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Effect Of Patient-Level Characteristics On Fluoroquinolone Susceptibility

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EFFECT OF PATIENT-LEVEL CHARACTERISTICS ON FLUOROQUINOLONE SUSCEPTIBILITY

by

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ABSTRACT

Antimicrobial stewardship programs are becoming more widespread to combat antibiotic resistance. This study aimed to evaluate the influence of patient-level characteristics on fluoroquinolone susceptibly among five gram-negative isolates to help better their implementation. We performed a retrospective analysis of patients over the age of 18 for five gram-negative isolates (*Acinetobacter species, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa*). We utilized Cox proportional hazards to determine the risk of patient-level characteristics, for both hospital and community-acquired infections, on fluoroquinolone resistance between 2016 and 2019. The population sample consisted of 8,285 patients receiving fluoroquinolones for at least one of the five organisms with 1,251 (15%) receiving FQ for more than one organism. In total, there were 12,055 cultures were positive for one of the organisms of interest. The model was adjusted for significant crude variables. There were 8,610 community-acquired infections (CAI), after adjustments females when compared with males saw a decrease risk of resistant *E. coli*. All ages when compared with 18-29 had an increased risk of resistant *E. coli*. Patients admitted from a physician's office with an *Acinetobacter* species infection had a decreased risk of FQ resistance, while patients admitted through a skilled nursing facility had an increased risk of resistant *E. coli, K.*

pneumoniae, and P. aeruginosa compared to those admitted not admitted through a healthcare facility. Several comorbidities, including chronic pulmonary disease, hemi or paraplegia, and patients with renal disease saw increased risks across varied organisms for FQ resistance. There were 3,445 hospital-acquired infections (HAI), after adjustments ages 30-39 and 40-49 when compared with 18-29 had an increased risk of resistance for *P. aeruginosa*. Patients with a length of stay of four or more weeks had an increased risk of resistant *K. pneumoniae* when compared with 2-3 week stay. Patients with chronic pulmonary disease or hemi or paraplegia had increased risks across various organisms. We have demonstrated several patient characteristics for both community and hospital-acquired infections that may increase the risk of FQ resistance among gram-negative isolates. These factors should be considered in the implementation of antimicrobial stewardship programs.

Keywords: fluoroquinolones, gram-negative, patient-characteristics

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Introduction

Antibiotics are imperative to treat infectious diseases; however, inappropriate antibiotic use can result in organisms becoming resistant. Specifically, their overuse can result in not only increased antibiotic resistance but also increased costs and incidence of side effects.[1] Antibiotic resistance can occur through multiple mechanisms (e.g., genetic mutations or DNA transfer) that can result in the antibiotic being ineffective on the organism.[2] The Centers for Disease Control estimates that more than 2.8 million antibiotic-resistant infections occur each year in the United States, resulting in 35,000 deaths.[3]

Fluoroquinolones (FQs) are an important class of antibiotics used to treat both community-acquired and hospital-acquired infections.[4] They are one of the most commonly prescribed antibiotics in the United States.[5,6] However, they are often prescribed in situations where antibiotics should not be used or FQs are not appropriate.[7,8] Gram-negative organisms were the primary focus of early FQs, but broad use has allowed for increased resistances.[9] FQ resistant *Escherichia coli* has been seen in nearly half of the World Health Organizations member states.[10] FQ over-prescriptions can result in increased morbidities such as urinary tract infections [11,12] as well as increased mortality through FQ-resistant infections.[13]

Antimicrobial stewardship programs aim to improve the utilization of antibiotics by reducing inappropriate use and dosages of antibiotics with the goal to improve patient susceptibility and reduce adverse health effects.[14] Many studies have demonstrated

improved outcomes after the implementation of an antimicrobial stewardship program.[15-18] An antimicrobial stewardship program restricting the use of FQs found improvements in the rate of susceptibility for *Acinetobacter species*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*; however, this study was limited by the use of aggregate data, and therefore susceptible to the aggregation bias (i.e., associations at the aggregate level may not hold at the person-level).[19] Patient characteristics have been demonstrated to influence antibiotic susceptibility. Recent studies have shown age as an important factor for antibiotic resistance with older patient having increased resistant infections. [20,21] Similarly, a higher Charlson comorbidity score was independently associated with an increase in antibiotic resistance.[22] Both community and hospital-acquired infections will need to be considered independently as there may be distinct differences in the risk of antibiotic resistance. [23,24] Community antibiotic use was associated with increased risk of resistant *E. coli*.[25,26] Additionally, a study of *Klebsiella pneumoniae* found higher rates of resistance among hospital-acquired infections when compared with community and healthcare associated infections.[27] With Antimicrobial stewardship programs becoming more widespread it is crucial to understand if specific patient characteristics are increasing the risk of antibiotic resistance. Therefore, we aimed to evaluate the influence of patient-level characteristics on fluoroquinolone susceptibility among five gram-negative isolates.

METHODS

Setting and Design

We performed a retrospective analysis of inpatients over the age of 18 at the University of Alabama at Birmingham (UAB) Hospital—a large, academic, tertiary-care medical center—who had a positive bacteria culture between 2016 and 2019. Five gram-negative isolates (*Acinetobacter species*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa)* were collected from cultures derived from several body sites including the blood, skin, respiratory tract, or urine. The organisms were categorized as either resistant or susceptible to the antibiotic class fluoroquinolones, which consisted of the two antibiotics ciprofloxacin and levofloxacin. If the same organism was collected multiple times within a two-month period from the same patient, we only included the first occurrence of the organism. Similarly, if conflicting susceptibility results of the same organism were reported for a patient on the same collection date, the organism was classified as resistant. In the analysis, patients with multiple organisms were analyzed for each organism separately. The infections were considered hospital-acquired if the organisms were cultured from a sample taken 72 or more hours after the patient's hospital admission date and community-acquired if a positive culture was taken prior to 72 hours. To determine which organisms the patient may have, the patient sample is placed on a culture plate that allows all five organisms to grow. Once there is bacterial growth, the sample can be further tested to determine the type of organism. To determine susceptibility, the minimum inhibitory concentration (MIC) for the five isolates was determined by Microscan (Beckman Coulter, Carlsbad, CA). The United States Clinical and Laboratory Standards Institute guidelines were used

to determine susceptibility breakpoints by microscan MIC breakpoints.

For community-acquired infections, the CDC's Social Vulnerability Index (SVI) was used to determine community-level characteristics at the census-tract level.[28] The SVI uses the United States census tract to collect data and determine the vulnerability in subdivisions of counties. Social vulnerability is made up of factors, including social conditions, poverty levels, vehicle access, or household environment that help illuminate factors influencing how a community would respond to a hazardous event. We utilized the SVI to analyze the patient community's percentage of housing with 10 or more units and housing with more than one person per room. In addition, we used percentile percentage rankings, between 0 and 1 with 1 being more vulnerable, to determine patient communities below the poverty estimate and without a high school diploma. The percentages and rankings were further categorized by their quartiles for analysis. We also used admission source to determine how the patient was admitted. The patient may have been admitted from a non-healthcare facility, physician's office, skilled nursing facility, or other facility (e.g. Court/law, healthcare facility, ambulatory surgery center).

For hospital-acquired infections, the length-of-stay in the hospital was measured in days and categorized as fewer than eight days, 8-14 days, 15-21 days, and 22 or more days. For community and hospital-acquired, the Charlson comorbidity index was used to determine the burden of comorbidities in this population for the bivariate analysis. Comorbidities were identified by ICD-10 codes and then weights were applied to determine the Charlson score. Comorbidities included myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, peptic ulcer disease, mild liver disease, diabetes

without complication, diabetes with complication, hemi/paraplegia, renal disease, malignancy, moderate or severe liver disease, metastatic solid tumor, and AIDS/HIV.[29] The Charlson score was categorized into four groups: 0, 1-2, 3-5, and 6 or more. Due to small population size races, other than White and Black, were categorized as Other race. Similarly, age was categorized into deciles beginning with 18 and 19, which were combined with the 20-29 group, and ending with age 80 or older.

Statistical Analysis

The chi-square test was used to analyze patient-level characteristics by susceptibility to fluoroquinolones. If the patient had any resistant organisms to fluoroquinolone, they were considered resistant for the purposes of the bivariate analyses. For multivariable analyses, the analyses were performed at the organism-level to evaluate the influence of patient characteristics per organism on fluoroquinolones. To obtain risk of resistance to fluoroquinolone, we used a Cox proportional hazard assuming similar time at risk for all variables. We adjusted the model for all significant variables in bivariate analyses. Collinearity diagnostics were performed by estimating variable inflation factors all of which were less than two; therefore, we have no evidence of meaningful collinearity issues. For the community-acquired model sex, race, age, percentile percentage of persons below the poverty estimate, and admission source. We chose to use individual comorbidities for the model rather than the Charlson score: myocardial infarction, dementia, chronic pulmonary disease, diabetes with complication, hemi-or-paraplegia, renal disease, and malignancies were added. While the hospital-acquired model included age, length of stay. Similarly, we chose to use individual comorbidities rather than the Charlson score: congestive heart failure, chronic pulmonary

disease, mild liver disease, diabetes with complication, hemi-or-paraplegia, and renal disease were analyzed. For all analyses, $p < 0.05$ was considered statistically significant, and SAS 9.4 (SAS Institute, Cary NC) was used.

RESULTS

The population sample consisted of 8,285 patients receiving fluoroquinolones for at least one of the five organisms with 1,251 (15%) receiving FQ for more than one organism. In total, there were 12,055 cultures were positive for one of the organisms of interest. Of these cultures, 45% (n=5,425) were positive for *Escherichia coli,* 23% (n=2,811) for *Klebsiella pneumoniae,* 21% (n=2,541) for *Pseudomonas aeruginosa*, 8% (n=953) for *Enterobacter cloacae*, and 3% (n=326) for *Acinetobacter* species.

Of the total patients, 71% had a community-acquired infection. For community-acquired infections, there were more females with more being susceptible to FQs (65%) than resistant (60%) (p=0.0002) (Table 1). There were no differences between susceptible and resistant for race; however, patients with a resistant organism were more often aged 60 to 69 (p=0.002). There were differences among admission source with 79% of susceptible and 74% of resistant patients admitted from a non-healthcare facility (p<.0001). Patients with a Charlson score of zero were more often susceptible (23%) than resistant (16%) while patients with a score of six or greater were more often resistant (27%) than susceptible (23%) to FQs (p <.0001). Those with a myocardial infarction were more often susceptible (16%) than resistant (14%) (p=0.03). However, patients were more often resistant with congestive heart failure (23% vs. 19%; p=0.001), peripheral vascular disease (9% vs. 7%; p=0.01), cerebrovascular disease (10% vs. 8%; p=0.01),

dementia (11% vs. 8%; p=0.002), chronic pulmonary disease (24% vs. 20%; p=0.003), diabetes with chronic complication (19% vs. 16%; 0.005), hemi or paraplegia (10% vs. 4%; p<.0001), or renal disease (26% vs. 21%; p<.0001) than susceptible to FQs.

For hospital-acquired infections, both susceptible and resistant patients were more often male, White, and age 60-69; however, no differences between susceptibility and resistance to FQs were significant (Table 2). A larger portion of patients had a length of stay of at least four weeks. Patients were more often resistant (44%) than susceptible (31%) with a length of stay of at least four weeks. There were no significant differences between resistance and susceptibility for Charlson comorbidity scores. However, patients were more often resistant with myocardial infarction (22% vs. 18%; p=0.05), congestive heart failure (29% vs. 24%; p=0.01), chronic pulmonary disease (27% vs. 21%; p=0.003), diabetes with chronic complications (20% vs. 15%; p=0.002), or renal disease (28% vs. 21%; p=0.001) than susceptible. However, patients with a metastatic solid tumor were more often susceptible (6%) than resistant (4%) to FQs (p=0.02).

Table 1. Patient characteristics by any organism resistance to fluoroquinolones among community-acquired infections

CHARACTERISTICS	SUSCEPTIBLE (n=4028) N (%)	RESISTANT (n=1855) N (%)	P-value
Sex			0.0002
Female	2607 (65)	1106 (60)	
Race			0.82
White	2193 (54)	1009 (54)	
Black	1673 (42)	765 (41)	
Other races	162 (4)	81 (4)	
Age			0.002
18-29	387 (10)	122 (7)	
30-39	353 (9)	162 (9)	
40-49	413 (10)	186 (10)	
50-59	732 (18)	315 (17)	
60-69	829 (21)	437 (24)	
70-79	674 (17)	335 (18)	
≥ 80	640 (16)	298 (16)	
Admission Source			<.0001
Non-healthcare facility	3192 (79)	1381 (74)	
Physician's office	706 (18)	319 (17)	
Skilled nursing facility	93 (2)	131 (7)	
Other	37 (1)	24 (1)	
PP below poverty estimate			0.16
0.0-0.25	1258 (31)	548 (30)	
0.26-0.50	905 (22)	461 (25)	
0.51-0.75	808 (20)	381 (21)	
0.76-1.0	1057 (26)	465 (25)	
PP without HS diploma			0.94
0.0-0.25	1340 (33)	484 (26)	
0.26-0.50	1034 (26)	433 (23)	
0.51-0.75	969 (24)	316 (17)	
0.76-1.0	684 (17)	621 (33)	
Percent of housing with ≥ 10 units			0.20
0.0-2.9	1945 (48)	890 (48)	
3.0- 9.9	999 (25)	496 (27)	
≥ 10	1084 (27)	469 (25)	
Percent of housing >1 per room			0.34
0.0-1.1	2002 (50)	895 (48)	
1.2-2.3	1016 (25)	462 (25)	
≥ 2.4	1010 (25)	498 (27)	
Charlson index			<.0001
0	928 (23)	303 (16)	
1-2	1235 (31)	568 (31)	
3-5	919 (23)	478 (26)	
6+	946 (23)	506 (27)	
Comorbidities			
Myocardial infarction	651 (16)	259 (14)	0.03
Congestive heart failure	750 (19)	418 (23)	0.001
Peripheral vascular disease	276 (7)	161 (9)	0.01
Cerebrovascular disease	311 (8)	180 (10)	0.01
Dementia	335 (8)	200 (11)	0.002
Chronic pulmonary disease	813 (20)	438 (24)	0.003
Rheumatic disease	173 (4)	75 (4)	0.66
Peptic ulcer disease	65 (2)	21 (1)	0.15
Mild liver disease	371 (9)	183 (10)	0.42
Diabetes without chronic complication	1041 (26)	508 (27)	0.21
Diabetes with chronic complication	642 (16)	351 (19)	0.005
Hemiplegia or paraplegia	148 (4)	192 (10)	<.0001
Renal disease	862 (21)	486 (26)	<.0001
Malignancy	484 (12)	203 (11)	0.23
Moderate or severe liver disease	104 (3)	45 (2)	0.72

Metastatic solid tumor	203 (5)	94 (5)	0.96
AIDS/HIV	57 (1)	25 (1)	0.84

P-values derived from Chi-square; PP=Percentile percentage, HS= High School, AIDS=acquired immunodeficiency syndrome, HIV= Human immunodeficiency virus

Table 2. Patient characteristics by any organism resistance to fluoroquinolones among hospital-acquired infections

CHARACTERISTICS	SUSCEPTIBLE (n=1748) N (%)	RESISTANT (n=654) N (%)	P-value
Sex			0.94
Female	773 (44)	288 (44)	
Race			0.93
White	1046 (60)	396 (61)	
Black	631 (36)	233 (36)	
Other races	71 (4)	25 (3)	
Age			0.18
18-29	161 (9)	49 (7)	
30-39	183 (10)	62 (9)	
40-49	200 (11)	96 (15)	
50-59	351 (20)	130 (20)	
60-69	432 (25)	154 (24)	
70-79	282 (16)	120 (18)	
≥ 80	139 (8)	43 (7)	
Length of Stay			<.0001
< 1 week	153 (9)	46 (7)	
1-2 weeks	429 (25)	122 (19)	
2-3 weeks	368 (21)	119 (18)	
3-4 weeks	261 (15)	78 (12)	
≥ 4 weeks	537 (31)	289 (44)	
Charlson index			0.13
0	319 (18)	100 (15)	
1-2	465 (27)	159 (24)	
3-5	408 (23)	170 (26)	
6+	556 (32)	225 (34)	
Comorbidities			
Myocardial infarction	323 (18)	144 (22)	0.05
Congestive heart failure	421 (24)	192 (29)	0.01
Peripheral vascular disease	208 (12)	75 (11)	0.77
Cerebrovascular disease	303 (17)	98 (15)	0.17
Dementia	93 (5)	34 (5)	0.91
Chronic pulmonary disease	371 (21)	176 (27)	0.003
Rheumatic disease	54 (3)	26 (4)	0.28
Peptic ulcer disease	48 (3)	24 (4)	0.24
Mild liver disease	166 (9)	69 (11)	0.44
Diabetes without chronic complication	471 (27)	190 (29)	0.30
Diabetes with chronic complication	264 (15)	134 (20)	0.002
Hemiplegia or paraplegia	232 (13)	84 (13)	0.78
Renal disease	372 (21)	182 (28)	0.001
Malignancy	279 (16)	97 (15)	0.50
Moderate or severe liver disease	76 (4)	30 (5)	0.80
Metastatic solid tumor	105 (6)	23 (4)	0.02
AIDS/HIV	22 (1)	5 (1)	0.31

P-values derived from Chi-square; AIDS=acquired immunodeficiency syndrome, HIV= Human immunodeficiency virus

Community-Acquired Infections

For community-acquired infections, there was a total of 8,610 community-acquired infections between 2016 and 2019. For crude results, females had a 21% decreased risk of resistant *E. coli* (RR: 0.79, 95% CI 0.71-0.87) and 32% decreased risk of resistant *K. pneumoniae* when compared with males (RR:0.68, 95% CI 0.55-0.84) (Table 3). When compared with 18 to 29-year-olds, ages 30 to 39 had a 37% increased risk of resistance (RR:1.37, 95% CI 1.06-1.76), ages 40 to 49 had a 38% increased risk resistance (RR: 1.38, 95% CI 1.08-1.77), ages 50 to 59 had a 55% increased risk resistance (RR:1.55, 95% CI 1.24-1.95), ages 60 to 69 had a 58% increased risk resistance (RR:1.58, 95% CI 1.27-1.96), ages 70 to 79 had a 65% increased risk resistance (RR:1.65, 95% CI 1.31-2.07), and ages 80 and over had a 60% increased risk resistance (RR: 1.60, 95% CI 1.27-2.00). Patients had a 17% increased risk of resistant *E. coli* when admitted through a physician's office when compared with a non-healthcare facility (RR: 1.17; 95% CI 1.02-1.35). Similarly, patients admitted through a skilled nursing facility had nearly a 3-fold increased risk for resistant *E. cloacae* (RR:2.87, 95% CI 1.20-6.86), 64% increased risk for resistant *E. coli* (RR:1.64, 95% CI 1.34-2.02), 2.3-fold increased risk for resistant *K. pneumoniae* (RR:2.27, 95% CI 1.60-3.23), and 54% increased risk for *P. aeruginosa* when compared with a non-healthcare facility (RR:1.54, 95% CI 1.12-2.12). There were no other significant results from other admission sources or other isolates.

Patients in communities with a percentile percentage below the poverty estimate of 0.26 to 0.50 had a 2-fold increased risk for resistant *E. cloacae* (RR:2.01, 95% CI 1.01-3.98) and 39% increased risk for resistant *K. pneumoniae* (RR:1.39, 95% CI 1.05-1.84) when compared with a percentile percentage of 0 to 0.25. For comorbidities,

patients with a Charlson score of one to two had a 3-fold increase risk of resistant *E. cloacae* (RR: 3.06, 95% CI 1.05-8.95) and 33% increase risk of resistant *E. coli* (RR:1.33, 95% CI 1.15-1.55) (Table 4) when compared with a score of zero. Additionally, patients with a score of three to five saw a 4.2-fold increase risk of resistant *E. cloacae* (RR: 4.15, 95% CI 1.43-12.01) and 47% increased risk of resistant *E. coli* (RR:1.47, 95% CI 1.26-1.72) when compared with a score of zero. Further, patients with a score of six or greater had a 49% increased risk of resistant *E. coli* when compared with a score of zero (RR: 1.49, 95% CI 1.28-1.74). Other isolates were not significant.

Patients with a myocardial infarction had a 36% decreased risk of resistant *K. pneumoniae* when compared to patients without a myocardial infarction (RR: 0.64,95% CI 0.47-0.89). Patients with dementia had a 19% increased risk of resistant *E. coli* compared to those without dementia (RR: 1.19, 95% CI 1.03-1.39). While patients with chronic pulmonary disease had an 85% increased risk of resistant *E. cloacae* compared to those without chronic pulmonary disease (RR: 1.85; 95% CI 1.09-3.14). Patients with diabetes with a chronic complication had a 16% increased risk of resistant *E. coli* compared to those without (RR: 1.16; 95% CI 1.02-1.31). Nearly all isolates had increased risk of resistance for patients with hemiplegia or paraplegia with *Acinetobacter* species having a 69% increased risk (RR:1.69, 95% CI 1.04-2.75), *E. coli* a 60% increased risk (RR:1.60, 95% CI 1.38-1.86), *K. pneumoniae* a nearly 3-fold increased risk (RR:2.57, 95% CI 2.02-3.27), *P. aeruginosa* a 110% increased risk (RR:2.10, 95% CI 1.72-2.56 compared to those without hemi or paraplegia). Patients with renal disease had a 21% increased risk of resistant *E. coli* compared to those without. Finally, patients with a malignancy had decreased resistant *P. aeruginosa* compared to those without a

malignancy (RR:0.60, 95% CI: 0.44-0.82). No other comorbidities saw significant risks for resistant isolates.

When adjusted for significant crude results, females compared to males had a 14% decreased risk of resistant *E. coli* (RR: 0.86, 95% CI 0.77-0.95) (Table 5). There were no significant risks for resistance between females and males for any other organisms. When compared with 18 to 29-year-olds, ages 30 to 39 had a 33% increased risk of resistance (RR:1.33, 95% CI 1.03-1.71), ages 40 to 49 had a 32% increased risk of resistance (RR: 1.32, 95% CI 1.03-1.69), ages 50 to 59 had a 51% increased risk of resistance (RR:1.51, 95% CI 1.20-1.90), ages 60 to 69 had a 55% increased risk of resistance (RR:1.55, 95% CI 1.23-1.94), ages 70 to 79 had a 63% increased risk of resistance (RR:1.63, 95% CI 1.28-2.07), and ages 80 and over had a 59% increased risk resistance (RR: 1.59, 95% CI 1.24-2.04) to FQ for *E. coli*. However, no other isolate had statistically significant risks. Patients admitted from a physician's office with an *Acinetobacter* species infection saw 79% decreased risk of resistance compared to those from a non-healthcare facility (RR: 0.21, 95% CI 0.05-0.87). While patients admitted from a skilled nursing facility had a 48% increased risk of resistant *E. coli* (RR:1.48, 95% CI 1.19-1.83), a 2.3-fold increased risk of resistant *K. pneumoniae* (RR:2.32, 95% CI 1.62-3.34), and a 65% increased risk of resistant *P. aeruginosa* (RR:1.65, 95% CI:1.18-2.29 when compared with patients not admitted from a healthcare facility. Patients admitted from a physician's office or other facility when compared with a non-healthcare facility had no significant risks. The percentile percentage below the poverty estimate saw no significant risks among any organism. As for comorbidities, patients with a myocardial infarction had a 14% and 35% decreased risk of FQ resistant for *E. coli*

(RR:0.86, 95% CI 0.74-0.99) and *K. pneumoniae* (RR:0.65, 95% CI 0.47-0.90) compared with patients without a myocardial infarction, respectively. While patients with chronic pulmonary disease had a 94% increased risk of resistant *E. cloacae* compared with patients without chronic pulmonary disease (RR:1.94, 95% CI 1.11-3.39). Patients with hemiplegia or paraplegia saw a 68% increased risk of resistant *E. coli* (RR:1.68, 95% CI 1.44-1.99), a 2-fold increased risk of resistant *K. pneumoniae* (RR: 2.22, 95% CI 1.67-2.94), and 97% increased risk of *P. aeruginosa* (RR:1.97, 95% CI 1.56-2.47) when compared with patients without this comorbidity. Finally, patients with renal disease had a 15% increased risk of resistant *E. coli* when compared with patients without renal disease (RR:1.15, 95% CI 1.01-1.31). No other comorbidities saw significant risks.

Table 3. Crude risk ratios (RRs) and associated 95% confidence intervals (CIs) for the association between patient demographics and resistance to fluoroquinolones by cultured organism for community-acquired infection between the years 2016 and 2019

CHARACTERISTICS	*Acinetobacter spp.* RR (95% CI)	*E. cloacae* RR (95% CI)	*E. coli* RR (95% CI)	*K. pneumoniae* RR (95% CI)	*P. aeruginosa* RR (95% CI)
Sex					
Male	Referent	Referent	Referent	Referent	Referent
Female	0.77 (0.45, 1.32)	0.99 (0.60, 1.63)	0.79 (0.71, 0.87)	0.68 (0.55, 0.84)	0.91 (0.77, 1.08)
Race					
White	Referent	Referent	Referent	Referent	Referent
Black	1.10 (0.66, 1.83)	1.23 (0.74, 2.05)	0.96 (0.87, 1.06)	1.18 (0.96, 1.46)	0.97 (0.82, 1.16)
Other races	0.87 (0.21, 3.69)	0.53 (0.07, 3.89)	0.92 (0.72, 1.17)	1.13 (0.67, 1.88)	1.47 (0.99, 2.18)
Age					
18-29	Referent	Referent	Referent	Referent	Referent
30-39	1.16 (0.51, 2.66)	3.91 (0.49, 32.22)	1.37 (1.06, 1.76)	0.66 (0.40, 1.09)	1.10 (0.81, 1.49)
40-49	0.80 (0.37, 1.71)	3.19 (0.41, 25.16)	1.38 (1.08, 1.77)	0.88 (0.56, 1.37)	1.05 (0.77, 1.42)
50-59	0.71 (0.32, 1.59)	1.72 (0.22, 13.40)	1.55 (1.24, 1.95)	0.65 (0.44, 1.01)	0.70 (0.52, 0.95)
60-69	0.73 (0.34, 1.56)	3.70 (0.50, 27.48)	1.58 (1.27, 1.96)	0.85 (0.57, 1.26)	0.83 (0.63, 1.11)
70-79	0.52 (0.15, 1.79)	1.72 (0.20, 14.67)	1.65 (1.31, 2.07)	0.61 (0.39, 0.95)	0.66 (0.49, 0.93)
≥ 80	1.03 (0.34, 3.11)	3.96 (0.50, 31.20)	1.60 (1.27, 2.00)	0.57 (0.37, 0.90)	0.62 (0.43, 0.89)
Admission Source					
Non-healthcare facility	Referent	Referent	Referent	Referent	Referent
Physician's office	0.21 (0.05, 0.85)	1.43 (0.84, 2.46)	1.17 (1.02, 1.35)	0.86 (0.62, 1.21)	0.87 (0.72, 1.06)
Skilled nursing facility	1.78 (0.81, 3.90)	2.87 (1.20, 6.86)	1.64 (1.34, 2.02)	2.27 (1.60, 3.23)	1.54 (1.12, 2.12)
Other	Undefined	Undefined	1.31 (0.83, 2.09)	0.88 (0.28, 2.73)	0.97 (0.40, 2.34)
PP below poverty estimate					
0.0-0.25	Referent	Referent	Referent	Referent	Referent
0.26-0.50	1.54 (0.74, 3.18)	2.01 (1.01, 3.98)	1.11 (0.97, 1.27)	1.39 (1.05, 1.84)	1.16 (0.93, 1.44)
0.51-0.75	1.05 (0.45, 2.48)	1.79 (0.86, 3.72)	1.06 (0.92, 1.22)	1.07 (0.77, 1.48)	1.00 (0.78, 1.28)
0.76-1.0	1.69 (0.82, 3.45)	0.85 (0.38, 1.95)	0.95 (0.83, 1.08)	1.24 (0.94, 1.64)	1.17 (0.94, 1.47)
PP without HS diploma					
0.0-0.25	Referent	Referent	Referent	Referent	Referent
0.26-0.50	1.26 (0.63, 2.48)	0.61 (0.30, 1.26)	0.94 (0.82, 1.07)	1.02 (0.79, 1.33)	0.99 (0.80, 1.23)
0.51-0.75	0.94 (0.46, 1.91)	0.93 (0.49, 1.76)	0.96 (0.83, 1.09)	1.03 (0.79, 1.34)	0.95 (0.75, 1.20)
0.76-1.0	1.45 (0.75, 2.82)	0.71 (0.35, 1.45)	0.92 (0.80, 1.07)	1.07 (0.80, 1.44)	1.27 (1.00, 1.61)
Percent of housing with ≥ 10 units					
0.0-2.9	Referent	Referent	Referent	Referent	Referent
3.0- 9.9	1.02 (0.57, 1.83)	1.20 (0.67, 2.13)	1.05 (0.94, 1.19)	1.05 (0.82, 1.34)	1.04 (0.85, 1.27)
≥ 10	0.92 (0.51, 1.67)	0.85 (0.44, 1.66)	1.01 (0.90, 1.14)	0.93 (0.72, 1.21)	0.94 (0.76, 1.15)
Percent of housing >1 per room					
0.0-1.1	Referent	Referent	Referent	Referent	Referent
1.2-2.3	1.08 (0.63, 1.87)	0.63 (0.31, 1.30)	0.98 (0.87, 1.11)	0.99 (0.77, 1.27)	0.95 (0.77, 1.17)
≥ 2.4	1.08 (0.56, 2.09)	1.40 (0.81, 2.43)	0.93 (0.83, 1.05)	1.09 (0.85, 1.41)	0.84 (0.84, 1.25)

RR and 95% CI derived from Cox regression; spp.=species, PP=Percentile percentage, HS=High school

Table 4. Crude risk ratios (RRs) and associated 95% confidence intervals (CIs) for the association between patient comorbidities and resistance to fluoroquinolones by cultured organism for community-acquired infection

CHARACTERISTICS	*Acinetobacter spp.* RR (95% CI)	*E. cloacae* RR (95% CI)	*E. coli* RR (95% CI)	*K. pneumoniae* RR (95% CI)	*P. aeruginosa* RR (95% CI)
Charlson index					
0	Referent	Referent	Referent	Referent	Referent
1-2	1.48 (0.60, 3.59)	3.06 (1.05, 8.95)	1.33 (1.15, 1.55)	1.34 (0.94, 1.91)	1.07 (0.84, 1.38)
3-5	1.87 (0.77, 4.56)	4.15 (1.43, 12.01)	1.47 (1.26, 1.72)	1.26 (0.89, 1.81)	1.05 (0.80, 1.37)
6+	1.22 (0.44, 3.36)	2.40 (0.80, 7.17)	1.49 (1.28, 1.74)	1.18 (0.83, 1.69)	0.95 (0.72, 1.26)
Comorbidities					
Myocardial infarction	0.48 (0.12, 1.96)	0.62 (0.27, 1.45)	0.95 (0.82, 1.09)	0.64 (0.47, 0.89)	0.81 (0.61, 1.06)
Congestive heart failure	1.30 (0.71, 2.38)	1.34 (0.75, 2.39)	1.09 (0.96, 1.22)	1.05 (0.82, 1.33)	0.97 (0.78, 1.21)
Peripheral vascular disease	1.18 (0.54, 2.57)	1.63 (0.83, 3.21)	1.17 (0.90, 1.39)	1.24 (0.87, 1.78)	0.74 (0.52, 1.04)
Cerebrovascular disease	1.02 (0.47, 2.24)	1.14 (0.42, 3.15)	1.18 (1.00, 1.39)	1.12 (0.80, 1.56)	1.04 (0.76, 1.44)
Dementia	1.44 (0.53, 3.97)	1.55 (0.56, 4.26)	1.19 (1.03, 1.39)	1.03 (0.72, 1.47)	1.01 (0.70, 1.45)
Chronic pulmonary disease	1.24 (0.68, 2.28)	1.85 (1.09, 3.14)	1.10 (0.97, 1.24)	1.14 (0.89, 1.46)	1.00 (0.83, 1.19)
Rheumatic disease	Undefined	1.45 (0.58, 3.63)	0.99 (0.78, 1.25)	1.02 (0.61, 1.71)	0.77 (0.46, 1.28)
Peptic ulcer disease	0.82 (0.11, 5.93)	2.31 (0.56, 9.45)	0.86 (0.56, 1.35)	0.68 (0.25, 1.82)	0.37 (0.10, 1.46)
Mild liver disease	1.16 (0.61, 2.22)	0.62 (0.23, 1.72)	1.07 (0.91, 1.26)	0.73 (0.51, 1.06)	0.94 (0.67, 1.31)
Diabetes without chronic complication	1.12 (0.65, 1.93)	1.64 (0.99, 2.73)	1.09 (0.98, 1.21)	0.99 (0.79, 1.24)	1.00 (0.83, 1.21)
Diabetes with chronic complication	0.62 (0.25, 1.55)	1.24 (0.69, 2.12)	1.16 (1.02, 1.31)	0.96 (0.74, 1.25)	0.98 (0.78, 1.23)
Hemiplegia or paraplegia	1.69 (1.04, 2.75)	2.19 (0.94, 5.08)	1.60 (1.38, 1.86)	2.57 (2.02, 3.27)	2.10 (1.72, 2.56)
Renal disease	0.83 (0.42, 1.62)	1.13 (0.64, 2.00)	1.21 (1.08, 1.35)	1.01 (0.80, 1.28)	0.93 (0.77, 1.14)
Malignancy	0.51 (0.16, 1.62)	0.55 (0.22, 1.36)	1.01 (0.85, 1.19)	0.69 (0.47, 1.00)	0.60 (0.44, 0.82)
Moderate or severe liver disease	Undefined	Undefined	1.22 (0.90, 1.65)	0.63 (0.30, 1.33)	0.71 (0.35, 1.42)
Metastatic solid tumor	Undefined	0.41 (0.10, 1.68)	1.10 (0.87, 1.40)	0.73 (0.44, 1.22)	0.79 (0.51, 1.22)
AIDS/HIV	1.24 (0.17, 8.95)	1.33 (0.18, 9.58)	0.92 (0.61, 1.38)	0.83 (0.31, 2.23)	1.23 (0.66, 2.29)

RR and 95% CI derived from Cox regression; spp.=species, AIDS=acquired immunodeficiency syndrome, HIV= Human immunodeficiency virus

Table 5. Adjusted risk ratios (RRs) and associated 95% confidence intervals (CIs) for the association between patient-level characteristics and resistance to fluoroquinolones among community-acquired infections

CHARACTERISTICS	*Acinetobacter Spp.*	*E. cloacae*	*E. coli*	*K. pneumoniae*	*P. aeruginosa*
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Sex					
Male	Referent	Referent	Referent	Referent	Referent
Female	0.79 (0.43, 1.47)	0.95 (0.56, 1.62)	0.86 (0.77, 0.95)	0.84 (0.67, 1.05)	0.98 (0.82, 1.17)
Age					
18-29	Referent	Referent	Referent	Referent	Referent
30-39	1.11 (0.44, 2.91)	3.56 (0.44, 28.75)	1.33 (1.03, 1.71)	0.71 (0.43, 1.18)	1.08 (0.79, 1.48)
40-49	0.76 (0.35, 1.66)	2.94 (0.37, 23.61)	1.32 (1.03, 1.69)	1.03 (0.66, 1.63)	1.11 (0.82, 1.51)
50-59	0.77 (0.34, 1.74)	1.62 (0.20, 12.97)	1.51 (1.20, 1.90)	0.85 (0.55, 1.32)	0.82 (0.60, 1.12)
60-69	1.07 (0.46, 2.41)	3.22 (0.42, 24.81)	1.55 (1.24, 1.94)	1.08 (0.71, 1.65)	0.97 (0.72, 1.30)
70-79	0.66 (0.16, 2.66)	1.67 (0.19, 14.81)	1.64 (1.29, 2.07)	0.86 (0.53, 1.39)	0.79 (0.56, 1.12)
≥ 80	1.01 (0.27, 4.16)	4.40 (0.52, 37.53)	1.60 (1.25, 2.04)	0.77 (0.46, 1.28)	0.72 (0.48, 1.07)
Admission Source					
Non-healthcare facility	Referent	Referent	Referent	Referent	Referent
Physician's office	0.21 (0.05, 0.87)	1.44 (0.83, 2.52)	1.15 (1.00, 1.33)	0.90 (0.64, 1.26)	0.95 (0.77, 1.16)
Skilled nursing facility	2.30 (0.90, 5.93)	2.55 (0.93, 7.01)	1.47 (1.19, 1.83)	2.32 (1.62, 3.34)	1.65 (1.18, 2.29)
Other	Undefined	Undefined	1.22 (0.76, 1.94)	0.92 (0.29, 2.88)	1.06 (0.44, 2.57)
PP below poverty estimate					
0.0-0.25	Referent	Referent	Referent	Referent	Referent
0.26-0.50	1.31 (0.61, 2.83)	1.98 (0.97, 4.05)	1.11 (0.97, 1.28)	1.23 (0.93, 1.64)	1.11 (0.89, 1.39)
0.51-0.75	0.97 (0.38, 2.52)	1.78 (0.83, 3.83)	1.08 (0.94, 1.26)	1.02 (0.73, 1.42)	0.97 (0.76, 1.25)
0.76-1.0	1.46 (0.67, 3.21)	0.81 (0.34, 1.91)	0.96 (0.84, 1.13)	1.06 (0.80, 1.42)	1.07 (0.85, 1.34)
Comorbidities					
Myocardial infarction	0.64 (0.14, 2.70)	0.59 (0.25, 1.40)	0.86 (0.74, 0.99)	0.65 (0.47, 0.90)	0.86 (0.65, 1.15)
Dementia	1.05 (0.26, 4.34)	0.97 (0.27, 3.48)	1.07 (0.90, 1.28)	1.18 (0.80, 1.76)	1.20 (0.79, 1.80)
Chronic pulmonary disease	1.41 (0.70, 2.83)	1.94 (1.11, 3.39)	1.12 (0.99, 1.27)	1.17 (0.91, 1.51)	1.15 (0.95, 1.40)
Diabetes with chronic complication	0.73 (0.25, 2.20)	1.40 (0.70, 2.78)	1.07 (0.93, 1.23)	1.00 (0.74, 1.34)	1.14 (0.88, 1.49)
Hemiplegia or paraplegia	1.60 (0.85, 3.01)	2.36 (0.93, 5.99)	1.68 (1.44, 1.99)	2.22 (1.67, 2.94)	1.97 (1.56, 2.47)
Renal disease	1.10 (0.48, 2.50)	0.92 (0.46, 1.83)	1.15 (1.01, 1.31)	1.15 (0.88, 1.51)	1.02 (0.81, 1.28)
Malignancy	0.68 (0.18, 2.56)	0.73 (0.28, 1.88)	0.99 (0.83, 1.17)	0.74 (0.50, 1.08)	0.73 (0.53, 1.00)

RR and 95% CI derived from Cox regression; spp.=specie, PP=Percentile percentage

Hospital-acquired infections

There were 3,445 hospital-acquired infections by the five organisms between 2016 and 2019. For crude results, patients who were 30 to 39 had an 89% increased risk (RR: 1.89, 95% CI 1.09-3.30) (Table 6) and patients 40 to 49 had a 75% increased risk of resistant *P. aeruginosa* (RR: 1.75, 95% CI 1.03-2.97) compared to patients 18 to 29. Patients with a length of stay of four or greater weeks had a 2.4-fold increased risk of *K. pneumoniae* compared to patients with a two to three week stay (RR: 2.40, 95% CI: 1.38-4.18). For comorbidities, patients with a Charlson score of three to five had a 49% increase risk of resistant *E. coli* compared with zero (RR: 1.49, 95% CI 1.06-2.10) (Table 7). While patients with a score of six or greater saw a 41% increase in the risk of *E. coli* compared to zero (RR:1.41, 95% CI 1.01-1.97). Patients with congestive heart failure had a 36% increased risk of resistant *E. coli* compared to those without congestive heart failure (RR:1.36, 95% CI 1.08-1.71). Additionally, those with mild liver disease had a 62% increased risk of resistant *K. pneumoniae* when compared to those without (RR: 1.62, 95% CI 1.01-2.59). Patients with diabetes with a chronic complication had an 80% increased risk for resistant *E. cloacae* compared to those without diabetes (1.80, 95% CI 1.06-3.07). While patients with hemiplegia or paraplegia had a 67% increased risk for *P. aeruginosa* resistant infections compared to those without hemi or paraplegia (RR: 1.67, 95% CI 1.22-2.30). Finally, patients with renal disease had a 32% increased risk of resistant *E. coli* (RR:1.32, 95% CI: 1.05-1.66) and 49% increased risk of *K. pneumoniae* (RR:1.49, 95% CI: 1.03-2.15) compared to those without renal disease.

After adjusting for all significant crude characteristics, infections from *P. aeruginosa* had a 78% increased risk for ages 30-39 (RR: 1.78, 95% CI 1.02-3.12) (Table 8) and 71%

for ages 40-49 (RR 1.71, 95% CI 1.00-2.93) compared with ages 18-29. However, other ages for *P. aeruginosa* as well as all other organisms had no significant risk differences when compared with ages 18-29. Patients with lengths of stay in the hospital of 4 or more weeks had a 109% increased risk of resistant *K. pneumoniae* when compared with a two to three-week length of stay (RR:2.09, 95% CI 1.19-3.66). Other lengths of stay compared with two to three weeks were not significant across all organisms. For patients with comorbidities, patients with chronic pulmonary disease had a 30% increased risk and a 34% increased risk compared with those without for FQ resistance among *E. coli* (RR:1.30, 95% CI 1.03-1.65) and *P. aeruginosa* (RR:1.34, 95% CI 1.02-1.77). Similarly, patients with hemiplegia or paraplegia had a 67% increased risk of resistant *P. aeruginosa* compared with those without (RR:1.67, 95% CI 1.20-2.32). All other organisms for chronic pulmonary disease and hemiplegia or paraplegia as well as comorbidities saw no significant risk differences.

Table 6. Crude risk ratios (RRs) and associated 95% confidence intervals (CIs) for the association between patient demographics and resistance to fluoroquinolones by cultured organism for hospital-acquired infection

CHARACTERISTICS	*Acinetobacter spp.* RR (95% CI)	*E. cloacae* RR (95% CI)	*E. coli* RR (95% CI)	*K. pneumoniae* RR (95% CI)	*P. aeruginosa* RR (95% CI)
Sex					
Male	Referent	Referent	Referent	Referent	Referent
Female	0.84 (0.52, 1.37)	1.02 (0.61, 1.71)	1.00 (0.82, 1.23)	0.81 (0.57, 1.16)	0.97 (0.75, 1.25)
Race					
White	Referent	Referent	Referent	Referent	Referent
Black	1.48 (0.84, 2.60)	0.94 (0.56, 1.59)	0.85 (0.68, 1.06)	1.26 (0.88, 1.80)	1.22 (0.94, 1.57)
Other races	1.13 (0.27, 4.80)	0.93 (0.23, 3.83)	0.85 (0.52, 1.38)	0.80 (0.29, 2.20)	1.52 (0.80, 2.90)
Age					
18-29	Referent	Referent	Referent	Referent	Referent
30-39	1.17 (0.41, 3.34)	0.63 (0.20, 1.91)	0.94 (0.57, 1.55)	2.35 (0.93, 5.96)	1.89 (1.09, 3.30)
40-49	1.55 (0.54, 4.41)	1.13 (0.46, 2.81)	1.17 (0.73, 1.86)	2.27 (0.91, 5.68)	1.75 (1.03, 2.97)
50-59	1.66 (0.68, 4.06)	0.91 (0.38, 2.17)	1.08 (0.70, 1.60)	2.02 (0.84, 4.82)	1.22 (0.72, 2.06)
60-69	1.89 (0.66, 5.39)	0.93 (0.40, 2.15)	1.09 (0.72, 1.66)	1.74 (0.73, 4.17)	1.20 (0.72, 2.01)
70-79	2.43 (0.82, 7.23)	0.87 (0.34, 2.25)	1.35 (0.80, 2.07)	1.61 (0.64, 4.05)	1.14 (0.66, 1.97)
≥ 80	0.81 (0.10, 6.58)	0.53 (0.11, 2.50)	0.99 (0.60, 1.66)	0.61 (0.15, 2.43)	1.22 (0.62, 2.37)
Length of Stay					
2-3 weeks	Referent	Referent	Referent	Referent	Referent
< 1 week	1.00 (0.12, 8.31)	Undefined	0.93 (0.63, 1.37)	1.10 (0.54, 2.26)	0.83 (0.53, 1.30)
1-2 weeks	0.92 (0.26, 3.27)	0.62 (0.25, 1.58)	0.90 (0.67, 1.20)	1.55 (0.77, 3.10)	0.95 (0.58, 1.55)
3-4 weeks	1.03 (0.38, 2.85)	0.93 (0.38, 2.26)	0.70 (0.46, 1.05)	0.90 (0.33, 2.49)	1.03 (0.59, 1.78)
≥ 4 weeks	0.85 (0.35, 2.05)	1.45 (0.76, 2.78)	1.11 (0.84, 1.47)	2.40 (1.38, 4.18)	1.37 (0.96, 1.97)

RR and 95% CI derived from Cox regression; spp.=species, RR=Risk ratio, CI=Confidence intervals, ≥=greater than or equal to

Table 7. Crude risk ratios (RRs) and associated 95% confidence intervals (CIs) for the association between patient comorbidities and resistance to fluoroquinolones by cultured organism for hospital-acquired infection

CHARACTERISTICS	*Acinetobacter spp.* RR (95% CI)	*E. cloacae* RR (95% CI)	*E. coli* RR (95% CI)	*K. pneumoniae* RR (95% CI)	*P. aeruginosa* RR (95% CI)
Charlson index					
0	Referent	Referent	Referent	Referent	Referent
1-2	0.75 (0.33, 1.71)	0.64 (0.30, 1.40)	1.28 (0.91, 1.81)	0.93 (0.51, 1.67)	1.36 (0.89, 2.11)
3-5	2.04 (0.10, 4.17)	1.11 (0.56, 2.18)	1.49 (1.06, 2.10)	0.94 (0.52, 1.71)	1.34 (0.87, 2.06)
6+	1.03 (0.48, 2.25)	0.93 (0.48, 1.81)	1.41 (1.01, 1.97)	1.25 (0.73, 2.14)	1.23 (0.81, 1.86)
Comorbidities					
Myocardial infarction	0.91 (0.41, 2.03)	1.14 (0.62, 2.09)	1.17 (0.91, 1.50)	1.15 (0.77, 1.73)	1.17 (0.87, 1.56)
Congestive heart failure	0.93 (0.46, 1.86)	1.15 (0.66, 2.02)	1.22 (0.97, 1.53)	1.47 (1.03, 2.11)	1.19 (0.91, 1.56)
Peripheral vascular disease	0.94 (0.34, 2.61)	0.91 (0.43, 1.90)	1.06 (0.78, 1.45)	0.93 (0.54, 1.59)	0.92 (0.61, 1.38)
Cerebrovascular disease	0.91 (0.41, 2.03)	1.23 (0.66, 2.29)	0.93 (0.70, 1.23)	0.90 (0.56, 1.43)	0.79 (0.53, 1.18)
Dementia	0.94 (0.23, 3.87)	1.30 (0.32, 5.32)	0.90 (0.56, 1.45)	0.85 (0.37, 1.93)	1.14 (0.64, 2.03)
Chronic pulmonary disease	1.07 (0.52, 2.21)	0.98 (0.52, 1.82)	1.36 (1.08, 1.71)	1.34 (0.91, 1.98)	1.23 (0.94, 1.60)
Rheumatic disease	Undefined	1.19 (0.29, 4.86)	1.27 (0.76, 2.13)	1.04 (0.43, 2.54)	1.20 (0.66, 2.20)
Peptic ulcer disease	1.44 (0.45, 4.63)	0.89 (0.22, 3.62)	1.43 (0.80, 2.43)	1.43 (0.67, 3.07)	1.03 (0.51, 2.07)
Mild liver disease	1.79 (0.87, 3.69)	1.34 (0.70, 2.56)	0.98 (0.67, 1.44)	1.62 (1.01, 2.59)	1.03 (0.67, 1.57)
Diabetes without chronic complication	1.13 (0.58, 2.20)	1.33 (0.79, 2.23)	1.12 (0.90, 1.41)	0.90 (0.61, 1.32)	0.93 (0.71, 1.23)
Diabetes with chronic complication	0.72 (0.29, 1.82)	1.80 (1.06, 3.07)	1.19 (0.92, 1.55)	1.46 (0.98, 2.18)	1.06 (0.78, 1.45)
Hemiplegia or paraplegia	1.52 (0.81, 2.86)	1.10 (0.54, 2.22)	0.85 (0.63, 1.15)	0.92 (0.55, 1.53)	1.67 (1.22, 2.30)
Renal disease	0.73 (0.31, 1.71)	1.68 (1.00, 2.82)	1.32 (1.05, 1.66)	1.49 (1.03, 2.15)	1.07 (0.81, 1.41)
Malignancy	0.65 (0.09, 4.73)	0.54 (0.23, 1.26)	1.04 (0.70, 1.37)	0.71 (0.40, 1.23)	0.83 (0.56, 1.22)
Moderate or severe liver disease	2.11 (0.90, 4.96)	1.43 (0.60, 3.12)	1.04 (0.57, 1.89)	0.78 (0.32, 1.90)	1.24 (0.68, 2.28)
Metastatic solid tumor	Undefined	0.37 (0.05, 2.63)	0.68 (0.40, 1.16)	0.56 (0.20, 1.51)	0.71 (0.36, 1.38)
AIDS/HIV	3.35 (0.46, 24.24)	Undefined	0.93 (0.35, 2.49)	1.44 (0.36, 5.80)	0.65 (0.16, 2.61)

RR and 95% CI derived from Cox regression; spp.=species, AIDS=acquired immunodeficiency syndrome, HIV= Human immunodeficiency virus

Table 8. Adjusted risk ratios (RRs) and associated 95% confidence intervals (CIs) for the association between patient-level characteristics and resistance to fluoroquinolones among hospital-acquired infections

CHARACTERISTICS	*Acinetobacter spp.* RR (95% CI)	*E. cloacae* RR (95% CI)	*E. coli* RR (95% CI)	*K. pneumoniae* RR (95% CI)	*P. aeruginosa* RR (95% CI)
Age					
18-29	Referent	Referent	Referent	Referent	Referent
30-39	1.11 (0.38, 3.20)	0.63 (0.21, 1.95)	0.91 (0.55, 1.51)	2.01 (0.79, 5.15)	1.78 (1.02, 3.12)
40-49	1.49 (0.50, 4.42)	1.05 (0.41, 2.69)	1.13 (0.71, 1.80)	1.95 (0.77, 4.94)	1.71 (1.00, 2.93)
50-59	1.63 (0.65, 4.14)	0.93 (0.37, 2.29)	1.05 (0.68, 1.63)	1.67 (0.68, 4.07)	1.19 (0.70, 2.04)
60-69	1.98 (0.64, 6.13)	0.91 (0.37, 2.21)	1.02 (0.67, 1.57)	1.34 (0.55, 3.28)	1.13 (0.66, 1.91)
70-79	2.52 (0.79, 8.02)	0.75 (0.28, 2.05)	1.21 (0.78, 1.88)	1.25 (0.48, 3.23)	1.11 (0.63, 1.95)
≥ 80	1.04 (0.12, 9.30)	0.49 (0.10, 2.42)	0.95 (0.56, 1.59)	0.59 (0.14, 2.40)	1.21 (0.60, 2.42)
Length of Stay					
2-3 weeks	Referent	Referent	Referent	Referent	Referent
< 1 week	1.04 (0.12, 9.27)	Undefined	0.93 (0.63, 1.38)	0.91 (0.33, 2.52)	1.03 (0.59, 1.79)
1-2 weeks	0.80 (0.22, 2.93)	0.66 (0.26, 1.70)	0.89 (0.66, 1.19)	1.09 (0.53, 2.25)	0.83 (0.53, 1.31)
3-4 weeks	0.96 (0.32, 2.93)	0.98 (0.39, 2.42)	0.71 (0.47, 1.06)	1.49 (0.74, 3.00)	0.97 (0.59, 1.60)
≥ 4 weeks	0.88 (0.34, 2.26)	1.51 (0.78, 2.91)	1.10 (0.83, 1.45)	2.09 (1.19, 3.66)	1.30 (0.90, 1.87)
Comorbidities					
Congestive heart failure	1.00 (0.46, 2.22)	0.80 (0.42, 1.54)	1.02 (0.79, 1.33)	1.19 (0.79, 1.79)	1.14 (0.84, 1.55)
Chronic pulmonary disease	0.91 (0.42, 1.97)	0.91 (0.48, 1.75)	1.30 (1.03, 1.65)	1.25 (0.83, 1.86)	1.34 (1.02, 1.77)
Mild liver disease	1.76 (0.81, 3.82)	1.13 (0.57, 2.24)	0.92 (0.63, 1.36)	1.38 (0.85, 2.23)	1.01 (0.65, 1.53)
Diabetes with chronic complication	0.69 (0.20, 2.34)	1.66 (0.87, 3.20)	0.97 (0.72, 1.32)	1.03 (0.63, 1.71)	1.10 (0.76, 1.59)
Hemiplegia or paraplegia	1.48 (0.76, 2.89)	1.19 (0.58, 2.48)	0.87 (0.64, 1.19)	0.98 (0.58, 1.64)	1.67 (1.20, 2.32)
Renal disease	0.83 (0.27, 2.58)	1.47 (0.77, 2.79)	1.24 (0.94, 1.65)	1.39 (0.87, 2.22)	1.02 (0.73, 1.44)

RR and 95% CI derived from Cox regression; spp.=species

Discussion

Our study demonstrates increased risk of FQ resistance across all five of the gram-negative isolates for different patient characteristics. Additionally, these differences are seen in both community and hospital acquired infections. For community-acquired infections an increase in the risk of resistant *E. coli* among older patients and decreased risk among females is similar to the findings of Erb et al. where they show males compared to females and patients over the age of 65 had increased odds of resistant *E. coli* among urine samples.[30] Conversely, our hospital-acquired infections only saw increases in risk for *P. aeruginosa* and for patients 30 to 39 and 40 to 49, but older patients had no significant increases in risk. Also, there were no significant increases in risk for any of the isolates across sex for Hospital-acquired infections. Our sample showed patients admitted from a skilled nursing facility had significant increases in risk of FQ resistant *E. coli* and *K. pneumoniae*. When compared with acute care facilities, skilled nursing facilities had more multi-occupancy rooms and less training in infection control and prevention.[31] Although, recent advancements in healthcare epidemiologic methods aim to combat this issue.[32] Comorbidities in both community and hospital-acquired infections saw increased risks for FQ infection. Community-acquired infections saw increases in patients with renal disease while hospital-acquired infections saw increases in patients with chronic pulmonary disease. They both saw increased risks for patients with Hemiplegia or paraplegia. Other studies have demonstrated increased risk of antibiotic resistance for patients with comorbidities.[33,34] However, our sample also shows a decrease in the risk of resistant *E. coli* and *K. pneumoniae* for patients with a myocardial infarction. Patient characteristics such as sex, age, and comorbidities were

more often seen as risks for FQ resistant than characteristics such as length of stay, admission type, or poverty level. These findings are similar to those found by de Lastours et al. where host factors rather than hospitalization or treatment specific factors were linked to increased risk of FQ resistance.[35]

Strengths of this study include the use of patient-level data rather than aggregate data to identify characteristics. Additionally, stratifying by hospital and community acquired infections allowed for independent observations of these settings. The hypothesis proposed by Lee at al. was demonstrated for continued resistance to FQ by *E. coli* in community-acquired infections.[19] Previous findings have also demonstrated increased FQ resistance for community-acquired isolates, but less so in hospital-acquired.[36-38] Our study also had several limitations, this was not a longitudinal design which prevents rates of resistant infections from being obtained. Additionally, small sample sizes for *Acinetobacter spp.* and *E. cloacae* after stratification may have impacted our power.

As the fight against antibiotic resistance continues, the need for antimicrobial stewardship programs will increase. A better understanding of the risk factors resulting in antibiotic resistance are paramount in their implementation. We have demonstrated several patient characteristics for both community and hospital-acquired infections that may increase the risk of FQ resistance among gram-negative isolates. Studies aimed at understanding how patient characteristics antibiotic susceptibility, especially among community-acquired infections, may be a crucial next step.

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APPENDIX

IRB APPROVAL LETTER

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
Office of the Institutional Review Board for Human Use

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APPROVAL LETTER

TO: Franks, Jeffrey A

FROM: University of Alabama at Birmingham Institutional Review Board
Federalwide Assurance # FWA00005960
IORG Registration # IRB00000196 (IRB 01)
IORG Registration # IRB00000726 (IRB 02)

DATE: 25-Feb-2020

RE: IRB-300004515
Effect of Patient-Level Characteristics on Fluoroquinolone Susceptibility

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The IRB reviewed and approved the Initial Application submitted on 25-Feb-2020 for the above referenced project. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services.

Type of Review: Exempt
Exempt Categories: 4
Determination: Exempt
Approval Date: 25-Feb-2020
Approval Period: No Continuing Review

Documents Included in Review:

- datacollection.200117
- exempt.clean.200225
- waiverauth.191213
- IRB PERSONNEL FORM