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Quantifying the Risk of Prosthetic Joint Infections Following Invasive Dental Procedures and the Effect of Antibiotic Prophylaxis

Brief Title – Prosthetic Joint Infections and Invasive Dental Procedures

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Statement of Institutional Review Board Approval or Waiver:

In this study we used data from the IBM® MarketScan® databases. Since MarketScan databases are statistically de-identified in compliance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA), and meet HIPAA limited-use dataset criteria, they are not subject to IRB-review (see 'Methods' section and Supplementary Appendix for further details).

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Brief Title – Prosthetic Joint Infections and Invasive Dental Procedures

Abstract

Background

Dentists face the expectations of orthopaedic surgeons and prosthetic joint patients to provide antibiotic prophylaxis (AP) before invasive dental procedures (IDPs) to reduce the risk of late prosthetic joint infection (LPJIs). This, 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.

Our aim was to identify any association between IDPs and LPJIs, and if AP reduces LPJI incidence following IDPs

Method:

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/Medicare-supplemental or Medicaid health cover and linked dental and prescription benefits data.

Results

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

Conclusion

This study 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 the development of antibiotic resistance. Dental AP use to prevent LPJI should, therefore, cease.

Keywords

Prosthetic joints, antibiotic prophylaxis, guidelines, prevention, dental procedures

Abbreviations:

AAOS = American Academy of Orthopaedic Surgeons
ADA = American Dental Association
AHA = American Heart Association
AP = Antibiotic prophylaxis
CPT = Current procedural terminology
ICD = International Classification of Disease
IDPs = Invasive dental procedures
LPJIs = Late prosthetic joint infections
NHS = National Health Service
NHSBSA = NHS Business Services Authority
OR = Odds ratio
PJIs = Prosthetic joint infections
UK = United Kingdom
US = United States of America

Introduction

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

LPJIs often results in prosthesis removal; less often, it can result in amputation or loss of life.[4] The cost of treating LPJIs is 4-6 times that of the original arthroplasty[5-8] and is projected at $1.62 billion annually in the US.[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 quickly, with ~4 million new hip and knee replacement operations projected annually in the US by 2030.[11]

Although LPJI incidence is relatively low, is the most common cause of joint failure following knee-replacements and the second most common after hip-replacements.[4, 12, 13] LPJI is mainly attributed to blood stream seeding of bacteria from another anatomical site,[14, 15] and this led orthopaedic surgeons in the US to recommend that patients with prosthetic-joints should be given AP before invasive dental procedures (IDPs).[16-18] None-the-less, there is scant data to support a causal-association between IDPs and LPJIs and AP efficacy in preventing LPJI has never been tested in a randomized controlled trial. Moreover, no association between IDPs and subsequent LPJIs was found in a recent UK study (where AP is not recommended).[19] However, this has not been confirmed in the US where dentists often prescribe AP to patients with prosthetic joints.

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

The aims of this study were to determine if there is a positive association between IDPs and subsequent LPJIs in two US populations, and if AP cover of IDPs reduces the incidence of LPJIs.

Materials and Methods

Data Source

The study was conducted in a US-healthcare population and reported following STROBE 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 (see supplementary appendix for more details on these). We also obtained data from the multi-State Medicaid database for patients who also had dental coverage. Since MarketScan databases are statistically de-identified in compliance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA), and meet HIPAA limited-use dataset criteria, they are not subject to IRB-review.[27] All enrollees ≥18 years with >16 months linked data (January 2000 - August 2015) were included. Data on individuals with linked medical, dental and prescription benefits between October 1st, 2009 and December 31st, 2019 who developed LPJIs were included.

LPJI hospital admissions

A cohort of individuals hospitalized with a LPJI between January 1st, 2010, and December 31st, 2019, were identified using primary ICD-9 code 996.66 or ICD-10 code T84.5. By reviewing each patient's records back to 2000, we identified the date and type of joint replaced using CPT, ICD-9, and ICD-10 joint replacement codes (Supplementary Appendix, Table S1). This allowed us to sub-analyse data by the type of joint replaced. Joint replacements were divided into (i) all, (ii) hip, (iii) knee, (iv) other, (v) multiple joint types, and (v) unknown. Unknown included all joint-replacements before 2000, or where data were missing, when no replacement-code-data were available. To ensure only LPJI patients were analysed, 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 following an earlier PJI admission as representing relapsing PJI.

Invasive Dental Procedures (IDP)

American Dental Association (ADA) CDT or ICD-9/10 procedure codes were used to classify dental procedures into: (i) Invasive-dental procedures (IDPs) – those dental procedures that involve manipulation of gingival tissue or the periapical region of the teeth, or perforation of the oral mucosa e.g. dental extractions, oral surgical procedures, scaling (supragingival or subgingival) and endodontic procedures, i.e. those dental procedures that the American Heart Association (AHA) guidelines recommend 'should' be covered by AP,[28, 29] (ii) Intermediate-dental procedures e.g. most restorative dental procedures, that may require AP cover when gingival manipulation is required to complete the procedure but do not require AP cover when the procedure can be completed without gingival manipulation. (iii) Non-IDPs, e.g., routine dental examination, dental radiographs, placement of removable prosthodontic or orthodontic appliances, for which AP is not recommended (Tables 1, Table S2).[28, 29] The most invasive procedure was ascribed to each visit. When treatment involved multiple visits, each was evaluated separately for procedures performed and AP cover.

Prescription benefits data were used to identify if AP was prescribed for each dental visit using previously validated methodology[30] (see also Supplemental Methods).

Previous studies have shown that >90% of distant infections associated with IDPs occur within 3-months, and this time-period is used widely to define distant site infections caused by IDPs.[4, 31-37] Hence, our choice of a 3-month risk-window for a causal relationship between IDPs and LPJIs (the case-period).

Case-Crossover Study

The case-crossover methodology was proposed by Maclure for studying the effect of transient events in triggering subsequent outcomes while simultaneously eliminating control selection bias and confounding because of constant within subject characteristics.[38] In case-crossover studies, individuals serve as their own control.

This study examined patients where the outcome was LPJIs and evaluated their exposure to IDPs. We compared IDP incidence in a pre-defined 3-month case-period occurring immediately before LPJI hospital-admission, with that in the preceding 12-month control-period (months 4-15).[38-40] To establish the chronicity of events, the monthly incidence of dental procedures over the 15-months before LPJI admission to hospital was plotted. Some case-crossover studies have compared case-periods with one or more control-periods of equal duration. However, Mittleman *et al* showed 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.[41] Using a 12-month control period also controls for seasonal and other time dependent effects.[41]

Statistical methods

Case-crossover analysis[38, 41] comparing exposure to dental procedures during the 3-month case-period immediately before LPJI admissions with the incidence of dental procedures 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).[41] 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 a 1-month and 2-month case period (and 12-month control-period)

Power Calculation

To ensure we had sufficient power to detect any clinically significant association or effect, we performed a power calculation (see supplementary appendix for details). This confirmed the study had >90% power to detect an odds ratio of 1.039, i.e., a 3.9% higher likelihood of dental-procedures, in the 3-month 'case-period' compared to the matched 'control-period'.

Results

Population Characteristics

The study identified 2,344 individuals who developed LPJI between January 1st, 2010, and December 31st, 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/Medicare supplemental cover and 1,184 had Medicaid cover (Table 1). Although the sex distribution was similar between the two populations, a much higher proportion of individuals with LPJI were over the age of 65 in the commercial/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 cover. The proportions of hip, knee and other prostheses affected by LPJI were not significantly different in the two populations, although the proportion where the type of joint affected was unknown was highest in the Medicaid group.

Incidence of different dental procedures over the 15 months before LPJI admission

In the 15 months preceding LPJI admission, 4,614 dental procedures, of which 1,821 (39.5%) were IDPs were performed, 3,445 in those in patients with commercial/Medicare supplemental cover (of which 1,460 (42.4%) were IDPs) and 1,169 in those with Medicaid cover (of which 361 (30.9%) were IDPs), see Table 1. Of the IDPs, 18.3% were covered by AP (19.3% in those with commercial/Medicare cover and 14.1% in those with Medicaid cover).

The monthly incidence of IDPs, intermediate, and non-invasive dental-procedures in the 15-months before LPJI hospital-admission were plotted for the combined populations and separately for those with commercial/Medicare supplemental cover and those with Medicaid cover (Figure 1). The incidence of procedures performed with and without AP cover were also plotted.

In none of the populations studied (combined, commercial/Medicare supplemental or Medicaid) did we detect a significant increase in the incidence of IDPs during the 3-month case period immediately before LPJI admission compared to the preceding 12-month control period (months 4-15 before LPJI admission), see Table 2. This was also the case when we used a 1-month or 2-month case-period (Tables S9 and S10). When we confined analysis to IDP that had been covered by AP, there was an increase in the incidence of these procedures in the 3 months before LJPI hospital admission (Table 2, Figure 1), but the increase was not significant. The same was true when a 1- or 2-month case-period was used (Tables S9 and S10). For IDP not covered by AP, rather than an increase, there was a small decrease in procedures in the 3 months before LPJI that was significant for the combined population (but not for the commercial/Medicare supplemental or Medicaid populations separately). There was also a small but significant fall in IDP not covered by AP when a 2-month case-period was used but the fall was not significant with a 1-month case-period (Tables S9 and S10).

The site of joint-replacement (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 (Tables S4-S8).

Discussion

In the 1970-80s, the use of AP to prevent infective endocarditis in "at risk" individuals undergoing IDPs became established. This led orthopaedic surgeons in the US to call for dentists to give AP to patients with prosthetic joints.[16-18, 42] In 1988, the American Dental Association (ADA) sponsored a workshop to address this issue. Although evidence to support its use was limited, they recommended AP until further evidence became available,[43, 44] and dentists widely adopted AP.[45] In 1997[46] and 2003[47] the ADA and American Academy of Orthopaedic Surgeons (AAOS) jointly published advisory statements. These recommended AP for 2 years after joint replacement but lifelong in patients with medical conditions that might put them at increased risk for LPJIs. In 2009, however, the AAOS unilaterally declared "the AAOS recommends that clinicians consider antibiotic prophylaxis for all total joint replacement patients prior to any invasive procedure that may cause bacteremia."[48] This caused dentists and their patients confusion.[20] The AAOS and ADA subsequently made several attempts, either together or alone, to produce guidance.[49-51] These efforts, however, only increased the confusion about whether to provide AP or not.[52-54] As a result, the ADA's Council on Scientific Affairs assembled a panel of experts to conduct a systematic review in 2014.[54] This recommended: "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. Orthopaedic 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.[55]

There is little microbiologic data to support a causal association between IDPs and LPJIs and there has never been a randomized controlled trial of AP to determine its safety and effectiveness. Unlike infective endocarditis where around 45% of cases are caused by oral streptococci, estimates suggest that oral streptococci are involved in <10% of LPJI cases.[4, 19, 21, 56-61]

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 *et al.*[62] performed a retrospective case review of 62 patients with LPJI knee infections and found 7 (11%) had a temporal association with IDPs. In a related study, LaPorte *et al*.[58] associated 3/52 (6%) LPJI hip infections with IDPs. However, neither study included a control group. In contrast, a case-control study by Kaandorp *et al*,[32] found 0/37 (0%) of LPJI patients 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 *et al*,[35] found only 4 (9.5%) had undergone IDPs in the preceding 3-months, compared to 15.9% of controls. However, differences were not statistically significant in either study. In another study of 303 PJI patients 48% had undergone IDPs in the previous 2 years compared with 34% of controls.[63] A sub-analysis of patients not given AP found 33 (11%) of the PJIs had IDPs in the preceding 2 years compared with 49 (14%) of the controls. None of the differences were statistically significant and each of these studies suffered from small sample size and lack of statistical power. The case-control studies also suffered from selection bias and risk-factor confounding between cases and controls. 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 suggested that AP was unlikely to be effective in preventing LPJIs. However, because this study was performed in the UK, where AP is not recommended, it was unable to directly confirm this.

The current study had >90% power to detect any clinically significant effect and confirmed the lack of association between IDPs and subsequent LPJIs in two different US populations, those with commercial/Medicare-supplemental cover and those with Medicaid cover. Furthermore, our study demonstrated that AP cover of IDPs had no significant effect in reducing the subsequent incidence of LPJIs.

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

Limitations

The MarketScan databases encompass a large sample of US employer-provided health insurance and Medicaid enrollees, however, our study only included those with medical, dental and prescription benefits cover. It is therefore unlikely to be representative of the entire US population.

The 996.66 ICD-9 and T84.5 ICD-10 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 (within 3 months of joint replacement). CDT and ICD-9/10 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 if a particular dental-procedure 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 i.e., 30-60 minutes before the procedure.[28, 29] 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 previously validated our methodology and demonstrated 88% (95% CI 82-92%) sensitivity and 96% (95% CI 94-97%) specificity for identification of AP prescribing and distinction from antibiotic use to treat infections.[30] Although the levels of AP cover of IDP that we identified were low, they are not much lower than in individuals at high-risk of IE,[64] where there are clear guidelines recommending AP cover,[28, 29] and dentists are more motivated to provide cover.[55, 65] Several other studies have also found poor compliance by US dentists with AP prescribing guidelines.[55, 66-68]

Conclusions

This study identified no association between IDPs and subsequent LPJIs, and no effect of AP cover of IDPs in reducing the subsequent risk of LPJIs. Our data, therefore, suggests that the continued use of AP poses an unnecessary adverse drug reaction risk to patients, and to the wider community due to its potential to promote the development of antibiotic resistance. The use of AP to prevent LPJI should therefore cease. Achieving this will likely require better communication between dentists and orthopaedic surgeons and a joint effort to support evidence-based antibiotic stewardship measures.[55]

Table 1. Characteristics of the study population

Characteristics	All Patients	Commercial/Medicare Supplemental Patients	Medicaid Patients
LPJI cases	N=2,344	N=1,160	N=1,184
Age			
18-34, n (%)	199 (8.5)	54 (4.7)	145 (12.3)
35-44, n (%)	247 (10.5)	58 (5.0)	189 (16.0)
45-54, n (%)	540 (23.0)	189 (16.3)	351 (29.7)
55-64, n (%)	812 (34.6)	368 (31.7)	444 (37.5)
65+, n (%)	546 (23.3)	491 (42.3)	55 (4.7)
Sex			
Male, n (%)	1194 (50.9)	601 (51.8)	593 (50.1)
Female, n (%)	1150 (49.1)	559 (48.2)	591 (49.9)
Prosthetic joint type			
Hip, n (%)	304 (13.0)	122 (10.5)	182 (15.4)
Knee, n (%)	759 (32.4)	412 (35.5)	347 (29.3)
Other, n (%)	55 (2.3)	25 (2.2)	30 (2.5)
Multiple, n (%)	398 (17.0)	254 (21.9)	144 (12.2)
Unknown, n (%)	828 (35.3)	347 (29.9)	481 (40.6)
Dental Procedures	N=4,614	N=3,445	N=1,169
IDP, n (%)	1,821 (39.5)	1,460 (42.4)	361 (30.9)
Intermediate, n (%)	797 (17.3)	551 (16.0)	246 (21.0)
Non-IDP, n (%)	1,996 (43.3)	1,434 (41.6)	562 (48.1)
Types of IDP	N=1,821	N=1,460	N=361
Scaling, n (%)	1,403 (77.0)	1,228 (84.1)	175 (48.5)

Extractions, n (%)	338 (18.6)	162 (11.1)	176 (48.8)
Endodontics, n (%)	78 (4.3)	63 (4.3)	15 (4.2)
Oral Surgery (inc biopsy, periodontal and implant surgery)	68 (3.7)	34 (2.3)	34 (9.4)
Procedures with AP cover			
IDP with AP cover, n (%)	333 (18.3)	282 (19.3)	51 (14.1)
Scaling with AP cover, n (%)	243 (17.3)	218 (17.8)	25 (14.3)
Extractions with AP cover, n (%)	69 (20.4)	44 (27.2)	25 (14.2)
Endodontics with AP cover, n (%)	19 (24.4)	16 (25.4)	<11 (20)
Oral Surgery with AP cover, n (%)	13 (19.1)	11 (32.4)	<11 (6)

Notes: IDP= Invasive dental procedures. More than one type of IDP may be performed at the same visit – hence values may total more than 100%. Please note that where the number of subjects was <11 in any cell, numbers were censored in compliance with data confidentiality requirements.

Table 2. Case-crossover analysis comparing the incidence of different dental procedures (with and without antibiotic prophylaxis (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/Medicare Supplemental LPJI Patients			Medicaid LPJI Patients		
	Case-Period Proc/m	Control-Period Proc/m	OR (95% CI) Unadjusted†, and adjusted* p values	Case-Period Proc/m	Control-Period Proc/m	OR (95% CI) Unadjusted†, and adjusted* p values	Case-Period Proc/m	Control-Period Proc/m	OR (95% CI) Unadjusted†, and adjusted* p values
Invasive - all	110.3	124.1	0.890 (0.790-1.002) p=0.054†, p=0.486*	89.3	99.3	0.896 (0.783-1.025) p=0.110†, p=0.99*	21.0	24.8	0.868 (0.674-1.117) p=0.271†, p=1*
Invasive - no AP cover	83.7	102.9	0.814 (0.711-0.932) p=0.003†, p=0.027*	67.7	81.2	0.829 (0.711-0.966) p=0.016†, p=0.144*	16.7	22.5	0.766 (0.576-1.020) p=0.068†, p=0.612*
Invasive - AP cover	26.3	21.1	1.252 (0979-1.601) p=0.073†, p=0.657*	21.7	18.1	1.197 (0.908-1.578) p=0.203†, p=1*	4.0	2.2	1.665 (0.924-3.000) p=0.089†, p=0.801*
Intermediate - all	41.0	56.2	0.750 (0.623-0.902) p=0.002†, p=0.018*	27.7	39	0.719 (0.572-0.905) p=0.005†, p=0.045*	13.3	17.2	0.812 (0.596-1.107) p=0.188†, p=1*
Intermediate - no AP cover	31.0	43.8	0.728 (0.589-0.901) p=0.003†, p=0.027*	21.3	30.3	0.716 (0.552-0.928) p=0.012†, p=0.108*	11.3	14.9	0.798 (0.570-1.116) p=0.188†, p=1*
Intermediate - AP cover	10.0	12.3	0.829 (0.572-1.203) p=0.323†, p=1*	6.3	8.7	0.737 (0.455-1.195) p=0.216†, p=1*	2.0	2.2	0.906 (0.403-2.036) p=0.812†, p=1*
Non-Invasive - all	114.0	137.8	0.842 (0.754-0.941) p=0.002†, p=0.018*	85.0	98.2	0.876 (0.770-0.997) p=0.046†, p=0.414*	29.0	39.6	0.760 (0.612-0.943) p=0.013†, p=0.117*
Non-Invasive - no AP cover	92.3	113.7	0.829 (0.733-0.938) p=0.003†, p=0.027*	67.7	79.2	0.867 (0.750-1.002) p=0.054†, p=0.486*	25.3	36.2	0.732 (0.581-0.921) p=0.008†, p=0.072*

Non-Invasive - AP cover	21.7	24.2	0.908 (0.706-1.170) p=0.456†, p=1*	17.3	19.1	0.918 (0.691-1.220) p=0.555†, p=1*	3.7	3.4	1.063 (0.572-1.976) p=0.846†, p=1*

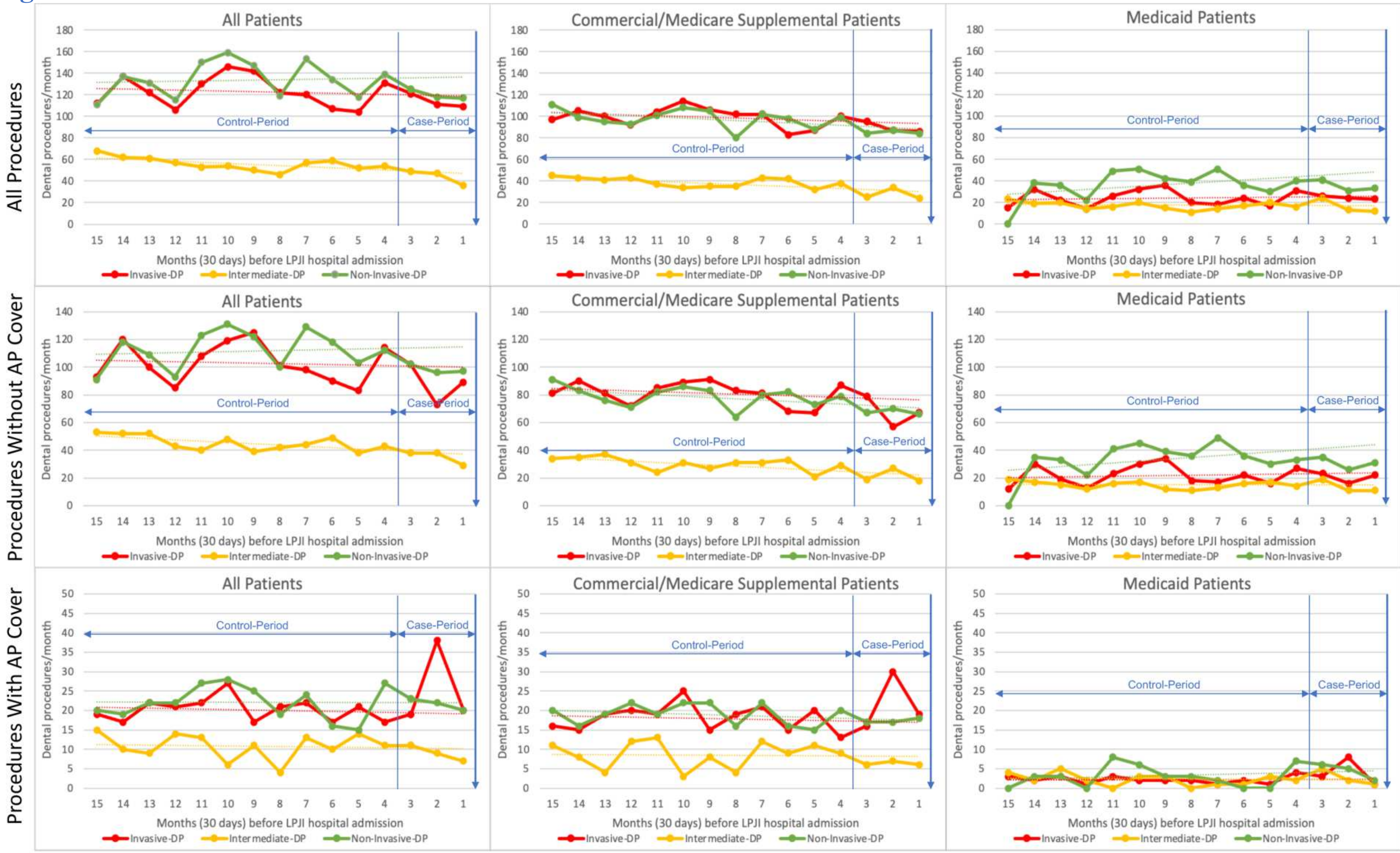
Notes: AP = antibiotic prophylaxis, LPJI = late prosthetic joint infection, OR = odds ratio, Proc/m = procedures per month. †Unadjusted p value, *adjusted p value using Bonferroni's correction for multiple comparisons.

Figure Legends

Figure 1. Incidence of invasive-, intermediate-, and non-invasive-dental procedures over the 15 months before late prosthetic joint infection (LPJI) hospital admission

Top row – plots for all dental procedures, Middle row - plots for dental procedures not covered by antibiotic prophylaxis (AP). Bottom row – plots for dental procedures covered by AP. Late prosthetic joint infection (LPJI) admission is denoted by the vertical blue arrow. The incidence of invasive- (red), intermediate- (yellow) and non-invasive- (green) dental procedures (DP) are plotted over 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 dental procedure type.

Figure 1


All Procedures
Procedures Without AP Cover
Procedures With AP Cover
All Patients
Commercial/Medicare Supplemental Patients
Medicaid Patients
Dental procedures/month
Control-Period
Case-Period
Months (30 days) before LPJI hospital admission
Invasive-DP
Intermediate-DP
Non-Invasive-DP

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