-9* code 590.x and the *ICD-10* code N10 and assessed risk factors for pyelonephritis and MDR pyelonephritis [36]. Second, we evaluated the association between the 3 sociodemographic variables and risk of MDR using UTI with any antimicrobial resistance (AMR) as the reference category.

RESULTS

The study population included 450 612 KPSC and 150 740 Sutter Health *E. coli* UTI patients identified with diagnosis codes and positive cultures in the outpatient setting between 2015 and 2017 and 970 135 KPSC and 333 320 Sutter Health frequency-matched controls. The majority of UTI cases were female and never-smokers, and they were a median age of 49 years (Table 1). At both KPSC and Sutter, UTI cases had more health care visits, a higher prevalence of type 2 diabetes, higher CCI scores, and more annual antibiotic orders than controls. At both health systems, cases were more likely to use Medicaid than controls but had similar prevalence of interpreter use and resided in census tracts with similar levels of socioeconomic deprivation. We observed low correlations (Spearman $\rho < .2$) between the 3 sociodemographic variables of interest (Supplementary Table 1).

Prevalence of Antibiotic Resistance

There were 325 286 *E. coli* UTI cultures (10.4% MDR) from 222 097 KPSC patients and 99 691 *E. coli* UTI cultures (12.8% MDR) from 72 101 Sutter Health patients. At both KPSC and Sutter Health, MDR *E. coli* isolates were more common among older adults, Hispanic individuals, single individuals, and those with type 2 diabetes (Table 2). At KPSC, we saw no relationship between patient sex and MDR prevalence, but at Sutter Health, men contributed 12.3% of MDR *E. coli* isolates and just 6.7% of non-MDR isolates. We observed moderate increases in prevalence of MDR among *E. coli* isolates between 2015 and 2017, especially at KPSC, and slightly higher prevalence of MDR among *E. coli* isolates in the summer and fall (Table 2).

Approximately 50% of isolates from KPSC and Sutter were susceptible to all 7 tested antibiotics (Figure 1). Resistance prevalence and patterns were similar at KPSC and Sutter Health. Ampicillin resistance was most common (44.7% and 40.6%, respectively), and nitrofurantoin resistance was least common (0.7% and 1.0%, respectively) (Table 3). Resistance to ampicillin alone (~13% of isolates) and resistance to ampicillin and TMP-SMZ together (~10% of isolates) were the most common resistance patterns (Figure 1). The most common MDR pattern was ampicillin, TMP-SMZ, and ciprofloxacin (~2.9% of isolates).

Sociodemographic Risk Factors for UTI

In adjusted models, we observed small negative associations between the 3 sociodemographic variables of interest and risk of UTI (Figure 2A). For example, Medicaid use was associated with a 0.9% and 0.6% reduction in risk of being a UTI case vs control at KPSC and Sutter Health, respectively.

Table 1. Demographic characteristics of Outpatient Urinary Tract Infection Cases and Controls at KPSC and Sutter Health, 2015–2017

	KPSC		Sutter	
	UTI Cases	Controls	UTI Cases	Controls
	n = 450 612	n = 970 135	n = 150 740	n = 333 320
Age, median (IQR), y	49 (31 to 66)	50 (32 to 66)	49 (32 to 68)	49 (32 to 67)
Sex				
Female	391 982 (87.0)	839 787 (86.6)	135 855 (90.1)	299 914 (90.0)
Male	58 630 (13.0)	130 348 (13.4)	14 885 (9.9)	33 406 (10.0)
Race/ethnicity				
Non-Hispanic				
Asian/PI	38 605 (8.6)	114 419 (11.8)	19 580 (13.0)	56 572 (17.0)
Black	38 317 (8.5)	94 188 (9.7)	5097 (3.4)	12 180 (3.7)
White	171 667 (38.1)	360 342 (37.1)	86 336 (57.3)	181 179 (54.4)
Hispanic	191 577 (42.5)	371 283 (38.3)	22 970 (15.2)	40 267 (12.1)
Other[a]	10 446 (2.3)	29 903 (3.1)	16 757 (11.1)	43 122 (12.9)
Smoking status				
Never	311 722 (69.2)	624 893 (64.4)	103 958 (69.0)	223 537 (67.1)
Former	86 697 (19.2)	162 619 (16.8)	31 651 (21.0)	60 987 (18.3)
Current	22 921 (5.1)	46 908 (4.8)	9931 (6.6)	17 488 (5.2)
Missing	29 272 (6.5)	135 715 (14.0)	5200 (3.4)	31 308 (9.4)
Marital status				
Married, domestic partner, common law	214 010 (47.5)	437 368 (45.1)	73 465 (48.7)	164 918 (49.5)
Single	135 456 (30.1)	303 447 (31.3)	42 937 (28.5)	92 522 (27.8)
Divorced, separated, widowed	66 864 (14.8)	122 007 (12.6)	22 605 (15.0)	41 702 (12.5)
Other or unknown	34 282 (7.6)	107 313 (11.1)	11 733 (7.8)	34 178 (10.3)
Season of encounter[b]				
Spring	108 627 (24.1)	235 555 (24.3)	36 719 (24.4)	82 115 (24.6)
Summer	116 221 (25.8)	235 620 (24.3)	38 418 (25.5)	79 482 (23.8)
Fall	118 739 (26.4)	247 636 (25.5)	38 823 (25.8)	85 686 (25.7)
Winter	107 025 (23.8)	251 324 (25.9)	36 780 (24.4)	86 037 (25.8)
Individuals with multiple UTIs		N/A		N/A
Year of first UTI				
2015	185 914 (41.3)		65 046 (43.2)	
2016	140 102 (31.1)		46 571 (30.9)	
2017	124 596 (27.7)		39 123 (26.0)	
UTI event diagnosis				
Diagnosis code with antibiotic	257 600 (57.2)		86 760 (57.6)	
E. coli culture	193 012 (42.8)		63 980 (42.4)	
No. of antibiotic orders per year, mean (SD)	0.9 (1.1)	0.4 (0.8)	0.6 (0.9)	0.2 (0.6)
No. of health care visits in the year before UTI or index date, median (IQR)	15 (6 to 30)	10 (3 to 21)	11 (4 to 23)	6 (2 to 14)
Charlsoxn Comorbidity Index, mean (SD)	1.1 (1.9)	0.8 (1.5)	0.5 (1.2)	0.3 (0.9)
Type 2 diabetes				
No	383 603 (85.1)	856 645 (88.3)	135 242 (89.7)	308 667 (92.6)
Yes	67 009 (14.9)	113 490 (11.7)	15 498 (10.3)	24 653 (7.4)
Medicaid use				
No	407 066 (90.3)	891 247 (91.9)	139 269 (92.4)	311 371 (93.4)
Yes	43 282 (9.6)	78 410 (8.1)	11 012 (7.3)	18 966 (5.7)
Missing	264 (0.1)	478 (<0.1)	459 (0.3)	2983 (0.9)
Required interpreter				
No	408 732 (90.7)	881 812 (90.9)	146 030 (96.6)	321 766 (96.5)
Yes	41 382 (9.2)	86 092 (8.9)	4393 (2.9)	10 155 (3.0)
Missing	496 (0.1)	2231 (0.2)	317 (0.2)	1399 (0.4)
Census tract sociodemographics,[c] median (IQR)				
Socioeconomic deprivation[d]	0.2 (–1.2 to 1.6)	0.3 (–1.2 to 1.6)	1.1 (–0.3 to 2.6)	1.4 (–0.1 to 3.0)
Agricultural workers, %	0.3 (0 to 1.0)	0.3 (0 to 1.0)	0.5 (0 to 2.0)	0.4 (0 to 1.7)
Population density, individuals/km^2	2642 (1354 to 4124)	2662 (1362 to 4148)	1964 (713 to 3030)	2052 (754 to 3178)

Abbreviations: IQR, interquartile range; KPSC, Kaiser Permanente Southern California; PI, Pacific Islander; UTI, urinary tract infection.

[a]Includes Native American or Alaskan, multiple races/ethnicities, other, and unknown.

[b]Seasons were defined as: Winter, Dec–Feb; Spring, Mar–May; Summer, Jun–Aug; Fall, Sept–Nov.

[c]Census tract–level sociodemographic variables from the 2011–2015 American Community Survey.

[d]Lower values indicate higher socioeconomic deprivation; the index was calculated from the following census tract–level variables: median household income, median value of owner-occupied housing units, proportion of households receiving interest, dividend, or net rental income, educational attainment (the proportion of adults ≥25 years of age with a high school diploma and the proportion of adults ≥25 years of age with completed college education), and occupation (the proportion of people employed in management, business, science, and arts occupations).

Table 2. Demographic Characteristics Associated With Outpatient MDR and Non-MDR Urine *E. coli* Isolates From KPSC and Sutter Health, 2015–2017

	KPSC		Sutter	
	MDR	Not MDR	MDR	Not MDR
	n = 33 838	n = 291 448	n = 12 793	n = 86 898
Age, median (IQR), y	62 (45 to 74)	58 (35 to 73)	66 (45 to 79)	54 (34 to 72)
Sex				
Female	28 706 (84.8)	247 373 (84.9)	11 218 (87.7)	81 038 (93.3)
Male	5132 (15.2)	44 075 (15.1)	1575 (12.3)	5860 (6.7)
Race/ethnicity				
Non-Hispanic				
Asian/PI	2673 (7.9)	22 773 (7.8)	1845 (14.4)	10 226 (11.8)
Black	2059 (6.1)	22 283 (7.6)	304 (2.4)	2422 (2.8)
White	12 222 (36.1)	126 298 (43.3)	7391 (57.8)	52 308 (60.2)
Hispanic	16 380 (48.4)	114 627 (39.3)	2041 (16.0)	12 885 (14.8)
Other[a]	504 (1.5)	5467 (1.9)	1212 (9.5)	9057 (10.4)
Smoking status				
Never	22 993 (68.0)	196 354 (67.3)	8233 (64.4)	58 928 (67.8)
Former	8215 (24.3)	68 063 (23.4)	3422 (26.7)	19 864 (22.9)
Current	1655 (4.9)	14 210 (4.9)	799 (6.2)	5305 (6.1)
Missing	975 (2.9)	12 821 (4.4)	339 (2.6)	2801 (3.2)
Marital status				
Married, domestic partner, common law	16 985 (50.2)	140 951 (48.4)	6086 (47.6)	41 827 (48.1)
Single	6995 (20.7)	74 778 (25.7)	2729 (21.3)	22 861 (26.3)
Divorced, separated, widowed	8147 (24.1)	58 260 (20.0)	3094 (24.2)	15 789 (18.2)
Other or unknown	1711 (5.1)	17 459 (6.0)	884 (6.9)	6421 (7.4)
Season of encounter[b]				
Spring	8347 (24.7)	71 879 (24.7)	3200 (25.0)	21 206 (24.4)
Summer	8597 (25.4)	74 868 (25.7)	3223 (25.2)	22 441 (25.8)
Fall	8663 (25.6)	75 204 (25.8)	3210 (25.1)	22 333 (25.7)
Winter	8231 (24.3)	69 497 (23.8)	3160 (24.7)	20 918 (24.1)
Year of culture				
2015	10 016 (29.6)	89 995 (30.9)	4231 (33.1)	28 584 (32.9)
2016	11 504 (34.0)	97 112 (33.3)	4230 (33.1)	28 676 (33.0)
2017	12 318 (36.4)	104 341 (35.8)	4332 (33.9)	29 638 (34.1)
No. of antibiotic orders per year, mean (SD)	2.0 (1.7)	1.3 (1.4)	1.6 (1.5)	0.9 (1.1)
No. of health care visits in the year before UTI or index date, median (IQR)	27 (10 to 49)	21 (8 to 40)	21 (8 to 39)	13 (5 to 28)
Charlson Comorbidity Index, mean (SD)	2.0 (2.4)	1.6 (2.2)	0.5 (1.2)	0.3 (0.9)
Type 2 diabetes				
No	25 127 (72.5)	237 358 (79.6)	135 242 (89.7)	308 667 (92.6)
Yes	9518 (27.5)	60 837 (20.4)	15 498 (10.3)	24 653 (7.4)
Medicaid use				
No	30 308 (87.5)	268 985 (90.2)	12 141 (94.9)	81 463 (93.7)
Yes	4296 (12.4)	28 895 (9.7)	622 (4.9)	5268 (6.1)
Missing	39 (0.1)	303 (0.1)	30 (0.2)	167 (0.2)
Required interpreter				
No	28 082 (83.0)	265 512 (91.1)	12 099 (94.6)	84 414 (97.1)
Yes	5715 (16.9)	25 616 (8.8)	672 (5.3)	2301 (2.6)
Missing	41 (0.1)	320 (0.1)	22 (0.2)	183 (0.2)
Census tract sociodemographics,[c] median (IQR)				
Socioeconomic deprivation[d]	0.1 (–1.4 to 1.5)	0.3 (–1.1 to 1.7)	1.0 (–0.5 to 2.6)	1.1 (–0.3 to 2.7)
Agricultural workers, %	0.3 (0 to 1.0)	0.3 (0 to 1.0)	0.6 (0 to 2.4)	0.5 (0 to 2.0)
Population density, individuals/km^2	2800 (1443 to 4321)	2527 (1316 to 4018)	1966 (776 to 2993)	1949 (711 to 2979)

Abbreviations: IQR, interquartile range; KPSC, Kaiser Permanente Southern California; PI, Pacific Islander; UTI, urinary tract infection.

[a]Includes Native American or Alaskan, multiple races/ethnicities, other, and unknown.

[b]Seasons were defined as: Winter, Dec–Feb; Spring, Mar–May; Summer, Jun–Aug; Fall, Sept–Nov.

[c]Census tract–level sociodemographic variables from the 2011–2015 American Community Survey.

[d]Lower values indicate higher socioeconomic deprivation; the index was calculated from the following census tract–level variables: median household income, median value of owner-occupied housing units, proportion of households receiving interest, dividend, or net rental income, educational attainment (the proportion of adults ≥25 years of age with a high school diploma and the proportion of adults ≥25 years of age with completed college education), and occupation (the proportion of people employed in management, business, science, and arts occupations).

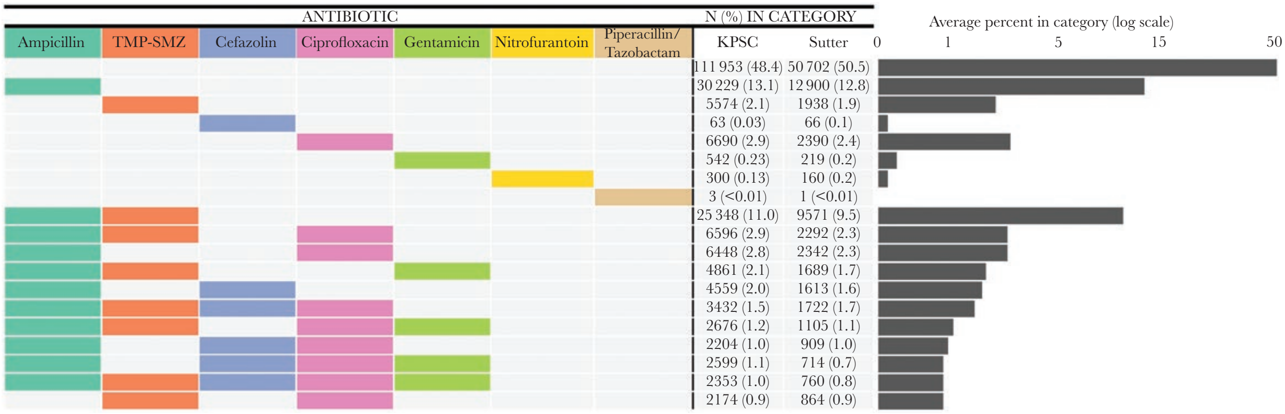

Figure 1. The most common outpatient urine *E. coli* isolate nonsusceptibility patterns at Kaiser Permanente Southern California and Sutter Health, 2015–2017. The first 7 rows show percent nonsusceptible (gray bar) to single antibiotics (colored rectangle), and the next 11 rows show percent nonsusceptible (gray bar) to combinations of antibiotics (colored rectangles). The number of isolates included includes those with any antibiotic susceptibility testing at each site.

This translated into ~7 fewer UTI cases per 1000 KPSC patients (95% CI, −9 to −5) and 5 fewer UTI cases per 1000 Sutter Health patients (95% CI, −8 to −2) due to Medicaid (Supplementary Figure 3A).

Sociodemographic Risk Factors for MDR *E. coli* UTI

Medicaid and requiring an interpreter were associated with an 8% and 36% increase in risk of MDR *E. coli* UTI at KPSC and a 9% and 28% increase at Sutter Health, respectively (Figure 2B). This translates into an absolute increase in risk of 8–33 additional MDR *E. coli* UTI cases per 1000 KPSC or Sutter Health patients (Supplementary Figure 3). High census tract–level deprivation was also associated with increased risk of MDR *E. coli* UTI at KPSC (RR, 1.04; 95% CI, 1.02 to 1.06) and Sutter Health (RR, 1.14; 95% CI, 1.10 to 1.17). In secondary analyses, we compared MDR UTI with AMR UTI and in general observed similar, though slightly attenuated, effect estimates (Supplementary Table 2).

Sociodemographic Risk Factors for Pyelonephritis

At KPSC, we identified 3076 episodes of outpatient pyelonephritis among 3011 patients (prevalence, 0.5% of total UTI), while at Sutter Health we identified 1770 episodes of outpatient pyelonephritis among 1612 patients (prevalence, 0.9% of total UTI). At both KPSC and Sutter Health, Medicaid use was associated with increased risk of having pyelonephritis vs not (RR, 1.13; 95% CI, 1.01 to 1.28; and RR, 1.18; 95% CI, 1.02 to 1.36, respectively). At KPSC, but not at Sutter, requiring an interpreter (RR, 1.19; 95% CI, 1.02 to 1.38) and high community deprivation (RR, 1.17; 95% CI, 1.09 to 1.26) were also associated with increased risk of having pyelonephritis (Supplementary Table 3). At KPSC, there were 1412 pyelonephritis cases with *E. coli* cultures (n = 172 [12.2%] were MDR) and 841 (n = 64 [7.6%] were MDR) at Sutter Health, not enough to perform regression analyses. Supplementary Table 4 shows counts of MDR by the 3 sociodemographic variables of interest; at KPSC, pyelonephritis cases who required an interpreter or lived in a high-deprivation community were more likely to be caused by MDR *E. coli,* and at Sutter we did not observe differences in MDR status by sociodemographic variables.

DISCUSSION

In this cross-sectional study from 2015 to 2017 on >600 000 outpatient UTI cases from 2 large health care systems in

Table 3. Nonsusceptibility of Outpatient Urine *E. coli* Isolates to Individual Antibiotics at KPSC and Sutter Health, 2015–2017

	KPSC (n = 325 344)		Sutter Health (n = 99 691)	
Antibiotic	Tested, No. (%)	Nonsusceptible of Tested, No. (%)	Tested, No. (%)	Nonsusceptible of Tested, No. (%)
Ampicillin	226 134 (69.5)	100 977 (44.7)	97 906 (98.2)	40 431 (40.6)
TMP-SMZ	226 079 (69.5)	58 322 (25.8)	97 875 (98.2)	22 419 (22.5)
Cefazolin	226 128 (69.5)	20 681 (9.1)	97 710 (98.0)	1981 (8.1)
Ciprofloxacin	226 135 (69.5)	38 660 (17.1)	97 909 (98.2)	15 238 (15.6)
Gentamicin	226 129 (69.5)	18 187 (8.0)	97 910 (98.0)	6724 (6.9)
Nitrofurantoin	226 108 (69.5)	1684 (0.7)	97 739 (98.0)	937 (1.0)
Piperacillin/tazobactam	226 032 (69.5)	4436 (2.0)	93 797 (94.1)	911 (1.0)

Abbreviations: KPSC, Kaiser Permanente Southern California; TMP-SMZ, trimethoprim/sulfamethoxazole.

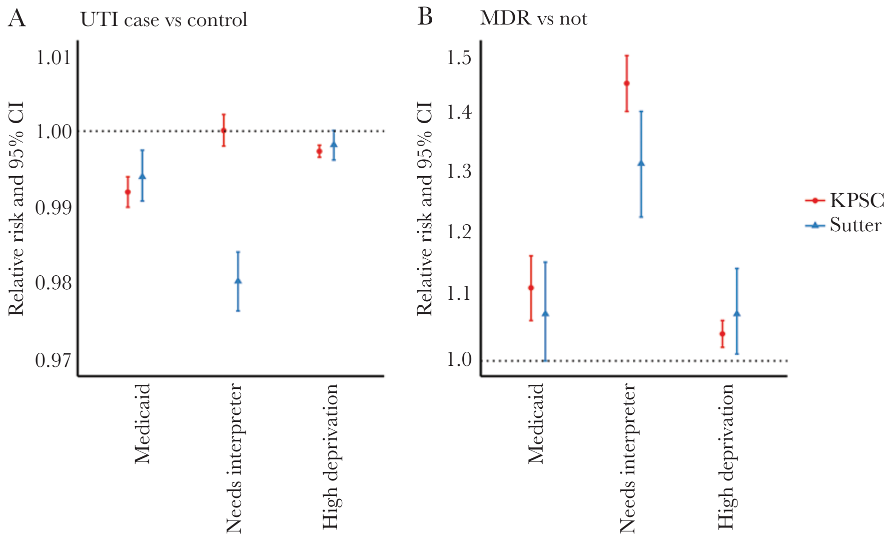

Figure 2. Relative risk of (A) outpatient urinary tract infection (UTI) and (B) multidrug-resistant (MDR) outpatient *E. coli* UTI by sociodemographic risk factors at Kaiser Permanente Southern California (KPSC) and Sutter Health, 2015–2017. Models were adjusted for patient age, sex, race/ethnicity, smoking status, marital status, season, year, annual health care visits and antibiotic orders, Charlson Comorbidity Index, type 2 diabetes, percent agricultural workers, and population density. Models for the main effects of Medicaid use, requiring an interpreter, and census tract–level socioeconomic deprivation each controlled for the other 2 factors. High deprivation was defined as living in a census tract in the first quartile of the deprivation index (score ≤–1.18 for KPSC or score ≤–0.33 for Sutter Health).

California, we observed a modest negative association between lower individual- and community-level SES and requiring an interpreter and UTI. Conversely, we found increased risk of MDR *E. coli* UTI consistently associated with Medicaid use, requiring an interpreter, and census tract–level deprivation. While multiple studies discuss the association between low SES and increased risk of antibiotic-resistant infection generally [15, 16], few studies have focused on antibiotic-resistant UTI [8, 17, 18, 21], and none have taken place in the United States.

Although lower than some national estimates, our rates of MDR UTI are consistent with other publications, ranging from 10.4% at KPSC to 12.8% at Sutter Health. Data from the Veterans Affairs Healthcare System from 2009 to 2013 on nearly 300 000 urine *E. coli* isolates (78% from men) found outpatient MDR rates between 3% to 7%, depending on the MDR definition used [37]. Sanchez et al. defined MDR as resistance to ≥3 agents and found a 17% prevalence of MDR in 2010 among >30 000 urine *E. coli* isolates from nationwide Surveillance Network data [5]. Different populations or slightly different definitions may explain the lower prevalence of MDR in California.

Prior studies have mainly focused on community-level SES factors as they relate to AMR infection. Literature from Europe consistently reports increased risk of any MDR infection related to living in a higher-deprivation community [15, 38], with 2 studies pointing to area-level deprivation as a risk factor for MDR UTI specifically [8, 17]. Another study from Australia, however, found no association between relative disadvantage and ceftriaxone-resistant UTI [18]. Increased antibiotic prescribing has been noted in more deprived neighborhoods [20], which could contribute to differences in prevalence of antibiotic-resistant infections.

Our findings suggest that individual-level SES and requiring an interpreter are important risk factors for MDR UTI and pyelonephritis. Use of Medicaid appeared to increase absolute risk of MDR UTI by ~10 cases per 1000 patients in both study populations, and requiring an interpreter was related to a 45% (KPSC) and a 31% (Sutter) increased risk of MDR UTI. Use of Medicaid was also associated with a 13% (KPSC) and 18% (Sutter) increased risk of pyelonephritis. To our knowledge, just 1 prior study, an analysis of pregnant women in India that did not assess resistance [21], has evaluated individual-level SES as a risk factor for UTI or bacteriuria. However, several studies have reported individual-level SES as a risk factor for other AMR infections in the United States [16].

SES may influence risk of MDR UTI through multiple pathways. We speculate that factors correlated with low individual- and area-level SES such as crowded living conditions or occupational and agricultural exposures may partially explain our findings [8, 14, 15, 18]. In our study population, we observed low correlation between Medicaid, community deprivation, and requiring an interpreter, indicating that these factors capture different facets of sociodemographic experience. Importantly, we hypothesize that requiring an interpreter proxies for extrinsic differences in exposure and not biological differences by race/ethnicity.

Requiring an interpreter may indicate differential exposure due to immigration status, linguistic isolation, antibiotic use or exposure, access to care (although we adjusted models for number of prior health care visits), recent travel or interaction with those who have traveled, diet, or other factors. In Australia, Chua et al. found increased risk of ceftriaxone-resistant UTI in regions with higher percentages of residents born in Southern and Eastern European, Middle Eastern, Asian, and North and Sub-Saharan African countries [18]. Travel to endemic areas, such as Asia, has previously been related to increased risk of MDR UTI [10].

With respect to UTI overall, we observed a slight reduction in risk related to sociodemographic factors. Research focused on pediatric populations in the United States [39] and Portugal [13] and pregnant women in India [21] has found increased risk of UTI related to lower individual- and area-level SES [21]. However, to our knowledge, no study has evaluated SES and UTI risk among nonpregnant adults. Related to other health conditions, studies among adults in high-income countries have reported mixed associations between SES and gastrointestinal infections [11], but increased odds of cold/influenza at lower levels of individual-level SES [40]. The observed protective effect of low SES and requiring an interpreter in our sample may reflect a reduced likelihood of these individuals seeking care for UTI, as uncomplicated UTI may resolve on its own. This mechanism is bolstered by our finding of consistently elevated risk of pyelonephritis (a more serious kidney infection) among lower-SES groups and those requiring an interpreter. Further, our analyses controlled for age, sex, type 2 diabetes, CCI, and prior antibiotic orders, factors that may explain the majority of variability in risk of UTI and account for much of the association between SES and UTI in our sample. Other unmeasured risk factors, such as sexual activity or consumption of chicken meat [9, 10], may be similar by sociodemographic group. These factors could explain the absence of SES disparities in UTI apparent for many other illnesses in the United States [41].

This study has limitations. While we included only outpatient-diagnosed UTI, we did not differentiate between health care– and community-acquired infection or include community-acquired UTI identified in the hospital setting (within the first 48 hours of hospitalization). This limits conclusions to the outpatient setting. Further, we compared MDR UTI to susceptible UTI; it is possible that risk factors for MDR overlap with those for any drug resistance. Because we relied on EHR data, we only captured patients who sought care, and we lacked access to a full suite of individual-level SES variables. While a prior study found Medicaid to reasonably proxy for individual-level SES [27], it did not capture all facets. In addition, requiring an interpreter may proxy for a range of factors that could differ by region. For example, in Southern California among Latino communities, requiring an interpreter may indicate differential health care access and frequent travel to countries with different antibiotic prescribing practices. Using data from 2 health care systems was a strength, although we could not harmonize these distinct populations and thus analyzed them separately. Differences in association observed by site may be explained by differences in patient populations, provider prescribing practices, or access to care (KPSC is an integrated health care system; Sutter is not). KPSC serves a much higher percentage of Hispanic patients, and ~9% of visits, vs 3% at Sutter, required an interpreter. Future studies that evaluate SES as a risk factor of MDR UTI across multiple health care systems or broad geographies should include stratified analyses to examine such differences.

In conclusion, individual- and area-level SES was related to increased risk of MDR UTI but not meaningfully associated with UTI overall. This suggests that clinicians seeing patients with UTI in the outpatient setting should consider geographic and sociodemographic characteristics of their patients when deciding to send a culture and selecting antibiotics. Improved capture of social determinants of health [42] and report-back to clinicians on geographic risk factors in the EHR can support this effort. Surveillance systems may also benefit from including SES data in their algorithms to target specific populations.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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