CPCSSN RCSSSP

Canadian Primary Care Sentinel Surveillance Network

Réseau canadien de surveillance sentinelle en soins primaires

Potentially Inappropriate Antibiotic Prescribing for Respiratory Tract Infections in Canadian Primary Care

Results from the Canadian Primary Care Sentinel Surveillance Network

April 2022

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Acknowledgements

The authors wish to recognize contributions to CPCSSN from the following:

Practice Based Research and Learning Network directors and scientists

Kris Aubrey-Bassler (Memorial University), David Barber (Queen's University), Simone Dahrouge (University of Ottawa), Neil Drummond (Universities of Calgary and Alberta), Kimberly Fairman (Institute of Circumpolar Research), Stephanie Garies (University of Calgary), Mathew Grandy (Dalhousie University), Michelle Griever (University of Toronto), Marie-Thérèse Lussier (Université de Montréal), Donna Manca (University of Alberta), Dee Mangin (McMaster University), Claude Richard (Université de Montréal), Alex Singer (University of Manitoba), Amanda Terry (Western University), Tyler Williamson (University of Calgary), Brianne Wood (Northern School of Medicine), Sabrina Wong (University of British Columbia) and Barbara Zelek (Northern School of Medicine).

Data managers

Kris Adamczyk, Baback Aliarazadeh, Charles Bruntz, Tao Chen, Michael Cummings, Brain Forst, Andy Gibb, Lorne Kinsella, Don White, Bill Peeler, Sara Sabri, Lena Schofield, Bedredine Sayah, Boglarka Soos, Matt Taylor, and Rick Truant.

Research assistants/associates

Aashka Bhatt, Allison Boileau, Kimberly Duerkson, Danica Goulet, Keri Harvey, Leanne Kosowan, Jennifer Lawson, Himasara Marasinghe, Walid Nacher, Rabiya Siddiqui, and Rebecca Theal.

Publication information

How to cite this publication

Wong ST, Morkem R, Leis J, Levinson W, Patey A, Durance A, Barber D. Potentially inappropriate antibiotic prescribing for respiratory tract infections in Canadian primary care: Results from the Canadian Primary Care Sentinel Surveillance Network. Kingston, ON: Canadian Primary Care Sentinel Surveillance Network; April 2022.

About CPCSSN

The Canadian Primary Care Sentinel Surveillance Network (CPCSSN) is an independent not-for-profit university-based consortium with an international reputation as a trusted source of primary care electronic medical record (EMR) data. Established in 2008, CPCSSN has developed a pan-Canadian primary care EMR data repository. CPCSSN has successfully built trusting relationships between primary care clinicians and researchers over the past 12 years. As of 2022, CPCSSN consisted of a network of 13 community-based primary care research and learning networks based in eight Canadian provinces (British Columbia, Alberta, Manitoba, Ontario, Quebec, Nova Scotia, Newfoundland) and one territory (Northwest Territories). There are other networks that have also started, including a network in Saskatchewan and one across Correctional Services Canada. CPCSSN draws on technological expertise to securely extract EMR data from primary care practices and includes close to 1,500 participating family physicians, nurse practitioners and other primary care clinicians and approximately 2 million patients. CPCSSN applies standardized ontologies and terminologies to transform data from various EMR vendors into a common data schema.

CPCSSN is supported through a diverse array of funding including peer-reviewed grants from federal agencies such as the Canadian Institutes of Health Research and the Public Health Agency of Canada, as well as other profit and not-for-profit organizations. CPCSSN is also supported with in-kind and direct funding support from the Canadian universities that host the regional networks.

About this report

This report represents a joint collaboration between CPCSSN and Choosing Wisely Canada (CWC). CWC is the national voice for reducing unnecessary tests and treatments in Canada. The CWC campaigns for health care providers and their organizations to adopt test and treatment guidelines that are supported by scientific evidence. This report has been prepared to support CPCSSN's mission for continued research in primary care with valuable insight and direction provided by CWC. This report aims to contribute to antimicrobial stewardship in Canada by showing baseline prescription patterns of antibiotics before and during the first year of the COVID-19 pandemic in Canada. Data are analyzed from the years 2019 and 2020 for those who had a visit to primary care for either a respiratory or urinary tract infection.

Contents

Abstract

Background and purpose

Respiratory tract infections (RTI) and urinary tract infections (UTI) are the leading causes of avoidable antimicrobial use in primary care. How the COVID-19 pandemic has impacted antibiotic prescribing practices across Canada is unknown. The purpose of this study was to examine rates of antibiotic prescribing for RTI and UTI in primary care during the first year of the pandemic (2020), compared to baseline in 2019.

Methods

Data were obtained from the Canadian Primary Care Sentinel Surveillance Network (CPCSSN), which includes 1,300 primary care clinicians and almost two million patients across Canada. We examined oral antibiotic prescribing for patients who were identified as having a primary care visit (virtual or in-person) for RTI or influenza-like illness (ILI), based on previously validated case definitions. The same analysis was repeated for UTI as a tracer condition. Antibiotic use considered avoidable for RTI was defined by Choosing Wisely Canada.

Results

A total of 1,692,876 patients with a valid birth year and sex documented and at least one visit to primary care in 2019 and 2020 were included. Patient visits for RTI decreased from 2.3% in 2019 to 1.6% in 2020 ($p<.0001$), as did patient visits for UTI (1.1% vs 0.7%, $p<.0001$). In 2019, 28.0% of patient visits for RTI were prescribed an antibiotic and this proportion decreased significantly to 20.6% in 2020 ($p<.0001$). The drop in antibiotic prescriptions for RTI was driven by a decrease in prescribing for common cold (13.6% vs. 11.3%, $p<.0001$) and for acute bronchitis/asthma (15.2% vs. 7.3%, $p<.0001$). In comparison, antibiotic prescribing for visits related to UTI increased marginally between 2019 and 2020 (71.6% vs. 72.3%, $p=0.007$).

Primary care providers that could be considered high prescribers (top quartile) were prescribing less often in 2020 (Q3=26.8%) than in 2019 (Q3=34.9%). This drop among the highest prescribers (top quartile) was most apparent for acute bronchitis/asthma and the common cold.

Conclusion

A significant decrease in antibiotic prescribing for RTI across primary care was observed during the first year of the COVID-19 pandemic, likely related to the changes in epidemiology and care delivery models in primary care. CPCSSN can provide pan-Canadian surveillance of antibiotic prescribing practices in primary care that can be used for provider feedback and quality improvement.

Introduction

The use, and often inappropriate use, of antimicrobials has been increasing since they were first introduced in the 1940s.[1] Consequently, there has been a global increase in antimicrobial resistance (AMR) which led to over 4.9 million deaths globally in 2019 and $1.4-$4.7 billion in costs to healthcare across North America and Europe.[1,2] In 2018 there were 5,400 deaths as a direct result of AMR in Canada.[3] While the emergence of AMR is a natural process, selection for these traits has been facilitated by the overuse of antimicrobial compounds in healthcare and agriculture.[4] Today, the number of resistant organisms, and the breadth of resistance of single organisms, is mounting to unprecedented levels.[5]

In humans, decreasing the inappropriate use of antibiotics can aid in curbing AMR. Much of these efforts in Canada have focused on acute care in hospitals.[6] Governments and healthcare institutions in high income countries have developed and implemented antimicrobial stewardship (AMS) programs.[7,8] These institutional programs have been effective and have resulted in reduced antibiotic utilization and AMR.[6,9]

In contrast, AMS programs outside of hospitals are less developed in Canada. The majority of antibiotic use in healthcare (90% by volume) occurs in the primary care setting, where many prescriptions are unindicated.[10,11] An Ontario cohort study found that, on average, 25% of antibiotic prescriptions by family physicians were avoidable.[12] In 2012, it was found that among those aged 65 years and older, the rate of antibiotic prescription for non-bacterial respiratory infections was as high as 46%.[13] As today's community member is tomorrow's patient, antibiotic use in this outpatient setting not only impacts AMR in the community but also antibiotic resistance in hospitals.

The COVID-19 pandemic has had a major impact upon primary care, as there was a more than 89% reduction in any preventive care visits and an approximate 25% reduction in the number of visits for diabetes and hypertension in 2019 compared to 2020.[14] Most primary care practices saw anywhere from a 30% to 70% reduction in visit volume during the first wave of the pandemic which undoubtedly contributed to decreased prescribing.[15] While there is minimal data released in peer-reviewed publications as of this writing, it is expected that the pandemic will have led to a dramatic change in the diagnosis and subsequent antibiotic treatment of RTIs, because, in most parts of the country, patients with respiratory symptoms no longer visited their primary care provider but instead visited COVID-19 assessment centres.

As primary care returns to in-person visits, more work is needed to understand how to decrease unnecessary interventions such as inappropriate antibiotic prescribing. Specific interventions, such as communication skills training, educational interventions, electronic decision support systems, and delayed prescribing, can lead to reductions in antimicrobial use.[16-18] In particular, the use of peer comparison, where primary care providers received feedback comparing their rate of antibiotic prescription to the 'top-performers', providers with the lowest prescription rate, was found to decrease

inappropriate antibiotic prescriptions by 16%.[11] However, before effective AMS programs can be tested and implemented within the primary care setting, baseline prescribing levels need to be known.

The goal of this work is to contribute to AMS in Canada by illuminating baseline prescribing patterns of antibiotics in primary care across a pan-Canadian primary care network. The objective of this work is to examine the patterns of antibiotic prescribing and specifically evaluate:

1. The proportion of respiratory tract infections (RTI), influenza-like illness (ILI), and urinary tract infection (UTI) episodes that were prescribed oral antibiotics in primary care in 2019 and 2020, and the potentially inappropriate prescribing of oral antibiotics.
2. The mean duration of oral antibiotics prescribed to patients in primary care to treat an episode of RTI, ILI or UTI, and how this compares to prescribing guidelines.

Methods

Study design

This is cross-sectional study compares the prescribing of antibiotics to patients in the calendar years 2019 and 2020, using pan-Canadian Canadian Primary Care Sentinel Surveillance Network (CPCSSN) data. The study sample for each year consists of patients with a valid sex and birth year in the database and a documented visit to their primary care provider within the year of study (2019 or 2020).

CPCSSN practice-based research and learning networks (n=13) across Canada contribute their data to create the country's largest repository of primary care electronic medical record (EMR) data. For this work, we used the point-of-care de-identified data from the fourth quarter (Q4) 2020 data extraction (all clinical data up to and including December 31, 2020). These data are transformed to a standard CPCSSN schema. The architecture and approach have been described previously, including data flow, quality, mapping, cleaning and de-identification.[19]

The data include information on patients' sociodemographic characteristics, providers, encounters, health conditions, risk factors, biometrics, laboratory results, procedures, medications, and referrals. We examined the data by patient, by encounter, and by episode (defined below).

Diagnostic groups

In each study year we identified patients who met the case definition for the following diagnostic groups: RTI (five syndromes), ILI, and UTI. Due to the overlapping symptomology of RTI and ILI, these two diagnostic groups were combined in the results section. A diagnosis of RTI, ILI, or uncomplicated UTI was determined using predefined algorithms (see Appendix). The RTI, ILI, and uncomplicated UTI diagnostic groups are not mutually exclusive.

RTI/ILI and uncomplicated UTI (herein referred to as UTI) were evaluated by patient, by encounter, and by episode:

- **By patient:** If a patient met the case criteria for RTI/ILI or UTI at least once in the study year they were counted as an RTI/ILI or UTI patient.
- **By encounter:** An encounter is defined as a unique visit date on which an RTI, ILI, or UTI diagnosis is determined (as per the case definitions). A patient can have one or many encounters for RTI/ILI or UTI.
- **By episode:** An RTI or ILI episode is defined as any visit, or series of visits, within 30 days of each other, on which an RTI or ILI diagnosis is determined (as per the case definitions). The grouping into episodes was evaluated for each RTI syndrome, and for ILI, separately.

  For example, this patient has four episodes of an RTI/ILI in 2019. Note that each RTI syndrome and ILI were not grouped together.

Patient	Diagnosis	Date	
0001	pharyngitis	01JAN2019	RTI/ILI episode
0001	pharyngitis	14JAN2019	
0001	sinusitis	21JAN2019	RTI/ILI episode
0001	bronchitis	16MAR2019	RTI/ILI episode
0001	flu	27MAR2019	RTI/ILI episode

  A UTI episode is defined as any visit, or series of visits within 10 days of each other, on which a UTI diagnosis is determined (as per the case definition).

In order to capture the RTI/ILI cases in 2020 that may have been COVID-19 cases misdiagnosed as RTI/ILI we evaluated the proportion of cases that also had a COVID-19 diagnosis within 30 days of the RTI/ILI diagnosis. This exploratory analysis will help highlight the amount of misclassification within this diagnostic group.

Prescribing

For each diagnostic group we measured the number and proportion of RTI/ILI and UTI episodes that received a prescription for an oral antibiotic (ATC code J01).

- **By episode:** If a patient was prescribed an antibiotic on the day of any of the encounters that comprise an RTI/ILI or UTI episode, or one day following an encounter, that episode was categorized as treated with antibiotics.

The number and duration of each antibiotic was evaluated for each episode of RTI/ILI or UTI. If a patient's RTI/ILI or UTI episode was treated with two different antibiotics the duration of each antibiotic was tabulated separately.

Analysis

The demographic and clinical characteristics of the patients in each diagnostic group are described. CPCSSN-validated case definitions were used, where appropriate.[20]

The proportion of episodes where an antibiotic was prescribed are described using frequencies and measures of central tendency, for each diagnostic group. Prescribing for all RTIs, as well as a breakdown by RTI syndrome, is reported. To understand the variation in prescribing rates by provider we tabulated the median prescribing rate as well as the upper and lower quantiles per provider for all RTIs, as well as for each syndrome.

In order to estimate inappropriate prescribing for RTI, each syndrome was evaluated separately, and treatment by demographic and clinical characteristics was evaluated. Inappropriate antibiotic prescriptions were based on Choosing Wisely Canada (CWC) recommendations.[21] CWC has created *Using Antibiotics Wisely,* a set of resources and materials to help clinicians choose wisely in practice.

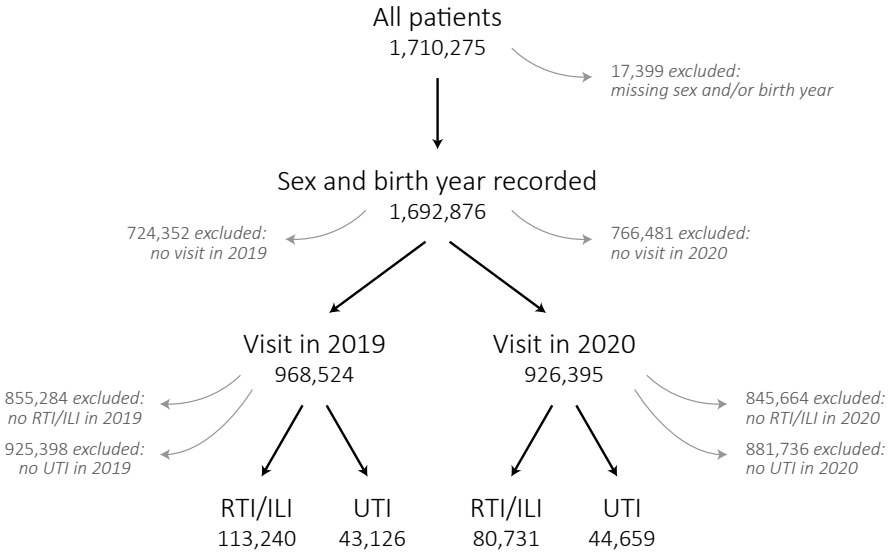
We examined the mean duration of the antibiotic prescribed for each syndrome. The duration of each antibiotic prescribed for both diagnostic groups, in each study year, was determined using the appropriate fields within the medication table of the CPCSSN database.

In order to estimate inappropriate prescribing for UTI, the type of antibiotic prescribed for each UTI episode was sorted into first-, second- or third-line categories based on prescribing guidelines.[21] The median duration of each antibiotic was also described as well as the prescribing rate.

Results

Figure 1 describes the 2019 and 2020 study populations. A comparable number of patients had a similar number of encounters with their primary care provider in 2019 compared to 2020. A total of 968,524 patients had 6,575,317 encounters in 2019 and 926,395 patients had 6,566,666 encounters in 2020. There was an absolute decrease of 32,509 in the number of patients diagnosed with at least one RTI/ILI. There was very little change in the number of patients diagnosed with at least one uncomplicated UTI.

Figure 1. Study inclusion flow chart



The demographic and clinical characteristics of the RTI/ILI and UTI study populations in 2019 are comparable to 2020 (Table 1). There was no difference in sex, but a small difference in the age distribution (more older adults), and location (more rural patients) of patients diagnosed with an RTI/ILI in 2020, compared to 2019 (p<.0001). There were significantly more patients with obesity, depression, and hypertension who were diagnosed with an RTI/ILI in 2020 compared to 2019. In the UTI group there was no change in the sex split, but a small difference in age distribution (less children) in patients diagnosed with a UTI in 2020 compared to 2019. Among those that had a UTI, there were significantly fewer with a diagnosis of chronic kidney disease, dyslipidemia, or osteoarthritis in 2020 compared to 2019.

There were a significantly lower number of RTI/ILI episodes (27.2% reduction in 2020, p<.0001); whereas, there was a small increase (7.7%) in the number of UTI episodes (Table 2).

Table 1. Demographic and clinical characteristics of study populations in 2019 and 2020

	RTI/ILI			UTI		
	2019 *n=113,240*	2020 *n=80,731*	p-value[a]	2019 *n=43,126*	2020 *n=44,659*	p-value[a]
Sex (%)						
Female	59.2	59.6	0.06	81.5	81.3	0.43
Age group (%)						
0-18	**30.8**	**26.4**	**<.0001**	**5.6**	**5.3**	**<.0001**
19-39	**22.5**	**23.7**		**20.6**	**20.9**	
40-64	**29.0**	**31.2**		**35.0**	**34.9**	
65+	**17.7**	**18.7**		**38.7**	**38.9**	
Rurality[b] (%)						
Urban	**82.8**	**82.1**	**<.0001**	81.6	81.3	0.17
Conditions/risk factors[c] (%)						
Chronic Kidney Disease	5.2	5.2	0.54	**13.2**	**12.7**	**<.0001**
Chronic Obstructive Pulmonary Disease	**3.0**	**2.8**	**0.04**	7.4	7.4	0.95
Dementia	1.7	1.6	0.73	5.4	5.2	0.32
Depression	**24.3**	**26.2**	**<.0001**	34.5	34.9	0.22
Diabetes Mellitus & Pediatric Diabetes Mellitus	**9.4**	**9.7**	**0.01**	16.9	17.0	0.76
Dyslipidemia	**29.9**	**30.7**	**0.0002**	**44.9**	**43.7**	**0.0004**
Epilepsy	1.4	1.5	0.10	1.8	1.8	0.66
Hypertension	**22.0**	**23.0**	**<.0001**	37.9	37.5	0.21
Non-Valvular Atrial Fibrillation	1.5	1.5	0.64	4.1	3.9	0.43
Obese	**16.6**	**17.8**	**<.0001**	21.2	21.6	0.15
Osteoarthritis	**14.6**	**15.0**	**0.03**	**25.9**	**25.1**	**0.007**
Parkinson's Disease	0.2	0.2	0.37	0.9	0.9	0.92
Pediatric Asthma	14.5	14.8	0.16	2.7	2.7	0.95

Bolding indicates statistically significant difference.
[a] Chi-square test
[b] In 2019, 1.8% of RTI/ILI patients and 2.0% of UTI patients were missing rurality. In 2020, 1.9% of RTI/ILI patients and 2.0% of UTI patients were missing rurality.
[c] All conditions are CPCSSN-validated conditions.

Table 2. Number of RTI/ILI and UTI episodes in 2019 and 2020

Type of infection	2019	2020	Difference, n (%)
RTI/ILI episodes[a]	144,231	100,561	-44,233 (27.2%)
UTI episodes[a]	57,466	60,844	+5,372 (7.7%)

[a] p<0.001

In order to understand the proportion of COVID-19 cases that were misclassified as RTI or ILI cases, we evaluated the total number of RTI and ILI encounters that had a COVID-19 diagnosis within 30 days. We found, across all CPCSSN networks, that less than 1% of patients with an RTI or ILI had a subsequent COVID-19 diagnosis recorded within the primary care medical record.

Prescriptions of antibiotics for RTI/ILI episodes decreased by 28.4% in 2020 (Table 3).

Table 3. Prescribing for RTI/ILI episodes in 2019 and 2020

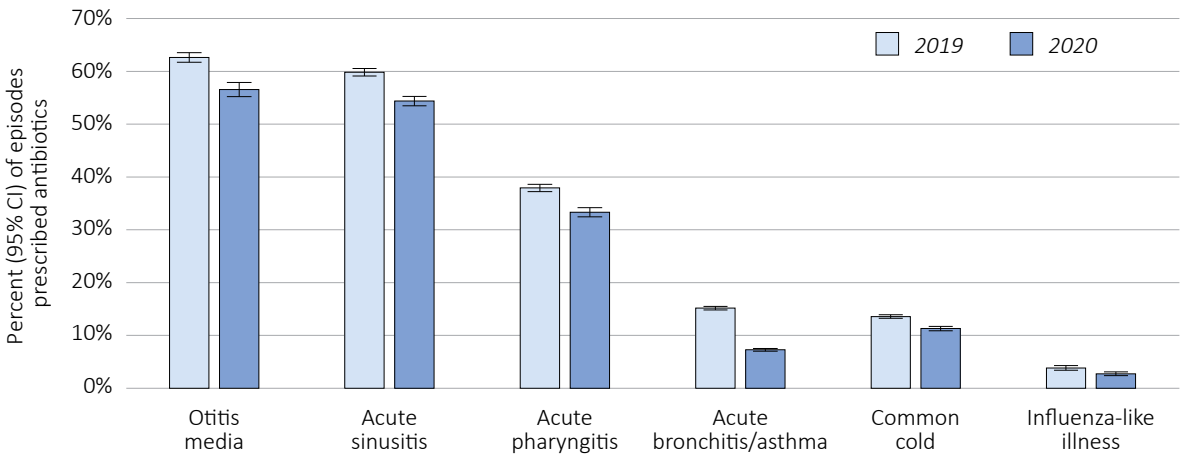
	2019		2020		Proportion Δ (% Δ)	p-value[a]
	%	*95% CI*	*%*	*95% CI*		
RTI/ILI episodes	26.7	[26.5, 27.0]	19.1	[18.9, 19.4]	-7.6 (-28.4%)	<.0001
Sex						
Male	25.4	[25.0, 27.5]	17.8	[17.5, 18.2]	-7.6% (-29.9%)	<.0001
Female	27.7	[27.4, 28.0]	20.0	[19.7, 20.3]	-7.7% (-27.8%)	<.0001
Age group						
0-18	29.0	[28.7, 29.5]	21.8	[21.3, 22.3]	-7.2% (-24.8%)	<.0001
19-39	24.2	[23.7, 24.7]	17.6	[17.2, 18.1]	-6.6% (-27.3%)	<.0001
40-64	27.5	[27.0, 27.9]	19.2	[18.8, 19.7]	-8.3% (-30.2%)	<.0001
65+	24.3	[23.7, 24.8]	17.1	[16.6, 17.7]	-7.2% (-29.6%)	<.0001
Rurality[b]						
Urban	26.0	[25.7, 26.2]	18.6	[18.3, 18.8]	-7.4% (-28.5%)	<.0001
Rural	30.6	[30.0, 31.2]	21.9	[21.3, 22.6]	-8.7% (-28.4%)	<.0001
Conditions/risk factors[c]						
Chronic Kidney Disease	24.9	[24.0, 26.0]	17.9	[16.8, 18.9]	-7.0% (-28.1%)	<.0001
Chronic Obstructive Pulmonary Disease	30.8	[29.4, 32.2]	26.6	[24.9, 28.4]	-4.2% (-13.6%)	<.0001
Dementia	19.5	[17.9, 21.1]	12.6	[11.1, 14.3]	-6.9% (-35.4%)	<.0001
Depression	27.3	[26.9, 27.8]	19.6	[19.1, 20.0]	-7.7% (-28.2%)	<.0001
Diabetes Mellitus & Pediatric Diabetes Mellitus	26.2	[25.5, 27.0]	18.7	[17.9, 19.5]	-7.5% (-28.6%)	<.0001
Dyslipidemia	26.3	[25.9, 26.7]	18.4	[18.0, 18.8]	-7.9% (-30.0%)	<.0001
Epilepsy	25.0	[25.5, 27.0]	19.1	[17.1, 21.1]	-5.9% (-23.6%)	<.0001
Hypertension	25.4	[25.0, 25.9]	17.5	[17.0, 18.0]	-7.9% (-31.1%)	<.0001
Non-Valvular Atrial Fibrillation	22.6	[20.9, 24.4]	15.9	[14.2, 17.9]	-6.7% (-29.6%)	<.0001
Obese	24.9	[24.4, 25.5]	17.8	[17.2, 18.3]	-7.1% (-28.5%)	<.0001
Osteoarthritis	26.2	[25.6, 26.8]	18.3	[17.7, 18.9]	-7.8% (-29.8%)	<.0001
Parkinson's Disease	22.0	[17.6, 27.0]	11.3	[7.6, 15.9]	-10.7% (-48.6%)	<.0001
Pediatric Asthma	21.0	[20.5, 21.5]	12.3	[11.8, 12.8]	-8.7% (-41.4%)	<.0001

All differences are statistically significant.
[a] Chi-square test
[b] In 2019, 1.8% of RTI/ILI patients were missing rurality. In 2020, 1.9% of RTI/ILI patients were missing rurality.
[c] All conditions are CPCSSN-validated conditions.

Evaluating prescribing by demographics and risk factors showed that while prescribing dropped significantly in all groups, there was some variation. Specifically, there was a larger decrease in prescribing to middle-aged and older adults compared to children (relative decrease of 24.8% in children, compared to a relative decrease of 30.2% in those 40-64 years old, and 29.6% decrease in those 65+ years old). There was no difference in prescribing rates for all RTI syndromes in rural locations compared to urban locations. However, when we evaluated RTI treatment by syndrome there was a stark, and significant, difference in prescribing for the common cold, with a relative decrease of 37.1% in urban areas, and an 11.6% increase in prescribing in rural locations. While there was a significant reduction in prescribing of antibiotics for RTI/ILI in all comorbid disease/risk factor groups, the smallest drop was seen in patients with chronic obstructive pulmonary disease (relative decrease of 13.6%), and the largest reduction was seen in patients with Parkinson's Disease (relative decrease of 48.6%), and pediatric asthma (relative decrease of 41.4%).

To establish the levels of potentially inappropriate prescribing for RTI, we evaluated RTI by syndrome, as several syndromes have no indication for antibiotics, meaning that the antibiotic prescribing rate should be zero (common cold and acute bronchitis/asthma) (Figure 2). We found that prescribing for the common cold dropped by 16.8% between 2019 and 2020 (13.6% to 11.3%, respectively, p<.0001). Prescribing for acute bronchitis/asthma dropped by 52.0% between 2019 and 2020 (15.2% to 7.9%, respectively, p<.0001)).

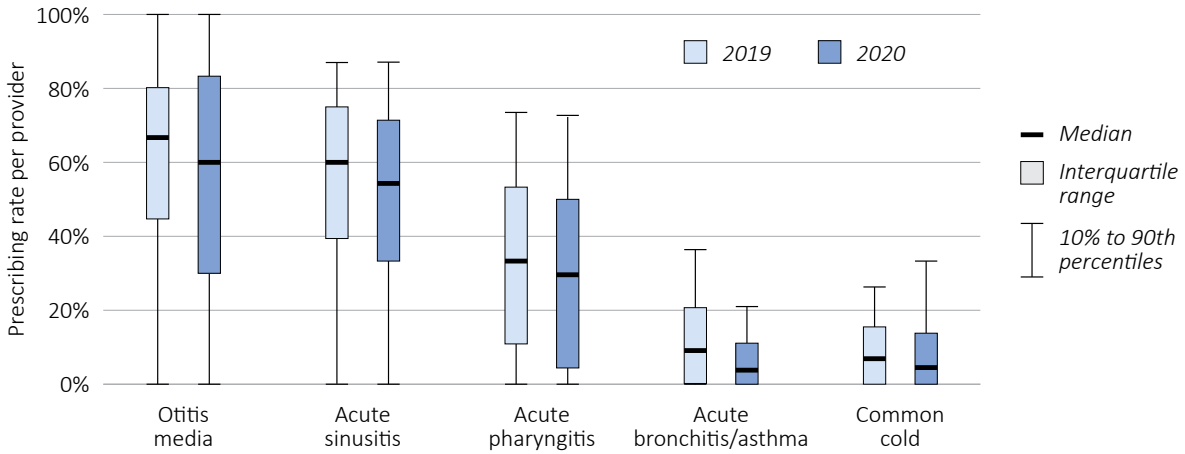
Figure 2. Prescribing for RTI, by syndrome, and ILI



There was a clinically and statistically significant (p<.0001) reduction in the average prescribing rate per provider in 2020 (median of 17.2) versus 2019 (median of 23.4) for all RTI syndromes (Figure 3a). Primary care providers that could be considered high prescribers (top quartile) were prescribing less often in 2020 (Q3=34.9%) than in 2019 (Q3=26.8%). The drop in average provider prescribing rates was most apparent for acute bronchitis/asthma and the common cold.

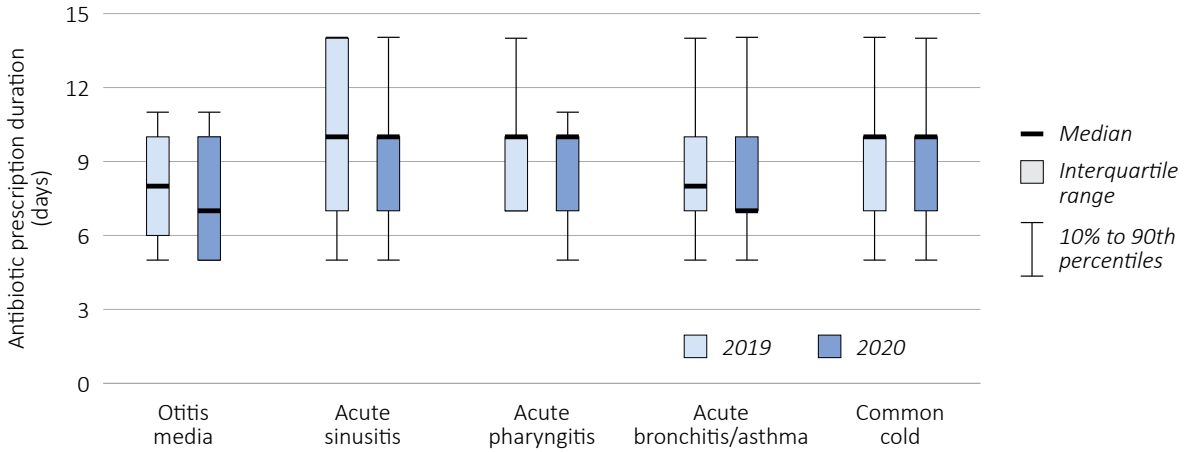
Among patients who did present to primary care and were diagnosed with an RTI there were fewer patients prescribed an antibiotic in 2020 compared to 2019. We found an absolute reduction of 45.8% unique patients prescribed an antibiotic in 2020 compared to 2019 (3.5% to 1.9%).

Figure 3a. Prescribing rate per provider for RTI, by syndrome



There was very little change in the length (duration) of the antibiotics prescribed for RTI in 2019 and in 2020 (Figure 3b). The median duration for an RTI prescription was 10 days (IQR, 3.0 days). An evaluation by syndrome shows that there was a slight decrease in the median prescribing duration for otitis media and acute bronchitis/asthma (eight days in 2019, compared to seven days in 2020).

Figure 3b. Duration of antibiotics prescribed for RTI, by syndrome



In contrast to RTI/ILI, there was no clinical or significant change in UTI incidence in 2019 compared 2020, and treatment remained relatively stable (Table 4). Over 80% of uncomplicated UTI episodes in 2019 and 2020 were treated appropriately with first-line antibiotics, and around 14% second-line antibiotics. Digging deeper into the specific antibiotics prescribed reveals that ciprofloxacin, a second-line antibiotic, was prescribed for approximately 10% of UTI episodes, in 2019 and in 2020. The median duration for each antibiotic (note, only the top five third-line antibiotics are displayed) are shown in Table 4. In both 2019 and 2020 over 80% of UTI episodes were prescribed a single antibiotic.

Unsurprisingly, a comparison of the encounter types (office versus virtual) in each study year revealed that virtual visits rose from 1.2% of visits in 2019 to 41.0% in 2020 for RTI visits, and from 3.0% of visits in 2019 to 53.2% in 2020 for UTI visits. Further analysis is planned to understand the impact virtual visits (online, via telephone, or email correspondence) had on prescribing practice compared to in-person visits at clinics.

Table 4. Prescribing for uncomplicated urinary tract infections

	2019			2020		
	n	% (95% CI)	Duration, median (IQR)	n	% (95% CI)	Duration, median (IQR)
UTI episodes	46,927			57,001		
First line antibiotics	29,646	81.8 (81.4-82.2)	2.0 (2.0)	36,289	82.9 (82.6-83.2)	1.0 (2.0)
Nitrofurantoin	21,702	59.9 (59.4-60.4)	7.0 (2.0)	25,940	59.3 (58.8-59.7)	5.0 (2.0)
Fosfomycin	4,142	11.4 (11.1-11.8)	1.0 (0)	5,734	13.1 (12.8-13.4)	1.0 (0.0)
Sulfamethoxazole and trimethoprim	3,802	10.5 (10.2-10.8)	3.0 (4.0)	4,615	10.6 (10.3-10.8)	3.0 (5.0)
Second line antibiotics	5,368	14.8 (14.4-15.2)	7 (4)	6,093	13.9 (13.6-14.2)	5.0 (6.0)
Ciprofloxacin	3,916	10.8 (10.5-11.1)	5.0 (4.0)	4,177	9.6 (9.3-9.8)	3.0 (6.0)
Amoxicillin	659	1.8 (1.7-2.0)	7.0 (3.0)	772	1.8 (1.6-1.9)	7.0 (3.0)
Cefalexin	560	1.5 (1.4-1.7)	7.0 (3.0)	805	1.8 (1.7-2.0)	7.0 (5.0)
Amoxicillin-clavulanate	226	0.6 (0.5-0.7)	10.0 (3.0)	325	0.7 (0.7-0.8)	7.0 (3.0)
Cefadroxil	7	0.02 (0.01-0.04)	7.0 (0)	14	0.03 (0.02-0.05)	6.0 (4.5)
Cefpodoxime	-			-		
Cefdinir	-			-		
Other antibiotics	1,233	3.4 (3.2-3.6)	7 (2)	1,374	3.1 (3.0-3.3)	5.0 (2.0)
Cefixime	326	0.9 (0.08-0.1)	7.0 (3.0)	521	1.2 (1.1-1.3)	7.0 (3.0)
Azithromycine	245	0.7 (0.6-0.8)	4.0 (4.5)	135	0.3 (0.3-0.4)	2.0 (4.0)
Metronidazole	159	0.4 (0.4-0.5)	7.0 (7.0)	175	0.4 (0.3-0.5)	7.0 (6.0)
Norfloxacin	117	0.3 (0.3-0.4)	7.0 (3.0)	142	0.3 (0.3-0.4)	7.0 (5.0)
Trimethoprim	77	0.3 (0.3-0.4)	3.0 (4.0)	130	0.3 (0.2-0.3)	3.0 (2.0)

Note: More than one type of antibiotic could have been prescribed per episode.

Discussion

This study compared antibiotic prescribing for RTI/ILI and UTI in primary care in Canada before and during the first year of the COVID-19 pandemic. Between 2019 and 2020 we found a similar number of total primary care visits by patients. The significant drop in the number of patients presenting to primary care with an RTI/ILI could be attributed to the change in epidemiology of RTI related to the COVID-19 pandemic and its associated public health measures. Reduced visits to primary care for RTI/ILI also translated to a large reduction in antibiotics being prescribed, but there was also a reduction in the antibiotic rate per episode when patients were seen. Specifically, the prescribing rate for asthma and acute bronchitis was cut in half and by almost 20% for the common cold. Some of this reduction may relate to presentations of COVID-19 where providers had heightened awareness that antibiotics were not indicated to treat mild infection, but this is currently unclear. Between 2019 and 2020 there was little change in the number of UTIs seen and treated by primary care, which serves as a tracer condition during the pandemic.

Anywhere from 25% to 68% of prescriptions are potentially avoidable across primary care settings.[22,23] Our study measured a large reduction in antibiotic prescribing between 2019 and 2020 for RTI/ILI with some indications that appropriateness improved particularly related to presentations of common cold and acute bronchitis. Approximately 16,000 fewer patients received an antibiotic prescription in 2020. Extrapolating our findings to the Canadian population of 38 million, there would be almost 100,000 fewer patients prescribed an antibiotic for RTI/ILI in primary care. As well, we postulate that some of this drop could be due to the increased patient awareness that antibiotics cannot treat a viral illness and therefore reduced the pressure to ask providers for an antibiotic prescription.

The reason that antibiotic prescribing for RTI/ILI increased in rural areas during the first year of the COVID-19 pandemic compared with the drop seen in urban areas is not known. One possibility is related to the differential impact of the pandemic which saw lower prevalence of COVID-19 in rural areas especially early on in the pandemic.[24]

In terms of patient groups with the least change in antibiotic prescribing, those with chronic obstructive pulmonary disease (COPD) saw the smallest reduction in antibiotics received for RTI (13.6% reduction for patients with COPD, compared to 28.4% reduction overall). The reason for this finding likely related to these patients having higher propensity for needing antibiotics overall, independent of the COVID-19 pandemic.

Increasing AMS in primary care, guided by pan-Canadian data on antibiotic prescribing patterns, has the potential to improve the health of Canadians. A silver lining of the pandemic is that there was a major decrease in antibiotic prescribing for RTI, with some indications that antibiotic prescribing for non-bacterial syndromes decreased. There is now an opportunity to sustain a decrease in antibiotic prescribing as Canada emerges from the pandemic. One potential target group for intervention is the

high-volume prescribers based on practice patterns observed before 2020. The top quartile of primary care provider prescribers, for example, were prescribing antibiotics for almost one out of every three patients presenting with RTI.

Peer feedback must be combined with behavioural change interventions in order to support successful practice changes. Choosing Wisely Canada is the national voice for reducing unnecessary tests and treatments in Canada.[25] National recommendations are already developed by professional societies that identify frequently overused tests and treatments that are not supported by scientific evidence and may expose patients to harm. In partnership with the College of Family Physicians of Canada, Choosing Wisely has developed clinical tools that can address the specific barriers to not prescribing antibiotics for viral RTI syndromes including delayed antibiotic prescriptions and viral prescription pads.[26] Another opportunity of focus aside from antibiotic initiation is the duration of therapy when antibiotics are prescribed. Our study found a median duration of 10 days for RTI, which exceeds the recommended maximum duration for most bacterial RTI syndromes.[27]

In this study, UTI was used as a tracer condition which did not see major changes in frequency or treatment as a result of the COVID-19 pandemic. We found that antibiotic choice and prescription duration was not always in line with guidelines, although this does not necessarily mean a certain agent was inappropriately used. Because the use of antibiotics for the treatment of UTI is often indicated, unlike in the case of RTI, the type and duration of antibiotics used is the most relevant factor. Second line antibiotics are appropriate under certain conditions, such as patients with allergies to first line agents, or patients with previous episodes of resistant infections.[21] This study found that ciprofloxacin is the most common second line drug being used. Although fluoroquinolones such as ciprofloxacin have been shown to be highly effective against UTIs, there is risk of severe adverse effects, and more research is needed to understand the reasons behind the high fluoroquinolone use given its increased risk profile.

Despite a lack of change in the rate of antibiotic prescriptions for UTI, there was a decrease in the duration of antibiotic prescription between 2019 and 2020 for many common antibiotics. For example, the median duration of a nitrofurantoin prescription dropped from seven days to five days; ciprofloxacin dropped from five days to three days; and amoxicillin-clavulanate prescriptions decreased from 10 days to seven days, which is all in line with guidelines.[21] While the cause of this decrease in the duration of the antibiotics prescribed for UTI between 2019 and 2020 is unknown, it is encouraging to see the durations more in line with guidelines.

Limitations

Using CPCSSN data to evaluate antimicrobial prescribing patterns in Canadian primary care has some limitations. There was some variation in the quality of the duration data. Missing data for duration for antibiotics prescribed for RTI/ILI was 31% in 2019 and 30% in 2020. For antibiotics prescribed for UTI, 41% were missing a duration in 2019 and 36% in 2020. The data can only report on what the provider has documented within the EMR; information not entered into a coded field within the medical record is not extracted nor evaluated which can lead to misclassification. However, validated case definitions were used to classify patients into the diagnostic groups, and these case definitions have been shown to have greater than 80% sensitivity and specificity.[20] The clinical records within the CPCSSN database do not contain information on any care or treatment received outside of the participating clinic. We may be undercounting the number of patients with RTI, ILI and UTI, and the number treated. This may be especially true in 2020 when there were COVID-19 assessment centres that were staffed with primary care providers offering care and treatment in provinces such as Ontario. However, this does not negate the finding of a significant reduction in provider prescribing rates to patients that did present to primary care with an RTI or ILI in 2020. The finding that less than one percent of patients diagnosed had a subsequent diagnosis of COVID-19 provides some indication that there may not be a large amount of misclassification of RTI and ILI cases. Another limitation was the amount of missing data in the medication field. However, the missing data are likely related to issues mapping the prescription data extracted from the electronic medical record to the CPCSSN schema. As such, the missingness is less likely to affect the estimate of duration as the sample size in this study was very large.

Conclusion

This study provides surveillance regarding the proportion of RTI/ILI and UTI episodes and patients prescribed oral antibiotics in primary care across a pan-Canadian network during 2019 and 2020. There is evidence of variability in practice at baseline at the provider level, and a significant decrease in prescribing for RTI during the first year of the COVID-19 pandemic. In contrast, antibiotic prescribing rates for UTI remained relatively stable. Having pan-Canadian data regarding antibiotic prescribing practices in primary care will be vital to advancing antimicrobial stewardship efforts in Canada.

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Appendix: Case definitions

RTI case definition

Each of the five following syndromes were defined as respiratory tract infections (RTI). In order to identify each syndrome, the following text and ICD-9 codes were included. Any visits associated with the exclusion text were not considered RTI related visits.

Syndrome	Inclusion criteria	Exclusion criteria
Otitis media (6 months-17 years)	381, 382	381.6, 381.7, 381. 8, 381.9
Uncomplicated pharyngitis	034, 463, 464, 462	Text includes: abscess, mononucleosis
Uncomplicated sinusitis	461	473
Upper respiratory tract infection – Common cold	460	
Acute bronchitis/Asthma (excluding COPD exacerbations)	466, 491, 492, 493, 496	COPD (as detected by CPCSSN case definition)

ILI case definition

A visit with any of the following was defined as an episode of influenza or influenza-like-illness:

1. A billing or encounter code for influenza: ICD-9 CM 487
   OR
2. An encounter diagnosis for influenza: ICD-9 CM 487.

UTI case definition

A visit with any of the following was defined as an episode of urinary tract infection:

1. A billing or encounter code for UTI: ICD-9 code 599
   OR
2. An encounter diagnosis for UTI: ICD-9 code 599
   OR
3. A prescription of any of the following medications:

Drug	ATC Code	Duration
Trimethoprim/sulfamethoxazole (TMP/SMX)	J01EE	Less than 4 days
Trimethoprim	J01EA01	Less than 4 days
Nitrofurantoin	J01XE01	Any
Ciprofloxacin	J01MA02	Less than 4 days
Fosfomycin	J01XX01	Any

CPCSSN  RCSSSP

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