

# Prevalence of antimicrobial use in a network of Canadian hospitals in 2002 and 2009

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**BACKGROUND:** Increasing antimicrobial resistance has been identified as an important global health threat. Antimicrobial use is a major driver of resistance, especially in the hospital sector. Understanding the extent and type of antimicrobial use in Canadian hospitals will aid in developing national antimicrobial stewardship priorities.

**METHODS:** In 2002 and 2009, as part of one-day prevalence surveys to quantify hospital-acquired infections in Canadian Nosocomial Infection Surveillance Program hospitals, data were collected on the use of systemic antimicrobial agents in all patients in participating hospitals. Specific agents in use (other than antiviral and antiparasitic agents) on the survey day and patient demographic information were collected.

**RESULTS:** In 2002, 2460 of 6747 patients (36.5%) in 28 hospitals were receiving antimicrobial therapy. In 2009, 3989 of 9953 (40.1%) patients in 44 hospitals were receiving antimicrobial therapy ( $P<0.001$ ). Significantly increased use was observed in central Canada (37.4% to 40.8%) and western Canada (36.9% to 41.1%) but not in eastern Canada (32.9% to 34.1%). In 2009, antimicrobial use was most common on solid organ transplant units (71.0% of patients), intensive care units (68.3%) and hematology/oncology units (65.9%). Compared with 2002, there was a significant decrease in use of first- and second-generation cephalosporins, and significant increases in use of carbapenems, antifungal agents and vancomycin in 2009. Piperacillin-tazobactam, as a proportion of all penicillins, increased from 20% in 2002 to 42.8% in 2009 ( $P<0.001$ ). There was a significant increase in simultaneous use of >1 agent, from 12.0% of patients in 2002 to 37.7% in 2009.

**CONCLUSION:** From 2002 to 2009, the prevalence of antimicrobial agent use in Canadian Nosocomial Infection Surveillance Program hospitals significantly increased; additionally, increased use of broad-spectrum agents and a marked increase in simultaneous use of multiple agents were observed.

**Key Words:** Antimicrobial use; Hospital; Prevalence

## La prévalence d'utilisation d'antimicrobiens dans un réseau d'hôpitaux canadiens en 2002 et 2009

**HISTORIQUE :** La résistance antimicrobienne croissante est une menace importante pour la santé dans le monde. L'utilisation d'antimicrobiens est un moteur de résistance majeur, particulièrement dans le milieu hospitalier. Il faut comprendre la portée et le type d'utilisation des antimicrobiens dans les hôpitaux canadiens pour établir les priorités nationales en matière de gouvernance antimicrobienne.

**MÉTHODOLOGIE :** En 2002 et 2009, dans le cadre de sondages de prévalence d'une journée visant à quantifier les infections nosocomiales dans les hôpitaux du Programme canadien de surveillance des infections nosocomiales, les chercheurs ont colligé des données sur l'utilisation des antimicrobiens systémiques par tous les patients des hôpitaux participants. Le jour du sondage, ils ont recueilli les agents précis utilisés (à part les antiviraux et les antiparasitaires) et l'information démographique relative aux patients.

**RÉSULTATS :** En 2002, 2 460 des 6 747 patients (36,5 %) de 28 hôpitaux recevaient un traitement antimicrobien. En 2009, 3 989 des 9 953 patients (40,1 %) de 44 hôpitaux recevaient un tel traitement ( $P<0,001$ ). L'utilisation avait beaucoup augmenté au centre du Canada (37,4 % à 40,8 %) et dans l'Ouest canadien (36,9 % à 41,1 %), mais pas dans l'Est canadien (32,9 % à 34,1 %). En 2009, l'utilisation d'antimicrobiens était plus courante dans les unités de transplantation d'organes pleins (71,0 % des patients), les unités de soins intensifs (68,3 %) et les unités d'hématologie-oncologie (65,9 %). Par rapport à 2002, on constatait en 2009 une diminution importante des céphalosporines de première et seconde générations et des augmentations marquées de carbapénèmes, d'antifongiques et de vancomycine. L'utilisation de piperacilline-tazobactam, en proportion de toutes les pénicillines, est passée de 20 % en 2002 à 42,8 % en 2009 ( $P<0,001$ ). L'utilisation simultanée de plus d'un agent a également connu une hausse importante, passant de 12,0 % des patients en 2002 à 37,7 % en 2009.

**CONCLUSION :** De 2002 à 2009, la prévalence d'utilisation d'antimicrobiens dans les hôpitaux du Programme canadien de surveillance des infections nosocomiales a considérablement augmenté. De plus, les chercheurs ont constaté une augmentation marquée d'agents à large spectre et d'utilisation simultanée de multiples agents.

**A**ntimicrobial resistance (AMR) in human bacterial pathogens has been identified as a public health problem of global significance (1-3). Hospitalized patients are at particular risk from antimicrobial-resistant pathogens due to the evolution of AMR after antimicrobial exposure and to the new acquisition of antimicrobial-resistant bacterial

strains, such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci and Enterobacteriaceae such as those with extended-spectrum beta-lactamases or carbapenemases. *Clostridium difficile* infection (CDI) is usually considered to be part of the same public health problem because it shares epidemiological characteristics

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**TABLE 1**  
**Antimicrobial use in Canadian Nosocomial Infection Surveillance Program hospitals in 2009: Patient characteristics**

Characteristic	Receiving antimicrobial therapy		
	Yes (n=3989)	No (n=5964)	P
Age, years, median (IQR)	62 (43–77)	68 (48–81)	<0.001
Male sex*	2145 (53.8)	2956 (49.9)	<0.001
Infant	213 (5.4)	518 (8.7)	<0.001
Child	329 (8.3)	293 (4.9)	<0.001
Adult	3435 (86.4)	5130 (86.3)	0.89
Type of ward†			
Medicine	1409 (35.3)	2500 (41.9)	<0.001
Surgery	1229 (30.8)	1810 (30.4)	0.62
Intensive care	411 (10.3)	191 (3.2)	<0.001
Neonatal intensive care	131 (3.3)	388 (6.5)	<0.001
Obstetrics/gynecology	49 (1.2)	118 (3.0)	0.004
Hematology/oncology	280 (7.0)	145 (2.4)	<0.001
Solid organ transplant	149 (3.7)	61 (1.0)	<0.001
Trauma/burn	44 (1.1)	48 (0.8)	0.13
Coronary care	41 (1.0)	192 (3.2)	<0.001
Neurosciences/neurosurgery	72 (1.8)	210 (3.5)	<0.001

Data presented as n (%) unless otherwise indicated. \*Data missing from 56 records; †Data missing from 53 records. IQR Interquartile range

with antimicrobial-resistant pathogens (ie, increasing incidence, association with antimicrobial therapy and primarily affecting hospitalized patients). In the United States, the Centers for Disease Control and Prevention (Georgia) estimates that a minimum of two million infections and 23,000 deaths annually are attributable to AMR, an additional 250,000 illnesses and 14,000 deaths result from CDI, and that most such infections occur in health care settings such as hospitals (2).

Antimicrobial use (AMU) is a major factor driving the occurrence of AMR and CDI. Consequently, antimicrobial stewardship (AS) has recently been established as a new form of clinical quality improvement. It has, as a core part of its mandate, the objective of improving the quality of antimicrobial therapy and, thereby, reducing selection pressures in bacteria favouring the development of AMR (4). AS activity can function at a local, regional/provincial, national or global level.

As in other aspects of public health, surveillance for AMR and AMU provides the information necessary for appropriate action. The Canadian Nosocomial Infection Surveillance Program (CNISP) has performed surveillance for selected antimicrobial-resistant organisms in hospitalized patients since 1994, and has documented the extent and trends over time of MRSA, vancomycin-resistant enterococci, extended-spectrum beta-lactamases, carbapenemase-producing microorganisms and CDI (5–13). In Canada, there are data regarding AMU in ambulatory settings (14–16) but there are little data regarding AMU in Canadian hospitals; this is an important deficiency of information because a considerable proportion of the AMR burden occurs within the hospital sector. In 2002, and again in 2009, CNISP performed one-day prevalence surveys to quantify hospital-acquired infections (HAI) among inpatients in network hospitals on that day (17,18). As part of these surveys, data were also collected on AMU in hospitalized patients. These data represent an important snapshot of information on AMU in hospitals in Canada that may reveal important evolving trends and inform national approaches to AS.

## METHODS

### Surveillance network

CNISP, a network of 54 acute care hospitals from 10 provinces, is a partnership between the Public Health Agency of Canada (PHAC) and the Canadian Hospital Epidemiology Committee, a group of hospital-based

physician infection prevention specialists. All CNISP hospitals have a university affiliation and provide primary, secondary and tertiary care to adult and/or pediatric patients. Seven hospitals were stand-alone pediatric centres. Surveillance for HAI and AMU in participating hospitals is considered to be within the mandate of hospital infection prevention and control programs and, therefore, does not constitute human research. In most participating hospitals, this surveillance activity does not require institutional review board review.

### AMU point prevalence

A point-prevalence survey of all adult and pediatric inpatients was conducted in CNISP hospitals in February 2002 and February 2009, excluding patients on psychiatric units or long-stay units associated with acute care hospitals. Data pertaining to one 24 h period were collected, entered manually into patient data-extraction forms and forwarded to PHAC for data entry and analysis. A unique identifier linked to the patient name was used only to identify patients at the participating hospital and was not transmitted to PHAC. Data elements collected included demographic information, age and sex, information on HAIs, microorganisms isolated, antimicrobials prescribed and use of additional (transmission-based) precautions. Systemic (intravenous or oral) antimicrobial agents in use on the survey day to treat or prevent bacterial, mycobacterial or fungal infections were identified by chart review and classified according to antimicrobial drug class.

### Data analysis

The CNISP hospitals were grouped according to region: western (British Columbia, Alberta, Saskatchewan and Manitoba); central (Ontario and Quebec); and eastern (Newfoundland and Labrador, New Brunswick, Prince Edward Island and Nova Scotia).

Each reported antimicrobial agent was grouped into its antimicrobial class using the Anatomical Therapeutic Chemical coding ([http://www.whocc.no/atc\\_ddd\\_index/](http://www.whocc.no/atc_ddd_index/)). To assess differences among patient populations, continuous variables were expressed using means and medians, and were compared using Student's t tests and Wilcoxon rank-sum tests as appropriate. All tests were two-tailed, and P values of 0.05 were considered to be statistically significant. All analyses were performed using SAS version 9.2 (SAS Inc, USA).

## RESULTS

In 2002, 6747 patients in 28 CNISP hospitals were surveyed; 2460 patients (36.5%) were receiving antimicrobial therapy. In 2009, 9953 patients in 44 hospitals were surveyed and 3989 (40.1%; P<0.001) were receiving therapy. According to region, antimicrobial prevalence significantly increased in central Canada (from 37.4% to 40.8%; P<0.01) and in western Canada (from 36.9% to 41.1%; P<0.001), but not in eastern Canada (32.9% to 34.1%; P=0.53). Table 1 describes the characteristics of surveyed patients in 2009, comparing those receiving antimicrobial therapy with those who were not receiving therapy. According to ward type, in 2009, antimicrobial therapy prevalence was highest on solid organ transplant wards (71.0%), hematology/oncology wards (65.9%, an increase from 53.6% in 2002; P<0.001) and intensive care units (68.3%). The prevalence of antimicrobial therapy was lowest on coronary care units (17.6%) and neonatal intensive care units (25.2%). From 2002 to 2009, prevalence increased significantly on surgery wards (34.6% to 40.4%) (Table 2). Table 3 compares the antimicrobial agents in use in 2002 with those in use in 2009 as a proportion of all agents used. Of the agents within the penicillin class, the proportion accounted for by pipercillin-tazobactam increased from 20% in 2002 to 42.8% in 2009 (P<0.001). Figure 1 shows the proportion of patients receiving >1 antimicrobial agent, which significantly increased between 2002 (12.0%) and 2009 (37.7%) (P<0.001). In 2009, among individuals on >1 agent (n=1505), there were 103 cases (7%) in which ≥2 of the same class of antimicrobial agent were in use.

**TABLE 2**  
Antimicrobial prevalence in 2002 and 2009 according to hospital ward type

Ward type	2002	2009	P
Medicine/pediatric medicine	1010 (34.7)	1409 (36.0)	0.044
Surgery	781 (34.6)	1229 (40.4)	<0.001
Intensive care	233 (65.6)	411 (68.3)	0.44
Neonatal intensive care	87 (24.3)	131 (25.2)	0.75
Obstetrics/gynecology	28 (22.8)	49 (29.3)	0.21
Hematology/oncology	158 (53.6)	280 (65.9)	<0.001
Solid organ transplant	71 (68.3)	149 (71.0)	0.62
Trauma/burn	39 (37.5)	44 (47.8)	0.14
Coronary care	50 (29.6)	41 (17.6)	0.53
Other	1 (10.0)	153 (36.3)	0.15
Neurosciences/neurosurgery		72 (25.5)	n/a

Data presented as n (%) unless otherwise indicated

## DISCUSSION

Sequential national prevalence surveys have been widely used to assess secular trends in the occurrence of health care-acquired infections and AMU worldwide as a cost-effective approach to obtaining national data to assist in determining priorities for action (19-23). The prevalence data included in the present report represent a useful assessment of AMU in CNISP hospitals at two points in time separated by seven years, from which evolving trends may be recognized. The data suggest that AMU is very high in hospitalized Canadians, and is increasing over time. This rising prevalence in inpatients in CNISP hospitals is in contrast to AMU in ambulatory settings, for which decreased use has been documented over a similar time period (24). These Canadian trends imply that greater national efforts are needed to examine and address the appropriateness of AMU within hospitals in Canada because hospitalized patients are exposed to high-intensity AMU, and antimicrobial-resistant pathogens often arise in hospitals due to antibiotic exposure or are transmitted within hospitals and subsequently selected by antimicrobial exposure.

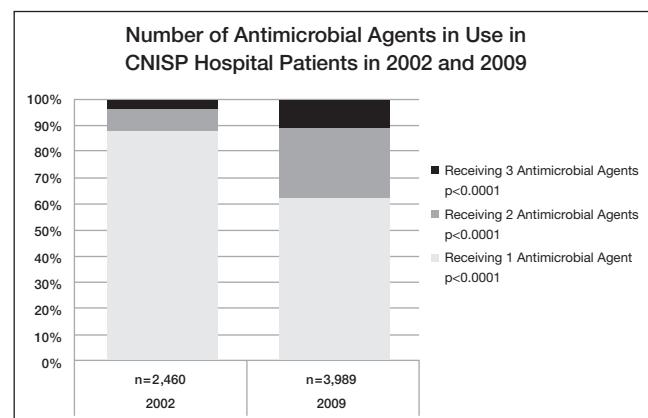
Within the group of patients receiving antimicrobial therapy, important trends may be developing. Patients surveyed in 2009 were significantly more likely to receive broad-spectrum antimicrobial agents than they were in 2002. Pipercillin-tazobactam, as a proportion of all penicillins, more than doubled in use. Use of carbapenems (imipenem, meropenem, ertapenem), often considered to be the last line of defense against invasive Gram-negative bacteria, remained low in 2009 (3.9% of all agents), but had increased from 2.6% in 2002. In contrast, use of narrower-spectrum agents such as first- and second-generation cephalosporins declined significantly. Furthermore, there was a marked increase in the prevalence of patients simultaneously receiving multiple antimicrobial agents.

Our data are silent regarding the appropriateness of AMU in CNISP hospitals. Having documented the spread of antimicrobial-resistant pathogens in CNISP hospitals, it is possible that increased AMU and increases in use of multiple agents simultaneously is, in part, a consequence as much as a cause of increasing AMR. The twofold increased use of vancomycin between the two surveys is likely a response to an increased prevalence of MRSA and CDI (6,8). In addition, increased use of broad-spectrum agents and antifungal therapy could reflect increasing acuity and complexity of hospital patients. Nevertheless, the data are concerning and point to a need for a better understanding of AMU in Canadian hospitals. More up-to-date information regarding AMU in CNISP hospitals would be an important first step. In addition, there is a need for information on the appropriateness of AMU in hospital clinical practice. Finally, research is required that provides a better understanding of factors driving the AMU trends we have observed, including assessment of forces that influence prescribing in hospitalized patients

**TABLE 3**  
Comparison of antimicrobial class use in Canadian Nosocomial Infection Surveillance Program hospitals: 2002 and 2009

Antimicrobial class	2002	2009	P
	(2864 patients)	(6048 patients)	
Penicillins	441 (15.4)	1023 (16.9)	0.07
Cephalosporins			
First generation	347 (12.01)	556 (9.2)	<0.001
Second generation	84 (2.9)	96 (1.6)	<0.001
Third generation	252 (8.8)	446 (7.4)	0.02
Carbapenems	73 (2.6)	238 (3.9)	<0.001
Fluoroquinolones	519 (18.1)	1055 (17.4)	0.43
Aminoglycosides	106 (3.7)	214 (3.5)	0.69
Macrolides	60 (2.1)	144 (2.4)	0.39
Tetracyclines	6 (0.2)	29 (0.5)	0.057
Antifungal agents	124 (4.3)	350 (5.8)	0.004
Antituberculous agents	52 (1.8)	102 (1.7)	0.66
Clindamycin	48 (1.7)	127 (2.1)	0.18
Metronidazole	256 (8.9)	530 (8.8)	0.79
Nitrofurantoin	7 (0.2)	46 (0.8)	0.003
Trimethoprim/ sulfamethoxazole	37 (1.3)	312 (5.2)	<0.001
Vancomycin	123 (4.3)	549 (9.1)	<0.001

Data presented as n (%) unless otherwise indicated



**Figure 1**) Number of antimicrobial agents in use in Canadian Nosocomial Infection Surveillance Program (CNISP) hospital patients in 2002 and 2009

in Canada. This information could then be used to develop appropriate national hospital AS strategies.

Prevalence surveys in other countries have assessed AMU. Our 2009 prevalence (40.1%) appears to be higher than a survey of 172 European hospitals conducted in 2009, which found a prevalence of 29.0% (21), and 32.4% found in three Australian hospitals surveyed in 2012 (22). A report from a 2007 survey in Scotland (25) showed an overall prevalence of AMU at 32.1% of 11,608 patients in acute care hospitals, with 12.6% overall receiving >1 agent. However, direct comparison of prevalence of AMU among countries – and even among hospitals – is hampered by the need to account for differences in survey methods, patient mix, acuity and local microbial ecology. Risk adjustment of AMU is an emerging field, and methods are being developed based on the types of hospital services provided, indexes of patient severity or combinations of both (26).

Our study was subject to limitations. The data reflect only two days of AMU in the same season separated by seven years. Pediatric hospitals were not included in our survey. While large numbers of patients

were surveyed, it is possible that the data over- or underestimate true AMU rates in Canadian hospitals. No data are available to fully characterize the trend between 2002 and 2009 – ie, whether a slow persistent increase or a sudden shift in utilization occurred. Similarly, we cannot comment on whether the change in AMU between 2002 and 2009 has continued. CNISP hospitals are primarily large tertiary care teaching institutions; these data may be expected to overestimate prevalence of AMU. While our data reflect some of the only publicly available information on AMU in Canadian hospitals, their shortcomings prevent full description of AMU trends in the hospital sector. Ideally, AMU data from a range of Canadian hospitals should be evaluated. As reviewed by Grant et al (27), there are significant gaps in AMR surveillance (particularly in the community sector) in Canada. Only a limited range of target pathogens have been surveyed in subsets of the Canadian hospital sector – primarily performed by our group. AMU surveillance is generally absent and that which occurs is not integrated with AMR surveillance, beyond that occurring within CNISP. Grant et al (26) recommend a range of initiatives, starting with establishment of a coordinated national cross-sectoral AMR and AMU surveillance system. We agree that better data on AMU within the hospital sector are needed.

## SUMMARY

Between 2002 and 2009, overall AMU prevalence in major Canadian hospitals significantly increased, and there were substantial shifts in type of agents used. These data can serve as a baseline for future prevalence studies and research into factors influencing the trends we observed.

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