carbapenems was correlated with the increased prevalence of HCAI-VRE. Overall, the results suggest that the relationship between antibiotic consumption and the occurrence of HCAI is complicated, and may vary depending on the different pathogens studied.

Second, even within the same class of antibiotics—fluoroquinolones—the association between each fluoroquinolone and the HCAI is quite different. In contrast to ciprofloxacin and levofloxacin, only the use of moxifloxacin was apparently associated with the incidence of HCAI-MRSA and HCAI-VRE in this study. The same situation was reported in previous studies,[6–8] i.e. the impact of different fluoroquinolones, such as ciprofloxacin and levofloxacin, on the antibiotic resistance rate varied.

In conclusion, this 6 year study at Chi Mei Medical Center found variation in the association between the prescription of fluoroquinolones, especially moxifloxacin, and the incidence of HCAI-MRSA and HCAI-VRE. It also reminds us of the importance of monitoring the consumption of each antimicrobial agent and its association with the resistance rate of each bacterium.

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Transparency declarations

None to declare.

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Fluoroquinolone use and fluoroquinolone-resistant *Pseudomonas aeruginosa* is declining in US academic medical centre hospitals

Amy L. Pakyz[1]*, Jin A. Lee[1], Mera A. Ababneh[1], Spencer E. Harpe[1], Michael J. Oinonen[2] and Ron E. Polk[1]

[1]Department of Pharmacotherapy and Outcomes Science, School of Pharmacy, Virginia Commonwealth University, Medical College of Virginia Campus, Richmond, VA, USA; [2]University HealthSystem Consortium, Chicago, IL, USA

*Corresponding author. Tel: +1-804-828-6027; Fax: +1-804-828-8359; E-mail: apakyz@vcu.edu

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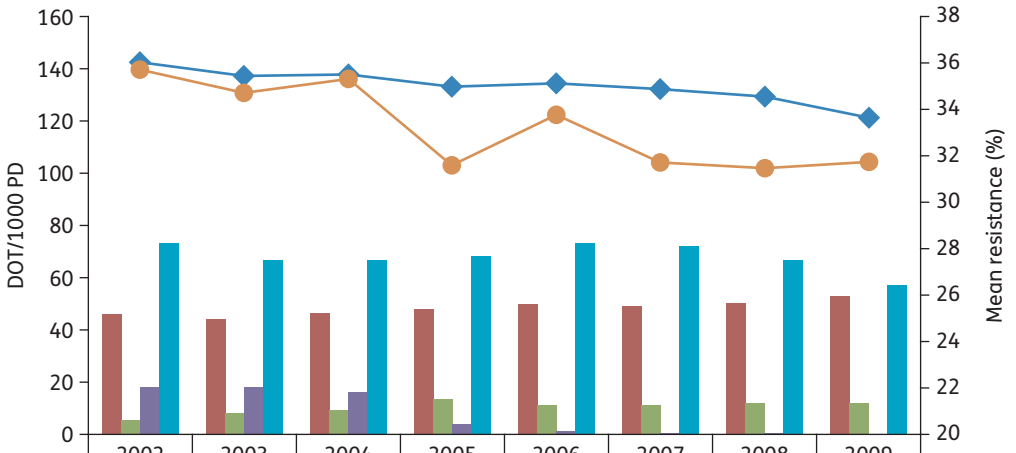
Sir,

Fluoroquinolone-resistant *Pseudomonas aeruginosa* is associated with a negative impact on patient outcome,[1] and treatment of these organisms can be challenging. Increases in fluoroquinolone-resistant *P. aeruginosa* have been reported across hospitals and these were related to fluoroquinolone use.[2–4] These studies were conducted in periods during which fluoroquinolone use was increasing; more recent data show that their use appears to be stabilizing or decreasing.[5]

The purpose of this study was to examine recent trends in fluoroquinolone-resistant *P. aeruginosa* and to determine relationships to fluoroquinolone use in US hospitals. This multi-year cross-sectional study used data from academic medical centres that participated in the University HealthSystem Consortium (UHC). Specifically, UHC member hospitals that subscribed to the Clinical Resource Manager (CRM) database provided drug usage and demographic data. Systemic fluoroquinolones (ciprofloxacin, gatifloxacin, moxifloxacin and levofloxacin) administered to adult patients (age $\geq$18 years) discharged from 1 January 2002 to 31 December 2009 from 20 hospitals were recorded as days of therapy (DOT) per 1000 patient days (PD). Resistance data (the proportion of ciprofloxacin-resistant isolates) were obtained from the antibiograms that hospitals provided. General linear mixed models were used to assess the significance of changes in antibiotic use and resistance. To assess the relationship between use of individual fluoroquinolones and fluoroquinolone-resistant *P. aeruginosa*, we used population-averaged longitudinal models, generalized estimating equation (GEE) models, to adjust for correlation among hospitals across time. Quasi-likelihood under the independence model criterion (QIC; an extension of Akaike's information criterion to the GEE method) was used to determine the best distribution and link functions, as well as the working correlation structure. Based on comparison of QIC values, a



	2002	2003	2004	2005	2006	2007	2008	2009
Ciprofloxacin	46	44	46	48	50	49	50	53
Moxifloxacin	5	8	9	13	11	11	12	11
Gatifloxacin	18	18	16	4	1	0	0	0
Levofloxacin	73	67	67	68	73	72	67	57
Total fluoroquinolone	142	137	138	133	135	132	129	121
Percent resistance	36	35	35	32	34	32	31	32

Figure 1. Trends in mean total and individual fluoroquinolone use (DOT/1000 PD) and fluoroquinolone-resistant *P. aeruginosa* (proportion of resistant isolates) in 20 US academic health centres from 2002 to 2009. The decline in total fluoroquinolone use and the proportion of resistance are statistically significant. This figure appears in colour in the online version of *JAC* and in black and white in the print version of *JAC*.

binomial distribution, logit link and an exchangeable working correlation structure were chosen for this model. We also controlled for the use of other Gram-negative antibacterials (carbapenems, third- and fourth-generation cephalosporins, β-lactam/β-lactamase inhibitor combinations and aminoglycosides). A P value <0.05 was considered significant and all tests were two-tailed. The statistical software used was SAS (version 9.2; SAS Institute, Cary, NC, USA). The Institutional Review Board at Virginia Commonwealth University approved this study.

Antibiotic-use data were available from all 20 hospitals for all 8 years. Antibiogram data were available from all 20 hospitals for at least 3 years, while 19 hospitals provided antibiogram data for ≥5 years and 12 provided data for all 8 years. Hospitals were located in all US geographical regions; the average hospital bed capacity was 536. From 2002 to 2009 there was a steady decrease in the mean use of fluoroquinolones: from 142 (SD=35) to 121 (SD=43) DOT/1000 PD; the trend was significant ($P=0.04$). See Figure 1. Across hospitals, the mean use of levofloxacin decreased, use of moxifloxacin increased, ciprofloxacin use was variable and gatifloxacin use fell to zero when it was withdrawn from the US market. The formulary mix of fluoroquinolones was diverse among hospitals and changed throughout the study period.

There was a significant decrease in the mean proportion of fluoroquinolone-resistant *P. aeruginosa*, from 36% in 2002 to 32% in 2009 ($P=0.01$; Figure 1). The GEE model results show that both ciprofloxacin use (coefficient=0.0030; $P=0.006$) and levofloxacin use (coefficient=0.0028; $P<0.0006$) were significantly related to the proportion of ciprofloxacin-resistant *P. aeruginosa*, while moxifloxacin use (coefficient=0.0011; $P=0.55$) and gatifloxacin use (coefficient=0.0013, $P=0.55$) were not significantly associated.

This hospital-level longitudinal study among a consortium of academic medical centres found several new findings concerning trends in fluoroquinolone use and resistance in *P. aeruginosa*. First, to the best of our knowledge, this is the only study to report a significant decline in the use of fluoroquinolones across a group of hospitals. Second, there was a significant decrease in the mean proportion of fluoroquinolone-resistant *P. aeruginosa*. Third, we found that both ciprofloxacin and levofloxacin use, but not that of moxifloxacin or gatifloxacin, was associated with the resistance proportion. One of the main differences in our study is that it reflects data from a more recent time period in which fluoroquinolone use was decreasing and overall resistance of *P. aeruginosa* to fluoroquinolones was decreasing. Our finding that moxifloxacin use was not related to the proportion of resistance may be related to its lower *in vitro* activity against *P. aeruginosa* compared with the other fluoroquinolones lacking a US FDA indication for *P. aeruginosa* infections. Its use in practice is preferred for the treatment of Gram-positive organisms. Hospitals that used moxifloxacin likely had another fluoroquinolone (e.g. ciprofloxacin) on the drug formulary for use against Gram-negative infections. The lack of association between gatifloxacin use and resistance may be due to its minimal use after 2006.

There are several limitations to this investigation. The relationships between fluoroquinolone use and resistance to *P. aeruginosa* represent the hospital-level perspective, not that of the patient. Therefore, the results may be subject to ecological bias,[6] meaning that findings may not reflect

patient-level relationships. Also, we did not account for any infection-control measures that may have influenced the development of fluoroquinolone-resistant *P. aeruginosa* within hospitals, and nor did we account for community fluoroquinolone use. In conclusion, fluoroquinolone use and fluoroquinolone-resistant *P. aeruginosa* are decreasing in US academic health centres. Despite the decline in use of fluoroquinolones, it may be prudent to continue to limit the use of these agents as a strategy to decrease the resistance of this important pathogen.

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Disclaimer

The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality, the National Center for Research Resources or the National Institutes of Health.

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