

# Antimicrobial Susceptibility of 27,123 Pathogens Isolated from Patients in Canadian Hospitals: CANWARD Study 2007 - 2011



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## UPDATED ABSTRACT

**Background:** CANWARD is a national, annual, ongoing study assessing pathogens causing infections in Canadian hospitals and their antimicrobial resistance patterns.

**Methods:** From 2007 through 2011, 27,123 pathogens were collected from tertiary-care centres from across Canada. Susceptibility testing was performed using CLSI broth microdilution methods.

**Results:** Of the 27,123 isolates collected in total, 45.2%, 29.6%, 14.8% and 10.4% were from blood, respiratory, urine and wound specimens, respectively. Patient demographics were as follows: 54.4/45.6% male/female, 12.8% ≤17yrs, 45.1% 18-64yrs and 42.1% ≥65yrs. Isolates were obtained from patients in medical and surgical wards 37.8%, emergency rooms 25.7%, clinics 18.0% and ICUs 18.5%. The most common pathogens were: *E. coli* 20.1%, *S. aureus* (MSSA) 15.4%, *P. aeruginosa* 8.0%, *S. pneumoniae* (SPN) 6.9%, *K. pneumoniae* 6.1%, *Enterococcus* spp. 5.9%, MRSA 4.7%, *H. influenzae* 3.8%, and *Enterobacter cloacae* 2.3%. Susceptibility rates (SR) for *E. coli* were: 100% meropenem (MER), 99.7% ertapenem (ERT), 97.7% piperacillin/tazobactam (P/T), 99.9% tigecycline (TGC), 93.7% ceftriaxone (CTR), 90.5% gentamicin (Gent), 77.9% ciprofloxacin (CIP) and 73.4% cotrimoxazole (T/S). SR for *P. aeruginosa* were: 93.1% colistin, 82.6% MER, 84.0% P/T, 83.5% ceftazidime (CAZ), 72.0% Gent and 71.9% CIP. SR for MRSA were: 100% daptomycin (DAP), 100% linezolid (LZD), 100% telavancin (TLV), 99.8% TGC, 99.9% vancomycin, 92.2% T/S and 48.2% clindamycin. Statistical analysis revealed that ESBL rates among *E. coli* and *K. pneumoniae* and VRE rates increased while MRSA rates declined over time. Fluoroquinolone resistance rates in *E. coli* also increased over time.

**Conclusions:** *E. coli*, MSSA, *P. aeruginosa*, SPN, *K. pneumoniae*, MRSA and *Enterococcus* spp. are the most common pathogens in Canadian hospitals. SR for *E. coli* were highest with MER, ERT P/T and TGC. SR for *P. aeruginosa* were highest with colistin, MER, P/T and CAZ. 100% susceptibility occurred in MRSA to DAP, LZD and TLV with 99.9% with vancomycin.

## INTRODUCTION

Pathogens causing antibiotic resistant infections is a Canadian and global crisis (1,2). Antibiotic resistant pathogens including methicillin-resistant *Staphylococcus aureus* (MRSA, community-associated and healthcare-associated), vancomycin-resistant *Enterococcus* species (VRE), penicillin-resistant *Streptococcus pneumoniae* (PRSP), extended spectrum β-lactamase (ESBL) producing *Escherichia coli* and *Klebsiella* species and fluoroquinolone-resistant and carbapenem-resistant *Enterobacteriaceae* and *Pseudomonas aeruginosa* are increasing in prevalence in Canada and around the world (1,2). Available therapeutic options for the treatment of these antibiotic resistant organisms are severely limited as these organisms frequently display a multidrug resistant (MDR) phenotype.

## PURPOSE

- To determine the pathogens associated with respiratory, urinary, bacteraemic and wound/IV site infections in Canadian patients affiliated with hospitals from 2007-2011, inclusive.
- To determine the prevalence of antimicrobial resistance in pathogens associated with respiratory, urinary, bacteraemic and wound/IV site infections in Canadian patients affiliated with hospitals from 2007-2011, inclusive.
- To assess the activity of antimicrobials against respiratory, urinary, bacteraemic and wound/IV site pathogens in Canadian patients affiliated with hospitals from 2007-2011, inclusive.

## MATERIALS & METHODS

**Participating Sites:** From January 2007 to December 2011, sentinel hospital sites (12 in 2007, 10 in 2008, 15 in 2009, 14 in 2010 and 15 in 2011) in major population centres in 8 of the 10 provinces in Canada were recruited (1,2). These sites were geographically distributed in a population based fashion.

**Bacterial Isolates:** Tertiary-care medical centres submitted pathogens from patients attending hospital clinics, emergency rooms, medical and surgical wards, and intensive care units. From January 2007 through December 2011, inclusive, each study site was asked to submit clinical isolates (consecutive, one per patient, per infection site) from inpatients and outpatients with respiratory, urine, wound, and bloodstream infections. The medical centres submitted "clinically significant" isolates from patients with a presumed infectious disease. Surveillance swabs, eye, ear, nose and throat swabs were excluded. We also excluded anaerobic organisms. Isolate identification was performed by the submitting site and confirmed at the reference site as required, based on morphological characteristics and antimicrobial susceptibility patterns. Isolates were shipped on Amies semi-solid transport media to the coordinating laboratory (Health Sciences Centre, Winnipeg, Canada), subcultured onto appropriate media, and stocked in skim milk at -80°C until minimum inhibitory concentration (MIC) testing was carried out. In 2007, 2008, 2009, 2010 and 2011; 7714, 5283, 5372, 4960 and 3794 isolates were collected, respectively (1,2).

**Antimicrobial Susceptibilities:** Following 2 subcultures from frozen stock, the *in vitro* activity of selected antimicrobials was determined by broth microdilution in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines (CLSI, 2009 M7-A8). Antimicrobial minimum inhibitory concentration (MIC) interpretive standards were defined according to CLSI breakpoints (M100-S21, 2011). Susceptibility testing could not be performed with all agents due to lack of space on the susceptibility panels. Antimicrobial agents were obtained as laboratory grade powders from their respective manufacturers. Stock solutions were prepared and dilutions made as described by CLSI (M7-A8, 2009). The MICs of the antimicrobial agents for the isolates were determined using 96-well custom designed microtitre plates. These plates contained doubling antimicrobial dilutions in 100µl/well of cation adjusted Mueller-Hinton broth and inoculated to a final concentration of approximately 5 × 10<sup>5</sup> CFU/ml then incubated in ambient air for 24 hours prior to reading. Colony counts were performed periodically to confirm inocula. Quality control was performed using ATCC QC organisms including: *S. pneumoniae* 49619, *S. aureus* 29213, *E. faecalis* 29212, *E. coli* 25922, and *P. aeruginosa* 27853.

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## REFERENCES

- Zhanel GG, DeCorby M, Adam HJ, et al. 2010. Antimicrobial Agents and Chemotherapy; 54(11): 4684-4693.
- Zhanel GG, Adam HJ, Low DE, et al. 2011. Diagnostic Microbiology and Infectious Diseases; 69: 291-306.

Table 1. Antimicrobial activity against the most common Gram-positive cocci isolated from Canadian hospitals

Organism (no. tested) / Antimicrobial Agent	% S	% I	% R	MIC ( $\mu$ g/mL)	MIC <sub>50</sub>	MIC <sub>90</sub>	Range
<i>Staphylococcus aureus</i> , MSSA (n=4177)							
Cefazolin	99.9	0.1	0.5	1	≤0.5 - 32		
Ciprofloxacin	85.9	3.0	11.1	0.5	8	≤0.06 - >16	
Clarithromycin	74.8	0.3	24.9	0.25	>32	≤0.12 - >16	
Clindamycin	92.5	0.4	7.1	≤0.12	0.25	≤0.12 - >8	
Daptomycin	100.0			0.12	0.25	≤0.03 - 1	
Gentamicin	97.8	0.1	2.1	≤0.5	1	≤0.5 - >32	
Linezolid	100.0			2	2	≤0.12 - 4	
Moxifloxacin	90.1	0.6	9.3	0.06	0.25	≤0.06 - >16	
Telavancin	100.0			0.25	0.5	≤0.06 - 1	
SXT	99.5	0.5	0.5	≤0.12	0.12	≤0.12 - >8	
Vancomycin	100.0			1	1	≤0.12 - 2	
<i>Staphylococcus aureus</i> , MRSA (n=1266)							
Cefazolin	100.0	64	≥128	1	-128		
Ciprofloxacin	13.7	0.3	85.9	≤16	>16	≤0.12 - >16	
Clarithromycin	12.2	0.1	87.7	≤32	>32	≤0.03 - >32	
Clindamycin	48.2	0.1	51.7	≤8	>8	≤0.12 - >8	
Daptomycin	100.0			0.25	0.25	≤0.06 - 1	
Gentamicin	91.0	0.1	8.9	≤0.5	1	≤0.5 - >32	
Linezolid	100.0			2	2	≤0.12 - 4	
Moxifloxacin	14.4	2.1	83.6	8	≤16	≤0.06 - >16	
Telavancin	100.0			0.5	0.06	≤0.1 - 1	
SXT	92.2	0.2	7.8	≤0.12	0.05	≤0.12 - >8	
Vancomycin	99.9	0.1	1	1	≤0.25	-4	
<i>Staphylococcus epidermidis</i> (n=568)							
AMC	82.0	18.0	1	8	≤0.06	-32	
Cefazolin	84.1	0.9	15.0	1	64	≤0.5 - >128	
Ciprofloxacin	71.5	8.0	20.5	4	≤32	≤1 - >32	
Cefepime	71.5	8	≥32	≤0.06	-32		
Ceftriaxone	57.0	23.2	19.7	>4	>4	≤1 - >4	
Ciprofloxacin	43.7	1.4	54.9	4	≤16	≤0.06 - >16	
Clarithromycin	31.2	1.2	67.6	≤16	>16	≤0.25 - >16	
Clindamycin	54.7	0.7	44.6	≤0.25	≤8	≤0.06 - >8	
Daptomycin	100.0			0.12	0.25	≤0.06 - 1	
Doripenem	45.7	10.6	43.7	4	≤32	≤0.06 - >32	
Ertapenem	84.7	0.1	18.0	1	64	≤0.5 - >128	
Gentamicin	84.1	0.9	15.0	1	64	≤0.5 - >128	
Linezolid	53.6	5.0	41.4	1	≤32	≤0.5 - >32	
Meropenem	68.0	10.0	22.0	2	32	≤0.12 - >32	
Moxifloxacin	45.4	7.0	47.5	1	≤16	≤0.06 - >16	
TZP	84.0	16.1	≤1	32	≤1 - >128		
Telavancin	0.25	0.5	≤0.06	1	1	≤0.12 - >8	
SXT	59.8	41.2	1	8	≤0.12 - 8		
Vancomycin	100.0	1	2	≤0.25	-4		
<i>Streptococcus pneumoniae</i> (n=1881)							
AMC	98.2	1.0	0.9	≤0.06	0.12	≤0.06 - 16	
Ceftriaxone <sup>b</sup>	99.3	0.5	0.2	≤0.06	0.12	≤0.06 - 4	
Cefuroxime	93.7	2.0	4.3	≤0.25	0.5	≤0.25 - >16	
Ciprofloxacin	98.3	0.1	0.1	≤0.03	0.06	≤0.06 - 16	
Clarithromycin	80.3	3.7	16.0	≤0.03	4	≤0.03 - >16	
Clindamycin	93.1	0.6	6.2	≤0.12	≤0.12	≤0.12 - >64	
Doripenem	99.9	0.1	0.03	0.06	0.03	≤0.03 - 2	
Doxycycline <sup>c</sup>	93.1	3.1	3.8	≤0.25	1	≤0.25 - >16	
Ertapenem	99.3	0.7	0.1	≤0.06	0.12	≤0.06 - 16	
Levofloxacin	65.5	1.1	33.5	2			