

CANADIAN ANTIMICROBIAL RESISTANCE SURVEILLANCE SYSTEM

UPDATE 2018



PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH



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

Également disponible en français sous le titre :

Système canadien de surveillance de la résistance aux antimicrobiens – mise à jour 2018

To obtain additional copies, please contact:

Public Health Agency of Canada

Address Locator 0900C2

Ottawa, ON K1A 0K9

Tel.: 613-957-2991

Toll free: 1-866-225-709

Fax.: 613-941-5366

TTY: 1-800-465-7735

E-mail: publications@canada.ca

This publication can be made available in alternative formats upon request.

© Her Majesty the Queen in Right of Canada, as represented by the Minister of Health, 2018

Publication date: November 2018

This publication may be reproduced for personal or internal use only without permission provided the source is fully acknowledged.

Cat.: HP37-21E-PDF

ISBN: 2369-0712

Pub.: 180540

CANADIAN ANTIMICROBIAL RESISTANCE SURVEILLANCE SYSTEM

Update 2018

TABLE OF CONTENTS

TABLE OF CONTENTS.....	I
GLOSSARY.....	III
INTRODUCTION.....	1
EXECUTIVE SUMMARY	2
Antimicrobial resistance.....	2
Carbapenemase-producing organisms	2
<i>Clostridioides difficile</i> infection	3
Methicillin-resistant <i>Staphylococcus aureus</i>	3
Vancomycin-resistant enterococci	4
<i>Neisseria gonorrhoeae</i>	4
Enteric bacteria from food sources and production animals	4
Highlights from new surveillance activities	5
Antimicrobial use	5
Antimicrobial use in humans	5
Antimicrobial use in food-producing animals, companion animals, and crops.....	6
Conclusion	6
Next steps.....	7
TECHNICAL ANNEX.....	8
Antimicrobial resistance and use	8
Carbapenemase-producing <i>Enterobacteriaceae</i>	10
<i>Clostridioides difficile</i>	12
Methicillin-resistant <i>Staphylococcus aureus</i>	15
Vancomycin-resistant enterococci.....	17
<i>Streptococcus pyogenes</i>	19
<i>Streptococcus pneumoniae</i>	20
<i>Neisseria gonorrhoeae</i>	21
<i>Mycobacterium tuberculosis</i>	23
Typhoidal <i>Salmonella enterica</i> (serovars Typhi and Paratyphi).....	24
Non-typhoidal <i>Salmonella enterica</i>	25
Resistance in enteric bacteria from food sources.....	26
1a. Generic <i>Escherichia coli</i> from chicken.....	27
1b. Generic <i>Escherichia coli</i> from pigs (pork).....	28
1c. Generic <i>Escherichia coli</i> from cattle (beef)	29
1d. Generic <i>Escherichia coli</i> from turkey	30
2a. <i>Salmonella</i> in chicken.....	31
2b. <i>Salmonella</i> in turkey	32
3a. <i>Campylobacter</i> spp. from chicken.....	33
3b. <i>Campylobacter</i> spp. from turkey	34
Surveillance Pilots	35

Hospital antibiogram data for <i>Escherichia coli</i>	35
The Community, Northern, and Rural Acute Care Point Prevalence Survey (CNAPP)	36
Human antimicrobial use in Canada	37
Overall results	37
Community pharmacy dispensing	38
Hospital purchasing	42
Prescribing in Indigenous and non-Indigenous populations	43
Antimicrobial recommendations by diagnoses	45
Increasing use of antimicrobials of high importance.....	46
Antimicrobials intended for use in animals and crops.....	48
Antimicrobial use in production and companion animals.....	48
Antimicrobial use in production animals	49
Antimicrobial use in grower-finisher pigs	49
Antimicrobial use in broiler chickens.....	49
Antimicrobial use in turkeys	50
Antimicrobial use in marine finfish.....	50
Antimicrobial use in companion animals.....	51
Route of administration	51
Indication for antimicrobial use in animals.....	51
Integration of data on antimicrobials intended for use in humans, animals, and crops.....	52
Integration of data on cephalosporin resistance in non-typhoidal <i>Salmonella</i> and generic <i>Escherichia coli</i>	54
Integration of data on fluoroquinolone resistance in <i>Campylobacter</i>	55
References.....	56
Appendix	57

GLOSSARY

AB	Alberta
AMMI	Association of Medical Microbiology and Infectious Disease
AMR	Antimicrobial resistance
AMU	Antimicrobial use
ARS	Antimicrobial-resistant <i>Streptococcus</i>
BC	British Columbia
BSI	Bloodstream infection
CA-CDI	Community-associated <i>Clostridioides difficile</i> Infections
CAHI	Canadian Animal Health Institute
CA-MRSA	Community-associated methicillin-resistant <i>Staphylococcus aureus</i>
CARSS	Canadian Antimicrobial Resistance Surveillance System
CCHS	Canadian Community Health Survey
CCS	Canadian CompuScript
CDH	Canadian Drugstore and Hospital
CDI	<i>Clostridioides difficile</i> infection
CDTI	Canadian Disease and Therapeutic Index
CHEC	Canadian Hospital Epidemiology Committee
CIDSC	Communicable and Infectious Disease Steering Committee
CIPARS	Canadian Integrated Program for Antimicrobial Resistance Surveillance
CMRSA	Canadian epidemic Methicillin Resistant <i>Staphylococcus aureus</i>
CNDSS	Canadian Notifiable Disease Surveillance System
CNISP	Canadian Nosocomial Infection Surveillance Program
CPE	Carbapenemase-producing <i>Enterobacteriaceae</i>
CPHLN	Canadian Public Health Laboratory Network
CPO	Carbapenamase-producing organisms
CRE	Carbapenem-resistant <i>Enterobacteriaceae</i>
CSC	Canadian CompuScript
CTBRS	Canadian Tuberculosis Reporting System
DDD	Defined Daily Dose
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESAG	Enhanced Surveillance for Antimicrobial Resistant Gonorrhea
ESBL	Extended-spectrum beta-lactamase
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	Europe
Framework	<i>Tackling Antimicrobial Resistance and Antimicrobial Use: A Pan-Canadian Framework for Action</i>
GLASS	Global Antimicrobial Resistance Surveillance System

GNB	Gram-negative Bacilli
HA-CDI	Healthcare-associated <i>Clostridioides difficile</i> infection
HA-MRSA	Healthcare-associated methicillin-resistant <i>Staphylococcus aureus</i>
J01	Antimicrobials for systemic use
Kg	Kilogram
KPC	<i>Klebsiella pneumoniae</i> carbapenemase
MB	Manitoba
MDR	Multidrug-resistant
MDR-TB	Multidrug-resistant Tuberculosis
mg/L	Milligrams per liter
MIA	Medically important antimicrobials
MIC	Minimum Inhibitory Concentration
MLST	Multiple-locus sequence typing
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
MSM	Men who have sex with men
NAAT	Nucleic Acid Amplification Test
NAP	North American pulse-field
NB	New Brunswick
NDM	New Delhi metallo-beta-lactamase
NIHB	Non-Insured Health Benefits
NL	Newfoundland
NML	National Microbiology Laboratory
NS	Nova Scotia
ON	Ontario
PCU	Population Correction Unit
PEI	Prince Edward Island
PHAC	Public Health Agency of Canada
PMRA	Pest Management Regulatory Agency
QC	Quebec
Rx	Prescription
SK	Saskatchewan
SME	<i>Serratia marcescens</i> carbapenemase (SME) producing organisms
STI	Sexually Transmitted Infections
TB	Tuberculosis
TE	Territories
TMP-SMX	Trimethoprim-Sulfamethoxazole
VRE	Vancomycin-resistant enterococci
WHO	World Health Organisation
XDR-TB	Extensively drug-resistant tuberculosis

INTRODUCTION

The Canadian Antimicrobial Resistance Surveillance System (CARSS) is Canada's national system for reporting on antimicrobial resistance and antimicrobial use. CARSS is one of the Public Health Agency of Canada (PHAC)'s commitments as part of the *Pan-Canadian Framework for Action on Antimicrobial Resistance and Antimicrobial Use*¹. CARSS integrates and synthesizes epidemiological and laboratory information from PHAC's surveillance systems that cover humans, food sources, and food-producing animals. By reporting findings on national antimicrobial resistance (AMR) and antimicrobial use (AMU), CARSS provides decision makers with evidence to support policy and programs to foster prudent AMU to prevent, limit, and control AMR in Canada.

All AMR and AMU content outlined in this report merit attention; however, significant changes in AMR and AMU that have a greater impact on public health are specifically highlighted. Also described are new initiatives such as the analysis of standardized hospital antimicrobial susceptibility (antibiogram) data for *Escherichia coli*; the results from a prevalence survey on AMR conducted in smaller non-academic acute care hospitals; and the analysis of the effect of AMU stewardship activities on animal populations.

The CARSS-Update 2018 replaces previously reported data with the most recent AMR and AMU surveillance information available. The surveillance results published by CARSS change from year to year, as data quality is improved (e.g., case reporting by hospitals), or as metrics become more accurate (e.g., antimicrobial purchasing data from hospitals, adjusted for antimicrobial returns over time). Therefore, when possible, the results should be referenced from the most recent CARSS publication. The surveillance systems and their methods, as well as the other data systems that informed the CARSS-Update 2018, are summarized later in this publication and are described in greater detail in the CARSS-2017 report².

The CARSS-Update 2018 is comprised of two parts: an Executive Summary, designed to highlight the most relevant AMR and AMU results; and a Technical Annex, that provides a more detailed look at AMR and AMU surveillance data. Within the Technical Annex there are three sections: an AMR section that focuses on priority organisms; an AMU section that focuses on antimicrobials intended for human use; and a section that contains information on antimicrobials intended for use in food-producing animals, companion animals, and crops.

EXECUTIVE SUMMARY

This Executive Summary provides an overview of the key findings from CARSS, summarizes the current state of surveillance on antimicrobial resistance (AMR) and antimicrobial use (AMU), and describes next steps.

Key findings from the Canadian Antimicrobial Resistance Surveillance System (CARSS)-Update 2018:

- Increase in colonization by carbapenemase-producing organisms in both hospitals and the community setting;
- Healthcare-associated *C. difficile* infection rates continue to decline;
- The rate of methicillin-resistant *Staphylococcus aureus* (MRSA) infections coming from the community has nearly doubled;
- MRSA bloodstream infections remain high in paediatric hospitals;
- Increasing rates of vancomycin-resistant enterococci infections are still being seen in hospitalized patients;
- Azithromycin resistance in *Neisseria gonorrhoeae* has doubled;
- Prescriptions for adults 60 years and older have continued to increase over time and represent the age group with the greatest use of antimicrobials;
- There was no reported use of fluoroquinolones or third-generation cephalosporins by sentinel chicken farms, consistent with recent policy changes that introduced a ban on the preventative use of Category I antimicrobials on poultry farms across Canada; and
- A decrease in the prevalence of resistance to third-generation cephalosporins was observed in non-typhoidal *Salmonella* spp. collected from chickens, chicken meat, and humans.

Antimicrobial resistance

Carbapenemase-producing organisms

The identification of New Delhi metallo-beta-lactamase (NDM) type carbapenemase-producing organisms (CPOs) in 2009 heralded a new era in emerging AMR. These organisms pose a serious public health threat due to their resistance to most antibiotics and their ability to transmit this resistance to other bacteria. Although CPO infection rates among hospitalized patients have remained low and unchanged for the past five years (0.03 infections per 10,000 patient-days since 2012), the rate of CPO colonization has increased by almost five-fold since 2014 (from 0.03 colonizations per 10,000 patient-days to 0.14 in 2017). Consistent with the trends seen in hospital settings, the number of CPO isolates submitted to provincial public health laboratories continued to increase in 2017 (889 isolates, compared to 779 in 2016), and rising CPO rates have also been reported in other jurisdictions³⁻⁷.

It is not clear whether the increase in CPO colonization rates in Canadian hospital sites is due to greater awareness and reporting as CPOs are now reportable to public health in three provinces (i.e. Ontario, British Columbia and Alberta), or whether it represents a true increase in the colonization rate among Canadians. Regardless of the reasons underlying the increasing rates of CPO colonization, this remains a significant finding.

***Clostridioides difficile* infection**

Over the past decade, Canadian hospitals have implemented a variety of infection prevention and control, antimicrobial stewardship, and quality improvement initiatives to address *Clostridioides difficile* infection (CDI; formerly known as *Clostridium difficile* infection). Healthcare-associated *C. difficile* infection (HA-CDI) rates have steadily decreased over time. In 2017, HA-CDI among hospitalized patients continued to decline, appearing to stabilize at a rate that is almost 40% lower compared to earlier years (3.85 per 10,000 patient-days in 2017, compared to 6.03 in 2012). Since 2015, when surveillance of community-associated (CA)-CDI began in sentinel hospitals, approximately one-third of all CDI cases have been identified as CA-CDI and this proportion remained similar in 2017.

Methicillin-resistant *Staphylococcus aureus*

The rate of methicillin-resistant *Staphylococcus aureus* infection reported by sentinel hospitals continued to increase, from 2.80 per 10,000 patient-days in 2012 to 3.17 in 2017. This trend appears to be driven by community-associated MRSA infections seen in hospitalized patients, increasing by over 60% from 2012 to 2017 (from 0.84 to 1.36 infections per 10,000 patient-days, respectively). Conversely, the rate of healthcare-associated MRSA infection continued to decrease in 2017 (1.65 per 10,000 patient-days, representing a 6% decrease from 1.74 per 10,000 patient-days in 2012).

The overall rate of healthcare-associated MRSA bloodstream infections (BSI) has increased in recent years, from 0.30 per 10,000 patient-days in 2012 to 0.44 in 2017. The previously noted increased rate of healthcare-associated MRSA BSI reported by paediatric hospitals has decreased slightly for the first time since 2013 (0.38 per 10,000 patient-days in 2017 from 0.42 in 2016). In contrast, the overall rate of MRSA BSI that originated in the community has more than doubled since 2012 (0.35 per 10,000 patient-days in 2017 versus 0.14 in 2012). Perhaps due to greater recognition of MRSA as a potential etiologic agent, all-cause mortality among patients with MRSA BSI has continued to decrease significantly (from 22 in 2012 to 16% in 2017).

All tested MRSA isolates remained universally susceptible to vancomycin and linezolid with less than 1% resistance to daptomycin. Of note, there has been a consistent annual decrease in clindamycin resistance, dropping from 84% in 2013 to 42% in 2017.

Vancomycin-resistant enterococci

Vancomycin-resistant enterococci (VRE) infections are typically resistant to multiple antibiotic classes which present health practitioners with limited treatment options. The rate of VRE BSIs in sentinel hospitals continued to rise, from 0.18 infections per 10,000 patient-days in 2016 to 0.23 in 2017. Surveillance data also indicate that the rate of non-BSI VRE infection (including urine and wounds) increased for the first time in 2017 (from 0.26 infections per 10,000 patients-days in 2016 to 0.34). Prior to 2017, the rate of non-BSI VRE infection had been decreasing each year since 2012.

VRE isolates from sentinel hospitals have demonstrated changes in resistance patterns. Over the past two years, daptomycin resistance has been increasing with current non-susceptibility detected in 9% of isolates. Changes in antimicrobial susceptibility were observed among aminoglycosides, with a substantial increase in resistance to high-level (H-L) gentamicin seen in 2017 (39% of isolates tested, compared to 14% in 2016). In contrast, the proportion of isolates with resistance to H-L streptomycin has decreased by 17% since 2014 (from 41% to 34% in 2017). Of note, 45% of VRE isolates were resistant to nitrofurantoin, one of the first-line drugs for treating enterococcal urinary tract infections (especially in the community); this is a three-fold increase from 2012. In 2017, VRE isolates were universally sensitive to linezolid.

Neisseria gonorrhoeae

In Canada, the rate of *Neisseria gonorrhoeae* infection has increased 20% from 55 cases per 100,000 population in 2015 to 65 in 2016. In 2016, fewer isolates were showing decreased susceptibility to cefixime and ceftriaxone (0.3% and 1.8%, respectively). However, the proportion of isolates resistant to azithromycin increased by over 50%, from 5% in 2015 to 7% in 2016. Extensively-drug resistant *N. gonorrhoeae* remains rare in Canada, with a single imported case reported in 2017⁸.

Enteric bacteria from food sources and production animals

Among enteric bacteria collected from chickens and chicken meat, there was a continued decrease in the prevalence of resistance to third-generation cephalosporins. The proportion of *E. coli* isolates from chicken meat that were resistant to ceftriaxone decreased from 28% in 2013 to 6% in 2017. In *Salmonella* spp. isolates from chicken meat tested at retail outlets, as well as in these isolates from chicken on sentinel farms, resistance to ceftriaxone was 6% in 2017 (decreased from over 20% in 2013). Over the same time period, there was also a significant decrease in ceftriaxone resistance in human non-typhoidal *Salmonella* spp. isolates (from 6% in 2013 to 4% in 2017).

Highlights from new surveillance activities

In 2016, standardized hospital antibiogram data for *Escherichia coli* (*E. coli*) were collected. There were minimal changes in resistance patterns from 2015 to 2016; however, in 2016 higher levels of non-susceptibility to sulfamethoxazole-trimethoprim (23%) and ciprofloxacin (19%) were still found.

A pilot study was conducted in 2017 among 30 northern, smaller community and rural acute care hospitals in nine Canadian provinces and all territories to assess the prevalence of AMR in non-academic healthcare settings. A survey conducted during one 24-hour period found MRSA, VRE, CPOs, extend-spectrum beta-lactamase-producing *Enterobacteriaceae* or CDI in approximately one quarter of patients who had a microbiological result available.

Antimicrobial use

Antimicrobial use in humans

In 2017, a combined total of 262,590 kilograms of antimicrobials were either dispensed through community pharmacies or purchased by hospitals, reflecting a total expenditure of approximately \$822 million. As in previous years, the majority of human antimicrobial use in Canada occurred in the community setting, where 92% of antimicrobials were dispensed through retail pharmacies. The remaining proportion (8%) was purchased for use by hospitals.

In the same year, a combined total of 19.5 Defined Daily Doses (DDDs) per 1,000 inhabitant-days was dispensed by community pharmacies or purchased by hospitals. Stated another way, this means that on an average day, 2% of the Canadian population could be receiving an antimicrobial to treat or prevent a bacterial infection.

Nationally, there was no observed change in the overall amount of antimicrobials dispensed in the community; however, as seen in previous years, community prescription rates varied by province. In 2017, the rate of prescriptions (per 1,000 inhabitants) was lower in all territories combined (358.6) and in British Columbia (569.3), and greater in Prince Edward Island/Newfoundland and Labrador (combined 970.2) compared to other provinces. Prescribing rate varied by antimicrobial, with amoxicillin remaining the most frequently community dispensed drug (164.0 prescriptions per 1,000 inhabitants).

Antimicrobial purchasing was twice as high in hospitals within Atlantic provinces as it was in Ontario in 2017. Canadians aged 60 years or older continued to receive antimicrobials at a rate nearly 60% greater than that seen among adults aged 15 to 59 years (923.1 prescriptions versus 577.3 prescriptions per 1,000 inhabitants) with prescription rates continuing to rise over time. Conversely, antimicrobial prescriptions among children under the age of 15 years continued to decrease, most recently from 610.0 prescriptions per 1,000 inhabitants in 2016 to 577.1 in 2017. Differences were seen in the indication for antimicrobial treatments among adults and children. The most common indications for antimicrobials in

adults were respiratory and urinary tract infections, whereas among children, 43% of antimicrobial recommendations were for treatment of otitis media.

Antimicrobial use in food-producing animals, companion animals, and crops

Surveillance of antimicrobial use in animals is an important component of an integrated approach towards addressing antimicrobial stewardship and antimicrobial resistance in Canada. The Canadian Animal Health Institute (CAHI) provides data to PHAC regarding the quantity of antimicrobials that are distributed for use in animals. In 2017, the total volume of these antimicrobials, excluding ionophores and chemical coccidiostats, was approximately 950,000 kilograms, or nearly four times the amount used in humans. The quantity of antimicrobials intended for use in animals was 11% lower than in 2016, and represents the lowest volume of sales since reporting began in 2006. Almost all antimicrobials were distributed for use in food-producing animals.

Overall, there was a significant increase in the number of sentinel farms reporting no use of medically important antimicrobials. In 2017, 32% of pig farms and 19% of chicken farms reported no use of these products, compared to 11% and 7% in 2016, respectively. There was no reported use of fluoroquinolones or third-generation cephalosporins by sentinel chicken farms, consistent with recent policy changes that introduced a ban on the preventative use of Category I antimicrobials on poultry farms across Canada.

Conclusion

The CARSS-Update 2018 highlights several critical areas requiring monitoring to inform research, stewardship, and infection prevention and control interventions. Future surveillance will require examining new data sources, leveraging existing information in novel ways, extending surveillance into different settings, and forming innovative partnerships. Ongoing collaborations with regional, provincial, territorial and federal health authorities, and other stakeholders, will improve surveillance for both antimicrobial resistant infections and the use of antimicrobials in Canada.

Next steps

In collaboration with partners, PHAC is continuing to strengthen AMR and AMU surveillance through the following initiatives:

- Targeted surveillance to better understand the rate of CPO colonization in the community through new initiatives with provincial and local partners;
- Expand surveillance activities to capture patients admitted to hospitals with AMR infections that are acquired in the community;
- Improve the representativeness of hospital-based AMR surveillance through enrolment of additional hospitals in remote areas;
- Align practices with international stakeholders by collecting data on all *Staphylococcus aureus* bloodstream infections as of 2018 (previously only MRSA BSI), so that the proportion of resistant infections can be determined;
- Collect antimicrobial susceptibility (antibiogram) data for *E. coli* infections as a first step to identify patterns of resistance for bacterial infections in health-care settings, with consideration being given to expanding the number of organisms captured in the surveillance initiative;
- Building on the success of the pilot projects, implement point prevalence studies to assess AMR and prescribing practices in northern and smaller community hospitals, as well as long term care facilities;
- Begin to develop an interactive data display and visualisation platform to show community-level antimicrobial susceptibility data (AMR-Net);
- Understand antimicrobial prescribing practices in the community through a cross-sectional survey that collects information related to in-home AMU practices, including compliance and patient understanding as to why and how the antimicrobial was prescribed; and
- Include results from freshwater finfish aquaculture AMU surveillance in future reports.

TECHNICAL ANNEX

Antimicrobial resistance and use

The following technical annex provides an update on available information on the priority organisms monitored under PHAC’s surveillance systems. The priority organisms included in the following CARSS-AMR 2018 technical annex are: carbapenemase-producing *Enterobacteriaceae*, *Clostridioides difficile* (formally known as *Clostridium difficile*), methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus* spp., *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Neisseria gonorrhoeae*, *Mycobacterium tuberculosis*, typhoidal *Salmonella enterica*, and non-typhoidal *Salmonella enterica*. This section also includes updates on AMR in bacteria recovered from retail meat (i.e., *Campylobacter* spp., *Salmonella* spp. and generic *E. coli*).

The technical annex also includes updates on antimicrobial use (AMU). With regard to antimicrobials intended for use in humans, data sources include antimicrobials dispensed through community pharmacies, as well as antimicrobials purchased by hospitals. For antimicrobials intended for use in animals (including fish) and crops, data sources include antimicrobials distributed for sale, and farm level data providing indications for antimicrobial use.

The following table aligns PHAC AMR surveillance results to the contributing surveillance program. Specific methodology and program design facets have been previously described in the 2017 CARSS report, and have been summarized in the appendix. Further information can be obtained from PHAC program specific reports, where available.

Organism	PHAC surveillance program	Key aspects of sampling/data collection
Carbapenemase-producing <i>Enterobacteriaceae</i>	The <i>Canadian Nosocomial Infection Surveillance Program</i> (CNISP)	Surveillance of select antimicrobial resistant organisms and healthcare-associated infections in 66 large acute care hospitals in 10 provinces. Representation of smaller community and northern hospitals is limited.
<i>Clostridioides difficile</i>		
Methicillin-resistant <i>Staphylococcus aureus</i>		
Vancomycin-resistant <i>Enterococcus</i> spp.		
<i>Streptococcus pyogenes</i>	The <i>National Surveillance of Invasive Streptococcal Disease</i>	Passive surveillance system monitoring antimicrobial susceptibilities in <i>S. pyogenes</i> and <i>S. pneumoniae</i> . Includes cultures and/or data submitted by public health laboratories covering all provinces and territories.
<i>Streptococcus pneumoniae</i>		
<i>Neisseria gonorrhoeae</i>	The <i>Antimicrobial-resistant Neisseria gonorrhoeae Surveillance System</i> and the <i>Enhanced Surveillance of Gonorrhoeae</i> (ESAG)	Antimicrobial susceptibilities of <i>N. gonorrhoeae</i> are monitored through submission of cultures and/or data from public health laboratories in 9 provinces and one territory. Three provinces participate in ESAG, which integrates laboratory data with enhanced epidemiologic case information, including risk factors and treatment.
<i>Mycobacterium tuberculosis</i>	The <i>Canadian Tuberculosis Reporting System</i> (CTBRS) and the <i>Canadian Tuberculosis Lab Surveillance System</i> (CTBLSS)	CTBRS and CTBLSS are case-based and isolate-based surveillance systems for TB in Canada, respectively, covering all 13 provinces and territories. TB drug resistance test results for all culture positive specimens are submitted annually to the CTBLSS by public health laboratories. CTBRS captures over 90% of all active TB cases in Canada, and includes epidemiologic data collected by provincial/territorial health authorities such as country of origin and treatment outcome.
Typhoidal and non-typhoidal <i>Salmonella enterica</i> spp. in humans	The <i>Canadian Integrated Program for Antimicrobial Resistance Surveillance</i> (CIPARS)	<i>Salmonella enterica</i> spp. isolates from humans are forwarded for antimicrobial susceptibility testing from public health laboratories in all 13 provinces and territories. This includes outbreak or non-outbreak associated isolates, but submission is voluntary and passive. All <i>S. Newport</i> and <i>S. Typhi</i> isolates are submitted. In 4 provinces with relatively higher number of samples, only isolates received in the first 15 days each month are sent on for antimicrobial susceptibility testing.
<i>Campylobacter</i> spp., <i>Salmonella enterica</i> spp. and <i>E. coli</i> in retail meat		Isolates are recovered from beef, pork, chicken, and turkey meat from randomly selected retail outlets in several regions across Canada. In 2017, this included four provinces.

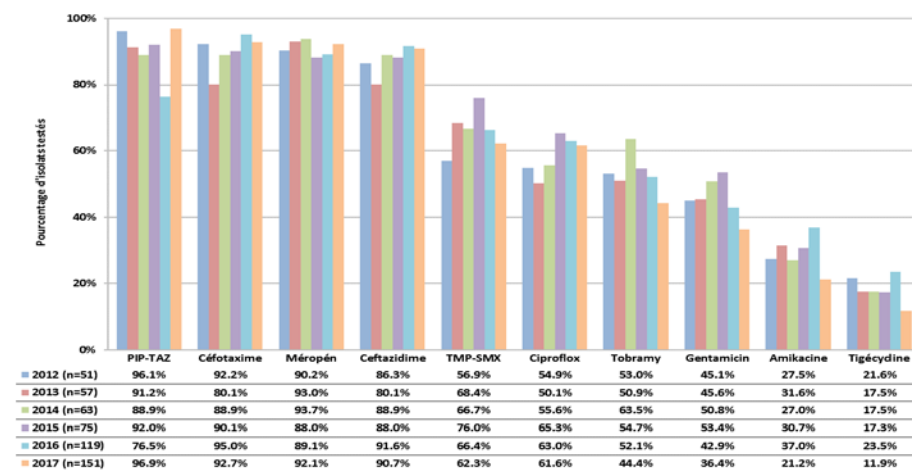
Carbapenemase-producing *Enterobacteriaceae*

Carbapenem class antimicrobials remain highly effective for treating infections caused by gram-negative bacilli. However, since 2009, there has been a trend in isolates producing carbapenemase, an enzyme that makes the organism resistant to carbapenem treatment. Infections caused by carbapenemase-producing *Enterobacteriaceae* (CPE) have limited treatment options and are often associated with poor outcomes.

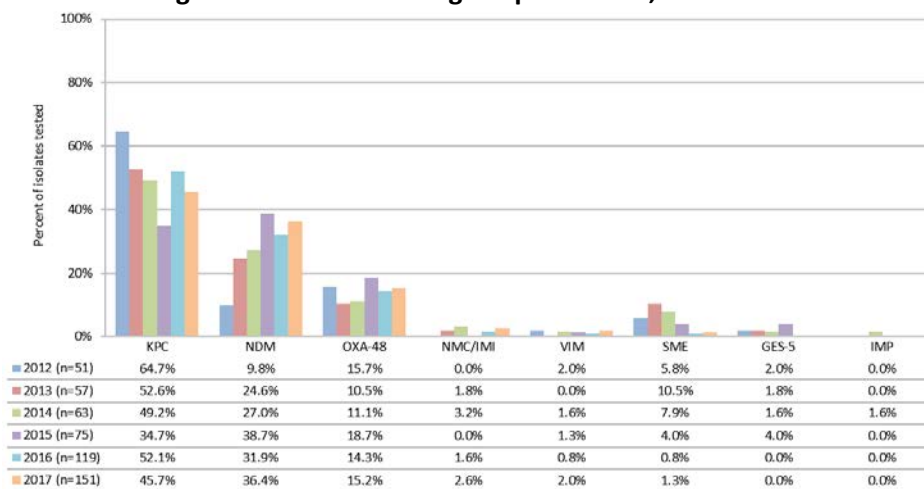
Overall, the number of CPE infections among hospitalized patients remained low (17 cases reported from 59 sentinel hospitals in 2017), and the rate of CPE infection among hospitalized patients remained stable at 0.03 cases per 10,000 patient-days from 2012 to 2017 (approximately one-thousand times lower than the 2017 infection rate of methicillin-resistant *Staphylococcus aureus*). However, CPE colonization rates among hospitalized patients increased by nearly five-fold since 2014 (from 0.03 cases per 10,000 patient-days in 2012 to 0.14 cases in 2017). This increase may be related to increased awareness, changes to screening practices, true increases in colonized cases including transmission within Canada, or a combination of these factors. The all-cause mortality rate for patients infected with a CPE from 2012 to 2017 was 18.3%. *Klebsiella pneumoniae* carbapenemase (KPC) continued to be the most common CPE gene (from 10% in 2012 to 46% in 2017), followed by New Delhi Metallo-beta-lactamase (from 65% in 2012 to 36% in 2017). Consistent with the trends in this report, the number of CPE isolates submitted to provincial public health laboratories continued to increase (from 779 in 2016 to 889 in 2017).

Figure 1: Rate of CPE cases (infections and colonizations) per 10,000 patient-days, 2012-2017



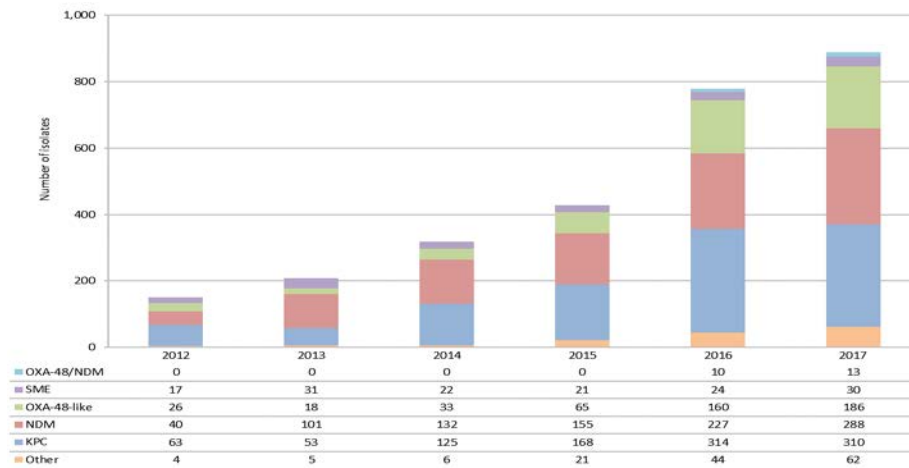
Figure 2: Selected CPE antimicrobial resistance patterns, 2012-2017

Note: PIP-TAZ = Piperacillin-Tazobactam; TMP-SMX = Trimethoprim-Sulfamethoxazole. *Total isolates tested for PIP-TAZ in 2017 = 130. All isolates were resistant to ampicillin, and all but one to cefazolin. All CPO isolates were screened for the *mcr*-type gene (an acquired gene associated with colistin resistance); positive results include one *E. coli* isolate in 2017 that also produced KPC-3.

Figure 3: CPE resistance gene prevalence, 2012-2017

Note: One isolate in 2013, two isolates in 2014, one isolate in 2015, two isolates in 2016, and five isolates in 2017 harboured both NDM and OXA-48 resistance genes.

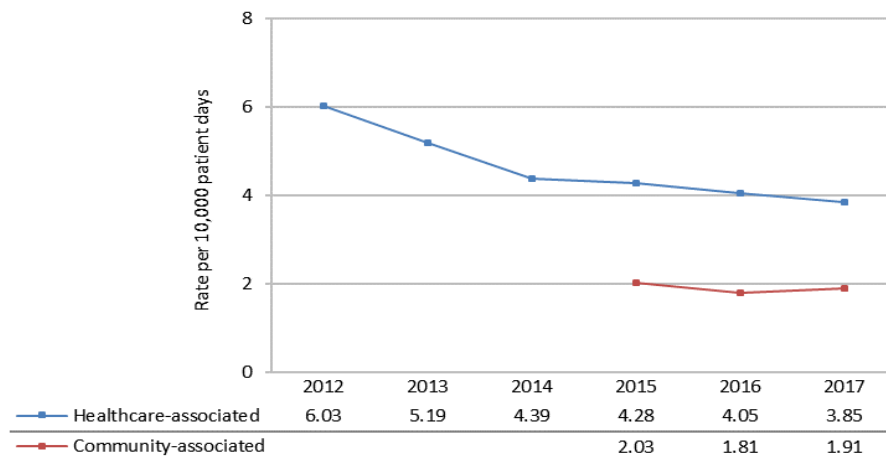
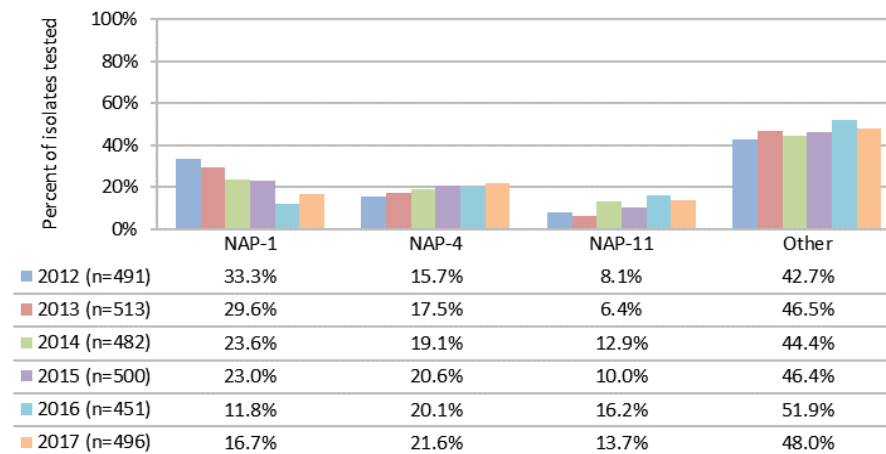
Figure 4: CPE isolates by resistance gene submitted to PHAC by the Canadian Public Health Laboratory Network, 2012-2017



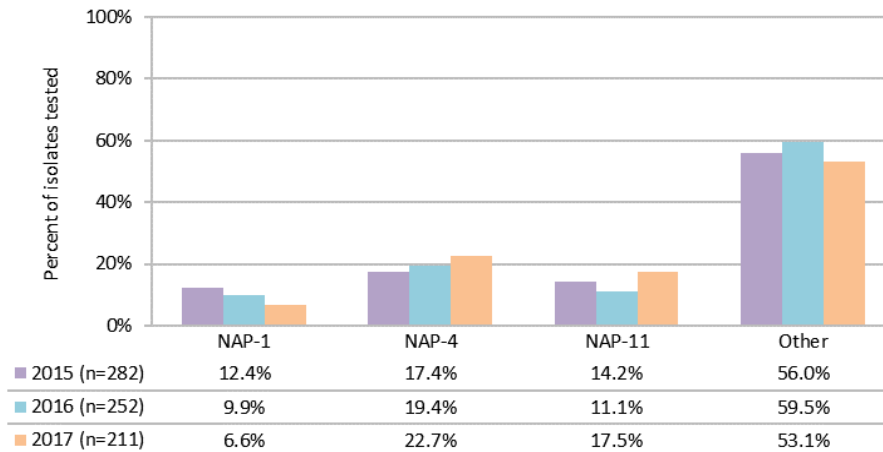
Clostridioides difficile

Clostridioides difficile (*C. difficile*) infection, formally known as *Clostridium difficile*, is an important cause of healthcare-associated infectious diarrhea in Canada, and is associated with the use of antibiotic therapies. Resistance to currently recommended antimicrobial therapies to *C. difficile* infection (CDI), including metronidazole and vancomycin, has not been observed. CDI has been a focus of antimicrobial stewardship and infection prevention and control activities among Canadian hospitals.

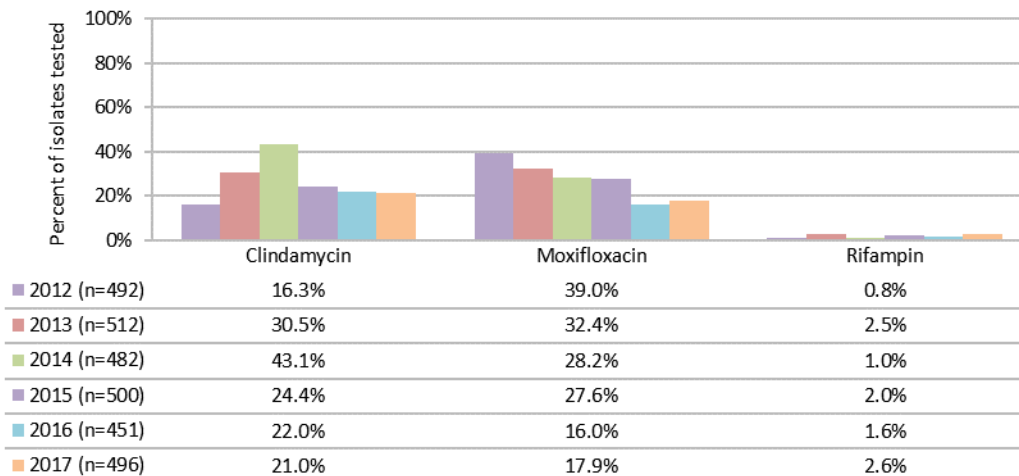
Among hospitalized patients diagnosed with healthcare-associated *C. difficile* infection (HA-CDI), the overall national rate continued to decrease; from 6.03 infections per 10,000 patient-days in 2012 to 3.85 in 2017 (a decrease of 36%). Attributable mortality among adults diagnosed with HA-CDI has decreased 30% since 2012 (from 4.6% to 3.2% in 2017). The most prevalent strain type for HA-CDI in 2017 remained NAP-4 (increasing from 16% in 2012 to 22% in 2017), while NAP-1 continued to decline (from 33% in 2012 to 17% in 2017). While surveillance for community-associated (CA)-CDI began in 2015, a similar trend was reported (NAP-4 increasing from 17% in 2015 to 23% in 2017, and NAP-1 decreasing from 12% in 2015 to 7% in 2017). As of 2017, approximately one third of all CDI cases were reported to be CA-CDI; a trend that aligns with reports published by international partners.

Figure 5: Rate of healthcare-associated (2012-2017) and community-associated (2015-2017) CDI**Figure 6: Healthcare-associated CDI strain type, 2012-2017**

Note: Strains reported as other NAP types include: NAP-2, NAP-3, NAP-5, NAP-6, NAP-7, NAP-8, NAP-9, NAP-10, NAP-12, and strains not assigned a NAP type.

Figure 7: Community-associated CDI strain type, 2015-2017

Note: Strains reported as other NAP types include: NAP-2, NAP-3, NAP-5, NAP-6, NAP-7, NAP-8, NAP-9, NAP-10, NAP-12, and strains not assigned a NAP type. The surveillance of community-associated CDI began in 2015.

Figure 8: Selected healthcare-associated *C. difficile* resistance patterns, 2012-2017

Note: Includes all cases identified among admitted patients acquired within a CNISP hospital. Isolates are collected for typing during a two-month period (March and April of each year) for adults (age 18 years and older) and year-round for children (age 1 year to less than 18 years old).

Methicillin-resistant *Staphylococcus aureus*

Infections caused by *Staphylococcus aureus* (*S. aureus*) are largely associated with skin and soft tissues, however bacterial pneumonia and BSIs are not uncommon. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a *S. aureus* that has acquired resistance to anti-staphylococcal beta-lactam antibiotics (e.g., methicillin, oxacillin, and cefazolin). Resistance to vancomycin has not been found in MRSA infections in Canada.

The overall MRSA infection rate (including bloodstream infections and clinical isolates) continued to increase (from 2.80 cases per 10,000 patient-days in 2012 to 3.17 in 2017) despite a 6% reduction in the rate of healthcare-associated MRSA (HA-MRSA) infections since 2012 (from 1.74 cases per 10,000 patient-days to 1.65 cases in 2017). This trend was primarily driven by a 62% increase in the community-associated (CA)-MRSA infection rate, from 0.84 cases per 10,000 patient-days in 2012 to 1.36 in 2017 (a trend also observed when measured by patient admissions). The overall rate of MRSA BSI remained stable from 2016 to 2017 (from 0.84 per 10,000 patient-days to 0.83), although MRSA BSI reported by paediatric-only hospitals remained higher than rates reported from 2012 to 2015. All-cause mortality among patients with MRSA BSI continued to decline, from 22 deaths per 100 cases in 2012 to 16 in 2017 (a reduction of 26%).

The proportion of MRSA identified as CMRSA2 (a strain more commonly attributed to healthcare-associated infections) decreased by 36% from 2012 to 2017, while the proportion identified as CMRSA10 (a strain more commonly attributed to community-associated infections) increased by 35% from 2012 to 2017. There has been a consistent annual decrease in clindamycin resistance, dropping from 83% of all MRSA isolates tested in 2013 to 42% in 2017, and rifampin remained highly active (1.3% in 2016).

Figure 9: Rate of healthcare-associated and community-associated MRSA infection, 2012-2017

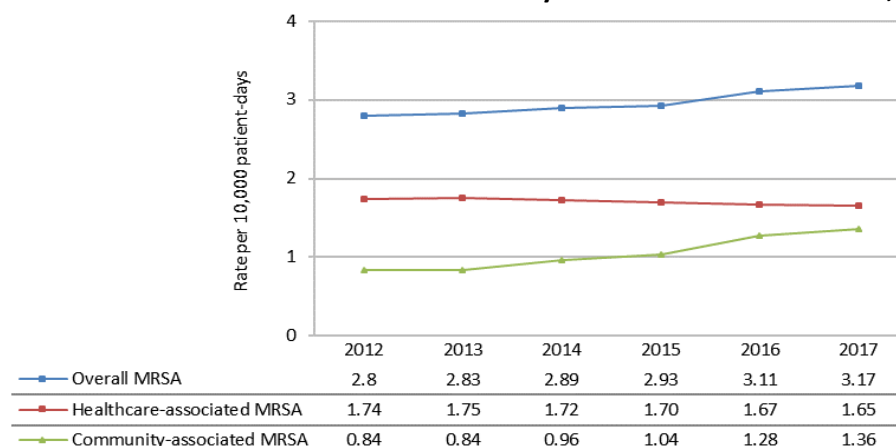
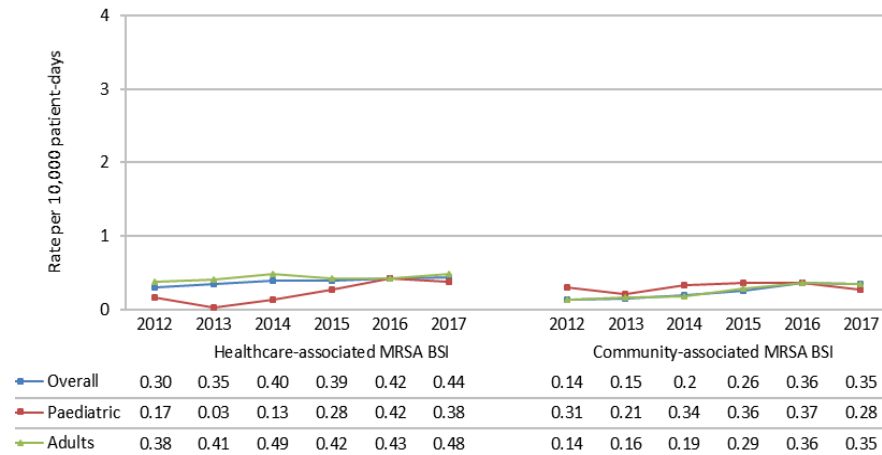


Figure 10: Rate of healthcare-associated and community-associated MRSA bloodstream infections (BSIs) (overall, adult and paediatric), 2012-2017



Note: Paediatric rates derived from participating stand-alone paediatric hospitals, and adult rates derived from participating stand-alone adult hospitals (mixed population hospitals excluded). Overall rates derived from all participating hospitals (stand-alone paediatric, stand-alone adult, and mixed population hospitals).

Figure 11: MRSA strain type, 2012-2017

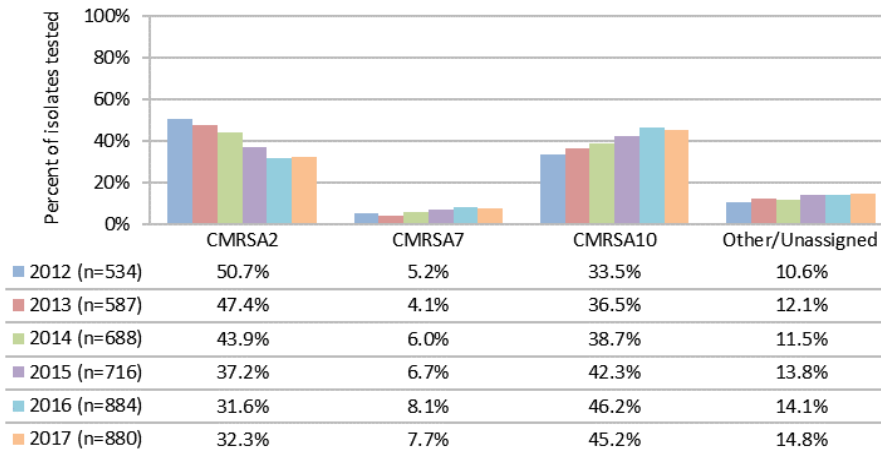
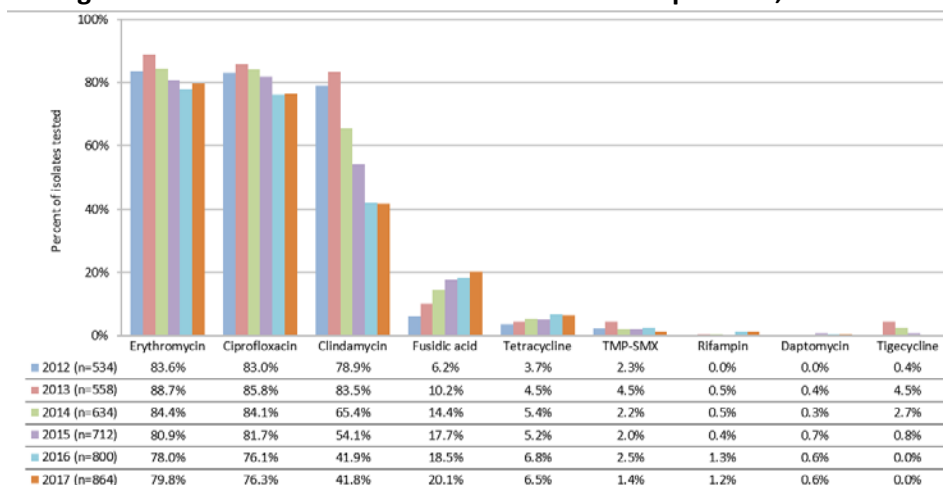


Figure 12: Selected MRSA antimicrobial resistance patterns, 2012-2017

Notes: Total # isolates tested for ciprofloxacin = 271 in 2014 and 104 in 2015. Total # isolates tested for clindamycin = 418 in 2013 and 572 in 2014. MRSA non-blood isolates (urine, respiratory, wound, surgical site) are collected from January to March of every year and blood isolates are collected year round. All MRSA isolates from 2013 to 2017 submitted to NML were susceptible to linezolid and vancomycin. TMP-SMX = Trimethoprim-sulfamethoxazole

Vancomycin-resistant enterococci

Enterococci bacteria are present as part of the normal gastrointestinal flora of both humans and animals, but can cause infections. Enterococci demonstrate a high degree of intrinsic antimicrobial resistance to commonly prescribed antibiotics (e.g., cephalosporins, anti-staphylococcal penicillins, and clindamycin). Vancomycin has long been considered a reliable antibiotic option for the treatment of infections caused by multidrug-resistant *Enterococcus*; however, the acquisition of high-level vancomycin resistance by enterococci has since left clinicians with more limited therapeutic options (e.g., aminoglycosides).

The overall rate of vancomycin-resistant Enterococci (VRE) increased from 0.43 in 2016 to 0.57 in 2017. The rate of VRE BSI increased 64% since 2015, from 0.14 infections per 10,000 patient-days in 2015 to 0.23 in 2017. Additionally, the rate of non-BSI VRE infection (e.g., urine, wound, other) increased for the first time since 2012, from 0.26 cases per 10,000 patient-days in 2016 to 0.34 in 2017 (an increase of 31%). While the proportion of VRE multi-locus sequence type (MLST) identified among VRE infections caused by *E. faecium* decreased since 2012 for ST117, ST18, and ST412, 62% of isolates reported in 2017 were ST1478 (compared to 11% in 2016, and only 5% in 2015). Among VRE BSI isolates, resistance to nitrofurantoin increased from 15% to 45% from 2012 to 2017, and high-level gentamicin resistance increased from 22% to 39% from 2012 to 2017.

Figure 13: Overall rate of VRE infection, VRE bloodstream infection (BSI) and VRE non-bloodstream infection (non-BSI), 2012-2017

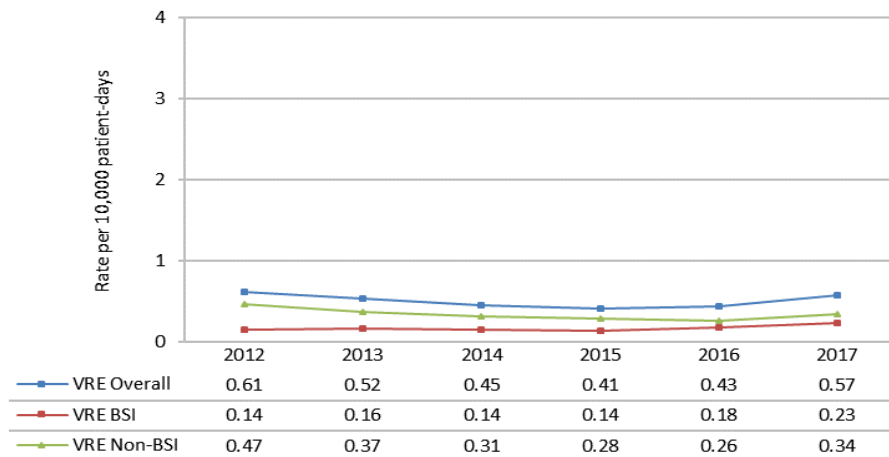
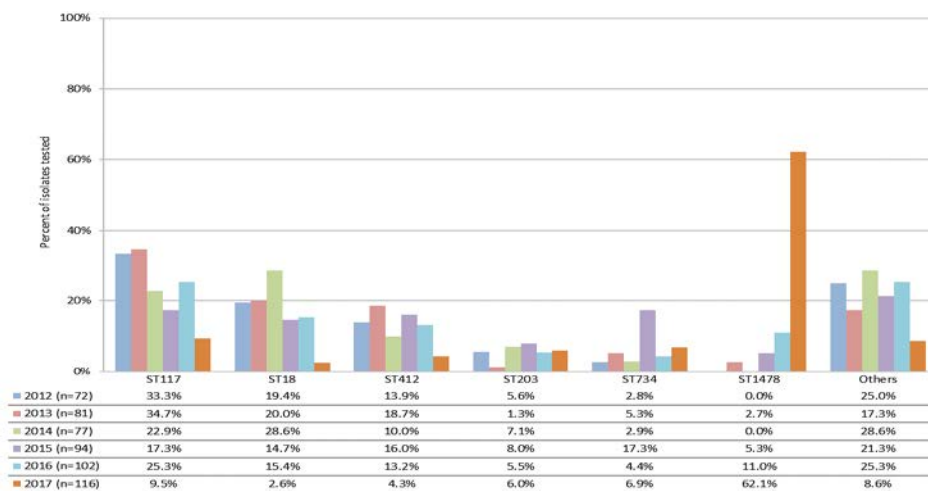
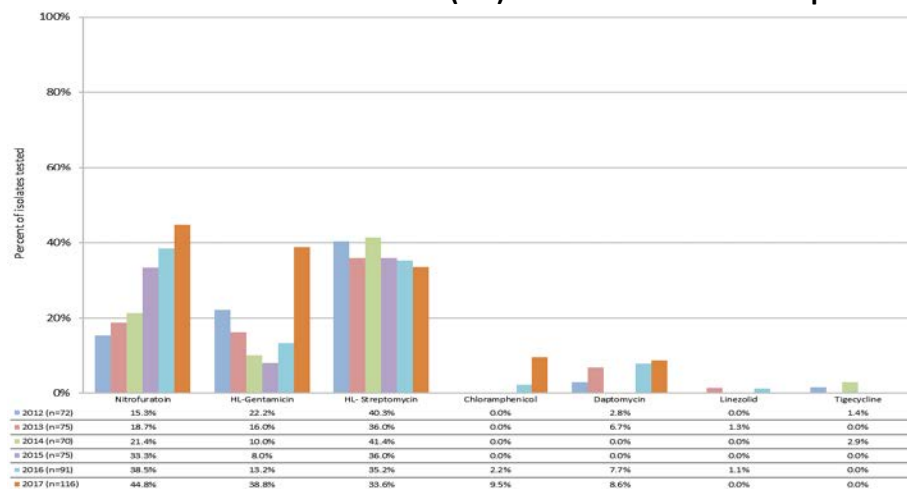


Figure 14: VRE strain type prevalence, 2012-2017



Note: Others include ST17, ST78, ST80, ST203, ST252, ST262, ST282, ST414, ST494, ST584, ST664, ST665, ST721, ST734, ST736, ST772, ST787, ST835, ST836, ST912, ST982, ST983, ST984, ST992, ST1032, ST1112, ST1113 and ST1265.

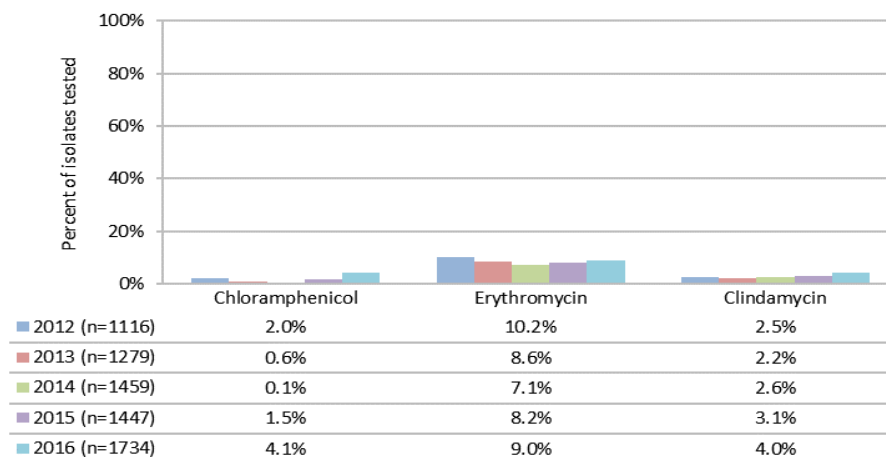
Figure 15: Selected VRE bloodstream infection (BSI) antimicrobial resistance patterns, 2012-2017

Note: The proportion of daptomycin resistance should be interpreted as non-susceptible. All isolates were resistant to ampicillin, levofloxacin, ciprofloxacin, and penicillin.

Streptococcus pyogenes

Streptococcus pyogenes (*S. pyogenes*), commonly referred to as Invasive Group A *Streptococcus* (IGAS), is a Gram positive bacteria responsible for many infections that vary in severity from mild skin infection, scarlet fever and “strep throat”, to bloodstream infections, necrotising fasciitis, and toxic shock. IGAS remains universally susceptible to penicillin class antimicrobials. In 2016, there has been little change in resistance rates to erythromycin or clindamycin at 9% and 4%, respectively.

The surveillance of invasive *S. pyogenes* is laboratory based and does not include the collection of demographic or population level data. Therefore, overall rates of infection are not available. Surveillance results include annual antimicrobial resistance patterns, as presented below.

Figure 16: Selected invasive *S. pyogenes* antimicrobial resistance patterns, 2012-2016

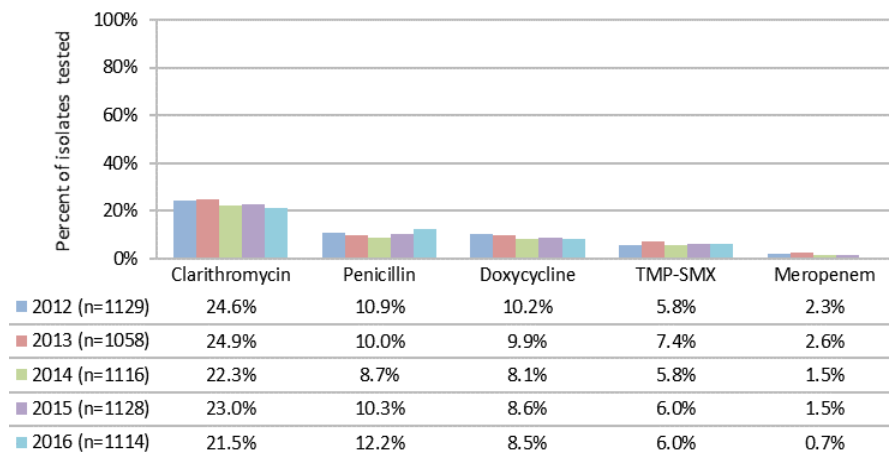
Note: All *S. pyogenes* isolates were susceptible to penicillin and vancomycin.

Streptococcus pneumoniae

Streptococcus pneumoniae (*S. pneumoniae*) is a bacterium that causes a variety of conditions, but can lead to life-threatening disease in susceptible individuals. While most infections are non-invasive and respond well to common antimicrobials, invasive infections can result in meningitis, bloodstream infection, and toxic shock syndrome. As some *S. pneumoniae* develop resistance to antimicrobial therapy, invasive infections can be difficult to treat. The prevention of infection by *S. pneumoniae* serotypes 6C and 19A (known to have higher rates of antimicrobial resistance) can be achieved by immunization with pneumococcal vaccines.

The surveillance of invasive *S. pneumoniae* is laboratory based and does not include the collection of demographic or population level data. Therefore, overall rates of infection are not available. Surveillance results include annual antimicrobial resistance patterns, as presented below. Penicillin resistance remained largely unchanged, reaching 12% in 2016, and the proportion of isolates classified as multidrug resistant (MDR) decreased from 8.0% in 2012 to 6.2% in 2016.

Figure 17: Selected *S. pneumoniae* antimicrobial resistance patterns, 2012-2016



Note: All *S. pneumoniae* isolates tested by PHAC were susceptible to vancomycin, ertapenem, daptomycin, linezolid, and tigecycline.

Neisseria gonorrhoeae

Neisseria gonorrhoeae (*N. gonorrhoeae*) is the causative agent of gonorrhea, the second most common sexually transmitted infection reported in Canada. In 2013, a decrease in susceptibility to cephalosporins prompted Canada to adopt combination therapy (i.e., azithromycin administered with ceftriaxone or cefixime) for gonorrhea as standard treatment. To date, combination therapy has not resulted in confirmed treatment failure for gonorrhea in Canada; however, treatment failure has been reported by the United Kingdom and Australia.

The overall rate of gonorrhea continued to increase in Canada, rising from 55 cases per 100,000 population in 2015 to 65 in 2016 (an increase of 18%). Of the 23,708 cases reported in 2016, only 4,538 (19%) were cultured, of which 65% were resistant to at least one antimicrobial being tested. The number of *N. gonorrhoeae* cultures being performed is in decline, due to the continued shift in diagnostic practice towards Nucleic Acid Amplification Testing (NAAT). This presents a challenge to laboratories monitoring the rates of antimicrobial resistance among *N. gonorrhoeae* isolates, as cultures are the gold standard for antimicrobial susceptibility testing.

With regard to the currently recommended antimicrobial therapy for gonorrhea, decreased susceptibility to cephalosporins declined from 2015 to 2016; cefixime (MIC \geq 0.25 mg/L) decreased from 1.9% in 2015 to 0.3% in 2016, and ceftriaxone (MIC \geq 0.125 mg/L) decreased from 3.5% in 2015 to 1.8% in 2016. However, resistance to azithromycin increased 53%; from 4.7% in 2015 to 7.2% in 2016.

In order to improve the understanding of current levels and trends of AMR gonorrhea in Canada and to provide better evidence to inform the development of treatment guidelines and public health interventions, PHAC launched the Enhanced Surveillance of Antimicrobial Resistant Gonorrhea (ESAG) in 2013. This enhanced laboratory-epidemiological linked surveillance program collects demographic information, risk behaviours, infection site, antimicrobial resistance and susceptibility, sequence typing, and prescribed treatment information. Treatment data collected by ESAG in 2016 indicated that the majority of cases were prescribed either the preferred or alternative therapies as proposed by the Canadian Guidelines of Sexually Transmitted Infections (CG-STI). Among gay, bisexual, and other men who have sex with men (gbMSM), 87% were prescribed either the preferred or alternative therapy proposed by the CG-STI for anogenital or pharyngeal infections. Among other adults, including females, transgender, and non-gbMSM males, there was a high level of adherence to the guidelines for anogenital infections (85%), and a lower level for pharyngeal infections (80%).

Figure 18: Percent of *N. gonorrhoeae* isolates demonstrating resistance to azithromycin or decreased susceptibility to cefixime or ceftriaxone, 2011-2016

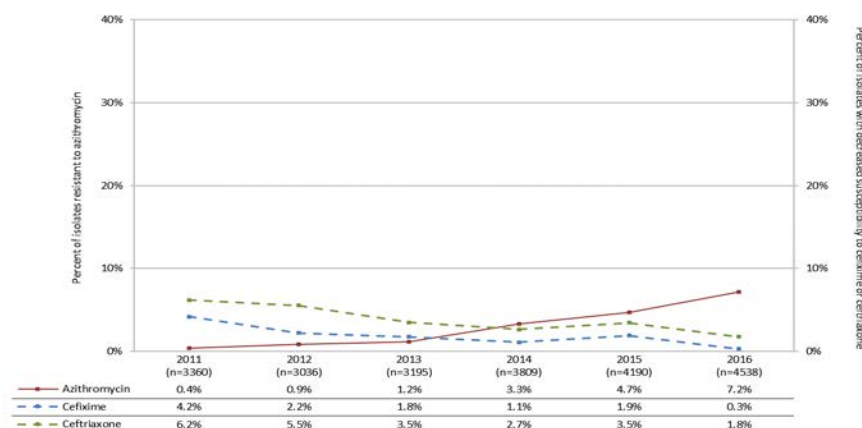
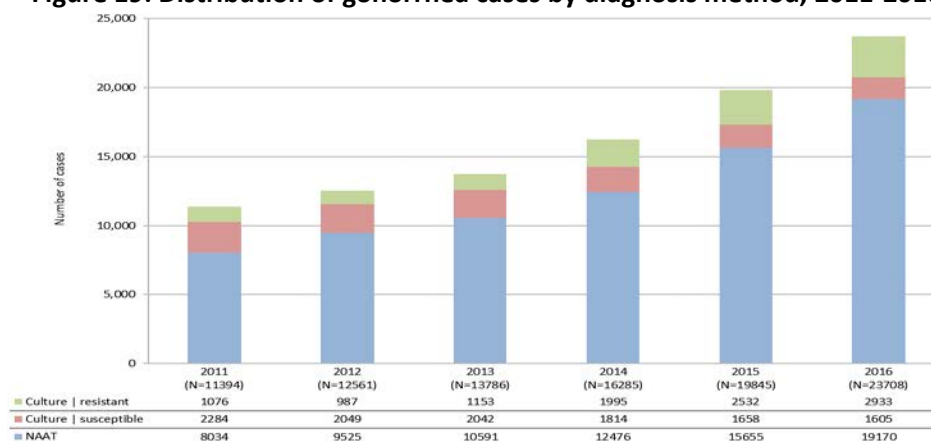


Figure 19: Distribution of gonorrhea cases by diagnosis method, 2011-2016



Notes: Culture | resistance = resistance to at least one of the following antimicrobials (penicillin, tetracycline, ciprofloxacin, azithromycin, erythromycin) or decreased susceptibility to cefixime or ceftriaxone. Culture | susceptible = susceptibility to all of the following antimicrobials (penicillin, tetracycline, ciprofloxacin, azithromycin, erythromycin, cefixime, ceftriaxone). NAAT = Nucleic Acid Amplification Testing.

Table 1: Prescribed treatment for gonorrhea by sexual behavior, ESAG (2016)

Infection Type	Treatment	gbMSM	Other adults	Overall
Anogenital	Preferred / Alternative	86.5%	84.7%	86.8%
	Other	8.4%	5.4%	9.3%
	No treatment information	4.8%	9.3%	3.7%
Pharyngeal	Preferred / Alternative	87.6%	79.4%	83.8%
	Other	11.4%	11.8%	6.5%
	No treatment information	1.0%	7.4%	9.0%

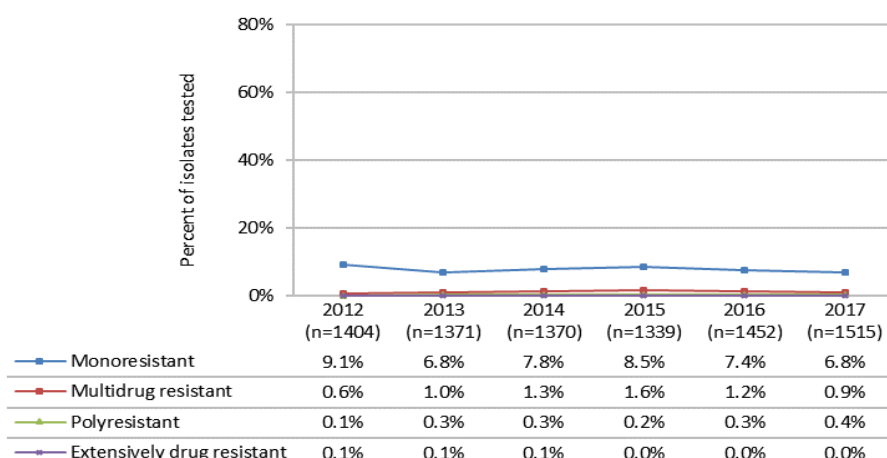
Note: 2016 ESAG results based on the stratified denominator by risk category from 758 overall cases. Guidelines for anogenital and pharyngeal infections (preferred and alternative treatments) are available in the 2017 CARSS Report.

Mycobacterium tuberculosis

Infection with *Mycobacterium tuberculosis* can lead to highly contagious and potentially serious disease that often invades the lungs and is spread through airborne droplets. People with active Tuberculosis (TB) require prolonged antibiotic treatment, and close contacts are investigated for evidence of TB infection. First-line drugs for treatment of infection include: isoniazid, rifampin, pyrazinamide and ethambutol. Multidrug-resistant *Mycobacterium* (MDR)-TB tuberculosis are bacterial strains that have resistance to isoniazid and rifampin, with or without resistance to other first-line drugs. Extensively drug-resistant (XDR)-TB strains have resistance to isoniazid and rifampin and any fluoroquinolone and at least one of the injectable second-line drugs. As a result of the challenge in treating MDR/XDR TB and the potential for transmission if untreated or partially treated, MDR-TB and XDR-TB are serious public health concerns, requiring careful monitoring and individualized treatment to ensure completion of therapy.

Similar to previous years, the 2017 rate of antimicrobial resistance among TB isolates remained low. Eight percent of TB isolates tested in 2017 had resistance to any of the first line anti-TB drugs. Of these, 84% were monoresistant (i.e., resistant to only one drug), 5% were polyresistant (i.e., resistant to more than one first line anti-TB drug, excluding the combination of isoniazid and rifampin) and 11% were MDR-TB. The last reported extensively drug-resistant isolate was reported in 2014. Trends in TB drug resistance have remained largely unchanged since 2007.

From 2006 through 2016, 2% of TB cases among Canadian born Indigenous persons were resistant to any of the first line anti-TB drugs, but there were no cases of MDR-TB in this group. Among Canadian born non-Indigenous cases of TB, 9% were resistant, of which 5% were MDR-TB. Drug resistance was highest among foreign born cases of TB over this time period, where 11% of cases had resistance, of which 14% of those with resistance were MDR-TB.

Figure 20: Percent of culture-positive TB cases by resistance profile, 2012-2017

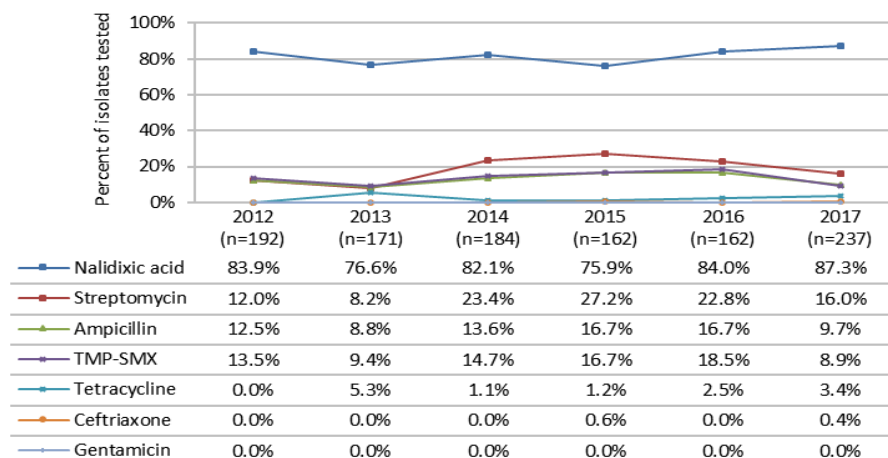
Notes: Total # isolates tested for pyrazinamide: 2012 = 1,175; 2013 = 1,187; 2014 = 1,142; 2015 = 1,141; 2016 = 1,254; 2017 = 1,272. Multidrug-resistant TB = resistance to isoniazid and rifampin, but does not meet the definition of extensively drug-resistant TB. Extensively drug-resistant TB = resistance to isoniazid and rifampin, any fluoroquinolone and at least one of three injectable second-line drugs (amikacin, capreomycin and kanamycin).

Typhoidal *Salmonella enterica* (serovars Typhi and Paratyphi)

Enteric fever is caused by *Salmonella enterica* serovars Typhi (*S. Typhi*) and Paratyphi (*S. Paratyphi*). It is an invasive febrile illness characterized by fever, rash, and diarrhea (or constipation). Children usually present with milder symptoms compared to adults. Serious complications, such as myocarditis or intestinal perforation, can also occur. First line empiric therapy has traditionally been a fluoroquinolone, with ciprofloxacin being the most commonly used. However, when deciding on the optimal empiric therapy, antimicrobial resistance patterns in travel destination countries should be considered. If fluoroquinolone resistance is suspected, an injectable third-generation cephalosporin is the empiric treatment of choice. Azithromycin is being increasingly used as an oral option to treat enteric fever because of the emergence of multidrug-resistant strains.

In 2017, 237 typhoidal isolates were tested for antimicrobial susceptibility; *S. Typhi* (80%), *S. Paratyphi* A (13%) and *S. Paratyphi* B^a (3%). The majority of typhoidal isolates tested in 2017 were recovered from blood samples (71%) and originated from residents of Ontario (50%), British Columbia (21%) and Alberta (14%). Overall, 87% of *S. typhoidal* isolates were resistant to nalidixic acid, and 22% were resistant to ciprofloxacin. One *S. Typhi* isolate was resistant to ceftriaxone and azithromycin, but no other typhoidal isolates demonstrated resistance to these two antimicrobials in 2017. A total of 12% of isolates were susceptible to all antimicrobials tested, whereas 11% were multiclass-resistant (i.e., resistant to ≥ 3 classes of antimicrobials). Generally, while the relative frequencies of resistance to the majority of the drug classes tested has fluctuated somewhat since 2012, the overall frequency of resistance has remained stable.

^a *Salmonella* Paratyphi B does not include *S. Paratyphi* B var. L (+) tartrate (+), formerly called *S. Paratyphi* var. Java.

Figure 21: Frequency of resistance to selected antimicrobials in typhoidal *Salmonella*, 2012-2017

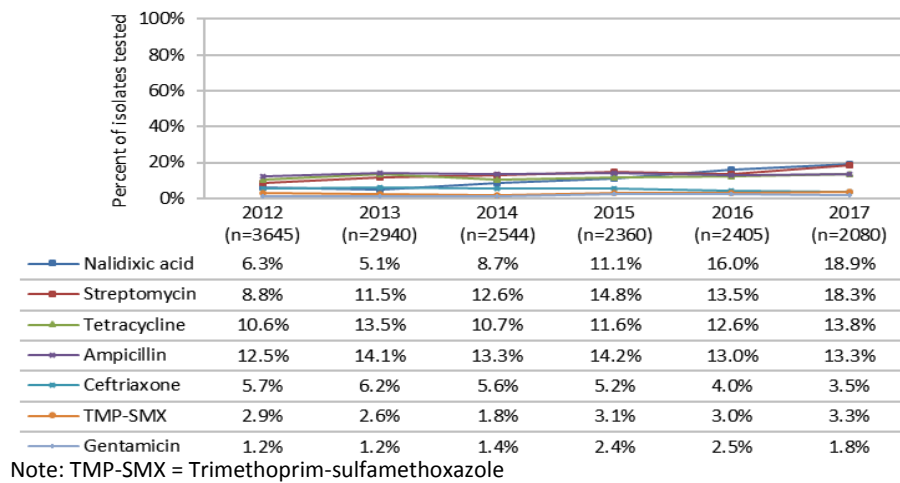
Note: TMP-SMX = Trimethoprim-sulfamethoxazole

Non-typhoidal *Salmonella enterica*

Non-typhoidal salmonellosis is a food-borne gastrointestinal disease caused many serovars of non-typhoidal *Salmonella enterica*. It is one of the primary causes of bacterial diarrheal disease in Canada. Most cases of salmonellosis are mild and resolve without treatment; however, it can be life-threatening in some cases. The severity of the disease depends on the susceptibility of the individual and the serovar of *Salmonella*.

In 2017, a total of 2,080 non-typhoidal *Salmonella* isolates from humans were submitted to PHAC for antimicrobial susceptibility testing, the majority of which were submitted by Ontario (33%) followed by Quebec (16%), Alberta (12%) and British Columbia (8%). *Salmonella* Enteritidis was the most common non-typhoidal serovar associated with human disease submitted for susceptibility testing (50%), followed by *S. Typhimurium* (15%) and *S. Heidelberg* (12%).

In 2017, the majority of the non-typhoidal *Salmonella* isolates submitted for antimicrobial susceptibility testing were recovered from stool samples (82%), followed by blood (6%) and urine (3%). A total of 38% of human non-typhoidal *Salmonella* isolates were resistant to one or more antimicrobials tested and 13% of isolates were resistant to three or more antimicrobial classes (i.e. multiclass-resistant). In 2017, nalidixic acid was the antimicrobial to which the largest proportion of isolates were resistant (19%), followed by streptomycin (18%), sulfisoxazole (14%), tetracycline (14%), and ampicillin (13%). Sixteen (<1%) non-typhoidal isolates were resistant to azithromycin, 2% were resistant to ciprofloxacin (data not shown), and 4% were resistant to ceftriaxone. No resistance to meropenem was detected in 2017. Increases have been observed in the frequency of non-typhoidal *Salmonella* isolates resistant to nalidixic acid (up from 6.3% in 2012 to 19% in 2017) and streptomycin (up from 9% in 2012 to 18% in 2017).

Figure 22: Frequency of resistance to selected antimicrobials in non-typhoidal *Salmonella*, 2012-2017

Resistance in enteric bacteria from food sources

PHAC monitors antimicrobial resistance in selected bacterial organisms (i.e., generic *E. coli*, *Campylobacter*, and *Salmonella*), in animals and food sources across Canada. The contamination of animals and animal products with antimicrobial-resistant bacteria has been identified as a source for human infection with resistant organisms, and these organisms are a frequent cause of food-borne outbreaks.

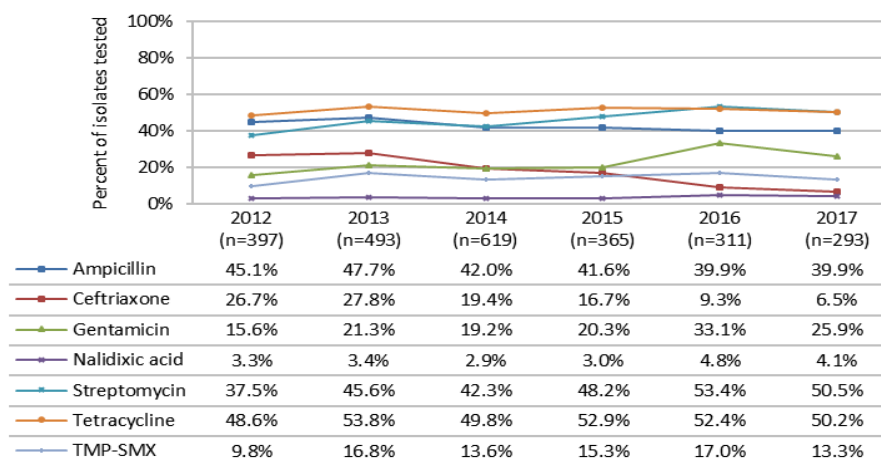
Many individuals infected with food-borne *E. coli*, *Salmonella*, and *Campylobacter* will develop diarrhea, fever, and abdominal cramps. In most cases, the illness is self-limited and antimicrobial treatment is not required. Some vulnerable individuals (e.g., the elderly, very young children and individuals with underlying medical conditions) may need to be treated and hospitalized. Pregnant women are also at increased risk of complications related to these organisms.

Sampling is focused on the major terrestrial food producing animal species consumed in Canada: chicken, pork, beef and turkey. The CARSS-Update 2018 summarizes the retail meat types for which bacterial isolation and antimicrobial susceptibility testing was conducted. Because human exposure to food animals or their products is highest in Canada via the consumption of retail meat, the data described below for generic *E. coli*, *Campylobacter*, and *Salmonella* are restricted to retail meat surveillance.

1a. Generic *Escherichia coli* from chicken

Of the 293 *E. coli* isolates recovered from 325 chicken meat samples collected from retail stores in 2017 (recovery risk of 90%), half (50%) were found to be resistant to tetracycline and streptomycin, followed by ampicillin (40%) and gentamicin (26%). One isolate was resistant to ciprofloxacin and no meropenem resistance was observed in 2017. Resistance to ceftriaxone (a third-generation cephalosporin) continued to decrease, from 27% in 2012 to 6% in 2017. Additional integrated information regarding ceftriaxone resistance from multiple enteric bacteria, including *E. coli* from chicken and humans, is summarized in the integration chapter, below.

Figure 23: Resistance to selected antimicrobials among generic *E. coli* isolated from chicken meat samples collected from retail stores, 2012-2017

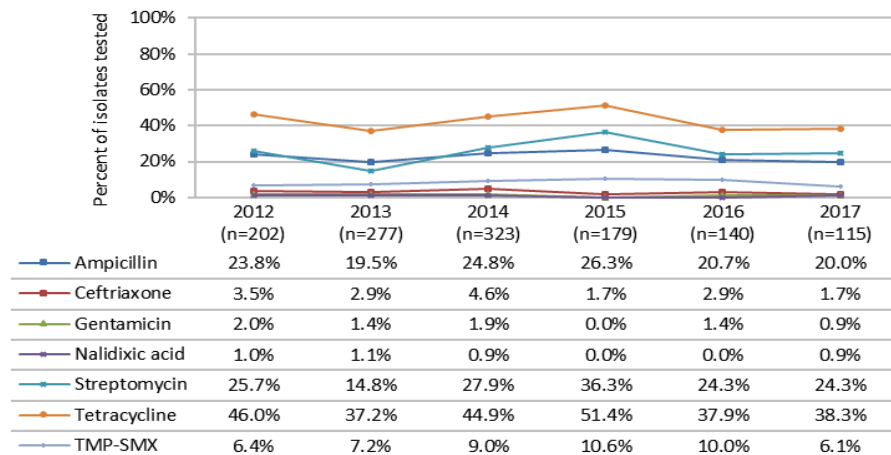


Note: TMP-SMX = Trimethoprim-sulfamethoxazole

1b. Generic *Escherichia coli* from pigs (pork)

Of the 115 *E. coli* isolates recovered from 647 pork meat samples collected from retail stores in 2017 (recovery risk of 17%), 38% were resistant to tetracycline. Two percent of isolates were resistant to ceftriaxone. Gentamicin and nalidixic acid was observed in a single isolate each (i.e. two separate isolates). No meropenem resistance was observed in 2017.

Figure 24: Resistance to selected antimicrobials among Generic *E. coli* isolated from pork meat samples collected from retail stores, 2012-2017

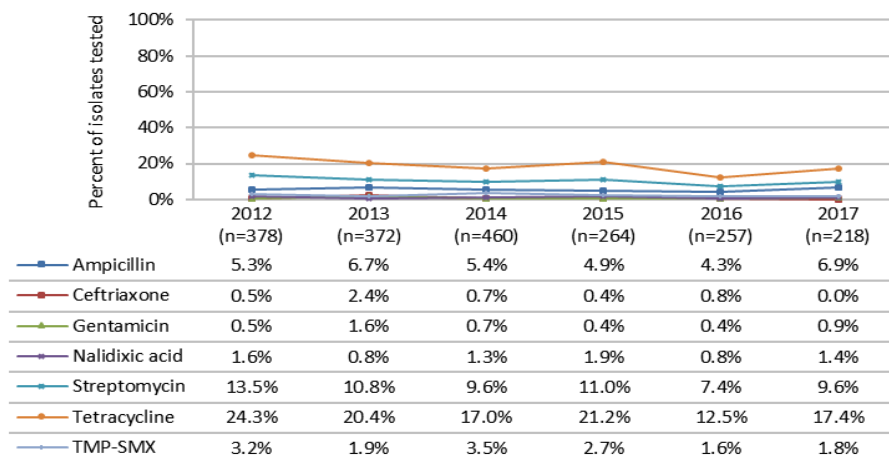


Note: TMP-SMX = Trimethoprim-sulfamethoxazole

1c. Generic *Escherichia coli* from cattle (beef)

Of the 218 *Escherichia coli* isolates recovered from 502 beef meat samples collected from retail stores in 2017 (recovery risk of 43%), 17% were resistant to tetracycline, and no isolates were resistant to ceftriaxone. One percent of isolates were resistant to gentamicin and one percent of isolates were resistant to nalidixic acid (separate isolates). One isolate was resistant to ciprofloxacin and another single isolate was resistant to azithromycin. No meropenem resistance was observed in 2017. In general, the levels of resistance have remained fairly stable since 2012, with a decrease in tetracycline resistance (from 24% in 2012 to 17% in 2017).

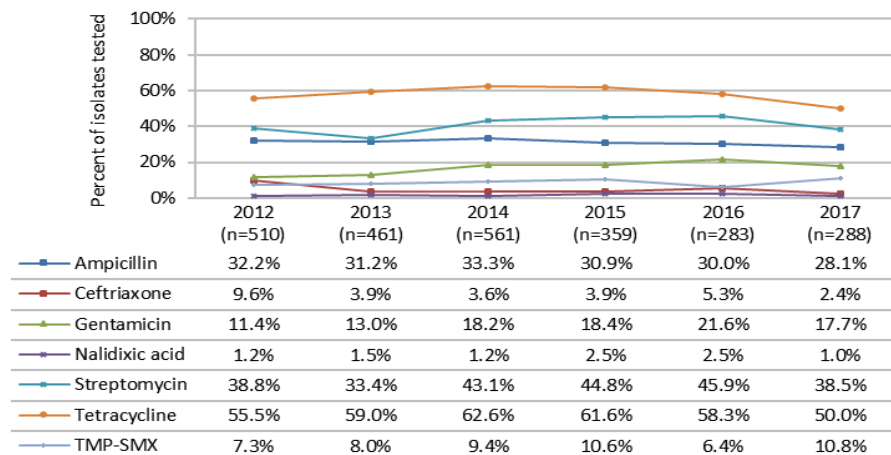
Figure 25: Resistance to selected antimicrobials among generic *E. coli* isolated from beef meat samples collected from retail stores, 2012-2017



1d. Generic *Escherichia coli* from turkey

Of the 288 *Escherichia coli* isolates recovered from 322 turkey meat samples collected from retail stores in 2017 (recovery risk of 89%), half (50%) were resistant to tetracycline, followed by streptomycin (39%), and ampicillin (28%). Two percent of isolates were resistant to ceftriaxone, compared to 10% of isolates resistant in 2012. Resistance to gentamicin was higher in 2017 (18%) compared to 2012 (11%). Two isolates were resistant to ciprofloxacin and one isolate was resistant to azithromycin. No meropenem resistance was observed in 2017.

Figure 26: Resistance to selected antimicrobials among generic *E. coli* isolated from turkey meat samples collected from retail stores, 2012-2017

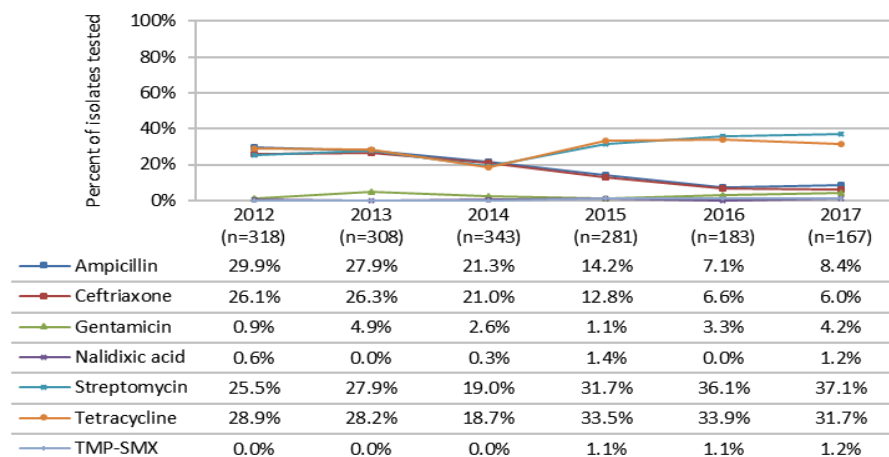


2a. *Salmonella* in chicken

Of the 167 *Salmonella* isolates recovered from 651 chicken meat samples collected from retail stores in 2017 (recovery risk of 26%), 59% were fully susceptible to all antimicrobials tested and 7% of isolates classified as multiclass-resistant (i.e., resistant to three or more antimicrobial classes). A total of 37% were resistant to streptomycin, followed by tetracycline (32%). Resistance to ceftriaxone decreased from 26% in 2012 to 6% in 2017. Additional integrated information regarding ceftriaxone resistance from multiple enteric bacteria, including *Salmonella* from chickens and humans, is summarized in the integration chapter below. Resistance to gentamicin increased from 1% in 2012 to 4% in 2017. In 2017, no resistance was observed to azithromycin or meropenem. Furthermore, no resistance to ciprofloxacin (an antimicrobial used in human medicine for treating severe and invasive salmonellosis) was observed.

Among retail chicken meat samples collected in 2017, the most common *Salmonella* serovars associated with resistance to third-generation cephalosporins were *S. Kentucky* and *S. Heidelberg*. Further information about third-generation cephalosporin resistance in non-typhoidal *Salmonella* is summarized in the integration chapter, below.

Figure 27: Resistance to selected antimicrobials among *Salmonella* spp. isolated from chicken meat samples collected at retail stores, 2012-2017

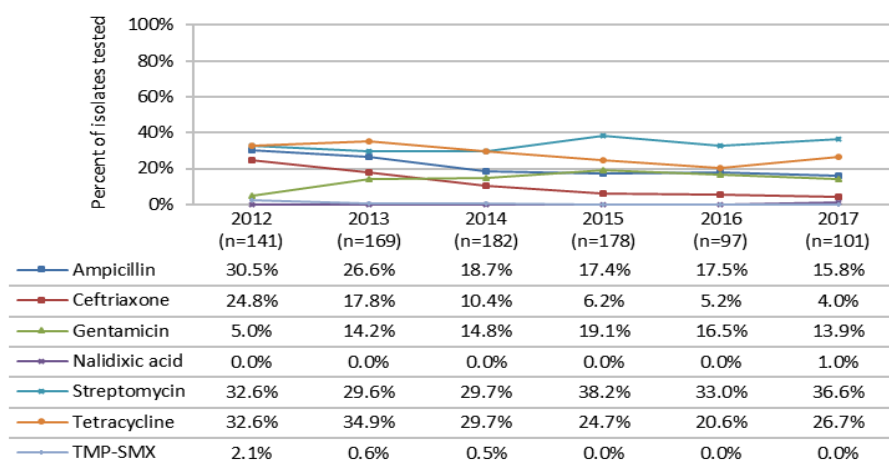


2b. *Salmonella* in turkey

Of the 101 *Salmonella* isolates recovered from 564 turkey meat samples collected from retail stores in 2017 (recovery risk of 18%), 56% were fully susceptible to all antimicrobials tested and 23% of isolates were classified as multiclass-resistant (i.e., resistant to three or more antimicrobial classes). A total of 37% of retail turkey *Salmonella* isolates were resistant to streptomycin, followed by tetracycline (27%). In 2017, ceftriaxone resistance decreased yet again to 4%, compared to 25% in 2012. No resistance was observed to azithromycin or meropenem. Furthermore, no resistance to ciprofloxacin (an antimicrobial used in human medicine for treating severe and invasive salmonellosis) was observed.

Resistance among *Salmonella* isolates is strongly influenced by serovars with some serovars more likely to demonstrate resistance than others. Although turkey and chicken are both poultry species, serovars recovered from turkey meat are generally quite different from those detected in retail chicken meat, thus the resistance profiles observed in turkey are also different. Among retail turkey meat, the *Salmonella* serovars associated with resistance to third-generation cephalosporins were serovars Agona, Bredeney, Brandenburg and Infantis unlike serovars Kentucky and Heidelberg driving this resistance in chicken meat.

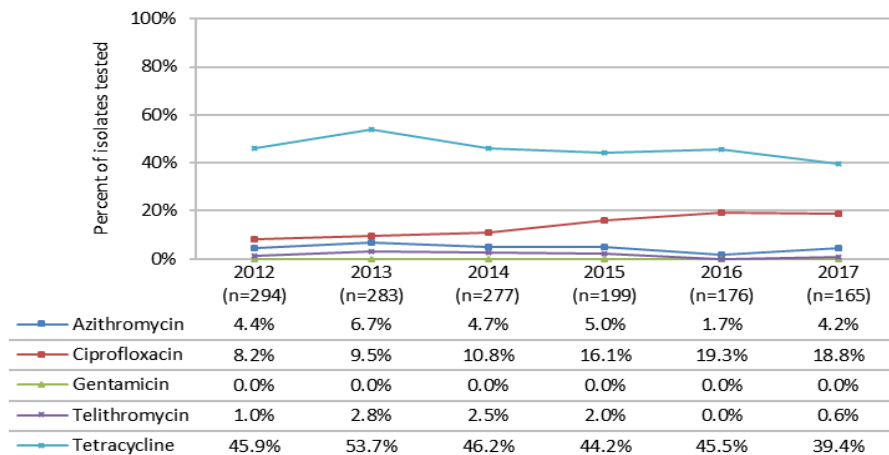
Figure 28: Resistance to selected antimicrobials among *Salmonella* spp. isolated from turkey meat samples collected at retail stores, 2012-2017



3a. *Campylobacter* spp. from chicken

Of the 165 *Campylobacter* spp. isolates recovered from 651 chicken meat samples collected from retail stores in Canada in 2017 (recovery risk of 25%), 39% were resistant to tetracycline. Resistance to ciprofloxacin was detected in 19% of isolates. Ciprofloxacin is considered to be an antimicrobial of very high importance in human medicine. Additionally, integrated information regarding fluoroquinolone (ciprofloxacin) resistance in *Campylobacter* spp. from chicken and humans is summarized in the integration chapter, below.

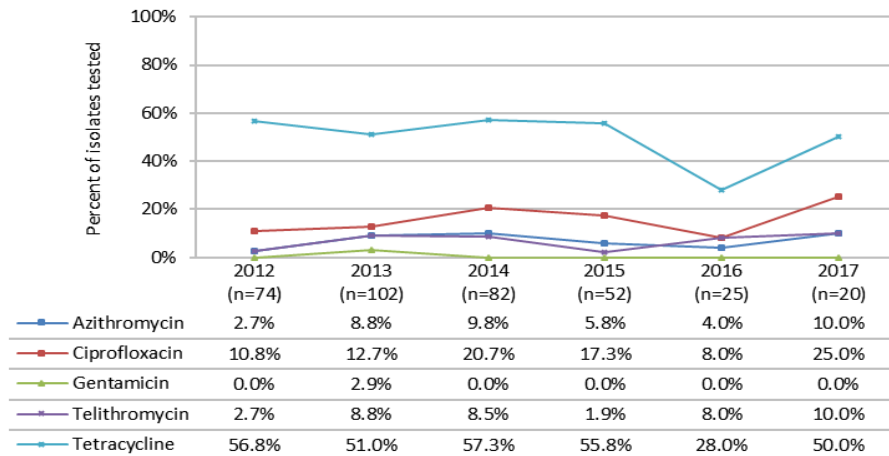
Figure 29: Resistance to selected antimicrobials among *Campylobacter* spp. isolated from chicken meat samples collected from retail stores, 2012 to 2017



3b. *Campylobacter* spp. from turkey

Of the 20 *Campylobacter* spp. isolates recovered from 278 turkey meat samples collected from retail stores in 2017 (recovery risk of 7%), 50% were resistant to tetracycline. Resistance to ciprofloxacin was detected in 25% of isolates and two isolates were resistant to telithromycin.

Figure 30: Resistance to selected antimicrobials among *Campylobacter* spp. isolated from turkey meat samples collected from retail stores, 2012 to 2017

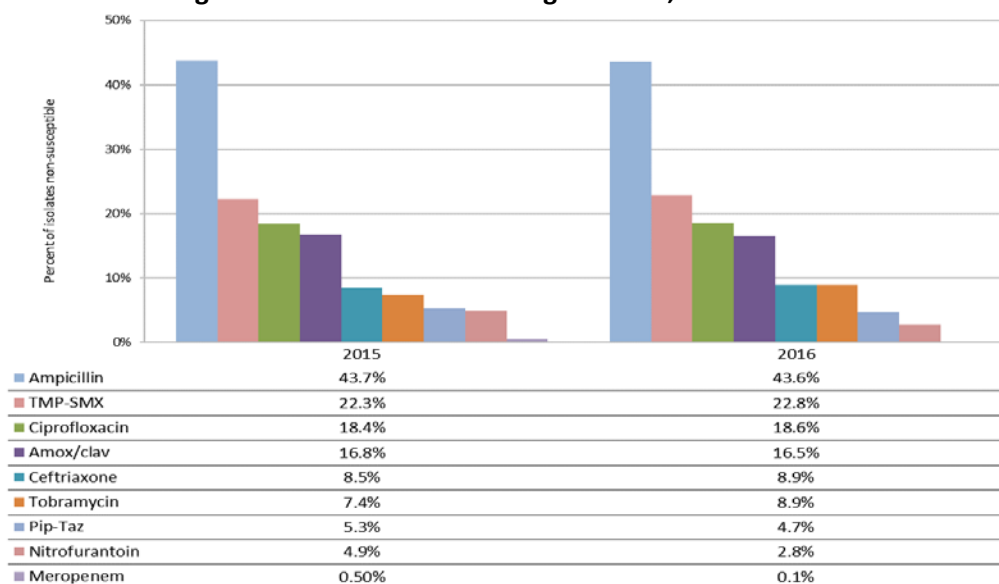


Surveillance Pilots

Hospital antibiogram data for *Escherichia coli*

In 2016, standardized hospital antibiogram data for *E. coli* were collected. There were minimal changes in resistance patterns from 2015 to 2016; however, the trend in non-susceptibility to two drugs commonly used for empiric treatment remained consistent (sulfamethoxazole-trimethoprim; 22% and 23% respectively), and ciprofloxacin (18% and 19%, respectively). Availability of these types of data will improve comparability of Canada's AMR trends to those found in other countries participating in the Global Antimicrobial Resistance Surveillance System (GLASS).

Figure 31: CNISP *E. coli* antibiogram data, 2015 and 2016



Note: PIP-TAZ = Piperacillin - Tazobactam; TMP-SMX = Trimethoprim-Sulfamethoxazole; Amox-clav = amoxicillin - clavulanic acid.

The Community, Northern, and Rural Acute Care Point Prevalence Survey (CNAPP)

The Public Health Agency of Canada monitors antimicrobial resistant organisms (ARO) in major urban hospitals in Canada, primarily through the Canadian Nosocomial Infection Surveillance Program (CNISP). Limitations associated with these data include a lack of information on ARO in smaller community and rural hospitals. The objective of this project was to describe the burden of ARO in Canadian acute-care hospitals located outside the CNISP network. PHAC conducted a point prevalence survey in a convenience sample of Canadian hospitals located in community, rural, or Northern regions. Data on inpatients pertaining to one 24-hour period were collected. Infections were classified as either acquired in the reporting facility (HAI) or community acquired. AROs captured by this study (i.e., targeted AROs) included methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), *Clostridioides difficile* infection (CDI), extended-spectrum beta-lactamase (ESBL) *Enterobacteriaceae*, and carbapenemase-producing organisms (CPO).

Thirty hospitals with a census of 2,237 patients were surveyed across nine Canadian Provinces and all Territories; 49% of the patients were male, and the median age was 72 ± 23 years. A total of 798 (36%) patients had at least one infection; 38.2% (n=305) pneumonia, 22.8% (n=182) urinary tract, 19% (n=152) skin and soft tissue, 8.4% (n=67) bacteremia, 7% (n=57) surgical site, 7% (n=53) viral respiratory tract, and 4% (n=31) CDI. The causative organism was known for 26% (n=206), of which 24% (n=49) were caused by a targeted ARO; 63% (n=31) CDI, 25% (n=12) MRSA, 8% (n=4) ESBL, and 4% (n=2) CPOs. Overall, 5% (n=101) of the patients had an HAI.

About one quarter of infections in which the pathogen was identified involved a targeted ARO. The burden of AROs in patients in Canadian hospitals located in community, rural, and Northern regions warrants further surveillance. The current hospital network was a useful addition to Canada's ability to monitor trends in ARO.

Human antimicrobial use in Canada

Information about antimicrobial use in Canadians comes from two primary data sources: (1) prescriptions dispensed by retail pharmacies in Canada (i.e., community pharmacy dispensing), and (2) antimicrobials purchased by Canadian hospitals (i.e., hospital purchasing). All data presented are for antimicrobials within the J01 class (i.e., antibacterials for systemic use, as described by the World Health Organization), with the addition of oral metronidazole, oral nystatin, and oral vancomycin. Please note that the 2017 CARSS report included only J01 antimicrobials with the addition of oral vancomycin. Unless otherwise specified, all data sources, methodologies, and metrics for AMU results presented in this report have been previously described in the 2017 CARSS report.

Overall results

The majority of human antimicrobial use in Canada continued to occur in the community setting, with approximately 92% of Defined Daily Doses (DDDs) in 2017 dispensed through community pharmacies; compared to 8% of DDDs purchased by hospitals. With regard to antimicrobial quantities, 222,257 kilograms of antimicrobials were dispensed through community pharmacies (more than 24 million prescriptions) and 40,333 kilograms were purchased by hospitals, for a total of 262,590 kilograms in 2017. This equates to a combined dispensation/purchasing of 19.5 DDDs per 1,000 inhabitant-days (i.e., roughly 2% of the Canadian population could be receiving an antimicrobial on an average day), with an estimated expenditure of approximately \$822 million (\$726 million in the community, \$96 million in hospital purchasing).

Stratified by Canadian provinces and territories, overall human antimicrobial use in 2017 (measured by DDDs, aggregated from both community pharmacy dispensations and hospital purchasing) was lowest in the territories, Québec, and British Columbia (BC); and highest in Prince Edward Island (PEI) and Newfoundland (NL) combined.

Figure 32: Defined daily doses (DDDs) per 1,000 inhabitant-days, hospital purchasing and community dispensation, 2012-2017

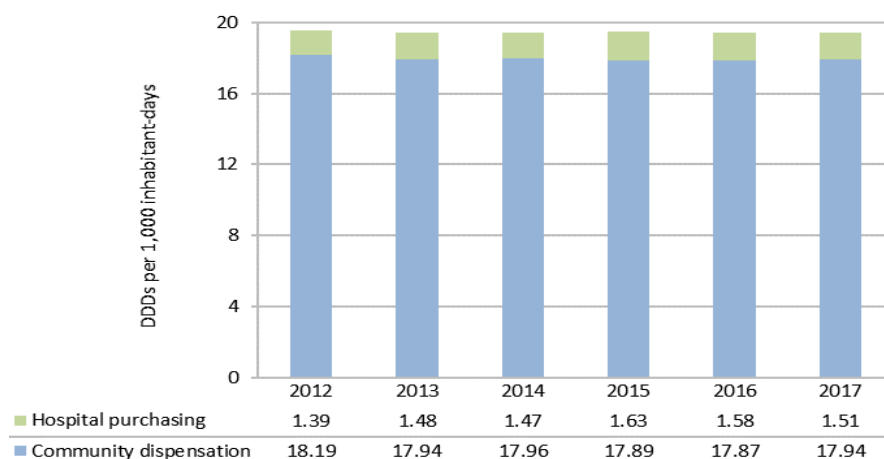
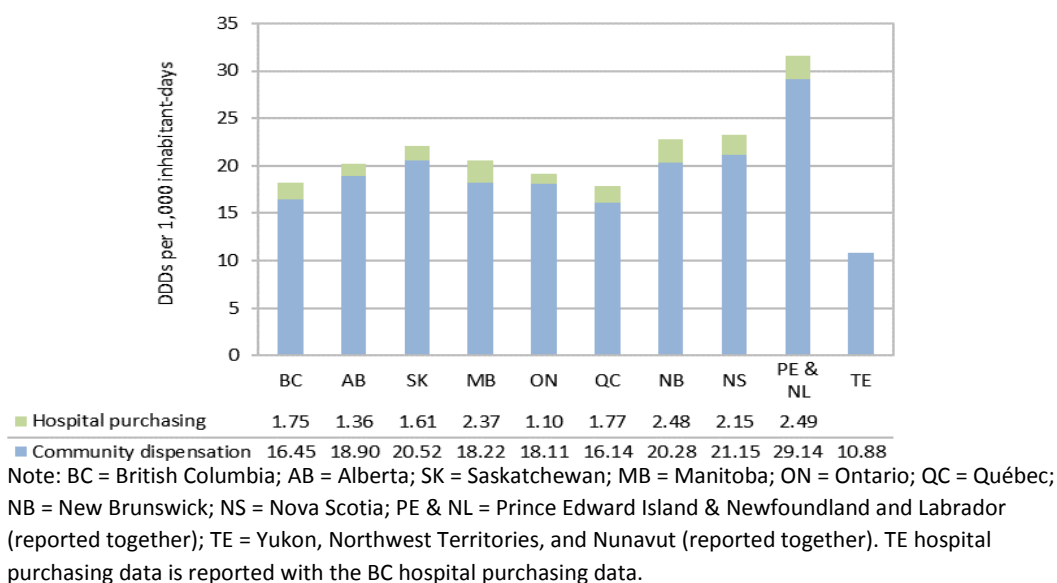


Figure 33: Provincial and Territorial distribution of defined daily doses (DDDs) per 1,000 inhabitant-days, hospital purchasing and community dispensation, 2017



Community pharmacy dispensing

In 2017, the dispensation of antimicrobials in the community by retail pharmacies remained nearly unchanged from 2016 when measured by prescriptions per 1,000 inhabitants, DDDs per population, and kilograms of active ingredient per population. Likewise, the top ten antimicrobials most frequently dispensed in the community remained similar in relative order from 2016 to 2017.

Stratified by Canadian Provinces and Territories, the rate of prescriptions per 1,000 inhabitants was highest in PEI and NL (reported together) and lowest in BC and the territories (reported together) in 2017 (970.2, 569.3, and 358.6 prescriptions per 1,000 inhabitants, respectively). While an overall reduction in the prescription rate per 1,000 inhabitants from 2016 to 2017 was reported by Saskatchewan (-8.8%), Alberta (-1.0%), Manitoba (-0.6%), British Columbia (-0.4%) and New Brunswick (-0.1%), increases were reported in Quebec (0.2%), Ontario (1.0%), Nova Scotia (1.3%), Prince Edward Island & Newfoundland and Labrador (2.9%), and the territories (13.9%). As such, the relative ranking by Province and Territory changed from 2016 to 2017.

Stratified by age group, Canadians aged 60 years or older received the most antibiotic prescriptions (923.1 prescriptions per 1,000 inhabitants); nearly 60% more than the per-capita rates among the 0-14 and 15-59 age groups. Also, prescription rates among those aged 60 or older continued to increase, from 863.4 per 1,000 inhabitants in 2012 to 923.1 prescriptions per 1,000 inhabitants in 2017. While specific antimicrobials prescribed varied across age groups, amoxicillin remained the most commonly prescribed antimicrobial in 2017 (55%, 22% and 17% of all prescriptions for Canadians aged 0-14, 15-59, and 60+, respectively).

Figure 34: Defined daily doses per 1,000 inhabitant-days, prescriptions per 1,000 inhabitants, and kilograms of active ingredient per 1,000 inhabitants for antimicrobials dispensed by community pharmacies, 2012-2017

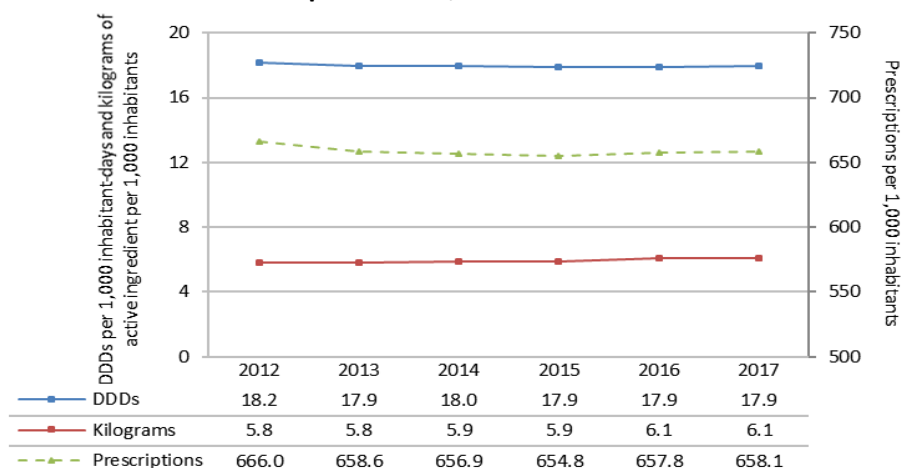


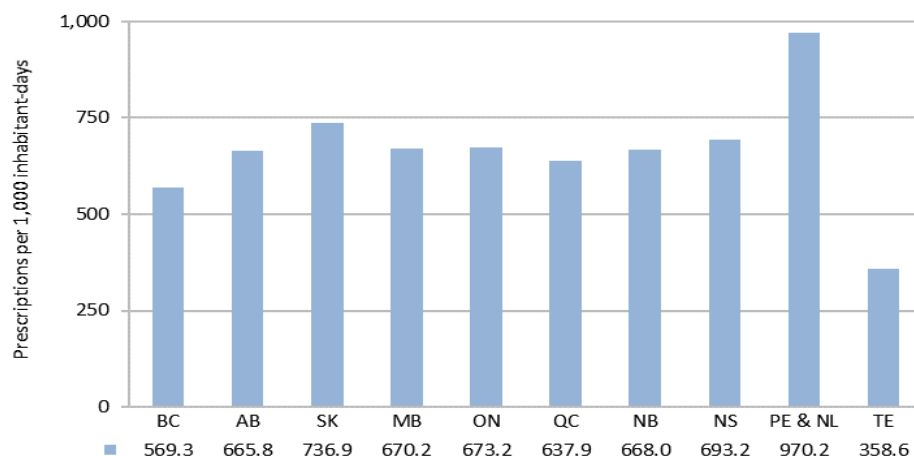
Table 2: Prescriptions dispensed by community pharmacies per 1,000 inhabitants for the 10 most commonly prescribed antimicrobials, 2012-2017

Antimicrobial	2012	2013	2014	2015	2016	2017
Amoxicillin	163.2	160.3	166.5	161.5	164.7	164.0
Azithromycin	59.9	56.3	56.9	59.5	63.4	66.0
Cephalexin	49.5	50.8	51.2	51.0	52.4	53.4
Ciprofloxacin	61.4	58.3	56.2	55.6	52.2	46.9
Amoxicillin and enzyme inhibitor	25.1	27.5	29.9	33.8	37.1	42.0
Nitrofurantoin	34.2	35.0	36.8	38.2	38.3	39.4
Sulfamethoxazole and trimethoprim	29.6	30.8	29.5	30.3	30.6	30.9
Clarithromycin	62.2	52.9	46.8	39.7	35.0	30.4
Doxycycline	16.7	18.6	20.4	23.1	24.8	27.6
Metronidazole	19.4	19.6	20.0	20.8	20.6	20.3
TOTAL	666.0	658.6	656.9	654.8	657.8	658.1

Table 3: Defined daily doses per 1,000 inhabitant-days for the 10 antimicrobials with the highest DDDs dispensed by community pharmacies, 2012-2017

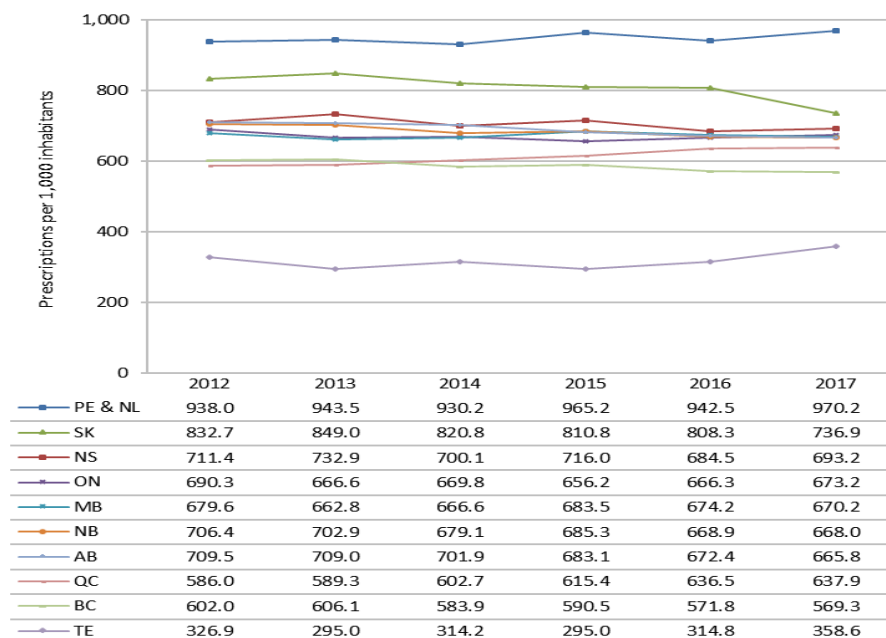
Antimicrobial	2012	2013	2014	2015	2016	2017
Amoxicillin	4.84	4.82	5.05	4.95	5.04	5.08
Doxycycline	1.31	1.40	1.50	1.68	1.79	1.95
Amoxicillin and enzyme inhibitor	0.91	1.01	1.11	1.27	1.40	1.59
Clarithromycin	2.64	2.28	2.04	1.75	1.54	1.36
Cephalexin	0.98	1.01	1.02	1.03	1.04	1.05
Azithromycin	1.01	0.85	0.85	0.89	0.93	0.99
Ciprofloxacin	1.17	1.11	1.07	1.06	1.00	0.90
Nitrofurantoin	0.78	0.78	0.80	0.82	0.81	0.81
Minocycline	0.87	0.82	0.75	0.68	0.61	0.56
Sulfamethoxazole and trimethoprim	0.56	0.54	0.54	0.52	0.51	0.52
TOTAL	18.19	17.94	17.96	17.89	17.87	17.94

Figure 35: Provincial and Territorial distribution of prescription rates per 1,000 inhabitants as dispensed by community pharmacies, 2017



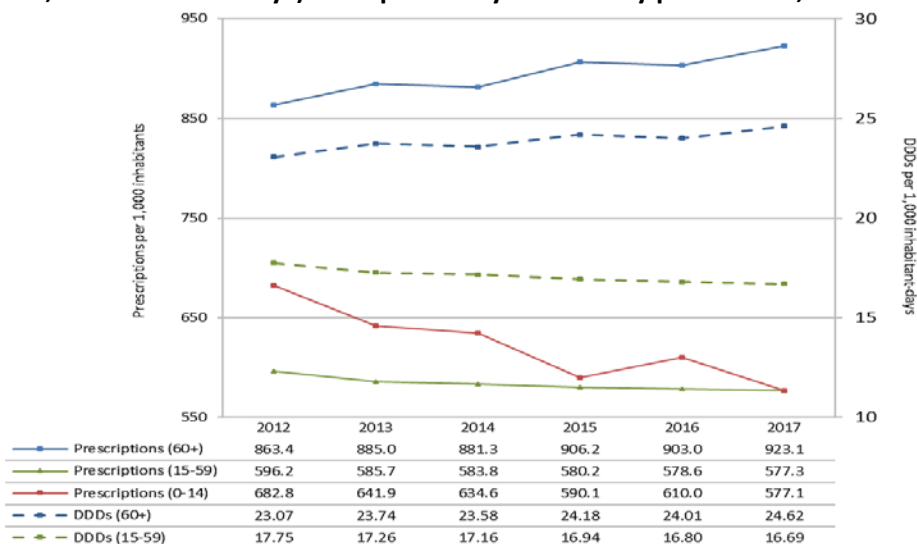
Note: BC = British Columbia; AB = Alberta; SK = Saskatchewan; MB = Manitoba; ON = Ontario; QC = Québec; NB = New Brunswick; NS = Nova Scotia; PE & NL = Prince Edward Island & Newfoundland and Labrador (reported together); TE = Yukon, Northwest Territories, and Nunavut (reported together).

Figure 36: Prescriptions per 1,000 inhabitants by Province and Territory as dispensed by community pharmacies, 2012-2017



Note: BC = British Columbia; AB = Alberta; SK = Saskatchewan; MB = Manitoba; ON = Ontario; QC = Québec; NB = New Brunswick; NS = Nova Scotia; PE & NL = Prince Edward Island & Newfoundland and Labrador (reported together); TE = Yukon, Northwest Territories, and Nunavut (reported together).

Figure 37: Patterns of antimicrobial use by age group (prescriptions per 1,000 inhabitants and DDDs per 1,000 inhabitant-days) as dispensed by community pharmacies, 2012-2017



Note: DDDs for age group 0-14 is excluded, as DDDs are not an appropriate measure for AMU in children.

Table 4: Prescriptions per 1,000 inhabitants for the top 5 most commonly prescribed prescriptions per age group, as dispensed from community pharmacies, 2012-2017

Age group	Rank	Antimicrobial	2012	2013	2014	2015	2016	2017
0 - 14	1	Amoxicillin	339.7	321.6	340.0	316.7	334.7	318.1
	2	Azithromycin	75.0	66.3	64.7	65.1	72.0	69.0
	3	Cephalexin	45.3	44.9	44.1	34.9	36.8	37.7
	4	Amoxicillin and enzyme inhibitor	31.6	32.9	33.5	33.5	33.1	35.6
	5	Clarithromycin	81.3	64.9	55.3	44.9	39.9	30.6
15 - 59	1	Amoxicillin	124.9	124.0	127.6	124.9	125.4	126.9
	2	Azithromycin	53.8	50.4	51.2	52.6	56.0	57.7
	3	Cephalexin	44.3	45.5	45.9	46.5	46.9	47.6
	4	Ciprofloxacin	55.5	52.0	49.7	48.7	45.1	39.8
	5	Amoxicillin and enzyme inhibitor	21.5	23.5	25.7	29.3	32.6	36.4
60 +	1	Amoxicillin	141.6	145.1	149.4	151.1	150.6	154.9
	2	Ciprofloxacin	126.1	120.0	114.9	113.3	107.0	96.6
	3	Azithromycin	66.7	66.0	67.3	74.6	77.1	85.3
	4	Cephalexin	68.5	71.0	71.4	75.2	77.8	79.2
	5	Nitrofurantoin	69.8	69.4	71.2	72.8	73.4	74.2

Hospital purchasing

The purchasing of antimicrobials by Canadian hospitals has remained stable from 2012 to 2017 (as measured by DDDs per 1,000 inhabitant-days and kilograms per 1,000 inhabitants). In 2017, 1.51 DDDs were purchased per 1,000 inhabitant-days (1.1 kilograms per 1,000 inhabitants). No single antimicrobial accounted for a large proportion of hospital purchasing over time.

Stratified by Canadian provinces and territories, Atlantic provinces and Manitoba reported the highest rate of antimicrobial purchasing in 2017, and Ontario reported the lowest (1.10 DDDs per 1,000 inhabitant-days).

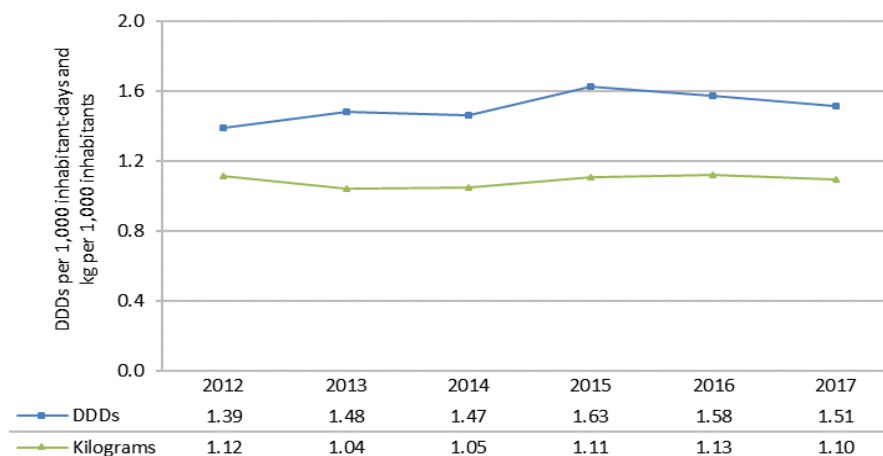
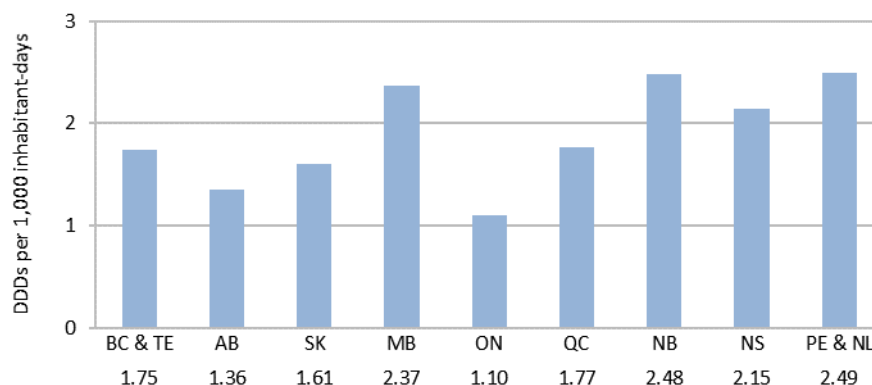
Figure 38: Defined daily doses (DDD) per 1,000 inhabitant-days and kilograms (kg) per 1,000 inhabitants for antimicrobials purchased by hospitals, 2012-2017

Figure 39: Provincial and Territorial distribution of defined daily doses (DDDs) per 1,000 inhabitant-days for antimicrobials purchased by hospitals, 2017



Note: BC = British Columbia; AB = Alberta; SK = Saskatchewan; MB = Manitoba; ON = Ontario; QC = Québec; NB = New Brunswick; NS = Nova Scotia; PE & NL = Prince Edward Island & Newfoundland and Labrador (reported together); TE = Yukon, Northwest Territories, and Nunavut (reported together).

Prescribing in Indigenous and non-Indigenous populations

Health Canada's Non-Insured Health Benefits (NIHB) Program provides coverage for Indigenous people when they are not insured elsewhere (including coverage relating to prescriptions), as guided by the provisions of the Canada Health Act. While the NIHB data only covers Indigenous people, not all Indigenous people access the service, and therefore some antimicrobial use among Indigenous people may be captured elsewhere (e.g., general community dispensing data).

These data currently represent the best opportunity to compare antimicrobial use among Indigenous and non-Indigenous peoples in Canada.

In 2017, a joint decision between PHAC and HC was made to remove NIHB data reporting from British Columbia for these analyses (the majority of Indigenous people hold alternate drug insurance through the First Nations Health Authority). These data are not available to PHAC or HC. Therefore, this removal affects both antimicrobial use and population values for historical data, and results presented here will differ from previous CARSS reports.

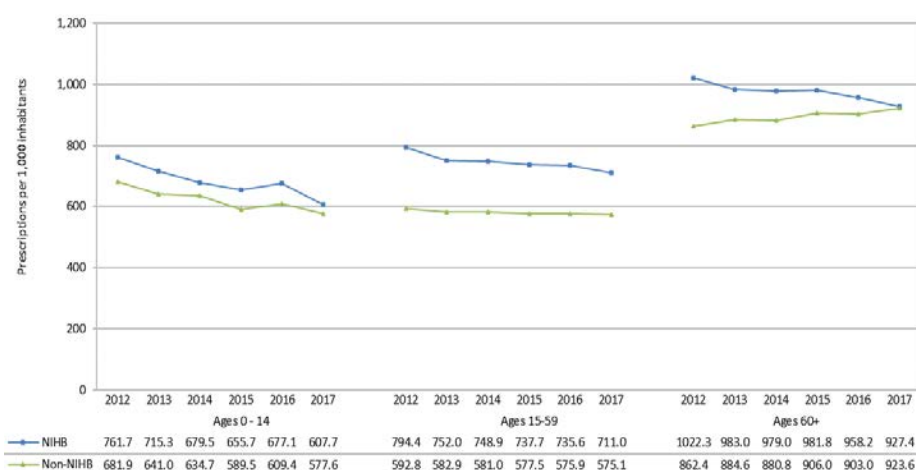
Overall, antimicrobial use within the Indigenous population was slightly higher than the non-NIHB population in 2017, with approximately 711 and 658 prescriptions dispensed per 1,000 inhabitants, respectively. However, over the 2011 to 2017 time frame, the NIHB population displayed a greater decline in prescribing than the non-NIHB population (16% decline as compared to 3%).

Figure 40: Defined daily doses per 1,000 inhabitant-days and prescriptions per 1,000 inhabitants for Indigenous (NIHB) and non-Indigenous populations (non-NIHB), 2012-2017



The decline in use among Indigenous populations from 2012 to 2017 can be attributed to reductions among all age groups. However, the most dramatic decline occurred among the 0-14 age group (25% decline). The 60+ age group continued to display the highest prescription rates. However, these rates were very close to the prescription rates among the non-Indigenous population. In contrast, prescribing rates among the 0-14 and 15-59 age groups were higher among the NIHB population than the non-NIHB population from 2012 to 2017.

Figure 41: Prescriptions per 1,000 inhabitants for Indigenous (NIHB) and non-Indigenous (non-NIHB) populations, by age group, 2012-2017



Antimicrobial recommendations by diagnoses

In 2017, more than 336 million diagnoses were estimated to be made by practitioners in Canada, resulting in an estimated 25.3 million antimicrobial recommendations.

Overall, an antimicrobial was mentioned in 7.5% of visits for all diagnoses combined. More visits were attributed to female patients than male patients (56% versus 44%). Also, more antimicrobial recommendations were recorded for female patients than male patients (59% versus 41%).

Similar to results seen from analysis of the community prescribing dataset, after adjusting for population size, antimicrobials were most likely recommended to the 65+ age group when looking at the number of recommendations per population. However, per visit, children 0-9 were most likely recommended an antimicrobial.

In 2017, the diagnoses that commonly received an antimicrobial recommendation varied by age group. In particular, 43% of antimicrobial recommendations made to children 0-9 years of age were to treat otitis media. In other age groups antimicrobial recommendations were distributed more evenly. In adults, upper respiratory tract and urinary tract infections were common diagnoses receiving an antimicrobial recommendation.

Figure 42: Proportion of antimicrobial recommendations per population and per visit, by age group, 2017.

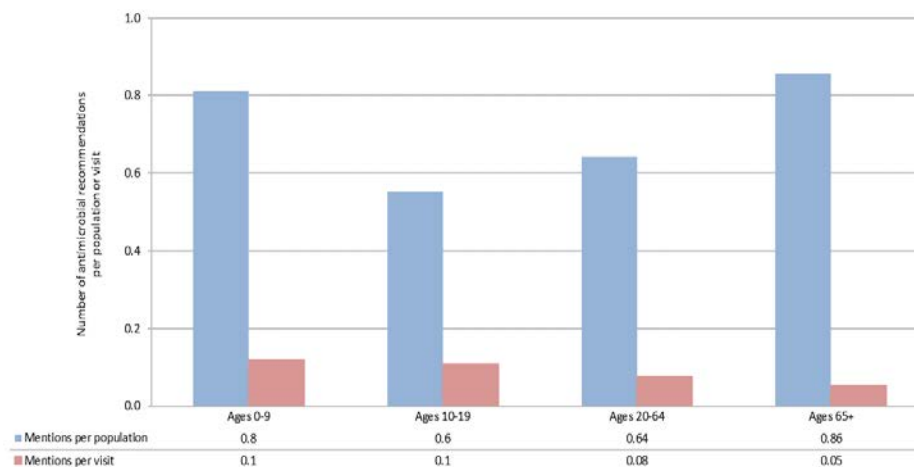


Table 5: Primary diagnoses for which antimicrobials were recommended in 2017, by age group

Age Group	Diagnosis or Diagnostic class	Percentage of total age-group antimicrobial recommendations
0 – 9	Otitis media	43
	Tonsillitis	8
	Infective disease (mainly <i>Streptococcus</i>)	8
	Pharyngitis	5
10 – 19	Otitis media	14
	Infective disease (mainly Streptococcal sore throat)	11
	Diseases of the genital/urinary system (mainly urinary tract infections of unspecified site)	9
	Pharyngitis	9
20-64	Diseases of the genital/urinary system (mainly urinary tract infections of unspecified site)	18
	Bronchitis	12
	Sinusitis	11
	Disease of the digestive system (e.g., proctocolitis, diverticulitis, periapical abscess)	6
65+	Diseases of the genital/urinary system (mainly urinary tract infections of unspecified site)	15
	Bronchitis	14
	Pneumonia	12
	Cellulitis	9

Increasing use of antimicrobials of high importance

The World Health Organization (WHO) has published a list of “reserve group” antibiotic products, which includes products that are intended to be used only in instances where all alternatives have failed^b.

The ‘antimicrobials of last resort’ available in Canada are as follows: aztreonam, cefepime, cefpirome, ceftaroline, colistin, daptomycin, intravenous fosfomycin, linezolid, polymyxin B, and tigecycline.

Despite direction to prescribe these products only when alternatives have failed, the use of these products has been increasing in Canada. This is suggested by a steady rise in hospital purchasing of these products. Use in the community setting has been more variable, with a peak in 2015, and an overall increase between 2012 and 2017.

The overall increase in use of antimicrobials of high importance has been driven by greater use of daptomycin, and to a lesser extent, aztreonam. No use of cefpirome, ceftaroline, intravenous fosfomycin, or polymyxin B was identified in 2017. This may indicate zero use of these products in Canada, or may indicate very low levels of use (so low that they may have been excluded due to potential for identification of prescribers and/or patients after data extrapolation).

^b World Health Organization. Essential medicines list. <http://www.who.int/mediacentre/news/releases/2017/essential-medicines-list/en/>

Figure 43: Defined Daily Doses (DDDs) per 1,000 inhabitant-days for antimicrobials of high importance purchased by hospitals and dispensed by pharmacies in Canada, 2012-2017

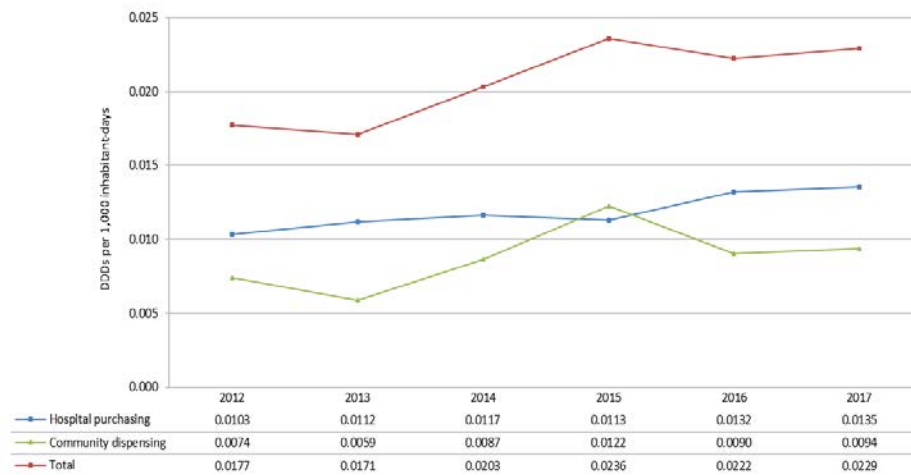
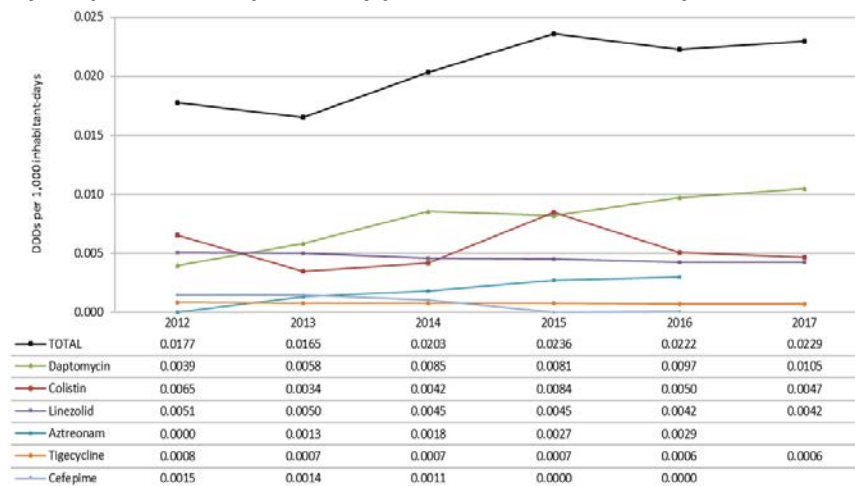


Figure 44: Defined Daily doses (DDDs) per 1,000 inhabitant-days for antimicrobials of high importance purchased by hospitals and dispensed by pharmacies in Canada, by antimicrobial, 2011-2017



Antimicrobials intended for use in animals and crops

The Canadian Animal Health Institute (CAHI) voluntarily provides data regarding antimicrobials distributed for sale for use in animals; CAHI represents manufacturers of animal health products and their members represent 95% of this market in Canada. At the time of writing, some of the CAHI member companies re-submitted their 2016 data; hence, the data included in this report differ slightly from the CAHI data presented previously. The CAHI reported quantities do not include antimicrobials imported for ‘own use’. Regulations restricting the own use importation practice came into effect in November 2017; hence, this practice could have occurred earlier in 2017. The CAHI’s quantities also do not include imported active pharmaceutical ingredients intended for further compounding. These data are expected to be captured by the Government of Canada in 2019.

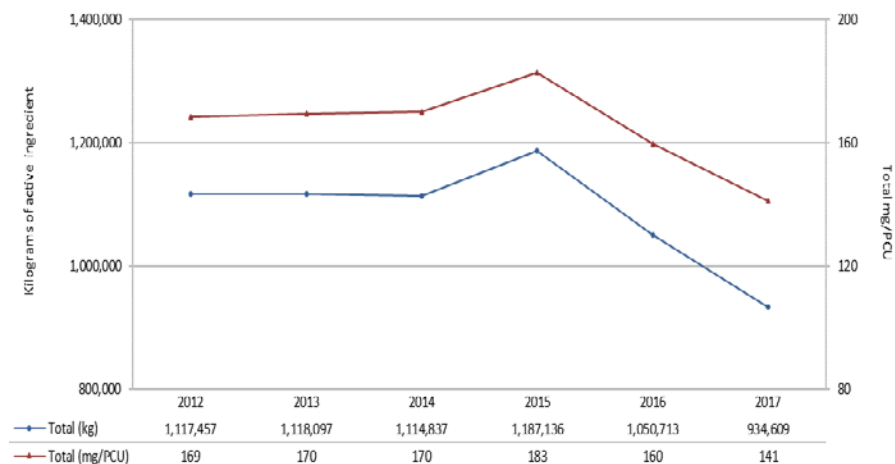
Antimicrobial use in production and companion animals

In 2017, approximately 950,000 kilograms of antimicrobials (excluding ionophores and chemical coccidiostats) were distributed for sale for use in animals by CAHI member companies. This volume was approximately 11% lower than in 2016 and the lowest reported since surveillance reporting began in 2006. The greatest decline from 2016 to 2017 occurred with the tetracyclines; a 95,241 kg decline equivalent to a 16% reduction.

The overall quantity of fluoroquinolones distributed for use in animals increased by 11% between 2016 and 2017. Fluoroquinolones are classified as “of very high importance to human medicine”, according to Health Canada’s Veterinary Drugs Directorate and as critically important antimicrobials according to the World Health Organization. In Canada, fluoroquinolones are licensed for use in certain animal species and come with recommendations against off-label use in other animal species due to AMR concerns.

The overall quantity of antimicrobials distributed is more meaningful when a denominator is applied to indicate how many animals these antimicrobials could potentially be given to. Additionally, animal species vary by weight. Therefore, both the number of animals and their weights need to be accounted for. When the standard weight in these calculations is based on an average weight of treatment, this denominator is known as the ‘population correction unit’ or ‘PCU’. Antimicrobial distribution/sales data adjusted by this denominator are reported as mg antimicrobial per kg animal. With this in mind, for production animals, the overall quantity of antimicrobials/PCU in Canada decreased by 12% since 2016; to the lowest reported since 2006 (using European standard animal weights).

Figure 45: Antimicrobials distributed for use in production animals over time; measured as kg of active ingredient and mg of active ingredient/population correction unit, 2012-2017



Note: The population data used for live horses was from 2010 and for fish was from 2016; more recent population data for these animal species were unavailable at the time of writing. Ionophores and chemical coccidiostats are not included in this figure. The data in this figure also do not include antimicrobials imported under the 'own use' provision or imported as active pharmaceutical ingredients used in compounding. The Total mg/PCU is calculated using the European standard.

Source: Canadian Animal Health Institute, Statistics Canada, Agriculture and Agri-Food Canada, Equine Canada, European Surveillance of Veterinary Antimicrobial Consumption.

Antimicrobial use in production animals

According to the 2017 data provided by CAHI member companies, the predominant classes of antimicrobials distributed for use in production animals (i.e., livestock, aquaculture, and horses) were the tetracyclines, “other antimicrobials” (avilamycin, bacitracin, chloramphenicol, chlorhexidine gluconate, florfenicol, fusidic acid, novobiocin, polymyxin B, tiamulin, bambamycin, and virginiamycin), beta-lactams (penicillins), and macrolides. Similar to 2016, these four antimicrobial classes represented approximately 87% of the volume of antimicrobials distributed for use in production animals.

Antimicrobial use in grower-finisher pigs

According to volunteer sentinel producers participating in CIPARS, the predominant classes of antimicrobials used in grower-finisher pigs in 2017 were tetracyclines, lincosamides, and macrolides. These antimicrobial classes represented over 78% of the total reported quantity of antimicrobials used in feed.

Antimicrobial use in broiler chickens

According to volunteer sentinel producers participating in CIPARS, the predominant classes of antimicrobials used in broiler chickens in 2017 were bacitracins, streptogramins, trimethoprim-sulfas, and orthosomycins. These antimicrobial classes represented over 88% of the total reported quantity of antimicrobial used.

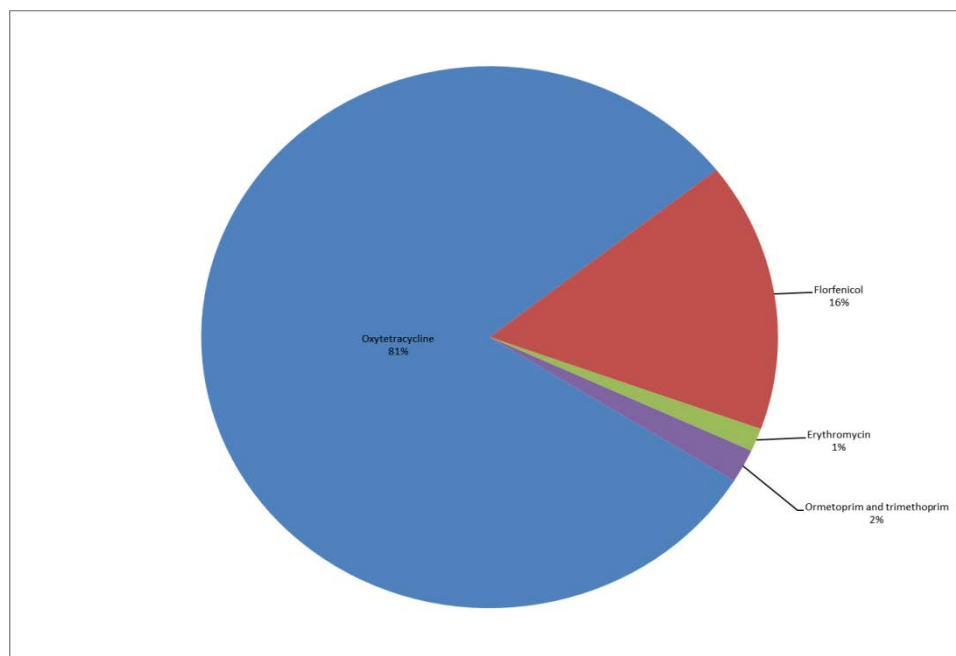
Antimicrobial use in turkeys

According to volunteer sentinel producers participating in CIPARS, the predominant classes of antimicrobials used in turkeys in 2017 were bacitracins, streptogramins, trimethoprim-sulfas, and macrolides. These antimicrobial classes represented over 96% of the total quantity of antimicrobials reported.

Antimicrobial use in marine finfish

Fisheries and Oceans Canada (DFO) requires industry owners and operators to report on their use of drugs and pesticides, including antimicrobials under the authority of the Aquaculture Activities Regulations authorized under the Fisheries Act. In an annual report, Aquaculture operators are required to report the quantity of drugs and pesticides used throughout the year at each location. From these data, the number of prescriptions and frequency of treatment is calculated, in addition to measures taken to avoid the need for their use. The most recent completed data are from 2016, but will be updated annually to reflect ongoing use. These data cover all marine finfish aquaculture facilities in Canada. Further information on the use of antimicrobials and other products by the aquaculture industry in Canada can be found on DFO's Aquaculture Public Reporting website.

Figure 46: Quantities (based on kg active ingredients) and type of antimicrobials used in marine finfish aquaculture in Canada, 2016



Source: Fisheries and Oceans Canada, 2018

Antimicrobial use in companion animals

According to the 2017 data provided by CAHI member companies, the predominant classes of antimicrobials distributed for use in companion animals were cephalosporins, beta-lactams, and trimethoprim-sulfas. This was similar to what was observed in 2016. These three classes represent approximately 95% of the volume of antimicrobials distributed for use in companion animals. PHAC is exploring the use of IQVIA data regarding the quantities of antimicrobials sold from human community pharmacies under veterinary prescription intended for use in companion animals.

Route of administration

Similar to previous years, CAHI data show that in 2017, antimicrobials were predominantly distributed for use in animals in feed (80%). Other less frequent routes of administration included water, injection, oral/topical, and intramammary (10%, 8%, 2%, <1%, respectively). Similar to the CAHI data, findings from farm surveillance (i.e., grower-finisher pigs, broiler chickens, and turkeys) indicate that the majority of antimicrobials were administered through feed.

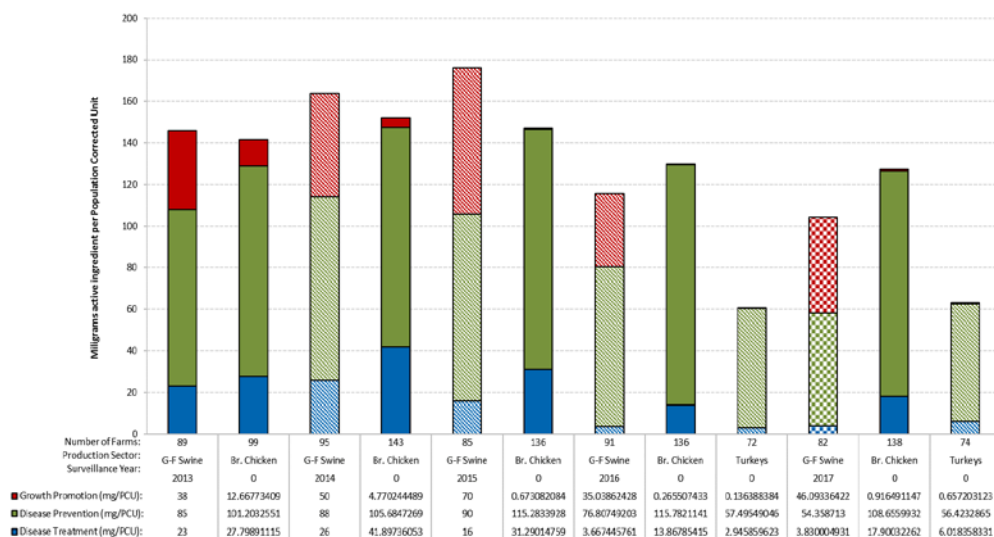
Indication for antimicrobial use in animals

In Canada, antimicrobials are used in animals to treat disease, prevent disease, or to promote growth (i.e., production claims), though there is pending action to remove the growth promotion claims of medically important antimicrobials.

In 2017, more farms participating in PHAC surveillance reported not using antimicrobials. Specifically, 32% and 19% of participating pig and chicken farmers, respectively, reported no use of medically important antimicrobials. This is a significant increase in the number of farmers reporting no use of medically important antimicrobials use compared to 2016, where the proportions were 11% and 7% of participating pig and chicken farmers, respectively. Similarly, among participating turkey farmers, 20% reported no use of medically important antimicrobials, an increase compared to 13% in 2016.

In 2017 the overall reported quantity of antimicrobial use in pigs declined; the proportion of antimicrobials used for disease prevention decreased to 52%, while the proportion of use for growth promotion increased to 44%. The overall quantity of antimicrobials used in chickens also declined, with little change in the proportion of use for treatment and prevention. Participating turkey farmers reported a small increase in the overall quantity of antimicrobial use; an increase in the proportion used for disease treatment to 10% and a decrease in the proportion used for disease prevention to 89%.

Figure 47: Trends in antimicrobials used on grower-finisher pig, broiler chicken and turkey sentinel farms, by reason for use, based on estimates of mg/PCU, 2012-2017



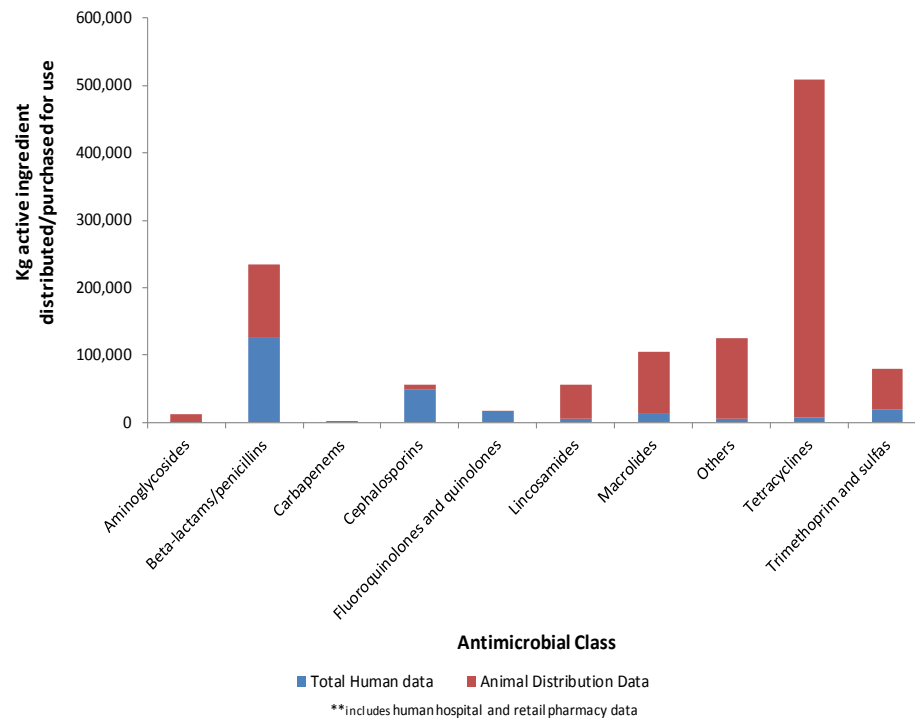
Source: CIPARS

Integration of data on antimicrobials intended for use in humans, animals, and crops

When measured by kilograms of active ingredient, approximately 77% of antimicrobials distributed or sold in 2017 were intended for production animals, 20% were for humans, 2% for crops and 1% for companion animals (data sources: CAHI; IQVIA and Health Canada; Pest Management Regulatory Agency, Health Canada; and CAHI, respectively). For context, there were approximately 20 times more animals in Canada in 2017 than people; this is an underestimate of the number of animals because the statistics on fish are reported as kg of fish, not number of live animals and hence cannot be included. After adjusting for underlying populations and average weights (i.e., mg drug/kg animal or mg drug/kg human), there were roughly 1.5 times more antimicrobials distributed for use in animals (using European standard average weights at treatment) than in humans.

Similar antimicrobials are used in humans and animals; however, some antimicrobial classes are sold or distributed more for use in humans than animals and vice-versa. By raw kilograms of antimicrobials, fluoroquinolones and cephalosporins are predominantly used in humans, and that macrolides and tetracyclines are used more frequently in animals. In Canada, carbapenems have never been licensed for use in animals.

Figure 48: Kilograms of antimicrobials distributed and/or sold for use in animals and humans, by antimicrobial class, 2017



Source: Canadian Animal Health Institute, IQVIA and Health Canada's Non-Insured Health Benefits (NIHB) program.

Note: Total Human Data includes human hospital and retail pharmacy data. Values for the animal data do not include antimicrobials imported under the 'own use' provision or imported as active pharmaceutical ingredients used in compounding. Ionophores and chemical coccidiostats are excluded. The macrolide class for humans includes the ketolides. Other antimicrobials for the animal data included: avilamycin, bacitracin, chloramphenicol, chlorhexidine gluconate, florfenicol, fusidic acid, novobiocin, polymyxin B, tiamulin, bambarmycin, and virginiamycin. Other antimicrobials for the human data included: bacitracin, chloramphenicol, colistimethate, colistin, daptomycin, fidaxomicin, fosfomicin, fusidic acid, linezolid, methenamine hippurate, methenamine mandelate, metronidazole, nitrofurantoin, polymyxin b, and vancomycin.

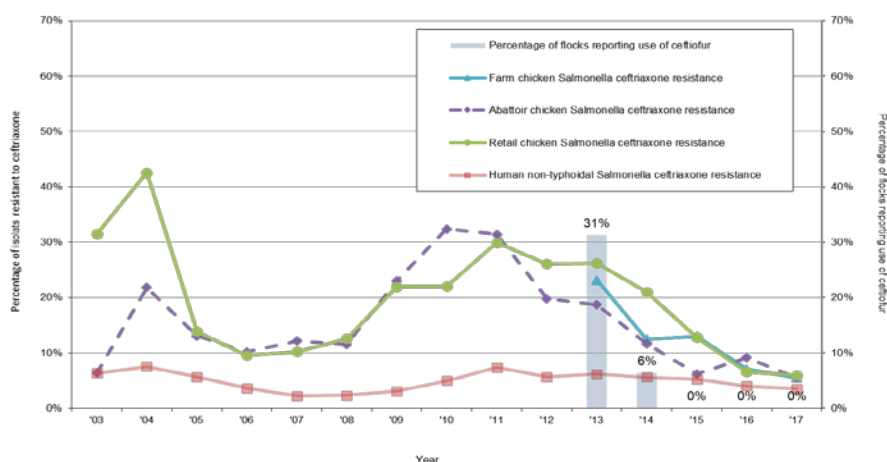
Integration of data on cephalosporin resistance in non-typhoidal *Salmonella* and generic *Escherichia coli*

Ceftriaxone is a Category I (i.e. very high importance to human medicine) antimicrobial that is used to treat a variety of human infections. Although ceftriaxone is not used in animals, similar drugs (e.g., ceftiofur) are used to treat and prevent a range of animal infections. In most situations, if an organism is resistant to one of these drugs, it will also be resistant to the other.

In the 2017 CARSS report, data from 2015-2016 illustrated a marked reduction in reported use of ceftiofur on broiler chicken farms (i.e. no reported use) and a general decrease in ceftriaxone resistance in *Salmonella* from humans, chickens, and chicken meat. Additionally, in mid-2014, the poultry industry implemented a national ban on the use of Category I antimicrobials, including ceftiofur, for disease prevention purposes. As in recent years, the industry-led initiative to eliminate the use of ceftiofur and all other Category I antimicrobials in poultry for disease prevention has appeared to have had the desired effect. In 2017, CIPARS data have again shown no reported use of ceftiofur in broiler chickens, as well as continued reduced resistance in *Salmonella* from chickens and chicken meat. This was also found in generic *E. coli* from these sample types (data not shown). In humans, most ceftriaxone resistance was observed in *Salmonella* Heidelberg isolates. In 2017, resistance to ceftriaxone in *Salmonella* Heidelberg isolates from humans dropped to 12%, down from 16% in 2016 (data not shown).

This trend will be monitored over time and the impact of this important intervention on resistance in *Salmonella* isolates from humans will also continue to be examined.

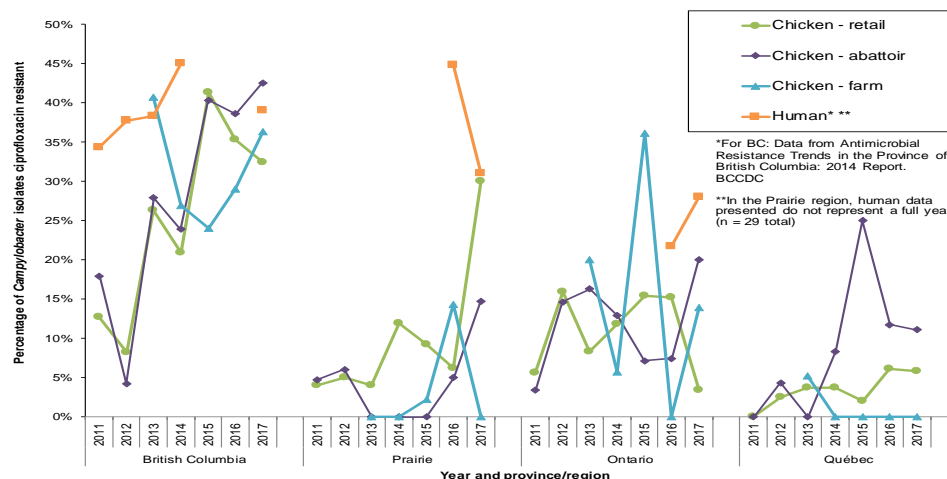
Figure 49: Reported use of ceftiofur on farms, and resistance to ceftriaxone in non-typhoidal *Salmonella* isolates from humans and chicken, 2003-2017



Integration of data on fluoroquinolone resistance in *Campylobacter*

Ciprofloxacin, a fluoroquinolone antimicrobial, is a category I antimicrobial (very high importance in human medicine). In 2016, ciprofloxacin resistance in *Campylobacter* from chicken continued to vary over time and across regions. The highest proportion of resistant isolates from chicken and chicken meat continued to be from British Columbia. More specifically, in 2016, resistance to ciprofloxacin among *Campylobacter* from chicken was highest in British Columbia for all surveillance components (farm, abattoir [slaughter] and retail). In 2016 and 2017, there was no reported fluoroquinolone use by participating sentinel chicken farms, which was consistent with the poultry industry's ban of Category I antimicrobials for disease prevention that began implementation in mid-2014. In 2016, antimicrobial resistance data for *Campylobacter* from humans, including ciprofloxacin, first became available through the FoodNet Canada program for two regions (Ontario, and the Prairie region - which for the human data only includes Alberta). These newly available human data are essential to begin to contextualize resistance data observed in food and food animals such as those described above. In 2017, data on ciprofloxacin-resistant *Campylobacter* from humans also became available in British Columbia through FoodNet Canada. Although data are limited and should be interpreted with caution, ciprofloxacin resistance among *Campylobacter* from humans was higher in British Columbia in 2017 compared to Alberta and Ontario. Ciprofloxacin resistance among *Campylobacter* from chicken was also highest in British Columbia, not only in retail meat samples but also at slaughter and from healthy chickens on-farm (Figure 50). With the availability of *Campylobacter* resistance data from humans as well as from food and food animals, this integrated story will continue to be monitored closely as new data arise.

Figure 50: Ciprofloxacin resistance among *Campylobacter* from humans and chicken sources, 2011-2017



References

1. Public Health Agency of Canada. Pan-Canadian framework for action on antimicrobial resistance. Can Commun Dis Rep. 2017; 43(11):217-9. <https://doi.org/10.14745/ccdr.v43i11a01> [Internet] Available from: <https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2017-43/ccdr-volume-43-11-november-2-2017/pan-canadian-framework-action-antimicrobial-resistance.html>
2. Public Health Agency of Canada. *Canadian Antimicrobial Resistance Surveillance System 2017 Report*. Public Health Agency of Canada; 2017. [Internet] Available from: <https://www.canada.ca/en/public-health/services/publications/drugs-health-products/canadian-antimicrobial-resistance-surveillance-system-2017-report-executive-summary.html>
3. Trepanier P, Mallard K, Meunier D, Pike R, Brown D, Ashby JP, et al. Carbapenemase-producing *Enterobacteriaceae* in the UK: a national study (EuSCAPE-UK) on prevalence, incidence, laboratory detection methods and infection control measures, J Antimicrob Chemother. 2017 Feb.1; 72 (2): 596–603, doi: 10.1093/jac/dkw414. <https://academic.oup.com/jac/article/72/2/596/2643145>
4. Samuelsen Ø, Overballe-Petersen S, Bjørnholt JV, Brisse S, Doumith M, Woodford N, et al. Molecular and epidemiological characterization of carbapenemase-producing *Enterobacteriaceae* in Norway, 2007 to 2014. PLoS ONE 2017; 12(11): e0187832. <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0187832>
5. Löfmark S, Sjöström K, Mäkitalo B, Edquist P, Tegmark Wisell K, Giske CG. Carbapenemase-producing *Enterobacteriaceae* in Sweden 2007-2013: Experiences from seven years of systematic surveillance and mandatory reporting. Drug Resist Updat. 2015 May; 20:29-38. doi: 10.1016/j.drup.2015.05.001. <https://www.sciencedirect.com/science/article/pii/S1368764615000229?via%3Dihub>
6. Livorsi DJ, Chorazy ML, Schweizer ML, Balkenende EC, Blevins AE, Nair R et al. A systematic review of the epidemiology of carbapenem-resistant *Enterobacteriaceae* in the United States. Antimicrob Resist Infect Control. 2018; 7:55. doi:10.1186/s13756-018-0346-9. <https://aricjournal.biomedcentral.com/articles/10.1186/s13756-018-0346-9>
7. Albiger B, Glasner C, Struelens M, Grundmann H, Monnet D, The European Survey of Carbapenemase-Producing *Enterobacteriaceae* (EuSCAPE) working group. Carbapenemase-producing *Enterobacteriaceae* in Europe: assessment by national experts from 38 countries, May 2015. Euro Surveill. 2015; 20(45): pii=30062. doi: <http://dx.doi.org/10.2807/1560-7917.ES.2015.20.45.30062>
8. Lefebvre B, Martin I, Demczuk W, Deshaies L, Michaud S, Labbé AC et al. Ceftriaxone-Resistant *Neisseria gonorrhoeae*, Canada, 2017. Emerg Infect Dis. 2018; 24(2):381-383. doi:10.3201/eid2402.171756. https://wwwnc.cdc.gov/eid/article/24/2/17-1756_article

Appendix

The following surveillance systems provided AMR results for this report:

1. *The Canadian Nosocomial Infection Surveillance Program (CNISP)*

Established in 1994, CNISP is a collaborative effort between PHAC and sentinel hospitals participating as members of the Canadian Hospital Epidemiology Committee (CHEC), a subcommittee of the Association of Medical Microbiology and Infectious Disease (AMMI) Canada. This program conducts surveillance on select antimicrobial-resistant organisms and healthcare-associated infections in 66 largely university-affiliated, acute-care hospitals in all provinces. No data are collected from the three territories.

2. *The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)*

Established in 2002, the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) collects, analyses, and communicates trends in antimicrobial use and in antimicrobial resistance for select bacteria from humans, animals, and retail meat across Canada. The bacteria under surveillance are known as enteric bacteria (they can be found in the intestines of people and animals) and can be transmitted between animals and people. Information from CIPARS supports measures to contain the emergence and spread of resistant bacteria among animals, food, and people, with the aim of prolonging the effectiveness of antimicrobials. Detailed methods of CIPARS activities can be found at http://publications.gc.ca/collections/collection_2017/aspc-phac/HP2-4-2015-eng.pdf.

3. *The Canadian Tuberculosis Reporting System (CTBRS) and The Canadian Tuberculosis Lab Surveillance System (CTBLSS)*

The CTBRS is a case-based surveillance system that uses data submitted by the provincial and territorial public health authorities to maintain non-nominal information on people diagnosed with active tuberculosis. The CTBLSS is an isolate-based surveillance system that uses data submitted by provincial TB laboratories to maintain information on the results of all unique TB isolates tested for drug resistance.

4. *The Antimicrobial-resistant Neisseria gonorrhoeae Surveillance System*

The *Antimicrobial-resistant Neisseria gonorrhoeae Surveillance System* has monitored antimicrobial susceptibilities of *N. gonorrhoeae* since 1985, through collaboration between the National Microbiology Laboratory (NML) and provincial laboratories.

5. *The Enhanced Surveillance of Gonorrhoeae (ESAG)*

The enhanced surveillance of Gonorrhoeae is an integrated epidemiology-laboratory surveillance system, designed to improve the understanding of current levels and trends of AMR gonorrhea in Canada, through partnership with Alberta, Manitoba, and Nova Scotia.

6. *The National Surveillance of Invasive Streptococcal Disease*

The *National Surveillance of Invasive Streptococcal Disease* is a passive surveillance system that monitors antimicrobial susceptibilities in *Streptococcus pneumoniae* and *Streptococcus pyogenes* isolated from sterile sites such as blood and spinal fluid. The surveillance is conducted through collaboration between the NML, provincial laboratories, the University of Manitoba, and the Canadian Antimicrobial Resistance Alliance.

In addition to the systems outlined above, PHAC's NML supports all AMR surveillance programs, providing data on molecular characterization and antimicrobial resistance. The NML also provides laboratory reference services to all provinces and territories, which assists with the detection of novel and emerging AMR organisms.

The following data sources are accessed to generate AMU results for this report:

1. Community AMU

The data presented are from two datasets: the Canadian CompuScript (CCS) dataset (purchased from IQVIA), and Health Canada's Non-Insured Health Benefits (NIHB) program. The CCS includes data collected from 59% of pharmacies in Canadian provinces, which are extrapolated to the universe of nearly 10,300 Canadian pharmacies. Data included are prescriptions dispensed by antimicrobial product, and the number of units dispensed by product.

The NIHB program data were acquired in order to present a picture of use among Indigenous populations in Canada. This dataset includes prescription counts and the number of units dispensed by product for all prescriptions dispensed under the program.

2. AMU by diagnosis

The Canadian Disease and Therapeutic index (CDTI) dataset, purchased from IQVIA, provides information about the patterns and treatments of disease encountered by office-based physicians (specialists and general practitioners, including those with offices in hospitals). Data from 652 physicians were available in 2017, and projection methods were used to extrapolate to the universe of approximately 62,743 Canadian physicians. At visits to these physicians during data collection periods, the physicians record all diagnoses made, as well as all drug products that are recommended (whether or not a prescription for that product is provided).

3. Hospital AMU

The Canadian Drugstore and Hospital (CDH) database, purchased from IQVIA, provides a measure of the dollar value and unit volume of pharmaceutical products purchased by nearly all Canadian hospitals. Data about purchases from pharmaceutical manufacturer warehouses/wholesalers are collected from over 839 hospitals, and are extrapolated to represent purchases made by over 1,001 hospitals across Canada.

4. AMU in animals and crops

The Canadian Animal Health Institute (CAHI) voluntarily provides CIPARS with data on the quantities of antimicrobial agents distributed by their member companies. Health Canada's Pest Management Regulatory Agency (PMRA) collects annual Canadian sales data from all pesticide manufacturers for antimicrobials intended for use on crops and provides these data to CIPARS. PHAC also collects information about antimicrobial use in broiler chickens, turkeys, and grower-finisher pigs through surveillance of sentinel farms.



PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH



Public Health
Agency of Canada

Agence de la santé
publique du Canada

Canada