

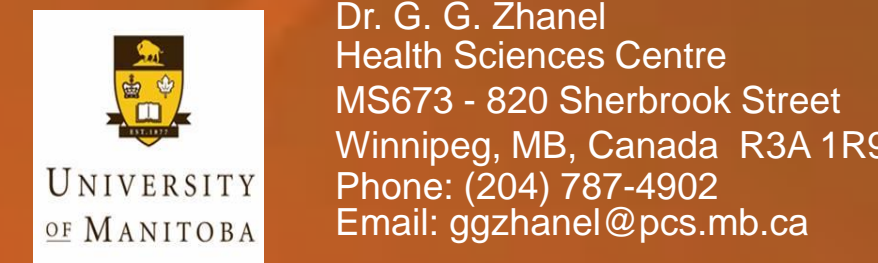
Antimicrobial Susceptibility of 39,816 Pathogens Isolated from Patients in Canadian Hospitals: CANWARD Study 2007-2015



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REVISED ABSTRACT

**Background:** CANWARD is a national, annual, Public Health Agency of Canada (PHAC) endorsed surveillance study assessing pathogens causing infections in Canadian hospitals and their antimicrobial resistance patterns. **Methods:** From 2007 to 2015, 39,816 pathogens were collected from tertiary-care hospitals across Canada. Antimicrobial susceptibility testing was performed using CLSI broth microdilution methods with >45 marketed and investigational agents. **Results:** Specimen source composition of the 39,816 isolates was 43.7% blood, 32.7% respiratory, 13.4% urine and 10.2% wound specimens. Patient demographic characteristics were: 54.5/45.5% male/female; 13.1/44.4/42.5% patients aged <17/18-64/≥65 years; and 38.0/24.9/19.0/18.1% patients located in medical and surgical wards/emergency rooms/ICUs/clinics. The most common pathogens were: *E. coli* (EC 19.6%), MSSA (16.6%), *P. aeruginosa* (PA 8.9%), *S. pneumoniae* (SPN 6.4%), *K. pneumoniae* (KP 6.1%), MRSA (4.6%), *H. influenzae* (4.1%), and *Enterococcus* spp. (4.0%). Susceptibility rates (SR) for EC were: 99.9% for meropenem (MER) and tigecycline (TGC), 99.7% ertapenem (ERT), 97.6% piperacillin-tazobactam (PTZ), 93.5% cefepime, 92.1% ceftazidime (CTR), 90.5% gentamicin (GEN), 76.9% ciprofloxacin (CIP) and 73.1% TMP-SMX (SXT). SR for PA were: 94.6% colistin, 84.4% PTZ, 83.0% ceftazidime (CAZ), 80.8% MER, 78.7% GEN and 74.7% CIP. SR for MRSA were: 100% for linezolid (LZD) and telavancin (TLV), 99.9% daptomycin (DAP) and vancomycin, 99.5% cefepime, 99.1% TGC, and 93.7% SXT. Rates of resistance in organisms between 2007-2015 increased significantly for ESBL-producing EC (3.4%-12.3%) as well as VRE (1.8%-4.4%), whereas MRSA rates (26.1%-19.4%) significantly declined. **Conclusions:** EC, MSSA, PA, SPN, KP, and MRSA are the most common pathogens in Canadian hospitals. SR for EC were highest for MER, TGC, ERT and PTZ. SR for PA were highest for colistin, PTZ, CAZ and MER. 99-100% of MRSA were susceptible DAP, LZD, TLV, cefepime and vancomycin.

MATERIALS & METHODS

**Participating Sites:** From January 2007 to December 2015, sentinel hospital sites (12 in 2007, 10 in 2008, 15 in 2009, 14 in 2010, 15 in 2011, 12 in 2012, 15 in 2013, 13 in 2014 and 13 in 2015) in major population centres in 8 of the 10 provinces in Canada were recruited. These sites were geographically distributed in a population based fashion: (BC [1 site], Alberta [1 site], Saskatchewan [1 site], Manitoba [1 site], Ontario [3-5 sites], Quebec [2-4 sites], Maritimes [1-2 sites]). **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 to October 2015, 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, as well as anaerobes, were excluded. 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, 2011, 2012, 2013, 2014 and 2015; 7714, 5283, 5374, 4960, 3788, 2803, 3511, 3174 and 3206 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 (M7-A10, 2015). Antimicrobial MIC interpretive standards were defined according to CLSI breakpoints (M100S, 2015). 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. 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 achieve a final concentration of approximately 5 x 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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INTRODUCTION

Antibiotic resistant infections is a Canadian and global crisis (1,2). Resistant pathogens including methicillin-resistant *Staphylococcus aureus* (MRSA - community associated (CA) and healthcare associated (HA)), 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. The ongoing goal of the CANWARD study is to assess pathogens associated with and antimicrobial resistance patterns in respiratory, bacteremic, urinary, and wound/IV site infections in Canadian hospitalized patients on medical/surgical wards (W), emergency rooms (ER), outpatient clinics (C) and intensive care units (ICU).

PURPOSE

- To determine the pathogens associated with respiratory, urinary, bacteremic and wound/IV site infections in Canadian patients affiliated with hospitals from 2007-2015, inclusive.
- To determine the prevalence of antimicrobial resistance in pathogens associated with respiratory, urinary, bacteremic and wound/IV site infections in Canadian patients affiliated with hospitals from 2007-2015, inclusive.
- To assess the activity of antimicrobials against respiratory, urinary, bacteremic and wound/IV site pathogens in Canadian patients affiliated with hospitals from 2007-2015, inclusive.

RESULTS

Table 1. National demographics of patients/isolates from CANWARD 2007-2015. Includes tables for Gender, Age Group, Ward Type, and Specimen Source.

Table 2. Antimicrobial activity against the most common Gram-positive cocci isolated from Canadian hospitals

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Table 3. Antimicrobial activity against the most common Gram-negative bacilli isolated from Canadian hospitals

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RESULTS

Table 4. The 20 most common organisms isolated from Canadian hospitals. Table listing Rank, Organism, and % of Total for the top 20 pathogens.

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CONCLUSIONS

- Of the 39,816 pathogens obtained, the most common were: *E. coli* 19.6%, *S. aureus* (MSSA) 16.6%, *P. aeruginosa* 8.9%, *S. pneumoniae* 6.3%, *K. pneumoniae* 6.1%, MRSA 4.6%, *H. influenzae* 4.1% and *Enterococcus* spp. (*E. faecalis* and *E. faecium*) 4.0%.
- Isolates were obtained from blood (43.7%), respiratory (32.7%), urine (13.4%) and wound specimens (10.2%) from patients on wards 38.0% (29.7% medical/8.3% surgical), ER 24.9%, ICU 19.0% and clinics 18.1%.
- Susceptibility rates for *E. coli* were: 99.9% meropenem and tigecycline, 99.7% ertapenem, 99.7% amikacin, 97.7% piperacillin/tazobactam, 95.3% ceftazidime, 93.5% cefepime, 92.1% ceftazidime, 92.1% ceftazidime, 76.9% ciprofloxacin and 73.1% trimethoprim/sulfamethoxazole.
- Susceptibility rates for *P. aeruginosa* were: 94.7% colistin, 91.9% amikacin, 84.4% doripenem, 84.4% piperacillin/tazobactam, 83.1% ceftazidime, 80.8% meropenem, 78.7% gentamicin and 74.7% ciprofloxacin.
- Susceptibility rates for MRSA were: 100% linezolid and telavancin, 99.9% daptomycin, 99.9% vancomycin, 99.5% cefepime, 99.1% TGC, 93.7% trimethoprim/sulfamethoxazole, 53.5% clindamycin, 17.0% ciprofloxacin and 15.0% for clarithromycin.

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