Eur J Clin Microbiol Infect Dis
DOI 10.1007/s10096-014-2264-y

ARTICLE

Escherichia coli antibiotic resistance in emergency departments. Do local resistance rates matter?

O. Grignon · E. Montassier · S. Corvec · D. Lepelletier · J.-B. Hardouin · J. Caillon · E. Batard · EDBAC Study Group

Received: 16 September 2014 / Accepted: 7 October 2014

Abstract Ciprofloxacin and cotrimoxazole are recommended to treat uncomplicated pyelonephritis and uncomplicated cystitis, respectively, provided that local resistance rates of uropathogens do not exceed specified thresholds (10 and 20 %, respectively). However, *Escherichia coli* resistance rates in Emergency Departments (ED) remain poorly described. Our objectives were to assess *E. coli* ciprofloxacin and cotrimoxazole resistance rates in EDs of a French administrative region, and to determine if resistance rates differ between EDs. This was a retrospective study of *E. coli* urine isolates sampled in ten EDs between 2007 and 2012. The following risk factors for resistance were tested using logistic regression: ED, sex, age, sampling year, sampling month. A total of 17,527 isolates were included. Ciprofloxacin local resistance rates (range, 5.3 % [95 % CI, 4.0–7.1 %] to 11.7 % [95 % CI, 5.2–23.2 %]) were ≤10 % in nine EDs in 2012. Five EDs were risk factors for ciprofloxacin resistance, as were male sex, age and sampling in April or October. Cotrimoxazole local resistance rates (range, 13.3 % [95 % CI, 6.3–25.1 %] to 20.4 % [95 % CI, 18.9–22.0 %]) were ≤20 % in seven EDs in 2012. Five EDs were risk factors for cotrimoxazole resistance, as were age, sampling between October and December, and sampling in 2011 and 2012. We found a significant variability of *E. coli* ciprofloxacin and cotrimoxazole resistance rates among EDs of a small region. These differences impact on the feasibility of empirical treatment of urinary tract infections with ciprofloxacin or cotrimoxazole in a given ED. Continuous local survey of antibacterial resistance in ED urinary isolates is warranted to guide antibacterial therapy of urinary tract infections.

The EDBAC Study Group is comprised of Rachid YOUSFI, Olivier LEMENAND, Olivier RAMBAUD, Claire BERTON, Philippe FRADIN, Claudie AUDRAIN, Sandra BOURDON, Jacques CHOUKROUN, Catherine VARACHE, Mohamed TOUIL, Edith JAOEN, Jean-Luc DESHAYES, Céline RAMANANTSOA, Bruno POUJOL, Pauline TOUROULT-JUPIN, Pierre-Marie ROY and Marie-Laure JOLY-GUILLOU.

Electronic supplementary material The online version of this article (doi:10.1007/s10096-014-2264-y) contains supplementary material, which is available to authorized users.

O. Grignon · E. Montassier · E. Batard
Emergency Department, Hôtel-Dieu, Centre Hospitalier Universitaire de Nantes, 1 Place Alexis-Ricordeau, 44000 Nantes, France

E. Montassier · S. Corvec · D. Lepelletier · J. Caillon · E. Batard (✉)
EA3826 Thérapeutiques Cliniques et Expérimentales des Infections, Faculté de Médecine & Pharmacie, Université de Nantes, 1 Rue Gaston-Veil, 44000 Nantes, France
e-mail: eric.batard@univ-nantes.fr

S. Corvec · D. Lepelletier · J. Caillon
Department of Microbiology and Infection Control, Hôtel-Dieu, Centre Hospitalier Universitaire de Nantes, 1 Place Alexis-Ricordeau, 44000 Nantes, France

J.-B. Hardouin
EA4275 SPHERE Biostatistics Pharmacoepidemiology and Human Science Research Team, Faculté de Médecine & Pharmacie, Université de Nantes, 1 Rue Gaston-Veil, 44000 Nantes, France

Introduction

Urinary tract infections (UTIs) account for a major proportion of Emergency Department (ED) visits and antibacterial therapy in the ED [1, 2]. Most of antibacterial therapies for UTI are started on an empirical basis, i.e. without antibiotic susceptibility tests. Ciprofloxacin is currently recommended for treating uncomplicated pyelonephritis in patients not requiring hospitalization where the prevalence of resistance of community uropathogens to fluoroquinolones is not known to exceed 10 % [3]. Moreover, cotrimoxazole is recommended for treating acute uncomplicated cystitis if local resistance rates of uropathogens causing acute uncomplicated cystitis do not

Published online: 23 October 2014

exceed 20 % [3]. European national data on antimicrobial resistance among uropathogens are available through the Antimicrobial Resistance Interactive Database (EARS-Net) of the European Centre for Disease Prevention and Control (www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx). However, these data are collected by health-care institutions (e.g. hospitals, rehabilitation centres and nursing homes), and thus may not reflect prevalence of resistance in EDs where most patients are admitted for community-acquired infection. Studies of antibiotic susceptibility of uropathogens in the ED are scarce, and mostly monocentric [4–7]. Variability of cotrimoxazole resistance rates among EDs has been suggested in a study conducted from 2000 to 2004 in 11 EDs located across the United States [8]. However, current resistance rates among uropathogens grown in the ED are poorly described, and it is not known whether, and to which extent, rates of antimicrobial resistance differ between EDs of a small region. Our objectives were to assess antibiotic resistance rates of *Escherichia coli* in EDs of a French administrative region, and to determine if resistance rates differ between them.

Methods

Study design and setting

This observational study was retrospectively conducted in ten public hospital EDs in the French region Pays de la Loire (area, 32,000 km²; census, 3,600,000 inhabitants). Median number of visits per ED was 41,227 (range 23,891–51,862) in 2012.

Selection of bacterial isolates

E. coli isolates were included if they were grown from urine that was sampled in the ED between January 2007 and December 2012, regardless the amount of bacteria. A single isolate was included per year and per patient. Any isolate was excluded if the patient's age or sex was not available, or if age was younger than 18 years.

Outcomes

Routine susceptibility tests were performed and interpreted as recommended by national guidelines of the French Society for Microbiology at the time they were carried out. During the whole study period, ciprofloxacin resistance was defined by a MIC for ciprofloxacin >1 mg/L, as recommended by the EUCAST 2014 clinical breakpoints. Cotrimoxazole resistance was defined as a MIC for trimethoprime >8 mg/L from 2007 to 2008, and >4 mg/L from 2009 to 2012. Amoxicillin and amoxicillin-clavulanate susceptibilities were defined by MICs ≤4 and ≤4/2 mg/L, respectively. As anonymous data of antibiotic susceptibility were transmitted by each participating microbiology laboratory to the investigators, no ethical approval was necessary.

Statistical analysis

Medians were reported with 1st and 3rd quartiles, means with SD, and proportions with 95 % confidence intervals. Risk factors for antibiotic resistance were analyzed using logistic regression. All variables were treated as categorical variables. For each variable, an answer category was chosen as a reference and answer categories that did not differ significantly were merged. Variables that were associated in univariate analysis with antibiotic susceptibility at a P-value≤0.20 were included for multivariate analysis. The threshold for statistical significance was 0.05. All analyses were performed using R software version 3.1.0 (2014-04-10) with the MASS package (http://CRAN.R-project.org).

Results

Patients and isolates characteristics

A total of 18,785 non duplicate isolates were eligible during the study period. Forty and 1,218 isolates were excluded due to missing demographic data and age <18 years, respectively. Hence 17,527 isolates were included (median number per ED, 1,350 [753–2,502]). Thirteen thousand five hundred ninety-eight patients were female (78 % [77–78 %]), and mean age was 62±24 years. Number of isolates steadily increased from 2,130 in 2007 to 3,548 in 2012. Grouping months across the 6 years of the study period, median number of isolates per month was 1,442 (1,415–1,486). Lowest and highest numbers of isolates were obtained respectively in February (1,259) and in August (1,704). Overall, susceptibility rates to amoxicillin, amoxicillin-clavulanate, cefotaxime, ciprofloxacin, gentamicin and cotrimoxazole were 56.7 % (55.9–57.4 %), 69.9 % (69.2–70.6 %), 97.6 % (97.3–97.8 %), 91.3 % (90.9–91.7 %), 96.3 % (96.0 %–96.6) and 81.4 % (80.8–82.0 %), respectively.

Ciprofloxacin resistance

Ciprofloxacin susceptibility test was unavailable for 30 isolates. Hence 17,497 isolates were analysed. Ciprofloxacin resistance rate slightly increased between 2007 and 2008, and was roughly steady between 2008 and 2012 (Fig. 1). Ciprofloxacin resistance rates for each ED are presented in Table 1 for the whole study period, and in web-only appendices for the year 2012 (see Electronic supplementary material).

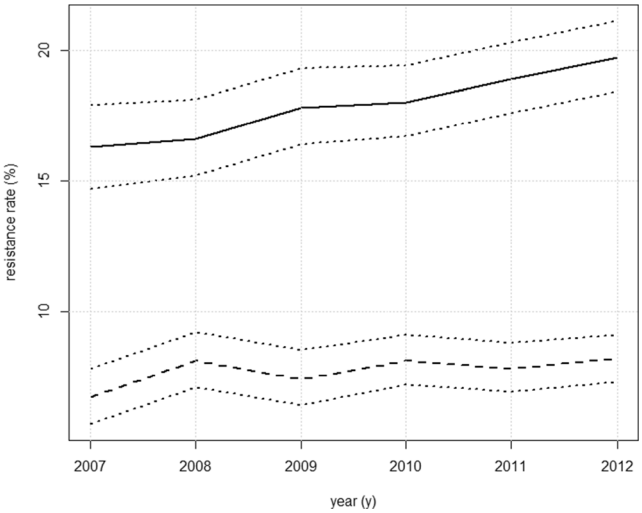

Fig. 1 Yearly trends of resistance rates in *Escherichia coli*. *Solid line* cotrimoxazole, *dashed line* ciprofloxacin, *point line* 95 % confidence interval

Ciprofloxacin resistance rates tended to be higher in April and October, and tended to be lower in August (Fig. 2). Ciprofloxacin resistance rates in females and males were respectively 7.0 % (6.6–7.4 %) and 10.5 % (9.6–11.5 %), and were statistically different (χ^2 test, $P<0.0001$). Ciprofloxacin resistance rate tended to increase along age classes (Fig. 3).

Age classes between 45 and 104, male sex, year 2012, urine sampling in April and in October and EDs A, B, C, G and J were significantly associated with ciprofloxacin resistance in univariate analysis (Table 2). The best model retained through multivariate analysis is shown in Table 2. Male sex, age classes between 45 and 104, urine sampled in April or October, and the ED of hospitals A, B, C, G or J were statistically significant independent risk factors for ciprofloxacin resistance.

Cotrimoxazole resistance

Cotrimoxazole susceptibility test was unavailable for 108 isolates. Hence, 17,419 isolates were included for analysis. Cotrimoxazole resistance rate increased steadily between 2007 and 2012 (Fig. 1). Resistance rates for each ED are presented in Table 1 for the whole study period, and in Supplementary file for year 2012 (see Electronic supplementary material). Cotrimoxazole resistance rates tended to be higher in October, November and December, and tended to be lower in May (Fig. 2). Cotrimoxazole resistance rates in females and males were respectively 17.7 % (17.1–18.4 %) and 19.3 % (18.1–20.1 %), and were statistically different (χ^2 test, $P<0.03$). Cotrimoxazole resistance rate tended to increase along age classes from 18–24 to 65–74, and tended to decrease from 65–74 to 95–104 (Fig. 3).

Fourteen variables were significantly associated with cotrimoxazole in univariate analysis: years 2011 and 2012, months April, July, August, October, November and December, male sex, and EDs A, C, F, H and J (Table 3). The best model retained through multivariate analysis is shown in Table 3. Age between 45 and 94, urine sampled between October and December, in years 2011 and 2012 and the ED of hospitals A, C, F, H and J were statistically significant independent risk factors for cotrimoxazole resistance (Table 3).

Further analyses showed that some EDs were independent risk factors for susceptibility to amoxicillin and for susceptibility to amoxicillin-clavulanate (electronic supplementary material, Tables 5–7, Figs. 4–6).

Table 1 Ciprofloxacin and cotrimoxazole resistance rates in *Escherichia coli* isolates of ten emergency departments, years 2007–2012

Emergency department	Ciprofloxacin		Cotrimoxazole	
	Tested isolates, *N*	Resistant isolates	Tested isolates, *N*	Resistant isolates
A	4,104	8.0 % (7.2–8.9 %)	4,104	17.9 % (16.8–19.1 %)
B	2,125	7.4 % (6.4–8.7 %)	2,065	16.2 % (14.6–17.9 %)
C	2,628	9.1 % (8.0–10.2 %)	2,621	20.4 % (18.9–22.0 %)
D	1,539	5.7 % (4.6–7.0 %)	1,537	16.0 % (14.2–18.0 %)
E	531	5.3 % (3.6–7.6 %)	531	16.6 % (13.6–20.1 %)
F	698	6.7 % (5.0–8.9 %)	694	18.7 % (15.9–21.9 %)
G	60	11.7 % (5.2–23.2 %)	60	13.3 % (6.3–25.1 %)
H	1,146	6.1 % (4.8–7.7 %)	1,145	17.3 % (15.2–19.6 %)
I	901	5.3 % (4.0–7.1 %)	901	13.9 % (11.7–16.3 %)
J	3,765	9.2 % (8.3 –10.1 %)	3,761	19.9 % (18.7–21.3 %)
All	17,497	7.8 % (7.4–8.2 %)	17,419	18.1 % (17.5–18.7 %)

Values given as estimate (95 % confidence interval)

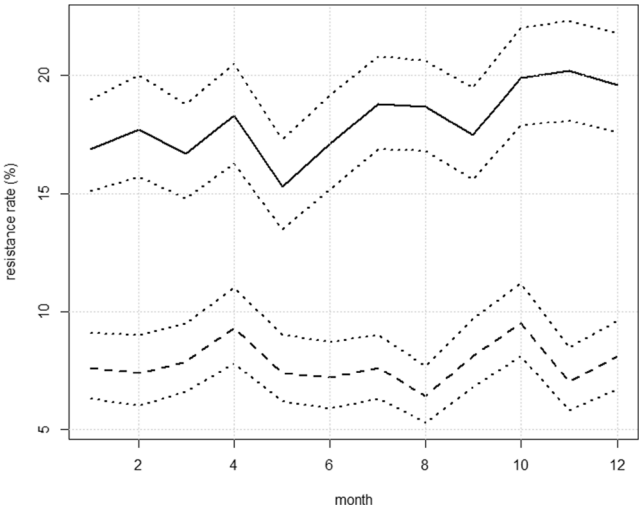

Fig. 2 Monthly resistance rates in *Escherichia coli*. *Solid line* cotrimoxazole, *dashed line* ciprofloxacin, *point line* 95 % confidence interval

Discussion

This work demonstrates that there are statistically significant differences in ciprofloxacin and cotrimoxazole *E. coli* resistance rates between EDs. For instance, in 2012, ciprofloxacin resistance rates ranged from <6 to >9 %. These results were obtained in a small area, as the maximal distance between participating EDs was 200 km (electronic supplementary material, Fig. 7). These differences were independent from other known risk factors for ciprofloxacin resistance such as year, sex and age. They were also independent from the month of urine sampling, a less well described risk factor for ciprofloxacin resistance. Incidentally, the high variability of monthly resistance rates, exemplified by ciprofloxacin resistance seasonality, is exploited by time-series analyses to demonstrate the relationship between antibiotic use and bacterial resistance [9–12]. Ciprofloxacin resistance in *E. coli* community-acquired hospital isolates has been linked with outpatient ciprofloxacin use in the same month and the month before, and with outpatient moxifloxacin use four months before [11]. In our study, higher rates of ciprofloxacin resistance in April and October may be due to fluctuations of fluoroquinolone use in the community in the preceding months. Interestingly, the ciprofloxacin resistance rates observed in this survey were far lower than those reported by the EARS-Net database for France, which reported an increase of fluoroquinolone resistance from 14.8 % in 2007 to 17.8 % in 2012 (www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx). This discrepancy is certainly explained by the origin of bacterial isolates, mostly community-acquired in our study, and hospital-acquired or healthcare-associated in the EARS-Net database. Indeed, ciprofloxacin resistance rates observed in this study were similar to those reported in a French community-based surveillance program [13]. Except in hospital G, in which very few isolates were grown, ciprofloxacin resistance rates were <10 % in all EDs in 2012. Hence, according to the IDSA/ESCMID guidelines, treating acute uncomplicated pyelonephritis with ciprofloxacin remained feasible in 2012 [3]. However, ciprofloxacin resistance was >9 % in four out of ten EDs, warranting continuous survey of bacterial resistance, in order to alter antibacterial therapy habits should this rate exceed 10 % in following years. Furthermore, decreasing use of fluroquinolones in the community and in the hospital setting through antibiotic stewardship programs may help to prevent the increase of ciprofloxacin resistance in the future [14–16].

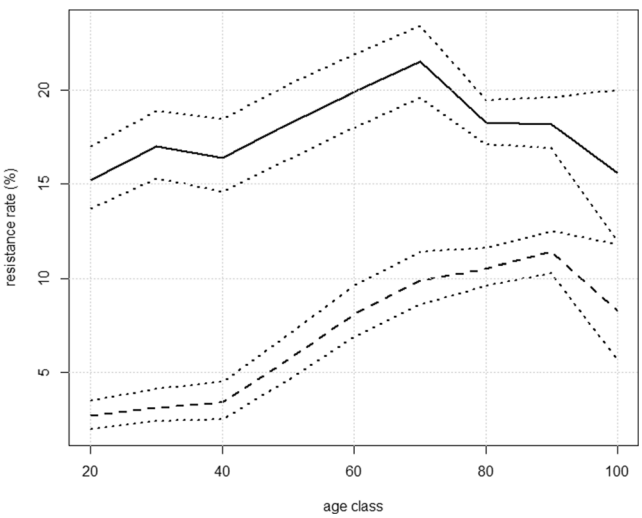

Fig. 3 Relationship between age and resistance rates in *Escherichia coli*. *Solid line* cotrimoxazole, *dashed line* ciprofloxacin, *point line* 95 % confidence interval. Age classes were 18–24, 25–34, 35–44, 45–54, 55–64, 65–74, 75–84, 85–94 and 95–104, and were respectively denominated 20, 30, 40, 50, 60, 70, 80, 90 and 100 (x-axis)

Our study also demonstrated differences in cotrimoxazole resistance rates among EDs, ranging in 2012 from 10.3 to 24.0 %. In 2012, seven out of the ten EDs of our study had cotrimoxazole resistance rate lower than 20 %. Hence, in these EDs, empirical treatment of uncomplicated acute cystitis with cotrimoxazole was feasible, according to the IDSA/ESCMID guidelines [3]. In other words, in some EDs, cotrimoxazole remained an alternative to nitrofurantoin, fosfomycin-trometamol and pivmecillinam for cystitis in 2012, thus providing a fluoroquinolone-sparing therapy when the latter are contra-indicated [17]. However, as cotrimoxazole resistance increased during the study period, and as some of these EDs had resistance rates close to 19–20 % in 2012, a continuous survey of resistance is warranted in order to stop prescribing cotrimoxazole should this rate exceed 20 % in following years.

Differences in ciprofloxacin resistance rates between EDs in a rather small area are consistent with inter-hospital variations of fluoroquinolone resistance prevalence that we previously reported in the same area [18]. The reasons why resistance rates of *E. coli* differ between EDs remain to be determined. First, there are probably differences in patient

Table 2 Risk factors for ciprofloxacin resistance in *Escherichia coli*

Univariate analysis			*P* value	Multivariate analysis			*P* value
Variable		OR		Variable		Adjusted OR	
Year	2007	Ref	–	Sex	Male	1.43 (1.26–1.62)	<0.001
	2008	1.24 (0.99–1.54)	0.059	Month	April or October	1.29 (1.12–1.48)	<0.001
	2009	1.11 (0.89–1.39)	0.36	Emergency department	A, B, C, G or J	1.47 (1.29–1.69)	<0.001
	2010	1.23 (0.99–1.52)	0.06	Age (years)	45–54	1.83 (1.39–2.4)	<0.001
	2011	1.18 (0.95–1.46)	0.13		55–64	2.66 (2.09–3.39)	<0.001
	2012	1.25 (1.01–1.54)	0.038		65–104	3.65 (3.08–4.36)	<0.001
Age class (years)	18–24	Ref	–				
	25–34	1.21 (0.82–1.8)	0.33				
	35–44	1.31 (0.88–1.96)	0.19				
	45–54	2.25 (1.58–3.24)	<0.001				
	55–64	3.3 (2.38–4.65)	<0.001				
	65–74	4.12 (3.01–5.74)	<0.001				
	75–84	4.4 (3.29–6.02)	<0.001				
	85–94	4.79 (3.57–6.57)	<0.001				
	95–104	3.38 (2.08–5.4)	<0.001				
Sex	Female	Ref	–				
	Male	1.57 (1.39–1.77)	<0.001				
Month	January	1.19 (0.91–1.58)	0.21				
	February	1.17 (0.88–1.56)	0.28				
	March	1.24 (0.94–1.63)	0.13				
	April	1.50 (1.15–1.95)	0.003				
	May	1.18 (0.89–1.55)	0.25				
	June	1.13 (0.85–1.5)	0.39				
	July	1.19 (0.91–1.56)	0.20				
	August	ref	–				
	September	1.29 (0.99–1.69)	0.06				
	October	1.54 (1.19–2)	0.001				
	November	1.10 (0.83–1.46)	0.49				
	December	1.28 (0.98–1.69)	0.071				
Emergency department	A	1.55 (1.15–2.14)	0.006				
	B	1.43 (1.03–2.01)	0.036				
	C	1.77 (1.3–2.46)	<0.001				
	D	1.08 (0.75–1.56)	0.68				
	E	0.99 (0.61–1.59)	0.96				
	F	1.28 (0.85–1.94)	0.24				
	G	2.35 (0.93–5.13)	0.047				
	H	1.16 (0.79–1.7)	0.45				
	I	Ref	–				
	J	1.79 (1.33–2.48)	<0.001				

OR>1 means that the variable is a predictive factor for ciprofloxacin resistance. Ref denotes reference

comorbidity between the EDs of our study. For example, only two hospitals (C and J) in our sample provide all types of care, including transplantation and cardiac and brain surgeries. Both hospitals were risk factors for ciprofloxacin resistance and for cotrimoxazole resistance in multivariate analyses. Second, resistance rates in the community may present spatial heterogeneity, even in a small area, as previously described in Sao Paulo, Brazil [19]. It would be plausible that resistance rates in the community surrounding one given ED influences resistance rates in the ED. Further studies—including more EDs than we used in this study—are needed to test these hypotheses.

Table 3 Risk factors for cotrimoxazole resistance in *Escherichia coli*

Univariate analysis			*P* value	Multivariate analysis			*P* value
Variable		OR		Variable		Adjusted OR	
Year	2007	Ref	–	Month	October, November or December	1.17 (1.07–1.27)	<0.001
	2008	1.03 (0.88–1.2)	0.73	Year	2011 or 2012	1.15 (1.06–1.24)	<0.001
	2009	1.11 (0.96–1.3)	0.16	Emergency department	A, F or H	1.17 (1.06–1.29)	0.003
	2010	1.13 (0.98–1.31)	0.10		C or J	1.35 (1.23–1.49)	<0.001
	2011	1.20 (1.04–1.39)	0.013	Age	45–54 or 75–94	1.15 (1.05–1.26)	0.003
	2012	1.26 (1.1–1.46)	0.001		55–74	1.37 (1.23–1.53)	<0.001
Age class	18–24	Ref	–				
	25–34	1.14 (0.95–1.36)	0.15				
	35–44	1.09 (0.91–1.32)	0.35				
	45–54	1.24 (1.03–1.49)	0.021				
	55–64	1.38 (1.16–1.64)	<0.001				
	65–74	1.52 (1.28–1.8)	<0.001				
	75–84	1.24 (1.07–1.45)	0.005				
	85–94	1.24 (1.06–1.44)	0.007				
	95–104	1.03 (0.74–1.4)	0.86				
Sex	Male	1.11 (1.01–1.21)	0.026				
Month	January	1.13 (0.93–1.38)	0.23				
	February	1.19 (0.97–1.47)	0.088				
	March	1.11 (0.91–1.36)	0.32				
	April	1.24 (1.02–1.51)	0.033				
	May	Ref	–				
	June	1.15 (0.94–1.4)	0.18				
	July	1.28 (1.06–1.55)	0.011				
	August	1.27 (1.05–1.54)	0.013				
	September	1.17 (0.96–1.43)	0.11				
	October	1.38 (1.14–1.67)	0.001				
	November	1.40 (1.15–1.7)	<0.001				
	December	1.35 (1.11–1.64)	0.002				
ED	A	1.36 (1.11–1.67)	0.004				
	B	1.20 (0.96–1.5)	0.11				
	C	1.59 (1.29–1.97)	<0.001				
	D	1.18 (0.94–1.5)	0.16				
	E	1.23 (0.91–1.66)	0.17				
	F	1.43 (1.09–1.87)	0.009				
	G	0.96 (0.41–1.95)	0.91				
	H	1.30 (1.02–1.66)	0.036				
	I	Ref	–				
	J	1.55 (1.26–1.91)	<0.001				

OR>1 means that the variable is a risk factor for cotrimoxazole resistance. Ref denotes reference

This work had three main limitations. First, we only included half of EDs of the study region, and did not report on year 2013, partly because some microbiology laboratories were not able to extract conveniently resistance data of their ED. As bacterial resistance increases worldwide with more and more problematical consequences, real-time monitoring of resistance rates should be implemented in hospitals at the ward level, in order to let clinicians tailor their antibacterial prescriptions to the most recent epidemiological data. Second, as microbiology lab files indicated only sex, age and sampling date, we could not take into account other risk factors of antibiotic resistance like urinary catheter, comorbidities and

previous antibacterial therapy. Furthermore, we did not restrict our study to patients with UTIs, and we certainly included subjects with asymptomatic bacteriuria. Hence, our results may not be exactly representative of bacterial resistance in patients with UTI. Patient-based studies would appropriately address these issues, although they are not well-adapted to epidemiological survey of bacterial resistance [8]. Third, we did not take into account uropathogens other than *E. coli*. We focused on *E. coli* because it is by far the most frequent bacterium causing community-acquired UTIs, and because other bacteria are more likely to cause asymptomatic bacterial colonization (for example, in patients with urinary catheter) than true UTIs [5–7].

In conclusion, this work shows significant differences in *E. coli* resistance rates between EDs of a small region. These differences influence the possibility of using ciprofloxacin and cotrimoxazole as empirical treatment of pyelonephritis or cystitis in a given ED, and highlight the necessity of implementing routine surveys of bacterial resistance in EDs.

Conflicts of interest None to declare.

References

1. Caterino JM, Ting SA, Sisbarro SG et al (2012) Age, nursing home residence, and presentation of urinary tract infection in U.S. emergency departments, 2001–2008. Acad Emerg Med 19:1173–1180
2. Elkharrat D, Brun-Ney D, Cordier B et al (2003) Prescriptions d'antibiotiques dans 34 services d'accueil et de traitement des urgences français Antimicrobial drugs prescribing in 34 french emergency department. Med Mal Infect 33:70–77
3. Gupta K, Hooton TM, Naber KG et al (2011) International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis 52:e103–e120
4. Lemort ML, Neuville S, Medus M et al (2006) Comparative susceptibility evolution in Escherichia coli from urinary tract infections in outpatients and inpatients at Perpignan hospital in 2002 and 2004. Pathol Biol (Paris) 54:427–430
5. Moffett SE, Frazee BW, Stein JC et al (2012) Antimicrobial resistance in uncomplicated urinary tract infections in 3 California EDs. Am J Emerg Med 30:942–949
6. Khawcharoenporn T, Vasoo S, Ward E et al (2012) High rates of quinolone resistance among urinary tract infections in the ED. Am J Emerg Med 30:68–74
7. Filiatrault L, McKay RM, Patrick DM et al (2012) Antibiotic resistance in isolates recovered from women with community-acquired urinary tract infections presenting to a tertiary care emergency department. Can J Emerg Med 14:295–305
8. Talan DA, Krishnadasan A, Abrahamian FM et al (2008) Prevalence and risk factor analysis of trimethoprim-sulfamethoxazole- and fluoroquinolone-resistant Escherichia coli infection among emergency department patients with pyelonephritis. Clin Infect Dis 47:1150–1158
9. Sun L, Klein EY, Laxminarayan R (2012) Seasonality and temporal correlation between community antibiotic use and resistance in the United States. Clin Infect Dis 55:687–694
10. Mahamat A, Lavigne JP, Fabbro-Peray P et al (2005) Evolution of fluoroquinolone resistance among Escherichia coli urinary tract isolates from a French university hospital: application of the dynamic regression model. Clin Microbiol Infect 11:301–306
11. Vernaz N, Huttner B, Muscionico D et al (2011) Modelling the impact of antibiotic use on antibiotic-resistant Escherichia coli using population-based data from a large hospital and its surrounding community. J Antimicrob Chemother 66:928–935
12. Gallini A, Degris E, Desplas M et al (2010) Influence of fluoroquinolone consumption in inpatients and outpatients on ciprofloxacin-resistant Escherichia coli in a university hospital. J Antimicrob Chemother 65:2650–2657
13. Thibaut S, Caillon J, Huart C et al (2010) Susceptibility to the main antibiotics of Escherichia coli and Staphylococcus aureus strains identified in community acquired infections in France (MedQual, 2004–2007). Med Mal Infect 40:74–80
14. Aldeyab MA, Harbarth S, Vernaz N et al (2012) The impact of antibiotic use on the incidence and resistance pattern of extended-spectrum beta-lactamase-producing bacteria in primary and secondary healthcare settings. Br J Clin Pharmacol 74:171–179
15. Gottesman BS, Carmeli Y, Shitrit P et al (2009) Impact of quinolone restriction on resistance patterns of Escherichia coli isolated from urine by culture in a community setting. Clin Infect Dis 49:869–875
16. Willemsen I, Cooper B, van Buitenen C et al (2010) Improving quinolone use in hospitals by using a bundle of interventions in an interrupted time series analysis. Antimicrob Agents Chemother 54:3763–3769
17. Slekovec C, Leroy J, Huttner A et al (2014) When the precautionary principle disrupts 3 years of antibiotic stewardship: nitrofurantoin in the treatment of urinary tract infections. J Antimicrob Chemother 69:282–284
18. Batard E, Ollivier F, Boutoille D et al (2013) Relationship between hospital antibiotic use and quinolone resistance in Escherichia coli. Int J Infect Dis 17:e254–e258
19. Kiffer CR, Camargo EC, Shimakura SE et al (2011) A spatial approach for the epidemiology of antibiotic use and resistance in community-based studies: the emergence of urban clusters of Escherichia coli quinolone resistance in Sao Paulo, Brasil. Int J Health Geogr 10:17