Population-Based Outpatient Antimicrobial Use in Newfoundland and Labrador, a Retrospective Cohort Study

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<td>Complete List of Authors:</td>
<td>Edwards, Ben; Memorial University, Medicine Wilson, Robert; Memorial University of Newfoundland, Medicine McDonald, Gerry; Eastern Health, Pharmacy Rudnick, Wallis; Public Health Agency of Canada Daley, Peter; Memorial University, Medicine</td>
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<td>antimicrobial use, antimicrobial resistance</td>
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**Abstract:**

Background: Population-based data on outpatient antimicrobial use (AMU) has not been reported from Newfoundland & Labrador (NL). We used pharmacy network prescription data to describe outpatient AMU in NL.

Methods: All outpatient antimicrobial prescriptions between June 2017 and June 2021 were retrospectively captured from the provincial pharmacy network, representing outpatients and long-term care facilities. Patient identifiers were removed. Prescriptions for parenteral and topical antimicrobials, antivirals, and antifungals were excluded. AMU was described using prescription rate and defined daily dose (DDD) rate.

Results: 1,586,534 prescriptions given to 394,708 individuals by 3,431 prescribers were analyzed. AMU rate was 757 prescriptions/1,000 inhabitants/year (7,392 DDD/1,000 inhabitants/year). Mean prescription duration was 10.4 days (SD=11.9). 1,095,611/1,586,534 (69.1%) prescriptions were from the WHO Aware 'Access' category. Prescription rate decreased from 878/1,000 inhabitants/year to 564/1,000 inhabitants/year (-35.8%, p<0.00001) over the study period, and mean DDD rate decreased from 8,589 DDD/1,000/year to 5,684 DDD/1,000/year (-33.8%, p<0.00001). The highest use antimicrobials were Amoxicillin (1,544 DDD/1,000/year), Doxycycline (877 DDD/1,000/year) and Ciprofloxacin (685 DDD/1,000/year). Prescribers wrote a mean of 102 (SD=248) prescriptions/year and three prescribers wrote >2,500 prescriptions/year. 9,203/394,708 (2.3%) of inhabitants received four or more prescriptions/year.
Interpretation: AMU rate in NL is 25% lower than previously described in national surveillance (9,857 DDD/1,000/year). AMU was in decline prior to COVID-19, and then decreased further during the pandemic. Targets for stewardship intervention include prolonged duration, high-rate prescribers, and high-rate inhabitants. Further research is needed to assess the appropriateness of prescriptions according to diagnosis.
The RECORD statement for pharmacoepidemiology (RECORD-PE) checklist of items, extended from the STROBE and RECORD statements, which should be reported in non-interventional pharmacoepidemiological studies using routinely collected health data.

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<td>Present key elements of study design early in the paper.</td>
<td>4.a: Include details of the specific study design (and its features) and report the use of multiple designs if used. 4.b: The use of a diagram(s) is recommended to illustrate key aspects of the study design(s), including exposure, washout, lag and observation periods, and covariate definitions as relevant.</td>
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<td>6.1: The methods of study population selection (such as codes or algorithms used to identify participants) should be listed in detail. If this is not possible, an explanation should be provided. 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. 6.3: If the study involved linkage of databases, consider use of a flow</td>
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<td>7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.</td>
<td>7.1.a: Describe how the drug exposure definition was developed. 7.1.b: Specify the data sources from which drug exposure information for individuals was obtained. 7.1.c: Describe the time window(s) during which an individual is considered exposed to the drug(s). The rationale for selecting a particular time window should be provided. The extent of potential left truncation or left censoring should be specified. 7.1.d: Justify how events are attributed to current, prior, ever, or cumulative drug exposure. 7.1.e: When examining drug dose and risk attribution, describe how current, historical or time on therapy are considered. 7.1.f: Use of any comparator groups should be outlined and justified. 7.1.g: Outline the approach used to handle individuals with more than one relevant drug exposure during the study period.</td>
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(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.

**Other analyses**

- Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses.

**Discussion**

### Key results

- Summarise key results with reference to study objectives.

**Limitations**

- Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.

**Interpretation**

- Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.

**Generalisability**

- Discuss the generalisability (external validity) of the study results.

**Other information**

### Funding

- Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.

### Accessibility of protocol, raw data, and programming code

- Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.

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RECORD=reporting of studies conducted using observational routinely collected data; RECORD-PE=RECORD for pharmacoepidemiological research; STROBE=strengthening the reporting of observational studies in epidemiology.
Antibiotic Use in Outpatient and Long-Term Care NL Populations between 2017-2020

Investigators: Benjamin Edwards, Dr. Robert Wilson, Gerry McDonald, Dr. Peter Daley

Name responsible for:
- Overall quality of study:
- Management of study:
- Quality control:
- Data entry and management:
- Analysis:
- Finances:
- Publication:

Introduction

Anti-microbial resistance is a growing problem throughout the world. In 2019, the WHO declared it to be one of the top 10 threats to global public health. One-in-four Canadians received at least one antibiotic course in 2018. In the same year, one anti-microbial resistant infection was reported to the Public Health Agency of Canada (PHAC) for every 180 people admitted to hospital. The use of antibiotics can also have many adverse effects including allergic reaction and C. difficile infection. Antimicrobial consumption by Canadians increased by 1.2% between 2014 and 2018. The Eastern Canadian provinces in particular are heavy utilizers of antibiotics, with Newfoundland and Labrador combined with Prince Edward Island consuming 9,857 defined daily doses (DDDs) annually per 1,000 inhabitants, the largest quantity of antimicrobials per capita in Canada. Excessive and inappropriate antibiotic use is one of the main drivers of antimicrobial resistance. Proper antimicrobial stewardship across different levels of care is a crucial aspect of containing this issue. Since 81% of antibiotics in NL are prescribed by family practitioners, this is a crucial area of focus. Another important area is long-term care facilities, as data from other areas of Canada suggest approximately 6% of LTC residents are on antibiotics at any given time. Analysis of Long-Term Care prescription data in NL has not yet been done and would provide insight into the trends specific to that population. The objective of this study is to describe population data from 2017-2020 and quantify the average duration of antibiotic prescriptions, prevalence of repeat prescriptions, and impact of COVID-19 on antimicrobial usage. Appropriate description of usage trends can direct the areas of focus for antimicrobial stewardship interventions.
Background and Significance

Long-term care populations are an important focus for antimicrobial stewardship. As mentioned above, in a study by Daneman et al., 5.9% of long-term care (LTC) residents were receiving antibiotics at the time of their point-prevalence assessment. Similarly, Marra et al. reported that 47-79% of residents are exposed to at least 1 antibiotic over a 12-month period. It was also reported that antibiotic utilization in long-term care facilities in Ontario did not change drastically between 2007 and 2014. Although usage of most antibiotics declined in that population, use of moxifloxacin, amoxicillin-clavulanate, doxycycline, and amoxicillin increased significantly. The three most prevalent antibiotics in both studies were nitrofurantoin, trimethoprim/sulfamethoxazole, and ciprofloxacin. The indications most frequently linked to prescription were urinary tract infection, and respiratory infections. Duration of antibiotic therapy also seemed to be a problem area in long-term care, where the majority of treatment courses were at least 10 days in duration (62.6%), and many exceeded 90 days (20.9%), suggesting chronic prophylaxis is common. There was a significant inter-facility variation as reported by Daneman et al., nearly 5-fold difference in antibiotic prevalence among residents in the lowest quintile (2.24±0.9% receiving antibiotics) as compared with the highest quintile (10.8±2.6% receiving antibiotics). In our NL population, there is a high rate of inappropriate antibiotic use for asymptomatic bacteriuria in long-term care facilities. Otherwise, there is a paucity of data on antibiotic usage in NL long term care populations and more research is needed in this area.

Family physicians are the primary prescribers for outpatient populations. Similar to LTC populations, a study by Tan et al. reported antibiotic use in outpatients remained stable from 2006-2015. It was also reported that antibiotic prescriptions dispensed by retail pharmacies increase by 5.6% between 2014 and 2018. The classes of antibiotics most commonly prescribed to outpatients as reported by Schwartz et al. were penicillins, macrolides, first-generation cephalosporins, and second-generation fluoroquinolones. In the Tan et al. population, among the prescriptions with associated diagnoses, upper respiratory tract infection was the most common, followed by urinary tract infections, then skin and soft tissue infections. However, for 65.7% of the prescriptions there was no associated diagnosis. Antibiotic usage variability was significant in many areas of outpatient populations. Schwartz reported significant variability by patient age and sex, with women aged 65 years and older receiving 985 antibiotics per 1000 population whereas men aged 18–64 years received 441 antibiotics per 1000 population. The same study reported women ≥ 65 years of age more commonly received treatment with antibiotics indicated for urinary tract infections (nitrofurantoin, second-generation fluoroquinolones, and trimethoprim and/or sulfonamides). Significant variability is also reported in prescribing rates between family physicians. Locally, there is a discrepancy in antibiotic prescribing between geographic regions (17% higher in rural areas), gender (52% higher in females), and between prescribers (20% of family physicians prescribe 58% of all oral antibiotics). The most common classes of antibiotics prescribed by family physicians in NL were very similar to those reported by Schwartz et al. NL also has a similar issue in high rates of prescription of
Nitrofurantoin and Ciprofloxacin to those ≥65. Use of fluoroquinolones, specifically Ciprofloxacin is high in NL, comprising 9% of all prescriptions by family physicians.\textsuperscript{12} Indications for outpatient antibiotic prescriptions are not collected in NL, as a result, little data is available regarding unnecessary antibiotic prescribing.\textsuperscript{10}

Across all studies the lack of significant decrease in antibiotic consumption, significant variability in antibiotic rates between subpopulations, and high prevalence of use of potentially unnecessary agents (e.g., Ciprofloxacin and Nitrofurantoin) in some populations suggest vast improvements may be made with further development of antimicrobial stewardship programs. These interventions are of particular importance as antimicrobial usage has remained relatively stable in Canada from 2001-2018.\textsuperscript{1,13} Several suggestions were made across studies about how to develop stewardship, including peer-comparison audit and feedback, clinical decision support, clinician education, strengthening systems for monitoring utilization, formulary restrictions, and public education. Some of these, specifically audit and feedback and academic detailing have been implemented locally with varied efficacy.

Areas of focus in the future may include use of decreasing use of reserve antibiotics (used for multi-drug resistant infections) and broad-spectrum quinolones, consistency in prescribing between facilities and prescribers, and decreasing overall antibiotic consumption. All of these issues are present in both outpatient and long-term care populations and have been described in our local population. Analysis of data from these populations at the provincial level and description of important variables such as repeat prescriptions provide a starting point for investigations regarding potential interventions.

**Research Question**

What is the rate of antimicrobial utilization in NL outpatient and long-term care populations between 2017-2020? Further, how has the rate changed over time, what is the average duration of antibiotics prescribed, what percentage of the antibiotic prescriptions were repeat prescriptions, and how has COVID-19 impacted the usage trend?

**Methodology**

Prescription data from the NLCHI database between 2017-2020 will be analyzed using SPSS software in a retrospective cross-sectional design. Resources and equipment required for this project include the NLCHI database and data analysis software. The timeline for this project is expected to be three months in length from June to August 2021. Subjects that will be included in analysis are Newfoundland and Labrador residents who received an antibiotic prescription between January 2017-December 2020. As this is a population level analysis, no inclusion criteria, exclusion criteria, or sample size calculations are necessary. The effect of missing data is expected to be minimal and will not need to be compensated for. No statistician to be consulted, no statistical testing will be used, and all analysis will be conducted by principal investigator.
Variables to be included in analysis are: MCP (nominal), gender (nominal), age (nominal), postal code (nominal), drug (nominal), dose (continuous), frequency (ordinal), duration (continuous), and route of administration (nominal). The trends to be analyzed are change in antimicrobial rate over time (outpatient and long-term care populations) and change as a result of COVID-19. Average duration and prevalence of repeat prescriptions will also be analyzed.

**Ethical Considerations**

The Newfoundland and Labrador Health Research Ethics Board (HREB) was consulted to determine if the project would require ethics approval. It was determined that since the project is a population level analysis with minimal risk to patients and patient health information ethics approval would not be required. However, there is still some risk of breach of confidentiality via release of patient health information given an identifier (MCP number) is a variable required in our project. Precautions will be taken regarding data access to, retention, and destruction including password protection, no physical copies of data, and database encryption.

Data will be managed and analyzed by digital interface. Access to database will be via NLCHI network. Accessible only via NLCHI and will be password protected, the principal investigator will have sole access. Data will be retained via the NLCHI database for 5 years following the project as per Memorial University protocol. After this period, the data will be securely deleted.

Benefits to the participants of this project are indirect in nature. They include helping curb antimicrobial resistance in the province and development of antimicrobial stewardship programs, as well as advancement of knowledge for future generations. No conflict of interest was declared by any investigator involved in the project. Consent of patients for use of this information is not required for this project.

The budget for this project includes a small fee required by NLCHI for access to database, to be funded by Quality of Care NL. Funding for principal investigator provided by MUN via Student Undergraduate Research Award (SURA). No other costs will be incurred.
References

Population-Based Outpatient Antimicrobial Use in Newfoundland and Labrador, a Retrospective Cohort Study.

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Abstract

Background: Population-based data on outpatient antimicrobial use (AMU) has not been reported from Newfoundland & Labrador (NL). We used pharmacy network prescription data to describe outpatient AMU in NL.

Methods: All outpatient antimicrobial prescriptions between June 2017 and June 2021 were retrospectively captured from the provincial pharmacy network, representing outpatients and long-term care facilities. Patient identifiers were removed. Prescriptions for parenteral and topical antimicrobials, antivirals, and antifungals were excluded. AMU was described using prescription rate and defined daily dose (DDD) rate.

Results: 1,586,534 prescriptions given to 394,708 individuals by 3,431 prescribers were analyzed. AMU rate was 757 prescriptions/1,000 inhabitants/year (7,392 DDD/1,000 inhabitants/year). Mean prescription duration was 10.4 days (SD=11.9). 1,095,611/1,586,534 (69.1%) prescriptions were from the WHO AWaRe ‘Access’ category. Prescription rate decreased from 878/1,000 inhabitants/year to 564/1,000 inhabitants/year (-35.8%, p<0.00001) over the study period, and mean DDD rate decreased from 8,589 DDD/1,000/year to 5,684 DDD/1,000/year (-33.8%, p<0.00001). The highest use antimicrobials were Amoxicillin (1,544 DDD/1,000/year), Doxycycline (877 DDD/1,000/year) and Ciprofloxacin (685 DDD/1,000/year). Prescribers wrote a mean of 102 (SD=248) prescriptions/year and three prescribers wrote >2,500 prescriptions/year. 9,203/394,708 (2.3%) of inhabitants received four or more prescriptions/year.

Interpretation: AMU rate in NL is 25% lower than previously described in national surveillance (9,857 DDD/1,000/year). AMU was in decline prior to COVID-19, and then decreased further during the pandemic. Targets for stewardship intervention include prolonged duration, high-rate prescribers, and high-rate inhabitants. Further research is needed to assess the appropriateness of prescriptions according to diagnosis.

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Introduction

Antimicrobial Resistance (AMR) has been defined among the top 10 threats to global public health by the WHO (1). AMR was responsible for 5,400 deaths and 880,000 days in hospital in Canada in 2018, costing the Canadian healthcare system $1.4 billion (2). Antimicrobial use (AMU) is the main driver of AMR (3,4). Canada does not have a national AMU surveillance system (5), although several provinces have reported (6–8). In 2020, the Canadian Antimicrobial Resistance Surveillance System report described Newfoundland & Labrador (NL) as the highest AMU rate among provinces in Canada (9). Further research also reports NL utilizing antimicrobials well above the national rate (10,11). However, these reports used data from Canadian CompuScript and IQVIA, not from representative provincial pharmacy networks. Population-based AMU rate has not been reported from NL.

Comprehensive description of AMU is the starting point to inform antimicrobial stewardship interventions in the outpatient setting, where the majority of AMU occurs. We performed an analysis of a population level dataset extracted from the Pharmacy Network to comprehensively describe outpatient AMU in NL and identify potential areas for stewardship intervention.

Methods

Research Protocol

Included as an appendix.

Study Design and Setting

We conducted a retrospective cohort study of AMU including all outpatient antimicrobial prescriptions given to residents of NL between June 1, 2017, and June 8, 2021. Prescriptions dispensed to patients in long-term care (LTC) facilities were also included.

Data Sources

In 2014, the Newfoundland and Labrador Centre for Health Information (NLCHI) created The Pharmacy Network, a province-wide system containing every outpatient prescription dispensed by community pharmacies in NL. The Pharmacy Network is a province-wide database used by community pharmacy staff to record and share medication information in the provincial drug information system. It enables authorized health professionals to access medication profiles in an online, real-time environment. Data quality issues in this database are proactively addressed and monitored on an ongoing basis by NLCHI.

Data was acquired from NLCHI (https://www.nlchi.nl.ca/). Exclusion criteria were applied as follows:

- Topical antimicrobials
- Antiviral agents
- Antifungal agents
- Antitubercular agents
- Parenteral antimicrobials
Variables collected from each prescription include age, gender, 6-digit postal code of patient’s home address, name of provider, and provincial drug coverage status. Antimicrobials were classified using the 2022 WHO Collaborating Centre for Drug Statistics Methodology Anatomical Therapeutic Chemical (ATC)/Defined Daily Dose (DDD) Classification Index.

AMU rate was reported in Defined Daily Doses (DDD) per 1000 inhabitants per year. DDD was calculated using the ATC/DDD Index (12). Population denominators were based on Statistics Canada population estimate data (13). AMU was also reported in prescriptions per 1000 inhabitants per year, using population estimates compiled by Statistics Canada and provincial census data (14,15). Urban Forward Sortation Areas (FSAs) were defined as all those encompassed within the St. John’s metropolitan area as per the Newfoundland and Labrador Statistics Agency (16). Rural FSAs were defined as all others in the province.

Statistical Analysis

Sample size was all available prescriptions. Analysis was performed using SPSS v25 (IBM, USA). Comparisons between AMU rates were made using t-test.

Ethics

Prescriptions were anonymized prior to analysis. The local health research ethics authority determined that ethics approval was not required for this project.

Reporting

This manuscript was reported according to the RECORD statement for pharmacoepidemiology studies.

Results

1,736,229 prescriptions were included in our database, and 149,515 (8.6%) were excluded, leaving 1,586,463 prescriptions included in our analysis (see Figure 1). This represented 394,708 individuals and 3,431 prescribers. The mean age was 47.7 years (+/-23.6). Sixty-one percent of prescriptions were dispensed to women. Twenty-six percent were beneficiaries of the provincial drug program, and 1.8% were admitted to LTC. The mean duration of therapy was 10.4 ± 11.9 days (see Table 1). Duration of therapy increased from 10.4 days in the first year of the study period to 10.9 days in the last year.

The mean DDD rate during the study period was 7,392 DDD/1,000 inhabitants/year, which decreased by 33.8% (p<0.00001) during 2017-2021. The first three years of the study period included 9.11% of this decrease. Comparing the first six months of the study period to the six months prior to the COVID-19 pandemic, outpatient antimicrobial use decreased from 8015 DDD/1,000 inhabitants/year to 7401 DDD/1,000 inhabitants/year. Following this 8.29% decline, there was a 28.7% decline at the same time period following the onset of the pandemic. The mean prescription rate over the study period was 757 prescriptions/1,000 inhabitants/year (see Figure 2). Prescription rate decreased from 878/1,000 inhabitants/year to 564/1,000 inhabitants/year (-35.8% (p<0.00001)). The first three years (prior to COVID-19 appearance in Canada) included 11.1% of this decrease.
The five highest use antimicrobials by DDD were Amoxicillin (1544 DDD/1,000/yr), Doxycycline (877 DDD/1,000/yr), Ciprofloxacin (685 DDD/1,000/yr), Azithromycin (570 DDD/1,000/yr), and Amoxicillin/Beta-Lactamase Inhibitor (562 DDD/1,000/yr) (see Figure 3). Usage of each individual antibiotic declined overall. Usage of Doxycycline and Amoxicillin/Beta-Lactamase Inhibitor increased slightly in the first three years, then declined in the final year of the study period.

AMU rate was highest among the cohort aged over 80 years (1313 Rx/1,000/yr, 12614 DDD/1,000/yr). AMU by prescription rate was lowest among the cohort aged 20-39 years (522 Rx/1,000/yr and AMU by DDD was lowest in the 0-19 cohort (4879 DDD/1,000/yr). The largest decrease in AMU was seen in the cohort aged 0-19 years, among both males and females (see Figure 4). The prescription rate for the cohort aged over 80 years decreased only slightly. Females received more antimicrobial prescriptions than males in every age category. AMU increased in the 65-79 years and 80+ years age categories in 2019-2020 before declining again in 2020-2021.

Ten percent of the study population received two or more antimicrobial prescriptions per year. Over 2% of the study population received four or more antimicrobial prescriptions per year, representing 14.8% of all prescriptions.

The majority of prescriptions (69.1%) were from the WHO AWARe ‘Access’ category, with 30.9% from the ‘Watch’ category and only 0.014% from the ‘Reserve’ category (Aztreonam, Linezolid, and Colistin).

Mean duration of therapy was very high and varied widely, suggesting there is a significant proportion of long-duration prescriptions (17).

The average DDD/1,000/year by postal code was 7,209 ± 983 (see Figure 5). The top three postal codes were A0A, A0J, and A1Y. Of 35 FSAs, two (A0A and A0J) were over 2 SD above the mean (see Figure 5). One postal code (A0P) was more than 2 SD below the mean. The average DDD/1000/yr of urban areas was 6850 ± 482 and the average DDD of rural areas was 7450 ± 1146.

Prescribers in NL wrote an average of 102 antimicrobial prescriptions per year and seven prescribers wrote >2,000 antimicrobial prescriptions per year. The top fifty prescribers wrote >1,000 antimicrobials prescriptions per year (see Figure 6).

Prescription rate reported by antimicrobial class is shown in Figure 7.

**Discussion**

This is the first population-based AMU rate report from NL, and the findings do not match with previous national reports. The 2019 period was reported by Crosby (10) as 950.2 prescriptions/1000/year in NL, but we observed 719-762 prescriptions/1000/year in 2019, a difference of over 20%. In fact, the AMU rate in NL is close to the AMU rate in other provinces. We would encourage the use of representative data to describe AMU in NL.
Antimicrobial prescription rate decreased 35.8% over the study period and mean DDD rate decreased by 33.8%. Much of this decline was associated with COVID-19, however, in the period prior to COVID-19 the prescription rate decreased by 11.1%. Additional NL data on family physician prescribing, showing a 9% decrease in the number of antimicrobials written by family physicians from 2016-2017 (the year prior to our study period) supports this trend (18). Other provinces have reported similar decreases, both before and after COVID-19 (7,19).

Decrease in AMU during COVID-19 may have been caused by reduction in access to care, willingness to seek care, measures to interrupt respiratory viral transmission, or observed decreases in non-COVID respiratory virus transmission due to COVID-19 (20–23). Decrease in AMU prior to COVID-19 may have been created by antimicrobial stewardship interventions already occurring in the province. The provincial Antimicrobial Stewardship Committee and Quality of Care NL have intervened in the community with physician audit and feedback, public campaigns on antibiotic utilization, and clinical decision support tools (24–26). Other explanations include demographic changes such as changes in attitudes toward AMU among younger people (27). Data from Saatchi et al supports this, reporting a decline in usage in BC since 2000 as well as a decrease in a similar timeframe between 2015-2018 (7). However, data from Manitoba shows usage increasing in that province between 2011 and 2016 (8). Kitano et al reported a decrease in AMU during the pandemic in Ontario (28) and Knight et al showed a decreased nationally associated with COVID-19 (29).

The top 5 most prescribed antimicrobials are consistent with other sources (8,9,30,31). Ciprofloxacin was the third most utilized drug at 685 DDD/1,000/yr. Despite previous evidence showing a decrease in usage in NL (32), it remains high. This is concerning given in 2016 an FDA advisory stated the harms of quinolones usually outweigh the benefits in uncomplicated infections, in addition to the prevalence of potentially inappropriate first line use in Canada (33,34). Ciprofloxacin was moved to special authorization status in NL in 2019 (35), requiring justification for use among patients included in the prescription drug program. Rate of usage of Doxycycline and Ciprofloxacin are higher than in other provinces (9,31).

AMU decreased across all age groups. The smallest decrease was seen in the 80+ age group. The largest decrease was seen in the 0-19 age group. At the beginning of the study period, males 0-19 received more prescriptions than males 40-64, however, at the end of the period they received the lowest amount, close to the rate among females 0-19. This trend is similar to the age cohort rates reported in Manitoba (8). AMU is high in both the 65-79 and 80+ age groups, 35.1% and 73.4% higher than the general population, respectively. Possible explanations include more frequent upper respiratory tract infections among older adults, or physician and patient concern about death due to upper respiratory tract infection among the elderly population.

Several postal codes were identified as having high usage rates and there was a wide variability between postal codes, ranging from 6046 DDD/1,000/year to 9281 DDD/1,000/year. Rural postal codes were found to have higher usage than urban postal codes (p<0.05). This is consistent with data from Quality of Care NL showing that the rate of antibiotic prescriptions was 17% higher in rural compared to urban regions (36).
Prescription rate per prescriber was highly skewed (Figure 6). Fifty prescribers prescribed more than 1,000 antimicrobial prescriptions per year. Quality of Care NL reported that in 2018, 20% of family physicians wrote 56% of all oral antimicrobials (18).

Areas of possible antimicrobial stewardship intervention in NL include prolonged duration, the high-rate population, high-rate prescribers, and high-rate postal codes. Further analysis may describe these groups in more detail. Reinforcing existing stewardship interventions such as peer comparison, while strengthening others like public education campaigns, may help optimize usage to prevent an increase in AMU after the pandemic.

Our study is limited by the lack of data on diagnosis. Therefore, we cannot comment on appropriateness. Our data set included prescriptions written by out of province prescribers and 2.39% of prescriptions were not associated with any prescriber, which may have biased the mean prescriptions per prescriber rate slightly downward. Since information on prescriber clinic setting and number of patients seen was not available, we cannot comment on individual prescriber practice variation which may explain the small number of very high-rate prescribers. Approximately 2.65% of prescriptions were associated with either an invalid, or out of province postal code. Our data relies on pharmacists entering the prescription information and as such could be vulnerable to human error. Patients admitted to LTC were included in analysis, although they represented a very small proportion of prescriptions. We are planning a separate analysis of LTC prescribing. Our results are generalizable to NL only.

Conclusion

AMU rate in NL is 25% lower than described in the CARSS report, and lower than reported in prior research. COVID-19 was associated with a significant reduction in AMU in NL coinciding with the onset of public health restrictions. Further antimicrobial stewardship in needed to maintain this drastic reduction and target high usage populations. Further research in needed targeting appropriateness of prescriptions and describing AMU among LTC inhabitants.

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Disclaimer

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Figure 1: Inclusion of Prescriptions

Records provided from NLCHI Database
(n = 1,736,229)

Records screened
(n = 1,736,229)

Records excluded:
Topical preparations (n = 118,320)
Antivirals (n = 29,970)
Parenteral preparations (n = 1,405)

Records included in analysis
(n = 1,586,534)
Table 1: Demographics

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<tr>
<td>Prescriptions, n</td>
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<td>Unique Individuals, n</td>
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<tr>
<td>Gender (%)</td>
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<tr>
<td>Female</td>
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<tr>
<td>Mean Age ± SD (years)</td>
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<tr>
<td>Mean Duration of Therapy ± SD (years)</td>
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<td>Insurance (%)</td>
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<tr>
<td>Provincial Drug Program</td>
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<tr>
<td>Other</td>
<td>73.8</td>
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<tr>
<td>Admitted to Long Term Care Facility (%)</td>
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<tr>
<td>Prescribers, n</td>
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</tbody>
</table>
Figure 2: AMU (Mean Prescriptions/1000/Yr)

- 2017 - 2018: 809
- 2018 - 2019: 762
- 2019 - 2020: 719
- 2020 - 2021: 519

- January 23 - First COVID-19 Case in Canada
- March 18 - COVID-19 Declared Public Health Emergency in NL

Figure 3: Top 5 Antimicrobials (DDD/1,000/Year)

- Amoxicillin
- Doxycycline
- Ciprofloxacin
- Azithromycin
- Amoxicillin and Beta-Lactamase Inhibitor

- 2017-2018
- 2018-2019
- 2019-2020
- 2020-2021

For Peer Review Only
Figure 4: AMU (Prescriptions/1000/Yr) by Sex and Age Category
Figure 5: AMU Map (DDD/1000/Yr)
Figure 6: Prescriptions per Year by Prescriber
Figure 7: Class AMU (DDD/1,000/Year)
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