



## COVER STORY

# The use of prophylactic antibiotics prior to dental procedures in patients with prosthetic joints

Evidence-based clinical practice guideline for dental practitioners—a report of the American Dental Association Council on Scientific Affairs

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In 2012, a panel of experts representing the American Academy of Orthopaedic Surgeons (AAOS) and the American Dental Association (ADA) (the 2012 Panel) published a systematic review and accompanying clinical practice guideline (CPG) entitled “Prevention of Orthopaedic



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## ABSTRACT

**Background.** A panel of experts (the 2014 Panel) convened by the American Dental Association Council on Scientific Affairs developed an evidence-based clinical practice guideline (CPG) on the use of prophylactic antibiotics in patients with prosthetic joints who are undergoing dental procedures. This CPG is intended to clarify the “Prevention of Orthopaedic Implant Infection in Patients Undergoing Dental Procedures: Evidence-based Guideline and Evidence Report,” which was developed and published by the American Academy of Orthopaedic Surgeons and the American Dental Association (the 2012 Panel).

**Types of Studies Reviewed.** The 2014 Panel based the current CPG on literature search results and direct evidence contained in the comprehensive systematic review published by the 2012 Panel, as well as the results from an updated literature search. The 2014 Panel identified 4 case-control studies.

**Results.** The 2014 Panel judged that the current best evidence failed to demonstrate an association between dental procedures and prosthetic joint infection (PJI). The 2014 Panel also presented information about antibiotic resistance, adverse drug reactions, and costs associated with prescribing antibiotics for PJI prophylaxis.

**Practical Implications and Conclusions.** The 2014 Panel made the following clinical recommendation: In general, for patients with prosthetic joint implants, prophylactic antibiotics are not recommended prior to dental procedures to prevent prosthetic joint infection. The practitioner and patient should consider possible clinical circumstances that may suggest the presence of a significant medical risk in providing dental care without antibiotic prophylaxis, as well as the known risks of frequent or widespread antibiotic use. As part of the evidence-based approach to care, this clinical recommendation should be integrated with the practitioner’s professional judgment and the patient’s needs and preferences.

**Key Words.** Antibiotic prophylaxis; evidence-based dentistry; practice guidelines; prostheses; joint replacement.

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Implant Infection in Patients Undergoing Dental Procedures: Evidence-based Guideline and Evidence Report.<sup>1-3</sup> The 2012 Panel initially considered 222 questions concerning the relationship between dental procedures, bacteremia (as an intermediate outcome), and the risk of developing a prosthetic joint infection (PJI) as a clinical end point. The 2012 Panel published a comprehensive evidence-based guideline. The release of this guideline was followed by calls to the ADA Member Service Center hotline request-



Supplemental material  
is available online.

ing additional clarification, which indicated that this guideline was 1 of the top 2 issues of concern to dental practitioners. Therefore, the ADA's Council on Scientific Affairs convened a panel of experts (the 2014 Panel) to provide dental professionals with a more specific and practical set of guidelines, the results of which are included in this article.

The 2014 Panel considered the direct evidence linking a PJI with a dental procedure but did not reevaluate intermediate outcomes, including bacteremia<sup>4</sup> from manipulation of oral mucosa. The full report of the 2012 Panel, which includes intermediate outcomes, is available online.<sup>1</sup> The 2014 Panel addressed the following clinical question: For patients with prosthetic joints, is there an association between dental procedures and PJI, and, therefore, should systemic antibiotics be prescribed before patients with prosthetic joint implants undergo dental procedures? In this article, we present the evidence to answer this question and provide clinical recommendations.

## EVIDENCE REVIEW

Because the 2012 Panel<sup>1</sup> conducted a comprehensive search of the biomedical literature and screened the results of the search according to defined inclusion and exclusion criteria, the 2014 Panel chose to use the literature selected by the 2012 Panel as the foundation of this CPG. In addition, the 2014 Panel updated the literature search and screening process to identify additional evidence. The methods are presented in Appendix 1 (available online at the end of this article). The 2014 Panel assessed each identified study according to the Critical Appraisal Skills Programme case-control critical appraisal tool<sup>5</sup> and then summarized the body of evidence to determine the level of certainty in the effect estimate and corresponding strength of the recommendation. Details about the process for generating clinical recommendations are in Appendix 2 (available online at the end of this article). The 2014 Panel did not conduct a meta-analysis because a meta-analysis of observational studies can produce precise, but possibly spurious, estimates of risk owing to the effects of confounding.<sup>6</sup>

In their systematic review,<sup>1</sup> the 2012 Panel identified 1 study that provided direct evidence about dental procedures as risk factors for developing prosthetic hip and knee implant infections. The study by Berbari and colleagues<sup>7</sup> was a case-control study of 339 patients with infected hip or knee prostheses (cases), and the authors matched them with 339 patients who did not have infected hip or knee prostheses (controls) and who were hospitalized in an orthopedic service at the Mayo Clinic Care Network (Rochester, MN) from December 2001 through May 2006. The authors reviewed and abstracted information from dental records to determine the association between the dental procedures (exposure) and hip and knee infections. Exposure was measured within the previous 6 months and 2 years before hospital admission and classified as low-risk dental procedures (fluoride treatment, restorative dentistry, and endodontic treatment) and high-risk dental procedures (periodontal treatment, extractions, treatment of a dental abscess, oral surgery, and dental hygiene), as defined by Berbari and colleagues.<sup>7</sup>

The authors controlled for confounding variables by matching control patients to case patients on the basis of joint arthroplasty location, resulting in exactly the same number of prosthetic hip ( $n = 164$ ) and knee ( $n = 175$ ) replacements among cases and controls. The authors also controlled for confounding by providing each patient with a yes versus no propensity score regarding whether the patient had had a dental visit during the period of data abstraction. The score took into account several covariates—including sociodemographic and behavioral information, comorbidities, and the American Society of Anesthesiologists score—that influenced a patient's propensity to visit a dentist. The authors also controlled for covariates such as antibiotic prophylaxis, sex, and joint effect. The regression models included all of these covariates and confounding variables.

The regression modeling used odds ratios (ORs), and the results showed no statistical association between having undergone high-risk dental procedures without antibiotics and PJIs at either 6-months (OR = 0.8; 95% confidence interval [CI], 0.4-1.7) or 2-years (OR = 0.8; 95% CI, 0.4-1.6) after the procedure. High-risk dental procedures with antibiotics were statistically significant at 6 months (OR = 0.5; 95% CI, 0.3-0.9), but not at 2 years (OR = 0.7; 95% CI, 0.5-1.1). All 4 of these ORs are below the null value of 1, indicating that case patients

**ABBREVIATION KEY.** AAOS: American Academy of Orthopaedic Surgeons. ADA: American Dental Association. CPG: Clinical practice guideline. PJI: Prosthetic joint infection.

had lower odds of having undergone dental procedures than did control patients.

The 2014 Panel identified 3 additional case-control studies via its updated literature search process.<sup>8-10</sup> The first study was by Skaar and colleagues.<sup>9</sup> They extracted data (*International Classification of Diseases, Ninth Revision, Clinical Modification* for procedures associated with hospital use in the United States: codes 81.5, 81.51, 81.52, 81.54, 81.56, 81.57, 81.80, 81.81, 81.84, 81.9, and 996.99) for the years 1997 through 2006 from the Medicare Current Beneficiary Survey. The nested case-control study included 168 participants who had undergone total arthroplasty—42 case participants who had PJIs matched according to age group, sex, and number of comorbid conditions with 126 control participants who did not. Dental data were based on patients' self-reports, which are susceptible to recall bias. The authors reported that control participants were more likely to have undergone invasive dental procedures than were case participants, although this result was not significant (main results were expressed as time to event with hazard ratios [HRs] and association with ORs: HR = 0.78 [95% CI, 0.18-3.39]; OR = 0.56 [95% CI, 0.18-1.74];  $P = .45$ ; neither the HR nor the OR was significant). Invasive dental procedures, as defined by Skaar and colleagues,<sup>9</sup> included teeth cleaning (including periodontal procedures), extractions, and endodontic procedures. The authors noted that the statistical power for their study was low. Despite the risk of bias, the study results appeared to be valid, generalizable, and consistent with those of other related studies in which investigators failed to demonstrate an association between dental procedures and PJI.

The second study also was a nested case-control study in which Swan and colleagues<sup>10</sup> addressed events associated with PJI. They identified 17 patients (of 1,641 who underwent arthroplasty between 1998 and 2006 in a tertiary referral center) in whom PJI developed more than 3 months postoperatively. The authors identified 51 control patients from a central institutional audit database, but it was unclear whether case and control participants were demographically similar. In addition, there was high susceptibility for recall bias because the exposure data were collected via telephone. The 2 factors most associated with PJI were having cellulitis or having more than 4 comorbidities. The authors used data for dental procedures as published in the article to create a 2×2 table and calculate the OR as 1.53 (95% CI, 0.13-18.03). We did not calculate a  $P$  value, but the CI was wide enough and includes the null value of 1; therefore, it failed to demonstrate an association between dental procedures and PJI.

The third study was a nested case-control study in which Jacobson and colleagues<sup>8</sup> recruited case participants from approximately 2,700 patients with prosthetic knee or hip joints that had been placed in 1 of 2 hospitals from 1970 through 1983. The authors

identified 30 case participants with late (> 6 months after implant placement) PJI and 100 control patients, although it was unclear whether or how the control patients were matched with the case patients. The authors reviewed dental charts, but they did not mention masking of data abstractors or the types of dental procedures that were performed. The authors did not account for any confounding factors such as age, sex, smoking status, or medical conditions. The authors performed a Fisher exact test, and from the published data we calculated an OR of 0.07 (95% CI, 0.01-0.56). This result provided evidence that there is an association between dental procedures and PJI; however, the OR and Fisher exact test results implied that those undergoing dental procedures were at lower risk of developing PJI. The methodological limitations of this study affect the validity and generalizability of its results; furthermore, the results are inconsistent with other studies in which investigators failed to show an association between dental procedures and PJI.

#### CLINICAL RECOMMENDATION AND RATIONALE

Using eTable 1 (available online at the end of this article) as a guide, the 2014 Panel judged with moderate certainty that there is no association between dental procedures and the occurrence of PJIs. The 2014 Panel made this judgment on the basis of the following 2 considerations. The first was consistency between results, in that the results of 3 of 4 studies failed to show an association between dental procedures and PJI, and the results of the fourth study showed a protective effect of dental procedures on PJI. The second was that although the number of studies was limited, it is unlikely that the results of the additional studies would have changed the conclusion. The 2014 Panel made the assumption that the evidence regarding hip and knee joint infections can be extrapolated to all joints on the basis of the morphologic and physiological characteristics of the tissues involved. This extrapolation is necessary for clinical relevance because, to our knowledge, no studies have been published addressing the relationship between dental treatment and infections of other types of prosthetic joints. Using the ADA's methods for generating clinical recommendation statements as described in eTable 2 (available online at the end of this article), when there is moderate certainty of no association, the strength of the recommendation is *against*. The term *against* means that evidence suggests not implementing this intervention or discontinuing ineffective procedures (eTable 3, available online at the end of this article).

On the basis of this rationale, the 2014 Panel makes the following clinical recommendation as depicted in the Sidebar at the end of the article: In general, for patients with prosthetic joint implants, prophylactic antibiotics are not recommended prior to dental procedures to prevent prosthetic joint infection. The practitioner and

patient should consider possible clinical circumstances that may suggest the presence of a significant medical risk in providing dental care without antibiotic prophylaxis, as well as the known risks of frequent or widespread antibiotic use.

This report is intended to assist practitioners with making decisions about the prophylactic use of antibiotics to prevent PJIs. The recommendations in this document are not intended to define a standard of care and rather should be integrated with the practitioner's professional judgment and the patient's needs and preferences.

### RISK FACTORS FOR DEVELOPING PROSTHETIC JOINT INFECTION INDEPENDENT OF DENTAL PROCEDURES

One case-control study<sup>7</sup> identified a number of nondental risk factors for developing PJI. In this study, Berbari and colleagues<sup>7</sup> evaluated both preoperative and postoperative factors associated with PJI. The most clinically relevant of these factors were postoperative, especially wound drainage after arthroplasty (OR = 18.7; 95% CI, 7.4-47.2). Other postoperative factors associated with PJI were wound hematoma after arthroplasty (OR = 2.5; 95% CI, 1.3-9.5) and postoperative urinary tract infection (OR = 2.7; 95% CI, 1.04-7.1). The OR for surgical site infection could not be calculated because there were no PJIs among the control subjects. Thus, the patients at the highest risk of developing PJI had drainage, an infection, or both after undergoing arthroplasty. There were no data regarding whether use of prophylactic antibiotics decreased the risk of developing PJIs in patients with these specific postoperative conditions.

Other conditions, as defined by Berbari and colleagues,<sup>7</sup> with significant ORs (ranging from 1.8 to 2.2) for PJI independent of dental procedures, were preoperative factors including prior operation/arthroplasty on the index joint, diabetes mellitus, and/or being immunocompromised (defined<sup>7</sup> as rheumatoid arthritis or current use of systemic steroids/immunosuppressive drugs or diabetes mellitus or presence of a malignancy or a history of chronic kidney disease). However, the magnitude of these ORs may not be clinically relevant. Observational studies such as those with a case-control design do not involve the use of randomization and are more prone to the effects of bias and confounding. Therefore, some epidemiologists maintain that in case-control studies significant ORs of less than 4 may not be large enough to be clinically relevant.<sup>11</sup> The upper limit of the 95% CIs for the preoperative factors did not include values of 4 or greater in the results of the case-control study by Berbari and colleagues.<sup>7</sup> Thus, although these factors were significant, the effects of these medical conditions on the risk of developing PJI may not be clinically relevant. Independent of having undergone a dental

procedure, it appears that postoperative factors such as drainage or infection after undergoing arthroplasty were associated more strongly with PJI than are having undergone previous surgery or arthroplasty of the index joint, being immunocompromised, or having a medical condition such as diabetes mellitus.

### FURTHER CONSIDERATIONS

The following considerations contribute to the argument against antibiotic prophylaxis.

**Antibiotic resistance.** There is a long-standing and increasing concern that repeated exposure to antibiotics is a risk factor for the development of resistant bacterial species (for example, penicillin-resistant streptococci).<sup>12-14</sup>

**Adverse drug reactions.** Although there are no data regarding the risk of developing a drug reaction from 1 dose of amoxicillin prescribed to prevent a distant site infection such as PJI, older data involving prophylaxis regimens that included intramuscular injections and multiple oral doses suggest that more people who are given antibiotic prophylaxis would experience drug reactions from penicillin-type drugs—some of which may be fatal—than would be prevented from developing PJI.<sup>15</sup> Of all allergens, penicillin is the most frequent medication-related cause of anaphylaxis in humans, and its use is the cause of approximately 75% of fatal anaphylaxis cases in the United States each year.<sup>16</sup> Other potential antibiotic-associated adverse reactions include nausea, vomiting, and diarrhea. There also is an increased risk of experiencing adverse reactions with increasing patient age (that is, in patients 70 years or older),<sup>17</sup> which is compounded by the increased frequency of arthroplasty in older patient cohorts.<sup>18</sup>

Prolonged treatment with antibiotics is associated with infections secondary to changes in the gastrointestinal microbial flora, which includes that involved in the development of oral thrush. For example, *Clostridium difficile* infection potentially can cause pseudomembranous colitis after patients are prescribed antibiotics to treat other infections.<sup>19</sup> Recognizing that a single dose of antibiotics for prophylaxis of PJI is unlikely to cause a *C difficile* infection, comprehensive dental care often involves multiple appointments over a short period. In addition, patients may have taken antibiotics for other medical conditions in the past, increasing their risk of experiencing changes in the gastrointestinal flora. The Centers for Disease Control and Prevention has estimated that annually there are approximately 250,000 people with *C difficile* infections that require hospitalization or already affect hospitalized patients, resulting in 14,000 deaths per year.<sup>20</sup> Investigators have identified clindamycin, cephalosporins, and fluoroquinolones as the inducing agents.<sup>19</sup>

**Cost.** The results of a 2013 report indicate that the annual cost of amoxicillin administered to patients with hip and knee prostheses before dental procedures in the United States may exceed \$50 million.<sup>21</sup>

## CONCLUSIONS

Evidence fails to demonstrate an association between dental procedures and PJI or any effectiveness for antibiotic prophylaxis. Given this information in conjunction with the potential harm from antibiotic

use, using antibiotics before dental procedures is not recommended to prevent PJI. Additional case-control studies are needed to increase the level of certainty in the evidence to a level higher than moderate. ■

## SUPPLEMENTAL DATA

Supplemental data related to this article can be found at <http://dx.doi.org/10.1016/j.adaj.2014.11.012>.

## Management of patients with prosthetic joints undergoing dental procedures

### Clinical Recommendation:

In general, for patients with prosthetic joint implants, prophylactic antibiotics are *not* recommended prior to dental procedures to prevent prosthetic joint infection.

For patients with a history of complications associated with their joint replacement surgery who are undergoing dental procedures that include gingival manipulation or mucosal incision, prophylactic antibiotics should only be considered after consultation with the patient and orthopedic surgeon.\* To assess a patient's medical status, a complete health history is always recommended when making final decisions regarding the need for antibiotic prophylaxis.

### Clinical Reasoning for the Recommendation:

- There is evidence that dental procedures are not associated with prosthetic joint implant infections.
- There is evidence that antibiotics provided before oral care do not prevent prosthetic joint implant infections.
- There are potential harms of antibiotics including risk for anaphylaxis, antibiotic resistance, and opportunistic infections like *Clostridium difficile*.
- The benefits of antibiotic prophylaxis may not exceed the harms for most patients.
- The individual patient's circumstances and preferences should be considered when deciding whether to prescribe prophylactic antibiotics prior to dental procedures.

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\* In cases where antibiotics are deemed necessary, it is most appropriate that the orthopedic surgeon recommend the appropriate antibiotic regimen and when reasonable write the prescription.

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1. American Academy of Orthopaedic Surgeons; American Dental Association. Prevention of orthopaedic implant infection in patients undergoing dental procedures: evidence-based guideline and evidence report. Rosemont, IL: American Academy of Orthopaedic Surgeons; 2012. Available at: [www.aaos.org/research/guidelines/PUDP/PUDP\\_guideline.pdf](http://www.aaos.org/research/guidelines/PUDP/PUDP_guideline.pdf). Accessed September 20, 2014.
2. Rethman MP, Watters W 3rd, Abt E, et al; American Academy of Orthopaedic Surgeons; American Dental Association. The American Academy of Orthopaedic Surgeons and the American Dental Association clinical practice guideline on the prevention of orthopaedic implant infection in patients undergoing dental procedures. *J Bone Joint Surg Am*. 2013;95(8):745-747.
3. Watters W 3rd, Rethman MP, Hanson NB, et al; American Academy of Orthopaedic Surgeons; American Dental Association. Prevention of orthopaedic implant infection in patients undergoing dental procedures. *J Am Acad Orthop Surg*. 2013;21(3):180-189.
4. Lockhart PB, Brennan MT, Sasser HC, Fox PC, Paster BJ, Bahrani-Mougeot FK. Bacteremia associated with toothbrushing and dental extraction. *Circulation*. 2008;117(24):3118-3125.
5. Critical Appraisal Skills Programme: making sense of evidence. Available at: [www.casp-uk.net/](http://www.casp-uk.net/). Accessed September 20, 2014.
6. Egger M, Smith GD, Altman DG. *Systematic Reviews in Health Care: Meta-analysis in Context*. 2nd ed. London, United Kingdom: BMJ; 2001.
7. Berbari EF, Osmon DR, Carr A, et al. Dental procedures as risk factors for prosthetic hip or knee infection: a hospital-based prospective case-control study (published correction appears in *Clin Infect Dis*. 2010;50[6]:944). *Clin Infect Dis*. 2010;50(1):8-16.
8. Jacobson JJ, Millard HD, Plezia R, Blankenship JR. Dental treatment and late prosthetic joint infections. *Oral Surg Oral Med Oral Pathol*. 1986; 61(4):413-417.
9. Skaar DD, O'Connor H, Hodges JS, Michalowicz BS. Dental procedures and subsequent prosthetic joint infections: findings from the Medicare Current Beneficiary Survey. *JADA*. 2011;142(12):1343-1351.
10. Swan J, Dowsey M, Babazadeh S, Mandaleson A, Choong PF. Significance of sentinel infective events in haematogenous prosthetic knee infections. *ANZ J Surg*. 2011;81(1-2):40-45.
11. Straus SE, Glaziou P, Richardson WS, Haynes RB. *Evidence-based Medicine: How to Practice and Teach It*. 4th ed. Edinburgh, United Kingdom: Elsevier Churchill Livingstone; 2011.
12. Helovuuo H, Hakkarainen K, Paunio K. Changes in the prevalence of subgingival enteric rods, staphylococci and yeasts after treatment with penicillin and erythromycin. *Oral Microbiol Immunol*. 1993;8(2): 75-79.
13. Leviner E, Tzukert AA, Benliel R, Baram O, Sela MN. Development of resistant oral viridans streptococci after administration of prophylactic antibiotics: time management in the dental treatment of patients susceptible to infective endocarditis. *Oral Surg Oral Med Oral Pathol*. 1987;64(4): 417-420.
14. Lockhart PB, Brennan MT, Fox PC, Norton HJ, Jernigan DB, Strausbaugh LJ. Decision-making on the use of antimicrobial prophylaxis for dental procedures: a survey of infectious disease consultants and review. *Clin Infect Dis*. 2002;34(12):1621-1626.
15. Bor DH, Himmelstein DU. Endocarditis prophylaxis for patients with mitral valve prolapse: a quantitative analysis. *Am J Med*. 1984;76(4): 711-717.
16. Neugut AI, Ghatak AT, Miller RL. Anaphylaxis in the United States: an investigation into its epidemiology. *Arch Intern Med*. 2001;161(1):15-21.
17. Faulkner CM, Cox HL, Williamson JC. Unique aspects of antimicrobial use in older adults. *Clin Infect Dis*. 2005;40(7):997-1004.
18. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am*. 2007;89(4):780-785.
19. Bartlett JG. Narrative review: the new epidemic of *Clostridium difficile*-associated enteric disease. *Ann Intern Med*. 2006;145(10): 758-764.
20. Centers for Disease Control and Prevention. Antibiotic/antimicrobial resistance: threat report 2013. Atlanta: Centers for Disease Control and Prevention; 2013;6, 51. Available at: [www.cdc.gov/drugresistance/threat-report-2013/](http://www.cdc.gov/drugresistance/threat-report-2013/). Accessed September 21, 2014.
21. Lockhart PB, Blizzard J, Maslow AL, Brennan MT, Sasser H, Carew J. Drug cost implications for antibiotic prophylaxis for dental procedures. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2013;115(3):345-353.