Investigation

Quantifying the risk of prosthetic joint infections after invasive dental procedures and the effect of antibiotic prophylaxis

Martin H. Thornhill, MBBS, BDS, PhD; Teresa B. Gibson, PhD; Cory Pack, BS; Bedda L. Rosario, PhD; Sarah Bloemers, MPH; Peter B. Lockhart, DDS; Bryan Springer, MD; Larry M. Baddour, MD

Supplemental material is available online.

ABSTRACT

Background. Dentists face the expectations of orthopedic surgeons and patients with prosthetic joints to provide antibiotic prophylaxis (AP) before invasive dental procedures (IDPs) to reduce the risk of late periprosthetic joint infections (LPJIs), despite the lack of evidence associating IDPs with LPJIs, lack of evidence of AP efficacy, risk of AP-related adverse reactions, and potential for promoting antibiotic resistance. The authors aimed to identify any association between IDPs and LPJIs and whether AP reduces LPJI incidence after IDPs.

Method. The authors performed a case-crossover analysis comparing IDP incidence in the 3 months immediately before LPJI hospital admission (case period) with the preceding 12-month control period for all LPJI hospital admissions with commercial or Medicare supplemental or Medicaid health care coverage and linked dental and prescription benefits data.

Results. Overall, 2,344 LPJI hospital admissions with dental and prescription records (n = 1,160 commercial or Medicare supplemental and n = 1,184 Medicaid) were identified. Patients underwent 4,614 dental procedures in the 15 months before LPJI admission, including 1,821 IDPs (of which 18.3% had AP). Our analysis identified no significant positive association between IDPs and subsequent development of LPJIs and no significant effect of AP in reducing LPJIs.

Conclusions. The authors identified no significant association between IDPs and LPJIs and no effect of AP cover of IDPs in reducing the risk of LPJIs.

Practical Implications. In the absence of benefit, the continued use of AP poses an unnecessary risk to patients from adverse drug reactions and to society from the potential of AP to promote development of antibiotic resistance. Dental AP use to prevent LPJIs should, therefore, cease.

Key Words. Prosthetic joints; antibiotic prophylaxis; guidelines; prevention; dental procedures.

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Replacing damaged and worn out joints with artificial joints is one of the great advances of modern medicine, and 2.9 million joints are replaced worldwide each year.[1,2] Periprosthetic joint infection (PJI) is a leading cause of prosthetic joint failure. Early infections ($\leq$ 3 months of surgery) are usually the result of surgical site contamination. In the 1950s, early infection rates were approximately 12%, but laminar airflow operating rooms and antibiotic prophylaxis (AP) before joint replacement reduced this to 1% to 2%.[3] Nonetheless, late periprosthetic joint infections (LPJIs) (occurring > 3 months after surgery) remain a continued focus of reduction strategies.

LPJI often results in prosthesis removal; less often, it can result in amputation or loss of life.[4] The cost of treating LPJIs is 4 through 6 times that of the original arthroplasty[5-8] and is projected at $1.62 billion annually in the United States.[9] This excludes any impact on a patient's quality of life or the societal costs of long-term disability.[10] The number of patients with prosthetic joints is rising, with approximately 4 million new hip and knee replacement operations projected annually in the United States by 2030.[11]

Although LPJI incidence is relatively low, it is the most common cause of joint failure after knee replacements and the second most common after hip replacements.[4,12,13] LPJI is mainly attributed to bloodstream seeding of bacteria from another anatomic site,[14,15] and this has led orthopedic surgeons in the United States to recommend that patients with prosthetic joints be prescribed AP before invasive dental procedures (IDPs).[16-18] However, there are scant data to support a causal association between IDPs and LPJIs, and, to our knowledge, AP efficacy in preventing LPJIs has never been tested in a randomized controlled trial. In addition, no association between IDPs and subsequent LPJIs was found in a 2022 study in the United Kingdom (where AP is not recommended).[19] However, this has not been confirmed in the United States, where dentists often prescribe AP to patients with prosthetic joints.

The cost of providing AP is approximately $59,640,000 annually in the United States.[20] However, this does not include the cost of adverse drug reactions to AP[21-23] or the possibility that AP may help promote the selection of antibiotic-resistant bacteria.[21,24,25]

The aims of our study were to determine whether there is a positive association between IDPs and subsequent LPJIs in 2 US populations and whether AP cover of IDPs reduces the incidence of LPJIs.

METHODS

Data source

Our study was conducted in a US health care population and reported following Strengthening the Reporting of Observational Studies in Epidemiology guidelines for cohort studies.[26] Data from the Commercial, Medicare Supplemental (for retirees with employer-paid Medicare supplemental insurance), Prescription Benefits, and Dental IBM MarketScan databases (integrating unidentifiable patient-level data) were linked (Appendix, available online at the end of this article, for more details). We also obtained data from the multistate Medicaid database for patients who also had dental coverage. Because MarketScan databases are statistically deidentified in compliance with the Health Insurance Portability and Accountability Act of 1996,[27] and meet Health Insurance Portability and Accountability Act limited-use data set criteria, they are not subject to institutional review board review. All enrollees 18 years and older with more than 16 months of linked data (January 2000-August 2015) were included. Data on patients with linked medical, dental, and prescription benefits from October 1, 2009, through December 31, 2019, who developed LPJIs were included.

LPJI hospital admissions

A cohort of patients hospitalized with an LPJI from January 1, 2010, through December 31, 2019, were identified using primary *International Classification of Diseases, Ninth Revision Clinical Modification* (ICD-9-CM)[31] code 996.66 or ICD-10-CM[32] code T84.5. When reviewing each patient's records back to 2000, we identified the date and type of joint replaced using *Current Procedural Terminology*,[30] ICD-9-CM, and *ICD-10 Procedure Coding System* (ICD-10-PCS)[33] joint replacement codes (Appendix and eTable 1, available online at the end of this article). This allowed us to subanalyze data according to the type of joint replaced. Joint replacements were divided into the following categories: all, hip, knee, other, multiple joint types, and unknown. Unknown included all joint replacements before 2000 when data were missing or when no replacement code data were available. To ensure only patients with LPJIs were analyzed, this information was also used to exclude patients admitted for joint infection within 3 months of their joint being replaced. We also excluded admissions for PJIs that occurred in the 12 months after an earlier PJI admission as representing relapsing PJI.

IDPs

American Dental Association (ADA) *Current Dental Terminology*[34] or ICD-9-CM[31] and ICD-10-PCS[33] procedure codes were used to classify dental procedures (DPs) as follows:

- IDPs, which are DPs that involve manipulation of gingival tissue or the periapical region of the teeth or perforation of the oral mucosa; for example, tooth extractions, oral surgical procedures, scaling (supragingival or subgingival), and endodontic procedures (i.e., those DPs that the American Heart Association guidelines recommend "should" be covered by AP)[29,35]

ABBREVIATION KEY

AAOS:	American Academy of Orthopaedic Surgeons.
ADA:	American Dental Association.
AP:	Antibiotic prophylaxis.
DP:	Dental procedure.
ICD-9-CM:	*International Classification of Diseases, Ninth Revision, Clinical Modification.*
ICD-10-PCS:	*ICD-10 Procedure Coding System.*
IDP:	Invasive dental procedure.
LPJI:	Late periprosthetic joint infection.
PJI:	Periprosthetic joint infection.

Table 1. Characteristics of the study population.

CHARACTERISTICS	ALL PATIENTS	COMMERCIAL/MEDICARE SUPPLEMENTAL PATIENTS	MEDICAID PATIENTS
LPJI* Cases, No.	2,344	1,160	1,184
Age Group, Y, No. (%)			
18-34	199 (8.5)	54 (4.7)	145 (12.3)
35-44	247 (10.5)	58 (5.0)	189 (16.0)
45-54	540 (23.0)	189 (16.3)	351 (29.7)
55-64	812 (34.6)	368 (31.7)	444 (37.5)
≥ 65	546 (23.3)	491 (42.3)	55 (4.7)
Sex, No. (%)			
Male	1,194 (50.9)	601 (51.8)	593 (50.1)
Female	1,150 (49.1)	559 (48.2)	591 (49.9)
Prosthetic Joint Type, No. (%)			
Hip	304 (13.0)	122 (10.5)	182 (15.4)
Knee	759 (32.4)	412 (35.5)	347 (29.3)
Other	55 (2.3)	25 (2.2)	30 (2.5)
Multiple	398 (17.0)	254 (21.9)	144 (12.2)
Unknown	828 (35.3)	347 (29.9)	481 (40.6)
Dental Procedures, No. (%)	4,614	3,445	1,169
IDP†	1,821 (39.5)	1,460 (42.4)	361 (30.9)
Intermediate	797 (17.3)	551 (16.0)	246 (21.0)
Non-IDP	1,996 (43.3)	1,434 (41.6)	562 (48.1)
Types of IDP, No. (%)	1,821	1,460	361
Scaling	1,403 (77.0)	1,228 (84.1)	175 (48.5)
Extractions	338 (18.6)	162 (11.1)	176 (48.8)
Endodontics	78 (4.3)	63 (4.3)	15 (4.2)
Oral surgery (including biopsy, periodontal and implant surgery)	68 (3.7)	34 (2.3)	34 (9.4)
Procedures With Antibiotic Prophylaxis Cover, No. (%)			
IDP	333 (18.3)	282 (19.3)	51 (14.1)
Scaling	243 (17.3)	218 (17.8)	25 (14.3)
Extractions	69 (20.4)	44 (27.2)	25 (14.2)
Endodontics	19 (24.4)	16 (25.4)	<11‡ (20)
Oral surgery	13 (19.1)	11 (32.4)	<11‡ (6)

* LPJI: Late prosthetic joint infection. † IDP: Invasive dental procedure. Because more than 1 type of IDP can be performed at the same visit, values may total more than 100%. ‡ When the number of patients was < 11 in any cell, numbers were censored in compliance with data confidentiality requirements.

- intermediate DPs, for example, most restorative DPs that may require AP cover when gingival manipulation is necessary to complete the procedure but do not require AP cover when the procedure can be completed without gingival manipulation
- non-IDPs, for example, routine dental examination, dental radiographs, and placement of removable prosthodontic or orthodontic appliances, for which AP is not recommended (Table 1 and eTable 2, available online at the end of this article)[29,35]

The most invasive procedure was ascribed to each visit. When treatment involved multiple visits, each was evaluated separately for procedures performed and AP cover. Data attrition steps are shown in eTable 3.

Prescription benefits data were used to identify whether AP was prescribed for each dental visit using previously validated methodology[28] (Appendix, available online at the end of this article).

Results of previous studies have shown that more than 90% of distant infections associated with IDPs occur within 3 months, and this period is used widely to define distant site infections caused by IDPs[4,36-42] and is why we chose a 3-month risk window for a causal relationship between IDPs and LPJIs (that is, the case period).

Case-crossover study

Maclure[43] proposed the case-crossover methodology for studying the effect of transient events in triggering subsequent outcomes while simultaneously eliminating control selection bias and confounding because of constant within-patient characteristics. In case-crossover studies, patients serve as their own control.

We examined patients when the outcome was LPJIs and evaluated their exposure to IDPs. We compared IDP incidence in a predefined 3-month case period occurring immediately before LPJI hospital admission with that in the preceding 12-month control period (months 4-15).[43-45] To establish the chronicity of events, the monthly incidence of DPs during the 15 months before LPJI hospital admission was plotted. In some case-crossover studies, researchers have compared case periods with 1 or more control periods of equal duration. However, Mittleman and colleagues[46] found that sampling the control period frequency over an entire year was twice as efficient as sampling control periods equal to the case period in length, even when many control periods were sampled. Using a 12-month control period also controlled for seasonal and other time-dependent effects.

Statistical methods

Case-crossover analysis[43,46] comparing exposure to DPs during the 3-month case period immediately before LPJI admissions with incidence of DPs in the preceding 12-month control period (months 4-15) was performed using conditional logistic regression (with fixed effects to control for time-invariant patient characteristics).[46] Because multiple comparisons were made, we calculated *P* values and then applied a Bonferroni correction. We have provided both the crude and Bonferroni-corrected *P* values (Table 2). As a sensitivity analysis, we repeated the analyses using 1-month and 2-month case periods and a 12-month control period.

Power calculation

To ensure that we had sufficient power to detect any clinically significant association or effect, we performed a power calculation (Appendix, available online at the end of this article). This confirmed that our study had greater than 90% power to detect an odds ratio of 1.039; that is, a 3.9% higher likelihood of DPs in the 3-month case period than the matched control period.

RESULTS

Population characteristics

We identified 2,344 patients who developed LPJIs from January 1, 2010, through December 31, 2019, for whom linked medical, dental, and prescription benefits data were available for at least 15 months before their LPJI hospital admission. Of them, 1,160 had commercial or Medicare supplemental coverage and 1,184 had Medicaid coverage (Table 1). Although the sex distribution was similar between the 2 populations, a much higher proportion of patients with LPJI were older than 65 years in the commercial or Medicare supplemental population (42.3%) than the Medicaid population (4.7%), as would be expected from the different age profiles of those eligible for Medicare or Medicaid. The proportions of hip, knee, and other prostheses affected by LPJIs were not significantly different in the 2 populations, although the proportion in which the type of joint affected was unknown was highest in the Medicaid group.

Incidence of different DPs during the 15 months before LPJI admission

In the 15 months preceding LPJI admission, 4,614 DPs were performed, of which 1,821 (39.5%) were IDPs, 3,445 were performed in patients with commercial or Medicare supplemental coverage (1,460 of these DPs [42.4%] were IDPs) and 1,169 were performed in patients with Medicaid

Table 2. Case-crossover analysis comparing the incidence of different dental procedures (with and without AP* cover) in the 3-month case period (months 1-3 before LPJI† admission) and the preceding 12-month control period (months 4-15 before LPJI admission).

DENTAL PROCEDURES	ALL LPJI PATIENTS			COMMERCIAL OR MEDICARE SUPPLEMENTAL LPJI PATIENTS			MEDICAID LPJI PATIENTS		
	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values
Invasive									
All	110.3	124.1	0.890 (0.790 to 1.002) .054, .486	89.3	99.3	0.896 (0.783 to 1.025) .110, .990	21.0	24.8	0.868 (0.674 to 1.117) .271, 1
No AP cover	83.7	102.9	0.814 (0.711 to 0.932) .003, .027	67.7	81.2	0.829 (0.711 to 0.966) .016, .144	16.7	22.5	0.766 (0.576 to 1.020) .068, .612
AP cover	26.3	21.1	1.252 (0979 to 1.601) .073, .657	21.7	18.1	1.197 (0.908 to 1.578) .203, 1	4.0	2.2	1.665 (0.924 to 3.000) .089, .801
Intermediate									
All	41.0	56.2	0.750 (0.623 to 0.902) .002, .018	27.7	39	0.719 (0.572 to 0.905) .005, .045	13.3	17.2	0.812 (0.596 to 1.107) .188, 1
No AP cover	31.0	43.8	0.728 (0.589 to 0.901) .003, .027	21.3	30.3	0.716 (0.552 to 0.928) .012, .108	11.3	14.9	0.798 (0.570 to 1.116) .188, 1
AP cover	10.0	12.3	0.829 (0.572 to 1.203) .323, 1	6.3	8.7	0.737 (0.455 to 1.195) .216, 1	2.0	2.2	0.906 (0.403 to 2.036) .812, 1
Noninvasive									
All	114.0	137.8	0.842 (0.754 to 0.941) .002, .018	85.0	98.2	0.876 (0.770 to 0.997) .046, .414	29.0	39.6	0.760 (0.612 to 0.943) .013, .117
No AP cover	92.3	113.7	0.829 (0.733 to 0.938) .003, .027	67.7	79.2	0.867 (0.750 to 1.002) .054, .486	25.3	36.2	0.732 (0.581 to 0.921) .008, .072
AP cover	21.7	24.2	0.908 (0.706 to 1.170) .456, 1	17.3	19.1	0.918 (0.691 to 1.220) .555, 1	3.7	3.4	1.063 (0.572 to 1.976) .846, 1

* AP: Antibiotic prophylaxis. † LPJI: Late prosthetic joint infection. ‡ Using Bonferroni correction for multiple comparisons.

coverage (361 of these DPs [30.9%] were IDPs) (Table 1). Of the IDPs, 18.3% were covered by AP (19.3% in patients with commercial or Medicare coverage and 14.1% in patients with Medicaid coverage).

The monthly incidence of IDPs, intermediate, and noninvasive DPs in the 15 months before LPJI hospital admission were plotted for the combined populations and separately for patients with commercial or Medicare supplemental coverage and patients with Medicaid coverage (Figure). The incidence of procedures performed with and without AP cover were also plotted.

In none of the populations studied (combined, commercial or Medicare supplemental, Medicaid) did we detect a significant increase in the incidence of IDPs during the 3-month case period immediately before LPJI admission compared with the preceding 12-month control period (months 4-15 before LPJI admission) (Table 2). This was also the case when we used a 1-month or 2-month case period (eTables 4 and 5, available online at the end of this article). When we confined analysis to IDPs that had been covered by AP, there was an increase in the incidence of these procedures in the 3 months before LPJI hospital admission (Table 2, Figure), but the increase was not significant. The same was true when a 1- or 2-month case period was used (eTables 4 and 5, available online at the end of this article). For IDPs not covered by AP, rather than an increase, there was a small decrease in procedures in the 3 months before LPJI, which was significant for the combined

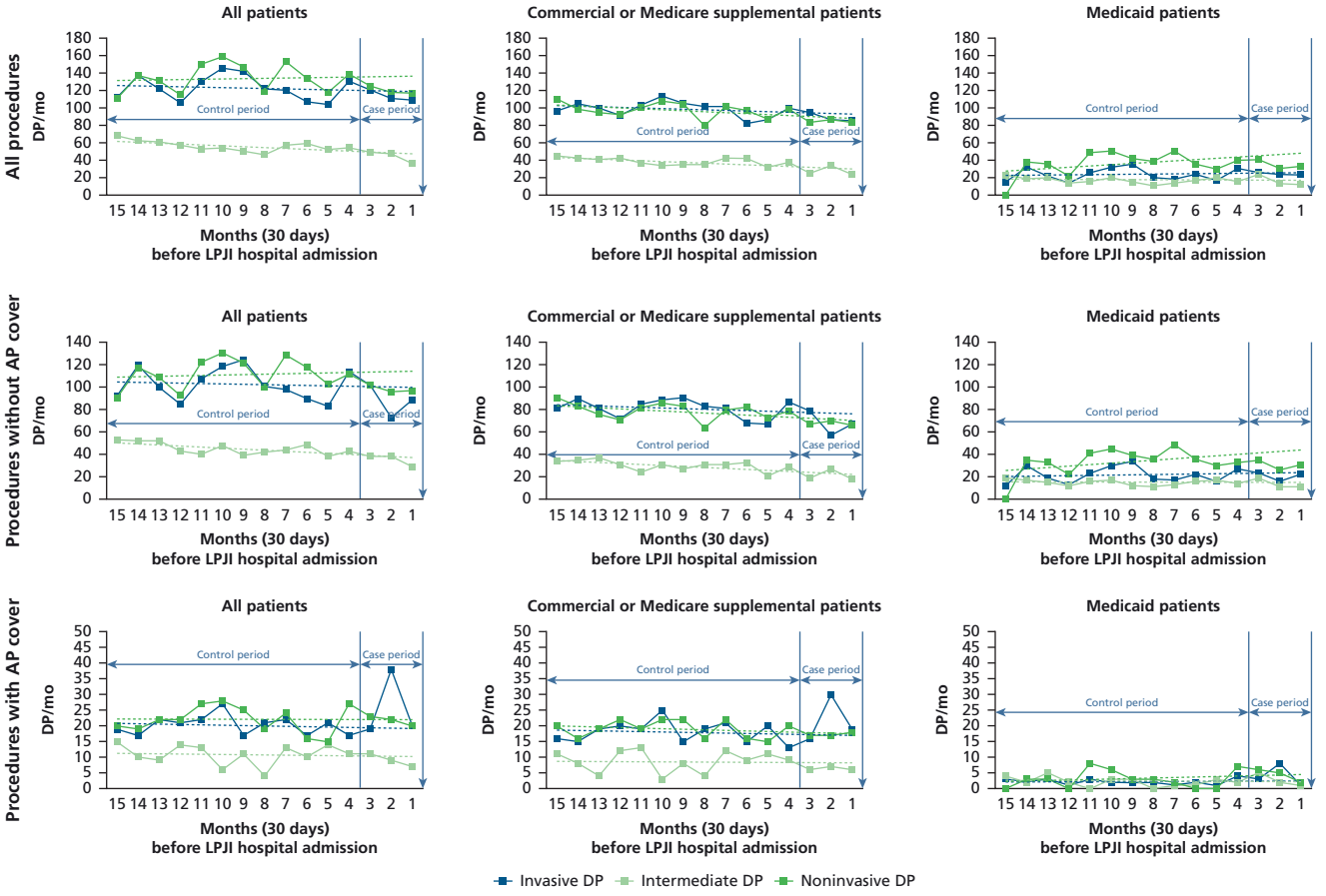

Figure. Incidence of invasive, intermediate, and noninvasive dental procedures (DPs) during the 15 months before late periprosthetic joint infection (LPJI) hospital admission. Top row: Plots for all DPs. Middle row: plots for DPs not covered by antibiotic prophylaxis (AP). Bottom row: plots for DPs covered by AP. LPJI admission is denoted by the vertical blue arrow. The incidence of invasive (blue), intermediate (light green), and noninvasive (green) DPs are plotted during the 15 months before LPJI admission, divided into a 3-month case period immediately before admission and a 12-month control period before that. Dotted lines show the trend of DP incidence for the control period extended into the case period for each DP type.

population (but not for the commercial or Medicare supplemental or Medicaid populations separately). There was also a small but significant fall in IDPs not covered by AP when a 2-month case period was used, but the fall was not significant with a 1-month case period (eTables 4 and 5, available online at the end of this article).

The site of joint replacement (that is, hip, knee, other, multiple, or unknown) had no effect on the relationship between IDPs and subsequent LPJIs, with no significant increase in IDPs in the 3 months before LPJI admission for any joint type and no significant effect of AP on this relationship (eTables 6 through 10, available online at the end of this article).

DISCUSSION

From the 1970s through the 1980s, the use of AP to prevent infective endocarditis in at-risk patients undergoing IDPs was established. This led orthopedic surgeons in the United States to call for dentists to prescribe AP to patients with prosthetic joints.[16-18,47] In 1988, the ADA sponsored a workshop to address this issue. Although evidence to support its use was limited, they recommended AP until additional evidence became available,[48,49] and dentists widely adopted AP.[50] In 1997[51] and 2003,[52] the ADA and American Academy of Orthopaedic Surgeons (AAOS), respectively, published joint advisory statements. These statements recommended AP for 2 years after joint replacement and for life in patients with medical conditions that might put them at increased risk of LPJIs. In 2009, however, the AAOS unilaterally declared "the AAOS recommends that clinicians consider antibiotic prophylaxis for total joint replacement patients … prior to any invasive procedure that may cause bacteremia."[53] This caused confusion for dentists and their patients.[20] The

AAOS and ADA subsequently made several attempts, either together or separately, to produce guidance.[54,55] These efforts, however, only increased the confusion about whether to provide AP.[56-58] As a result, the ADA's Council on Scientific Affairs assembled a panel of experts to conduct a systematic review in 2014.[58] They recommended the following: "In general, for patients with prosthetic joint implants, prophylactic antibiotics are not recommended prior to dental procedures." Unfortunately, this advice lacked AAOS support. As a result, confusion persists among dentists and their patients about the use of AP. Orthopedic surgeons continue to advocate for their patients to receive AP when undergoing IDPs and, for fear of being considered negligent, many dentists continue to provide it.[59]

There are few microbiological data to support a causal association between IDPs and LPJIs and, to our knowledge, there has never been a randomized controlled trial of AP to determine its safety and effectiveness. Unlike infective endocarditis, in which oral streptococci causes approximately 45% of cases, estimates suggest that oral streptococci are involved in fewer than 10% of LPJI cases.[4,19,21,60-65]

For AP to be effective, there must be a positive causal association between IDPs and LPJIs. Six studies have attempted to evaluate this possibility. In 1977, Waldman and colleagues[66] performed a retrospective case review of 62 patients with LPJIs of the knee and found 7 (11%) had a temporal association with IDPs. In a related study, LaPorte and colleagues[62] associated 3 of 52 (6%) LPJIs of the hip with IDPs. However, neither study included a control group. In contrast, in a case-control study, Kaandorp and colleagues[37] found 0 of 37 patients (0%) with LPJIs had undergone an IDP in the preceding 3 months, but 10% of controls had. In a similar study of 42 Medicare patients with LPJIs, Skaar and colleagues,[40] found 9.5% had undergone IDPs in the preceding 3 months compared with 15.9% of control patients. However, differences were not statistically significant in either study. In another study of 303 patients with PJIs, 48% had undergone IDPs in the previous 2 years compared with 34% of control patients.[67] Researchers performing a subanalysis of patients not given AP found that 33 of the patients with PJIs (11%) had undergone IDPs in the preceding 2 years compared with 49 (14%) of the control patients. None of the differences were statistically significant, and each of these studies had a small sample size and lacked statistical power. There was also selection bias and risk factor confounding between case and control patients in the case-control studies. In contrast, the largest case-crossover study of 9,427 LPJI episodes had more than sufficient power to detect a clinically significant effect and found no significant association between IDPs and subsequent LPJIs.[19] These data strongly suggest that AP was unlikely to be effective in preventing LPJIs. However, because the study was performed in the United Kingdom, where AP is not recommended, investigators were unable to confirm this directly.

Our study had a greater than 90% power to detect any clinically significant effect and confirmed the lack of association between IDPs and subsequent LPJIs in 2 different US populations, those with commercial or Medicare supplemental coverage and those with Medicaid coverage. Furthermore, we found that AP cover of IDPs had no statistically significant effect in reducing the subsequent incidence of LPJIs.

Although the lack of association between IDPs and LPJIs and lack of effect of AP were similar in the commercial or Medicare supplemental and Medicaid populations, there were some differences in the DPs performed and use of AP. Although a smaller proportion of all DPs performed on Medicaid patients were IDPs compared with commercial or Medicare supplemental patients (30.9% and 42.2%, respectively), a much high proportion of IDPs in Medicaid patients were extractions and oral surgery procedures (48.8% and 9.4%, respectively) than in commercial or Medicare supplemental patients (11.1% and 2.3%, respectively). Conversely, fewer IDPs were scaling procedures in Medicaid patients than in commercial or Medicare supplemental patients (48.5% and 84.1%, respectively). These findings suggest regular, ongoing preventative oral health care is more common in the commercial or Medicare supplemental population, and urgent and reactive care is more common in the Medicaid population. The proportion of IDPs (including all IDP subtypes) that were covered by AP was also lower in the Medicaid population than the commercial or Medicare supplemental population (14.1% and 19.3%, respectively).

Our study has some limitations. The MarketScan databases encompass a large sample of US employer-provided health insurance and Medicaid enrollees; however, we only included those with

medical, dental, and prescription benefits coverage. It is therefore unlikely to be representative of the entire US population.

The 996.66 ICD-9-CM[31] and T84.5 ICD-10-CM[32] codes identify PJIs, but do not identify the joint infected or distinguish between early and late PJIs. To determine this, we searched each patient's record for earlier admissions for joint replacement to exclude early PJIs, which are defined as occurring within 3 months of joint replacement. *Current Dental Terminology*[34] and ICD-9-CM and ICD-10-PCS joint replacement codes enabled us to identify the type of joint replaced, and this was used to subdivide cases. However, because we could only access records after January 2000, if joint replacement occurred before that or was not recorded, then we did not know the type of joint replaced and had to record it as "unknown."

Varying dental AP-prescribing strategies (particularly use of a single prescription for multiple courses) made it difficult to verify whether a particular DP was covered. Even when AP was prescribed as a single dose immediately before a procedure, we could not verify that it had been taken or that it was taken at the correct time, that is 30 to 60 minutes before the procedure.[29,35] Similarly, even when there was no evidence of AP prescribing, it is possible that a patient was provided AP by another means. However, we have validated our methodology previously and had 88% (95% CI, 82% to 92%) sensitivity and 96% (95% CI, 94% to 97%) specificity for identification of AP prescribing and distinction from antibiotic use to treat infections.[28] Although the levels of AP cover of IDPs that we identified were low, they are not much lower than those in patients at high risk of infective endocarditis,[28] for which there are clear guidelines recommending AP cover,[29,35] and dentists are more motivated to provide AP cover.[59,68] Several other studies have also found poor compliance with AP prescribing guidelines among US dentists.[59,69-71]

CONCLUSIONS

We did not identify any association between IDPs and subsequent LPJIs or any effect of AP cover of IDPs in reducing the subsequent risk of LPJIs. Our data suggest that continued use of AP poses the unnecessary risks of adverse drug reaction to patients and potential to promote the development of antibiotic resistance in the wider community. The use of AP to prevent LPJIs should therefore cease. Achieving this will likely require better communication between dentists and orthopedic surgeons and a joint effort to support evidence-based antibiotic stewardship measures.[59] ■

SUPPLEMENTAL DATA

Supplemental data related to this article can be found at https://doi.org/10.1016/j.adaj.2022.10.001.

Dr. Thornhill is a professor of translational research in dentistry, Unit of Oral and Maxillofacial Medicine Surgery and Pathology, School of Clinical Dentistry, University of Sheffield, Sheffield, UK, and an associate professor, Department of Oral Medicine, Carolinas Medical Center–Atrium Health, Charlotte, NC. Address correspondence to Dr. Thornhill, Unit of Oral and Maxillofacial Medicine Surgery and Pathology, University of Sheffield School of Clinical Dentistry, Claremont Crescent, Sheffield S10 2TA, UK, email m.thornhill@sheffield.ac.uk.

Dr. Gibson is a senior director of Health Outcomes Research and Data Science, IBM Watson Health, Ann Arbor, MI.

Mr. Pack is a data analyst, IBM Watson Health, Ann Arbor, MI.

Dr. Rosario is a statistician, IBM Watson Health, Ann Arbor, MI.

Ms. Bloemers is a research assistant, IBM Watson Health, Ann Arbor, MI.

Dr. Lockhart is a research professor, Department of Oral Medicine, Carolinas Medical Center–Atrium Health, Charlotte, NC.

Dr. Springer is a joint replacement surgeon, OrthoCarolina, Charlotte, NC.

Dr. Baddour is a professor of infectious diseases, Division of Infectious Diseases, Department of Medicine and Department of Cardiovascular Diseases, Mayo Clinic College of Medicine, Rochester, MN.

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research team, their views may not reflect any views expressed in this article.

ORCID Numbers. Martin H. Thornhill: https://orcid.org/0000-0003-0681-4083; Bedda L. Rosario: https://orcid.org/0000-0001-8795-4242; Peter B. Lockhart: https://orcid.org/0000-0003-3293-3430. For information regarding ORCID numbers, go to http://orcid.org.

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APPENDIX

Data source

The IBM MarketScan databases integrate deidentified patient-level health data across a series of health care–related databases. We linked data, including prescription benefits data, from the MarketScan Commercial (private health insurance coverage provided mainly via employers as a benefit for their employees), Medicare supplemental (top-up health insurance employer-provided coverage for their retirees to improve the basic coverage Medicare provides), and dental (insurance cover for private oral health care) databases.[e1,e2] We also accessed the MarketScan multistate Medicaid database and identified patients in receipt of Medicaid services that included medical, dental, and prescription benefits, for inclusion in the study. Because the MarketScan data are deidentified in compliance with the Health Insurance Portability and Accountability Act of 1996[27] and meet limited-use data set criteria, studies using the data are exempt from institutional review board review. All enrollees older than 18 years; with more than 16 months of linked medical, dental, and prescribing data from October 1, 2009, through December 31, 2019; and who developed late periprosthetic joint infections (LPJIs) were included in the study.

Identifying whether invasive dental procedures (IDPs) were covered by antibiotic prophylaxis (AP)

Prescription benefits data were used to identify whether each dental procedure was likely to have been covered by AP using methodology described previously[28] and outlined briefly here. For each patient in the cohort, that patient's prescription benefits data were searched for AP prescriptions matching the 2007 recommendations from the American Heart Association.[29] These were identified in the database using the following prescribing criteria:

- mode of antibiotic delivery: oral
- antibiotic: amoxicillin, clindamycin, cephalexin, azithromycin, or clarithromycin
- dosage: 2 g of amoxicillin, 600 mg of clindamycin, 2 g of cephalexin, 500 mg of azithromycin, or 500 mg of clarithromycin

In our earlier study, we identified that dentists often prescribed multiple courses of AP cover as a single prescription to ensure that patients had sufficient supplies to cover several invasive dental procedure visits; that is, to avoid the patient having to fill a separate prescription for each invasive dental procedure visit.[28] They also often prescribed at the end of a course of dental treatment so that the patient would have supplies available in advance for a future course of dental treatment. To address these eventualities, we evaluated several different algorithms against the reference standard of the actual prescribing and dental records of 80 patients at high risk of infective endocarditis, 40 patients at moderate risk of infective endocarditis, and 40 patients at low or unknown risk of infective endocarditis. The algorithm that best identified when an invasive dental procedure was likely to have been covered by AP included the 3 prescribing criteria above, when the number of days' supply of the antibiotic was 5 or fewer and the time between the prescription fill date and the invasive dental procedure date was 73 or fewer when the number of days' supply was 1, 146 or fewer when number of days' supply was 2, 219 or fewer when number of days' supply was 3, 292 or fewer when number of days' supply was 4 or 365 or fewer when number of days' supply was 5. Results from using this algorithm had 88% (95% CI, 82% to 92%) sensitivity and 96% (95% CI, 94% to 97%) specificity for identifying when a dental procedure was likely to have been covered by AP,[28] and this was the algorithm we used in the our study to determine whether a dental procedure was likely to have been covered by AP.

Power calculation

The method for sample size evaluation for multiple matched case-control studies using a quantitative covariate was provided by Lachin.[e3] This sample size calculation is relevant to case-crossover studies. The input variables for the calculation were

- n (number of sets [each set contains nD cases and nH controls]) = 2,344 (number of LPJI infections)
- Power = 0.90
- σ (SD of the quantitative exposure variable) = 0.707, 1, 1.414, 1.732, 2
- nD (number of cases per set) = 3

- nH (number of controls per set) = 12
- R^2 (coefficient of determination) = 0
- $\alpha = .05$

Producing the following power calculations, assuming a range of values for the SD of the quantitative exposure of interest, as defined above:

- LPJIs: n = 2,344
- Total: n = 35,160
- Case periods: n = 7,032
- Control periods: n = 28,128
- Variance of continuous exposure: 0.5, 1, 2, 3, 4
- SDs of quantitative exposure: 0.707, 1, 1.414, 1.732, 2
- Odds ratios: 1.056, 1.039, 1.028, 1.023, 1.020

Assuming the SD of the quantitative exposure variable of interest is 1 and each set of matched case-controls consists of 3 cases (3 case months) and 12 matched controls (12 control months), a total of 2,344 matched sets (2,344 LPJI hospital admissions with linked dental data) will provide greater than 90% power to detect an odds ratio of 1.039, that is, a 3.9% higher likelihood of dental procedures in the 3-month risk period than the matched control period.

e1. IBM Watson Health. *The IBM MarketScan Research Databases for Life Sciences Researchers: Data Brochure*. IBM Watson Health; April 2019.
e2. IBM Watson Health. *The Truven Health MarketScan Databases for Health Services Researchers: White Paper*. IBM Watson Health; April 2019.
e3. Lachin JM. Sample size evaluation for a multiply matched case-control study using the score test from a conditional logistic (discrete Cox PH) regression model. *Stat Med*. 2008;27(14):2509-2523.

eTable 1. CPT,* ICD-9-CM,† and ICD-10-PCS‡ procedure codes for identifying when a prosthetic joint replacement occurred and what type of joint was involved.

PROCEDURES	CPT	ICD-9-CM	ICD-10-PCS
Hip Joint Replacement (Arthroplasty)	27125, 27130, 27132, 27134, 27137, 27138	00.70, 00.71, 00.72, 00.73, 81.51, 81.52, 81.53 V43.64	All codes starting: 0SR901-0SR906 and 0SR90J Or: 0SRB01-0SRB06 and 0SRB0J Or: 0SRA00-0SRA03 and 0SRA0J Or: 0SRE00-0SRE03 and 0SRE0J Or: 0SRR01-0SRR03 and 0SRR0J Or: 0SRS01-0SRS03 and 0SRS0J
Knee Joint Replacement (Arthroplasty)	27445, 27446, 27447, 27486, 27487, 27488	00.80, 00.81, 00.82, 00.83, 00.84, 81.54, 81.55 V43.65	All codes starting: 0SRC0J-0SRC0N and 0SRC06 Or: 0SRD0J-0SRD0N and 0SRD06
Other Joint Replacement (Arthroplasty)	23470, 23472, 23473, 23474, 24360,24361, 24362, 24363, 24365, 24366, 24370, 24371, 25240, 25442, 25446, 26530, 26531, 27700, 27702, 27703, 27704,	81.56, 81.57, 81.59, 81.73, 81.80, 81.81, 81.84, 81.88, 81.97 V43.60, V43.61, V43.62, V43.63, V43.66, V43.69	All codes starting: 0RR0-0RR9 and 0RRA-0RRX Or: 0SR0-0SR8 and 0SRF-0SRQ
All Joint Replacements (Arthroplasties)	All of the above	All of the above	All of the above

* CPT: *Current Procedural Terminology*.[30] † ICD-9-CM: *International Classification of Diseases, Ninth Revision, Clinical Modification*.[31] ‡ ICD-10-PCS: *ICD-10 Procedure Coding System*.[33]

eTable 2. CDT* and ICD-9-CM† procedure codes for invasive, intermediate, and noninvasive dental procedures, and codes for specific types of invasive dental procedure.

PROCEDURES	CDT CODES	ICD-9-CM CODES
Dental Procedures		
Invasive dental procedure codes (those procedures that "should" be covered by AP‡)	D0180, D0472-4, D1110, D1120, D3221, D3310, D3320, D3330, D3332-3, D3346-8, D3351-3, D3410, D3421, D3425-32, D3450, D3460, D3470, D3910, D3920, D4210-2, D4230-1, D4240-1, D4245, D4249, D4260-1, D4263-8, D4270, D4273-8, D4283, D4341-2, D4346, D4355, D4381, D4910, D4921, D6010-3, D6040, D6050, D6080-1, D6100-4, D7111, D7140, D7210, D7220, D7230, D7240-1, D7250-1, D7260-1, D7270, D7272, D7280, D7282-3, D7285-6, D7290-5, D7310-1, D7320-1, D7340, D7350, D7410-5, D7465, D7440-1, D7450-1, D7460-1, D7471-3, D7485, D7490, D7510-1, D7520-1, D7530, D7540, D7550, D7560, D7610, D7630, D7671, D7710, D7730, D7770, D7941, D7943-50, D7952-3, D7955, D7960, D7963, D7970-2, D7981-3, D7991, D7996-8	2301, 2309, 2311, 2319, 235, 236, 2370-3, 240, 2411-2, 242, 2431-2, 2439, 244, 245, 246, 2491, 2499, 2502, 251, 252, 253, 254, 2551, 2559, 2591-4, 2599, 260, 2612, 2621, 2629-32, 2641-2, 2649, 270, 271, 2721-4, 2731-2, 2741-3, 2749, 2751-7, 2759, 2761-4, 2769, 2771-3, 2779, 2791-2, 2799, 9654
Intermediate dental procedure codes (those procedures that "may" be covered by AP)	D0120, D0150, D2150, D21601, D2330-2, D2335, D2390, D2392-4, D2520, D2530, D2542-4, D2620, D2630, D2642-4, D2651-2, D2662-4, D2710, D2712, D2720-2, D2740, D2750-2, D2780-3, D2790-2, D2794, D2799, D2929-34, D2960-2, D4999, D6051-2, D6055-7, D6065-7, D6075-7, D6545, D6548-9, D6600-15, D6624, D6634, D6710, D6720-2, D6740, D6750-2, D6780-3, D6790-4, D7620, D7640, D7650, D7660, D7670, D7680, D7720, D7740, D7750, D7760, D7771, D7780	232, 233, 2341, 2342, 2343, 2349
Noninvasive dental procedure codes (those procedures for which there is no AP recommendation)	All CPT dental procedure codes not listed as being red or yellow.	All ICD-9 dental procedure codes not listed as being red or yellow.
Specific Types of Invasive Dental Procedure		
Scaling	D1110, D1120, D4341-2, D4346, D4355, D4381, D4910, D4921,	9654
Extractions	D7111, D7140, D7210, D7220, D7230, D7240-1, D7250-1,	2301, 2309, 2311, 2319,
Endodontic procedures	D3221, D3310, D3320, D3330, D3332-3, D3346-8, D3351-3, D3410, D3421, D3425-32, D3450, D3460, D3470, D3910, D3920,	2370-3
Surgical procedures (including oral and periodontal surgical procedures and biopsies)	D0472-4, D4210-2, D4230-1, D4240-1, D4245, D4249, D4260-1, D4263-8, D4270, D4273-8, D4283, D7260-1, D7270, D7272, D7280, D7282-3, D7285-6, D7290-5, D7310-1, D7320-1, D7340, D7350, D7410-5, D7465, D7440-1, D7450-1, D7460-1, D7471-3, D7485, D7490, D7510-1, D7520-1, D7530, D7540, D7550, D7560, D7610, D7630, D7671, D7710, D7730, D7770, D7941, D7943-50, D7952-3, D7955, D7960, D7963, D7970-2, D7981-3, D7991, D7996-8	240, 2411-2, 242, 2431-2, 2439, 244, 245, 246, 2491, 2499, 2502, 251, 252, 253, 254, 2551, 2559, 2591-4, 2599, 260, 2612, 2621, 2629-32, 2641-2, 2649, 270, 271, 2721-4, 2731-2, 2741-3, 2749, 2751-7, 2759, 2761-4, 2769, 2771-3, 2779, 2791-2, 2799

* CDT: *Current Dental Terminology*.[34] † ICD-9-CM: *International Classification of Diseases, Ninth Revision, Clinical Modification*.[31]
‡ AP: Antibiotic prophylaxis.

eTable 3. Data attrition steps.

ATTRITION STEPS	ALL PATIENTS, NO.	COMMERCIAL OR MEDICARE SUPPLEMENTAL PATIENTS, NO.	MEDICAID PATIENTS, NO.
Enrolled in Database at Least 1 Month 2009-2019	197,924,079	168,855,655	29,068,424
Had Drug Coverage Entire Time Enrolled	158,902,117	133,102,194	25,799,923
17 Years or Older as of January 1, 2019	128,847,010	113,344,362	15,502,648
Dental Coverage at Least 1 Month 2007-2019	36,797,581	21,294,933	15,502,648

	PEOPLE, NO.	EVENTS, NO.	PEOPLE, NO.	EVENTS, NO.	PEOPLE, NO.	EVENTS, NO.
Inpatient PJI* Admission 2009-2019	13,682	23,873	9,202	14,976	4,480	8,897
15 Months Continuous Enrollment Required Before PJI	11,117	18,839	7,952	12,809	3,165	6,030
Require No Joint Replacement Within 3 Months of PJI	2,979	3,060	1,827	1,876	1,152	1,184
Require Dental Cover Entire 15 Months Before PJI	2,285	2,344†	1,133	1,160†	1,152	1,184†
Prosthetic Joint Type Present						
Hip only	NA‡	304	NA	122	NA	182
Knee only	NA	759	NA	412	NA	347
Other joint only	NA	55	NA	25	NA	30
Multiple joints	NA	398	NA	254	NA	144
Unknown	NA	828	NA	347	NA	481

* PJI: Periprosthetic joint infection. † These are the values left after the sequential attrition steps that are used in the analysis. ‡ NA: Not applicable.

eTable 4. Case-crossover analysis comparing the incidence of different dental procedures (with and without AP* cover) in the 1-month case period (month 1 before LPJI† admission) and the preceding 12-month control period (months 2-13 before LPJI admission).

DENTAL PROCEDURES	ALL LPJI PATIENTS			COMMERCIAL OR MEDICARE SUPPLEMENTAL LPJI PATIENTS			MEDICAID LPJI PATIENTS		
	Case Period, Procedures/ mo	Control Period, Procedures/ mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/ mo	Control Period, Procedures/ mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/ mo	Control Period, Procedures/ mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values
Invasive									
All	102	121.8	0.839 (0.687 to 1.024) .085, .765	86.0	97.7	0.877 (0.703 to 1.095) .248, 1	16.0	24.2	0.698 (0.432 to 1.128) .142, 1
No AP cover	79.0	98.9	0.801 (0.639 to 1.005) .055, .495	67.0	78.3	0.853 (0.664 to 1.095) .248, 1	12.0	20.6	0.620 (0.356 to 1.082) .092, .828
AP cover	23.0	22.8	1.007 (0.664 to 1.528) .974, 1	19.0	19.3	0.983 (0.616 to 1.568) .942, 1	4.0	3.4	1.11 (0.453 to 2.721) .819, 1
Intermediate									
All	39.0	52.6	0.760 (0.556 to 1.038) .085, .765	24.0	36.6	0.655 (0.443 to 0.998) .049, .441	15.0	16.0	0.949 (0.591 to 1.525) .829, 1
No AP cover	29.0	41.2	0.725 (0.505 to 1.041) .082, .738	18.0	28.4	0.645 (0.405 to 1.029) .066, .594	11.0	12.8	0.886 (0.506 to 1.549) .670, 1
AP cover	10.0	11.4	0.887 (0.481 to 1.636) .701, 1	6.0	8.2	0.739 (0.327 to 1.673) .469, 1	4.0	3.2	1.170 (0.479 to 2.855) .730, 1
Noninvasive									
All	107.0	133.8	0.817 (0.678 to 0.985) .034, .306	84.0	95.0	0.893 (0.72 to 1.105) .299, 1	23.0	38.8	0.631 (0.424 to 0.939) .023, .207
No AP cover	85.0	109.7	0.795 (0.644 to 0.980) .032, .288	66.0	76.1	0.879 (0.692 to 1.116) .289, 1	19.0	33.6	0.605 (0.390 to 0.937) .024, .216
AP cover	22.0	24.1	0.923 (0.613 to 1.389) .701, 1	18.0	18.9	0.956 (0.606 to 1.508) .847, 1	4.0	5.2	0.807 (0.317 to 2.053) .652, 1

* AP: Antibiotic prophylaxis. † LPJI: Late periprosthetic joint infection. ‡ Using Bonferroni correction for multiple comparisons.

eTable 5. Case-crossover analysis comparing the incidence of different dental procedures (with and without AP* cover) in the 2-month case period (months 1-2 before LPJI† admission) and the preceding 12-month control period (months 3-14 before admission).

DENTAL PROCEDURES	ALL LPJI PATIENTS			COMMERCIAL OR MEDICARE SUPPLEMENTAL LPJI PATIENTS			MEDICAID LPJI PATIENTS		
	Case Period, Procedures/ mo	Control Period, Procedures/ mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/ mo	Control Period, Procedures/ mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/ mo	Control Period, Procedures/ mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values
Invasive									
All	106.0	123.2	0.861 (0.746 to 0.994) .041, .369	86.5	99.2	0.868 (0.739 to 1.021) .088, .792	19.5	24.1	0.834 (0.611 to 1.140) .255, 1
No AP cover	78.0	101.6	0.77 (0.652 to 0.909) .002, .018	62.0	81.1	0.76 (0.629 to 0.918) .004, .036	16.0	20.5	0.806 (0.571 to 1.137) .219, 1
AP cover	28.0	21.5	1.283 (0968 to 1.701) .083, .747	24.5	18.1	1.355 (0993 to 1.849) .055, .495	3.5	3.4	1.0 (0.487 to 2.052) 1, 1
Intermediate									
All	42.5	54.0	0.804 (0.647 to 0.999) .049, .441	29.0	37.3	0.785 (0.600 to 1.027) .077, .693	13.5	16.7	0.842 (0.584 to 1.214) .357, 1
No AP cover	33.0	42.1	0.801 (0.626 to 1.025) .078, .702	22.5	29.1	0.784 (0.579 to 1.062) .116, 1	10.5	13.0	0.837 (0.550 to 1.274) .407, 1
AP cover	9.5	11.9	0.818 (0.521 to 1.286) .384, 1	6.5	8.2	0.794 (0.450 to 1.403) .428, 1	3.0	3.7	0.861 (0.412 to 1.803) .692, 1
Noninvasive									
All	113.5	135.0	0.855 (0.749 to 0.976) .021, .189	85.5	96.0	0.900 (0.772 to 1.049) .178, 1	28.0	39.0	0.747 (0.575 to 0.971) .029, .261
No AP cover	92.5	110.8	0.850 (0.735 to 0.984) .030, .270	68.0	77.2	0.892 (0.751 to 1.059) .191, 1	24.5	33.7	0.757 (0.572 to 1.001) .051, .459
AP cover	21.0	24.2	0.883 (0.651 to 1.198) .425, 1	17.5	18.8	0.936 (0.668 to 1.312) .702, 1	3.5	5.3	0.697 (0.335 to 1.450) .334, 1

* AP: Antibiotic prophylaxis. † LPJI: Late periprosthetic joint infection. ‡ Using Bonferroni correction for multiple comparisons.

eTable 6. Case-crossover analysis comparing the incidence of different dental procedures (with and without AP* cover) in the 3-month case period (months 1-3 before LPJI† admission) and the preceding 12-month control period (months 4-15 before LPJI admission) for patients with prosthetic hip joints developing LPJI.

DENTAL PROCEDURES	ALL LPJI PATIENTS			COMMERCIAL OR MEDICARE SUPPLEMENTAL LPJI PATIENTS			MEDICAID LPJI PATIENTS		
	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values
Invasive									
All	14.3	13.7	1.048 (0.752 to 1.461) .783, 1	12	9.2	1.298 (0.891 to 1.893) .175, 1	2.3	4.4	0.549 (0.254 to 1.185) .127, 1
No AP cover	11.3	10.8	1.044 (0.721 to 1.513) .818, 1	9.7	7	1.377 (0.904 to 2.097) .137, 1	1.7	4.1	0.432 (0.176 to 1.063) .068, .612
AP cover	3.0	2.8	1.058 (0.509 to 2.201) .879, 1	2.3	2.2	1.037 (0.454 to 2.368) .932, 1	0.7	0.3	2.00 (0.366 to 10.919) .423, 1
Intermediate									
All	7.7	7.1	1.074 (0.694 to 1.663) .749, 1	5.3	4.2	1.223 (0.721 to 2.075) .455, 1	2.3	2.8	0.836 (0.382 to 1.828) .653, 1
No AP cover	4.7	4.9	0.951 (0.538 to 1.682) .864, 1	3.3	2.9	1.130 (0.577 to 2.211) .722, 1	2.0	2.3	0.863 (0.364 to 2.044) .737, 1
AP cover	3.0	2.2	1.297 (0.659 to 2.554) .452, 1	2	1.3	1.397 (0.904 to 2.097) .137, 1	0.3	0.5	0.725 (0.108 to 4.865) .741, 1
Noninvasive									
All	12.0	16.4	0.756 (0.539 to 1.059) .104, .936	9.7	8.7	1.103 (0.747 to 1.631) .621, 1	2.3	7.8	0.334 (0.157 to 0.709) .004, .036
No AP cover	10.0	12.8	0.801 (0.552 to 1.160) .240, 1	8	6.2	1.255 (0.808 to 1.950) .313, 1	2.0	7.2	0.315 (0.140 to 0.708) .005, .045
AP cover	2.0	3.6	0.606 (0.273 to 1.348) .220, 1	1.7	2.4	0.739 (0.312 to 1.749) .492, 1	0.3	0.6	0.571 (0.070 to 4.644) .601, 1

* AP: Antibiotic prophylaxis. † LPJI: Late periprosthetic joint infection. ‡ Using Bonferroni correction for multiple comparisons.

eTable 7. Case-crossover analysis comparing the incidence of different dental procedures (with and without AP* cover) in the 3-month case period (months 1-3 before LPJI† admission) and the preceding 12-month control period (months 4-15 before LPJI admission) for patients with prosthetic knee joints developing LPJI.

DENTAL PROCEDURES	ALL LPJI PATIENTS			COMMERCIAL OR MEDICARE SUPPLEMENTAL LPJI PATIENTS			MEDICAID LPJI PATIENTS		
	Case Period, Procedures/ mo	Control Period, Procedures/ mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/ mo	Control Period, Procedures/ mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/ mo	Control-Period, Procedures/ mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values
Invasive									
All	36.3	42.8	0.844 (0.684 to 1.041) .113, 1	33	36.2	0.907 (0.726 to 1.133) .390, 1	3.3	6.6	0.505 (0.261 to 0.978) .043, .387
No AP cover	26.3	34.3	0.763 (0.598 to 0.973) .029, .261	24.3	28.8	0.840 (0.650 to 1.085) .181, 1	2.3	6.0	0.388 (0.178 to 0.846) .017, .153
AP cover	10.0	8.5	1.177 (0.783 to 1.770) .434, 1	8.7	7.4	1.168 (0.755 to 1.805) .486, 1	1.0	0.6	1.73 ().442 to 6.779) .431, 1
Intermediate									
All	12.7	18.5	0.702 (0.502 to 0.981) .038, .342	8.3	13.7	0.624 (0.413 to 0.944) .026, .234	4.3	4.8	0.907 (0.513 to 1.602) .737, 1
No AP cover	11.7	14.2	0.831 (0.585 to 1.180) .301, 1	8.3	10.5	0.808 (0.535 to 1.222) .313, 1	3.7	4.3	0.86 (0.463 to 1.597) .633, 1
AP cover	1.0	4.2	0.249 (0.079 to 0.790) .018, .162	0.0	3.2	0.000 (0, infinity) .989, 1	0.7	0.5	1.266 (0.298 to 5.378) .749, 1
Noninvasive									
All	43.7	45.3	0.968 (0.810 to 1.157) .719, 1	34.7	35.2	0.987 (0.807 to 1.208) .902, 1	9.0	10.2	0.903 (0.616 to 1.324) .601, 1
No AP cover	34.3	35.8	0.965 (0.788 to 1.181) .729, 1	27.3	27.3	1.000 (0.795 to 1.257) 1, 1	7.7	9.2	0.854 (0.565 to 1.292) .455, 1
AP cover	9.3	9.6	0.979 (0.674 to 1.422) .910, 1	7.3	7.8	0.947 (0.621 to 1.444) .801, 1	1.3	0.9	1.372 (0.479 to 3.924) .556, 1

* AP: Antibiotic prophylaxis. † LPJI: Late periprosthetic joint infection. ‡ Using Bonferroni correction for multiple comparisons.

eTable 8. Case-crossover analysis comparing the incidence of different dental procedures (with and without AP* cover) in the 3-month case period (months 1-3 before LPJI† admission) and the preceding 12-month control period (months 4-15 before LPJI admission) for patients with other types of prosthetic joint developing LPJI.

DENTAL PROCEDURES	ALL LPJI PATIENTS			COMMERCIAL OR MEDICARE SUPPLEMENTAL LPJI PATIENTS			MEDICAID LPJI PATIENTS		
	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values
Invasive									
All	2.7	2.2	1.189 (0.535 to 2.640) .671, 1	1.3	1.9	0.695 (0.241 to 2.005) .501, 1	1.3	0.3	4.147 (1.014 to 16.954) .048, .432
No AP cover	1.7	1.3	1.235 (0.465 to 3.277) .672, 1	0.3	1.1	0.325 (0.043 to 2.435) .274, 1	1.3	0.2	5.333 (1.194 to 23.829) .028, .252
AP cover	1.0	0.9	1.089 (0.307 to 3.860) .895, 1	1.0	0.8	1.196 (0.332 to 4.303) .784, 1	0.0	0.1	0 (0 to infinity) .997, 1
Intermediate									
All	1.3	1.5	0.886 (0.295 to 2.660) .829, 1	0.3	1.2	0.277 (0.036 to 2.135) .218, 1	1.0	0.3	3.094 (0.675 to 14.188) .146, 1
No AP cover	1.3	1.0	1.341 (0.427 to 4.209) .615, 1	0.3	0.8	0.436 (0.054 to 3.502) .435, 1	1.0	0.2	4 (0.807 to 19.818) .090, 0.81
AP cover	0.0	0.5	0.000 (0.000 to infinity) .996, 1	0.0	0.4	0.000 (0 to infinity) .997, 1	0.0	0.1	0 (0 to infinity) .997, 1
Noninvasive									
All	3.3	2.8	1.161 (0.591 to 2.282) .665, 1	1.7	2.1	0.824 (0.336 to 2.021) .672, 1	1.7	0.8	2.375 (0.754 to 7.484) .140, 1
No AP cover	2.7	2.2	1.195 (0.574 to 2.489) .634, 1	1.0	1.5	0.727 (0.244 to 2.171) .568, 1	1.7	0.7	2.681 (0.833 to 8.630) .098, 0.882
AP cover	0.7	0.7	1.000 (0.205 to 4.873) 1, 1	0.7	0.6	1.151 (0.229 to 5.780) .864, 1	0.0	0.1	0 (0 to infinity) .997, 1

* AP: Antibiotic prophylaxis. † LPJI: Late periprosthetic joint infection. ‡ Using Bonferroni correction for multiple comparisons.

eTable 9. Case-crossover analysis comparing the incidence of different dental procedures (with and without AP* cover) in the 3-month case period (months 1-3 before LPJI† admission) and the preceding 12-month control period (months 4-15 before LPJI admission) for patients with multiple prosthetic joint types developing LPJI.

DENTAL PROCEDURES	ALL LPJI PATIENTS			COMMERCIAL OR MEDICARE SUPPLEMENTAL LPJI PATIENTS			MEDICAID LPJI PATIENTS		
	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values
Invasive									
All	22.7	24.9	0.905 (0.690 to 1.186) .468, 1	19.0	22.1	0.851 (0.633 to 1.144) .286, 1	3.7	2.8	1.283 (0.658 to 2.501) .465, 1
No AP cover	16.0	19.2	0.829 (0.604 to 1.138) .246, 1	13.0	16.9	0.757 (0.533 to 1.076) .121, 1	3.3	2.2	1.444 (0.716 to 2.912) .305, 1
AP cover	6.7	5.8	1.170 (0.700 to 1.954) .550, 1	6.0	5.2	1.172 (0.682 to 2.015) .566, 1	0.3	0.6	0.562 (0.067 to 4.684) .594, 1
Intermediate									
All	7.0	11.3	0.632 (0.403 to 0.992) .046, .414	4.7	8.9	0.531 (0.306 to 0.923) .025, .225	2.3	2.4	0.97 (0.449 to 2.096) .938, 1
No AP cover	4.0	7.9	0.519 (0.287 to 0.938) .030, 0.270	2.7	6.5	0.417 (0.202 to 0.860) .018, .162	2.0	1.4	1.371 (0.562 to 3.343) .488, 1
AP cover	3.0	3.4	0.889 (0.448 to 1.765) .738, 1	2.0	2.4	0.838 (0.358 to 1.963) .018, 1	0.3	1.0	0.406 (0.062 to 2.663) .347, 1
Noninvasive									
All	19.7	27.4	0.730 (0.557 to 0.957) .023, .207	15.0	22.8	0.676 (0.498 to 0.918) .012, .108	4.7	4.6	1.019 (0.561 to 1.850) .951, 1
No AP cover	15.7	21.5	0.747 (0.554 to 1.008) .056, .504	11.0	17.7	0.652 (0.459 to 0.926) .017, .153	4.7	3.8	1.224 (0.667 to 2.248) .514, 1
AP cover	4.0	5.9	0.678 (0.368 to 1.247) .211, 1	4.0	5.2	0.777 (0.420 to 1.435) .420, 1	0.0	0.8	0 (0 to infinity) .992, 1

* AP: Antibiotic prophylaxis. † LPJI: Late periprosthetic joint infection. ‡ Using Bonferroni correction for multiple comparisons.

eTable 10. Case-crossover analysis comparing the incidence of different dental procedures (with and without AP* cover) in the 3-month case period (months 1-3 before LPJI† admission) and the preceding 12-month control period (months 4-15 before LPJI admission) for patients developing LPJI when the type of prosthetic joint is unknown.

DENTAL PROCEDURES	ALL LPJI PATIENTS			COMMERCIAL OR MEDICARE SUPPLEMENTAL LPJI PATIENTS			MEDICAID LPJI PATIENTS		
	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values	Case Period, Procedures/mo	Control Period, Procedures/mo	Odds Ratio (95% CI) Unadjusted, Adjusted‡ *P* Values
Invasive									
All	34.3	40.4	0.859 (0.699 to 1.055) .147, 1	24.0	29.8	0.801 (0.621 to 1.034) .089, .801	10.3	10.6	0.978 (0.704 to 1.300) .895, 1
No AP cover	28.3	37.2	0.770 (0.613 to 0.967) .024, .216	20.3	27.4	0.736 (0.559 to 0.971) .030, .270	8.0	9.9	0.84 (0.570 to 1.240) .381, 1
AP cover	5.7	3.1	1.635 (0.997 to 2.680) .051, .459	3.7	2.4	1.447 (0.752 to 2.785) .268, 1	2.0	0.6	2.105 (0.872 to 5.000) .098, .882
Intermediate									
All	12.3	17.8	0.727 (0.522 to 1.013) .059, .531	9.0	11.0	0.821 (0.544 to 1.239) .347, 1	3.3	6.8	0.589 (0.326 to 1.066) .080, .720
No AP cover	9.3	15.8	0.632 (0.432 to 0.923) .018, .162	6.7	9.7	0.698 (0.436 to 1.116) .133, 1	2.7	6.6	0.505 (0.260 to 0.982) .044, .396
AP cover	3.0	2.0	1.428 (0.695 to 2.934) .333, 1	2.3	1.3	1.846 (0.724 to 4.706) .199, 1	0.7	0.2	4.69 (0.579 to 38.009) .148, 1
Noninvasive									
All	35.3	45.8	0.788 (0.645 to 0.963) .020, .180	24.0	29.5	0.823 (0.642 to 1.054) .123, 1	11.3	16.3	0.73 (0.519 to 1.026) .070, .630
No AP cover	29.7	41.4	0.738 (0.594 to 0.917) .006, .054	20.3	26.4	0.783 (0.599 to 1.023) .072, .648	9.3	15.2	0.655 (0.451 to 0.951) .026, .234
AP cover	5.7	4.4	1.247 (0.746 to 2.083) .400, 1	3.7	3.1	1.183 (0.610 to 2.294) .620, 1	2.0	1.1	1.603 (0.679 to 3.783) .282, 1

* AP: Antibiotic prophylaxis. † LPJI: Late prosthetic joint infection. ‡ Using Bonferroni correction for multiple comparisons.