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**Title: An evaluation of dental antibiotic prescribing practices in the United States**

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## Background

Antibiotics are the most commonly used medications for the treatment and prevention of bacterial infections, and account for \$10.7 billion in healthcare expenditure in the United States (US).<sup>1,2</sup> However, antibiotic misuse is widespread in outpatient and inpatient clinical settings. For example, the Centers for Disease Control and Prevention (CDC) conservatively estimate that 47 million prescriptions for antibiotics (30% of all outpatient antibiotic prescriptions) are unnecessary.<sup>3</sup> Excessive antibiotic use contributes to the development of antibiotic-resistant bacteria, such as *Clostridium difficile* and carbapenem-resistant Enterobacteriaceae, which are recognized as urgent threats to the US healthcare system. Serious antibiotic-resistant bacteria are estimated to cause 23,000 deaths and 2 million illnesses in the US annually.<sup>1</sup>

A number of organizations have initiated strategies to improve antibiotic utilization, including the CDC, which has set a national goal to reduce the number of inappropriate antibiotic prescriptions by half by the year 2020.<sup>4</sup> In 2003, the CDC launched the *Get Smart about Antibiotics* campaign, aimed at educating healthcare providers and consumers about appropriate antibiotic prescribing and use.<sup>5</sup> More recently, the CDC released guidance to hospitals,<sup>6</sup> nursing homes,<sup>7</sup> and outpatient clinics<sup>8</sup> on how to improve antibiotic prescribing practices. As of January 1<sup>st</sup> 2017, The Joint Commission (a national hospital accreditation agency in the US) requires that all acute-care hospitals have an antimicrobial stewardship program to improve antibiotic prescribing practices.<sup>9</sup> Moreover, the Centers for Medicare and Medicaid Services (CMS) has proposed formal antibiotic stewardship programs in all acute-care hospitals as a condition of

participation.<sup>10</sup> Many of these initiatives are aimed at physicians, but antibiotic prescribing practices by other healthcare providers, including dentists, are likely to be closely evaluated in the future.

There is a lack of published data on the antibiotic prescribing practices of dentists. Current studies suggest that inappropriate antibiotic prescribing by dentists may be common. For example, a self-reported survey of dentists found that 70% of dentists reported inappropriate prescription of prophylactic antibiotics prior to a dental procedure.<sup>11</sup> Moreover, dentists' adherence to current antibiotic prescribing guidelines likely remain suboptimal. In a case-based survey, adherence to prescribing guidelines among pediatric dentists in North Carolina varied by 10-42%.<sup>12</sup> In a UK study of antibiotic prescribing among general dental practices, only 19% of antibiotics were prescribed in situations where their use was indicated by clinical guidelines. A similar study in the oral surgery acute dental clinic of a major London hospital reported only 30% of antibiotic prescriptions complied with clinical guidelines.<sup>13</sup>

To our knowledge, there has been only one nation-wide epidemiologic investigation of antibiotic prescribing practices by dentists in the U.S.<sup>14</sup> Roberts et al reported data on the number and type of antibiotics prescribed by general dentists. However, there is little data on the antibiotic prescribing practices among dental specialists for prophylaxis *versus* treatment purposes and the length of antibiotic treatment courses prescribed by dentists. In this study we evaluated the antibiotic prescribing practices of dentists in the US by analyzing dental antibiotic prescription claims data for a large nationally representative sample of commercially-insured individuals.

## **Methods**

Express Scripts Holding Company (ESHC) is the largest independent prescription benefits manager in the United States, with detailed prescription data for over 80 million American lives. Data on outpatient antibiotic prescriptions from dentists from January 1, 2015 through December 31, 2015 was obtained from the ESHC database. Data included prescribing dental provider specialty and location, as well as the prescribed antibiotic's name, dose, and days' supply (treatment duration). Members with missing claims information, including provider information, were excluded. Topical antibiotics, systemic or topical antifungals, antiparasitics, and antivirals were excluded. Antibiotics with the same active ingredient, but a different formulation (e.g., extended release tablets) were combined. Antimicrobials with antibacterial properties (e.g., methenamine) were included.

Provider specialties were ranked by percentage of total antibiotic prescriptions, and the top 10 were displayed (Table 1). For this initial analysis, general dentists and all dental specialists were grouped together. The number of prescribers, prescriptions, patients, and eligible beneficiaries in the database were also obtained. The number of eligible beneficiaries was defined as the total number of individuals within the ESHC database at the midpoint of the 2015 calendar year. In other words, this value represents the number of individuals who are eligible for prescription benefit coverage through ESHC. This number does not reflect the number of people who received dental care or filled any antibiotic prescriptions. The percentage of total prescribers was calculated by

dividing the number of providers within each specialty by the total number of prescribers. The percentage of antibiotic prescriptions was calculated using a similar method. The number of antibiotic prescriptions per prescriber was calculated to evaluate for high-volume antibiotic prescribing groups with fewer providers and low-volume antibiotic prescribing groups with several providers.

We reviewed the most common antibiotics prescribed by all dental providers and stratified the results by dental specialty. The number of dental specialty prescribers, number of prescriptions, number of patients, the rate of prescriptions per provider, and the rate ratio of antibiotic prescriptions compared to general dentists were analyzed from the available data. Antibiotic selection was explored by listing the top 10 most commonly prescribed antibiotics for each dental specialty. Pairwise chi-square tests were conducted to compare prescribing rates by specialty with general dentists.

Antibiotic treatment duration (number of days) was presented in a histogram. In order to distinguish antibiotic prescriptions provided for prophylaxis purposes from those provided for treatment purposes we defined antibiotic prophylaxis prescriptions as those written for  $\leq 1$  days' supply of antibiotics, and we defined treatment prescriptions as those written for  $> 1$  days' supply of antibiotics. US maps were used to evaluate for variation in state-level antibiotic prescribing practices for overall antibiotic use, antibiotic use for prophylaxis, and antibiotic use for treatment purposes. Antibiotic prescriptions were calculated by antibiotic prescription count per 100,000 eligible beneficiaries in each state to adjust for variation in the state population.

The analyses were performed with SAS (v9.4, Cary, NC, USA) and R (v3.3.1). This study was approved by the Washington University's Human Research Protection Office.

## **Results**

A total of 22,299,629 antibiotic prescriptions were prescribed by 866,916 providers out of the 38,988,099 eligible member database for the calendar year 2015. On average, 0.57 antibiotics were prescribed per beneficiary in 2015. Accounting for 17.93% of providers (155,462), dentists prescribed the third highest number of antibiotics (2,937,494 prescriptions) (Table 1). After adjusting for number of prescriptions per provider, dentists prescribed fewer antibiotics than most medical specialties (18.90 prescriptions per provider), and ranked ninth among the top 10 antibiotic prescribing specialties by prescription count, after obstetric and gynecologic providers (20.72 prescriptions per provider).

When examining antibiotic prescriptions by dental providers only, the most common antibiotics prescribed were amoxicillin, clindamycin, penicillin, azithromycin, and cephalexin (Figure 1). However, several unusual antibiotics were identified including erythromycin, an agent that is no longer recommended in the American Dental Association (ADA) guidelines, which was identified as the 10<sup>th</sup> most-commonly prescribed antibiotic. Prescriptions that lack significant antimicrobial activity against typical oral flora were also identified. Atypical antibiotics prescribed that are not optimal

for treating oral infections included drugs like ciprofloxacin (n=14,451; 0.49%), trimethoprim-sulfamethoxazole (n=3,318; 0.11%), nitrofurantoin (n=835; 0.03%), and methenamine (n=59; <0.01%).

There was a significant variation in antibiotic prescribing practices by dental specialty (Table 2). Although general dentists prescribed the highest volume of antibiotics, they had lower prescribing rates than some other dental specialists. As a specialty, Oral and Maxillofacial Pathology was much more likely to prescribe antibiotics than other dental specialties. Other high-volume dental prescribing specialties included Oral and Maxillofacial Surgery, Oral and Maxillofacial Radiology, Endodontics, and Periodontics. Orthodontists prescribed the fewest antibiotics per prescriber.

All dental providers commonly prescribed broad spectrum antibiotics, such as clindamycin and amoxicillin-clavulanate. However, antibiotic prescribing patterns varied by dental specialty for several antibiotics (Table 3). For example, periodontists prescribed doxycycline more than their peers, whereas orthodontists prescribed azithromycin more often. Interestingly, oral and maxillofacial surgeons more frequently prescribed narrower spectrum antibiotics such as penicillin and amoxicillin compared to other dental specialties.

A histogram depicting antibiotic prescription duration demonstrated that most antibiotics were prescribed for 5, 7, or 10 days (Figure 2a). There were very few prescriptions for fewer than 5 days; some prescriptions for 30 days or longer were identified, but these were rare. These findings were largely driven by amoxicillin, which showed a similar prescribing pattern (Figure 2b). Histograms stratified by common antibiotics demonstrated similar findings (Supplemental Figure). Amoxicillin, the most common antibiotic prescribed in our data, was generally written for 7 or 10 days. Similar prescribed durations were demonstrated for penicillin and amoxicillin-clavulanate. Azithromycin, clindamycin and cephalexin – recommended alternatives to amoxicillin for endocarditis prophylaxis – were rarely prescribed with fewer than 5 days of supply.

Significant variation in antibiotic prescribing rates are demonstrated by state maps (Figures 3a, 3b, and 3c). Specifically, overall antibiotic prescribing, and antibiotic prescribing rates for treatment, were highest in the southern regions (Alabama, Mississippi, Louisiana, and Arkansas) and the Northeast (New York, Massachusetts, and New Jersey). In contrast, prescribing rates for antibiotic prophylaxis were highest in the Great Plains (Kansas, Nebraska, Iowa, and South Dakota).

## **Discussion**

To our knowledge, this study is the first to provide national estimates for antibiotic treatment selection by both general dentists and dental specialists in the United States. When taken together, general dentists and dental specialists are the third highest

prescribers of antibiotics in the nation by volume. This study is also the first to examine dental antibiotic treatment duration in the US. Results of this study suggest that most antibiotics prescribed by dentists in the United States are likely for the treatment of odontogenic infections, rather than antibiotic prophylaxis. Many treatment courses utilize broad-spectrum agents such as amoxicillin-clavulanate and clindamycin. This study demonstrated that dentists occasionally prescribed antibiotics unsuited for antibiotic prophylaxis or the treatment of dental infections and with spectra of antimicrobial activity suited only for non-dental conditions, such as urinary tract infections.

Several studies have previously demonstrated that antibiotic prescribing among dentists is comparable to many medical specialties. Using national antibiotic prescribing estimates for the US in 2011, Hicks et al. identified that general dentists were responsible for 10% of antibiotic prescriptions and were the 4<sup>th</sup> highest prescriber of antibiotics in the US by volume.<sup>15</sup> In fact, general dentists in that study prescribed slightly fewer antibiotics than pediatricians (12%) and internal medicine physicians (12%). Dentists in other countries also contribute to a large percentage of antibiotic prescriptions. For example, dentists provided approximately 11.3% of all outpatient antibiotic prescriptions in British Columbia, Canada in 2013<sup>16</sup> and nearly 10% of all antibiotic prescribing in primary care in England.<sup>17</sup>

Antibiotic prescribing among dentists appears to be increasing in some countries. National antibiotic prescribing rates increased by 50% among dental practitioners in

Australia between 2001 and 2012.<sup>18</sup> Similar findings were observed in British Columbia, Canada, where dental antibiotic prescribing increased over 60% between 1996 and 2013, whereas overall antibiotic prescribing by physicians declined;<sup>19</sup> by the end of the study, the proportion of all antibiotics prescription by dentists increased from 6.7% to 11.3%. This rise in antibiotic prescriptions among dentists may be related to a number of reasons. First, individuals may be receiving better access to dental care. Second, dental providers may be performing more procedures to salvage infected teeth - rather than performing extractions. Finally, as the patient population ages, dental problems are likely becoming more common. However, regardless of the prescribing trends, some of these antibiotic prescriptions may be unnecessary.

To our knowledge, no studies have evaluated individual dental antibiotic prescriptions to determine how often antibiotics are prescribed inappropriately in the US; however, two surveys demonstrate that inappropriate antibiotic prescribing is common.<sup>11,12</sup>

Furthermore, significant geographic variation in antibiotic prescribing practices, suggests that inappropriate antibiotic prescribing is a national problem. For example, general dentists in the District of Columbia prescribed nearly twice as many antibiotics as general dentists in Delaware.<sup>14</sup> In the UK, inappropriate antibiotic prescribing appears to be common.<sup>13,20</sup> For example, in a 2016 cross-sectional study analyzing antibiotic prescribing of 568 patients among general dentists, less than 20% of antibiotics were prescribed in situations consistent with clinical guidelines.<sup>21</sup> However, these issues are not limited to just the US and UK, inappropriate antibiotic prescribing practices among dentists is a worldwide problem.<sup>22-24</sup>

Self-described issues that contribute to unnecessary antibiotic prescriptions among dentists include antibiotics to treat dental pain associated with periapical abscesses, increase in use of dental implants, slow adoption of guidelines, decreasing skill-set of the average dentist, use of antibiotics as a substitute for surgery, aging populations, and increased competition (more dentists per capita).<sup>16,25</sup> Other important factors include failure of previous operative treatment, shortage of clinical time, and patient pressure.<sup>21,26</sup>

Inappropriate antibiotic prescriptions have important costs. Unnecessary antibiotic use contributes to the selection of multidrug resistant organisms,<sup>27</sup> wastes healthcare resources,<sup>28</sup> and likely leads to a significant number of adverse patient events annually.<sup>29,30</sup> Thornhill et al. identified that even short antibiotic treatment durations associated with endocarditis prophylaxis are associated with adverse reactions, including *Clostridium difficile*.<sup>31</sup> Furthermore, narrower spectrum agents, such as amoxicillin had a significantly safer side effect profile for patients than clindamycin.

Several investigators have explored methods to improve antibiotic prescribing practices among dentists. Through a combination of audit, education and feedback on prescribing practices in England, Chate et al. reduced antibiotic use by 43% among 212 general dental providers.<sup>32</sup> A similar audit, education and feedback intervention in a London hospital dental department, improved antibiotic prescribing guideline compliance from 30% to 80%. Several other studies have also demonstrated improvements in antibiotic

prescribing practices after antimicrobial stewardship interventions.<sup>13,20,33,34</sup> These audit and feedback interventions appear to be well-received by participants. In a follow-up survey after an antibiotic audit and feedback intervention, a majority of general dentists found the experience to be both understandable and worthwhile.<sup>35</sup>

Additional studies are required to better evaluate antibiotic prescribing behavior among dentists in the US. Specific areas for further investigation include longitudinal prescribing trend analyses, evaluations of indeterminate antibiotic treatment durations (e.g., 2-4 days' supply) and prolonged treatment durations (e.g., beyond 10 days), better insights into prescriber behavior rationale, and the effect of antimicrobial stewardship interventions – such as audit and feedback in the US. Ultimately, improved antibiotic prescribing may likely require a combination of clear treatment guidelines by the ADA and/or the CDC along with comprehensive antimicrobial stewardship efforts targeted to dental prescribers.

Our study had some limitations. First, despite using one of the largest prescription databases available in the US, our cohort only included privately insured Americans and may not be generalizable to the entire US population. Specifically, most individuals with commercial insurance benefits tend to be younger and employed, married to someone who is employed, or the child of someone who has private insurance. Second, only claims that were processed and reimbursed by the payer were included in the analysis. Some enrollees may have paid for their antibiotic prescriptions without using their

insurance benefits. In particular, shorter duration (and less expensive) antibiotic prescriptions, such as antibiotics for prophylaxis may be under-represented in our data. Third, the prescription claims data lacked diagnosis or indication information. As a result, it was difficult to determine if prolonged antibiotic treatment durations were being prescribed for prophylaxis for several days following a dental procedure, non-specific conditions such as undifferentiated dental pain, or non-dental conditions like sinusitis, upper respiratory tract infections, urinary tract infections, or skin and soft tissue infections. Finally, the antibiotic prescriptions in this study are limited to those processed by one large pharmacy benefit management company and do not provide a complete picture of the antibiotic prescribing patterns for a dental provider. Thus, antibiotic prescription rates per provider do not represent the true national prescribing rates for the average dental provider.

## **Conclusions**

Our findings suggest that dentists and dental specialists are significant contributors to outpatient antibiotic prescriptions in the US. Many of these antibiotic prescriptions are written for prolonged periods of time and include broad-spectrum antibiotics. Some prescribed antibiotics appear to be for non-dental infections or unsuitable for treating dental infections. Further analyses are needed to understand, and eventually improve, antibiotic selection practices among dental providers.

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Table 1. Top 10 Antibiotic Prescribing Specialties within the Express Scripts Incorporated Database in 2015.

Rank	Specialty	No. of Prescribers	Percent of Total Prescribers	No. of Rxs	Percent of Total Rxs	No. of Patients	Rxs/Prescriber in Express Scripts	No. of Eligible Patients
1	Family Medicine	97,322	9.9%	6,543,124	20.4%	4,168,730	67.2	43,285,147
2	Internal Medicine	155,686	15.8%	4,561,532	14.2%	2,605,633	29.3	43,285,147
3	Dentists and Dental Specialties	157,016	15.9%	3,280,809	10.2%	2,325,880	20.9	43,285,147
4	Pediatrics	53,770	5.4%	2,568,436	8.0%	1,562,212	47.8	43,285,147
5	Emergency Medicine	42,814	4.3%	1,445,066	4.5%	1,196,345	33.8	43,285,147
6	Dermatology	10,839	1.1%	809,045	2.5%	356,288	74.6	43,285,147

7	Obstetrics & Gynecology	34,228	3.5%	766,007	2.4%	526,182	22.4	43,285,147
8	Urology	9,203	0.9%	646,674	2.0%	326,808	70.3	43,285,147
9	Otolaryngology	9,192	0.9%	448,645	1.4%	310,243	48.8	43,285,147
10	Surgery	24,323	2.5%	266,584	0.8%	180,940	11.0	43,285,147

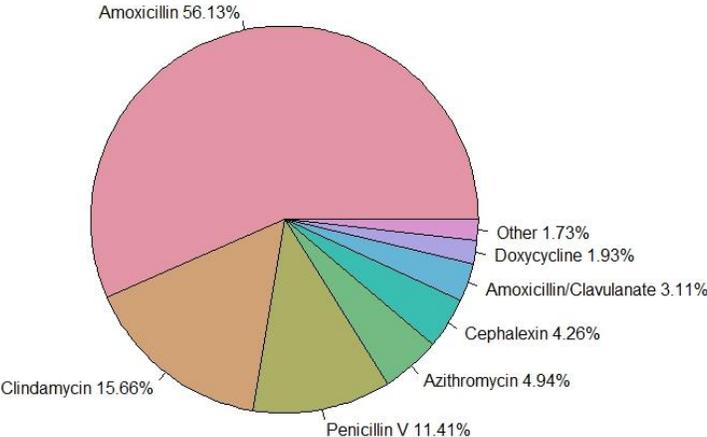
Table 2. Antibiotic Prescription Data by Dental Specialty within the Express Scripts Incorporated Database in 2015.

<b>Dental Specialty</b>	<b>Number of Prescriptions</b>	<b>Number of Prescribers</b>	<b>Prescriptions per Prescriber</b>	<b>Percent of Prescriptions (%)</b>
Dentist (general)	2,068,734	131,664	15.71	74.07%
Oral and Maxillofacial Surgery	349,247	5,485	63.67	12.50%
Periodontics	171,696	4,325	39.7	6.15%
Endodontics	145,546	4,197	34.68	5.21%
Oral and Maxillofacial Pathology	27,020	404	66.88	0.97%
Prosthodontics	18,206	1,775	10.26	0.65%
Dental Public Health	5,201	419	12.41	0.19%
Pediatric Dentistry	3,985	1,464	2.72	0.14%
Orthodontics and Dentofacial Orthopedics	2,702	969	2.79	0.10%
Oral and Maxillofacial Radiology	579	10	57.9	0.02%
<b>Total</b>	<b>2,792,916</b>	<b>150,712</b>	<b>18.53</b>	<b>100%</b>

Table 3. Most Common Antibiotics Prescribed by Dental Specialty within the Express Scripts Incorporated Database in 2015.

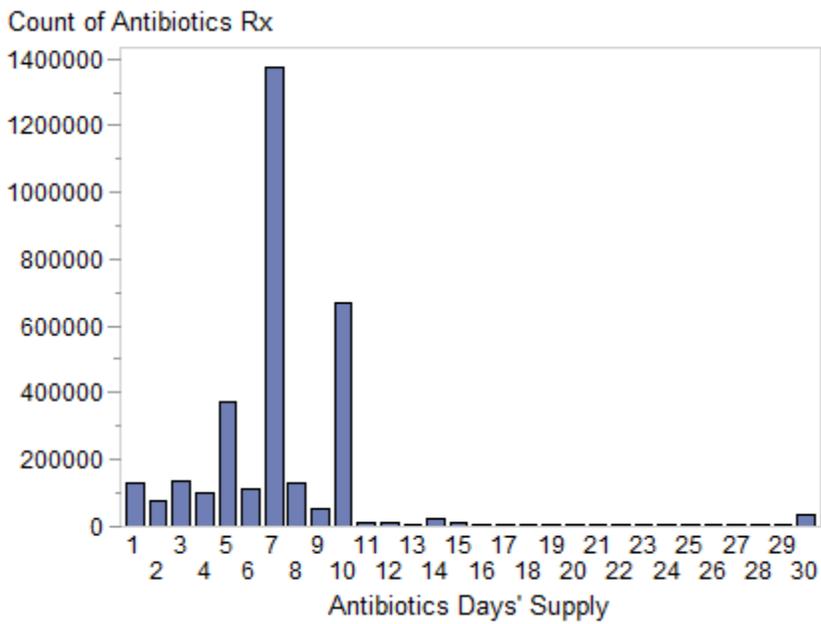
Antibiotic Rank	Dentist (general)	Oral and Maxillofacial Surgery	Periodontics	Endodontics	Oral and Maxillofacial Pathology	Pediatric Dentistry	Prosthodontics	Dental Public Health	Orthodontics and Dentofacial Orthopedics	Oral and Maxillofacial Radiology
1	Amoxicillin (56%)	Amoxicillin (58%)	Amoxicillin (60%)	Amoxicillin (47%)	Amoxicillin (56%)	Amoxicillin (50%)	Amoxicillin (63%)	Amoxicillin (53%)	Amoxicillin (33%)	Amoxicillin (79%)
2	Clindamycin (16%)	Clindamycin (15%)	Doxycycline (10%)	Clindamycin (23%)	Penicillin V (16%)	Azithromycin (19%)	Clindamycin (15%)	Clindamycin (17%)	Azithromycin (27%)	Clindamycin (12%)
3	Penicillin V (12%)	Penicillin V (14.5%)	Clindamycin (9%)	Penicillin V (12%)	Clindamycin (13%)	Penicillin V (8%)	Penicillin V (6%)	Penicillin V (15%)	Clindamycin (12%)	Azithromycin (3.0%)
4	Azithromycin (5%)	Amoxicillin/Clavulanate (4.5%)	Azithromycin (7%)	Amoxicillin/Clavulanate (6%)	Azithromycin (4.7%)	Clindamycin (7.6%)	Azithromycin (5.97%)	Cephalexin (4.1%)	Penicillin V (4.9%)	Amoxicillin/Clavulanate (2.6%)
5	Cephalexin (4.8%)	Azithromycin (3.3%)	Amoxicillin/Clavulanate (3.5%)	Azithromycin (5.6%)	Cephalexin (3.4%)	Amoxicillin/Clavulanate (3.6%)	Amoxicillin/Clavulanate (2.9%)	Azithromycin (4.0%)	Amoxicillin/Clavulanate (4.6%)	Penicillin V (1.6%)
6	Amoxicillin/Clavulanate (2.6%)	Cephalexin (2.9%)	Penicillin V (3.4%)	Cephalexin (3.1%)	Amoxicillin/Clavulanate (3.1%)	Cephalexin (3.4%)	Cephalexin (2.8%)	Amoxicillin/Clavulanate (2.2%)	Cephalexin (4.0%)	Ciprofloxacin (0.7%)
7	Doxycycline (1.6%)	Doxycycline (0.6%)	Metronidazole (2.4%)	Metronidazole (2.0%)	Doxycycline (1.2%)	Ciprofloxacin (2.3%)	Doxycycline (1.4%)	Doxycycline (2.0%)	Doxycycline (3.8%)	Levofloxacin (0.4%)
8	Metronidazole (0.8%)	Metronidazole (0.5%)	Cephalexin (2.2%)	Ciprofloxacin (0.4%)	Ciprofloxacin (0.5%)	Doxycycline (1.5%)	Metronidazole (0.8%)	Ciprofloxacin (1.0%)	Ciprofloxacin (3.0%)	Cephalexin (0.2%)
9	Ciprofloxacin (0.5%)	Ciprofloxacin (0.3%)	Ciprofloxacin (0.7%)	Doxycycline (0.36%)	Metronidazole (0.48%)	Sulfamethoxazole/Trimethoprim (1.0%)	Ciprofloxacin (0.6%)	Metronidazole (0.7%)	Sulfamethoxazole/Trimethoprim (1.8%)	Metronidazole (0.2%)
10	Erythromycin (0.4%)	Levofloxacin (0.3%)	Levofloxacin (0.3%)	Levofloxacin (0.2%)	Levofloxacin (0.3%)	Levofloxacin (0.7%)	Erythromycin (0.5%)	Erythromycin (0.6%)	Metronidazole (1.5%)	n/a

Figure 1. Top 10 Antibiotics Prescribed by Dentists within the Express Scripts Incorporated Database in 2015.



Other: Metronidazole (0.89%), Erythromycin base (0.33%)

Figure 2a. Histogram of Days' Supply of All Antibiotics Prescribed by Dentists within the Express Scripts Incorporated Database in 2015.



Note. Dental claims are truncated to 30 days' supply.

Figure 2b. Histogram of Days' Supply of Amoxicillin Prescribed by Dentists within the Express Scripts Incorporated Database in 2015.

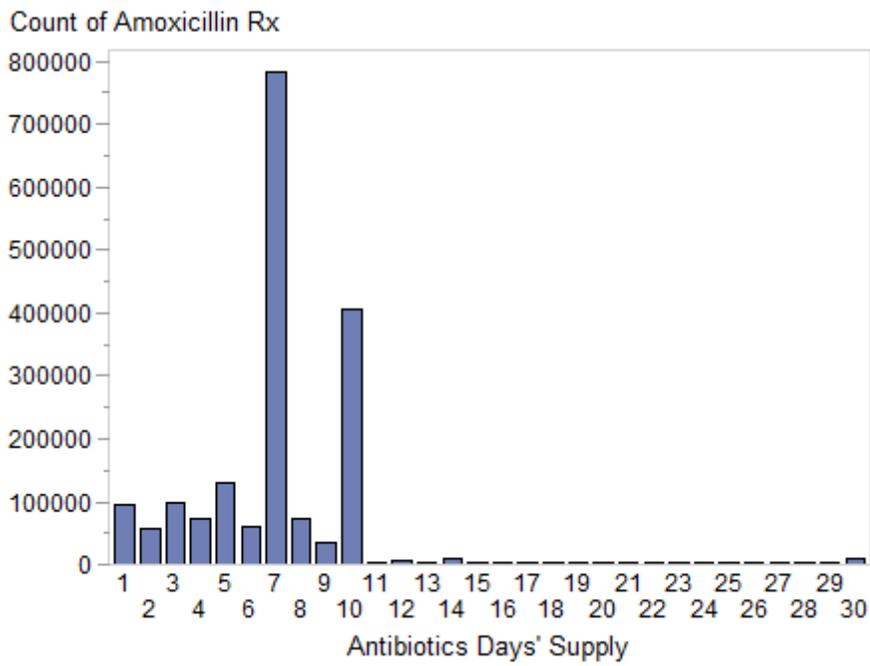


Figure 3a. Map of All Antibiotics Prescribed by Dentists within the Express Scripts Incorporated Database in 2015.

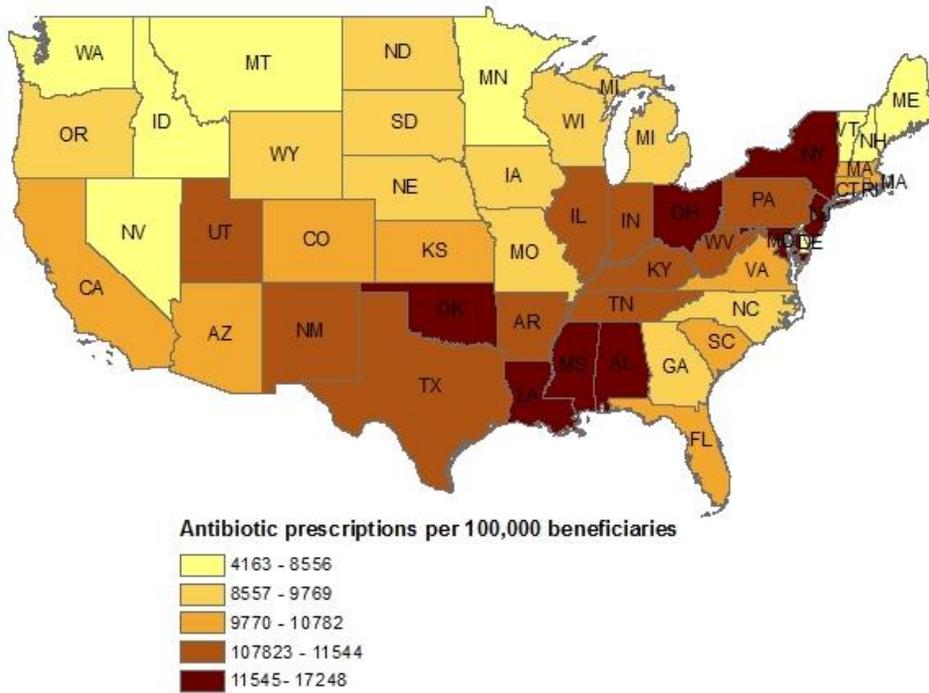


Figure 3b. Map of Dental Antibiotic Prescriptions (prophylaxis) by State, 2015

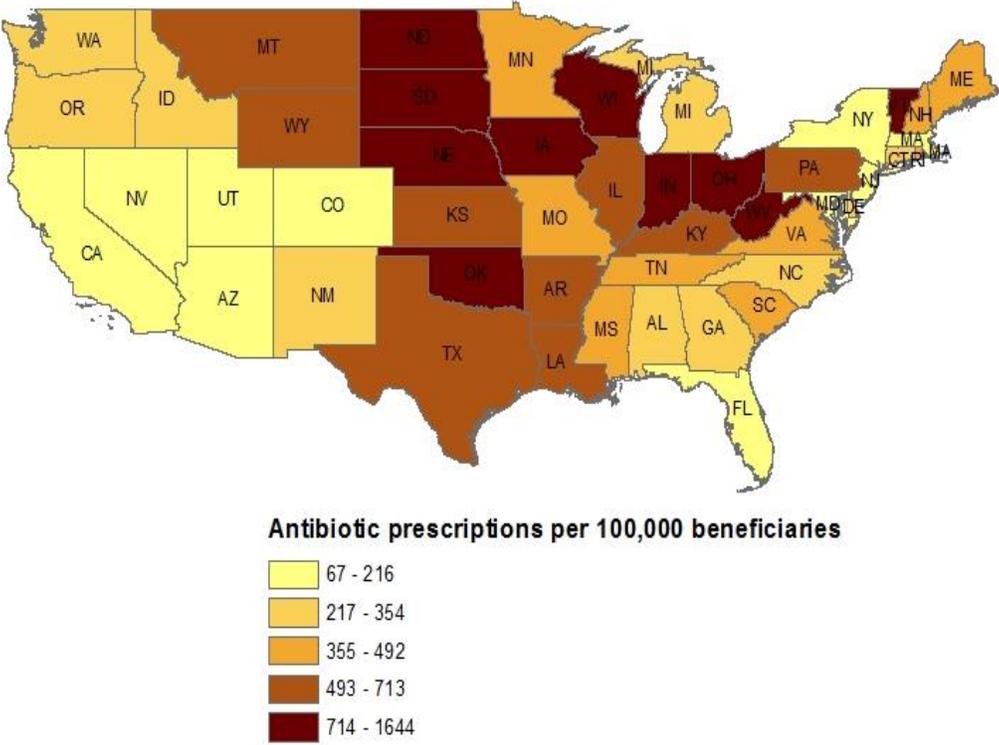
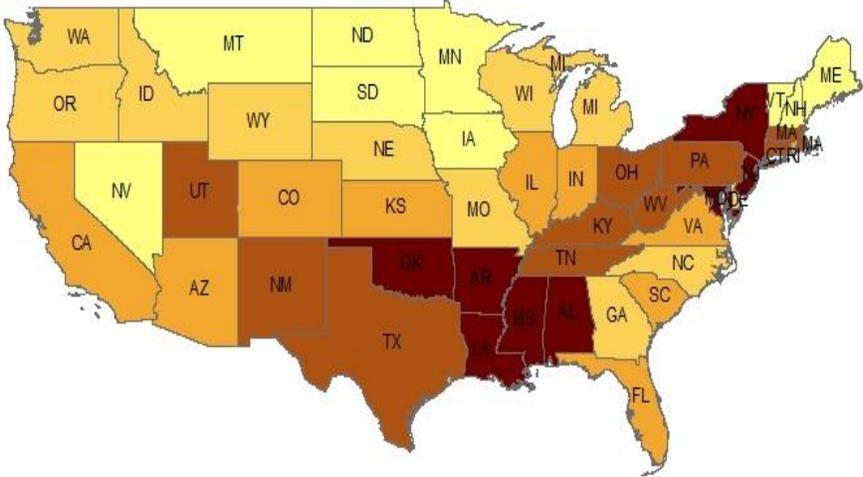
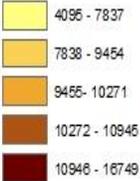


Figure 3c. Map of Dental Antibiotic Prescriptions (treatment) by State, 2015

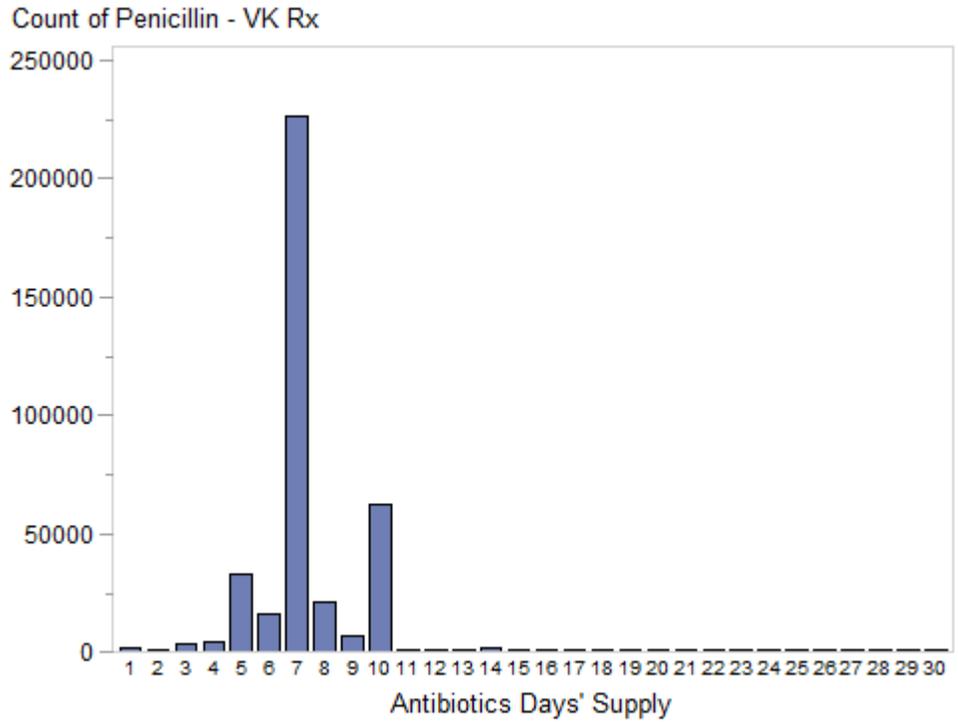


Antibiotic prescriptions per 100,000 beneficiaries

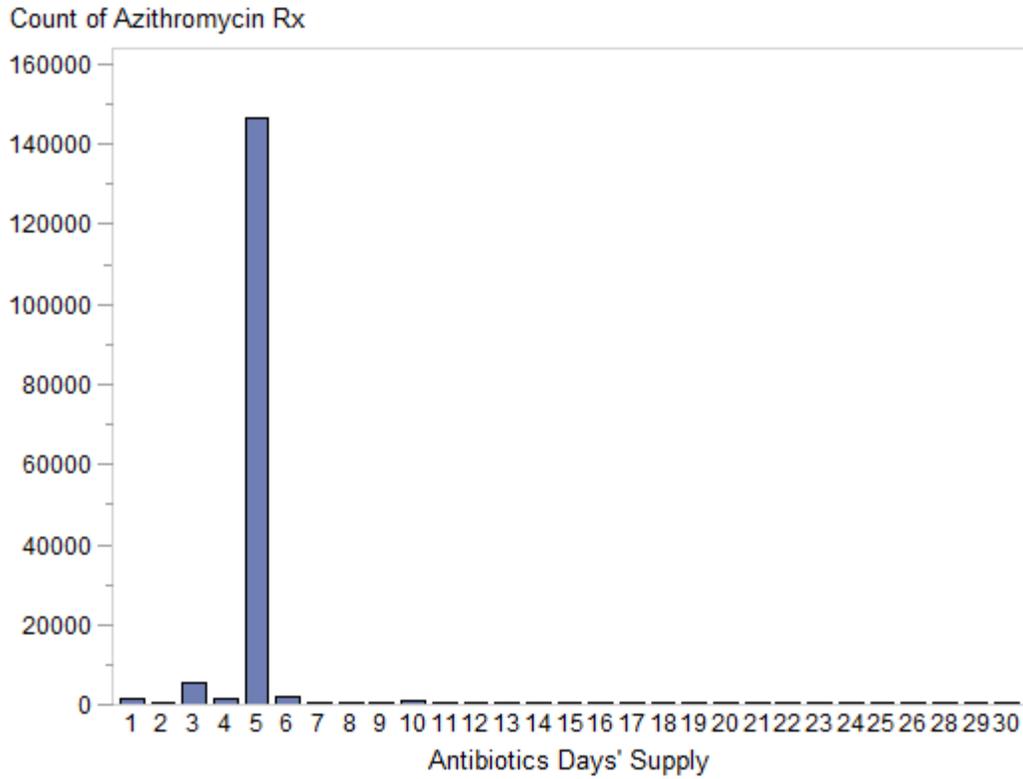


Supplementary Appendix:

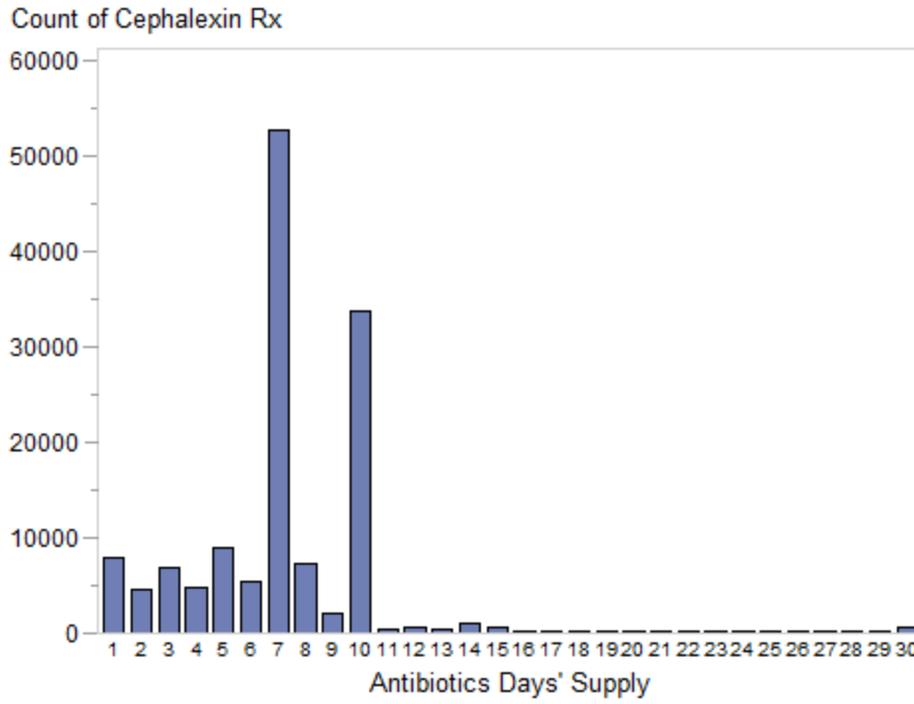
Histogram of Days' Supply of Penicillin Prescribed by Dentists within the Express Scripts Incorporated Database in 2015.



Histogram of Days' Supply of Azithromycin Prescribed by Dentists within the Express Scripts Incorporated Database in 2015.



Histogram of Days' Supply of Cephalexin Prescribed by Dentists within the Express Scripts Incorporated Database in 2015.



Histogram of Days' Supply of Clindamycin Prescribed by Dentists within the Express Scripts Incorporated Database in 2015.

