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Prescribing of Antibiotic Prophylaxis to Prevent Infective Endocarditis

Brief Title – Antibiotic Prophylaxis of Infective Endocarditis

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Abstract

Background:

In 2007, the American Heart Association (AHA) recommended that antibiotic prophylaxis (AP) be restricted to those at high-risk of complications due to infective endocarditis (IE) undergoing invasive dental procedures. We aimed to estimate the appropriateness of AP prescribing by type of dental procedure performed in those at high-risk, moderate-risk or low/unknown-risk of IE complications.

Methods:

Eighty high-risk, 40 moderate-risk and 40 low/unknown-risk cases were randomly selected from patients with linked dental, healthcare and prescription benefits data in the IBM® MarketScan® Databases, one of the largest US healthcare convenience data samples. Prescription and dental procedure data were analysed independently by two clinicians to determine if AP of each dental visit was likely, possible or unlikely.

Results:

In those at high-risk, 64% of invasive dental procedures were unlikely to have received AP and in 32/80 (40%) high-risk cases there was no evidence of AP for any dental visit. When AP was prescribed, several different strategies were used to provide coverage for multiple dental visits including multi-day courses, multi-dose prescriptions and refills, sometimes leading to oversupply of antibiotics.

Conclusions:

AP prescribing practices were inconsistent, did not always meet the highest antibiotic stewardship standards and made retrospective evaluation difficult. Nonetheless, for those at high-risk of IE complications, there appears to be a concerning level of under prescribing of AP for invasive dental procedures.

Practical Implications:

Some dentists may be failing to fully comply with AHA recommendations to provide AP cover for all invasive dental procedures in those at high-risk of IE complications.

Keywords:
Infective endocarditis, antibiotic prophylaxis, dental procedures, guidelines, prevention, antibiotic stewardship, risk,

Abstract word count: 249/250 words

Abbreviations:

ADA = American Dental Association
AHA = American Heart Association
AP = Antibiotic prophylaxis
CDT = Current Dental procedure Terminology
ICD = International Classification of Diseases
IE = Infective endocarditis
NPV = Negative predictive value
PPV = Positive predictive value
US = United States of America

Introduction

The American Heart Association (AHA) issued the first guidelines on the use of antibiotic prophylaxis (AP) before invasive dental procedures to prevent IE in 1955.[1] However, there has never been a randomized controlled trial to prove the efficacy of AP in IE prevention[2] and it has been argued that daily activities such as toothbrushing, flossing, mastication, etcetera, pose a greater risk for IE than invasive dental procedures.[3] This, along with concerns about the risk of adverse drug reactions and the development of antibiotic resistance, has led guideline committees to limit those for whom AP is recommended. As a result, the AHA recommended in 2007 that AP be restricted to those undergoing invasive dental procedures who are at highest-risk from complications of IE.[4]

Although several studies have investigated the impact of this guideline change on the incidence of IE, only two have examined the impact on AP prescribing.[5, 6] Both identified a large reduction in AP prescribing for those at moderate-risk of IE, for whom AP was no longer recommended. However, these groups also identified a significant reduction in AP prescribing for those at high-risk, for whom AP is recommended.[5, 6] Neither study evaluated if AP was appropriately prescribed.

Only one US study has attempted to quantify inappropriate AP prescribing. This group used a large administrative database to determine that 81% of AP prescribing for dental visits was inappropriate.[7] However, these data combined the analysis of inappropriate prescribing of AP to prevent prosthetic joint infections and IE. Furthermore, this study was not designed to investigate whether AP was appropriately prescribed to those who should receive it.[7]

The aim of the current study was to estimate the appropriateness of AP prescribing before dental procedures to prevent IE in a random sample of individuals at high-risk, moderate-risk, or low/unknown-risk of complications from IE selected from a large commercial claims database. A secondary aim was to evaluate the sensitivity and specificity of different protocols for automatic identification of when AP was prescribed to cover a dental procedure in large data sets, such as the MarketScan Database, in order to facilitate subsequent large-scale studies.

Methods

Data Source:

The IBM® MarketScan® Databases are a collection of HIPAA-compliant data sets that integrate de-identified patient-level health data across the different databases. Because data are statistically-deidentified in a HIPAA-compliant manner to protect patient privacy, studies using the data are exempt from IRB review. The databases provide one of the largest convenience US healthcare data samples with over 255 million unique patients since 1995, including 41.2 million individuals in the last full data year.[8, 9] For this study, we linked data from the IBM® Market Scan Commercial, Medicare Supplemental, Dental and Prescription Benefits data sets.[8, 9] Enrollees over the age of 18 years, with linked data for the period January 1st, 2000 through August 31st, 2015 were included in the study. Together, these data provided a large nationally representative data sample of Americans with employer-provided health insurance.[8, 9] Data were included up to August 31st, 2015; after this date, medical diagnosis and medical/dental procedure coding changed from ICD-9 to ICD-10 and codes were not always transferrable or equivalent.

IE-risk stratification and identification of IE admissions:

The database was queried from January 2000 to identify any ICD-9 or CPT diagnosis or procedure codes that would have placed an individual at high- or moderate-risk of complications from IE as defined by the 2007 AHA guidelines (Supplemental Tables S1-S3).[4, 10] Individuals not identified as moderate- or high-risk were considered to be at unknown/low-risk of IE.

IE hospital admissions were identified using diagnosis codes (ICD-9 code 421.0, 421.1 or 421.9, primary or secondary discharge diagnoses). Previously described methods were used to ensure single continuous episodes of IE were counted only once.[11] After an enrollee had an IE-related hospital admission, they were considered at high-risk for complications of future episodes of IE.

Selection of Cases:

From all individuals who had fully linked dental, prescription benefits and commercial medical or Medicare Supplemental data for January 1st, 2011 through August 31st, 2014, a computer algorithm randomly selected 80 individuals at high-risk of complications from IE, 40 at moderate-risk and 40 at low/unknown-risk. Selecting individuals between these dates ensured that there was an 11-year period to determine if an individual had diagnoses or procedures that would put them at high- or moderate-risk from complications of IE and that there was at least one year to study AP coverage of dental procedures.

Invasive Dental Procedures:

AHA guidelines provide a definition of dental procedures that should be covered by AP in those at highest risk of IE complications (see supplemental Table S4).[4] The American Dental Association (ADA) Code on Dental Procedures and Nomenclature (CDT codes)[12] and ICD-9 procedure codes[13] were used to identify types of dental procedure performed. These codes were scrutinised by 4 dentists who divided the codes into 3 categories; (i) codes identifying 'red procedures', i.e. invasive procedures that 'should' be covered with AP for those at high-risk of IE complications,[4] (ii) codes identifying 'yellow procedures', i.e. invasive dental procedures that 'may' be covered with AP on some occasions and not on others and (iii) codes identifying 'green procedures', i.e. non-invasive dental procedures where there is no recommendation for AP cover. When there were differences in opinion about grading of CDT and ICD-9 codes, agreement was reached through consensus discussion. Grading of CDT and ICD-9 codes is shown in supplemental Tables S5-S7. When a dental visit included multiple procedures, the most invasive procedure was ascribed to that visit, i.e. red dental procedures took precedence, followed by yellow and then green procedures.

Prescribing data and manual identification of when a dental visit was covered by AP:

Prescribing data available for each case included, the name, fill date, number of day's supply, metric quantity, strength, dose prescribed and refill number for all antibiotic prescriptions. Each dental visit was independently evaluated by two clinicians blind to a patient's risk status and nature of the dental procedure performed to determine if it was likely, possible or unlikely that visit had been covered by AP. Where there was disagreement, a third clinician arbitrated the case to achieve consensus. For AP to be considered 'likely' or 'possible', a prescription had to be an oral antibiotic at a dose, or multiple of the dose, recommended for AP purposes by the AHA guidelines, i.e. amoxicillin 2g, clindamycin 600mg, cephalexin 2g, azithromycin 500mg or clarithromycin 500mg. All prescriptions were considered invalid after 1 year and all prescriptions for more than 5 day's supply of antibiotic were considered unlikely to be for AP purposes. Both the number of AP prescriptions and, because some prescriptions covered multiple courses of AP (by providing several days' supply or multiples of the recommended dose), the number of courses of AP prescribed were examined.

Automated identification of AP cover of a dental visit using computer algorithms:

The study also evaluated the performance of 3 AP algorithms (Table 1) against manual chart review (gold standard). Since the gold standard outcome was 'likely', 'possible', or 'unlikely' covered by AP, but the algorithms produced a binary ('covered' *vs* 'not covered') outcome, we calculated the sensitivity etc of each algorithm against two alternative 'gold standard' binary outcomes (a) 'likely' *vs* 'possible' or 'unlikely' or (b) 'likely' or 'possible' *vs* 'unlikely'.

Results

Patient characteristics

The study comprised 160 cases: 80 high-risk, 40 medium-risk and 40 low/unknown-risk cases. The high-risk group included 63% who were men and the mean age (65 years) was significantly higher than the mean age of all cases (59 years). In contrast, the low/unknown-risk group contained 60% women and the mean age (47 years) was significantly lower than that for all cases (Table 2).

There was no significant difference in the number of days of study or number of dental visits per patient available for us to examine among the different risk groups. The number of red dental visits studied was significantly higher for the moderate-risk group than for all cases, but there were no other significant differences in the number of different types of dental visit (red, yellow, green) between the patient risk groups.

The most common factor for being high-risk was prior heart valve replacement in 69/80 cases (86%), of whom 45 (56%) were men, followed by previous IE in 11/80 (14%) of cases. Native valve abnormalities accounted for 37/40 (93%) of those at moderate-risk of IE complications. In addition, there was one case each of rheumatic heart disease (female), hypertrophic cardiomyopathy (female) and congenital valve disease (male).

Antibiotic prophylaxis (AP)

Despite each case containing several red procedure visits, there was no evidence that a dental visit was covered in 32/80 (40%) of those at high-risk for IE complications. This included 13/30 (43%) women and 19/80 (24%) men. In the remaining 48/80 high-risk individuals, there was evidence that AP was likely to have been given on at least one occasion. In all 80 high-risk individuals, only 125/468 (27%) of red dental visits, i.e. visits that should be covered by AP, were likely to have been (Figure 1). A further 44/468 (9%) were possibly covered and 299/468 (64%) were unlikely to have been covered.

When analysis was confined to the 48 high-risk cases with evidence of AP being prescribed on at least one occasion, it was likely that only 125/290 (43%) of red dental visits were covered with AP. A further 44/290 (15%) were possibly covered and 121/290 (42%) were unlikely to have been covered.

For yellow dental visits, where dentists have some discretion about when AP should be given, 19% of visits were likely to have been covered with AP, 7% possibly covered and 74% were unlikely to have been covered in the entire high-risk group of 80 cases. In the 48-case group, when those with no evidence of AP prescribing were excluded, 39% of yellow procedure visits were likely to have been covered, 15% possibly covered and 46% were unlikely to have been covered. Even though there is no recommendation to cover green procedure dental visits, 5% were likely and 9% possibly covered in the entire high-risk group. In the restricted high-risk group, 9% were likely and 16% possibly covered by AP.

In those at moderate-risk of IE complications, for whom AP is not recommended, only 22/410 (5%) dental visits were likely and 11/410 (3%) possibly covered by AP. Of 376 dental visits recorded in those at low/unknown-risk, only 5 were likely to have been covered by AP, all of which were for the same patient (Figure 1).

IE development following invasive dental procedures

Two individuals, one man and one woman, underwent hospital admission with an IE diagnosis following a dental visit. In both cases, the individuals had not been identified as high-risk or moderate-risk of complications before they developed IE. Both, however, had a record of undergoing a red D1110 dental prophylaxis (supragingival scaling) procedure that was unlikely to have been covered by AP in the 4 months preceding the IE diagnosis. In one case, IE admission occurred 8 days following dental prophylaxis, and 11 weeks after in the other. Having become high-risk as a result of IE, both continued to receive dental treatment that was tracked. In one case, this continued for 41 months after IE diagnosis, during which 8 red, 2 yellow and 10 green dental visits occurred of which only 1 red and 1 green visit were likely to have been covered by AP; both of these visits occurred more than 3 years after the IE diagnosis was made. In the other case, dental visit data continued for 13 months after the IE diagnosis, during which there were 3 red and one yellow dental visit. On each occasion, there was no evidence that AP was likely to have been prescribed.

Types of dental procedures performed

Across the different risk groups, scaling accounted for the vast majority (80-90%) of red procedures performed (Figure 2). Extractions were the next most common, followed by endodontic treatments. Figure 3 shows the percentage of the different types of red procedure that were likely, possibly, or unlikely to have been covered with AP. In those at high-risk, the percentage of visits likely to have been covered with AP was highest (at 50%) for oral surgery procedures, implant procedures and periodontal probing. It was lower for extractions (38% likely and 7% possible), endodontic treatment (31% likely and 4% possible) and all types of scaling (25% likely and 10% possible). However, coverage of subgingival scaling procedures was higher (34% likely and 10% possible) than for supragingival scaling (24% likely and 10% possible).

In those at moderate-risk, i.e. those for whom the AHA recommended AP should have ceased, 5/40 (13%) were likely to have been given AP and 2/40 (5%) possibly received AP. In those at low/unknown-risk, for whom AP has never been recommended, only 1 individual received AP (for 5 D1110 – dental prophylaxis visits and one visit for a two surfaced composite restoration of a posterior tooth (D2392)).

Types of AP prescription issued

Amoxicillin was the most frequently prescribed antibiotic, accounting for 147/196 (75%) of all AP prescriptions and 359/489 (73%) of all AP courses prescribed (Figure 4). This was followed by clindamycin (17% of prescriptions), clarithromycin (4%), azithromycin (3%), and cephalexin (1%).

Although, a prescription for 1 day's supply of AP was the most common, it accounted for only 35% of all AP prescriptions. Three days' supply (3 courses) was the next most common, accounting for 29% of AP prescriptions, but prescriptions for 2, 4 and 5 days were also common. Indeed, multi-day prescriptions were the norm for cephalexin, azithromycin and clarithromycin. Figure 4 shows the proportion of all AP prescriptions by antibiotic and number of day's supply prescribed.

Sensitivity and specificity of automated protocols for detecting AP cover of dental visits

The performance of the three automated algorithms is displayed in Table 3. Of note, algorithm A has already been used in a 'big data' study of the appropriateness of AP prescriptions before dental procedures.[7] This algorithm had high specificity (100%) but very low sensitivity (25%) for correctly identifying when AP had been prescribed. That is, the prescriptions it identified were highly likely to be for AP, but it also frequently missed situations when AP had been correctly prescribed. The other two protocols were developed for future studies to try to improve sensitivity while retaining good specificity. Although Algorithm B demonstrated improved sensitivity (54%) over Algorithm A, while retaining good specificity (99%), sensitivity was still poor. Algorithm C, however, significantly improved sensitivity (88%) with only a small further reduction in specificity (96%).

Discussion

The finding that there was no evidence of AP being prescribed before any dental procedure in 40% of high-risk patients is striking. When all high-risk patients are considered, 64% of red dental procedures were unlikely to have been covered with AP. This suggests significant under prescribing of AP. It is unclear if this lack of compliance with the AHA recommendations is consistent with continued widespread confusion about AP in general,[14, 15] a lack of awareness of patient comorbidities,[14, 15] prescriber inertia, patient non-adherence or limitations with the use of administrative data.

Our findings are consistent with those of a large French study that reported only 50% of invasive dental procedures were covered by AP in patients at high-risk of complications from IE.[16] However, that study accepted all antibiotic prescriptions that might have activity against oral streptococci in the 21 days before an invasive dental procedure as evidence of AP coverage, regardless of duration or dose prescribed. The actual level of AP prescribing was likely lower. These findings are also consistent with the 15-20% decline in AP prescribing for those at high-risk from IE complications following the 2007 changes in AHA recommendations.[5, 6]

The under prescribing and fall in AP observed in those at high-risk may reflect difficulties experienced by dentists in distinguishing between high-risk and moderate-risk cardiac conditions, as identified in a recent systematic review[14] and questionnaire survey of US dentists.[15] However, high-risk cases in our study had either a replacement heart-valve or a previous history of IE and should not have been difficult to identify.

Survey data suggest that delayed adoption of evidence-based practices and confusion may be contributing to our observations[14, 15, 17] A 2010 survey of 878 US dentists reported that 70% had one or more patients who continued to receive AP before invasive dental procedures, even though it was no longer recommended,[17] and a more recent survey of US dentists identified confusion about which patients should receive AP.[15]

Scaling procedures accounted for the vast majority of dental procedures that might require AP in dental offices. These were divided into those mainly involving supragingival scaling (Table S7) and those that involved subgingival scaling or root planning. The ratio of supragingival to subgingival procedures was highest in those at high-risk, less in those at moderate-risk and lowest in those at low/unknown-risk. This may suggest that dentists were attempting to be less invasive with dental cleaning in those at highest-risk. In addition, supragingival scaling was less likely to be covered by AP than subgingival scaling and root planning, further suggesting that dentists may regard supragingival scaling as less invasive. A recent study, however, demonstrated that there is no significant difference in size or magnitude of bacteremia that characterizes supragingival scaling and dental extractions,[18] suggesting supragingival scaling is of significant invasiveness. Of interest, the two individuals who developed IE after an invasive dental procedure in the current investigation did so after uncovered supragingival scaling.

Amoxicillin 2g accounted for the majority of all AP prescriptions with penicillin alternatives accounting for 22%. Our study could not distinguish if amoxicillin alternatives were prescribed due to a history of penicillin allergy or for other reasons. However, of the penicillin alternative prescriptions dispensed, 20 (51%) occurred in individuals who at other times were prescribed amoxicillin AP. Only on two occasions was the penicillin alternative prescribed in the 3 weeks following an amoxicillin prescription. This suggests that penicillin alternatives are frequently prescribed, even when a patient does not have a history of penicillin allergy. Given the comparative safety of AP prophylaxis with amoxicillin,[19] and the greater risk of adverse drug reactions with alternatives,[19, 20] this raises antibiotic stewardship concerns.

This study also suggested that while some dentists issue a separate prescription for each AP course, others prescribe multi-day courses, multiples of the normal AP dose or permit prescription refills to provide patients with supplies they need to cover multiple dental visits. There are several potential concerns with this. First, from a study perspective, this makes it more difficult to determine if a dental visit was covered by AP. This is particularly the case with longer duration prescriptions e.g. 5-days, when there is also uncertainty whether the prescribed course of antibiotics was intended to treat an infection or to provide AP cover for multiple dental visits. Individually examining dental treatment codes for each visit and timing of prescriptions, however, often made it possible to establish if a prescription was intended for treatment or AP purposes.

While multi-day prescriptions may reduce cost for patients, they raise a number of antibiotic stewardship issues that include: 1) will patients remember to take AP for a future dental visit up to a year later; 2) will they take the required single dose; 3) will the antibiotic be within its use-by-date; 4) will patients take the antibiotic for non-AP purposes? Some patients in our cohort were clearly issued antibiotics more frequently than needed (e.g. 3-5 day courses prescribed each time a patient had a red-procedure dental visit). Another possibility is that some dentists are not following the single dose recommendation for AP cover, as identified in some questionnaire surveys.[14]

The current investigation was used to validate three algorithms to identify when a dental visit or procedure was covered by AP in large data studies and determine their sensitivity and specificity.

Study Limitations

The data described here are based on the case histories of patients selected randomly form populations at high-risk, moderate-risk or low/unknown-risk of IE. Because they were selected randomly, it is assumed that that they represent all such patients, but that may not be the case. As described above, the different strategies used by dentists to prescribe AP, particularly the practice of covering multiple courses of AP with a single prescription, made it difficult to verify when or whether a particular dental visit was covered. Even when a single dose of AP was prescribed immediately before an invasive dental procedure visit, we could not be certain that the patient took AP. Similarly, even when there was no evidence that an antibiotic prescription was issued, we cannot be certain that the patient was not provided AP by some other means, e.g. by the dentist dispensing the antibiotic from their office without a prescription record. For these reasons, we chose to use the terms “likely”, “possible” and “unlikely” to describe the probability that AP was prescribed rather than using more definitive categorical terms.

Although our study suggests significant levels of under-prescribing of AP to those at high-risk of IE complications undergoing invasive dental procedures, we have to caution that it is possible we have underestimated AP prescribing due to non-recorded direct dispensing of AP by dentists. The level of this practice would have to be high, however, to account for there being no AP records in 40% of high-risk individuals, or for AP cover to have been likely for only 26.7% of high-risk red dental visits. Ultimately, the best way to capture dental antibiotic prescribing practices is likely via a prospective process that incorporates patient comorbidities, antibiotic prescriptions data (including both pharmacy and in-office), dental procedure, and indication for prescription. These data would help provide baseline information to drive future antibiotic stewardship interventions.

Conclusions

This study identified significant under-prescribing of AP in individuals at high-risk of IE complications undergoing invasive dental procedures. Of the invasive dental procedures performed, scaling accounted for the majority (80-90%). The study also identified a number of different prescribing strategies to provide AP, particularly for repeat dental visits, some of which may not be consistent with modern antibiotic stewardship recommendations. In addition, this study validates, for the first time, the sensitivity and specificity of algorithms to identify AP prescribing in ‘big data’ studies.

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Table 1. The definition of the different algorithms used for identifying when antibiotic prophylaxis has been prescribed in large administrative datasets.

Parameter	Algorithm A	Algorithm B	Algorithm C
Antibiotics	Any systemic antibiotic	Oral amoxicillin, clindamycin, cephalexin azithromycin or clarithromycin	Oral amoxicillin, clindamycin, cephalexin azithromycin or clarithromycin
Dosage*	Any	2g for amoxicillin, 600 mg for clindamycin, 2g for cephalexin, 500mg for azithromycin or 500mg for clarithromycin	2g for amoxicillin, 600 mg for clindamycin, 2g for cephalexin, 500mg for azithromycin or 500mg for clarithromycin
Days supply	≤2	≤3	≤5
Time (days) between fill date and visit date	≤7	≤30 where day's supply = 1 ≤60 where day's supply = 2 ≤90 where day's supply = 3	≤73 where day's supply = 1 ≤146 where day's supply = 2 ≤219 where day's supply = 3 ≤292 where day's supply = 4 ≤365 where day's supply = 5

Note: Data parameters available for each prescription included: drug name, fill date, number of day's supply, metric quantity, strength, and refill number. *Dosage = metric quantity/day's supply x strength

Table 2. Patient characteristics.

	High-Risk Patients	Moderate-Risk Patients	Low/Unknown-Risk Patients	All Patients
No of cases	80	40	40	160
Female Sex %	37.5%	47.5%	60%	45.6%
Age				
Mean (SD)	65.1 (13.4)*	60.1 (15.11)	46.9 (15.0)*	59.3 (16.0)
Median (IQR)	67.0 (59.0-76.0)	60.0 (49.0-71.0)	49.0 (32.0-58.0)	61.0 (49.0-70.0)
Study duration for each patient (days)				
Mean (SD)	1104 (473)	1199 (337)	1015 (437)	1105 (436)
Median (IQR)	1173 (696-1394)	1255 (932-1451)	1078 (703-1361)	1196 (830-1392)
Total number of dental visits/patient studied				
Mean (SD)	9.8 (5.3)	10.1 (4.1)	9.4 (5.7)	9.8 (5.1)
Median (IQR)	10 (6-13)	10 (8-13)	9 (5-12)	9 (6-13)
Red dental visits/patient				
Mean (SD)	5.8 (3.0)	7.3 (2.6)	5.8 (3.0)	6.2 (3.5)
Median (IQR)	6 (4-8)	7 (5-9)	6 (3-8)	6 (4-8)
Yellow dental visits/patient				
Mean (SD)	1.7 (2.1)	1.5 (1.5)	1.6 (1.5)	1.6 (1.8)
Median (IQR)	1 (0-2)	1 (0-3)	1 (0-2)	1 (0-2)
Green dental visits/patient				
Mean (SD)	2.3(2.4)	1.4 (1.9)	1.6 (2.0)	1.9 (2.2)
Median (IQR)	2 (0-3)	1 (0-2)	1 (0-2)	1 (0-3)

*Significantly different from the mean for all cases ($p<0.05$).

Table 3. The performance of different algorithms for identifying when antibiotic prophylaxis (AP) has been prescribed in large administrative datasets.

	AP Likely *v* AP Possible or AP Unlikely	AP Likely or AP Possible *v* AP Unlikely
Algorithm A		
Sensitivity	25.4% (19.4%-32.1%)	18.0% (13.6%-23.0%)
Specificity	100% (99.7%-100%)	100% (99.7%-100%)
PPV	100%	100%
NPV	90.6% (89.8%-91.2%)	85.3% (84.6%-86.0%)
+ Likelihood ratio	N/A	N/A
- Likelihood ratio	0.75 (0.69-0.81)	0.82 (0.78-19.31)
Algorithm B		
Sensitivity	53.9% (46.6%-61.1%)	42.5% (36.6%-48.6%)
Specificity	99.0% (98.3%-99.4%)	99.9% (99.5%-100%)
PPV	88.1% (81.3%-92.7%)	98.3% (93.5%-99.6%)
NPV	93.9% (93.0%-94.7%)	89.2% (88.2%-90.2%)
+ Likelihood ratio	53.15 (31.09-90.96)	276.40 (68.73-111.63)
- Likelihood ratio	0.47 (0.40-0.54)	0.58 (0.52-0.64)
Algorithm C		
Sensitivity	87.6% (82.1%-91.9%)	75.8% (70.3%-80.8%)
Specificity	95.5% (94.3%-96.5%)	98.2% (97.3%-98.8%)
PPV	73.2% (68.0%-77.8%)	89.6% (85.2%-92.8%)
NPV	98.2% (97.4%-98.8%)	95.1% (94.0%-96.0%)
+ Likelihood ratio	19.50 (15.21-25.02)	41.10 (27.50-61.44)
- Likelihood ratio	0.13 (0.09-0.19)	0.25 (0.20-0.30)

Figure legends:

Figure 1.

Percent of different levels of invasiveness of dental procedures where antibiotic prophylaxis (AP) coverage was likely, possible or unlikely for those at high-risk, moderate-risk or low/unknown-risk of complications from infective endocarditis (IE).

Figure 2.

The proportion of all red invasive dental procedures characterized by periodontal probing, all types of dental scaling (sub-divided by codes representing mainly supragingival scaling and those in which subgingival scaling is also required), periodontal surgery, dental extractions, endodontic treatments, oral surgery procedures and implant related invasive procedures.

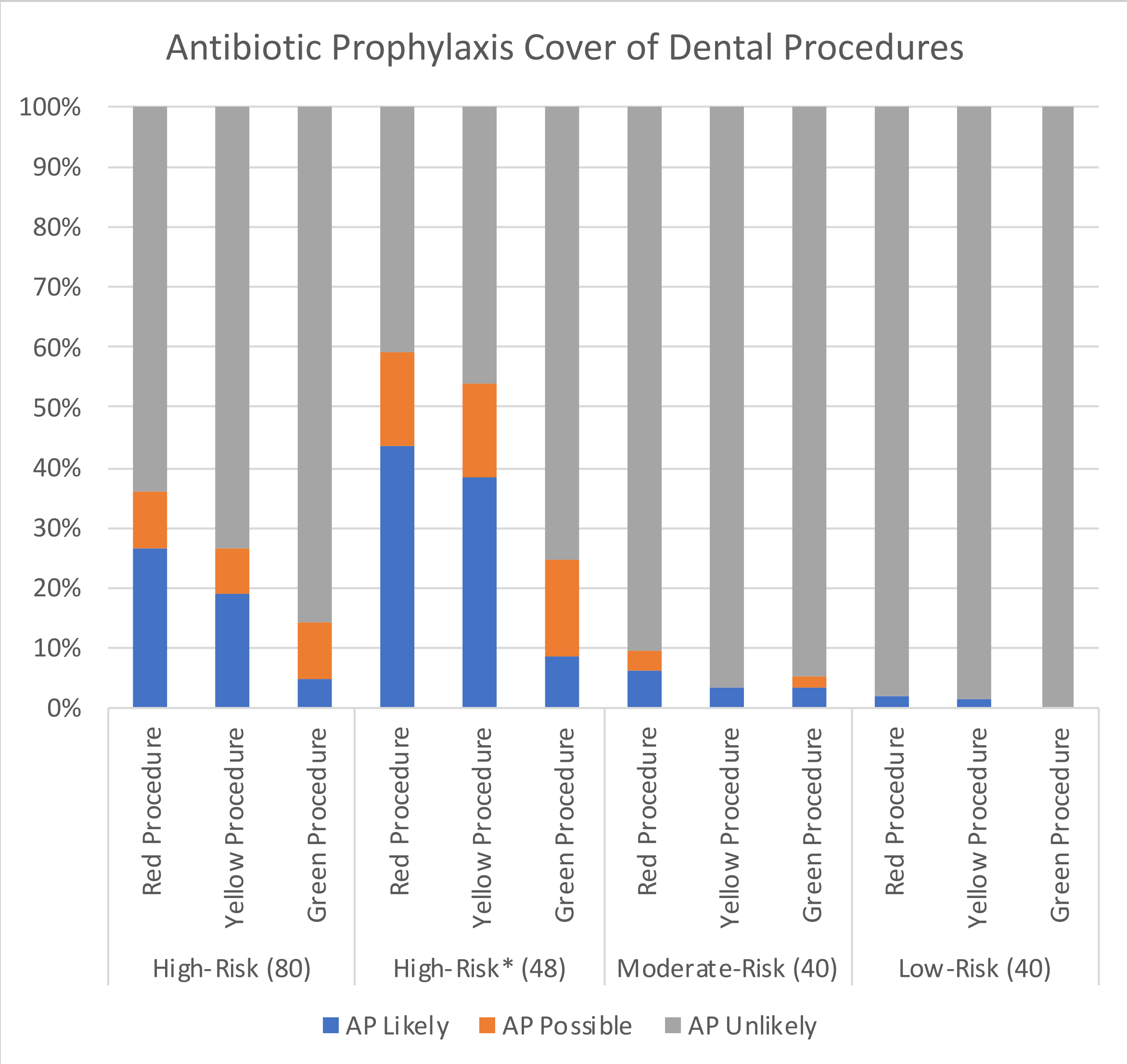
Figure 3.

The proportion of different red invasive dental procedures, i.e. periodontal probing, all types of dental scaling (sub-divided by codes representing mainly supragingival scaling and those in which subgingival scaling is also required), periodontal surgery, dental extractions, endodontic treatments, oral surgery procedures and implant related invasive procedures, where antibiotic prophylaxis (AP) coverage was likely, possible or unlikely for those at high-risk, moderate-risk or low/unknown-risk of complications from infective endocarditis (IE).

Figure 4.

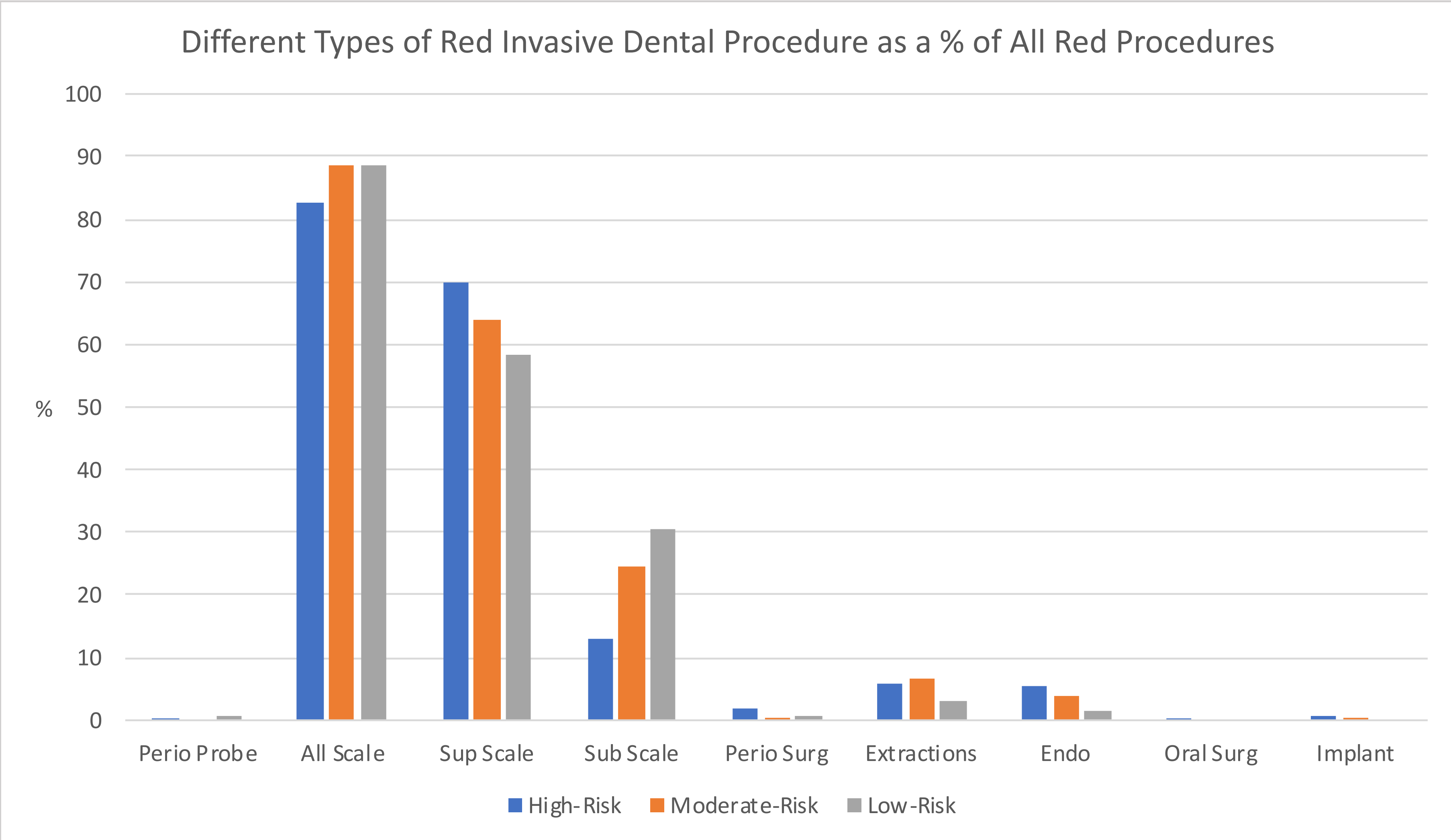
Antibiotic type and number of days prescribed as a percentage of all antibiotic prophylaxis (AP) prescriptions.

Figure 1



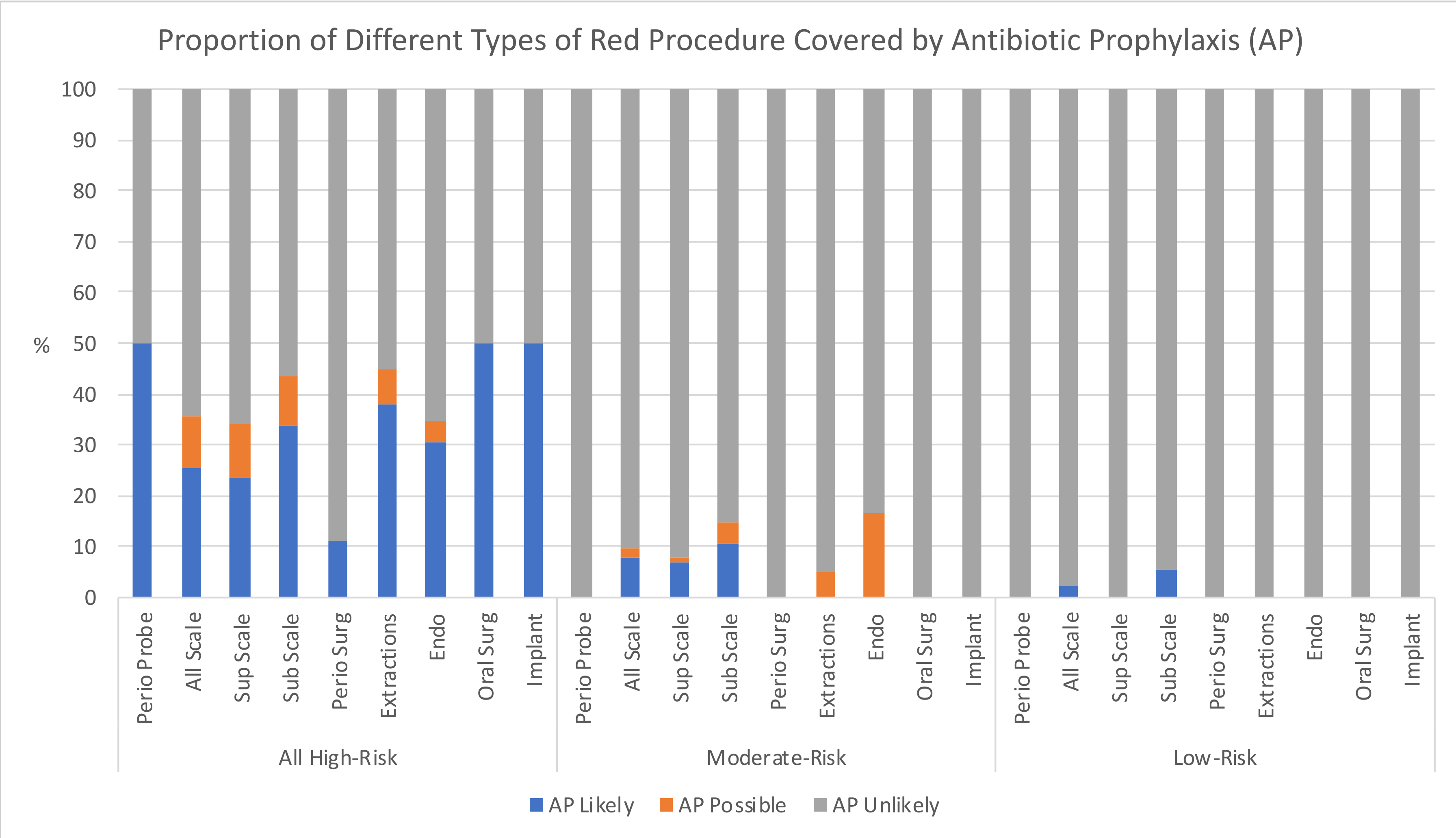
*Excluding the 32 high-risk individuals for whom there was no evidence of AP coverage for any dental visit/procedure.

Figure 2



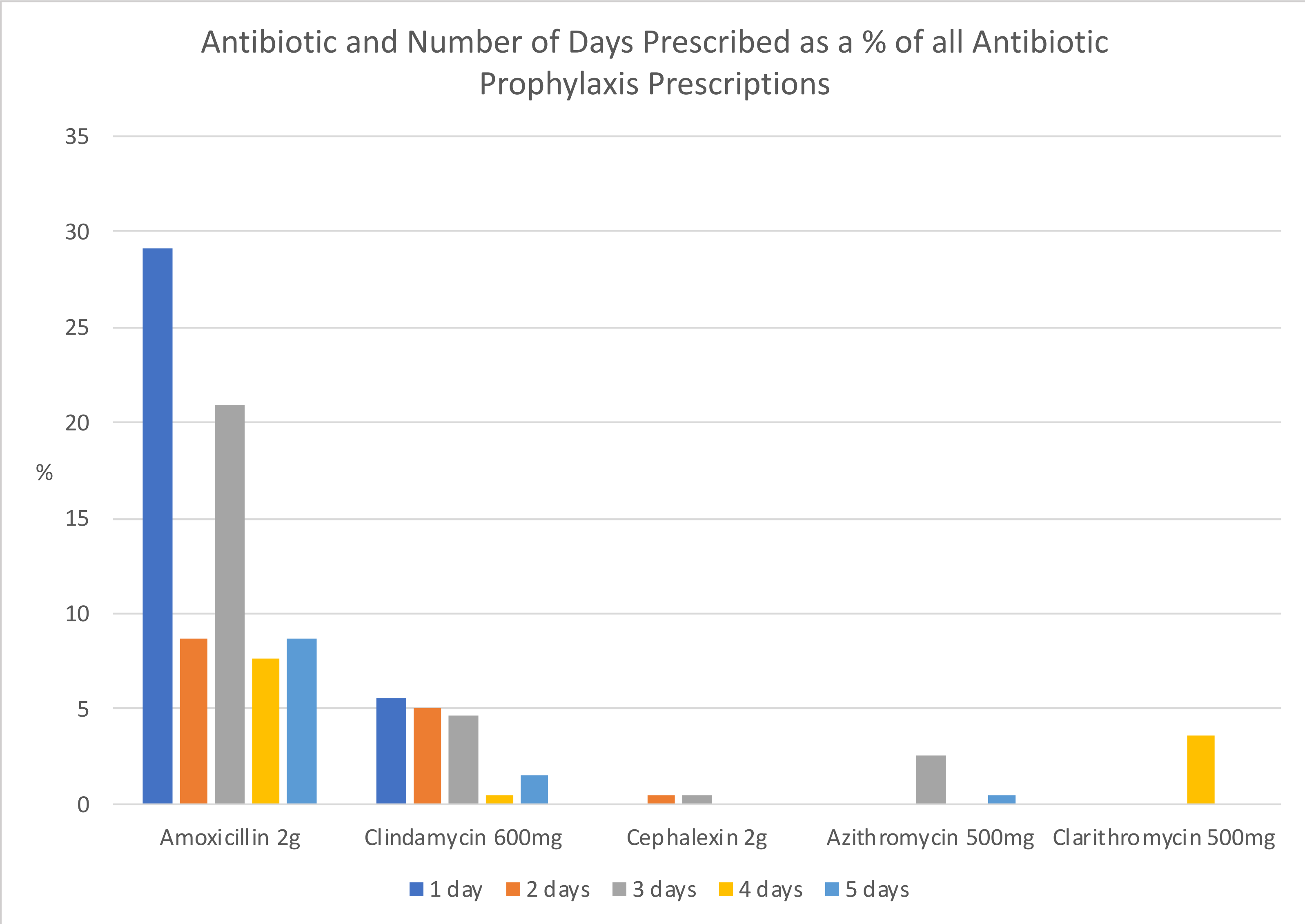
Different Types of Red Invasive Dental Procedure as a % of All Red Procedures
100
90
80
70
60
50
40
30
20
10
0
%
Perio Probe
All Scale
Sup Scale
Sub Scale
Perio Surg
Extractions
Endo
Oral Surg
Implant
High-Risk
Moderate-Risk
Low-Risk

Figure 3



Proportion of Different Types of Red Procedure Covered by Antibiotic Prophylaxis (AP)
100
90
80
70
60
%
50
40
30
20
10
0
Perio Probe
All Scale
Sup Scale
Sub Scale
Perio Surg
Extractions
Endo
Oral Surg
Implant
All High-Risk
Moderate-Risk
Low-Risk
AP Likely
AP Possible
AP Unlikely

Figure 4



Antibiotic and Number of Days Prescribed as a % of all Antibiotic Prophylaxis Prescriptions
35
30
25
20
%
15
10
5
0
Amoxicillin 2g
Clindamycin 600mg
Cephalexin 2g
Azithromycin 500mg
Clarithromycin 500mg
1 day
2 days
3 days
4 days
5 days