Patterns of dental antibiotic prescribing in 2017: Australia, England, United States, and British Columbia (Canada)

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Abstract

Objective: Our objective was to compare patterns of dental antibiotic prescribing in Australia, England, and North America (United States and British Columbia, Canada).


Participants: Patients receiving an antibiotic dispensed by an outpatient pharmacy.

Methods: Prescription-based rates adjusted by population were compared overall and by antibiotic class. Contingency tables assessed differences in the proportion of antibiotic class by country.

Results: In 2017, dentists in the United States had the highest antibiotic prescribing rate per 1,000 population and Australia had the lowest rate. The penicillin class, particularly amoxicillin, was the most frequently prescribed for all countries. The second most common agents prescribed were clindamycin in the United States and British Columbia (Canada) and metronidazole in Australia and England. Broad-spectrum agents, amoxicillin-clavulanic acid, and azithromycin were the highest in Australia and the United States, respectively.

Conclusion: Extreme differences exist in antibiotics prescribed by dentists in Australia, England, the United States, and British Columbia. The United States had twice the antibiotic prescription rate of Australia and the most frequently prescribed antibiotic in the US was clindamycin. Significant opportunities exist for the global dental community to update their prescribing behavior relating to second-line agents for penicillin allergic patients and to contribute to international efforts addressing antibiotic resistance. Patient safety improvements will result from optimizing dental antibiotic prescribing, especially for antibiotics associated with resistance (broad-spectrum agents) or C. difficile (clindamycin). Dental antibiotic stewardship programs are urgently needed worldwide.

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Antibiotic resistance is a major public health burden driven by the unnecessary use of antibiotics. Dentists contribute significantly to global antibiotic use and are responsible for an estimated 10% of all antibiotics prescribed to humans. The FDI World Dental Federation has highlighted the overwhelming case for restricting the use of antibiotics to only when absolutely necessary. High rates of dental overprescribing in relation to national guidelines have been identified in Australia, England, and the United States. Comparing appropriateness between countries is difficult, however, because guidelines for therapeutic and prophylactic uses of antibiotics by dentists differ markedly around the world. Unexplained differences in patterns of antibiotic use have been employed as a means of assessing unnecessary use of antibiotics; England’s UK 5-year national action plan identifies priority actions to reduce variation in antibiotic prescribing between healthcare organizations. Studies of antibiotic prescribing patterns by general dentists in individual countries have been widely undertaken. In North America, an increasing trend has been identified in British
Columbia, Canada, and in the United States. By contrast, Australia and England have experienced a reducing trend. In this study, we compared patterns of dental antibiotic prescribing during 2017 in several regions of the world: Australia, England, and North America (United States and British Columbia, Canada).

Method

This study was a population-level analysis of dental antibiotic prescribing between January 1 and December 31, 2017. Metrics to assess the quantity of antibiotic use were selected from an international consensus of outpatient quantity metrics. Prescriptions per defined population counts the number of antibiotic items without considering the daily dose or duration of the antibiotic course.

Dispensed systemic antibiotic prescriptions from outpatient pharmacies, community, and mail-service pharmacies prescribed by dentists in Australia, England, the United States and British Columbia were included. The drugs were grouped by class: penicillins, cephalosporins, lincosamides (which includes clindamycin), macrolides (which includes erythromycin and azithromycin), nitroimidazoles (which includes metronidazole), tetracyclines, and others (which includes trimethoprim with sulfamethoxazole, spiramycin, and quinolones).

Data sources

Data for antibiotics dispensed by pharmacists to dental patients in Australia were accessed from the Department of Health relating to the Pharmaceutical Benefits Scheme and the Repatriation Pharmaceutical Benefits Scheme. Greater than 90% of these prescriptions are from the community setting, which is the main source of dental prescriptions. The 2017 mid-year population size (24,598,900) was obtained from the Australian Bureau of Statistics.

Data for antibiotics dispensed by community pharmacists to dental patients in England were accessed from the National Health Service Digital Prescription Cost Analysis. These data relate only to antibiotics prescribed to dental patients who receive care through the publicly funded National Health Service. The 2017 mid-year population size (55,619,430) was obtained from the UK Office for National Statistics.

The US data relating to antibiotics prescribed by dentists were obtained from IQVIA LRX and included those who were commercially insured, used Medicare or Medicaid, and who paid cash. These data included 92% of all outpatient prescriptions dispensed in the United States. The 2017 population size (325,147,121) was obtained from the US Census Bureau.

Prescribing data relating to dentists in British Columbia were obtained from the BC Ministry of Health, PharmaNet, a database capturing 99% of outpatient prescriptions in the province. The 2017 mid-year population size (4,817,160) was obtained from Statistics Canada.

No ethics approval was required from the Australian Department of Health because these data were publicly available to facilitate health policy research and analysis. Data from England were available via request to the National Health Service under the UK Freedom of Information Act 2000. Use of the National Health Service Business Services Authority data sets is licensed under the terms of the Open Government License for Public Sector Information. The University of Illinois at Chicago Investigational Review Board deemed that this study was exempt from review and informed consent. The University of British Columbia Institutional Review Board approved the protocol used in this study (no. HO9-00650).

Outcomes

Three outcomes for each country were described: (1) rate per 1,000 population of antibiotic prescription items dispensed, (2) relative proportions of each antibiotic class, and (3) rate per 1,000 population of each antibiotic type.

Statistical analysis

Data and statistical analyses were conducted using SAS version 9.4 statistical software (SAS Institute, Cary, NC). Comparison of proportions of prescriptions and each specific antibiotic by country were analyzed using the χ² or the Fisher exact test, and a 2-sided P value ≤ .05 was considered significant.

Results

In 2017, dentists in the United States prescribed 23.6 million antibiotic items, 3.0 million in England, 0.8 million in Australia, and 0.3 million in British Columbia. As shown in Figure 1, dentists in the United States had the highest rate of antibiotic use (72.6 antibiotic items per 1,000 population) and Australia had the lowest rate of antibiotic use (33.2 antibiotic items per 1,000 population) during 2017.

Relative proportions of each antibiotic class

As shown in Table 1, the penicillin class of antibiotics was the most prescribed in each country (highest at 80.5% in British Columbia and lowest at 66.8% in England). Nitroimidazoles (ie, metronidazole) comprised the second most frequently prescribed class of antibiotics in England (28.4%) and Australia (13.2%). Lincosamides (ie, clindamycin) comprised the second most frequently prescribed class of antibiotics in the United States (14.3%) and British Columbia (12.4%). Macrolides comprised the third most frequently prescribed class of antibiotics in the United States. Cephalosporins were prescribed more often in the United States (3.9%) and Australia (3.0%) than in British Columbia (0.8%) and England (0.2%). Tetracyclines were rarely prescribed in any of the countries.

Rate per 1,000 population by antibiotic type

As shown in Figure 2, the highest rate of antibiotic prescribing per 1,000 population in each country was amoxicillin; British Columbia had the highest rate (46.3 prescription items per 1,000 population) and Australia had the lowest rate (21.3 per 1,000 population) (Table 2). The rate of prescribing for the broader-spectrum antibiotic amoxicillin-clavulanic acid was highest in Australia (3.8 per 1,000 population) and lowest in England (0.3 per 1,000 population). The narrowest-spectrum antibiotic, pentoxyphenylpenicillin, was most commonly prescribed in the United States (6.8 per 1,000 population) and least commonly in England (0.2 per 1,000 population).

Metronidazole was the second most frequently used antibiotic in Britain (15.2 prescription items per 1,000 population) and Australia (4.4 per 1,000 population). Clindamycin was the second most frequently used antibiotic in the United States (10.4 items per 1,000 population) and British Columbia (8.1 per 1,000 population). The rate of cephalaxin use was highest in the United States (2.7 per 1,000 population) and lowest in England (0.1 per 1,000 population). Macrolides were rarely used in Australia or British Columbia; in the United States, azithromycin was the most prescribed macrolide (3.1 per 1,000 population) and in England it was erythromycin (1.9 per 1,000 population). Doxycycline was the
most prescribed tetracycline; the highest rate was in the United States (0.9 items per 1,000 population) and the lowest rates were in Australia and England (both 0.1 per 1,000 population).

Discussion
In 2017, wide variation existed in the patterns of antibiotic prescribing by dentists. The rate per 1,000 population in the United States was twice that in Australia, which had the lowest prescribing rate. Although amoxicillin was the most prescribed dental antibiotic in all 4 countries, clindamycin was the second most prescribed dental antibiotic in the United States and British Columbia compared to metronidazole in Australia and England. Other broad-spectrum agents, such as amoxicillin-clavulanate and macrolides (eg, azithromycin), which have higher resistance potential, were also used by dentists.

The variation in the rates of antibiotic prescribing among the 4 countries does not seem to be explained by differences in dental health, but it may be related to differences in the prophylactic use of dental antibiotics aiming to protect people at risk of distance site infections during operative dental procedures. Similar levels of dental health have been previously described using well-established epidemiological outcomes measures of oral health including missing teeth, edentulousness, number of carious teeth, and degree of caries experience. Many factors are known, however, to influence dental antibiotic prescribing, including access to dental treatment and the existence of (or knowledge about) national guidelines. Further research to explain the reasons for the significant variation identified is needed.

Variation in national guidelines: Indications
Dental antibiotic guidelines around the world for therapeutic indications are generally based on the principles of draining infections and removing the cause, with procedures such as dental extraction. For the prevention of conditions such as infective endocarditis, antibiotic prophylaxis (a single oral dose of amoxicillin 3 g or clindamycin 600 mg) is indicated by guidance in most countries, including Australia, the United States, and Canada; but it is not routinely recommended by guidelines used in England. The extent to which this fundamental difference in guideline philosophy accounts for differences between England and the other nations in this study is unclear, although it is likely to be relatively small. In the United States, high rates of prophylactic overprescribing (not in accordance with guidelines) are known to occur. Suggested explanations include the perioperative use of antibiotics to prevent complications of oral surgery procedures, such as the placement of dental implants and the removal of third molars.

Ensuring that national guidelines are clear about therapeutic, prophylactic, and perioperative indications will be important to reducing variation in the rates of dental antibiotic prescribing internationally.

Variation in antibiotic types
Although amoxicillin is the most prescribed antibiotic in each of the 4 countries, in Norway and Sweden the most prescribed antibiotic is phenoxymethylpenicillin and in Japan cephalosporins and macrolides are most often prescribed. Macrolides were prescribed by dentists in all 4 countries studied: erythromycin most often in England and azithromycin most often in the United States. The World Health Organization (WHO) has introduced 3 classifications of antibiotics as part of its efforts to tackle antibiotic resistance: the AWARe classification (ie, Access, Watch, Reserve). Antibiotics which offer the best therapeutic value while minimizing the potential for resistance are included in the ‘Access’ group. Antibiotics that are prone to selecting for resistance are included in the ‘Watch’ group. Watch-group antibiotics (including...
macrolides) should be prioritized in antibiotic stewardship programs to minimize their use.23

High levels of resistance to erythromycin are associated with bacteria commonly isolated from odontogenic infections and increased incidence of side-effects (eg, gastrointestinal adverse effects) and drug interactions in some parts of the world.24 Dental antibiotic stewardship programs, which focus on reducing the unnecessary use of antibiotics generally and optimizing the use of macrolide antibiotics specifically, are needed worldwide.

Adverse drug reactions to oral antibiotics commonly prescribed by dentists are also important considerations. Common antibiotic-related adverse reactions include nausea, vomiting and diarrhea. More serious outcomes include allergy, anaphylaxis, bacterial resistance, and Clostridoides difficile infection. Clindamycin use in dentistry has been associated with a significant number of nonfatal and fatal adverse drug reactions,30 and community-associated Clostridoides difficile infections have been related to dental use of clindamycin in the United States.31 Our finding that clindamycin was prescribed in the United States and British Columbia far more often than in England is significant and highlights the importance of a review of dental antibiotic guidelines to ensure that they consider the risks as well as the benefits for patients.

Patient-reported penicillin allergy is the reason dentists in Australia and the United States prescribe clindamycin.25,26 In England, macrolides are recommended for patients who are allergic or unable to tolerate penicillin or metronidazole antibiotics.27 This problem is significant because penicillin allergy is reported in 10%–20% of patients, yet a high percentage of penicillin allergy labels on medical records are likely to be erroneous.35 Providing pathways for dentists to refer patients for penicillin-allergy testing and, where possible, desensitization, offers a potential solution to this problem.36
Updating and implementing national guidelines

The importance of national dental antibiotic guidelines that consider the local context including rates of resistance to antibiotics to particular antibiotics, the availability of quality-assured antibiotics, and access to dental services has been highlighted by the FDI World Dental Federation. In particular, guidelines appropriate in high-income countries may not be appropriate in low- and middle-income countries where access to dentistry and high-quality antibiotics may differ. As a result, dental antibiotic prescribing guidelines around the world will continue to vary.

Antibiotic stewardship measures aim to optimize antibiotic prescribing in accordance with national guidelines. They have been advocated as one way that dental teams can contribute to global efforts to tackle antibiotic resistance. Because factors driving antibiotic prescribing decisions are complex and numerous, there is no ‘one size fits all’ solution: combinations of clinical audits, feedback, and educational outreach visits have been shown to be particularly effective in primary dental care. A systematic review of metrics for evaluating antibiotic stewardship programs across primary health care revealed that dental studies focused solely on rates of antibiotic prescribing, whereas a wider set of outcomes, such as adverse outcomes and patient satisfaction, were employed in other primary healthcare settings. Further research to develop international consensus for a set of dental antibiotic stewardship core outcomes is needed.

This study had several limitations. Each nation collects and reports its antibiotic prescribing data in different ways. The data reported in this study for Australia, England, and British Columbia were obtained from public health data sources, whereas US data are proprietary. As highlighted in a similar study across Northern Europe, the figures for each country are known to be underestimates of the total number of antibiotics prescribed to dental patients and, in particular, the English data do not include prescriptions for patients receiving private treatment. This factor also applies to the Australian data, although these numbers are estimated to be low because all common antibiotics prescribed for dental treatment are listed on the Pharmaceutical Benefits Scheme. In contrast, the British Columbia PharmaNet captures all outpatient prescriptions, irrespective of payer, and there is reasonable confidence that it captures most dental use.

Importantly, these data include only antibiotics dispensed by pharmacists. Around the world, not all antibiotics are supplied to patients by pharmacists. In England, private dentists can supply antibiotics directly to patients, and while the actual quantity is unknown, it has been estimated that this may represent another 25% of dental antibiotics that are currently uncounted. Dentists in Australia may also dispense antibiotics directly, although dental dispensing of medicines is thought to be rare. Regulations in Canada and the United States prevent dentists from supplying antibiotics. However, in many countries (especially low-to-middle-income countries), >60% of antibiotics can be purchased directly without a prescription and not necessarily through a pharmacy. The inability to quantify the potentially numerous antibiotics supplied directly is a significant issue, and high-priority action is required to ensure that systems are in place to monitor all antibiotic use in all countries, irrespective of payer or supplier.

Fig. 2. Relative proportions of each antibiotic type by country.
Although the routinely collected data included in this study were assessed to be the best available to quantify the amount of antibiotics dispensed to dental patients, it was not possible to assess the indication (eg, therapeutic or prophylactic use) for the prescription, nor to assess the appropriateness of prescribing. Furthermore, differences between national guidelines make it difficult to compare antibiotic prescribing between countries. The necessity for national guidelines that consider the local context, such as patterns of resistant bacteria and access to dental procedures (as advocated by the FDI World Dental Federation), present considerable difficulty in drawing conclusions about rates of overprescribing across the international dental community. Further research is needed to identify how best to present international comparisons for dental antibiotic prescribing to drive quality improvements using the proposed core outcome set for dental antimicrobial stewardship.

In conclusion, concerning differences exist in the patterns of dental antibiotic prescribing around the world. Significant

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Australia</th>
<th>England</th>
<th>United States</th>
<th>British Columbia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Penicillins</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin prescription items, no.</td>
<td>524,166</td>
<td>1,959,346</td>
<td>14,607,292</td>
<td>223,057</td>
</tr>
<tr>
<td>Rate per 1,000 population (95% CI)</td>
<td>21.3 (21.3–21.4)</td>
<td>35.2 (35.2–35.3)</td>
<td>44.9 (44.9–44.5)</td>
<td>46.3 (46.1–46.5)</td>
</tr>
<tr>
<td>Amoxicillin/Clavulanic acid prescription items, no.</td>
<td>92,903</td>
<td>15,578</td>
<td>710,856</td>
<td>7,954</td>
</tr>
<tr>
<td>Rate per 1,000 population (95% CI)</td>
<td>3.8 (3.8–3.8)</td>
<td>0.3 (0.3–0.3)</td>
<td>2.2 (2.2–2.2)</td>
<td>1.7 (1.6–1.7)</td>
</tr>
<tr>
<td>Phenoxymethylpenicillin prescription items, no.</td>
<td>11,197</td>
<td>12,873</td>
<td>2,194,226</td>
<td>20,999</td>
</tr>
<tr>
<td>Rate per 1,000 population (95% CI)</td>
<td>0.5 (0.4–0.5)</td>
<td>0.2 (0.2–0.2)</td>
<td>6.8 (6.8–6.8)</td>
<td>4.4 (4.3–4.4)</td>
</tr>
</tbody>
</table>

| **Cephalosporins**                      |           |         |               |                  |
| Cefalexin prescription items, no.       | 24,056    | 5,593   | 886,761       | 2,515            |
| Rate per 1,000 population (95% CI)      | 1.0 (1.0–1.0) | 0.1 (0.1–0.1) | 2.7 (2.7–2.7) | 0.5 (0.5–0.5) |
| Other cephalosporins prescription items, no. | 676 | 627 | 32,794 | 102 |
| Rate per 1,000 population (95% CI)      | 0.0 (0.0–0.0) | 0.0 (0.0–0.0) | 0.1 (0.1–0.1) | 0.0 (0.0–0.0) |

| **Lincosamides**                        |           |         |               |                  |
| Clindamycin prescription items, no.     | 41,324    | 14,253  | 3,367,880     | 38,866           |
| Rate per 1,000 population (95% CI)      | 1.7 (1.7–1.7) | 0.3 (0.3–0.3) | 10.4 (10.4–10.4) | 8.1 (8.0–8.1) |

| **Macrolides**                          |           |         |               |                  |
| Azithromycin prescription items, no.    | ...       | 2,236   | 1,021,272     | 3,363            |
| Rate per 1,000 population (95% CI)      | ...       | 0.0 (0.0–0.0) | 3.1 (3.1–3.1) | 0.7 (0.7–0.7) |
| Erythromycin prescription items, no.    | 9,598     | 107,047 | 40,268        | 2,096            |
| Rate per 1,000 population (95% CI)      | 0.4 (0.4–0.4) | 1.9 (1.9–1.9) | 0.1 (0.1–0.1) | 0.4 (0.4–0.4) |
| Other Macrolides prescription items, no. | 1,422 | 7,654 | 19,432 | 1,614 |
| Rate per 1,000 population (95% CI)      | 0.1 (0.1–0.1) | 0.1 (0.1–0.1) | 0.1 (0.1–0.1) | 0.3 (0.3–0.3) |

| **Nitroimidazoles**                     |           |         |               |                  |
| Metronidazole prescription items, no.   | 108,041   | 846,207 | 206,682       | 8,651            |
| Rate per 1,000 population (95% CI)      | 4.4 (4.4–4.4) | 15.2 (15.2–15.3) | 0.6 (0.6–0.6) | 1.8 (1.8–1.8) |

| **Tetracyclines**                       |           |         |               |                  |
| Doxycycline prescription items, no.     | 1,719     | 4,611   | 301,508       | 2,008            |
| Rate per 1,000 population (95% CI)      | 0.1 (0.1–0.1) | 0.1 (0.1–0.1) | 0.9 (0.9–0.9) | 0.4 (0.4–0.4) |
| Tetracycline prescription items, no.     | ...       | 914     | 3,874         | 199              |
| Rate per 1,000 population (95% CI)      | ...       | 0.0 (0.0–0.0) | 0.0 (0.0–0.0) | 0.0 (0.0–0.0) |
| Other tetracyclines prescriptions, no.  | ...       | 491     | 11,304        | 48               |
| Rate per 1,000 population (95% CI)      | ...       | 0.0 (0.0–0.0) | 0.0 (0.0–0.0) | 0.0 (0.0–0.0) |

| **Other**                               |           |         |               |                  |
| Other antibiotic prescription items, no. | 642       | ...     | 165,440       | 1,432            |
| Rate per 1,000 population (95% CI)      | 0.0 (0.0–0.0) | ... | 5 (0.5–0.5) | 0.3 (0.3–0.3) |

Note. CI, confidence interval.
opportunities exist for the global dental community to contribute to international efforts to tackle antibiotic resistance, including by changing from broad-spectrum antibiotics (eg, amoxicillin/clavulanate) to narrower-spectrum antibiotics (eg, phenoxymethylpenicillin) and by reducing the use of WHO ‘Watch’ antibiotics (eg, azithromycin). The dental profession can also contribute to improvements in patient safety by minimizing the use of antibiotics associated with increased adverse drug reactions (eg, clindamycin) by reviewing guidelines, auditing compliance, and assisting in efforts to delabel people who identify as penicillin allergic. Dental antibiotic stewardship programs are urgently required as part of national responses to delivering the WHO global action plan on tackling antimicrobial resistance. Further research to understand locally relevant factors driving unnecessary dental antibiotic prescribing in each country is needed to support the development of context-appropriate stewardship solutions to the global problem of antibiotic resistance. To enable improvements in the quality of dental antibiotic prescribing around the world, it is vital that governments ensure that they have systems to capture all data relating to antibiotic prescribing, irrespective of payer or supplier.

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