

# Risk Factors for Multi- and Extreme-Drug Resistance in 4806 *Escherichia coli* Isolates in Canadian Hospitals – Results from CANWARD 2007-2010

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## ABSTRACT

**Objective:** We analysed demographic factors associated with antimicrobial resistance to key antimicrobials, multidrug resistance (MDR, resistance to  $\geq 3$  different drug classes) and extreme drug resistance (XDR,  $\geq 5$  different drug classes) in *E. coli* isolates obtained from across Canada between 2007 and 2010.

**Methods:** Clinically significant *E. coli* isolates were collected from Jan. 2007 to Dec. 2010 as part of the national CANWARD surveillance study. Susceptibility testing was performed using CLSI broth dilution methods. Regression models were used to identify factors (age, inpatient status, gender, urinary tract source) associated with resistance to fluoroquinolones (FQ), gentamicin (GM), piperacillin-tazobactam (PT), ceftriaxone (CRO) and trimethoprim-sulfamethoxazole (SXT), MDR and XDR.

**Results:** Resistance rates were 5.9% for CRO, 21.4% for FQ, 9.1% for GM, 26.3% for SXT and 2.4% for PT. 18.9% of isolates were MDR and 5.5% of isolates were XDR. Inpatient status and increasing age were the most important predictors of MDR with male gender having a small but statistically significant association with MDR. Resistance to antibiotics was consistently associated with inpatient status and for some antimicrobials, increasing age and male gender were also notable associations. A particularly strong association between fluoroquinolone resistance and increasing age was observed. Inpatient status was the only factor significantly associated with XDR.

**Conclusions:** Important risk factors for *E. coli* resistance, MDR and XDR in Canadian hospitals were increasing age, male gender and inpatient status.

## BACKGROUND

Antimicrobial resistance is a growing problem among Gram-negative isolates worldwide. *E. coli* is the most commonly isolated clinically relevant gram-negative organism in most healthcare settings (1,2). Resistance rates are increasing and multi-drug resistant (MDR, concurrent resistance to agents from  $\geq 3$  different antimicrobial classes) isolates are common (3). Appropriate empiric antimicrobial choice must take into account local resistance patterns and other demographic variables such as patient age, site and severity of infection, gender, previous antimicrobial use, stay in hospitals or personal care homes, and colonization with antimicrobial resistant organisms (1,2). The purpose of this study was to provide an in-depth analysis of patient factors associated with drug resistance in *E. coli* isolates from patients in Canadian hospitals.

## MATERIALS & METHODS

Isolates were collected as part of the CANWARD study between January 2007 and December 2010. 15 centers in 8 provinces contributed clinically relevant isolates. A total of 17,065 isolates were submitted in the study period of which 4806 were *E. coli*. Susceptibility testing was done using broth microdilution in accordance with the CLSI M07-A8 documents and susceptibility was according to CLSI M100-S21. Full factorial stepwise logistic regression using the bayesian information criterion for model optimization was used to model effects of inpatient status, age, urinary tract source and gender on resistance to fluoroquinolones, gentamicin, piperacillin-tazobactam, ceftriaxone, trimethoprim-sulfamethoxazole, MDR (resistance to  $\geq 3$  antibiotic classes) and XDR (resistance to  $\geq 5$  antibiotic classes).

## RESULTS

**TABLE 1:** Distribution of gender, patient location, specimen source and age of patients with isolates tested.

	N (%)
Male	1845 (38.4)
Female	2961 (61.6)
Inpatient	2145 (44.6)
Outpatient	2661 (55.4)
Blood	2381 (49.5)
Urine	1952 (40.6)
Wound	174 (3.6)
Respiratory	299 (6.2)
$\leq 17$ years	513 (10.7)
18 – 64 years	1995 (41.5)
$\geq 65$ years	2298 (47.8)

**TABLE 2:** Antibiotics tested by broth microdilution and percent susceptible according to CLSI M100-S21

	Percent susceptible (n=4806)
Amikacin	99.6
Amoxicillin-clavulanate*	90.1
Cefazolin	69.9
Ceftriaxone	94.1
Ciprofloxacin	76.6
Ertapenem*	99.5
Gentamicin	90.9
Meropenem	100
Piperacillin-tazobactam	97.6
Tigecycline	99.9
Trimethoprim-sulfamethoxazole	73.7
Isolates resistant to $\geq 3$ classes (MDR)	18.9
Isolates resistant to $\geq 5$ classes (XDR)	5.5

\*n = 3805

**TABLE 3:** Variables found to be significantly associated with resistance to fluoroquinolones, gentamicin, piperacillin-tazobactam, ceftriaxone, trimethoprim-sulfamethoxazole, multi-drug resistance and extreme drug resistance. No variables were associated with resistance to other antimicrobials tested (see Table 2).

	Variable associated with resistance: OR (95%CI)
Fluoroquinolones	Age >64 versus < 18: 7.2 (4.7 – 11.6) Inpatient: 1.5 (1.3 – 1.8) Male: 1.5 (1.3 – 1.8)
Ceftriaxone	Inpatient: 2.1 (1.6 – 2.7) Age >64 versus < 18: 2.3 (1.4 – 4.1)
Gentamicin	Inpatient: 1.5 (1.2 – 1.8) Male: 1.5 (1.2 – 1.9)
Trimethoprim-sulfamethoxazole	Inpatient: 1.2 (1.0 – 1.3) Non-urine isolate: 1.2 (1.1 – 1.4)
Isolates resistant to $\geq 3$ classes (MDR)	Male : 1.4 (1.2 – 1.6) Inpatient : 1.8 (1.5 – 2.1) Age >64 versus < 18: 2.6 (1.9 – 3.7)
Isolates resistant to $\geq 5$ classes (XDR)	Inpatient : 1.8 (1.2 – 2.6)

## CONCLUSIONS

❖ In this study, male gender was independently associated with resistance to fluoroquinolones, gentamicin and multi-drug resistance.

❖ In this study, inpatients were significantly more likely to have an *E. coli* isolate resistant to fluoroquinolones, ceftriaxone, gentamicin, trimethoprim-sulfamethoxazole. Inpatients were also more likely to have infections caused by multi-drug resistant and extremely-drug resistant isolates.

❖ Inpatient status was the only independent factor observed to be associated with extreme-drug resistance in this study.

❖ Age  $\geq 65$  was associated with multi-drug resistant isolates and isolates resistant to ceftriaxone and fluoroquinolones. The association with fluoroquinolone resistance was particularly strong.

❖ Isolation from the urinary tract was not independently associated with resistance to any antimicrobial, multi-drug resistance nor extreme drug resistance.

## ACKNOWLEDGEMENTS

We acknowledge the contributions of the directors and technologists of the contributing site microbiology laboratories.

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