Prevalence of antimicrobial-resistant pathogens in Canadian hospitals: Results of the Canadian Ward Surveillance Study (CANWARD 2007)

George G Zhanel PhD[1,2,3], James A Karlowsky PhD[1,3], Mel DeCorby MSc[1,3], Kim A Nichol MSc[3], Aleksandra Wierzbowski MSc[1,3], Patricia J Baudry MSc[1,3], Philippe Lagacé-Wiens MD[1,3], Andrew Walkty MD[1,3], Frank Schweizer PhD[4], Heather Adam PhD[5], Melissa McCracken MSc[6], Michael R Mulvey PhD[6], The Canadian Antimicrobial Resistance Alliance (CARA), Daryl J Hoban PhD[1,3]

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BACKGROUND: Canadian hospitals as well as hospitals worldwide are increasingly faced with antibiotic-resistant pathogens, including multidrug-resistant (MDR) strains.
OBJECTIVES: To assess the prevalence of pathogens, including the resistance genotypes of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE) and extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* in Canadian hospitals, as well as their antimicrobial resistance patterns.
METHODS: Bacterial isolates were obtained between January 1, 2007, and December 31, 2007, inclusive, from patients in 12 hospitals across Canada as part of the Canadian Ward Surveillance Study (CANWARD 2007). Isolates were obtained from bacteremic, urinary, respiratory and wound specimens and underwent antimicrobial susceptibility testing. Susceptibility testing was assessed using the Clinical and Laboratory Standards Institute broth microdilution method.
RESULTS: In total, 7881 isolates were recovered from clinical specimens of patients attending Canadian hospitals. The 7881 isolates were collected from respiratory (n=2306; 29.3%), blood (n=3631; 46.1%), wounds/tissue (n=617; 7.8%) and urinary (n=1327; 16.8%) specimens. The 10 most common organisms isolated from 76.5% of all clinical specimens were *E coli* (21.6%), methicillin-susceptible *S aureus* (13.9%), *Streptococcus pneumoniae* (8.9%), *Pseudomonas aeruginosa* (8.0%), *Klebsiella pneumoniae* (5.8%), MRSA (4.9%), *Haemophilus influenzae* (4.3%), coagulase-negative staphylococci/*Staphylococcus epidermidis* (4.0%), *Enterococcus* species (3.0%) and *Enterobacter cloacae* (2.1%). MRSA made up 26.0% (385 of 1480) of all *S aureus* (genotypically, 79.2% of MRSA were health care-associated MRSA and 19.5% were community-associated MRSA), and VRE made up 1.8% of all enterococci (62.5% of VRE had the *van*A genotype). ESBL-producing *E coli* occurred in 3.4% of *E coli* isolates. The CTX-M type was the predominant ESBL, with CTX-M-15 as the predominant genotype. With MRSA, no resistance was observed to daptomycin, linezolid, tigecycline and vancomycin, while resistance rates to other agents were: clarithromycin 91.4%, clindamycin 61.8%, fluoroquinolones 88.6% to 89.6%, and trimethoprim-sulfamethoxazole 12.2%. With *E coli*, no resistance was observed to ertapenem, meropenem and tigecycline, while resistance rates to other agents were: amikacin 0.1%, cefazolin 14.2%, cefepime 2.0%, ceftriaxone 8.9%, gentamicin 10.6%, fluoroquinolones 23.6% to 24.5%, piperacillin-tazobactam 1.3% and trimethoprim-sulfamethoxazole 26.6%. Resistance rates with *P aeruginosa* were: amikacin 7.6%, cefepime 11.7%, gentamicin 20.8%, fluoroquinolones 23.4% to 25.1%, meropenem 8.1% and piperacillin-tazobactam 7.3%. A MDR phenotype (resistance to three or more of cefepime, piperacillin-tazobactam, meropenem, amikacin or gentamicin, and ciprofloxacin) occurred frequently in *P aeruginosa* (10.6%) but uncommonly in *E coli* (1.2%), *K pneumoniae* (1.5%), *E cloacae* (0%) or *H influenzae* (0%).
CONCLUSIONS: *E coli*, *S aureus* (methicillin-susceptible and MRSA), *S pneumoniae*, *P aeruginosa*, *K pneumoniae*, *H influenzae* and *Enterococcus* species are the most common isolates recovered from clinical specimens in Canadian hospitals. The prevalence of MRSA was 26.0% (of which genotypically, 19.5% was community-associated MRSA), while VRE and ESBL-producing *E coli* occurred in 1.8% and 3.4% of isolates, respectively. A MDR phenotype is common with *P aeruginosa* in Canadian hospitals.

Key Words: *Canadian hospitals; Resistance; Surveillances*

La prévalence des pathogènes résistant aux antimicrobiens dans les hôpitaux canadiens : Les résultats de l'étude CANWARD 2007 sur la surveillance des services aux hospitalisés canadiens

HISTORIQUE : Les hôpitaux nord-américains et du monde entier affrontent de plus en plus des pathogènes résistant aux antibiotiques, y compris des souches multirésistantes.
OBJECTIFS : Évaluer la prévalence des pathogènes, y compris la résistance des génotypes du staphylocoque doré méthicillinorésistant (SARM), des entérocoques résistant à la vancomycine (ERV) et de l'*Escherichia coli* producteur de bêta-lactamase à large spectre (BLLS) dans les hôpitaux canadiens, ainsi que leurs modes de résistance antimicrobienne.
MÉTHODOLOGIE : On a obtenu les isolats bactériens entre le 1er janvier et le 31 décembre 2007, inclusivement, auprès de patients de 12 hôpitaux du Canada dans le cadre de l'étude CANWARD 2007 sur la surveillance des services aux hospitalisés canadiens. On a prélevé les isolats dans des échantillons bactériémiques, urinaires, respiratoires et de plaies, qui 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 : On a prélevé au total 7 881 isolats d'échantillons cliniques de patients qui fréquentaient des hôpitaux canadiens. Ces 7 881 isolats ont été prélevés sur des échantillons respiratoires (n=2 306;

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[1]*Department of Medical Microbiology, Faculty of Medicine;* [2]*Departments of Medicine and* [3]*Clinical Microbiology, Health Sciences Centre;* [4]*Department of Chemistry, Faculty of Science, University of Manitoba, Winnipeg, Manitoba;* [5]*University of Toronto, Toronto, Ontario;* [6]*Nosocomial Infections Branch, National Microbiology Laboratory, Winnipeg, Manitoba*
Correspondence: Dr George G Zhanel, Clinical Microbiology, Health Sciences Centre, MS673-820 Sherbrook Street, Winnipeg, Manitoba, R3A 1R9. Telephone 204-787-4902, fax: 204-787-4699, e-mail ggzhanel@pcs.mb.ca

29,3 %), sanguins (n=3 631; 46,1 %), de plaies ou de tissus (n= 617; 7.8 %) et urinaires (n=1 327; 16,8 %). Les dix principaux organismes isolés dans 76,5 % de tous les échantillons cliniques étaient l'*E coli* (21,6 %), le staphylocoque doré susceptible à la méthicilline (13,9 %), le *Streptococcus pneumoniae* (8,9 %), le *Pseudomonas aeruginosa* (8,0 %), le *Klebsiella pneumoniae* (5,8 %), le SRAM (4,9 %), l'*Haemophilus influenzae* (4,3 %), les staphylocoques négatifs à la coagulase ou le *Staphylococcus epidermidis* (4,0 %), les espèces d'entérocoques (3,0 %) et l'*Enterobacter cloacae* (2,1 %). Le SRAM représentaient 26,0 % (385 des 1 480 échantillons) de tous les staphylocoques dorés (d'un point de vue génotypique, 79,2 % des SRAM étaient d'origine nosocomiale et 19,5 %, d'origine non nosocomiale) et les ERV, 1,8 % de tous les entérocoques (62,5 % des ERV possédaient le génotype *vanA*). L'*E coli* producteur de BLLS s'observait dans 3,4 % des isolats d'*E coli*. Le type CTX-M était le BLLS prédominant, et le CTX-M-15, le génotype prédominant. Pour ce qui est du SRAM, on n'a pas observé de résistance à la daptomycine, au limézolide, à la tygécycline et à la vancomycine, tandis que le taux de résistance aux autres agents s'établissait comme suit : clarithromycine 91,4 %, clindamycine 61,8 %, fluoroquinolones 88,6 % à 89,6 %, et triméthoprim-sulfaméthoxazole 12,2 %. L'*E coli* n'était pas résistant à l'ertapénem, au méropénem et à la tigécycline, tandis que le taux de résistance aux autres agents s'établissait comme suit : amikacine 0,1 %, céfazoline 14,2 %, céfépime 2,0 %, ceftriaxone 8,9 %, gentamicine 10,6 %, fluoroquinolones 23,6 % à 24,5 %, pipéracilline-tazobactam 1,3 % et triméthoprim-sulfaméthoxazole 26,6 %. Le taux de résistance au *P aeruginosa* se déclinait comme suit : amikacine 7,6 %, céfépime 11,7 %, gentamicine 20,8 %, fluoroquinolones 23,4 % à 25,1 %, méropénem 8,1 % et pipéracilline-tazobactam 7,3 %. Un phénotype multirésistant (à trois médicaments ou plus parmi la céfépime, la pipéracilline-tazobactam, le méropénem, l'amikacine ou la gentamicine et la ciprofloxacine) se produisait souvent dans les cas de *P aeruginosa* (10,6 %), mais rarement dans ceux d'*E coli* (1,2 %), de *K pneumoniae* (1,5 %) d'*E cloacae* (0 %) ou de *H influenzae* (0 %).

CONCLUSIONS : L'*E coli*, le staphylocoque doré (susceptible à la méthicilline et le SARM), le *S pneumoniae*, le *P aeruginosa*, le *K pneumoniae*, le *H influenzae* et les espèces d'entérocoques sont les principaux isolats prélevés dans les échantillons cliniques d'hôpitaux canadiens. La prévalence du SARM y était de 26,0 % (qui, du point de vue du génotype, s'associait à un SARM non nosocomial dans 19,5 % des cas), tandis que les ERV et l'*E coli* producteur de BLLS s'observaient dans 1,8 % et 3,4 % des isolats, respectivement. Un phénotype multirésistant est courant en cas de *P aeruginosa* dans les hôpitaux canadiens.

Infections caused by antimicrobial-resistant bacteria are rising in Canada and the United States, which underscores the need for continued surveillance, appropriate antimicrobial prescribing, prudent infection control and new treatment alternatives (1-3). Commonly described antimicrobial-resistant 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 increasing in prevalence in all regions of Canada, the United States and globally (4-11). Frequently, these antibiotic-resistant organisms display a multidrug-resistant (MDR) phenotype, which further limits treatment options (2,4,11).

The purpose of the Canadian Ward Surveillance Study (CANWARD 2007) was to assess the prevalence of pathogens, including the resistance genotypes of MRSA, VRE and ESBL, causing infections in Canadian hospitals, as well as their antimicrobial resistance patterns. The present report is the first national, prospective surveillance study assessing antimicrobial resistance in Canadian hospitals.

METHODS

Bacterial isolates

The CANWARD 2007 study included 12 medical centres from all regions of Canada (www.can-r.ca). From January 1, 2007, to December 31, 2007, inclusive, each centre collected and submitted clinical isolates from patients attending hospital clinics, emergency rooms (ERs), medical and surgical wards, and intensive care units (ICUs). Each centre was asked to submit clinical isolates (consecutive, one organism/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 coordinating laboratory (Health Sciences Centre, Winnipeg, Manitoba) on Amies charcoal swabs, subcultured onto appropriate media, and stocked in skim milk at –80°C until minimum inhibitory concentration (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 (3,11,12). For all antimicrobials tested, MIC interpretive standards were defined according to 2006 CLSI breakpoints. 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 higher (R).

Characterization of MRSA, ESBL-producing *E coli* and VRE

MRSA: Potential MRSA isolates were confirmed using the CLSI disk diffusion method and *mec*A polymerase chain reaction (PCR). All isolates of MRSA were tested for Panton-Valentine leukocidin and typed using pulsed-field gel electrophoresis (PFGE) following the Canadian standardized protocol to assess whether the isolates were CA-MRSA or HA-MRSA (13-16). PFGE fingerprints were analyzed with BioNumerics version 3.5 (Applied Maths, USA) using a position tolerance of 1.0 and an optimization of 1.0. Strain relatedness was determined as previously described (17). Fingerprints were compared with the national MRSA fingerprint database and were grouped into one of 10 Canadian epidemic MRSA (CMRSA-1 to CMRSA-10) as previously described (15). In the present study, CA-MRSA and HA-MRSA were defined genotypically and not epidemiologically. Any MRSA with a CMRSA-7 (USA400/MW2) or CMRSA-10 (USA300) genotype was labelled as CA-MRSA, while all other genotypes (eg, CMRSA-1 [USA600], CMRSA-2 [USA100], CMRSA-4 [USA200]) were labelled as HA-MRSA.

ESBL testing: Any *E coli* or *Klebsiella* species with a ceftriaxone MIC of 1 µg/mL or greater was identified as a potential ESBL producer as specified by CLSI. ESBL producers were confirmed using the CLSI double disk diffusion method and retested for MIC to both ceftriaxone and ceftazidime (18). PCR and DNA sequence analysis was used to identify bla_{SHV}, bla_{TEM} and $bla_{CTX\text{-}M}$ genes among isolates, as previously described (7,8,18).

VRE: Potential VRE isolates were confirmed using CLSI vancomycin disk diffusion testing and underwent *van*A and *van*B PCR as well as DNA fingerprinting to assess genetic similarity, as previously described (10,19).

RESULTS

Patient demographics and specimen types

A total of 7881 isolates recovered from clinical specimens were collected from hospitals across Canada; 54.7% (4311 of 7881) of isolates were collected from males while 45.3% (3570 of 7881) were from females. Patient age breakdown was: 17 years or younger, 11.7% (926 of 7881); 18 to 64 years, 47.3% (3726 of 7881); and 65 years and older, 41.0% (3229 of 7881). Organisms were obtained from respiratory specimens (29.3%; 2306 of 7881), blood (46.1%; 3631 of 7881), wounds/tissue (7.8%; 617 of 7881) and urine (16.8%; 1327 of 7881).

Most common organisms isolated in Canadian hospitals

Table 1 describes the 20 most common organisms isolated in hospitals across Canada. The most common Gram-positive cocci included MSSA, *S pneumoniae*, MRSA, coagulase-negative staphylococci/*Staphylococcus epidermidis* and *Enterococcus* species, which together represented 34.7% of all isolates. The most common Gram-negative bacilli included *E coli*, *P aeruginosa*, *Klebsiella pneumoniae*, *Haemophilus influenzae* and *Enterobacter cloacae*, which together made up 41.8% of all organisms from hospitals across Canada.

TABLE 1
The 20 most common organisms isolated from Canadian hospitals

Ranking	Organism	Isolates, n	% of total
1	*Escherichia coli*	1701	21.6
2	MSSA	1095	13.9
3	*Streptococcus pneumoniae*	702	8.9
4	*Pseudomonas aeruginosa*	633	8.0
5	*Klebsiella pneumoniae*	455	5.8
6	MRSA	385	4.9
7	*Haemophilus influenzae*	342	4.3
8	CNS/*Staphylococcus epidermidis*	317	4.0
9	*Enterococcus* spp	237	3.0
10	*Enterobacter cloacae*	166	2.1
11	*Enterococcus faecalis*	161	2.0
12	*Proteus mirabilis*	119	1.5
13	*Streptococcus agalactiae*	116	1.5
14	*Serratia marcescens*	108	1.4
15	*Stenotrophomonas maltophilia*	107	1.4
16	*Streptococcus pyogenes*	105	1.3
17	*Candida albicans*	103	1.3
18	*Klebsiella oxytoca*	100	1.3
19	*Moraxella catarrhalis*	93	1.2
20	*Streptococcus viridans*	66	0.8
	Other*	770	9.8
Total		7881	100.0

**Other:* Achromobacter *species (spp),* Acinetobacter *spp,* Aeromonas *spp,* Bacillus *spp,* Burkholderia *spp,* Candida *spp,* Chryseobacterium *spp,* Citrobacter *spp,* Corynebacterium *spp,* Dermabacter *spp,* Enterobacter *spp,* Enterococcus *spp,* Flavobacterium *spp,* Gemella *spp,* Gordonia *spp,* Haemophilus *spp,* Klebsiella *spp,* Kluyvera *spp,* Kocuria *spp,* Listeria *spp,* Micrococcus *spp,* Morganella *spp,* Neisseria *spp,* Pantoea *spp,* Proteus *spp,* Providencia *spp,* Pseudomonas *spp,* Raoultella *spp,* Rhodococcus *spp,* Roseomonas *spp,* Salmonella *spp,* Sphingobacterium *spp,* Serratia *spp,* Staphylococcus *spp,* Stomatococcus *spp,* Streptococcus *spp,* Yersinia *spp. CNS Coagulase-negative staphylococci; MRSA Methicillin-resistant* Staphylococcus aureus; *MSSA Methicillin-susceptible* S aureus

Most common organisms isolated by specimen site

Table 2 describes the 10 most common isolates recovered from clinical specimens from the four specimen sites, including respiratory, blood, wounds/tissue and the urinary tract. Within the respiratory tract, *S pneumoniae*, MSSA and MRSA were the most common Gram-positive cocci, accounting for 42.4% of isolates. For Gram-negative bacilli, *P aeruginosa, H influenzae*, *E coli*, *Moraxella catarrhalis*, *Stenotrophomonas maltophilia*, *K pneumoniae* and *Serratia marcescens* represented 46.9% of isolates obtained. Among blood culture isolates, Gram-positive cocci, including MSSA, coagulase-negative staphylococci/*S epidermidis*, *S pneumoniae*, MRSA and *E faecalis* made up 35.8% of organisms isolated in Canadian hospitals. The most common Gram-negative bacilli isolated from blood included *E coli*, *K pneumoniae*, *P aeruginosa* and *E cloacae*, which made up 35.7% of all isolates. For wounds/tissue, Gram-positive cocci, including MSSA, MRSA, *Streptococcus pyogenes*, coagulase-negative staphylococci/*S epidermidis* and *Enterococcus* species made up 58.7% of the total isolates. The most common Gram-negative bacilli isolated from wounds/tissue were *P aeruginosa*, *E coli*, *E cloacae* and *K pneumoniae*, which made up 25.7% of all isolates. From the urinary tract the most commonly isolated organisms were Gram-negative bacilli, including *E coli*, *K pneumoniae*, *Proteus mirabilis*, *P aeruginosa*, *E cloacae* and *Klebsiella oxytoca*, which made up 74.7% of isolates. Gram-positive cocci obtained from the urinary tract most commonly included *Enterococcus* species, coagulase-negative staphylococci/*S epidermidis*, *Streptococcus agalactiae* and MSSA, which made up 19.0% of isolates.

Characteristics of MRSA

Of the 385 MRSA (26.0% of all *S aureus*) isolated from hospitals in Canada, 19.5% were CA-MRSA and 79.2% were HA-MRSA, as determined by PFGE; 1.3% of MRSA could not be genotypically classified. CA-MRSA belonged to PFGE types CMRSA10/USA300 (66.7%) and CMRSA7/USA400 (33.3%); PFGE types identified among HA-MRSA included CMRSA2/USA100/800 (81.6%), CMRSA6 (13.1%), CMRSA1/USA600 (3.3%), CMRSA5/USA500 (1.3%), CMRSA3 (0.3%) and CMRSA9 (0.3%). Panton-Valentine leukocidin was detected in 94.7% of CA-MRSA and 0.7% of HA-MRSA. More data on MRSA in CANWARD 2007 are described by Nichol et al (20) in the present supplement.

Characteristics of ESBL *E coli*

Fifty-three of 1560 (3.4%) *E coli* were ESBL producers. ESBL-producing *E coli* ranged from 1.1% in ERs, 1.9% in ICUs, 3.3%

TABLE 2
The 10 most common organisms isolated by specimen site in Canadian hospitals

Ranking	Organism	Isolates, n	% of total
Respiratory (n=2306 or 29.3%)			
1	*Streptococcus pneumoniae*	471	20.4
2	MSSA	383	16.6
3	*Pseudomonas aeruginosa*	380	16.5
4	*Haemophilus influenzae*	321	13.9
5	MRSA	125	5.4
6	*Escherichia coli*	102	4.4
7	*Moraxella catarrhalis*	91	3.9
8	*Stenotrophomonas maltophilia*	79	3.4
9	*Klebsiella pneumoniae*	61	2.6
10	*Serratia marcescens*	51	2.2
	Other	242	10.7
Total		2292	100.0
Blood (n=3631 or 46.1%)			
1	*E coli*	797	21.9
2	MSSA	485	13.4
3	*K pneumoniae*	266	7.3
4	CNS/*Staphylococcus epidermidis*	257	7.1
5	*S pneumoniae*	232	6.4
6	MRSA	172	4.7
7	*Enterococcus faecalis*	154	4.2
8	*P aeruginosa*	148	4.1
9	*Candida albicans*	103	2.8
10	*Enterobacter cloacae*	88	2.4
	Other	929	25.7
Total		3631	100.0
Wounds/Tissue (n=617 or 7.8%)			
1	MSSA	203	32.9
2	MRSA	77	12.5
3	*P aeruginosa*	63	10.2
4	*E coli*	57	9.2
5	*Streptococcus pyogenes*	31	5.0
6	CNS/*S epidermidis*	26	4.2
7	*Enterococcus* species	25	4.1
8	*E cloacae*	21	3.4
9	*Streptococcus agalactiae*	20	3.2
10	*K pneumoniae*	18	2.9
	Other	76	12.4
Total		581	100.0
Urine (n=1327 or 16.8%)			
1	*E coli*	751	56.6
2	*Enterococcus* species	175	13.2
3	*K pneumoniae*	112	8.4
4	*Proteus mirabilis*	49	3.7
5	*P aeruginosa*	43	3.2
6	CNS/*S epidermidis*	29	2.2
7	*S agalactiae*	27	2.0
8	MSSA	21	1.6
9	*E cloacae*	19	1.4
10	*Klebsiella oxytoca*	19	1.4
	Other	82	6.3
Total		1327	100.0

CNS Coagulase-negative staphylococci; MRSA Methicillin-resistant Staphylococcus aureus; *MSSA Methicillin-susceptible* S aureus

in hospital clinics, 6.2% in medical wards and 7.9% in surgical wards. ESBL-producing *E coli* were identified from 11 of the 12 sites, and the prevalence ranged from 0% to 9.3% among participating hospitals. Of the 53 ESBL-producing *E coli*, 51 (96.2%) were of the CTX-M genotype with 28 (52.8%) $bla_{\text{CTX-M-15}}$, 17 (32.1%) $bla_{\text{CTX-M-14}}$, two (3.8%) $bla_{\text{CTX-M-27}}$ and one (1.9%) each of $bla_{\text{CTX-M-3}}$, $bla_{\text{CTX-M-24}}$, $bla_{\text{CTX-M-65}}$, bla_{SHV2a} and an unknown. More data on ESBL-producing *E coli* in CANWARD 2007 are described by Baudry et al (21) in the present supplement.

Characteristics of VRE

Of the 1.8% VRE (eight of 450 of all *Enterococci* species) isolated, 62.5% displayed a *van*A genotype, while 37.5% displayed a *van*B genotype. All VRE were *E faecium*.

Antimicrobial susceptibility

Antimicrobial resistance rates (per cent of isolates determined to be intermediate and resistant) for the most common Gram-positive cocci based on specimen source are listed in Table 3. With MRSA, no resistance was observed to daptomycin, linezolid, tigecycline and vancomycin. Nitrofurantoin (urinary indication only) proved to be active against MRSA as well, with 0% resistance (Table 3). Resistance rates with MRSA were: clarithromycin 91.4%, clindamycin 61.8%, fluoroquinolones 88.6% to 89.6%, and trimethoprim-sulfamethoxazole (SXT) 12.2% (Table 3). The lowest rates of resistance with MRSA occurred in wound specimens with clindamycin and SXT (Table 3). With methicillin-resistant *S epidermidis* (MRSE), no resistance was observed to daptomycin, linezolid and vancomycin. No Food and Drug Administration (USA) breakpoints are available for tigecycline and MRSE, but when MRSA breakpoints were applied, MRSE resistance was 0% with tigecycline. Resistance rates with MRSE were: clarithromycin 90.0%, clindamycin 90.0%, fluoroquinolones 95.0% to 100%, and SXT 75.0% (Table 3). With *S pneumoniae*, no resistance was observed to vancomycin or linezolid. Resistance rates with *S pneumoniae* were: fluoroquinolones 0.6% to 4.3%, ceftriaxone 0.1%, carbapenems 0.1% to 0.3%, clarithromycin 12.9%, clindamycin 5.7% and SXT 7.0% (Table 3). Resistance rates for all agents tested were higher in *S pneumoniae* obtained from respiratory versus blood specimens (Table 3). With *E faecalis*, no resistance was observed to vancomycin, daptomycin and tigecycline (using *E faecalis* breakpoints). Resistance rates with *E faecalis* were: fluoroquinolones 31.8% to 35.1%, linezolid 1.3% (intermediate resistance only) and nitrofurantoin (urinary indication only) 1.2% (intermediate resistance only) (Table 3). Higher resistance for tested agents was observed with *E faecium* compared with *E faecalis* including vancomycin, with resistance of 12.0% (Table 3).

Antimicrobial resistance rates (per cent of isolates determined to be intermediate and resistant) for the most common Gram-positive cocci based on hospital ward location are listed in Table 4. With *S aureus* (MSSA), resistance rates for fluoroquinolones, clarithromycin, clindamycin and SXT were not influenced by ward location, with similar rates in hospital clinics, ERs, ICUs, and medical and surgical wards (Table 4). Resistance rates with MRSA obtained from the ER were lower versus other hospital areas for fluoroquinolones, clindamycin and SXT (Table 4). With *S pneumoniae*, limited differences occurred with beta-lactams, fluoroquinolones and SXT per hospital ward location, likely due to low resistance rates overall for these agents. *S pneumoniae* resistance with clarithromycin and clindamycin occurred in all hospitals areas (Table 4).

TABLE 3
Resistance rates for the most common gram-positive cocci isolated from Canadian hospitals based on specimen source

Organism and Source	% of isolates (%I/%R)																
	CFZ	CPM	CTR	PTZ	ETP	MER	CIP	LEV	MXF	CLR	CD	LZD	TGC	SXT	FD	DAP	VAN
S. aureus																	
MSSA																	
All	0.2/0	0.4/0	0.6/0	0.1/0	0.3/0	0/0	4.2/12.0	0.3/9.9	0.5/9.4	0.6/26.2	0.4/8.6	0/0	0/0	0/0.7	0/0	0/0	0/0
Blood	0/0	0.2/0	0.2/0	0/0	0/0	0/0	2.7/11.9	0/10.5	0.4/10.1	0.4/24.5	0.2/7.6	0/0	0/0	0/0.6	0/0	0/0	0/0
Urine	0/0	0/0	0/0	0/0	na	0/0	0/42.9	0/33.3	4.8/28.6	4.8/33.3	0/19.0	0/0	0/0	0/9.5	na	0/0	0/0
Wound	0.5/0	0.5/0	1.5/0	0.5/0	4.3/0	0/0	3.4/6.9	0/5.9	0.5/5.4	0.5/21.7	0/5.9	0/0	0/0	0/0	0/0	0/0	0/0
Respiratory	0/0	0.3/0	0.8/0	0/0	0/0	0/0	6.8/13.1	0.8/10.2	0.5/9.7	0.8/30.4	0.8/10.7	0/0	0/0	0/0.8	0/0	0/0	0/0
MRSA																	
All	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0.3/89.6	0/89.1	0.5/88.6	0/91.4	0.3/61.8	0/0	0/0	0/12.2	0/0	0/0	0/0
Blood	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0/91.1	0/89.9	0.6/89.3	0/93.5	0/65.1	0/0	0/0	0/10.1	0/0	0/0	0/0
Urine	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0/93.7	0/93.7	0/93.7	0/87.5	0/68.7	0/0	0/0	0/12.5	na	0/0	0/0
Wound	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	1.3/81.6	0/81.6	0/81.6	0/89.5	1.3/42.1	0/0	0/0	0/6.6	0/0†	0/0	0/0
Respiratory	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0/91.9	0/91.9	0.8/91.1	0/90.3	0/68.5	0/0	0/0	0/18.5	0/0†	0/0	0/0
S. epidermidis																	
MSSE																	
All	0/0	8.3/4.6	27.8/2.8	0/1.8	7.1/16.7	5.6/2.8	0/52.8	1.8/50.9	7.4/43.5	1.8/64.8	0/38.9	0/0	-	0/41.7	0/0	0/0	0/0
Blood	0/0	8.6/4.8	28.8/2.9	0/1.9	7.1/16.7	5.8/2.9	0/51.9	1.9/50.0	7.7/42.3	1.9/64.4	0/38.5	0/0	-	0/42.3	0/0	0/0	0/0
Urine	na	na	na	na	na	na	na	na	na	na	na	na	-	na	na	na	na
Wound	na	na	na	na	na	na	na	na	na	na	na	na	-	na	na	na	na
Respiratory	na	na	na	na	na	na	na	na	na	na	na	na	-	na	na	na	na
MRSE																	
All	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0/100	0/100	5.0/95.0	0/90.0	0/90.0	0/0		0/75.0	na	0/0	0/0
Blood †	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0/100	0/100	5.3/94.7	0/89.5	0/89.5	0/0	-	0/73.7	na	0/0	0/0
Urine	na	na	na	na	na	na	na	na	na	na	na	na	-	na	na	na	na
Wound	na	na	na	na	na	na	na	na	na	na	na	na	-	na	na	na	na
Respiratory	na	na	na	na	na	na	na	na	na	na	na	na	-	na	na	na	na
S. pneumoniae																	
All	-	-	0.1/0.1	-	0/0.1	2.4/0.3	0/4.3	0/0.6	0.3/0.6	6.1/12.9	0.1/5.7	0/0	-	6.7/7.0	-	-	0/0
Blood	-	-	0/0	-	0/0	0.5/0	0/1.4	0/0	0/0	5.6/7.0	0/3.3	0/0	-	6.4/5.0	-	-	0/0
Urine	-	-	na	-	na	na	na	na	na	na	na	na	-	na	-	-	na
Wound	-	-	na	-	na	na	na	na	na	na	na	na	-	na	-	-	na
Respiratory	-	-	0.2/0.2	-	0/0.2	3.4/0.5	0/5.7	0/0.9	0.5/0.9	6.4/15.7	0.2/6.8	0/0	-	6.8/7.9	-	-	0/0
E. faecalis																	
All	-	-	-	-	-	-	26.6/35.1	0/31.8	-	-	-	1.3/0	0/0	-	1.2/0	0/0	0/0
Blood	-	-	-	-	-	-	25.8/36.7	0/33.3	-	-	-	1.4/0	0/0	-	1.2/0	0/0	0/0
Urine	-	-	-	-	-	-	na	na	-	-	-	na	na	-	na	na	na
Wound	-	-	-	-	-	-	na	na	-	-	-	na	na	-	na	na	na
Respiratory	-	-	-	-	-	-	na	na	-	-	-	na	na	-	na	na	na
E. faecium																	
All	-	-	-	-	-	-	5.2/82.8	3.4/79.3	-	-	-	8.6/0	-	-	32.4/27.0	0/0	0/12.0
Blood	-	-	-	-	-	-	5.4/82.1	3.6/78.6	-	-	-	5.4/0	-	-	32.4/27.0	0/0	0/8.9
Urine	-	-	-	-	-	-	na	na	-	-	-	na	-	-	na	na	na
Wound	-	-	-	-	-	-	na	na	-	-	-	na	-	-	na	na	na
Respiratory	-	-	-	-	-	-	na	na	-	-	-	na	-	-	na	na	na

**based on oxacillin susceptibility; na no isolates within criteria / insufficient numbers for analysis; †data based on 10-19 isolates; '-' indicates no defined breakpoints. I intermediate; R resistant; CFZ cefazolin; CPM cefepime; CTR ceftriaxone; CLR clarithromycin; CD clindamycin; LZD linezolid; TGC tigecycline; CIP ciprofloxacin; LEV levofloxacin; MXF moxifloxacin; MER meropenem; PTZ piperacillin/tazobactam; ETP ertapenem; SXT trimethoprim/sulfamethoxazole; FD nitrofurantoin; DAP daptomycin; VAN vancomycin*

E faecalis and *E faecium* resistance occurred in all hospital areas (Table 4).

Antimicrobial resistance rates (per cent of isolates determined to be intermediate and resistant) for the most common Gram-negative bacilli based on specimen source are listed in Table 5. With *E coli*, no resistance was observed to ertapenem, meropenem and tigecycline (Table 5). Resistance rates with *E coli* were: amoxicillin-clavulanate 1.2%, cefazolin 14.2%,

TABLE 4
Resistance rates for the most common gram-positive cocci isolated from Canadian hospitals based on ward location

Organism and Location	% of isolates (%I/%R)														
	CFZ	CPM	CTR	PTZ	ETP	MER	CIP	LEV	MXF	CLR	CD	LZD	TGC	SXT	FD	DAP	VAN
S. aureus																	
MSSA																	
All	0.2/0	0.4/0	0.6/0	0.1/0	0.3/0	0/0	4.2/12.0	0.3/9.9	0.5/9.4	0.6/26.2	0.4/8.6	0/0	0/0	0/0.7	0/0	0/0	0/0
Clinic	0/0	0/0	0.8/0	0/0	0/0	0/0	9.6/11.7	0.4/8.3	0.8/7.5	0/33.7	0.8/12.1	0/0	0/0	0/0.4	0/0	0/0	0/0
ER	0.3/0	1.0/0	1.0/0	0.3/0	0.7/0	0/0	2.7/9.3	0.3/8.6	1.0/7.6	0.3/21.6	0.7/6.6	0/0	0/0	0/1.0	0/0	0/0	0/0
ICU	0/0	0/0	0/0	0/0	0/0	0/0	3.3/8.7	0.5/6.0	0/6.0	1.1/17.5	0/6.0	0/0	0/0	0/0	0/0	0/0	0/0
Medical	0.3/0	0.3/0	0.3/0	0/0	0/0	0/0	1.7/18.2	0/15.7	0.3/15.4	1.4/30.4	0/10.8	0/0	0/0	0/0.7	0/0	0/0	0/0
Surgical	0/0	0/0	0/0	0/0	0/0	0/0	4.9/8.5	0/8.5	0/8.5	0/25.6	0/3.7	0/0	0/0	0/1.2	0/0	0/0	0/0
MRSA																	
All	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0.3/89.6	0/89.1	0.5/88.6	0/91.4	0.3/61.8	0/0	0/0	0/12.2	0/0	0/0	0/0
Clinic	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0/87.2	0/87.2	2.0/89.8	0/89.4	2.1/48.9	0/0	0/0	0/14.9	0/0†	0/0	0/0
ER	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0/84.7	0/83.5	1.2/82.3	0/94.1	0/48.2	0/0	0/0	0/3.5	0/0	0/0	0/0
ICU	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0/84.7	0/84.7	1.4/83.3	0/84.7	0/69.4	0/0	0/0	0/25.0	0/0†	0/0	0/0
Medical	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0/94.2	0/93.4	0/93.4	0/92.0	0/70.1	0/0	0/0	0/10.9	0/0	0/0	0/0
Surgical	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	2.3/95.4	0/95.4	0/95.4	0/97.7	0/63.6	0/0	0/0	0/9.1	0/0†	0/0	0/0
S. epidermidis																	
MSSE																	
All	0/0	8.3/4.6	27.8/2.8	0/1.8	7.1/16.7	5.6/2.8	0/52.8	1.8/50.9	7.4/43.5	1.8/64.8	0/38.9	0/0	-	0/41.7	0/0	0/0	0/0
Clinic †	0/0	0/1.0	10.0/0	0/0	na	0/0	0/60.0	0/60.0	0/60.0	0/60.0	0/40.0	0/0	-	0/30.0	na	0/0	0/0
ER	0/0	0/0	20.0/0	0/0	10.0/0†	0/0	0/30.0	0/30.0	5/45.0	0/30.0	0/30.0	0/0	-	0/25.0	0/0†	0/0	0/0
ICU	0/0	17.1/2.9	51.4/2.9	0/0	na	11.4/2.9	0/57.1	2.9/54.3	5.0/25.0	5/45.0	0/48.6	0/0	-	0/62.9	na	0/0	0/0
Medical	0/0	6.4/9.7	16.1/6.4	0/3.2	0/18.7†	6.4/6.4	0/48.4	3.2/45.2	6.4/38.7	0/85.7	0/48.6	0/0	-	0/32.3	0/0†	0/0	0/0
Surgical †	0/0	8.3/0	16.7/0	0/8.3	na	0/0	0/83.3	0/83.3	16.7/66.7	0/66.7	0/33.3	0/0	-	0/41.7	na	0/0	0/0
MRSE																	
All	0/100*	0/100*	0/100*	0/100*	0/100*	0/100*	0/100	0/100	5.0/95.0	0/90.0	0/90.0	0/0		0/75.0	na	0/0	0/0
Clinic	na	na	na	na	na	na	na	na	na	na	na	na	-	na	na	na	na
ER	na	na	na	na	na	na	na	na	na	na	na	na	-	na	na	na	na
ICU	na	na	na	na	na	na	na	na	na	na	na	na	-	na	na	na	na
Medical	na	na	na	na	na	na	na	na	na	na	na	na	-	na	na	na	na
Surgical	na	na	na	na	na	na	na	na	na	na	na	na	-	na	na	na	na
S. pneumoniae																	
All	-	-	0.1/0.1	-	0/0.1	2.4/0.3	0/4.3	0/0.6	0.3/0.6	6.1/12.9	0.1/5.7	0/0	-	6.7/7.0	-	-	0/0
Clinic	-	-	0/0	-	0/0	4.5/0	0/9.0	0/0.9	0/1.8	3.6/17.9	0/6.2	0/0	-	2.6/9.6	-	-	0/0
ER	-	-	0.4/0	-	0/0	1.7/0	0/3.0	0/0.8	0.4/0.8	6.4/11.1	0.4/5.1	0/0	-	8.5/6.8	-	-	0/0
ICU	-	-	0/0	-	0/0	0.9/0	0/1.9	0/0	0/0	6.5/5.6	0/1.9	0/0	-	5.6/6.5	-	-	0/0
Medical	-	-	0/0.6	-	0/0.6	2.9/1.2	0/2.9	0/0	0/0	8.2/17.1	0/8.2	0/0	-	8.7/5.8	-	-	0/0
Surgical	-	-	0/0	-	0/0	3.4/0	0/13.8	0/3.4	3.6/0	0/10.3	0/6.9	0/0	-	0/6.4	-	-	0/0
E. faecalis																	
All	-	-	-	-	-	26.6/35.1	0/31.8	-	-	-	-	1.3/0	0/0	-	1.2/0	0/0	0/0
Clinic †	-	-	-	-	-	26.7/40.0	0/33.3	-	-	-	-	6.7/0	0/0	-	0/0	0/0	0/0
ER	-	-	-	-	-	33.3/10.0	0/10.0	-	-	-	-	0/0	0/0	-	0/0	0/0	0/0
ICU	-	-	-	-	-	17.1/45.7	0/40.0	-	-	-	-	0/0	0/0	-	5.3/0	0/0	0/0
Medical	-	-	-	-	-	29.3/37.9	0/34.5	-	-	-	-	1.7/0	0/0	-	0/0	0/0	0/0
Surgical †	-	-	-	-	-	25.0/43.7	0/43.7	-	-	-	-	0/0	0/0	-	0/0	0/0	0/0
E. faecium																	
All	-	-	-	-	-	5.2/82.8	3.4/79.3	-	-	-	8.6/0	-	-	32.4/27.0	0/0	0/0	0/12.0
Clinic	-	-	-	-	-	na	na	-	-	-	na	-	-	na	na	na	na
ER	-	-	-	-	-	-	na	na	-	-	na	-	-	na	na	na	na
ICU †	-	-	-	-	-	0/90.0	0/90.0	-	-	-	na	-	-	-	37.5/12.5	0/0	0/0
Medical	-	-	-	-	-	15.0/75.0	5.0/70.0	-	-	-	5.0/0	-	-	18.7/31.2	0/0	0/0	0/0
Surgical	-	-	-	-	-	6.7/46.7	0/46.7	-	-	-	7.7/0	-	-	-	0/0	0/0	0/3.3

** based on oxacillin susceptibility; na no isolates within criteria / insufficient numbers for analysis; † data based on 10–19 isolates; '-' indicates no defined breakpoints. I intermediate; R resistant; CFZ cefazolin; CPM cefepime; CTR ceftriaxone; CLR clarithromycin; CD clindamycin; LZD linezolid; TGC tigecycline; CIP ciprofloxacin; LEV levofloxacin; MXF moxifloxacin; MER meropenem; PTZ piperacillin/tazobactam; ETP ertapenem; SXT trimethoprim/sulfamethoxazole; FD nitrofurantoin; DAP daptomycin; VAN vancomycin*

cefepime 2.0%, ceftriaxone 8.9%, gentamicin 10.6%, fluoroquinolones 23.6% to 24.5%, piperacillin-tazobactam 1.3% and SXT 26.6% (Table 5). Resistance rates for beta-lactams and *E coli* was highest in isolates obtained from wound specimens (Table 5). Resistance rates with *P aeruginosa* were: amikacin 7.6%, cefepime 11.7%, gentamicin 20.8%, fluoroquinolones 23.4% to 25.1%, meropenem 8.1%, piperacillin-tazobactam 7.3% and colistin (polymyxin E) 2.2% (Table 5). Resistance rates with aminoglycosides were highest in *P aeruginosa* obtained from respiratory specimens and highest with fluoroquinolones in urinary and respiratory *P aeruginosa* (Table 5). With *K pneumoniae*, no resistance was observed to ertapenem and meropenem (Table 5). Resistance rates with *K pneumoniae* were: cefazolin 6.8%, ceftriaxone 3.1%, cefepime 2.2%, fluoroquinolones 4.2% to 6.6%, amikacin 0.4%, gentamicin 2.9%, piperacillin-tazobactam 2.0%, tigecycline 1.5% and SXT 8.6%.

Antimicrobial resistance rates (per cent of isolates determined to be intermediate and resistant) for the most common Gram-negative bacilli based on hospital ward location are

TABLE 5
Resistance rates for the most common gram-negative bacilli isolated from Canadian hospitals based on specimen source

Organism and Source	% of isolates (%I/%R)																
	A/C	CFZ	CPM	CTR	FOX	ETP	MER	PTZ	AMK	GEN	CIP	LEV	MXF	COL	FD	SXT	TGC
E.coli																	
All	8.5/1.2	3.8/14.2	2.8/2.0	1.9/8.9	3.8/3.8	0/0	0/0	1.1/1.3	0.3/0.1	0.5/10.6	0.3/24.5	0.8/23.6	-	-	3.2/1.2	0/26.6	0.2/0
Blood	6.6/1.3	3.5/9.1	1.8/1.0	1.9/4.5	3.1/2.4	0/0	0/0	0.7/1.1	0.1/0.2	0.6/9.4	0.2/22.0	0.1/21.9	-	-	2.4/0.7	0/29.0	0/0
Urine	11.1/0	3.7/18.0	3.6/2.9	1.9/12.9	6.8/6.0	0/0	0/0	1.5/1.3	0.5/0	0.4/11.5	0.4/25.4	1.5/23.6	-	-	6.0/3.4	0/23.6	0.3/0
Wound	38.5/7.7†	5.3/35.1	8.8/5.3	3.5/22.8	7.7/30.8†	0/0†	0/0	0/5.3	1.7/0	0/17.5	0/29.8	0/28.1	-	-	7.7/0†	0/29.8	1.7/0
Respiratory	21.4/0†	4.9/13.7	2.0/1.0	2.0/4.9	0/7.1†	0/0†	0/0	1.0/1.0	0/0	0/9.8	0/34.3	1.0/33.3	-	-	0/0†	0/27.4	0/0
P.aeruginosa																	
All	-	-	20.8/11.7	40.9/35.2	-	-	4.1/8.1	0/7.3	7.0/7.6	19.0/20.8	10.6/23.4	13.4/25.1	-	10.2/2.2	-	0/85.5	-
Blood	-	-	14.3/4.1	44.9/37.4	-	-	6.1/5.4	0/4.8	2.0/1.4	6.8/9.5	5.4/15.6	8.8/17.7	-	10.2/2.0	-	0/95.2	-
Urine	-	-	13.9/9.3	44.2/37.2	-	-	4.6/9.3	0/9.3	2.3/9.3	9.3/20.9	9.3/32.6	7.0/39.5	-	na	-	0/100	-
Wound	-	-	14.3/7.9	58.7/33.3	-	-	1.6/11.1	0/6.3	1.6/1.6	27.0/7.9	3.2/20.6	7.9/22.2	-	na	-	0/96.8	-
Respiratory	-	-	25.3/15.5	36.0/34.5	-	-	3.7/8.4	0/8.2	10.3/10.8	23.4/27.4	14.0/25.8	16.8/26.8	-	10.5/2.6	-	0/78.2	-
K.pneumoniae																	
All	5.0/1.0	1.8/6.8	0.2/2.2	0.4/3.1	4.5/4.0	0/0	0/0	1.3/2.0	0/0.4	0.4/2.9	0.9/6.6	2.0/4.2	-	-	33.2/31.2	0/8.6	4.0/1.5
Blood	3.7/0	1.1/4.1	0/1.1	0/1.1	4.3/1.2	0/0	0/0	0.7/1.9	0/0	0.7/1.5	0/3.8	1.9/1.9	-	-	35.0/30.1	0/6.8	1.9/1.9
Urine	8.3/0	2.7/11.7	0.9/3.6	0.9/7.2	4.2/20.8	0/0	0/0	1.8/1.8	0/0.9	0/4.5	2.7/14.4	3.6/9.0	-	-	25.0/41.7	0/13.5	4.5/1.8
Wound †	na	0/11.1	0/5.6	5.6/5.6	na	na	0/0	0/0	0/5.6	0/11.1	0/11.1	0/11.1	-	-	na	0/16.7	5.6/0
Respiratory	20.0/10.0†	3.3/8.2	0/3.3	0/3.3	10.0/10.0†	0/0†	0/0	3.3/3.3	0/0	0/3.3	1.6/3.3	0/3.3	-	-	10.0/30.0†	0/4.9	11.5/0
E.cloacae																	
All	20.8/70.8	3.6/91.0	0/0	3.6/18.1	8.3/43.1	0/0	0/0	8.4/9.0	0/0	0/3.6	0.6/7.8	4.2/3.0	-	-	38.9/6.9	0/8.4	5.4/1.2
Blood	20.0/70.0	5.7/88.6	0/0	5.7/15.9	10.0/40.0	0/0	0/0	9.1/6.8	0/0	0/2.3	0/6.8	2.3/3.4	-	-	36.7/8.3	0/5.7	6.8/1.1
Urine †	na	5.3/94.7	0/0	0/15.8	na	na	0/0	5.3/10.5	0/0	0/5.3	5.3/10.5	10.5/0	-	-	na	0/10.5	5.3/5.3
Wound	na	0/95.2	0/0	0/14.3	na	na	0/0	9.5/4.8	0/0	0/4.8	0/4.8	4.8/0	-	-	na	0/9.5	4.8/0
Respiratory	na	0/92.1	0/0	2.6/26.3	na	na	0/0	7.9/15.8	0/0	0/5.3	0/10.5	5.3/5.3	-	-	na	0/13.2	2.6/0
H.influenzae																	
All	0/0.3	-	0/0	0/0.3	-	0/0.3	0/0.3	0/0.3	-	-	0/0	0/0	0/0	-	-	4.4/12.1	-
Blood †	0/0	-	0/0	0/0	-	0/0	0/0	0/0	-	-	0/0	0/0	0/0	-	-	0/0	-
Urine	na	-	na	na	-	na	na	na	-	-	na	na	na	-	-	na	-
Wound	na	-	na	na	-	na	na	na	-	-	na	na	na	-	-	na	-
Respiratory	0/0.3	-	0/0	0/0.3	-	0/0.3	0/0.3	0/0.3	-	-	0/0	0/0	0/0	-	-	4.7/12.8	-

Na no isolates within criteria / insufficient numbers for analysis; †data based on 10-19 isolates; ' - ' indicates no defined breakpoints. I intermediate; R resistant; A/C amoxicillin/clavulanate; CFZ cefazolin; CPM cefepime; CTR ceftriaxone; FOX cefoxitin; ETP ertapenem; MER meropenem; PTZ piperacillin/tazobactam; AMK amikacin; GEN gentamicin; CIP ciprofloxacin; LEV levofloxacin; MXF moxifloxacin; COL colistin; FD nitrofurantoin; SXT trimethoprim/sulfamethoxazole; TGC tigecycline

TABLE 6
Resistance rates for the most common gram-negative bacilli isolated from Canadian hospitals based on ward location

Organism and Location	% of isolates (%I/%R)																
	A/C	CFZ	CPM	CTR	FOX	ETP	MER	PTZ	AMK	GEN	CIP	LEV	MXF	COL	FD	SXT	TGC
E.coli																	
All	8.5/1.2	3.8/14.2	2.8/2.0	1.9/8.9	3.8/3.8	0/0	0/0	1.1/1.3	0.3/0.1	0.5/10.6	0.3/24.5	0.8/23.6	-	-	3.2/1.2	0/26.6	0.2/0
Clinic	4.1/1.4	5.2/18.9	2.8/3.1	2.8/11.9	2.7/11.0	0/0	0/0	1.1/1.4	1.0/0	0.3/11.2	0/25.2	1.1/23.8	-	-	2.7/4.1	0/25.9	0/0
ER	3.4/0.8	2.3/7.6	0.9/0.5	1.4/3.2	2.3/2.3	0/0	0/0	0.9/0.7	0.1/0	0.5/6.5	0/16.7	0.1/16.4	-	-	3.0/0.8	0/22.4	0/0
ICU	7.0/1.4	4.4/10.0	1.9/1.2	1.2/5.6	4.2/1.4	0/0	0/0	0.6/1.9	0/0	0.6/10.6	0.6/21.2	2.5/20.0	-	-	1.4/0	0/23.1	0/0
Medical	15.8/1.8	4.2/20.3	5.2/3.6	2.7/13.8	6.7/4.3	0/0	0/0	1.3/1.9	0.2/0.4	0.2/13.6	0/33.1	0.6/31.7	-	-	4.3/0.6	0/32.7	0.6/0
Surgical	28.6/0	5.3/19.1	4.6/2.3	0.8/16.0	3.6/3.6	0/0	0/0	1.5/1.5	0.8/0	1.5/19.1	3.0/34.3	1.5/33.6	-	-	3.6/3.6	0/30.5	0/0
P.aeruginosa																	
All	-	-	20.8/11.7	40.9/35.2	-	-	4.1/8.1	0/7.3	7.0/7.6	19.0/20.8	10.6/23.4	13.4/25.1	-	10.2/2.2	-	0/85.5	-
Clinic	-	-	19.8/17.6	36.3/28.0	-	-	3.3/7.7	0/8.2	13.7/19.8	19.2/35.2	11.0/25.8	11.0/25.3	-	7.1/0†	-	0/69.8	-
ER	-	-	15.8/4.0	40.6/28.7	-	-	3.0/2.0	0/3.0	4.9/1.0	15.8/13.9	5.9/15.8	4.0/19.8	-	9.5/0	-	0/88.1	-
ICU	-	-	29.8/15.4	35.6/51.0	-	-	6.7/19.2	0/11.5	4.8/2.9	19.2/19.2	11.5/25.0	23.1/26.9	-	6.1/6.0	-	0/90.4	-
Medical	-	-	21.1/8.8	44.3/36.6	-	-	4.1/6.2	0/6.2	4.6/2.6	19.1/14.9	12.4/25.8	16.0/27.8	-	14.0/2.3	-	0/93.8	-
Surgical	-	-	15.4/9.6	55.8/36.5	-	-	3.8/5.8	0/7.7	0/5.8	23.1/9.6	9.6/17.3	11.5/21.1	-	na	-	0/94.2	-
K.pneumoniae																	
All	5.0/1.0	1.8/6.8	0.2/2.2	0.4/3.1	4.5/4.0	0/0	0/0	1.3/2.0	0/0.4	0.4/2.9	0.9/6.6	2.0/4.2	-	-	33.2/31.2	0/8.6	4.0/1.5
Clinic	0/0†	6.2/10.4	0/0	2.1/4.2	0/5.9†	0/0†	0/0	0/0	0/0	0/4.2	4.2/10.4	4.2/4.2	-	-	29.4/41.2†	0/14.6	2.1/2.1
ER	0/0	0/0	0/0.8	0/0	4.8/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	-	-	34.9/27.0	0/5.6	0.8/1.6
ICU	8.9/0	2.5/10.0	0/1.2	0/2.5	2.2/2.2	0/0	0/0	3.7/2.5	0/0	0/1.2	2.5/2.5	1.2/1.2	-	-	37.8/33.3	0/2.5	5.0/0
Medical	8.5/1.7	0.7/8.8	0/3.4	0/4.0	3.4/6.8	0/0	0/0	1.3/3.4	0/0	1.3/4.0	0/9.5	2.7/6.1	-	-	30.5/33.9	0/10.8	8.1/1.3
Surgical	6.7/6.7†	3.8/9.4	1.9/5.7	1.9/7.5	20.0/13.3†	0/0†	0/0	1.9/3.8	0/3.8	0/7.5	0/17.0	3.8/13.2	-	-	26.7/20.0†	0/13.2	0/3.8
E.cloacae																	
All	20.8/70.8	3.6/91.0	0/0	3.6/18.1	8.3/43.1	0/0	0/0	8.4/9.0	0/0	0/3.6	0.6/7.8	4.2/3.0	-	-	38.9/6.9	0/8.4	5.4/1.2
Clinic	na	4.8/90.5	0/0	0/14.3	na	na	0/0	0/9.5	0/0	0/0	0/0	0/0	-	-	na	0/0	0/0
ER	40.0/46.7†	3.8/88.5	0/0	3.8/15.4	0/40.0†	0/0†	0/0	7.7/7.7	0/0	0/3.8	0/7.7	3.9/3.9	-	-	53.3/0†	0/7.7	3.9/3.9
ICU	10.5/78.9†	2.2/93.5	0/0	6.5/17.4	5.3/42.1†	0/0†	0/0	6.5/10.9	0/0	0/4.3	2.2/8.7	4.3/4.3	-	-	26.3/15.8†	0/10.9	10.9/0
Medical	21.0/73.7†	6.5/91.3	0/0	2.2/23.9	10.5/47.4†	0/0†	0/0	15.2/8.7	0/0	0/2.2	0/8.7	4.3/2.2	-	-	31.6/5.3†	0/13.0	4.3/0
Surgical	20.0/70.0†	0/88.9	0/0	3.7/14.8	10.0/20.0†	0/0†	0/0	7.4/7.4	0/0	0/7.4	0/11.1	7.4/3.7	-	-	50.0/0†	0/3.7	3.7/3.7
H.influenzae																	
All	0/0.3	-	0/0	0/0.3	-	0/0.3	0/0.3	0/0.3	-	-	0/0	0/0	0/0	-	-	4.4/12.1	-
Clinic	0/0	-	0/0	0/0	-	0/0	0/0	0/1.2	-	-	0/0	0/0	0/0	-	-	8.3/8.3	-
ER	0/0	-	0/0	0/0	-	0/0	0/0	0/0	-	-	0/0	0/0	0/0	-	-	3.6/17.9	-
ICU	0/2.2	-	0/0	0/0	-	0/2.0	0/2.0	0/0	-	-	0/0	0/0	0/0	-	-	2.2/11.1	-
Medical	0/0	-	0/0	0/0	-	0/0	0/0	0/0	-	-	0/0	0/0	0/0	-	-	2.7/12.3	-
Surgical	0/0	-	0/0	0/3.4	-	0/0	0/0	0/0	-	-	0/0	0/0	0/0	-	-	3.4/6.9	-

na no isolates within criteria / insufficient numbers for analysis; †data based on 10-19 isolates; ' - ' indicates no defined breakpoints. I intermediate; R resistant; A/C amoxicillin/clavulanate; CFZ cefazolin; CPM cefepime; CTR ceftriaxone; FOX cefoxitin; ETP ertapenem; MER meropenem; PTZ piperacillin/tazobactam; AMK amikacin; GEN gentamicin; CIP ciprofloxacin; LEV levofloxacin; MXF moxifloxacin; COL colistin; FD nitrofurantoin; SXT trimethoprim/sulfamethoxazole; TGC tigecycline

listed in Table 6. With *E coli* and *K pneumoniae*, resistance rates for penicillins, cephalosporins, fluoroquinolones, aminoglycosides and SXT were highest from medical and surgical ward specimens and lowest in ER specimens (Table 6). With *P aeruginosa*, resistance rates were highest in ICU specimens for penicillins, cephalosporins, carbapenems, fluoroquinolones and colistin (Table 6). Aminoglycoside resistance with *P aeruginosa* was highest in hospital clinics, which included cystic fibrosis clinics (Table 6).

MDR

MDR was assessed in Gram-negative organisms only, because no accepted definition exists for Gram-positive organisms (Table 7). MDR for Gram-negative organisms was defined as resistance to three or more of the following: cefepime, piperacillin-tazobactam, meropenem, amikacin or gentamicin, and ciprofloxacin (adapted from reference 1). The MDR phenotype was most common in *P aeruginosa* at 10.6%. A MDR phenotype occurred in 1.2% of *E coli*, 1.5% of *K pneumoniae*, and 0% of *E cloacae* and *H influenzae* (Table 7).

TABLE 7
Multidrug-resistant (MDR) phenotypes in Canadian hospitals

Organism	Total isolates, n	MDR isolates, n (%)
Escherichia coli	1701	21 (1.2)
Pseudomonas aeruginosa	633	67 (10.6)
Klebsiella pneumoniae	455	7 (1.5)
Enterobacter cloacae	166	0 (0)
Haemophilus influenzae	329	0 (0)

MDR for Gram-negative bacilli defined as resistant to three or more of the following: cefepime, piperacillin/tazobactam, meropenem, amikacin or gentamicin, and ciprofloxacin

DISCUSSION

The CANWARD study was the first national, prospective surveillance study assessing antimicrobial resistance in hospitals across Canada. This national surveillance study involving 12 medical centres in major population centres in seven of the 10 provinces in Canada collected isolates from blood, respiratory, wound and urinary specimens. Unlike previous studies that documented that more than one-half of all isolates recovered from clinical specimens in hospitals were from the respiratory tract, the CANWARD study could not make such a conclusion because it was set up to collect isolates from a variety of specimen sources to assess antimicrobial resistance patterns, rather than assessing the prevalence of infectious diseases in Canadian hospitals (1,3). It has previously been reported that of the deaths associated with heath care-associated infections in American hospitals (National Nosocomial Infections Surveillance [NNIS], 2002), approximately 36.3% were respiratory, 31.0% were bloodstream, 13.2% were urinary tract and 8.3% were surgical site (wound) infections (22). We report that the 10 most common isolates recovered from 76.5% of all clinical specimens in hospitals across Canada were *E coli*, MSSA, *S pneumoniae*, *P aeruginosa*, *K pneumoniae*, MRSA, *H influenzae*, coagulase-negative staphylococci/*S epidermidis*, *Enterococcus* species and *E cloacae* (Table 1). Our data are in keeping with previous reports that Gram-positive cocci including MSSA, *S pneumoniae*, MRSA and *Enterococcus* species are the most common Gram-positive isolates recovered from clinical specimens in North American hospitals (3,23). The recent report by Lockhart et al (1) that the most common Gram-negative bacilli isolated from American institutions from 1993 to 2004 were *P aeruginosa*, *E coli*, *K pneumoniae* and *E cloacae* is also consistent with our findings.

In all hospitals involved in the CANWARD study, MSSA and MRSA were important isolates recovered from clinical specimens including bacteremia, respiratory tract specimens and wound/tissue specimens. MRSA made up 26.0% of all staphylococci and, surprisingly, 19.5% of all MRSA in Canadian hospitals were CA-MRSA. In a previous study involving 19 ICUs across Canada (3), we reported that 9.1% of all MRSA were CA-MRSA. Thus, it is clear that CA-MRSA genotypes are rapidly spreading across Canadian hospitals. The most common CA-MRSA genotypes continue to be CMRSA10/USA300 (66.7%) and CMRSA7/USA400 (33.3%), which is consistent with previous reports (4,11,13,15). The most common HA-MRSA genotypes in Canadian hospitals were CMRSA2/USA100/800 (81.6%) and CMRSA6 (13.1%), which has also been previously documented (4,11,13,15). The CANWARD study also showed that VRE made up only 1.8% of all enterococci with the *van*A genotype (mostly *E faecium*) making up 62.5% of all VRE. The present study, as well as previous work, confirms that *E faecium* carrying *van*A is the predominant genotype in North America (10,11,19). The low level of VRE across Canada has been previously documented and shows the lack of spread of VRE across the country (10,11). Whether the low level of VRE in Canadian hospitals reflects the use of active surveillance programs, which have been reported to prevent VRE colonization and bacteremia, is unknown (24,25). A recent Australian study has reported that aggressive hand hygiene does not only reduce the incidence of MRSA infections but can also lower MRSA bacteremia (26).

The CANWARD study found that 3.4% of *E coli* were ESBL producers. Most concerning was that ESBL-producing *E coli* were isolated from all hospital areas (ie, ERs, ICUs, hospital clinics, and medical and surgical wards). In addition, because ESBL-producing *E coli* were identified in 11 of the 12 sites, and because 90.6% of the isolates displayed an MDR phenotype, it is strongly suspected that MDR ESBL-producing *E coli* are now firmly established in Canadian hospitals. This study showed that the CTX-M genotype ($bla_{\text{CTX-M-15}}$ and $bla_{\text{CTX-M-14}}$) was the predominant genotype in Canadian hospitals. Other studies assessing ESBL-producing *E coli* have shown that the CTX-M genotype is spreading rapidly in both community and hospital settings (5,7,8,11,18,27,28). Pitout et al (8) investigated the molecular epidemiology of ESBL-producing *E coli* collected from 2000 to 2005, inclusive, in the Calgary Health Region. These investigators reported that 64% (354 of 552) of ESBL-producing *E coli* were PCR-positive for $bla_{\text{CTX-M}}$ genes, with CTX-M-14 (59.6%) and CTX-M-15 (36.2%) reported most commonly. Our study highlights the rapid spread of MDR ESBL CTX-M-15 *E coli* in Canadian hospitals. This MDR phenotype may be spreading rapidly due to the extensive use of third-generation cephalosporins and fluoroquinolones.

The present study showed that with the exception of MRSA, where resistance to fluoroquinolones, clindamycin and

SXT was lower in the ER compared with other hospital locations, little differences in resistance rates with Gram-positive cocci were observed among various hospital locations. This is consistent with previous studies where higher resistance rates in the ICU as well as medical and surgical wards have been reported with Gram-negative bacilli but not Gram-positive cocci (1,3,29,30). In agreement with previous studies, we found that resistance rates with *E coli* and *K pneumoniae* were highest from medical and surgical ward specimens and lowest in ER specimens, whereas with *P aeruginosa*, resistance rates were highest in the ICU (1,3,30). The reason that resistance rates were high in clinics is because these primarily represented hospital specialty clinics such as cystic fibrosis clinics rather than acute care outpatient clinics.

With MRSA, resistance rates were very high with fluoroquinolones, macrolides (such as clarithromycin) and clindamycin, but lower with SXT (12.2%). These resistance rates are consistent with previous reports (3,15). Thus, SXT still represents a reasonable empirical treatment for mild to moderate infections (eg, skin and soft tissue infections) caused by CA-MRSA or HA-MRSA. All MRSA were susceptible to vancomycin, linezolid, tigecycline and daptomycin. It should be stated that even though only four of 385 (1.0%) MRSA demonstrated vancomycin MICs of 2 µg/mL, unlike others, we did not assess the prevalence of heteroresistant vancomycin-intermediate *S aureus* by population analysis profiling (31). A recent analysis from Detroit identified 8.3% (of 917 strains assessed from 2003 to 2007) of MRSA as heteroresistant vancomycin-intermediate *S aureus* (31). All MRSE were susceptible to vancomycin, linezolid, tigecycline and daptomycin, while no *Enterococcus* species proved to be resistant to tigecycline or daptomycin. The lowest rates of resistance for Gram-negative bacilli occurred with amikacin, cefepime, ertapenem (except *P aeruginosa*), meropenem and piperacillin-tazobactam, which is consistent with previous reports (1,3,30). The low resistance with amikacin likely reflects the low usage of aminoglycosides in favour of the fluoroquinolones in Canada and the United States over the past decade. In contrast, fluoroquinolone resistance was high with *E coli* (23.6% to 24.5%) and *P aeruginosa* (23.4% to 25.1%), which is consistent with other reports (1,3,30), and reflects extensive fluoroquinolone usage (27). A recent report documented increasing prevalence of MDR Gram-negative bacilli in American ICUs (1). Although our definition of MDR for Gram-negative bacilli (resistance to three or more of the following: cefepime, piperacillin-tazobactam, meropenem, amikacin or gentamicin, and ciprofloxacin), was slightly more restrictive, our MDR rates of 10.6% with *P aeruginosa* were somewhat higher than previously reported in the United States, at 9.3% (1). In contrast, MDR rates in Canadian hospitals of 1.2% with *E coli*, 0% with *E cloacae*, and 1.5% with *K pneumoniae* are lower than those in American institutions at 2.0%, 5.9% and 13.3%, respectively. Why MDR rates are higher in Canada with *P aeruginosa* and lower with Enterobacteriaceae (*E coli*, *E cloacae* and *K pneumoniae*) is unclear, but may be due to the lower prevalence of ESBL-producing Enterobacteriaceae in Canada (3,11). MDR ESBL-producing *E coli* were all susceptible to the carbapenems, ertapenem and meropenem, as well as tigecycline.

The limitations of the CANWARD study are numerous, including the fact that we cannot be certain that all clinical specimens represented active infection. As in our previous CAN-ICU study (3,11), 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, duplicate swabs, eye, ear, nose and throat swabs, and genital cultures. Another limitation is that we do not have admission date data for each patient and clinical specimen, thus were not able to provide a more accurate description of community versus nosocomial onset. In the present study, CA-MRSA and HA-MRSA were defined genotypically and not epidemiologically. Any MRSA with a CMRSA-7 (USA400/MW2) or CMRSA-10 (USA300) genotype were labelled as CA-MRSA while all other genotypes (eg, CMRSA-1 [USA600], CMRSA-2 [USA100], CMRSA-4 [USA200]) were labelled as HA-MRSA. It is known epidemiologically that CA-MRSA genotypes can be associated with health care-associated infections and that HA-MRSA can be associated with community-associated infections (13). *E coli* and *K pneumoniae* were screened for potential ESBL production using only ceftriaxone, which, although consistent with CLSI guidelines, may have missed some SHV-producing *K pneumoniae* strains by not also testing ceftazidime. Whether this accounted for the reduced number of ESBL-producing *K pneumoniae* versus ESBL-producing *E coli* is unclear. 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 the present study.

CONCLUSIONS

E coli, *S aureus* (MSSA and MRSA), *S pneumoniae*, *P aeruginosa*, *K pneumoniae*, *H influenzae* and *Enterococcus* species are the most common isolates recovered from clinical specimens in Canadian hospitals. The prevalence of MRSA was 26.0% (of which genotypically, 19.5% was CA-MRSA), VRE 1.8% and ESBL-producing *E coli* 3.4% of isolates. A MDR phenotype is common with *P aeruginosa* in Canadian hospitals.

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APPENDIX 1

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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/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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