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Antibiotic Prophylaxis and Incidence of Endocarditis Before and After the 2007 AHA Recommendations

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ABSTRACT

BACKGROUND The American Heart Association updated its recommendations for antibiotic prophylaxis (AP) to prevent infective endocarditis (IE) in 2007, advising that AP cease for those at moderate risk of IE, but continue for those at high risk.

OBJECTIVES The authors sought to quantify any change in AP prescribing and IE incidence.

METHODS High-risk, moderate-risk, and unknown/low-risk individuals with linked prescription and Medicare or commercial health care data were identified in the Truven Health MarketScan databases from May 2003 through August 2015 (198,522,665 enrollee-years of data). AP prescribing and IE incidence were evaluated by Poisson model analysis.

RESULTS By August 2015, the 2007 recommendation change was associated with a significant 64% (95% confidence interval [CI]: 59% to 68%) estimated fall in AP prescribing for moderate-risk individuals and a 20% (95% CI: 4% to 32%) estimated fall for those at high risk. Over the same period, there was a barely significant 75% (95% CI: 3% to 200%) estimated increase in IE incidence among moderate-risk individuals and a significant 177% estimated increase (95% CI: 66% to 361%) among those at high risk. In unknown/low-risk individuals, there was a significant 52% (95% CI: 46% to 58%) estimated fall in AP prescribing, but no significant increase in IE incidence.

CONCLUSIONS AP prescribing fell among all IE risk groups, particularly those at moderate risk. Concurrently, there was a significant increase in IE incidence among high-risk individuals, a borderline significant increase in moderate-risk individuals, and no change for those at low/unknown risk. Although these data do not establish a cause-effect relationship between AP reduction and IE increase, the fall in AP prescribing in those at high risk is of concern and, coupled with the borderline increase in IE incidence among those at moderate risk, warrants further investigation. (J Am Coll Cardiol 2018;■:■–■) © 2018 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

AHA = American Heart Association

AP = antibiotic prophylaxis

CI = confidence interval

ESC = European Society of Cardiology

ICD = International Classification of Disease

IE = infective endocarditis

NICE = National Institute for Health and Care Excellence

Infective endocarditis (IE) is a life-threatening infection with high morbidity and ~30% first-year mortality (1). Although uncommon, a large number of individuals with predisposing cardiac conditions are at increased risk of IE (2). Preventing IE in those at risk has been the focus of international guidelines since the American Heart Association (AHA) first advocated antibiotic prophylaxis (AP) before invasive medical and dental procedures in 1955 (3). However, there has never been a trial of AP to define its efficacy (4). This, and concerns about the risk of adverse reactions and the development of antibiotic resistance, led to reductions in the populations of individuals targeted for AP. In 2007, the AHA recommended AP be restricted to those at high risk of IE and its complications who were undergoing invasive dental procedures (5). The European Society of Cardiology (ESC) published similar guidance in 2009 (6), whereas the U.K. National Institute for Health and Care Excellence (NICE) recommended the complete cessation of AP in 2008 (7).

Following the NICE recommendation, Dayer et al. (8) demonstrated an 89% fall in AP prescribing in England and a significant increase in IE. Similar studies were performed following the 2007 AHA (9–16) and 2009 ESC (17,18) recommendation changes, with varying results. Importantly, however, none of these studies included data on the impact of the recommended changes on AP prescribing.

The aim of this investigation was to quantify changes in AP prescribing and IE incidence following the 2007 AHA recommendations in individuals at high, moderate, or unknown/low risk of IE, using commercial and Medicare data and linked prescription benefit data from the Truven Health MarketScan databases that cover a large proportion of the U.S. population.

METHODS

The MarketScan databases are a collection of HIPAA (Health Insurance Portability and Accountability Act)-compliant datasets that integrate deidentified patient-level health data across commercial health insurance, Medicare supplemental insurance, and Medicaid programs covering physician office visits, inpatient and outpatient hospital services, and outpatient prescription drug coverage (19,20). They provide one of the largest U.S. health care data samples with 240 million covered lives and 32 billion service records (19,20). The commercial data include employees, spouses, and dependents covered by employer-sponsored private health insurance involving more than 260 employers and 40 health plans (19,20). Medicare data have been gathered from supplemental Medicare programs, where a secondary payer to Medicare exists, typically employer-based retiree health insurance. The Medicaid data cover 44 million enrollees from multiple states (20).

All commercial insurance, Medicare, and Medicaid enrollees over the age of 18 years, with linked prescription benefit data, were identified for the period May 1, 2003, through August 31, 2015. Preliminary analysis identified a large age distribution change in enrollees with Medicaid-covered prescription drug benefits in January 2006, due to transfer of Medicare-eligible persons (mainly persons >65 years of age) to the newly instituted Medicare Part D prescription drug coverage (Online Figure 1). Thus, Medicaid data were unreliable for studying longitudinal change and were excluded from this investigation. The change, however, did not impact Medicare supplemental insurance data. Together, the MarketScan Commercial and Medicare Supplemental databases provide a large nationally representative data sample of Americans with employer-provided health insurance (19,20).

For each enrollee, AP prescriptions were identified as defined by the AHA recommendations (a single oral dose of amoxicillin 2 g, clindamycin 600 mg, cephalexin 2 g, azithromycin 500 mg, or clarithromycin 500 mg) (5), and IE hospital admissions were identified using diagnosis International Classification of Disease (ICD) 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 once (21). The database was searched back to January 2000 to identify any ICD-9 or CPT (Current Procedural Terminology) diagnosis or procedure codes occurring before an IE admission that would have

Association's Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease; helped produce the 2007 American Heart Association guideline on prevention of infective endocarditis; and has served as a consultant for Boston Scientific. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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placed an individual at high or moderate risk of IE (Online Tables 1 and 2) (5,22). Patients who did not develop IE were categorized in the same way if any of the relevant codes appeared in their records between January 2000 and August 2015. After an enrollee had an IE-related hospital admission, they were considered at high risk for further new episodes of IE. New IE episodes were distinguished from readmissions by only accepting IE admissions >6 months apart as new episodes (2,23). Individuals not identified as moderate or high risk were considered to be at unknown/low risk of IE.

We also quantified the total reimbursed inpatient payment costs to all providers of care (hospitals, physicians, and any ancillary payments) for each continuous period of IE hospital admission (including transfers between hospitals for treatment of the same episode of IE) and the total reimbursed amount to pharmacies for each AP prescription.

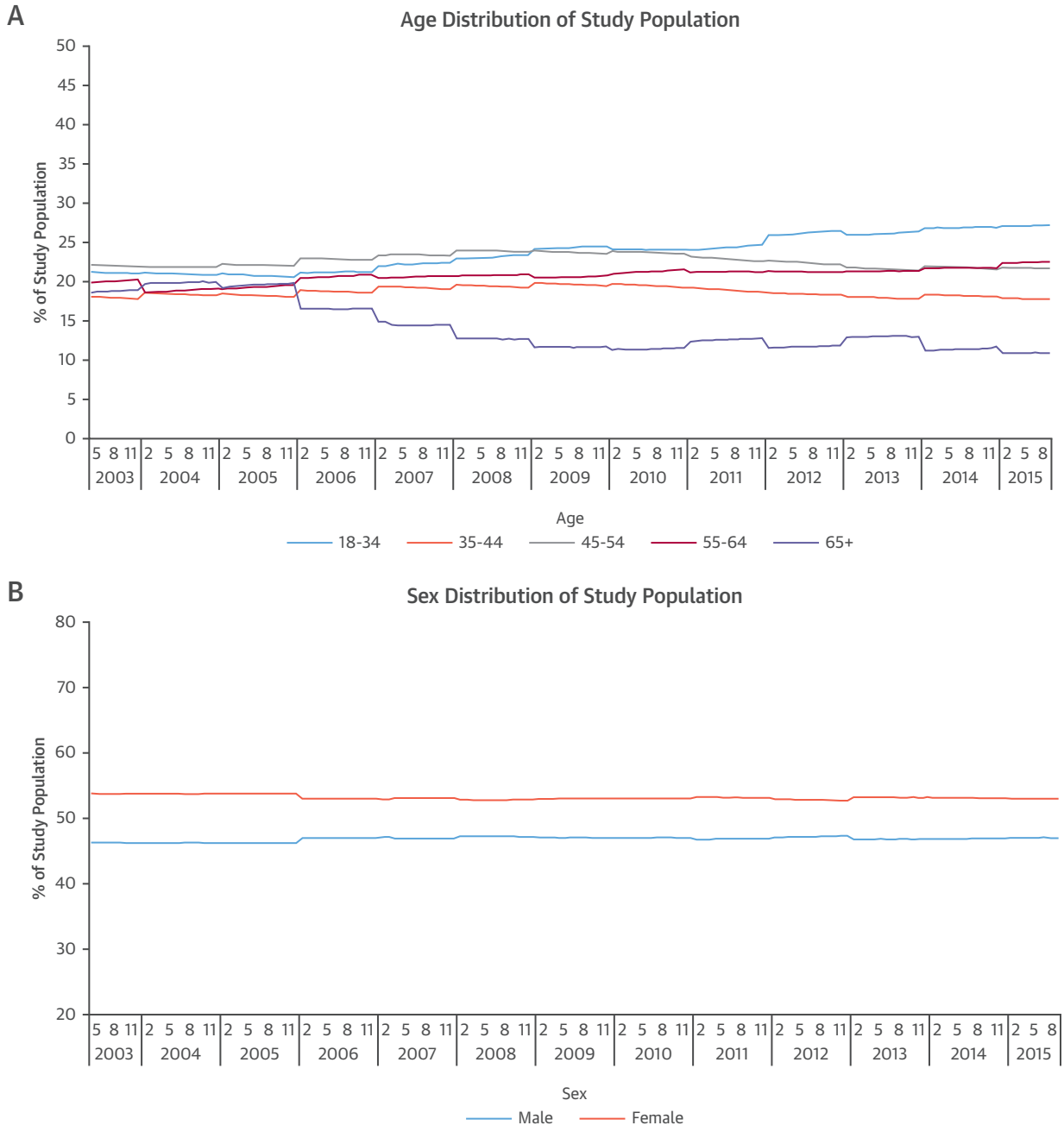
The AHA AP recommendations were first available online on April 19, 2007, but were not published in hard copy until October 2007 (5). Most dentists would not have been aware of the changes until a summary was published in the *Journal of the American Dental Association* in June 2007 (24). Previous studies, however, have shown that it can take 18 months following guideline change for new AP recommendations to be widely adopted (8,21). For descriptive purposes, the data were therefore divided into 3 periods: 1) pre-recommendation (May 1, 2003, through April 31, 2007); 2) transition (18 months from May 1, 2007, through October 31, 2008); and 3) post-recommendation (November 1, 2008, through August 31, 2015). To evaluate for any change, Poisson regression models with exponential conditional means and first-order residual autocorrelation were used so that they imposed a multiplicative relationship between the outcome and the explanatory variables, to model any change in the event rate (events/population) for both AP prescribing and IE incidence using the number of enrollees as a weight (see the Online Methods, for details). The models allowed for pre-recommendation time trends that were linear on the linked (logarithmic) scale. The shift from the pre-recommendation period to transition period was modeled with an intercept change and time trend change; the shift from the transition period to post-recommendation period was modeled with a second slope change but no intercept change. Age group and sex interactions were included as controls to account for demographic influences. The event rates were analyzed separately for high-risk, moderate-risk, and unknown/low-risk enrollees. The Poisson model analysis provided estimates for the level of AP prescribing or IE incidence that would result if the pre-recommendation change trends continued into the future without other factors intervening. By comparing the predicted AP and IE incidence figures in the transition or post-recommendation period estimated from the Poisson model, with and without the 2007 AHA recommendation change in effect, we obtained estimates for the size of changes in AP prescribing rates and IE admission rates associated with the recommendation change, controlling for pre-existing time trends and patient composition. Thus, the Poisson models allowed us to estimate the effect of the recommendations change on level of AP prescribing and IE incidence at specific times after the recommendations change, that is, the difference in the level of AP prescribing or IE incidence/month/100,000 enrollees estimated by the fitted regression models with and without the recommendations in effect.

RESULTS

POPULATION DEMOGRAPHICS. Age and sex distributions of the study population over time are shown in **Figure 1**. Changes in the different health care coverage populations over time are shown in Online Figures 1 to 3. The study included 198,522,665 enrollee-years of data of which 1,266,695 (0.64%) were high risk, 11,733,117 (5.91%) moderate risk, and 185,522,852 (93.45%) unknown/low risk. The ratio of moderate-risk/high-risk enrollees remained relatively constant (**Figure 2**). In the last year of the study, 0.83% of enrollees were high risk and 7.21% were moderate risk. The proportion of high-risk and moderate-risk individuals was higher among Medicare than commercial health care enrollees (Online Figures 4 to 6). In total, there were 20,340 episodes of IE and 1,910,544 AP prescriptions issued. The breakdown of this by risk and health insurer type is show in **Table 1**.

AP PRESCRIBING. In the pre-recommendation period, AP prescribing was decreasing for all risk types (**Central Illustration**). The fall was steeper within the transition period with a shallower downward trend in the post-recommendation period. The Poisson model analyses allowed us to compare the predicted level of AP prescribing at specific time points during the transition and post-recommendation periods with the Poisson model estimate of what the level of AP prescribing would have been at each time point had the pre-recommendation trend in prescribing continued unaltered (**Figure 3**, Online Table 3). By August 2015, there was a 20% overall reduction (0.80 proportional change; 95% confidence interval [CI]: 0.68 to 0.96) in

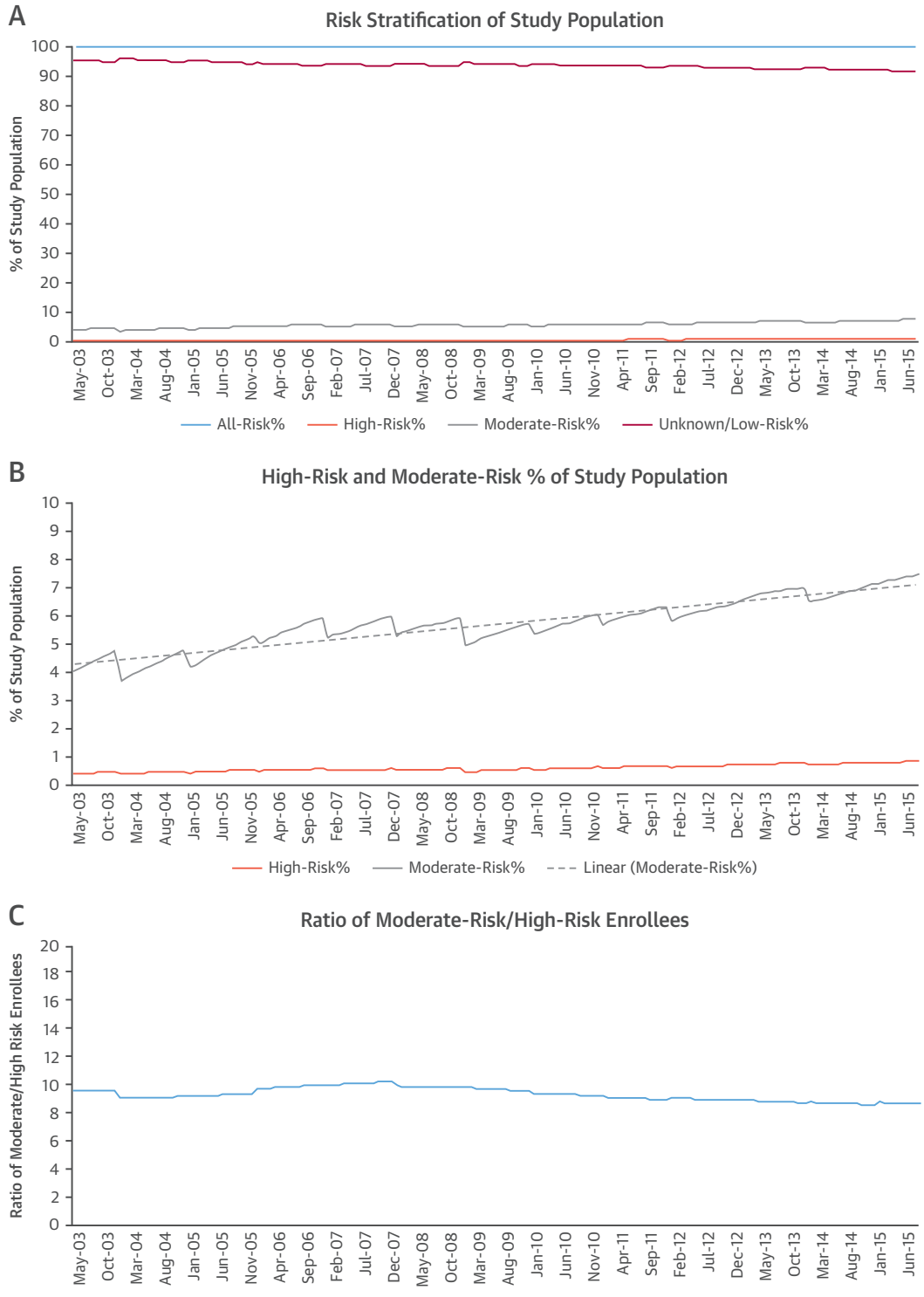
FIGURE 1 **Age and Sex Distribution of Study Population**



Age **(A)** and sex **(B)** distributions of the study population over time.

AP prescribing for individuals at high risk compared with the Poisson model estimate of what AP prescribing would have been had the pre-recommendation trend in AP prescribing continued unaltered, a 64% reduction (0.36 proportional change; 95% CI: 0.32 to 0.41) for those at moderate risk and a 52% reduction (0.48 proportional change; 95% CI: 0.42 to 0.54) for low/unknown-risk individuals. These trends equated to a decrease of 186 (95% CI: 51 to 321) from the Poisson estimate of 953 (95% CI: 818 to 1,088) AP prescriptions/month/100,000 to 767 AP prescriptions/month/100,000 for

FIGURE 2 **The Risk Stratification of the Study Population**



The infective endocarditis (IE) risk stratification of the study population **(A)** with the proportion of the study population at high risk or moderate risk of IE shown in greater detail **(B),** with the linear trend line **(dashed)** for those at moderate risk of IE. Changes in the ratio of those at moderate risk/high risk are also shown **(C)**.

TABLE 1 Number of Enrollees, Cases of IE, and Prescriptions of AP

	Enrollee-Years	IE*	IE/100,000 Enrollee-Years	AP†	AP/100,000 Enrollee-Years
Commercial enrollees					
High-risk	751,556	2,442	324.93	84,980	11,307.21
Moderate-risk	6,661,771	2,680	40.23	233,671	3,507.64
Unknown/low-risk	164,125,685	6,723	4.10	855,424	521.20
Total	171,539,012	11,845	6.91	1,174,075	684.44
Medicare enrollees					
High-risk	515,139	2,211	429.20	62,258	12,085.66
Moderate-risk	5,071,347	2,865	56.49	218,489	4,308.30
Unknown/low-risk	21,397,167	3,149	15.98	455,722	2,129.82
Total	26,983,653	8,495	31.48	736,469	2,729.32
Commercial + Medicare enrollees					
High-risk	1,266,695	4,653	367.33	147,238	11,623.79
Moderate-risk	11,733,117	5,545	47.26	452,160	3,853.71
Unknown/low-risk	185,522,852	10,142	5.47	1,311,146	706.73
Total	198,522,665	20,340	10.25	1,910,544	962.38

*Number of infective endocarditis (IE) cases identified between May 1, 2003, and August 31, 2015. †Number of antibiotic prophylaxis (AP) prescriptions filled between May 1, 2003, and August 31, 2015.

those at high risk, a decrease of 297 (95% CI: 223 to 371) from an estimate of 464 (95% CI: 390 to 538) AP prescriptions/month/100,000 to 167 AP prescriptions/month/100,000 for those at moderate risk and a decrease of 45 (95% CI: 25 to 64) from an estimate of 86 (95% CI: 66 to 105) AP prescriptions/month/100,000 to 41 AP prescriptions/month/100,000 for those at low/unknown risk of IE.

INCIDENCE OF IE. IE incidence was declining in the pre-recommendation period. The rate of decline was highest in individuals at high risk, intermediate for moderate risk, and lowest for low/unknown-risk individuals. In the post-recommendation period, although there remained a slight downward trend in all 3 groups, the rate of decrease was less. Poisson model analyses (**Figure 3**) showed that, compared with the pre-recommendation period, there was an increase in IE incidence in high- and moderate-risk populations in the post-recommendation period relative to what would have been expected without the recommendation change. By August 2015, we estimated there had been a 177% increase (2.77 proportional change; 95% CI: 1.66 to 4.61) above what would have been expected in IE incidence in those at high risk, a 75% increase (1.75 proportional change; 95% CI: 1.03 to 3.00) in the moderate-risk group and no significant increase in the low/unknown-risk group (1.12 proportional change; 95% CI: 0.71 to 1.76). These changes equated to an increase of 19.53 (95% CI: 14.22 to 24.84) from the model-based estimate of 11.04 (95% CI: 5.73 to 16.35) IE cases/month/100,000 to 30.57 IE cases/month/100,000 among those at high risk of IE, an increase of 1.47 (95% CI: 0.44 to 2.50) from an estimate of 1.94 (95% CI: 0.91 to 2.97) IE cases/month/100,000 to 3.41 IE cases/month/100,000 among those at moderate risk of IE and no significant increase in the low/unknown-risk group (0.04 IE case/month/100,000; 95% CI: −0.12 to 0.20).

COST OF INPATIENT IE CARE AND AP PRESCRIPTIONS. The reimbursed costs for inpatient IE care/10,000 enrollees rose throughout the period of study (**Figure 4A**), despite an overall reduction in IE cases. This was because the cost of treating IE cases (**Figure 4B**) increased from an average of $43,978 in the first year to $92,413 in the last year of the study. By contrast, reimbursed AP prescription costs/10,000 enrollees fell (**Figure 4A**) throughout the study. This was partly because of the fall in AP prescribing but also because the reimbursed cost of each AP prescription fell from an average of $5.36 in the first year of the study to $2.00 in the last year. Separate reimbursement costs for commercial, Medicare, and Medicaid providers are provided online (Online Table 4, Online Figure 7).

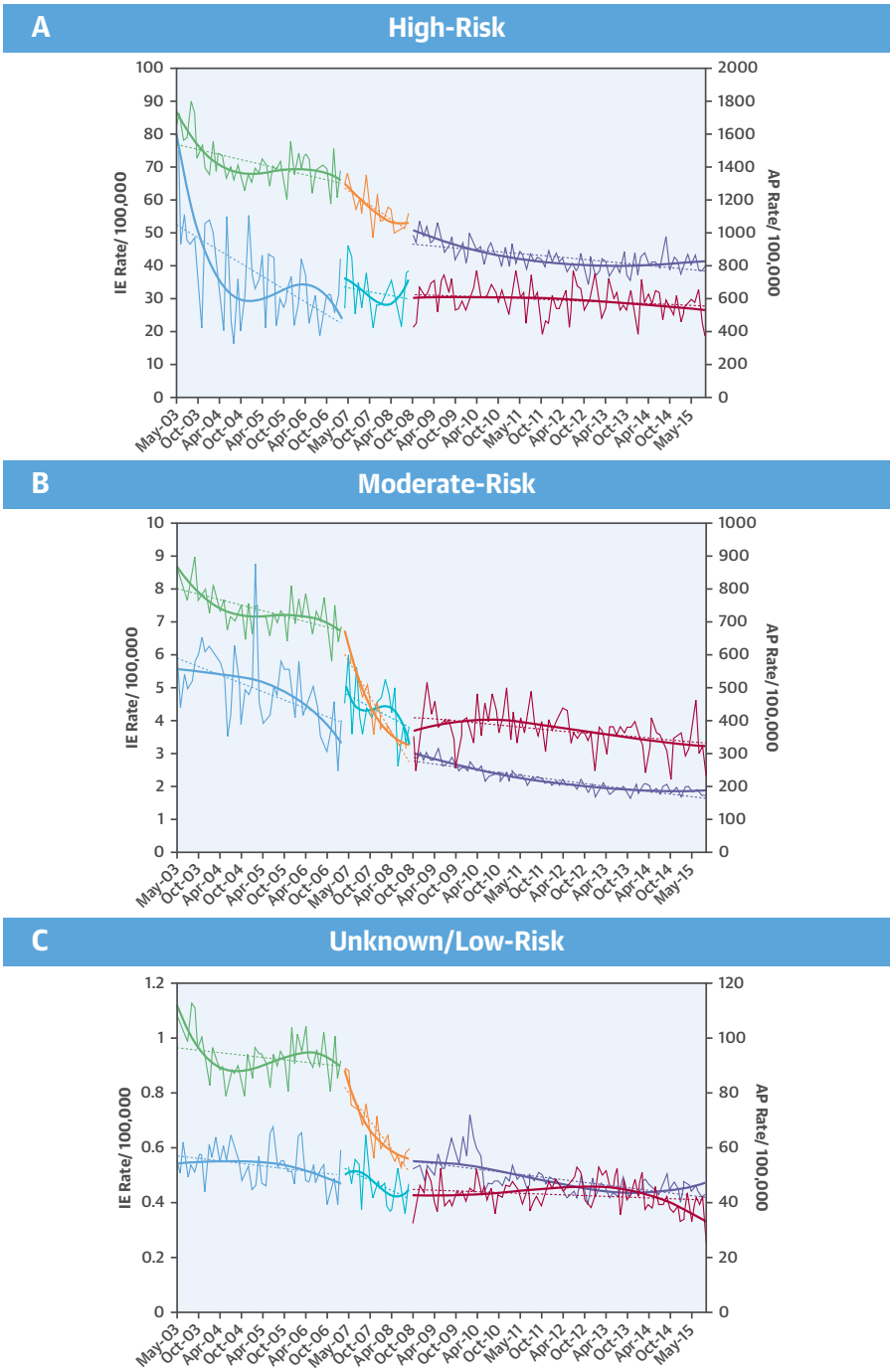
DISCUSSION

This study provides an estimate of the proportions of the U.S. population at moderate (7.21%) or high risk (0.83%) of IE (**Central Illustration**). The proportion of Medicare enrollees at high or moderate risk of IE was much higher than for commercial health care enrollees (Online Figures 4 to 6). This difference may, in part, be due to the older age of patients in the Medicare population with a typically higher burden of chronic valvular disease and cardiac implantable electronic devices. This may also explain the higher overall IE incidence in Medicare patients (**Table 1**).

There was a decline in IE incidence in all 3 risk categories of patients in the period between May 2003 and the change in AHA AP recommendations in April 2007. This may reflect introduction of the modified Duke criteria in April 2000 (25) and increased use of transesophageal echocardiography for IE diagnosis (26). Both interventions increased diagnostic specificity and reduced the number of "definite" IE cases diagnosed by excluding some cases previously considered "possible." Previous studies have reported conflicting trends in IE incidence over the period of the current study (9-16).

AP prescribing before 2007 declined for all 3 risk categories. There was a relatively steep decline between May 2003 and October 2004, followed by a

CENTRAL ILLUSTRATION **Changes in AP Prescribing and IE Incidence**



Thornhill, M.H. et al. J Am Coll Cardiol. 2018;■(■):■-■.

Antibiotic prophylaxis (AP) prescriptions issued/100,000 enrollees **(thin continuous green, orange, and purple lines)** and incidence of infective endocarditis (IE)/100,000 enrollees **(thin continuous blue, cyan, and red lines)** for those at **(A)** high risk, **(B)** moderate risk, and **(C)** unknown/low risk of IE. The curves are divided into 3 periods representing the pre-recommendations change period (May 1, 2003, to April 31, 2007; **green lines** for AP, **blue** for IE), transition period (May 1, 2007, to October 31, 2008; **orange lines** for AP, **cyan** for IE), and post-recommendations change period (November 1, 2008, to August 31, 2015; **purple lines** for AP, **red** for IE). In each case, the monthly data **(thin continuous lines)**, straight trend line **(dashed lines)**, and third-order polynomial curve **(thick continuous line)** are shown.

slight increase. The factors responsible for these trends are not entirely clear. AP prescribing patterns for individuals with low/unknown risk of IE suggest the possibility of some overprescribing that decreased over time. The 1997 AHA recommendations (22), in place before 2007, advised AP for moderate- and high-risk individuals. They also included a more complex list of cardiac conditions and a more extensive list of medical and dental procedures for which AP was recommended. By 2003 to 2004, these recommendations had been in place for several years, and many clinicians were aware of views subsequently embedded in the 2007 guidelines (5), that is, that many patients with cardiac conditions previously included for AP did not need it. Moreover, there was little evidence to support the use of AP for many of the medical procedures previously recommended for coverage, (e.g., genitourinary, gastrointestinal, hepatobiliary, ear, nose, and throat, respiratory tract interventions). These observations, along with concerns about the risk of adverse drug reactions and selection of drug resistance, may have contributed to the pre-2007 fall in AP prescribing.

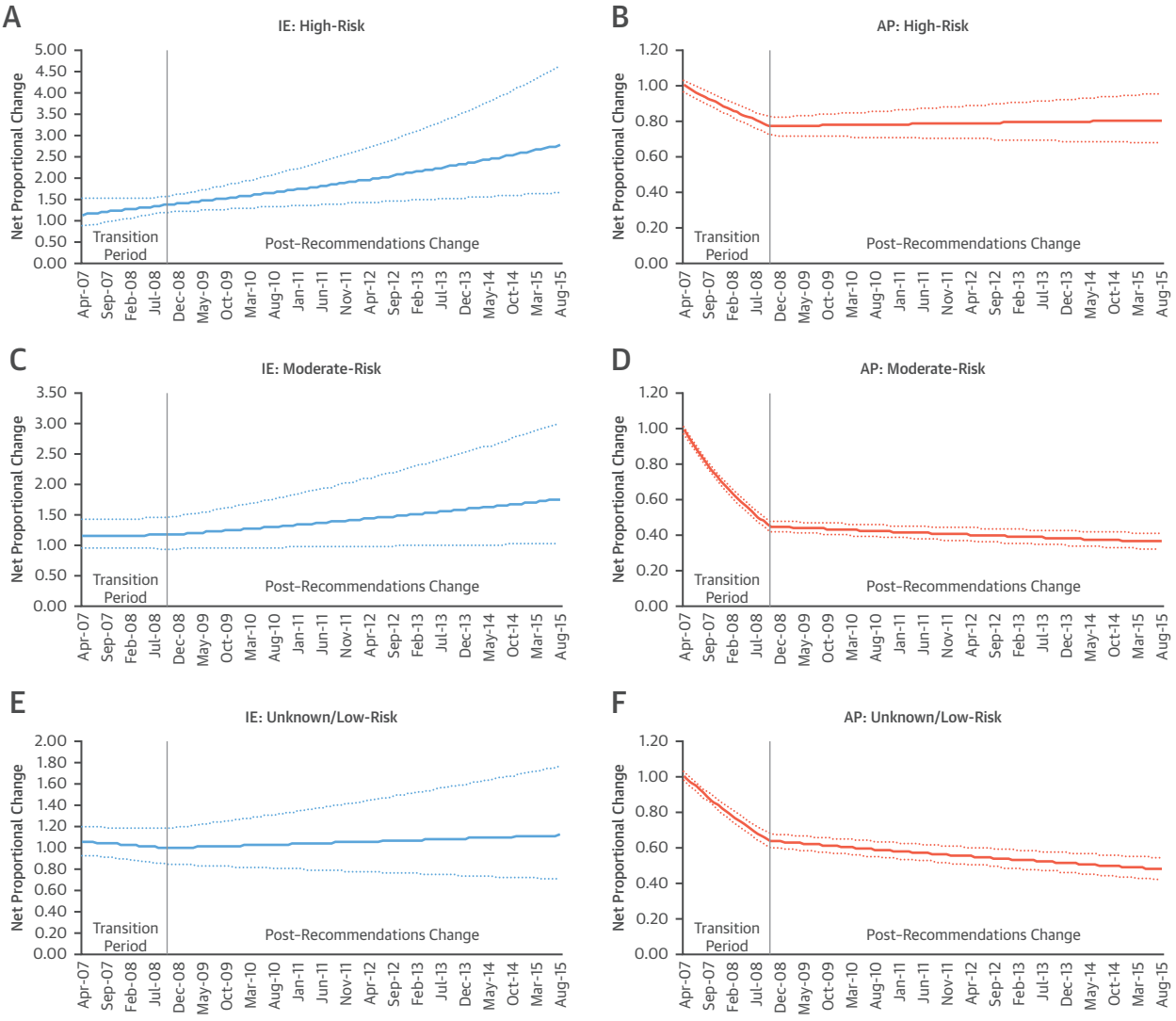
Following publication of the 2007 AHA recommendations (5), there was a significant reduction in AP prescribing. Consistent with the new recommendations, the greatest reduction was among those at moderate risk of IE. AP prescribing in this subset did not, however, fall to zero, with 2,036 AP prescriptions/month/100,000 enrollees still being prescribed by August 2015. Similarly, for those at low/unknown risk of IE, 6,064 AP prescriptions/month/100,000 enrollees were still being prescribed by August 2015. More concerning, however, was the fall of 186 (95% CI: 51 to 321) AP prescriptions/month/100,000 among high-risk individuals. This suggests that despite attempts to simplify recommendations, there is still confusion among clinicians about which patients should and should not receive AP (27–29). A population-based study of AP use in Olmsted County, Minnesota, also demonstrated a fall in AP prescribing for high-risk patients following publication of the 2007 AHA recommendations (30). This may reflect difficulty among dentists in identifying patients at high versus moderate risk, or lack of knowledge about current recommendations. To better understand the factors responsible for the fall in AP prescribing in those at high risk, and the persistence of AP prescribing in those at moderate or low -risk of IE, a questionnaire-based survey has been launched to further investigate the AP prescribing practices of dentists.

Following the recommendations change, there was an increase in IE incidence relative to the period before the change. This was greatest in high-risk individuals, much less in those at moderate risk, despite the much greater reduction in AP prescribing, and nonexistent in individuals at low/unknown risk. Although this does not establish a causal relationship between AP prescribing and IE prevention, our data provide support for the 2007 AHA guidelines that recommend against AP in those with no predisposing cardiac condition, that is, those at low/unknown risk. In individuals at high risk, a modest fall in AP prescribing occurred at the same time as a relatively large increase in IE incidence. These observations would lend support to the current AHA and ESC recommendations that high-risk individuals should receive AP. For those at moderate risk of IE, a much larger fall in AP prescribing occurred at the same time as a small increase in IE incidence, which only reached statistical significance 80 months after the recommendation change, that is, December 2013 (**Figure 3C**, Online Table 3). This suggests that AP is likely to be less effective, if it is effective at all, in the majority of individuals at moderate risk of IE and provides support for the current AHA and ESC recommendations not to give AP to those at moderate risk. It does raise the possibility, however, that a small number of individuals currently considered at moderate risk, such as those with certain other predisposing comorbidities or specific cardiac anomalies, such as bicuspid aortic valve or mitral valve prolapse (31), could benefit from AP and highlights the need for a more detailed evaluation of risk among those currently considered at moderate risk (2).

The cost of treating IE admissions more than doubled between 2000 and 2015 from $43,978 to $92,413, whereas the cost of AP prescriptions more than halved from $5.36 to $2.00. If one assumes that AP is effective, then this would have increased the potential cost effectiveness of AP 5-fold. A recent full health-economic analysis of the effect of the recommendation changes in the United Kingdom found that AP was likely to be highly cost-effective for those at high risk of IE and, depending on the degree of AP efficacy and precise level of risk, could be cost-effective for some patients at moderate risk (32). Nonetheless, it is important that factors other than cost-effectiveness are considered in any decision to recommend AP, such as the potential development of adverse consequences of the infection, antibiotic-related adverse events, and antibiotic resistance.

Numerous studies have attempted to evaluate the change in IE incidence before and after the 2007 AHA recommendations (9–16). These studies have used different methodologies and produced different results as to whether IE incidence has increased,

FIGURE 3 **Change in IE Incidence and AP Prescribing After Compared With Before the Change in Recommendations**

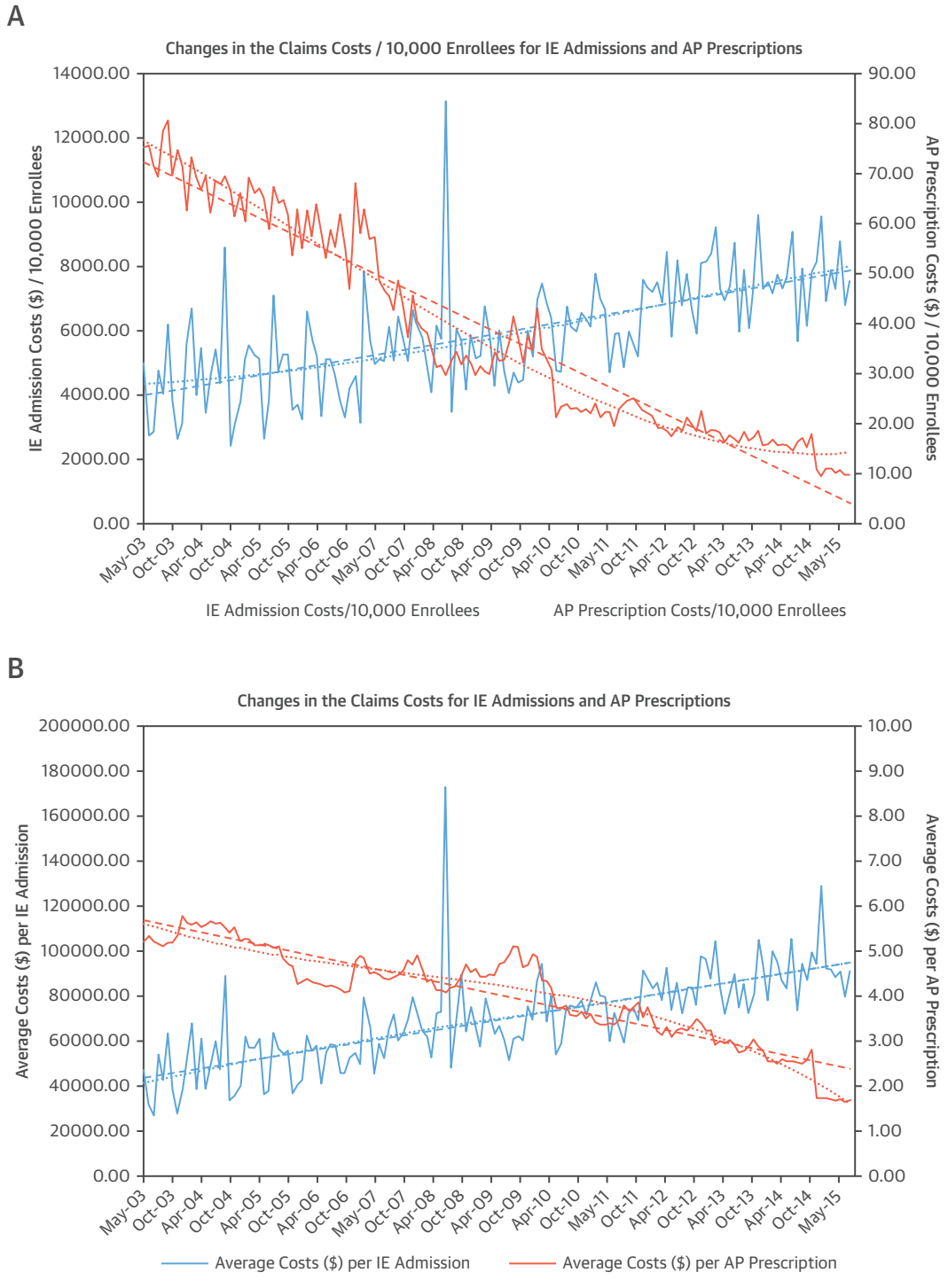


Poisson model analyses showing the proportional monthly change in infective endocarditis (IE) incidence **(A, C, E)** and antibiotic prophylaxis (AP) prescribing **(B, D, F)** during the transition and post-recommendations change periods compared with the period before the recommendation changes for those at high risk **(A, B)**, moderate-risk **(C, D),** or unknown/low risk **(E, F)**. A value of 1 represents no change; values >1 represent an increase and values <1 represent a decrease. The **solid lines** represent the mean change, and the **dotted lines** represent the upper and lower 95% confidence intervals (CIs).

decreased, or remained stable. Some of these investigations even included an examination of the same population (the National Inpatient Sample) and yet reported different results (10,11,13). None have included an evaluation of the concurrent effect of the recommended changes for prescribing AP. The present study is the first to examine the concurrent effects of the recommendation changes on AP prescribing and IE incidence. It is also the first to stratify these changes into the different categories of individual affected, that is, those at high, moderate, and low/unknown risk for IE.

STUDY LIMITATIONS. The data are derived from administrative databases, which are susceptible to misclassification, particularly given that IE diagnosis can be challenging. Nonetheless, a recent study, using ICD-10 codes, equivalent to the ICD-9 codes used in this study, found an administrative database had 0.95 sensitivity (95% CI: 0.86 to 0.99) and 1.0

FIGURE 4 Changes in IE and AP Claims Costs



Claims costs per 10,000 enrollees for IE hospital admissions and AP prescriptions **(A)** and the average claims cost per IE admission and per AP prescription **(B)**. Monthly IE admission costs shown with a **solid blue line** and AP prescription costs with a **solid orange line**. In each case, the linear trend line is shown in the same color **dashed line** and the third-order polynomial curve in the same color **dotted line**. Abbreviations as in Figure 3.

specificity (95% CI: 1.0 to 1.0) for identification of modified Duke criteria definite IE cases (33). Furthermore, coding is performed by trained coding specialists and is based on diagnoses at discharge rather than at admission. Administrative databases also allow larger sample sizes than clinical databases and capture IE hospitalizations in community as well as tertiary hospitals and thereby avoid referral bias. The MarketScan databases provide a very large, nationally representative, sample of Americans with employer-provided health insurance (19,20,34), including Medicare supplementary insurance, but may not generalize to those without employer-provided insurance or the U.S. population as a whole.

This study used CPT and ICD-9 codes to identify those at moderate- or high-risk of IE. To optimize identification of these individuals, we accepted any record (inpatient, outpatient, physician's office. etc.) where 1 of these conditions was recorded at any time before an IE admission (or at any time for those with no IE admissions). Nonetheless, if the only record of a predisposing procedure or condition occurred before January 2000, it would be missed, and they would be considered as low/unknown risk. This could account for some of the AP prescribing and IE incidence identified in this low/unknown-risk group. Nonetheless, the level of AP prescribing, and IE incidence, was small in the low/unknown-risk group compared with the other 2 groups and, despite a decrease in AP prescribing, no increase was seen in IE incidence, suggesting that any misclassification was likely not significant. On the other hand, misclassification could have resulted in an underestimation of the number of individuals at moderate- or high-IE risk.

It would have been of great interest to determine whether the observed increases in IE incidence were due to oral streptococci. Unfortunately, microbiological data are not a component of the MarketScan databases. Furthermore, there are no ICD-9 codes that specifically identify oral streptococci. In addition, recording of ICD-9 supplementary codes that might help identify causal organisms was not a requirement of the health care coverage plans studied. Recording of causal organism data was as low as 25%, and varied over time, between health care coverage plans and among risk groups, making analysis unreliable. The inpatient IE reimbursement health care costs used in this study do not take into account the full health-economic costs resulting from on-going illness, the impact on the patient's quality of life, or the individual, family, and societal costs of chronic illness, unemployment, or premature death (32). Similarly, the AP prescribing costs do not take into account the costs associated with adverse drug reactions (35) or the risk of promoting the selection of antibiotic-resistant bacteria.

Finally, although this study focused on the value of AP coverage of invasive dental procedures to prevent IE, it is likely that more cases of oral streptococcal IE occur as a result of daily activities such as tooth brushing, flossing, and mastication, particularly in those with poor oral hygiene or periodontal disease (36). AP does not, therefore, reduce the importance of maintaining good oral hygiene in the prevention of IE.

CONCLUSIONS

Although our data do not establish a cause-effect relationship between reduction in AP use and increase in IE incidence, they do provide support for the current AHA and ESC recommendations that focus AP on those at high risk of IE. Given the importance that these recommendations place on AP use in this patient subgroup, the fall in AP prescribing in those at high risk is of concern and warrants investigation. The borderline significant IE increase in those at moderate risk of IE, despite a large fall in AP prescribing, is concordant with current guidance that suggests that AP is unlikely to be of benefit in this group as a whole; however, further investigation into specific heart valve conditions within the moderate-risk group may be warranted.

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PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE: Following publication of the American Heart Association/American Dental Association recommendations on antibiotic prophylaxis, more restrictive prescribing of antibiotic prophylaxis was accompanied by an increased incidence in cases of infective endocarditis.

TRANSLATIONAL OUTLOOK: Further studies are needed to determine whether the observed association is causal and, if so, how best to revise recommendations for antibiotic prophylaxis to prevent endocarditis while minimizing the adverse consequences of overprescribing antibiotics.

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KEY WORDS antibiotic prophylaxis, dental procedures, guidelines, infective endocarditis, prevention

APPENDIX For an expanded Methods section as well as supplemental figures and tables, please see the online version of this paper.