Antimicrobial susceptibility of 6685 organisms isolated from Canadian hospitals: CANWARD 2007

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GG Zhanel, M DeCorby, KA Nichol, et al. Antimicrobial susceptibility of 6685 organisms isolated from Canadian hospitals: CANWARD 2007. Can J Infect Dis Med Microbiol 2009;20(Suppl A):20A-30A

BACKGROUND: Antimicrobial resistance is a growing problem in North American hospitals as well as hospitals worldwide.
OBJECTIVES: To assess the antimicrobial susceptibility patterns of commonly used agents against the 20 most common organisms isolated from Canadian hospitals.
METHODS: In total, 7881 isolates were obtained between January 1, 2007, and December 31, 2007, from 12 hospitals across Canada as part of the Canadian Ward Surveillance Study (CANWARD 2007). Of these, 6685 isolates (20 most common organisms) obtained from bacteremic, urinary, respiratory and wound specimens underwent antimicrobial susceptibility testing. Susceptibility testing was assessed using the Clinical and Laboratory Standards Institute broth microdilution method.
RESULTS: The most active (based upon minimum inhibitory concentration [MIC] data only) agents against methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus epidermidis* (MRSE) were dalbavancin, daptomycin, linezolid, telavancin, tigecycline and vancomycin, with MICs required to inhibit the growth of 90% of organisms (MIC_{90}) of 0.06 µg/mL and 0.06 µg/mL, 0.25 µg/mL and 0.25 µg/mL, 4 µg/mL and 1 µg/mL, 0.25 µg/mL and 0.25 µg/mL, 0.5 µg/mL and 0.25 µg/mL, and 1 µg/mL and 2 µg/mL, respectively. The most active agents against vancomycin-resistant enterococci were daptomycin, linezolid and tigecycline with MIC_{90}s of 2 µg/mL, 4 µg/mL and 0.12 µg/mL, respectively. The most active agents against *Escherichia coli* were amikacin, cefepime, ertapenem, meropenem, piperacillin-tazobactam and tigecycline with MIC_{90}s of 4 µg/mL, 2 µg/mL, 0.06 µg/mL or less, 0.12 µg/mL or less, 4 µg/mL and 1 µg/mL, respectively. The most active agents against extended-spectrum beta-lactamase-producing *E coli* were ertapenem, meropenem and tigecycline with MIC_{90}s of 0.12 µg/mL or less, 0.12 µg/mL or less and 1 µg/mL, respectively. The most active agents against *Pseudomonas aeruginosa* were amikacin, cefepime, meropenem and piperacillin-tazobactam with MIC_{90}s of 32 µg/mL, 32 µg/mL, 8 µg/mL and 64 µg/mL, respectively. The most active agents against *Stenotrophomonas maltophilia* were tigecycline and trimethoprim-sulfamethoxazole and levofloxacin with MIC_{90}s of 8 µg/mL, 8 µg/mL and 8 µg/mL, respectively. The most active agents against *Acinetobacter baumannii* were amikacin, fluoroquinolones (eg, levofloxacin), meropenem, and tigecycline with MIC_{90}s of 2 µg/mL or less, 1 µg/mL, 4 µg/mL and 2 µg/mL, respectively.
CONCLUSIONS: The most active agents versus Gram-positive cocci from Canadian hospitals were vancomycin, linezolid, daptomycin, tigecycline, dalbavancin and telavancin. The most active agents versus Gram-negative bacilli from Canadian hospitals were amikacin, cefepime, ertapenem (not *P aeruginosa*), meropenem, piperacillin-tazobactam and tigecycline (not *P aeruginosa*). Colistin (polymyxin E) was very active against *P aeruginosa* and *A baumannii*.

Key Words: *Canadian hospitals; Resistance; Susceptibility*

La susceptibilité aux antimicrobiens de 6 685 organismes isolés dans des hôpitaux canadiens : CANWARD 2007

HISTORIQUE : La résistance aux antimicrobiens est un problème croissant dans les hôpitaux nord-américains et du monde entier.
OBJECTIFS : Évaluer les modes de susceptibilité aux antimicrobiens d'agents souvent utilisés contre les 20 principaux organismes isolés dans des hôpitaux canadiens.
MÉTHODOLOGIE : Au total, on a recueilli 7 881 isolats entre le 1er janvier et le 31 décembre 2007 dans 12 hôpitaux du Canada, dans le cadre de l'étude CANWARD 2007 sur la surveillance des services aux hospitalisés canadiens. De ce nombre, 6 685 isolats (les 20 principaux organismes) prélevés dans des échantillons bactériémiques, urinaires, respiratoires et de plaies ont subi un test de susceptibilité aux antimicrobiens. On a évalué ce test au moyen de la méthode de microdilution en milieu liquide du *Clinical and Laboratory Standards Institute*.
RÉSULTATS : Les agents les plus actifs (d'après les données de concentration minimale inhibitrice [CMI] seulement) contre le staphylocoque doré méthicillinorésistant (SARM) et le *Staphylococcus epidermidis* méthicillinorésistant (SERM) étaient la dalbavancine, la daptomycine, le linézolide, la télavancine, la tigécycline et la vancomycine, les CMI nécessaires pour inhiber la croissance de 90 % des organismes (CMI_{90}) étant de 0,06 µg/mL et 0,06 µg/mL, 0,25 µg/mL et 0,25 µg/mL, 4 µg/mL et 1 µg/mL, 0,25 µg/mL et 0,25 µg/mL, 0,05 µg/mL et 0,25 µg/mL et 1 µg/mL et 2 µg/mL, respectivement. Les agents les plus actifs contre les entérocoques résistant à la vancomycine étaient la daptomycine, le linézolide et la tigécycline, avec une CMI_{90} de 2 µg/mL, 4 µg/mL et 0,12 µg/mL, respectivement. Les agents les plus actifs contre l'*Escherichia coli* étaient l'amikacine, le céfépime, l'ertapénem, le méropénem, la pipéracilline-tazobactam et la tigécycline, avec une CMI_{90} de 4 µg/mL, 2 µg/mL, 0,06 µg/mL ou moins, 0,12 µg/mL ou moins, 4 µg/mL et 1 µg/mL, respectivement. Les agents les plus actifs contre l'*E coli* producteur de

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bêta-lactamase à large spectre étaient l'ertapénem, le méropénem et la tigécycline, avec une CMI_{90} de 0,12 µg/mL ou moins, 0,12 µg/mL ou moins et 1 µg/mL, respectivement. Les agents les plus actifs contre le *Pseudomonas aeruginosa* étaient l'amikacine, le céfépime, le méropénem et la pipéracilline-tazobactam, avec une CMI_{90} de 32 µg/mL, 32 µg/mL, 8 µg/mL et 64 µg/mL, respectivement. Les agents les plus actifs contre le *Stenotrophomonas maltophilia* étaient la tigécycline, le triméthoprim-sulfaméthoxazole et la lévoflocacine, avec une CMI_{90} de 8 µg/mL, 8 µg/mL et 8 µg/mL, respectivement. Les agents les plus actifs contre l'*Acinetobacter baumannii* étaient l'amikacine, les fluoroquinolones (p. ex., la lévofloxacine), le méropénem et la tigécycline, avec une CMI_{90} de 2 µg/mL ou moins, 1 µg/mL, 4 µg/mL et 2 µg/mL, respectivement.

CONCLUSIONS : Les agents les plus actifs contre les cocci gram positifs des hôpitaux canadiens étaient la vancomycine, le linézolide, la daptomycine, la tigécycline, la dalbavancine et la télavancine. Les agents les plus actifs contre les bacilles gram négatifs des hôpitaux canadiens étaient l'amikacine, le céfépime, l'ertapénem (sauf pour le P aeruginosa), le méropénem, la pipéracilline-tazobactam et la tigécycline (sauf pour le *P aeruginosa*). La colistine (polymyxine E) était très active contre le *P aeruginosa* et l'*A baumannii*.

Hospitals in North America as well as hospitals worldwide are facing the growing presence of infections caused by antimicrobial-resistant as well as multidrug-resistant (MDR) pathogens (1-4). Pathogens including methicillin-resistant *Staphylococcus aureus* (MRSA; community-associated [CA-MRSA] and health care-associated [HA-MRSA]), vancomycin-resistant *Enterococcus* species (VRE), penicillin-resistant *Streptococcus pneumoniae*, extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella* species, and fluoroquinolone-resistant and carbapenem-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* are growing in prevalence in Canada, the United States and globally (5-10). Treatment options of antimicrobial-resistant organisms can be severely limited because these organisms frequently display a MDR phenotype (3,4).

We recently reported on the antimicrobial activity of commonly used agents against 3931 organisms isolated from intensive care units in Canada (11). The purpose of the present study was to assess the in vitro activity (minimum inhibitory concentrations required to inhibit the growth of 50% and 90% of organisms [MIC_{50} and MIC_{90}]) of commonly prescribed antimicrobials against the 20 most common organisms (6685 isolates) obtained from patients in hospitals across Canada.

METHODS

Bacterial isolates

Study isolates were obtained as part of the Canadian Ward Surveillance Study (CANWARD 2007). The CANWARD study included 12 medical centres from all regions of Canada (www.can-r.ca). The precise methods of isolate collection are explained in detail in the first paper of the present supplement (12). In brief, from January 1, 2007, to December 31, 2007, inclusive, each centre collected and submitted clinical isolates from patients attending hospital clinics, emergency rooms, medical and surgical wards, and intensive care units. Each centre was asked to submit clinical isolates (consecutive, one organism per infection site per patient) from blood (360 isolates collected as 30 consecutive/month for each of the 12 months), respiratory (n=200), urine (n=100), and wound/intravenous (n=50) infections. All organisms were identified at the originating centre using local site criteria and were deemed clinically significant. In total, 7881 isolates were collected. Isolates were shipped to the reference laboratory (Health Sciences Centre, Winnipeg, Manitoba) on Amies charcoal swabs, subcultured onto appropriate media, and stocked in skim milk at –80°C until MIC testing was carried out.

Antimicrobial susceptibilities

Susceptibility testing was carried out using microbroth dilution in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines (11,13). For all antimicrobials tested, MIC interpretive standards were defined according to CLSI breakpoints (CLSI 2006). Susceptibility testing could not be performed with all agents due to lack of space on the susceptibility panels. Thus, susceptibility testing was not performed with *P aeruginosa* for ceftazidime, tobramycin and imipenem. The following interpretive breakpoints (Food and Drug Administration, USA) were used for tigecycline susceptible (S), intermediate (I) and resistant (R): *S aureus* (methicillin-susceptible [MSSA] and MRSA) 0.5 µg/mL or less (S); *Enterococcus faecalis* (vancomycin susceptible), 0.25 µg/mL or less (S); Enterobacteriaceae, 2 µg/mL or less (S), 4 µg/mL (I), and 8 µg/mL or greater (R). No breakpoints are presently available for dalbavancin and telavancin.

Characterization of MRSA, ESBL-producing Enterobacteriaceae and VRE

MRSA: Potential MRSA isolates were confirmed and tested as previously described (10). All isolates of MRSA were typed using pulsed-field gel electrophoresis following the Canadian standardized protocol to assess whether the isolates were CA-MRSA or HA-MRSA (9,10,14,15).

ESBL testing: Potential *E coli* or *Klebsiella* species. ESBL producers were identified and tested as previously described (10).

VRE: Potential VRE isolates were confirmed using CLSI vancomycin disk diffusion testing and underwent *van*A and *van*B polymerase chain reaction as well as DNA fingerprinting to assess genetic similarity, as previously described (7,10).

RESULTS

Patient demographics and specimen types

A total of 7881 organisms (the 20 most common organisms, representing 6685 isolates, underwent susceptibility testing) were obtained from bacteremic, urinary, respiratory and wound specimens from hospitals across Canada. The patient demographics associated with these isolates have been described (12).

Most common organisms isolated from Canadian hospitals

The 20 most common organisms isolated from hospitals across Canada included 3178 Gram-positive cocci: MSSA, *S pneumoniae*, MRSA, coagulase-negative staphylococci/*Staphylococcus epidermidis*, and *Enterococcus* species, as well as 3507 Gram-negative bacilli including *E coli*, *P aeruginosa*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, *Enterobacter cloacae* and *Proteus mirabilis* (12).

Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)

In vitro activity of various antimicrobials against MSSA, MRSA (including HA-MRSA and CA-MRSA), coagulase-negative

staphylococci/*S epidermidis* (including both methicillin-susceptible [MSSE] and methicillin-resistant [MRSE] *S epidermidis*), *S pneumoniae*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Enterococcus faecalis* and *E faecium* including VRE is displayed in Table 1. Limited resistance was observed against MSSA with the exception of clarithromycin (26.2%), fluoroquinolones (range 9.5% to 12.0%) and clindamycin (8.6%) (Table 1). One hundred per cent susceptibility was observed with cefazolin, daptomycin, ertapenem, linezolid, meropenem, piperacillin-tazobactam, tigecycline and vancomycin. Dalbavancin and telavancin were active with MIC_{90}s of 0.06 µg/mL and 0.5 µg/mL, respectively. Resistance rates with MRSA were 87.9% to 89.0% to fluoroquinolones, 90.5% to clarithromycin, 61.2% to clindamycin and 12.3% to trimethoprim-sulfamethoxazole (TMP-SMX). The most active agents tested against MRSA were vancomycin, daptomycin, linezolid and tigecycline with 100% susceptibility and MIC_{90}s of 1 µg/mL, 0.25 µg/mL, 4 µg/mL and 0.5 µg/mL, respectively (Table 1). Dalbavancin and telavancin were active against MRSA with MIC_{90}s of 0.06 µg/mL and 0.25 µg/mL, respectively. Betalactams, ertapenem, meropenem, fluoroquinolones, clindamycin, clarithromycin and TMP-SMX were more active versus CA-MRSA than HA-MRSA (Table 1). The activity of dalbavancin, daptomycin, linezolid, telavancin, tigecycline and vancomycin did not change between HA-MRSA and CA-MRSA. Against MSSE, resistance was observed with clarithromycin at 64.8%, clindamycin 38.9%, fluoroquinolones 43.5% to 52.8% and TMP-SMX 41.7% (Table 1). One hundred per cent susceptibility was observed with daptomycin, linezolid and vancomycin. Dalbavancin and telavancin were active against MSSE with MIC_{90}s of 0.06 µg/mL and 0.25 µg/mL, respectively. The most active agents tested against MRSE were vancomycin, daptomycin and linezolid with 100% susceptibility and MIC_{90}s of 2 µg/mL, 0.25 µg/mL and 1 µg/mL, respectively (Table 1). Dalbavancin, tigecycline and telavancin were active against MRSE with MIC_{90}s of 0.06 µg/mL, 0.25 µg/mL and 0.25 µg/mL, respectively.

With *S pneumoniae*, limited resistance was observed with the exception of clarithromycin at 13.0%, clindamycin at 5.8%, doxycycline at 4.4%, fluoroquinolones (range 0.6% to 4.4%) and TMP-SMX at 7.1% (Table 1). One hundred per cent susceptibility was observed with linezolid and vancomycin with MIC_{90}s of 1 µg/mL and 0.25 µg/mL or less, respectively (Table 1). Dalbavancin, tigecycline and telavancin were active against *S pneumoniae* with MIC_{90}s of 0.03 µg/mL or less, 0.03 µg/mL or less and 0.06 µg/mL or less, respectively. Against *E faecalis*, ciprofloxacin and levofloxacin resistance was 35.1% and 31.8%, respectively. All *E faecalis* were susceptible to daptomycin, tigecycline and vancomycin. Dalbavancin and telavancin were active against *E. faecalis* with MIC_{90}s of 1 µg/mL and 1 µg/mL, respectively. Against *E faecium*, ciprofloxacin and levofloxacin resistance was 82.8% and 79.3%, respectively, while vancomycin resistance was 3.3%. All *E faecium* were susceptible to daptomycin and tigecycline (Table 1). Dalbavancin and telavancin were active against *E faecium* with MIC_{90}s of 0.25 µg/mL and 0.5 µg/mL, respectively. The most active agents tested against VRE were daptomycin, linezolid and tigecycline with MIC_{90}s of 2 µg/mL, 4 µg/mL and 0.12 µg/mL, respectively. Dalbavancin and telavancin demonstrated limited

TABLE 1
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)

	% S	% I	% R	MIC_{50}	MIC_{90}	Range Min	Range Max
Methicillin-susceptible *Staphylococcus aureus* (n=1095)							
Cefazolin	100			≤0.5	1	≤0.5	2
Cefepime	99.8	0.2		4	8	≤1	16
Ceftriaxone	99.6	0.4		4	4	1	16
Ciprofloxacin	83.7	4.2	12	0.5	8	≤0.06	>16
Clarithromycin	73.2	0.6	26.2	≤0.25	>16	≤0.03	>32
Clindamycin	91	0.4	8.6	≤0.25	0.25	≤0.12	>8
Dalbavancin	No BP			0.06	0.06	≤0.03	0.25
Daptomycin	100			0.12	0.25	≤0.06	1
Ertapenem	100			0.25	0.25	0.12	0.5
Levofloxacin	89.7	0.3	10	0.25	4	≤0.06	>32
Linezolid	100			2	4	≤0.12	4
Meropenem	100			≤0.12	0.12	≤0.06	1
Moxifloxacin	90	0.6	9.5	≤0.06	1	≤0.06	>16
Nitrofurantoin	100			16	16	≤0.5	32
Piperacillin/ Tazobactam	100			≤1	≤1	≤1	8
Telavancin	No BP			0.25	0.5	≤0.06	1
Tigecycline	100			0.25	0.25	≤0.03	0.5
TMP/SMX	99.3		0.7	≤0.12	≤0.12	≤0.12	16
Vancomycin	100			1	1	≤0.25	2
Methicillin-resistant *S aureus* (MRSA) (n=385)							
Cefazolin			100.0*	64	>128	0.5	>128
Cefepime			100.0*	>32	>128	2	>256
Ceftriaxone			100.0*	>64	>256	2	>256
Ciprofloxacin	10.8	0.2	89	>16	>16	0.25	>16
Clindamycin	38.6	0.3	61.2	>8	>8	≤0.12	>8
Clarithromycin	9.5		90.5	>16	>32	≤0.12	>32
Dalbavancin	No BP			0.06	0.06	≤0.03	0.12
Daptomycin	100			0.12	0.25	0.12	1
Ertapenem			100.0*	8	>32	0.12	>32
Levofloxacin	11.6		88.4	>32	>32	0.12	>32
Linezolid	100			2	4	0.25	4
Meropenem			100.0*	8	>32	0.12	>64
Moxifloxacin	11.6	0.5	87.9	8	>16	≤0.06	>16
Nitrofurantoin	100			16	16	8	32
Piperacillin/ Tazobactam			100.0*	32	128	≤1	256
Telavancin	No BP			0.25	0.25	0.12	1
Tigecycline	100			0.25	0.5	≤0.03	0.5
TMP/SMX	87.7		12.3	≤0.12	8	≤0.12	>8
Vancomycin	100			1	1	≤0.25	2
Health care-associated MRSA (n=285)							
Cefazolin			100.0*	128	>128	1	>128
Cefepime			100.0*	256	>256	4	>32
Ceftriaxone			100.0*	>256	>256	2	>64
Ciprofloxacin	2.1		97.9	>16	>16	0.25	>16
Clindamycin	25.3	0.3	74.4	>8	>8	≤0.25	>8
Clarithromycin	3.2		96.8	>16	>16	≤0.25	>16
Dalbavancin	No BP			0.06	0.06	≤0.03	0.12
Daptomycin	100			0.12	0.25	0.12	1
Ertapenem			100.0*	16	>32	0.5	>32
Levofloxacin	2.1		97.9	>32	>32	0.12	>32
Linezolid	100			2	4	0.25	4
Meropenem			100.0*	8	>32	0.25	>32

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TABLE 1 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)

	% S	% I	% R	MIC_{50}	MIC_{90}	Range Min	Range Max
Health care-associated MRSA (n=285) – CONTINUED							
Moxifloxacin	2.1	0.4	97.5	8	>16	≤0.06	>16
Nitrofurantoin	100			16	16	8	32
Piperacillin/ Tazobactam			100.0*	64	128	2	256
Telavancin	No BP			0.25	0.25	0.12	1
Tigecycline	100			0.25	0.5	0.12	0.5
TMP/SMX	83.9		16.1	≤0.12	>8	≤0.12	>8
Vancomycin	100			1	1	≤0.25	2
Community-associated MRSA (n=71)							
Cefazolin			100.0*	8	32	1	128
Cefepime			100.0*	32	>32	8	>32
Ceftriaxone			100.0*	32	>64	16	>64
Ciprofloxacin	38	1.4	60.6	16	>16	0.25	>16
Clindamycin	90.1		9.9	≤0.25	≤0.25	≤0.25	>8
Clarithromycin	28.2		71.8	>16	>16	≤0.25	>16
Dalbavancin	No BP			0.06	0.06	≤0.03	0.12
Daptomycin	100			0.12	0.5	0.12	0.5
Ertapenem			100.0*	2	4	0.25	8
Levofloxacin	42.3		57.7	4	8	0.12	16
Linezolid	100			2	2	1	4
Meropenem			100.0*	1	4	0.25	8
Moxifloxacin	42.3	1.4	56.3	2	2	≤0.06	4
Nitrofurantoin	100			16	16	16	16
Piperacillin/ Tazobactam			100.0*	16	32	2	64
Telavancin	No BP			0.25	0.25	0.12	0.5
Tigecycline	100			0.25	0.25	0.06	0.25
TMP/SMX	100			≤0.12	≤0.12	≤0.12	1
Vancomycin	100			1	1	0.5	1
Coagulase-negative staphylococci (n=182)							
Cefazolin	84.8	1.1	14.1	1	64	≤0.5	>128
Cefepime	71.7	9.8	18.5	4	128	≤1	>128
Ceftriaxone	69.4	14.3	16.3	8	>256	0.5	>256
Ciprofloxacin	38.8	1	60.2	16	>16	0.12	>16
Clarithromycin	43.9	2	54.1	16	>16	0.12	>32
Clindamycin	71.4		28.6	≤0.25	>8	≤0.12	>8
Dalbavancin	No BP			≤0.03	0.06	≤0.03	0.12
Daptomycin	100			0.12	0.25	≤0.06	0.5
Ertapenem	83.3		16.7	0.5	>4	0.12	>4
Levofloxacin	39.8	4.1	56.1	8	>32	≤0.06	>32
Linezolid	100			1	1	≤0.12	4
Meropenem	75.5	9.2	15.3	1	16	≤0.06	32
Moxifloxacin	42.9	6.1	51	2	>16	≤0.06	>16
Piperacillin/ Tazobactam	88.8		11.2	≤1	16	≤1	256
Telavancin	No BP			0.12	0.12	≤0.06	0.12
Tigecycline	No BP			0.25	0.5	0.06	1
TMP/SMX	64.3		35.7	0.5	8	≤0.12	>8
Vancomycin	100			1	2	0.5	2
***Staphylococcus epidermidis* (n=135)**							
Cefazolin	83.1	1.5	15.4	1	64	≤0.5	128
Cefepime	72.3	6.9	20.8	4	>32	≤0.25	128
Ceftriaxone	58.6	22.6	18.8	8	>64	≤0.25	>256
Ciprofloxacin	39.9		60.1	8	>16	≤0.06	>16

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TABLE 1 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)

	% S	% I	% R	MIC_{50}	MIC_{90}	Range Min	Range Max
***Staphylococcus epidermidis* (n=135) – CONTINUED**							
Clarithromycin	29.3	1.5	69.2	>16	>32	≤0.03	>32
Clindamycin	51.9		48.1	≤0.25	>8	≤0.12	>8
Dalbavancin	No BP			≤0.03	0.06	≤0.03	0.12
Daptomycin	100			0.12	0.25	≤0.03	0.25
Ertapenem	63.6	5.5	30.9	2	>32	0.12	>32
Levofloxacin	39.8	2.3	57.9	8	>32	0.12	>32
Linezolid	100			1	1	≤0.12	2
Meropenem	77.4	4.5	18.1	1	32	≤0.06	64
Moxifloxacin	42.1	6.8	51.1	2	>16	≤0.06	>16
Nitrofurantoin	100			8	16	2	16
Piperacillin/ Tazobactam	85		15	≤1	16	≤1	128
Telavancin	No BP			0.12	0.25	≤0.06	0.25
Tigecycline	No BP			0.25	0.5	≤0.03	0.5
TMP/SMX	51.9		48.1	2	8	≤0.12	>8
Vancomycin	100			1	2	≤0.25	2
Methicillin-susceptible *S epidermidis* (n=108)							
Cefazolin	100			1	4	≤0.5	8
Cefepime	87.1	8.3	4.6	4	16	≤0.25	64
Ceftriaxone	69.4	27.8	2.8	8	16	≤0.25	128
Ciprofloxacin	47.2		52.8	4	>16	≤0.06	>16
Clarithromycin	33.3	1.9	64.8	>16	>32	≤0.03	>32
Clindamycin	61.1		38.9	≤0.25	>8	≤0.12	>8
Dalbavancin	No BP			≤0.03	0.06	≤0.03	0.12
Daptomycin	100			0.12	0.25	≤0.03	0.25
Ertapenem	76.2	7.1	16.7	0.5	8	0.12	32
Levofloxacin	47.2	1.9	50.9	4	>32	0.12	>32
Linezolid	100			0.5	1	≤0.12	2
Meropenem	91.7	5.6	2.8	1	4	≤0.06	32
Moxifloxacin	49.1	7.4	43.5	1	4	≤0.06	>16
Nitrofurantoin	100			8	16	2	16
Piperacillin/ Tazobactam	98.2		1.9	≤1	2	≤1	16
Telavancin	No BP			0.12	0.25	≤0.06	0.25
Tigecycline	No BP			0.25	0.5	≤0.03	0.5
TMP/SMX	58.3		41.7	1	>8	≤0.12	>8
Vancomycin	100			1	2	≤0.25	2
Methicillin-resistant *S epidermidis* (n=20)							
Cefazolin			100.0*	64	128	32	128
Cefepime			100.0*	64	128	32	128
Ceftriaxone			100.0*	256	>256	64	>256
Ciprofloxacin			100	>16	>16	8	>16
Clarithromycin	10		90	>16	>32	0.12	>32
Clindamycin	10		90	>8	>8	≤0.12	>8
Dalbavancin	No BP			≤0.03	0.06	≤0.03	0.06
Daptomycin	100			0.12	0.25	≤0.06	0.25
Ertapenem			100.0*	>32	>32	16	>32
Levofloxacin			100	>32	>32	4	>32
Linezolid	100			1	1	0.5	1
Meropenem			100.0*	32	32	16	64
Moxifloxacin		5	95	>16	>16	1	>16
Nitrofurantoin	100			16	16	8	16
Piperacillin/ Tazobactam			100.0*	16	64	8	128

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TABLE 1 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)

	% S	% I	% R	MIC_{50}	MIC_{90}	Range Min	Range Max
Methicillin-resistant *S epidermidis* (n=20) – CONTINUED							
Telavancin	No BP			0.25	0.25	0.12	0.25
Tigecycline	No BP			0.25	0.25	0.06	0.5
TMP/SMX	25		75	4	8	≤0.12	8
Vancomycin	100			1	2	1	2
***Streptococcus pneumoniae* – all (n=702)**							
Amoxicillin/ Clavulanate	99.4	0.4	0.2	≤0.06	0.12	≤0.06	8
Cefuroxime	95.4	2.1	2.5	≤0.25	≤0.25	≤0.25	>16
Ceftriaxone	99.7	0.1	0.2	</0.06	0.12	≤0.06	4
Ciprofloxacin	95.6		4.4	1	2	≤0.06	>16
Clarithromycin	80.9	6.1	13	≤0.03	2	≤0.03	>32
Clindamycin	94	0.2	5.8	≤0.12	≤0.12	≤0.12	>8
Dalbavancin	No BP			≤0.03	≤0.03	≤0.03	0.12
Daptomycin	No BP			≤0.06	0.12	≤0.06	0.12
Doxycycline	93	2.6	4.4	≤0.25	1	≤0.25	>16
Ertapenem	99.8		0.2	≤0.06	≤0.06	≤0.06	4
Levofloxacin	99.4		0.6	0.5	1	≤0.06	32
Linezolid	100			0.5	1	≤0.12	2
Meropenem	97.1	2.6	0.3	≤0.06	≤0.06	≤0.06	2
Moxifloxacin	99.1	0.3	0.6	0.12	0.25	≤0.06	8
Penicillin	79.1	15.7	5.2	0.06	0.25	≤0.03	8
Piperacillin/ Tazobactam	No BP			≤1	≤1	≤1	4
Telavancin	No BP			≤0.06	≤0.06	≤0.06	0.12
Telithromycin	100			0.015	0.3	≤0.008	0.5
Tigecycline	No BP			≤0.03	≤0.03	≤0.03	0.12
TMP/SMX	86.2	6.7	7.1	≤0.12	1	≤0.12	>8
Vancomycin	100			≤0.25	≤0.25	≤0.25	0.5
***Streptococcus pyogenes* (n=105)**							
Ceftriaxone	100			≤0.06	≤0.06	≤0.06	≤0.06
Ciprofloxacin	No BP			1	2	0.25	4
Clarithromycin	90.4		9.6	≤0.03	0.12	≤0.03	>32
Clindamycin	97.3		2.7	≤0.12	≤0.12	≤0.12	>8
Dalbavancin	No BP			≤0.03	≤0.03	≤0.03	≤0.03
Daptomycin	100			≤0.03	0.06	≤0.03	0.12
Ertapenem	100			≤0.06	≤0.06	≤0.06	≤0.06
Levofloxacin	98.6	1.4		0.5	1	0.25	4
Linezolid	100			1	1	0.5	2
Meropenem	100			≤0.06	≤0.06	≤0.06	≤0.06
Moxifloxacin	No BP			0.12	0.25	≤0.06	0.5
Piperacillin/ Tazobactam	No BP			≤1	≤1	≤1	≤1
Telavancin	No BP			≤0.06	≤0.06	≤0.06	≤0.06
Tigecycline	100			≤0.03	0.06	≤0.03	0.12
TMP/SMX	No BP			≤0.12	≤0.12	≤0.12	0.25
Vancomycin	100			0.5	0.5	≤0.25	0.5
***Streptococcus agalactiae* (n=116)**							
Ceftriaxone	100			≤0.06	≤0.06	≤0.06	0.25
Ciprofloxacin	No BP			1	2	0.5	>16
Clarithromycin	75	3.4	21.6	≤0.03	>32	≤0.03	>32
Clindamycin	85.2	2.3	12.5	≤0.12	>8	≤0.12	>8
Dalbavancin	No BP			≤0.03	≤0.03	≤0.03	≤0.03
Daptomycin	100			0.12	0.12	≤0.03	0.12
Ertapenem	100			≤0.06	≤0.06	≤0.06	≤0.06

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TABLE 1 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)

	% S	% I	% R	MIC_{50}	MIC_{90}	Range Min	Range Max
***Streptococcus agalactiae* (n=116) – CONTINUED**							
Levofloxacin	97.7		2.3	1	1	0.5	>32
Linezolid	100			1	1	≤0.12	2
Meropenem	100			≤0.06	≤0.06	≤0.06	≤0.06
Moxifloxacin	No BP			0.12	0.25	≤0.06	4
Nitrofurantoin	No data						
Piperacillin/ Tazobactam	No BP			≤1	≤1	≤1	≤1
Telavancin	No BP			≤0.06	≤0.06	≤0.06	≤0.06
Tigecycline	100			0.06	0.12	≤0.03	0.12
TMP/SMX	No BP			≤0.12	≤0.12	≤0.12	0.25
Vancomycin	100			0.5	0.5	≤0.25	0.5
***Enterococcus*, nonspeciated (n=237)**							
Cefazolin	No BP			32	128	≤0.5	>128
Cefepime	No BP			64	>128	≤0.25	>128
Ceftriaxone	No BP			256	>256	≤0.25	>256
Ciprofloxacin	31	24.6	44.4	2	>16	≤0.06	>16
Clarithromycin	No BP			>16	>16	≤0.03	>32
Clindamycin	No BP			>8	>8	≤0.12	>8
Dalbavancin	No BP			0.06	0.12	≤0.03	0.5
Daptomycin	100			0.5	1	≤0.03	2
Ertapenem	No BP			8	>32	≤0.06	>32
Levofloxacin	58.2	0.4	41.4	2	>32	≤0.06	>32
Linezolid	95.7	4.3		2	2	≤0.12	4
Meropenem	No BP			8	16	≤0.06	>64
Moxifloxacin	No BP			0.5	>16	≤0.06	>16
Nitrofurantoin	84	8	8	8	64	≤0.5	128
Piperacillin/ Tazobactam	No BP			4	16	≤1	>512
Telavancin	No BP			0.5	1	≤0.06	1
Tigecycline	No BP			0.12	0.25	≤0.03	1
Vancomycin	99.1	0.9		1	2	≤0.25	>8
***Enterococcus faecalis* (n=161)**							
Cefazolin	No BP			32	128	0.5	>128
Cefepime	No BP			>32	128	≤0.25	>128
Ceftriaxone	No BP			>64	>256	≤0.25	>256
Ciprofloxacin	38.3	26.6	35.1	2	>16	0.25	>16
Clarithromycin	No BP			2	>32	0.06	>32
Clindamycin	No BP			>8	>8	≤0.12	>8
Dalbavancin	No BP			0.06	0.06	≤0.03	0.25
Daptomycin	100			0.5	1	≤0.06	2
Ertapenem	No BP			8	16	0.25	>32
Levofloxacin	68.2		31.8	2	>32	0.25	>32
Linezolid	98.7	1.3		2	2	0.5	4
Meropenem	No BP			4	8	≤0.06	>32
Moxifloxacin	No BP			0.5	16	≤0.06	>16
Nitrofurantoin	98.8	1.2		8	16	2	64
Piperacillin/ Tazobactam	No BP			4	8	≤1	512
Telavancin	No BP			0.5	1	≤0.06	1
Tigecycline	100			0.12	0.25	0.06	0.25
Vancomycin	100			1	2	0.5	4
***Enterococcus faecium* (n=60)**							
Cefazolin	No BP			>128	>128	32	>128
Cefepime	No BP			>32	>128	2	>128

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TABLE 1 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-positive cocci)

	% S	% I	% R	MIC_{50}	MIC_{90}	Range Min	Range Max
***Enterococcus faecium* (n=60) – CONTINUED**							
Ceftriaxone	No BP			>64	>256	0.5	>256
Ciprofloxacin	12.1	5.1	82.8	>16	>16	1	>16
Clarithromycin	No BP			>32	>32	0.5	>32
Clindamycin	No BP			>8	>8	≤0.12	>8
Dalbavancin	No BP			0.12	0.25	≤0.03	>16
Daptomycin	100			1	2	0.12	2
Ertapenem	No BP			>32	>32	4	>32
Levofloxacin	17.2	3.5	79.3	>32	>32	1	>32
Linezolid	91.4	8.6		2	2	1	4
Meropenem	No BP			>32	>64	4	>64
Moxifloxacin	No BP			>16	>16	≤0.25	>16
Nitrofurantoin	40.6	32.4	27	64	128	8	128
Piperacillin/ Tazobactam	No BP			512	>512	2	>512
Telavancin	No BP			0.12	0.5	≤0.06	4
Tigecycline	100			0.12	0.12	0.06	0.5
Vancomycin	88.3		11.7	0.5	>8	≤0.25	>8
Vancomycin-resistant enterococci (n=8)†							
Cefazolin	No BP			>128	>128	>128	>128
Cefepime	No BP			>128	>128	>32	>128
Ceftriaxone	No BP			>256	>256	>64	>256
Ciprofloxacin			100	>16	>16	>16	>16
Clarithromycin	No BP			>16	>32	2	>32
Clindamycin	No BP			>8	>8	≤0.25	>8
Dalbavancin	No BP			0.5	>16	0.06	>16
Daptomycin	100			1	2	0.25	2
Ertapenem	No BP			>32	>32	>32	>32
Levofloxacin	No BP		100	>32	>32	>32	>32
Linezolid	75	25		2	4	1	4
Meropenem	No BP			>64	>64	>32	>64
Moxifloxacin	No BP			>16	>16	>16	>16
Nitrofurantoin		50	50	64	128	64	128
Piperacillin/ Tazobactam	No BP			>512	>512	>512	>512
Telavancin	No BP			0.12	4	0.12	4
Tigecycline	No BP			0.06	0.12	0.06	0.12
Vancomycin			100	>8	>8	>8	>8

**Based upon oxacillin susceptibility; †5 van*A *and 3* van*B. I intermediate; Max Maximum; $MIC_{50/90}$ Minimum inhibitory concentrations (in µg/mL) required to inhibit 50%/90% of organisms; Min Minimum; No BP No Clinical and Laboratory Standards Institute (or Food and Drug Administration for tigecycline) -approved breakpoints defined; R resistant; S susceptible*

activity against VRE with MIC_{90}s of greater than 16 µg/mL and 4 µg/mL, respectively.

Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-negative bacilli)

The in vitro activity of various antimicrobials against *E coli* (including ESBL-producing *E coli*), *P aeruginosa*, *K pneumoniae*, *H influenzae*, *E cloacae*, *P mirabilis*, *Serratia marcescens*, *S maltophilia*, *Klebsiella oxytoca*, *Moraxella catarrhalis* and *A baumannii* is displayed in Table 2. For *E coli*, resistance rates were: TMP-SMX 26.6%, ciprofloxacin and levofloxacin 24.5% and 23.6%, respectively, and cefazolin 14.2% (Table 2). Limited resistance occurred with ceftriaxone 8.9%, gentamicin 10.6%, nitrofurantoin 1.2%, piperacillin-tazobactam 1.3% and cefepime 2.0%. One hundred per cent susceptibility was observed with ertapenem and meropenem, while 99.8% of *E coli* were susceptible to tigecycline (Table 2). Thus, the most active agents against *E coli* were amikacin, amoxicillin-clavulanate, cefepime, ertapenem, meropenem, piperacillin-tazobactam and tigecycline with MIC_{90}s of 4 µg/mL, 8 µg/mL, 2 µg/mL, 0.06 µg/mL or less, 0.12 µg/mL or less, 4 µg/mL and 1 µg/mL, respectively. ESBL-producing *E coli* displayed 92.5% resistance to ciprofloxacin, 67.9% resistance to TMP-SMX and 58.5% resistance to gentamicin. All ESBL-producing *E coli* were susceptible to ertapenem, meropenem, nitrofurantoin and tigecycline, with MIC_{90}s of 0.12 µg/mL, 0.12 µg/mL or less, 32 µg/mL and 1 µg/mL, respectively. The most active agents tested against *P aeruginosa* were piperacillin-tazobactam, meropenem, colistin (polymyxin E) and amikacin, with 92.7%, 87.8%, 87.6% and 85.4% susceptibility and MIC_{90}s of 64 µg/mL, 8 µg/mL, 4 µg/mL and 32 µg/mL, respectively (Table 2). Resistance with *P aeruginosa* was high with fluoroquinolones 23.4% to 25.1% and gentamicin 20.8%. All agents were active against *H influenzae* except TMP-SMX, with 12.1% resistance. For *K pneumoniae*, resistance rates were: TMP-SMX 8.8%, cefazolin 7.0%, fluoroquinolones 4.2% to 6.6%, piperacillin-tazobactam 2.0%, tigecycline 1.7% and ceftriaxone 3.1%. One hundred per cent susceptibility occurred with ertapenem and meropenem as well as 99.6% with amikacin (Table 2). With *E cloacae*, resistance rates were: cefazolin 91.0%, ceftriaxone 18.1%, TMP-SMX 8.4%, piperacillin-tazobactam 9.1%, gentamicin 3.6%, fluoroquinolones 3.0% to 7.8% and tigecycline 1.2%. One hundred per cent susceptibility occurred with amikacin, cefepime, ertapenem and meropenem (Table 2). With *P mirabilis*, resistance rates were: cefazolin 5.0%, TMP-SMX 9.2%, fluoroquinolones 7.6% to 9.2% and gentamicin 3.4%. One hundred per cent susceptibility occurred with cefepime, ceftriaxone, ertapenem, meropenem and piperacillin-tazobactam (Table 2). With *S marcescens*, resistance rates were: cefazolin 99.1%, TMP-SMX 2.8%, fluoroquinolones 4.7% to 7.5%, ceftriaxone 2.8%, gentamicin 4.7%, and piperacillin-tazobactam 0.9%. With *S marcescens*, 100% susceptibility occurred with cefepime, ertapenem and meropenem, while 99.1% were susceptible to amikacin (Table 2). The most active agents tested against *S maltophilia* were TMP-SMX and levofloxacin with 75.5% and 65.1% susceptibility, respectively, and MIC_{90}s of 8 µg/mL and 8 µg/mL, respectively. The remaining agents demonstrated high rates of resistance (61.5% to 97.2%). Tigecycline was active with MIC_{50}s and MIC_{90}s of 2 µg/mL and 8 µg/mL, respectively. All agents were very active against *M catarrhalis*. With *K oxytoca*, all agents were very active except cefazolin, with 17.0% resistance. The most active agents tested against *A baumannii* were amikacin, gentamicin, levofloxacin and meropenem with 92.0% susceptibility for all four agents, and MIC_{90}s of 2 µg/mL or less, 1 µg/mL, 1 µg/mL and 4 µg/mL, respectively. Tigecycline was active with MIC_{50}s and MIC_{90}s of 0.5 µg/mL and 2 µg/mL, respectively.

DISCUSSION

The CANWARD study was the first national, prospective surveillance study assessing antimicrobial activity against pathogens from Canadian hospitals, including hospital clinics,

TABLE 2
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-negative bacilli)

	% S	% I	% R	MIC_{50}	MIC_{90}	Range Min	Range Max
***Escherichia coli* (n=1701)**							
Amikacin	99.5	0.4	0.1	≤2	4	≤2	>64
Amoxicllin/ Clavulanate	90.3	8.5	1.2	4	8	0.5	32
Cefazolin	82.1	3.7	14.2	2	64	≤0.5	>128
Cefepime	95.2	2.8	2	≤1	2	≤0.25	>128
Cefoxitin	92.4	3.8	3.8	4	8	≤0.06	>128
Ceftriaxone	89.2	1.9	8.9	≤1	16	≤0.25	>256
Ciprofloxacin	75.2	0.3	24.5	≤0.06	>16	≤0.06	>16
Colistin	No BP			0.5	1	≤0.06	>16
Ertapenem	100			≤0.06	≤0.06	≤0.06	1
Gentamicin	88.9	0.5	10.6	≤0.5	16	≤0.5	>32
Levofloxacin	75.7	0.8	23.6	≤0.06	16	≤0.06	>32
Meropenem	100			≤0.12	≤0.12	≤0.06	0.5
Moxifloxacin	No BP			≤0.06	>16	≤0.06	>16
Nitrofurantoin	95.7	3.1	1.2	16	32	≤0.5	>256
Piperacillin/ Tazobactam	97.6	1.1	1.3	2	4	≤1	>512
Tigecycline	99.8	0.2		0.25	1	0.06	4
TMP/SMX	73.4		26.6	≤0.12	>8	≤0.12	>8
Extended-spectrum beta-lactamase *E coli* (n=53)							
Amikacin	94.3	3.8	1.9	4	16	≤2	>64
Amoxicllin/ Clavulanate	60.4	37.7	1.9	8	16	4	16
Cefazolin			100	128	>128	128	>128
Cefepime	45.3	30.2	24.5	16	>32	≤1	>32
Cefoxitin	92.4	5.7	1.9	8	8	4	>32
Ceftriaxone	3.8	15.1	81.1	>64	>64	2	>64
Ciprofloxacin	7.5		92.5	>16	>16	≤0.06	>16
Colistin	No BP			1	1	0.25	2
Ertapenem	100			≤0.06	0.12	≤0.06	0.25
Gentamicin	41.5		58.5	32	>32	≤0.5	>32
Levofloxacin	7.5		92.5	16	32	≤0.06	>32
Meropenem	100			≤0.12	≤0.12	≤0.12	≤0.12
Moxifloxacin	No BP			>16	>16	≤0.06	>16
Nitrofurantoin	96.2	3.8		16	32	8	32
Piperacillin/ Tazobactam	92.4	5.7	1.9	4	16	≤1	>512
Tigecycline	100			0.5	1	0.25	2
TMP/SMX	32.1		67.9	>8	>8	≤0.12	>8
***Pseudomonas aeruginosa* (n=633)**							
Amikacin	85.4	7	7.6	8	32	≤2	>64
Amoxicllin/ Clavulanate	No BP			>32	>32	1	>32
Cefazolin	No BP			>128	>128	16	>128
Cefepime	67.4	20.9	11.7	8	32	≤0.25	>128
Cefoxitin	No BP			>32	>32	2	>32
Ceftriaxone	23.9	40.9	35.2	32	256	≤0.25	>256
Ciprofloxacin	66	10.6	23.4	0.5	16	≤0.06	>16
Colistin	87.6		12.4	2	4	0.5	>16
Ertapenem	No BP			8	32	0.12	>32
Gentamicin	60.2	19	20.8	4	>32	≤0.5	>32
Levofloxacin	61.5	13.4	25.1	2	16	≤0.06	>32
Meropenem	87.8	4.1	8.1	0.5	8	≤0.06	>64
Moxifloxacin	No BP			4	>16	≤0.06	>16

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TABLE 2 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-negative bacilli)

	% S	% I	% R	MIC_{50}	MIC_{90}	Range Min	Range Max
***Pseudomonas aeruginosa* (n=633) – CONTINUED**							
Nitrofurantoin	No BP			>256	>256	16	>256
Piperacillin/ Tazobactam	92.7		7.3	4	64	≤1	>512
Tigecycline	No BP			>16	>16	0.25	>16
TMP/SMX	14.5		85.5	>8	>8	≤0.12	>8
***Klebsiella pneumoniae* (n=455)**							
Amikacin	99.6		0.4	≤2	≤2	≤2	>64
Amoxicllin/ Clavulanate	93.5	5	1.5	2	8	1	>32
Cefazolin	91.2	1.8	7	2	8	≤0.5	>128
Cefepime	97.8	0.2	2	≤1	≤1	≤0.25	128
Cefoxitin	91	4.5	4.5	4	8	1	>32
Ceftriaxone	96.2	0.7	3.1	≤1	≤1	≤0.25	>256
Ciprofloxacin	92.5	0.9	6.6	≤0.06	0.5	≤0.06	>16
Colistin	No BP			0.5	1	0.12	>16
Ertapenem	100			≤0.06	≤0.06	≤0.06	2
Gentamicin	96.7	0.4	2.9	≤0.5	≤0.05	≤0.5	>32
Levofloxacin	93.8	2	4.2	≤0.06	1	≤0.06	>32
Meropenem	100			≤0.12	≤0.12	≤0.06	0.25
Moxifloxacin	No BP			0.12	1	≤0.06	>16
Nitrofurantoin	35.1	33.2	31.7	64	128	8	>256
Piperacillin/ Tazobactam	96.7	1.3	2	2	8	≤1	>512
Tigecycline	94.3	4	1.7	1	2	0.25	>16
TMP/SMX	91.2		8.8	≤0.12	2	≤0.12	>8
***Haemophilus influenzae* (n=342)**							
Amoxicillin/ Clavulanate	99.7		0.3	0.5	1	≤0.06	8
Cefepime	100			≤0.25	≤0.25	≤0.25	2
Ceftriaxone	99.7		0.3	≤0.06	≤0.06	≤0.06	>4
Ciprofloxacin	100			≤0.015	≤0.015	≤0.015	0.5
Ertapenem	99.7		0.3	≤0.03	0.12	≤0.03	>4
Gentamicin	No BP			1	2	≤0.5	16
Levofloxacin	100			≤0.015	0.03	≤0.015	0.5
Meropenem	99.7		0.3	≤0.06	0.12	≤0.06	2
Moxifloxacin	100			≤0.015	0.06	≤0.015	0.5
Piperacillin/ Tazobactam	99.7		0.3	≤1	≤1	≤1	2
Tigecycline	No BP			0.12	0.5	≤0.03	4
TMP/SMX	83.5	4.4	12.1	≤0.12	4	≤0.12	>8
***Enterobacter cloacae* (n=166)**							
Amikacin	100			≤2	≤2	≤2	16
Amoxicillin/ Clavulanate	8.4	20.8	70.8	32	>32	2	>32
Cefazolin	5.4	3.6	91	128	>128	1	>128
Cefepime	100			≤1	2	≤0.25	8
Cefoxitin	48.6	8.3	43.1	16	>32	4	>32
Ceftriaxone	78.3	3.6	18.1	≤1	>64	≤0.25	>256
Ciprofloxacin	91.6	0.6	7.8	≤0.06	0.5	≤0.06	>16
Colistin	No BP			0.5	16	0.12	>16
Ertapenem	100			≤0.06	0.5	≤0.06	2
Gentamicin	96.4		3.6	≤0.5	1	≤0.5	>32
Levofloxacin	92.8	4.2	3	≤0.06	1	≤0.06	32
Meropenem	100			≤0.12	≤0.12	≤0.06	0.5

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TABLE 2 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-negative bacilli)

	% S	% I	% R	MIC_{50}	MIC_{90}	Range Min	Range Max
***Enterobacter cloacae* (n=166) – CONTINUED**							
Moxifloxacin	No BP			0.12	0.5	≤0.06	>16
Nitrofurantoin	54.2	38.9	6.9	32	64	16	256
Piperacillin/ Tazobactam	82.5	8.4	9.1	2	64	≤1	512
Tigecycline	93.4	5.4	1.2	1	1	0.25	16
TMP/SMX	91.6		8.4	≤0.12	1	≤0.12	>8
***Proteus mirabilis* (n=119)**							
Amikacin	99.2	0.8		4	8	≤2	32
Amoxicillin/ Clavulanate	97.1		2.9	1	4	0.5	32
Cefazolin	86.6	8.4	5	8	16	1	64
Cefepime	100			≤1	≤1	≤0.25	2
Cefoxitin	91.2	8.8		4	8	2	16
Ceftriaxone	100			≤1	≤1	≤0.25	4
Ciprofloxacin	82.4	8.4	9.2	≤0.06	2	≤0.06	>16
Colistin	No BP			>16	>16	>16	>16
Ertapenem	100			≤0.06	≤0.06	≤0.06	0.12
Gentamicin	95.8	0.8	3.4	1	2	≤0.5	>32
Levofloxacin	88.2	4.2	7.6	0.12	4	≤0.06	>32
Meropenem	100			≤0.12	≤0.12	≤0.06	0.25
Moxifloxacin	No BP			0.5	16	0.12	>16
Nitrofurantoin		5.9	94.1	128	128	64	256
Piperacillin/ Tazobactam	100			≤1	≤1	≤1	2
Tigecycline	10.1	35.3	54.6	8	8	1	16
TMP/SMX	90.8		9.2	≤0.12	2	≤0.12	>8
***Serratia marcescens* (n=108)**							
Amikacin	99.1	0.9		≤2	4	≤2	32
Amoxicillin/ Clavulanate	2.6	30.8	66.6	32	>32	4	>32
Cefazolin	0.9		99.1	>128	>128	2	>128
Cefepime	100			≤1	≤1	≤0.25	8
Cefoxitin	7.7	53.8	38.5	16	>32	4	>32
Ceftriaxone	92.5	4.7	2.8	≤1	≤1	≤0.25	>64
Ciprofloxacin	88.8	3.7	7.5	0.12	2	≤0.06	16
Colistin	No BP			>16	>16	>16	>16
Ertapenem	100			≤0.06	≤0.06	≤0.06	0.5
Gentamicin	91.6	3.7	4.7	≤0.5	1	≤0.5	>32
Levofloxacin	90.6	4.7	4.7	0.12	2	≤0.06	16
Meropenem	100			≤0.12	≤0.12	≤0.06	2
Moxifloxacin	No BP			0.25	4	≤0.06	>16
Nitrofurantoin		2.6	97.4	256	>256	64	>256
Piperacillin/ Tazobactam	94.4	4.7	0.9	2	8	≤1	128
Tigecycline	61.7	32.7	5.6	2	4	0.12	>16
TMP/SMX	97.2		2.8	0.5	1	≤0.12	8
***Stenotrophomonas maltophilia* (n=107)**							
Amikacin*	16	8.5	75.5	>64	>64	≤2	>64
Amoxicillin/ Clavulanate	No BP			>32	>32	4	>32
Cefazolin	No BP			>128	>128	128	>128
Cefepime*	4.7	6.6	88.7	64	128	≤0.25	>128
Cefoxitin	No BP			>32	>32	8	>32
Ceftriaxone*	0.9	1.9	97.2	256	>256	8	>256

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TABLE 2 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-negative bacilli)

	% S	% I	% R	MIC_{50}	MIC_{90}	Range Min	Range Max
***Stenotrophomonas maltophilia* (n=107) – CONTINUED**							
Ciprofloxacin*	6.6	24.5	68.9	4	>16	≤0.06	>16
Colistin*	26.9	11.6	61.5	8	>16	0.25	>16
Ertapenem	No BP			>32	>32	0.12	>32
Gentamicin*	17	4.7	78.3	32	>32	≤0.5	>32
Levofloxacin	65.1	14.2	20.7	2	8	≤0.06	>32
Meropenem*	5.7	1.9	92.4	>64	>64	≤0.06	>64
Moxifloxacin	No BP			1	8	0.12	>16
Nitrofurantoin	No BP			>256	>256	32	>256
Piperacillin/ Tazobactam*	3.8	14.1	82.1	256	>512	16	>512
Tigecycline	No BP			2	8	0.25	16
TMP/SMX	75.5		24.5	1	8	≤0.12	>8
***Klebsiella oxytoca* (n=100)**							
Amikacin	100			≤2	≤2	≤2	16
Amoxicillin/ Clavulanate	96.9	3.1		2	4	1	16
Cefazolin	60	23	17	8	32	≤0.5	>128
Cefepime	99	1		≤1	≤1	≤0.25	16
Cefoxitin	96.9	3.1		2	4	1	16
Ceftriaxone	94	6		≤1	≤1	≤0.25	32
Ciprofloxacin	95	2	3	≤0.06	0.12	≤0.06	16
Colistin	No BP			0.5	1	0.25	2
Ertapenem	100			≤0.06	≤0.06	≤0.06	≤0.06
Gentamicin	97	2	1	≤0.5	≤0.5	≤0.5	>32
Levofloxacin	96	2	2	≤0.06	0.12	≤0.06	8
Meropenem	100			≤0.12	≤0.12	≤0.06	0.12
Moxifloxacin	No BP			0.12	0.25	≤0.06	>16
Nitrofurantoin	75	21.9	3.1	32	64	8	128
Piperacillin/ Tazobactam	90	1	9	2	16	≤1	>512
Tigecycline	99		1	0.5	2	0.25	8
TMP/SMX	95		5	≤0.12	≤0.12	≤0.12	>8
***Moraxella catarrhalis* (n=93)**							
Amikacin							
Amoxicillin/ Clavulanate	No BP			0.12	0.25	≤0.06	0.5
Cefazolin							
Cefepime							
Cefoxitin							
Ceftriaxone	No BP			0.25	1	≤0.06	1
Ciprofloxacin	No BP			≤0.06	≤0.06	≤0.06	0.12
Colistin							
Ertapenem	No BP			≤0.06	≤0.06	≤0.06	0.12
Gentamicin							
Levofloxacin	No BP			≤0.06	≤0.06	≤0.06	0.12
Meropenem	No BP			≤0.06	≤0.06	≤0.06	≤0.06
Moxifloxacin	No BP			≤0.06	≤0.06	≤0.06	0.25
Nitrofurantoin							
Piperacillin/ Tazobactam	No BP			≤1	≤1	≤1	≤1
Tigecycline	No BP			0.12	0.25	0.06	0.5
TMP/SMX	No BP			≤0.12	2	≤0.12	>8

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TABLE 2 – CONTINUED
Antimicrobial activity against the 20 most common organisms isolated from Canadian hospitals (Gram-negative bacilli)

	% S	% I	% R	MIC_{50}	MIC_{90}	Range Min	Range Max
***Acinetobacter baumannii* (n=25)**							
Amikacin	92		8	≤2	≤2	≤2	>64
Amoxicillin/ Clavulanate	No BP			8	32	2	>32
Cefazolin	No BP			>128	>128	64	>128
Cefepime	84	8	8	4	16	≤1	>128
Cefoxitin	No BP			>32	>32	8	>32
Ceftriaxone	24	68	8	16	32	4	>256
Ciprofloxacin	88		12	0.25	4	0.12	32
Colistin	No BP			1	2	1	2
Ertapenem	No BP			4	8	2	>32
Gentamicin	92		8	≤0.5	1	≤0.5	>32
Levofloxacin	92		8	0.25	1	≤0.06	>16
Meropenem	92		8	0.5	4	≤0.12	32
Moxifloxacin	No BP			0.12	0.5	≤0.06	8
Nitrofurantoin	No BP			>256	>256	256	>256
Piperacillin/ Tazobactam	76	12	12	4	>128	≤1	>512
Tigecycline	No BP			0.5	2	0.12	4
TMP/SMX	84		16	≤0.12	>8	≤0.12	>8

**Non-Enterobacteriaceae breakpoints used. Colistin (polymyxin E); I Intermediate; Max Maximum; $MIC_{50/90}$ Minimum inhibitory concentrations (in µg/mL) required to inhibit 50%/90% of organisms; Min Minimum; No BP No Clinical and Laboratory Standards Institute (or Food and Drug Administration for tigecycline) -approved breakpoints defined; R Resistant; S Susceptible; TMP-SMX Trimethoprim-sulfamethoxazole*

emergency rooms, medical and surgical wards, and intensive care units. A total of 7881 organisms were obtained between January 1, 2007, and December 31, 2007, inclusive. Of the 7881 organisms, 6885 (87.4%) represented the 20 most common organisms isolated from hospitals in Canada and underwent antimicrobial susceptibility testing.

The most active agents (based upon MIC data only) against the 3178 Gram-positive organisms tested were vancomycin, linezolid, daptomycin, tigecycline, dalbavancin and telavancin (Table 1). It should be mentioned that listing agents as most active based solely upon MIC is not accurate because potency depends both upon the agent's pharmacokinetics as well as in vitro susceptibility (ie, pharmacodynamics). Vancomycin was active against MSSA and MRSA with MIC_{90}s of 1 µg/mL and 1 µg/mL, respectively. Only six of 1095 (0.55%) MSSA and four of 385 (1.0%) MRSA demonstrated vancomycin MICs of 2 µg/mL. No MSSA or MRSA with vancomycin MICs of 4 µg/mL or greater were obtained. This is consistent with previous data that has reported that vancomycin continues to be active against MSSA and MRSA in Canada (4,9,11). It must however be stated that no population analysis profiling was performed on any MRSA to assess for heteroresistant vancomycin-intermediate *S aureus*. Against MSSE and MRSE, vancomycin was less active compared with MSSA and MRSA. The MIC_{90}s for both MSSE and MRSE were 2 µg/mL. This reduced vancomycin activity against MSSE and MRSE versus MSSA and MRSA has also been previously documented (9,16). In this study, as well as with previous data, vancomycin continues to be very active against all *Streptococcus* species, with all isolates displaying MICs of 1 µg/mL or less (9,17). Vancomycin was less active against *E faecalis* and *E faecium* with 0% and 11.7% of strains resistant, respectively. As has been reported elsewhere, the predominant VRE genotype in North America continues to be *van*A (4,7).

Linezolid was active against MSSA and MRSA with 100% of isolates demonstrating susceptibility with MICs 4 µg/mL or less (Table 1). No difference in linezolid activity was observed between HA-MRSA and CA-MRSA. Linezolid was more active against MSSE and MRSE in comparison with MSSA and MRSA, with all isolates demonstrating linezolid MICs of 1 µg/mL or less (Table 1). Linezolid's continued excellent activity against MSSA/MRSA and MSSE/MRSE has been previously documented (11,16,17). As has been previously documented, linezolid continues to be active against *Streptococcus* species with all isolates displaying MICs of 2 µg/mL or less (11,17). Linezolid was less active against *E faecalis* and *E faecium*, with 1.3% and 8.6% of strains demonstrating intermediate resistance, respectively. This rate of linezolid resistance in *E faecium* is consistent with previous reports (17-19).

Daptomycin was active against MSSA and MRSA with 100% of isolates demonstrating susceptibility, with MICs of 1 µg/mL or less (Table 1). No difference in daptomycin activity was observed between HA-MRSA and CA-MRSA. Daptomycin was equally active against MSSE and MRSE compared with MSSA and MRSA, with all isolates demonstrating daptomycin MICs of 0.25 µg/mL or less. Daptomycin's excellent activity against MSSA/MRSA and MSSE/MRSE has been previously documented (11,16). As has been previously reported (11,16), daptomycin was active against *Streptococcus* species with isolates displaying MICs of 0.12 µg/mL or less. Daptomycin was active against *E faecalis*, *E faecium* and VRE, with 100% susceptibility and all isolates displaying MICs of 2 µg/mL or less (Table 1). Daptomycin-resistant enterococci species continue to be rare (18) and have not been documented in Canada. From these data, it is clear daptomycin is a very active agent against all Gram-positive organisms causing infections in Canadian hospitals.

Tigecycline was active against MSSA and MRSA with 100% of isolates demonstrating susceptibility, with MICs of 0.5 µg/mL or less (Table 1). No difference in tigecycline activity was observed between HA-MRSA and CA-MRSA. Tigecycline was equally active against MSSE and MRSE compared with MSSA and MRSA, with all isolates demonstrating tigecycline MICs of 0.5 µg/mL or less. Tigecycline's excellent activity against MSSA/MRSA and MSSE/MRSE has been previously documented (11,19). As has been previously reported, tigecycline was very active against *Streptococcus* species, with all isolates displaying MICs of 0.12 µg/mL or less (11,19). Tigecycline was very active against *E faecalis*, *E faecium* and VRE, with all isolates displaying MICs of 0.5 µg/mL or less (Table 1). From these data, it is clear tigecycline is a very active agent against all Gram-positive organisms causing infections in Canadian hospitals.

Dalbavancin was active against MSSA and MRSA with 100% of isolates demonstrating MICs of 0.25 µg/mL or less (Table 1). No difference in dalbavancin activity was observed between HA-MRSA and CA-MRSA. Dalbavancin was equally active against MSSE and MRSE, with all isolates demonstrating

MICs of 0.12 µg/mL or less. Dalbavancin's excellent activity against MSSA/MRSA and MSSE/MRSE has been previously documented (11,20). As has been previously reported (11,20), dalbavancin was active against *Streptococcus* species with isolates displaying MICs of 0.12 µg/mL or less. Dalbavancin was active against *E faecalis*, but displayed less activity against *E faecium* and VRE (Table 1).

Telavancin was active against MSSA and MRSA with 100% of isolates demonstrating MICs of 1 µg/mL or less (Table 1). No difference in telavancin activity was observed between HA-MRSA and CA-MRSA. Telavancin was equally active against MSSE and MRSE, with all isolates demonstrating MICs of 0.25 µg/mL or less. Telavancin's excellent activity against MSSA/MRSA and MSSE/MRSE has been previously documented (20,21). As has been previously reported (21), telavancin was active against *Streptococcus* species with isolates displaying MICs of 0.12 µg/mL or less. Telavancin was active against *E faecalis*, but displayed less activity against *E faecium* and VRE (Table 1). It has been previously documented that telavancin is active against VanB *Enterococcus* species, but not VanA *Enterococcus* species (21).

The most active (based on MIC only) agents against the 3507 Gram-negative bacilli obtained from Canadian hospitals were amikacin, cefepime, ertapenem (not *P aeruginosa*), meropenem, piperacillin-tazobactam and tigecycline (not *P aeruginosa*) (Table 2). Amikacin was very active against *E coli* (including ESBL-producing strains) with 99.5% of strains testing susceptible with an MIC_{90} of 4 µg/mL. Likewise, amikacin proved to be very active against all other Enterobacteriaceae tested (Table 2). Against *P aeruginosa*, amikacin proved to be one of the most active agents tested, with 85.4% of strains testing susceptible with MIC_{90} of 32 µg/mL. Against *A baumannii*, amikacin *P aeruginosa* was very active with 92.0% of strains being susceptible with MIC_{90} of 2 µg/mL or less. The excellent activity of amikacin against both Enterobacteriaceae as well as nonfermenters isolated from patients in hospitals, including in the intensive care unit, is not surprising because the reduced usage of aminoglycosides in favour of fluoroquinolones over the past 15 years has resulted in maintained activity of aminoglycosides in the setting on increasing fluoroquinolone resistance (4,19,22). Thus, amikacin represents a potential option for the treatment of infections caused by Gram-negative bacilli resistant to other less toxic agents.

In the present study, we reported that cefepime, ertapenem, meropenem and piperacillin-tazobactam were very active against Gram-negative bacilli isolated from patients in Canadian hospitals. These agents were active against Enterobacteriaceae including against *E coli* (only ertapenem and meropenem were active against ESBL-producing strains). Against *P aeruginosa*, resistance was piperacillin-tazobactam 7.3%, meropenem 8.1% and cefepime 11.7%. Previous investigators have reported the ongoing excellent activity of these agents versus Gram-negative bacilli isolated from hospitalized patients (4,19,22). Colistin was found to be very active against *E coli* (including ESBL strains) with MIC_{90} of 1 µg/mL. Colistin was also very active against *Klebsiella* species, *E cloacae* and *P mirabilis*. Against *P aeruginosa*, resistance to colistin was 12.4% with an MIC_{90} of 4 µg/mL (Table 2). Against *A baumannii*, colistin was also very active, with an MIC_{90} of 2 µg/mL (Table 2). These data are consistent with other reports of the promising potential of colistin for Gram-negative bacilli such as *P aeruginosa* and *A baumannii* (23,24).

Tigecycline demonstrated 99.8% susceptibility versus *E coli* (100% versus ESBL-producing strains) and was also active against other Enterobacteriaceae including *K pneumoniae*, *E cloacae*, *S marcescens* and *K oxytoca* (Table 2). Tigecycline was not active against *P mirabilis* and *P aeruginosa*. Tigecycline also proved to be active against *S maltophilia* and *A baumannii* organisms frequently resistant to other antimicrobial classes (Table 2). The activity of tigecycline against Gram-negative bacilli (with the exception of *P aeruginosa*) has been previously reported and supports the potential to use this agent for the treatment of infections caused by non-*Pseudomonas* Gram-negative bacilli in hospitalized patients (11,19).

The present study has several limitations, including the fact that we can not be certain that all clinical specimens represented active infection. In the CANWARD study, we asked centres to obtain 'clinically significant' specimens from patients with a presumed infectious disease. Although all of the isolates may not represent actual infection from patients, we believe that most do because we excluded all surveillance swabs and duplicate swabs, as well as eye, ear, nose and throat swabs and genital cultures. In addition, we do not have admission date data for each patient/clinical specimen, thus were not able to provide a more accurate description of community versus nosocomial onset. Finally, susceptibility testing was not performed for all antimicrobial agents due to lack of space on the susceptibility panels utilized. It is recognized that data on antimicrobials such a ceftazidime, imipenem, tobramycin and others would be beneficial, because different hospital formularies stock these and other antimicrobials not tested in this study.

CONCLUSIONS

The most active agents versus Gram-positive cocci from Canadian hospitals were vancomycin, linezolid, daptomycin, tigecycline, dalbavancin and telavancin. The most active agents versus Gram-negative bacilli from Canadian hospitals were amikacin, cefepime, ertapenem (not *P aeruginosa*), meropenem, piperacillin-tazobactam and tigecycline (not *P aeruginosa*). Colistin was very active against *P aeruginosa* and *A baumannii*.

ACKNOWLEDGEMENTS: This paper was presented in part at the 48th Interscience Conference on Antimicrobial Agents and Chemotherapy-ICAAC (2008) in Washington, DC. Funding for the CANWARD 2007 study was provided in part by the University of Manitoba, Health Sciences Center in Winnipeg, National Microbiology Laboratory-Health Canada, Abbott, Affinium Inc, Astellas, Bayer, Janssen Ortho Inc, Merck, Oryx, Pfizer Canada, TaiGen, Targanta and Wyeth Inc. Special thanks to Nancy Laing, Barb Weshnoweski, Ravi Vashisht, Lisa Bittner and Haley Butcher for technological assistance. The authors thank M Tarka for expert secretarial assistance. The authors thank the investigators and laboratory site staff at each medical centre that participated in the CANWARD 2007 study: Vancouver Hospital, Vancouver, British Columbia – Dr D Roscoe; University of Alberta Hospitals, Edmonton, Alberta – Dr R Rennie; Royal University Hospital, Saskatoon, Sascatchewan – Dr J Blondeau; Health Sciences Centre, Winnipeg, Manitoba – Drs D Hoban and G Zhanel; Mount Sinai Hospital, Toronto, Ontario – Dr S Poutanen;

Children's Hospital of Eastern Ontario, Ottawa, Ontario – Dr F Chan; London Health Sciences Centre, London, Ontario – Dr Z Hussain; St Joseph's Hospital, Hamilton, Ontario – Dr C Lee; Hopital Maisonneuve-Rosemont, Montreal, Quebec – Dr M Laverdiere; Montreal General Hospital, Montreal, Quebec – Dr V Loo; Royal Victoria Hospital, Montreal, Quebec – Dr V Loo; QEII Health Sciences Centre, Halifax, Nova Scotia – Drs K Forward and R Davidson. CANWARD data are also displayed at www.can-r.ca, the official Web site of the Canadian Antimicrobial Resistance Alliance (CARA).

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