Manitoba Centre for Health Policy

Outpatient Antibiotic Prescribing by Manitoba Clinicians

Autumn 2021

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About the Manitoba Centre for Health Policy

The Manitoba Centre for Health Policy (MCHP) is located within the Department of Community Health Sciences, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba. The mission of MCHP is to provide accurate and timely information to healthcare decision-makers, analysts and providers, so they can offer services that are effective and efficient in maintaining and improving the health of Manitobans. Our researchers rely upon the unique Manitoba Population Research Data Repository (Repository) to describe and explain patterns of care and profiles of illness and to explore other factors that influence health, including income, education, employment, and social status. This Repository is unique in terms of its comprehensiveness, degree of integration, and orientation around an anonymized population registry.

Members of MCHP consult extensively with government officials, healthcare administrators, and clinicians to develop a research agenda that is topical and relevant.

This strength, along with its rigorous academic standards, enables MCHP to contribute to the health policy process. MCHP undertakes several major research projects, such as this one, every year under contract to Manitoba Health and Seniors Care. In addition, our researchers secure external funding by competing for research grants. We are widely published and internationally recognized. Further, our researchers collaborate with a number of highly respected scientists from Canada, the United States, Europe, and Australia.

We thank the Research Ethics Board on the Bannatyne Campus at the University of Manitoba for their review of this project. MCHP complies with all legislative acts and regulations governing the protection and use of sensitive information. We implement strict policies and procedures to protect the privacy and security of anonymized data used to produce this report and we keep the provincial Health Information Privacy Committee informed of all work undertaken for Manitoba Health and Seniors Care.

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Abbreviations

aOR	Adjusted Odds Ratios
ASP	Antimicrobial Stewardship Program
ATC	Anatomical Therapeutic Chemical Classification
COPD	Chronic Obstructive Pulmonary Disease
SARS-CoV-2	Coronavirus currently causing the COVID-19 pandemic
DDD	Defined Daily Dose
DPIN	Drug Program Information Network
ESAC-Net	European Surveillance of Antibiotic Consumption Network
GAS	Group A Streptococcus
ICD	International Classification of Diseases
IQR	Interquartile Range
MCHP	Manitoba Centre for Health Policy
MHSC	Manitoba Health and Seniors Care
PCP	Primary Care Provider
SEFI-2	Socioeconomic Factor Index-2
SSTI	Skin and Soft Tissue Infections
URTI	Upper Respiratory Tract Infection
UTI	Urinary Tract Infections

Executive Summary

Introduction

Antibiotics are essential life-saving medications in modern medicine. They are part of a larger overall group of medications called “antimicrobials” and are used to treat bacterial infections. Without the curative power of antibiotics, many routine medical procedures and minor infections would be very risky. However, with the overuse of antibiotics, antibiotic resistance is increasing, and infections are becoming more difficult to treat. As antibiotic resistance becomes more widespread, more patients will succumb to antibiotic-resistant infections.

Antimicrobial stewardship programs (ASP) are quality improvement programs that aim to reduce unnecessary antibiotic use without impacting appropriate use. The vast majority of antibiotic use in Manitoba is among outpatients (outside of hospitals), where it is conservatively estimated that 30% of antibiotics are unnecessary [1,2]. This report focuses on outpatient antibiotic use in Manitoba.

Research Objectives

- **Objective 1:** Examine trends for antibiotic use (or dispensation) in Manitoba from 2011-16:
  - by age group and health region, using dispensations per 1,000 people per day;
  - using the European Surveillance of Antibiotic Consumption Network (ESAC-Net) quality indicators.
- **Objective 2:** Examine patterns of health services use of patients prescribed antibiotics in Manitoba by looking at:
  - the relationship between ambulatory care physician visits and antibiotic dispensations;
  - the characteristics of physician-prescribed dispensations not linked to a health care contact;
  - the characteristics of dispensations of antibiotics prescribed by non-physician health care professionals;
  - the relationship between diagnosis codes provided by ambulatory primary care physicians and antibiotic dispensations to ascertain appropriateness of antibiotic use.
- **Objective 3:** Develop a framework for providing antibiotic prescribing feedback at the individual practitioner level.

Data Source and Methods

MCHP's Manitoba Population Research Data Repository was used to characterize the use of oral antibiotic medications in the outpatient setting by a Manitoba cohort from 2011-2016 (excluding personal care home residents, those with a Child and Family Services address, and wards of public trustees who have a mailing address of the office that represents them, but their postal code of residence is unknown). Antibiotics were classified by their mechanism of action according to the Anatomical Therapeutic Chemical (ATC) classification (see the MCHP Concept Dictionary for a full definition http://mchp-appserv.cpe.umanitoba.ca/viewDefinition.php?definitionID=102254). The Drug Program Information Network (DPIN) data that was used identifies dispensations of drugs (i.e., filled prescriptions). Prescriptions that went unfilled and medications dispensed without a prescription were not included. Results are presented for adults (15 years and older) and children, as well as by smaller age groups and by health region of residence when looking at overall dispensation trends. Linkage of antibiotic dispensations to outpatient physician visits and hospital discharges was undertaken to further examine patterns of use. International Classification of Diseases (ICD-9-CM) codes were used to identify the diagnosis (billing) code associated with the antibiotic dispensation and categorized according to the objectives above. This approach has some limitations, specifically that the diagnosis code may not necessarily represent the indication for the antibiotic but has been previously used in published studies and antibiotic stewardship programs. Multi-level regression models were run to look for associations between physician and patient characteristics and antibiotic dispensations. Dispensation rates were also examined at the individual prescriber level (de-identified) in order to ascertain the ability of the data to provide a prescriber-level feedback report, comparing dispensation rates to peer rates.

Notes About Terminology

It should be noted that this report captures dispensations of antibiotics only. When we use the term 'antibiotic use', we mean antibiotic dispensations by pharmacies, thus indicating the initial prescription written by the provider and intended for use by the patient based on filling the prescription.

A broad-spectrum antibiotic is one that is effective against a wide range of bacteria, often multiple types such as gram-positive and gram-negative. A narrow-spectrum antibiotic is effective against a smaller range of bacteria. In general, the narrowest-spectrum antibiotic should be used whenever possible, because broader-spectrum antibiotics lead to more selection pressure for antibiotic resistance.

Dispensation Patterns for Antibiotics in Manitoba

The percentage of the Manitoba population who filled at least one prescription increased from 6.5% in 2011 to 6.6% in 2016, and while this difference may seem small, it amounted to over 67,000 more prescriptions in 2016 than 2011. Age- and sex-adjusted dispensation rates are reported per 1,000 people per day by any prescriber, by drug class, subclass and for some individual antibiotics. In 2016, the overall dispensation rate in adults was slightly higher and in children it was slightly lower than in 2011. The most commonly dispensed antibiotics in 2016 were β-lactam penicillins (35.0%), macrolides (23.9%), quinolones (13.7%) and cephalosporins (11.2%) (Table E.1). Dispensation rates for all antibiotics varied by age group and were highest in those under five years old and 65 years and older. There was seasonal variation with more antibiotics dispensed in the winter months compared to summer months, a pattern that was more pronounced in younger age groups. Rates differed by health region, with Prairie Mountain Health having the highest rate of

dispensations overall. Northern Health Region had differing patterns depending on drug class (some classes were dispensed at lower rates compared to Manitoba overall and some higher). This may reflect differences in which antibiotics are dispensed directly from nursing stations (which are not captured in our data) compared to those requiring a prescription (which are captured).

Table E.1: Key Findings by Drug Class

Drug Class	Examples of Drugs in this Class	Percent of Total Antibiotics Dispensed in 2016	Findings
J01A - Tetracyclines	- doxycycline - tetracycline	5.6%	- used mostly in adults, in whom dispensation rates were higher in 2016 than 2011
J01C - Beta-Lactam Penicillins	- amoxicillin - amoxicillin and clavulanate	35%	- highest use in children under age 10 and with pronounced seasonal variation - use was higher for adults 65 and older in 2016 than 2011 - no consistent pattern over time in other age groups
J01D - Cephalosporins	- cephalexin - cefuroxime	11.2%	- highest use in children aged 1-4 - Rates were slightly lower in 2016 than 2011 in children under age 10 but slightly higher for older age groups
J01E - Sulfonamides and Trimethoprims	- trimethoprim and sulfamethoxazole	4.9%	- higher rates in adults than children - use was higher in 2016 than 2011 for all ages under 65 years - Large variation in rates were seen in children due to varied availability of the oral suspension.
J01F - Macrolides, Lincosamides and Streptogramins	- azithromycin - clindamycin	23.9%	- highest use in children aged 1-4 and in adults aged 15 and older with wide seasonal variation - use in general was lower in 2016 than 2011 in all age groups except 10-14 year olds
J01M - Quinolones	- ciprofloxacin - levofloxacin	13.7%	- this class is rarely used in children - use for adults aged 65 and older was almost 3 times that of use in younger adults - use was lower in 2016 than 2011, and this was E9more pronounced in older adults

Dispensation Trends using the European Surveillance of Antibiotic Consumption Network Quality Indicators

This analysis compares antibiotic dispensation using quality indicators for community consumption of antibiotics developed by the European Centre for Disease Prevention and Control under the European Surveillance of Antibiotic Consumption Network (ESAC-Net). These indicators measure antibiotic use as defined daily doses (DDD) per 1,000 people per day rather than the dispensations per 1,000 people per day reported in the previous results. Age- and sex-adjusted results for 2016 were compared to 2011 (Table E.2). Results across health regions are also presented in Chapter 3. It should be noted that changes in population health over time may lead to justifiable changes in antibiotic use. For some indicators, differences may look large due to wide confidence intervals; all significant differences are indicated as such.

Results comparing 2016 indicators to 2011 indicators:

Table E.2: Comparing Antibiotic Consumption 2011-2016

ESAC-Net Indicator	Value by year (% or ratio)		Interpretation of the Change from 2011-2016
	2011	2016	
Consumption of β-lactamase-sensitive penicillins expressed as a percent of total consumption of total antibacterials	1.9%	1.5%	Indicates less prudent use
Consumption of β-lactamase inhibitor penicillin combinations as percent of total antimicrobials	4.4%	6.8%	Indicates less prudent use
Consumption of third- and fourth-generation cephalosporins as percent of total antimicrobials	0.3%	0.1%	Indicates more prudent use
Consumption of fluoroquinolones as percent of total antimicrobials	10.6%	10.1%	Did not change
Ratio of broad spectrum to narrow spectrum penicillins, cephalosporins and macrolides	2.7	2.6	Did not change
Seasonal Variation in Total Antibacterial Use (% increased use in winter compared to summer)	16.2%	10.3%	Indicates more prudent use
Seasonal variation in quinolone use	3.4%	-10.9%	Trend towards change: Higher use in winter, changed to higher use in summer

Relationship Between Ambulatory Care Physician Visits and Antibiotic Dispensations

We examined the relationship between ambulatory care physician visits[1] and antibiotic dispensations. Antibiotic dispensations were considered to be related to that visit, and thus linked, if they occurred within five days. Due to data limitations, only physician visits (but not visits to nurse practitioners or other practitioners) could be linked directly to dispensations. While there are limitations to the use of ICD-9-CM codes to ascertain the reason for antibiotic dispensation, these codes are used extensively in the literature and studies have demonstrated a demonstrated correlation of 50-80% compared to chart review/clinical databases [3–5].

There were 36,634,945 qualifying ambulatory care physician visits in the years 2011-2016. Overall, 8.44% of ambulatory care physician visits were linked to an outpatient antibiotic dispensation; 10.95% of ambulatory primary care visits and 1.34% of other ambulatory visits were linked to antibiotic dispensations. In 2016, slightly lower rates of ambulatory care physician visits were associated with antibiotic dispensations than 2011.

Dispensation rates were highest for Prairie Mountain Health in all years and lowest in Northern Health Region. Rates were lowest for seniors age 65+ years and highest for children ages 1-4.

Characteristics of Physician-Prescribed Dispensations not Linked to a Health Care Contact

Understanding why an antibiotic dispensation might not be linked to a health care contact is important for interpreting and generalizing the results for linked dispensations. An antibiotic dispensation might be unlinked, that is no physician visit was identifiable in the 5 days preceding the dispensation for different reasons. Examples include that no health care contact occurred, a contact may have occurred but not been captured in the data (due to non-billing physicians) or because the antibiotic was prescribed by a non-physician. Data discriminating non-physician-

1 Ambulatory visits include almost all contacts with physicians; this includes office visits, walk-in clinics, home visits, emergency department visits and visits to outpatient departments.

prescribed dispensations from physician-prescribed dispensations were only available from 2014 onwards, thus this objective uses data from 2014-2016 only.

Overall, 74.1% of prescriptions were linked with a hospital discharge or physician visit. While this report is focused on outpatient use, for this particular analysis we included prescriptions that could be associated with a hospital discharge (within two days). Unlinked dispensations were more likely to be adult (than paediatric) and differed by health region with Northern Health Region having the highest number of dispensations not associated with a health care contact (almost double that of some other regions) and Prairie Mountain Health having the lowest. Tetracyclines as a class were the most likely to be unlinked, with macrolides[2] and β-lactam penicillins were most likely to be linked. There was a statistically significant difference in the percentage of unlinked dispensations between the years 2014 and 2016, but it was less than 1%.

Further testing looking at detailed physician and patient characteristics demonstrated differences between linked and unlinked dispensations across all of the characteristics we measured.

Characteristics of Dispensations of Antibiotics Prescribed by Non-Physician Health Care Professionals

From 2014 onwards, the type of prescriber could be identified from the DPIN data. Table E.3 presents the distribution of prescriber type in all dispensations. Patterns of antibiotic classes prescribed reflect the common conditions seen by these practitioners.

Table E.3: Antibiotic Dispensations by Type of Prescribing Healthcare Professional, 2014-2016

Healthcare Professionals	Antibiotic Dispensations	
	Count	Percent
Physicians	2,240,581	87.04
Dentists	239,802	9.32
Nurse Practitioners	88,942	3.46
Pharmacists	3,950	0.15
Optometrists	733	0.03
Midwives	202	0.01
Other	56	<0.01

Relationship between Diagnosis Codes Provided by Ambulatory Primary Care Physicians and Antibiotic Dispensations to Ascertain Appropriateness of Antibiotic Use

Benchmark conditions for which antibiotics may have been prescribed were divided into conditions that generally do not require antibiotics and conditions that may require antibiotics. A statistical multi-level model examining all available factors known to be predictors of antibiotic dispensations was run to identify important patterns.

Results for Conditions That Generally Do Not Require Antibiotics

These conditions included acute bronchitis, asthma/allergic rhinitis, cough and upper respiratory tract infection (URTI, common cold) [6–11]. There was a wide variability in the dispensation of antibiotics for the conditions in this category. Dispensations for acute bronchitis were highest in all age groups (over 60% in all age groups except for children under age one), and the other three conditions had much lower dispensation rates (all less than 30%) with variability by age and condition. There was wide variability across physicians in how often they prescribed antibiotics for URTI and acute bronchitis, with narrower variability for asthma/allergic rhinitis and cough.

In 2016, dispensation rates were significantly higher in most age groups than in 2011. For asthma/allergic rhinitis, rates were significantly higher in most age groups. For cough, there was a variable pattern; however, in adults, the rates were significantly higher. For URTI, rates were significantly lower in all age groups except age 65+, where they were higher.

The adjusted model examining characteristics associated with the odds of an antibiotic dispensation for conditions that generally do not require antibiotics demonstrated greater antibiotic use when the physician had a higher

2 Macrolides, lincosamides and streptogramin class of antibiotics

patient load, the physician practice was in Prairie Mountain Health, there were more patient comorbidities, and patient socioeconomic status was lower. Visits to the majority of care provider, seeing a paediatrician (for children), and the dispensation occurring in the summer months compared to the winter months were associated with lower use of antibiotics. The majority of care provider was identified (for patients with at least 3 visits) as the provider seen for 50% of primary care visits.

Results for Conditions That May Require Antibiotics

These conditions included acute laryngitis/tracheitis, acute otitis media, pharyngitis, pneumonia and sinusitis. For all but laryngitis/tracheitis, rates of antibiotic use were highest in late childhood and were lower in adulthood than in childhood. Rates were similar among these conditions, varying from approximately 45-60%. For laryngitis/tracheitis, rates were lower (approximately 20%) and highest in adulthood. With the exception of pneumonia, where quinolones were the second most common antibiotic, classes dispensed tended to be macrolides and penicillins, with penicillins more common in younger age groups and macrolides more common as age increased. Quinolones were seen in all conditions in adults; there was a small representation of the cephalosporins, but other antibiotics were substantially less commonly used. There was wide variability across physicians in how often they dispensed antibiotics for all conditions in this group.

In 2016, rates were significantly lower for acute laryngitis/tracheitis than in 2011 and higher for acute otitis media, pharyngitis, and pneumonia, except in patients aged 65+. There was no change for sinusitis.

In this category of conditions, clinical factors such as patient age, socioeconomic status and comorbidities influenced whether antibiotics were prescribed; as expected, these factors were associated with differences in dispensation rates in the models. However, similar to the models for conditions which generally do not require antibiotics, visits to the majority of care provider and prescriptions by a paediatrician were associated with moderately lower odds of a dispensation and a physician having a higher patient load and having received their training outside of Canada/United States was associated with higher dispensation odds. There was some seasonality, but the odds ratios were relatively low. There was no seasonality for pneumonia, a finding that requires further investigation.

For three conditions, acute otitis media, pharyngitis and pneumonia, models were also run to examine characteristics associated with dispensation of an inappropriate type of antibiotic. For acute otitis media 23.4% and for pharyngitis 30.4% of antibiotics dispensed were an inappropriate type. Appropriateness of antibiotic choice for pneumonia was only examined in children, and in 52.4% of dispensations it was inappropriate.

A Framework for Providing Antibiotic Prescribing Feedback at the Individual Practitioner Level

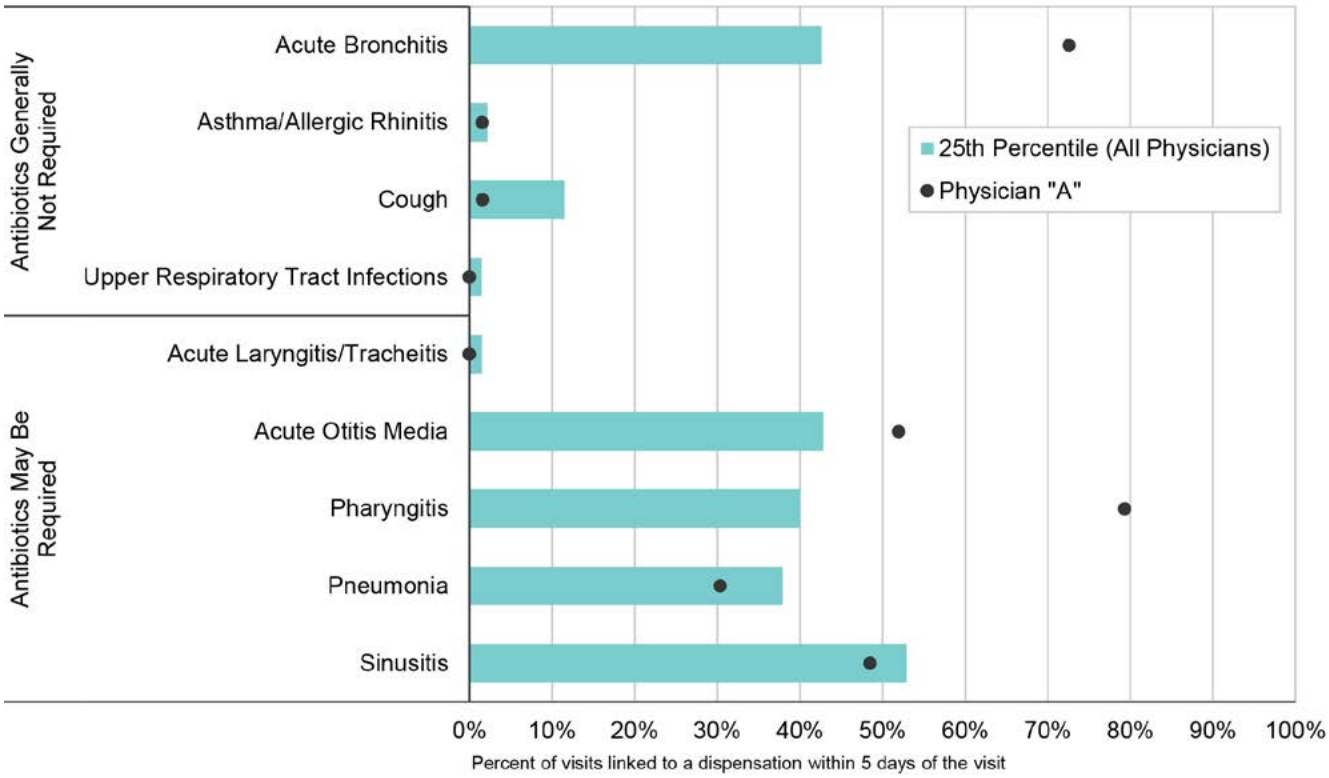
For each condition where antibiotics are generally not required (4 conditions) or may be required (5 conditions), the percentage of visits that were linked to an antibiotic dispensation for each individual primary care provider (PCP) (family physician or paediatrician) from 2014 to 2016 was calculated. This allowed us to identify how many prescribers are frequent or infrequent prescribers for each condition by comparing them to their peers. PCPs with less than ten visits for a specific condition were excluded from this particular analysis.

Over 90% of PCPs were included in the analysis for at least two conditions and over 70% were included in the analysis for three or more conditions within each group of conditions. Frequent prescribers were those who prescribed antibiotics more often than the lowest 25% of their peers. Infrequent prescribers were those who prescribed antibiotics less often than 25% of their peers. Results demonstrated that very few PCPs behaved in an 'all or none' manner. That is, they may have prescribed frequently for some conditions within a group, but not all. Similarly, they may have prescribed infrequently for some conditions but not all. Approximately half of PCPs did not achieve the benchmark, that is having a prescriber rate under the 25th percentile, in at least one condition (within a group of conditions). Conversely, half of the PCPs were not frequent prescribers in any condition (within each group). Approximately 20% of the PCPs were frequent prescribers in two or more of the conditions (within each group).

Example of a Prescriber Feedback Report

This example compares the PCPs' rates of dispensations to the 25th percentile for all primary care physicians (see Figure E.1). Providing prescribers with feedback comparing their practice to their peers is an evidence-supported method of improving appropriate antibiotic use [12,13].

Figure E.1: Report Card for Primary Care Physician "A" by Appropriateness of Antibiotic Dispensation, 2014-2016



Conclusions and Recommendations

Antibiotic use in older adults requires attention:

Antibiotic use in adults is increasing in Manitoba, especially in adults age 65+.

Recommendation: While some of the increase may be appropriate (due to increasing illness), outpatient ASPs should ensure they include older adults in their planning.

Antibiotic use in younger adults is increasing, often in conditions that do not require antibiotics:

Across most indicators of prudent use, rates were higher in 2016 than in 2011 for dispensations of antibiotics to adults age 15-64.

Recommendation: Acute bronchitis and pneumonia are common in adults and may be conditions to target for antibiotic stewardship strategies.

Antibiotic use in children is greater than necessary and often not aligned with evidence-informed recommendations:

Antibiotic use in children showed variable trends in Manitoba, with some increases from 2011-2016 when examined by condition.

Recommendation: ASPs targeting antibiotic use in children should focus on conditions identified as having the highest inappropriate usage, such as pneumonia, pharyngitis and acute otitis media.

Canadian recommendations are not being consistently followed for what needs antibiotics or what type of antibiotic is needed:

For many conditions, the type of antibiotics dispensed is not in keeping with Canadian recommendations.

Recommendation: ASPs for these conditions should address not just antibiotic use but choice of antibiotic, emphasizing that non-first line antibiotics may be less beneficial and may contribute to antibiotic resistance and side effects.

Rates of broad-spectrum antibiotic use might be higher than needed:

Mixed results were seen for use of broad-spectrum compared to narrow-spectrum antibiotics.

Recommendation: Attention should be paid to reducing use of broader-spectrum penicillins such as amoxicillin/clavulanic acid where appropriate and encouraging use of narrower-spectrum penicillins such as amoxicillin.

It's not just physicians that rescribe antibiotics:

Approximately 15% of antibiotics dispensed were prescribed by non-physicians; over 9% of total antibiotics dispensed were from dentists.

Recommendation: Outpatient ASPs need to include non-physicians in their planning, messaging and programming. Data systems should allow for ongoing audit and feedback of all prescribers.

Certain primary care physician characteristics are consistently associated with higher dispensation rates:

There were some physician characteristics consistently associated with higher antibiotic dispensation rates.

Recommendation: Planning and implementing of ASPs should include consultation with physicians from higher use populations, which in our study included older physicians, physicians trained outside of Canada/United States and physicians with a higher patient volume.

Higher continuity of care is associated with less antibiotic dispensation:

Visits to a majority of care provider were associated with less dispensation of antibiotics, and when dispensed, the antibiotics were more likely to be appropriate.

Recommendation: Address system issues which limit access to and accessibility of PCPs. Encourage patients to seek care from their most responsible physician when possible, especially for what appear to be minor conditions "just requiring an antibiotic".

There are significant differences in antibiotic dispensations by health region:

Dispensation rates varied by health region for many conditions and antibiotic classes. Rates were consistently higher for Prairie Mountain Health.

Recommendation: Health regions can use the data provided to tailor programs within their region. Additional data by health region are available in the online supplement (http://mchp-appserv.cpe.umanitoba.ca/supp.php/ASP_Online_Supplement-Main_TOC.htm).

Prescriber-specific feedback reports are feasible with the data available:

Examples of feedback reports are provided in this report. Individual prescriber-level data demonstrate that approximately half of primary care physicians in Manitoba do not achieve the benchmark of dispensation rates less than the 25th percentile in at least one condition (within each group of conditions).

Recommendation: A program to provide prescribers with regular, sustained and specific feedback on their antibiotic prescribing in comparison to their peers is recommended as an evidence supported method of improving antibiotic use.

Chapter 1: Introduction

Antibiotics are essential life-saving medications in modern medicine. Antibiotics specifically treat bacterial infections and are part of the larger overall terminology of “antimicrobials”, which also includes antivirals for viral infections, antifungals for fungal and yeast infections, and antiparasitics for parasites. Without the curative power of antibiotics, many routine medical therapies and procedures such as transplants, cancer chemotherapy, routine surgeries and obstetrical care would simply not be possible or would be very risky due to the risk of life-threatening infections.

While Canada-wide numbers are not available, reports from the United States indicate that each year at least 1.7 million people (or 1 in every 200 people) develop a severe blood stream infection called sepsis and would die without access to effective antibiotics. In Manitoba, approximately 4,000 pregnancies per year require a caesarean section delivery [14] and need effective antibiotics to prevent infection [15]. In Canada, some estimates have suggested that post-cesarean-section infection rates are almost 3%. In 1942, Mrs. Anne Miller of Connecticut was near death following blood sepsis after a miscarriage in a New York hospital [16]. She became the first civilian successfully treated with the antibiotic penicillin. She received roughly the equivalent of a tablespoon of antibiotic, which at the time was about half of all that drug available in the United States. Prior to this, she would have died.

Now, as antibiotic resistance becomes more common and new antibiotic development begins to lag, these infections are much more difficult to treat. Patients today are at much higher risk of succumbing to infections due to antibiotic resistance since antibiotics were first used.

Where Are Antibiotics Used?

Antibiotics are used in human medicine, as well as in veterinary care, aquaculture, and even in plant agriculture [17]. The amounts used outside of human medicine are substantial, since they are used for various reasons including animal disease treatment, disease prevention and growth promotion. In 2016, almost one million kg of antimicrobials considered important for medical use in Canada were distributed for use in animals, both in livestock and companion animals [18]. On a global scale, the consumption of antimicrobials for use in livestock is estimated to increase by 66% by 2030 to approximately 105,000 tons [17]. Overuse and misuse of antibiotics in animal and agricultural sectors is a concern for human health because of the increasing evidence that misuse substantially drives antimicrobial resistance to medically important pathogens in animals and

humans. There have been reports of livestock-associated methicillin-resistant Staphylococcus aureus infecting people who have no exposure to the livestock industry [19], as well as multidrug-resistant urinary tract E. coli infections from poultry [20].

Antibiotics are given to patients in hospitals and other inpatient settings, but the vast majority of antibiotics are prescribed to people in the community or in an ambulatory setting. In 2017, 262,590 kg of antibiotics were dispensed through community pharmacies or given to patients in hospitals in Canada, at a cost of almost $822 million [18]. Around 90% of all antibiotic use occurs in the outpatient setting, including doctors' offices, community pharmacies and walk-in clinics, and emergency rooms [15,18,21]. Overall, antibiotics are prescribed in almost 15% of visits to a clinician.

Who Is Receiving Antibiotics?

Available data collected through the Public Health Agency of Canada in 2017 shows that on average, about 2% of the entire Canadian population is dispensed an antibiotic prescription annually [18]. Regional variation exists in Canada across provinces and territories. Rates of prescribing are highest in Prince Edward Island and Newfoundland (reported together) at 970.2 prescriptions per 1,000 people, and lowest in British Columbia at 569.3 per 1,000 people.

Variation also exists across different age groups. Prescribing to children and for young infants has historically been considered to be an important driver of total antibiotic prescribing. In recent years, this trend has been shown to be changing. Recent work from the United States has shown that rates of outpatient oral antimicrobial prescribing in paediatrics is down 13% from 2011 to 2016, but in the same period, rates in adults have actually increased 2%, with high overall rates in adults age 65+ [22].

What Do We Know About Inappropriate Antibiotic Prescribing?

A range of clinicians (not just physicians) can prescribe antibiotics. In Manitoba, dentists, nurse practitioners, pharmacists and midwives can all prescribe antibiotics. All types of prescribers have been implicated in overprescribing or inappropriately prescribing all classes of commonly used antibiotics. Inappropriate prescribing of antibiotics can mean treatment that is too long in duration or the wrong drug for the diagnosis, or antibiotics for a diagnosis where antibiotics are not needed. These inappropriate prescribing behaviours result in patients receiving antibiotics that may very well be harmful to them with no benefit. In addition to promoting antibiotic-resistant strains, antibiotics can have direct side effects, including bone marrow suppression, heart dysrhythmias, various types of skin reactions from mild to severe, and gastrointestinal (GI) effects ranging from simple diarrhea to possible Clostridium difficile diarrhea disease, which in some cases is severe enough to lead to hospitalization, colectomy or death [21]. Any of these side effects can lead to additional interactions with the health care system. Antibiotics also account for more than 20% of all emergency room visits due to medication side effects [23].

Many studies have conservatively estimated rates of inappropriate antibiotic prescribing in the ambulatory setting to be at least 30% of all prescriptions [1,2]. Many of these prescriptions are for physician-diagnosed conditions that are due to viruses and do not require antibiotics (runny noses, colds, simple cough and/or sore throat, bronchitis, etc.). Why do prescribers over-prescribe antibiotics? Clinical psychologists and behavioural scientists have attempted to gain insight into this through direct observations, focus groups and surveys, often in the inpatient setting. While lack of basic medical knowledge can be a reason, psychosocial reasons are strong drivers [21]. Common themes center around prescribers' beliefs that they should appear competent and capable in front of a patient, not wanting patients to feel time was "wasted" by not getting something, that by giving an antibiotic they are decreasing the risk of something bad happening and the often-mistaken belief by the clinician that the patient is "demanding" antibiotics when they are actually misinterpreting verbal cues for additional information [24]. Inappropriate prescribing behaviour can also be driven by interpersonal factors among clinicians, including hierarchy and the influence of senior colleagues, not wanting to alter or give feedback on the prescribing behaviours of others, and the belief that one does not over-prescribe antibiotics ("It's not me, it's them…") [25].

What Can Be Done to Improve Antibiotic Prescribing?

Quality improvement programs can address issues of inappropriate antibiotic prescribing. These programs are collectively referred to as antimicrobial stewardship programs or ASPs. There is no universal definition or model for ASPs. The overall theme is one of quality and patient safety so that the right antibiotic is given at the right dose and duration and only when needed [26]. The strongest evidence-based strategies for ASPs are in the form of prospective audit with feedback to stakeholders on prescribing behaviour and other metrics. This and other forms of persuasive and behaviour-nudging interventions have been shown to lower rates of inappropriate antibiotic prescribing without negatively impacting appropriate forms of antibiotic prescribing [12,13].

Since the vast majority of antibiotic prescribing occurs in the ambulatory setting, implementing and improving antimicrobial stewardship in ambulatory settings is of

paramount importance. To date, there are few experiences published on how to best implement a successful and sustainable outpatient ASP, but some have successfully started using audit with feedback, Electronic Patient Record reminders and public accountability posters [27,28].

To date, no systematic or comprehensive review of outpatient antibiotic use has been conducted in Manitoba, and Manitobans lack the benefit of a regional or provincial outpatient ASP. In order to contribute to optimal antibiotic use and protect Manitobans, this report will establish baseline measures on recent outpatient antibiotic use in the province. In addition, prescribing as it relates to indication, either appropriate or inappropriate, will be assessed, albeit within the limitations of the data available. Finally, the potential impact of various patient- and prescriber-level factors will be assessed. Taking all these results together, we will also demonstrate how a theoretical outpatient ASP using a prospective audit and feedback model could leverage existing data housed at the Manitoba Centre for Health Policy (MCHP) to provide regular reports to providers on their antibiotic prescribing in an attempt to nudge behaviour in the right direction.

This report examines the use of oral antibiotics in the outpatient setting in Manitoba. It includes an in-depth exploration of the use and prescribing patterns of this group of medications with a view to understanding the potential factors influencing use from multiple perspectives, including those of prescribers, patients and regional health authorities. The overarching goal is to identify targets and methods for antimicrobial stewardship interventions using the data available in the Manitoba Population Research Data Repository (https://umanitoba.ca/manitoba-centre-for-health-policy/data-repository#data-list-and-data-descriptions).

Research Objectives

Research objectives were operationalized in conjunction with Manitoba Health and Seniors Care and interested prescribers and stakeholders within the context of data available in MCHP's prescription and health care databases.

Our specific research objectives include:

- **Objective 1:** Examine patterns of antibiotic use (or dispensation) in Manitoba from 2011-16:
    - by age group and health region, using dispensations per 1,000 people per day;
    - using the European Surveillance of Antibiotic Consumption Network (ESAC-Net) quality indicators.
- **Objective 2:** Examine patterns of health services use of patients prescribed antibiotics in Manitoba by looking at:
    - the relationship between ambulatory care physician visits and antibiotic dispensations;
    - the characteristics of physician-prescribed dispensations not linked to a health care contact;
    - the characteristics of dispensations of antibiotics prescribed by non-physician health care professionals;
    - the relationship between diagnosis codes provided by ambulatory primary care physicians and antibiotic dispensations to ascertain appropriateness of antibiotic use.
- **Objective 3:** Develop a framework for providing antibiotic prescribing feedback at the individual practitioner level.

Organization of the Chapters

Each chapter begins with a brief introduction to the topic and any terminology that requires explanation. Any methods specific to the chapter are outlined. For some chapters, we have noted when extra data are available in the online supplement which can be accessed from http://mchp-appserv.cpe.umanitoba.ca/supp/ASP_Online_Supplement-Main_TOC.pdf. Detailed definitions, including data sources, data years, diagnoses and drug codes, are provided in Appendix 1 of the online supplement. The key findings for that chapter are summarized with graphs/figures where appropriate to illustrate the results. A conclusion or summary finishes each chapter. Recommendations that stem from the data are included in chapters as appropriate, and in a summary Conclusions and Recommendations chapter. Additional results are available in Appendix 2 online.

Chapter 2: Methods

Data Sources

Data for this report were derived from anonymized health care administrative data contained in the Manitoba Population Research Data Repository at MCHP (https://umanitoba.ca/manitoba-centre-for-health-policy/data-repository#data-list-and-data-descriptions). The Repository houses individual-level administrative data for virtually all Manitobans from a variety of sources across several domains, including health. All records in the Repository are de-identified (no names or addresses attached) and Personal Health Information Numbers (PHINs) and other identifiers are scrambled to protect confidentiality. All results are reported as aggregated values; any values based on one to five individuals are suppressed.

We used the following databases from the Repository: the Manitoba Health Insurance Registry (demographic information like age, sex and postal codes); prescription dispensation records from outpatient dispensaries through Manitoba Health's Drug Program Information Network (DPIN); Medical Services (physician billing claims; ICD-9-CM codes); hospital discharge abstracts (reason for hospitalization; ICD-10-CA codes); Vital Statistics; and Statistics Canada's public use files from the 2016 Census (Table 2.1).

We linked Manitobans' prescription data to specific diagnoses from their encounters with the health care system (e.g., physician visits, hospitalizations) using each person's scrambled health identification number (PHIN). We used data from January 1st to December 31st from 2011-2016. In this report, the first quarter (Q1) of each year was January to March, the second quarter (Q2) April to June, the third quarter (Q3) July to September and the fourth quarter (Q4) was October to December. For more information on linking prescription dispensations to health care encounters please refer to the Technical Appendix in the online supplement.

Table 2.1: Data Sources for this Report

Databases	Data years used	Data fields
Manitoba Health, Seniors & Active Living		
Canadian Census (public-use files)	1996, 2001, 2006, 2011	Community-level data on key socioeconomic characteristics.
Drug Program Information Network Data	2011-2016	For example, DIN, dispensing date (PRVDDT), quantity, days supply, SCRPHIN birthdate, sex.
Hospital Discharge Abstracts	2011-2016	For example, Diagnosis Codes for target condition, comorbid conditions and baseline variables.
Manitoba Health Insurance Registry	2011-2016	For example, coverage start date, coverage, end date, postal code, birthdate, SCRPHIN, cancellation code, sex.
Medical Services	2011-2016	For example, Diagnosis Codes for target condition, comorbid conditions and baseline variables.
Provider Registry	2011-2016	For example, Provider type for prescriptions.
Long Term Care Utilization History	2011-2016	Users, admissions, services, wait times, level of care, characteristics, facilities
Manitoba Families		
Child & Family Services: Applications and Intake	2011-2016	All fields involved in children in care and families receiving protection and support services from CFS

Categorization of Medications

All oral formulations (e.g., tablet, capsule, liquid) of an antibiotic available in Canada were considered. Injectable and topical formulations were excluded. Antibiotics were classified according to their mechanism of action according to the Anatomical Therapeutic Chemical (ATC) classification. Antibiotics included in this report are outlined in Table 2.2; a more detailed table is available in the Technical Appendix in the online supplement.

Combination antibiotics such as amoxicillin/clarithromycin were treated either as two different drug classes when examining classes dispensed (as in Chapters 3-4) or as one prescription (as in Chapters 5-7). The use of intravenous antibiotics (vancomycin/fidomycin) orally to treat certain gastrointestinal conditions were excluded from some analyses as noted in each particular section.

Table 2.2: Anatomical Therapeutic Chemical (ATC) Classification for Antibiotics Included in this Study

Drug Class	Drug Subclass	Drugs
J01 -All Oral Antibiotics		
J01A - Tetracyclines		doxycycline tetracycline minocycline
J01C - β-Lactam Penicillins		amoxicillin ampicillin penicillin cloxacillin amoxicillin and clavulanate
J01D - Cephalosporins	J01DB - first generation	cephalexin cefadroxil cefaclor cefprozil cefuroxime
	J01 DC second generation	
J01E - Sulfonamides and Trimethoprims		trimethoprim trimethoprim and sulfamethoxazole
J01F - Macrolides, Lincosamides and Streptogramins		erythromycin clarithromycin azithromycin clindamycin spiramycin
J01M - Quinolones		ofloxacin norfloxacin, levofloxacin moxifloxacin ciprofloxacin
J01X - Other Antibiotics		linezolid fosfomycin nitrofurantoin methenamine Metronidazole includes P01AB01 and J01XD

Notes: Combination antibiotics such as amoxicillin/clarithromycin are treated either as two different drug classes or as on prescription depending on the indicator under study.
Oral antibiotics (vancomycin/fidomycin) are excluded from this report

Population

All individuals with coverage under the provincial health insurance plan were included in the analysis, except those residing in long-term care facilities (LTC), those who were public wards, or those with a Child and Family Services postal code. Results are provided for either quarterly or annual populations. The quarterly population excluded LTC residents from the quarter in which they entered LTC and from subsequent quarters. The annual population is the population from the third calendar quarter excluding LTC residents from the year during which they entered LTC and all subsequent years. Out-of-province patients who received antibiotic prescriptions were not included in the numerator or denominator.

If other exclusions apply to specific indicators in this report, they will be noted in the relevant section.

Demographic Characteristics

For most outcomes, antibiotic dispensation results are reported by:

- **Age**
  - Paediatric (under age 15) versus adults (age 15 and older)
  - Age groups (under age one, 1-4, 5-9, 10-14, 15-64, 65+)

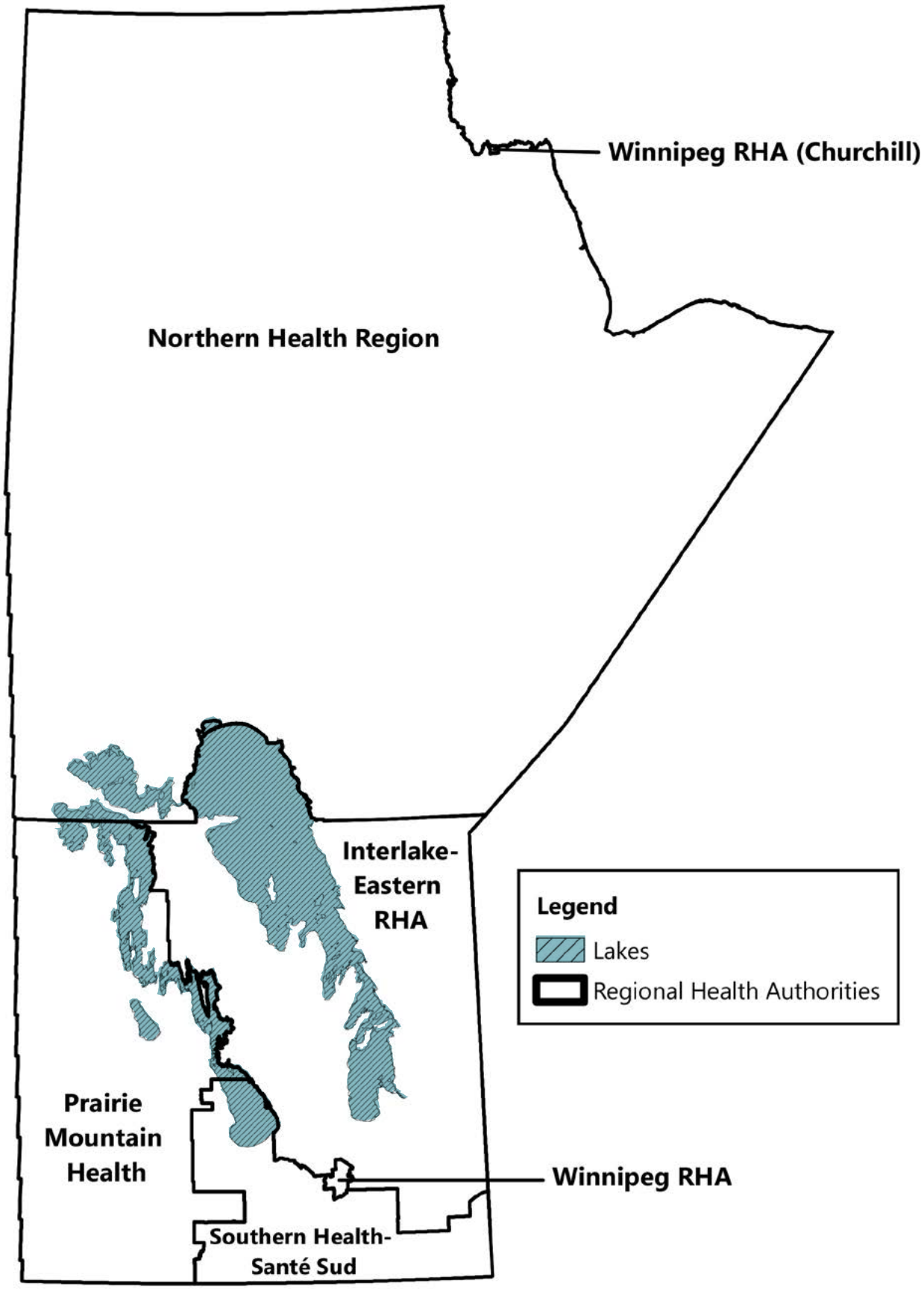
  Age 15 was used as the adult cut-off as this is the usual age at which an 'adult' dosage is used for antibiotic dispensations.

- **Regional Health Authority (RHA) or Health Region**
  - Southern Health-Santé Sud
  - Winnipeg RHA
  - Prairie Mountain Health
  - Interlake-Eastern RHA
  - Northern Health Region

Health regions of residence (based on postal codes) are reported because funding for the provincial health care system is allocated to the five RHAs in Manitoba (Figure 2.1). Health regions are listed in figure legends in order of the lowest (at the top of the legend) to the highest (bottom of legend) premature mortality rate (i.e., death before age 75). The reason we order them this way is because the premature mortality rate indicator serves as a proxy for poor health status: regions with a high premature mortality rate are often sicker. In a universal needs-based healthcare system, regions with higher premature mortality require more care, and therefore use more healthcare services. It is reasonable to expect that these regions would also exhibit higher dispensation rates for antibiotics.

Additional descriptive variables are used in Chapters 5 and 6 to look at the relationship between physician and patient characteristics and antibiotic dispensations. See the methods section in those chapters for further details.

Figure 2.1: Map of Regional Health Authorities in Manitoba, 2016



Prescriber Details

Many different types of health care providers prescribe antibiotics in Manitoba. Physicians can be generally divided into specialists (both surgical and non-surgical) and primary care providers (PCP). PCPs include family physicians and paediatricians. While paediatricians provide both primary care and specialist care in Manitoba, for this report they are combined with the PCPs as we could not distinguish paediatric specialists from those providing primary care in the data. In addition to physicians, the drug dispensation data include prescriptions by nurse practitioners, dentists, midwives, optometrists and pharmacists. Data prior to 2014 do not allow us to differentiate by prescriber type, but from 2014 onwards we are able to distinguish between type of prescriber. Prescriptions by physicians can be linked directly to an individual physician, whereas prescriptions by other prescribers can only be linked to a prescriber type. In Chapters 3-4 of this report, when we look at antibiotic dispensations without considering health care contacts, all dispensation data are included (2011-2016). Due to data limitations, it is not possible to link non-physician dispensations to non-physician visits, i.e., it is not possible to link prescriptions to a nurse practitioner visit. Thus, for the analyses in Chapter 5 and onwards, the specific methods describe which types of dispensations were included as well as the years of data that were used.

Ambulatory Care Physician Visits

Ambulatory care physician visits include all outpatient contacts with a physician, either a PCP (family physician/ paediatrician) or a specialist. In Chapter 5, all ambulatory care physician visits are included. In Chapters 6-7, we analyze dispensations for specific indications and only ambulatory care visits to PCPs are included.

Further information on methods can be found prior to each section and in the Technical Appendix in the online supplement.

Categorizing Appropriateness of Antibiotic Use

While the available data and analyses undertaken do not provide sufficient detail to audit every encounter and prescription and adjust for multiple comorbidities and conditions, the linkage of the ICD-9-CM diagnosis codes supplied by the physician at a visit to a dispensed prescription can be taken as indication for the antibiotic. This approach allows patterns of use both at the population and practitioner level to be examined. However, it has some limitations. The main limitation is that ambulatory visits have only one diagnosis code assigned by the practitioner and this approach assumes that is the indication for the dispensed antibiotic. It is possible that a visit addressed multiple issues with the diagnosis code reflecting one issue and the antibiotic reflecting a different issue. Despite these limitations, this approach is frequently used in the published literature. Comparisons to chart or clinical data review demonstrate that the correlation between the ICD9-CM code and the prescriber's indication is between 50-80% [3–5] and varies by indication. Antibiotics dispensed following a visit that was not captured in the Repository, mostly due to visits to physicians who do not bill or capture their visits via shadow billing, cannot be classified. We have divided individual diagnosis codes, or groups of codes representing single conditions, into three categories: generally do not require antibiotics, may require antibiotics, and generally require antibiotics. These categories are based on published literature and professional guidelines as outlined in each section. This report focuses on patterns in the first two categories as we are examining ways to encourage more prudent (usually decreased) use. Examining whether antibiotics were prescribed when they would be indicated by the diagnosis code is outside the scope of this report, but we have included this information in the online supplement.

It should be noted that this report captures dispensations of antibiotics only. We use the term 'antibiotic use' to indicate dispensations by pharmacies, thus indicating the initial prescription written by the provider and intended use by the patient based on filling the prescription. The Repository data cannot capture prescriptions that were provided but not filled, or prescriptions that were filled and then the antibiotics were not taken by the patient.

Rates and Adjustments

A rate refers to the number of events or individuals with a characteristic of interest during a given period per number of individuals or events observed in this period. Many health-related events can happen to a given person more than once. For example, the physician visit rate shows how often individuals visit physicians each year (that is, number of visits per individual in a year). Where an indicator covers a period longer than one year, the rate is annualized (calculated as an average rate in a year).

The rates in most graphs by health region in this report have been statistically adjusted to account for the different age and sex composition of the different populations that are compared. This adjustment allows for fair comparisons among areas with different population characteristics. Adjusted rates show what each area's rate would have been if the populations had the same age and sex composition as the Manitoba population in 2011. Adjusted rates do not tell you how many actual people or events are being reported in that indicator. If an area has a very different age and sex composition compared to Manitoba,

the adjusted rate may give you an overestimate or underestimate of the actual number of people or events reported. Adjusted rates are essential for comparisons between populations because they provide the context to understand the results.

Significance of the Results

If a difference is “statistically significant” or an indicator is “statistically different” between two groups, then this difference is large enough that we are confident it is not just due to chance. Statistical significance describes how much confidence to put in the results. When you see a large difference that is NOT statistically significant, it is telling you that this rate is probably not different from the comparison rate and that it could fluctuate greatly from year to year. This could be due to the finding being based on small numbers (either a small number of events, or a small underlying population) so it could change from year to year and may be higher, similar or lower than the comparison the next time it is measured. All of the graphs show statistical significance, using numbers or symbols that are explained in the corresponding footnotes below the graphs.

When an “s” appears on a graph or next to a health region, this indicates that we cannot report the finding because it is based on a small number of individuals or events (1 to 5) that could potentially be identified. In this case, we “suppress” this finding (referred to as data suppression or suppressed data).

Chapter 3:
Dispensation Trends for Antibiotics in Manitoba

In this section, we report on antibiotic dispensations by any prescriber per 1,000 people per day. While multiple measures are used in the literature to examine outpatient antibiotic use, this one was chosen as it was easy to understand, easy to compare to other regions/countries and widely used in the literature [29]. We examined dispensation patterns of all oral antibiotics with the exception of oral vancomycin, and we did not examine antifungal or antiviral drugs or individual oral antibiotics with dispensation counts too low to report (e.g., sulfamethoxazole).

Analyses of dispensation trends were based on data from the Drug Program Information Network, which captures information about filled prescriptions (i.e., dispensations) for all drugs including antibiotics. Unfilled prescriptions and medications dispensed directly without a prescription (e.g., from a public health clinic or nursing station) were not captured in our findings. Therefore, our findings potentially underestimate antibiotic use in Manitoba, especially in the Northern Health Region where services are often provided at nursing stations.

It should be noted that this report captures dispensations of antibiotics only. We use the term ‘antibiotic use’ to indicate dispensations by pharmacies, thus indicating the initial prescription written by the provider and intended use by the patient based on filling the prescription. The Repository data cannot capture prescriptions that were provided but not filled or prescriptions that were filled and then the antibiotics were not taken by the patient.

When discussing types of antibiotics, the terms broad-spectrum and narrow-spectrum are sometimes used. A broad-spectrum antibiotic is one that is effective against a wide range of bacteria, often multiple types such as gram-positive and gram-negative. A narrow-spectrum antibiotic is effective against a smaller range of bacteria. In general, the narrowest-spectrum antibiotic should be used, as broader-spectrum antibiotics lead to more pressure for antibiotic resistance.

We examined the dispensation patterns of oral antibiotics by age group for children and adults and by health region and overall for Manitoba. For all classes, most subclasses, and some individual drugs, the report presents a summary of crude rates by age-group and the age- and sex-adjusted rates for children and adults. Complete results are available in Appendix 1. Counts and crude rates are available in the online supplement for this report. For select subclasses and individual drugs, all findings are presented in the online supplement.

Antibiotics Overall (J01):

- Tetracycline Class (J01A)
- β-Lactam Penicillin Class (J01C)
  - Extended-Spectrum Penicillin Subclass (J01CA)
    - Amoxicillin (J01CA04) – mostly in online supplement
  - β-Lactamase-Sensitive Penicillin Subclass (J01CE) – in online supplement only
  - β-Lactamase-Resistant Penicillin Subclass (J01CF)
  - β-Lactamase Inhibitor/Penicillin Combination Subclass (J01CR)
    - Amoxicillin/Clavulanic Acid (J01CR02) – mostly in online supplement
- Cephalosporin Class (J01D)
  - First Generation Cephalosporin Subclass (J01DB) – in online supplement only
    - Cephalexin (J01DB01) – mostly in online supplement
  - Second Generation Cephalosporin Subclass (J01DC) – in online supplement only
    - Cefuroxime (J01DC02) – mostly in online supplement
- Sulfonamide and Trimethoprim Class (J01E)
  - Trimethoprim/Sulfamethoxazole (J01EE01) – mostly in online supplement
- Macrolide, Lincosamide and Streptogramin Class (J01F)
  - Azithromycin (J01FA10) – mostly in online supplement
- Quinolone Class (J01M)
  - Ciprofloxacin (J01MA02) – mostly in online supplement
- Other Antibiotic Class (J01X)
  - Metronidazole (J01XD01) – in online supplement only
  - Nitrofurantoin (J01XE01)

Graphs are not presented for all findings, only where appropriate to illustrate key findings or patterns.

Antibiotics Overall (J01)

The size of the total population of Manitoba increased by 7.3% from 2011 to 2016 (from 1,244,202 people to 1,335,336 people). Over this time period, the total number of antibiotic dispensations in Manitoba increased by 8.3% (from 810,833 to 878,416). A total of 6.5% of Manitobans filled a prescription for antibiotics in 2011 compared to 6.6% of Manitobans in 2016. In 2016, the distribution of dispensed antibiotics by class were β-lactam penicillins (35.0%), macrolides (23.9%), quinolones (13.7%), cephalosporin antibacterials (11.2%), tetracyclines (5.6%), sulfonamide and trimethoprims (4.9%) and other (5.7%).

Key Findings by Age Group

- Dispensation rates in Manitoba varied across age groups:
  - Rates for ages 10-14 were consistently lower than for other age groups.
  - Rates for children under 5 years and adults ages 65 and older were higher than for other age groups.
- Dispensation rates varied seasonally from summer to winter quarters in all age groups:
  - Seasonal variation was more pronounced in the two youngest age groups and less so among those ages 10+.
- There were small but statistically significant changes in rates from 2011 to 2016 in all age groups:
  - The rates for groups younger than 15 years decreased slightly in 2016, while rates for ages 15+ increased.

Key Findings by Health Region

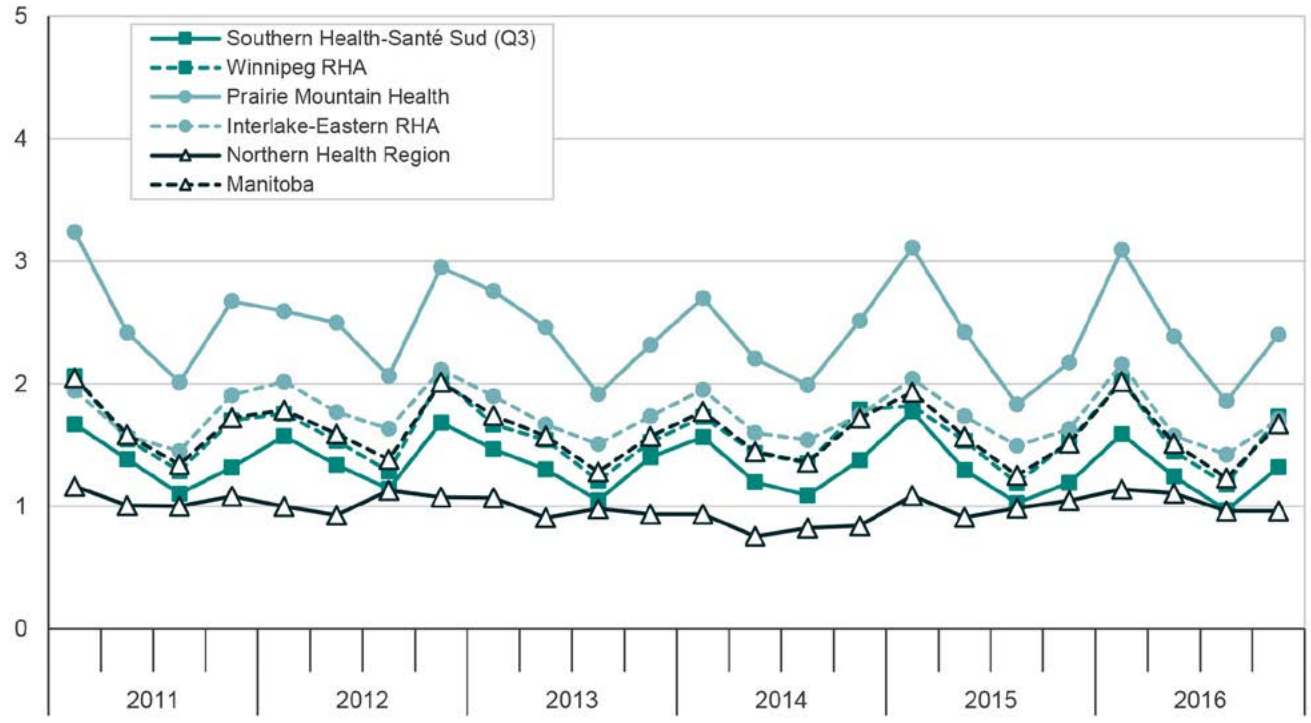
- All ages:
  - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters, while rates in Interlake-Eastern RHA were significantly higher than the provincial average in most quarters.
  - Rates in Southern Health-Santé Sud were significantly lower than the Manitoba average in all quarters, and rates in Northern Health Region were lower than the provincial average in some quarters.

- Rates in Prairie Mountain Health were higher than all other regions in all time periods, followed by rates in Interlake-Eastern RHA; rates in Southern Health-Santé Sud were lower than other regions in most time periods, with similarly low rates in Northern Health Region in some quarters.
- Rates in Winnipeg RHA were comparable to the Manitoba average in all time periods.
- Overall, rates for all regions and Manitoba in 2011 were not significantly different from rates in 2016.

- Alternative approaches to investigating trends in antibiotic dispensation:
  - After accounting for socioeconomic status (SEFI-2) and comorbidities (Charlson Index score) in addition to age and sex of the population, the findings changed very little (see online supplement). Therefore, only age and sex adjustments were used when looking at dispensation trends by age group and health region across antibiotic classes, subclasses and individual drugs.
  - Another well-established approach for group comparisons is the use of relative rates, where the group with the lowest rate is used as a benchmark for comparison to other groups [30,31]. Regional relative rates and 95% confidence intervals showed that dispensation rates in all health regions were significantly higher than rates in Southern Health-Santé Sud, with relative rates ranging from 1.07 to 1.48 (online supplement)[3].
- Adults:
  - Dispensation trends among adults were similar to those of the overall population.
  - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters, and rates in Interlake-Eastern RHA were significantly higher than the provincial average in almost all quarters.
  - Rates in Southern Health-Santé Sud were significantly lower than the Manitoba average in all quarters, while rates in Northern Health Region were lower than the provincial average in very few quarters.
  - Prairie Mountain Health had the highest and Southern Health-Santé Sud the lowest rates when compared with other regions.
  - Overall, rates for adults in all regions (except Northern Health Region) and Manitoba in 2011 were not significantly different from rates in 2016:
    - Rates in Northern Health Region in the third quarter of 2016 were significantly higher than the rates in the corresponding quarter in 2011.
- Children (Figure 3.1):
  - Dispensation trends among children were similar to those for the whole population with some small exceptions.
  - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters, while rates in Interlake-Eastern RHA were rarely significantly higher than the provincial average.
  - Rates in Southern Health-Santé Sud were significantly lower than the Manitoba average in some quarters, while rates in Northern Health Region were lower in all quarters.
  - Prairie Mountain Health had the highest and Northern Health Region the lowest rates when compared with other regions.
  - Overall, rates for children in all regions (except Southern Health-Santé Sud) and Manitoba in 2011 were not significantly different from rates in 2016:
    - Rates in Southern Health-Santé Sud in the third quarter of 2016 were significantly lower than the rates in the corresponding quarter in 2011.

3 Relative rates for antibiotic classes, subclasses and individual drugs are available in the online supplement.

Figure 3.1: Quarterly Dispensation Rates for Antibiotics Overall (J01) for Children by Health Region
Age- and sex-adjusted rates per 1,000 people ages 0-14 per day



(Q1,2,3,4) - Indicates statistically significant differences between corresponding quarters in 2011 and 2016 ($p<0.05$).

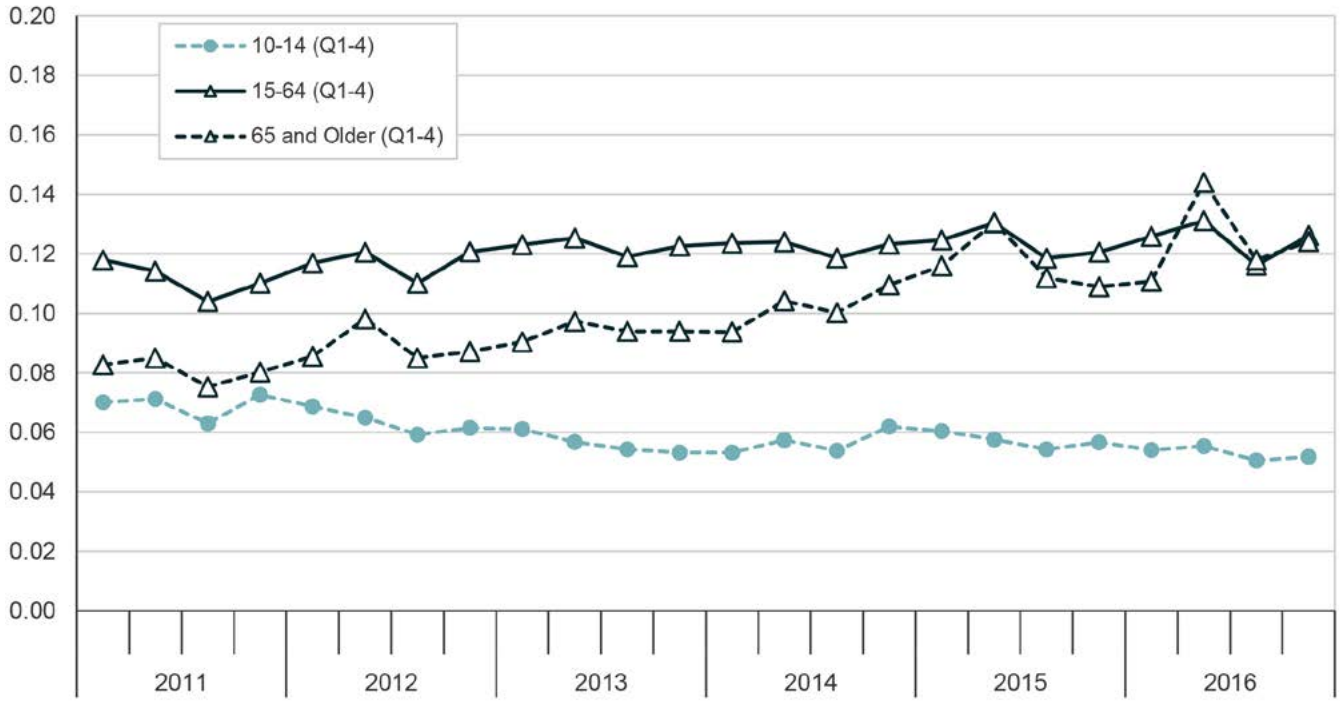
Tetracycline Antibiotics (J01A)

The tetracycline drug class includes antibiotics such as doxycycline, minocycline and tetracycline [32], and made up 5.6% of antibiotic dispensations in 2016. These antibiotics are broad-spectrum and act against gram-positive and gram-negative bacteria, spirochetes and obligate intracellular bacteria (e.g., chlamydia, rickettsia, and mycoplasma) [33,34]. Tetracyclines are indicated to treat gynecological, genitourinary, respiratory, intestinal infections, dermatological conditions, Lyme disease and soft-tissue infections [35]. These antibiotics are mostly avoided in younger children, so we are only showing results for children ages 10-14 for Manitoba overall.

Key Findings by Age Group:

- Dispensation rates in adults (ages 15 and older) were consistently higher than those for children ages 10-14.
- Rates for children under age 10 were suppressed due to small numbers.
- Dispensation rates did not appear to have any seasonal variation.
- There were small but statistically significant changes in rates from 2011 to 2016 in all age groups shown in Figure 3.2:
  - The rates for children ages 10-14 were lower in 2016 than 2011, while rates for people ages 15-64 and 65 and older were higher in 2016.

Figure 3.2: Quarterly Dispensation Rates for Tetracyclines (J01A) by Age Group*
Crude rates per 1,000 people per day



* Rates for ages under 10 are not shown due to low numbers.
(Q1,2,3,4) - Indicates statistically significant differences between corresponding quarters in 2011 and 2016 ($p<0.05$).

Key Findings by Health Region for Adults:

- Dispensation rates and patterns over time for adults were comparable across health regions:
  - Only the rates in Northern Health Region in the second quarter of 2011 and Prairie Mountain Health in the second quarter of 2016 were significantly higher than the Manitoba average.
- Seasonal variation was not consistent across regions; some regions exhibited peaks in the summer quarters.
- Overall, rates for adults in all regions and Manitoba in 2016 were significantly higher than rates in most quarters of 2011.

β-Lactam Penicillins (J01C)

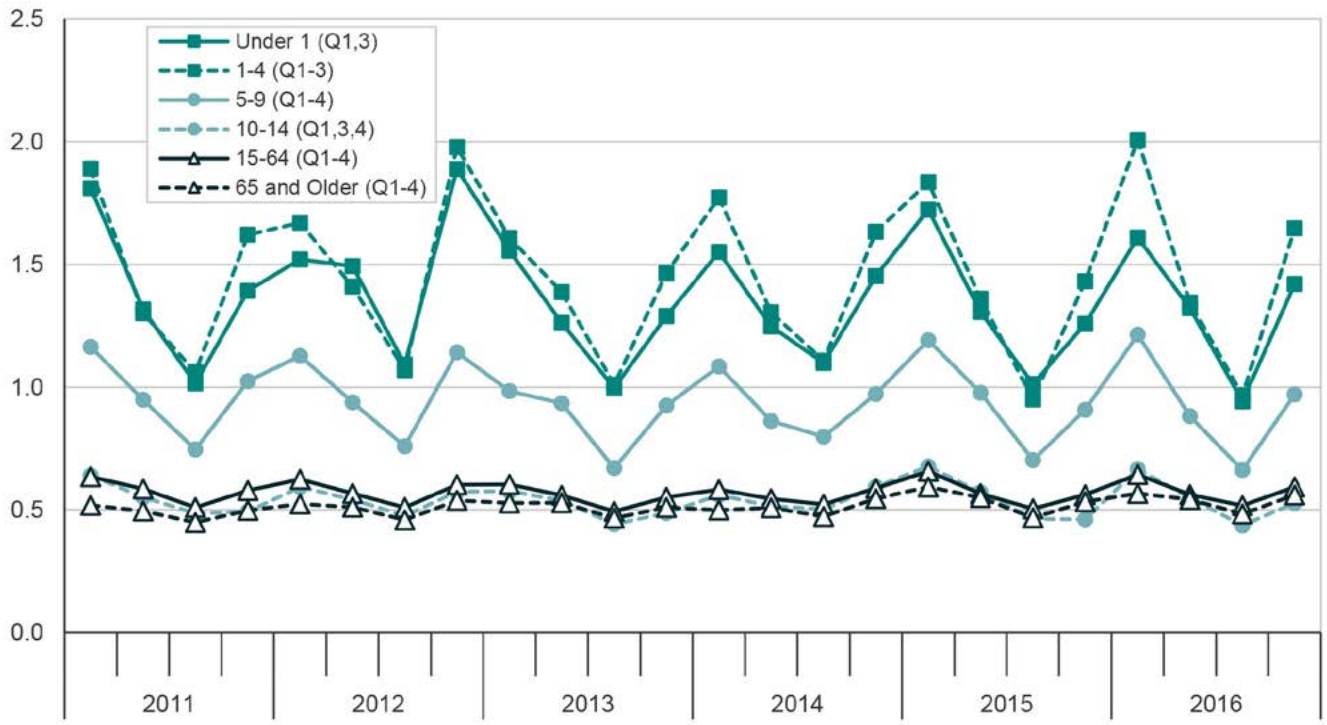
This drug class includes common antibiotics such as penicillin, amoxicillin, cloxacillin and β-lactamase inhibitor combinations such as amoxicillin/clavulanic acid [32]. It made up 35.0% of dispensed antibiotic prescriptions in Manitoba in 2016. This drug class is most active against gram-positive bacteria and is indicated to treat bacterial infections such as lower respiratory tract infections, strep throat and otitis media. The drugs are used in both children and adults.

Key Findings by Age Group (Figure 3.3):

- Overall, dispensation rates for β-lactam penicillins were consistently higher than rates for all other antibiotic classes.
- Dispensation rates in Manitoba varied across age groups:
  - Rates for children ages under 10 were consistently considerably higher than for older age groups.
  - Rates for age groups under 1 and 1-4 years were comparable in most quarters, with the exception of slightly lower rates for ages under 1 in most winter quarter peaks.
  - Rates for age group 5-9 were consistently lower than for ages under 5.
  - Rates for age groups 10 and older were comparable over time.
- Dispensation rates varied seasonally from summer to winter quarters in all age groups:
  - Seasonal variation was more pronounced in the three youngest age groups and less so in ages 10 and older.
- There were small but statistically significant changes in rates from 2011 to 2016 in all age groups:
  - The rates for ages 65 and older increased over time in all quarters.
  - The rates for other age groups in 2016 fluctuated relative to 2011 rates, with no consistent increases or decreases.

Figure 3.3: Quarterly Dispensation Rates for β-Lactam Penicillins (J01C) by Age Group

Crude rates per 1,000 people per day



(Q1,2,3,4) - Indicates statistically significant differences between corresponding quarters in 2011 and 2016 (p<0.05).

Key Findings by Health Region:

- Adults:
  - Among adults, dispensation rates of β-lactam penicillins were consistently higher than rates for all other antibiotics.
  - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters, and rates in Northern Health Region were significantly higher than the provincial average in several quarters.
  - Rates in Southern Health-Santé Sud were significantly lower than the Manitoba average in all quarters.
  - Prairie Mountain Health had the highest and Southern Health-Santé Sud the lowest rates when compared with other regions.
  - Dispensation rates exhibited seasonal variation across regions.
  - Overall, rates for adults in all regions (except Prairie Mountain Health and Northern Health Region) in some quarters of 2011 were significantly different from rates in 2016:
    - Rates in Winnipeg RHA increased over time in most quarters.
    - Rates in Interlake-Eastern RHA and Manitoba increased in some quarters, while rates in Southern Health-Santé Sud decreased in one quarter.
- Children:
  - Dispensation rates among children varied considerably across regions:
    - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters.
    - Rates in Northern Health Region were significantly lower than the provincial average in all quarters, and rates in Southern Health-Santé Sud were lower than the average in most quarters.
    - The rates in Prairie Mountain Health were considerably higher than other regions, while the rates in Northern Health Region were the lowest rates.
  - Rates in all regions exhibited seasonal variation, though with a smaller magnitude in Northern Health Region.
  - Rates in some quarters of 2016 in Southern Health-Santé Sud, Interlake-Eastern RHA and Northern Health Region were significantly different than rates in 2011, with no consistent increasing or decreasing pattern.

Subclasses

The high proportion of dispensations of β-lactam penicillins compared to other antibiotics and the considerable differences in indications across subclasses warrant a more detailed look at dispensation trends of commonly dispensed subclasses of β-lactam penicillins.

Extended-Spectrum Penicillins (J01CA)

This subclass includes relatively narrow-spectrum penicillin-based antibiotics. The most representative dispensed drug from this subclass is amoxicillin. It is considered first line therapy for many common ambulatory infections, especially in children [36]. It also comes in suspension form, which is much more accessible and palatable than some other related medications.

Key Findings by Age Group:

- Dispensation trends for the extended-spectrum penicillin subclass are similar to those for the β-lactam penicillin class:
  - Rates varied across age groups.
  - The highest rates were for age groups under 5, followed by rates for ages 5-9.
  - Rates for age groups under 1 and 1-4 years were comparable in most quarters, with the exception of slightly lower rates for ages under 1 in most winter quarter peaks.
  - Rates for age groups 10 and older were quite similar over time, though rates for ages 65 and older appear to be consistently lower.
- Seasonal variation was seen in the age groups but was more pronounced among children under age 10.
- There were small but statistically significant changes in rates from 2011 to 2016 in all age groups, though not always in all quarters:
  - The rates for age groups 10-14 and 65 and older increased in all quarters.
  - The changes in the remaining age groups were not consistent increases or decreases across all quarters of 2016.

Key Findings by Health Region:

- Adults:
  - Regional dispensation trends for extended-spectrum penicillins among adults were similar to the trends for β-lactam penicillin class.
  - Rates in Prairie Mountain Health appeared to be consistently higher than rates in other regions and Manitoba overall; however, only rates in a few quarters in 2011-2013 were significantly higher than the Manitoba average.

- Rates in Southern Health-Santé Sud appeared to be consistently lower than those for other regions and Manitoba overall; however, the rates for Southern Health-Santé Sud were not significantly different from the Manitoba average.
- Dispensation rates exhibited seasonal variation across regions.
- There were no statistically significant changes in rates from 2011 to 2016 in any of the regions.

- Children:
  - Regional dispensation trends for extended-spectrum penicillins among children closely matched the trends for the β-lactam penicillin class.
  - Dispensation rates among children varied considerably across regions:
    - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters.
    - Rates in Northern Health Region were significantly lower than the provincial average in all quarters, and rates in Southern Health-Santé Sud were lower than the average in most quarters.
    - The rates in Prairie Mountain Health were considerably higher than other regions, while the rates in Northern Health Region were the lowest.
  - Rates in all regions exhibited seasonal variation, though with a smaller magnitude in Northern Health Region.
  - Rates in Interlake-Eastern RHA in the first two quarters of 2016 were higher than those in 2011.
  - Rates in some quarters in 2016 in Northern Health Region were significantly different than those in 2011, with no consistent increasing or decreasing pattern.

β-Lactamase Inhibitor Combinations (J01CR)

The most well-known drug in this subclass is amoxicillin/clavulanic acid, a drug with a broader application than amoxicillin (a member of the extended-spectrum penicillin subclass). It is used to treat infections found or expected to be resistant to amoxicillin. Most other medications in this subclass are intravenous and not captured in this report.

Key Findings by Age Group:

- Dispensation rates for β-lactamase inhibitor combinations were lower and followed different patterns than rates for the extended-spectrum penicillins:
  - The patterns in rates varied over time across age groups, whereby no age groups exhibited consistently lower or higher rates over the entire study period.
  - After the second quarter in 2014, the rates in people ages 65 and older remained the highest among all age groups, followed by age groups 15-64 and 1-4; rates for the remaining age groups were comparable over time.
  - In 2011, β-lactamase inhibitor combinations were most commonly dispensed among children under 5, while the rates in 2016 were highest in ages 15 and older.
- Seasonal variation was seen in all age groups but was more pronounced in some age groups and time periods.
- There were small but statistically significant changes in rates from 2011 to 2016 in all age groups, though not always in all quarters:
  - The rates for age groups 10-14, 15-64 and 65 and older increased over time.
  - The rates in age groups under age 10 decreased in some quarters.

Key Findings by Health Region:

- Adults:
  - Regional dispensation rates for β-lactamase inhibitor combinations among adults were lower and followed different patterns than rates for extended-spectrum penicillins.
  - Dispensation rates varied across regions:
    - Rates were significantly higher than the Manitoba average for Prairie Mountain Health (all years), Interlake-Eastern RHA (2011-2013), and Northern Health Region (some quarters in 2016).
    - Rates in Winnipeg RHA were significantly lower than the provincial average until the second quarter of 2013, while rates in Southern Health-Santé Sud were below the average in some quarters in 2015-2016.
    - Overall, Prairie Mountain Health had consistently higher rates than other regions, followed by Interlake-Eastern RHA until 2015:
      - Northern Health Region had the second highest rates in most quarters in 2015-2016.

- Seasonal variation in dispensation rates was inconsistent, with more pronounced winter peaks in 2015-2016.
- Dispensation rates increased significantly from 2011 to 2016 in all regions.

- Children:
  - Regional dispensation rates for β-lactamase inhibitor combinations among children were lower and followed different patterns than rates for extended-spectrum penicillins.
  - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters, followed by rates in Interlake-Eastern RHA in some quarters in 2013-2016.
  - Rates in Winnipeg RHA were significantly lower than the provincial average in all quarters, and rates in Southern Health-Santé Sud were lower than the average in most quarters.
  - Rates in Southern Health-Santé Sud and Winnipeg RHA were consistently lower than other regions.
  - There was no well-defined seasonal variation across regions or over time.
  - Rates in Prairie Mountain Health decreased significantly in the first two quarters of 2016, when compared with 2011; other regions had few significant differences in quarterly rates between 2011 and 2016, without any consistent overall increase or decrease.

β-Lactamase-Resistant Penicillins (J01CF)

A very commonly dispensed drug from this subclass is cloxacillin. This antibiotic is effective against staphylococcal bacteria and is often used to treat skin infections.

Key Findings by Age Group:

- β-lactamase-resistant penicillins were dispensed less frequently than extended-spectrum penicillins and β-lactamase inhibitor combinations.
- Rates increased with age, with the highest rates observed in adults (ages 15 and older) throughout the entire study period.
- Seasonal variation was less pronounced and differed from the typical winter peaks and summer lows seen in other antibiotics.
- Dispensation rates among adults decreased over time, with statistically significant declines from 2011 to 2016 in all quarters and age groups.

Key Findings by Health Region:

- Adults:
  - Regional dispensation rates for β-lactamase-resistant penicillins among adults were lower and followed different patterns than rates for β-lactamase inhibitor combinations and extended-spectrum penicillins.
  - Dispensation rates were comparable across most regions, with the exception of Prairie Mountain Health and Northern Health Region:
    - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters.
    - Rates in Northern Health Region were higher than the provincial average in some quarters of 2011-2012 and lower in all quarters of 2014-2016.
  - Seasonal variation was less pronounced and differed from the typical winter peaks and summer lows seen in other antibiotics; peaks in rates occurred in the late summer quarters and lows in the winter quarters.
  - Dispensation rates decreased significantly from 2011 to 2016 in all regions.
- Children:
  - Regional dispensation rates for β-lactamase-resistant penicillins among children were lower than those for adults.
  - Dispensation rates were also lower and had different patterns than rates for β-lactamase inhibitor combinations and extended-spectrum penicillins.
  - Rates were comparable across most regions and quarters, with the exception of Prairie Mountain Health:
    - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in most quarters.
    - Rates in Northern Health Region were significantly higher than the provincial average in two quarters in 2011, but lower in one quarter in 2016.
    - Rates in Winnipeg RHA were significantly lower than the provincial average in 2011, as well as in some quarters of 2012, 2014 and 2016.
    - Similarly, rates in Southern Health-Santé Sud were lower than the average in very few quarters in 2014-2016.

- Seasonal variation was not well-defined and seemed to differ from the winter highs and summer lows typical for other β-lactam penicillins; peaks in rates were seen mostly in the late summer quarters.
- Dispensation rates decreased significantly from 2011 to 2016 in all regions.

Cephalosporins (J01D)

This drug class contributed 11.2% of antibiotic dispensations in Manitoba in 2016. Cephalosporins are indicated to treat lower respiratory tract infections, as well as skin and soft tissue infections (SSTI) in children and adults. This class is often divided into first, second and third generation cephalosporins. Earlier generations are often used to treat gram-positive bacterial infections and to boost action of third generation cephalosporins against gram-negative bacteria. Commonly dispensed oral cephalosporins include cephalexin, cefixime, and cefuroxime[32].

Key Findings by Age Group:

- Cephalosporins were the fourth most commonly dispensed class of antibiotics.
- Rates varied across age groups:
  - The highest rates overall were for ages 1-4, followed by ages under 1 in some winter quarters or ages 65 and older in some late summer quarters.
  - Dispensation rates were lowest in ages 10-14.
- Seasonal variation was inconsistent across age groups, with ages under 4 exhibiting peaks in some late summer and some winter quarters; other age groups mostly exhibited peaks in late summer quarters.
- There were small but statistically significant changes in rates from 2011 to 2016 in all age groups, though not always in all quarters:
  - The rates for ages under 10 decreased over time, while rates for ages 10 and older increased slightly in 2016.

Key Findings by Health Region

- Adults:
  - Despite the seemingly comparable regional dispensation rates, regional trends followed a ranking similar to other antibiotics:
    - Rates in Prairie Mountain Health were significantly higher than the provincial average in all quarters, followed by rates in Interlake-Eastern RHA in most quarters.
    - Rates in Winnipeg RHA were significantly lower than the Manitoba average in most quarters, and rates in Southern Health-Santé Sud were lower in some quarters.
  - Dispensation rates exhibited seasonal variation in all regions, except Prairie Mountain Health:
    - The seasonal patterns were similar to those for β-lactamase-resistant penicillins.
  - Overall, rates for adults in Southern Health-Santé Sud, Winnipeg RHA and Interlake-Eastern RHA in 2011 were significantly different from rates in 2016, though not always in all quarters:
    - Rates in Winnipeg RHA increased over time in all quarters.
    - Rates in Southern Health-Santé Sud increased in some quarters, while rates in Interlake-Eastern RHA decreased in one quarter.
- Children:
  - Dispensation rates among children varied considerably across regions, especially compared to trends among adults:
    - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters.
    - Rates in Interlake-Eastern RHA were significantly higher than the provincial average in most quarters.
    - Rates in Southern Health-Santé Sud and Northern Health Region were significantly lower than the provincial average in most quarters, and rates in Winnipeg RHA were lower in two quarters.
  - Dispensation rates exhibited seasonal variation in all regions:
    - Seasonal peaks in Prairie Mountain Health were inconsistent, with peaks in some winter quarters.
    - Seasonal peaks in other regions were in late summer quarters, with the exception of Northern Health Region where rates varied considerably over time.
  - Rates in Winnipeg RHA decreased significantly from 2011 to 2016 in all quarters, while rates in some quarters in Prairie Mountain Health, Interlake-Eastern RHA, Northern Health Region and Manitoba decreased significantly.

Sulfonamides and Trimethoprims (J01E)

This class contributed 4.9% of antibiotic dispensations in Manitoba in 2016. Sulfonamides and trimethoprims are active against some gram-positive bacteria (including methicillin-resistant Staphylococcus aureus) and gram-negative bacteria and are indicated to treat urinary tract infections (UTI) [32]. The most commonly dispensed drug in this class is the combination drug sulfamethoxazole/trimethoprim. The considerably lower dispensation rates for children can be attributed in part to a lack of availability in paediatric formulations of sulfamethoxazole/trimethoprim starting in approximately 2017 [37] and continuing intermittently [38].

Key Findings by Age Group

- Overall, dispensation rates for this class are the lowest among all that we examined.
- Dispensation rates in Manitoba varied greatly across most age groups:
  - Overall, dispensation rates for adults (ages 15 and older) were much higher than those for children.
  - Older adults (65 and older) had the highest rates, almost double those for adults in the 15-64 age group; the latter was twice as high as the rates for ages 10-14.
  - Rates for age groups under 10 were comparable in most quarters, with the exception of slightly higher rates for ages 1-4 from the second quarter in 2012 until the first quarter in 2014 and in 2015.
- Dispensation rates varied over time in older adults (ages 65 and older) and children under age 10, without a clear seasonal pattern:
  - Rates for children under age 10 varied drastically over time, with large gaps between peaks and lows.
- There were small but statistically significant changes in rates from 2011 to 2016 in all age groups, though not in all quarters:
  - Rates increased significantly from 2011 to 2016 in all ages under 65, with the greatest increases in ages under 10.
  - Rates for older adults (65 and older) remained unchanged in all quarters in 2016 relative to 2011 with the exception of the first quarter.

Key Findings by Health Region:

- Adults:
  - Rates among adults in Northern Health Region were considerably higher than the provincial average, with consistent significant differences in all quarters.
  - Rates in Prairie Mountain Health and Interlake-Eastern RHA were significantly higher than the Manitoba average in several quarters in 2014-2016.
  - Rates in Southern Health-Santé Sud were significantly lower than the average in two quarters in 2016.
  - Dispensation rates varied over time in all regions, with a suggestion of late summer peaks.
  - Overall, rates for adults in all regions (except Southern Health-Santé Sud) in 2016 were significantly higher than rates in 2011:
    - The highest increase in rates was seen in Interlake-Eastern RHA.
    - Rates in Southern Health-Santé Sud in 2016 were comparable to 2011.
- Children:
  - Dispensation rates among children followed a similar regional pattern as rates among adults:
    - Rates in Northern Health Region were significantly higher than the provincial average in almost all quarters.
    - Rates in Prairie Mountain Health were higher than the Manitoba average in most quarters, while rates in Interlake-Eastern RHA were higher in two quarters.
    - Rates in Southern Health-Santé Sud and Winnipeg RHA were mostly similar to the Manitoba average, being only lower in few quarters.
  - Rates in all regions exhibited large differences between peaks and lows that often spanned several quarters; the peaks spanned about two years (2012-2013 and 2015-2016):
    - These patterns might be attributed to manufacturing shortages that resulted in lower availability and dispensation [39,40].
  - The rates in all regions increased significantly and considerably from 2011 to 2016:
    - The highest increases were seen in Northern Health Region and Prairie Mountain Health.

Macrolides, Lincosamides and Streptogramins (J01F)

Macrolides, lincosamides and streptogramins contributed 23.9% of dispensed antibiotic prescriptions in Manitoba in 2016. This drug class includes commonly prescribed antibiotics such as erythromycin, clarithromycin, clindamycin and azithromycin [32]. These antibiotics are active against a range of bacteria. For macrolides, this includes atypical bacteria such as mycoplasmas, pertussis, and chlamydia. Drugs in this class are indicated to treat upper and lower respiratory tract infections in children and adults but are generally considered second line after β-lactam agents. These antibiotics are also used instead of penicillins and cephalosporins in the presence of an allergy. Clindamycin has activity against gram-positive bacteria; it also has anaerobic activity. Therefore, it can be used to treat skin and soft tissue and bone and joint infections, intra-abdominal infections, and infections of the head and neck, including dental and oral cavity infections.

Key Findings by Age Group:

- Dispensation rates for this drug class were the second highest overall:
  - The only exception was rates for adults ages 15 and older, which were comparable to dispensation rates for β-lactam penicillins.
- Dispensation rates in Manitoba varied across age groups:
  - Rates for adults (ages 15 and older) and younger children (ages 1-4) were higher than other age groups.
  - The lowest rates overall were for ages 10-14, followed closely by other child age groups in 2014-2016.
- Strong seasonal variation was exhibited in all age groups, with winter peaks and summer lows:
  - This pattern was similar to the seasonality exhibited in dispensations of β-lactam penicillins.
- Dispensation rates across all age groups, except ages 10-14, exhibited a significant decrease from most quarters in 2011 to 2016:
  - The rates for ages 10-14 decreased only in one quarter.
  - The decline in dispensation rates was biggest in ages under 4.

Key Findings by Health Region:

- Adults:
  - Prairie Mountain Health had the highest dispensation rates, followed by Interlake-Eastern RHA; Southern Health-Santé Sud had the lowest dispensation rates among all the regions:
    - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters, and rates in Interlake-Eastern RHA were higher than the average in most quarters.
    - Rates in Southern Health-Santé Sud were significantly lower than the Manitoba average in all quarters.
    - Rates in Northern Health Region fluctuated over time, significantly higher in some quarters and significantly lower in others.
  - Dispensation rates exhibited strong seasonal variation across all regions, with winter peaks and summer lows:
    - Seasonal variation was less pronounced in Northern Health Region in 2012-2014.
  - Overall, rates for adults in all regions (except Prairie Mountain Health) and Manitoba overall in some quarters of 2011 were significantly different from rates in 2016:
    - The rates in Southern Health-Santé Sud, Winnipeg RHA, Northern Health Region and Manitoba overall decreased in the second quarter of 2016.
    - Rates in Interlake-Eastern RHA decreased in most quarters of 2016.
- Children:
  - Dispensation rates among children varied considerably across regions:
    - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters, while rates in Interlake-Eastern RHA were above the average in some quarters.
    - Rates in Northern Health Region were significantly lower than the provincial average in all quarters, and rates in Southern Health-Santé Sud were lower than the average in most quarters.
  - Rates in all regions except Northern Health Region exhibited strong seasonal variation, with winter peaks and summer lows.
  - Rates in 2011 in all regions and Manitoba overall exhibited significant differences from rates in 2016:
    - The rates in all regions decreased over time, with the greatest decline in Prairie Mountain Health.

Quinolones (J01M)

Quinolones contributed 13.7% of antibiotic dispensations in Manitoba in 2016. This drug class includes commonly dispensed antibiotics such as ciprofloxacin and levofloxacin [32]. These drugs have broad coverage against different types of bacteria and are indicated to treat gram-negative bacteria in the setting of UTIs, intra-abdominal infections, some infectious diarrhea, and in some cases, respiratory infections or bone and joint infections. Some members of this class have activity against atypical organisms and Mycobacterium tuberculosis. Quinolones are rarely prescribed to children in typical outpatient settings given historical data from animal studies that demonstrated harm, leading to very small dispensation rates in ages under 15 (data not shown). Thus, findings are presented only for adults (ages 15 and older).

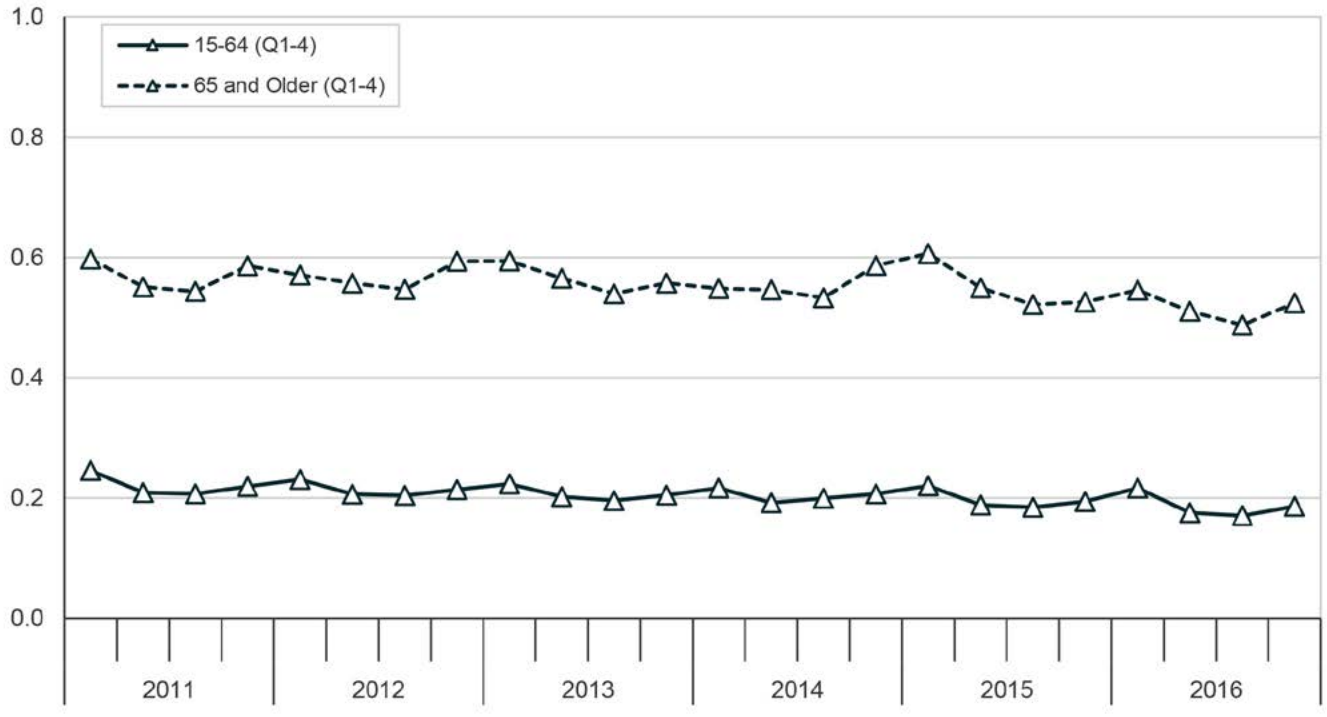
Key Findings for Adults by Age Group

- Dispensation rates for this drug class (among adults) were third highest overall:
  - When compared with rates for macrolides, lincosamides and streptogramins, this drug class had higher rates for older adults (ages 65 and older) and lower rates for younger adults (ages 15-64).
- Dispensation rates among older adults were almost three times higher than rates for younger adults.
- Seasonal variation was exhibited in older adults, though not consistently throughout the study period and with small winter peaks and summer lows:
  - This pattern was similar but much less pronounced that the seasonality exhibited in dispensations of β-lactam penicillins, macrolides, lincosamides and streptogramins.
- Dispensation rates for both age groups exhibited a significant decrease from 2011 to 2016; the decline in rates in 2016 was greater among older adults.

Key Findings for Adults by Health Region:

- Prairie Mountain Health had the highest dispensation rates, followed by Interlake-Eastern RHA; Northern Health Region and Southern Health-Santé Sud had the lowest dispensation rates among the regions:
  - Rates in Prairie Mountain Health were significantly higher than the Manitoba average in all quarters, and rates in Interlake-Eastern RHA were higher than the average in most quarters.
  - Rates in Southern Health-Santé Sud and Northern Health Region were significantly lower than the Manitoba average in most quarters.
- Dispensation rates exhibited seasonal variation across all regions, with small winter peaks and summer lows:
  - Seasonal variation was less pronounced and less consistent in Northern Health Region in 2011-2013.
- Dispensation rates in all regions (except Northern Health Region) and Manitoba overall decreased significantly from 2011 to 2016.

Figure 3.4: Quarterly Dispensation Rates for Quinolones (J01M) by Age Group*
Crude rates per 1,000 people per day



* Rates for ages under 15 are not shown due to small numbers.
(Q1,2,3,4) - Indicates statistically significant differences between corresponding quarters in 2011 and 2016 ($p<0.05$).

Other Antibiotics (J01X)

This group of antibiotics contributed 5.7% of antibiotic dispensations in Manitoba in 2016. It includes drugs not captured in classes J01A to J01M. The most commonly dispensed antibiotics in this group include nitrofurantoin and metronidazole [32]. Nitrofurantoin is active against gram-negative bacteria and is indicated to treat uncomplicated UTIs or as prophylaxis. Metronidazole is active against anaerobic bacteria. This drug is used to treat intra-abdominal infections, trichomoniasis, C. difficile diarrheal disease, bacterial vaginosis, some intestinal parasite infections and to control flares of Crohn's disease. Drugs in this class are prescribed mostly to adults. Dispensations among children (ages 1-14) were very low and declined in some quarters from 2011 to 2016 for ages 1-9 (data not shown). Thus, only results for adults are presented in this section.

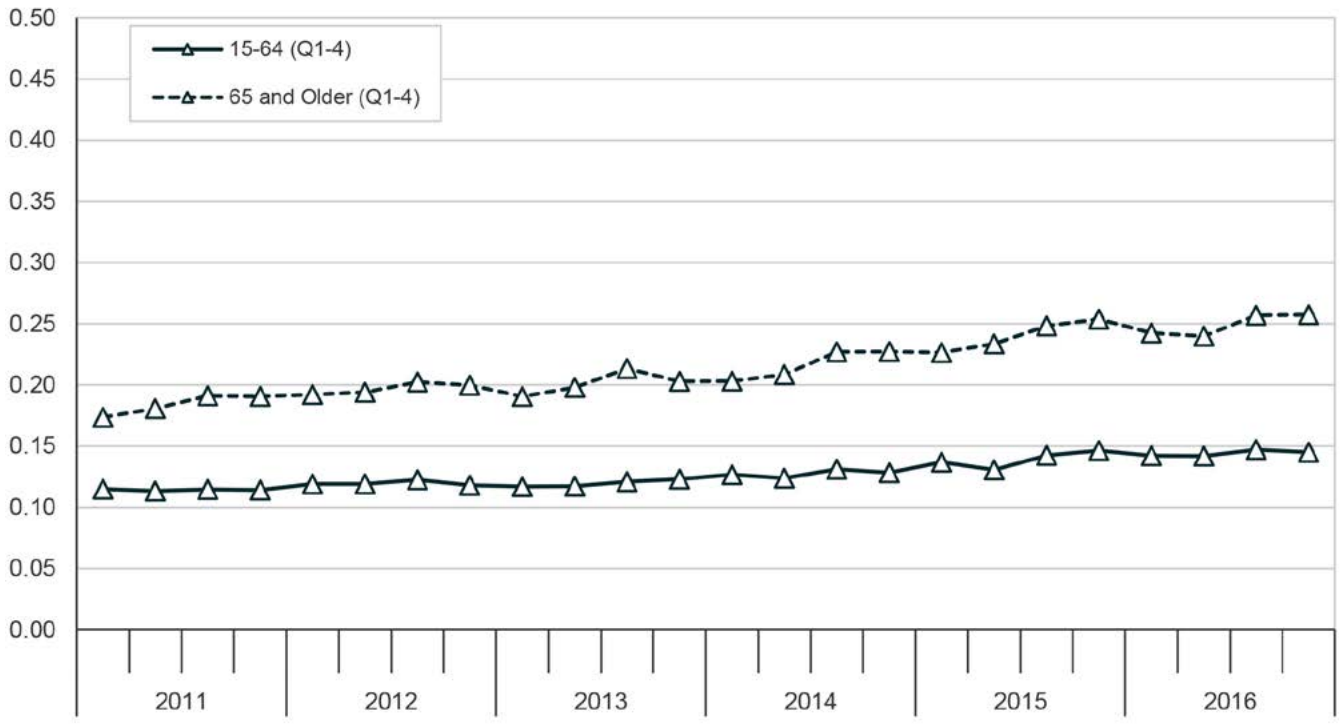
Key Findings for Adults by Age Group (Figure 3.5):

- Dispensation rates for this drug class (among adults) were low, and only higher than tetracyclines and sulfonamides overall:
  - Dispensation rates for this class were comparable to rates for sulfonamides and trimethoprims.
  - Rates for this class among younger adults were comparable to rates for tetracyclines but almost twice as high as older adults.
- Dispensation rates among older adults were almost twice as high as rates for younger adults.
- No seasonal variation was seen in the dispensation patterns.
- Dispensation rates for both age groups increased significantly from 2011 to 2016 (all quarters), with larger increases among older adults:
  - This pattern is consistent with the increases in tetracycline dispensations among adults.

Key Findings for Adults by Health Region:

- Northern Health Region had the highest dispensation rates, followed by Interlake-Eastern RHA and Prairie Mountain Health; Southern Health-Santé Sud had the lowest dispensation rates in most quarters:
  - Rates in Northern Health Region and Interlake-Eastern RHA were significantly higher than the Manitoba average in most quarters, and rates in Prairie Mountain Health were higher than the average in some quarters.
  - Rates in Southern Health-Santé Sud were significantly lower than the Manitoba average in most quarters.
- No seasonal variation was seen across regions.
- Dispensation rates in all regions and Manitoba overall increased significantly from 2011 to 2016:
  - The highest increases in dispensation rates were seen in Southern Health-Santé Sud and Interlake-Eastern RHA.

Figure 3.5: Quarterly Dispensation Rates for Other Antibiotics (J01X) by Age Group
Crude rates per 1,000 people per day



* Rates for ages under 15 are not shown due to small numbers.
(Q1,2,3,4) - Indicates statistically significant differences between corresponding quarters in 2011 and 2016 ($p<0.05$).

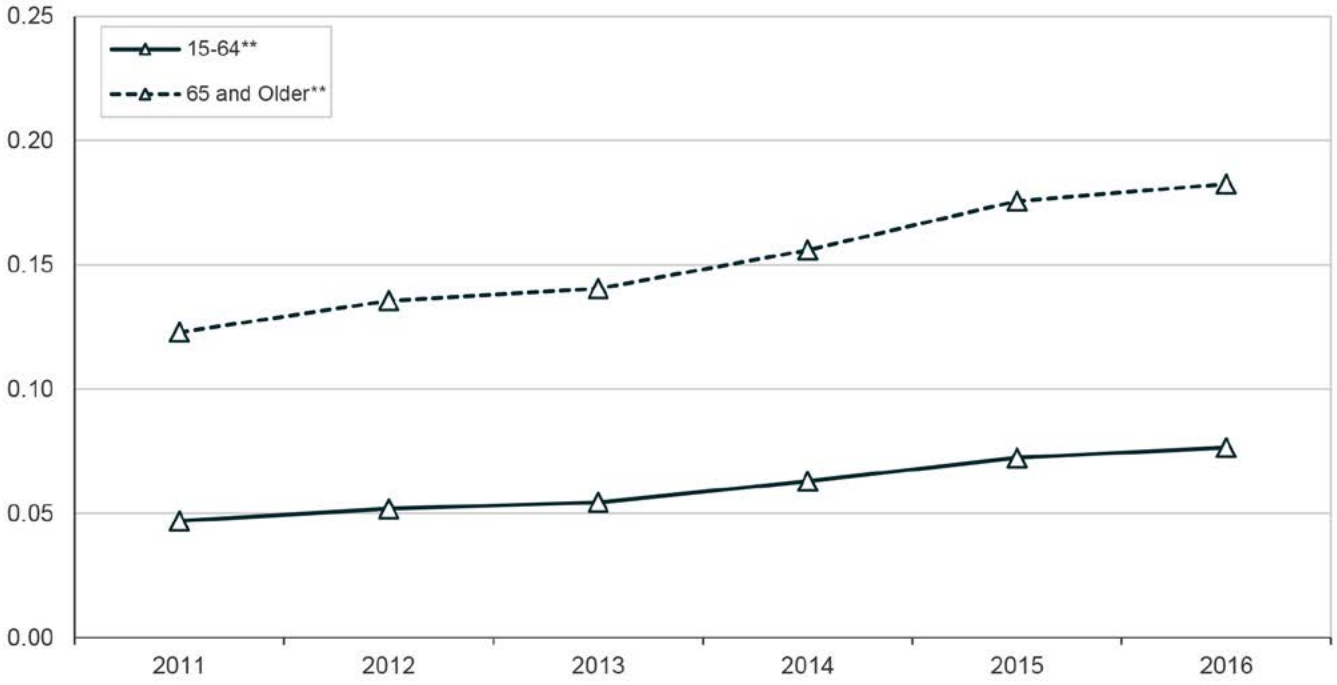
Nitrofurantoin (J01XE01)

Nitrofurantoin is one of the most commonly dispensed drugs in the group of other antibiotics (J01X). This drug is part of the subclass nitrofuran derivatives (J01XE). It is used only for uncomplicated UTIs, for which it is a recommended first-line choice [41]. Findings for nitrofurantoin are presented as annual rates instead of quarterly rates due to small counts. This drug is prescribed mostly to adults, leading to very low dispensation rates for children. Some dispensations were seen for children ages 1-14, with a statistically significant increase from 2011 to 2016 in ages 10-14 (data not shown). Therefore, only data for adults are presented in this report.

Dispensation rates of nitrofurantoin were almost three times higher among older adults when compared with younger adults (Figure 3.6). The rates in both age groups increased significantly over time, with greater increases among older adults.

Figure 3.6: Annual Dispensation Rates for Nitrofurantoin (J01XE01) by Age Group*

Crude rates per 1,000 people per day



* Rates for ages under 10 are not shown due to small numbers. Rates for age groups under 1 and 10-14 in 2011 were statistically significantly different from rates in 2016 ($p<0.05$).

** Indicates statistically significant differences between rates in 2011 and 2016 ($p<0.05$).

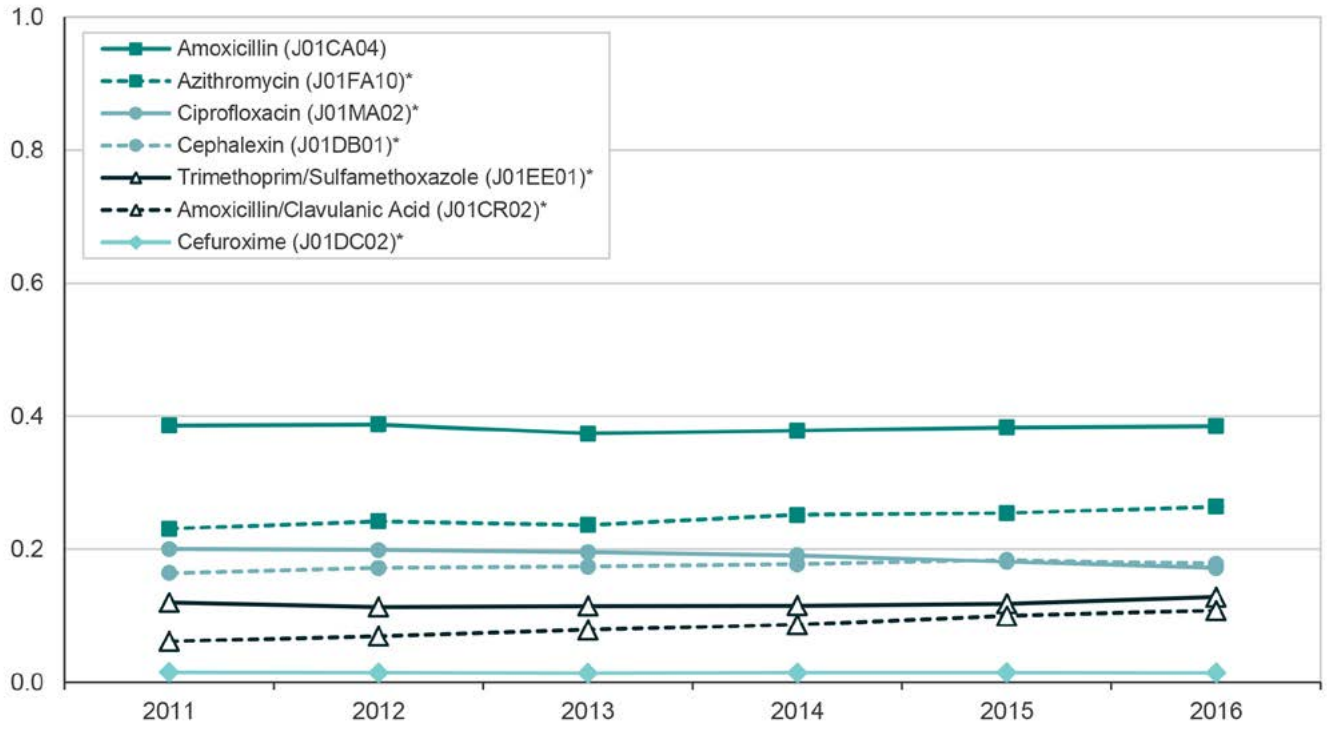
Commonly Dispensed Individual Antibiotics

This section presents findings for commonly used antibiotics in outpatient practice. Amoxicillin, amoxicillin/clavulanic acid, azithromycin, cefuroxime, cephalexin, and trimethoprim/sulfamethoxazole are often prescribed to both children and adults [32]. Ciprofloxacin is often prescribed to adults. Dispensation rates are shown as annual averages due to the smaller number of dispensations of individual drugs when compared with dispensations at the class and subclass levels.

Key Findings by Age Group:

- Adults (Figure 3.7):
  - Dispensation rates for amoxicillin (β-lactam penicillin class) were consistently higher than the rates for other drugs.
  - Rates for amoxicillin, which is a member of the class of macrolides, lincosamides, and streptogramins, were almost twice as high as the rates for the next most commonly dispensed antibiotics (azithromycin and ciprofloxacin).
  - The rates of all of these drugs, except amoxicillin, exhibited a significant change from 2011 to 2016:
    - The rates of cefuroxime and ciprofloxacin decreased over time, with a greater decline in ciprofloxacin.
    - The rates of all other drugs increased over time, with the greatest increases seen for amoxicillin/clavulanic acid and azithromycin.

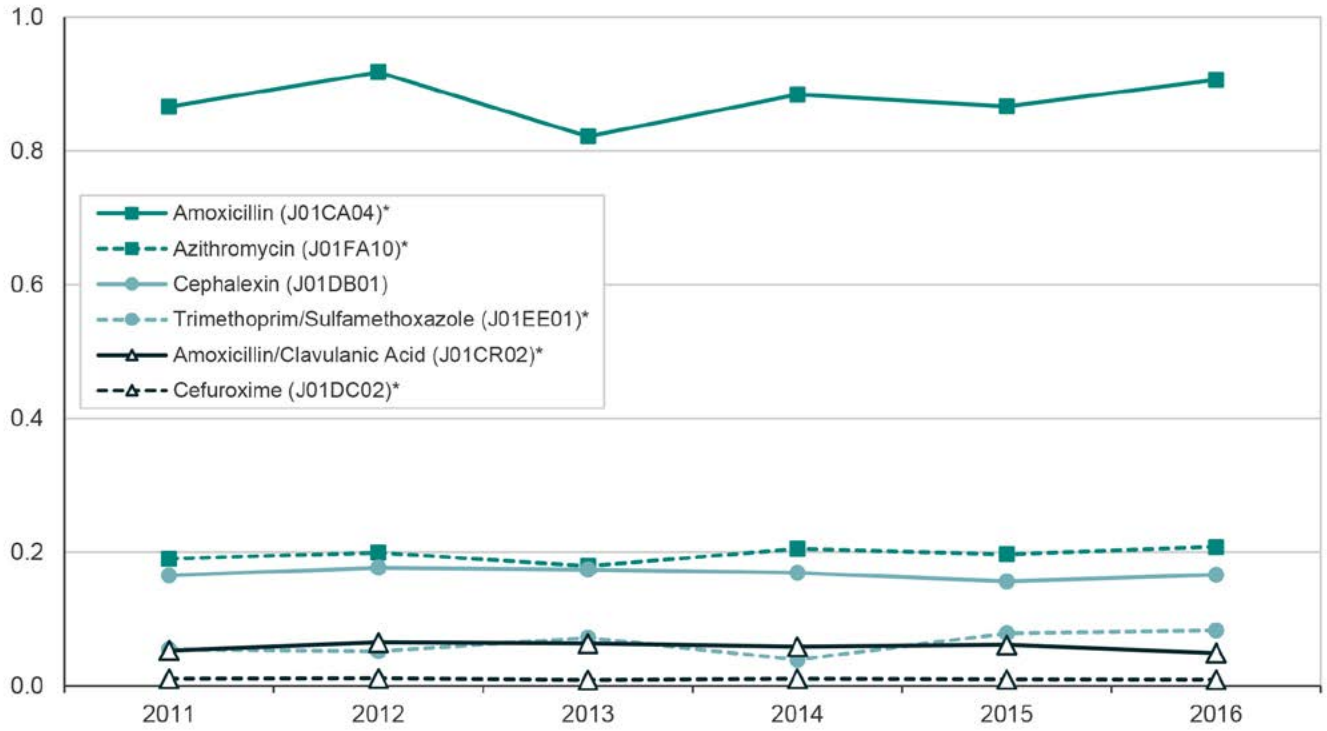
Figure 3.7: Annual Dispensation Rates for Commonly Dispensed Antibiotics for Adults
Crude rates per 1,000 people ages 15 and older per day



* Indicates statistically significant differences between rates in 2011 and 2016 ($p<0.05$).

- Children (Figure 3.8):
  - Dispensation rates of amoxicillin (β-lactam penicillin class) were also consistently higher among children when compared with the rates for other drugs.
  - Amoxicillin dispensation rates were over four times higher than the rates of the second most commonly dispensed drug (azithromycin) and more than five times higher than the third most commonly dispensed drug (cephalexin).
  - The rates of all of these drugs, except cephalexin, exhibited a significant change from 2011 to 2016:
    - The rates of amoxicillin/clavulanic acid and cefuroxime decreased slightly over time, with a greater decline in amoxicillin/clavulanic acid.
    - The rates of all other drugs increased over time, with the greatest increases seen for amoxicillin and trimethoprim/sulfamethoxazole.

Figure 3.8: Annual Dispensation Rates for Commonly Dispensed Antibiotics for Children
Crude rates per 1,000 people ages 0-14 per day



* Indicates statistically significant differences between rates in 2011 and 2016 ($p<0.05$).

Summary and Discussion

This chapter describes population-level use of outpatient prescription oral antibiotics in Manitoba with comparisons by health region and age group. It demonstrates a few consistent patterns and offers some insight into overall prescribing practices. It forms the basis for a more detailed analysis at the individual visit, diagnosis, and prescriber level for the rest of the report.

For comparisons by health region, similar patterns were seen across all classes and subclasses of antibiotics. When compared between health regions, with the exception of the Northern Health Region, dispensation rates decreased in the order of Prairie Mountain Health, Interlake-Eastern RHA, Manitoba overall, Winnipeg RHA, and Southern Health-Santé Sud, when differences were present. The Northern Health Region behaved differently across antibiotic classes and age groups (adults vs children). Northern Health Region had the highest or second highest dispensation rates for sulfonamides and trimethoprims (adults and children), β-lactam penicillins (adults), and other antibiotics (adults). Dispensation rates for Northern Health Region were among the lowest for tetracyclines (adults), β-lactam penicillins (children), cephalosporins (children), macrolides, lincosamides and streptogramins (adults and children), and quinolones (adults). This is likely due to differences in which antibiotics are dispensed in nursing stations or health centres without a prescription compared to those requiring a prescription. Even after age and sex adjustments, there were significant consistent patterns which may be indicative of areas for ASPs to target.

Patterns by age group followed the expected use patterns for antibiotics based on common indications, age restrictions and bacteria being treated in different age groups. β-lactam and cephalosporin antibiotics rates were highest in children to cover predominantly upper and lower respiratory infections with gram-positive bacteria, with tetracyclines, macrolides and quinolones highest in adults covering a broader range of bacteria including the atypical bacteria. For some indications where more than one antibiotic class/sub-class is appropriate, prescriptions to children depend on the availability and palatability of oral suspensions, as was seen in greater use of cephalosporins compared to β-lactamase-resistant penicillins such as cloxacillin.

There were some significant changes over time. Dispensation rates of antibiotics overall have decreased slightly in children (ages under 15) and increased in adults (ages 15+). β-lactamase-resistant penicillins decreased over time mostly in adults, while β-lactam inhibitor combinations increased over time. An opposite and promising pattern seen in children was the decreasing use of β-lactam inhibitor combinations, such as amoxicillin/clavulanic acid paired with increasing use of the preferable penicillins such as amoxicillin (the extended-spectrum subclass). There was a significant increase over time in dispensations of other antibiotics, and when individual drugs were examined, this suggested that this is due to increased use of nitrofurantoin. The use of sulfonamides increased in all groups, as did the macrolides. Changes in patterns of use over time are also affected by changes in population health status and infectious disease outbreaks. Quinolone use in adults showed a small decrease over time. This may be related to recent messaging campaigns encouraging stewardship of quinolone use. Some recent publications have led to Black Box warnings from the Food and Drug Administration in the United States, as they relate to quinolone use and risk for serious and potentially irreversible serious adverse effects including tendon rupture, peripheral neuropathy, exacerbations of myasthenia gravis, cardiac conduction effects, and aneurysm rupture [42].

The descriptive information this chapter presented is essential to help establish benchmarks for future antimicrobial stewardship initiatives to target and to compare the effect of future interventions.

Chapter 4:
Quality Indicators for Antibiotic Consumption in the Community

The European Centre for Disease Prevention and Control under the European Surveillance of Antibiotic Consumption Network (ESAC-Net) has established several quality indicators for the consumption of antibiotics in the community. ESAC-Net is a network of national surveillance systems throughout Europe [43]. ESAC-Net collects and analyses data on antibiotic consumption over time in hospitals and in the community in member countries of the European Union, European Economic Area and European Free Trade Association. ESAC-Net data are used as a reference dataset by various jurisdictions.

In this chapter, we report on the standard ESAC-Net indicators for outpatient systemic antibiotics [44], comparing Manitoba to Europe. Some of these indicators divide antibiotics into broad- and narrow-spectrum antibiotics. A broad-spectrum antibiotic is one that is effective against a wide range of bacteria, often multiple types such as gram-positive and gram-negative. A narrow-spectrum antibiotic is effective against a smaller range of bacteria. In general, the narrowest-spectrum antibiotic should be used as broader-spectrum antibiotics lead to more resistance.

The ESAC-Net indicators include:

- Relative consumption of antibiotics
    - The following groupings of antibiotics as a percentage of total antibiotics:
        - β-lactamase-sensitive penicillins
        - β-lactam inhibitor combinations
        - Third and fourth generation cephalosporins
        - Fluoroquinolones
    - Consumption of broad- vs. narrow-spectrum antibiotics
        - Ratio of broad-spectrum (β-lactam inhibitor combinations/second generation cephalosporins/third generation cephalosporins/non-erythromycin macrolides) to narrow-spectrum (β-lactamase-sensitive penicillins/1st generation cephalosporins/erythromycin) penicillins, cephalosporins and macrolides
    - Seasonal variation in antibiotic consumption
        - Percent increase in daily dose dispensations from the summer quarters (April-June and July-September) to the winter quarters (January-March and October-December) in a 12-month period starting in July

Methods

The ESAC-Net indicators use a method of capturing antibiotic use called a defined daily dose (DDD), and it is reported as a value of DDD per 1,000 people per day. The DDD is calculated by taking the daily amount of prescribed antibiotics and dividing it by a standard daily dose for that antibiotic. For example, if the standard dose of an antibiotic is 1,000 g per day, and someone is dispensed 1,500 g per day, they are receiving 1.5 DDD per day. Results are reported for all of Manitoba (except for quinolones which are rarely prescribed for children) to allow for comparison to the ESAC-Net indicators. This method of capturing antibiotic use has some issues with paediatric formulations where doses are volume-based, based on the weight of the patient, and the dispensed volume includes overage. Thus, we present results for adults only in the online supplement. Even in adults, a "standard" dose of antibiotic may vary by the particular infection being treated.

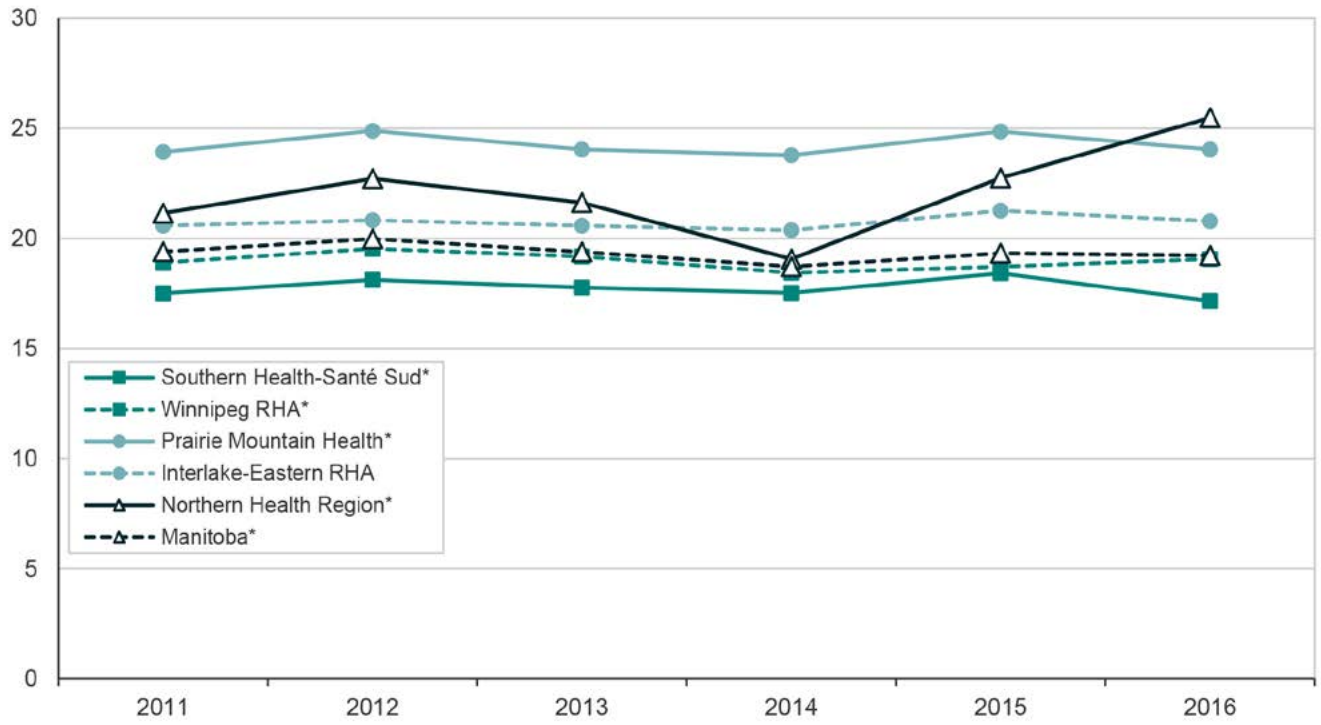
Age- and sex-adjusted results are presented. Statistical comparisons between the health regions and all of Manitoba and between 2016 and 2011 are reported.

Further data with these indicators is available in Appendix 2. Comparisons to the 2016 ESAC-Net data are included in the introduction to each indicator [44]. Results are for all prescribers captured in the DPIN data. The cohort is the standard cohort defined in Chapter 2. Even though it is difficult to estimate the ideal target, one could argue that the lowest prescribing regions likely do not have excess mortality from under prescribing and therefore would be a reasonable benchmark.

Defined Daily Dose for Antibiotics Overall by Health Region

Figure 4.1 presents dispensations of antibiotics by DDD/1,000 people/day. In 2016 the Manitoba rate was 19.22. The ESAC-Net data show that DDD/1,000 people/day rates range from 9.2 (Netherlands) to 31.0 (Greece) [44]. Crude rates and counts are available in the online supplement for this report.

Figure 4.1: Annual Defined Daily Dose Dispensation Rates for Antibiotics Overall (J01) by Health Region, 2011-2016
Age- and sex-adjusted rate per 1,000 people per day



* Indicates statistically significant differences between rates in 2011 and 2016 ($p<0.05$).

ESAC-Net Quality Indicators

This section provides age- and sex-adjusted results for select ESAC-Net quality indicators for all Manitobans and prescribers, overall (Table 4.1) and by health region (Figures 4.2-4.4). Additional information for all Manitobans overall and by health region, as well as for adults overall and by health region, are available in the online supplement for this report.

Table 4.1: Rates for ESAC-Net Quality Indicators of Antibiotic Consumption in Manitoba, 2011-2016
Age- and sex-adjusted rates for all Manitobans and all prescribers

Year	ESAC-Net* Quality Indicators of Antibiotic Consumption (Average Rate and 95% Confidence Intervals)						
	Relative Consumption (Antibiotic Class Relative to Antibiotics Overall)				Broad vs. Narrow Spectrum	Seasonal Variation (Increase from Summer to Winter)	
	β-Lactamase-Sensitive (J01CE) †	β-Lactamase Inhibitor/Penicillin Combination (J01CR)**	Third- and fourth-generation cephalosporins (J01DD & J01DE)**	Fluoroquinolones (J01MA)**	Antibiotics Overall (J01)**	Antibiotics Overall (J01)**	Quinolone Class (J01M)**
	%	%	%	%	Ratio	%	%
2011	1.94 (1.93-1.95)	4.39 (4.37-4.40)	0.31 (0.30-0.31)	10.56 (10.54-10.58)	2.66 (2.65-2.66)	16.22 (16.12-16.33)	3.39 (3.10-3.69)
2012	1.75 (1.45-2.12)	4.78 (4.39-5.21)	0.28 (0.22-0.36)	10.00 (7.99-12.50)	2.72 (2.53-2.92)	8.11 (4.21-12.17)	77.59 (43.36-119.99)
2013	1.58 (1.30-1.91)	5.41 (4.97-5.89)	0.28 (0.21-0.35)	9.94 (7.95-12.44)	2.64 (2.46-2.84)	10.93 (6.92-15.09)	64.36 (32.76-103.48)
2014	1.59 (1.31-1.93)	6.01 (5.52-6.55)	0.17 (0.13-0.21)	11.03 (8.81-13.79)	2.65 (2.46-2.84)	9.70 (5.74-13.82)	136.14 (90.49-192.72)
2015	1.56 (1.29-1.89)	6.43 (5.91-7.00)	0.09 (0.07-0.11)	9.88 (7.90-12.35)	2.63 (2.44-2.82)	15.00 (10.85-19.32)	107.56 (67.43-157.30)
2016	**1.50 (1.24-1.82)**	**6.81 (6.26-7.42)**	**0.13 (0.10-0.17)**	10.14 (8.11-12.69)	2.64 (2.46-2.84)	**10.28 (6.30-14.42)**	-10.90 (-27.92-10.14)

* ESAC-Net represents the European Surveillance of Antibiotic Consumption Network (ESAC-Net).
** Lower values indicate more prudent use
† higher values indicate more prudent use
Bolded values indicate statistically significant differences between 2011 and 2016 ($p<0.01$).

Relative Consumption of Antibiotics

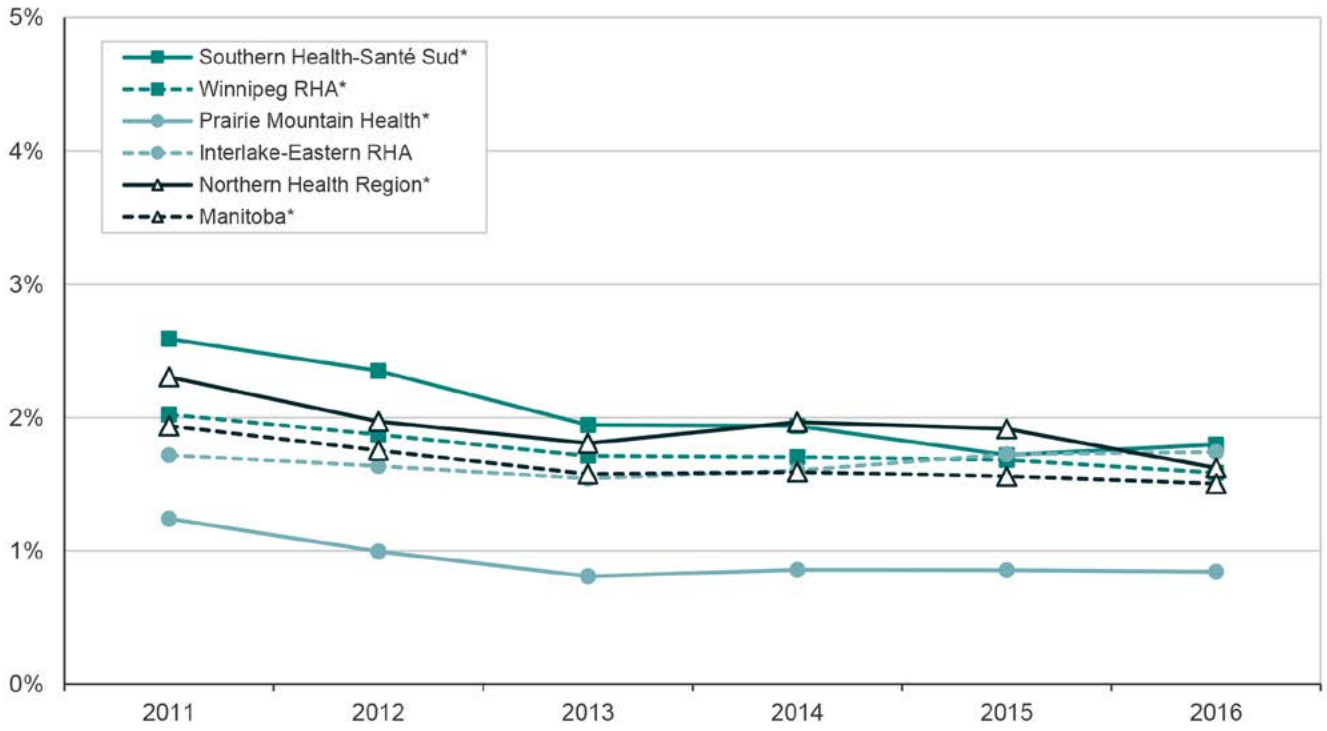
Consumption of β-Lactamase-Sensitive Penicillins Expressed as a Percent of Total Consumption of otal Antibacterials

This indicator examines the percentage of total antibiotic use that is due to the narrow-spectrum β-lactamase-sensitive penicillins. For this indicator, a higher number indicates more use of narrow-spectrum antibiotics, which is felt to be more prudent use. This indicator ranges widely in the ESAC-Net data from less than 0.1% (Italy, Luxembourg, Portugal) to 27.5% (Sweden).

Key findings (Figure 4.2):

- Rates varied by health region, ranging from 0.84 to 1.8% in 2016.
- Rates in Prairie Mountain Health were lower than the Manitoba rate.
- Rates in Southern Health-Santé Sud were higher than the Manitoba rate in 2011 and 2012, but not in other years.
- All health regions worsened (indicated by a decrease), except for Interlake-Eastern RHA, which did not change.

Figure 4.2: Annual Consumption of β-Lactamase-Sensitive Penicillins (J01CE) as Percent of Total Antimicrobials (J01) by Health Region
Age- and sex-adjusted percent, all ages, all prescribers



* Indicates statistically significant differences between rates in 2011 and 2016 (p<0.05).

Relative Consumption of Antibiotics

Consumption of β-Lactamase-Sensitive Penicillins Expressed as a Percent of Total Consumption of Total Antibacterials

This indicator examines the percentage of total antibiotic use that is due to the narrow-spectrum β-lactamase-sensitive penicillins. For this indicator, a higher number indicates more use of narrow-spectrum antibiotics, which is felt to be more prudent use. This indicator ranges widely in the ESAC-Net data from less than 0.1% (Italy, Luxembourg, Portugal) to 27.5% (Sweden).

Key findings (Figure 4.2):

- Rates varied by health region, ranging from 0.84 to 1.8% in 2016.
- Rates in Prairie Mountain Health were lower than the Manitoba rate.
- Rates in Southern Health-Santé Sud were higher than the Manitoba rate in 2011 and 2012, but not in other years.
- All health regions worsened (indicated by a decrease), except for Interlake-Eastern RHA, which did not change.

Consumption of β-Lactamase Inhibitor Penicillin Combinations as Percent of Total Antimicrobials

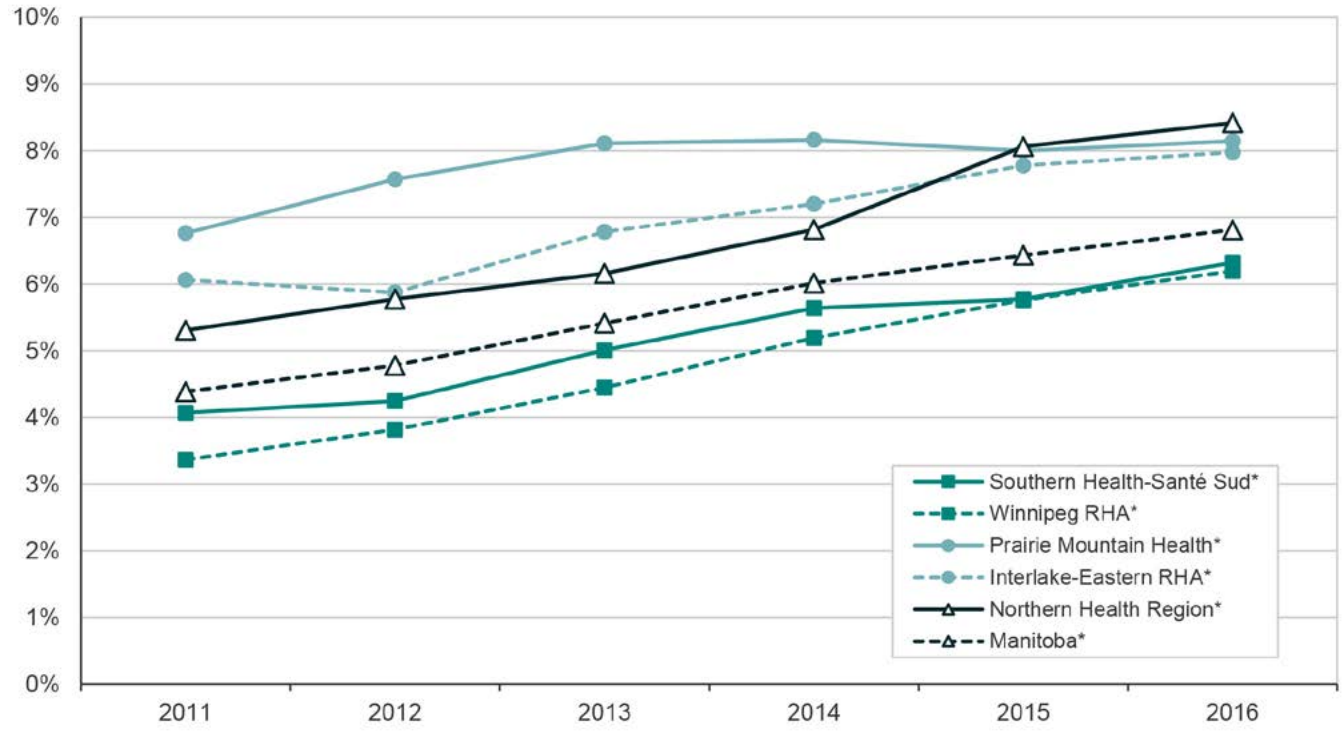
This indicator looks at the percentage of penicillin/inhibitor combinations such as amoxicillin/clavulanic acid as a percentage of all antibiotics. This category of combination antibiotic is a broad-spectrum agent, and general prudent use of this type of antibiotic would have a lower value. This indicator ranges widely in the ESAC-Net data from less than 0.1% (Finland) to 36.4% (Portugal).

Key findings (Figure 4.3):

- Rates varied slightly by health region, ranging from 6.2% to 8.4% in 2016.
- Rates for Prairie Mountain Health, Northern Health Region and Interlake-Eastern RHA were higher than the Manitoba rate.
- Rates for Winnipeg RHA were lower than the Manitoba rate in 2011-2014, and for Southern Health-Santé Sud in in 2012.
- All health regions worsened (indicated by an increase) over time.

Figure 4.3: Annual Consumption of β-Lactamase Inhibitor Penicillin Combinations (J01CR) as Percent of Total Antimicrobials (J01) by Health Region

Age- and sex-adjusted percent, all ages, all prescribers



* Indicates statistically significant differences between rates in 2011 and 2016 ($p<0.05$).

Consumption of Third and Fourth Generation Cephalosporins as Percent of Total Antimicrobials

This indicator looks at the percentage of total antibiotic use that is third and further generation cephalosporins such as cefixime and cefdinir. These drugs are used to treat primarily gram-negative infections, are considered broader-acting in their spectrum, and compromise a very small amount overall of outpatient oral antibiotic use. In general, prudent use of antibiotics would be indicated by a lower value. This indicator ranges widely in the ESAC-Net data from less than 0.1% (multiple countries) to 8.9% (Italy).

Key findings:

- Rates by health region were very close in 2016, ranging from 0.08% to 0.25%.
- Rates were higher for Interlake-Eastern RHA than the Manitoba rate, and they were higher in earlier years for all regions except the north.
- Rates were lower for the north than the Manitoba rate only in 2016.
- Use in all regions improved (indicated by a decrease) over time.

Consumption of Fluoroquinolones as Percent of Total Antimicrobials

This indicator which is from the fluoroquinolone subclass looks at the percentage of total antibiotic use, such as ciprofloxacin and levofloxacin. In general, prudent use of antibiotics would be indicated by a lower value. This indicator ranges widely in the ESAC-Net data from less than 2.3% (Norway) to 16.8% (Hungary).

Key findings:

- Rates by health region were close in 2016, ranging from 7.02% to 11.18%.
- No regional rates were significantly higher than the Manitoba rate, and only the Northern Health Region had a lower rate.
- There was no significant change in rates between 2011 and 2016.

Broad- and Narrow-Spectrum Antibiotic Consumption

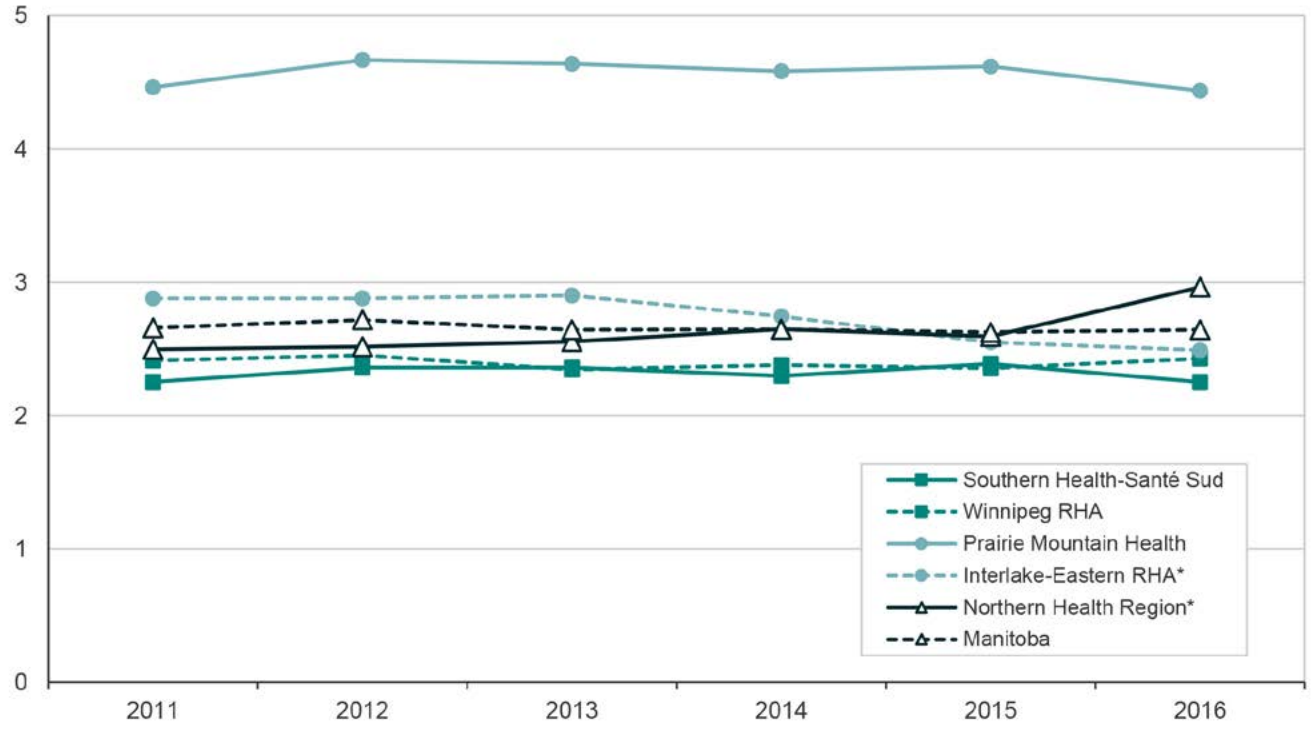
Ratio of Broad-Spectrum to Narrow-Spectrum Penicillins, Cephalosporins and Macrolides

This indicator looks at the ratio of broad- to narrow-spectrum antibiotics in the commonly used outpatient classes. In general, prudent use of antibiotics would be indicated by a lower value. This indicator ranges widely in the ESAC-Net data from 0.16 (Norway) to 624.04 (Greece). Note that a value less than one indicates less broad-spectrum use than narrow-spectrum use. Values over one indicates greater broad-spectrum use than narrow-spectrum use.

Key findings (Figure 4.4):

- Most health region ratios were close together, except for Prairie Mountain Health, which was much higher, ranging from 2.49-4.44 in 2016.
- All health regions had values greater than 1.00 at all time points
- Prairie Mountain Health in all years and Northern Health Region in 2016 were higher than the Manitoba rate.
- Ratios were only lower than the Manitoba rate for Winnipeg RHA and Southern Health-Santé Sud in most time periods.
- Ratios for Interlake-Eastern RHA improved (indicated by a decrease) in 2016 compared to 2011, and for Northern Health Region worsened (indicated by an increase).

Figure 4.4: Annual Ratio of Broad-Spectrum (J01CR, J01DR, J01DD, J01F-FA01) to Narrow-Spectrum Penicillins, Cephalosporins and Macrolides (J01CE, J01DB, J01FA01) by Health Region
Age- and sex-adjusted percent, all ages, all prescribers



* Indicates statistically significant differences between ratios in 2011 and 2016 ($p<0.05$).

Seasonal Variation in Antibiotic Consumption

Seasonal Variation in Total Antibacterial Use

Seasonal variation compares the use of antibiotics in the winter to that in the summer and is expressed as how much higher use is in the winter compared to the summer. In this indicator, all types of oral antibiotics are included. For these analyses, winter is considered January-March and October-December, with summer encompassing April-June and July-September for a 12-month period starting in July to account for one winter season. Thus '2011' for output actually starts in July 2010. Increased prescribing is well described during winter/colder months, and some seasonal variation is expected, but with prudent antibiotic use it should be minimal and large values are suggestive of overprescribing for viral respiratory illnesses [45]. Patients presenting with respiratory illness during winter months are in general more likely to have primary viral illness, and subsequently may develop secondary bacterial infections. However, this risk of secondary infections is often over-estimated by prescribers [28]. In the ESAC-Net data, this varies widely from 8.6% (Denmark) to 47.4% (Latvia).

Key findings:

- The values in 2016 between the health regions ranged from 7.8% to 13.5%.
- In the adjusted model, the Northern Health Region in 2012/2013 had a negative value suggesting higher rates in summer compared to winter.
- Regional rates were similar to the Manitoba rates, only varying occasionally in some years.
- Seasonal variation decreased significantly in 2016 compared to 2011 for all health regions, except Southern Health-Santé Sud where there was a trend (p=0.055).

Seasonal Variation in Quinolone Use

Seasonal variation compares the use of antibiotics in the winter to that in the summer and is expressed as how much higher use is in the winter compared to the summer. In this indicator, variations in the quinolone class are described. For these analyses, winter is considered January-March and October-December, with summer encompassing April-June and July-September for a 12-month period starting in July to account for one winter season. Thus '2011' for output actually starts in July 2010. Some seasonal variation is expected, but with prudent antibiotic use it should be minimal and large values are suggestive of overprescribing for viral respiratory illnesses or other infectious syndromes [45]. Due to very low DDD rates in children affecting model fit, results are shown for this indicator for adults only. In the ESAC-Net data this varies widely from 0.4% (United Kingdom) to 47.3% (Hungary).

Key findings:

- In 2016, the health regions varied between 8.6% and 34.1%.
- Rates were similar to the Manitoba rates, only varying occasionally in some years for Prairie Mountain Health, Interlake-Eastern RHA and Northern Health Regions (see Appendix Table 2.5).
- Seasonal variation did not change for any health region in 2016 compared to 2011.

Summary and Discussion

The antibiotic use indicators in this chapter demonstrate similar patterns to those seen in Chapter 3 when antibiotic use was examined by class and subclass. In general, there were small differences between the health regions with Prairie Mountain Health and Interlake-Eastern RHA having fewer desirable results than the Manitoba rates for the β-lactam indicators, and Southern Health-Santé Sud having more desirable outcomes in these indicators. There is some question about the validity of the Northern Health Region indicators, as suggested by the inverse seasonal variation, and the unknown quantity of antibiotics dispensed from nursing stations without a prescription. For the cephalosporin, fluoroquinolone and seasonal variation indicators there were few differences between health regions, and any seen were small.

Changes over time were variable but consistent between health regions. For the β-lactam related indicators, there was a small change towards less prudent use. For the cephalosporin indicators, there was a change towards more prudent use. For fluoroquinolone use, both as a percentage and for seasonal variation, there was no change. For seasonal variation overall, there was a small decrease, a desirable change.

In comparison to the average European rates, Manitoba rates tended more towards the desirable ranges, with the exception of seasonal variation, where results were more mid-range. However, many countries have rates considerably more desirable than Manitoba's. Countries with more variable seasonal weather, and thus more seasonal variation in viral illnesses tended to have higher rates [45–47], as applies to Manitoba. Direct comparisons would require adjustment for characteristics affecting antibiotic use such as age, sex, morbidities and socioeconomic status [48]; however the data as they stand identify areas for further attention and study.

Chapter 5:
Relationship between Health Care Service Use and Antibiotic Dispensations to Manitobans

Characterizing outpatient antibiotic use and identifying inappropriate use requires data on the indication (or reason) for the prescription. These data are obtained by linking a drug dispensation to a health care contact and the diagnosis code assigned during that contact. The linkage can be done either starting with health care contacts and seeing how many contacts can be linked to an antibiotic dispensation or starting with dispensed antibiotics and seeing how many can be linked to a health care contact. These two approaches provide different information and will be explored in this chapter. The results of linkage of health care contacts to specific diagnoses are presented in Chapter 6.

Relationship between Ambulatory Care Physician Visits and Antibiotic Dispensations

While many different kinds of health care contacts can result in an antibiotic prescription, here we focus on outpatient care or ambulatory care visits. Outpatient care is care provided to community-dwelling Manitobans who visit a health care practitioner in an outpatient setting; it excludes Manitobans residing in personal care homes and who are hospitalized. Prescriptions filled at hospital discharge to be taken at home would typically also be captured under outpatient care; however, our focus in this report is on antibiotics dispensed in the community, so we have excluded this subset of prescriptions. Many studies have reported that the outpatient setting is where the vast majority (>90%) of antibiotic prescribing occurs [18].

Methods

All ambulatory care physician visits were identified for the Manitoba cohort described in Chapter 2 for 2011-2016. For these analyses, we included oral fidaxomicin and vancomycin to maximize the accuracy of the linkage, and combination drugs such as amoxicillin/clarithromycin are treated as one single dispensation. While ambulatory care visits usually include nurse practitioner visits as well as physician visits, we were unable to link nurse practitioner prescriptions to health care visits in the relevant datasets; thus, only ambulatory care physician visits could be examined. Emergency department visits were also included as ambulatory care visits.

Our analyses build on previously published data that used a five-day window for ambulatory care physician visits [49] (i.e., the dispensation of antibiotics occurred within five days of the linked physician visit). When

we explored using a longer linkage window, the proportion of linkages did not significantly increase, and so we chose to retain the five-day window to maintain consistency with published literature. Details of this sensitivity analysis can be found in the online supplement.

Ambulatory care physician visits can be to different types of physicians, such as family physicians, paediatricians or other specialists. In this report, ambulatory care visits to primary care providers (PCPs) include those to family physicians or paediatricians; all other physician types are categorized as 'other'.

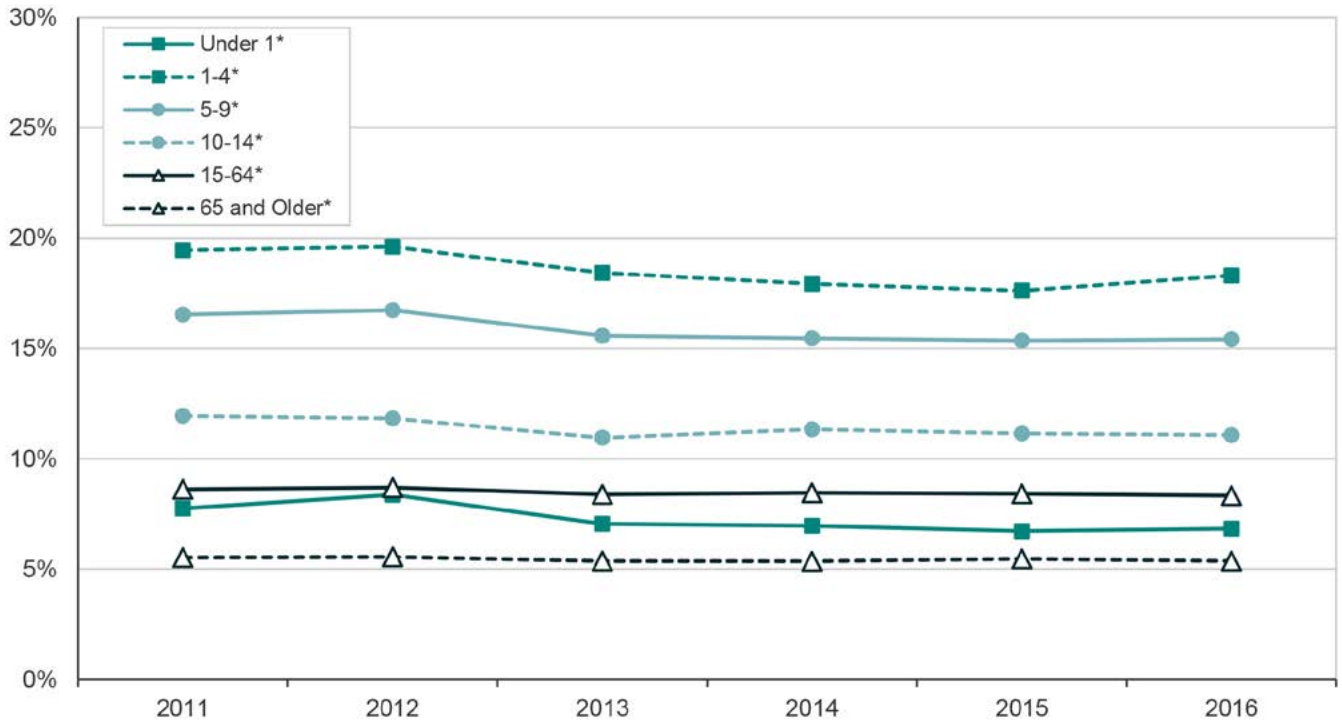
Results

In Manitoba, there were 36,634,945 qualifying ambulatory care physician visits in 2011-2016. Overall, 8.44% of those visits were linked to an antibiotic dispensation. When we looked at ambulatory PCP and other ambulatory care visits separately, we found that 10.95% of PCP visits were linked to antibiotic dispensations, while only 1.34% of other ambulatory care visits were linked to antibiotic dispensations. In 2016, the percentage of ambulatory care visits associated with an antibiotic dispensation was slightly but significantly lower than in 2011 (8.3% vs 8.7%). Numerical results for the graphs as well as further detail on associated billing codes can be found in Appendix 3.

Results by Age Group (Figure 5.1):

- Rates of antibiotic dispensation were lowest for seniors age 65+ and highest for children ages 1-4.
- In all age groups, dispensation rates were slightly but significantly lower in 2016 compared to 2011.

Figure 5.1: Percent of Ambulatory Physician Visits Resulting in Antibiotic Dispensations by Age Group
Crude percent of visits with a dispensation within five days

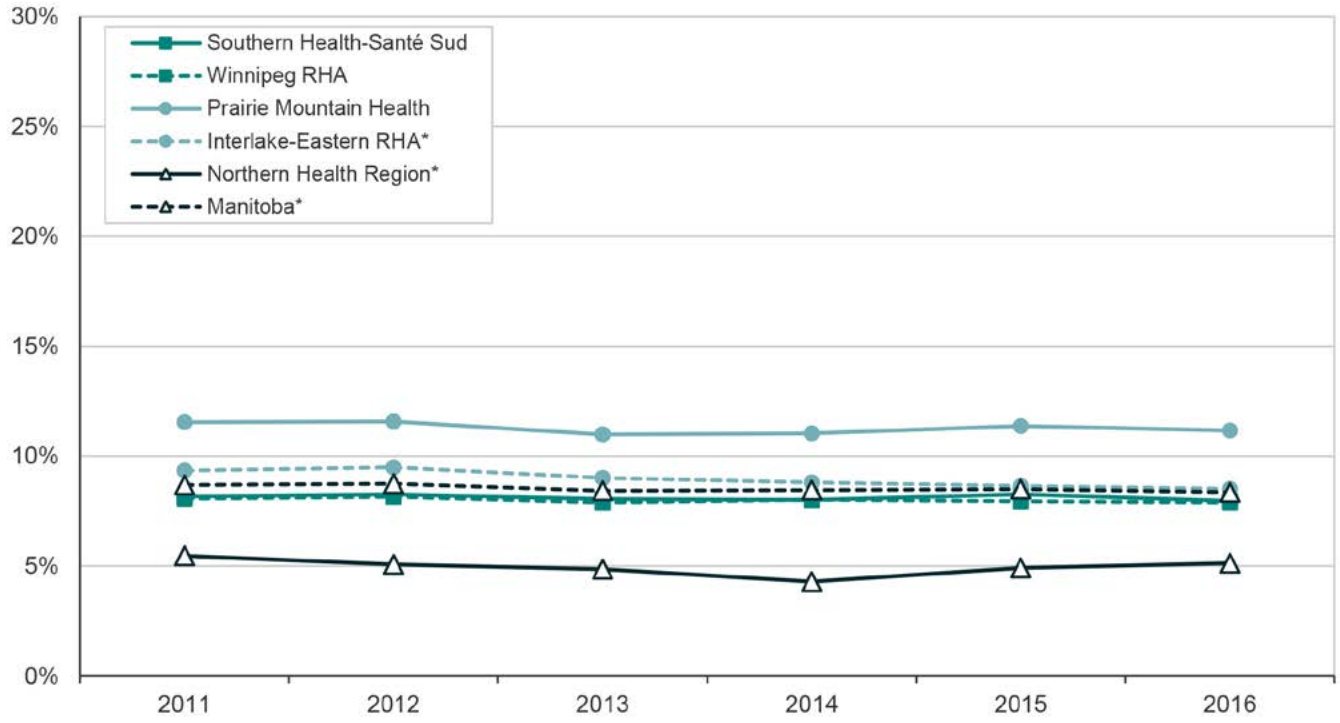


* Indicates statistically significant differences between rates in 2011 and 2016 (p<0.05).

Results by Health Region (Figure 5.2):

- Rates were highest in Prairie Mountain Health and lowest in Northern Health Region.
- Rates were significantly higher in Prairie Mountain Health than the Manitoba average in all years, and significantly higher in Interlake-Eastern RHA for 2011-2013.
- Rates in Southern Health-Santé Sud were lower than the Manitoba average (except 2015), and also lower in Winnipeg RHA and Northern Health Region.
- In 2016, rates were slightly but significantly lower in Interlake-Eastern RHA, Northern Health Region and Manitoba overall compared to 2011.
    - There was no significant change between regions.

Figure 5.2: Percent of Ambulatory Physician Visits Resulting in Antibiotic Dispensations by Health Region
Age- and sex-adjusted percent of visits with a dispensation within five days



* Indicates statistically significant differences between rates in 2011 and 2016 (p<0.05).

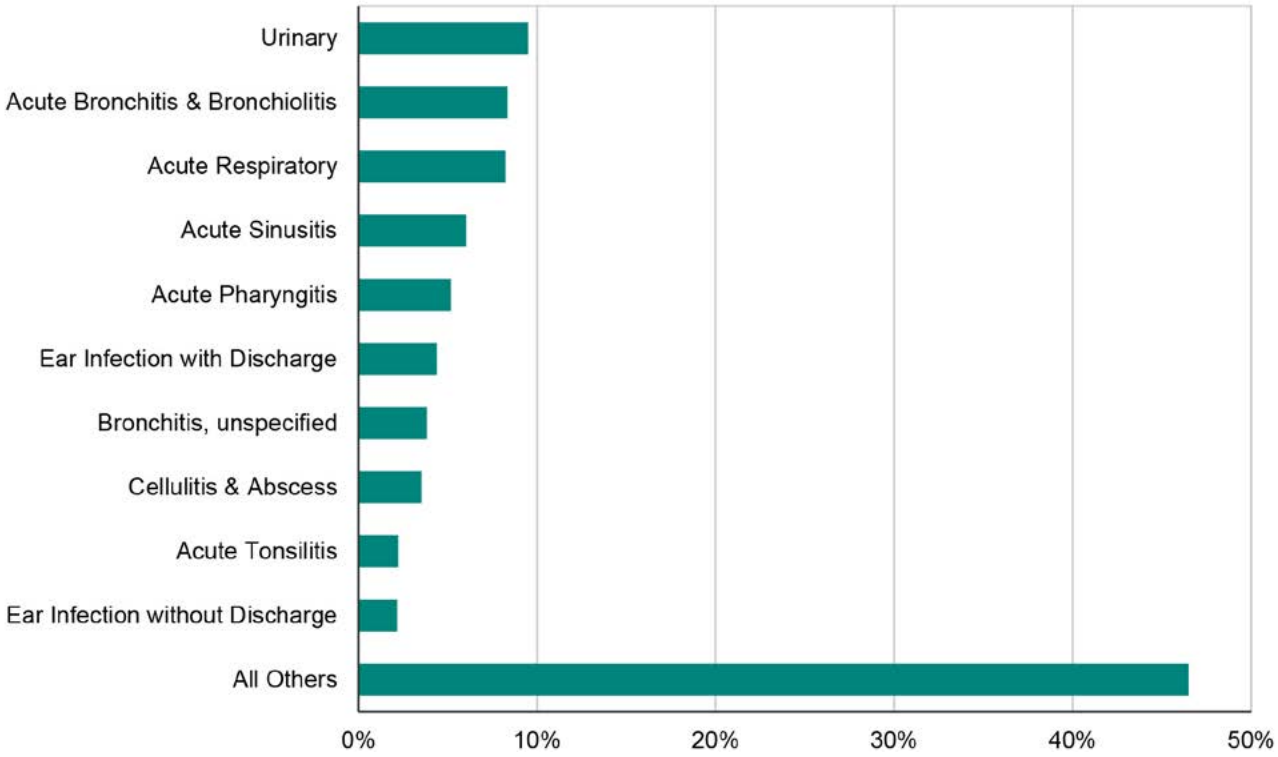
Most Common Diagnosis Codes for Ambulatory Care Physician Visits Associated with Antibiotic Dispensations

- Diagnosis codes below are taken directly from the ICD-9-CM (Figure 5.3).
- Overall:
  - Only two of the 10 most commonly diagnosed conditions, 'urinary' and 'cellulitis & abscess', generally require antibiotics.
  - Two other common conditions, 'acute sinusitis' and 'acute bronchitis & bronchiolitis', generally do not require antibiotics.
  - The remaining six most common diagnosis codes represent conditions that may require antibiotics, depending on other factors.
- Age Groups:
  - In general, the most common diagnosis codes resulting in antibiotic dispensation are similar amongst the individual age groups to those seen in the whole population, but with differing order.
  - In the paediatric age groups, respiratory codes, including ear infections, predominate.
  - In the adult age groups, 'urinary' is the most common code, with skin infections more common in this group than in the younger age groups.
  - 'Pneumonia' as a code is only seen in the 10 most common codes in the 65+ age group.
  - 'Hypertension' is also one of the 10 most common codes in the 65+ age group. This underlines one of the limitations of using diagnosis codes to ascertain the indication for antibiotics, as previously mentioned.

Conclusion

The number of ambulatory care physician visits associated with antibiotic dispensations is a crude measure of antibiotic use. It is affected by antibiotic prescribing patterns and the underlying reasons for physician visits for different age groups and populations. We see this most clearly in the breakdown by patient age, as children are more frequently seen for infectious symptoms. However, in the under one-year-old age group, where frequent health supervision visits occur, rates of antibiotic dispensations are lower. In adults, especially older adults, rates are lower again as more of their visits are for management of chronic health care issues such as diabetes and cardiovascular disease. The appearance of hypertension as a visit diagnosis associated with an antibiotic dispensation in adults 65 and older suggests visits for multiple issues, since antibiotics are not prescribed for hypertension. Some visits linked to infectious concerns may have been missed because only one diagnosis code can be assigned per visit. This may also be true for children under the age of one year.

Figure 5.3: Most Common Diagnosis Codes for Ambulatory Physician Visits Resulting in Antibiotic Dispensations, 2016
Crude percent of visits with a dispensation within five days



The appearance of two conditions which generally do not require antibiotics in the ten most common diagnosis codes associated with an antibiotic dispensation, acute sinusitis and acute bronchitis & bronchiolitis, supports the need for the additional modelling we performed to look at the appropriateness of antibiotic use and related factors (Chapter 6).

Characteristics of Physician-Prescribed Dispensations Not Linked to a Health Care Contact

Not all antibiotic dispensations can be linked to a health care contact. The reasons why this may be the case potentially include the way care was provided (e.g., by telephone consultation, which was not recorded in the data prior to the SARS-CoV-2 pandemic) or because the dispensation was a refill of a previous prescription and there was no health care contact associated with the refill. As well, if the visit resulting in the prescription was from a non-billing practitioner who did not shadow bill, the visit would not show up in our data.

We can compare the characteristics of antibiotic dispensations that could be linked to a health care contact (a physician visit or hospital discharge) to those that could not be linked. These analyses are important for understanding more fully how antibiotics are prescribed and to examine the limitations in interpreting the data on dispensations linked to a health care contact. In this analysis, we included all dispensations from community pharmacies as well as dispensations associated with a hospital discharge within the previous two days.

Methods

This analysis is limited to data from 2014-2016 and to physician-prescribed antibiotics only. The reason for this is that dispensations by non-physicians cannot be linked to health care contacts in the DPIN data since the physician's unique College of Physicians and Surgeons number is used for this linkage and only physicians are assigned such a number. This means that other providers, such as nurse practitioners, midwives, pharmacists and dentists, cannot be individually linked to prescriptions or dispensations. Prior to 2014, provider type was also not differentiated in the data, and so we could not distinguish between physicians and other health care providers. We did however include all types of physician visits and all types of physician (family physicians and specialists).

Antibiotics dispensed to individuals in the study cohort that could not be linked to either a hospital discharge within the preceding two days or to an ambulatory physician visit within the last five days were considered unlinked. The percentage of unlinked dispensations for each characteristic were compared using a Chi-square or t-test, as appropriate. Significance was set at $p<0.05$ with Bonferroni adjustment.

Results

A summary of the results is provided here, with additional output in the online supplement, including:

- Counts and crude percents of linked and unlinked dispensations by:
  - Characteristics of patients and physicians and dispensations for children.
  - Characteristics of patients and physicians and dispensations for adults.
  - Dispensations by drug class and health region of residence for Manitobans overall.
  - Characteristics of patients and physicians and dispensations of each drug class for Manitobans overall.

Antibiotics Overall

From 2014 to 2016, there were 2,240,581 antibiotic dispensations in the study cohort, of which 74.1% (n=1,660,355) could be linked to either a physician visit or hospital discharge. Unlinked dispensations differed from linked dispensations across all characteristics.

Unlinked dispensations were more likely to be adult than paediatric, and patterns differed across health regions, with Northern Health Region almost twice as high as the other health regions and Prairie Mountain Health the lowest (Table 5.1). There was a statistical but not clinically significant difference (less than 1%) between 2014 and 2016. The proportions of linked and unlinked dispensations also differed by drug class, with tetracyclines the highest and macrolides, lincosamides and streptogramins the lowest (but less than 1% lower than the β-lactam penicillins).

Table 5.1: Characteristics of Antibiotic Dispensations by Linkage to Health Care Contact, 2014-2016
Counts and percent of dispensations

Characteristics	Antibiotic Dispensations by Linkage to Ambulatory Physician Visits			
	Linked		Unlinked	
	Count	Percent	Count	Percent
Age Group (Years)*				
Children (0-14)	322,047	80.99	75,572	19.01
Adults (15 and Older)	1,338,308	72.62	504,654	27.38
Patient Residence*				
Southern Health-Santé Sud	201,708	73.48	72,818	26.53
Winnipeg RHA	948,266	75.81	302,498	24.19
Prairie Mountain Health	309,731	79.96	77,612	20.04
Interlake-Eastern RHA	154,984	70.42	65,103	29.58
Northern Health Region	45,666	42.34	62,195	57.66
Dispensation Year*				
2014	546,341	74.24	189,575	25.76
2015	554,201	74.13	193,381	25.87
2016	559,813	73.94	197,270	26.06
Drug Class*				
Tetracyclines (J01A)	61,463	43.10	81,150	56.90
Beta-Lactam Penicillins (J01C)	571,945	82.50	121,311	17.50
Cephalosporins (J01D)	216,286	73.44	78,212	26.56
Sulfonamides and Trimethoprims (J01E)	87,474	57.98	63,388	42.02
Macrolides, Lincosamides and Streptogramins (J01F)	412,086	82.96	84,668	17.04
Quinolones (J01M)	202,563	69.32	89,668	30.68
Other Antibiotics (J01X) and Unclassified**	108,538	64.26	61,829	35.74
Overall	**1,660,355**	**100.00**	**580,226**	**100.00**

* Indicates a statistically significant difference in the distribution of linked and unlinked antibiotic dispensations among category groups ($p<0.05$).
** Includes the drugs amoxicillin/clarithromycin, fidaxomicin, and vancomycin.

Adults

For adults, the number and proportion of unlinked dispensations differed across all patient and physician characteristics. Unlinked dispensations were more likely among patients age 65 and older, male patients, patients from the Northern Health Region, those with a higher Charlson Comorbidity Score, and those with a higher SEFI-2 score. (SEFI-2 is an area-level measure of socioeconomic status that uses census data on income, education, single parent households and unemployment; a higher score indicates lower socioeconomic status). Unlinked dispensations were also associated with female physicians, younger physicians, lower physician visit rates per day, physician practice location in Northern Health Region, the physician having a salary or mixed remuneration model, the physician providing some hospital-based care, having completed medical training in Canada or the United States, the visit not being a majority of care physician visit, occurring in a more recent year of dispensation, and drug class (tetracyclines being the most likely to be unlinked). For unlinked dispensations, we could not assign patients to a most responsible PCP, and thus the majority of care provider metric was used: among patients who had at least 3 visits to a physician, if they had at least 50% of these visits to the same provider, that was their majority of care provider.

Children

For children, unlinked dispensations differed across all patient and physician characteristics. Unlinked dispensations were more likely in the youngest age group (under one year), female patients, patients from the Northern Health Region, those living in a household with a higher number of children, children who had been in care of Child and Family Services, children with a higher Charlson Comorbidity Score and those with a higher SEFI-2 score (indicating lower socioeconomic status). Unlinked dispensations were also associated with female physicians, younger physicians, lower physician visit rates per day, physician practice location in Northern Health Region, the physician having a salary or mixed remuneration model, the physician providing some hospital-based care, having completed medical training in Canada or the United States, the visit not being to the majority of care physician, prescribed by a paediatrician, having been dispensed in 2015, and drug class (tetracyclines and unclassified being the most likely to be unlinked).

Antibiotic Class

When linkage rates were compared between health regions and stratified by drug class, a similar pattern was seen across all drug classes. Northern Health Region had the highest rates of unlinked dispensations across all drug classes. The remaining health regions were statistically different from the Manitoba rate, but most differences were less than 10%. It is not expected that all dispensations would be linkable to a visit, as some conditions such as recurrent UTIs, acne, or prophylactic antibiotics would not necessarily require a physician visit.

Conclusion

A significant proportion of antibiotic dispensations cannot be linked to a health care contact, and thus the appropriateness of the antibiotic prescribing cannot be ascertained from this information. We did however note that unlinked antibiotic dispensations differ from linked dispensations by patient and physician characteristics, and thus the results of our analyses may not be broadly generalizable. The results in this section demonstrate the need for further analyses to ascertain appropriateness of antibiotic use; these analyses will use data on antibiotic dispensations linked to physician visits and will take into account several additional factors.

Characteristics of Dispensations of Antibiotics Prescribed by Other Health Care Professionals

While physicians account for most antibiotic prescriptions to Manitobans, other professionals can also prescribe antibiotics and these dispensations (identified by type of prescriber but not individual prescriber) are captured in the DPIN data from 2014 onwards.

Methods

Dispensations of drugs prescribed by non-physicians and dispensed to the study cohort from 2014 to 2016 were included in this analysis. We examined all antibiotics listed in Chapter 3. Results are presented for information only; no statistical analysis was undertaken.

Results

Dentists accounted for almost 10% of dispensations, nurse practitioners accounted for approximately 3.5%, and other practitioners made up the remaining small proportions (Table 5.2).

Table 5.2: Antibiotic Dispensations by Type of Prescribing Healthcare Professional, 2014-2016

Healthcare Professionals	Antibiotic Dispensations	
	Count	Percent
Physicians	2,240,581	87.04
Dentists	239,802	9.32
Nurse Practitioners	88,942	3.46
Pharmacists	3,950	0.15
Optometrists	733	0.03
Midwives	202	0.01
Other	56	<0.01

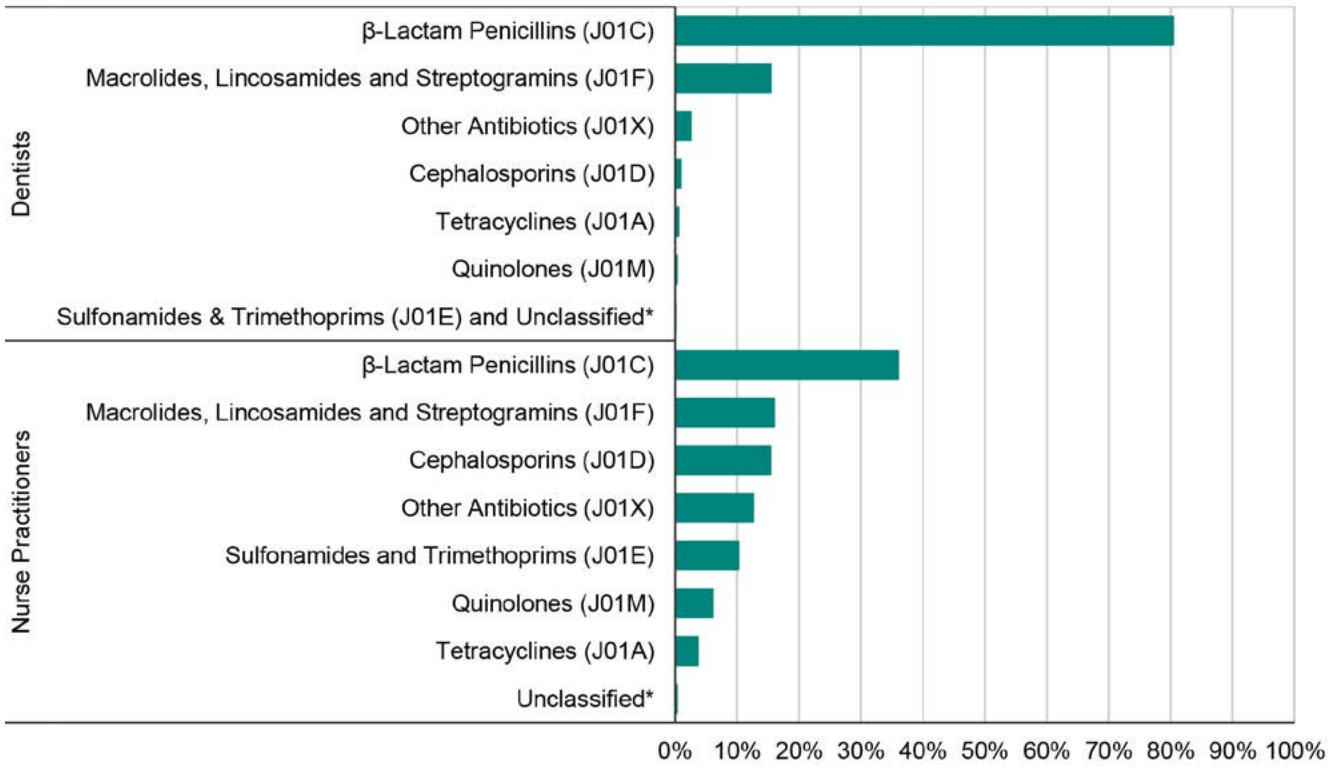
Prescribed by Dentists

An examination of the drug classes prescribed by dentists revealed that over 80% were β-lactam penicillins (as expected for management of oral bacteria), with macrolides the second most common (most likely representing substitution for penicillin allergy) (Figure 5.4).

Prescribed by Nurse Practitioners

Nurse practitioner antibiotic class prescriptions occurred in the same general pattern as the distribution of antibiotic classes for all Manitoba. β-lactam and cephalosporin antibiotics accounted for over half of dispensations from nurse practitioner prescribing (Figure 5.4).

Figure 5.4: Percent of Dispensations for Antibiotics Prescribed by Dentists and Nurse Practitioners by Drug Class, 2014-2016



Conclusion

Non-physician prescribers contribute almost 15% of antibiotic dispensations. Patterns of antibiotic classes prescribed reflect the common conditions seen by these practitioners. Antimicrobial stewardship needs to include non-physicians in its messaging and programming.

Chapter 6:
Relationship between Diagnosis Codes Provided by Ambulatory Primary Care Physicians and Antibiotic Dispensations: Ascertaining Appropriateness of Antibiotic Use

Introduction

A basic premise of antimicrobial stewardship is supporting prudent use of antibiotics, thereby limiting unnecessary antibiotic use while ensuring that antibiotics are prescribed when needed. The decision to prescribe antibiotics depends on the condition or illness being treated, but also on other factors such as the patient's underlying condition(s), availability of follow-up care, and local patterns of antibiotic resistance. These other factors also influence decisions around whether to prescribe antibiotics and the choice of drug. Due to the interplay of these complexities and the information available in administrative data, we would not expect a perfect match between diagnoses by physicians in the billing record and 'appropriateness' of antibiotic use. Physicians choose the most applicable diagnosis code for each patient visit; however, a single code does not capture all aspects of the health care visit, especially if multiple issues are dealt with in one visit. Even for illnesses that are always viral in nature, such as the common cold, where the number of dispensations linkable to this diagnosis should be very low and should not vary widely between PCPs, it will never be zero.

Taking these factors into account, we have chosen some benchmark conditions and divided them into three categories:

1. **Conditions that generally do not require antibiotics,** including both non-infectious (such as asthma/allergic rhinitis) and infectious illnesses usually caused by viruses (such as acute bronchitis, cough and upper respiratory tract infection (URTI) or the 'common cold').
2. **Conditions which may require antibiotics,** such as those where the clinical presentation, patient factors such as age and underlying conditions, or identification of a bacterial source might indicate antibiotics. Conditions in this group include acute otitis media (ear infection), pharyngitis (sore throat, including 'strep throat'), sinusitis, tracheitis/laryngitis, and pneumonia.
3. **Conditions that usually require antibiotics.** To consider appropriateness of antibiotic choice, we examined two conditions which almost always require antibiotics, SSTIs UTIs.

Presentation of Findings

In this chapter, we present key findings for each of the benchmark conditions by calculating the percent of visits resulting in an antibiotic dispensation by age group (2011 vs 2016) and showing the distribution of dispensed drug classes in 2016. We also present the distribution of visits resulting in a dispensation at the prescriber level (as well as median and the interquartile range). This tells us how many prescribers are frequent or infrequent prescribers for that condition. For some conditions, we present additional analyses looking at appropriateness of antibiotic choice.

For the first two categories, conditions which generally do not require antibiotics and conditions that may require antibiotics, we then present adjusted odds ratios (aOR) from a multi-level model of characteristics associated with less appropriate prescribing practices. This analysis includes all of the factors that are known to or could possibly influence whether an antibiotic would or should be prescribed for that category of conditions. The model accounts for these factors at the same time and then outputs how that factor influences receipt of antibiotics as aOR. A higher aOR means that the characteristic is more likely to be associated with receipt of antibiotics, and a lower aOR means that the characteristic is less likely to be associated with an antibiotic dispensation. For some conditions, we present additional analyses looking at appropriateness of antibiotic choice. The online supplement includes models for each individual condition within the category.

Appendix 4 provides additional findings:

- Age- and sex-adjusted percent of linked ambulatory primary care physician visits by health region, condition and drug appropriateness.

The online supplement for this section provides counts and crude rates for the following analyses:

- Count and crude percent of linked ambulatory primary care physician visits by age group, condition and drug appropriateness.
- Count and crude percent of linked ambulatory primary care physician visits by health region, condition and drug appropriateness.
- Count and crude percent of linked dispensations by drug class, condition and drug appropriateness.
- Count and crude percent of linked dispensations by drug class, age group, condition and drug appropriateness.
- Age- and sex-adjusted odds ratios and p-values for predictors of antibiotic dispensations among children and adults by condition.
- Age- and sex-adjusted odds ratios and p-values for predictors of inappropriate antibiotic dispensations among children and adults by condition.

Methods

The analyses were conducted using data from calendar years 2011 and 2016 for the entire eligible Manitoba population (as described in Chapter 2) except for the multi-level models. Multiple visits by the same patient to the same physician on the same day were excluded (1.3% of total visits), visits associated with a dispensation that also linked to a hospitalization (0.15% of total visits) were excluded, as were visits that linked to multiple dispensations (0.22%). Of the total visit count, 1,164,306 visits had a diagnostic code of interest. These were then limited to ambulatory primary care physician visits only. Dispensations of oral vancomycin and fidaxomicin were included. Combination drugs were treated as one prescription.

Descriptive information is presented for dispensed drug classes. The difference between 2011 and 2016 was tested by calculating the rate ratio and 95% confidence intervals for the two years' rates and seeing if this ratio was statistically different from 1.0 using a Z-test. For analyses looking at appropriateness of antibiotic choice, the proportion of each category was compared to the proportion of appropriate use using the binomial exact test – 2 sided. We considered proportions significantly different if the p-value <0.05.

Multi-Level Modelling

The probability of an antibiotic dispensation resulting from an ambulatory primary care physician visit for a condition that does generally require antibiotics or may occasionally require antibiotics was estimated in a multivariable multi-level logistic regression model for visits from 2014-2016. Patient and provider characteristics included in the multi-level model were chosen based on published literature on factors associated with antibiotic use and from characteristics available in the Repository that might be associated with patterns of antibiotic use [50]. The characteristics varied slightly between the adult model and children's model. Patient characteristics included age group, patient sex, SEFI-2 (a measure of socioeconomic status), Charlson Comorbidity score, number of children in the household (for children's model only), whether the practitioner was the patient's majority of care provider, and whether the child had been in care of Child and Family Services (for children's model only). Physician characteristics included physician age, physician practice location, fee-for-service remuneration model compared to salary/mixed, whether the physician provided some hospital-based care, whether they had received medical training in Canada/United States compared to elsewhere, and average number of visits per day to the physician (as a measure of patient load). A patient was deemed to have seen their majority of care provider when that patient had more than 50% of their primary care visits to that provider. Patients with too few visits (less than three in three years) to assign a majority of care provider formed an additional group. Both models also looked at the effect of seasonality comparing antibiotic use in summer (April-October) to winter (November-March) months. The children's model also examined whether visits to a paediatrician differed from those to a family physician. For these models, we considered a p value of <0.01 as significant due to the multiple variables under investigation. See the Technical Appendix in the online supplement for further details on how these variables were constructed.

Conditions That Generally Do Not Require Antibiotics

This section discusses four conditions that generally do not require antibiotics. A description of each condition is provided before the results. A brief summary of the results then is presented (more details are available in the Technical Appendix in the online supplement).

Acute Bronchitis

Acute bronchitis is a non-specific condition that results in a productive cough and is sometimes associated with some shortness of breath. It is often termed a 'chest cold.' It is generally self-limiting and treated symptomatically, resolving without specific treatment 85% of the time. Treatment with antibiotics is not generally recommended unless underlying chronic lung disease, such as Chronic Obstructive Pulmonary Disease (COPD), often called emphysema, is present [6,7]. Numerous well-designed clinical studies have shown that for otherwise healthy patients, antibiotics for acute bronchitis are not needed, but the prescribing rate has remained very high for many years despite this professional guidance [8].

Only 2.44% of people with acute bronchitis who were dispensed antibiotics also had a diagnosis for COPD over the preceding two years. Among the four conditions we examined that generally do not require antibiotics, acute bronchitis had the highest rate of dispensations at 73.0% (95% CI 71.6-74.4%).

Figure 6.1 shows antibiotic dispensations to people with acute bronchitis as percentage of visits by age group:

Rates of dispensations increased by age group until ages 5-9.

Rates were similar for ages 5-9, 10-14 and 14-65.

- Rates were a bit lower for the 65+ age group compared to lower age groups (except under 1).
- When 2016 was compared to 2011, rates in 2016 were higher for:
  - The under one-year-old group, 1-4 year olds, and 15-64 year olds.
  - No other changes over time were seen.

Looking at the dispensed class of antibiotic revealed that:

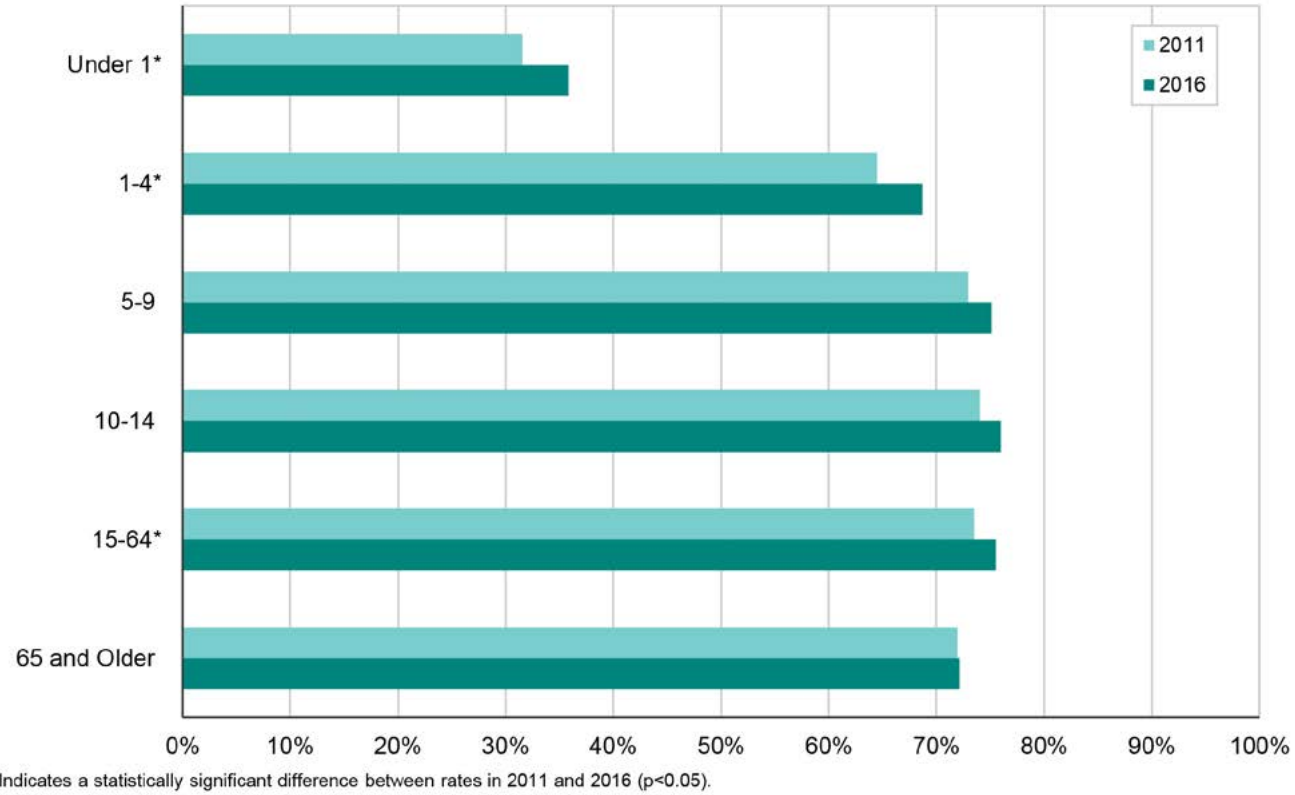
- Macrolides[4] were most commonly dispensed, followed by β-lactam penicillins.
  - Other classes made up only a small percentage.
- Different age groups had a different ratio of β-lactam penicillins to macrolides. Younger age groups had more β-lactam penicillins than macrolides, and this trend reversed in older age groups.
- A small proportion of quinolone dispensations were seen in the 15-64 and 65+ age groups.

The distribution of visits resulting in an antibiotic dispensation by practitioner demonstrated that:

- The median percentage of dispensations for all practitioners was 66.7% with an interquartile range (IQR) of 42.6-80.5%. Among the four conditions we examined that generally do not require antibiotics, this was the largest range.

Figure 6.1: Antibiotic Dispensations Linked to Primary Care Ambulatory Physician Visits for Acute Bronchitis, by Age Group (Years)

Crude percent of visits with a dispensation within five days



* Indicates a statistically significant difference between rates in 2011 and 2016 ($p<0.05$).

4 Macrolides, lincosamides and streptogramin class of antibiotics

Asthma or Allergic Rhinitis

Asthma exacerbations (i.e., a worsening of asthma symptoms) and allergic rhinitis (runny nose from allergies) are non-infectious in origin and should not be treated with antibiotics [9].

The overall rate of antibiotic dispensations following visits for this condition was 9.7% (95% CI 9.2-10.2%) in 2016.

Figure 6.2 shows antibiotic dispensations as percentage of visits by age group:

- Rates were relatively similar across age groups, but slightly higher under age 5.
- When 2016 was compared to 2011, dispensation rates significantly decreased in all age groups except ages 5-9, where it did not change.

Looking at class of antibiotics, we see similar patterns to those for acute bronchitis:

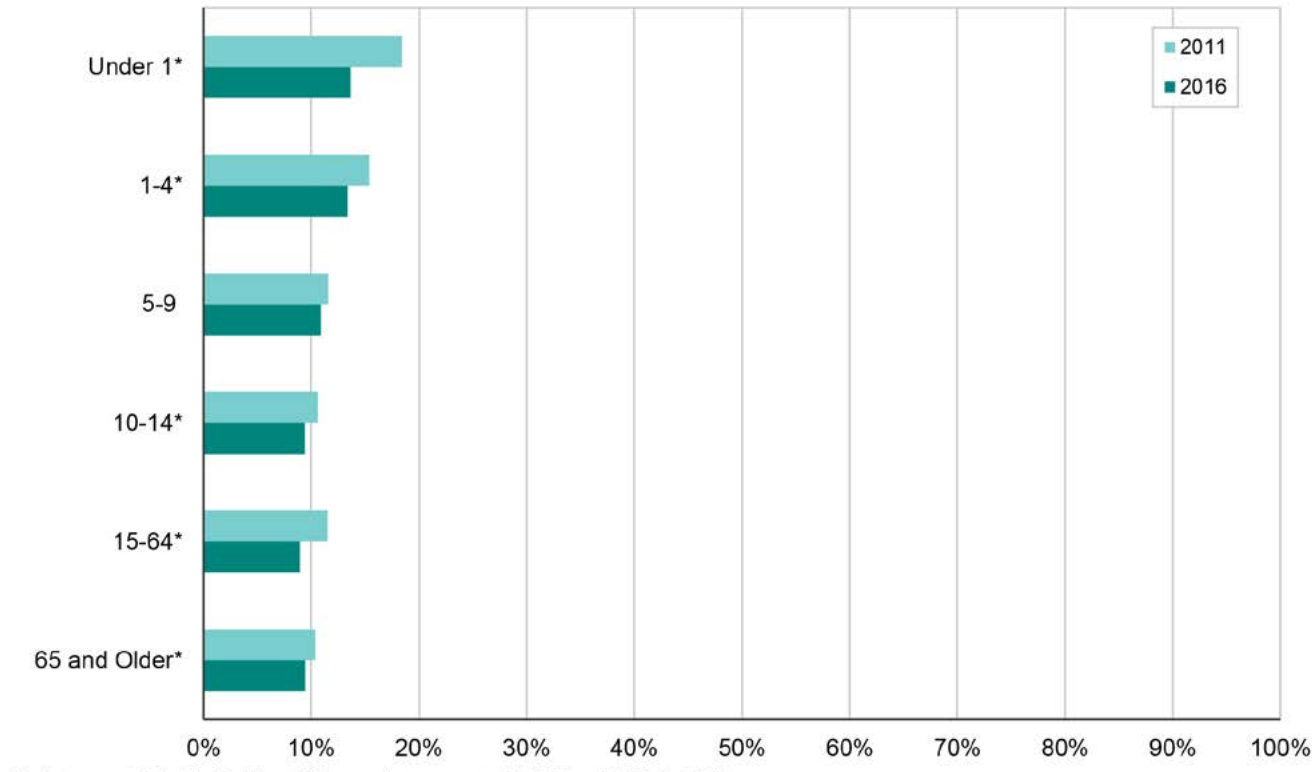
- Overall, macrolides[5] were most commonly dispensed, followed by β-lactam penicillins.
    - Other classes made up only a small percentage.
- Different age groups had a different ratio of β-lactam penicillins to macrolide. Younger age groups had more β-lactam penicillins dispensed than macrolides, and this trend reversed in older age groups.
- A small proportion of quinolone dispensations were seen in the 15-64 and 65+ age groups.

The distribution of visits resulting in an antibiotic dispensation by practitioner revealed that:

- The median percentage of dispensations for all practitioners was 5.7% with an IQR of 2.2-11.1%. [illegible]atively narrow distribution, and some practitioners wrote zero prescriptions for this condition.

Figure 6.2: Antibiotic Dispensations Linked to Primary Care Ambulatory Physician Visits for Asthma/Allergic Rhinitis, by Age Group (Years)

Crude percent of visits with a dispensation within five days



* Indicates a statistically significant difference between rates in 2011 and 2016 (p<0.05).

5 Macrolides, lincosamides and streptogramin class of antibiotics

Cough

Cough is a non-specific diagnosis, a symptom of an underlying condition that may or may not require antibiotics and may or may not be infectious in origin. When it is a manifestation of an underlying condition requiring antibiotics, it should be captured as such with a specific diagnosis provided, rather than referring to the symptom of cough.

The overall percentage of visits for this condition that resulted in an antibiotic dispensation was 12.2% (95% CI 11.7-12.8%) in 2016.

Figure 6.3 shows antibiotic dispensations as percentage of visits by age group:

- The highest dispensation rates were in the 1-4 year old age group, and rates decreased as age groups increased.
- Rates were lower in 2016 for ages 1-4 years compared to 2011.
- Rates were higher in 2016 for ages 15 years and older compared to 2011.

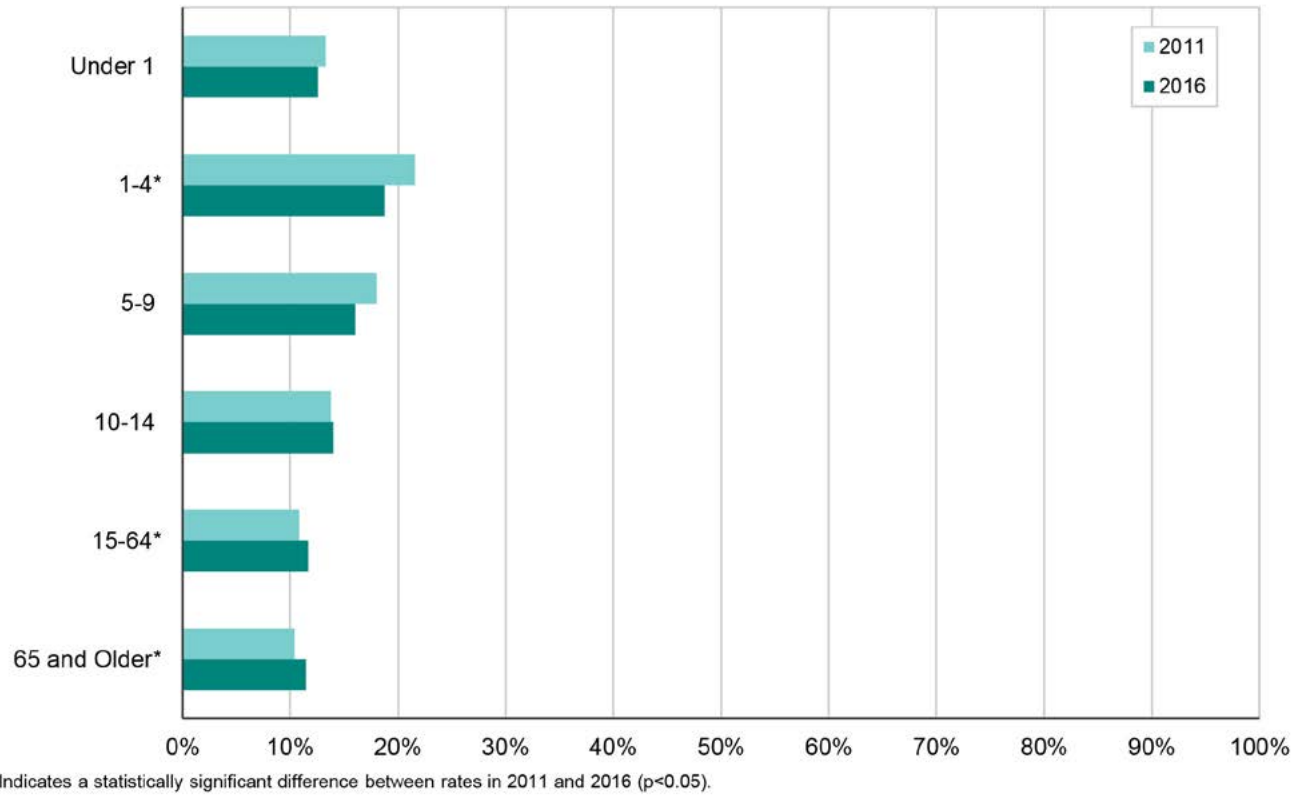
Looking at the class of antibiotics dispensed, we observed similar patterns to those for acute bronchitis and asthma/allergic rhinitis:

- Overall, macrolides[6] were the most common antibiotic dispensed, followed by β-lactam penicillins.
    - Other classes made up only a small percentage.
- Different age groups had different ratios of β-lactam penicillins to macrolides. Younger age groups had more β-lactam penicillins than macrolides, and this trend reversed in older age groups.
- A small proportion of quinolone dispensations were seen in the 15-64 and 65+ age groups.

The distribution of visits resulting in an antibiotic dispensation by practitioner revealed:

- The median percentage of dispensations for all practitioners was 5.9% with an IQR of 2.7-11.5%. This is a relatively narrow distribution, similar to that for asthma/allergic rhinitis. Some practitioners wrote zero prescriptions for this condition.

Figure 6.3: Antibiotic Dispensations Linked to Primary Care Ambulatory Physician Visits for Cough, by Age Group (Years)
Crude percent of visits with a dispensation within five days



* Indicates a statistically significant difference between rates in 2011 and 2016 (p<0.05).

6 Macrolides, lincosamides and streptogramin class of antibiotics

Upper Respiratory Tract Infection (URTI)

URTIs, most commonly termed the 'common cold', are caused by a variety of different respiratory viruses and do not need antibiotics.

The overall percentage of visits for this condition that resulted in an antibiotic dispensation was 15.2% in 2016.

Figure 6.4 shows dispensations as percentage of visits by age group:

- Rates of antibiotic dispensation were low in children under 1 year, and somewhat higher but similar in the rest of the paediatric age groups.
- Rates increased as age increased.
- Compared to 2011, rates in 2016 were lower in all age groups except age 65+, where they were higher, and in the age 5-9 group, where there was no change.

Looking at class of antibiotics dispensed, we observed that:

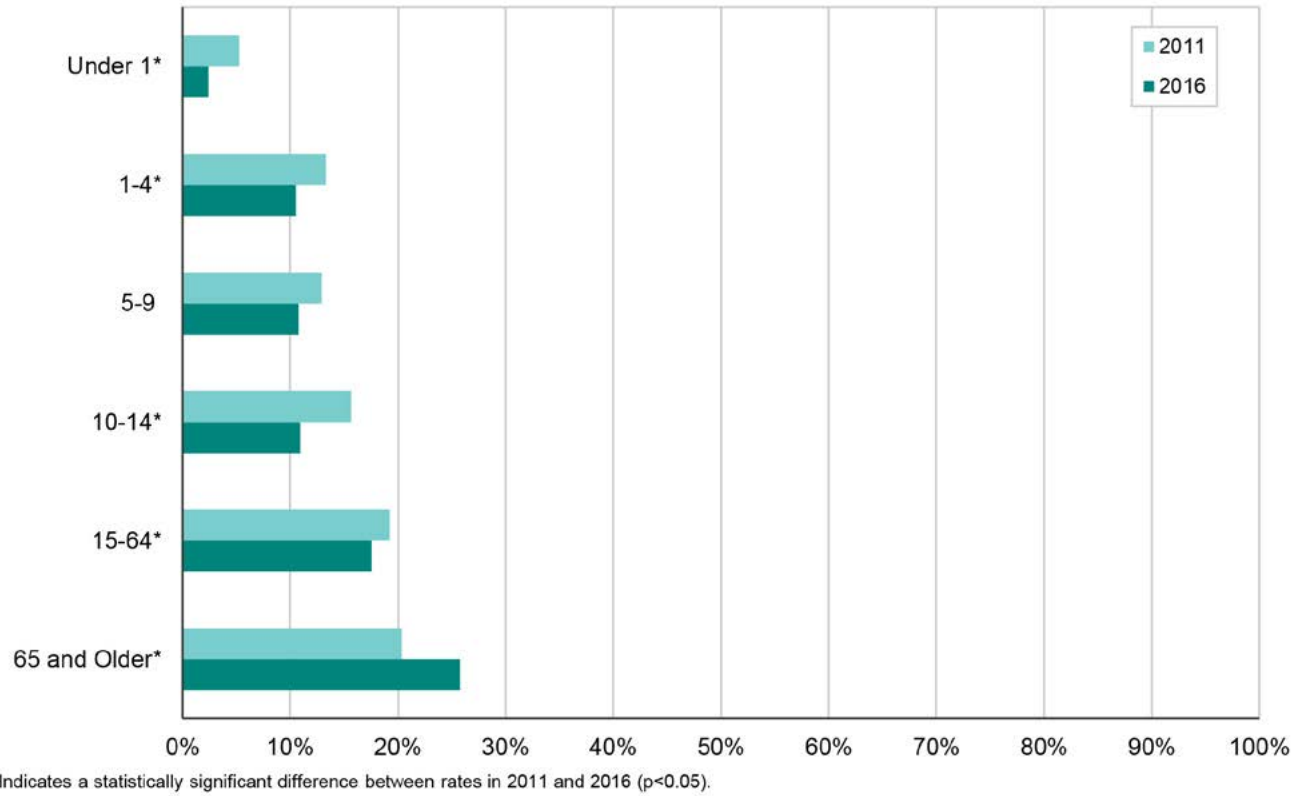
- The pattern differed from the three previous conditions, as β-lactam penicillins were the most commonly dispensed antibiotic, followed by macrolides[7].
    - Other classes made up only a small percentage.
- The ratio of β-lactam penicillins to macrolides was relatively similar across age groups.
- A small proportion of quinolone dispensations were seen in the 15-64 and 65+ age groups.

The distribution of visits resulting in an antibiotic dispensation by practitioner revealed that:

- The median percentage of dispensations for all practitioners was 8.5% with an IQR of 1.5-22.9%. Among conditions that generally do not require antibiotics, this was the second largest range.
- The upper half of practitioners in this range were widely spaced; the 90th percentile was at 44%.

Figure 6.4: Antibiotic Dispensations Linked to Primary Care Ambulatory Physician Visits for Upper Respiratory Tract Infection, by Age Group (Years)

Crude percent of visits with a dispensation within five days



* Indicates a statistically significant difference between rates in 2011 and 2016 (p<0.05).

7 Macrolides, lincosamides and streptogramin class of antibiotics

Multi-Level Modelling for Conditions That Generally Do Not Require Antibiotics

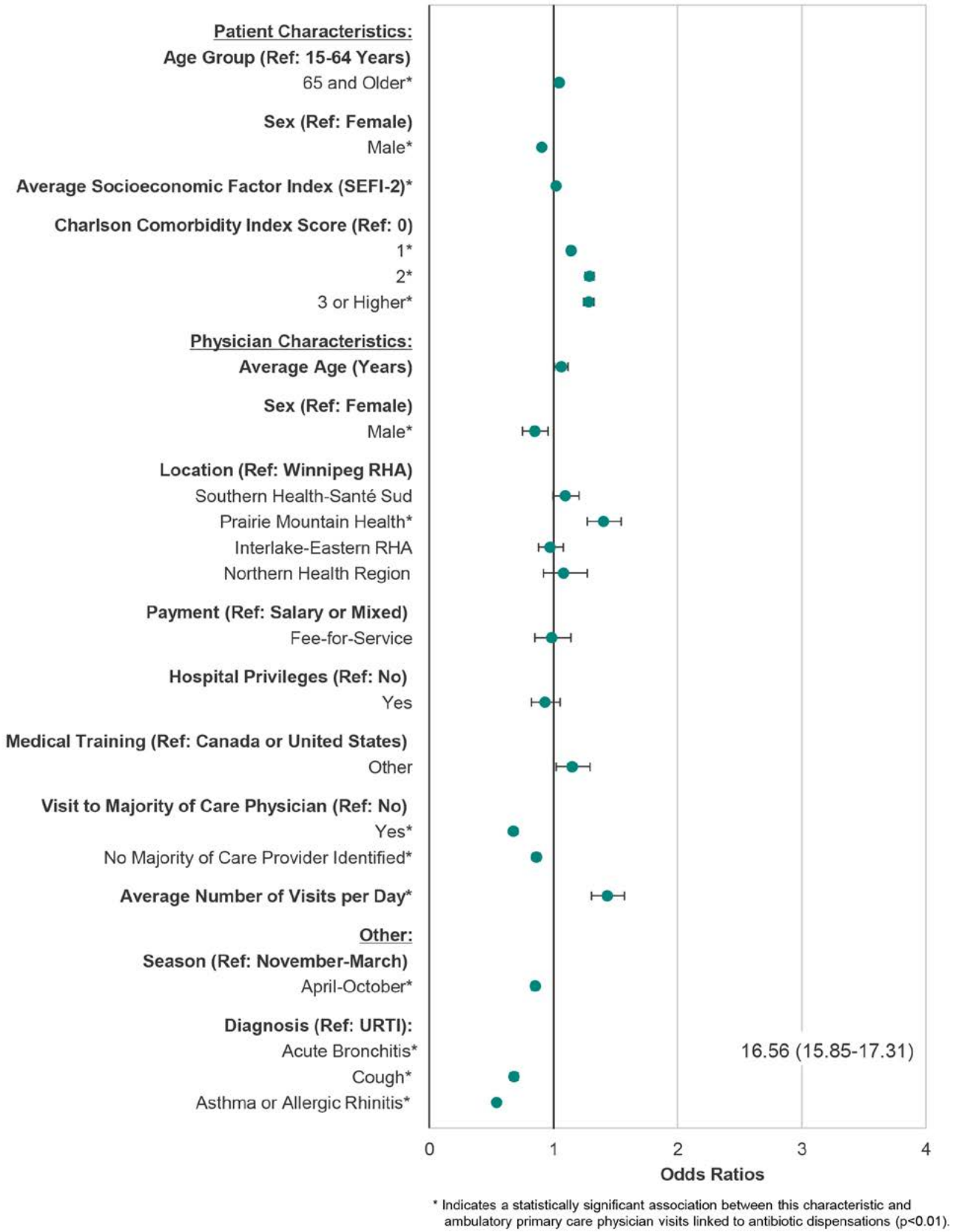
A model was developed to identify which patient and physician characteristics were significantly associated with dispensation of antibiotics for the four conditions in this category. The model generates aOR, which tell us how likely a characteristic was to be associated with a dispensation after adjusting for each factor in the model.

For adults, the following characteristics were significantly associated with an antibiotic dispensation following a visit for a condition that generally does not require antibiotics (see Figure 6.5):

- Higher odds of antibiotic dispensation:
    - Physician location in Prairie Mountain Health compared to Winnipeg RHA (aOR 1.40, 95% CI 1.27-1.54).
    - Higher number of visits per day, a measure of patient load (aOR 1.43, 95% CI 1.31-1.57).
    - Patient age 65+ compared to 15-64 years (aOR 1.05, 95% CI 1.02-1.07).
    - Charlson Index of 1 (aOR 1.14, 95% CI 1.12-1.16), 2 (aOR 1.29, 95% CI 1.25-1.32) or 3+ (aOR 1.28, 95% CI 1.24-1.33) compared to 0.
    - Higher SEFI-2 score, indicating lower socioeconomic status (aOR 1.02, 95% CI 1.01-1.03)
    - Acute bronchitis compared to URTI (aOR 16.56, 95% CI 15.85-17.31).
- Lower odds of antibiotic dispensation:
    - Male compared to female physician sex (aOR 0.85, 95% CI 0.75-0.96).
    - Male compared to female patient sex (aOR 0.91, 95% CI 0.89-0.92).
    - Drug prescribed by the patient's majority of care provider (aOR 0.68, 95% CI 0.66-0.69).
    - Too few visits to assign a patient to a majority of care provider (aOR 0.86, 95% CI 0.83-0.89).
    - Summer compared to winter months (aOR 0.85, 95% CI 0.84-0.87).
    - Cough (aOR 0.68, 95% CI 0.65-0.71) or asthma/allergic rhinitis (aOR 0.54, 95% CI 0.52-0.57) compared to URTI.

Figure 6.5: Association Between Patient and Physician Characteristics and Dispensations of Antibiotics for Conditions that Generally Do Not Require Antibiotics in Adults

Age- and sex-adjusted odds ratios (average and 95% confidence intervals), patient ages 15 and older



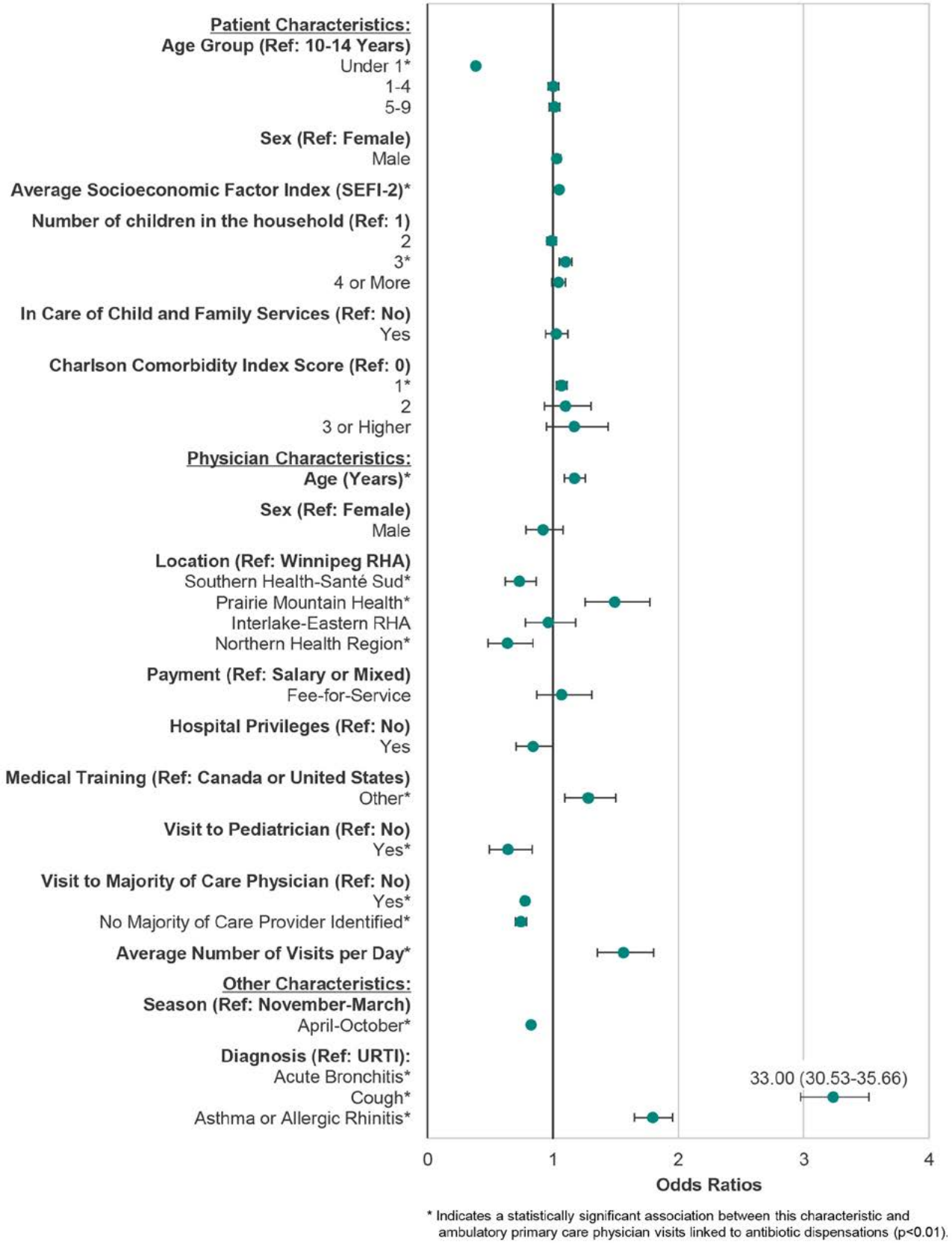
* Indicates a statistically significant association between this characteristic and ambulatory primary care physician visits linked to antibiotic dispensations ($p<0.01$).

For children, the following characteristics were significantly associated with an antibiotic dispensation following a visit for a condition that generally does not require antibiotics (see Figure 6.6):

- Higher odds of antibiotic dispensation:
  - Older physician age (aOR 1.17, 95% CI 1.09-1.26).
  - Physician location in Prairie Mountain Health compared to Winnipeg RHA (aOR 1.49, 95% CI 1.26-1.78).
  - Physician training outside of Canada/United States (aOR 1.28, 95% CI 1.09-1.50).
  - Higher number of visits per day, a measure of patient load (aOR 1.56, 95% 1.35-1.80).
  - Charlson Index of 1 compared to 0 (aOR 1.07, 95% CI 1.03-1.11).
  - 3 children in the home compared to 1 (aOR 1.10, 95% CI 1.05-1.15).
  - Higher SEFI-2 score, indicating lower socioeconomic status (aOR 1.05, 95% CI 1.03-1.07).
  - Acute bronchitis (aOR 33.00, 95% CI 30.53-35.67), cough (aOR 3.24, 95% CI 2.98-3.52), or asthma/allergic rhinitis (aOR 1.80, 95% CI 1.65-1.95) compared to URTI.
- Lower odds of antibiotic dispensation:
  - Physician located in Northern Health Region (aOR 0.64, 95% CI 0.48-0.84) or Southern Health-Santé Sud (aOR 0.73, 95% CI 0.62-0.87) compared to Winnipeg RHA.
  - Paediatrician compared to family physician (aOR 0.64, 95% CI 0.49-0.83).
  - Patient age 0-1 years compared to 10-14 years (aOR 0.38, 95% CI 0.36-0.41).
  - Prescribed by the patient's majority of care provider (aOR 0.78, 95% CI 0.75-0.81).
  - Too few visits to assign a patient a majority of care provider (aOR 0.74, 95% CI 0.70-0.79).
  - Summer compared to winter months (aOR 0.83, 95% CI 0.80-0.85).

Figure 6.6: Association Between Patient and Physician Characteristics and Dispensations of Antibiotics for Conditions that Generally Do Not Require Antibiotics in Children

Age- and sex-adjusted odds ratios (average and 95% confidence intervals), patient ages 0-14



* Indicates a statistically significant association between this characteristic and ambulatory primary care physician visits linked to antibiotic dispensations ($p<0.01$).

Models were also run by individual conditions (results available in the online supplement). Patterns of association were similar to the overall model. For URTI, the confidence intervals were wider than in other models, suggesting more variability (these individual level results are in the online supplement). Acute bronchitis was notably different in that a higher Charlson Index was not associated with any change in antibiotic dispensation.

Summary

For respiratory conditions that generally do not require antibiotics [6–11], we found wide variability in dispensation of antibiotics between the different conditions. Dispensation of antibiotics was highest for acute bronchitis in all age groups: over 60% of visits in all age groups (except for children under one year) resulted in a prescription. Meanwhile, the other three conditions we examined had much lower dispensation rates (all less than 30%) with differing variability by age and condition. Macrolide and penicillin antibiotics were most commonly dispensed in all of these conditions; quinolones were seen in adults, and some cephalosporins were also dispensed, with a few other classes also represented but substantially less common. In general, penicillins were more common in younger children and macrolides were more common in older children and adults. There was wide variability across physicians in how often they prescribed antibiotics for URTI and acute bronchitis, but much narrower variability for asthma/allergic rhinitis and cough.

Compared to 2011, dispensation rates in 2016 were significantly higher (or trended towards higher) for acute bronchitis and were lower for asthma/allergic rhinitis in all age groups. For cough, the pattern was variable; however, in adults, the rates were significantly higher in 2016. For URTI, dispensation rates were lower in 2016 than in 2011 in all age groups, except 65+ where they were higher.

For most physician and patient characteristics we examined, the results were consistent with those previously reported in the literature [51]. Both the adult and paediatric models demonstrated higher odds of an antibiotic being prescribed in association with higher physician visits per day (a measure of patient load) and physician practice in Prairie Mountain Health. Higher Charlson Index scores (indicative of greater comorbidity) and lower socioeconomic status were also associated with higher odds of antibiotic dispensation. It should be noted that because of limitations associated with using billing codes to look at antibiotic use, these results might reflect at least some physician visits where antibiotics actually were indicated for the patient's condition. However, it is unexpected that the Charlson Index was not associated with antibiotic dispensation in patients with acute bronchitis. The reason for these unexpected findings could be that individuals with COPD, the most common comorbidity influencing antibiotic use in acute bronchitis patients, made up a very small percentage of visits because their visits are captured under a different ICD-9-CM code (for chronic bronchitis). Acute bronchitis as a condition had substantially higher odds of being associated with an antibiotic dispensation than the other conditions in the model.

Majority of care provider visits were significantly associated with lower dispensation rates. Dispensations were significantly lower in summer compared to winter in both adults and children, but the aORs were very low, suggesting that they did not account for a lot of the differences in prescribing. For children, care from a paedatrician as compared to a family physician has been reported as a significant factor in receiving an antibiotic prescription [52]; in our study, it was associated with a significantly lower odds of dispensation in the overall model and in the acute bronchitis model.

Fee-for-service practice and having provided some hospital-based care (a proxy for hospital privileges) were chosen due to their reported significance in the literature; they were not significantly associated with antibiotic dispensation in the overall model and rarely in the individual models.

Both adult and children in Prairie Mountain Health had higher odds of receiving an antibiotic prescription, consistent with the higher antibiotic dispensation rates in that region seen throughout this report. This finding suggests that those higher rates are not due to differences in patient populations between different the health regions but are specific to prescribing practices in Prairie Mountain Health. Northern Health Region had lower dispensation rates for children than other regions However, this is likely an artifact of the data, as morbidity is higher in this region than others; previous results in this report have demonstrated that the Northern Health Region data behave differently and should be interpreted with caution.

Conditions That May Require Antibiotics

In this section, we examine five conditions for which antibiotics would be indicated in certain individuals due to factors such as presenting symptoms, age or underlying health conditions (more details are available in the Technical Appendix in the online supplement). A discussion of the factors influencing the decision to use antibiotics for each condition precedes the results. In some models, type of antibiotic is also assessed, and for some conditions, especially those where the preferred antibiotic is from the penicillin group, the 'appropriate' antibiotic choice must include the accepted alternatives for patient allergy. Unfortunately, the Repository data do not document allergies. Thus, we had to make some assumptions about what constitutes an acceptable deviation by comparing dispensation rates of the chosen antibiotic to population-based allergy rates, and it is therefore somewhat uncertain whether or not that antibiotic was chosen because of allergy.

Acute Laryngitis or Tracheitis

Acute laryngitis is infection/inflammation of the larynx (voice box) and tracheitis is infection/inflammation of the trachea (airway); both present as hoarseness and/or loss of voice with or without airway obstruction. These conditions may be caused by infection or factors like environmental stress; their incidence is relatively low. Two other conditions that may present very similarly are epiglottitis and diphtheria; both carry a risk of fatal airway obstruction but are rarely seen now that they have been essentially eliminated by routine childhood vaccination.

For patients who present with laryngitis or tracheitis, have specific bacterial etiologies, and are appropriately diagnosed (usually via direct airway visualization), antibiotics would be indicated [53]. However, in an outpatient setting, these diagnoses are often non-specific. Milder clinical presentations of laryngitis may include symptoms similar to sore throat and are generally due to upper respiratory viruses if symptoms of laryngitis predominate.

The overall percentage of visits for this condition that resulted in an antibiotic dispensation in 2016 was the lowest among the five we examined at 24.4% (95% CI 22.7-26.2%) of visits.

Figure 6.7 shows antibiotic dispensations as percentage of visits by age group:

- Dispensation rates increased by age group until the age 15+ groups.
- Rates were similar for both adult age groups.
- In 2016, rates were higher in age groups 10 years and older than in 2011.

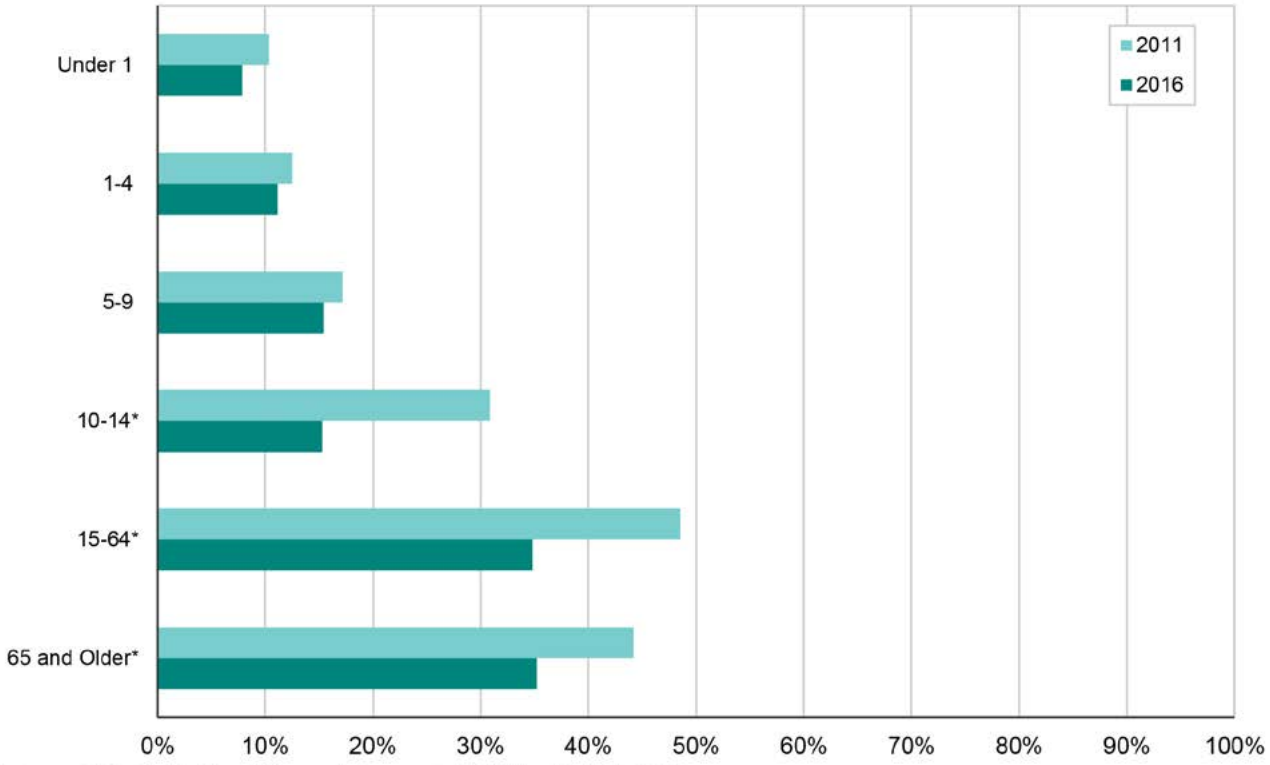
Looking at class of antibiotics dispensed demonstrated that:

- Macrolides[8] were most common followed by β-lactam penicillins.
    - Other classes made up only a small percentage.
- Different age groups had different ratios of β-lactam penicillins to macrolides. Younger age groups had more β-lactam penicillins than macrolides, and this trend reversed in older age groups.
- A small proportion of quinolone dispensations was seen in the 15-64 and 65+ age groups.

The distribution of visits resulting in an antibiotic dispensation by practitioner demonstrated that:

- The median percentage of dispensations for all practitioners was 10.0% with an IQR of 1.5-35.0%.
- Some practitioners wrote zero prescriptions.
- The lower half of the distribution had more variability than the upper half.

Figure 6.7: Antibiotic Dispensations Linked to Primary Care Ambulatory Physician Visits for Acute Laryngitis/Tracheitis, by Age Group (Years)
Crude percent of visits with a dispensation within five days



* Indicates a statistically significant difference between rates in 2011 and 2016 (p<0.05).

8 Macrolides, lincosamides and streptogramin class of antibiotics

Acute Otitis Media

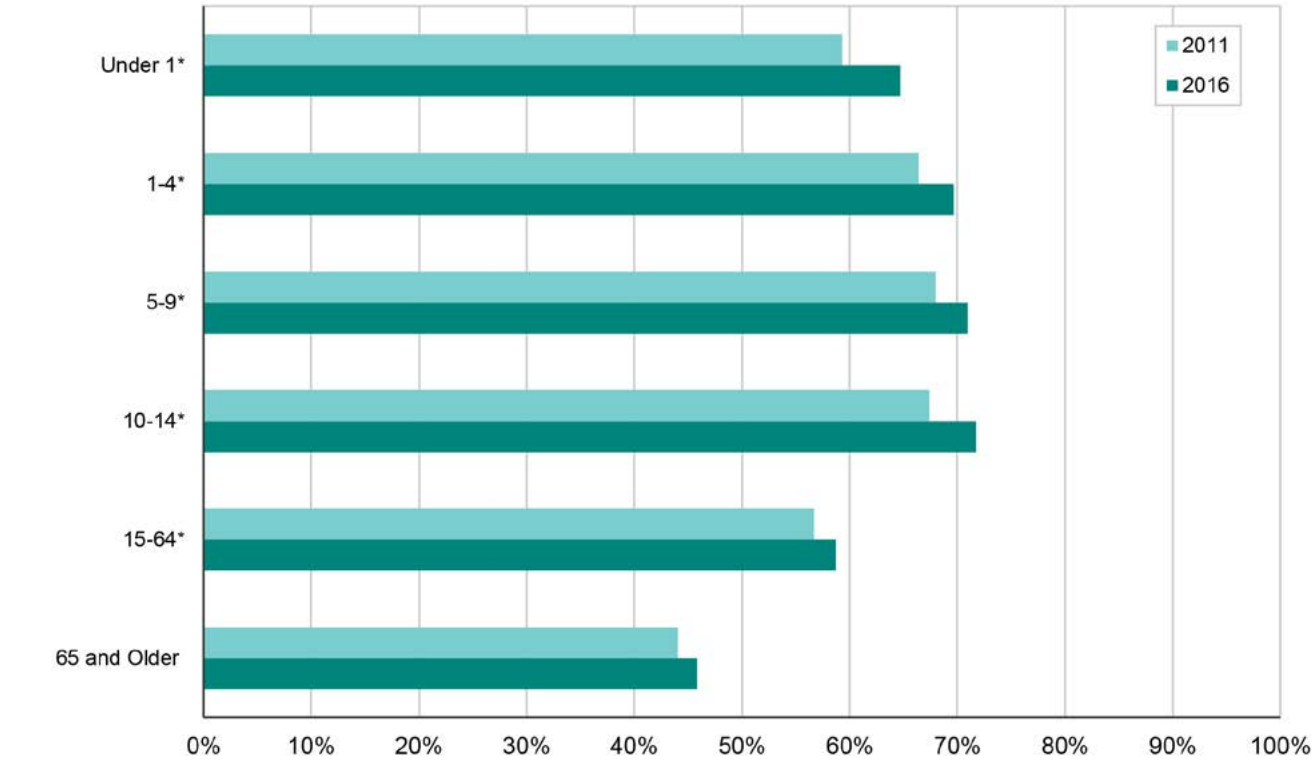
Current guidelines for management of paediatric acute otitis media (ear infection) recommend pain management for all children. Antibiotics are indicated if the ear drum is perforated or if a middle ear effusion is present and the child is moderately to severely ill (severe ear pain, severe systemic symptoms or greater than 48 hours of symptoms). Other presentations should be observed for 24-48 hours and reassessed for treatment. For most cases, amoxicillin is the antibiotic of choice, or cephalosporins or macrolides if the patient has a penicillin allergy [36,54,55]. As acute otitis media is rare in adults, adult treatment is more individualized.

In 2016, 65.1% (95% CI 64.2-66.1%) of all visits with a diagnosis of acute otitis media were associated with an antibiotic dispensation. In children, this percentage ranged from 65-72% (depending on age group), and for adults it was 58%.

Figure 6.8 shows antibiotic dispensations as percentage of visits by age group:

- Dispensation rates were relatively similar across the paediatric age groups, but slightly lower in children under 1 year than in older children.
- Adult dispensation rates were lower than paediatric rates, and adults 65+ had lower rates than 15-64-year-olds.
- In 2016, rates were higher for all age groups (except 65+ years) than in 2011.

Figure 6.8: Antibiotic Dispensations Linked to Primary Care Ambulatory Physician Visits for Acute Otitis Media, by Age Group (Years)
Crude percent of visits with a dispensation within five days



* Indicates a statistically significant difference between rates in 2011 and 2016 (p<0.05).

Looking at class of antibiotics dispensed demonstrated that:

- Overall, β-lactam penicillins were the most common class dispensed, and macrolides were second most common
    - Cephalosporin antibiotics were dispensed about half as often as macrolides.
- All age groups had higher use of β-lactam penicillins than macrolides; cephalosporin use was relatively stable.
- A small proportion of quinolone dispensations were seen in the 15-64 and 65+ age groups.

The distribution of visits resulting in an antibiotic dispensation by practitioner demonstrated that:

- The median percentage of dispensations for all practitioners was 58.5% with an IQR of 42.9-71.9%.
- Visits in the lower half of the distribution were spaced slightly wider than in the upper half.

Further statistical modelling was undertaken to look at whether antibiotics that were dispensed for acute otitis media were the appropriate choice. An appropriate antibiotic choice for acute otitis media was defined as extended-spectrum penicillins (includes amoxicillin), β-lactamase inhibitor combinations (includes amoxicillin/clavulanic acid) or second generation cephalosporins. We examined children only since guidelines for antibiotic choice for acute otitis media in adults are not available. We did however, generate an exploratory model using the children's guidelines for adults – there results are available in the online supplement.

An inappropriate antibiotic was dispensed in 18% of the visits in which antibiotics was dispensed to children with acute otitis media.

The following characteristics were significantly associated with higher odds of a child being prescribed an inappropriate choice of antibiotic:

- Male patient sex (aOR 1.07, 95% CI 1.02-1.12).
- A Charlson Index of 1 compared to 0 (aOR 1.28, 95% CI 1.20-1.36).
- Older physician age (aOR 1.25, 95% CI 1.16-1.35).
- Physician practice in Southern Health-Santé Sud (aOR 1.46, 95% CI 1.20-1.77) or Prairie Mountain Health (aOR 1.74, 95% CI 1.42-2.13) compared to Winnipeg RHA.
- Prescribed by the patient's majority of care physician (aOR 1.22, 95% CI 1.15-1.29).

The following characteristics were significantly associated with lower odds of a child being prescribed an inappropriate choice of antibiotic:

- Patient age under 1 year (aOR 0.61; 95% CI 0.55-0.68), ages 1-4 (aOR 0.79, 95% CI 0.73-0.85), or age 5-9 (aOR 0.76, 95% CI 0.71-0.83) compared to ages 10-14.
- Higher SEFI-2 score, indicating lower socioeconomic status (aOR 0.93, 95% CI 0.90-0.96).
- Number of children in the home 3 (aOR 0.90, 95% CI 0.84-0.97) or 4+ (aOR 0.86, 95% CI 0.79-0.93) compared to 1.
- Physicians who provide some hospital-based care (aOR 0.77, 95% CI 0.63-0.93).
- Prescribed by a paediatrician instead of a family physician (aOR 0.62, 95% CI 0.46-0.82).
- Too few visits to assign a majority of care physician (aOR 0.61, 95% CI 0.55-0.67).

Pharyngitis

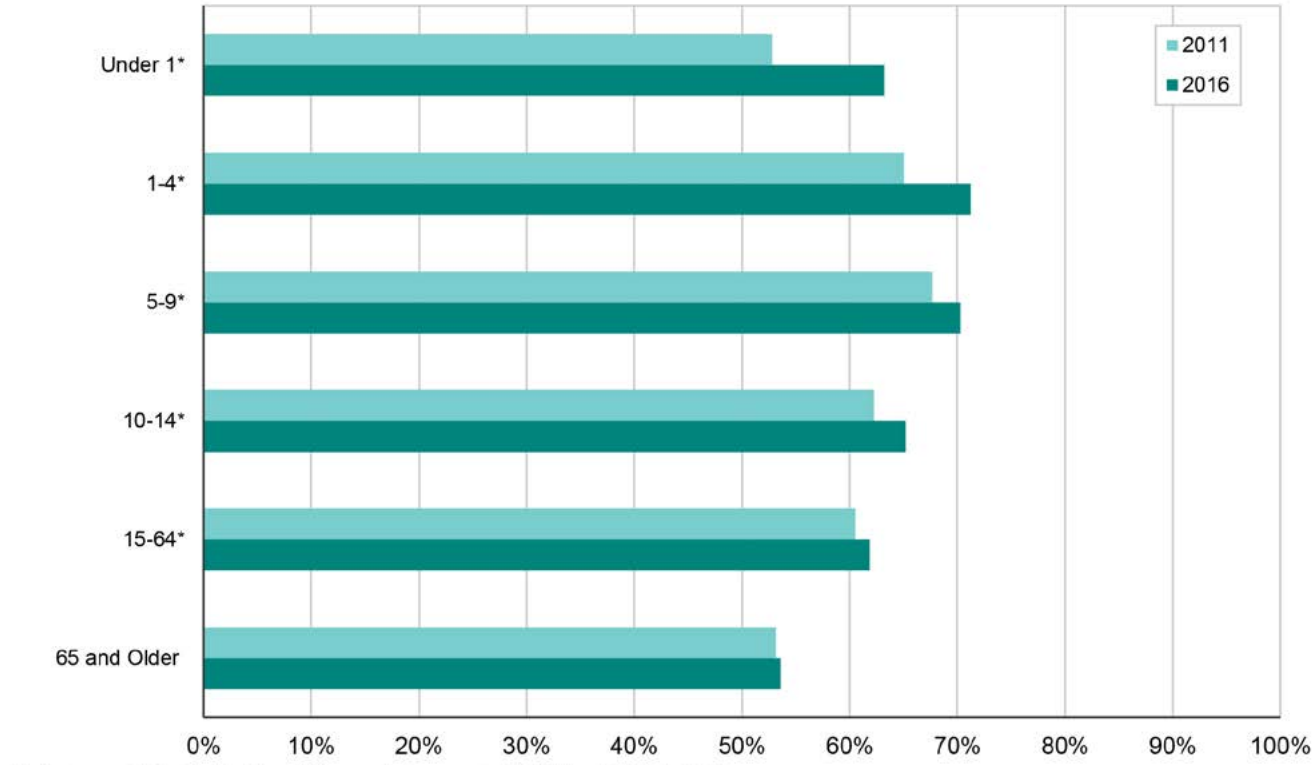
Commonly referred to as 'sore throat', pharyngitis can be caused by bacteria or viruses. Pharyngitis can be a symptom associated with many viral URTIs or a specific bacterial infection. The most important specific diagnosis a physician needs to make (especially in children) is streptococcal sore throat, which is caused by Group A Streptococcus (GAS) and requires treatment with penicillin to reduce the risk of rheumatic fever and other complications. Adult patients with streptococcal pharyngitis should also receive antibiotics. Approximately 10% of adult cases of pharyngitis and up to ~30% of cases in children are caused by GAS, depending on age, season and exposure to other children or carriers. Most other sore throats in the outpatient setting do not require antibiotic treatment [56].

In 2016, an antibiotic was dispensed after 64.1% (95% CI 63.3-64.9%) of visits coded as pharyngitis.

Figure 6.9 shows dispensations as percentage of visits by age group:

- Dispensation rates were lower in the under age 1 and 10-14-year-old age groups compared to other paediatric rates.
- Adult rates were lower than paediatric rates, and rates for adults age 65+ were lower than for ages 15-64.
- In 2016, rates were higher for all age groups (except 65+ years) than in 2011.

Figure 6.9: Antibiotic Dispensations Linked to Primary Care Ambulatory Physician Visits for Pharyngitis, by Age Group (Years)
Crude percent of visits with a dispensation within five days



* Indicates a statistically significant difference between rates in 2011 and 2016 (p<0.05).

Looking at class of antibiotics dispensed demonstrated that:

- Overall, β-lactam penicillins were the most common class dispensed, and macrolides were the second most common.
- All age groups had higher use of β-lactam penicillins than macrolides; cephalosporin use was variable.
- A very small proportion of quinolone dispensations were seen in the 15- 64 and 65+ age groups.

The distribution of visits resulting in an antibiotic dispensation by practitioner demonstrated that:

- The median percentage of dispensations for all practitioners was 57.1% with an IQR of 40.0-72.0%.
- Visits in the lower half of the distribution were spaced slightly wider than in the upper half.

Further statistical modelling was done to look at whether antibiotics that were dispensed for pharyngitis were the appropriate choice. Since the almost sole indication for antibiotic treatment in pharyngitis is GAS, the antibiotic of choice is penicillin or amoxicillin. Among visits where antibiotics were dispensed for pharyngitis, 30.4% were inappropriate.

Models were also run allowing a different antibiotic to be substituted with a cephalosporin or macrolide in case of penicillin allergy. In those models, 8.7% of visits were linked to inappropriate antibiotic choice; and the rate of 'appropriate' use was higher. The detailed results of these models are presented in the online supplement.

In the model not allowing substitution for allergy, the following characteristics were significantly associated with higher odds of an inappropriate choice of antibiotic for **adults:**

- Physician practice in Prairie Mountain Health (aOR 1.45, 95% CI 1.24-1.70) compared to Winnipeg RHA.
- Receipt of medical training outside of Canada/ United States (aOR 1.50, 95% CI 1.24-1.70).
- Higher physician visits per day, a measure of patient load (aOR 1.23, 95% CI 1.11-1.37).
- Patient age 65+ years compared to 15-64 years (aOR 1.18, 95% CI 1.10-1.27).
- A Charlson Index of 1 (aOR 1.17, 95% CI 1.12-1.22), 2 (aOR 1.34, 95% CI 1.23-1.46) or 3 (aOR 1.43, 95% CI 1.26-1.62) compared to 0.
- Prescribed by the patient's majority of care provider (aOR 1.14, 95% CI 1.10-1.18).

In the model **no**t allowing substitution for allergy, the following characteristics were significantly associated with lower odds of an inappropriate choice of antibiotic for adults:

- Physician practice in Southern Health-Santé Sud (aOR 0.74, 95% CI 0.63-0.86) compared to Winnipeg RHA.
- Too few visits to assign a majority of care provider (aOR 0.75, 95% CI 0.71-0.79).
- Higher SEFI-2 score, indicating lower socioeconomic status (aOR 0.93, 95% CI 0.91-0.95).
- In the model not allowing substitution for allergy, the following characteristics were significantly associated with higher odds of an inappropriate choice of antibiotic for children:
- Physician practice in Interlake Eastern RHA (aOR 1.65, 95% CI 1.31-2.06) or Prairie Mountain Health (aOR 1.86, 95% CI 1.53-2.25) compared to Winnipeg RHA.
- Receipt of medical training outside of Canada/ United States (aOR 1.36, 95% CI 1.14-1.62).
- A Charlson Index of 1 (aOR 1.23, 95% CI 1.15-1.31) or 2 (aOR 1.43 95% CI 1.09-1.87) compared to 0.
- Prescribed by the patient's majority of care provider (aOR 1.14, 95% CI 1.08-1.21).

In the model **not** allowing substitution for allergy, the following characteristics were significantly associated with lower odds of an inappropriate choice of antibiotic for children:

- Patient age group 0-1 years (aOR 0.50, 95% CI 0.41-0.62), 1-4 years (aOR 0.72, 95% CO 0.68-0.77) or 5-9 years (aOR 0.77, 95% CI 0.73-0.81) compared to 10-14 years.
- Too few visits to assign a majority of care provider (aOR 0.66, 95% CI 0.60-0.72).
- Number of children in the home 3 (aOR 0.88, 95% CI 0.82-0.94) or 4+ (aOR 0.82, 95% CI 0.75-0.89) compared to 1.
- Higher SEFI-2 score, indicating lower socioeconomic status (aOR 0.90, 95% CI 0.88-0.93).

Pneumonia

Pneumonia includes both bacterial and viral infections of the lower respiratory tract. Many different bacteria and viruses can cause pneumonia with symptoms of varying severity. Many people with pneumonia require hospitalization and many may receive intravenous antibiotics. Choice of antibiotics for community-acquired pneumonia in outpatients depends on the age and other health conditions of the person. In children, especially younger children under age five, pneumonia is likely to be viral. But in older age groups, community-acquired

pneumonia is most likely to be caused by gram-positive bacteria like Streptococcus pneumoniae and atypical bacteria like mycoplasma. Guidelines exist for the choice of antibiotics to treat pneumonia in children and adults [57,58].

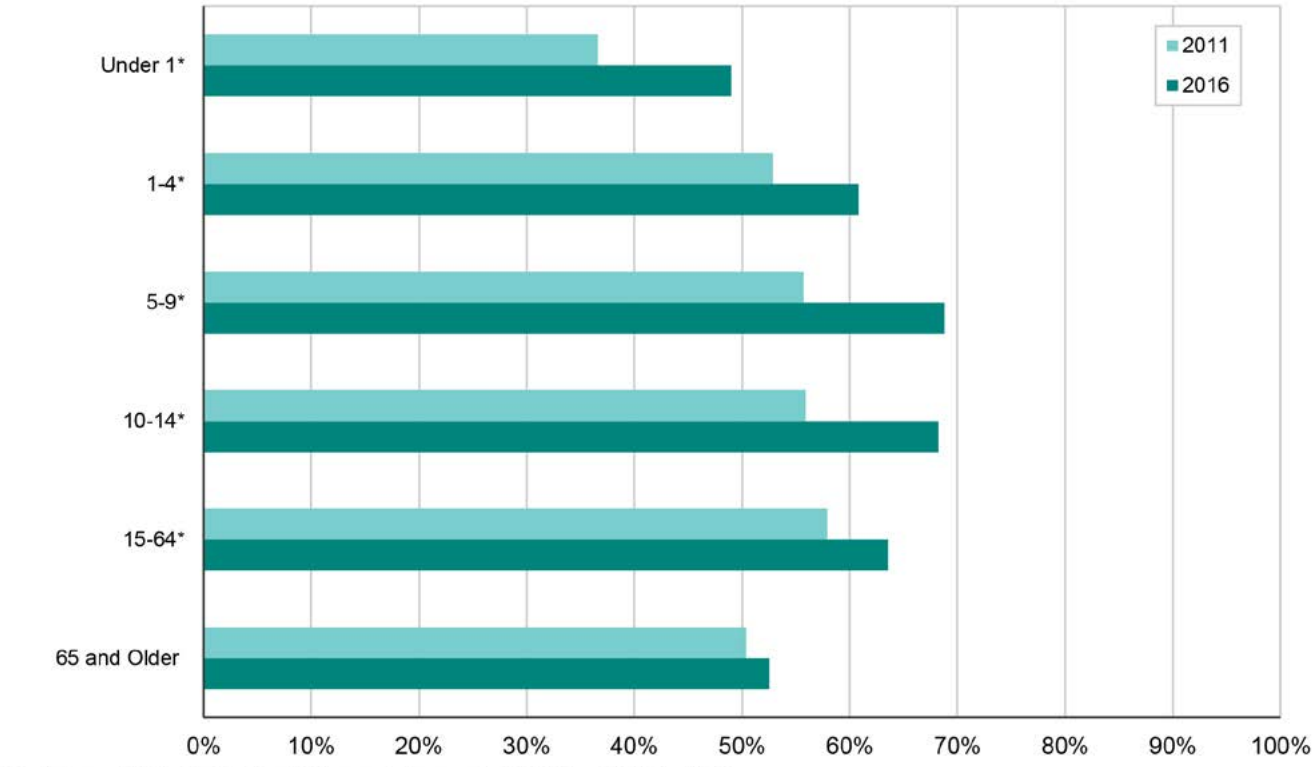
There are separate diagnosis codes for viral and bacterial pneumonia. We did some preliminary statistical modelling to look at antibiotic dispensations in patients coded for viral vs bacterial pneumonia and found extremely high rates of antibiotic dispensations in the viral pneumonia group, even surpassing those for bacterial pneumonia in some age groups. Consultation with the advisory group and practitioners on the research team revealed this was most likely due to coding of most pneumonia as viral (regardless of whether it was actually viral or bacterial), and thus for our analyses, we combined all pneumonia codes and did not distinguish between viral and bacterial. This is a limitation of using ICD diagnosis codes as antibiotic indications and may limit the usefulness of these results.

In 2016, an antibiotic was dispensed with in 60.4% (95% CI 58.7-62.1%) of visits with a diagnosis of pneumonia.

Figure 6.10 shows dispensations as percentage of visits by age group:

- Antibiotic dispensation rates increased steadily with age group until the 65 and older group, where they were slightly lower than in the 15-64-year-old group.
- In 2016, rates were higher than in 2011 for all age groups except 65+ years.

Figure 6.10: Antibiotic Dispensations Linked to Primary Care Ambulatory Physician Visits for Pneumonia, by Age Group (Years)
Crude percent of visits with a dispensation within five days



* Indicates a statistically significant difference between rates in 2011 and 2016 (p<0.05).

Looking at class of antibiotics dispensed demonstrated that:

- Overall, macrolides were the most common class dispensed, and β-lactams and quinolones had similar dispensation rates in second place.
- The use of macrolides increased with age, as did the use of quinolones, but β-lactam antibiotics were more common than macrolides in children under 5 years.

The distribution of visits resulting in an antibiotic dispensation by practitioner demonstrated that:

- The median percentage of dispensations for all practitioners was 53.2% with an IQR of 37.9-67.9%.
- Visits in the lower half of the distribution were spaced slightly wider than in the upper half.

Further statistical modelling was done to look at whether antibiotics that were dispensed to children for pneumonia were the appropriate choice. Current guidelines recommend the use of amoxicillin unless atypical pneumonia (such as mycoplasma) is suspected, where a macrolide would be used instead. Substitution for allergy would generally be a second generation cephalosporin such as cefuroxime or possibly macrolides (but macrolides should be less often recommended due to evolving resistance patterns) [54].

An inappropriate antibiotic is defined as any antibiotic other than those in subclass extended-spectrum (including amoxicillin) and β-lactamase sensitive (such as penicillin). In older children ages 10-14, some use of macrolides would be appropriate as mycoplasma emerges as a pathogen.

Models were run to look at all children and children ages 0-5 only (available in the online supplement), but since they yielded similar results, only the results for all children are presented. An inappropriate antibiotic was dispensed in 32.8% of visits and in 52.4% of dispensations. In the model looking at children ages 0-5 only, an inappropriate antibiotic was dispensed in 23.7% of visits and in 40.4% of dispensations.

The following characteristics were significantly associated with:

- Higher odds of an inappropriate antibiotic dispensation:
  - Physician practice in Prairie Mountain Health (aOR 2.62, 95% CI 1.56-4.39) compared to Winnipeg RHA.
  - A Charlson Index of 1 (aOR 1.44, 95% CI 1.25-1.66) compared to 0.
  - Older physician age (aOR 1.48, 95% CI 1.24-1.76).
  - Higher physician visits per day, a measure of patient load (aOR 1.33, 95% CI 1.07-1.65).
- Lower odds of an inappropriate antibiotic dispensation:
  - Patient age group under 1 year (aOR 0.10, 95% CI 0.07-0.13), 1-4 years (aOR 0.18, 95% CI 0.15-0.21) or 5-9 years (aOR 0.39, 95% CI 0.32-0.47) compared to 10-14 years.
  - Too few visits to assign a majority of care provider (aOR 0.66, 95% 0.60-0.72).
  - Number of children in the home 3 (aOR 0.88, 95% CI 0.82-0.94) or 4+ (aOR 0.82, 95% CI 0.75-0.89) compared to 1.
  - Higher SEFI-2 score, indicating lower socioeconomic status (aOR 0.90, 95% CI 0.88-0.93).

Sinusitis

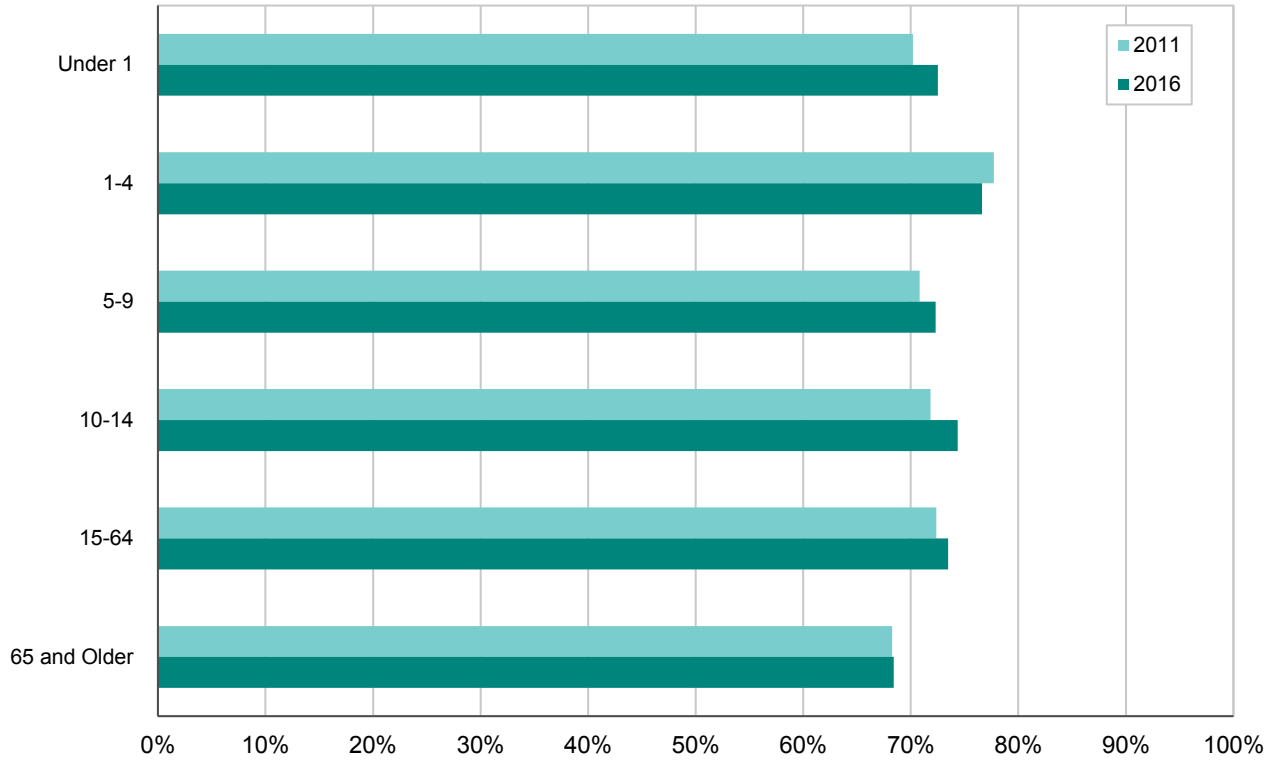
Sinusitis is a general term for an infection of the sinuses, which are air-filled spaces connected to the nasal cavity in the skull and facial bones. Infections can be caused by viruses or bacteria. Acute bacterial sinusitis is suspected when symptoms of purulent nasal discharge with blockage and facial pain/headache have persisted for at least ten days or worsened after initial improvement. Management includes watchful waiting for another week or antibiotics. Due to the predominance of gram-positive bacteria such as Streptococcus pneumoniae and Haemophilus influenzae causing bacterial sinusitis, treatment with amoxicillin is recommended as first line if antibiotics are prescribed [59,60].

In 2016, an antibiotic was dispensed in 72.9% (95% CI 71.8-74.0%) of visits with a diagnosis of sinusitis.

Figure 6.11 shows dispensations as percentage of visits by age group:

- Antibiotic dispensation rates were lowest in children under 1 year and in adults ages 65 and older.
- Rates were roughly similar in the other age groups.
- There was no significant change in any age group between 2011 and 2016.

Figure 6.11: Antibiotic Dispensations Linked to Primary Care Ambulatory Physician Visits for Sinusitis, by Age Group (Years)
Crude percent of visits with a dispensation within five days



* Indicates a statistically significant difference between rates in 2011 and 2016 (p<0.05).

Looking at class of antibiotics dispensed demonstrated that:

- Overall, β-lactams were the most common class and macrolides were the second most common.
- The use of macrolides increased with age as use of β-lactam antibiotics decreased.
    - Cephalosporin use was seen in younger age groups.
    - Quinolone use was seen in the adult age groups.

The distribution of visits resulting in an antibiotic dispensation by practitioner demonstrated that:

- The median percentage of dispensations for all practitioners was 68.7% with an IQR of 52.9-80.0%.
- The visits in the lower half of the distribution were wider spaced than in the upper half.

Multi-Level Modelling for Conditions That May Require Antibiotics

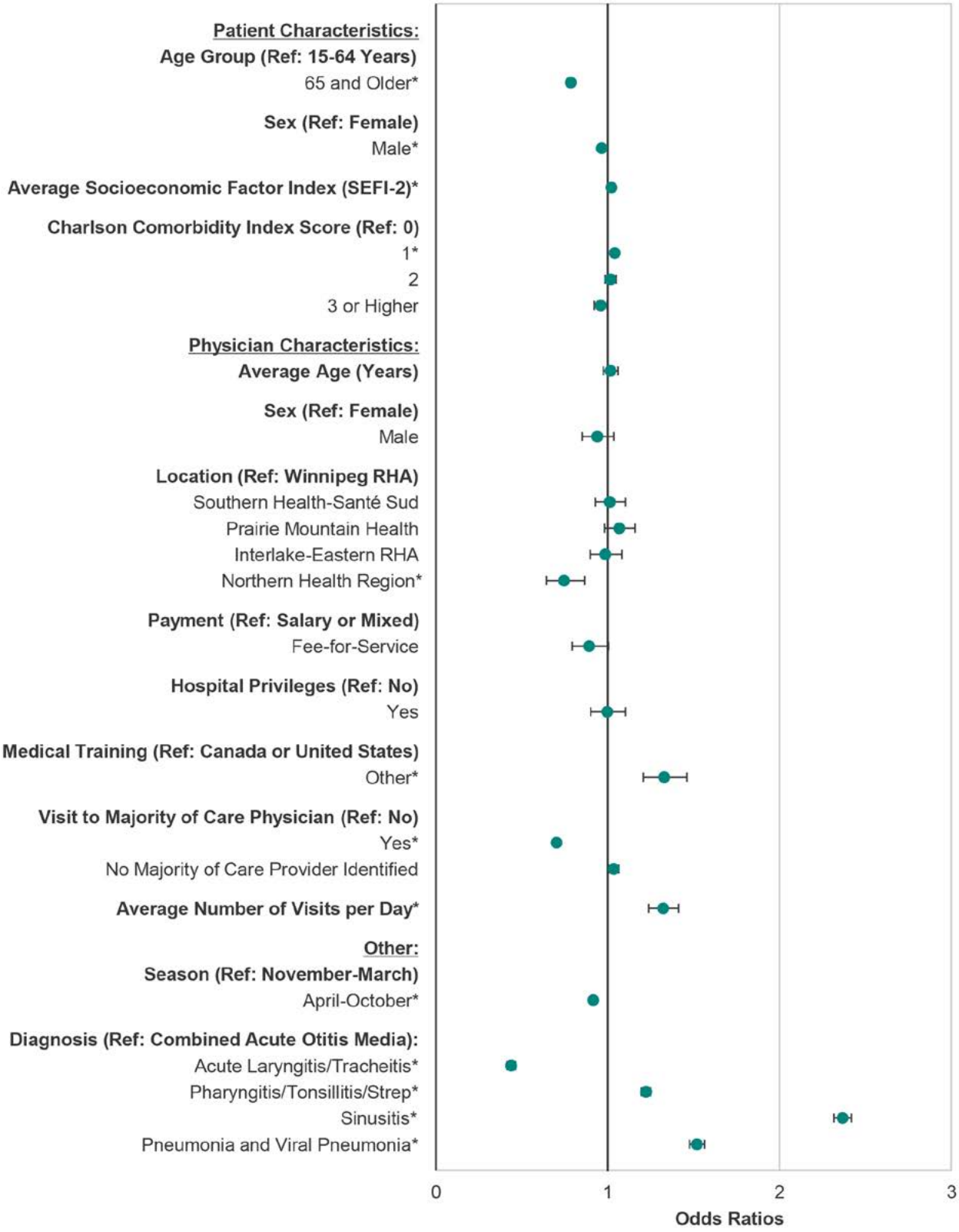
A model was developed to identify which patient and physician characteristics were significantly associated with dispensation of antibiotics for the five conditions in this category. The model generates aOR, which tell us how likely a characteristic was to be associated with a dispensation after adjusting for each factor in the model.

For adults, the following characteristics were significantly associated with (see Figure 6.12):

- Higher odds of antibiotic dispensation:
    - Receipt of medical training outside of Canada/ United States (aOR 1.33, 95% CI 1.21-1.46).
    - More visits per day, a measure of patient load (aOR 1.32, 95% CI 1.24-1.41).
    - Patient age 65+ compared to 15-64 years (aOR 1.05, 95% CI 1.02-1.07).
    - A Charlson Index of 1 compared to 0 (aOR 1.04, 95% CI 1.02-1.06).
    - Higher SEFI-2 score, indicating lower socioeconomic status (aOR 1.02, 95% CI 1.01-1.03).
    - Diagnosis of pharyngitis (aOR 1.22, 95% CI 1.20-1.25), sinusitis (aOR 2.37, 95% CI 2.32-2.42) or pneumonia (aOR 1.52, 95% CI 1.48-1.56), each compared to acute otitis media.
- Lower odds of antibiotic dispensation:
    - Physician location in Northern Health Region compared to Winnipeg RHA (aOR 0.75, 95% CI 0.64-0.87).
    - Patient age 65+ compared to 15-64 (aOR 0.79, 95% CI 0.77-0.80).
    - Male compared to female patient sex (aOR 0.96, 95% CI 0.95-0.98).
    - Prescribed by the patient's majority of care provider (aOR 0.70, 95% CI 0.69-0.71).
    - Summer compared to winter months (aOR 0.91, 95% CI, 0.90-0.93).

Figure 6.12 Association Between Patient and Physician Characteristics and Dispensations of Antibiotics for Conditions that May Require Antibiotics in Adults

Age- and sex-adjusted odds ratios (average and 95% confidence intervals), patient ages 15 and older



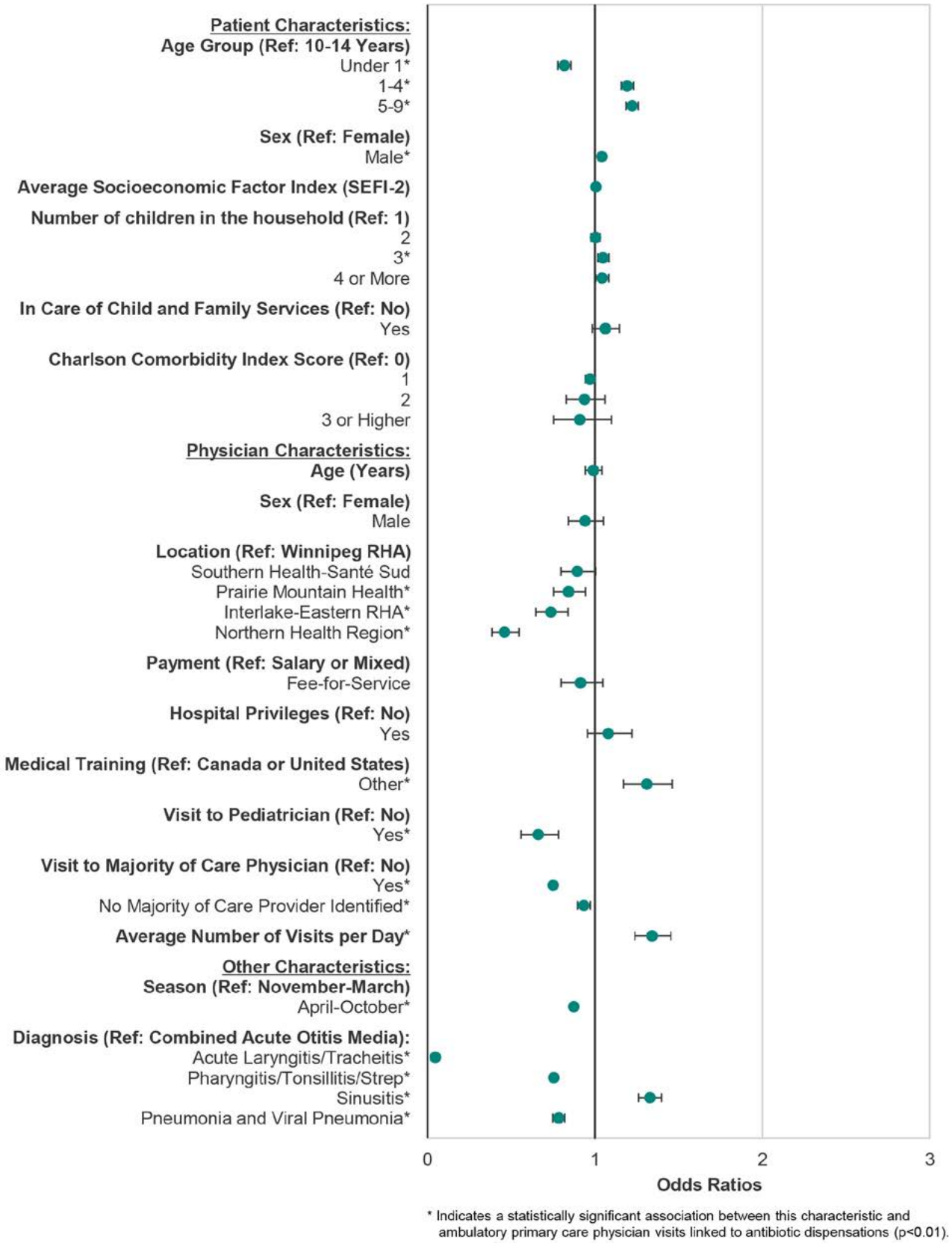
* Indicates a statistically significant association between this characteristic and ambulatory primary care physician visits linked to antibiotic dispensations ($p<0.01$).

For children, the following characteristics were significantly associated with (see Figure 6.13):

- Higher odds of antibiotic dispensation:
    - Physician training outside of Canada/United States (aOR 1.31, 95% CI 1.17-1.46).
    - More visits per day, a measure of patient load (aOR 1.34, 95% CI 1.24-1.45).
    - Patient age group 1-4 years (aOR 1.19, 95% CI 1.16-1.23) or 5-9 years (aOR 1.22, 95% CI 1.19-1.26) compared to 10-14 years.
    - Male patient sex compared to female (aOR 1.04, 95% CI 1.02-1.06).
    - Three children in the home compared to 1 (aOR 1.05, 95% CI 1.02-1.08).
    - Sinusitis compared to acute otitis media (aOR 1.33, 95% CI 1.26-1.40).
- Lower odds of antibiotic dispensation:
    - Physician location in Interlake-Eastern RHA (aOR 0.74, 95% CI 0.65-0.84), Northern Health Region (aOR 0.46, 95% CI 0.39-0.55) or Prairie Mountain Health (aOR 0.84, 95% CI 0.75-0.94) compared to Winnipeg RHA.
    - Paediatrician prescribed instead to family physician (aOR 0.66, 95% CI 0.56-0.78).
    - Patient age less than 1 year compared to 10-14 years (aOR 0.82, 95% CI 0.78-0.86).
    - Prescribed by the patient's majority of care provider (aOR 0.75, 95% CI 0.73-0.77).
    - Too few visits to assign a patient a majority of care provider (aOR 0.93, 95% CI 0.90-0.97).
    - Summer compared to winter months (aOR 0.88, 95% CI 0.80-0.85).
    - Acute laryngitis/tracheitis (aOR 0.05, 95% CI 0.04-0.05), pharyngitis (aOR 0.75, 95% CI 0.74-0.77) or pneumonia (aOR 0.78, 95% CI 0.75-0.82) compared to acute otitis media.

Figure 6:13: Association Between Patient and Physician Characteristics and Dispensations of Antibiotics for Conditions that May Require Antibiotics in Children

Age- and sex-adjusted odds ratios (average and 95% confidence intervals), patient ages 0-14



* Indicates a statistically significant association between this characteristic and ambulatory primary care physician visits linked to antibiotic dispensations ($p<0.01$).

We also ran multi-level models for each individual condition (results available in the online supplement). Patterns of association between antibiotic dispensation and patient/physician characteristics were similar to the overall models shown above, except that seasonality was not significantly associated with antibiotic dispensations for pneumonia in the children's model (aOR 0.93, 95%CI 0.86-1.02).

Summary

For all of the conditions we examined that might require antibiotics (except laryngitis/tracheitis), antibiotic dispensation rates peaked in late childhood and then declined until they were lower in adulthood than in childhood; the dispensation rates were similar among conditions, ranging from approximately 45-60%. For laryngitis/tracheitis, dispensation rates were lower than for the other four conditions and peaked in adulthood.

The most common antibiotic classes prescribed tended to be macrolides and penicillins, with penicillins more common in younger age groups, and macrolides more common as age increased, except for pneumonia, where quinolones were the second most common antibiotic class. Quinolones were prescribed for all conditions in adults. There was also a small representation of the cephalosporins. Other antibiotics were substantially less common. How often physicians dispensed different antibiotics was widely variable across all five conditions.

In 2016, dispensation rates were significantly lower for acute laryngitis/tracheitis and higher for acute otitis media (trend only for age 65+), pharyngitis (trend only for age 65+) and pneumonia (trend only for age 65+) compared to 2011. There was no change between these two time points in dispensation rates for sinusitis.

We saw some associations between patient and provider characteristics and antibiotic dispensations that reflected whether an antibiotic was indicated or not, such as patient age, socioeconomic status and comorbidities. However, similar to the models in the previous section (conditions which generally do not require antibiotics), visits to the majority of care provider and prescriptions by a paediatrician were associated with moderately lower odds of dispensation, and higher patient load was associated with higher odds. There was some seasonality in dispensing, but the odds ratios were relatively low even when they were significant. There was no seasonality in dispensing antibiotics for pneumonia, a finding that requires further investigation.

Receipt of medical training outside of Canada/United States was associated with higher odds of a prescription. This is possibly due to differing spectrums of disease presentation and the need for antibiotic treatment in other countries. Fee-for-service practice and providing some hospital-based care were indicators we selected because of their reported significance in the literature – however, we saw very little association between them and antibiotic dispensation.

We saw no associations between children having been in care of Child and Family Services and higher antibiotic prescribing rates – this indicator was tested out of concern that children in care may receive fragmented health care and thus have higher morbidity.

Rates of inappropriate antibiotic choice were high for all of the conditions we modeled, especially for pneumonia, where over half of antibiotics dispensed were an inappropriate type. For pharyngitis, when we allowed substitution of a different antibiotic in case of allergies to penicillin, the rate of inappropriate antibiotic prescribing dropped from 30.4% to 8.7%; however, the true rate of penicillin allergy is likely lower than that. Approximately 10-20% of the overall population is labeled allergic to penicillin, but when formal allergy assessments are done, well over 90% of these "allergic" patients are able to safely tolerate penicillin-class antibiotics [61,62].

Conditions That Usually Require Antibiotics

The role of antimicrobial stewardship is to encourage appropriate choice of antibiotic, targeted to the local resistance patterns and usually targeted against particular bacteria. In order to comment on whether antibiotic dispensation rates are appropriate, we would need to model dispensation patterns in a such a way that we can discriminate the initial health care contact from follow-up or other related visits that occur after the initial diagnosis and antibiotic dispensation – however, this level of detail was outside the scope of this report. Thus, we modeled two conditions that usually require antibiotics to look at the class of antibiotic dispensed, limiting these analyses to looking at only the most common inappropriate class of antibiotics and what patient/physician characteristics they were associated with (more details are available in the Technical Appendix in the online supplement).

Skin and Soft Tissue Infections (SSTIs)

Skin and soft tissue infections are caused by a variety of bacteria, including streptococcus and staphylococcal species. In patients with underlying conditions such as diabetes or immune disorders, other bacteria may also play a role [63]. Some less severe infections may be treated with a topical antibiotic and would not be captured in the analyses in this report. Quinolones are considered to be an inappropriate choice for SSTI [64].

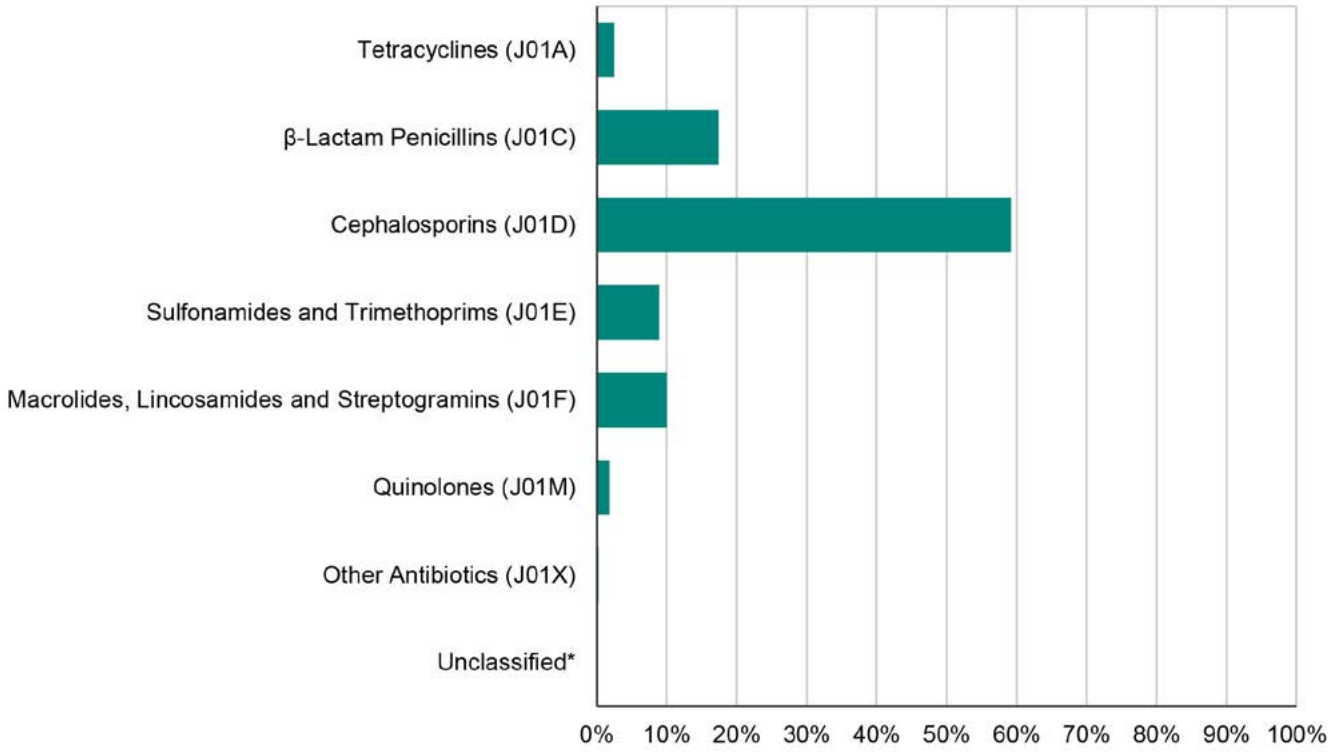
In 2016, an oral antibiotic was dispensed following a diagnosis of an SSTI in 53.4% (95% CI 52.6-54.3%) of physician visits.

The distribution of antibiotic classes (shown in Figure 6.14) demonstrates a predominance of cephalosporin antibiotics dispensed to SSTI patients. When broken down by age group, the patterns were similar across the paediatric age groups. In adults, quinolones accounted for just over 1.18% of antibiotics dispensed; this finding makes sense given that quinolones are not appropriate for SSTI.

We planned to run a multi-level model to examine factors associated with dispensation of a quinolone antibiotic for SSTIs (inappropriate choice); however, due to low numbers, this analysis was not possible. Further detail is available in the online supplement.

Figure 6.14: Antibiotic Dispensations Linked to Ambulatory Visits to Primary Care Physicians for Skin and Soft Tissue Infections, by Drug Class, 2016

Crude percent of total dispensations within five days of a visit



* Includes the drugs amoxicillin/clarithromycin, fixadomicin and vancomycin.

Urinary Tract Infections (UTIs)

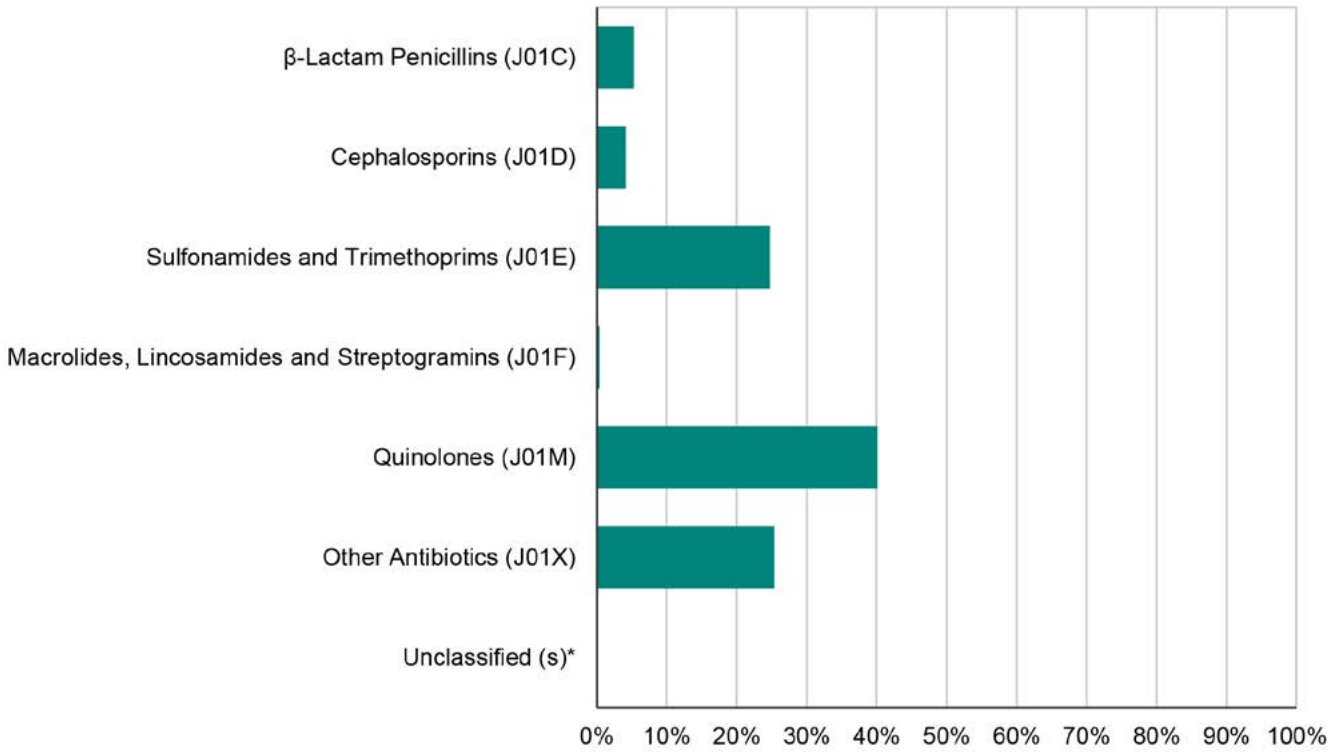
Urinary tract or 'bladder' infections are usually caused by gram-negative bacteria, with 75-95% of uncomplicated infections in adults caused by E. coli. A simple or uncomplicated UTI, also termed acute cystitis, involves infection of the bladder and urethra only, whereas a complicated UTI may include the kidneys (upper urinary tract) as well. Antibiotic choice for UTIs is influenced by local antibiotic resistance patterns, the degree of illness at presentation and the presence of underlying conditions. Clinical guidelines suggest the use of trimethoprim-sulfamethoxazole (sulfonamides class) as first line for uncomplicated UTIs in adults, or nitrofurantoin if there are concerns about bacterial resistance. Treatment in adults is often undertaken without a urine culture. Care provided solely by telephone or self-diagnosis in patients with recurrent UTIs is an accepted practice [65]. In children, a urine culture is part of the investigation and is ultimately used to guide therapy. Due to the difficulty in excluding the possibility of a complicated UTI in younger children, first line treatment may be intravenous, and if oral antibiotics are given, the choice of antibiotic type depends on local resistance patterns [66]. Macrolides are considered an inappropriate antibiotic choice for UTIs [41,66]. Quinolones are effective, but they are wider-spectrum than other choices and are therefore not typically recommended for UTI [67].

In 2016, antibiotics were dispensed with a diagnosis of UTI in 64.2% (95% CI 62.0-66.5%) of visits.

Figure 6.15 illustrates the distribution of antibiotic classes and demonstrates that quinolone antibiotics were the most frequently dispensed. When broken down by age group, the patterns were similar across the paediatric age groups with cephalosporins and sulfonamides predominating. In adults and children age ten and over, sulfonamides, quinolones, and "other" antibiotics (including nitrofurantoin) were most commonly represented. Macrolides made up a very small percentage and were not easily discriminated in the figure (0.21% of dispensations).

We planned to run a multi-level model to examine factors associated with dispensation of a quinolone antibiotic for UTIs; however, due to low numbers, this analysis was not possible. Further detail is available in the online supplement.

Figure 6.15: Antibiotic Dispensations Linked to Ambulatory Visits to Primary Care Physicians for Urinary Tract Infections, by Drug Class, 2016
Crude percent of total dispensations within five days of a visit



* Includes the drugs amoxicillin/clarithromycin, fixadomicin and vancomycin.
s Indicates data suppressed due to small numbers.

Summary

For both conditions in this category, both of which generally require antibiotics, the incidence of dispensation of an inappropriate antibiotic was quite low and thus we were not able to model it. The dispensation rates for both conditions were lower than expected, and in some cases, they were lower than for the other two categories of conditions (where antibiotics generally were not indicated). The relatively high rate of quinolone dispensation for UTI in adults was of concern as this class of medications is not generally recommended [63].

Conclusions and Recommendations

This chapter identifies patterns of antibiotic dispensation as they relate to diagnosis codes assigned at an ambulatory primary care visit, highlighting areas for targeted outpatient antimicrobial stewardship and previously unrecognized concerns that should continue to be monitored.

Dispensation of antibiotics where they are generally not indicated

Rates of antibiotic dispensation were relatively low for all conditions where they were generally not indicated, except for acute bronchitis, identifying it as a target for ASPs. Multi-level models and sensitivity analyses suggested that the high rates of dispensations for this condition were not due to underlying comorbidities, since comorbid COPD accounted for less than 3% of the dispensations; dispensations were also not associated with the Charlson Comorbidity Index. It is concerning that antibiotic dispensation rates for this condition are also increasing over time. For this category of conditions as a whole, higher dispensation rates were consistently associated with older physician age and higher patient load, and these factors should be taken into consideration when planning intervention strategies.

Dispensation of antibiotics where they may be indicated

Antibiotic dispensation rates were relatively high for this category of conditions (with the exception of laryngitis/tracheitis), and in many cases, rates were higher than for conditions which nearly always require antibiotics. While it is not possible to identify clearly whether antibiotics were strictly needed at each health care contact using the available data, the wide variability among practitioners and consistent identification of physician characteristics associated with higher odds of dispensations (even after adjusting for patient factors) suggest that lower rates could be achieved. For this group of conditions, physician characteristics associated with higher odds of an antibiotic dispensation included higher patient load and receipt of medical training outside of Canada/United States, perhaps reflecting differing patterns of antibiotic use and guidelines in other countries. Some physicians may benefit from educational interventions.

Changes from 2011-2016

It is concerning that in most indicators where a difference in dispensation rates occurred from 2011 to 2016, it was usually higher in 2016, especially in adults. This pattern was seen in both categories of conditions described above and warrants further study to examine the underlying reasons and to develop targeted interventions.

Antibiotic choice

For the respiratory conditions we examined, the general patterns of antibiotic choice reflect the treatment of the specific bacteria that commonly infect the respiratory tract. However, the antibiotics prescribed were often broader spectrum than required, and thus inappropriate as per guidelines. This type of prescribing was most pronounced in the treatment of pneumonia in children. While some use of macrolide antibiotics is acceptable in older children, dispensation rates of non-penicillin or cephalosporin antibiotics were quite high. These are broader spectrum antibiotics than should be used, therefore considered inappropriate. In the multi-level modelling, non-penicillin or cephalosporin antibiotic (or inappropriate) dispensation was associated with older physician age, Charlson comorbidity score of 1, physician location in Prairie Mountain Health, and a higher physician visit rate. Interestingly, among these characteristics, only higher physician age was associated with dispensation of any antibiotic. While dispensation of antibiotics overall was lower in paediatrician visits and majority of care provider visits, these characteristics were not significantly associated with decreased use of inappropriate antibiotics. Choice of antibiotic and indications for antibiotic use in paediatric pneumonia are identified as areas for intervention.

Rates of inappropriate antibiotic choice for SSTIs and UTIs were low and are not currently identified as areas for intervention. However, use of quinolones for UTIs was possibly higher than needed, and may be a target for intervention or further study.

Chapter 7:
Prescriber-Level Outcomes and an Example of a Prescriber Feedback Report

As noted in the introduction, the reasons why some physicians have higher antibiotic dispensation rates, even when their patients have similar characteristics, are multi-factorial and not fully understood. While variability in physicians' basic medical knowledge can be a reason for different dispensation rates, psychosocial reasons are also suspected to be strong drivers of inappropriate prescribing behaviour [21], as are hierarchical relationships between clinicians, the influence of senior or teaching colleagues, and the belief that one does not over-prescribe antibiotics ("It's not me, it's them…") [25]. The strongest evidence-based ASP strategies are prospective audits with feedback to stakeholders on prescribing behaviour and other metrics. This and other forms of persuasive and behaviour-nudging interventions have been shown to lower rates of inappropriate antibiotic prescribing without negatively impacting appropriate forms of antibiotics prescribing [12,13].

One of the objectives of this report was to explore the feasibility of using the data in the Repository to give Manitoba physicians individual-level feedback on their prescribing patterns that could be compared to their peers. This practice is becoming more common where physician overprescribing occurs, such as for opioids [68].

In this chapter, we report prescribing outcomes at the individual level and the distribution of frequent and infrequent prescribers in the different categories of appropriate antibiotic prescribing. We also provide an example of what a prescriber feedback report could look like.

Methods

For each PCP in the study cohort and for each condition examined in Chapter 6 for which the physician had at least 10 visits from 2014-2016, we calculated the percentage of visits to the physician that could be linked to an antibiotic dispensation. If a physician had fewer than ten visits for a condition, we did not examine that condition for that individual. We calculated the distribution of each eligible condition, identifying the 25th, 50th and 75th percentiles of ambulatory primary care physician frequency of prescribing. The number of physicians who were frequent (>75th percentile) prescribers and infrequent (<25th percentile) prescribers for the conditions in each category are presented below. The benchmark was set at less than the 25th percentile.

Results

In the study cohort, there were 1,159 ambulatory PCPs eligible for at least one condition. Among these physicians, 61.4% were eligible in all four conditions in the 'generally does not require antibiotics' category, 12.8% were eligible for three conditions, 16.9% for two conditions and 9.0% for only one condition. For the 'may require antibiotics category', 27.3% of physicians were eligible for all five conditions, 37.4% were eligible for four conditions, 17.5% were eligible for three conditions, 9.5% for two conditions and 8.4% for only one condition.

Table 7.1 presents the percentage of primary care physicians who were frequent or infrequent prescribers in one or more conditions in each category. These findings demonstrate that very few prescribers behaved in an 'all or none' manner. That is, they may have prescribed frequently for some conditions within a category but not others. Similarly, they may have prescribed infrequently for some conditions but not all. Approximately half of all physicians we examined did not achieve the benchmark for at least one condition in a category. Conversely, half of the physicians were not a frequent prescriber for any condition in a category. Approximately 20% of the prescribers were frequent prescribers for two or more of the conditions in each category.

Table 7.1: Frequent and Infrequent Prescribers of Antibiotics Among Ambulatory Primary Care Physicians, by Appropriateness of Antibiotic Dispensation and Number of Conditions, 2014-2016

Physicians with 10 or more visits per condition that resulted in dispensations within 5 days

Number of Conditions	Eligible Prescribers	Ambulatory Primary Care Physicians Linked to Antibiotic Dispensations			
		Frequent Prescribers*		Infrequent Prescribers**	
		N	%	N	%
Antibiotics Generally Not Required					
None	1,229	604	49.15	668	54.35
1+	1,229	439	35.72	334	27.18
2+	1,119	145	12.96	168	15.01
3-4†	911	41	4.50	59	6.48
Antibiotics May Be Required					
None	1,159	503	43.40	590	50.91
1+	1,159	391	33.74	273	23.55
2+	1,062	159	14.97	160	15.07
3+	952	83	8.72	90	9.45
4-5†	749	23	3.07	46	6.14

* Above the 75th percentile of physicians with visits for each condition that are linked to antibiotic dispensations.

** Below the 25th percentile of physicians with visits for each condition that are linked to antibiotic dispensations.

† Categories were combined due to small numbers.

An Example of a Prescriber Feedback Report

We generated an example of a feedback report for an individual prescriber, comparing their dispensation rate to their peers'. In this example, we used the 25th percentile of PCPs as the benchmark for appropriate prescribing, but this value could be adjusted to any benchmark percentile as needed. We also included all PCPs in this example, but the output could be adjusted to include only paediatricians or family physicians.

Figures 7.1 and 7.2 show data generated for this report, representing real practitioners in Manitoba, and demonstrating the variable prescribing practices across different conditions. Depending on the software used to generate the report, the visual representation could vary.

Figure 7.1: Report Card for Primary Care Physician "A" by Appropriateness of Antibiotic Dispensation, 2014-2016

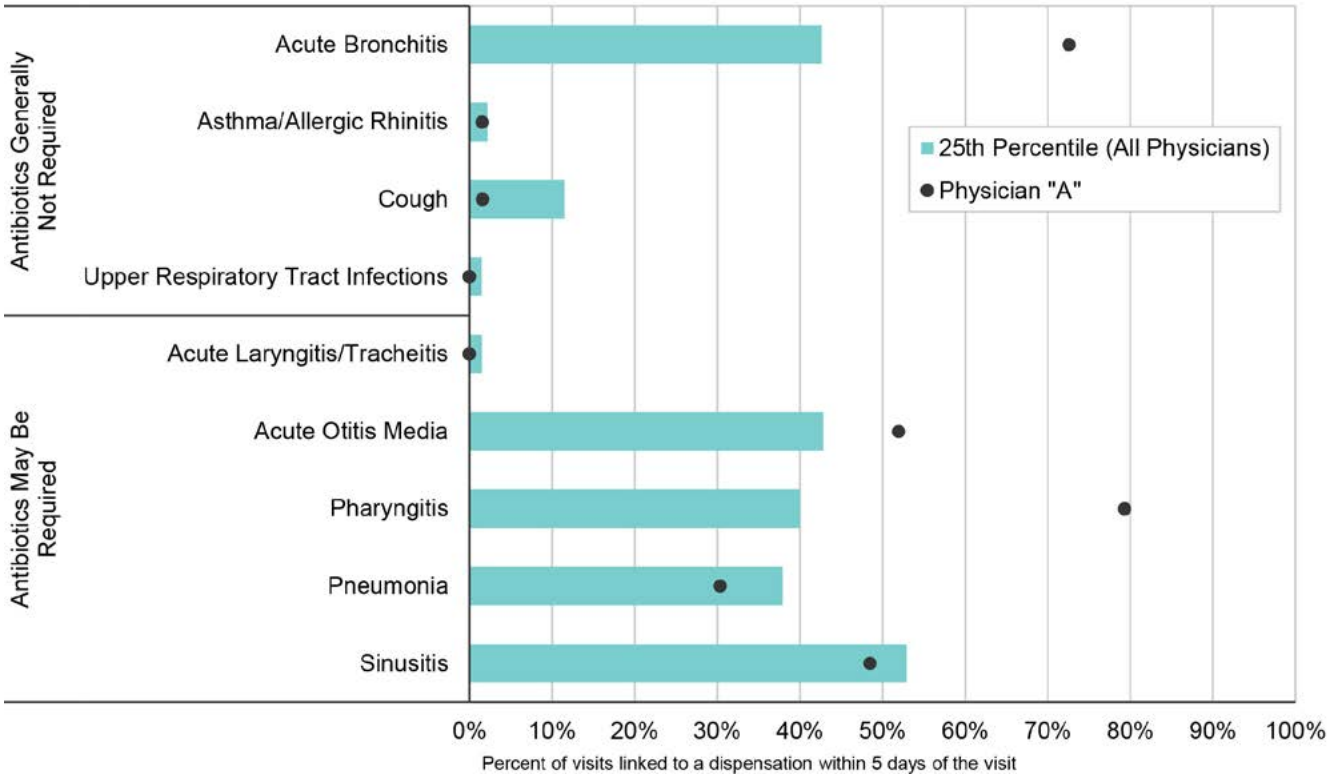
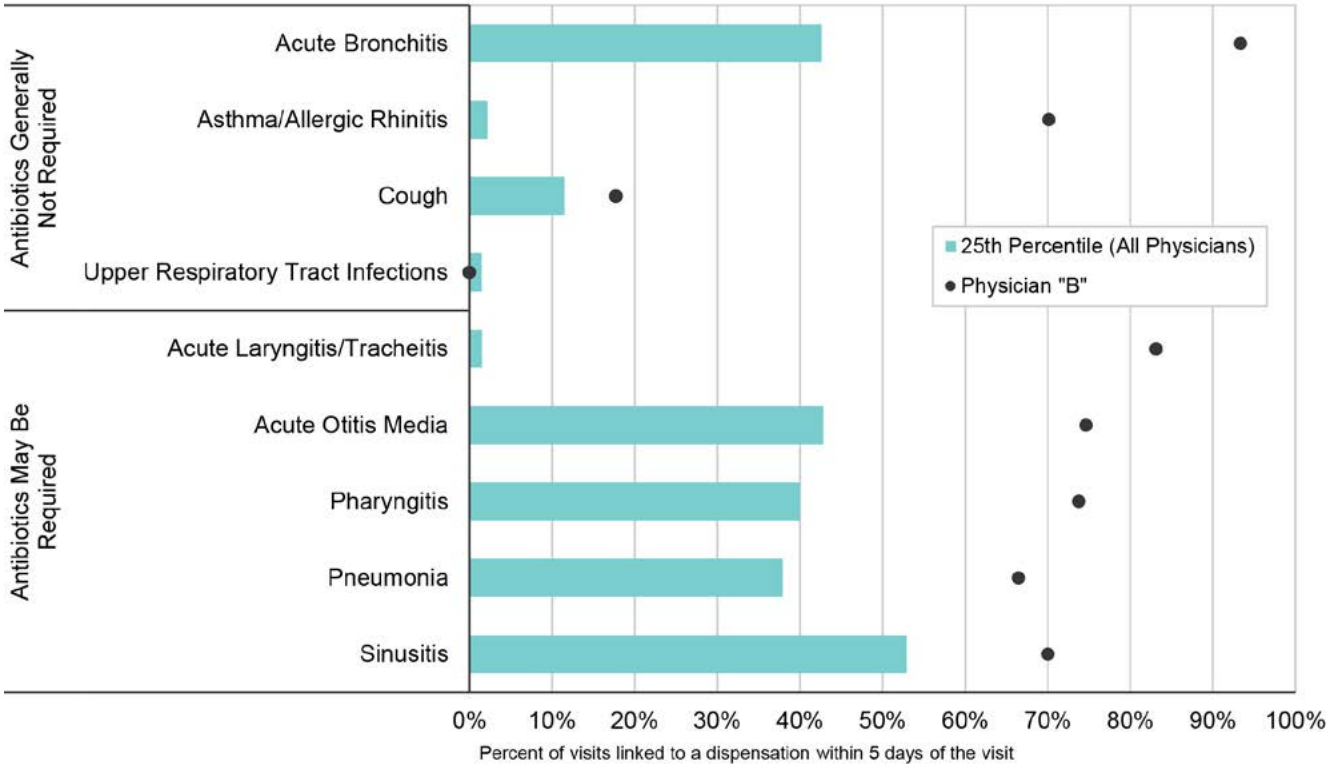


Figure 7.2: Report Card for Primary Care Physician "B" by Appropriateness of Antibiotic Dispensation, 2014-2016



Summary

Examining appropriateness of antibiotic dispensations at the prescriber level demonstrates that there is within-prescriber variability in appropriateness of antibiotic use across groups of conditions, both for conditions that generally do not require antibiotics and for those that may require antibiotics. It is feasible to use data from the Repository to generate prescriber feedback reports, which have been shown to be effective at changing prescribing behaviour with sustained investment over time.

In a study from Pennsylvania, quarterly audit and feedback reports to paediatricians across a large practice network resulted in a 12.5% decrease of inappropriate broad-spectrum antibiotic prescribing over one year [12]. However, once the study closed and the funding to supply the reports was withdrawn, the behavioural nudge was gone, and inappropriate prescribing reverted to pre-intervention levels [69]. Prescriber audits with feedback reports often have their largest impact when combined with other interventions, such as public commitment posters, communication training for prescribers, and electronic medical record reminders/suggestions. As part of one multipronged approach to reducing outpatient antimicrobial use, a study from the United States demonstrated a reduction in inappropriate antimicrobial prescribing from 20% to 4% [13]. In another study, researchers used a combination of online modules, webinars and video teaching vignettes in addition to prescriber feedback reports over a three-year period. Over this long study period, there was a 7% sustained drop in inappropriate antibiotic prescribing for acute respiratory tract infections [70]. If extrapolated to all paediatricians in the United States, this would result in a reduction of 1.5 million antibiotic prescriptions for children with this type of infection.

The Repository data could be used to generate feedback reports as one part of a strategy to reduce inappropriate antibiotic use in Manitoba.

Chapter 8:
Conclusions and Recommendations

Objectives regarding outpatient antibiotic use in Manitoba from 2011 to 2016:

- Comparing Manitoba trends in antibiotic use to worldwide statistics using the European Surveillance of Antibiotic Consumption Network (ESAC-Net) quality indicators
- Examining patterns of health service use in Manitoba, which involved linking antibiotic dispensations to diagnosis codes to assess appropriateness of use and associated factors
- Exploring data at the provider level to ascertain the feasibility of individual provider feedback reports

Chapter 2 outlines the limitations of the data and the report, but it is worth restating the main limitations here. We could only examine antibiotic dispensations (filled prescriptions) but not prescriptions that were written and not filled – this means we may have underestimated how many antibiotics were prescribed. However, even with this limitation, dispensation rates were higher than optimal with wide discrepancies between regions, age groups and providers. We were also unable to identify prescriptions that were filled but not actually taken by the patient, but this is less important to our study because we focused on prescribing practices, not patient behaviour. The other major limitation of the study is the use of ICD-9-CA codes to identify the reason for the antibiotic dispensation. While research suggests the validity of this approach is somewhat variable, it is still widely used, is useful for demonstrating changes in response to interventions aimed at improving antibiotic prescribing behaviour, and remains the best choice at the population level due to its wide coverage and relative ease of use.

Future research on antibiotic stewardship in the community should regularly assess trends over time and investigate in more detail the factors associated with less-than-optimal antibiotic use and possible interventions for the conditions with the highest rates of misuse.

The summary of our findings, major conclusions and recommendations are presented in this chapter.

Antibiotic use among adults is increasing in Manitoba, especially among adults age 65+

Overall rates of antibiotic use increased from 2011 to 2016 among adults. Use of tetracylines, β-lactams (including penicillins and cephalosporins) and sulfonamides was higher in adults in 2016 compared to 2011, while only macrolides and quinolones were lower in adults.

Recommendation

Outpatient ASPs should include prescribing for older adults in their planning.

Antibiotic use among younger adults is increasing, often for conditions that do not require antibiotics

For conditions that generally do not require antibiotics, antibiotic dispensation rates for acute bronchitis and cough increased from 2011-2016. Dispensations for acute bronchitis were not related to patient co-morbidities. For conditions that may require antibiotics, dispensation rates increased for younger adults (ages 15-64) for acute otitis media, pharyngitis, and pneumonia. Higher antibiotic use is associated with increasing antibiotic resistance.

Recommendation

Acute bronchitis and pneumonia are common in adults and may be important conditions to target with antibiotic stewardship programs.

Antibiotic use in children is greater than necessary and often not aligned with evidence-informed recommendations

While rates of antibiotic use overall in children decreased slightly from 2011 to 2016, use of β-lactam penicillins did not change. Seasonal variation in antibiotic use, the bulk of which occurs in children, as measured by the ESAC-Net indicator, was lower in 2016 than 2011. Inappropriate choice of antibiotic was common. For conditions that generally do not need antibiotics, such as acute bronchitis in younger children, rates were higher in 2016 than 2011. For acute otitis media, pharyngitis and pneumonia, rates were also higher in 2016 than 2011. This puts children at risk for both adverse effects from antibiotics as well as furthers antibiotic resistance.

Recommendation

ASPs targeting antibiotic use in children should concentrate on conditions identified as having the highest antibiotic use, such as pneumonia, pharyngitis and acute otitis media, and should also address choice of antibiotic, which was frequently inappropriate.

Canadian recommendations for the conditions that need antibiotics, or the type of antibiotic needed are not being consistently followed

We saw substantial use of inappropriate antibiotics and/or antibiotics reserved for special circumstances as per guidelines. This was most pronounced in treatment of pneumonia in children, where rates of any antibiotic use were high (approximately 50%); an inappropriate antibiotic was dispensed in 52.4% of dispensations in children less than 15 years old and 40.4% of dispensations in children under five years old. While some use of macrolide antibiotics is acceptable in older children, rates of non-penicillin or cephalosporin antibiotics were high.

In all ages, acute otitis media was treated with an inappropriate antibiotic in 23.4% of health care visits in which an antibiotic was dispensed, and pharyngitis was treated with an inappropriate antibiotic 30.4% of the time (8.7% if all of the substitutions occurred because of allergy). Use of quinolones for UTIs was possibly higher than needed at 40.1%, as quinolones are not recommended as the first choice for treating UTIs.

Recommendation

ASPs for paediatric pneumonia and otitis media in all ages should address not only high rates of antibiotic use but frequent inappropriate choice of antibiotic and should emphasize that non-recommended antibiotics may be less effective, have more adverse effects, and are likely to drive antibiotic resistance.

There are mixed results for use of broad-spectrum vs narrow-spectrum antibiotics

Using the ESAC-Net quality indicators, we demonstrated increasing use of broader-spectrum penicillins and decreasing use of narrower-spectrum penicillins. A reduction in broad-spectrum cephalosporins was seen, but there was no change in the ratio of commonly used broad- to narrow-spectrum antibiotics as a group (penicillins, cephalosporins, macrolides) from 2011-2016. This is inappropriate as the narrowest spectrum of antibiotic is generally more appropriate.

Recommendation

ASPs should pay attention to reducing use of broader-spectrum penicillins such as amoxicillin/clavulanic acid where appropriate and encouraging use of narrower-spectrum penicillins such as amoxicillin.

It's not just physicians who prescribe antibiotics

In 2014-2016, approximately 15% of antibiotics dispensed were prescribed by non-physicians. Dentists accounted for 9.3% and nurse practitioners for 3.5% of prescribers, with other health care professionals making up the rest.

Recommendation

Outpatient ASPs need to include non-physicians in their discussions, planning, messaging and programming. Data systems should allow for ongoing audit and feedback of all prescribers.

Certain primary care physician characteristics are consistently associated with higher dispensation rates

After adjusting for patient characteristics, dispensations for conditions that generally do not require antibiotics were consistently associated with older physician age and higher physician visit rates (indicating higher patient load). Dispensations for conditions that may require antibiotics were consistently associated with receipt of medical training outside of Canada/United States and higher patient load.

Recommendation

The planning and implementation stages of ASPs should include consultation with older physicians, physicians trained outside of Canada/United States and physicians with high patient loads.

Visits to a majority of care provider are associated with lower antibiotic dispensation rates, and when dispensed, are more likely to be appropriate

For almost all conditions we examined, a physician who saw a patient for more than 50% of the patient's primary care visits was less likely to prescribe that patient antibiotics than a physician who was not the majority of care provider. Having a majority of care provider was also associated with a decreased likelihood of the patient receiving an inappropriate antibiotic for pharyngitis and acute otitis media, but not for pneumonia.

Recommendation

Address system issues that limit access to PCPs. Encourage patients to seek care from their most responsible physician when possible, especially for what appear to be minor conditions that "just require an antibiotic".

Dispensation rates vary by health region for many conditions and antibiotic classes

Prairie Mountain Health had consistently higher antibiotic dispensation rates. For specific indicators patterns varied for other Health Regions. In Northern Health Region, patterns of dispensation were variable and there were known differences in prescribing practices due to care at nursing stations.

Recommendation

Health regions in Manitoba can use the data provided in this report to tailor their regional programs. Additional data are available for each individual health region in the online supplement.

Prescriber-level feedback reports are feasible with the data available

Examples of antibiotic prescribing feedback are provided in this report. Prescriber-level data demonstrate that approximately half of primary care physicians do not achieve the benchmark of dispensation rates in the lowest 25th percentile for at least one condition (within each category of conditions). Approximately 20% of prescribers are frequent prescribers (higher than the 75th percentile) in two or more conditions (within each category).

Recommendation

A program to provide prescribers with regular, sustained and specific feedback on their antibiotic prescribing in comparison to their peers is recommended as an evidence supported method of improving antibiotic use.

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Appendix 1: Additional Dispensation Trends (Chapter 3)

All Antibiotics (J01)

Appendix Table 1.1: Statistical Comparisons of Quarterly Dispensation Rates for Antibiotics Overall (J01) by Health Region
Age- and sex-adjusted rates per 1,000 people per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**1.72**	1.91	**2.63**	2.06	1.86	1.98
2	**1.55**	1.70	**2.28**	**1.90**	1.76	1.77
3	**1.39**	1.54	**2.04**	**1.79**	1.69	1.62
4	**1.55**	1.77	**2.41**	**2.00**	1.76	1.83
2012						
1	**1.67**	1.85	**2.47**	**2.12**	**1.69**	1.92
2	**1.55**	1.71	**2.32**	**1.95**	1.69	1.78
3	**1.43**	1.57	**2.13**	**1.89**	1.77	1.67
4	**1.69**	1.88	**2.58**	**2.08**	**1.76**	1.94
2013						
1	**1.64**	1.86	**2.45**	**2.10**	**1.77**	1.93
2	**1.57**	1.73	**2.32**	**1.94**	**1.67**	1.80
3	**1.44**	1.54	**2.07**	**1.80**	1.68	1.63
4	**1.57**	1.70	**2.26**	**1.92**	1.69	1.77
2014						
1	**1.63**	1.77	**2.39**	**2.01**	**1.67**	1.84
2	**1.51**	1.67	**2.21**	**1.91**	**1.52**	1.73
3	**1.47**	1.67	**2.11**	**1.88**	**1.60**	1.72
4	**1.62**	1.87	**2.37**	2.00	**1.61**	1.89
2015						
1	**1.83**	1.97	**2.67**	**2.22**	**1.79**	2.05
2	**1.59**	1.73	**2.32**	**1.99**	**1.64**	1.81
3	**1.44**	1.59	**2.03**	**1.80**	1.72	1.66
4	**1.51**	1.72	**2.22**	**1.94**	1.80	1.77
2016						
1	**1.71**	1.94	**2.59**	**2.19***	1.90	2.00
2	**1.52**	1.69	**2.29**	**1.90**	1.81	1.77
3	**1.40**	1.59	**2.06**	**1.78**	**1.79**	1.65
4	**1.58**	1.83	**2.34**	1.95	1.75	1.86

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Appendix Table 1.2: Statistical Comparisons of Quarterly Dispensation Rates for Antibiotics Overall (J01) for Adults by Health Region
Age- and sex-adjusted rates per 1,000 people ages 15 and older per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**1.72**	1.88	**2.49**	2.09	2.07	1.96
2	**1.59**	1.74	**2.25**	**1.98**	**1.99**	1.82
3	**1.46**	1.61	**2.05**	**1.87**	**1.90**	1.68
4	**1.60**	1.78	**2.35**	**2.02**	1.96	1.85
2012						
1	**1.69**	1.87	**2.44**	**2.14**	1.91	1.95
2	**1.60**	1.75	**2.27**	**1.99**	1.92	1.82
3	**1.50**	1.64	**2.14**	**1.95**	**1.96**	1.73
4	**1.69**	1.84	**2.49**	**2.07**	1.97	1.92
2013						
1	**1.68**	1.90	**2.38**	**2.15**	1.98	1.96
2	**1.63**	1.77	**2.28**	**2.00**	1.90	1.84
3	**1.53**	1.62	**2.10**	**1.86**	**1.90**	1.71
4	**1.61**	1.74	**2.24**	**1.96**	1.92	1.81
2014						
1	**1.64**	1.77	**2.32**	**2.03**	1.90	1.85
2	**1.58**	1.72	**2.20**	**1.99**	1.76	1.79
3	**1.56**	1.74	**2.13**	**1.96**	1.84	1.80
4	**1.68**	1.89	**2.33**	**2.06**	1.85	1.93
2015						
1	**1.83**	2.01	**2.55**	**2.25**	2.00	2.08
2	**1.65**	1.77	**2.29**	**2.05**	1.86	1.86
3	**1.54**	1.68	**2.08**	**1.87**	**1.94**	1.75
4	**1.58**	1.76	**2.23**	**2.01**	**2.03**	1.83
2016						
1	**1.73**	1.92	**2.46**	**2.19**	2.12	1.99
2	**1.58**	1.75	**2.27**	**1.98**	**2.02**	1.83
3	**1.51**	1.68	**2.10**	**1.87**	**2.04***	1.75
4	**1.63**	1.86	**2.32**	2.00	1.99	1.90

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Appendix Table 1.3: Statistical Comparisons of Quarterly Dispensation Rates for Antibiotics Overall (J01) for Children by Health Region
Age- and sex-adjusted rates per 1,000 people ages 0-14 per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**1.67**	2.06	**3.24**	1.95	**1.16**	2.05
2	1.38	1.55	**2.42**	1.57	**1.01**	1.58
3	**1.10**	1.29	**2.01**	1.45	**1.00**	1.34
4	**1.32**	1.70	**2.67**	1.91	**1.08**	1.72
2012						
1	1.57	1.76	**2.59**	2.02	**1.00**	1.79
2	**1.34**	1.53	**2.50**	1.77	**0.93**	1.59
3	**1.14**	1.29	**2.07**	**1.63**	**1.13**	1.38
4	**1.68**	2.05	**2.95**	2.12	**1.08**	2.01
2013						
1	**1.47**	1.67	**2.76**	1.90	**1.07**	1.74
2	**1.30**	1.54	**2.46**	1.67	**0.91**	1.57
3	**1.05**	1.21	**1.91**	**1.51**	**0.98**	1.28
4	1.40	1.52	**2.32**	1.74	**0.94**	1.57
2014						
1	1.57	1.73	**2.70**	1.95	**0.94**	1.77
2	**1.20**	1.43	**2.21**	1.60	**0.75**	1.45
3	**1.09**	1.35	**1.99**	1.54	**0.82**	1.36
4	**1.38**	1.79	**2.51**	1.74	**0.84**	1.72
2015						
1	1.77	1.82	**3.11**	2.04	**1.09**	1.93
2	**1.30**	1.53	**2.42**	1.73	**0.91**	1.57
3	**1.03**	1.19	**1.83**	**1.50**	**0.99**	1.25
4	**1.19**	1.53	**2.18**	1.63	**1.05**	1.52
2016						
1	**1.59**	2.03	**3.10**	2.16	**1.14**	2.02
2	**1.24**	1.45	**2.39**	1.58	**1.11**	1.51
3	**0.97***	1.18	**1.86**	1.42	**0.96**	1.23
4	**1.32**	1.73	**2.40**	1.71	**0.96**	1.67

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Tetracyclines (J01A)

Appendix Table 1.4: Statistical Comparisons of Quarterly Dispensation Rates for Tetracyclines (J01A) for Adults by Health Region
Age- and sex-adjusted rates per 1,000 people ages 15 and older per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	0.11	0.12	0.12	0.10	0.10	0.11
2	0.12	0.11	0.12	0.11	**0.09**	0.11
3	0.10	0.10	0.11	0.10	0.09	0.10
4	0.11	0.11	0.11	0.10	0.09	0.11
2012						
1	0.11	0.11	0.12	0.12	0.10	0.11
2	0.12	0.11	0.14	0.13	0.11	0.12
3	0.10	0.11	0.11	0.11	0.11	0.11
4	0.11	0.12	0.12	0.11	0.12	0.11
2013						
1	0.11	0.12	0.12	0.12	0.12	0.12
2	0.12	0.12	0.14	0.13	0.12	0.12
3	0.12	0.11	0.13	0.11	0.11	0.12
4	0.12	0.12	0.13	0.11	0.12	0.12
2014						
1	0.12	0.12	0.13	0.11	0.11	0.12
2	0.12	0.12	0.14	0.13	0.10	0.12
3	0.12	0.12	0.13	0.12	0.11	0.12
4	0.13	0.12	0.14	0.12	0.13	0.13
2015						
1	0.13	0.13	0.14	0.13	0.12	0.13
2	0.15	0.13	0.17	0.15	0.12	0.14
3	0.12	0.12	0.15	0.12	0.13	0.13
4	0.12	0.12	0.13	0.12	0.13	0.12
2016						
1	0.13	0.13	0.14*	0.12*	0.13*	0.13
2	0.15*	0.13	**0.19***	0.15*	0.16*	0.15*
3	0.12*	0.12*	0.14*	0.13*	0.15*	0.13*
4	0.12	0.13*	0.14*	0.13*	0.15*	0.13*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

β-Lactam Penicillins (J01C)

Appendix Table 1.5: Statistical Comparisons of Quarterly Dispensation Rates for β-Lactam Penicillins (J01C) for Adults by Health Region
Age- and sex-adjusted rates per 1,000 people ages 15 and older per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**0.56**	0.59	**0.81**	0.60	0.65	0.62
2	**0.51**	0.55	**0.76**	0.59	**0.64**	0.57
3	**0.45**	0.48	**0.66**	0.50	**0.62**	0.51
4	**0.49**	0.55	**0.76**	0.57	**0.65**	0.57
2012						
1	**0.55**	0.59	**0.80**	0.62	0.61	0.61
2	**0.51**	0.55	**0.74**	0.55	0.62	0.57
3	**0.45**	0.49	**0.67**	0.51	**0.57**	0.51
4	**0.54**	0.57	**0.83**	0.57	0.60	0.60
2013						
1	**0.53**	0.58	**0.77**	0.59	0.61	0.60
2	0.53	0.55	**0.74**	0.54	0.58	0.57
3	**0.45**	0.49	**0.64**	0.48	**0.55**	0.50
4	**0.50**	0.53	**0.74**	0.56	0.58	0.56
2014						
1	**0.52**	0.56	**0.74**	0.59	0.60	0.58
2	**0.49**	0.53	**0.71**	0.56	0.54	0.55
3	**0.44**	0.52	**0.65**	0.54	0.54	0.53
4	**0.51**	0.60	**0.74**	0.61	0.56	0.60
2015						
1	**0.58**	0.65	**0.86**	0.68	0.63	0.66
2	**0.50**	0.57	**0.75**	0.60	0.58	0.59
3	**0.42**	0.51	**0.62**	0.53	0.56	0.51
4	**0.47**	0.56	**0.70**	0.62	**0.64**	0.58
2016						
1	**0.55**	0.63*	**0.80**	0.68*	0.67	0.64
2	**0.47***	0.57	**0.71**	0.59	0.61	0.58
3	**0.43**	0.52*	**0.65**	0.53	**0.60**	0.53
4	**0.50**	0.60*	**0.73**	0.62*	0.60	0.61*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Appendix Table 1.6: Statistical Comparisons of Quarterly Dispensation Rates for β-Lactam Penicillins (J01C) for Children by Health Region

Age- and sex-adjusted rates per 1,000 people ages 0-14 per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**1.03**	1.30	**1.73**	1.11	**0.68**	1.23
2	0.85	0.96	**1.33**	0.87	**0.53**	0.94
3	**0.63**	0.77	**1.07**	0.77	**0.56**	0.76
4	**0.79**	1.09	**1.42**	1.09	**0.63**	1.03
2012						
1	1.03	1.17	**1.43**	1.15	**0.61**	1.12
2	0.83	0.98	**1.42**	1.01	**0.55**	0.97
3	**0.62**	0.77	**1.12**	0.84	**0.53**	0.77
4	**1.01**	1.31	**1.70**	1.20	**0.62**	1.23
2013						
1	0.90	1.06	**1.60**	1.09	**0.55**	1.05
2	**0.77**	0.98	**1.43**	0.93	**0.48**	0.95
3	**0.58**	0.71	**1.05**	0.75	**0.47**	0.71
4	0.89	0.96	**1.29**	0.99	**0.48**	0.95
2014						
1	1.02	1.15	**1.57**	1.18	**0.53**	1.12
2	**0.71**	0.92	**1.32**	0.94	**0.44**	0.89
3	**0.63**	0.84	**1.13**	0.88	**0.43**	0.80
4	**0.83**	1.15	**1.45**	1.07	**0.46**	1.06
2015						
1	1.14	1.22	**1.81**	1.29	**0.62**	1.23
2	**0.80**	0.98	**1.39**	1.08	**0.54**	0.97
3	**0.55**	0.72	**1.00**	0.83	**0.48**	0.71
4	**0.72**	0.99	**1.20**	1.00	**0.55**	0.92
2016						
1	**1.02**	1.34	**1.75**	1.38*	**0.63**	1.27
2	**0.76**	0.94	**1.30**	0.94	**0.65***	0.93
3	**0.53***	0.70	**0.99**	0.75	**0.45***	0.69
4	**0.84**	1.13	**1.31**	1.03	**0.52***	1.04

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Extended-Spectrum Penicillins (J01CA)

Appendix Table 1.7: Statistical Comparisons of Quarterly Dispensation Rates for Extended Spectrum Penicillins (J01CA) for Adults by Health Region

Age- and sex-adjusted rates per 1,000 people ages 15 and older per day

Year and Quarter	Age- and Sex0Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	0.39	0.45	0.56	0.40	0.45	0.45
2	0.32	0.38	0.48	0.38	0.43	0.39
3	0.27	0.32	0.41	0.30	0.39	0.33
4	0.33	0.39	**0.51**	0.36	0.45	0.40
2012						
1	0.37	0.43	**0.55**	0.39	0.38	0.43
2	0.34	0.39	**0.49**	0.35	0.42	0.39
3	0.30	0.33	0.42	0.32	0.35	0.34
4	0.37	0.42	**0.55**	0.37	0.41	0.43
2013						
1	0.36	0.43	0.52	0.38	0.41	0.42
2	0.38	0.40	0.47	0.34	0.38	0.40
3	0.30	0.34	0.41	0.29	0.37	0.34
4	0.33	0.39	**0.50**	0.36	0.41	0.39
2014						
1	0.35	0.40	0.49	0.39	0.39	0.40
2	0.34	0.38	0.47	0.37	0.37	0.39
3	0.29	0.36	0.40	0.34	0.36	0.35
4	0.35	0.43	0.49	0.40	0.35	0.42
2015						
1	0.40	0.46	0.58	0.44	0.40	0.46
2	0.35	0.40	0.49	0.38	0.38	0.40
3	0.28	0.34	0.38	0.32	0.34	0.34
4	0.32	0.39	0.46	0.39	0.42	0.39
2016						
1	0.36	0.44	0.52	0.43	0.43	0.44
2	0.31	0.40	0.46	0.37	0.37	0.39
3	**0.27**	0.35	0.42	0.33	0.37	0.35
4	0.34	0.41	0.47	0.39	0.39	0.41

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Appendix Table 1.8: Statistical Comparisons of Quarterly Dispensation Rates for Extended Spectrum Penicillins (J01CA) for Children by Health Region

Age- and sex-adjusted rates per 1,000 people ages 0-14 per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**0.90**	1.17	**1.49**	0.99	**0.53**	1.09
2	0.74	0.86	**1.12**	0.74	**0.40**	0.82
3	**0.54**	0.69	**0.91**	0.68	**0.41**	0.67
4	**0.70**	0.97	**1.21**	0.99	**0.50**	0.91
2012						
1	0.93	1.05	**1.26**	1.02	**0.49**	1.00
2	0.76	0.89	**1.24**	0.94	**0.44**	0.88
3	**0.55**	0.71	**0.93**	0.74	**0.44**	0.69
4	**0.93**	1.18	**1.51**	1.08	**0.51**	1.10
2013						
1	0.84	0.98	**1.42**	0.98	**0.45**	0.96
2	**0.70**	0.89	**1.25**	0.81	**0.39**	0.85
3	**0.53**	0.64	**0.92**	0.64	**0.36**	0.63
4	0.80	0.87	**1.14**	0.88	**0.38**	0.85
2014						
1	0.93	1.05	**1.38**	1.07	**0.45**	1.02
2	**0.65**	0.85	**1.17**	0.84	**0.36**	0.81
3	**0.57**	0.79	**0.98**	0.78	**0.36**	0.74
4	**0.76**	1.06	**1.30**	0.96	**0.36**	0.96
2015						
1	1.07	1.12	**1.63**	1.19	**0.50**	1.13
2	**0.73**	0.90	**1.26**	0.95	**0.45**	0.88
3	**0.52**	0.65	**0.87**	0.74	**0.39**	0.64
4	**0.65**	0.88	**1.04**	0.89	**0.44**	0.82
2016						
1	**0.96**	1.23	**1.57**	1.24*	**0.53**	1.16
2	**0.70**	0.88	**1.19**	0.86*	**0.56***	0.86
3	**0.48**	0.65	**0.87**	0.66	**0.39**	0.63
4	**0.76**	1.04	**1.14**	0.96	**0.42***	0.94

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

β-Lactamase Inhibitor Combinations (J01CR)

Appendix Table 1.9: Statistical Comparisons of Quarterly Dispensation Rates for β-Lactamase Inhibitor Combinations (J01CR) for Adults by Health Region

Age- and sex-adjusted rates per 1,000 people ages 15 and older per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	0.06	**0.04**	**0.12**	**0.10**	0.07	0.06
2	0.05	**0.05**	**0.12**	**0.09**	0.08	0.06
3	0.05	**0.04**	**0.11**	**0.09**	0.08	0.06
4	0.06	**0.05**	**0.11**	**0.09**	0.07	0.06
2012						
1	0.06	**0.05**	**0.12**	**0.11**	0.07	0.07
2	0.06	**0.05**	**0.12**	**0.09**	0.08	0.07
3	0.06	**0.05**	**0.13**	0.09	**0.10**	0.07
4	0.06	**0.06**	**0.15**	**0.11**	0.09	0.08
2013						
1	0.07	**0.06**	**0.15**	**0.12**	0.10	0.08
2	0.07	0.07	**0.14**	**0.11**	0.10	0.08
3	0.06	0.06	**0.13**	**0.10**	0.08	0.08
4	0.07	0.06	**0.14**	**0.11**	0.09	0.08
2014						
1	0.07	0.07	**0.14**	0.10	0.09	0.08
2	0.07	0.07	**0.14**	0.11	0.10	0.09
3	0.07	0.08	**0.14**	0.11	0.10	0.09
4	0.08	0.09	**0.15**	0.13	0.11	0.10
2015						
1	0.10	0.10	**0.18**	0.14	0.15	0.12
2	0.08	0.09	**0.16**	0.13	0.12	0.10
3	**0.07**	0.08	**0.14**	0.11	**0.12**	0.09
4	**0.08**	0.10	**0.15**	0.13	0.12	0.11
2016						
1	0.09*	0.11*	**0.18***	0.15*	0.15*	0.12*
2	**0.08***	0.10*	**0.16***	0.13*	**0.16***	0.11*
3	0.08*	0.09*	**0.14***	0.11	**0.15***	0.10*
4	**0.09***	0.12*	**0.17***	0.14*	0.14*	0.12*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).

* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Appendix Table 1.10: Statistical Comparisons of Quarterly Dispensation Rates for β-Lactamase Inhibitor Combinations (J01CR) for Children by Health Region

Age- and sex-adjusted rates per 1,000 people ages 0-14 per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**0.05**	**0.05**	**0.16**	0.06	0.05	0.06
2	0.04	**0.04**	**0.14**	0.06	0.04	0.05
3	**0.03**	**0.03**	**0.11**	**0.06**	0.05	0.04
4	**0.03**	**0.03**	**0.12**	0.06	0.05	0.05
2012						
1	0.05	**0.04**	**0.15**	0.07	0.05	0.06
2	**0.04**	**0.05**	**0.16**	0.07	0.07	0.06
3	**0.04**	**0.03**	**0.16**	0.08	0.07	0.06
4	**0.05**	**0.06**	**0.18**	0.08	0.07	0.08
2013						
1	**0.04**	**0.05**	**0.17**	**0.09**	0.05	0.07
2	**0.05**	**0.05**	**0.18**	0.07	0.05	0.07
3	0.05	**0.04**	**0.12**	**0.09**	0.06	0.06
4	0.05	**0.04**	**0.12**	**0.08**	0.05	0.06
2014						
1	**0.04**	**0.05**	**0.13**	0.07	0.05	0.06
2	**0.04**	**0.04**	**0.13**	0.08	0.05	0.06
3	**0.04**	**0.04**	**0.13**	**0.08**	0.05	0.05
4	**0.04**	**0.04**	**0.14**	0.07	0.06	0.06
2015						
1	**0.04**	**0.05**	**0.16**	0.09	0.08	0.07
2	**0.04**	**0.04**	**0.15**	**0.10**	0.07	0.06
3	**0.04**	**0.04**	**0.11**	0.07	0.07	0.06
4	**0.04**	**0.04**	**0.11**	0.07	0.07	0.06
2016						
1	**0.04**	**0.03***	**0.11***	**0.08***	0.06	0.05*
2	0.04	**0.03**	**0.11***	**0.07**	0.06*	0.05
3	0.03	**0.03**	**0.10**	**0.06**	0.05	0.04
4	0.04	**0.04***	**0.12**	0.05	0.07	0.05

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

β-Lactamase-Resistant Penicillins (J01CF)

Appendix Table 1.11: Statistical Comparisons of Quarterly Dispensation Rates for β-Lactamase-Resistant Penicillins (J01CF) for Adults by Health Region

Age- and sex-adjusted rates per 1,000 people ages 15 and older per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	0.04	0.04	**0.06**	0.04	0.06	0.04
2	0.05	0.04	**0.07**	0.05	0.06	0.05
3	0.05	0.04	**0.08**	0.05	**0.08**	0.05
4	0.04	0.03	**0.06**	0.04	**0.06**	0.04
2012						
1	0.04	0.03	**0.06**	0.03	**0.05**	0.04
2	0.04	0.04	**0.06**	0.04	0.05	0.04
3	0.04	0.04	**0.06**	0.04	0.04	0.04
4	0.04	0.03	**0.05**	0.03	0.03	0.03
2013						
1	0.03	0.03	**0.04**	0.03	0.03	0.03
2	0.03	0.03	**0.06**	0.03	0.03	0.03
3	0.04	0.03	**0.05**	0.03	0.03	0.03
4	0.03	0.02	**0.04**	0.03	0.02	0.03
2014						
1	0.03	0.02	**0.04**	0.02	**0.02**	0.03
2	0.03	0.02	**0.04**	0.03	**0.01**	0.03
3	0.03	0.02	**0.05**	0.03	**0.01**	0.03
4	0.02	0.02	**0.04**	0.02	**0.01**	0.02
2015						
1	0.02	0.02	**0.04**	0.02	**0.01**	0.02
2	0.03	0.02	**0.04**	0.02	**0.01**	0.02
3	0.03	0.02	**0.04**	0.03	**0.01**	0.03
4	0.02	0.02	**0.04**	0.02	**0.01**	0.02
2016						
1	0.02*	0.02*	**0.03***	0.02*	**0.01***	0.02*
2	0.02*	0.02*	**0.04***	0.02*	**0.01***	0.02*
3	0.02*	0.02*	**0.04***	0.02*	**0.01***	0.02*
4	0.02*	0.02*	**0.04***	0.02*	**0.01***	0.02*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Appendix Table 1.12: Statistical Comparisons of Quarterly Dispensation Rates for β-Lactamase-Resistant Penicillins (J01CF) for Children by Health Region

Age- and sex-adjusted rates per 1,000 people ages 0-14 per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	0.03	**0.02**	0.03	0.03	**0.04**	0.03
2	0.03	**0.02**	**0.05**	0.03	0.03	0.03
3	0.03	**0.02**	0.05	0.03	**0.07**	0.03
4	0.02	**0.01**	**0.04**	0.01	0.03	0.02
2012						
1	0.02	0.01	0.03	0.02	0.02	0.02
2	0.01	0.01	**0.03**	0.02	0.01	0.01
3	0.02	0.01	0.02	0.02	0.02	0.01
4	0.01	**0.00**	**0.01**	0.01	0.01	0.01
2013						
1	0.01	0.00	**0.01**	0.01	0.01	0.01
2	0.01	0.00	**0.01**	0.01	0.01	0.01
3	0.01	0.01	**0.02**	0.01	0.01	0.01
4	0.01	0.00	**0.01**	0.00	0.01	0.01
2014						
1	0.01	0.00	**0.01**	0.00	0.00	0.00
2	0.00	0.00	**0.01**	0.01	0.00	0.01
3	0.01	**0.01**	**0.02**	0.01	0.00	0.01
4	**0.01**	**0.00**	**0.01**	0.01	0.00	0.01
2015						
1	0.00	0.01	**0.01**	0.01	0.00	0.01
2	0.01	0.00	**0.01**	0.01	0.00	0.01
3	**0.01**	0.01	**0.03**	0.02	0.02	0.02
4	0.01	0.01	0.01	**0.01**	0.01	0.01
2016						
1	0.01*	0.00*	0.01*	0.01*	0.00*	0.01*
2	0.01*	0.00*	**0.01***	0.00*	0.00*	0.01*
3	0.01*	**0.01***	**0.02***	0.01*	**0.00***	0.01*
4	**0.01***	**0.00***	**0.01***	0.00*	s	0.01*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
s Indicates suppression due to small numbers.
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Cephalosporins (J01D)

Appendix Table 1.13: Statistical Comparisons of Quarterly Dispensation Rates for Cephalosporins (J01D) for Adults by Health Region
Age- and sex-adjusted rates per 1,000 people ages 15 and older per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**0.16**	**0.17**	**0.27**	**0.22**	0.19	0.19
2	0.19	**0.18**	**0.26**	**0.24**	**0.23**	0.20
3	0.20	**0.19**	**0.27**	**0.26**	0.23	0.21
4	0.18	**0.18**	**0.27**	**0.23**	0.21	0.20
2012						
1	**0.18**	**0.17**	**0.27**	**0.23**	0.19	0.19
2	0.19	**0.19**	**0.27**	**0.26**	0.20	0.21
3	0.21	**0.20**	**0.28**	**0.28**	0.24	0.23
4	**0.17**	**0.18**	**0.26**	0.21	0.21	0.19
2013						
1	**0.17**	**0.18**	**0.24**	**0.22**	0.21	0.19
2	**0.18**	0.20	**0.25**	**0.25**	0.20	0.21
3	0.23	**0.21**	**0.27**	**0.26**	0.23	0.23
4	0.19	**0.18**	**0.26**	0.22	0.20	0.20
2014						
1	0.18	**0.17**	**0.24**	**0.22**	0.18	0.19
2	0.20	**0.19**	**0.25**	**0.25**	0.19	0.21
3	0.21	0.21	**0.26**	**0.25**	0.22	0.23
4	0.19	**0.19**	**0.26**	0.22	0.19	0.20
2015						
1	0.20	0.19	**0.25**	0.21	0.18	0.20
2	0.21	**0.20**	**0.26**	**0.25**	0.22	0.22
3	0.22	0.22	**0.27**	**0.26**	0.25	0.23
4	**0.18**	**0.18**	**0.25**	**0.22**	**0.23**	0.20
2016						
1	**0.18***	**0.18***	**0.27**	0.21	0.20	0.20
2	0.20	**0.20***	**0.27**	**0.24**	0.22	0.21
3	0.22*	0.21*	**0.27**	0.24	0.22	0.22
4	**0.18**	0.19*	**0.27**	0.21*	0.19	0.20

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Appendix Table 1.14: Statistical Comparisons of Quarterly Dispensation Rates for Cephalosporins (J01D) for Children by Health Region
Age- and sex-adjusted rates per 1,000 people ages 0-14 per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**0.19**	0.26	**0.56**	0.29	**0.19**	0.28
2	**0.19**	0.23	**0.45**	0.29	**0.20**	0.26
3	**0.22**	0.26	**0.47**	**0.36**	0.24	0.29
4	**0.20**	0.23	**0.53**	**0.34**	**0.20**	0.27
2012						
1	**0.19**	0.23	**0.47**	**0.34**	**0.16**	0.26
2	**0.20**	0.22	**0.45**	**0.32**	**0.16**	0.25
3	**0.24**	**0.25**	**0.44**	**0.42**	0.30	0.29
4	**0.21**	0.26	**0.46**	0.33	**0.18**	0.27
2013						
1	**0.19**	0.23	**0.40**	**0.32**	0.22	0.25
2	**0.21**	0.24	**0.39**	0.31	**0.17**	0.25
3	**0.23**	0.25	**0.39**	**0.39**	0.24	0.28
4	**0.19**	0.22	**0.38**	**0.30**	**0.19**	0.24
2014						
1	**0.19**	0.21	**0.40**	0.28	**0.16**	0.23
2	0.22	0.23	**0.41**	**0.30**	**0.13**	0.25
3	0.23	0.25	**0.41**	**0.33**	**0.21**	0.27
4	0.23	0.22	**0.43**	0.24	**0.15**	0.24
2015						
1	0.23	**0.22**	**0.51**	0.25	**0.17**	0.25
2	**0.19**	0.22	**0.42**	0.24	**0.16**	0.24
3	0.20	0.20	**0.36**	**0.29**	0.22	0.23
4	**0.15**	0.17	**0.38**	0.21	0.19	0.20
2016						
1	**0.19**	0.23*	**0.51**	0.24	0.21	0.26
2	**0.20**	0.20*	**0.46**	0.25	**0.19**	0.24
3	0.21	0.22*	**0.42**	**0.31**	0.21	0.25*
4	**0.18**	0.20*	**0.45***	0.24*	**0.15***	0.23*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Sulfonamides and Trimethoprims (J01E)

Appendix Table 1.15: Statistical Comparisons of Quarterly Dispensation Rates for Sulfonamides and Trimethoprims (J01E) for Adults by Health Region

Age- and sex-adjusted rates per 1,000 people ages 15 and older per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	0.12	0.11	0.13	0.13	**0.20**	0.12
2	0.12	0.11	0.12	0.13	**0.19**	0.12
3	0.12	0.12	0.13	0.13	**0.20**	0.12
4	0.12	0.11	0.13	0.12	**0.19**	0.12
2012						
1	0.12	0.12	0.13	0.13	**0.19**	0.12
2	0.11	0.11	0.11	0.11	**0.17**	0.11
3	0.12	0.10	0.12	0.12	**0.20**	0.12
4	0.12	0.11	0.12	0.13	**0.20**	0.12
2013						
1	0.11	0.11	0.12	0.11	**0.18**	0.11
2	0.11	0.11	0.12	0.11	**0.18**	0.12
3	0.12	0.12	0.14	0.14	**0.20**	0.13
4	0.12	0.11	0.13	0.12	**0.20**	0.12
2014						
1	0.12	0.11	0.13	0.12	**0.18**	0.12
2	0.12	0.11	0.12	0.13	**0.16**	0.12
3	0.13	0.12	0.13	0.14	**0.19**	0.13
4	0.12	0.11	**0.14**	0.13	**0.18**	0.12
2015						
1	0.12	0.12	0.13	0.14	**0.17**	0.12
2	0.11	0.11	0.13	**0.14**	**0.16**	0.12
3	0.12	0.12	**0.15**	**0.15**	**0.21**	0.13
4	0.12	0.11	0.13	0.13	**0.20**	0.12
2016						
1	0.11	0.11	0.14	0.13	**0.20**	0.12
2	**0.12**	0.12*	0.14*	**0.16***	**0.22***	0.13*
3	**0.13**	0.13*	**0.16***	**0.17***	**0.21**	0.14*
4	0.12	0.12	**0.15***	**0.16***	**0.22**	0.13*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Appendix Table 1.16: Statistical Comparisons of Quarterly Dispensation Rates for Sulfonamides and Trimethoprims (J01E) for Children by Health Region

Age- and sex-adjusted rates per 1,000 people ages 0-14 per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	0.09	0.08	0.12	0.11	0.09	0.09
2	0.06	0.06	0.08	0.06	0.08	0.06
3	0.03	0.03	0.04	0.04	**0.05**	0.03
4	0.02	0.02	0.03	0.04	**0.05**	0.03
2012						
1	0.02	0.02	0.04	**0.05**	**0.04**	0.03
2	0.04	0.04	**0.06**	0.05	**0.06**	0.04
3	0.06	0.05	0.08	0.06	**0.11**	0.06
4	0.07	0.06	0.08	0.08	**0.10**	0.07
2013						
1	0.06	0.06	**0.09**	0.07	**0.10**	0.07
2	0.06	0.06	**0.10**	0.08	**0.10**	0.07
3	0.06	0.06	**0.10**	0.08	**0.12**	0.07
4	0.06	0.06	**0.10**	0.09	**0.11**	0.07
2014						
1	0.05	0.05	**0.09**	0.05	**0.08**	0.06
2	0.02	0.02	**0.04**	0.03	**0.04**	0.03
3	0.02	0.02	0.03	0.03	**0.04**	0.02
4	0.04	**0.03**	**0.07**	0.06	**0.08**	0.05
2015						
1	0.06	0.05	**0.10**	0.07	**0.10**	0.07
2	0.06	0.05	**0.10**	0.08	0.08	0.06
3	0.07	**0.06**	**0.14**	**0.13**	**0.15**	0.09
4	0.08	0.08	**0.13**	0.11	**0.17**	0.10
2016						
1	0.07	0.07	**0.13**	0.10	**0.14***	0.09
2	0.06	**0.06**	**0.10**	0.09*	**0.13***	0.07
3	**0.07***	**0.07***	**0.14***	0.12*	**0.18***	0.09*
4	0.06*	0.07*	**0.13***	0.10*	**0.14***	0.08*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Macrolides, Lincosamides and Streptogramins (J01F)

Appendix Table 1.17: Statistical Comparisons of Quarterly Dispensation Rates for Macrolides, Lincosamides and Streptogramins (J01F) for Adults by Health Region

Age- and sex-adjusted rates per 1,000 people ages 15 and older per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**0.38**	0.49	**0.63**	0.52	0.50	0.49
2	**0.29**	0.41	**0.49**	**0.46**	**0.47**	0.41
3	**0.24**	0.33	**0.39**	**0.39**	**0.38**	0.33
4	**0.32**	0.46	**0.56**	**0.51**	0.42	0.45
2012						
1	**0.36**	0.48	**0.59**	**0.57**	**0.42**	0.48
2	**0.29**	0.41	**0.50**	**0.48**	0.41	0.41
3	**0.24**	0.34	**0.45**	**0.42**	**0.40**	0.35
4	**0.38**	0.49	**0.64**	**0.55**	**0.43**	0.49
2013						
1	**0.38**	0.51	**0.62**	**0.58**	**0.45**	0.51
2	**0.31**	0.41	**0.55**	**0.46**	0.39	0.41
3	**0.24**	0.31	**0.42**	**0.37**	**0.39**	0.32
4	**0.31**	0.42	**0.52**	**0.49**	0.42	0.42
2014						
1	**0.33**	0.43	**0.58**	**0.52**	0.42	0.44
2	**0.28**	0.39	**0.50**	**0.45**	0.39	0.39
3	**0.27**	0.38	**0.46**	**0.42**	0.38	0.37
4	**0.33**	0.47	**0.56**	0.49	**0.39**	0.46
2015						
1	**0.40**	0.52	**0.67**	**0.58**	**0.45**	0.52
2	**0.30**	0.39	**0.51**	**0.45**	0.41	0.39
3	**0.25**	0.33	**0.41**	0.35	**0.38**	0.33
4	**0.30**	0.40	**0.51**	**0.44**	0.42	0.40
2016						
1	**0.36**	0.49	**0.62**	**0.52**	0.47	0.48
2	**0.27***	0.36*	**0.48**	0.39*	0.40*	0.36*
3	**0.23**	0.33	**0.40**	0.35*	**0.41**	0.33
4	**0.31**	0.44	**0.53**	0.44*	0.40	0.43

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Appendix Table 1.18: Statistical Comparisons of Quarterly Prescription Rates for Macrolides, Lincosamides and Streptogramins (J01F) for Children by Health Region

Age- and sex-adjusted rates per 1,000 people ages 0-14 per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**0.33**	0.38	**0.80**	0.40	**0.20**	0.41
2	**0.25**	0.26	**0.53**	0.33	**0.18**	0.29
3	**0.19**	0.20	**0.41**	0.25	**0.15**	0.23
4	**0.26**	0.32	**0.65**	0.40	**0.21**	0.35
2012						
1	0.30	0.30	**0.61**	**0.44**	**0.17**	0.34
2	**0.23**	0.27	**0.52**	**0.35**	**0.15**	0.29
3	**0.19**	0.20	**0.39**	**0.27**	**0.18**	0.23
4	0.36	0.39	**0.68**	0.47	**0.17**	0.41
2013						
1	0.29	0.29	**0.63**	0.39	**0.19**	0.34
2	0.23	0.24	**0.51**	0.31	**0.15**	0.27
3	**0.14**	0.17	**0.34**	**0.25**	**0.14**	0.19
4	0.24	0.25	**0.51**	**0.34**	**0.16**	0.28
2014						
1	0.29	0.29	**0.61**	**0.41**	**0.15**	0.33
2	0.22	0.23	**0.41**	0.30	**0.13**	0.25
3	**0.19**	0.22	**0.39**	0.27	**0.14**	0.24
4	**0.25**	0.36	**0.53**	0.36	**0.15**	0.34
2015						
1	0.32	0.31	**0.64**	0.40	**0.18**	0.35
2	0.24	0.25	**0.48**	0.31	**0.13**	0.28
3	0.19	0.18	**0.31**	0.22	**0.14**	0.20
4	**0.21**	0.26	**0.44**	0.29	**0.14**	0.27
2016						
1	**0.28***	0.36	**0.67***	0.42	**0.17***	0.37
2	**0.20***	0.22*	**0.48**	0.25*	**0.14***	0.25*
3	**0.14***	0.17*	**0.28***	**0.22**	**0.12***	0.18*
4	**0.21***	0.30	**0.49***	0.31*	**0.15***	0.30*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Quinolones (J01M)

Appendix Table 1.19: Statistical Comparisons of Quarterly Dispensation Rates for Quinolones (J01M) for Adults by Health Region
Age- and sex-adjusted rates per 1,000 people ages 15 and older per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**0.27**	0.29	**0.40**	0.33	**0.26**	0.30
2	**0.24**	0.26	**0.35**	**0.29**	**0.22**	0.27
3	**0.23**	0.25	**0.34**	**0.32**	0.24	0.26
4	**0.25**	0.27	**0.37**	**0.32**	**0.22**	0.28
2012						
1	**0.25**	0.28	**0.37**	**0.32**	**0.22**	0.29
2	**0.23**	0.26	**0.35**	**0.30**	**0.23**	0.27
3	**0.23**	0.25	**0.33**	**0.32**	0.24	0.26
4	**0.24**	0.26	**0.36**	**0.33**	**0.23**	0.27
2013						
1	**0.25**	0.28	**0.37**	**0.32**	**0.22**	0.29
2	**0.24**	0.25	**0.34**	**0.31**	0.24	0.26
3	**0.23**	0.24	**0.33**	**0.28**	0.23	0.25
4	**0.24**	0.25	**0.33**	**0.30**	**0.23**	0.26
2014						
1	**0.24**	0.26	**0.35**	**0.30**	**0.24**	0.27
2	**0.22**	0.25	**0.32**	**0.28**	**0.21**	0.25
3	**0.22**	0.25	**0.33**	**0.29**	**0.23**	0.26
4	**0.24**	0.26	**0.34**	**0.30**	**0.23**	0.27
2015						
1	**0.26**	0.27	**0.36**	**0.32**	**0.25**	0.28
2	**0.22**	0.24	**0.32**	0.27	**0.21**	0.25
3	0.22	0.23	**0.31**	0.25	0.24	0.24
4	**0.22**	0.24	**0.33**	0.26	0.23	0.25
2016						
1	**0.24***	0.26*	**0.35***	**0.32**	0.26	0.27*
2	**0.21***	0.22*	**0.30***	0.25*	0.22	0.23*
3	0.21*	0.21*	**0.29***	0.24*	0.25	0.22*
4	0.22*	0.23*	**0.33***	0.26*	0.23	0.24*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Other Antibiotics (J01X)

Appendix Table 1.20: Statistical Comparisons of Quarterly Dispensation Rates for Other Antibiotics (J01X) for Adults by Health Region
Age- and sex-adjusted rates per 1,000 people ages 15 and older per day

Year and Quarter	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011						
1	**0.11**	0.11	**0.14**	**0.16**	**0.16**	0.12
2	**0.11**	0.11	**0.14**	**0.16**	0.15	0.13
3	**0.10**	0.12	**0.15**	**0.15**	**0.15**	0.13
4	**0.11**	**0.11**	**0.16**	**0.16**	**0.15**	0.13
2012						
1	**0.11**	0.12	**0.16**	0.15	**0.17**	0.13
2	**0.11**	0.12	**0.16**	0.15	**0.16**	0.13
3	**0.11**	0.13	**0.16**	0.15	**0.17**	0.14
4	**0.11**	0.12	**0.15**	**0.15**	**0.17**	0.13
2013						
1	**0.11**	0.12	**0.15**	**0.15**	**0.17**	0.13
2	**0.11**	0.12	0.15	**0.16**	**0.16**	0.13
3	**0.11**	0.13	0.15	**0.16**	**0.16**	0.13
4	0.12	0.12	0.14	**0.16**	**0.16**	0.13
2014						
1	**0.12**	0.13	**0.16**	**0.16**	**0.18**	0.14
2	**0.11**	0.12	**0.16**	**0.16**	**0.17**	0.13
3	0.13	0.13	0.16	**0.17**	**0.17**	0.14
4	0.13	0.13	0.16	**0.16**	**0.17**	0.14
2015						
1	0.13	0.14	0.16	**0.17**	**0.18**	0.14
2	0.13	0.13	0.15	**0.18**	**0.17**	0.14
3	0.14	0.14	0.17	**0.18**	**0.18**	0.15
4	0.15	0.15	0.17	**0.20**	**0.19**	0.16
2016						
1	0.15*	0.14*	0.17*	**0.19***	0.18	0.16*
2	0.14*	0.15*	0.16*	**0.18***	**0.18***	0.15*
3	0.15*	0.15*	0.17*	**0.18***	**0.19***	0.16*
4	0.14*	0.15*	0.18	**0.18**	**0.20***	0.16*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

Appendix 2: Additional Quality Indicators for Antibiotic Consumption in the Community (Chapter 4)

Defined Daily Dose for Antibiotics Overall (J01) by Health Region

Appendix Table 2.1: Statistical Comparisons of Annual Defined Daily Dose Dispensation Rates for Antibiotics Overall (J01) by Health Region, 2011-2016

Age- and sex-adjusted rates per 1,000 people per day

Year	Age- and Sex-Adjusted Rates by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011	17.51	18.91	**23.93**	20.58	21.14	19.40
2012	18.11	19.53	**24.89**	20.83	**22.72**	19.98
2013	17.77	19.18	**24.04**	20.57	**21.62**	19.38
2014	17.53	18.44	**23.78**	20.37	19.06	18.72
2015	18.42	18.72	**24.85**	21.26	**22.74**	19.33
2016	**17.16***	19.07*	**24.04***	20.78	**25.48***	19.22*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in this quarter is statistically significantly different from the corresponding quarter in 2011 ($p<0.05$).

ESAC-Net Quality Indicators

Indicators of Relative Consumption

Consumption of β-lactamase-sensitive penicillins expressed as a percent of total consumption of total antibacterials

Appendix Table 2.2: Annual Consumption of β-Lactamase-Sensitive Penicillins (J01CE) as Percent of Total Antibacterials (J01) by Health Region

Age- and sex-adjusted percent, all ages, all prescribers

Year	Age- and Sex-Adjusted Percents by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011	**2.59**	2.02	**1.24**	1.72	2.30	1.94
2012	**2.35**	1.87	**1.00**	1.64	1.97	1.75
2013	1.94	1.71	**0.81**	1.54	1.81	1.58
2014	1.94	1.70	**0.86**	1.60	1.97	1.59
2015	1.72	1.68	**0.85**	1.72	1.92	1.56
2016	1.80*	1.59*	**0.84***	1.74	1.62*	1.50*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate (p<0.01).
* Indicates health region's rate in 2011 is statistically significantly different from the rate in 2016 (p<0.05).

Consumption of β-lactamase inhibitor penicillin combinations as percent of total antimicrobials

Appendix Table 2.3: Annual Consumption of β-Lactamase-Sensitive Penicillin Combinations (J01CR) as Percent of Total Antibacterials (J01) by Health Region

Age- and sex-adjusted percent, all ages, all prescribers

Year	Age- and Sex-Adjusted Percents by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011	4.07	**3.36**	**6.76**	**6.06**	**5.31**	4.39
2012	**4.24**	**3.81**	**7.57**	**5.87**	**5.77**	4.78
2013	5.01	**4.45**	**8.11**	**6.78**	**6.16**	5.41
2014	5.64	**5.19**	**8.16**	**7.20**	**6.82**	6.01
2015	5.77	5.76	**8.00**	**7.78**	**8.06**	6.43
2016	6.32*	6.20*	**8.15***	**7.98***	**8.42***	6.81*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate (p<0.01).
* Indicates health region's rate in 2011 is statistically significantly different from the rate in 2016 (p<0.05).

Consumption of third- and fourth-generation cephalosporins as percent of total antimicrobials

Appendix Table 2.4: Annual Third- and Fourth-Generation Cephalosporins (J01DD and J01DE) as Percent of Total Antibacterials (J01) by Health Region

Age- and sex-adjusted percent, all ages, all prescribers

Year	Age- and Sex-Adjusted Percents by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011	**0.22**	**0.21**	**0.45**	**0.82**	0.24	0.31
2012	**0.16**	0.21	0.28	**0.86**	0.26	0.28
2013	**0.19**	0.23	0.27	**0.72**	0.21	0.28
2014	0.13	0.13	0.16	**0.42**	0.18	0.17
2015	0.08	0.06	**0.13**	**0.13**	0.08	0.09
2016	0.16*	0.10*	0.16*	**0.25***	**0.08***	0.13*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in 2011 is statistically significantly different from the rate in 2016 ($p<0.05$).

Consumption of fluoroquinolones as percent of total antimicrobials

Appendix Table 2.5: Annual Consumption of Fluoroquinolones (J01MA) as Percent of Total Antibacterials (J01) by Health Region

Age- and sex-adjusted percent, all ages, all prescribers

Year	Age- Sex-Adjusted Percents by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011	10.10	10.58	11.03	10.18	**7.43**	10.56
2012	9.70	10.64	9.18	8.67	7.56	10.00
2013	10.22	9.87	9.30	9.56	8.54	9.94
2014	10.31	11.12	11.12	9.65	**7.57**	11.03
2015	8.42	10.43	10.30	8.40	**7.29**	9.88
2016	8.18	11.18	9.32	8.33	**7.02**	10.14

Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).
* Indicates health region's rate in 2011 is statistically significantly different from the rate in 2016 ($p<0.05$).

Indicators of Broad- and Narrow-Spectrum Antibiotic Consumption

Ratio of broad-spectrum to narrow-spectrum penicillins, cephalosporins and macrolides

Appendix Table 2.6: Annual Ratio of Broad-Spectrum (J01CR, J01DR, J01DD, J01F-FA01) to Narrow-Spectrum Penicillins, Cephalosporins and Macrolides (J01CE, J01DB, J01FA01) by Health Region

Age- and sex-adjusted percent, all ages, all prescribers

Year	Age- and Sex-Adjusted Ratios by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011	**2.25**	**2.41**	**4.46**	2.88	2.50	2.66
2012	**2.36**	**2.45**	**4.67**	2.88	2.52	2.72
2013	**2.36**	**2.34**	**4.64**	2.90	2.56	2.64
2014	**2.30**	**2.38**	**4.58**	2.74	2.65	2.65
2015	2.39	**2.36**	**4.62**	2.55	2.59	2.63
2016	**2.25**	2.43	**4.44**	2.49*	**2.96***	2.64

Bold indicates health region's ratio is statistically significantly different from the Manitoba ratio (p<0.01).
* Indicates health region's ratio in 2011 is statistically significantly different from the ratio in 2016 (p<0.05).

Indicators of Seasonal Variation in Antibiotic Consumption

Seasonal Variation in Total Antibacterial (J01) Use

Appendix Table 2.7: Annual Seasonal Variation in Total Antibacterial (J01) Use: Percent Change from Summer to Winter Quartes by Health Region

Age- and sex-adjusted percent change from summer (April-June, July-September) to winter quarters (January-March, October-December) in a 12-month period starting in July, all ages, all prescribers

Year	Age- and Sex-Adjusted Percent by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011	18.73	17.10	17.51	17.64	13.92	16.22
2012	8.16	9.91	11.22	13.35	**-5.95**	8.11
2013	13.07	12.77	12.53	10.65	**2.26**	10.93
2014	14.72	9.33	12.42	11.60	7.01	9.70
2015	15.04	15.93	16.42	12.28	15.40	15.00
2016	9.72*	11.64*	10.58*	13.45	7.81*	10.28*

Bold indicates health region's seasonal variation is statistically significantly different from the Manitoba seasonal variation (p<0.01).
* Indicates health region's seasonal varition in 2011 is statistically significantly different from the seasonal variation in 2016 (p<0.05).

Seasonal Variation in Quinolone Use (J01M)

Appendix Table 2.8: Annual Seasonal Variation in Quinolone (J01M) Use among Adults: Percent Change from Summer to Winter Quarters by Health Region

Age- and sex-adjusted percent change from summer (April-June, July-September) to winter quarters (January-March, October-December) in a 12-month period starting in July, all ages, all prescribers

Year	Age- and Sex-Adjusted Percent by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011	20.43	7.02	**28.02**	**26.38**	9.06	9.33
2012	9.45	10.03	10.16	8.20	11.62	5.02
2013	12.76	6.59	13.11	1.57	1.08	2.82
2014	12.72	7.20	18.01	12.51	**23.19**	6.23
2015	23.32	16.70	9.34	19.59	25.35	12.58
2016	13.43	8.56	**26.22**	**34.14**	17.78	9.21

Bold indicates health region's seasonal variation is statistically significantly different from the Manitoba seasonal variation ($p<0.01$).
* Indicates health region's seasonal varition in 2011 is statistically significantly different from the seasonal variation in 2016 ($p<0.05$).

Appendix 3: Relationship between Health Care Service Use and Antibiotic Dispensations (Chapter 5)

Relationship between Ambulatory Care Physician Visits and Antibiotic Dispensations

Appendix Table 3.1: Statistical Comparisons of Percent of Ambulatory Physician Visits Resulting in Antibiotic Dispensations by Health Region

Age- and sex-adjusted percent of visits with a dispensation within five days

Year	Age- and Sex-Adjusted Percent by Health Region					
	Southern Health-Santé Sud	Winnipeg RHA	Prairie Mountain Health	Interlake-Eastern RHA	Northern Health Region	Manitoba
2011	**8.17**	**8.07**	**11.54**	**9.35**	**5.47**	8.69
2012	**8.27**	**8.16**	**11.58**	**9.50**	**5.09**	8.75
2013	**8.05**	**7.89**	**10.99**	**9.01**	**4.86**	8.44
2014	**8.00**	**8.03**	**11.03**	8.81	**4.29**	8.45
2015	8.26	**7.96**	**11.38**	8.64	**4.92**	8.50
2016	**7.96**	**7.90**	**11.17**	8.52*	**5.14***	8.36*

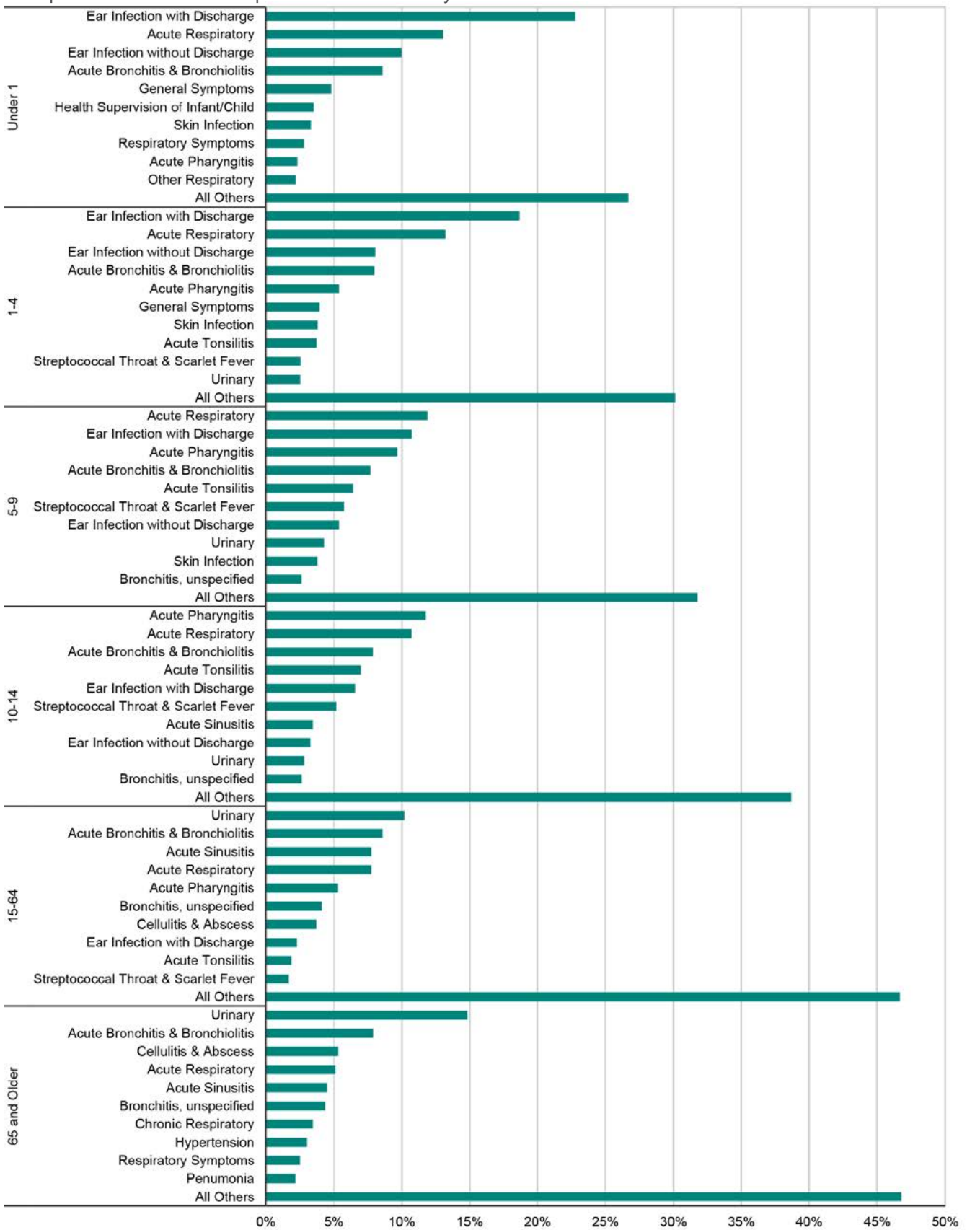
Bold indicates health region's rate is statistically significantly different from the Manitoba rate ($p<0.01$).

* Indicates statistically significantly differences between rates in 2011 and 2016 ($p<0.05$).

Most Common Diagnosis Codes for Ambulatory Physician Visits Associated with Antibiotic Dispensations

Appendix Figure 3.1: Most Common Diagnosis Codes for Ambulatory Physician Visits Resulting in Antibiotic Dispensations by Age Group, 2016

Crude percent of visits with a dispensation within five days

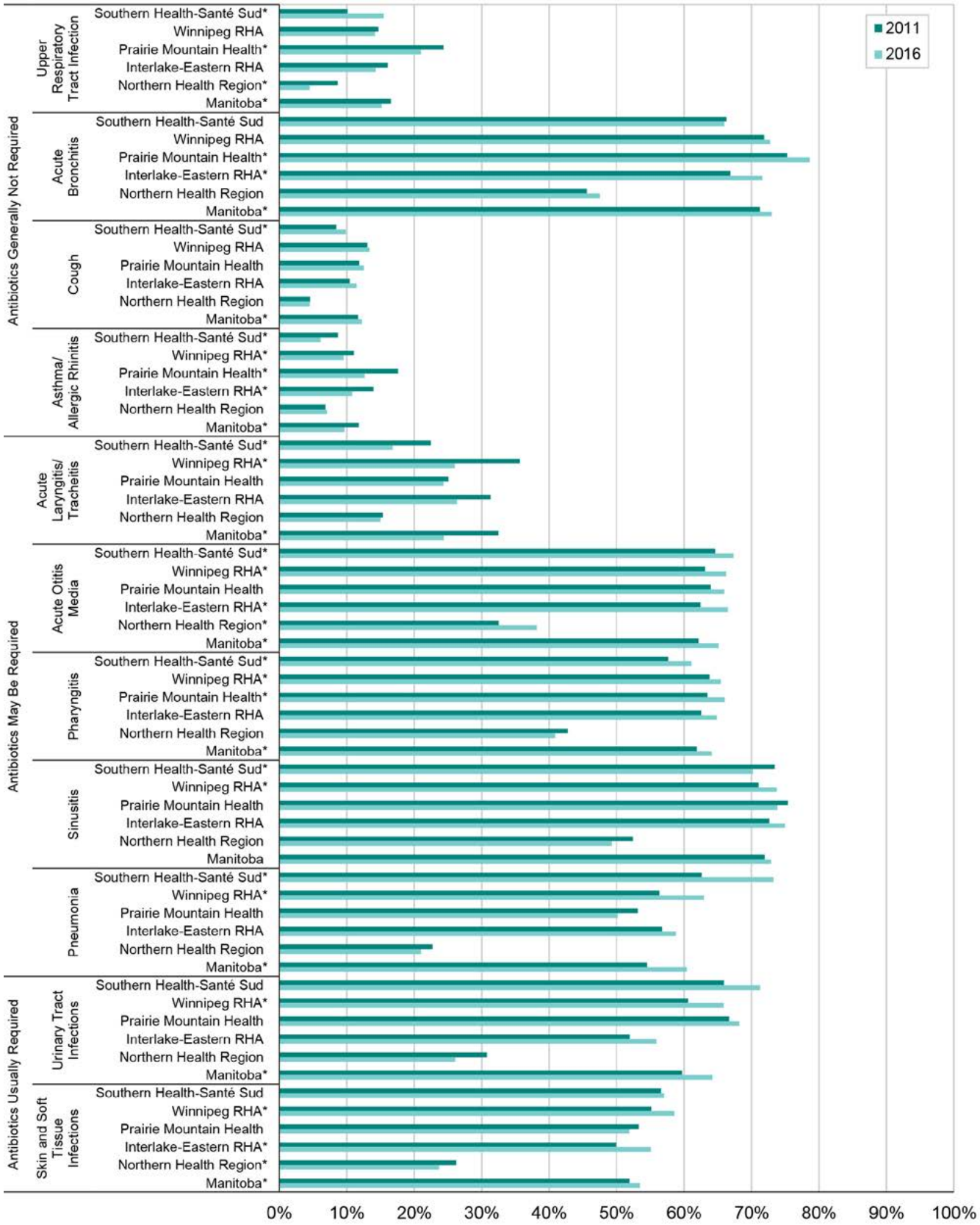


Appendix 4: Relationship between Diagnosis Codes Provided by Ambulatory Primary Care Physicians and Antibiotic Dispensations to Ascertain Appropriateness of Antibiotic Use (Chapter 6)

Overall

Appendix Figure 4.1: Ambulatory Primary Care Physician Visits Resulting in Antibiotic Dispensation by Patient Diagnosis and Health Region, 2011 and 2016

Age- and sex-adjusted percent of visits with a dispensation within five days



* Indicates a statistically significant difference between rates in 2011 and 2016 ($p<0.05$).

Conditions That Generally Do Not Require Antibiotics

Appendix Table 4.1: Statistical Comparisons of Percent of Ambulatory Primary Care Physician Visits Resulting in Antibiotic Dispensation for Conditions That Generally Do Not Require Antibiotics, by Health Region

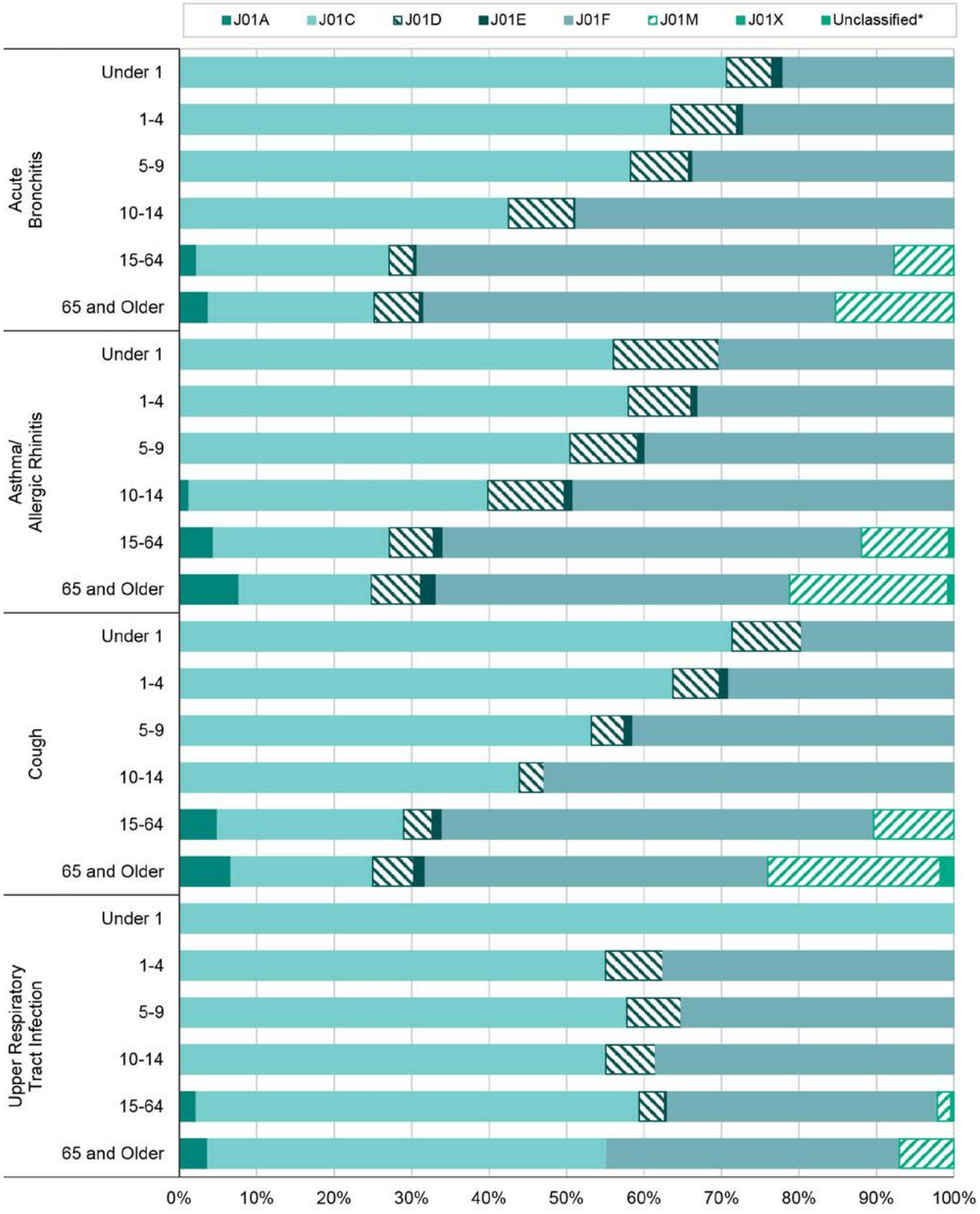
Age- and sex-adjusted percent of visits with antibiotic dispensation within five days

Year	ESAC-Net* Quality Indicators of Antibiotic Consumption (Average Rate and 95% Confidence Intervals)						
	Relative Consumption (Antibiotic Class Relative to Antibiotics Overall)				Broad vs. Narrow Spectrum	Seasonal Variation (Increase from Summer to Winter)	
	β-Lactamase-Sensitive (J01CE) †	β-Lactamase Inhibitor/Penicillin Combination (J01CR)**	Third- and fourth-generation cephalosporins (J01DD & J01DE)**	Fluoroquinolones (J01MA)**	Antibiotics Overall (J01)**	Antibiotics Overall (J01)**	Quinolone Class (J01M)**
	%	%	%	%	Ratio	%	%
2011	1.94 (1.93-1.95)	4.39 (4.37-4.40)	0.31 (0.30-0.31)	10.56 (10.54-10.58)	2.66 (2.65-2.66)	16.22 (16.12-16.33)	3.39 (3.10-3.69)
2012	1.75 (1.45-2.12)	4.78 (4.39-5.21)	0.28 (0.22-0.36)	10.00 (7.99-12.50)	2.72 (2.53-2.92)	8.11 (4.21-12.17)	77.59 (43.36-119.99)
2013	1.58 (1.30-1.91)	5.41 (4.97-5.89)	0.28 (0.21-0.35)	9.94 (7.95-12.44)	2.64 (2.46-2.84)	10.93 (6.92-15.09)	64.36 (32.76-103.48)
2014	1.59 (1.31-1.93)	6.01 (5.52-6.55)	0.17 (0.13-0.21)	11.03 (8.81-13.79)	2.65 (2.46-2.84)	9.70 (5.74-13.82)	136.14 (90.49-192.72)
2015	1.56 (1.29-1.89)	6.43 (5.91-7.00)	0.09 (0.07-0.11)	9.88 (7.90-12.35)	2.63 (2.44-2.82)	15.00 (10.85-19.32)	107.56 (67.43-157.30)
2016	**1.50 (1.24-1.82)**	**6.81 (6.26-7.42)**	**0.13 (0.10-0.17)**	10.14 (8.11-12.69)	2.64 (2.46-2.84)	**10.28 (6.30-14.42)**	-10.90 (-27.92-10.14)

* ESAC-Net represents the European Surveillance of Antibiotic Consumption Network (ESAC-Net).
** Lower values indicate more prudent use
† higher values indicate more prudent use
Bolded values indicate statistically significant differences between 2011 and 2016 ($p<0.01$).

Appendix Figure 4.2: Antibiotic Dispensations Linked to Ambulatory Visits to Primary Care Physicians for Conditions That Generally Do Not Require Antibiotics, by Age Group (Years) and Drug Class, 2016

Crude percent of total dispensations within five days of a visit



* Includes the drugs amoxicillin/clarithromycin, fixadomicin and vancomycin.

Conditions That May Require Antibiotics

Appendix Table 4.2: Statistical Comparisons of Percent of Ambulatory Primary Care Physician Visits Resulting in Antibiotic Dispensation for Conditions That May Require Antibiotics, by Health Region

Age- and sex-adjusted percent of visits with antibiotic dispensation within five days

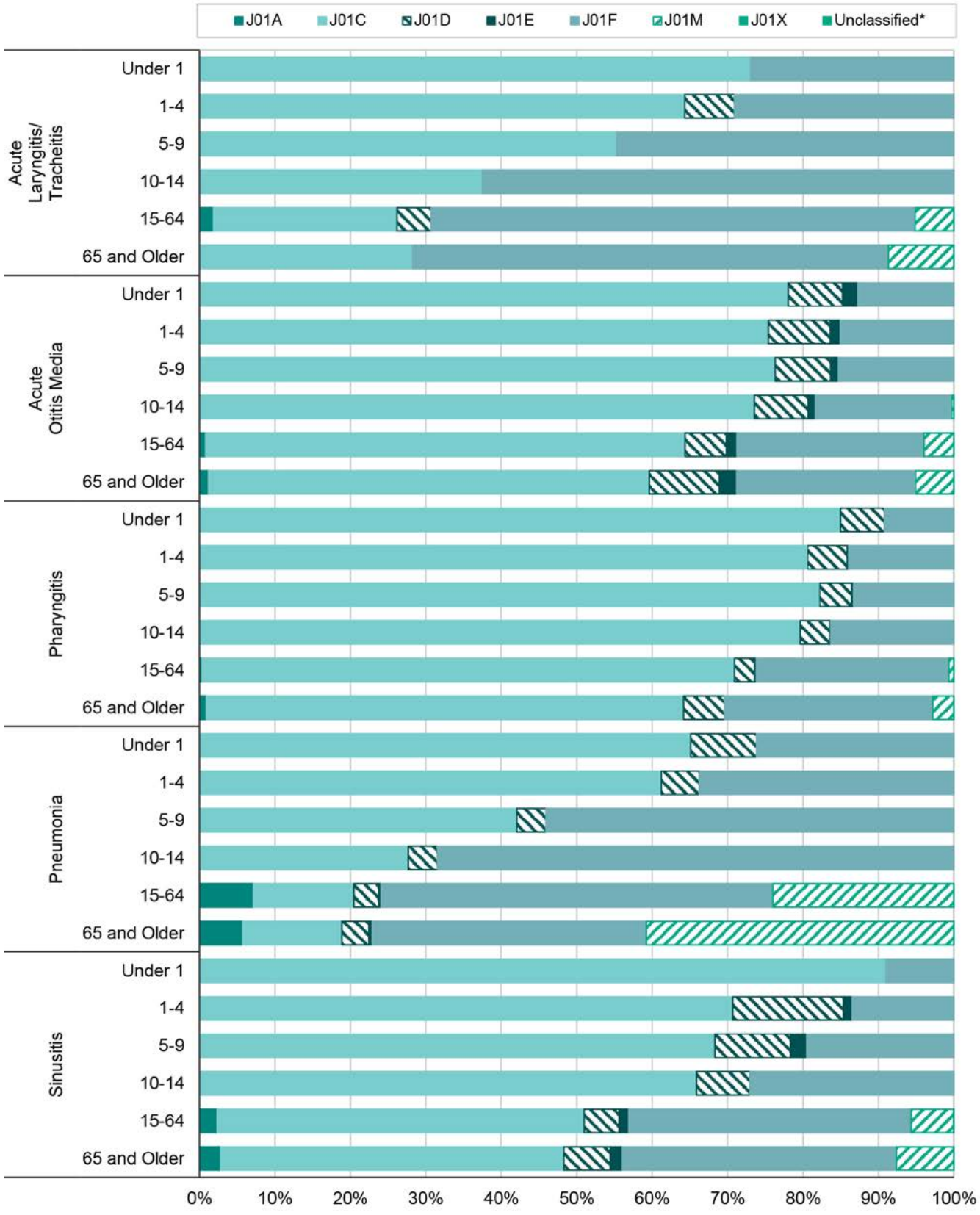
Health Region	Percent of Ambulatory Physician Visits Resulting in Antibiotic Dispensation	
	2011	2016
Acute Laryngitis/Tracheitis		
Southern Health-Santé Sud	**22.45***	**16.81***
Winnipeg RHA	**35.64***	26.01*
Prairie Mountain Health	**25.12**	24.33
Interlake-Eastern RHA	31.30	26.32
Northern Health Region	**15.33**	15.04
Manitoba	32.51*	24.37*
Acute Otitis Media		
Southern Health-Santé Sud	**64.62***	67.33*
Winnipeg RHA	63.12*	66.27*
Prairie Mountain Health	63.94	65.98
Interlake-Eastern RHA	62.46*	66.53*
Northern Health Region	**32.53***	**38.19***
Manitoba	62.12*	65.11*
Pharyngitis		
Southern Health-Santé Sud	**57.66***	**61.10***
Winnipeg RHA	**63.75***	**65.44***
Prairie Mountain Health	63.46*	66.05*
Interlake-Eastern RHA	62.59	64.89
Northern Health Region	**42.72**	**40.88**
Manitoba	61.87*	64.07*
Sinusitis		
Southern Health-Santé Sud	73.44*	70.23*
Winnipeg RHA	71.02*	73.73*
Prairie Mountain Health	**75.42**	73.84
Interlake-Eastern RHA	72.63	75.01
Northern Health Region	**52.43**	**49.27**
Manitoba	71.97	72.88
Pneumonia		
Southern Health-Santé Sud	**62.64***	**73.28***
Winnipeg RHA	56.33*	**62.95***
Prairie Mountain Health	53.12	**50.18**
Interlake-Eastern RHA	56.73	58.80
Northern Health Region	**22.71**	**20.99**
Manitoba	54.52*	60.38*

Bold indicates health region's rate is statistically significantly differentfrom the Manitoba rate ($p<0.01$).

* Indicates statistically significantly differences between rates in 2011 and 2016 ($p<0.05$).

Appendix Figure 4.3: Antibiotic Dispensations Linked to Ambulatory Visits to Primary Care Physicians for Conditions That May Require Antibiotics, by Age Group (Years) and Drug Class, 2016

Crude percent of total dispensations within five days of a visit



* Includes the drugs amoxicillin/clarithromycin, fixadomicin and vancomycin.

Conditions That Usually Require Antibiotics

Appendix Table 4.3: Statistical Comparisons of Percent of Ambulatory Primary Care Physician Visits Resulting in Antibiotic Dispensation for Conditions That Usually Require Antibiotics, by Health Region

Age- and sex-adjusted percent of visits with antibiotic dispensation within five days

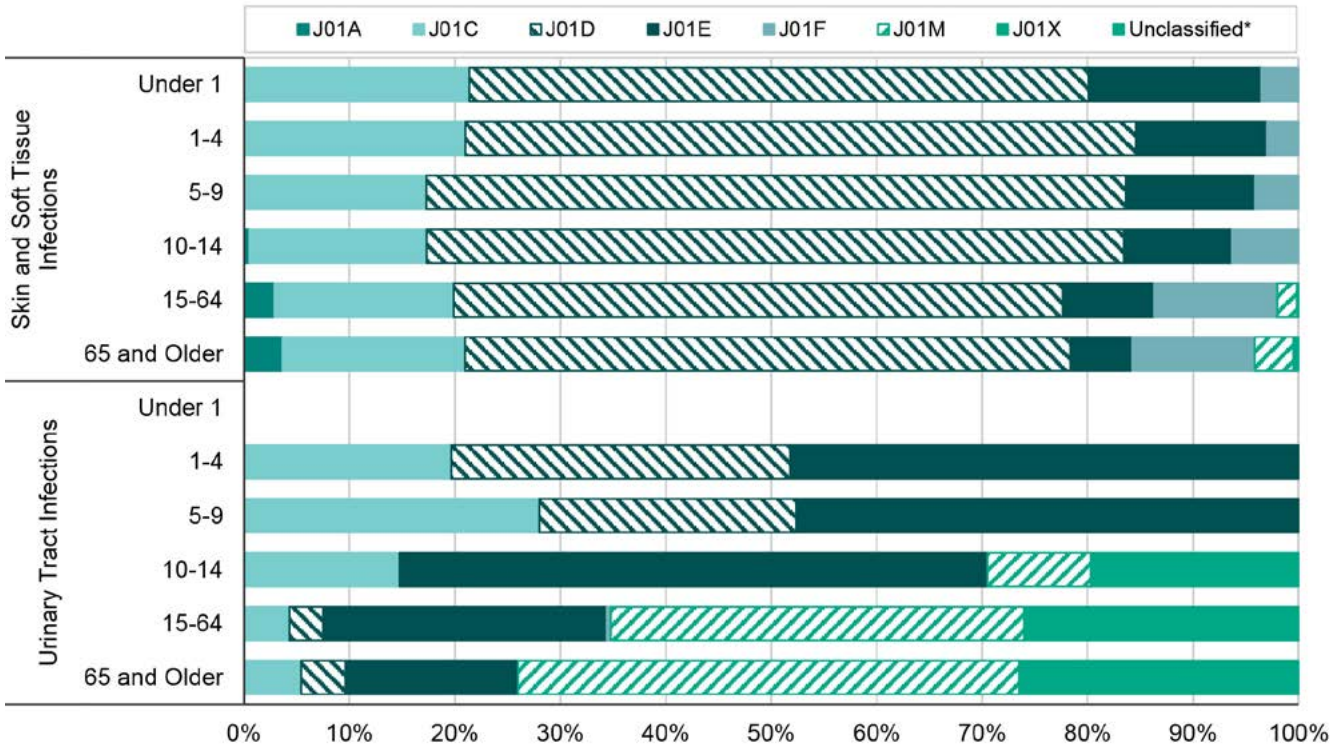
Health Region	Percent of Ambulatory Physician Visits Resulting in Antibiotic Dispensation	
	2011	2016
Urinary Tract Infections		
Southern Health-Santé Sud	65.92	**71.29**
Winnipeg RHA	60.61*	65.87*
Prairie Mountain Health	**66.70**	68.19
Interlake-Eastern RHA	**51.97**	**55.92**
Northern Health Region	**30.78**	**26.08**
Manitoba	59.73*	64.21*
Skin and Soft Tissue Infections		
Southern Health-Santé Sud	**56.56**	**57.06**
Winnipeg RHA	**55.12***	**58.54***
Prairie Mountain Health	53.27	51.89
Interlake-Eastern RHA	50.00*	55.03*
Northern Health Region	**26.24***	**23.71***
Manitoba	51.93*	53.43*

Bold indicates health region's rate is statistically significantly different from the Manitoba rate (p<0.01).

* Indicates statistically significantly differences between rates in 2011 and 2016 (p<0.05).

Appendix Figure 4.4: Antibiotic Dispensations Linked to Ambulatory Visits to Primary Care Physicians for Conditions That Usually Require Antibiotics, by Age Group (Years) and Drug Class, 2016

Crude percent of total dispensations within five days of a visit



* Includes the drugs amoxicillin/clarithromycin, fixadomicin and vancomycin.

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