Development, Validation and Application of a Machine Learning Algorithm to Standardize Antibiotic Prescribing Records in a pan-Canadian Primary Care EMR Database: Describing Patterns of Pediatric Antibiotic Prescribing

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Abstract

Background

Most antibiotics dispensed by community pharmacies in Canada are prescribed by family physicians. Primary care electronic medical records (EMR) are an important source for understanding antibiotic prescribing patterns. Using EMR data for secondary purposes can be challenging due to variable data quality. This study used antibiotic prescriptions as an exemplar to investigate a machine learning approach for cleaning and coding antibiotic prescription data in a pan-Canadian primary care EMR database.

Methods

There were 16,119 unique prescription names in any antibiotic category in the Canadian Primary Care Sentinel Surveillance Network database. A semi-supervised classification model was developed using reference standard labels derived from the Health Canada Drug Product Database. The resulting Anatomical Therapeutic Chemical codes assigned to the medication records were verified manually to determine whether the algorithm correctly classified the medication.

Results

Overall, the algorithm performed very well compared to the reference standard (sensitivity 99.5%, specificity 92.4%, PPV 98.6%, NPV 97.0%). In a pediatric cohort receiving at least one antibiotic prescription from their primary care provider at any time (N=312,739), just over half were male (51.1%) and most lived in an urban setting (78.4%). Penicillins were the most prescribed type of antibiotic in the previous year (56.2% of all antibiotics prescribed to pediatric patients), with antibiotic prescribing generally decreasing since 2016.

Interpretation

Machine learning is a novel way to accurately standardize prescribing records from large primary care EMR datasets. Access to cleaned EMR data can support important secondary uses, including community-based antibiotic prescribing surveillance and practice improvement.

Introduction

High quality medical record data are essential for their primary purpose of supporting clinical care, as well as for important secondary uses such as clinical quality improvement studies, disease surveillance and research. Pharmacoepidemiological research traditionally relies on administrative databases such as Canada's National Prescription Drug Utilization Information System (NPDUIS)[1] or provincial or regional sources such as the Pharmaceutical Information Network (PIN) in Alberta.[2] While these databases have the advantage of covering nearly entire populations, they contain information for dispensed medications only, and not prescriptions that were issued but not filled. Dispensing data can also be challenging to use, as they may be constrained by different types of drug coverage for various age groups across time and geography. With an estimated 85% of family physicians reporting use of an electronic medical record (EMR) system in their practice,[3] the data contained within primary care EMRs provide a novel opportunity to better understand prescribing patterns, health care delivery, and patient care in the community, where the majority of health system encounters occur.[4] However, the value of EMR data for any purpose, especially when derived from multiple providers, systems or jurisdictions, can be limited, as its quality is highly variable and advanced processing and data standardization are usually required before analysis can take place.[8]

We selected antibiotic prescribing as the exemplar to model a novel approach to cleaning and standardizing EMR data. Nearly two-thirds of all antibiotics dispensed by community pharmacies in Canada are prescribed by family physicians.[5] Primary care EMR data is the only source of information about prescribed medications (not just what was dispensed in a pharmacy), which can help address important gaps in understanding antibiotic prescribing.[6] Children are especially at high risk for receiving potentially inappropriate prescribed medications, for whom estimates suggest twice as many antimicrobials are prescribed for respiratory tract infections as are expected in an outpatient setting.[7]

The primary objective of this study was therefore to build and validate a machine-learning tool to structure and code antibiotic prescription data in a pan-Canadian primary care EMR database. Our secondary objective was to describe the patterns of antibiotic prescribing for a pediatric population in primary care using the newly classified antibiotic medication data. This work aims to provide a fundamental first step towards building an antibiotic prescribing surveillance system for Canada by improving the quality of prescribed medication data available for population health surveillance, practice quality improvement studies and clinical research. It also serves to demonstrate an efficient and effective process for improving EMR data quality in general.

Methods

Data source

The Canadian Primary Care Sentinel Surveillance Network (CPCSSN) began in 2008 with a mandate to build a repository of de-identified primary care EMR data available for research, surveillance and quality improvement[4,9] CPCSSN currently extracts EMR data from over 1,400 sentinel family practices across Canada, including longitudinal information from nearly two million Canadians. The CPCSSN data included in this study were collected within seven provinces – British Columbia, Alberta, Manitoba, Ontario, Quebec, Nova Scotia and Newfoundland and Labrador. The data for this study were extracted from 12 different EMR systems on June 30, 2020 as part of CPCSSN's routine biannual extractions. Included are patient demographics, physical measurements (e.g., height, weight, blood pressure), prescribed medications, symptoms and diagnoses recorded during patient visits, billing claims, and laboratory results.[10] Extensive cleaning, coding, and processing algorithms have been built specifically for the CPCSSN dataset to manage variable data quality, since EMRs are designed for direct patient care and not for secondary purposes.[8,10,11] For example, medication data were previously standardized using a simple pattern-matching approach that assigned codes to medication names using

the Anatomical Therapeutical Chemical (ATC) Classification system.[12] Whilst this approach is effective, it is cumbersome and expensive to implement and update regularly. Our study used all medication data within the CPCSSN database (approximately 42 million records containing 2.4 million unique medication names), which included records dating from 1981 up to 2020, although most medication records (95%) were from 2008 onwards.

For the machine learning-based classifier developed for this study, the Health Canada Drug Product Database (DPD)[13] was used as the reference standard to which all prescription medications in the CPCSSN database were mapped. The DPD, which is updated nightly, contains all drug products approved for human use in Canada and is available in comma-separated values (CSV) format from the Health Canada website.[13]

Machine learning model

The *FastText* open-source library (version 0.9.2) was used to develop the machine learning model for cleaning and coding the unstructured prescribing text in the CPCSSN database.[14,15] *FastText* was selected for its efficiency when using standard computing infrastructure, as well as its ability to leverage morphemes, such as prefixes or suffixes, when training word embedding models. A large corpus of uncoded medication name text (n=2,419,786) selected from the CPCSSN database to include all antibiotic medications was used to train a skip-gram word representation model; this approach aims to predict the context (or surrounding) words given a target word. This was then used to build a semi-supervised classification model using multinomial logistic regression, with labels derived from the Health Canada DPD. The training dataset (n=151,296 records) included values sourced from the DPD, such as brand and generic names, in addition to medication names in the CPCSSN database that had been previously coded to a relatively high degree of accuracy using simple pattern and prefix matching from the DPD. We iteratively refined the model through 5 rounds of review. At each round the team

was engaged to evaluate whether the model was appropriate and to review sources of potential disagreement between the classification from the model and the reference standard.

Validation

All 16,119 unique prescription names present in any antibiotic category were drawn from the CPCSSN data; this accounted for 159 unique ATC codes for antibiotics. After the algorithm was applied to the data, a trained reviewer manually reviewed each of the 16,119 prescription instances to confirm whether it had assigned the correct ATC code, given the medication name, strength, dose, frequency, and route information available in the original record. In the case where the reviewer was unsure whether the match was correct, a consensus was sought with two other study members. The sensitivity, specificity, positive predictive and negative predictive values were calculated, comparing the algorithm-derived output to the reviewer's verification.

Statistical analysis

A descriptive analysis was then used to understand antibiotic prescribing rates among a pediatric population aged 18 years and younger in the national CPCSSN database. Age groups were calculated using year of birth, sex was described as reported in the patient EMR, residence was categorized as rural if the second digit of the patient postal code was equal to 0 and urban if the second digit was greater than 0, thus adhering to Canada Post's own urban or rural classification. Antibiotic medications were defined according to ATC code groups representing antibiotics (full list of codes in Supplementary Table 1). *PostgreSQL 11* was used for the descriptive analysis.

Ethics approval

This study received approval from the Conjoint Health Research Ethics Board at the University of Calgary (REB20-1316).

Results

Figure 1 reports the validity of the machine learning algorithm as compared to manual review of each prescription record (i.e., whether the record was assigned the correct ATC code). Overall, the algorithm performed very well compared to the reference standard, with sensitivity 99.5%, specificity 92.4%, PPV 98.6% and NPV 97.0%. In total, there were 270 records that were inaccurately classified (false positives and false negatives). In a simple post-hoc analysis of these 270 records, we found that some did not refer to antibiotics, some were misclassified as a different antibiotic, and some were the wrong medication entirely.

Table 1 summarizes the demographic characteristics of the pediatric cohort (N=312,739). Among those who had received at least one antibiotic prescription at any time from their primary care provider, most were male (51.1%) and living in an urban setting (78.4%). Penicillins were the most prescribed type of antibiotic (56.2%) (Table 1), with antibiotic prescribing in general decreasing since 2016 (Figure 2).

Interpretation

This study presents a method for cleaning, coding, and standardizing prescribed medication records in a primary care EMR database. The machine learning-based classifier accurately mapped the unstructured information in the EMR to the correct entry in the DPD. We also present the antibiotic prescribing patterns among pediatric patients who had an encounter with a primary care provider who contributed to the CPCSSN database. We focused this work on antibiotic prescribing, as it is a common activity in primary care and is also one of the more complex prescription records, in terms of having several medication classes, multiple routes (e.g., creams, pills), and is often compounded with other medications. This new method will be used to expand our standardization processes to include other types of medications in the CPCSSN database. Since machine learning is highly dependent on the

training data used, our access to a large pan-Canadian data source reinforces confidence that this method will be able to accurately classify additional medication data from various regions and different EMR systems. With the use of Health Canada's DPD as the reference standard, this ensures that newly approved medications will be immediately included in our classifier in the future.

The trends in pediatric antibiotic prescribing were not surprising, with seasonal fluctuations and an overall decrease in prescribing rates over the previous four years. This is consistent with patterns observed in other countries[16,17] and reflects the significant efforts of the national Choosing Wisely campaign to reduce antibiotic prescribing.[18] Further, antibiotic prescribing may have trailed off as a result of the COVID-19 pandemic possibly due to a reduction in conditions requiring antibiotics or through decreased visits to family physicians.

The use of coded EMR data from primary care practices provides a novel and efficient way to conduct antibiotic prescribing and other health surveillance in Canada. In the future, we may link regional CPCSSN data with administrative health data, such as PIN, to create more robust datasets that capture a more complete trajectory of diagnoses, prescriptions, and dispensed medications. This work will also inform the development of machine learning methods to code and classify the rest of the prescribed medication data in CPCSSN, as well as other types of data in EMRs such as diagnoses, medical procedures and referrals. The potential of this approach to improve EMR data quality for almost every secondary purpose is clearly significant.

Limitations

While CPCSSN is a unique data source for national pharmacoepidemiology, it is not without limitations. It does not include all practices, providers or patients, rather it is a sample of providers willing to contribute de-identified EMR data for surveillance and research. Generally, the CPCSSN

database is reasonably representative of patients (with slight over-representation of females and older adults) and providers (who are more often younger, female and in an academic practice).[19] Secondly, the machine learning algorithm developed here may not be directly portable to other data sources or settings; however, given that 12 different primary care EMR systems were included in this database, from several provincial contexts, we are relatively confident in the robustness of the model. Lastly, the machine learning model only classifies prescribed medications listed on the DPD. There may be other non-prescription medications in the medication table, as well as notes unrelated to medications (e.g., compression stockings, massage therapy recommendation, etc.), that would not be classified using this approach.

Conclusion

We developed a machine learning algorithm that classifies unstructured antibiotic medication data from primary care with a high degree of accuracy. When applied to the national CPCSSN database, this will help to provide more robust data for pharmacoepidemiology, research and clinical quality improvement, and will be transferrable to other conditions and other data in the record.

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Data Sharing

The CPCSSN database is accessible to researchers for approved uses. To submit a data access request or to find out more about the data access fees, data dictionary, and other information, visit: http://cpcssn.ca/dar/

Abbreviations

ATC	Anatomical Therapeutic Chemical (classification)
CPCSSN	Canadian Primary Care Sentinel Surveillance Network
CSV	Comma-Separated Values
DPD	Drug Product Database
EMR	Electronic Medical Record
NPDUIS	National Prescription Drug Utilization Information System
NPV	Negative Predictive Value
PIN	Pharmaceutical Information Network
PPV	Positive Predictive Value

Table 1. Demographic characteristics and antibiotic prescriptions for pediatric patients receiving at least one antibiotic prescription within primary care practices in Canada.

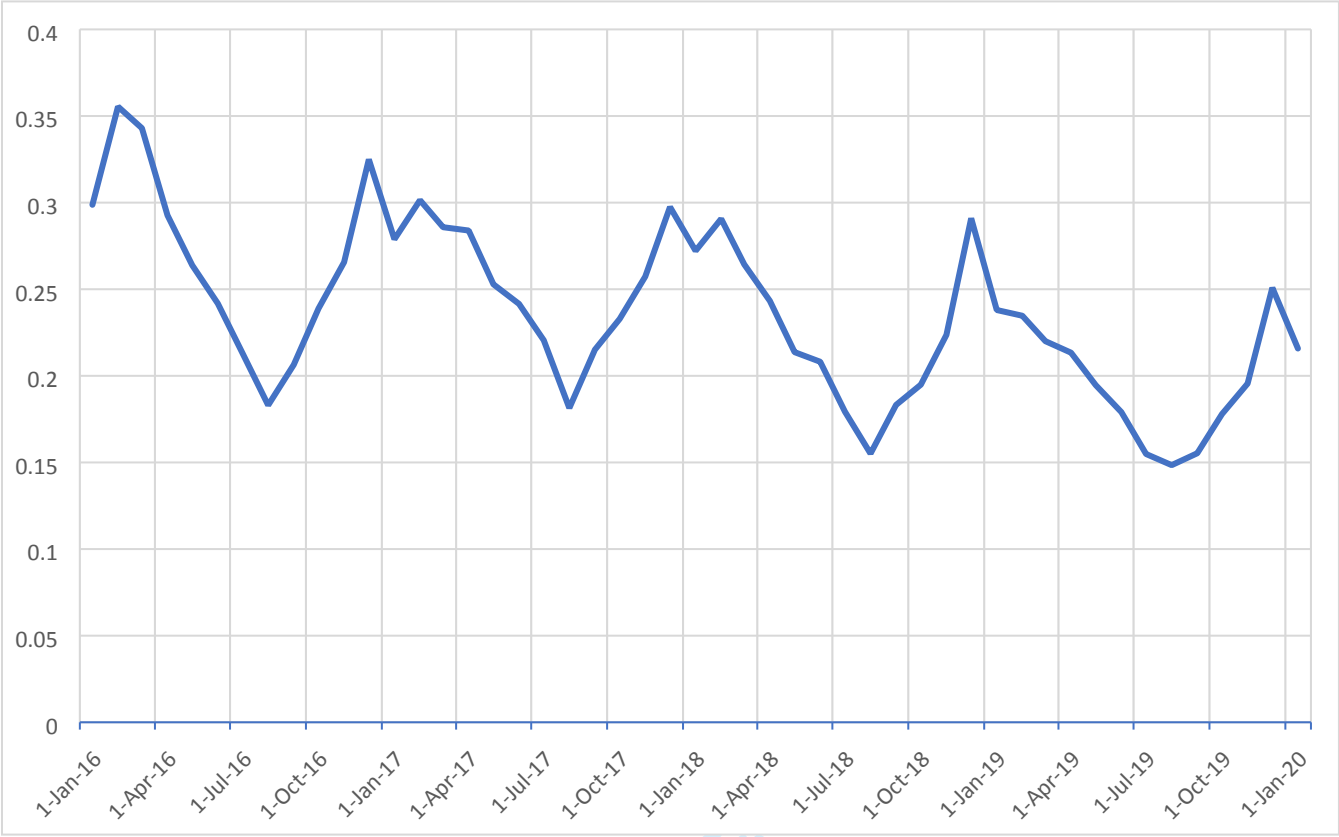
Characteristics	**Number of patients, n (%) N=312,739**
Age group (in years)	
0-4	55,449 (17.7)
5-9	93,117 (29.8)
10-14	94,465 (30.2)
15-18	69,708 (22.3)
Sex	
Female	152,468 (48.8)
Male	159,939 (51.1)
Missing sex	332 (0.1)
Residence*	
Rural	52,238 (16.7)
Urban	245,244 (78.4)
Missing postal code	15,257 (4.9)
Types of antibiotics prescribed at least once in previous year	
Any type of antibiotic	16,251 (5.2)
Penicillins	9,132 (2.9)
Cephalosporins	3,858 (1.2)
Macrolides	2,106 (0.7)
Sulfonamides	786 (0.3)

*Based on second digit of postal code, where 0=rural and >0=urban.

Figure 1. Confusion matrix comparing the machine learning algorithm to the reviewer confirmation of ATC-coded antibiotic medications in the CPCSSN database.

		Human Review			
		Yes	No		
CPCSSN Algorithm	Yes	13,451 True Positive (TP)	197 False Positive (FP)	PPV 98.6	Total Positive 13,648
	No	73 False Negative (FN)	2,398 True Negative (TN)	NPV 97.0	Total Negative 2,471
		Sensitivity 99.5	Specificity 92.4		

Figure 2. Antibiotic prescribing as a proportion of total medications prescribed by month for patients 18 years and younger (January 2016 to January 2020).



Supplementary Table 1. List of antibiotic-specific ATC codes.

ATC Code	Medication Name
A01AB22	Doxycycline
A01AB23	Minocycline
A07AA02	Nystatin
A07AA06	Paromomycin
A07AA09	Vancomycin
A07AA11	Rifaximin
A07AA12	Fidaxomicin
D06AA02	Chlortetracycline
D06AA04	Tetracycline
D06AX01	Fusidic Acid
D06AX04	Neomycin
D06AX05	Bacitracin
D06AX07	Gentamicin
D06AX09	Mupirocin
D06AX13	Retapamulin
D06AX14	Ozenoxacin
D06AX30	Combinations of Antibiotics
D06AX55	"Bacitracin, Combinations"
D06BA01	Silver Sulfadiazine
D06BA03	Mafenide
D06BA51	"Silver Sulfadiazine, Combinations
D06BX01	Metronidazole
D07CA01	Hydrocortisone and Antibiotics
D07CA02	Methylprednisolone and Antibiotics
D07CB01	Triamcinolone and Antibiotics
D07CB05	Flumetasone and Antibiotics
D07CC01	Betamethasone and Antibiotics
D07CC05	Fluocinonide and Antibiotics
D10AF01	Clindamycin
D10AF51	"Clindamycin, Combinations"
D10AF52	"Erythromycin, Combinations"
D10AF53	"Chloramphenicol, Combinations"
G01AA01	Nystatin
G01AA10	Clindamycin
G01AA51	"Nystatin, Combinations"
G01AF01	Metronidazole
J01AA01	Demeclocycline
J01AA02	Doxycycline
J01AA07	Tetracycline
J01AA08	Minocycline
J01AA09	Rolitetracycline
J01AA12	Tigecycline
J01BA01	Chloramphenicol
J01CA01	Ampicillin
J01CA02	Pivampicillin
J01CA04	Amoxicillin
J01CA06	Bacampicillin
J01CA08	Pivmecillinam
J01CA12	Piperacillin
J01CA13	Ticarcillin
J01CA51	"Ampicillin, Combinations"
J01CE01	Benzylpenicillin
J01CE02	Phenoxymethylpenicillin

J01CE08	Benzathine Benzylpenicillin
J01CE09	Procaine Penicillin
J01CE10	Benzathine Phenoxymethylpenicillin
J01CE30	Combinations
J01CF	Beta-Lactamase Resistant Penicillins
J01CF02	Cloxacillin
J01CF05	Flucloxacillin
J01CR02	Amoxicillin and Beta-Lactamase Inhibitor
J01CR03	Ticarcillin and Beta-Lactamase Inhibitor
J01CR05	Piperacillin and Beta-Lactamase Inhibitor
J01DB01	Cefalexin
J01DB03	Cefalotin
J01DB04	Cefazolin
J01DB05	Cefadroxil
J01DC01	Cefoxitin
J01DC02	Cefuroxime
J01DC03	Cefamandole
J01DC04	Cefaclor
J01DC05	Cefotetan
J01DC10	Cefprozil
J01DD01	Cefotaxime
J01DD02	Ceftazidime
J01DD04	Ceftriaxone
J01DD07	Ceftizoxime
J01DD08	Cefixime
J01DD13	Cefpodoxime
J01DE01	Cefepime
J01DF01	Aztreonam
J01DH02	Meropenem
J01DH03	Ertapenem
J01DH04	Doripenem
J01DH51	Imipenem and Cilastatin
J01DI01	Ceftobiprole Medocaril
J01DI54	Ceftolozane and Beta-Lactamase Inhibitor
J01EA01	Trimethoprim
J01EB02	Sulfamethizole
J01EB04	Sulfapyridine
J01EB05	Sulfafurazole
J01EC01	Sulfamethoxazole
J01EC02	Sulfadiazine
J01EE01	Sulfamethoxazole and Trimethoprim
J01EE02	Sulfadiazine and Trimethoprim
J01FA01	Erythromycin
J01FA02	Spiramycin
J01FA09	Clarithromycin
J01FA10	Azithromycin
J01FA15	Telithromycin
J01FF01	Clindamycin
J01FF02	Lincomycin
J01FG02	Quinopristin and Dalfopristin
J01GA01	Streptomycin
J01GB01	Tobramycin
J01GB03	Gentamicin
J01GB05	Neomycin
J01GB06	Amikacin
J01GB07	Netilmicin

J01MA01	Ofloxacin
J01MA02	Ciprofloxacin
J01MA06	Norfloxacin
J01MA11	Grepafloxacin
J01MA12	Levofloxacin
J01MA13	Trovafloxacin
J01MA14	Moxifloxacin
J01MA15	Gemifloxacin
J01MA16	Gatifloxacin
J01MB02	Nalidixic Acid
J01RA02	"Sulfonamides, Combinations With Other Antibacterials (Excl. Trimethoprim)"
J01XA01	Vancomycin
J01XA03	Telavancin
J01XA04	Dalbavancin
J01XB01	Colistin
J01XB02	Polymyxin B
J01XC01	Fusidic Acid
J01XD01	Metronidazole
J01XE01	Nitrofurantoin
J01XX01	Fosfomycin
J01XX04	Spectinomycin
J01XX05	Methenamine
J01XX08	Linezolid
J01XX09	Daptomycin
J01XX10	Bacitracin
J01XX11	Tedizolid
J01XX55	"Methenamine, Combinations"
J02AA01	Amphotericin B
J04	Antimycobacterials
J04AA02	Sodium Aminosalicylate
J04AB01	Cycloserine
J04AB02	Rifampicin
J04AB04	Rifabutin
J04AB30	Capreomycin
J04AC01	Isoniazid
J04AC51	"Isoniazid, Combinations"
J04AK01	Pyrazinamide
J04AK02	Ethambutol
J04AM05	"Rifampicin, Pyrazinamide and Isoniazid"
J04BA01	Clofazimine
J04BA02	Dapsone
P01AB01	Metronidazole
S01AA	Antibiotics
S01AA01	Chloramphenicol
S01AA02	Chlortetracycline
S01AA07	Framycetin
S01AA09	Tetracycline
S01AA11	Gentamicin
S01AA12	Tobramycin
S01AA13	Fusidic Acid
S01AA17	Erythromycin
S01AA26	Azithromycin
S01AA30	Combinations of Different Antibiotics
S01AB04	Sulfacetamide
S01AB54	"Sulfacetamide, Combinations"
S01AE01	Ofloxacin

S01AE03	Ciprofloxacin
S01AE06	Gatifloxacin
S01AE07	Moxifloxacin
S01AE08	Besifloxacin
S01CA01	Dexamethasone and Antiinfectives
S01CA02	Prednisolone and Antiinfectives
S01CA03	Hydrocortisone and Antiinfectives
S01CA05	Betamethasone and Antiinfectives
S01CA07	Fluorometholone and Antiinfectives
S02AA01	Chloramphenicol
S02AA14	Gentamicin
S02AA30	"Antiinfectives, Combinations"
S02CA02	Flumetasone and Antiinfectives
S02CA03	Hydrocortisone and Antiinfectives
S02CA05	Fluocinolone Acetonide and Antiinfectives
S02CA06	Dexamethasone and Antiinfectives
S03AA07	Ciprofloxacin
S03AA30	"Antiinfectives, Combinations"

ATC=Anatomical Therapeutic Chemical (classification system)