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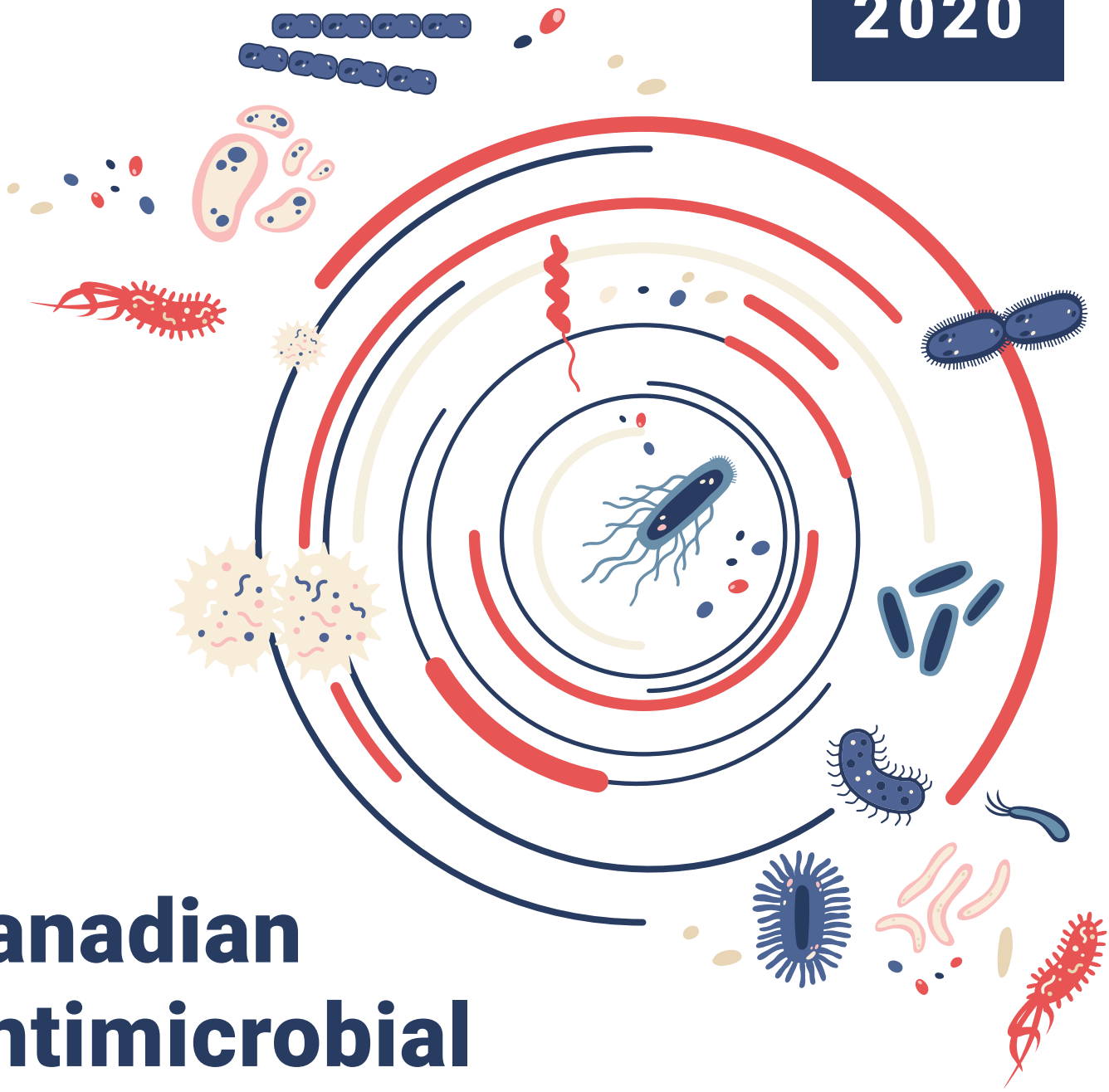

Canadian Antimicrobial Resistance Surveillance System Report

Public Health Agency of Canada
Agence de la santé publique du Canada

Canada

TO PROMOTE AND PROTECT THE HEALTH OF CANADIANS THROUGH LEADERSHIP, PARTNERSHIP, INNOVATION AND ACTION IN PUBLIC HEALTH.

— Public Health Agency of Canada

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Canadian Antimicrobial Resistance Surveillance System Report

Protecting and Empowering Canadians to Improve Their Health

TABLE OF CONTENTS

GLOSSARY

AMR	Antimicrobial resistance
AMU	Antimicrobial use
ARO	Antimicrobial-resistant organism
AST	Antimicrobial susceptibility testing
ATC	Anatomical therapeutic chemical
BSI	Bloodstream infection
CA	Community-associated
CAHI	Canadian Animal Health Institute
CARSS	Canadian Antimicrobial Resistance Surveillance System
CDI	*Clostridioides difficile* Infection
CIPARS	Canadian Integrated Program for Antimicrobial Resistance Surveillance
CNDSS	Canadian Notifiable Disease Surveillance System
CNISP	Canadian Nosocomial Infection Surveillance Program
CPE	Carbapenemase-producing Enterobacteriaceae
CTBLSS	Canadian Tuberculosis Laboratory Surveillance System
DDD	Defined Daily Dose
DDDvetCa	Veterinarian-Defined Daily Dose Canadian standard
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
eSTREP	National Laboratory Surveillance of Invasive Streptococcal Disease
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
GAS	Group A *Streptococcus pyogenes*
GASP–Canada	Gonococcal Antimicrobial Surveillance Program – Canada

HA	Healthcare-associated
Kg	Kilogram
KPC	*Klebsiella pneumoniae* carbapenemase
MDR	multidrug-resistant
mg/PCU	Milligrams per population correction unit
MIC	Minimum inhibitory concentration
MLST	Multi-locus sequence typing
MRSA	Methicillin-resistant *Staphylococcus aureus*
NAP	North American pulse type
NDM	New Delhi metallo-β-lactamase
NIHB	Non-Insured Health Benefits
NML	National Microbiology Laboratory
OXA	Oxacillinase
PCU	Population correction unit
PHAC	Public Health Agency of Canada
PMRA	Pest Management Regulatory Agency
SME	*Serratia marcescens* enzyme
ST	Sequence type
TB	Tuberculosis (*Mycobacterium tuberculosis*)
VRE	Vancomycin-resistant *Enterococcus*
WHO	World Health Organization
XDR	Extensively drug-resistant

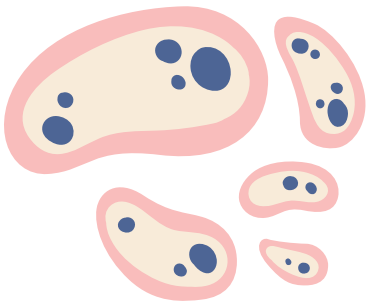

1

CHAPTER 1

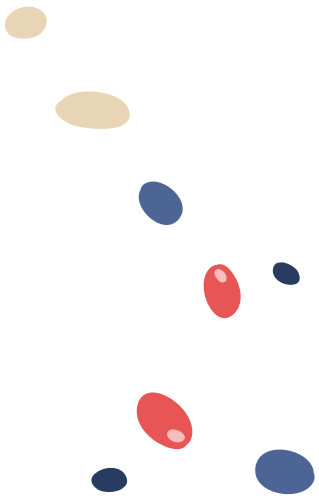
FOREWORD

Antimicrobials are important medical therapies that have come to define modern medicine. Their unnecessary use and overuse can promote the emergence of antimicrobial resistance (AMR) – that is, the ability of organisms to overcome the effects of the drugs designed to kill them. The spread of antimicrobial-resistant organisms (AROs), sometimes referred to as superbugs, jeopardizes infection control and the success of common medical procedures, which can leave patients vulnerable to infection. These procedures, including caesarean sections, hip replacements and chemotherapy, are performed on thousands of Canadians each day.

Many Canadians have already experienced a serious infection caused by an ARO or know someone who has. In 2018, one AMR infection was reported to the Public Health Agency of Canada (PHAC) for every 180 people admitted to hospital; for some of these infections, one in five patients died[1]. In another recent publication, the Council of Canadian Academies estimated that "ARO infections contributed to 14,000 Canadian deaths in 2018 alone[2]."



We rely on the continued effectiveness of antimicrobials – one-in-four Canadians received at least one antibiotic course in 2018[3]. We know, however, that some antimicrobials are used unnecessarily, which contributes to AMR[4]. The growing trend of AMR is a problem that no single entity can solve on its own.



PHAC is contributing to the body of evidence that forms the basis of our knowledge of AMR. Through detection and monitoring, surveillance enables effective infection prevention and control measures (the foundational strategy to limit the spread of organisms in hospitals and the community) thereby reducing the overall need for antimicrobials. Similarly, surveillance identifies where antimicrobials are being used excessively, allowing for targeted stewardship activities that reduce inappropriate prescribing and use. Surveillance also measures the outcome of interventions, such as reducing AMR infection rates and decreasing inappropriate antimicrobial use.

This surveillance report highlights a number of concerning trends in Canada. Together, we need to take action to address these issues and preserve antimicrobial effectiveness now and into the future.


2

CHAPTER 2

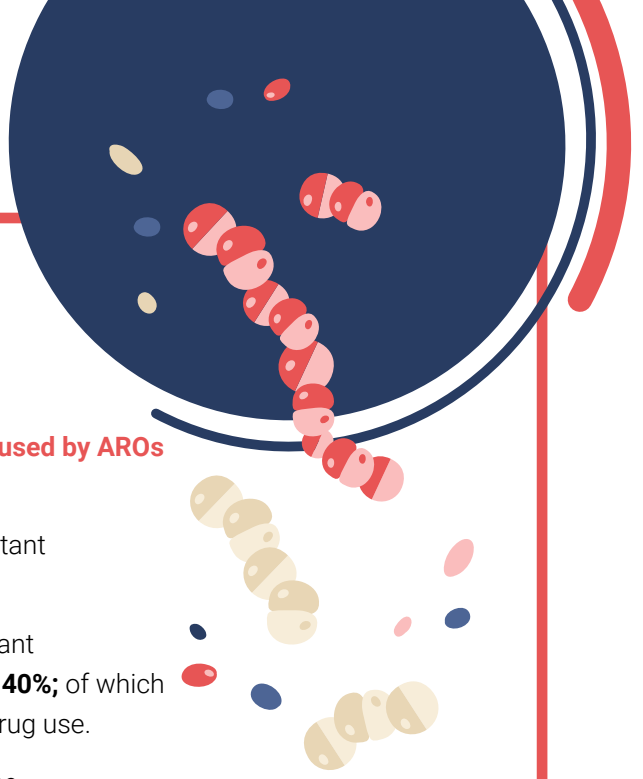
EXECUTIVE SUMMARY

This 2020 Canadian Antimicrobial Resistance Surveillance System (CARSS) Report provides a detailed assessment of antimicrobial resistance (AMR) in Canada. This report also provides recent information on the amount of antimicrobials used in humans and animals, as antimicrobial use (AMU) is one of the key drivers of AMR.

The methodology used for this report prioritizes AMR and AMU data acquired by the Public Health Agency of Canada (PHAC) and its partners. These data are often characterized by a high degree of national representation, but are not fully comprehensive. While this publication does not include projections as a result of mathematical modeling or the calculation of cost estimates, the timely availability of these data complement the existing body of evidence:

1. Globally, infections caused by AROs are becoming more frequent, leading to increased illness, death and rising healthcare costs[5].

2. Indicators show that the situation is worsening in Canada.



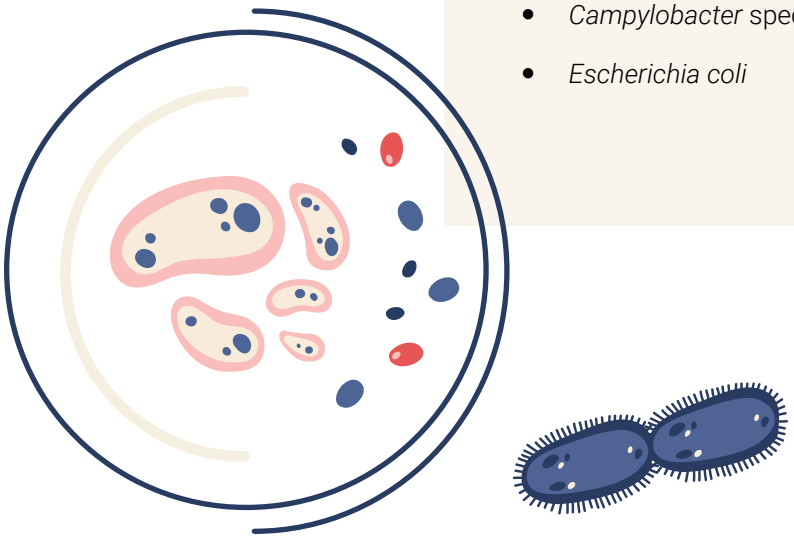
Between 2014 and 2018:

- The rate of potentially fatal **bloodstream infections (BSI) caused by AROs increased.**
    - The rate of healthcare-associated vancomycin-resistant ***Enterococcus*** **(VRE) BSI more than doubled.**
    - The rate of community-associated methicillin-resistant ***Staphylococcus aureus*** **(MRSA) BSI increased by 140%;** of which nearly half the cases are associated with injection drug use.
    - Approximately **20% of patients diagnosed** with these antimicrobial-resistant BSIs **died within 30 days of diagnosis.**
- The **effectiveness of carbapenems** (a class of antimicrobial important for the treatment of multidrug-resistant infections) **is threatened by a nine-fold increase** in the number of patients testing positive for carbapenem-resistant organisms without signs of infection.
- The proportion of **multidrug-resistant gonorrhea infections doubled.**
- In *Salmonella* Typhi/Paratyphi (Typhoid fever) infections, **ceftriaxone resistance** increased from nearly undetectable levels **to 3%.**
- **Antimicrobial use in humans continues to increase.**
    - Antimicrobial **prescription rates** for Canadians aged **65 years and older continued to increase**, particularly in women.
    - Antimicrobial purchasing by **hospitals increased by nearly 30%.**
    - Although the use of "Reserve" antimicrobials[6] (antimicrobials that should be reserved for treating multidrug-resistant infections) was <1% of **all antimicrobials consumed by humans in Canada, their use increased by nearly 10%.**
    - The use of **carbapenems increased by more than 120%** in the community setting (noting a near doubling in the use of ertapenem).
- While the kilograms of antimicrobials distributed for use in **animals** decreased by 11%, **there was a 6% increase between 2017 and 2018.**

This publication contributes to the body of evidence needed to inform the development of effective antimicrobial stewardship and infection prevention and control strategies, which work towards limiting the rise of AMR infections.

Priority antimicrobial-resistant organisms in Canada:

- Methicillin-resistant *Staphylococcus aureus*
- Vancomycin-resistant *Enterococcus*
- Carbapenemase-producing Enterobacteriaceae
- *Clostridioides difficile*
- *Neisseria gonorrhoeae*
- *Mycobacterium tuberculosis*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*
- Typhoidal and non-typhoidal *Salmonella enterica*
- *Acinetobacter* species
- *Campylobacter* species
- *Escherichia coli*




3

CHAPTER 3

INTRODUCTION

Surveillance as the foundation for effective action

As the number of antimicrobial-resistant infections increase, the amount of effective antimicrobial options available to treat these infections grows smaller. In order to intervene appropriately and ensure the longevity of existing antimicrobials, we rely on surveillance systems capable of detecting and monitoring emerging threats.

Comprehensive surveillance provides the data we need to:

- Inform interventions that prevent the spread of antimicrobial-resistant organisms and consequent infections.
- Guide the appropriate use of antimicrobials to limit the emergence of resistance.
- Create opportunities for innovative research and development.
- Measure the impact of stewardship and infection prevention and control activities.

The Canadian Antimicrobial Resistance Surveillance System (CARSS) is Canada's national system for reporting on antimicrobial resistance (AMR) and antimicrobial use (AMU). CARSS synthesizes and integrates epidemiological and laboratory information from Public Health Agency of Canada (PHAC) surveillance programs across the human and agricultural sectors to provide high quality national data on AMR and AMU.

Building on surveillance excellence

No one country, level of government or single sector can slow the growing problem of AMR on its own. Preserving the effectiveness of existing antimicrobial drugs will be achieved through collaboration among governments and partners in healthcare, animal health, agri-food, industry, academia, professional associations and the general public.

Through investment, innovation and partnerships, PHAC has increased its ability to provide evidence to guide the development of effective antimicrobial stewardship and infection prevention and control strategies.

New surveillance initiatives:

- The national surveillance of healthcare-associated infections has expanded to represent nearly one-third of all acute care hospital beds in Canada.
- Point prevalence data from two surveys in community hospital and long-term care facilities benchmarked the burden of antimicrobial-resistant organisms (ARO) and AMU in these facility types.
- AMR in the community sector has been examined through a pilot project using electronic medical records covering 75,000 patients to look at patterns of resistance in urinary tract infections and how they are treated.
- Enhanced *Neisseria gonorrhoeae* surveillance has expanded to better examine the epidemiology behind the increased rates of infection, target public health interventions and improve treatment guidelines.
- Epidemiologic and laboratory support for local health regions has improved our understanding of the community transmission of multidrug-resistant organisms.
- The implementation of whole genome sequencing at the National Microbiology Laboratory will help identify factors associated with food production and AMR.
- An integrated electronic platform is being developed to share standardized laboratory resistance data from federal and provincial public health laboratories. This will provide a near-comprehensive data source on national resistance patterns and an early warning system for emerging resistant pathogens.

- The amount of antimicrobials sold for use in food producing and companion animals is now reported to Health Canada as a legislated requirement, complementing PHAC efforts to expand the species-specific surveillance of farm-level AMU in all major terrestrial food animal species (i.e. broiler chickens, turkeys, grower–finisher pigs, beef cattle and dairy cattle).
- Strategic collaborations between PHAC and Fisheries and Oceans Canada has led to inclusion of AMU information from land-based and freshwater net pen operations. This enhances previous integration with data from Fisheries and Oceans Canada for marine based aquaculture operations, as well as information from Health Canada's Pest Management Regulatory Agency on antimicrobials sold for use as pesticides on food crops.
- Interim recommendations for public health laboratories have been published on the reporting of multidrug-resistant and extensively drug-resistant organisms.

Collaboration needed to fill surveillance gaps

Surveillance conducted by PHAC and its partners provides high quality and reliable data on AMR and AMU. However, the surveillance of AMR in humans is primarily restricted to hospitalized individuals, which limits data on AMR and the appropriateness of antimicrobial prescribing in people who access local community healthcare. In addition, only minimal information is available on AMR and AMU in Indigenous populations and data on underlying socioeconomic factors associated with infections caused by AROs are not readily available.

Regarding the animal, agriculture and food sector, surveillance gaps also remain. For example, the scope of retail meat sampling across the country was limited to 4 provinces in 2018 – two of which were only partially covered. Data collection from on-farm and abattoirs is also not comprehensive, requiring additional collaboration with industry partners. These limitations are important because the general population of Canadians may be exposed to AMR from the food chain via meat and poultry contaminated with AROs, and many areas are currently unrepresented.

Finally, while PHAC is committed to applying a One Health perspective on the emergence of AMR, there is limited data regarding environmental surveillance – a necessary component of any One Health framework.

Recently identified and emerging threats

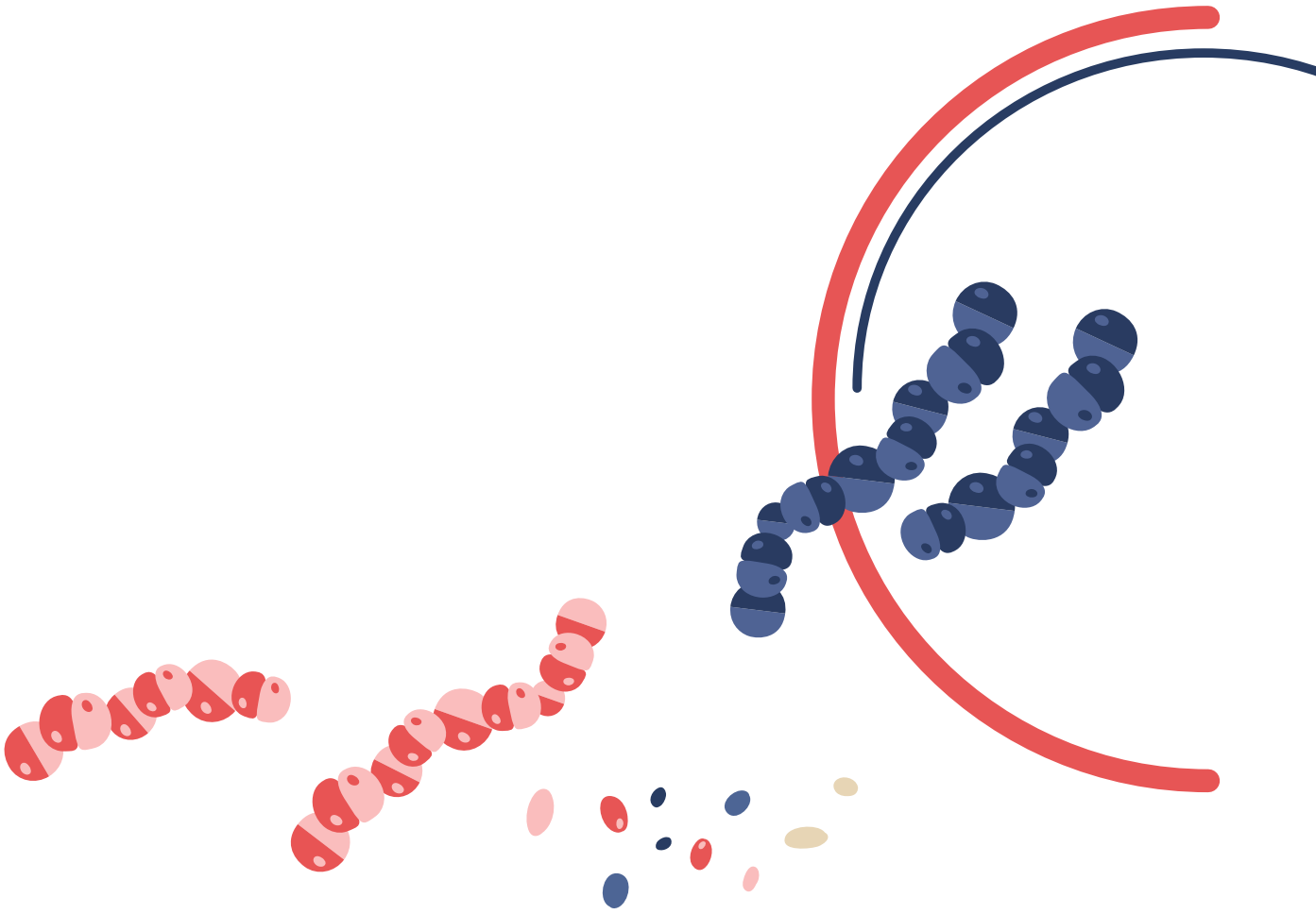
It is challenging to secure reliable and cost-effective surveillance data to identify and monitor novel or rare AROs. However, emerging threats are being detected by integrating the results of existing surveillance programs, innovative ad-hoc activities, collaboration with PHAC partners and/or the use of auxiliary systems. While these results are not fully examined within this report, the following findings merit attention.

- *Candida auris (C. auris)*, a fungal pathogen often resistant to antifungal drugs, has been detected in Canada. Between 2012 and September 2019, 24 cases of *C. auris* have been reported to PHAC, some of which were multidrug-resistant.
- In 2017 and 2018, the first ceftriaxone-resistant cases of *Neisseria gonorrhoeae* were reported in Canada (associated with travel to South-East Asia). Their presence in Canada threatens the continued effectiveness of currently recommended therapy.
- Carbapenemase genes have been detected in *Acinetobacter* isolated from patients in the healthcare setting (41 cases between 2014 and 2018). This represents a threat to the continued effectiveness of carbapenems — a class of antimicrobial used to treat multidrug-resistant infections.
- The frequency of highly drug resistant *Salmonella enterica* isolated from animals (diseased and healthy), select additional nodes in the food chain (abattoir samples and retail meat) and human sources has reached unprecedented levels (*n*=132 in 2018). These organisms are resistant to at least six of seven antimicrobial classes tested.
- Resistance to nalidixic acid is being identified more frequently in *Salmonella* Enteritidis isolated from broiler chickens. This is worth noting because resistance to nalidixic acid is extremely rare in chickens and may be a precursor to fluoroquinolone resistance — a class of antimicrobials that is very important to human medicine[7].

Action needs to continue

As written by the Council of Canadian Academies in their recent publication *When Antibiotics Fail*, "Antimicrobial resistance is a looming public health threat and potential economic disaster in Canada. The implications of inaction are significant for Canadian society and the economy"[8].

PHAC continues to work with its partners to ensure that high quality and timely data on AMR and AMU are readily available for those who need it most. Surveillance data and information is necessary to guide our collective efforts in effective infection prevention and control, antimicrobial stewardship, new research and future innovation to combat AMR.



4

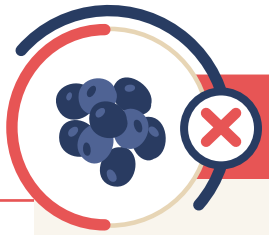
CHAPTER 4

KEY FINDINGS

Trend Summary

Methicillin-resistant *Staphylococcus aureus* bloodstream infection	2014–2018	Getting Worse
Vancomycin-resistant *Enterococcus* bloodstream infection	2014–2018	Getting Worse
Carbapenemase-producing Enterobacteriaceae	2014–2018	Getting Worse
Clostridioides difficile infection	2015–2018	Getting Better
Multidrug-resistant *Neisseria gonorrhoeae* infection (gonorrhea)	2014–2018	Caution
Drug-resistant *Mycobacterium tuberculosis* infection	2014–2018	Stable
Streptococcus pneumoniae (invasive pneumococcal disease)	2013–2017	Stable
Streptococcus pyogenes (group A *Streptococcus)*	2013–2017	Stable
Antimicrobial use in humans	2014–2018	Caution
Antimicrobial use in animals	2014–2018	Caution

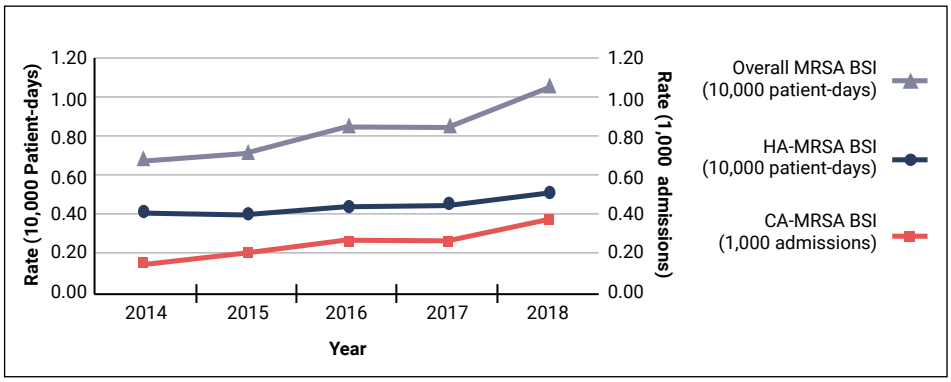
METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* BLOODSTREAM INFECTION



Trend: Getting Worse

Key Findings:

- The rate of community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infection (BSI) increased by 140% between 2014 and 2018.
- All-cause mortality was high for cases of MRSA-BSI; 20% of patients died within 30 days of diagnosis between 2014 and 2018.
- All MRSA blood isolates were susceptible to vancomycin and linezolid.



Between 2014 and 2018

62–65 **Canadian surveillance hospitals reported:**

2,913 cases of MRSA-BSI

555 deaths

Source:

- The Canadian Nosocomial Infection Surveillance Program (CNISP)

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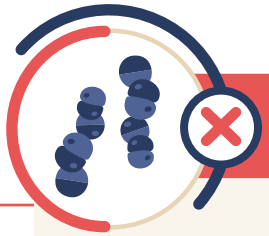
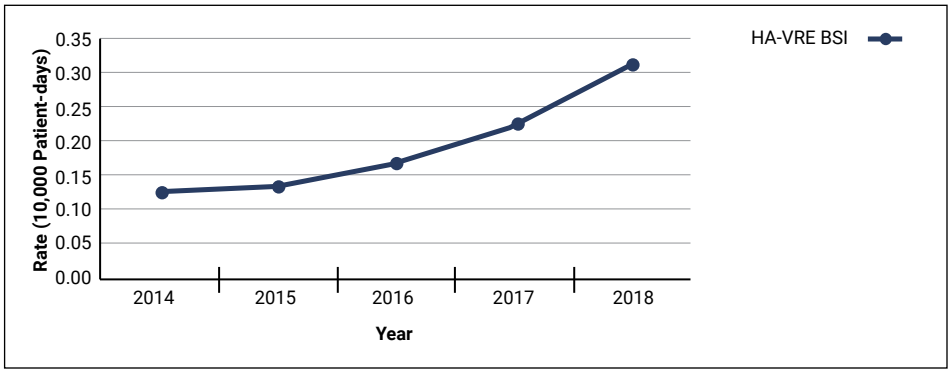
VANCOMYCIN-RESISTANT *ENTEROCOCCUS* BLOODSTREAM INFECTION



Trend: Getting Worse

Key Findings:

- The rate of healthcare-associated (HA) vancomycin-resistant *Enterococcus* (VRE) bloodstream infection (BSI) more than doubled between 2014 and 2018.
- All-cause mortality was high for cases of HA-VRE-BSI; 31% of patients died within 30 days of diagnosis between 2014 and 2018.
- The rapid emergence of *Enterococcus faecium (E. faecium)* sequence type 1478 was associated with rising levels of resistance to important antimicrobials (i.e. gentamicin and daptomycin).



Between 2014 and 2018

57–62 **Canadian surveillance hospitals reported:**

649 cases of VRE-BSI

202 deaths

Source:

- The Canadian Nosocomial Infection Surveillance Program (CNISP)

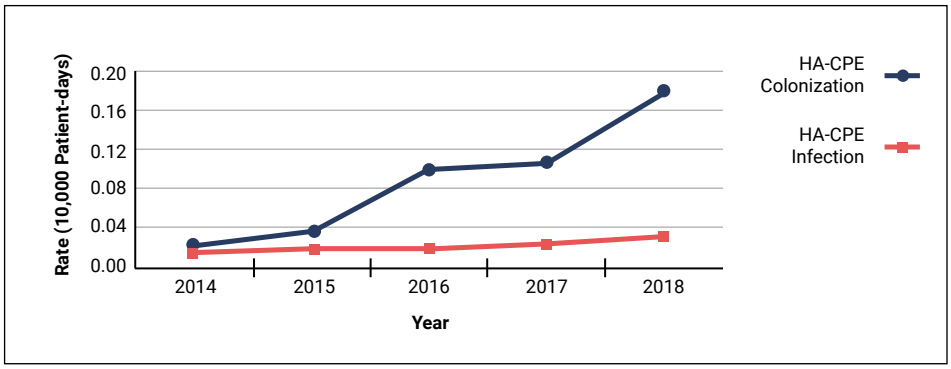
Public Health Agency of Canada | Agence de la santé publique du Canada

CARBAPENEMASE-PRODUCING ENTEROBACTERIACEAE

Trend: **Getting Worse**

Key Findings:

- Between 2014 and 2018, Canadian hospitals reported a nine-fold increase in patients colonized with healthcare-associated (HA) carbapenemase-producing Enterobacteriaceae (CPE).
- All-cause mortality was high for cases of HA-CPE infection; 16% of patients died within 30 days of diagnosis between 2014 and 2018.
- HA-CPE cases are often associated with international travel and international healthcare exposure; however, domestic nosocomial transmission appears to be increasing.



Between 2014 and 2018

57–59 Canadian surveillance hospitals reported:

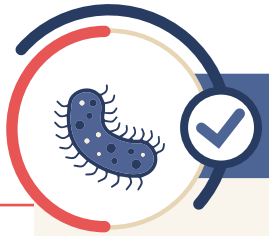
292	HA-colonizations
73	HA-infections
365	total cases of HA-CPE
16	deaths

Source:

- The Canadian Nosocomial Infection Surveillance Program (CNISP)

Public Health Agency of Canada / Agence de la santé publique du Canada

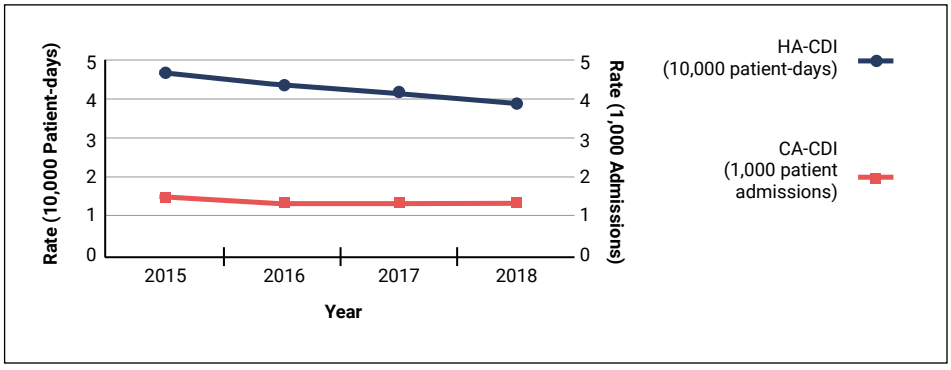
CLOSTRIDIOIDES DIFFICILE INFECTION



Trend: **Getting Better**

Key Findings:

- The rate of healthcare-associated (HA) *Clostridioides difficile (C. difficile)* infection (CDI) decreased by 15% between 2015 and 2018.
- All-cause mortality for cases of HA-CDI was 10% between 2015 and 2018 (attributable mortality was 3%).
- Approximately one-third of CDI identified among inpatients of participating hospitals were attributed to the community (CA).



Between 2015 and 2018

53–68 Canadian surveillance hospitals reported:

16,034	cases of CDI (HA+CA)
1,361	deaths (estimated)
362	attributable to CDI (estimated)

Source:

- The Canadian Nosocomial Infection Surveillance Program (CNISP)

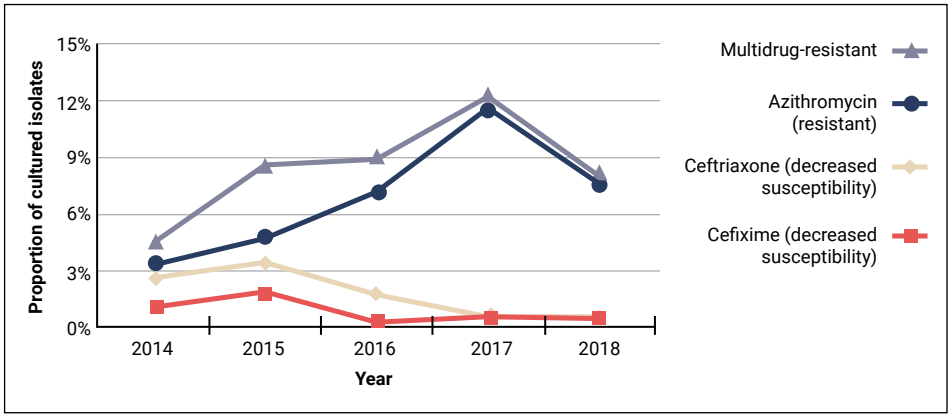
Public Health Agency of Canada / Agence de la santé publique du Canada

MULTIDRUG-RESISTANT *NEISSERIA GONORRHOEAE* INFECTION (GONORRHEA)

Trend: Caution

Key Findings:

- The number of gonorrhea diagnoses in Canada nearly doubled between 2014 and 2018.
- The proportion of multidrug-resistant (MDR) *Neisseria gonorrhoeae* (GC) isolates increased by 78% between 2014 and 2018.
- In 2018, seven extensively drug-resistant (XDR) *Neisseria gonorrhoeae* isolates were identified in Canada.



Between 2014 and 2018

117,906 cases of gonorrhea

2,030 MDR-GC infections reported to PHAC

10,414 estimated number of MDR-GC infections in Canada

Source:

- The Gonococcal Antimicrobial Surveillance Program (GASP-Canada) and the Canadian Notifiable Disease Surveillance System.

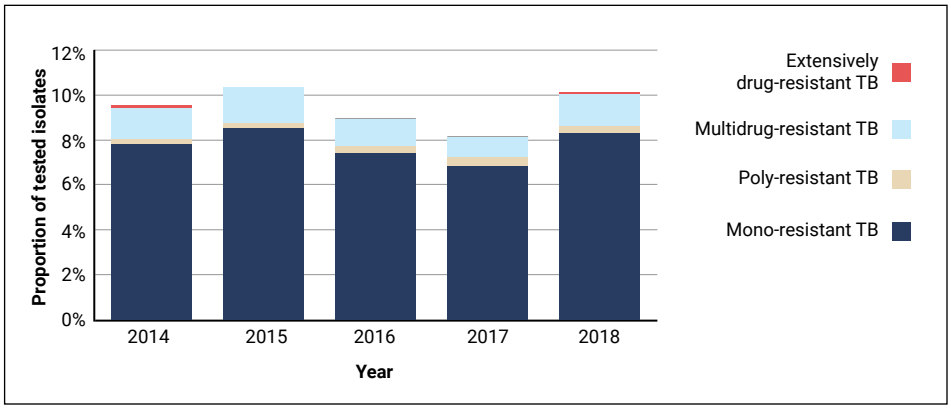
Public Health Agency of Canada | Agence de la santé publique du Canada

DRUG-RESISTANT *MYCOBACTERIUM TUBERCULOSIS* INFECTION

Trend: Stable

Key Findings:

- Between 2014 and 2018, the rate of *Mycobacterium tuberculosis* (TB) infection in Canada remained stable at approximately 4.8 per 100,000 population.
- In 2018, the proportion of culture-positive TB isolates resistant to any first-line drug was 10%.
- In 2018, the first case of extensively drug-resistant TB since 2014 was identified.



Between 2014 and 2018

7,129 culture-positive TB cases

663 resistant culture-positive TB cases

Source:

- The Canadian Tuberculosis Laboratory Surveillance System.

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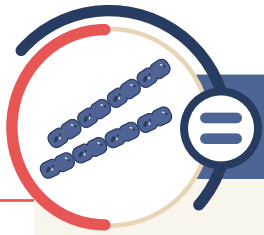
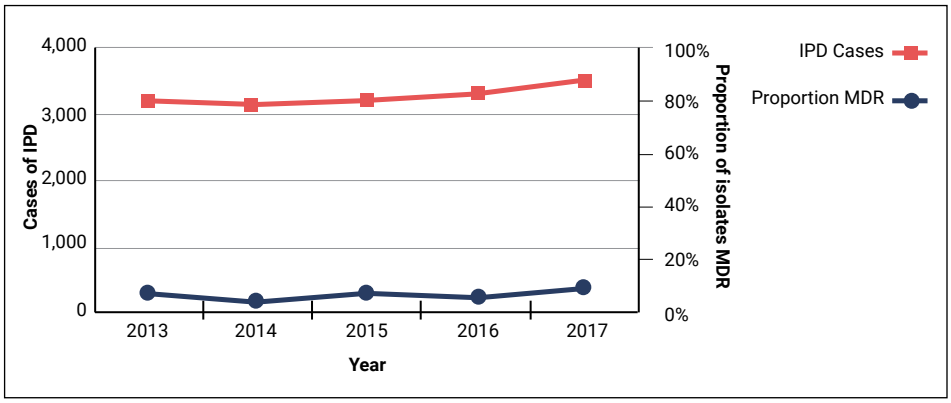
STREPTOCOCCUS PNEUMONIAE INVASIVE PNEUMOCOCCAL DISEASE (IPD)



Trend: Stable

Key Findings:

- The proportion of invasive *Streptococcus pneumoniae (S. pneumoniae)* isolates resistant to penicillin increased by 49% between 2013 and 2017.
- The proportion of invasive *S. pneumoniae* isolates classified as multidrug-resistant (MDR) increased by 26% between 2013 and 2017.
- Infections caused by multidrug-resistant (MDR) *S. pneumoniae* serotypes 19A and 19F may be prevented using existing pneumococcal vaccines.



Between 2013 and 2017

16,341	cases of IPD
389	MDR-IPD reported to PHAC
1,154	estimated number of MDR-IPD in Canada
10,414	estimated number of MDR-GC infections across Canada

Source:

- The National Surveillance of Invasive Streptococcal Disease (eSTREP) and the Canadian Notifiable Disease Surveillance System (CNDSS)

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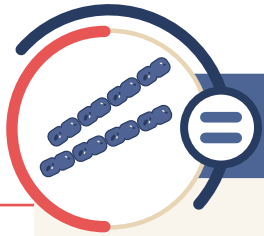
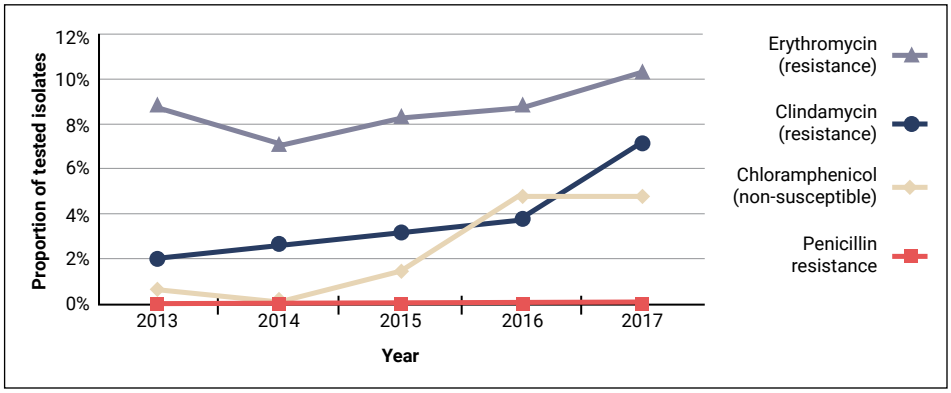
STREPTOCOCCUS PYOGENES GROUP A *STREPTOCOCCUS* (GAS)



Trend: Stable

Key Findings:

- Between 2013 and 2017, the incidence rate of invasive group A *Streptococcus pyogenes* (GAS) infection increased by 42%.
- Between 2013 and 2017, the proportion of *S. pyogenes* isolates resistant to erythromycin increased to 10%; resistance to clindamycin increased to 7%.
- All *S. pyogenes* isolates tested remained susceptible to penicillin.



Between 2013 and 2017

10,039	cases of GAS
0	cases resistant to penicillin

Source:

- The National Surveillance of Invasive Streptococcal Disease (eSTREP) and the Canadian Notifiable Disease Surveillance System (CNDSS)

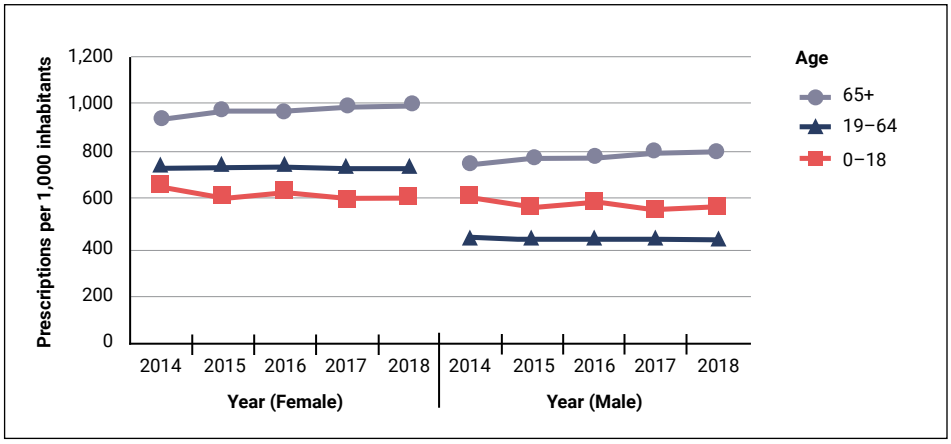
Public Health Agency of Canada | Agence de la santé publique du Canada

ANTIMICROBIAL USE IN HUMANS

Trend: **Caution**

Key Findings:

- Consumption of antimicrobials by humans increased by 1.2% between 2014 and 2018.
- The use of antimicrobials that should be reserved for suspected or confirmed multidrug-resistant infections increased by nearly 10% between 2014 and 2018 (overall use remained less than 1%).
- In 2018, Canada consumed the 12th lowest quantity of antimicrobials compared to the latest data from 29 European countries.



Estimated in 2018:

6,388	antibiotic doses consumed per 1,000 inhabitants
24.2 M	antibiotic prescriptions dispensed
$825 M	total antibiotic expenditure

Source:

- IQVIA (Canadian CompuScrip and Canadian Drugstore and Hospital Purchases datasets), Indigenous Services Canada, Statistics Canada, and the World Health Organization.

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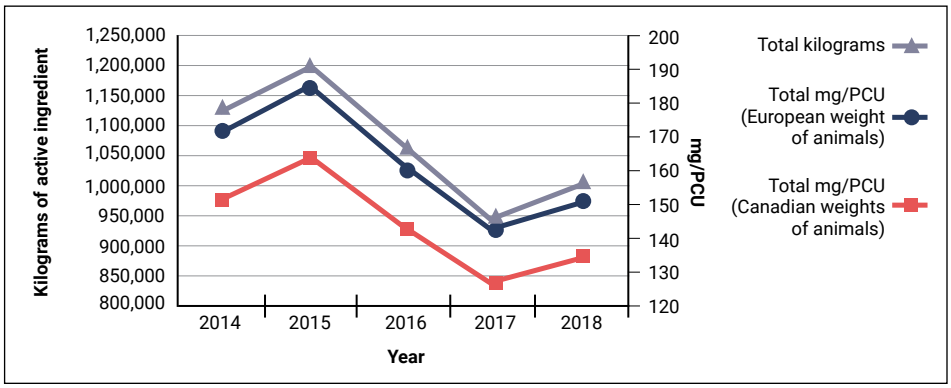
ANTIMICROBIAL USE IN ANIMALS

Trend: **Caution**

Key Findings:

- Between 2017 and 2018, the weight in kilograms of antimicrobial active ingredient distributed for use in animals increased by 6%.
- Between 2017 and 2018, declines in antimicrobial use (AMU) were reported by grower–finisher pig and broiler chicken sentinel farms.
- In 2018, Canada distributed the sixth highest quantity of antimicrobials intended for use in animals compared to the latest data from 31 European countries.



In 2018

1 M kg	kilograms of antibiotics distributed

Source:

- The Canadian Integrated Program for Antimicrobial Resistance Surveillance, the Canadian Animal Health Institute and the European Surveillance of Veterinary Antimicrobial Consumption

Note: PCU (Population correction unit) accounts for the size of the animal population, including the number and average weight at treatment. Mg/PCU (milligrams per PCU) is the mg of antimicrobials sold or used in animals divided by the population correction unit. Excludes ionophores and chemical coccidiostats.

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CHAPTER 5

TECHNICAL ANNEX

The data presented in this report are compiled from laboratory reference services and five Public Health Agency of Canada (PHAC) surveillance programs, which represent collaborations that extend into government, healthcare, industry, academia and professional associations. This technical annex intends to provide an overview of national data on antimicrobial resistance (AMR) and antimicrobial use (AMU) in the human sector and AMU in animals and agriculture. The data in this report replaces previously reported data, as PHAC works to improve data quality, integrate more data sources and update surveillance methodology.

1. The Canadian Nosocomial Infection Surveillance Program (CNISP) is an active sentinel surveillance network of acute care hospitals that integrates information from epidemiological, laboratory and pharmaceutical sources. CNISP currently represents nearly one-third of all acute care beds and an estimated one-third of all discharges in Canada, with participation from hospitals in all provinces. For this publication, date of diagnosis is considered the date of first positive culture or date of laboratory confirmation. This report includes CNISP information on:

    - Methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections[1]
    - Vancomycin-resistant *Enterococcus* (VRE) bloodstream infections
    - Carbapenemase-producing Enterobacteriaceae (CPE) infections and colonizations
    - *Clostridioides difficile* infections (CDI)
    - Antibiogram data on *Escherichia coli* and *Acinetobacter* spp.
    - Ward-specific AMU in adult inpatients of participating hospitals

1 MRSA strain typing and antimicrobial susceptibility testing was conducted in part by the Sunnybrook Health Sciences Centre.

2. The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) monitors resistance in enteric bacteria in humans, animals and food as well as AMU in animals, with a focus on bacteria and antimicrobials of public health importance. This report includes CIPARS information on:

    - Typhoidal and non-typhoidal *Salmonella enterica* recovered from humans, the data for which are a product of an enhanced, passive surveillance collaboration with provincial public health laboratories. Participation is voluntary and some provinces only submit a subset of isolates according to a sampling protocol.
    - *Salmonella, Campylobacter* and generic *Escherichia coli* recovered from retail meat and poultry, the data for which are a product of an active and standardized surveillance system.
    - Antimicrobials distributed for use in animals, the data for which are a product of a voluntary partnership between the Canadian Animal Health Institute and PHAC. Data on antimicrobials sold for use on crops are provided by Health Canada's Pest Management Regulatory Agency. Farm-level AMU information is provided by sentinel farms (terrestrial species) and Fisheries and Oceans Canada (all aquaculture operations).

3. The Gonococcal Antimicrobial Surveillance Program – Canada (GASP–Canada) is a passive collaboration with provincial public health laboratories. Participation in the surveillance of *Neisseria gonorrhoeae* is voluntary and uses standardized laboratory methods. Denominators were established by data submissions from provincial and territorial public health laboratories.

4. The Canadian Tuberculosis Laboratory Surveillance System (CTBLSS) is a passive collaboration with provincial public health laboratories. Participation in the surveillance of *Mycobacterium tuberculosis* is voluntary and uses standardized laboratory methods.

5. The National Laboratory Surveillance of Invasive Streptococcal Disease (eSTREP) is a passive collaboration with provincial public health laboratories (including data contributions from the Toronto Invasive Bacterial Diseases Network, the Alberta Provincial Public Health Laboratory and Laboratoire de santé publique du Québec). Participation in the surveillance of *Streptococcus pneumoniae* and *Streptococcus pyogenes* is voluntary, with some provinces only submitting a subset of isolates according to a sampling protocol. National statistics were developed through the integration of data from the Canadian Noti iable Disease Surveillance System and Statistics Canada. Antimicrobial susceptibility testing was performed by the Health

Sciences Centre at the University of Manitoba and the Canadian Antimicrobial Resistance Alliance and included *Streptococcus pneumoniae* isolates submitted from Saskatchewan, Manitoba, Ontario, Quebec, Nova Scotia, Prince Edward Island, New Brunswick and Newfoundland and Labrador.

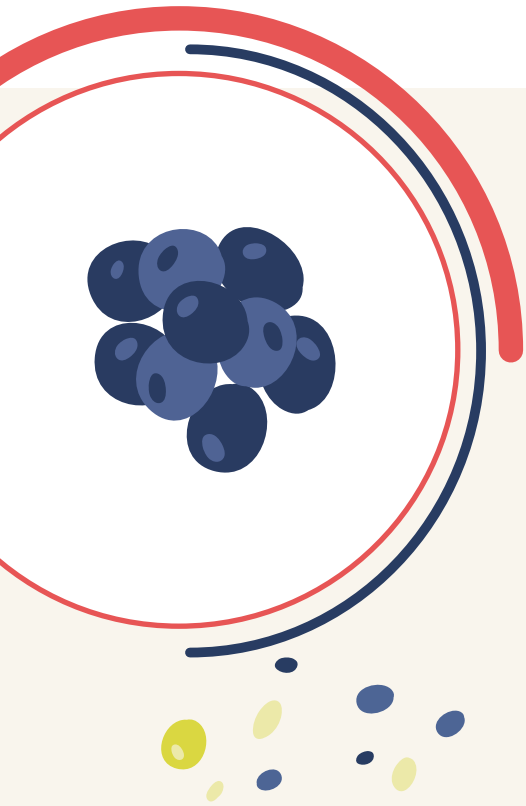
6. The National Microbiology Laboratory (NML) supports all AMR surveillance programs, providing data on molecular characterization and antimicrobial susceptibility testing. The NML also provides laboratory reference services to all provinces and territories which assists with the detection of novel and emerging antimicrobial-resistant organisms.

The presentation of antimicrobial susceptibility testing was visualized using Excel 2016 (standard conditional formatting).

Table 1: Chapter summary of data included in the report, listing the organism, contributing surveillance program, data years, and associated sector

Chapter	Source	Data years	Sector(s)
Methicillin-resistant *Staphylococcus aureus*	CNISP	2014–2018	Healthcare and community
Vancomycin-resistant *Enterococcus*	CNISP	2014–2018	Healthcare
Carbapenemase-producing Enterobacteriaceae	CNISP	2014–2018	Healthcare
Clostridioides difficile	CNISP	2015–2018	Healthcare and community
Neisseria gonorrhoeae	GASP–Canada	2014–2018	Community
Mycobacterium tuberculosis	CTBLSS	2014–2018	Community
Streptococcus pneumoniae	eSTREP	2013–2017	Community
Streptococcus pyogenes	eSTREP	2013–2017	Community
Resistance in *Escherichia coli* and *Acinetobacter* spp.	CNISP	2016-2018*	Healthcare and community combined (Antibiogram)
Salmonella enterica (serovars Typhi, Paratyphi and non-typhoidal)	CIPARS	2014–2018	Community (Antibiogram)
Resistance in enteric bacteria from food sources (*Salmonella*, *E. coli*, and *Campylobacter*)	CIPARS	2014–2018	Food chain (Antibiogram)
Antimicrobial use in humans	CARSS	2014–2018	Healthcare and community
Antimicrobial use in animals and on crops in Canada	CIPARS	2014–2018	Agriculture

Abbreviations: CNISP, Canadian Nosocomial Infection Surveillance Program; GASP–Canada, Gonococcal Antimicrobial Surveillance Program – Canada; CTBLSS, Canadian Tuberculosis Laboratory Surveillance System; eSTREP, National Laboratory Surveillance of Invasive Streptococcal Disease; CIPARS, Canadian Integrated Program for Antimicrobial Resistance Surveillance; CARSS, Canadian Antimicrobial Resistance Surveillance System.
*only 2018 data were available for ***Acinetobacter*** spp.



Methicillin-resistant *Staphylococcus aureus*

Key findings

- The rate of community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infection (BSI) increased by 140% between 2014 and 2018.
- All-cause mortality was high for cases of MRSA-BSI; 20% of patients died within 30 days of diagnosis between 2014 and 2018.
- All MRSA blood isolates were susceptible to vancomycin and linezolid.

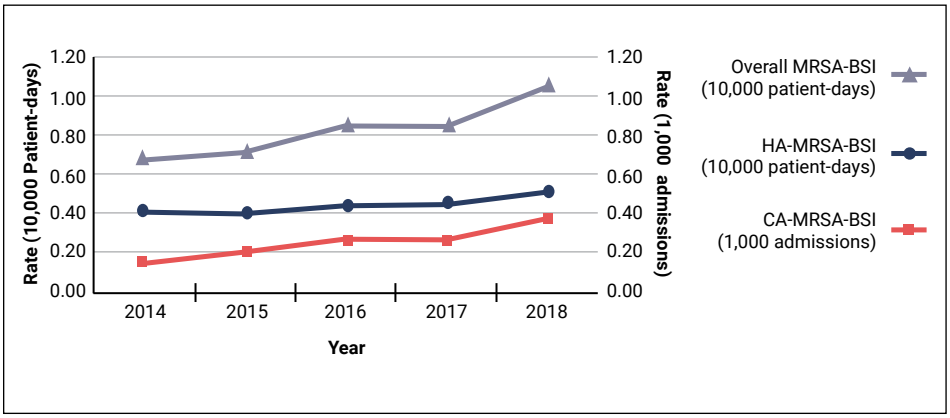
MRSA-BSI overall results

Between 2014 and 2018, the rate of MRSA-BSI increased from 0.66 to 1.05 cases per 10,000 patient-days (*n*=448 to *n*=767). This was largely driven by an increase in cases attributed to the community, from 0.15 to 0.36 cases per 1,000 admissions (*n*=137 to *n*=359). All-cause mortality was high across the five years, with death within 30 days of diagnosis in 19.5% (*n*=555/2,842) of MRSA-BSIs.

Methods

Data presented were restricted to cases of MRSA-BSI reported to the Canadian Nosocomial Infection Surveillance Program (CNISP) by 62 to 65 hospitals between 2014 and 2018. Healthcare-associated (HA) cases are reported per 10,000 patient-days and community-associated (CA) cases are reported per 1,000 hospital admissions. All-cause mortality calculations excluded cases where source of acquisition was unavailable; data on attributable mortality was not collected. Further methodology and case definitions have been previously described by CNISP[9] .

Figure 1: Incidence rate of healthcare-associated (HA) and community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infection (BSI), Canada, 2014 – 2018



Healthcare-associated MRSA-BSI results

Between 2014 and 2018, the rate of HA-MRSA-BSI increased from 0.40 to 0.51 cases per 10,000 patient-days (*n*=274 to *n*=369). All-cause mortality was high across the five years, with death within 30 days of diagnosis in 24.3% (*n*=362/1,491) of HA-MRSA-BSIs.

In 2018, laboratory results were available for 90.5% (*n*=334/369) of reported HA-MRSA-BSIs. Between 2014 and 2018, the proportion of strain type CMRSA 2 decreased from 66.7% (*n*=146/219) to 38.0% (*n*=127/334), CMRSA 10 increased from 22.8% (*n*=50/219) to 35.6% (*n*=119/334) and CMRSA 7 increased from 2.3% (*n*=5/219) to 7.5% (*n*=25/334).

Between 2014 and 2018, all HA-MRSA blood isolates were susceptible to vancomycin (the most used antimicrobial in this setting) and less than 1% were non-susceptible to daptomycin. In 2018, of those antimicrobials that may be used as part of treatment for non-bloodstream MRSA infections, no resistance to linezolid was detected and the prevalence of resistance to tetracycline (4.5%), trimethoprim-sulfamethoxazole (0.9%) and rifampin (0.9%) was low. Between 2014 and 2018, resistance to clindamycin decreased from 75.5% to 50.3%.

Table 2: Antimicrobial resistance patterns from healthcare-associated methicillin-resistant *Staphylococcus aureus* blood isolates, Canada, 2014–2018

	Proportion (%) of resistant isolates per year				
Year	**2014**	**2015**	**2016**	**2017**	**2018**
Isolates tested (*n*)	**218**	**219**	**273**	**296**	**334**
Ciprofloxacin	96.8	80.4	78.4	77.0	74.6
Clindamycin	75.5	66.7	48.0	47.6	50.3
Daptomycin*	0.5	0.0	1.1	0.7	0.0
Linezolid	0.0	0.0	0.0	0.0	0.0
Rifampin	0.5	0.5	2.6	1.0	0.9
Tetracycline	2.8	3.2	4.8	5.4	4.5
Tigecycline*	2.8	0.9	0.0	0.0	0.0
Trimethoprim-sulfamethoxazole	1.4	1.8	1.5	1.4	0.9
Vancomycin	0.0	0.0	0.0	0.0	0.0

Some antimicrobials are presented for epidemiological purposes only. A subset of isolates were tested against clindamycin (2014) and ciprofloxacin (2014, 2015).
*Non-susceptible.

Community-associated MRSA-BSI results

Between 2014 and 2018, the rate of MRSA-BSI arising from a community infection but detected in hospital inpatients increased from 0.15 to 0.36 cases per 1,000 admissions (*n*=137 to *n*=359). All-cause mortality in community-associated cases was lower than for HA cases across the five years: death within 30 days of diagnosis was reported in 14.3% (*n*=167/1,171) of CA-MRSA-BSIs.

In 2018, laboratory results were available for 93.0% (*n*=334/359) of CA-MRSA-BSIs identified among hospital inpatients. Between 2014 and 2018, the proportion of strain type CMRSA 2 decreased from 18.9% (*n*=23/122) to 17.7% (*n*=59/334), CMRSA 10 decreased from 61.5% (*n*=75/122) to 56.9% (*n*=190/334) and CMRSA 7 increased from 8.2% (*n*=10/122) to 9.3% (*n*=31/334).

Between 2014 and 2018, all CA-MRSA blood isolates were susceptible to vancomycin (the most used antimicrobial in this setting) and less than 1% were non-susceptible to daptomycin. In 2018, the prevalence of resistance to

antimicrobials that may be used as part of treatment for non-bloodstream MRSA infections remained low for trimethoprim-sulfamethoxazole (3.3%) and rifampin (0.9%) and a higher prevalence of resistance to tetracycline (9.9%) was observed compared to HA-MRSA-BSI isolates. Between 2014 and 2018, resistance to clindamycin decreased from 42.1% to 33.2%.

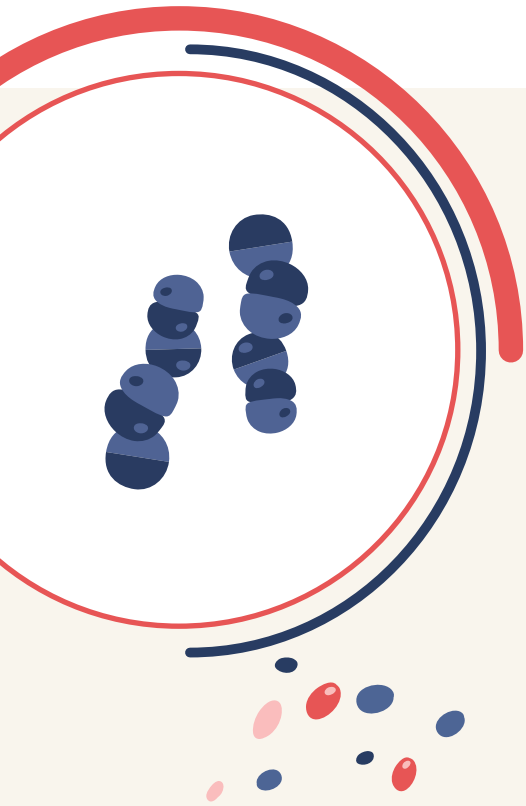
Table 3: Antimicrobial resistance patterns from community-associated methicillin-resistant *Staphylococcus aureus* blood isolates, Canada, 2014–2018

	Proportion (%) of resistant isolates per year				
Year	**2014**	**2015**	**2016**	**2017**	**2018**
Isolates tested (*n*)	**122**	**154**	**228**	**232**	**334**
Ciprofloxacin	77.8	81.1	75.4	76.3	69.2
Clindamycin	42.1	36.4	39.5	36.6	33.2
Daptomycin*	0.0	0.6	0.9	1.3	0.0
Linezolid	0.0	0.0	0.0	0.0	0.0
Rifampin	0.0	0.6	1.3	2.6	0.9
Tetracycline	7.4	3.9	7.5	7.8	9.9
Tigecycline*	0.8	0.6	0.0	0.0	0.0
Trimethoprim-sulfamethoxazole	1.6	1.3	2.6	1.3	3.3
Vancomycin	0.0	0.0	0.0	0.0	0.0

A subset of isolates were tested against clindamycin (2014) and ciprofloxacin (2014, 2015). Some antimicrobials are presented for epidemiological purposes only.
*Non-susceptible.

Table 4: Methicillin-resistant *Staphylococcus aureus* epidemic strain type associations

Canadian standard	American standard	Sector
CMRSA2	USA100/USA800	Historically healthcare-associated
CMRSA7	USA400	Historically community-associated
CMRSA10	USA300	



Vancomycin-resistant *Enterococcus*

Key findings

- The rate of healthcare-associated (HA) vancomycin-resistant *Enterococcus* (VRE) bloodstream infection (BSI) more than doubled between 2014 and 2018.
- All-cause mortality was high for cases of HA-VRE-BSI; 31% of patients died within 30 days of diagnosis between 2014 and 2018.
- The rapid emergence of *Enterococcus faecium (E. faecium)* sequence type (ST) 1478 was associated with rising levels of resistance to important antimicrobials (i.e. gentamicin and daptomycin).

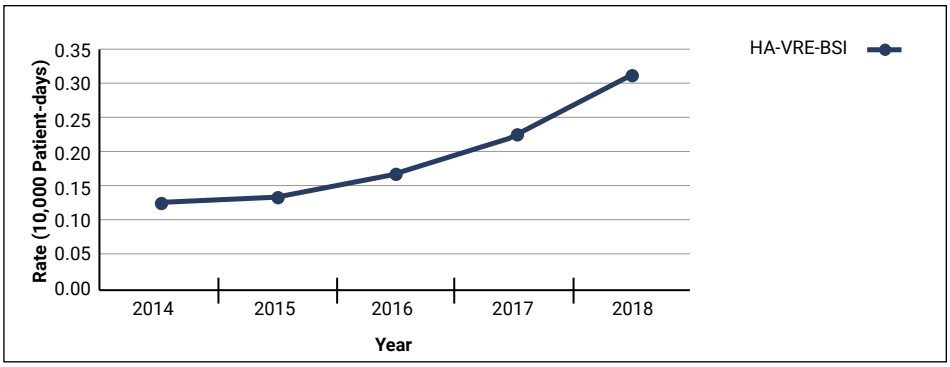
Healthcare-associated VRE-BSI results

Between 2014 and 2018, the rate of HA-VRE-BSI increased from 0.12 to 0.31 cases per 10,000 patient-days (*n*=84 to *n*=219). All-cause mortality remained high across the five years, with death within 30 days of diagnosis in 31.1% (*n*=202/649) of all cases.

Methods

Data presented were restricted to cases of HA-VRE-BSI reported to CNISP by 57 to 62 reporting hospitals between 2014 and 2018. All-cause mortality calculations excluded cases where source of acquisition was unavailable; data on attributable mortality was not collected. Multi-locus sequence typing (MLST) and antimicrobial susceptibility testing were only conducted on associated *Enterococcus faecium* blood isolates. Community-associated (CA) VRE-BSIs (approximately 5% of all reported VRE-BSIs) were excluded from this report. Further methodology and case definitions have been previously described by CNISP[10].

Figure 2: Incidence rate of healthcare-associated (HA) vancomycin resistant *Enterococcus* (VRE) bloodstream infection (BSI), Canada, 2014-2018



The organisms identified as causing HA-VRE-BSI were *E. faecium* (98.6%, *n*=216) and *E. faecalis* (1.4%, *n*=3). Of the eligible *E. faecium* cases reported in 2018, MLST and antimicrobial susceptibility testing results were available for 73.1% (*n*=158/216). ST1478 (which was first identified in Canada in 2013) has rapidly emerged as the predominant sequence type, representing 42.4% (*n*=67/158) of all *E. faecium* isolates submitted in 2018.

Between 2014 and 2018, daptomycin non-susceptibility increased from 0.0% to 7.6%, resistance to high-level gentamicin increased from 9.4% to 43.0% and resistance to linezolid increased from 0.0% to 1.3%.

Table 5: Antimicrobial resistance patterns from healthcare-associated vancomycin-resistant *Enterococcus faecium* blood isolates, Canada, 2014–2018

	Proportion (%) of resistant isolates per year				
Year	**2014**	**2015**	**2016**	**2017**	**2018**
Isolates tested (*n*)	**64**	**73**	**83**	**109**	**158**
Ampicillin	100.0	100.0	100.0	100.0	100.0
Chloramphenicol	0.0	0.0	2.4	9.2	2.5
Ciprofloxacin	100.0	100.0	100.0	100.0	100.0
Daptomycin*	0.0	0.0	8.4	9.2	7.6
Erythromycin	92.2	95.9	90.4	94.5	95.6
Gentamicin (high-level)	9.4	8.2	14.5	38.5	43.0
Levofloxacin	100.0	100.0	100.0	100.0	98.7
Linezolid	0.0	0.0	1.2	0.0	1.3
Nitrofurantoin	20.3	31.5	36.1	45.0	29.1
Penicillin	100.0	100.0	100.0	100.0	100.0
Quinupristin-dalfopristin	7.8	2.7	9.6	7.3	10.1
Rifampin	76.6	94.5	94.0	94.5	89.2
Streptomycin (high-level)	39.1	35.6	34.9	34.9	31.6
Tetracycline	53.1	60.3	51.8	57.8	63.9
Tigecycline	1.6	0.0	0.0	0.0	0.6

Some antimicrobials are presented for epidemiological purposes only.
*Non-susceptible.

Carbapenemase-producing Enterobacteriaceae

Key findings

- Between 2014 and 2018, Canadian hospitals reported a nine-fold increase in patients colonized with healthcare-associated (HA) carbapenemase-producing Enterobacteriaceae (CPE).
- All-cause mortality was high for cases of HA-CPE infection; 16% of patients died within 30 days of diagnosis between 2014 and 2018.
- HA-CPE cases are often associated with international travel and international healthcare exposure; however, domestic nosocomial transmission appears to be increasing.

Methods

Data presented were restricted to cases (as a result of infection or colonization) of genotypically-confirmed HA-CPE reported to the Canadian Nosocomial Infection Surveillance Program (CNISP) by 57 to 59 reporting hospitals between 2014 and 2018. CPE were identified at participating hospitals through phenotypic or genotypic methods (or a combination of both) and sent to the National Microbiology Laboratory (NML) for confirmation and reference testing. All CPE isolates harboured known carbapenemase genes.

The infection rate, colonization rate and proportions of identified carbapenemases were calculated for HA-CPE infections and colonizations and excluded cases where source of acquisition was unknown. The definition for the term "healthcare-associated" included domestic and international healthcare exposures. All-cause mortality was calculated for infected inpatients and excluded cases where source of acquisition was unknown; data on attributable mortality was not collected.

Antimicrobial susceptibility testing results represent all CPE isolates (including clinical and screening isolates from inpatients and outpatients) submitted between 2014 and 2018; duplicates (i.e. isolates from the same patient where the organism and the carbapenemase were the same) were excluded. Some patients harboured multiple carbapenemases. Further methodology and case definitions have been previously described by CNISP[11].

Due to their ability to readily spread and colonize patients in healthcare environments, preventing the transmission of these organisms is a major public health initiative and coordinated international effort are needed.

Robert A Bonomo, Eileen M Burd, John Conly, et al. Clin Infect Dis. 2018[12]

Healthcare-associated HA-CPE results

Between 2014 and 2018, the rate of HA-CPE infections among inpatients remained low and stable (0.02 to 0.03 per 10,000 patient-days, *n*=10 to *n*=21); in contrast, the rate of HA-CPE colonization among inpatients increased from 0.02 to 0.18 per 10,000 patient-days (*n*=14 to *n*=119). While some of this increase may be the result of heightened awareness and the implementation of hospital-specific screening practices, the increased detection of cases is of concern for Canadian hospitals. All-cause mortality remained high among inpatients across the five years, with death within 30 days of diagnosis in 16.4% (*n*=12/73) of all HA-CPE infections. In 2018, 39.3% (*n*=46/117) of patients identified with HA-CPE travelled outside of Canada within the past 12 months. Of the HA-CPE cases reported in 2018 who travelled outside of Canada within the past 12 months, 84.1% (*n*=37/44) reported receipt of medical care while abroad.

In 2018, 147 carbapenemase confirmation results were available from 140 HA-CPE inpatient cases (some patients harboured multiple carbapenemases). The proportion of carbapenemases identified as *Klebsiella pneumoniae* carbapenemase (KPC) was 54.4% (*n*=80/147); New Delhi metallo-β-lactamase (NDM) 23.1% (*n*=34/147); Oxacillinase (OXA-48) 9.5% (*n*=14); and *Serratia marcescens* enzymes (SME) 2.0% (*n*=3).

Figure 3: Incidence rates of healthcare-associated (HA) carbapenemase-producing Enterobacteriaceae (CPE) colonizations and infections per 10,000 patient-days, Canada, 2014–2018

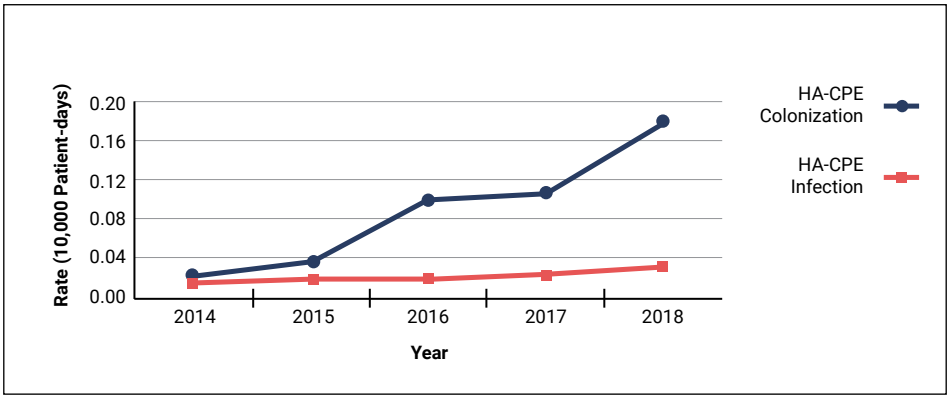
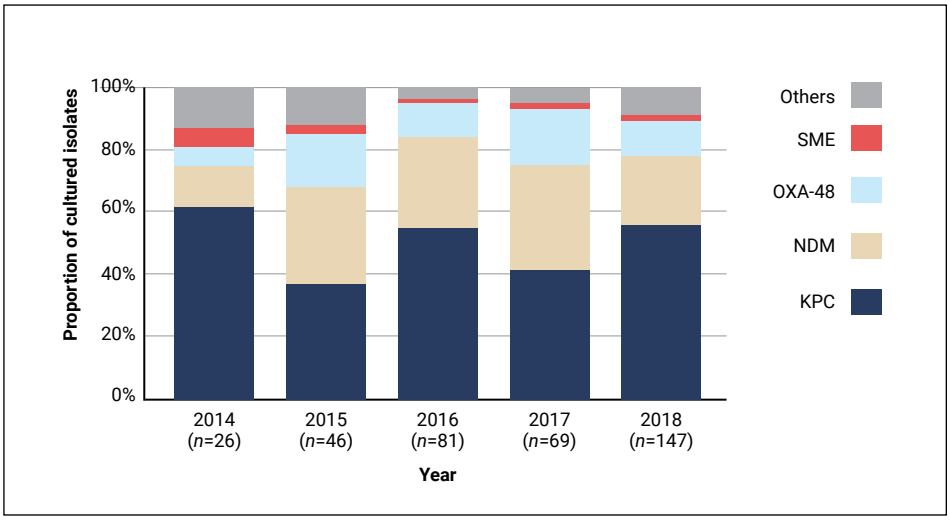


Figure 4: Carbapenemase genes in healthcare-associated carbapenemase-producing Enterobacteriaceae infections and colonizations, Canada, 2014–2018

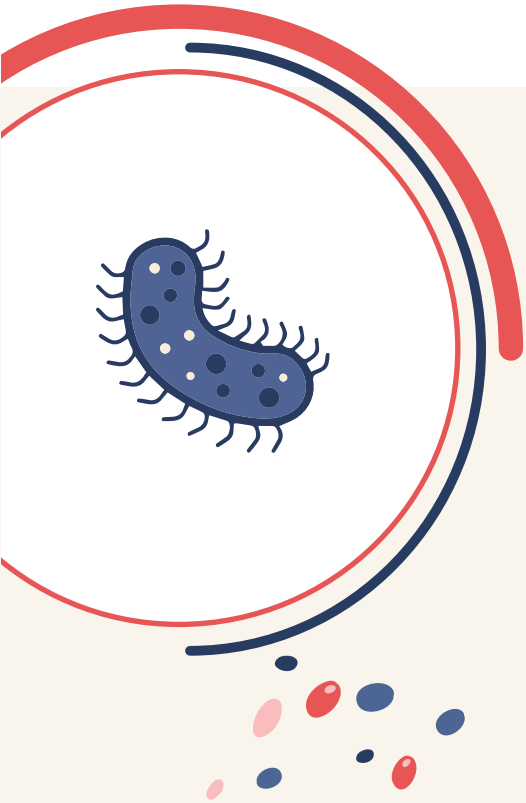


In 2018, antimicrobial susceptibility testing results were available for 227 CPE isolates sent to the NML from CNISP hospitals (i.e. clinical, screening and reference testing isolates from inpatient and outpatient settings). The proportion of resistance remained high for the majority of antimicrobials tested.

Table 6: Antimicrobial resistance patterns of carbapenemase-producing Enterobacteriaceae isolates, Canada, 2014–2018

	Proportion (%) of resistant isolates per year				
Year	**2014**	**2015**	**2016**	**2017**	**2018**
Isolates tested (*n*)	**67**	**81**	**162**	**187**	**227**
Amikacin	25.4	27.2	25.9	17.1	18.5
Cefotaxime	88.1	87.7	90.7	89.8	86.3
Ceftazidime	88.1	85.2	85.8	85.6	84.1
Ciprofloxacin	73.1	79.0	82.7	73.8	69.2
Gentamicin	50.7	49.4	38.3	34.2	34.4
Meropenem	94.0	85.2	86.4	85.0	87.2
Piperacillin-tazobactam	89.4	98.7	95.9	96.4	95.0
Tigecycline	16.4	16.0	19.8	9.6	12.8
Tobramycin	62.7	49.4	46.3	38.0	44.1
Trimethoprim-sulfamethoxazole	67.2	72.8	63.6	60.4	62.6

A subset of isolates were tested against piperacillin-tazobactam for years 2014–2018. All isolates harboured known carbapenemase genes (some demonstrated in vitro susceptibility to meropenem). Some antimicrobials are presented for epidemiological purposes only.



Clostridioides difficile

Key findings

- The rate of healthcare-associated (HA) *Clostridioides difficile (C. difficile)* infection (CDI) decreased by 15% between 2015 and 2018.
- All-cause mortality for cases of HA-CDI was 10% between 2015 and 2018 (attributable mortality was 3%).
- Approximately one-third of CDI identified among inpatients of participating hospitals were attributed to the community (CA).

Healthcare-associated CDI results

Between 2015 and 2018, the rate of HA-CDI decreased from 4.6 to 3.9 cases per 10,000 patient-days (*n*=3,136 to *n*=2,809). All-cause mortality within 30 days of diagnosis was 9.8% across the four years (attributable mortality was 2.5%).

Methods

Data presented were restricted to cases reported to the Canadian Nosocomial Infection Surveillance Program (CNISP) by 53 to 68 reporting hospitals between 2015 and 2018. Results were stratified by source of acquisition (i.e. healthcare-associated and community-associated), with unknowns excluded. Cases eligible for combined clinical and laboratory surveillance (e.g. mortality, molecular typing and antimicrobial susceptibility testing) were those identified in adults during March or April and year-round in children. CA-CDI is defined as symptoms occurring less than 72 hours after admission without history of hospitalization or any other healthcare exposure within the previous 12 weeks. Mortality calculations excluded cases where the source of acquisition was unknown. The associations between *C. difficile* North American pulsed field (NAP) types and ribotypes are referenced at the end of this chapter. Further methodology and case definitions have been previously described by CNISP[13].

Combined clinical and laboratory results were available for 86.5% (*n*=475/549) of eligible HA-CDI. NAP-4 associated ribotype strains were predominant in 2018, representing 22.1% (*n*=105/475) of isolates; NAP-11 and NAP-1 associated ribotype strains 15.4% (*n*=73/475) and 9.3% (*n*=44/475) of isolates, respectively. Low levels of *C. difficile* ribotypes associated with livestock (i.e. 078 and 126) were detected (2.1% in 2018).

Table 7: Antimicrobial resistance patterns of healthcare-associated *Clostridioides difficile* isolates, Canada, 2015–2018

	Proportion (%) of resistant isolates per year			
Year	**2015**	**2016**	**2017**	**2018**
Isolates tested (*n*)	**540**	**494**	**526**	**475**
Clindamycin	25.0	22.1	21.9	47.4
Metronidazole	0.0	0.0	0.0	0.2
Moxifloxacin	28.1	17.2	18.6	12.4
Rifampin	2.0	1.6	2.5	1.7
Vancomycin	0.0	0.0	0.0	0.0

One metronidazole resistant isolate was identified in 2018. The increase in clindamycin resistance in 2018 represents a reclassification (an increase in samples with MIC values of 6-8 mg/L; high-level clindamycin resistance remained stable). Some antimicrobials are presented for epidemiological purposes only.

Community-associated CDI results

Between 2015 and 2018, the rate of CA-CDI in patients admitted to participating hospitals decreased from 1.5 to 1.3 cases per 1,000 patient-admissions (*n*=1,034 for both years). All-cause mortality within 30 days of diagnosis was 4.9% across the four years (attributable mortality was 1.6%).

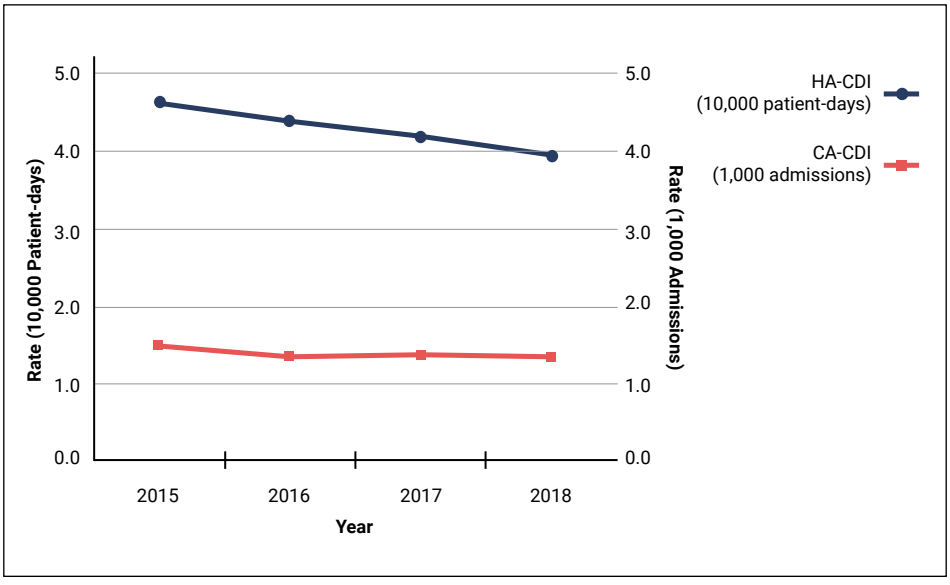
Combined clinical and laboratory results were available for 90.7% (*n*=156/172) of eligible CA-CDI. NAP-4 associated ribotype strains were predominant in 2018, representing 21.8% (*n*=34/156) of isolates; NAP-11 and NAP-1 associated ribotype strains 17.3% (*n*=27/156) and 3.8% (*n*=6/156) of isolates, respectively. Low levels of *C. difficile* ribotypes associated with livestock (i.e. 078 and 126) were detected (0.6% in 2018).

Table 8: Antimicrobial resistance patterns of community-associated *Clostridioides difficile* isolates, Canada, 2015–2018

	Proportion (%) of resistant isolates per year			
Year	**2015**	**2016**	**2017**	**2018**
Isolates tested (*n*)	**205**	**163**	**150**	**156**
Clindamycin	28.8	22.1	22.7	52.6
Metronidazole	0.0	0.0	0.0	0.0
Moxifloxacin	16.1	11.0	10.7	7.1
Rifampin	1.5	0.6	0.7	1.3
Vancomycin	0.0	0.0	0.0	0.0

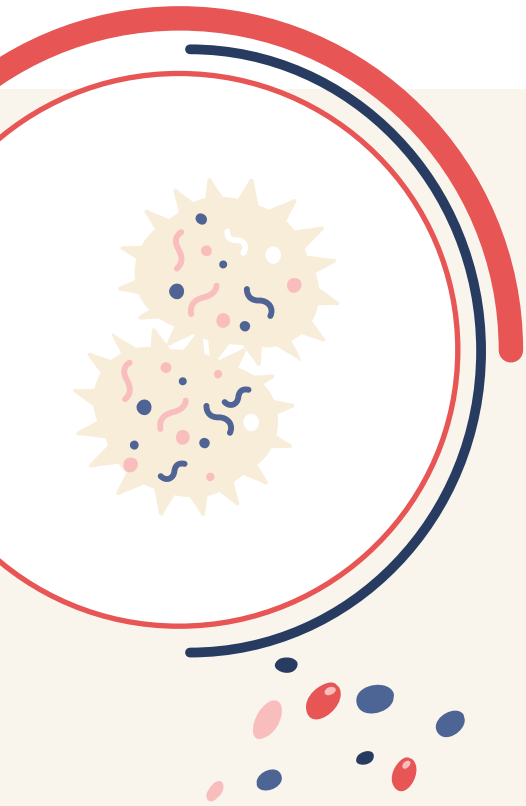
The increase in clindamycin resistance in 2018 represents a reclassification (an increase in samples with MIC values of 6-8 mg/L; high-level clindamycin resistance remained stable). Some antimicrobials are presented for epidemiological purposes only.

Figure 5: Incidence rate of healthcare-associated (HA) *Clostridioides difficile* infection (CDI) per 10,000 patient-days and community-associated (CA) CDI per 1,000 patient admissions , Canada, 2015–2018



North American pulsed field type (NAP) and ribotype associations

NAP classifications	ribotypes
NAP-1	027, 176, 075
NAP-4	020, 014, 076, 629
NAP-11	106, 103, 024



Neisseria gonorrhoeae

Key findings

- The number of gonorrhea diagnoses in Canada nearly doubled between 2014 and 2018.
- The proportion of multidrug-resistant (MDR) *Neisseria gonorrhoeae (N. gonorrhoeae)* isolates increased by 78% between 2014 and 2018.
- In 2018, seven extensively drug-resistant (XDR) *N. gonorrhoeae* isolates were identified in Canada.

Gonorrhea results

Between 2014 and 2018, the number of cases of gonorrhea diagnosed in Canada nearly doubled, from 45.9 to 79.5 cases per 100,000 inhabitants. In 2018, antimicrobial susceptibility results were available via cultured isolates for an estimated 19.3% of all diagnoses (*n*=5,607/29,034). The remainder (80.7%) were diagnosed using molecular methods (e.g. Nucleic Acid Amplification Testing [NAAT]) that did not allow for antimicrobial susceptibility testing. Proportionally, the number of gonorrhea diagnoses with accompanying cultured isolates decreased by 17.5% between 2014 (*n*=5,607/29,034) and 2018 (*n*=3,809/16,285).

Methods

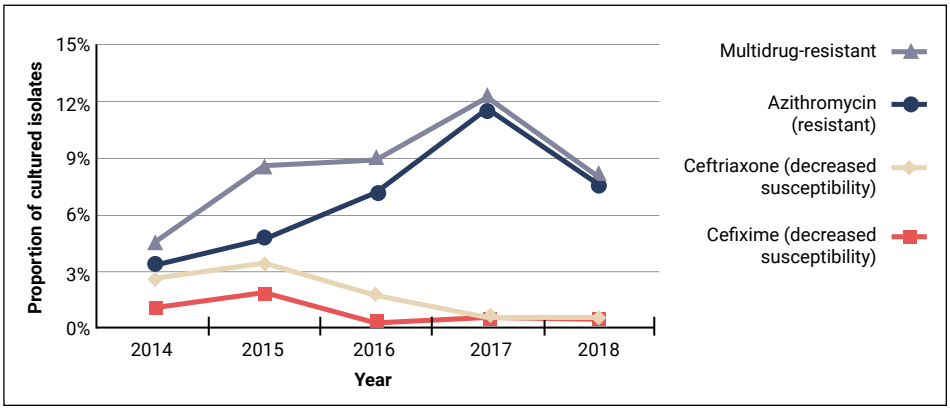
Data presented were restricted to *N. gonorrhoeae* isolates submitted or reported to the Gonococcal Antimicrobial Surveillance Program – Canada (GASP–Canada) between 2014 and 2018 and cases reported to the Canadian Notifiable Disease Surveillance System (CNDSS) between 2014 and 2017 (total cases reported in 2018 was unavailable at the time of publication and therefore 2017 data were used). The proportion of resistance was calculated using the total number of isolates cultured (excluding duplicates). Further methodology and case definitions have been previously described by GASP–Canada[14].

Between 2014 and 2018, the proportion of MDR *N. gonorrhoeae* isolates increased from 4.5% (*n*=172/3,809) to 8.0% (*n*=448/5,607), noting that the proportion reached 12.2% (*n*=645/5,290) in 2017. Between 2014 and 2018, the proportion of XDR *N. gonorrhoeae* isolates increased from 0.03% (*n*=1/3,809) to 0.12% (*n*=7/5,607).

Contributing to these increases was a 123.5% increase in the proportion of isolates resistant to azithromycin, from 3.4% (*n*=128/3,809) to 7.6% (*n*=427/5,607) between 2014 and 2018. In 2018, the proportion of *N. gonorrhoeae* isolates demonstrating resistance or decreased susceptibility to cefixime or ceftriaxone remained below 1% (*n*=27 and 31, respectively).

Between 2012 and 2018, GASP–Canada identified 26 *N. gonorrhoeae* isolates that demonstrated co-resistance or decreased susceptibility to the antimicrobials recommended as dual therapy for the treatment of gonorrhea (i.e. azithromycin in combination with cefixime or ceftriaxone) in Canada. Additionally, the first ceftriaxone-resistant cases of *N. gonorrhoeae* were reported in Canada in 2017 and 2018. These highly resistant isolates of *N. gonorrhoeae* represent an emerging public health threat.

Figure 6: Proportion of resistance or decreased susceptibility to antimicrobials in *Neisseria gonorrhoeae* isolates, Canada, 2014–2018



Neisseria gonorrhoeae drug resistance definitions

- Multidrug-resistant (MDR): isolates with decreased susceptibility or resistance to one currently recommended therapy (a cephalosporin or azithromycin), plus resistance to at least two other antimicrobials (penicillin, tetracycline, erythromycin and/or ciprofloxacin).
- Extensively drug-resistant (XDR): decreased susceptibility or resistance to two currently recommended therapies (a cephalosporin and azithromycin), plus resistance to at least two other antimicrobials (penicillin, tetracycline, erythromycin and/or ciprofloxacin).

Mycobacterium tuberculosis

Key findings

- Between 2014 and 2018, the rate of *Mycobacterium tuberculosis* (TB) infection in Canada remained stable at approximately 4.8 per 100,000 population.
- In 2018, the proportion of culture-positive TB isolates resistant to any first-line drug was 10%.
- In 2018, the first case of extensively drug-resistant TB since 2014 was identified.

TB Results

Between 2014 and 2018, the incidence rate of TB infection remained stable at 4.7 to 4.8 per 100,000 population (*n*=1,651 to *n*=1,797).

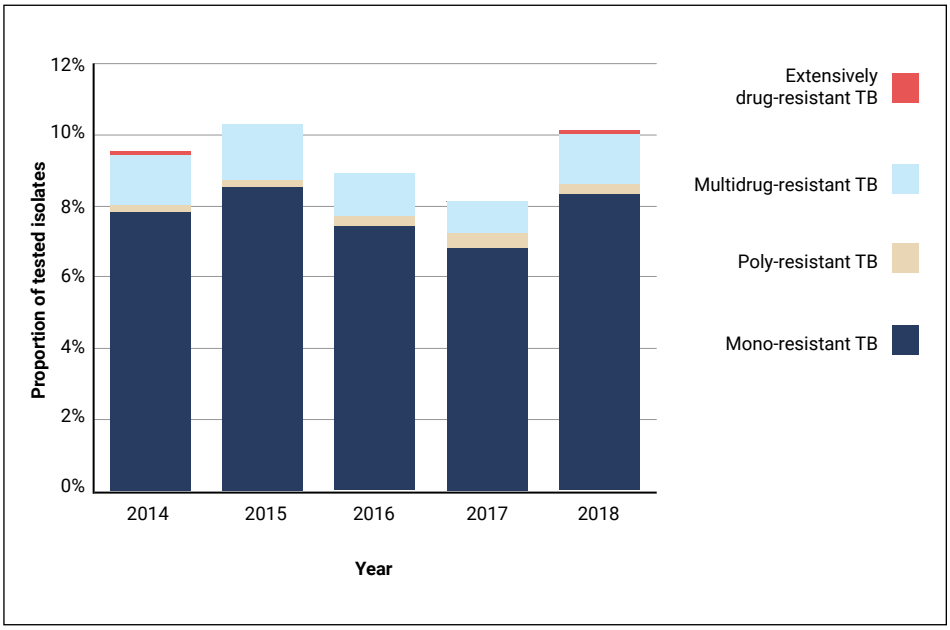
Antimicrobial susceptibility results were available for 99.4% (*n*=1,459/1,468) of all the culture-positive TB infections reported in 2018. Between 2014 and 2018, the annual proportion of TB isolates resistant to any first-line anti-TB medications increased from 9.5% (*n*=130/1,368) to 10.1% (*n*=148/1,459).

Methods

Data presented were restricted to culture-positive cases of TB reported to the Canadian Tuberculosis Laboratory Surveillance System (CTBLSS) between 2014 and 2018. National statistics on TB (e.g. annual incidence rate per 100,000 inhabitants per year) were developed through the integration of data from Statistics Canada. Further methodology and case definitions have been previously described by CTBLSS[15].

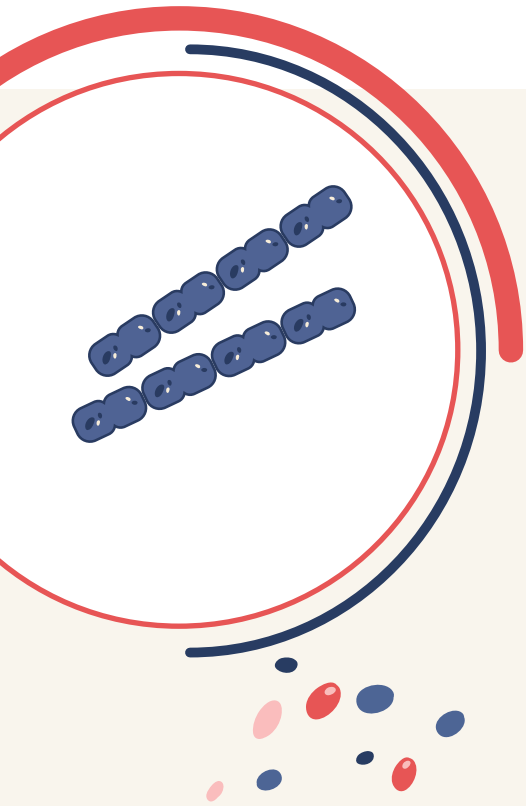
In 2018, the proportion of monoresistant TB isolates was 8.3% (*n*=121/1,458), polyresistant TB isolates was less than 1% (*n*=5/1,458), multidrug-resistant TB isolates was 1.4% (*n*=22/1,458) and extensively drug-resistant was less than 1% (*n*=1/1,458, the first since 2014).

Figure 7: Proportion of monoresistant, polyresistant, multidrug-resistant, and extensively drug-resistant *Mycobacterium tuberculosis* (TB) isolates, Canada, 2014–2018



Tuberculosis (TB) drug resistance definitions

- First-line anti-TB medications: isoniazid, rifampin, ethambutol and pyrazinamide.
- Monoresistant TB: resistance to one first-line anti-tuberculosis medication.
- Polyresistant TB: resistance to more than one first-line anti-tuberculosis medication (excluding the combination of isoniazid and rifampin).
- Multidrug-resistant TB: resistance to isoniazid and rifampin, with or without resistance to other anti-tuberculosis medications.
- Extensively drug-resistant TB: resistance to isoniazid, rifampin and any fluoroquinolone and at least one of the following injectable second-line drugs (amikacin, capreomycin, or kanamycin).



Streptococcus pneumoniae

Key findings

- The proportion of invasive *Streptococcus pneumoniae (S. pneumoniae)* isolates resistant to penicillin increased by 49% between 2013 and 2017.
- The proportion of invasive *S. pneumoniae* isolates classified as multidrug-resistant increased by 26% between 2013 and 2017.
- Infections caused by multidrug-resistant *S. pneumoniae* serotypes 19A and 19F may be prevented using existing pneumococcal vaccines.

Invasive *S. pneumoniae* results

Between 2013 and 2017, the incidence rate of invasive disease due to *S. pneumoniae* increased from 9.1 to 9.5 per 100,000 population (*n*=3,185 to *n*=3,477).

Antimicrobial susceptibility results were available for 32.5% (*n*=1,129/3,477) of all invasive isolates identified in 2017. The resistance profile of *S. pneumoniae* serotypes associated with antimicrobial resistance (i.e. 19F, 6C, 19A, 15A, 23A, 23B and 35B) remained largely unchanged from previous years; however, between 2013 and 2017, the overall proportion of isolates resistant to penicillin (using meningitis resistance breakpoints) increased from 10.0% to 14.9% and multidrug resistance increased from 7.6% (*n*=80/1,058) to 9.6% (*n*=108/1,129).

Methods

Data presented were restricted to invasive *S. pneumoniae* isolates submitted to the National Laboratory Surveillance of Invasive Streptococcal Disease (eSTREP) between 2013 and 2017. Meningitis related isolates were regarded as most invasive, followed by blood and then other sterile sites. Penicillin resistance was defined using parenteral meningitis breakpoints. Multidrug resistance was defined as resistance to three or more classes of antimicrobials tested. Further methodology and case definitions have been previously described by eSTREP[16].

Infection by some antimicrobial-resistant *S. pneumoniae* serotypes (e.g. 19A, 19F) can be prevented through the use of pneumococcal vaccines.

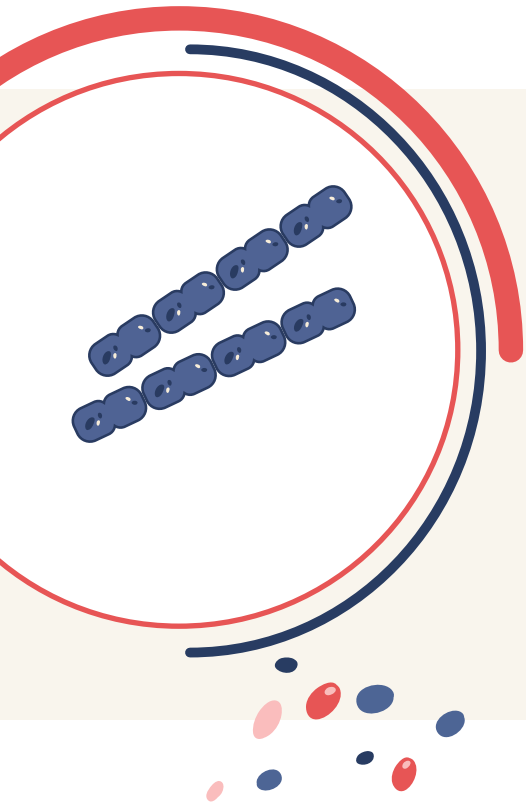
Table 9: Antimicrobial resistance patterns in *Streptococcus pneumoniae* isolates, Canada, 2013–2017

	Proportion (%) of resistant isolates per year				
Year	**2013**	**2014**	**2015**	**2016**	**2017**
Isolates tested (*n*)	**1,057**	**1,116**	**1,128**	**1,114**	**1,129**
Amoxicillin-clavulanic acid	0.7	0.7	0.3	0.1	0.4
Ceftriaxone	0.7	0.2	0.1	0.4	0.7
Cefuroxime	4.7	4.7	5.1	5.4	6.4
Chloramphenicol	10.0	8.7	10.3	12.2	14.9
Ciprofloxacin	1.4	1.9	0.4	0.6	1.1
Clarithromycin	24.8	22.3	23.0	21.5	25.7
Clindamycin	5.9	4.5	5.9	4.2	7.9
Doxycycline	9.8	8.1	8.6	8.5	10.7
Levofloxacin	0.6	0.9	0.4	0.3	0.4
Meropenem	2.6	1.5	1.5	0.7	1.6
Penicillin	10.0	8.7	10.3	12.2	14.9
Trimethoprim-sulfamethoxazole	7.4	5.8	6.0	5.9	6.8

Penicillin and ceftriaxone resistance using parenteral meningitis resistance breakpoints; cefuroxime resistance using parenteral breakpoints. Some antimicrobials are presented for epidemiological purposes only.

In Canada, *Streptococcus pneumoniae* remains one of the leading causes of infectious disease including pneumonia, meningitis, bacteremia and otitis media. Although the widespread use of pneumococcal conjugate vaccines (PCVs) in Canadian children has reduced the incidence of pneumococcal diseases associated with vaccine-serotypes, rapid increase of non-vaccine serotypes in carriage and pneumococcal infections is of great concern to clinicians.

Xianding Deng, Deirdre Church, Otto G Vanderkooi, et al. Expert Rev. Anti-infect. Ther. 2013.[17]



Streptococcus pyogenes

Key findings

- Between 2013 and 2017, the incidence rate of invasive group A *Streptococcus pyogenes* (GAS) infection increased by 42%.
- Between 2013 and 2017, the proportion of *S. pyogenes* isolates resistant to erythromycin increased to 10%; resistance to clindamycin increased to 7%.
- All *S. pyogenes* isolates tested remained susceptible to penicillin.

Invasive GAS results

Between 2013 and 2017, the incidence rate of invasive GAS infection in Canada increased from 4.8 to 6.8 cases per 100,000 population (*n*=1,665 to *n*=2,486).

Antimicrobial susceptibility testing was conducted on 93.7% (*n*=2,330/2,486) of all GAS infections identified in 2017. All *S. pyogenes* isolates remained susceptible to penicillin and vancomycin. Between 2013 and 2017, the proportion of *S. pyogenes* resistant to erythromycin increased from 8.6% to 10.3%; resistance to clindamycin increased from 2.2% to 7.2%; and non-susceptibility to chloramphenicol increased from 0.7% to 4.8%.

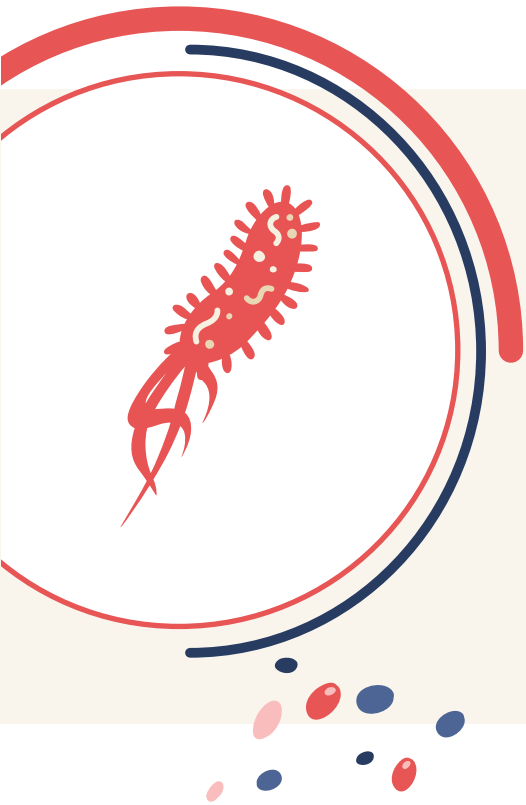
Methods

Data presented were restricted to *S. pyogenes* isolates submitted to the National Laboratory Surveillance of Invasive Streptococcal Disease (eSTREP) between 2013 and 2017. Further methodology and case definitions have been previously described by eSTREP[18].

Table 10: Antimicrobial resistance patterns in *Streptococcus pyogenes* isolates, Canada, 2013–2017

	Proportion (%) of resistant isolates per year				
Year	**2013**	**2014**	**2015**	**2016**	**2017**
Isolates tested (*n*)	**1,287**	**1,460**	**1,453**	**1,768**	**2,330**
Chloramphenicol*	0.7	0.1	1.5	4.7	4.8
Clindamycin	2.2	2.6	3.2	3.9	7.2
Erythromycin	8.6	7.1	8.3	8.8	10.3
Penicillin	0.0	0.0	0.0	0.0	0.0
Vancomycin	0.0	0.0	0.0	0.0	0.0

Some antimicrobials are presented for epidemiological purposes only.
*Non-susceptible.



Resistance in *Escherichia coli* and *Acinetobacter* spp.

Key findings

- In 2018, the proportion of *Acinetobacter* spp. isolates non-susceptible to meropenem was 5%.
- Between 2015 and 2018, the proportion of *Escherichia coli (E. coli)* non-susceptible to carbapenems was <1% for blood and urine isolates.

Antibiogram results: *E. coli* (blood)

Between 2016 and 2018, non-susceptibility to ciprofloxacin in *E. coli* blood isolates remained stable (from 26.1% to 26.8%), piperacillin-tazobactam increased (from 6.9% to 13.0%) and trimethoprim-sulfamethoxazole increased (from 26.6% to 30.7%). In 2018, non-susceptibility to carbapenems remained less than 1%. Full antibiogram results are presented in Table 11.

Methods

Data presented are hospital-level antibiogram data on all inpatient and outpatient clinical *E. coli* and *Acinetobacter* spp. isolates submitted by participating CNISP hospital laboratories (including blood, urine and other clinical isolates such as respiratory, skin, soft tissue and surgical sites). Duplicate isolates were removed as per Clinical and Laboratory Standards Institute guidelines; however, standardization between participating hospitals was not assessed. As of 2018, there was no minimum number of isolates required for hospital reporting; prior to 2018, the minimum cut off for reporting was 30 isolates per hospital.

Table 11: Non-susceptibility patterns in *Esherichia coli* blood isolates, Canada, 2014–2018

	Proportion (%) of resistant isolates per year		
Year	**2016**	**2017**	**2018**
Number of participating hospital laboratories	**11**	**15**	**24**
Amikacin	0.5	0.2	0.6
Amoxicillin-clavulanate	19.5	23.7	24.7
Ampicillin	51.7	58.0	55.2
Cefazolin (for systemic use)	36.2	47.1	33.0
Ceftriaxone	13.2	13.2	15.8
Ciprofloxacin	26.1	26.9	26.8
Ertapenem	0.4	0.2	0.3
Gentamicin	10.6	10.6	10.7
Imipenem		0.2	0.7
Meropenem	0.1	0.0	0.3
Piperacillin-tazobactam	6.9	11.6	13.0
Tobramycin	12.7	12.3	10.2
Trimethoprim-sulfamethoxazole	26.6	28.0	30.7

Some antimicrobials are presented for epidemiological purposes only. The number of isolates tested varies by antimicrobial and year. For years 2016, 2017, and 2018 (*n*): amikacin (574 | 761 | 1,462); amoxicillin-clavulanate (406 | 1,017 | 1,761); ampicillin (834 | 1,192 | 2,116); cefazolin (474 | 547 | 1,671); ceftriaxone (822 | 1,185 | 2,101); ciprofloxacin (834 | 1,189 | 2,116); ertapenem (667 | 597 | 1,499); gentamicin (834 | 1,143 | 2,113); imipenem (0 | 466 | 684); meropenem (761 | 834 | 2,008); piperacillin-tazobactam (834 | 1,135 | 2,099); tobramycin (801 | 1,151 | 2,068); trimethoprim-sulfamethoxazole (492 | 1,123 | 1,731).

Antibiogram results: *E. coli* (urine)

Between 2016 and 2018, non-susceptibility to ciprofloxacin in *E. coli* urine isolates decreased (from 19.4% to 17.7%), piperacillin-tazobactam increased (from 4.0% to 6.0%) and trimethoprim-sulfamethoxazole decreased (from 24.5% to 21.5%). In 2018, non-susceptibility to carbapenems remained less than 1%. Full antibiogram results are presented in Table 12.

Table 12: Non-susceptibility patterns in *Esherichia coli* urine isolates, Canada, 2014–2018

	Proportion (%) of resistant isolates per year		
Year	**2016**	**2017**	**2018**
number of participating hospital laboratories	**17**	**50**	**25**
Amikacin	0.1	0.2	0.1
Amoxicillin-clavulanate	16.3	15.4	18.2
Ampicillin	45.7	42.6	45.7
Cefazolin (for systemic use)	31.5	16.9	23.9
Cefazolin (marker for oral use)	21.4	28.0	14.2
Cefoxitin	5.6	6.4	6.8
Ceftriaxone	7.8	6.5	9.5
Ciprofloxacin	19.4	16.7	17.7
Ertapenem	0.2	0.1	0.4
Gentamicin	8.0	7.6	7.9
Imipenem	0.6	0.1	0.7
Meropenem	0.2	0.1	0.0
Nitrofurantoin	3.2	3.0	3.2
Piperacillin-tazobactam	4.0	5.2	6.0
Tobramycin	9.9	8.5	8.1
Trimethoprim-sulfamethoxazole	24.5	21.8	21.5

Some antimicrobials are presented for epidemiological purposes only. The number of isolates tested varies by antimicrobial and year. For years 2016, 2017, and 2018 (*n*): amikacin (19,790 | 17,590 | 16,493); amoxicillin-clavulanate (17,991 | 27,812 | 21,836); ampicillin (22,387 | 31,346 | 26,379); cefazolin (3,800 | 12,657 | 19,900); cefazolin (13,854 | 8,550 | 10,133); cefoxitin (8,846 | 12,464 | 6,509); ceftriaxone (13,617 | 22,261 | 25,085); ciprofloxacin (22,376 | 31,252 | 26,377); ertapenem (14,342 | 23,817 | 18,897); gentamicin (22,393 | 29,965 | 26,407); imipenem (6,798 | 11,900 | 10,259); meropenem (15,181 | 22,894 | 22,470); nitrofurantoin (25,885 | 43,943 | 26,164); piperacillin-tazobactam (19,790 | 26,715 | 25,052); tobramycin (18,367 | 28,041 | 25,129); trimethoprim-sulfamethoxazole (22,378 | 31,340 | 23,888).

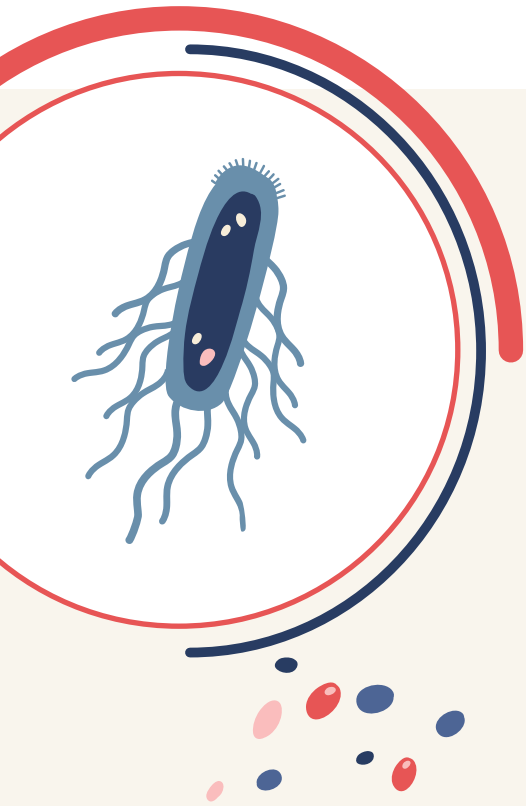
Antibiogram results: *Acinetobacter* spp.

In 2018, non-susceptibility to meropenem in *Acinetobacter* spp. was 4.7%. Full antibiogram results are presented in Table 13.

Table 13: Non-susceptibility patterns in *Acinetobacter* spp. isolates, Canada, 2014–2018

	Proportion (%) of resistant isolates per year
Year	**2018**
number of participating hospital laboratories	**39**
Ceftazidime	13.6
Ciprofloxacin	5.5
Gentamicin	5.8
Meropenem	4.7
Piperacillin-tazobactam	12.6
Tobramycin	3.4

Some antimicrobials are presented for epidemiological purposes only. The number of isolates tested varies by antimicrobial and year. For 2018 (*n*): ceftazidime (381); ciprofloxacin (381); gentamicin (380); meropenem (341); piperacillin-tazobactam (380); tobramycin (380).



Typhoidal and non-typhoidal *Salmonella enterica*

Key findings

- Between 2014 and 2018, the frequency of *Salmonella* Typhi/Paratyphi resistant to ceftriaxone increased from nearly undetectable levels to 3%.
- Between 2014 and 2018, the frequency of typhoidal *Salmonella* resistant to ciprofloxacin increased by 34%.
- In 2018, 11% of typhoidal *Salmonella* were resistant to three or more classes of antimicrobials.
- In 2018, 13% of non-typhoidal *Salmonella* were resistant to three or more classes of antimicrobials.

Antibiogram results: Typhoidal *Salmonella enterica* (Typhi and Paratyphi)

The number of typhoidal *S. enterica* isolates submitted for laboratory testing increased from 184 to 278 between 2014 and 2018. In 2018, 87.4% (*n*=243/278) of submitted typhoidal *S. enterica* isolates were Typhi, 11.1% (*n*=31/278) were Paratyphi A and 1.4% (*n*=4/278) were Paratyphi B. Where the site of isolation was known, the majority were cultured from blood (71.8%, *n*=196/273).

Methods

Data presented were restricted to isolates of *Salmonella enterica* (serovars Typhi, Paratyphi and several non-typhoidal serovars) associated with human infection submitted to the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) between 2014 and 2018. National statistics on infection rates were not assessed. Further methodology has been previously described by CIPARS[19].

The relative frequencies of resistance in the submitted typhoidal *S. enterica* isolates remained stable for most antimicrobials between 2014 and 2018; however, increases were noted in ceftriaxone (from undectectable to 2.9%), ciprofloxacin (from 13.7% to 18.4%) and nalidixic acid (from 82.1% to 87.8%). No resistance to azithromycin was identified. A total of 10.8% (*n*=30/278) of *S. enterica* isolates were multiclass-resistant (i.e. resistant to three or more classes of antimicrobials) and less than 1% (*n*=2/278) were resistant to at least six of the seven antimicrobial classes tested.

Table 14: Antimicrobial resistance patterns in *Salmonella enterica* Typhi and Paratyphi isolated from humans, Canada, 2014–2018

	Proportion (%) of resistant isolates per year				
Year	**2014**	**2015**	**2016**	**2017**	**2018**
Isolates tested (*n*)	**184**	**162**	**162**	**237**	**278**
Ampicillin	13.6	16.7	16.7	9.7	11.2
Azithromycin	0.0	0.0	0.0	0.0	0.0
Ceftriaxone	0.0	0.6	0.0	0.4	2.9
Chloramphenicol	14.8	16.6	17.9	8.1	10.8
Ciprofloxacin	13.7	10.4	14.2	22.1	18.4
Gentamicin	0.0	0.0	0.0	0.0	0.4
Nalidixic acid	82.1	75.9	84.0	87.3	87.8
Streptomycin	23.4	27.2	22.8	16.0	18.7
Tetracycline	1.1	1.2	2.5	3.4	1.4
Trimethoprim-sulfamethoxazole	14.7	16.7	18.5	8.9	10.4

Some antimicrobials are presented for epidemiological purposes only.

Antibiogram results: Non-typhoidal *Salmonella enterica*

The number of non-typhoidal *S. enterica* isolates submitted for laboratory testing decreased from 2,544 to 2,190 between 2014 and 2018. In 2018, 50.5% (*n*=1,107/2,190) of non-typhoidal *S. enterica* isolates submitted were Enteritidis, 13.7% (*n*=299/2,190) Typhimurium and 10.7% (*n*=234/2,190) Heidelberg. The majority were recovered from stool samples (84.5%, *n*=1,851/2,190), blood (6.8%, n=149/2,190) and urine (5.3%, *n*=116/2,190).

Between 2017 and 2018, the proportion of non-typhoidal *S. enterica* isolates resistant to nalidixic acid decreased from 18.8% to 15.2% and resistance to tetracycline increased from 13.7% to 16.2%. No resistance to meropenem was identified. The overall frequency of resistance in the remaining antimicrobial

classes remained relatively stable. In 2018, 31.8% (*n*=696/2,190) of non-typhoidal *S. enterica* isolates were resistant to one or more antimicrobials tested and 13.3% (*n*=291/2,190) were multiclass-resistant (i.e. resistant to three or more classes of antimicrobials tested).

Table 15: Antimicrobial resistance patterns in non-typhoidal *Salmonella enterica* isolated from humans, Canada, 2014–2018

	Proportion (%) of resistant isolates per year				
Year	**2014**	**2015**	**2016**	**2017**	**2018**
Isolates tested	**2,544**	**2,360**	**2,405**	**2,080**	**2,190**
Ampicillin	13.3	14.2	13.0	13.3	13.4
Ceftriaxone	5.6	5.2	4.0	3.5	2.8
Chloramphenicol	4.4	4.5	4.7	7.4	7.8
Ciprofloxacin	1.0	0.7	1.7	1.8	2.2
Gentamicin	1.4	2.4	2.5	1.8	2.4
Meropenem	0.0	0.0	0.0	0.0	0.0
Nalidixic acid	8.7	11.1	16.0	18.9	15.2
Streptomycin	12.6	14.8	13.5	18.3	14.7
Tetracycline	10.7	11.6	12.6	13.8	16.2
Trimethoprim-sulfamethoxazole	1.8	3.1	3.0	3.3	4.6

Some antimicrobials are presented for epidemiological purposes only.

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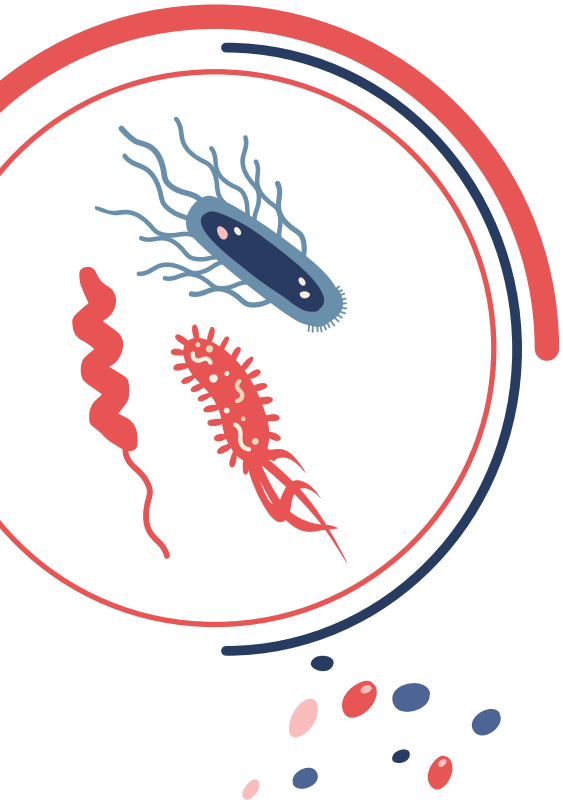
6

CHAPTER 6

RESISTANCE IN ENTERIC BACTERIA FROM FOOD SOURCES



Key findings

- Azithromycin resistance in *Campylobacter* species isolated from retail chicken meat remains low (13.6%), but increased nearly three-fold between 2014 and 2018.
- Ceftriaxone resistance in *Salmonella* isolated from retail chicken meat decreased by 55% between 2014 and 2018.

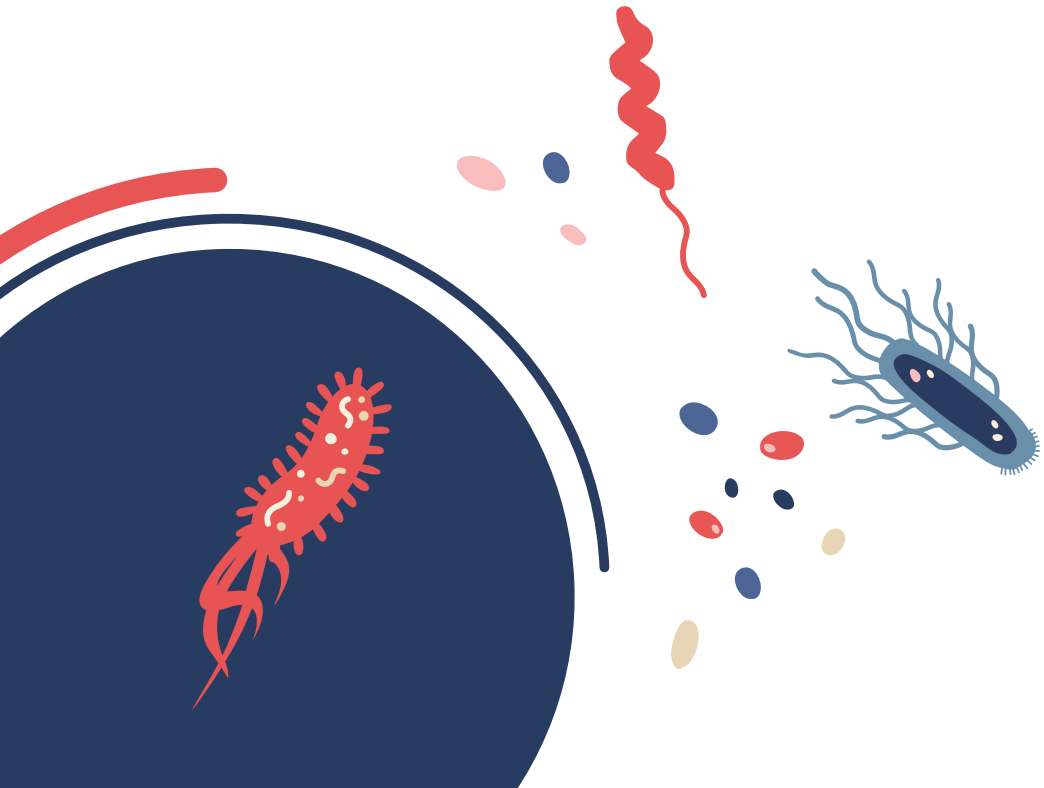
Methods

Data presented include isolates from the following sources between 2014 and 2018: generic *Escherichia coli (E. coli)* recovered from retail beef, chicken, pork and turkey meat; isolates of *Campylobacter* recovered from retail chicken meat; and isolates of *Salmonella* recovered from retail chicken and turkey meat. Excluded from this report were surveillance activities conducted on healthy animals on farms, healthy animals at slaughter and clinical (diagnostic) isolates. These results and further details on methodology are available in the CIPARS Report[20].

Antibiogram results: *E. coli*, *Campylobacter* and *Salmonella*

Between 2014 and 2018, the number of attempted isolate recoveries from retail meat decreased from 6,799 to 2,316, inclusive of *E. coli* (*n*=3,423 to *n*=1,126), *Campylobacter* (*n*=1,149 to *n*=406) and *Salmonella* (*n*=2,227 to *n*=784).

The proportion of resistance to azithromycin in *Campylobacter* spp. isolated from retail chicken meat increased from 4.7% to 13.6% between 2014 and 2018. The proportion of resistance to ceftriaxone in *Salmonella* isolated from retail chicken meat decreased from 21.0% to 9.4%. The proportion of resistance to ciprofloxacin in *E. coli* isolated from retail pork increased from undetectable levels to 2.0% between 2014 and 2018, nalidixic acid increased from 0.9% to 3.9% and tetracycline decreased from 44.9% to 29.4%. Full antibiogram results are presented in Tables 16 – 19.



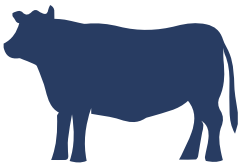


Table 16: Antimicrobial resistance patterns in *Escherichia coli (E. coli)* isolates recovered from retail beef meat samples, Canada, 2014–2018

		Proportion (%) of resistant isolates per year				
Organism	**Antimicrobial**	**2014**	**2015**	**2016**	**2017**	**2018**
E. coli	**(*n*) positive (% recovery)**	**464 (50%)**	**280 (43%)**	**257 (49%)**	**218 (43%)**	**122 (39%)**
	Ampicillin	5.4	4.9	4.3	6.9	5.7
	Ceftriaxone	0.7	0.4	0.8	0.0	0.0
	Chloramphenicol	4.6	2.3	2.7	5.1	4.1
	Ciprofloxacin	0.0	0.0	0.0	0.5	0.0
	Gentamicin	0.7	0.4	0.4	0.9	0.8
	Nalidixic acid	1.3	1.9	0.8	1.4	2.5
	Streptomycin	9.6	11.0	7.4	9.6	9.0
	Tetracycline	17.0	21.2	12.5	17.4	16.4
	Trimethoprim-sulfamethoxazole	3.5	2.7	1.6	1.8	4.9

Some antimicrobials are presented for epidemiological purposes only.

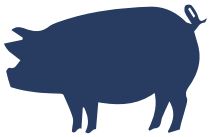


Table 17: Antimicrobial resistance patterns in *Escherichia coli (E. coli)* isolates recovered from retail pork meat samples, Canada, 2014–2018

		Proportion (%) of resistant isolates per year				
Organism	**Antimicrobial**	**2014**	**2015**	**2016**	**2017**	**2018**
E. coli	**(*n*) positive (% recovery)**	**339 (30%)**	**191 (24%)**	**140 (21%)**	**115 (18%)**	**51 (13%)**
	Ampicillin	24.8	26.3	20.7	20.0	19.6
	Ceftriaxone	4.6	1.7	2.9	1.7	2.0
	Chloramphenicol	7.1	7.8	7.9	5.2	2.0
	Ciprofloxacin	0.0	0.0	0.0	0.0	2.0
	Gentamicin	1.9	0.0	1.4	0.9	3.9
	Nalidixic acid	0.9	0.0	0.0	0.9	3.9
	Streptomycin	27.9	36.3	24.3	24.3	21.6
	Tetracycline	44.9	51.4	37.9	38.3	29.4
	Trimethoprim-sulfamethoxazole	9.0	10.6	10.0	6.1	7.8

Some antimicrobials are presented for epidemiological purposes only.

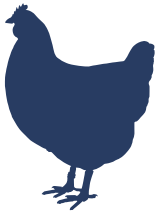


Table 18: Antimicrobial resistance patterns in *Escherichia coli (E. coli), Campylobacter,* and *Salmonella* isolates recovered from retail chicken meat samples, Canada, 2014–2018

		Proportion (%) of resistant isolates per year				
Organism	**Antimicrobial**	**2014**	**2015**	**2016**	**2017**	**2018**
Campylobacter	**(*n*) positive (% recovery)**	**294 (26%)**	**203 (25%)**	**176 (27%)**	**165 (25%)**	**103 (25%)**
	Azithromycin	4.7	5.0	1.7	4.2	13.6
	Ciprofloxacin	10.8	16.1	19.3	18.8	13.6
	Gentamicin	0.0	0.0	0.0	0.0	0.0
	Tetracycline	46.2	44.2	45.5	39.4	25.2
E. coli	**(*n*) positive (% recovery)**	**626 (92%)**	**402 (93%)**	**311 (93%)**	**293 (90%)**	**180 (88%)**
	Ampicillin	42.0	41.6	39.9	39.9	37.2
	Ceftriaxone	19.4	16.7	9.3	6.5	6.7
	Chloramphenicol	6.1	6.0	4.2	4.4	6.1
	Ciprofloxacin	0.0	0.0	1.0	0.3	0.0
	Gentamicin	19.2	20.3	33.1	25.9	31.1
	Nalidixic acid	2.9	3.0	4.8	4.1	4.4
	Streptomycin	42.3	48.2	53.4	50.5	60.0
	Tetracycline	49.8	52.9	52.4	50.2	48.3
	Trimethoprim-sulfamethoxazole	13.6	15.3	17.0	13.3	23.3
Salmonella	**(*n*) positive (% recovery)**	**348 (30%)**	**297 (37%)**	**183 (28%)**	**167 (26%)**	**130 (32%)**
	Ampicillin	21.3	14.2	7.1	8.4	9.4
	Ceftriaxone	21.0	12.8	6.6	6.0	9.4
	Chloramphenicol	0.6	0.3	0.6	0.0	0.8
	Ciprofloxacin	0.0	0.0	0.0	0.0	0.0
	Gentamicin	2.6	1.1	3.3	4.2	3.1
	Nalidixic acid	0.3	1.4	0.0	1.2	0.8
	Streptomycin	19.0	31.7	36.1	37.1	44.1
	Tetracycline	18.7	33.5	33.9	31.7	40.2
	Trimethoprim-sulfamethoxazole	0.0	1.1	1.1	1.2	2.4

Some antimicrobials are presented for epidemiological purposes only.

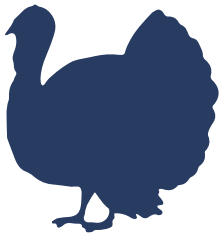


Table 19: Antimicrobial resistance patterns in *Escherichia coli (E. coli)* and *Salmonella* isolates recovered from retail turkey meat samples, Canada, 2014–2018

		Proportion (%) of resistant isolates per year				
Organism	**Antimicrobial**	**2014**	**2015**	**2016**	**2017**	**2018**
E. coli	**(*n*) positive (% recovery)**	**572 (87%)**	**381 (92%)**	**283 (87%)**	**288 (89%)**	**179 (88%)**
	Ampicillin	33.3	30.9	30.0	28.1	27.4
	Ceftriaxone	3.6	3.9	5.3	2.4	2.8
	Chloramphenicol	4.1	5.6	5.3	3.5	3.9
	Ciprofloxacin	0.7	1.1	0.4	0.7	0.6
	Gentamicin	18.2	18.4	21.6	17.7	11.7
	Nalidixic acid	1.2	2.5	2.5	1.0	2.2
	Streptomycin	43.1	44.8	45.9	38.5	31.8
	Tetracycline	62.6	61.6	58.3	50.0	50.3
	Trimethoprim-sulfamethoxazole	9.4	10.6	6.4	10.8	7.3
Salmonella	**(*n*) positive (% recovery)**	**189 (18%)**	**185 (26%)**	**96 (16%)**	**101 (18%)**	**114 (30%)**
	Ampicillin	18.7	17.4	17.5	15.8	8.9
	Ceftriaxone	10.4	6.2	5.2	4.0	1.8
	Chloramphenicol	11.0	15.1	0.0	19.8	0.0
	Ciprofloxacin	0.0	0.0	0.0	0.0	0.0
	Gentamicin	14.8	19.1	16.5	13.9	7.1
	Nalidixic acid	0.0	0.0	0.0	1.0	0.0
	Streptomycin	29.7	38.2	33.0	36.6	25.9
	Tetracycline	29.7	24.7	20.6	26.7	20.5
	Trimethoprim-sulfamethoxazole	0.5	0.0	0.0	0.0	1.8

Some antimicrobials are presented for epidemiological purposes only.


7

CHAPTER 7

ANTIMICROBIAL USE BY HUMANS IN CANADA

Key findings

- Consumption of antimicrobials by humans increased between 2014 and 2018.
- The use of antimicrobials that should be reserved for suspected or confirmed multidrug-resistant infections[2] increased by nearly 10% between 2014 and 2018 (overall use remained less than 1%).
- In 2018, Canada consumed the 12th lowest quantity of antimicrobials compared to the latest data from 29 European countries (one position worse than in 2015).

2 As defined by the World Health Organization's AWaRe classification.

Methods

Data on human antimicrobial consumption in Canada were acquired from the Public Health Agency of Canada, Indigenous Services Canada and IQVIA (a provider of pharmaceutical sales and dispensing information in over 100 countries). Near-comprehensive coverage of Canadian antimicrobial consumption by humans (including some information on indication of use) was achieved using five datasets:

Healthcare sector:

- The IQVIA-owned Canadian Drugstore and Hospital Purchases dataset contains the projected unit volume and cost estimates for pharmaceutical products sold to all Canadian hospitals by manufacturers and wholesalers. The projection was derived from purchasing information collected from a representative sample of 780 hospitals (from a sampling frame of 940 hospitals) extrapolated through proprietary geographical projection methods. The most recent data presented (for 2017 and 2018) are subject to adjustment for product returns. Due to small sample sizes or unique purchasing trends, data from some jurisdictions have been combined.
- The Public Health Agency of Canada's Canadian Nosocomial Infection Surveillance Program (CNISP) collected data on the quantity of all antimicrobials distributed to adult inpatients admitted to a subset of 21 participating hospitals in 2018. Data were stratified by ward and age. Long-term care units were excluded.

Community sector:

- The IQVIA-owned Canadian CompuScript dataset contains the projected unit volume, number of prescriptions and cost estimates for pharmaceutical products dispensed through all Canadian retail pharmacies located in the provinces (i.e. the community sector). The projection was derived from dispensing information collected from a representative sample of 6,000 pharmacies (from a sampling frame of 10,000 pharmacies) extrapolated through proprietary geographical projection methods. Due to small sample sizes or unique dispensing trends, data from some jurisdictions have been combined.
- The Non-Insured Health Benefits (NIHB) claims data (operated by Indigenous Services Canada) contains the unit volume and number of prescriptions for pharmaceutical products claimed by Indigenous populations. This was used to estimate antimicrobial consumption in the territories. Due to small sample sizes, data from the represented jurisdictions were combined.
- The IQVIA-owned Canadian Disease and Therapeutic Index contains indication of use data on patient visits in outpatient settings (i.e. not during a hospital admission), including the number of visits, the number of visits per condition, the number of visits with a mention of an antimicrobial and the antimicrobial mentioned. A total of 650 physicians (representative of all medical specialties) were sampled in 2018 and the annual burden was projected using the number of days sampled and the number of doctors sampled within each specialty.

All data presented were restricted to antimicrobials used for systemic use (i.e. J01 products, as defined by the 2019 World Health Organization [WHO] Collaborating Centre for Drug Statistics Methodology Anatomical Therapeutic Chemical [ATC] Classification Index, which does not include topical antibiotics, antifungal, or antiviral medications) in addition to oral vancomycin, oral fidaxomicin, oral colistin and oral metronidazole. Antimicrobials not listed in the WHO ATC index were

excluded (e.g. oral penicillin G and inhalant levofloxacin). The primary outcome metric was Defined Daily Dose (DDD) per 1,000 inhabitants. This was developed through the integration of (1) IQVIA data sources; (2) Indigenous Services Canada data sources; (3) the WHO Collaborating Centre for Drug Statistics Methodology 2019 ATC and DDD index; and (4) census population data provided by Statistics Canada. Antibiotics included in each antimicrobial class (i.e. ATC grouping) are listed in Appendix A.

Data limitations include the following: error values for the estimated point values were not provided by IQVIA; antimicrobial products consumed in low volume or through unique distribution mechanisms were not well represented and may have been censored; and antimicrobial consumption trends were not available for individuals (e.g. consecutive prescriptions or prescriptions-per-person were not possible to assess).

Terminology

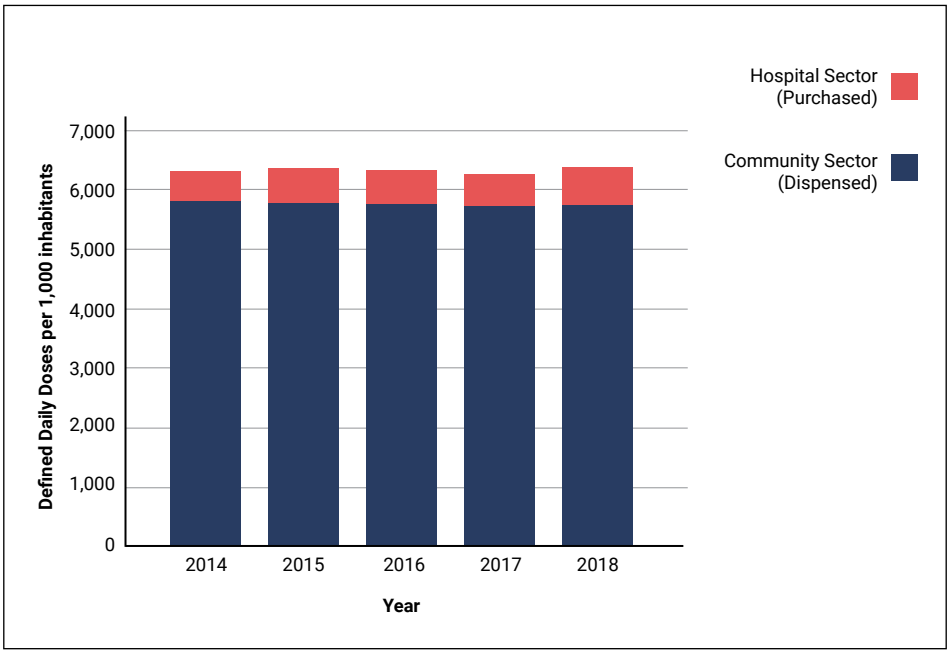
- **Defined Daily Dose (DDD):** The assumed average maintenance dose per day for an antimicrobial drug used for its main indication in adults. DDDs provide a fixed unit of measurement independent of price, currencies, package size and strength, enabling the researcher to assess trends in drug consumption and to perform comparisons between population groups.
- **Defined Daily Dose (DDD) per 1,000 inhabitants:** The estimated number of Defined Daily Doses standardized to the Canadian population.
- **Defined Daily Dose (DDD) per 1,000 inhabitant-days:** The estimated number of DDDs standardized to the Canadian population and the number of days in the year.
- **Total prescriptions:** The estimated number of prescriptions dispensed by retail pharmacies in Canada (excludes inpatient drug dispensations).
- **Prescriptions per 1,000 inhabitants:** The estimated number of prescriptions standardized to the Canadian population.
- **Total prescription costs:** Estimated total costs to the consumer (including mark-ups and dispensing fees).
- **Community sector:** Antimicrobial dispensing occurring in the community setting (outside of the inpatient setting). This includes retail pharmacies located in hospitals.
- **Healthcare sector:** Antimicrobials purchased for use in the hospital setting (primarily inpatient).
- **Antimicrobial recommendation:** Recommendations during a visit to a physician for an antimicrobial that may or may not lead to a prescription filled at a retail pharmacy.

Overall human antimicrobial consumption: National perspective

Between 2014 and 2018, annual antimicrobial consumption (including antimicrobials dispensed by community retail pharmacies and antimicrobials purchased by hospitals) by people in Canada increased from 17.3 to 17.5 DDDs per 1,000 population-days (i.e. 17.5 antimicrobial doses consumed each day for every 1,000 inhabitants or 6,388 antimicrobial doses consumed annually for every 1,000 inhabitants). This trend was driven by a 28.6% increase in purchasing of antimicrobials by hospitals (from 1.4 to 1.8 DDDs per 1,000 inhabitant-days, subject to returns adjustment) compared to a 1.3% decrease in retail dispensing (from 15.9 to 15.7 DDDs per 1,000 inhabitant-days).

In 2018, 89.8% of DDDs were dispensed in the community sector through retail pharmacies and the remaining 10.2% were purchased by hospitals. The estimated cost of all antimicrobials consumed (purchased by hospitals and dispensed in the community) increased between 2014 and 2018, from $809 to $825 million (adjusted for inflation).

Figure 8: National human consumption of antimicrobials, purchased by hospitals and dispensed by retail pharmacies, Canada, 2014–2018



Overall human antimicrobial consumption: Regional perspective

In 2018, the eastern provinces consumed the largest quantity of antimicrobials per capita. Newfoundland and Labrador combined with Prince Edward Island consumed 9,857.0 DDDs annually per 1,000 inhabitants and Nova Scotia and New Brunswick consumed 7,752.8 and 7,350.3 DDDs annually per 1,000 inhabitants, respectively. The lowest consumption of antimicrobials per capita was in the territories combined (1,738.9 DDDs annually per 1,000 inhabitants[3]), British Columbia (5,866.4 DDDs annually per 1,000 inhabitants) and Quebec (5,905.5 DDDs annually per 1,000 inhabitants).

Human antimicrobial consumption: Top antimicrobial classes

In 2018, the top five classes of antimicrobials consumed were extended-spectrum penicillins (1,266.7 DDDs annually per 1,000 inhabitants), tetracyclines (1,234.8 DDDs annually per 1,000 inhabitants), macrolides (872.7 DDDs annually per 1,000 inhabitants), fluoroquinolones (550.2 DDDs annually per 1,000 inhabitants) and first-generation cephalosporins (481.3 DDDs annually per 1,000 inhabitants).

3 Retail pharmacy distribution data only.

Figure 9: Annual human consumption of the top five classes of antimicrobials, purchased by hospitals and dispensed by retail pharmacies, Canada, 2018

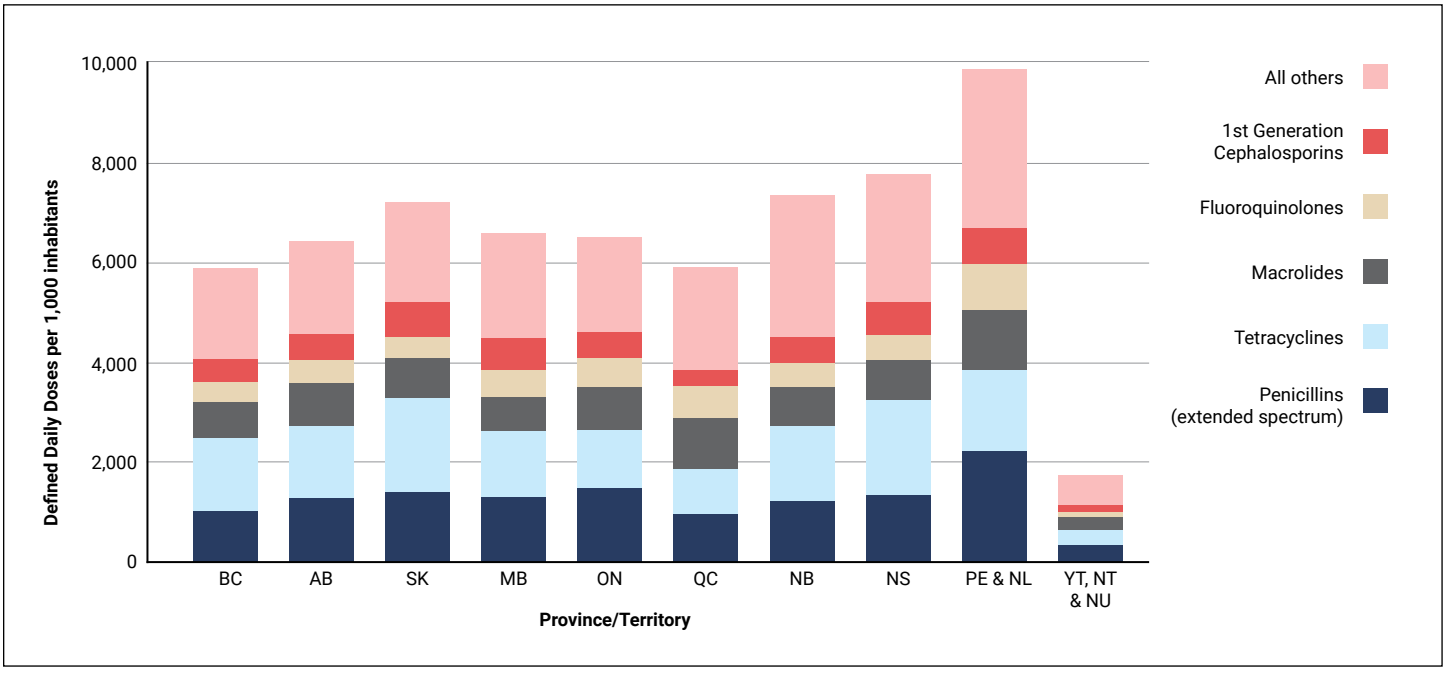


Table 20: Antimicrobial molecules by class

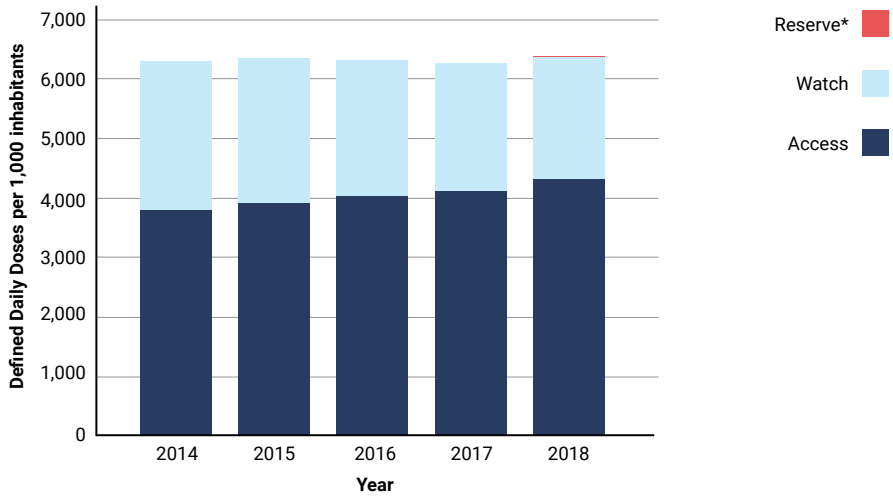
Antimicrobial class	Antimicrobial molecules
Extended-spectrum penicillins	Amoxicillin
	Ampicillin
	Piperacillin
Tetracyclines	Doxycycline
	Minocycline
	Tetracycline
	Tigecycline
Macrolides	Azithromycin
	Clarithromycin
	Erythromycin
	Spiramycin
Fluoroquinolones	Ciprofloxacin
	Gatifloxacin
	Levofloxacin
	Moxifloxacin
	Norfloxacin
	Ofloxacin
First-generation cephalosporins	Cefadroxil
	Cefazolin
	Cephalexin

Overall human antimicrobial consumption: AWaRe categorization

WHO AWaRe "Reserve" antibiotics[21] are defined as drugs that should be reserved for the treatment of suspected or confirmed multidrug-resistant organisms. The consumption of these antibiotics was less than 1% of all DDDs per 1,000 inhabitants in 2018 in Canada; however, the consumption of these antibiotics increased by 9.3% (from 7.5 to 8.2 DDDs per 1,000 inhabitants) between 2014 and 2018. This was largely driven by an increase of 35.9% in the purchasing of reserve category antimicrobials by Canadian hospitals (from 3.9 to 5.3 DDDs per 1,000 inhabitants, subject to returns adjustment), particularly a 58.3% increase in purchasing of daptomycin (from 2.4 to 3.8 DDDs per 1,000 inhabitants, subject to returns adjustment). This increase was not explained by a decrease in the use of vancomycin.

The consumption of WHO AWaRe "Watch" antibiotics, defined as antibiotics that have high resistance potential, made up 32.4% of all DDDs per 1,000 inhabitants in 2018. This compares to 67.5% "Access" antibiotics, which includes antibiotics that are active against many common susceptible pathogens and have lower resistance potential.

Figure 10: Annual human consumption of antimicrobials purchased by hospitals and dispensed by retail pharmacies in Canada, using the AWaRe antimicrobial classification (World Health Organization), 2014–2018



* The annual human consumption of Reserve class antimicrobials for years 2014, 2015, 2016, 2017, and 2018 was 7.5, 9.1, 7.3, 7.7, and 8.2 Defined Daily Doses per 1,000 inhabitants.

Table 21: Examples of antimicrobials included in the World Health Organization's AWaRe categories

AWaRe Category	Example antimicrobials
Reserve	Ceftazidime-avibactam
	Ceftolozane-tazobactam
	Daptomycin
	Linezolid
	Tigecycline
Watch	Azithromycin
	Ciprofloxacin
	Ertapenem
	Piperacillin-tazobactam
	Vancomycin (intravenous)
Access	Amikacin
	Amoxicillin-clavulanic acid
	Cefazolin
	Doxycycline
	Trimethoprim-sulfamethoxazole

Overall human antimicrobial consumption: International perspective

The European Surveillance of Antimicrobial Consumption Network (ESAC-Net), one of the largest internationally standardized surveillance systems measuring antimicrobial consumption, collects and reports data on the quantity of J01 antimicrobials consumed in the community and hospital sectors in European countries. These data, reported in DDDs per 1,000 inhabitant-days, were comparable to Canadian human antimicrobial consumption data.

Overall, Canada was the 12th lowest consumer of antimicrobials per capita in 2018 compared to the 29 European countries reporting to ESAC-Net. Canada consumed nearly twice the amount of antimicrobials consumed by the Netherlands (the country with the lowest consumption) and about half the amount consumed by Greece (the country with the highest consumption).

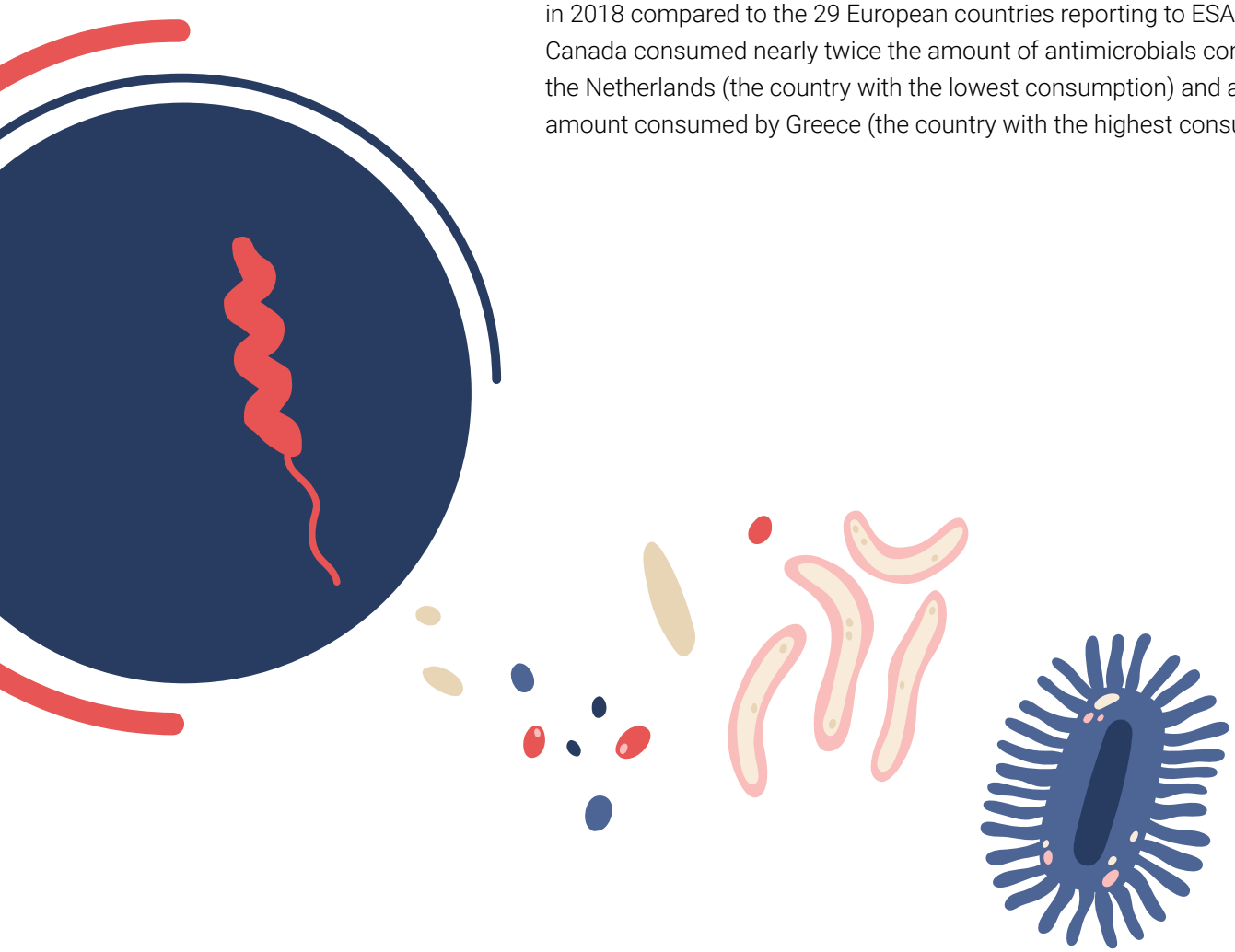
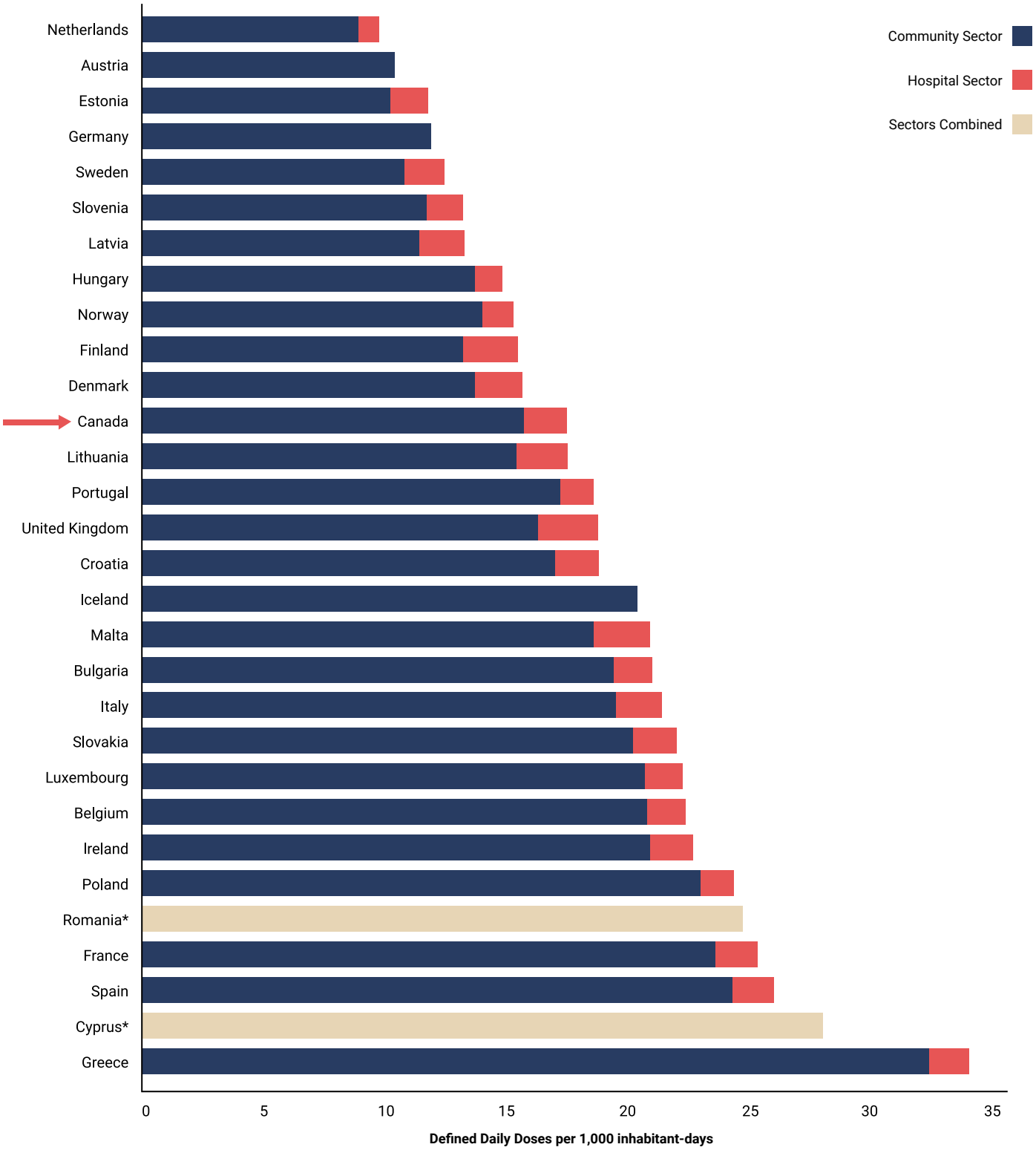


Figure 11: Consumption of antimicrobials per capita (Defined Daily Doses per 1,000 inhabitant-days), Canada and 29 European countries, 2018



Source: the European Centre for Disease Prevention and Control and the Public Health Agency of Canada. Canadian estimates include vancomycin, metronidazole, colistin, and fidaxomicin.

Community sector human antimicrobial consumption: Defined Daily Doses dispensed

Between 2014 and 2018, dispensation of antimicrobials by Canadian retail pharmacies decreased from 15.9 to 15.7 DDDs per 1,000 inhabitant-days (i.e. 15.7 antimicrobial doses consumed each day for every 1,000 inhabitants or 5,735.3 antimicrobial doses consumed annually for every 1,000 inhabitants). The proportion of total DDDs dispensed in Canada attributed to the community sector decreased from 91.9% in 2014 to 89.8% in 2018.

In 2018, the top five classes of antimicrobials dispensed by Canadian retail pharmacies were extended-spectrum penicillins (1,244.7 DDDs annually per 1,000 inhabitants), tetracyclines (1,088.2 DDDs annually per 1,000 inhabitants), macrolides (817.5 DDDs annually per 1,000 inhabitants), fluoroquinolones (482.0 DDDs annually per 1,000 inhabitants) and first-generation cephalosporins (427.5 DDDs annually per 1,000 inhabitants). This trend was consistent when stratified by sex for the top four classes of antimicrobials dispensed in 2018; the fifth most dispensed antimicrobial for females was nitrofurantoin (550.0 DDDs annually per 1,000 inhabitants), compared to first-generation cephalosporins dispensed to males (422.1 DDDs annually per 1,000 inhabitants).

Figure 12: Top five community-dispensed antimicrobials by sex, Canada, 2014–2018

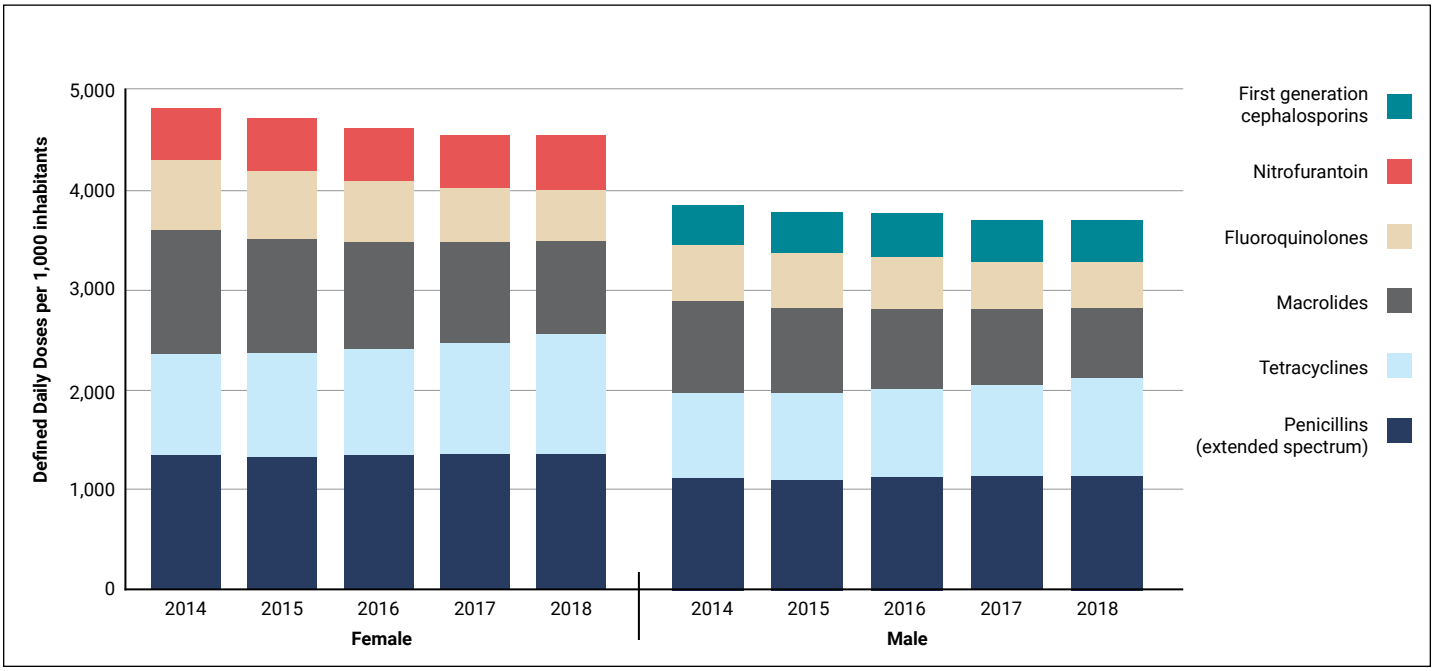


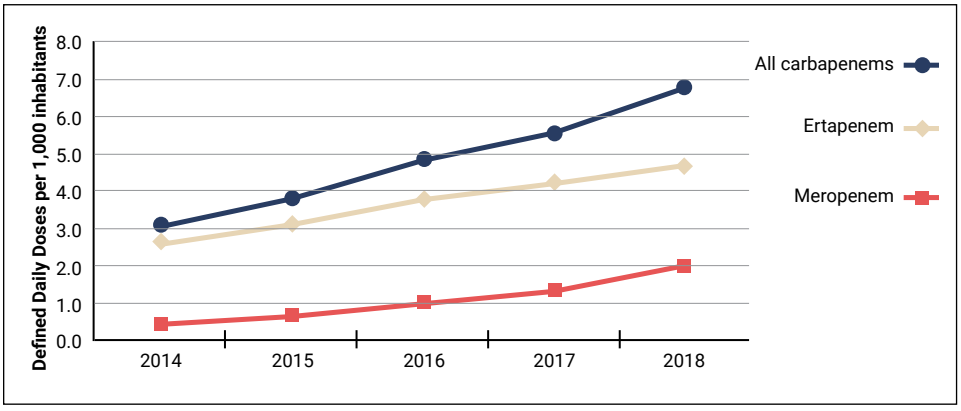
Table 22: Antimicrobial molecules by class

Antimicrobial class	Antimicrobial molecules
Extended-spectrum penicillins	Amoxicillin
	Ampicillin
	Piperacillin
Tetracyclines	Doxycycline
	Minocycline
	Tetracycline
	Tigecycline
Macrolides	Azithromycin
	Clarithromycin
	Erythromycin
	Spiramycin
Fluoroquinolones	Ciprofloxacin
	Gatifloxacin
	Levofloxacin
	Moxifloxacin
	Norfloxacin
	Ofloxacin
First-generation cephalosporins	Cefadroxil
	Cefazolin
	Cephalexin

Community sector human antimicrobial consumption: Carbapenems dispensed

The consumption of carbapenems (a class of antimicrobial used to treat multidrug-resistant infections) in the community setting increased from 3.0 to 6.8 DDDs per 1,000 inhabitants between 2014 and 2018. This appears to be driven by the increased consumption of ertapenem, from 2.6 to 4.7 DDDs per 1,000 inhabitants between 2014 and 2018.

Figure 13: Carbapenems dispensed in the community, Canada, 2014–2018

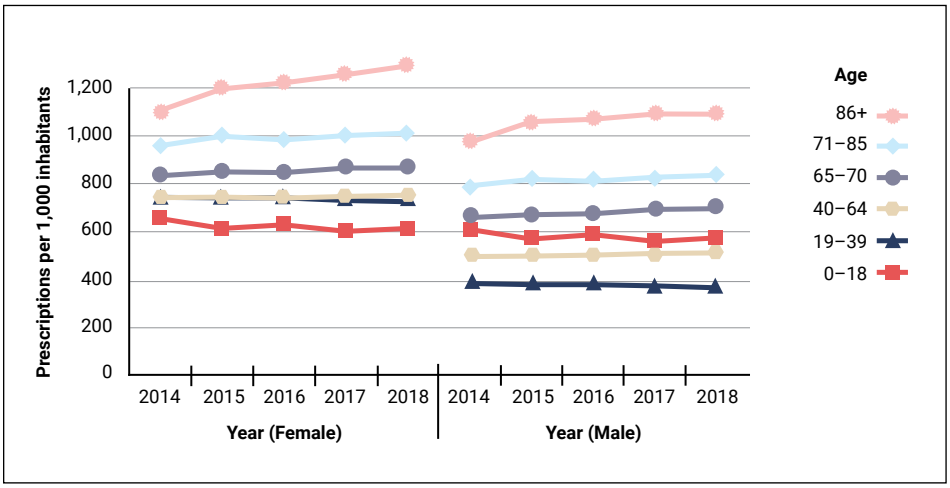


Community sector human antimicrobial consumption: Prescriptions dispensed

The number of prescriptions dispensed by retail pharmacies in Canada increased by 5.7% between 2014 and 2018 (*n*=22.9 million to *n*=24.2 million). This increase was less than 1% when standardized by population size (647.6 to 653.3 prescriptions per 1,000 inhabitants per year).

In 2018, those aged 0 to 18 years received 17.6% (*n*=4.3 million) of all dispensed prescriptions; those aged 19 to 64 years received 56.5% (*n*=13.7 million); and those aged 65 years or more received 25.7% (*n*=6.2 million). When standardized by population size, those aged 0 to 18 years received 595.3 annual prescriptions per 1,000 inhabitants; those aged 19 to 64 received 593.2; and those aged 65 years or more received 911.5. Stratified by sex, females received more prescriptions annually than males (769.2 compared to 533.5 prescriptions per 1,000 inhabitants, respectively). This trend was consistent across all age categories.

Figure 14: Community-dispensed antimicrobial prescriptions per 1,000 inhabitants, by age and sex, Canada, 2014–2018



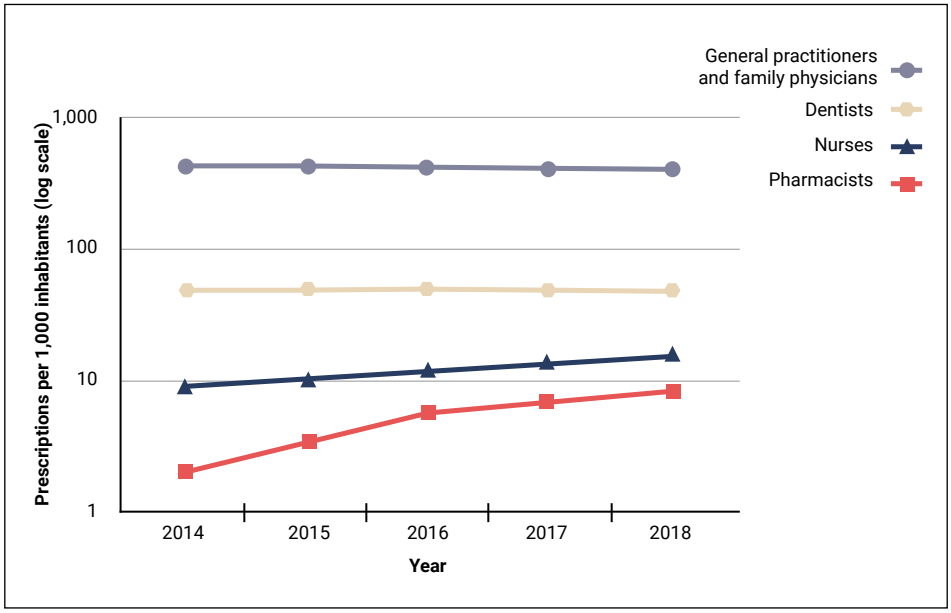
Community sector human antimicrobial consumption: Prescription origins

In 2018, the majority of prescriptions (63.8%) originated from family physicians and general practitioners (416.2 prescriptions per 1,000 inhabitants), compared to 36.2% for all other medical and non-medical subspecialties combined (236.5 prescriptions per 1,000 inhabitants).

Between 2014 and 2018, the number of prescriptions per 1,000 inhabitants originating from family physicians and general practitioners declined from 428.3 to 416.2. Of non-physician prescribers in Canada, the number of prescriptions per 1,000 inhabitants originating from dentists remained stable (48.1 to 48.5 prescriptions); those originating from nurses increased from 8.9 to 14.9; and those originating from pharmacists increased from 2.0 to 8.3.

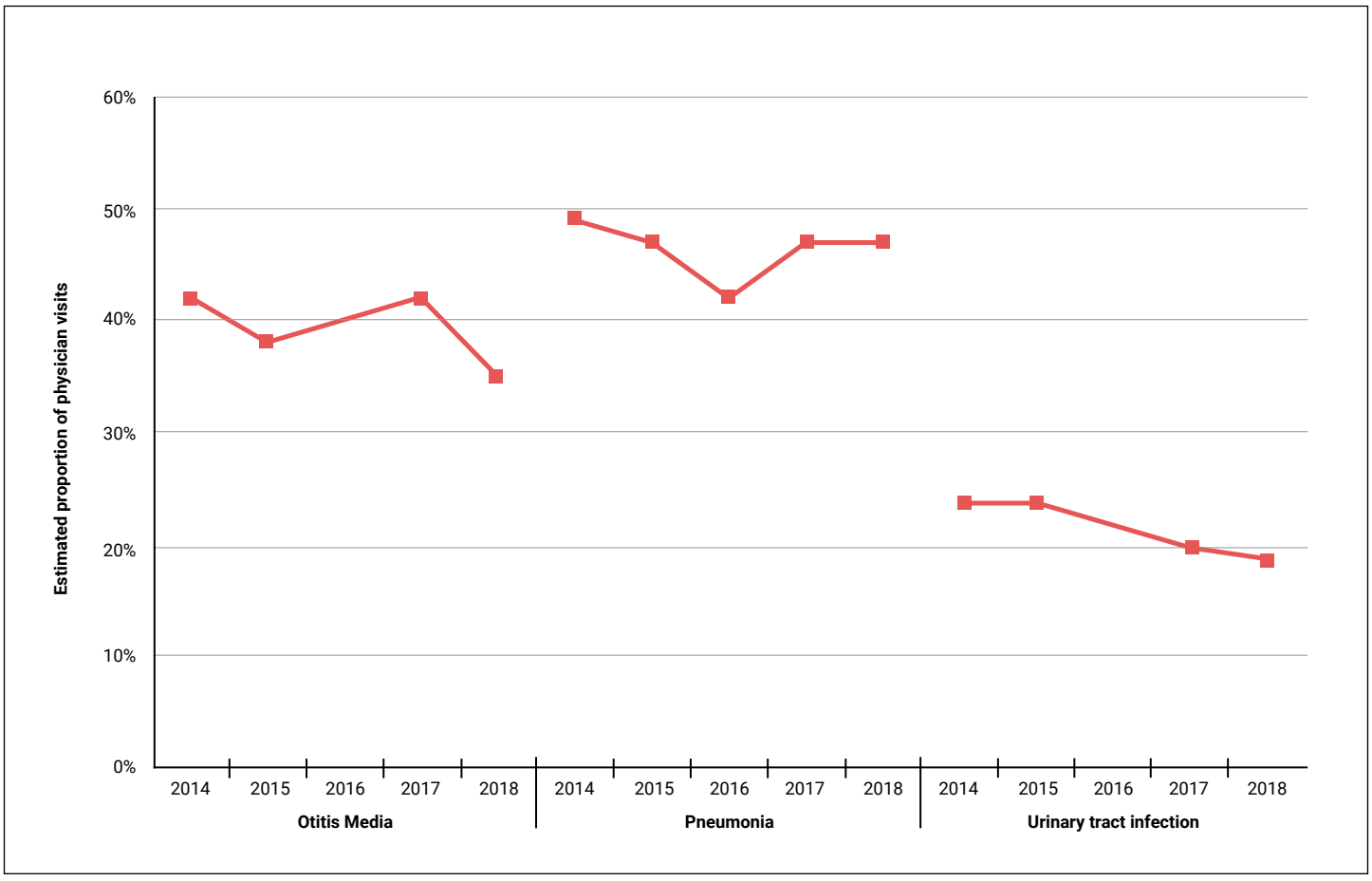
On average, each family physician and general practitioner was responsible for 355 filled prescriptions in 2017, compared to dentists (77), pharmacists (6) and nurses (1).

Figure 15: Community-dispensed antimicrobial prescriptions per 1,000 inhabitants, by specialty, Canada, 2014–2018 (log scale)



Between 2014 and 2018, the proportion of otitis media diagnoses that resulted in a recommendation for antimicrobials decreased from 42.2% to 35.5%; the proportion of pneumonia diagnoses that resulted in a recommendation for antimicrobials was stable (48.8% to 46.9%), noting a decrease observed in 2016 (41.8%); the proportion of urinary tract infection diagnoses that resulted in a recommendation for antimicrobials decreased from 24.1% to 19.5%.

Figure 16: Estimated proportion of physician visits that resulted in a mention of antimicrobials, Canada, 2014–2018



Hospital sector human antimicrobial consumption: Defined Daily Doses purchased

Between 2014 and 2018, purchasing of antimicrobials by Canadian hospitals increased from 1.4 to 1.8 DDDs per 1,000 inhabitant-days (i.e. 1.8 DDDs purchased each day for every 1,000 inhabitants or 652.7 DDDs purchased annually for every 1,000 inhabitants, subject to returns adjustment). The proportion of total DDDs purchased by Canadian hospitals increased from 8.1% in 2014 to 10.2% in 2018.

The number of antimicrobial doses purchased by Canadian hospitals increased by 33.0% between 2014 and 2018 (*n*=18.2 million to *n*=24.2 million), or 27.4% when standardized by population size (512.3 to 652.7 doses purchased per 1,000 inhabitants).

In 2018, Canadian hospitals purchased the following quantities of antimicrobials: ceftriaxone (50.6 DDDs annually per 1,000 inhabitants), azithromycin (46.6 DDDs annually per 1,000 inhabitants), ciprofloxacin (45.6 DDDs annually per 1,000 inhabitants), cefazolin (35.2 DDDs annually per 1,000 inhabitants), and piperacillin-tazobactam (25.9 DDDs annually per 1,000 inhabitants). Increases in the purchasing of doxycycline and penicillin G were also identified, and are currently being investigated.

Hospital sector human antimicrobial consumption: Defined Daily Doses dispensed

In 2018, 21 CNISP hospitals reported all medications dispensed to adult inpatients by ward. The top five antimicrobials distributed in non-intensive care units were cefazolin (114.6 DDDs per 1,000 patient-days), piperacillin-tazobactam (41.8 DDDs per 1,000 patient-days), metronidazole (39.5 DDDs per 1,000 patient-days), ceftriaxone (39.1 DDDs per 1,000 patient-days) and ciprofloxacin (33.3 DDDs per 1,000 patient-days).

The top five antimicrobials distributed in intensive care units were cefazolin (232.9 DDDs per 1,000 patient-days), piperacillin-tazobactam (208.4 DDDs per 1,000 patient-days), vancomycin (oral and parenteral, 176.7 DDDs per 1,000 patient-days), meropenem (144.7 DDDs per 1,000 patient-days) and ceftriaxone (133.3 DDDs per 1,000 patient-days).


8

CHAPTER 8

ANTIMICROBIAL USE IN ANIMALS AND ON CROPS IN CANADA

Key findings

- Between 2017 and 2018, the weight in kilograms of antimicrobial active ingredient distributed for use in animals increased by 6%.
- Between 2017 and 2018, declines in antimicrobial use (AMU) were reported by grower–finisher pig and broiler chicken sentinel farms.
- In 2018, Canada distributed the sixth highest quantity of antimicrobials intended for use in animals compared to the latest data from 31 European countries.

Methods

Data on antimicrobial consumption by animals were provided by the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) and included contributions from the following:

- Data from 95% of animal health product manufacturers were voluntarily provided by the Canadian Animal Health Institute (CAHI) and included the kilograms of antimicrobials distributed for sale for use in production animals (including horses) and companion animals, and the routes of antimicrobial administration.
- AMU by animal species was voluntarily provided by 333 sentinel farms participating in CIPARS (141 broiler chicken flocks, 95 turkey flocks and 97 grower–finisher pig herds, 2018 data) and Fisheries and Oceans Canada (all land-based and freshwater net pen facilities and marine aquaculture operations, 2017 data).
- Information on the quantities of antimicrobials sold for use as pesticides on crops was provided by Health Canada's Pest Management Regulatory Agency (PMRA).

Antimicrobial quantities excluded active pharmaceutical ingredients imported for further compounding, ionophores and chemical coccidiostats.

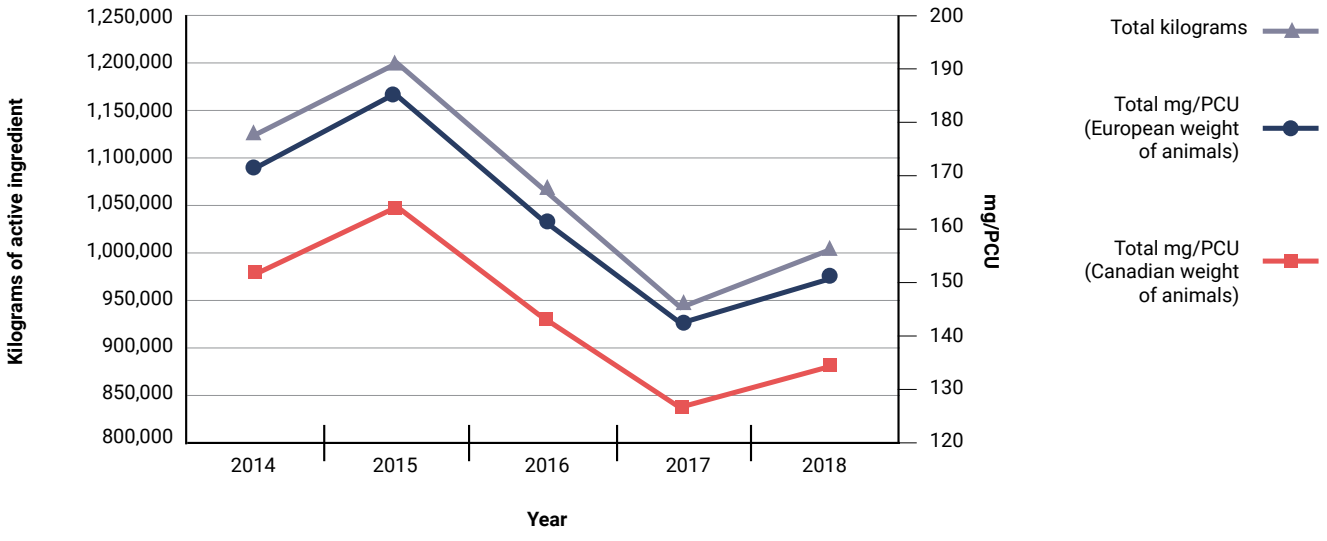
Terminology

- **Kilograms (kg) of antimicrobials distributed for sale:** The weight of antimicrobial active ingredients distributed for (or used) in animals.
- **Population correction unit (PCU):** also referred to as a measure of biomass, the PCU accounts for the size of the population, including the number and weight of animals or people in the population. For animal PCU, the weight is the estimated average weight of the animal at time of treatment.
- **Milligrams per population correction unit (mg/PCU):** The quantities of antimicrobials sold or used in animals divided by the PCU. This metric is interpreted as milligrams of antimicrobial per kilogram of animal.
- **Defined Daily Dose for animals (DDDvetCA)[22]:** The assumed average dose per kg animal per species per day. The 'CA' indicator in DDDvetCA refers to Canadian dose standards.
- **Defined Daily Doses (DDDvetCA) per 1,000 animal-days at risk:** The number of DDDvetCAs standardized by the total animals and the number of days at risk corresponding to the production period. This calculation is animal species-specific.

Animal antimicrobial consumption: National perspective

Between 2014 and 2018, the annual quantity of antimicrobials distributed for use in animals decreased from 1.13 million to 1.00 million kilograms, noting an increase from 0.95 million to 1.00 million between 2017 and 2018. This overall trend was consistent when the quantity was measured as mg/PCU using both Canadian and European standard weights of animals. This increase was primarily driven by an increase of 12% in the quantity of tetracyclines, from 501,582 to 560,643 kilograms between 2017 and 2018. Of note was an increase of 6% in the reported distribution of fluoroquinolones (a class of antimicrobials categorized as having very high importance to human medicine and is only licensed for use in certain animal species in Canada[23]) from 640 to 677 kilograms between 2017 and 2018. However, the quantities of fluoroquinolones distributed in 2018 did not surpass quantities reported in 2015 (860 kilograms).

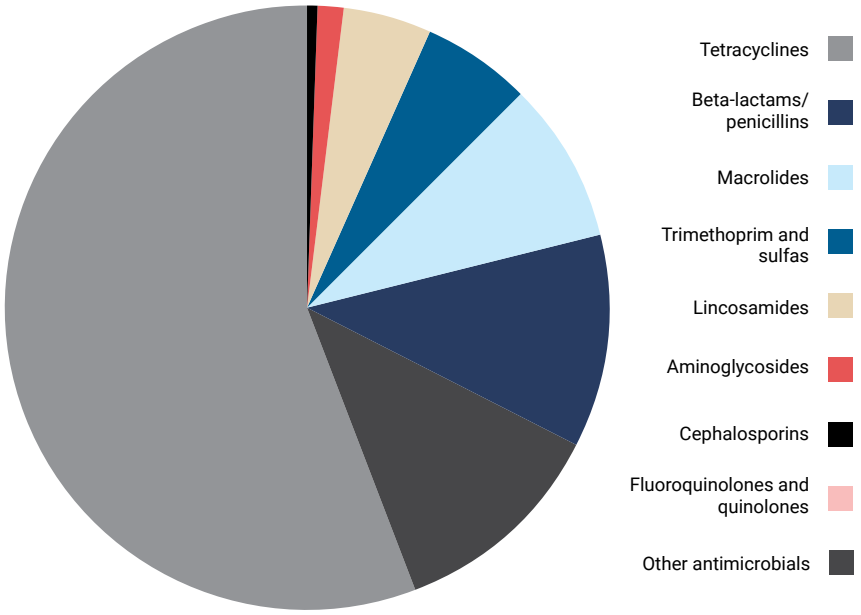
Figure 17: Annual quantity of antimicrobials distributed for use in animals, Canada, 2014–2018



The population data for live horses was from 2010 and for fish was from 2017.
Source: The Canadian Animal Health Institute, Statistics Canada, Agriculture and Agri-Food Canada, Equine Canada, and the European Surveillance of Veterinary Antimicrobial Consumption.
Abbreviations: mg, milligram; PCU, population correction unit

In 2018, the top five classes of antimicrobial active ingredient distributed for use in animals (excluding the "other antimicrobials" grouping) were tetracyclines (560,643 kilograms), β-lactams/penicillins (113,653 kilograms), macrolides (87,221 kilograms), trimethoprim and sulfas (57,865 kilograms) and lincosamides (47,228 kilograms).

Figure 18: Kilograms of antimicrobial active ingredient distributed for use in animals, Canada, 2018



Other antimicrobials include: Avilamycin, bacitracins, bambermycin, chloramphenicol, chlorhexidine gluconate, florfenicol, fusidic acid, novobiocin, polymixin B, tiamulin, and virginiamycin

Animal antimicrobial use: Trends by animal species

For broiler chicken flocks, AMU (excluding ionophores and chemical coccidiostats) decreased from 501 to 483 DDDvetCa per 1,000 chicken-days, between 2014 and 2018. The largest decrease was reported by farms in Ontario (from 587 to 487 DDDvetCa per 1,000 chicken-days), Quebec (from 587 to 524 DDDvetCa per 1,000 chicken-days) and Alberta, Saskatchewan and Manitoba (combined, from 424 to 403 DDDvetCa per 1,000 chicken-days); however, an increase was reported by farms in British Columbia, from 365 to 549 DDDvetCa per 1,000 chicken-days. In 2018, the predominant classes of antimicrobials used were bacitracins, penicillins and trimethoprim-sulfas. The quantity of antimicrobials used for growth promotion decreased to zero between 2014 and 2018.

For grower–finisher pig herds, AMU in feed (excluding ionophores) decreased from 290 to 171 DDDvetCa per 1,000 pig-days, between 2014 and 2018. The largest decrease was reported by farms in Quebec (from 255 to 94 DDDvetCa per 1,000 pig-days), followed by Alberta, Saskatchewan and Manitoba (combined, from 308 to 193 DDDvetCa per 1,000 pig-days) and Ontario (from 294 to 192 DDDvetCa per 1,000 pig-days). In 2018, the predominant classes of antimicrobials used were tetracyclines, lincosamides and macrolides.

For turkey flocks, AMU (excluding ionophores and chemical coccidiostats) increased from 102 to 109 DDDvetCa per 1,000 turkey-days, between 2016 and 2018. A decrease was reported by farms in Ontario (from 149 to 110 DDDvetCa per 1,000 turkey-days) and increases were reported by farms in British Columbia (from 85 to 121 DDDvetCa per 1,000 turkey-days) and Quebec (from 66 to 84 DDDvetCa per 1,000 turkey-days). In 2018, the predominant classes of antimicrobials used were bacitracins, streptogramins and trimethoprim-sulfas. The quantity of antimicrobials used for growth promotion (adjusted for population and weight) decreased to zero between 2014 and 2018.

For marine finfish and land-based and freshwater net pen facilities, only tetracycline (oxytetracycline), florfenicol and trimethoprim-sulfonamides were reported to be used.

For companion animals (not including horses), the predominant classes of antimicrobials distributed for use were cephalosporins, penicillins and the trimethoprim-sulfonamides.

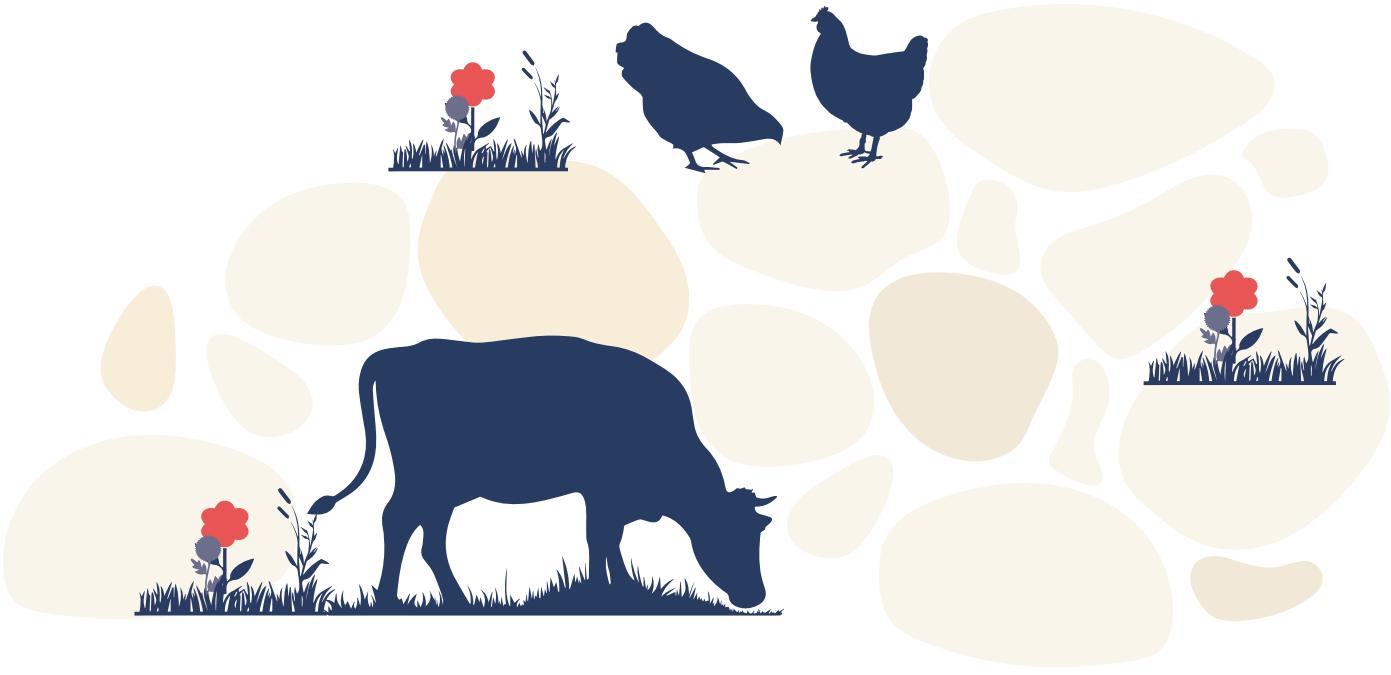
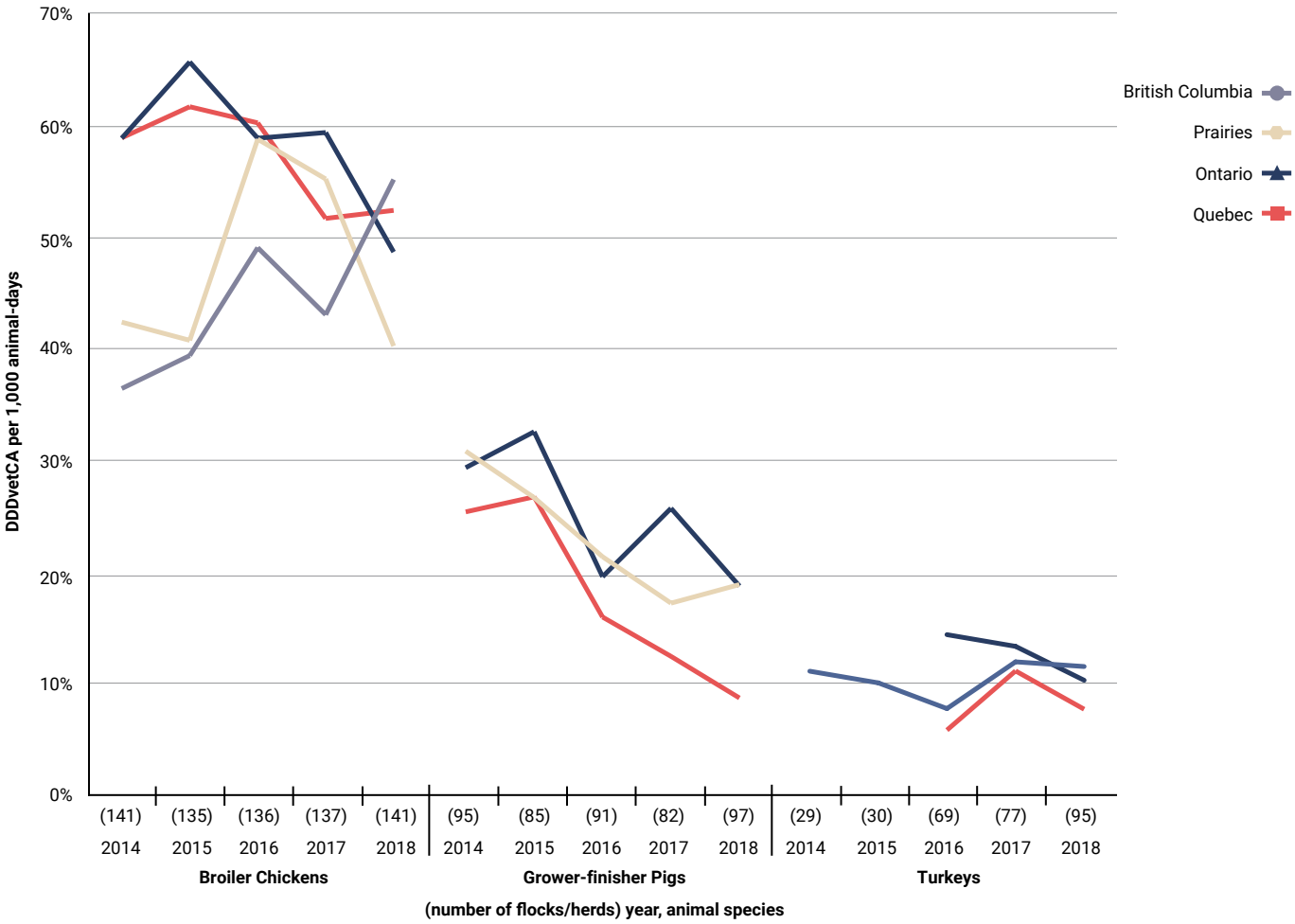


Figure 19: Quantity of antimicrobials used in broiler chickens, pigs (via feed), and turkeys on sentinel farms, Canada, 2014–2018



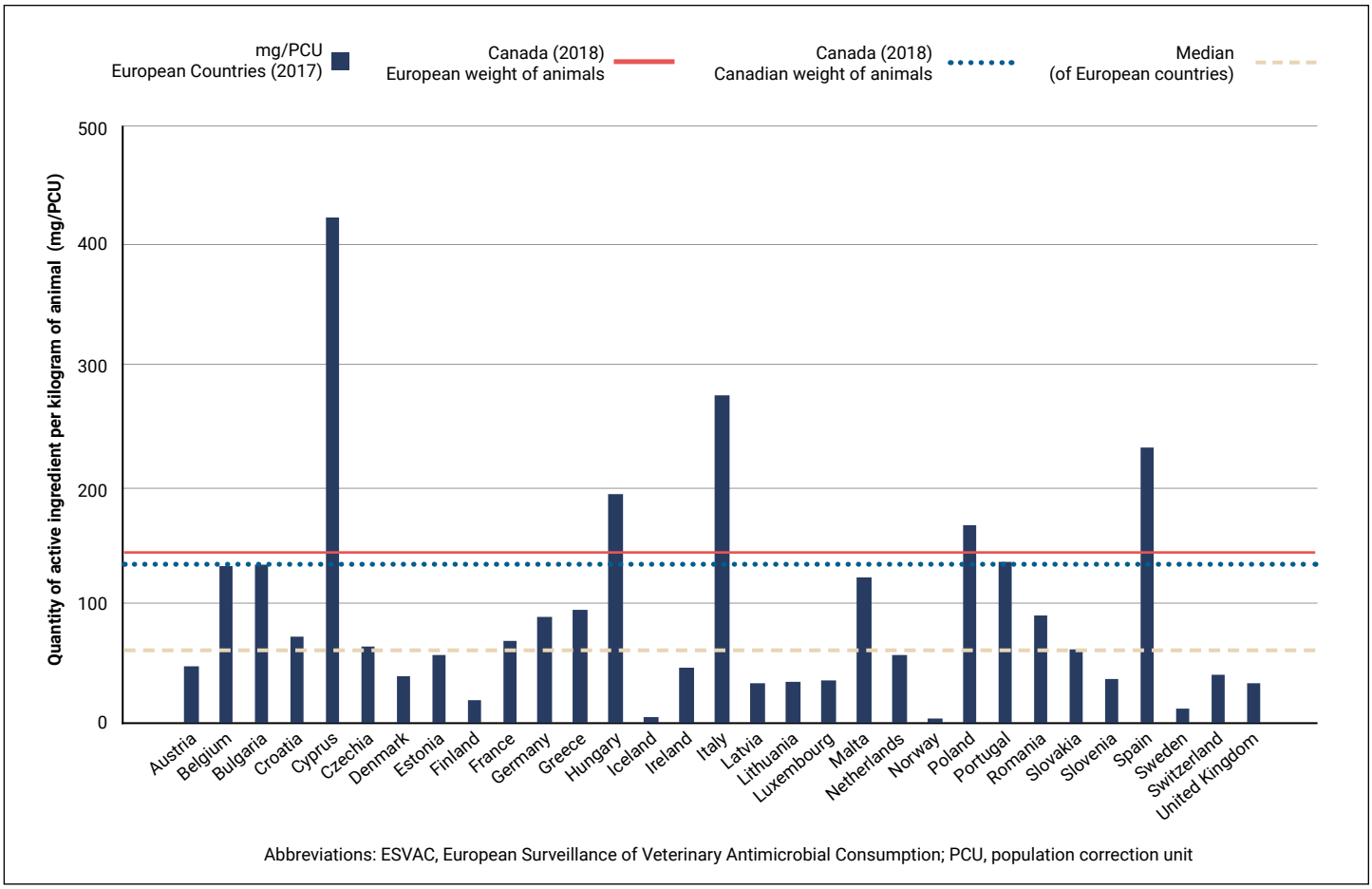
Abbreviations: DDDvetCA - the assumed average dose per kg animal per species per day (using Canadian dose standards).

Animal antimicrobial consumption: International perspective

The European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) Network collects and reports data on the quantity of antimicrobials sold and/or distributed for use in animals for 31 European countries[24]. These data are reported in mg/PCU and were the best publicly available source of data for country-specific international comparisons at the time of publication.

Overall, Canada distributed and/or sold the sixth highest quantity of antimicrobials intended for use in animals (2018 data, using European standard animal weights) when compared to the 31 European countries in the ESVAC Network (2017 data). Canada sold 48 times more antimicrobials than Norway (the country with the lowest sales) and three times less than Cyprus (the country with the highest sales).

Figure 20: Antimicrobials intended for use in animals, Canada and 31 ESVAC Network countries



Abbreviations: ESVAC, European Surveillance of Veterinary Antimicrobial Consumption; PCU, population correction unit


9

CHAPTER 9

DATA INTEGRATION HIGHLIGHTS

Key findings

- In 2018, a total of 1.28 million kilograms of active antimicrobial ingredient were consumed in Canada (including humans, animals and crops).
- Between 2013 and 2018, the frequency of resistance to third-generation cephalosporins in *Salmonella* isolated from broiler chickens and humans decreased. This was associated with a national ban on the use of antimicrobials of very high importance to human health for disease prevention in chickens, voluntarily implemented by the Canadian poultry industry.

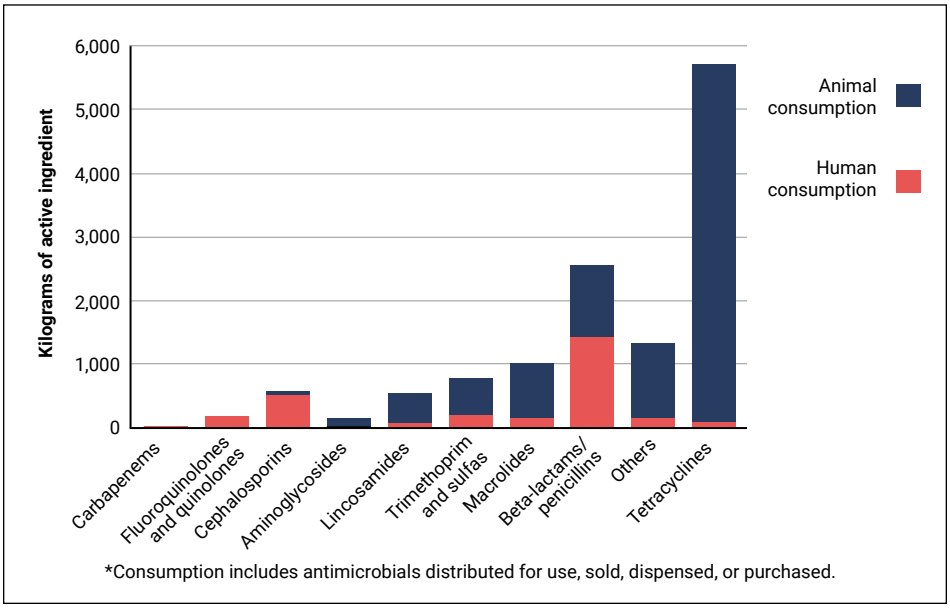
Total antimicrobial consumption in Canada

The total kilograms of active antimicrobial ingredient consumed (including antimicrobials distributed, sold, dispensed, or purchased) in the human and animal sectors can be calculated through the integration of data sourced from IQVIA, Health Canada and the Canadian Animal Health Institute.

In 2018, a total of 1.28 million kilograms of active antimicrobial ingredient was consumed in Canada. The animal sector represented 79%, the human sector represented 21%, and antimicrobials intended for use in crops represented <1%. However, there were approximately 21 animals for every human in Canada (an underestimate, as the number of fish receiving antimicrobials is only reported in kilograms and therefore cannot be included).

While similar antimicrobial classes were consumed in the animal and human sectors, the distribution of use varied. The weight in kilograms of tetracyclines, macrolides, trimethoprim and sulfas, lincosamides and aminoglycosides were predominately consumed in the animal sector; whereas cephalosporins and fluoroquinolones were predominately consumed in the human sector. The weight in kilograms of β-lactams/penicillins consumed was more evenly divided between the animal sector and the human sector (0.14 and 0.11 million kilograms of active antimicrobial ingredient, respectively). In Canada, carbapenems have never been licensed for use in animals.

Figure 21: Kilograms of antimicrobials consumed* in the animal and human sectors, Canada, 2018



Ceftriaxone resistance in broiler chicken flocks and people

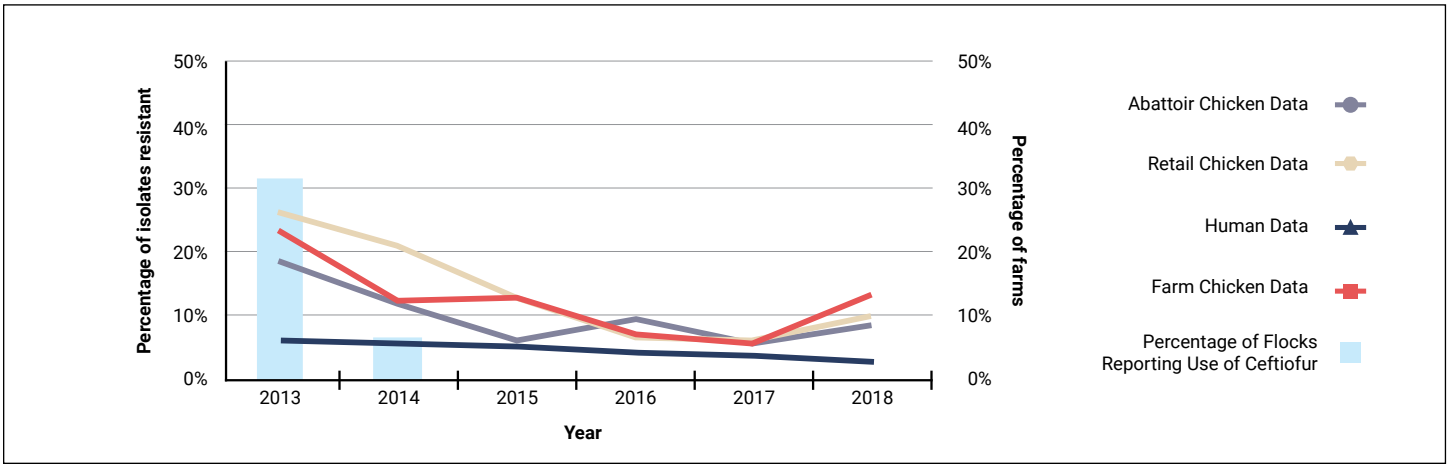
The impact of antimicrobial stewardship interventions in the Canadian food chain can be investigated by integrating data from sentinel farm surveillance (antimicrobial use) and antimicrobial susceptibility testing results of isolates recovered from sentinel farms, abattoirs, retail meat and people with zoonotic enteric bacterial illness.

In 2014, the Canadian poultry industry implemented a national ban on the use of antimicrobials of very high importance to human health (i.e. Category I antimicrobials, as defined by Health Canada[25]) for disease prevention, including the use of third-generation cephalosporins (e.g. ceftiofur). Since 2015, there has been no reported use of ceftiofur in sentinel broiler chicken flocks, as well as an overall decrease in observed resistance to third-generation cephalosporins (e.g. ceftriaxone) in *Salmonella* isolated from chickens and chicken meat.

> Although ceftriaxone is not used in animals in Canada, organisms can develop resistance to ceftriaxone through exposure to similar drugs (e.g. ceftiofur). In most situations, if an organism is resistant to one of these drugs, it will be resistant to the other.

The reduction in ceftiofur use in broiler chicken flocks and associated overall decrease in ceftriaxone resistance in *Salmonella* isolates from chickens and humans is a good example of a successful intervention to limit antimicrobial resistance. However, between 2017 and 2018, resistance to ceftriaxone increased in *Salmonella* isolated from broiler chickens (from 6.0% to 13.0%). This increase is currently being investigated and highlights the need for ongoing surveillance.

Figure 22: Reduction in reported use of ceftiofur on farm and changing resistance to ceftriaxone in non-typhoidal *Salmonella* from humans and chicken sources, Canada, 2013–2018




10

CHAPTER 10

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11

CHAPTER 11

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12

CHAPTER 12

APPENDICES

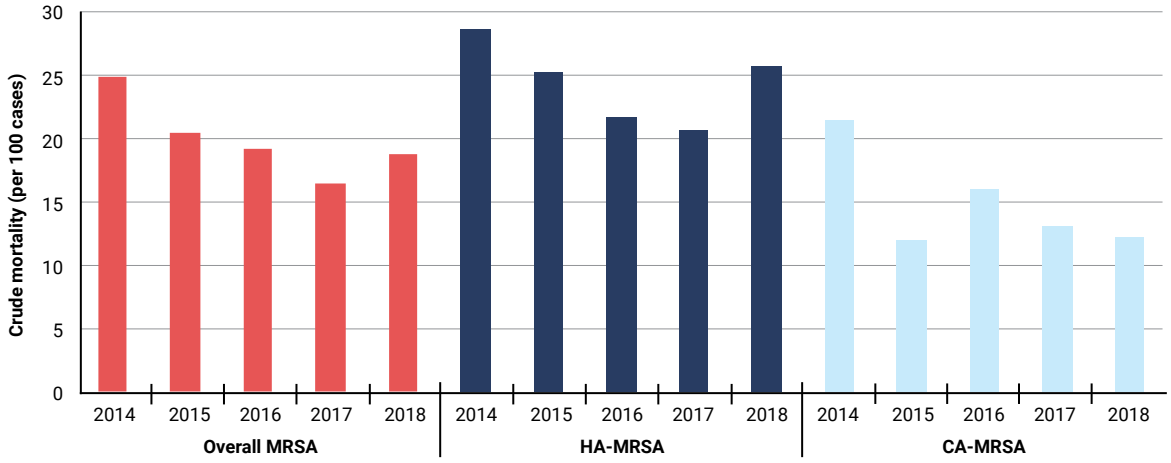
Appendix A: Antibiotics included in each antimicrobial class (i.e. ATC grouping) – Human sector

Atc4	Atc4 description	Atc5	Atc5 description	Molecule
A07a	Intestinal anti-infectives	A07aa	Antibiotics	Fidaxomicin
				Vancomycin
J01a	Tetracyclines	J01aa	Tetracyclines	Doxycycline
				Minocycline
				Tetracycline
				Tigecycline
J01b	Amphenicols	J01ba	Amphenicols	Chloramphenicol
J01c	Beta-lactam antibacterials, penicillins	J01ca	Penicillins with extended spectrum	Amoxicillin
				Ampicillin
				Piperacillin
		J01ce	Beta-lactamase sensitive penicillins	Penicillin g
				Penicillin v
		J01cf	Beta-lactamase resistant penicillins	Cloxacillin
				Dicloxacillin
				Flucloxacillin
				Oxacillin
		J01cr	Combinations of penicillins, incl. Beta-lactamase inhibitors	Amoxicillin:clavulanic acid
				Clavulanic acid:ticarcillin
				Piperacillin
				Piperacillin:tazobactam
J01d	Other beta-lactam antibacterials	J01db	First-generation cephalosporins	Cefadroxil
				Cefazolin
				Cephalexin
		J01dc	Second-generation cephalosporins	Cefaclor
				Cefoxitin
				Cefprozil
				Cefuroxime
		J01dd	Third-generation cephalosporins	Cefixime
				Cefotaxime
				Ceftazidime
				Ceftriaxone
		J01de	Fourth-generation cephalosporins	Cefepime
		J01df	Monobactams	Aztreonam
		J01dh	Carbapenems	Cilastatin:imipenem
				Ertapenem
				Meropenem
		J01di	Other cephalosporins and penems	Ceftobiprole medocaril
				Ceftolozane:tazobactam

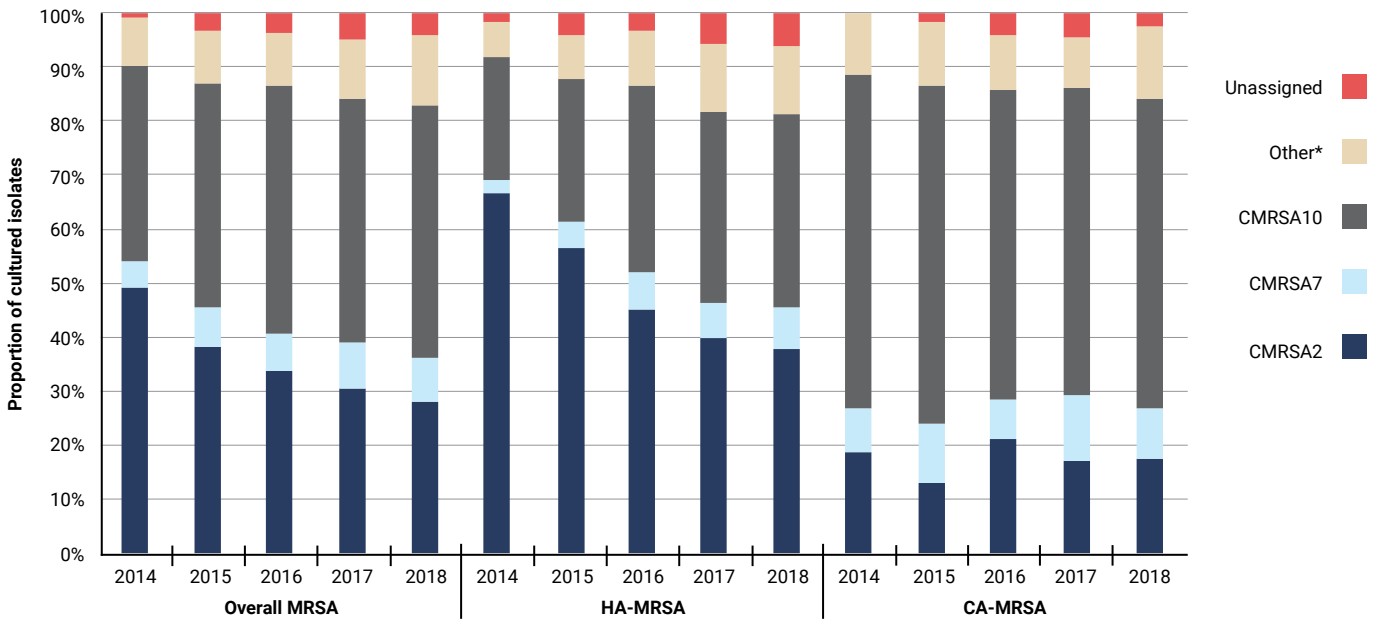
Atc4	Atc4 description	Atc5	Atc5 description	Molecule
J01e	Sulfonamides and trimethoprim	J01ea	Trimethoprim and derivatives	Trimethoprim
		J01ec	Intermediate-acting sulfonamides	Sulfadiazine
				Sulfamethoxazole
		J01ee	Combinations of sulfonamides and trimethoprim, incl. Derivatives	Sulfamethoxazole:trimethoprim
J01f	Macrolides, lincosamides and streptogramins	J01fa	Macrolides	Azithromycin
				Clarithromycin
				Erythromycin
				Erythromycin ethylsuccinate
				Spiramycin
		J01ff	Lincosamides	Clindamycin
				Lincomycin
J01g	Aminoglycoside antibacterials	J01ga	Streptomycins	Streptomycin
		J01gb	Other aminoglycosides	Amikacin
				Gentamicin
				Tobramycin
J01m	Quinolone antibacterials	J01ma	Fluoroquinolones	Ciprofloxacin
				Gatifloxacin
				Levofloxacin
				Moxifloxacin
				Norfloxacin
				Ofloxacin
J01x	Other antibacterials	J01xa	Glycopeptide antibacterials	Telavancin
				Vancomycin
		J01xb	Polymyxins	Colistin
				Polymyxin b
		J01xc	Steroid antibacterials	Fusidic acid
		J01xd	Imidazole derivatives	Metronidazole
		J01xe	Nitrofuran derivatives	Nitrofurantoin
		J01xx	Other antibacterials	Bacitracin
				Daptomycin
				Fosfomycin
				Linezolid
				Methenamine
P01a	Agents against amoebiasis and other protozoal diseases	P01ab	Nitroimidazole derivatives	Metronidazole

Appendix B: Supplementary Figures

Crude mortality for overall, healthcare-associated (HA) and community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infection, Canada, 2014–2018

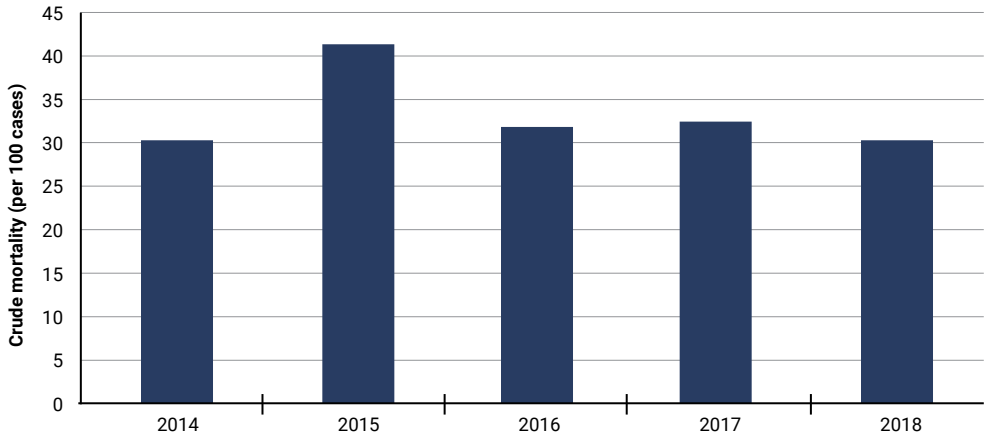


Strain types of overall, healthcare-associated (HA), and community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA) blood isolates, Canada, 2014–2018

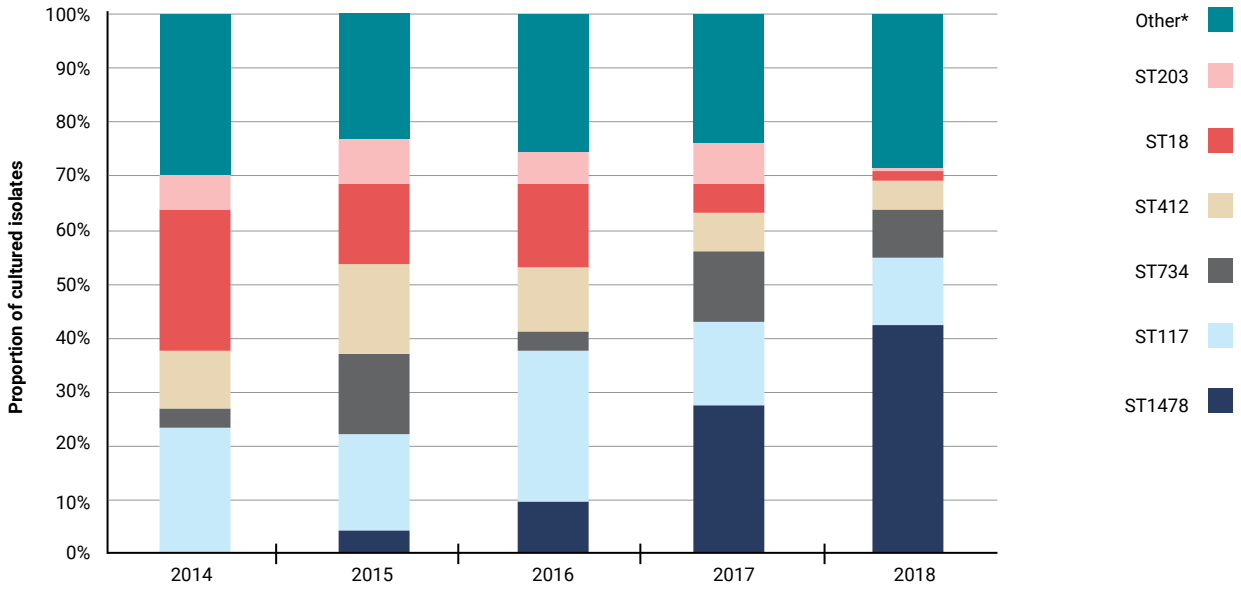


*Other strain types from 2014 to 2018 include CMRSA 1, CMRSA 3/6, CMRSA 4, CMRSA 5, CMRSA 8, ST72, ST88, ST97, ST398, ST772, USA 700, USA 1000, USA 1100 and European.

Crude mortality for healthcare-associated vancomycin-resistant *Enterococcus* bloodstream infection, Canada, 2014–2018

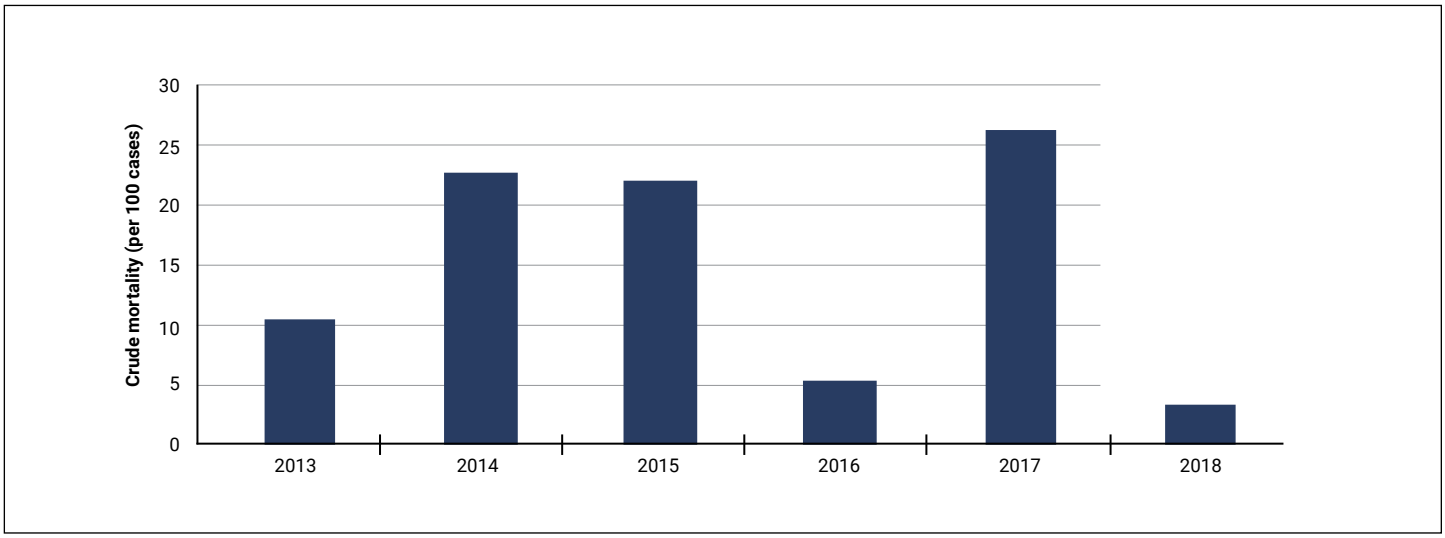


Sequence types of healthcare-associated vancomycin-resistant *E. faecium* blood isolates, Canada, 2014–2018

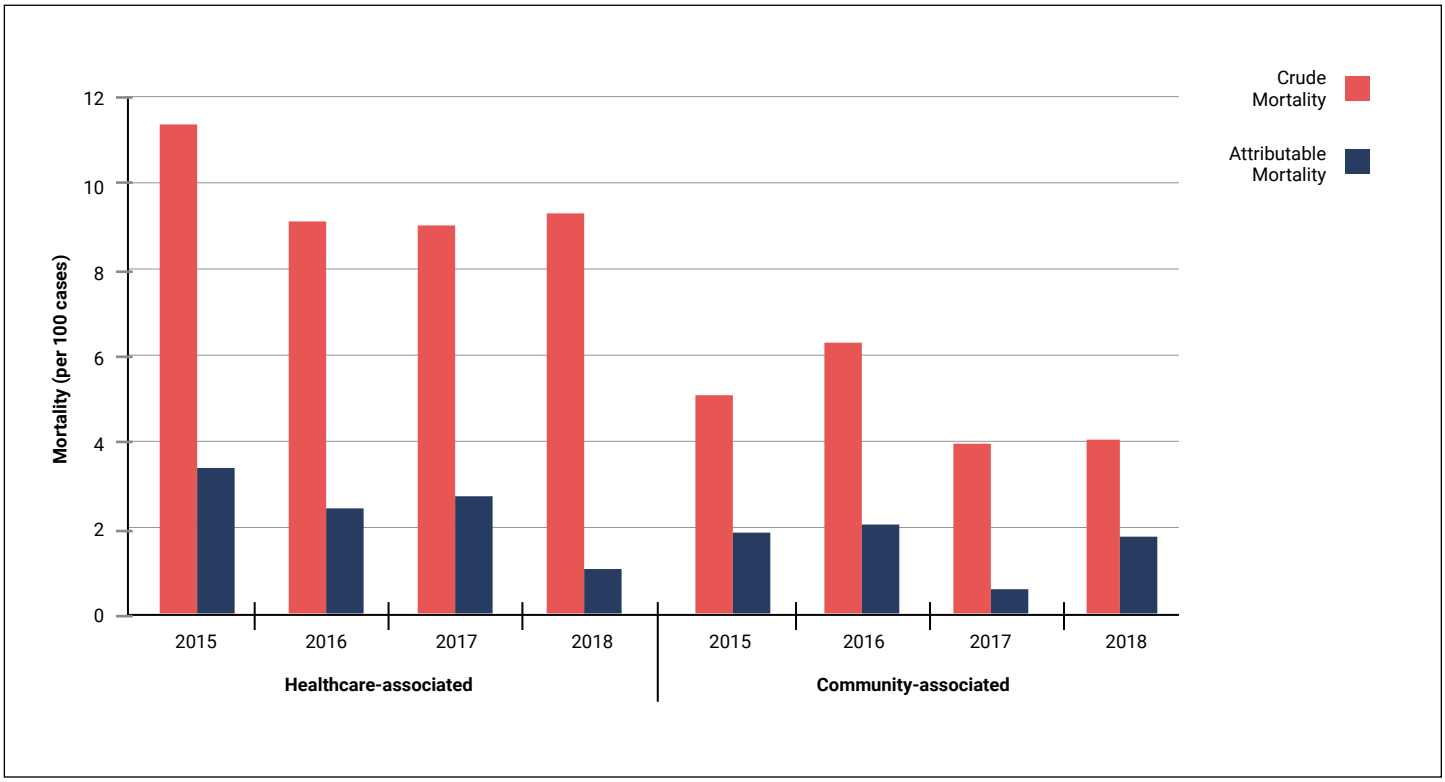


Note: "Other" include ST16, ST17, ST56, ST78, ST80, ST154, ST192, ST233, ST252, ST262, ST280, ST282, ST375, ST414, ST494, ST584, ST612,ST662,ST663, ST664, ST665, ST721, ST736, ST750, ST761, ST772, ST787, ST802, ST835, ST836, ST912, ST982, ST983, ST984, ST992, ST1032, ST1112, ST1113, ST1265, ST1421, ST1424, ST1497, ST1587, and ST1612.

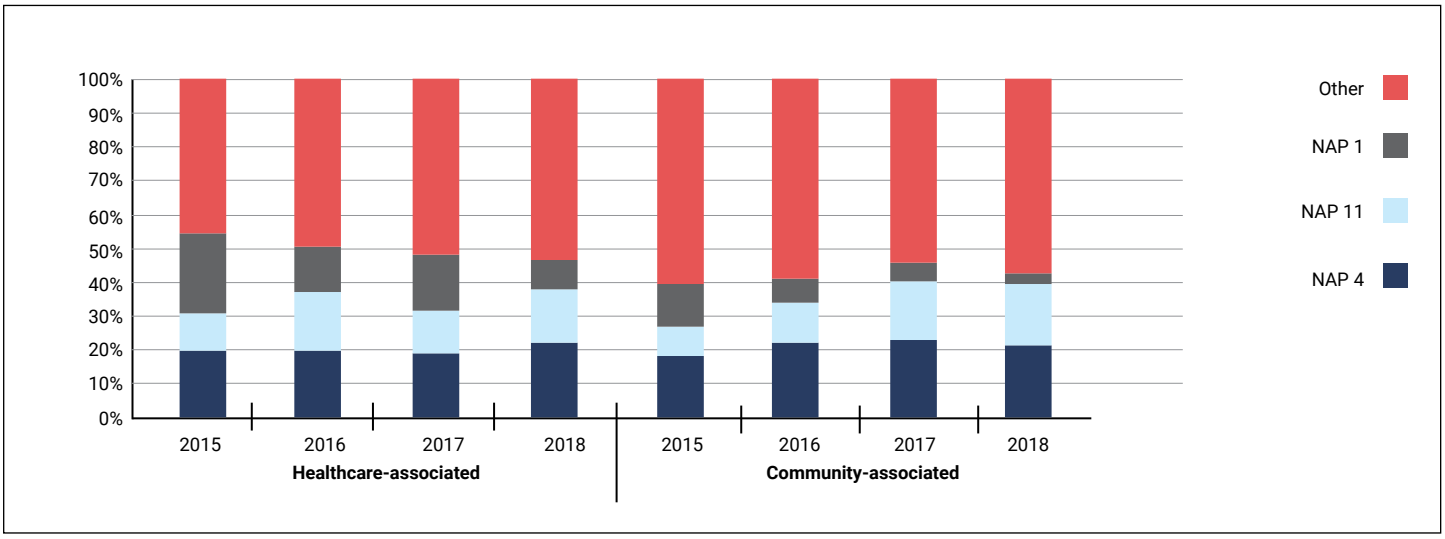
Crude mortality for healthcare-associated carbapenemase-producing Enterobacteriaceae infection, Canada, 2014–2018



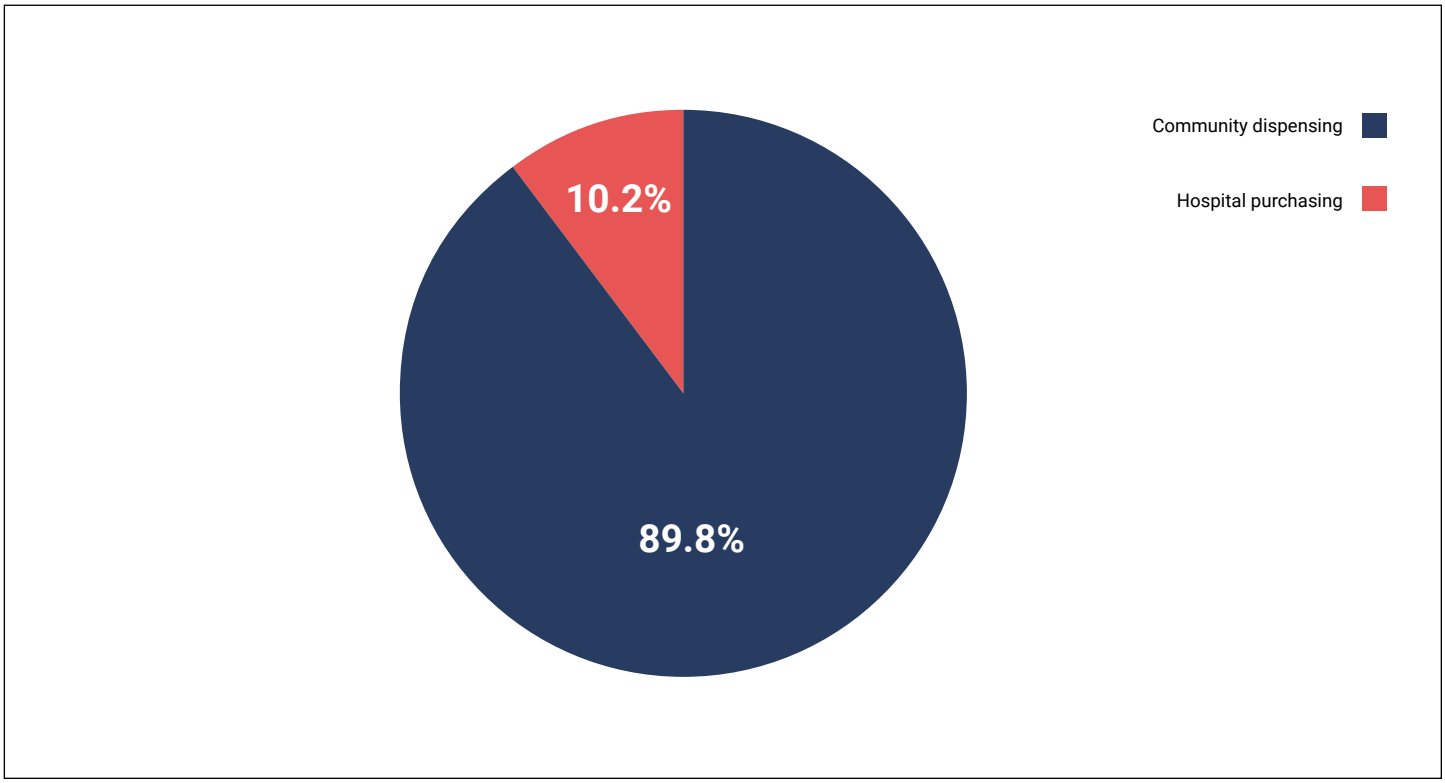
Crude and attributable mortality for healthcare-associated and community-associated *Clostridioides difficile* infection, Canada, 2015–2018



North American pulsed field (NAP) type of healthcare-associated and community-associated *Clostridioides difficile* infection, Canada, 2015–2018



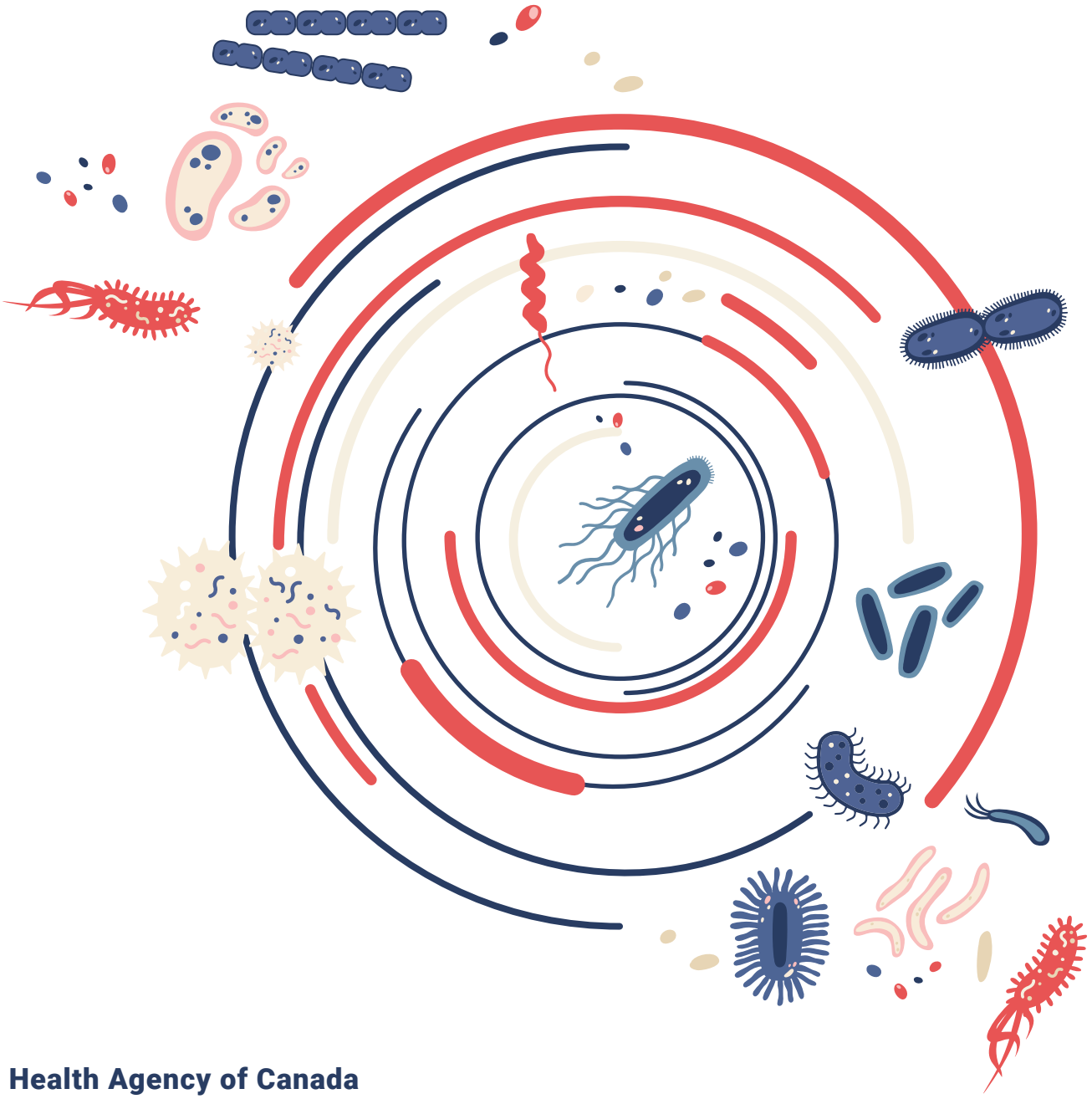
National human consumption of antimicrobials (Defined Daily Doses per 1,000 inhabitants), purchased by hospitals and dispensed by retail pharmacies, Canada, 2018



Appendix C: Participating CNISP Hospitals

Hospital Name	City	Province
Alberta Children's Hospital	Calgary	AB
BC Children's Hospital	Vancouver	BC
BC Women's Hospital	Vancouver	BC
Bridgepoint Active Healthcare	Toronto	ON
Burin Peninsula Health Care Centre	Burin	NL
Carbonear General Hospital	Carbonear	NL
Children's Hospital of Eastern Ontario (CHEO)	Ottawa	ON
Children's Hospital of Western Ontario	London	ON
Civic Campus, Ottawa Hospital	Ottawa	ON
Dartmouth General Hospital	Halifax	NS
Dr. G.B. Cross Memorial Hospital	Clarenville	NL
Foothills Medical Centre	Calgary	AB
General Campus, Ottawa Hospital	Ottawa	ON
General Hospital & Miller Centre	St. John's	NL
General Hospital, Hamilton Health Sciences Centre	Hamilton	ON
Halifax Infirmary	Halifax	NS
Health Sciences Centre-Winnipeg	Winnipeg	MB
Hôpital Maisonneuve-Rosemont	Montréal	QC
Hospital for Sick Children	Toronto	ON
Hôtel-Dieu de Québec	Québec	QC
IWK Health Centre	Halifax	NS
Janeway Children's Hospital and Rehabilitation Centre	St. John's	NL
Jurvinski Hospital and Cancer Center, Hamilton Health Sciences Centre	Hamilton	ON
Kelowna General Hospital	Kelowna	BC
Kingston General Hospital	Kingston	ON
Lachine Hospital, McGill University Health Centre	Montréal	QC
Lion's Gate	North Vancouver	BC
McMaster Children's Hospital, Hamilton Health Sciences Centre	Hamilton	ON
Montreal Children's Hospital, McGill University Health Centre	Montréal	QC
Montreal General Hospital, McGill University Health Centre	Montréal	QC
Montreal Neurological Institute, McGill University Health Centre	Montréal	QC
Mount Sinai Hospital	Toronto	ON
Nanaimo Regional General Hospital	Nanaimo	BC
North York General Hospital	Toronto	ON
Pasqua Hospital	Regina	SK
Peter Lougheed Centre	Calgary	AB

Hospital Name	City	Province
Powell River General Hospital	Powell River	BC
Prince County Hospital	Summerside	PE
Princess Margaret	Toronto	ON
Queen Elizabeth Hospital	Charlottetown	PE
Regina General Hospital	Regina	SK
Rehabilitation Centre	Halifax	NS
Richmond General Hospital	Richmond	BC
Rockyview General Hospital	Calgary	AB
Royal Jubilee	Victoria	BC
Royal University Hospital	Saskatoon	SK
Royal Victoria Hospital, McGill University Health Centre	Montréal	QC
Sechelt Hospital (formerly St. Mary's)	Sechelt	BC
SMBD - Jewish General Hospital	Montréal	QC
South Health Campus	Calgary	AB
Squamish General Hospital	Squamish	BC
St Joseph's Healthcare	Hamilton	ON
St. Clare's Mercy Hospital	St. John's	NL
St. Paul's Hospital	Saskatoon	SK
Stollery Children's Hospital	Edmonton	AB
Sudbury Regional Hospital	Sudbury	ON
Sunnybrook Hospital	Toronto	ON
The Moncton Hospital	Moncton	NB
Toronto General Hospital	Toronto	ON
Toronto Western Hospital	Toronto	ON
UBC Hospital	Vancouver	BC
University Hospital	London	ON
University Hospital of Northern BC	Prince George	BC
University of Alberta Hospital	Edmonton	AB
University of Manitoba Children's Hospital	Winnipeg	MB
University of Ottawa Heart Institute, Ottawa Hospital	Ottawa	ON
Vancouver General Hospital (VGH)	Vancouver	BC
Veterans Memorial Building	Halifax	NS
Victoria General	Halifax	NS
Victoria General Hospital	Victoria	BC
Victoria Hospital	London	ON
Western Memorial Regional Hospital	Corner Brook	NL



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