SUPPLEMENTAL MATERIAL

Supplementary-Appendix:

Endocarditis, Invasive Dental Procedures and Antibiotic Prophylaxis Efficacy in Medicaid Patients

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Abbreviations:

ADA = American Dental Association
AHA = American Heart Association
AP = Antibiotic prophylaxis
CCI = Charlson comorbidity index
CPT = Current procedural terminology
CDT = Common dental terminology
ESC = European Society of Cardiology
HIPAA = Health Insurance Portability and Accountability Act
ICD = International Classification of Disease
IDPs = Invasive dental procedures
IE = Infective endocarditis
IDU = Injection drug use
IRB = Institutional review board
NNP = Number needed to prevent
Non-IDPs = Non-invasive dental procedures
OR = Odds ratio
STROBE = Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines for cohort studies
USA = United States of America

Supplementary-Methods:

Data Source:

The IBM® MarketScan® databases integrate de-identified patient-level health-data across a series of healthcare related databases. We studied the Multi-State Medicaid (basic health cover provided in some states for those without medical insurance) database and, for comparison, linked data from the employer-funded Commercial (private health insurance cover provided mainly by employers as a benefit for their employees), Medicare-Supplemental (top up health insurance cover provided by employers for their retirees to improve the basic cover provided by Medicare), prescription benefits and Dental (insurance cover for private dental care) databases. Because the MarketScan® data are deidentified in compliance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA), and meet limited-use dataset criteria, studies using the data are exempt IRB review.(US Department for Health and Human Services, 1996) All enrollees over 18, with more than 16 months of linked medical, dental and prescribing data from January 2000 through August 2015 were included.

We only included data until August 2015, because in October 2015 the US transitioned from using ICD-9 to ICD-10 diagnosis and procedure codes. This change caused major disruption to the recording of diagnoses and procedures because ICD-10 codes don't always translate directly into corresponding ICD-9 codes. Indeed, numerous studies using US coding data that spanned the changeover period have reported significant disruption to the recording of the incidence or prevalence of specific diagnoses. Hence, to avoid this disruption and to ensure data integrity and continuity we confined our study to the period before October 2015. Changes to the recording of CPT (medical procedure codes) and CDT (dental procedure codes) after October 2015 caused further disruption that could have affected the data used in this study.

IE admissions and IE-risk stratification:

ICD-9 or CPT diagnosis/procedure codes were used to identify individuals as being at high-IE-risk (Tables S1 and S3) or moderate-IE-risk (Tables S1 and S4) as defined by the AHA guidelines.(Dajani et al., 1997; W. Wilson et al., 2007; W. R. Wilson et al., 2021) Individuals not so identified were considered at low/unknown-IE-risk.

IE-hospital-admissions were identified using ICD-9 421.0, 421.1 or 421.9, primary or secondary discharge diagnosis codes. Previously described methods were used to ensure single continuous IE-episodes were only counted once.(M. H. Thornhill et al., 2011) After IE-admission, enrollees were considered at high-risk for future IE episodes. New episodes were distinguished from readmissions by only accepting IE-admissions >6 months apart.(Chu et al., 2005; M. H. Thornhill et al., 2018)

Invasive Dental-Procedures:

The American Dental Association (ADA) Code on Dental Procedures and Nomenclature (CDT codes)(American Dental Association (ADA), 2019) and ICD-9 procedure codes(Centers for Disease Control and Prevention (CDC), 2019) were used to classify 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 AHA guidelines recommend 'should' be covered by AP,(W. Wilson et al., 2007; W. R. Wilson et al., 2021) (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 S2 and S5).(W. Wilson et al., 2007; W. R. Wilson et al., 2021) When a dental visit included multiple-procedures, the most invasive was ascribed to that visit. We also sub-analysed IDPs using codes specific for dental scaling, extractions, endodontic and surgical-procedures (periodontal and oral surgical) (Table S5).

Prescription benefits data were used to identify whether each dental procedure was likely to have been AP-covered or not using methodology previously described(M.H. Thornhill et al., 2020) and briefly outlined here. For each patient in the cohort, that patient's prescription benefits data was searched for antibiotic prophylaxis (AP) prescriptions matching the 2007 AHA recommendations.(W. Wilson et al., 2007) These were identified in the database using the following prescribing criteria (a) mode of antibiotic delivery – oral, (b) antibiotic – amoxicillin, clindamycin, cephalexin, azithromycin or clarithromycin, (c) dosage - 2g for amoxicillin, 600 mg for clindamycin, 2g for cephalexin, 500mg for azithromycin or 500mg for clarithromycin. Our earlier study identified that dentists often prescribed multiple courses of AP cover as a single prescription, in order to ensure that patients had sufficient supplies to cover several invasive dental procedure visits i.e. to avoid the patient having to fill a separate prescription for each invasive dental procedure visit. 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 gold standard of the actual prescribing and dental records of 80 patients at high IE-risk, 40 moderate-risk and 40 low-unknown risk patients. The algorithm that best identified when an invasive dental procedure was likely to have been covered by AP included the 3 elements above (a-c) where the number of day's supply of the antibiotic was ≤5 and the time between the prescription fill date and the invasive dental procedure date was ≤73 where the number of day's supply = 1, ≤146 where day's supply = 2, ≤219 where day's supply = 3, ≤292 where day's supply = 4 or ≤365 where day's supply = 5. Using this algorithm had 88% (95% CI 82-92%) sensitivity and 96% (95% CI 94-97%) specificity for identifying when a dental procedure was likely to have been covered by AP[29] and this was the algorithm employed in the current study to determine if a dental procedure was likely to have been covered by AP or not.(M.H. Thornhill et al., 2020)

Cohort Study:

We studied the entire 1,678,190 Medicaid cohort of individuals, >18, with linked medical/dental/prescription data. For demographic comparison we also examined 7.9 million individuals with employer provided Commercial/Medicare-Supplemental health cover and linked dental and prescription benefits data. All individuals were stratified by IE-risk and followed until study end, death or the end of linked data cover. Individuals could move from a lower- to higher-risk stratification depending on the occurrence of risk-related diagnoses or procedures.

We quantified IE-incidence in the 30-day exposure period following dental-procedures, and repeated the analysis using a 4-month exposure period. Crude incidence rates were adjusted for differences between cases and controls for age, sex or Charlson comorbidity index (CCI).(Charlson, Pompei, Ales, & MacKenzie, 1987) To model the IE-outcome we used Firth correction penalized logistic regression because the outcome of interest is rare.(Doerken, Avalos, Lagarde, & Schumacher, 2019) Firth logistic regression - a penalized-likelihood statistical method. This method was introduced to address the possibility of rare outcomes causing small sample size bias (particularly in some sub-analyses) when using traditional maximum likelihood logistic regression that can lead to the non-convergence of regression estimates.(Doerken et al., 2019; Firth, 1991) The odds of IE following an IDP or intermediate-dental

procedure, or a sub-type of IDP i.e. dental extraction, oral surgical procedure, scaling or endodontic procedure was estimated by comparing the IE-incidence with the IE-incidence following a non-IDP (the control group for this purpose) to test the null hypothesis that there is no increase in the incidence of IE in the 30-days (or 4-months) following an invasive dental procedure (the dental procedures model). We also compared IE-incidence following dental-procedures with or without AP cover to test the null hypothesis that AP does not reduce the incidence of IE in the 30-days (or 4-months) following a dental procedure (the antibiotic prophylaxis model). For both models we set a $p<0.05$ criterion for determining significance but we first applied a Bonferroni correction to the p values to account for situations where multiple comparisons were performed. We also calculated the number of procedures that needed to be covered by AP to prevent one case of IE, i.e. the number needed to prevent (NNP).

Case-Crossover Study

The case-crossover design was first proposed by Maclure for studying the effect of transient events in triggering subsequent outcomes while eliminating control selection bias and confounding by constant within subject characteristics, each individual acting as their own control.(Maclure, 1991) We identified all IE-hospital-admissions and quantified monthly exposure to different dental-procedures in the 16-months prior to IE-hospital-admission. This data was plotted (Figures 1 and S1) to identify the timing of any association between IDPs and IE-admission. These revealed a higher incidence of IDPs in the month before IE-admission than at any other time. We therefore performed a case-crossover analysis(Maclure, 1991; Mittleman, Maclure, & Robins, 1995) comparing the 1-month (30 day) exposure or case period immediately before IE-hospital-admission with the 12-month (months 2-13) control period before that, using conditional logistic regression with fixed effects for patient ID (to control for time invariant patient characteristics over the duration of the study). Mittleman *et al* have shown that sampling the control frequency over a full-year prior to the case period is twice as efficient as sampling control periods of equal duration to the case period, even when many such control periods are sampled and the 12-month control period reduces any periodic time-dependent effects in the control period.(Mittleman et al., 1995) Because other case-crossover studies examining the association between IDPs and IE have used a longer case period, usually 3-4 months,(Chen et al., 2015; Porat Ben-Amy, Littner, & Siegman-Igra, 2009) we repeated the analysis using a 4-month case period and 12-month control period (months 5-16). Bonferroni correction was also applied to p values where multiple comparisons were made.

Table S1. Cardiac conditions used to classify individuals as being at high or moderate IE-risk

High IE-Risk
Previous history of Infective endocarditis
Presence of prosthetic cardiac valve (including transcatheter valves)
Prosthetic material used for valve repair (including annuloplasty and percutaneous valve procedures using prosthetic material)
Unrepaired cyanotic congenital heart disease
Congenital heart disease in which palliative shunts or conduits were used
Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by transcatheter during the first 6 months after the procedure only.
Moderate IE-Risk
Rheumatic heart disease
Non-rheumatic valve disease (including mitral valve prolapse)
Congenital valve anomalies (including aortic stenosis)
Hypertrophic cardiomyopathy

Notes: Adapted from the American Heart Association guidelines.(Dajani et al., 1997; W. Wilson et al., 2007; W. R. Wilson et al., 2021) More extensive details of all diagnoses and procedures (including the relevant ICD-9-CM diagnosis and procedure codes and CPT procedure codes) included in the definition of those at high or moderate IE-risk are provided in Supplemental Tables S3 and S4.

Table S2. Examples of invasive-dental procedures (IDPs), intermediate-dental procedures and non-invasive dental procedures (non-IDPs)

Invasive-Dental Procedures (IDPs) – procedures that should be covered by AP
Dental extractions (including surgical removal of impacted teeth and residual tooth roots)
Oral surgery procedures (including biopsies, periodontal surgery, implant surgery and other oral surgery and maxillofacial procedures involving oral soft tissues or bone)
Scaling procedures (including dental prophylaxis, periodontal scaling and root planning, periodontal maintenance and gingival irrigation or delivery of antimicrobial agents into the diseased gingival crevice)
Endodontic treatment (including pulpal debridement, endodontic treatment and re-treatment, apexification/recalcification, apicectomy and peri-radicular procedures)
Intermediate-Dental Procedures – procedures that may or may not require AP cover
Restorative dental procedures (fillings, inlays, crowns and bridges) and oral examination procedures that may on occasion involve gingival manipulation (when AP cover should be provided), but on other occasions do not involve gingival manipulation (when AP should not be provided).
Non-Invasive-Dental Procedures (non-IDPs)
Oral examinations not involving manipulation of the gingival or apical tissues
Dental radiographs
Placement of removable prosthodontic or orthodontic appliances
Adjustment of orthodontic appliances and placement of orthodontic brackets

Notes: Based on American Heart Association guidelines.(W. Wilson et al., 2007; W. R. Wilson et al., 2021) More extensive details of the dental procedures (including the relevant American Dental Association CDT and ICD-9 procedure codes) used to define invasive-dental procedures (IDPs), intermediate-dental procedures and non-IDPs, and each category of IDP (extractions, oral surgical procedures, scaling and endodontic treatments) are provided in Supplemental Table S5.

Table S3. ICD-9-CM Diagnosis and Procedure Codes, and CPT Outpatient Procedure codes used to identify 'high risk' cardiac conditions

Cardiac Condition	ICD-9-CM Codes (and CPT outpatient procedure codes)
Previous IE	**ICD-9 Diagnostic Code:** 4210 acute and subacute bacterial endocarditis 4211 acute and subacute infective endocarditis (in diseases classified elsewhere) 4219 acute endocarditis, unspecified
Prosthetic cardiac valve	**ICD-9 Procedure Codes:** 3505 endovascular replacement of aortic valve 3506 transapical replacement of aortic valve 3507 endovascular replacement of pulmonary valve 3508 transapical replacement of pulmonary valve 3509 endovascular replacement of unspecified heart valve 3520 open and other replacement of unspecified heart valve 3521 open and other replacement of aortic valve with tissue graft 3522 open and other replacement of aortic valve 3523 open and other replacement of mitral valve with tissue graft 3524 open and other replacement of mitral valve 3525 open and other replacement of pulmonary valve with tissue graft 3526 open and other replacement of pulmonary valve 3527 open and other replacement of tricuspid valve with tissue graft 3528 open and other replacement of tricuspid valve 3583 total repair of truncus arteriosus **CPT Procedure Codes:** 0256T Implantation of catheter-delivered prosthetic aortic heart valve; endovascular approach 0257T Implantation of catheter-delivered prosthetic aortic heart valve; open thoracic approach (eg, transapical, transventricular) 0258T Transthoracic cardiac exposure (eg, sternotomy, thoracotomy, subxiphoid) for catheter-delivered aortic valve replacement; without cardiopulmonary bypass 0268T Implantation of catheter-delivered prosthetic pulmonary valve, endovascular approach 0318T Implantation of catheter-delivered prosthetic aortic heart valve, open thoracic approach, (eg, transapical, other than transaortic) 33361 Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; percutaneous femoral artery approach 33362 Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; open femoral artery approach 33363 Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; open axillary artery approach 33364 Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; open iliac artery approach 33365 Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; transaortic approach (eg, median sternotomy, mediastinotomy) 33366 Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; transapical exposure (eg, left thoracotomy) 33405 Replacement, aortic valve, with cardiopulmonary bypass; with prosthetic valve other than homograft or stentless valve 33406 Replacement, aortic valve, with cardiopulmonary bypass; with allograft valve (freehand) 33410 Replacement, aortic valve, with cardiopulmonary bypass; with stentless tissue valve 33411 Replacement, aortic valve; with aortic annulus enlargement, noncoronary sinus 33412 Replacement, aortic valve; with transventricular aortic annulus enlargement (Konno procedure) 33413 Replacement, aortic valve; by translocation of autologous pulmonary valve with allograft replacement of pulmonary valve (Ross procedure) 33430 Replacement, mitral valve, with cardiopulmonary bypass 33465 Replacement, tricuspid valve, with cardiopulmonary bypass 33475 Replacement, pulmonary valve 33477 Transcatheter pulmonary valve implantation, percutaneous approach, including pre-stenting of the valve delivery site, when performed 33496 Repair of non-structural prosthetic valve dysfunction with cardiopulmonary bypass (separate procedure) **ICD-9 Diagnostic Codes:** 99602 mechanical complication due to heart valve prosthesis 99671 other complications due to heart valve prosthesis V433 heart valve replaced by other means

Prosthetic material used for valve repair	**ICD-9 Procedure Codes:** 3533 annuloplasty 3597 percutaneous mitral valve repair with implant **CPT Procedure Codes:** 0343T Transcatheter mitral valve repair percutaneous approach including transseptal puncture when performed; initial prosthesis 0344T Transcatheter mitral valve repair percutaneous approach including transseptal puncture when performed; additional prosthesis (es) during same session (List separately in addition to code for primary procedure) 33391 Valvuloplasty, aortic valve, open, with cardiopulmonary bypass; complex (eg, leaflet extension, leaflet resection, leaflet reconstruction, or annuloplasty) 33418 Transcatheter mitral valve repair, percutaneous approach, including transseptal puncture when performed; initial prosthesis 33419 Transcatheter mitral valve repair, percutaneous approach, including transseptal puncture when performed; additional prosthesis(es) during same session (List separately in addition to code for primary procedure) 33426 Valvuloplasty, mitral valve, with cardiopulmonary bypass; with prosthetic ring 33427 Valvuloplasty, mitral valve, with cardiopulmonary bypass; radical reconstruction, with or without ring 33464 Valvuloplasty, tricuspid valve; with ring insertion 33468 Tricuspid valve repositioning and plication for Ebstein anomaly 33478 Outflow tract augmentation (gusset), with or without commissurotomy or infundibular resection 33600 Closure of atrioventricular valve (mitral or tricuspid) by suture or patch 33602 Closure of semilunar valve (aortic or pulmonary) by suture or patch 33612 Repair of double outlet right ventricle with intraventricular tunnel repair; with repair of right ventricular outflow tract obstruction 33860 Ascending aorta graft, with cardiopulmonary bypass, includes valve suspension, when performed 33861 Ascending aorta graft, with cardiopulmonary bypass, with or without valve suspension; with coronary reconstruction 33863 Ascending aorta graft, with cardiopulmonary bypass, with aortic root replacement using valved conduit and coronary reconstruction (eg, Bentall) 33864 Ascending aorta graft, with cardiopulmonary bypass with valve suspension, with coronary reconstruction and valve-sparing aortic root remodeling (eg, David Procedure, Yacoub Procedure)
Unrepaired cyanotic congenital heart disease (CHD)	**ICD-9 Diagnostic Codes:** 7450 common truncus 74510 complete transposition of great vessels 74511 double outlet right ventricle 74519 other transposition of great vessels 7452 tetralogy of Fallot 7453 common ventricle 74560 endocardial cushion defects 7457 cor biloculare 74741 total anomalous pulmonary venous connection
CHC in whom a palliative shunt or conduit has been used	**ICD-9 Procedure Codes:** 3541 enlargement of existing arterial septal defect 3542 creation of septal defect in heart 3591 interatrial transposition of venous return 3592 creation of conduit between right ventricle and pulmonary artery 3593 creation of conduit between left ventricle and aorta 3594 creation of conduit between atrium and pulmonary artery 390 systemic to pulmonary shunt 3921 caval-pulmonary artery anastomosis **CPT Procedure Codes:** 33404 Construction of apical-aortic conduit 33606 Anastomosis of pulmonary artery to aorta (Damus-Kaye-Stansel procedure) 33608 Repair of complex cardiac anomaly other than pulmonary atresia with ventricular septal defect by construction or replacement of conduit from right or left ventricle to pulmonary artery 33610 Repair of complex cardiac anomalies (eg, single ventricle with subaortic obstruction) by surgical enlargement of ventricular septal defect 33611 Repair of double outlet right ventricle with intraventricular tunnel repair; 33612 Repair of double outlet right ventricle with intraventricular tunnel repair; with repair of right ventricular outflow tract obstruction

	33615 Repair of complex cardiac anomalies (eg, tricuspid atresia) by closure of atrial septal defect and anastomosis of atria or vena cava to pulmonary artery (simple Fontan procedure) 33617 Repair of complex cardiac anomalies (eg, single ventricle) by modified Fontan procedure 33619 Repair of single ventricle with aortic outflow obstruction and aortic arch hypoplasia (hypoplastic left heart syndrome) (eg, Norwood procedure) 33697 Complete repair tetralogy of Fallot with pulmonary atresia including construction of conduit from right ventricle to pulmonary artery and closure of ventricular septal defect 33735 Atrial septectomy or septostomy; closed heart (Blalock-Hanlon type operation) 33736 Atrial septectomy or septostomy; open heart with cardiopulmonary bypass 33737 Atrial septectomy or septostomy; open heart, with inflow occlusion 33750 Shunt; subclavian to pulmonary artery (Blalock-Taussig type operation) 33755 Shunt; ascending aorta to pulmonary artery (Waterston type operation) 33762 Shunt; descending aorta to pulmonary artery (Potts-Smith type operation) 33764 Shunt; central, with prosthetic graft 33766 Shunt; superior vena cava to pulmonary artery for flow to 1 lung (classical Glenn procedure) 33767 Shunt; superior vena cava to pulmonary artery for flow to both lungs (bidirectional Glenn procedure) 33768 Anastomosis, cavopulmonary, second superior vena cava (List separately in addition to primary procedure) 33774 Repair of transposition of the great arteries, atrial baffle procedure (eg, Mustard or Senning type) with cardiopulmonary bypass; 33775 Repair of transposition of the great arteries, atrial baffle procedure (eg, Mustard or Senning type) with cardiopulmonary bypass; with removal of pulmonary band 33776 Repair of transposition of the great arteries, atrial baffle procedure (eg, Mustard or Senning type) with cardiopulmonary bypass; with closure of ventricular septal defect 33777 Repair of transposition of the great arteries, atrial baffle procedure (eg, Mustard or Senning type) with cardiopulmonary bypass; with repair of subpulmonic obstruction 33782 Aortic root translocation with ventricular septal defect and pulmonary stenosis repair (ie, Nikaidoh procedure); without coronary ostium reimplantation 33783 Aortic root translocation with ventricular septal defect and pulmonary stenosis repair (ie, Nikaidoh procedure); with reimplantation of 1 or both coronary ostia 33786 Total repair, truncus arteriosus (Rastelli type operation) 33918 Repair of pulmonary atresia with ventricular septal defect, by unifocalization of pulmonary arteries; without cardiopulmonary bypass 33920 Repair of pulmonary atresia with ventricular septal defect, by construction or replacement of conduit from right or left ventricle to pulmonary artery 92992 Atrial septectomy or septostomy; transvenous method, balloon (eg, Rashkind type) (includes cardiac catheterization) 92993 Atrial septectomy or septostomy; blade method (Park septostomy) (includes cardiac catheterization)
Completely repaired CHD defect with prosthetic material or device, whether placed by surgery or catheter intervention, **during first 6 months after the procedure only.**	**ICD-9 Procedure Codes:** 3550 repair of unspecified septal defect of heart with prosthesis 3551 repair of atrial septal defect with prosthesis, open technique 3552 repair of atrial septal defect with prosthesis, closed technique 3553 repair of ventricular septal defect with prosthesis, open technique 3554 repair of endocardial cushion defect with prosthesis 3555 repair of ventricular septal defect with prosthesis, closed technique 3560 repair of unspecified septal defect of heart with tissue graft 3561 repair of atrial septal defect with tissue graft 3562 repair of ventricular septal defect with tissue graft 3563 repair of endocardial cushion defect with tissue graft 3570 other and unspecified repair of unspecified septal defect of heart 3571 other and unspecified repair of atria septal defect 3572 other and unspecified repair of ventricular septal defect 3573 other and unspecified repair of endocardial cushion defect 3581 total repair of tetralogy of Fallot 3582 total repair of total anomalous pulmonary venous connection 3584 total correction of transposition of great vessels 3598 other operations on septa of heart **CPT Procedure Codes** 0166T Transmyocardial transcatheter closure of ventricular septal defect, with implant; without cardiopulmonary bypass 0167T Transmyocardial transcatheter closure of ventricular septal defect, with implant; with cardiopulmonary bypass 33545 Repair of postinfarction ventricular septal defect, with or without myocardial resection 33641 Repair atrial septal defect, secundum, with cardiopulmonary bypass, with or without patch 33645 Direct or patch closure, sinus venosus, with or without anomalous pulmonary venous drainage

	33647 Repair of atrial septal defect and ventricular septal defect, with direct or patch closure 33660 Repair of incomplete or partial atrioventricular canal (ostium primum atrial septal defect), with or without atrioventricular valve repair 33665 Repair of intermediate or transitional atrioventricular canal, with or without atrioventricular valve repair 33670 Repair of complete atrioventricular canal, with or without prosthetic valve 33675 Closure of multiple ventricular septal defects; 33676 Closure of multiple ventricular septal defects; with pulmonary valvotomy or infundibular resection (acyanotic) 33677 Closure of multiple ventricular septal defects; with removal of pulmonary artery band, with or without gusset 33681 Closure of single ventricular septal defect, with or without patch; 33684 Closure of single ventricular septal defect, with or without patch; with pulmonary valvotomy or infundibular resection (acyanotic) 33688 Closure of single ventricular septal defect, with or without patch; with removal of pulmonary artery band, with or without gusset 33692 Complete repair tetralogy of Fallot without pulmonary atresia; 33694 Complete repair tetralogy of Fallot without pulmonary atresia; with transannular patch 33710 Repair sinus of Valsalva fistula, with cardiopulmonary bypass; with repair of ventricular septal defect 33770 Repair of transposition of the great arteries with ventricular septal defect and subpulmonary stenosis; without surgical enlargement of ventricular septal defect 33771 Repair of transposition of the great arteries with ventricular septal defect and subpulmonary stenosis; with surgical enlargement of ventricular septal defect 33778 Repair of transposition of the great arteries, aortic pulmonary artery reconstruction (eg, Jatene type); 33779 Repair of transposition of the great arteries, aortic pulmonary artery reconstruction (eg, Jatene type); with removal of pulmonary band 33780 Repair of transposition of the great arteries, aortic pulmonary artery reconstruction (eg, Jatene type); with closure of ventricular septal defect 33781 Repair of transposition of the great arteries, aortic pulmonary artery reconstruction (eg, Jatene type); with repair of subpulmonic obstruction 93580 Percutaneous transcatheter closure of congenital interatrial communication (ie, Fontan fenestration, atrial septal defect) with implant 93581 Percutaneous transcatheter closure of a congenital ventricular septal defect with implant

Notes:

1. Patients at “high-risk” of developing IE were identified by determining whether they had been diagnosed with a “high-risk” condition (ICD-9 codes) or undergone a “high risk” procedure (ICD-9 or CPT procedure codes) at any time before they first developed IE or at any-time for those who did not develop IE during the study period (within the available healthcare records for that individual).
2. Since the AHA guidelines consider patients with congenital heart disease repaired with prosthetic material to be high risk only for the first 6 months after the procedure, they were treated as high-risk for the first 6 months after the procedure only.

Table S4. ICD-9-CM Diagnosis and Procedure Codes, and CPT Outpatient Procedure codes used to identify 'moderate risk' cardiac conditions

Cardiac Condition	ICD-9-CM Codes
Previous Rheumatic Fever	**ICD-9 Diagnostic Codes:** 390 rheumatic fever without heart involvement 3910 acute rheumatic pericarditis 3911 acute rheumatic endocarditis 3912 acute rheumatic myocarditis 3918 other acute rheumatic heart disease 3919 acute rheumatic heart disease, unspecified 3920 rheumatic chorea with heart involvement 3929 rheumatic chorea without heart involvement 3941 rheumatic mitral insufficiency 3940 mitral stenosis 3942 mitral stenosis with insufficiency 3949 other unspecified mitral disease 3950 rheumatic aortic stenosis 3951 rheumatic aortic insufficiency 3952 rheumatic aortic stenosis with insufficiency 3959 other and unspecified aortic rheumatic diseases 3960 mitral and aortic stenosis 3961 mitral stenosis and aortic insufficiency 3962 mitral insufficiency and aortic stenosis 3963 mitral insufficiency and aortic insufficiency 3968 multiple involvement of mitral and aortic valves 3969 mitral and aortic valve disease unspecified 3970 diseases of tricuspid valve 3971 rheumatic diseases of pulmonary valve 3979 rheumatic diseases of endocardium, valve unspecified 39890 rheumatic heart disease, unspecified 39899 other rheumatic heart diseases
Non-Rheumatic Valve Disease	**ICD-9 Diagnostic codes:** 4240 mitral valve disorders 4241 aortic valve disorders 4242 tricuspid valve disorders specified as non-rheumatic 4243 pulmonary valve disorders
Hypertrophic cardiomyopathy	**ICD-9 Diagnostic Codes:** 42511 hypertrophic obstructive cardiomyopathy 42518 other hypertrophic cardiomyopathy
Congenital valve anomalies	**ICD-9 Diagnostic codes:** 74600 congenital pulmonary valve anomaly, unspecified 74601 atresia of pulmonary valve, congenital 74602 stenosis of pulmonary valve, congenital 74609 other congenital anomalies of pulmonary valve 7461 tricuspid atresia and stenosis, congenital 7462 Ebstein's anomaly 7463 congenital stenosis of aortic valve 7464 congenital insufficiency of aortic valve 7465 congenital mitral stenosis 7466 congenital mitral insufficiency 7467 hyperplastic left heart syndrome 74681 sub-aortic stenosis 74683 infundibular pulmonic stenosis 74689 other specified congenital heart anomalies of heart

Notes: Patients at "moderate risk" of developing IE were identified by determining whether they had been diagnosed with a "moderate risk" condition (ICD-9 codes) at any time before they first developed IE or at any-time for those who did not develop IE during the study period (within the available healthcare records for that individual).

Table S5. CDT and ICD-9 IDP, intermediate-dental procedure and non-IDP Codes, and Codes for Specific Types of IDP

Analyses	CDT Codes	ICD-9 Codes
All Invasive Dental Procedure (IDP) Codes i.e. those procedures that 'should' be covered by AP according to the 2007 AHA recommendations	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
All Intermediate Dental Procedure Codes i.e. those procedures that 'may' be covered by AP according to the 2007 AHA recommendations	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
Non-IDP codes i.e. 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.
Codes For Specific Types of IDP		
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 surgical procedures, periodontal surgery 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,

Table S6. Cohort Study, Dental Procedures Model - Crude IE Incidence Within 1-Month (30 days) of a Dental Procedure.

IE Risk	High IE-Risk Individuals				Moderate IE-Risk Individuals				Low/Unknown IE-Risk Individuals			
Type of Dental Procedure	Procedures (n)	IE (n)	Crude IE/million proc	OR (95%CI)	Procedures (n)	IE (n)	Crude IE/million proc	OR (95%CI)	Procedures (n)	IE (n)	Crude IE/million proc	OR (95%CI)
All	26,877	49	1,823.1		266,711	28	105.0		4,962,603	59	11.9	
Control; non-invasive dental proc. (non-IDPs)	8,823	4	453.4	1	89,439	10	111.8	1	1,390,003	12	8.6	1
Intermediate-dental proc.	4,632	2	431.8	0.952 (0.174-5.208)	41,847	1	23.9	0.214 (0.027-1.669)	987,956	11	11.1	1.290 (0.569-2.924)
Invasive-dental proc. (IDPs)	13,422	43	3,203.7	7.092 (2.545-19.608) p=0.005	135,425	17	125.5	1.122 (0.514-2.451)	2,584,644	36	13.9	1.613 (0.840-3.106)
Types of IDP												
- Scaling	7,026	1	142.3	0.314 (0.035-2.809),	59,094	3	50.8	0.454 (0.125-1.650)	1,486,315	10	6.7	0.779 (0.337-1.805)
- Extractions	6,029	39	6,468.7	14.286 (5.128-40.000), p<0.0001	72,861	14	192.1	1.718 (0.763-3.876)	1,012,541	22	21.7	2.519 (1.245-5.076), p=0.03
- Endodontic	403	0			3,548	0			110,916	0		
- Surgical	745	13	17,449.7	38.462 (12.658-125.000), p<0.0001	6,922	4	577.9	5.181 (1.621-16.393), p=0.01	91,936	9	97.9	11.364 (4.785-27.027), p=0.02

Notes: Crude data without adjustment for differences in the age, sex and Charlson Comorbidity Index (CCI) score between cases and controls. Surgical Procedures includes both oral surgery and periodontal surgery procedures. IDP = invasive-dental procedures, IE = infective endocarditis, Non-IDPs = non-invasive dental procedures, OR = odds ratio Proc = procedure. OR significantly higher than control non-invasive dental procedure (non-IDPs) value. Bonferroni corrected p values shown where p<0.05 (other p values not significant).

Table S7. Cohort Study, Antibiotic Prophylaxis Model - Crude IE Incidence Within 1-Month (30 days) of Dental Procedures Covered or Not Covered by Antibiotic Prophylaxis.

Medicaid Patients							
IE Risk	AP / No AP	High IE-Risk Individuals		Moderate IE-Risk Individuals		Low/Unknown IE-Risk Individuals	
Type of Dental Procedure		Crude IE/million proc	OR (95%CI), p NNP	Crude IE/million proc	OR (95%CI), p	Crude IE/million proc	OR (95%CI), p
Non-IDPs	AP	601.7	1.513 (0.137-16.696)	249.9	2.097 (0.445-9.873)		
	No AP	397.8		119.3			
Intermediate-dental proc.	AP	0	<0.001 (<0.001->999.999)			86.3	11.014 (2.848-42.593)
	No AP	806.8				7.8	
IDPs	AP	864.6	0.178 (0.055-0.581), p<0.05	140.6	1.017 (0.231-4.476)	20.5	1.441 (0.346-6.005)
	No AP	4,830.2		138.3		14.2	
Types of IDP							
Scaling	AP			0	<0.001 (<0.001->999.999)	22.2	3.327 (0.422-26.255)
	No AP			45.1		6.7	
Extractions	AP	2,290.1	0.248 (0.076-0.810), p<0.05	262.5	1.300 (0.288-5.863)	20.8	0.931 (0.125-6.938)
	No AP	9,179.6		202.1		22.3	
Endodontic	AP						
	No AP						
Surgical	AP	5,618.0	0.284 (0.036-2.261), p<0.05	1,319.3	2.346 (0.244-22.579)	185.4	1.887 (0.236-15.084)
	No AP	19,480.5		562.9		98.3	

Notes: Surgical Procedures includes both oral surgery and periodontal surgery procedures. AP = antibiotic prophylaxis, IDPs = invasive dental procedures, IE = infective endocarditis, Non-IDPs = non-invasive dental procedures, Proc. = procedure, OR = odds ratio. AP significantly reduced IE incidence compared to no AP, Bonferroni corrected p values shown where p<0.05 (other p values not significant).

Table S8. Cohort Study, Dental Procedures Model - Adjusted IE Incidence Within 4-Months of a Dental Procedure.

Medicaid Patients												
IE Risk	**High IE-Risk Individuals**				**Moderate IE-Risk Individuals**				**Low/Unknown IE-Risk Individuals**			
Type of Dental Procedure	Procedures (n)	IE (n)	Adjusted IE/million proc	OR (95%CI)	Procedures (n)	IE (n)	Adjusted IE/million proc	OR (95%CI)	Procedures (n)	IE (n)	Adjusted IE/million proc	OR (95%CI)
All	26,877	113	5,188.0		266,711	125	586.7		4,962,603	216	58.7	
Control; non-IDPs	8,823	34	3,966.3	1	89,439	51	583.4	1	1,390,003	79	57.6	1
Intermediate-dental proc.	4,632	18	4,050.3	1.079 (0.599-1.881)	41,847	21	520.4	0.923 (0.545-1.510)	987,956	54	55.5	1.141 (0.802-1.612)
IDPs	13,422	84	6,383.8	1.707 (1.154-2.579), p<0.05	135,425	81	609.4	1.062 (0.751-1.516)	2,584,644	155	60.6	1.192 (0.911-1.572)
Types of IDP												
- Scaling	7,026	20	3,019.5	0.893 (0.499-1.561)	59,094	17	304	0.586 (0.327-1.001)	1,494,978	37	26	0.571 (0.380-0.845)
- Extractions	6,029	60	10,234.3	2.563 (1.695-3.940), p<0.0005	72,861	61	858	1.405 (0.970-2.041)	1,012,541	110	110	1.847 (1.386-2.471), p=0.04
- Endodontic	403	1	3,926.7	1.010 (0.113-3.829)	3,548	2	727	1.336 (0.274-3.965)	110,916	4	41	0.971 (0.318-2.264)
- Surgical	745	18	25,668.6	6.182 (3.416-10.839), p<0.0001	6,922	10	1,566	2.311 (1.117-4.344)	91,936	27	305	3.966 (2.512-6.079), p=0.006

Notes: Adjusted data corrected for differences in the age, sex and Charlson Comorbidity Index (CCI) score between cases and controls. Surgical procedures includes both oral surgery and periodontal surgery procedures. IDPs = invasive-dental procedures, IE = infective endocarditis, Non-IDPs = non-invasive dental procedures, Proc = procedure, OR = odds ratio. OR significantly higher than control non-invasive dental procedures (non-IDPs) value, Bonferroni corrected p values shown where p<0.05 (other p values not significant).

Table S9. Cohort Study, Antibiotic Prophylaxis Model - Adjusted IE Incidence Within 4-Months of Dental Procedures Covered or Not Covered by Antibiotic Prophylaxis.

Medicaid Patients							
IE Risk	AP / No AP	High IE-Risk Individuals		Moderate IE-Risk Individuals		Low/Unknown IE-Risk Individuals	
Type of Dental Procedure		Adjusted IE/million proc	OR (95%CI), p	Adjusted IE/million proc	OR (95%CI), p	Adjusted IE/million proc	OR (95%CI), p
Non-IDPs	AP	4,793.8	1.001 (0.408-2.186)	715.6	1.060 (0.385-2.383)	68.1	0.973 (0.269-2.467)
	No AP	4,969.4		614.9		59.1	
Intermediate-dental proc	AP	3,150.9	0.525 (0.135-1.546)	876.7	2.655 (0.674-8.011)	105.0	1.555 (0.425-4.037)
	No AP	6.063.8		444.6		54.1	
IDPs	AP	4,881.7	0.606 (0.338-1.029)	1,118.8	1.858 (1.020-3.191)	57.1	0.704 (0.263-1.502)
	No AP	8,094.1		573.6		63.5	
Types of IDP							
Scaling	AP	4,045.9	1.441 (0.494-4.171)	652.7	2.167 (0.544-6.675)	82.6	2.234 (0.601-5.978)
	No AP	2,498.6		293.5		26.1	
Extractions	AP	7,500.8	0.575 (0.268-1.109)	1,561.9	1.823 (0.904-3.392)	53.0	0.405 (0.085-1.160)
	No AP	13,508.7		809.8		118.8	
Endodontic	AP			5,064.3	9.419 (0.728-120.072)		
	No AP			918.8			
Surgical	AP	15,567.9	0.469 (0.091-1.570)	3,811.3	2.023 (0.380-7.412)	298.4	0.902 (0.101-3.451)
	No AP	32,486.4		1,891.5		336.4	

Notes: Adjusted data corrected for differences in the age, sex and Charlson Comorbidity Index (CCI) score between cases and controls. Surgical procedures includes both oral surgery and periodontal surgery procedures. AP = antibiotic prophylaxis, IDPs = invasive-dental procedures, IE = infective endocarditis, Non-IDPs = non-invasive dental procedures, Proc. = procedure, OR = odds ratio. AP significantly reduced IE incidence compared to no AP, Bonferroni corrected p values shown where $p<0.05$ (other p values not significant) – in this case none were significant.

Table S10. Cohort Study, Dental Procedures Model - Crude IE Incidence Within 4-Months of a Dental Procedure.

Medicaid Patients												
IE Risk	**High IE-Risk Individuals**				**Moderate IE-Risk Individuals**				**Low/Unknown IE-Risk Individuals**			
Type of Dental Procedure	Procedures (n)	IE (n)	Crude IE/million proc	OR (95%CI)	Procedures (n)	IE (n)	Crude IE/million proc	OR (95%CI)	Procedures (n)	IE (n)	Crude IE/million proc	OR (95%CI)
All	26,877	113	4,204.3		266,711	125	468.7		4,962,603	216	43.5	
Control; non-IDPs	8,823	34	3,853.6	1	89,439	51	570.2	1	1,390,003	79	56.8	1
Intermediate-dental proc.	4,632	18	3,886.0	1.008 (0.569-1.789)	41,847	21	501.8	0.880 (0.529-1.462)	987,956	54	54.7	0.962 (0.680-1.359)
IDPs	13,422	84	6,258.4	1.629 (1.092-2.427)	135,425	81	598.1	1.049 (0.739-1.490)	2,584,644	155	60.0	1.055 (0.805-1.383)
Types of IDP												
- Scaling	7,026	20	2,846.6	0.738 (0.424-1.284)	59,094	17	287.7	0.504 (0.291-0.873)	1,486,315	37	24.9	0.438 (0.296-0.647)
- Extractions	6,029	60	9,951.9	2.597 (1.704-3.968), p<0.01	72,861	61	837.2	1.468 (1.012-2.132)	1,012,541	110	108.6	1.912 (1.433-2.551)
- Endodontic	403	1	2,481.4	0.643 (0.088-4.717)	3,548	2	563.7	0.988 (0.241-4.065)	110,916	4	36.1	0.635 (0.232-1.733)
- Surgical	745	18	24,161.1	6.410 (3.597-11.364), p<0.0001	6,922	10	1,444.7	2.538 (1.287-5.000)	91,936	27	293.7	5.181 (3.344-8.000), p<0.05

Notes: Crude data without adjustment for differences in the age, sex and Charlson Comorbidity Index (CCI) score between cases and controls. Surgical procedures include both oral surgery and periodontal surgery procedures. IDPs = invasive-dental procedures, IE = infective endocarditis, Non-IDPs = non-invasive dental procedures, Proc = procedure, OR = odds ratio. OR significantly higher than control non-IDP value, Bonferroni corrected p values shown where p<0.05 (other p values not significant).

Table S11. Cohort Study, Antibiotic Prophylaxis Model - Crude IE Incidence Within 4-Months of Dental Procedures Covered or Not Covered by Antibiotic Prophylaxis.

Medicaid Patients							
IE Risk	AP / No AP	High IE-Risk Individuals		Moderate IE-Risk Individuals		Low/Unknown IE-Risk Individuals	
Type of Dental Procedure		Crude IE/million proc	OR (95%CI), p NNP	Crude IE/million proc	OR (95%CI), p	Crude IE/million proc	OR (95%CI), p
Non-IDPs	AP	4,211.8	0.920 (0.394-2.149)	624.8	1.075 (0.423-2.728)	56.9	0.995 (0.313-3.160)
	No AP	4,574.4		581.3		57.2	
Intermediate-dental proc.	AP	2,425.2	0.461 (0.131-1.621)	666.7	1.754 (0.495-6.218)	86.3	1.676 (0.521-5.389)
	No AP	5,244.1		380.2		51.5	
IDPs	AP	4,611.0	0.588 (0.337-1.028)	1,054.7	1.908 (1.079-3.374)	51.2	0.820 (0.336-2.000)
	No AP	7,813.6		553.1		62.4	
Types of IDP							
Scaling	AP	3,423.0	1.455 (0.491-4.311)	491.5	1.954 (0.536-7.128)	66.5	1.949 (0.590-6.440)
	No AP	2,085.2		248.2		24.4	
Extractions	AP	6,870.2	0.550 (0.268-1.130)	1,444.0	1.768 (0.907-3.445)	41.6	0.326 (0.080-1.322)
	No AP	12,908.8		771.7		116.1	
Endodontic	AP	0		2,040.8	12.012 (0.690-209.123)	0	
	No AP	5,025.1		382.9		40.2	
Surgical	AP	11,236.0	0.388 (0.086-1.748)	2,638.5	1.748 (0.367-8.328)	185.4	0.615 (0.083-4.541),
	No AP	28,138.5		1,500.9		307.1	

Notes: Surgical procedures include both oral surgery and periodontal surgery procedures. AP = antibiotic prophylaxis, IDPs = invasive dental procedures, IE = infective endocarditis, Non-IDPs (non-invasive dental procedures), Proc. = procedure, OR = odds ratio. AP significantly reduced IE incidence compared to no AP, Bonferroni corrected p values shown where $p<0.05$ (other p values not significant). Note, there are no significant reductions in crude 4-month IE incidence comparing AP to no AP.

Table S12. Case-Crossover Analysis Using 4-Month Case Period (months 0-4 before IE admission) and 12-Month Control Period (months 5-16 before IE admission) – Dental Procedures Model.

Case-Crossover Analysis of Individuals Who Developed Infective Endocarditis (IE)									
Prior IE Risk	High IE-Risk Individuals			Moderate IE-Risk Individuals			Low/Unknown IE-Risk Individuals		
No of Dental Procedures	Proc/m in 4m Case Period	Proc/m in 12m Control Period	Odds Ratio (95% CI)	Proc/m in 4m Case Period	Proc/m in 12m Control Period	Odds Ratio (95% CI)	Proc/m in 4m Case Period	Proc/m in 12m Control Period	Odds Ratio (95% CI)
Non-invasive dental proc (non-IDPs)	27.5	23.8	1.164 (0.93, 1.456)	14.2	9.7	1.492 (1.081, 2.06)	20.8	25.8	0.802 (0.628, 1.024)
Intermediate-dental proc.	8	8.6	0.931 (0.624, 1.388)	5.2	2.1	2.564 (1.426, 4.607)	9.5	7.5	1.27 (0.867, 1.859)
Invasive-dental proc. (IDPs)	28.8	17.2	1.692 (1.343, 2.131), p<0.01	13.5	6.6	2.076 (1.464, 2.945), p<0.05	16.5	19.2	0.855 (0.649, 1.126)
Scaling	6.5	6.2	1.04 (0.664, 1.629)	2.2	1.5	1.502 (0.674, 3.346)	2.8	5.4	0.506 (0.267, 0.96)
Extractions	21.5	10.8	2.005 (1.523, 2.639), p<0.001	10.2	4.4	2.353 (1.559, 3.55), p<0.05	12.2	13.6	0.901 (0.653, 1.242)
Endodontic	0.2	1.1	0.227 (0.03, 1.747)	0.5	0.2	3 (0.423, 21.297)	0.2	0.7	0.372 (0.046, 2.992)
Surgical	5	1.2	4.032 (2.06, 7.891), p<0.0001	2	1	2.018 (0.82, 4.969)	4.5	2	2.268 (1.227, 4.193)

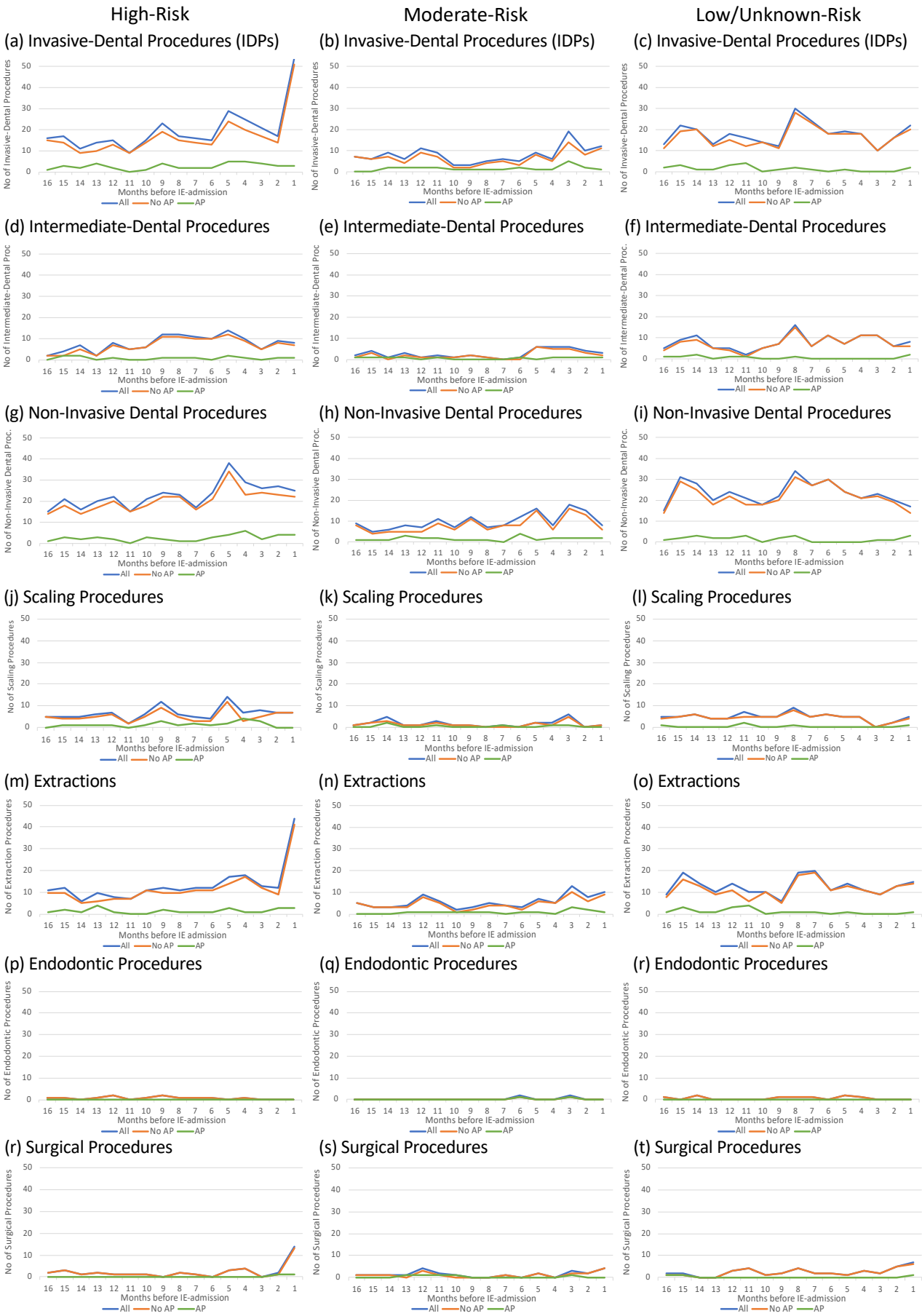
Notes: IDP = invasive-dental procedures, IE = infective endocarditis, m = month, non-IDPs = non-invasive dental procedures, proc = procedures. Surgical Procedures includes both oral surgery and periodontal surgery procedures. OR for case period significantly higher than for control period, Bonferroni corrected p values shown where p<0.05 (other p values not significant).

Table S13. Case-Crossover Analysis Using 4-Month Case Period (months 0-4 before IE admission) and 12-Month Control Period (months 5-16 before IE admission) – Antibiotic Prophylaxis Model.

Case-Crossover Analysis of Individuals Who Developed Infective Endocarditis (IE)									
Prior IE Risk	**High IE-Risk Individuals**			**Moderate IE-Risk Individuals**			**Low/Unknown IE-Risk Individuals**		
Type of Dental Procedure	Proc/m in 4m Case Period	Proc/m in 12m Control Period	Odds Ratio (95% CI)	Proc/m in 4m Case Period	Proc/m in 12m Control Period	Odds Ratio (95% CI)	Proc/m in 4m Case Period	Proc/m in 12m Control Period	Odds Ratio (95% CI)
Non-IDPs - AP	3.8	2.2	1.741 (0.919, 3.299)	2.2	2.1	1.084 (0.497, 2.361)	1.2	1.5	0.832 (0.308, 2.249)
Non-IDPs – No AP	23.8	21.6	1.104 (0.869, 1.403)	12	7.6	1.602 (1.123, 2.283)	19.5	24.2	0.8 (0.621, 1.03)
Non-IDPs, AP v No AP			1.577 (0.797-3.119)			0.678 (0.288-1.594)			1.039 (0.373-2.897)
Intermediate-dental proc. – AP	0.8	0.8	1 (0.27, 3.7)	1	0.6	1.73 (0.501, 5.975)	0.5	0.4	1.2 (0.233, 6.185)
Intermediate-dental proc – No AP	7.2	7.8	0.925 (0.608, 1.406)	4.2	1.5	2.873 (1.473, 5.602)	9	7.1	1.274 (0.861, 1.885)
Intermediate-dental proc., AP v No AP			1.081 (0.274-4.266)			0.607 (0.149-2.473)			0.942 (0.175-5.086)
IDPs – AP	4.2	2.2	1.9 (1.032, 3.496)	2.2	1.4	1.602 (0.708, 3.625)	0.5	1.5	0.332 (0.077, 1.433)
IDPs – No AP	24.5	14.9	1.659 (1.293, 2.128), p<0.01	11.2	5.2	2.206 (1.497, 3.249)	16	17.8	0.9 (0.679, 1.193)
IDPs, AP v No AP			1.147 (0.594-2.216)			0.727 (0.294-1.794)			0.369 (0.083-1.635)
Scale - AP	1.8	1.2	1.504 (0.605, 3.739)	0.5	0.3	1.5 (0.275, 8.189)	0.2	0.2	1 (0.104, 9.614)
Scale – No AP	4.8	5.1	0.934 (0.557, 1.567)	1.8	1.2	1.502 (0.605, 3.727)	2.5	5.2	0.482 (0.247, 0.941)
Scale AP v No AP			1.61 (0.565-4.583)			0.999 (0.146-6.849)			2.07 (0.196-21.910)
Extract - AP	2.5	1.3	1.887 (0.852, 4.175)	1.5	0.8	2.01 (0.713, 5.672)	0.2	1.3	0.187 (0.025, 1.41)
Extract – No AP	19	9.5	2.021 (1.508, 2.709), p<0.01	8.8	3.7	2.424 (1.548, 3.795), p<0.01	12	12.2	0.979 (0.705, 1.36)
Extract AP v No AP			0.934 (0.401-2.178)			0.829 (0.268-2.568)			0.191 (0.025-1.479)
Endo- AP				0.2	0.1	3 (0.188, 47.963)			
Endo – No AP	0.2	1.1	0.227 (0.03, 1.747)	0.2	0.1	3 (0.188, 47.963)	0.2	0.7	0.372 (0.046, 2.992)
Endo AP v No AP						1 (0.020-50.397)			
Surg – AP	0.8	0	481644 (0, 3.954e+202)	0.2	0.3	0.742 (0.08, 6.887)	0.2	0.1	3 (0.188, 47.963)
Surg - No AP	4.2	1.2	3.426 (1.707, 6.876), p<0.05	1.8	0.7	2.631(0.953, 7.267)	4.2	1.9	2.236 (1.19, 4.2)
Surg AP v No AP			140595 (0-1.155e+202)			0.282 (0.024-3.263)			1.342 (0.078-23.027)

Notes: AP = antibiotic prophylaxis, Endo = endodontic procedures, Extract = extractions, IDP = invasive-dental procedure, IE = infective endocarditis, m = month, non-IDPs = non-invasive dental procedures, proc = number of dental procedures, Scale = scaling procedures, Surg = surgical procedures, v = versus (compared with). Surgical procedures includes both oral surgery and periodontal surgery procedures. AP odds significantly reduced when compared with No AP odds, Bonferroni corrected p values shown where p<0.05 (other p values not significant).

Figure S1. Incidence of different types of dental procedure over the 16-months before IE-hospital-admission (0 months = admission date) in the **Medicaid population**



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