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Concise Communication

Estimating the cost of inappropriate antibiotic prophylaxis prior to dental procedures

Cynthia L. Gong PharmD, PhD[1,2], Anh Duong BS[3] and Kenneth M. Zangwill MD[4]

[1]Division of Neonatology, Fetal & Neonatal Institute, Children's Hospital Los Angeles, Los Angeles, California, [2]Department of Pediatrics, Keck School of Medicine, University of Southern California, Los Angeles, California, [3]Alfred E. Mann School of Pharmacy, University of Southern California, Los Angeles, California and [4]Division of Pediatric Infectious Diseases, Department of Infection Prevention and Control, and The Lundquist Institute at Harbor-UCLA Medical Center, Torrance, California

Abstract

Inappropriate dental antibiotic prescriptions to prevent infective endocarditis in the United States results in ~$31 million in excess costs to the healthcare system and patients. This includes out-of-pocket costs ($20.5 million), drug costs ($2.69 million) and adverse event costs (eg, *Clostridioides difficile* and hypersensitivity) of $5.82 million (amoxicillin), $1.99 million (clindamycin), and $380,849 (cephalexin).

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Since 2007, the American Heart Association, with input from the American Dental Association, has limited the target populations for antibiotic prophylaxis prior to dental procedures for the prevention of infective endocarditis to only those with cardiac conditions at highest risk.[1] This guidance reflected an acknowledgment of the lack of evidence on effectiveness of prophylaxis in preventing infective endocarditis, concerns about drug-associated adverse events, and development of bacterial resistance. The guideline recommends prophylaxis only prior to dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa in patients with valvular heart disease; patients with selected congenital heart conditions; and patients with previous, relapsed, or recurrent infective endocarditis.[1]

Although overall antibiotic use in this setting has declined substantially since 2007, inappropriate use remains an ongoing problem.[2] Several analyses have shown that ~5 of every 6 dental prophylactic prescriptions are inconsistent with guidelines.[3,4] In this study, we estimated costs associated with this practice behavior from a healthcare payer perspective.

Methods

Based on 2018 census data, we modeled adults aged ≥18 years in the United States who had a dental visit with an antibiotic prescribed over a 1-year period. According to published data from large cohorts, ~83.1% of these prescriptions are considered inappropriate.[2–4] We considered only amoxicillin, cephalexin, and clindamycin because they account for 94% of the prescribed drugs in the dental setting.[2–5] We calculated the costs of drug-related adverse effects by estimating the likelihood of the most impactful adverse events related to dental antibiotic prophylaxis: *Clostridioides difficile* infection and anaphylaxis or severe hypersensitivity requiring an emergency department (ED) visit or hospitalization.[5–7] When possible, we used estimates derived from studies specific to antibiotics given for dental prophylaxis to reduce the likelihood of overestimating the probability of adverse effects. For *C. difficile* infection, we calculated the proportion of cases that would be treated outpatient versus inpatient.[8] We applied a highly conservative definition to calculate the risk of hypersensitivity or anaphylaxis to only include the most severe reactions requiring an ED visit or hospitalization.[5,7,9,10] We also evaluated the potential risk of infective endocarditis if inappropriate antibiotic prescribing did not occur.[11,12]

We used the reported incidence of infective endocarditis among those without known predisposing cardiac conditions undergoing dental procedures,[11] and we extrapolated this value to a population-wide estimate based on the incidence of infective endocarditis according to predetermined diagnostic criteria.[12] The cost of adverse effects was determined by costs reported per the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project based on *International Classification of Disease, Ninth Revision* (ICD-9) codes, ICD-10 codes, and Clinical Classifications Software Refined (CCSR) codes, and drug treatment cost based on the Veterans' Affairs Federal Supply Schedule pricing. We also estimated patient burden based on average prescription drug copay. Finally, we performed one-way sensitivity analyses to assess the robustness of our results to changes in model parameters. All costs are reported in 2022 USD. Probability and cost parameters are reported in Table 1.

Results

In our base case, we estimate that among 253,815,197 US adults aged ≥18 years, 167,010,400 (65.8%) have a dental visit each year. Among them, 7,965,084 (4.8%) receive prophylactic antibiotics.[3] Among those receiving prophylactic antibiotics, 6,617,132 (83.1%)

Corresponding author: Cynthia L. Gong; Email: gongc@usc.edu

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Table 1. Clinical and Cost-Related Parameters and Values Used for Cost Estimation

Parameter	Base[a]	Min[a]	Max[a]	Reference	Notes
Dental visits, %					
Those with dental visits	65.8	52.6	79.0	2018 Census Data	National Center for Health Statistics[b]
Those with antibiotics prescribed	4.77	4.39	7.51	Suda et al[3]	
Inappropriate use, %					
Those with dental visits	83.1	48.6	88.8	Suda et al[2–4]	Multiple sources
Drug distribution, %					
Amoxicillin	71.9	68.9	74.8	Suda et al[2–4]	Based on aggregate national data sources[c]
Clindamycin	15.1	13.8	16.2		
Cephalexin	5.2	0.8	8.2		
Other	7.9	6.4	9.4		
Drug costs (single prophylactic dose)					
Amoxicillin	$0.21	$0.16	$0.25	VA FSS[d]	Represents the average cost based on several national drug codes (manufacturer and quantity per bottle)
Clindamycin	$1.14	$0.52	$3.46		
Cephalexin	$0.65	$0.56	$0.83		
Other	$0.67	$0.42	$1.51		
Average copay	$3.10	$0.15	$9.73	GoodRx[e]	
AE *Clostridioides difficile* outpatient, %					
Outpatient cases	40.0	31.0	61.0	Ofori et al[8]	
AE amoxicillin risk					
C. difficile overall	0.0197	0.0071	0.0618	Gross et al,[5] Wilson et al,[6] Liang et al[9]	Derived from 3 studies, 2 of which were specific to evaluating ADEs after dental prophylaxis
C. difficile hospitalization	0.0118	0.0049	0.0241	Calculated	
C. difficile outpatient	0.0079	0.0022	0.0377	Calculated	
Anaphylaxis or hypersensitivity	0.00112	0.00090	0.00134	Gross et al,[5] Thornhill et al,[7] Liang et al[9]	
AE clindamycin risk					
C. difficile overall	0.0277	0.0014	0.5645	Gross et al,[5] Wilson et al,[6] Thornhill et al,[7] Liang et al[9]	Derived from 4 studies, 3 of which were specific to dental prophylaxis
C. difficile hospitalization	0.0166	0.0010	0.2201	Calculated	
C. difficile outpatient	0.0111	0.0004	0.3443	Calculated	
Anaphylaxis or hypersensitivity	0.00479	0.00503	0.00024	Gross et al,[5] Thornhill et al,[7] Liang et al[9]	
AE cephalosporin risk					
C. difficile overall	0.0186	0.0149	0.0223	Gross et al[5]	
C. difficile hospitalization	0.0112	0.0103	0.0087	Calculated	
C. difficile outpatient	0.0074	0.0046	0.0136	Calculated	
Anaphylaxis or hypersensitivity	0.00049	0.00039	0.00059	Macy et al[10]	
Adverse effect costs					
C. difficile hospitalization	$9,509	$9,330	$9,689	AHRQ[f]	Calculated based on ICD and CCSR codes
C. difficile outpatient	$33.27	$22.51	$54.02	VA FSS[d]	
Anaphylaxis or hypersensitivity	$8,512	$8,108	$8,916	AHRQ[f]	

(*Continued*)

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Table 1. (*Continued*)

Parameter	Base[a]	Min[a]	Max[a]	Reference	Notes
Endocarditis risk					
No known predisposing cardiac conditions, antibiotic prophylaxis	0.00002	0.00002	0.00002	Duval et al,[11] Quan et al[12]	Extrapolated based on risk of IE after dental procedure, and applied to overall population IE rates
No known predisposing cardiac conditions no antibiotic prophylaxis	0.00007	0.00007	0.00008	Duval et al,[11] Quan et al[12]	
Endocarditis cost	$40,665	$38,059	$43,271	AHRQ[f]	Calculated based on ICD and CCSR codes

Note. ADE, adverse drug event; AE, adverse event; AQRH, Agency for Healthcare Research and Quality; VA FSS, Department of Veterans' Affairs Federal Supply Schedule; IE, infective endocarditis; ICD, *International Classification of Diseases*; CCSR, Clinical Classifications Software Refined.
[a]Units as specified per row.
[b]Health, United States, 2019. US National Center for Health Statistics website. https://www.ncbi.nlm.nih.gov/books/NBK569310/. Published 2021. Accessed July 11, 2022.
[c]Thompson W, Teoh L, Hubbard CC, et al. Patterns of dental antibiotic prescribing in 2017: Australia, England, United States, and British Columbia (Canada). *Infect Control Hosp Epidemiol* 2022;43:191–198.
[d]VA National Acquisition Center contract catalog search tool. Veterans' Affairs website. https://www.vendorportal.ecms.va.gov/nac/Pharma/List. Accessed April 30, 2023.
[e]Prescription Prices, Coupons & Pharmacy Information. GoodRx website. https://www.goodrx.com/. Accessed May 3, 2023.
[f]Clinical Classifications Software Refined (CCSR) for ICD-10-CM diagnoses. Healthcare Cost and Utilization Project. Agency for Healthcare Research and Qualitywebsite. https://www.hcup-us.ahrq.gov/toolssoftware/ccsr/dxccsr.jsp#download. Published 2022. Accessed July 12, 2022.

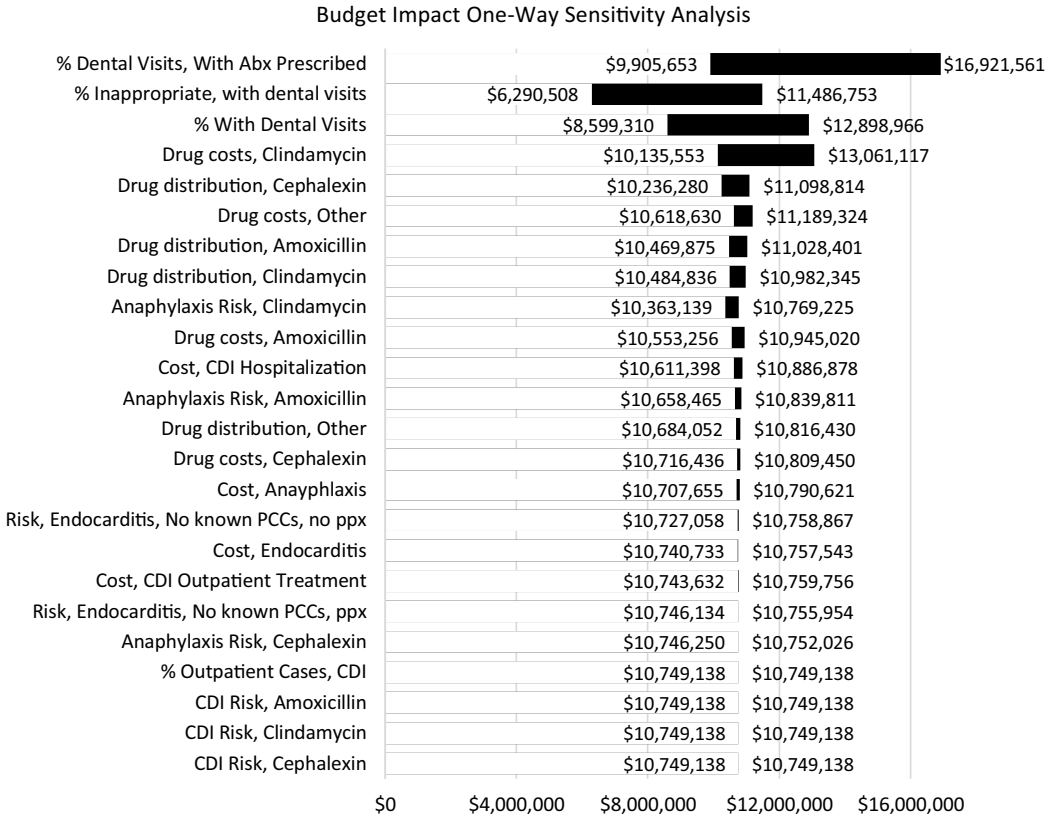

Figure 1. One-Way Sensitivity Analysis for Overall Budget Impact

are inappropriately prescribed antibiotic prophylaxis. This practice incurs ~$10.8 million in excess healthcare costs per year, or $1,620 per 1,000 dental visits. This includes antibiotic use amounting to $2.69 million per year, and adverse effect costs of $5.82 million, $1.99 million, and $380,849 for amoxicillin, clindamycin, and cephalexin, respectively. Inappropriate prophylaxis leads to an excess 768 inpatient *C. difficile* cases annually and up to 103 cases of severe hypersensitivity or anaphylaxis requiring hospitalization, amounting to $7.30 million and $874,584, respectively. If no inappropriate antibiotic use occurs, we estimate an excess of ~3 cases of infective endocarditis, or $131,149 per year. The antibiotic prescriptions further amount to $20,500,703 in patient out-of-pocket expenses per year.

One-way sensitivity analyses indicated that the percentage of dental visits in which an antibiotic was prescribed had the largest impact on the total excess costs associated with inappropriate antibiotic prescribing, followed by the percentage of inappropriate antibiotic prophylaxis prescribed (Fig. 1). The next-largest impacts were the drug costs for each antibiotic followed by the distribution of drugs used for prophylaxis, though these parameters had minimal (<5%) impacts on the overall costs. For key clinical outcomes (CDI, anaphylaxis, and endocarditis cases), the most sensitive parameter was also the percentage of dental visits in which an antibiotic was prescribed, followed by percentage of inappropriate antibiotics prescribed and percentage of individuals aged >18 years with a dental visit (Supplementary Fig. 1 online).

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For CDI and anaphylaxis, this was followed by the distribution of antibiotics prescribed. For endocarditis, this was followed by the risk of endocarditis among those with no predisposing cardiac conditions, with and without prophylaxis (Supplementary Fig. 1 online).

Discussion

The burden of inappropriate use of antibiotics in dentistry for prevention of infective endocarditis prophylaxis in the United States has been well described. At least 75% of such prescriptions are not consistent with published guidelines. The potential impacts of this reality, however, are unclear. These might include clinically meaningful adverse events from the antibiotic taken, the development of and spread of antibiotic resistance, and/or the costs associated with each. The direct medical costs associated with the above have not been reported in dentistry. Inappropriate antibiotic prescriptions for dental prophylaxis cost the US healthcare system and patients >$31 million per year, the former due primarily to adverse effects associated with even just a single dose of antibiotics; drug costs alone make up ~25% of the total healthcare system burden.

Although indications for prophylaxis have been substantially narrowed, prevention of infective endocarditis remains the goal for the high-risk groups for whom it is still recommended. Therefore, we also considered the potential costs under the assumption that had inappropriate antibiotics not been prescribed, some cases of endocarditis may have occurred. We estimated that at most, there may be an excess of up to three cases, incurring a trivial direct cost burden in aggregate, nationally.

The study had several limitations. The datasets used to assess inappropriate antibiotic prescribing (specifically) did not include the uninsured, and they reflected nonprobability samples of data[2] or select populations (eg, Veterans' Affairs).[3] However, each data set referenced is national in scope and links dental claims with medical and prescription claims of patients enrolled in both medical and dental health plans, with similarly concluded high rates of inappropriate dental prophylaxis. In addition, our estimates of endocarditis risk after a dental procedure were extrapolated from studies in France and England. Thus, the calculated incidence of endocarditis used in our model may not represent the true incidence in the United States. Lastly, our estimates do not contain costs associated with antibiotics not included in our analysis; indirect costs associated with adverse effects; pharmacist time spent filling the drug and counseling a patient; patient time lost to pick up a prescription; or the impact of unnecessary antibiotic use promoting community antibiotic resistance, which is very difficult to robustly assess.

Overall, while the estimated costs associated with inappropriate antibiotic use in dentistry may not be significant, dentists account for 6%–10% of all antibiotic prescriptions in the United States,[3] resulting in a nontrivial burden of preventable adverse effects.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/ice.2023.126

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References

1. Wilson WR, Gewitz M, Lockhart PB, *et al.* Prevention of *viridans* group streptococcal infective endocarditis: a scientific statement from the American Heart Association. *Circulation* 2021;143:E963–E978.
2. Suda KJ, Calip GS, Zhou J, *et al.* Assessment of the appropriateness of antibiotic prescriptions for infection prophylaxis before dental procedures, 2011 to 2015. *JAMA Netw Open* 2019;2:e193909.
3. Suda KJ, Fitzpatrick MA, Gibson G, *et al.* Antibiotic prophylaxis prescriptions prior to dental visits in the Veterans' Health Administration (VHA), 2015–2019. *Infect Control Hosp Epidemiol* 2022;43:1565–1574.
4. Hubbard CC, Evans CT, Calip GS, Zhou J, Rowan SA, Suda KJ. Appropriateness of antibiotic prophylaxis before dental procedures, 2016–2018. *Am J Prev Med* 2022;62:943–948.
5. Gross AE, Suda KJ, Zhou J, *et al.* Serious antibiotic-related adverse effects following unnecessary dental prophylaxis in the United States. *Infect Control Hosp Epidemiol* 2021;42:110–112.
6. Wilson GM, Evans CT, Fitzpatrick MA, *et al. Clostridioides difficile* infection following dental antibiotic prescriptions in a cohort of US veterans. *Infect Control Hosp Epidemiol* 2023;44:494–496.
7. Thornhill MH, Dayer MJ, Prendergast B, Baddour LM, Jones S, Lockhart PB. Incidence and nature of adverse reactions to antibiotics used as endocarditis prophylaxis. *J Antimicrob Chemother* 2015;70:2382–2388.
8. Ofori E, Ramai D, Dhawan M, Mustafa F, Gasperino J, Reddy M. Community-acquired *Clostridium difficile*: epidemiology, ribotype, risk factors, hospital and intensive care unit outcomes, and current and emerging therapies. *J Hosp Infect* 2018;99:436–442.
9. Liang EH, Chen LH, Macy E. Adverse reactions associated with penicillins, carbapenems, monobactams, and clindamycin: a retrospective population-based study. *J Allergy Clin Immunol Pract* 2020;8:1302–1313.
10. Macy E, Contreras R. Adverse reactions associated with oral and parenteral use of cephalosporins: a retrospective population-based analysis. *J Allergy Clin Immunol* 2015;135:745–752.
11. Duval X, Alla F, Hoen B, *et al.* Estimated risk of endocarditis in adults with predisposing cardiac conditions undergoing dental procedures with or without antibiotic prophylaxis. *Clin Infect Dis* 2006;42:e102–e107.
12. Quan TP, Muller-Pebody B, Fawcett N, *et al.* Investigation of the impact of the NICE guidelines regarding antibiotic prophylaxis during invasive dental procedures on the incidence of infective endocarditis in England: an electronic health records study. *BMC Med* 2020;18:84.