Title: The 2018 Global Point Prevalence Survey of Antimicrobial Consumption and Resistance in 47 Canadian Hospitals

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Abstract

Background

Patient-level surveillance of antimicrobial use (AMU) in Canadian hospitals is needed to reduce antimicrobial overuse and misuse and was piloted in 2017 amongst 14 hospitals in Canada. Continued surveillance is needed to identify trends and opportunities for interventions and measure the impact of interventions. The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS) is an international collaborative to monitor antimicrobial use and resistance in hospitals worldwide. This paper presents the results of the 2018 Global-PPS in Canadian hospitals.

Methods

Canadian adult, pediatric and neonatal hospitals (n=118) were invited to participate in this web-based cross-sectional survey. All surveys except for one institution were performed in the 2018 calendar year. All in-patient wards in each hospital were surveyed according to the Global-PPS methodology.

Results

Forty-seven of 118 (40%) hospitals participated in the survey. Of 13 272 patients included, 4447 (33.5%) received a total of 6171 antimicrobials. Overall, 74.1% (n=4832) of antimicrobials were for therapeutic use, 12.6% (n=825) were for medical prophylaxis, 8.9% (n=578) were for surgical prophylaxis (SP), 2.2% (n=143) for other use and 2.3% (n=147) were for unidentified reasons.

Interpretation

AMU is overall similar to what was previously reported in Canada (33.5%). Documentation of indication for therapeutic use was high (87%). Rational use of antimicrobials adhered to guidelines (84%) and seemingly prioritized single dose of SP. Though guideline availability was lower in the Atlantic Provinces, new protocols have since been implemented.

Introduction

Antimicrobial resistance (AMR) is a substantial threat to public health[1] and increases mortality, morbidity and healthcare cost[2]. Antimicrobial overuse and misuse accelerates AMR development[1,3]. A global response is warranted to ensure rational antimicrobial use (AMU) given that AMR is commutable between countries. In 2017, Canada has released the *Framework for Action* on AMR and AMU to reinforce its strategy on AMR and to complement the World Health Organisation *Global Action Plan on Antimicrobial Resistance*[4,5]. Surveillance of AMU is a core component of the *Framework for Action,* as it allows trend monitoring and identification of areas of concerns. The Canadian Nosocomial Infection Surveillance Program (CNISP) monitors AMU in participating hospitals using daily defined doses (DDDs) with monthly data points[6]. However, this method lacks patient-level and qualitative information; most notably the indication, appropriate choice, dosing and duration of antimicrobials, which are required to interpret quantitative aspects and guide stewardship interventions[7]. Patient-level surveillance of AMU is a key factor in reducing antimicrobial overuse and misuse. Recently, CNISP has published the results of 3 national point-prevalence surveys (PPSs), limited to healthcare-acquired infections (HAIs)[8]. In Canada, patient-level AMU surveillance performed on a national level has been done through a pilot PPS in 2017 which only included 14 hospitals[9]. A broader Canadian sample will allow for trend identification, evaluation of impact of interventions and benchmarking in the future.

The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS) is an international collaborative created in 2014 to monitor antimicrobial use and resistance in hospitals worldwide. Global-PPS locally documents, on a single day, patient-level antimicrobial prescribing practices. The advantage of the Global-PPS's standardized surveillance method is that it is adapted to all types of hospitals and allows data comparison locally, nationally and internationally. Global-PPS identifies areas of improvement and, through repeat surveys, measures the impact of interventions. This article presents the results of the 2018 Global-PPS in Canadian hospitals.

Methods

Objective and Design

The objective of this cross-sectional study was to evaluate antimicrobial use and resistance in Canadian hospitals. The primary outcome was to measure antimicrobial prescribing rates, antimicrobial indications and agent selection in medical, surgical and intensive care wards. The secondary outcome was to measure resistance rates and compare results to the 2017 Global-PPS survey. In order to ensure comparability between Global-PPS studies, the methodology employed in this study was the same as the 2017 pilot survey[10].

Setting and Participants

Adult, pediatric and neonatal hospitals in Canada were invited to participate in the 2018 Global-PPS through the CNISP, the Association of Medical Microbiology and Infectious Disease Canada and the *Association des Médecins Microbiologistes-Infectiologues du Québec*. Surveys were performed between June and December 2018; one hospital performed the study beginning January 2019. All in-patient wards were surveyed once on a single day; however, different wards could be surveyed on separate days. Wards were not surveyed on a weekend or a holiday. Surgical wards were not surveyed on a day following a weekend or holiday in order to better represent a routine weekday regarding information on the duration of surgical prophylaxis (SP).

On the day of the survey, detailed data was collected for all admitted inpatients receiving an antimicrobial as of 0800 h. A patient was considered receiving an antimicrobial if the agent was one of the following: systemic antibiotics, antibiotics used as intestinal anti-infectives, systemic antimycotics and antifungals, antituberculosis agents, nitroimidazole derivatives and antiprotozoals used as antibiotic agents, antivirals and antimalarials. Topical antimicrobials were excluded.

Participation in the Global-PPS was either considered exempt as quality assurance projects or approved by the research ethics boards at participating hospitals if required by institution-specific policies.

Data collection

A physician, pharmacist or nurse with some infectious disease training performed the survey. An administrator per site provided oversight to ensure survey completion. The necessary detailed information was retrieved from medical charts and was not discussed with the ward staff nor was direct feedback provided to enhance objective data collection. The Global-PPS utilizes a uniform standardized surveillance method for all hospitals.

Data collected for each patient on antimicrobial therapy included age, weight, gender and antimicrobial agent. For each antimicrobial received, the following information was collected: dose, route, diagnosis, indication, and a set of quality indicators such as diagnosis documented in the chart at the start of the antimicrobial, local guideline compliance, stop/review date documented and whether therapy was empirical or targeted. The treating physician's diagnosis was recorded based on standardized categories[11]. Type of indication was categorized based on standardized definitions and included: community-acquired infection (CAI), healthcare-associated infection (HAI), surgical prophylaxis (SP) as one dose, one day or more than one day, medical prophylaxis (MP) defined as prophylaxis not related to surgery (e.g. antifungals for chemotherapy), other, and unknown[11]. If therapy was targeted, the targeted multidrug resistance type was recorded. Finally, biomarker data were recorded (C-reactive protein, procalcitonin or other) if they supported prescribing decisions. Antibiotics were categorized using the World Health Organization AWaRe classification[12].

Data analysis

Antimicrobial consumption data is presented in terms of proportions and/or 95% confidence interval (CI). Prevalence of antimicrobial prescribing is presented as the proportion of patients on at least one antimicrobial compared to the number of inpatients on the ward. A patient on single or multiple antimicrobials had the same weight in the

numerator. Biomarker data and dose differences between patients for the same antimicrobial were not analyzed.

Results

Forty-seven of 118 Canadian hospitals participated in the 2018 Global-PPS and data from all hospitals were included in the study. The median (interquartile range) hospital size was 276 (157-465.5) beds. Thirty hospitals were university-affiliated centers. Eleven hospitals were from Western Canada (BC and SK), 22 from Central Canada (ON and QC) and 14 from the Atlantic Provinces (NB, NL, NS and PE). Nine hospitals were primary care centers (10.0% of patients), 15 were secondary care centers (29.7% of patients) and 23 were tertiary/specialized care centers (60.3% of patients). Two tertiary care centers were exclusively pediatric centers. Overall, 802 units and 13 272 patients were included in the survey; about 1 in every 6 acute care beds in Canada were surveyed[13]. Table 1 presents baseline patient characteristics (age of neonates was not recorded due to privacy reasons).

Antimicrobial Prevalence

Of the 13 272 admitted inpatients, 4447 (33.5%; 95% CI, 30.7%-36.2%) received a total of 6525. Almost one-third (29.3%) of patients in primary care centers received antimicrobials, 31.0% in secondary care centers and 35.4% in tertiary/specialized care centers (Table 2). 34% of adults, 35.8% of pediatric patients and 15.7% of neonates received at least one antimicrobial (Table 3). Therapeutic use was highest in primary and secondary care centers (80.1% and 80.5% respectively), while medical prophylaxis in tertiary/specialized centers was more than double that of other hospital types (Table 2).

Therapeutic use

Therapeutic use accounted for the majority of antimicrobial prescriptions (74.1% in adults, 65.1% in pediatric patients and 58.1% in neonates [Table 4-5a/b]); treatment being targeted in 39.4% of cases. Overall, 29.6% of antimicrobials were for respiratory tract (1431/4832), 11.5% for urinary (554/4832) 11.0% for intra-abdominal (531/4832), 10.3% (496/4832) for skin and soft tissue (496/4832) and 7.3% for bone and joint (355/4832) infections (Table 6). The overall prevalence of patients presenting HAIs was

9.2% (1225/13272); 9.5% (1184/12438) in adults and 4.9% (41/834) in pediatric/neonatal wards. Community-acquired pneumonia (CAP) accounted for 14.4% (694/4832) of antimicrobials while healthcare-acquired pneumonia (HAP) accounted for 9.1% (438/4832). Empirical treatment accounted for 60.6% (2926/4832) of all antimicrobials for therapeutic use and targeted treatment accounted for 39.4% (1906/4832). Of 3014 antimicrobials for CAIs, 1896 (62.9%) were empirical treatment and 1118 (37.1%) were targeted treatment. Of the 1818 antimicrobials for HAIs, 1030 (56.7%) were empirical treatment and 788 (43.3%) were targeted treatment.

Medical prophylaxis

Antibiotics were the most commonly prescribed antimicrobials for MP (52.0%, 429/825; Supplementary Table 1). Antivirals were the second most prescribed (26.7%, 220/825). Combination of sulfonamides and trimethoprim was the most prescribed agent (22.4%, 185/825).

Surgical prophylaxis

Cefazolin accounted for the majority of surgical antimicrobial prophylaxis prescriptions (69.7%). Overall, 36% of patients received a single dose of SP, 33% received prophylaxis for a duration of 1 day and 32% for more than 1 day. Supplementary Material Table 2 presents antimicrobial prevalence by SP site in wards.

Antimicrobial Class Prevalence

Antibiotics accounted for 83.6% of antimicrobials prescribed (5454/6525; Table 7). Penicillins with β-lactamase inhibitors (19.1%, 1042/5454), 1st generation cephalosporins (13.4%, 730/5454), 3rd generation cephalosporins (11.1%, 606/5454) and fluoroquinolones (10.7%, 583/5454) were the most common antibiotics prescribed. Individually, piperacillin with β-lactamase inhibitors (12.3%), cefazolin (9.7%), ceftriaxone (8.1%), vancomycin (6.9%) and ciprofloxacin (5.9%) were the most commonly prescribed antimicrobials. For the treatment of pneumonia, the combination of a penicillins with a β-lactamase inhibitor (27.2%) or 3rd generation cephalosporin monotherapy (19.3%) or fluoroquinolone monotherapy (12.5%) accounted for more than half of the antibiotics prescribed. Antivirals

(7.3%), antifungals (7.2%), antimalarial agents (1.1%) and antituberculosis agents (0.7%) respectively followed antibiotics in prevalence. Antimicrobials indication for HAI and CAI is described in Fig.1a/b and Fig.2.

Antibiotic stewardship

A diagnosis/indication was documented in the patient's file at the initiation of 87% antimicrobials (5699/6525). Sixty-three percent of antimicrobials had a stop/review date documented in the patient's file. Local guidelines were present to guide 75% of prescriptions and 84% of prescriptions were judged as complying with the recommended antimicrobial choice. Compliance to guideline was highest in Western Canada (86.7%) and lowest in Atlantic Provinces (71.5%). Stewardship data is presented in Table 4.

Antimicrobial Resistance

A total of 353 multidrug resistant organisms (MDROs) were identified in the 3548 patients for which AMU was for therapeutic use (9.9%). Of those, 16.7% (186/1116), 7.5% (135/1731), and 6.1% (37/611) were in the Western, Central and Atlantic regions of Canada. The most frequent MDROs were methicillin-resistant *Staphylococcus aureus* (MRSA) (23.2%, 82/353). The prevalence of patients presenting an MRSA infection was 4.6%, 1.7% and 0.2% in the Western, Central and Atlantic regions of Canada, respectively. Resistance rate are presented based on targeted treatment in Table 8.

Interpretation

This study is the largest nationwide PPS to measure AMU using patient-level data in Canada and serves as a benchmark for future Global-PPS studies. The data provided in this study is considered representative of the Canadian population as it included 18% of acute care beds in hospitals spanning the 3 major regions of Canada and 7/10 provinces. AMU on medical, surgical and intensive care wards is similar to those previously reported in Canada. As seen in the 2017 pilot study[9], respiratory tract infections accounted for the majority of infections treated in all wards except for surgical wards, where intra-abdominal infections were most prevalent. The proportion of antimicrobial use varied significantly between indications. For CAP, 3rd generation cephalosporins were the most commonly

used antimicrobials while penicillins with β-lactamase inhibitors were most prevalent for the treatment of HAP. Agent selection for CAP and HAP is similar to previously reported worldwide and European rates[11]. However, lower use of penicillins with β-lactamase inhibitors was reported in the United-States, where levofloxacin alone predominated in CAP and HAP[11].

From 2002 to 2017, a significant decrease in HAI prescriptions has been observed in Canada[8]. When comparing our results to the 2017 survey[9], this decrease appears to have been maintained in 2018. At patient level, similar rates of HAIs have been reported worldwide in 2015[11] and in Europe in 2016-2017[14]. Our data indicates that piperacillin-tazobactam is ahead of cefazolin in terms of AMU compared to previous observations[6]. We observe a general continuation in the order of most used antimicrobials between 2016 and 2018 in Canada. A major decrease in fluoroquinolone use was previously observed in Canadian hospital part of the CNISP network[6]. Relative to PPSs performed in 2002, 2009 and 2017, our results are in line with this trend[9,15].

The proportion of patients receiving a single dose of SP has more than tripled in 2018, whereas receiving SP for more than one day has decreased by 20%[9]. In Europe, SP for more than 1 day represents 54% of SP prescription[14] while 31% was reported in this study. Our results indicate a trend towards SP being administered for no more than one day in Canada. On any given day, the indication for a prescription was identified in the vast majority of cases (87%). However, a significant proportion of antimicrobial prescription in the Atlantic Canadian Provinces were not guided by local guidelines (53% vs. 25% national average); their implementation could help reduce misuse and/or overuse in this region. Moreover, higher guideline availability appears to correlate with higher rates of targeted treatments in this study (Table 4). Nevertheless, almost identical compliance to guidelines was observed in 2018 compared to previous Canadian[9] and European rates[14]. Despite similar compliance, the decrease in antimicrobial use in pediatric patients and neonates, combined with the seemingly prioritized single dose of SP over SP for more than one day may indicate a more rational use of antimicrobial across Canada. However, further evaluation should be performed to assess the impact of these changes.

As seen in the 2017 survey, MRSA is still the most frequently treated MDRO[9]. The rate of MRSA infection has been increasing since 2012 and this trend is believed to be driven by the increasing rate of community-acquired MRSA[16]. A significant proportion of MDROs were identified in the western Canadian regions (16.7% vs. 9.9% national average). MDROs were generally more uncommon in the Atlantic Provinces. The lower prevalence of MRSA in the Atlantic (0.2% vs. 2.3% national average) appears to correlate with the lower empirical use of vancomycin in these regions (2.6% vs. 4.6% national average). Indeed, as vancomycin is usually recommended when treating an MRSA infection[17], the prevalence of vancomycin being driven by the prevalence of MRSA is plausible. This association is maintained for the rest of Canada.

Future PPSs will be performed to establish meaningful trends in AMU across Canadian hospitals by region, hospital types and individual hospitals. Higher rates of AMU and lower rates of HAIs are reported in the United-States[18,19], however, the difference in reporting methodology and period between surveys prevent rigorous comparison between countries. When similar methodology is used, antimicrobial prevalence reported in this study (33.5% of patients; 95% CI, 30.7%-36.2%) is in line with previously reported global and European rates[11,14].

Limitations

The main limitation of PPSs is inherent to the method of a cross-sectional survey, namely the interpretation of data acquired at a single point in time. Although day-to-day variations occur, PPSs have moderate correlation with antimicrobial consumption measured in DDD for the month and season of the PPS[20]. However, surveys were performed between June and December (one in January), which may partially correct for seasonal variation. The PPS was carried out at centers where identification of microorganism and stewardships programs are mostly available, introducing selection and representiveness bias; performing a PPS in hospitals where this expertise is not available is of future interest. A total of 14 hospitals participated in the 2017 survey while 47 participated in 2018; comparison may be limited. Differences in surveyors, regarding

compliance to guideline, may also be a source of bias. A missing component of the survey was the validity of the infectious disease diagnosis. The surveyor recorded what the physician intended to treat as recorded in the medical files, which is not based on clinical case definitions provided with the Global-PPS protocol. A substantial proportion of inappropriate use is due to inaccurate diagnosis[21]; however, it is currently beyond the scope of the Global-PPS. Future areas of considerations include the use of diagnostic codes and stewardship, graded appropriateness and collection of data regarding allergies to antimicrobials.

Conclusion

This study provided valid and reliable results on antimicrobial prescribing practices in Canadian hospitals. The results will support national and local stewardship programs. Though AMU was overall similar to what was previously reported in Canada, a more rational use of antimicrobials may be put forward with the seemingly decreased prevalence of AMU in pediatric and neonatal patients combined to the prioritized SP as one dose rather than for more than a day. Adherence to guideline was high throughout Canada (84%), howbeit their availability was lower in the Atlantic Provinces. New protocols have since been developed in these regions. Further PPSs will allow for more robust trend identification and evaluation of interventions.

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Item category	Checklist Item	Manuscript page
Design	Describe survey design	4
IRB	IRB approval	6
	Informed consent	Not applicable
	Data protection	Described in referenced protocol
Recruitment process	Open survey versus closed survey	5
	Contact mode	5
	Advertising the survey	Not applicable
Survey administration	Web/E-mail	5
	Context	5
	Mandatory/voluntary	6
	Incentive	Not applicable
	Time/Date	5
	Randomization of items or questionnaire	Described in referenced protocol
	Adaptive questioning	Described in referenced protocol
	Number of items	Described in referenced protocol
	Number of screens	Described in referenced protocol
	Completeness check	Described in referenced protocol
	Review step	Described in referenced protocol
Response rates	Unique site visitor	6
	View rate	Not applicable
	Participation rate	7
	Completion rate	Same as participation rate
Preventing multiple entries	Cookie used	Described in referenced protocol
	IP check	Described in referenced protocol
	Log file analysis	Described in referenced protocol
	Registration	Described in referenced protocol
Analysis	Handling of incomplete questionnaires	Not applicable
	Questionnaire submitted with an atypical timestamp	5
	Statistical correction	Not applicable

Section
Method - Objective and Design
Method - Setting and Participants
Not applicable
Method - Objective and Design
Method - Setting and Participants
Method - Setting and Participants
Not applicable
Method - Setting and Participants
Method - Objective and Design
Method - Objective and Design
Not applicable
Method - Setting and Participants
Method - Objective and Design
Method - Objective and Design
Method - Objective and Design
Method - Objective and Design
Method - Objective and Design
Method - Objective and Design
Method - Data collection
Not applicable
Results
Results
Method - Objective and Design
Method - Objective and Design
Method - Objective and Design
Method - Objective and Design
Not applicable
Method - Setting and Participants
Not applicable

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Completed
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Yes
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Yes
Objectives	3	State specific objectives, including any prespecified hypotheses	Yes (and in methods)
Methods			
Study design	4	Present key elements of study design early in the paper	Yes
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Yes
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Yes
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Yes
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Yes
Bias	9	Describe any efforts to address potential sources of bias	Yes
Study size	10	Explain how the study size was arrived at	Yes
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Yes
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Yes
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	Not applicable
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Not applicable
		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes
		(b) Give reasons for non-participation at each stage	Not applicable

		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes
		(b) Indicate number of participants with missing data for each variable of interest	Not applicable
Outcome data	15*	Report numbers of outcome events or summary measures	Yes
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes
		(*b*) Report category boundaries when continuous variables were categorized	Yes
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Table 1. Baseline Patient Characteristics

	Average Age ± Standard Deviation, years	**Male, %**
Adult (n=12 438)	64.0 ± 17.9	54.8
Pediatric (n=427)	7.6 ± 7.6	59.1
Neonatal (n=407)	Not assessable	72.1

Table 2. Overall Antimicrobial Prevalence and Use by Hospital Type

	All types	**Primary**	**Secondary**	**Tertiary and Specialized**
Number of patients, N	13 272	1325	3947	8000
Number of patients receiving antimicrobials, N (%)	4447 (33.5)	388 (29.3)	1225 (31.0)	2834 (35.4)
Number of antimicrobials received, N	6525	518	1635	4372
Therapeutic Use, N (%)	4832 (74.1)	415 (80.1)	1316 (80.5)	3101 (70.9)
Medical Prophylaxis, N (%)	825 (12.6)	33 (6.4)	101 (6.2)	691 (15.8)
Surgical Prophylaxis, N (%)	578 (8.9)	38 (7.3)	156 (9.5)	384 (8.8)
Other, or Unknown, N (%)	290 (4.4)	32 (6.2)	62 (3.8)	196 (4.5)

Table 3. Overall Antimicrobial Prevalence by Ward Type in Adult, Pediatric and Neonatal Patients

Adult	**All wards**	**AMW**	**HO-AMW**	**T-AMW**	**P-AMW**	**ASW**	**AICU**
Number of patients on ward, N	12 438	7686	420	142	159	3083	948
Number of patients receiving antimicrobials, N (%)	4230 (34.0)	2031 (26.4)	205 (48.8)	113 (79.6)	91 (57.2)	1318 (42.8)	472 (49.8)
Number of antimicrobials received, N	6171	2753	387	305	196	1755	775
Pediatric and Neonatal	**All wards**	**PMW**	**GNMW**	**HO-PMW**	**PSW**	**PICU**	**NICU**
Number of patients on ward, N	834	307	151	25	57	38	256
Number of patients receiving antimicrobials, N (%)	217 (26.0)	81 (26.4)	7 (4.6)	21 (84.0)	24 (42.1)	21 (55.3)	63 (24.6)
Number of antimicrobials received, N	354	115	14	46	32	39	108

Table 4. Regional documentation for indications, planned duration or review, and adherence to local guidelines

	Total	West	Central	Atlantic
Number of antimicrobials received, N	6525	2092	3372	1061
Reasons in notes, N (%)	5699 (87.3)	1899 (90.8)	2922 (86.7)	878 (82.8)
Stop/Review date, N (%)	4106 (62.9)	1357 (64.9)	2095 (62.1)	564 (53.2)
Antimicrobials for therapeutic use, N	4832	1572	2462	798
Targeted treatments, N (%)	1906 (39.4)	716 (45.5)	936 (38.0)	254 (31.8)
Guidelines compliance, N (%)				
Yes[a]	3928 (84.3)	1474 (86.7)	2125 (85.0)	329 (71.5)
No information, diagnosis missing	224 (3.5)	65 (3.2)	118 (3.5)	41 (3.9)
No guidelines available	1604 (24.7)	281 (13.7)	763 (22.6)	560 (52.8)

[a]The rate of positive compliance is calculated as opposed to negative guideline compliance, excluding if information or guideline was missing

Table 5a. Antimicrobial Use by Ward Type for Adult, Pediatric and Neonatal Wards

Adult	**All wards**	**AMW**	**HO-AMW**	**T-AMW**	**P-AMW**	**ASW**	**AICU**
Total number of antimicrobials	6171	2753	387	305	196	1755	775
Therapeutic Use, N (%)	4610 (74.7)	2319 (84.2)	199 (51.4)	123 (40.3)	156 (79.6)	1205 (68.7)	608 (78.5)
Medical Prophylaxis, N (%)	749 (12.1)	227 (8.2)	175 (45.2)	178 (58.4)	37 (18.9)	73 (4.2)	59 (7.6)
Surgical Prophylaxis, N (%)	567 (9.2)	86 (3.1)	4 (1.0)	0 (0.0)	1 (0.5)	403 (23.0)	73 (9.4)
Other or Unknown, N (%)	245 (4.0)	121 (4.4)	9 (2.3)	4 (1.3)	2 (1.0)	74 (4.2)	35 (4.5)
Pediatric and Neonatal	**All wards**	**PMW**	**GNMW**	**HO-PMW**	**PSW**	**PICU**	**NICU**
Total number of antimicrobials	354	115	14	46	32	39	108
Therapeutic Use, N (%)	222 (62.7)	90 (78.3)	12 (87.5)	17 (37.0)	20 (62.5)	24 (61.5)	59 (54.6)
Medical Prophylaxis, N (%)	76 (21.5)	7 (6.1)	2 (14.3)	24 (52.2)	4 (12.5)	9 (23.1)	30 (27.8)
Surgical Prophylaxis, N (%)	11 (3.1)	3 (2.6)	0	0	5 (15.6)	0	3 (2.8)
Other or Unknown, N (%)	45 (12.7)	15 (13.0)	0	5 (10.9)	3 (9.4)	6 (15.4)	16 (14.8)

Abbreviations: AMW, adult medical ward; HO-AMW, hematology-oncology-AMW, T-AMW, transplant-AMW; P-AMW, pneumology-AMW; ASW, adult surgical ward; AICU, adult intensive care unit

Table 5b. Antimicrobial Use by Region

	Total	West	Central	Atlantic
Total number of antimicrobials	6525	2092	3372	1061
Therapeutic Use, N (%)	4832 (74.1)	1572 (75.1)	2462 (73.0)	798 (75.2)
Medical Prophylaxis, N (%)	825 (12.6)	241 (11.5)	467 (13.8)	117 (11.0)
Surgical Prophylaxis, N (%)	578 (8.9)	198 (9.5)	293 (9.7)	87 (8.2)
Other or Unknown, N (%)	290 (4.4)	81 (3.9)	150 (4.4)	59 (5.6)

Table 6. Number of Antimicrobials for Community-Acquired and Hospital-Acquired Infectious Disease Indications

Indication	Adults			Pediatric and Neonatal		
	Total, N	CAI, %	HAI, %	Total, N	CAI, %	HAI, %
Overall	4610	62.0	38.0	222	70.3	29.7
Central Nervous System	108	67.6	32.4	20	80.0	20.0
Eye	8	87.5	12.5	1	100	0
Ear, Nose, Throat	142	47,2	52,8	15	93.3	6.7
Lung	57	78,9	21,1	3	100	0
Upper Respiratory Tract	31	87,1	12,9	0	NA	NA
Bronchitis	134	85,1	14,9	2	100	0
Pneumonia	1100	61,2	38,8	32	65.6	34.4
Tuberculosis	66	100	0	0	NA	NA
Cardiovascular	139	57,6	42,4	1	0	100
GI Tract	260	43,1	56,9	8	75.0	25.0
Intra-Abdominal	516	65,9	34,1	15	73.3	26.7
Skin and Soft Tissue	484	66,7	33,3	11	54.5	45.5
Bone and Joint	341	65,7	34,3	12	91.7	8.3
Lower Urinary Tract	300	48,7	51,3	1	0	100
Upper Urinary Tract	240	59,6	40,4	12	91.7	8.3
Obstetric/Gynaecologic (female)	46	73,9	26,1	0	NA	NA
Genitourinary (male)	16	50,0	50,0	0	NA	NA
BAC	143	56,6	43,4	13	38.5	61.5
Sepsis	109	42,2	57,8	48	60.4	39.6
HIV	116	100	0	0	NA	NA
FN	104	38,5	61,5	14	71.4	28.6
PUO/PUO-HO	48	45,8	54,2	9	88.9	11.1
Lymphatic	3	100	0	0	NA	NA
Other	70	68,6	31.4	3	33.3	66.7
Unknown	29	69,0	31,0	2	50.0	50.0

Abbreviations: CAI, community-acquired infectious disease; HAI, hospital-acquired infectious disease; GI, gastrointestinal; BAC, bacteremia with no clear anatomical site; FN, fever in neutropenic patient; PUO, pyrexia of unknown origin; PUO-HO, PUO in hematology-oncology patient; NA, not applicable

Table 7a. Antimicrobial Prevalence by Region

	Total	West	Central	Atlantic
Total number of antimicrobials	6525	2092	3372	1061
Antibiotics, N	5454	1729	2801	924
Antifungals, N	473	144	264	65
Antivirals, N	477	179	250	48
Antituberculosis agents, N	47	26	13	8
Antimalarial agents, N	72	13	44	15
Other, N	46	10	25	11
Antibiotics by Class, %				
Penicillins with β-lactamase inhibitors	19,1	19,3	20,0	16,1
Penicillins with extended spectrum	1,8	1,5	2,1	1,3
β-lactamase-resistant penicillins	1,4	2,1	0,8	1,7
β-lactamase-sensitive penicillins	2,4	2,1	2,4	2,8
1st generation cephalosporins	13,4	14,6	12,2	14,7
2nd generation cephalosporins	1,6	1,5	1,4	2,6
3rd generation cephalosporins	11,1	13,3	9,5	12,0
4th generation cephalosporins	0,1	0,1	0,2	0,0
5th generation cephalosporins	0,1	0,2	0,1	0,0
Carbapenems	5,0	4,2	6,0	3,8
Fluoroquinolones	10,7	8,9	11,4	11,8
Aminoglycosides	2,1	1,0	2,9	1,7
Macrolides	4,0	4,0	3,8	4,3
Tetracyclines	2,5	2,0	2,7	2,5
Clindamycin	1,3	1,3	1,5	1,0
Metronidazole	5,3	5,9	4,1	7,9
Combinations of sulfonamides and trimethoprim	5,7	4,7	6,2	6,0
Linezolid	0,4	0,9	0,1	0,2
Vancomycin PO	2,5	2,0	2,8	2,4
Vancomycin IV	5,8	6,9	6,0	3,4
Nitrofurantoin	1,1	1,0	0,9	1,7
Colistin	0,3	0,1	0,4	0,0
Daptomycin	0,5	0,7	0,5	0,0
Rifamycins	1,1	1,1	1,1	1,0
Other	0,7	1,0	0,1	0,2

Table 7b. Antimicrobial Prevalence by Class in Adult, Pediatric and Neonatal Wards

Adult	**All wards**	**AMW**	**HO-AMW**	**T-AMW**	**P-AMW**	**ASW**	**AICU**
Total number of antimicrobials	6171	2753	387	305	196	1755	775
Antibiotics, N	5153	2354	213	137	150	1621	678
Antifungals, N	442	144	85	78	11	65	59
Antivirals, N	457	196	86	79	15	49	32
Antituberculosis agents, N	45	11	2	4	19	6	3
Antimalarial agents, N	72	47	1	6	1	14	3
Other, N	2	1	0	1	0	0	0
Antibiotics by Class, %							
Penicillins with β-lactamase inhibitors	19,7	18,1	28,2	21,2	16,7	20,8	20,6
Penicillins with extended spectrum	1,0	0,9	0,5	0,0	0,0	1,0	1,3
β-lactamase-resistant penicillins	1,4	1,9	0,5	0,0	0,0	1,2	1,0
β-lactamase-sensitive penicillins	2,3	3,5	2,3	0,7	2,0	1,2	0,9
1st generation cephalosporins	13,8	9,8	2,8	1,5	2,7	24,2	10,9
2nd generation cephalosporins	1,6	2,6	0,0	0,0	1,3	1,0	0,6
3rd generation cephalosporins	10,8	13,0	3,3	4,4	8,0	8,3	13,3
4th generation cephalosporins	0,2	0,0	0,5	0,0	0,7	0,2	0,1
5th generation cephalosporins	0,1	0,1	0,0	0,0	0,0	0,1	0,4
Carbapenems	5,1	4,0	8,9	10,2	8,0	3,3	10,2
Fluoroquinolones	11,1	12,4	14,6	8,8	15,3	10,9	5,9
Aminoglycosides	1,3	1,1	0,5	1,5	4,0	1,5	1,2
Macrolides	4,1	5,3	0,9	3,6	10,0	1,9	4,9
Tetracyclines	2,6	4,1	0,0	0,7	4,7	1,8	1,2
Clindamycin	1,4	1,5	0,9	0,0	0,7	1,4	1,5
Metronidazole	5,4	4,0	3,8	0,7	2,7	8,8	4,6
Combinations of sulfonamides and trimethoprim	5,6	5,6	14,6	28,5	10,0	2,7	4,7
Linezolid	0,4	0,4	0,0	0,0	1,3	0,4	0,3
Vancomycin PO	2,6	3,1	3,8	5,1	0,7	1,8	2,2
Vancomycin IV	5,9	4,8	10,8	8,8	2,7	4,5	11,4
Nitrofurantoin	1,1	1,4	0,9	0,0	0,0	1,2	0,4
Colistin	0,3	0,1	0,0	2,9	2,7	0,1	0,3
Daptomycin	0,5	0,5	0,9	0,0	0,0	0,5	0,6
Rifamycins	1,1	0,9	0,0	0,0	4,0	1,4	1,0
Other	0,8	0,8	1,4	1,5	2,0	0,6	0,4
Pediatric and Neonatal	**All wards**	**PMW**	**GNMW**	**HO-PMW**	**PSW**	**PICU**	**NICU**
Total number of antimicrobials	354	115	14	46	32	39	108
Antibiotics, N	301	106	14	30	32	33	86
Antifungals, N	31	2	0	12	0	5	12
Antivirals, N	20	6	0	3	0	1	10
Antituberculosis agents, N	2	1	0	1	0	0	0
Antibiotics by Class, %							
Penicillins with β-lactamase inhibitors	8,3	8,5	0,0	20,0	9,4	18,2	1,2
Penicillins with extended spectrum	15,6	9,4	50,0	0,0	6,3	9,1	29,1
β-lactamase-resistant penicillins	1,7	0,0	0,0	0,0	0,0	0,0	5,8
β-lactamase-sensitive penicillins	4,7	7,5	0,0	0,0	6,3	3,0	3,5
1st generation cephalosporins	7,0	11,3	0,0	0,0	18,8	0,0	3,5
2nd generation cephalosporins	1,3	0,9	0,0	0,0	0,0	0,0	3,5
3rd generation cephalosporins	16,9	29,2	0,0	6,7	15,6	18,2	8,1
Carbapenems	4,0	1,9	0,0	3,3	6,3	9,1	4,7
Fluoroquinolones	2,7	2,8	0,0	6,7	6,3	3,0	0,0
Aminoglycosides	15,9	9,4	50,0	3,3	6,3	6,1	30,2
Macrolides	2,0	2,8	0,0	3,3	0,0	6,1	0,0
Tetracyclines	0,3	0,9	0,0	0,0	0,0	0,0	0,0
Clindamycin	0,7	1,9	0,0	0,0	0,0	0,0	0,0
Metronidazole	3,7	2,8	0,0	0,0	15,6	3,0	2,3
Combinations of sulfonamides and trimethoprim	7,0	2,8	0,0	36,7	6,3	15,2	0,0

Linezolid	2	1	0	1	0	0	0
Vancomycin PO	1	0	0	1	0	3	
Vancomycin IV	16	4	0	1	1	0	7
Nitrofurantoin	1	1	0	0	0	0	0
Rifampicin	1	0	0	1	0	0	0
Other	4	2	0	2	0	0	0

Abbreviations: AMW, adult medical ward; HO-AMW, hematology-oncology-AMW, T-AMW, transplant-AMW; P-AMW, pneumology-AMW; ASW, adult surgical ward; AICU, adult intensive care unit

Table 8. Antimicrobial Resistance Rates

Multidrug-resistant organism	Total number of patients treated for MDRO, N	Overall prevalence of MDRO[a], %	West[a], %	Central[a], %	Atlantic[a], %
MRSA	82	5.6	9.5	4.2	0.5
MRCoNS	33	2.2	2.2	2.5	1.4
VRE	10	0.7	0.7	0.8	0
ESBL-producing Enterobacteriaceae	41	2.8	4.1	1.5	3.7
3-ceph	60	4.1	4.9	2.7	6.8
CRE	5	0.3	0.9	0	0
ESBL-NF	22	1.5	2.2	1.3	0.5
CR-NF	25	1.7	1.7	1.8	1.4
Other MDRO	75	5.1	8.4	3.4	2.7

[a]Number of patients treated for MDRO on number of patients receiving antimicrobials for targeted use

Abbreviations: MDRO, multidrug-resistant organism; MRSA, methicillin-resistant *Staphylococcus aureus*; MRCoNS, methicillin-resistant coagulase negative staphylococci; VRE, Vancomycin-resistant enterococci; ESBL, bacteria producing extended-spectrum beta-lactamases; 3-ceph, 3rd generation cephalosporin resistant *Enterobacteriales*; CRE, carbapenem-resistant *Enterobacteriale*; ESBL-NF, ESBL-producing non-fermenter Gram-negative bacilli; CR-NF, carbapenem-resistant non-fermenter Gram-negative bacilli.

Supplementary Material Table 1. Antimicrobial Prevalence by Medical Prophylaxis Site for Adult, Pediatric and Neonatal Wards

Adult	**All wards**	**AMW**	**HO-AMW**	**T-AMW**	**P-AMW**	**ASW**	**AICU**
Total number of antimicrobials prescribed for medical prophylaxis, N	749	227	175	178	37	73	59
Prophylaxis site, N							
Fever in a neutropenic patient	2	0	2	0	0	0	0
General medical prophylaxis without targeting a specific site	425	86	158	115	9	27	30
Medical prophylaxis for maternal risk factors	6	6	0	0	0	0	0
Other	15	7	1	0	3	0	4
Bone and Joint	16	9	0	1	0	6	0
Central Nervous System	3	2	0	0	0	1	0
Cardiovascular System	3	3	0	0	0	0	0
Ear, Nose, Throat	16	3	0	10	0	0	3
Gastrointestinal Tract	57	23	1	11	1	13	8
Obstetrics or Gynecological	7	3	0	0	0	4	0
Respiratory Tract	165	64	11	40	24	12	14
Urinary Tract	30	19	1	0	0	10	0
Tuberculosis	1	0	0	1	0	0	0
Unknown	3	2	1	0	0	0	0
Pediatric and Neonatal	**All wards**	**PMW**	**GNMW**	**HO-PMW**	**PSW**	**PICU**	**NICU**
Total number of antimicrobials prescribed for medical prophylaxis, N	76	7	2	24	4	9	30
Prophylaxis site, N							
General medical prophylaxis without targeting a specific site	28	0	0	16	1	3	8

Medical prophylaxis for newborn risk factors	14	0	2	0	0	0	12
Respiratory Tract	13	3	0	6	0	4	0
Urinary Tract	4	2	0	0	0	0	2
PUO/PUO-HO	6	2	0	2	2	0	0
Bacteremia with no clear anatomic site and no shock	10	0	0	0	0	2	8
Skin, soft tissue	1	0	0	0	1	0	0

Abbreviations: AMW, adult medical ward; HO-AMW, hematology-oncology-AMW, T-AMW, transplant-AMW; P-AMW, pneumology-AMW; ASW, adult surgical ward; AICU, adult intensive care unit

Supplementary Material Table 2. Antimicrobial Prevalence by Surgical Prophylaxis Site for Adult, Pediatric and Neonatal Wards

Adult	**All wards**	**AMW**	**HO-AMW**	**T-AMW**	**P-AMW**	**ASW**	**AICU**
Total number of antimicrobials prescribed for surgical prophylaxis, N	567	86	4	0	1	403	73
Prophylaxis site, N							
General surgical prophylaxis without targeting a specific site	11	0	4	0	0	7	0
Other	2	0	0	0	0	0	2
Bone and Joint	176	10	0	0	0	158	8
Central Nervous System	29	4	0	0	0	14	11
Cardiovascular System	107	19	0	0	0	44	44
Ear, Nose, Throat	31	3	0	0	0	26	2
Gastrointestinal Tract	78	6	0	0	0	67	5
Obstetrics or Gynecological	68	38	0	0	0	30	0
Respiratory Tract	7	0	0	0	1	6	0
Urinary Tract	58	6	0	0	0	51	1
Pediatric and Neonatal	**All wards**	**PMW**	**GNMW**	**HO-PMW**	**PSW**	**PICU**	**NICU**
Total number of antimicrobials prescribed for surgical prophylaxis, N	11	3	0	0	5	0	3
Prophylaxis site, N							
Bone and Joint	2	0	0	0	2	0	0
Ear, Nose, Throat	1	0	0	0	1	0	0
Gastrointestinal Tract	8	3	0	0	2	0	3

Abbreviations: AMW, adult medical ward; HO-AMW, hematology-oncology-AMW, T-AMW, transplant-AMW; P-AMW, pneumology-AMW; ASW, adult surgical ward; AICU, adult intensive care unit

Fig. 1a

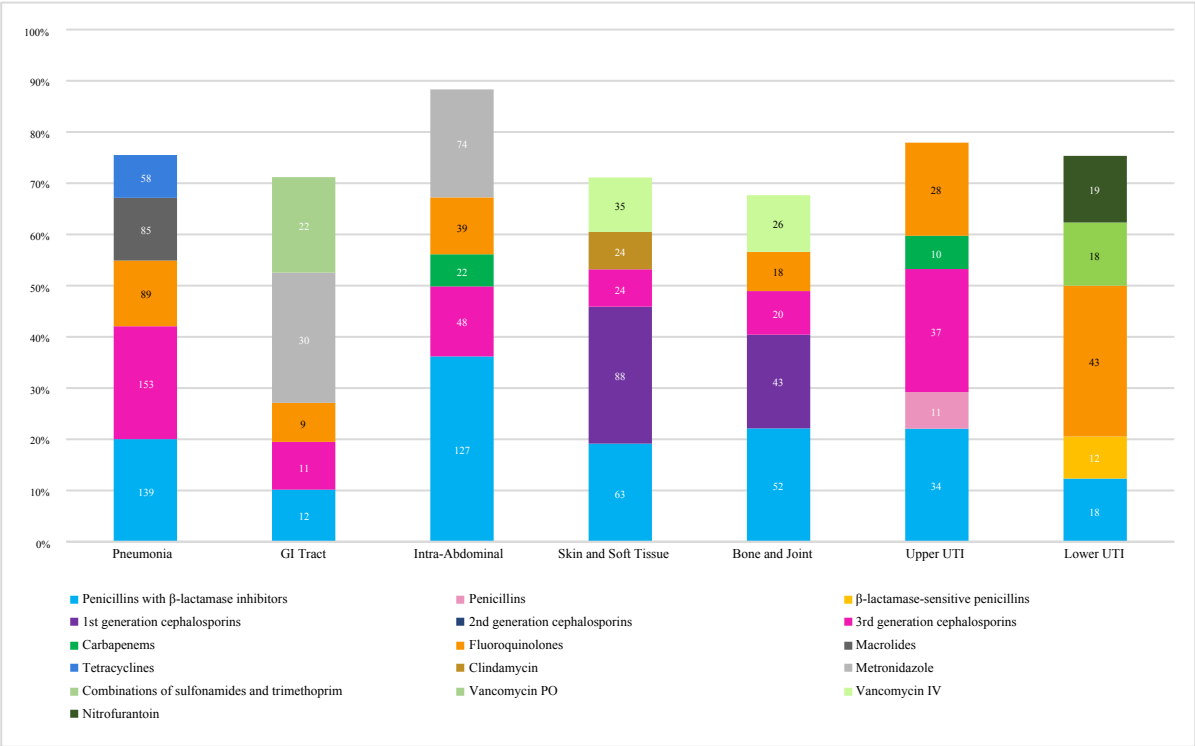
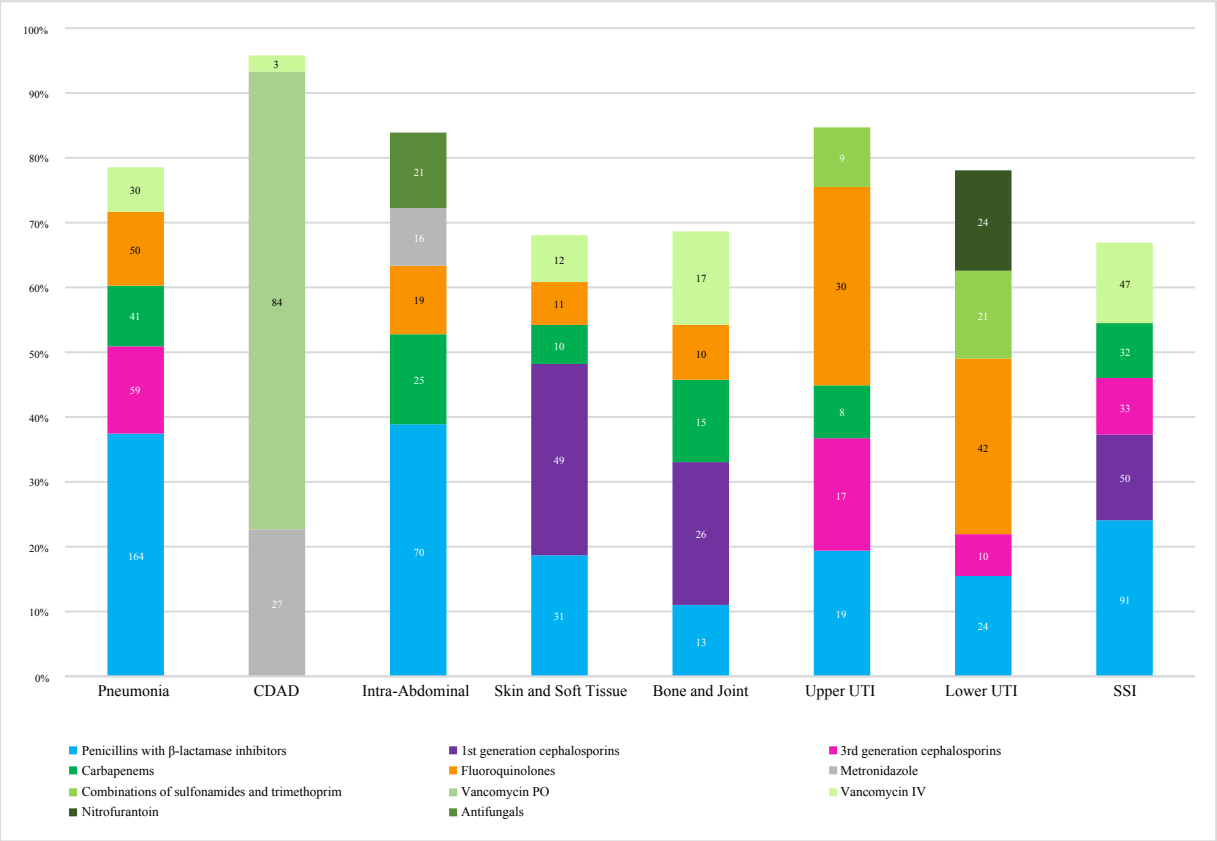


Fig. 1b


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Pneumonia
CDAD
Intra-Abdominal
Skin and Soft Tissue
Bone and Joint
Upper UTI
Lower UTI
SSI
164
59
41
50
30
27
84
3
70
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19
16
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31
49
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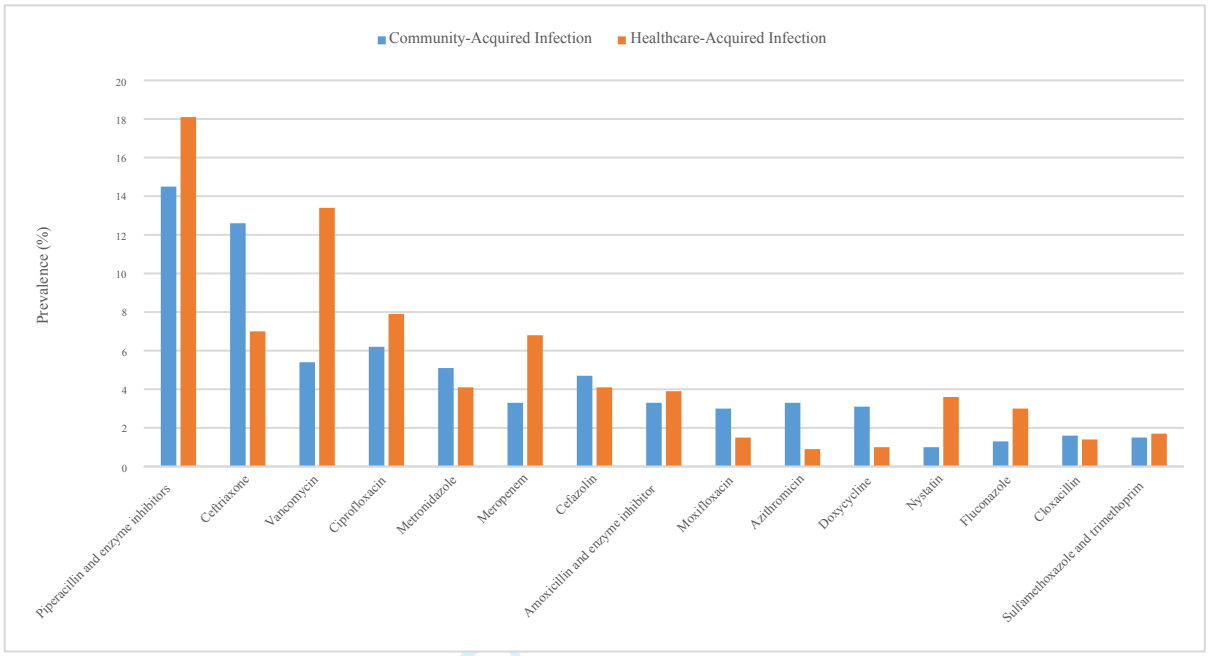
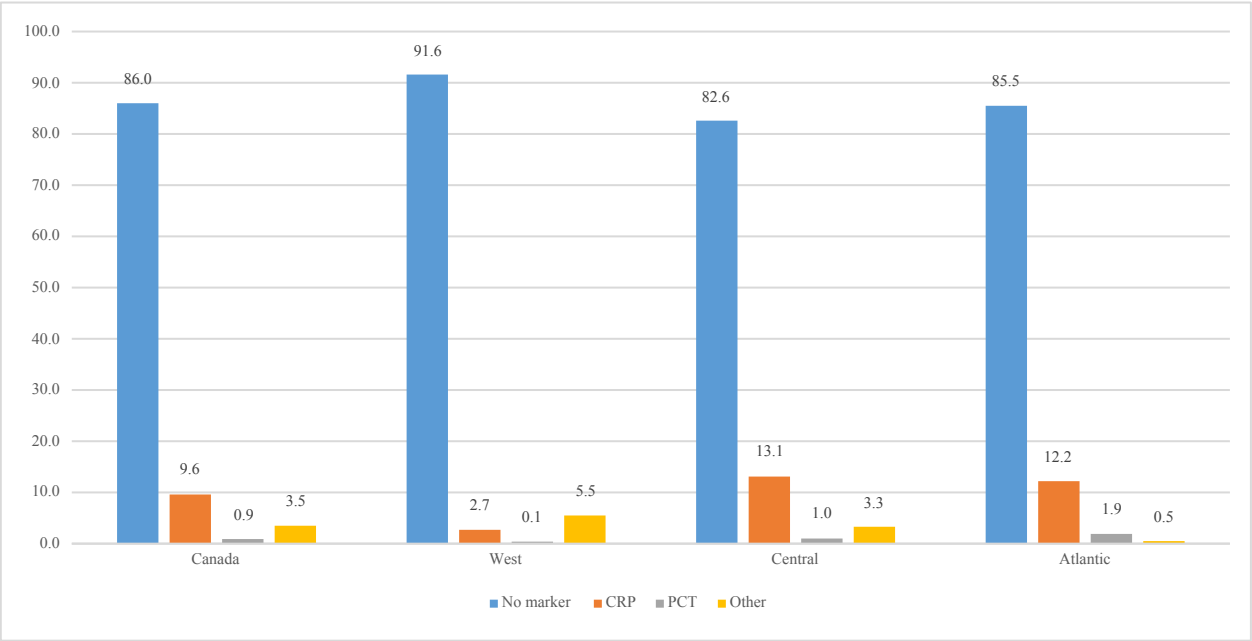
17
19
17
8
30
9
24
10
42
21
24
91
50
33
32
47
Penicillins with β-lactamase inhibitors
1st generation cephalosporins
3rd generation cephalosporins
Carbapenems
Fluoroquinolones
Metronidazole
Combinations of sulfonamides and trimethoprim
Vancomycin PO
Vancomycin IV
Nitrofurantoin
Antifungals

Fig.2 (supplemental)



	Community-A	Healthcare-Acquired Infection
Piperacillin and enzyme inhibitors	14.5	18.1
Ceftriaxone	12.6	7
Vancomycin	5.4	13.4
Ciprofloxacin	6.2	7.9
Metronidazole	5.1	4.1
Meropenem	3.3	6.8
Cefazolin	4.7	4.1
Amoxicillin and enzyme in	3.3	3.9
Moxifloxacin	3	1.5
Azithromicin	3.3	0.9
Doxycycline	3.1	1
Nystatin	1	3.6
Fluconazole	1.3	3
Cloxacillin	1.6	1.4
Sulfamethoxazole and trir	1.5	1.7

Fig. 3 (supplemental)



	Canada	West	Central	Atlantic
No marker	86.0	91.6	82.6	85.5
CRP	9.6	2.7	13.1	12.2
PCT	0.9	0.1	1.0	1.9
Other	3.5	5.5	3.3	0.5