1 **Title Page** 2 3 Title: Population-based Assessment of Antibiotics Prescribing by Dentists in Manitoba – A Longitudinal Analysis 4 5 6 **Authors:** Aaron Quach BSc (Pharm), DMD Candidate<sup>1</sup> (ORCID ID 0000-0003-2408-466X) 7 Kevin J Friesen, MScPharm<sup>2</sup> (ORCID ID 0000-0002-6038-550X) 8 9 Jamie Falk, PharmD<sup>2</sup> (ORCID ID 0000-0003-4029-320X) Robert J Schroth, DMD, PhD<sup>1,4,5</sup> (ORCID ID 0000-0002-6262-5378) 10 Shawn Bugden, MSc, PharmD<sup>2,3</sup> (ORCID ID 0000-0002-9842-5909) 11 <sup>1</sup> Dr. Gerald Niznick College of Dentistry, Rady Faculty of Health Sciences, University of 12 Manitoba 13 <sup>2</sup>College of Pharmacy, Rady Faculty of Health Sciences, University of Manitoba 14 <sup>3</sup> School of Pharmacy, Memorial University of Newfoundland 15 <sup>4</sup>Children's Hospital Research Institute of Manitoba 16 <sup>5</sup>Shared Health Inc. 17 18 Abstract Word Count: 248 19 Total Word Count: 2607 20 21 22 23 24 **Corresponding Author:** 25 Shawn Bugden School of Pharmacy, Memorial University 26 300 Prince Phillip Drive 27 28 St John's NL Canada A1B 3V6 Email: shawn.bugden@mun.ca 29 Phone: 709-727-3629 30 31 Fax: 204-864-4819 32

34 Abstract 35 36 **Background:** 37 Antibiotic surveillance/stewardship programs have become important tools to promote optimal antibiotic 38 use. Dental prescribing of antibiotics is a significant contributor to overall antibiotic use but has received 39 limited assessment and review at the population level. 40 Methods: 41 Antibiotic prescriptions dispensed from 2014-2019 were evaluated in this longitudinal population-based study conducted in Manitoba, Canada. Antibiotic rates were adjusted for population numbers (per 1000 42 43 persons). Linear regression was used to assess trends over time for dentists and physicians. 44 **Results:** 45 Over the study period, 405,124 antibiotic prescriptions written by dentists were dispensed, representing 9.1% of all antibiotic prescriptions. Physician antibiotic prescribing dropped over time while dentist 46 47 prescribing remained unchanged (60.1 prescriptions/1000 persons). More than a quarter (27.0%) had 48 potentially inappropriate durations longer than a week. 49 Penicillins were most commonly prescribed (amoxicillin (64.1%), penicillin V (15.0%)). While limited prescriptions were written for the broader spectrum amoxicillin/clavulanate (1.9%), there was a modest 50 51 increase over time of 12.5% per year (p<0.0015). 52 Analysis by region and income showed relatively consistent results except for northern remote regions 53 where higher rates of dental prescribing were seen. 54 **Conclusions:** 55 Dental prescribing of antibiotics in Manitoba is stable but higher than national averages with some 56 indications of increased use of broad-spectrum antibiotics. This is in contrast to a significant decline of 57 overall antibiotic prescribing by physicians. 58 **Practical Implications:** 59 Current data suggest that limiting prescription duration, evaluating the need for a prescription, and increasing scrutiny of the need for broad-spectrum antibiotics may improve the overall quality of dental 60 61 antibiotic prescribing. 62 63 64 **Keywords:** Antibiotics, Dentists, Prescribing, antibiotic stewardship 65 66

# **Background**

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Antibiotic resistance is considered a serious threat to global public health by the World Health Organization (WHO). Increasing resistance rates to common infections have been observed worldwide, highlighting a need for antibiotic surveillance and stewardship programs. Across North America there have been a variety of action plans over the past decade seeking to address the problem of antimicrobial resistance by focusing on surveillance, stewardship, and innovation.<sup>2,3</sup> The appropriateness of dental use of antibiotics has been brought into question as a potential problem considering increasing resistance rates and a lack of treatment guidelines.<sup>4</sup> However, despite dentists accounting for 3-13% of all antibiotic prescribing,<sup>5–9</sup> these programs and recommendations often fail to include dentists or focus only on hospital dental practice. 10,11 Studies looking at dental prescribing have found increasing rates in North America (United States and Canada)<sup>8,12</sup> but decreasing rates have been found in England and Australia.7,9 Limited guidelines for antibiotic prescribing in dentistry as well as slow or incomplete application of existing guidelines have been suggested as a reason for inappropriate antibiotic initiation amongst dentists. 5,6,8,13,14 Choice of therapeutic antibiotic and duration is another area lacking clear guidance. 15 While various reviews highlight penicillin V as a preferred option due to its narrow spectrum and the lack of evidence of amoxicillin superiority, <sup>16,17</sup> the broader spectrum amoxicillin is more commonly prescribed.<sup>6–9,13</sup> The American Association of Endodontics (AAE) states that practitioners should minimize the use of broad spectrum antibiotics. 18 However, both the AAE and the ADA prefer amoxicillin over penicillin V due to its broader spectrum and more favorable dosing interval. 18,19 Although the ADA does list penicillin V as an alternative first line agent. In this paper, the population level data (Manitoba, Canada) for all filled antibiotic prescriptions written by dentists over a 5-year period was examined. The aim of our study was to evaluate the trends in

antibiotic prescribing by dentists and consider the impact of the focus on antibiotic stewardship on current dental antibiotic prescribing.

### Methods

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Antibiotic prescribing by dental professionals in the Province of Manitoba, Canada was assessed for the interval between April 1, 2014 and March 31, 2019. Administrative health care data including prescription dispensation records and the Manitoba Health registry were evaluated using a serial crosssectional design. Trends in dentist prescribing patterns were contrasted with those of physicians over the same time. Manitoba has a universal health care system, with all physician visits and hospitalizations provided at no cost. While dental services are not covered by the system, prescriptions written by dentists are either paid directly by patients, covered by private insurance, or fully covered by public insurance once individuals have paid their annual, income-based deductible. The administrative data generated is gathered and stored in the Manitoba Population Research Data Repository, which has been previously described in the literature and is used extensively for health, social science, education, and justice research.20,21 As dental services are not covered by the Manitoba health care system, the data on services rendered are not collected and stored in the Data Repository. However, dispensed prescriptions written by dentists, as with all other prescriptions, are collected and can be distinguished from prescriptions written by other health care professionals. All individual level data stored in the repository contains a unique, scrambled identifier allowing for the cross-linking of data across the many databases available. Oral antibiotic prescriptions dispensed in the province during the study period were identified using ATC codes starting with "J01" or with the code "P01AB01", which is an alternative ATC code for

metronidazole. The days supply field was used to describe the distribution of antibiotic treatment

length. Prescriptions were classified by prescriber into four categories: dentist, physician, nurse practitioner, or other (pharmacists, midwives, optometrists, and unknown). Rates of antibiotic use were adjusted for population numbers and expressed as units per 1000 persons.

Antibiotic prescriptions were also broken down into mutually exclusive categories based on drug or drug class. These categories were amoxicillin alone, penicillin, clindamycin, amoxicillin/clavulanate, macrolides, metronidazole, and miscellaneous. Numbers of prescriptions for each category were summarized by year.

User demographics, including age, sex, and geography were determined using the Manitoba Health registry. Postal codes were used in conjunction with Canada census data to assign individuals to income quintiles based on the average neighborhood income of each user.

Descriptive statistics were used to summarize rates of use and changes between 2014/15 and 2018/19.

Ordinary linear regression was used to assess trends in antibiotic prescribing by physicians and dentists, as well as to test for trends over time in the use of individual drug classes.

# Results

Over the period of April 2014 – March 2019, 4,452,767 oral antibiotic prescriptions were dispensed by community pharmacies in Manitoba (approximately 890,000 per year, population 1,369,852 in 2018). There were 405,124 dentist prescriptions accounting for 9.1% of the antibiotics dispensed during the study period, with physicians accounting for 87.0%, nurse practitioners 3.7%, and other prescribers contributing the remaining 0.2%. Overall, a 4.4% decrease in prescriptions was seen from 2014/15 to 2018/19, despite the population in the province increasing by 4.1% over the same period. Breaking down rates of antibiotic prescriptions by prescriber type reveals that the decline was driven by a significant drop in physician antibiotic prescribing over time ( $\beta$  = -13.21, t=-5.33 p<0.05; R<sup>2</sup>=0.90) (Figure 1). The rate of dental prescribing, meanwhile, was virtually unchanged over the study period ( $\beta$  = -

0.321, t=-0.82 p=0.47; R<sup>2</sup>=0.18). Overall, the annual rate of dental prescribing of antibiotics averaged 60.1 prescriptions per 1000 people. Men (56.8 prescriptions per 1000 persons) had significantly lower annual rate than women (63.3 prescriptions per 1000 persons)(p < 0.0001). There was also significant variation in the annual dental prescribing by age ( $\leq$ 18 – 25.8, 19 to 40 – 63.1, 41 to 59 76.7,  $\geq$ 60 74.6 prescriptions per 1000 people; ANOVA F=1182, p<0.0001).

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(7.8%) of the prescriptions were for only 1 or 2 days and may have been indicated for prophylaxis. Over a quarter of the prescriptions (27.0%) were written for durations longer than 7 days (Figure 2).

144 As a class, penicillin antibiotics accounted for the overwhelming majority of dental antibiotic 145 prescriptions accounting for 81.0% of all dental antibiotics prescribed during the study. Amoxicillin was 146 the most commonly prescribed antibiotic (64.1%) followed by penicillin V (15.0%), and clindamycin 147 (12.1%) (Figure 3). There were modest but non-significant increases in amoxicillin (62.0% to 66.8%) and 148 non-significant declines in penicillin V prescribing (15.9% to 12.8%) as a proportion of the total over 149 time. While use was relatively low (1.9%), the proportion of dental antibiotic prescriptions for 150 amoxicillin/clavulanate increased over time (1.7% to 2.4%). In relative terms, this translates to 151 approximately a 12.5% ( $\beta$  =0.10, t=3.23 p<0.05; $R^2$ =0.78) increase in amoxicillin/clavulanate prescribing 152 per year. Of note, physician prescribing of amoxicillin/clavulanate also increased by approximately 153 10.6% per year ( $\beta$  = 2.89, t=11.17 p<0.0015, R<sup>2</sup>= 0.98) during the study. For macrolides, the overall 154 proportion of antibiotic prescribing was 2.9%, but this declined during the study from 3.3% to 2.5%. In 155 relative terms, this represents a decrease of approximately 6.2% per year ( $\beta$  =-0.13, t=-21.17 p<0.001; 156 R<sup>2</sup>=0.99) in macrolide prescribing. The most common macrolide prescribed was azithromycin (62.5%)

followed by erythromycin (29.3%) and clarithromycin (8.2%).

An analysis of the rate of dental antibiotic prescriptions was conducted by region and the income quintile of the patients. In most regions, there was little difference in the rate of dental prescribing by income quintile and no appreciable change over time. However, the Northern Region showed higher prescribing rates, considerable variation in the rate of antibiotic prescribing by income quintile and a modest increase in the rate of antibiotic prescribing over time (Figure 4).

### Discussion

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From April 2014 through March 2019, Manitoba dentists prescribed 9.1% of all outpatient antibiotics. While physician prescribing of antibiotics declined during this period, there was no significant decline in dental prescriptions. Amoxicillin was the most commonly prescribed antibiotic. While the use of narrow spectrum penicillin V trended downward, there was a significant increase in the prescribing of amoxicillin/clavulanate during the study period. Overall, the results are not alarming but suggest that there may be room for improvement in antibiotic stewardship in dental prescribing. It is concerning that there was no evidence of the decline in dental antibiotic usage as seen with physician antibiotic prescribing. In addition, antibiotic stewardship programs encourage the use of narrow spectrum firstline agents, so even a modest increase in the use of the broad spectrum amoxicillin/clavulanate is an area of potential concern. Prescription duration was also mostly ≤7days as recommended, 16,19 but more than a quarter were for durations of longer than 7 days, which is another area of concern. The overall stable level of antibiotic prescribing found in this study can be contrasted to an assessment conducted in British Columbia, Canada where a greater decrease in physician prescribing was seen (18% decline) and dental antibiotic prescribing was increasing (62% increase).8 However, the British Columbia study considered a time period (1996 to 2013) prior to the start of this study. The Canadian Antimicrobial Resistance Surveillance System Report also reported a rise in dental antibiotic prescribing

from 31.3 prescriptions per 1,000 inhabitants in 2010 to 48.2 in 2014.<sup>22</sup> However, similar to what was

found in this study, dental antibiotic prescribing was relatively stable from 2014 to 2018 with a prescribing rate of 48.5 prescriptions per 1,000 inhabitants in 2018.<sup>23</sup> Data from the reports also show that on a national level, dentists provided 4.7% of outpatient antibiotic prescriptions in 2010. This peaked in 2014 with dentists prescribing 7.7% of antibiotics and remained stable with a rate of 7.4% in 2018.<sup>22,23</sup> Comparatively for the 2014-2019 period, Manitoba dentists prescribed more antibiotics both as percentage of total antibiotic prescribing (9.1% Manitoba vs. 7.4% Canada) and as a population-adjusted rate (60.1 Manitoba vs. 48.5 Canada in prescriptions/1000 people).

Study of dental antibiotic prescribing in the United States has shown some indications of a rise in antibiotic prescribing with one study showing a small rise from 1996 to 2013 with an adjusted odd ratio of 1.10.<sup>12</sup> However, both stable rates (2013-2015) and decreasing rates (2005-2010) have also been reported.<sup>24,25</sup> Internationally, England and Australia have both reported decreasing dental prescribing for 2010-2017 and 2013-2016, respectively.<sup>7,9</sup>

Across the populations of the countries studied above, amoxicillin dominates dental prescribing accounting for 56-79% of antibiotic prescriptions. <sup>6-9,13</sup> While this study found penicillin V and clindamycin to be the next more commonly prescribed, drug choice after amoxicillin varied across jurisdictions. A U.S. study and the Canadian British Columbia study found clindamycin and penicillin V to be the second and third most frequently prescribed antibiotic by dentists. <sup>8,13</sup> However, the next most common antibiotics were metronidazole and amoxicillin/clavulanate in Australia, and metronidazole and erythromycin in England. <sup>7,9</sup> A concerning increase in amoxicillin/clavulanate prescriptions was also noted in several studies. <sup>7–9</sup> Dental coverage and accessibility might differ considerably between jurisdictions, which may have considerable effects on the prescribing habits of dentists and impact the validity of comparisons across regions.

The higher level of dental antibiotic prescribing found in this study is of some concern given the global imperative to reduce and optimize antibiotic use. One possible explanation for this could be more people seeking emergency dental care instead of regular dental care in the province. Most dentists in Manitoba are graduates of the University of Manitoba DMD program, it is possible that antibiotic stewardship is not emphasized as strongly in the curriculum as other schools. Although we were unable to directly assess appropriateness, improper prescribing has the potential to be a significant contributor to the total number of dental antibiotics. In a 2017 survey in British Columbia, at least 30% of 116 general dentist and 36 endodontist respondents would prescribe antibiotics for the 6 of 7 scenarios in which antibiotics were not indicated. A

We estimated about 7.8% of dental antibiotics were prescribed for prophylaxis. Data limitations

prevented a detailed assessment of the appropriateness of these prescriptions. However, a 2015 survey of Alberta dentists and dental hygienists on the 2007 AHA infective endocarditis prophylaxis guidelines found heterogeneous results, with some respondents prescribing for procedures or conditions that did not warrant prophylaxis and others failing to prescribe when indicated. Suggested reasons included prescriber disagreement with guidelines, guideline vagueness, or difficulty remembering guidelines. Patient or physician preference is also cited as a reason for continued prophylaxis when not indicated. Given these results, it seems likely that over-prescribing of antibiotics may be occurring in dentistry and suggests a need for ongoing support, guidance, and guideline application approaches for dental antibiotic prescribing. In 2019, the ADA released a clinical practice guideline on antibiotic use for pulpal dental pain and intraoral swelling. Although the effect of these guidelines on prescribing is not yet known, the implementation of guidelines can have a profound impact on prescribing habits. After the NICE 2008 guidelines were introduced recommending the cessation of antibiotic prophylaxis for infective endocarditis prevention in England, there was a 78.6% reduction in prophylaxis prescriptions

over the following 24 months.<sup>27</sup> Antibiotic prophylaxis for third molar extraction and implant placement

is common practice but remains controversial. <sup>28</sup> Further studies and guidance on the use of antibiotics in periodontal surgery, oral surgery, extractions, and implant placement may also help reduce unwarranted antibiotics. It is worth noting that the Canadian Association of Hospital Dentists and Choose Wisely Canada have developed a resource that includes clear language on antimicrobial stewardship (<a href="https://choosingwiselycanada.org/hospital-dentistry/">https://choosingwiselycanada.org/hospital-dentistry/</a>).

In most regions, there was little impact of income on the rate of dental antibiotic prescribing. The Northern Region, however, showed higher antibiotic prescribing, an increase in prescribing over time, and rates that differed by income quintile. This area would be characterized as rural and remote and is known to have more limited access to dental service with few dental specialists. One possible explanation for this could be the use of antibiotics in lieu of definitive dental treatment or to manage infections in emergency style dentistry due to irregular access to dental services. In support of this idea, the COVID-19 pandemic limited access to dental services around the world. Data from England suggest that this limited access was associated with an increase in dental antibiotic prescribing by 25%.<sup>29</sup> In Australia, however, this pandemic period of limited access was associated with a 16% decrease in antibiotic prescribing.<sup>30</sup> Further investigation is required to evaluate the relationship between income, access and dental antibiotic prescribing.

This study has a number of strengths and limitations. A strength of this study is the ability of the Manitoba Centre for Health Policy Repository to capture all filled prescriptions at community pharmacies with the Drug Program Information Network (DPIN), allowing for the use of complete population-level data for a full 5 years. The study was also able to assess dental antibiotic prescribing by income quintile. We believe this is a novel finding and may offer insight to prescribing patterns and access in rural/remote and underserviced areas. There are also important limitations. The most important is that dental care is not publicly funded in Canada and no diagnostic codes for dental work are tracked in the provincial administrative data. Therefore, prescriptions from dentists cannot be linked

to a specific indication. In addition, there are no records of prescriptions written but not filled or of antibiotics given in hospital. The study was also limited by the lack of antibiotic resistance information to assess the appropriateness of broader spectrum antibiotics.

### Conclusion

Dental prescribing of antibiotics in Manitoba is stable but higher than national averages with some indication of increased use of broad-spectrum antibiotics. This is in contrast to a significant decline of overall antibiotic prescribing by physicians. Further efforts are necessary to enhance the support of dentists in the application of best practices related to the initiation, selection, and appropriate duration of antibiotics.

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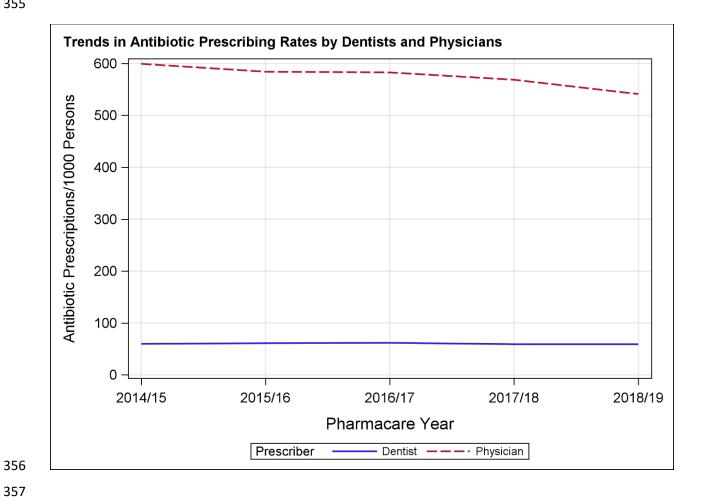
The authors acknowledge the Manitoba Centre for Health Policy for use of data contained in the Population Health Research Data Repository under project #2019/2020-22. The results and conclusions are those of the authors and no official endorsement by the Manitoba Centre for Health Policy, Manitoba Health, Senior and Active Living, or other data providers is intended or should be inferred. Data used in this study are from the Population Health Research Data Repository housed at the Manitoba Centre for Health Policy, University of Manitoba and were derived from data provided by Manitoba Health, Seniors and Active Living and the Manitoba Centre for Health Policy, University of Manitoba and were derived from data provided by Manitoba. This project was funded by a grant from the University of Manitoba. Aaron Quach received a BScDent Studentship from the Manitoba Medical Service Foundation. At the time of this study Dr. Schroth currently held a Canadian Institutes of Health Research Embedded Clinician Researcher salary award.

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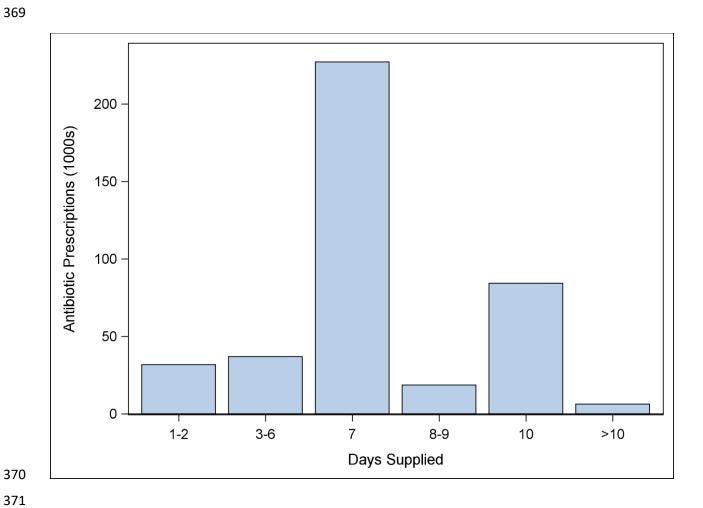
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368 Figure 2.



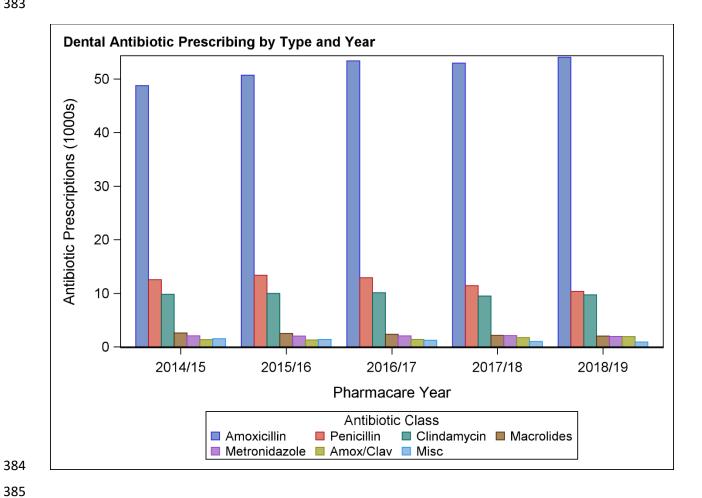


Figure 4.

Antibiotic prescription rates by income quintile: Northern Manitoba vs rest of province. Income quintiles are ordered from lowest (quintile 1) to highest (quintile 5) income level

