Budget Impact of Appropriate Low-Dose Aspirin Use for Primary and Secondary Cardiovascular Event Prevention in the Managed Care Setting

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ABSTRACT

BACKGROUND: Cardiovascular disease remains the leading cause of death in adults in the United States and constitutes a substantial portion of overall national health expenditures. Aspirin is generally recommended for primary cardiovascular event prevention based on a given patient's underlying cardiovascular event risk profile, particularly for those aged 50-69 years with a 10-year risk of coronary heart disease of $\geq 10\%$. Evidence-based clinical guidelines are in agreement for secondary prevention consisting of lifelong, low-dose aspirin therapy following a cardiovascular event. Despite these recommendations, research suggests suboptimal concordance between guidelines and clinical practice.

OBJECTIVE: To evaluate the budget impact of appropriate low-dose aspirin use for primary and secondary cardiovascular event prevention compared with current rates of low-dose aspirin use.

METHODS: An economic model measuring budget spend for cardiovascular events, aspirin, and aspirin-related adverse events was developed from the perspective of a U.S. payer. The model compared current rates of aspirin use to appropriate rates of aspirin use according to guideline recommendations for both primary and secondary cardiovascular event prevention.

RESULTS: For a hypothetical plan with 1 million members, an estimated 18,026 patients were on aspirin therapy for primary cardiovascular event prevention, while guidelines recommend that 55,788 patients should have been on aspirin therapy for this indication. Optimal aspirin use in the primary cardiovascular event prevention population reduced the number of nonfatal myocardial infarctions (MIs; -367), ischemic strokes (-232), and deaths (-60), with an increase in the number of gastrointestinal bleeds (169) and hemorrhagic strokes (98). Evidence-based guideline-compliant use of aspirin for primary cardiovascular event prevention resulted in total cost savings of approximately \$4.2 million over a 5-year time horizon. For secondary cardiovascular event prevention, an estimated 48,663 patients were on aspirin, while clinical guidelines recommend that 71,316 patients should have been on aspirin therapy for this indication. Optimal aspirin use in secondary cardiovascular event prevention reduced the number of nonfatal MIs (-515), ischemic strokes (-375), and deaths (-217), with an increase in the number of gastrointestinal bleeds (98) and hemorrhagic strokes (58). Evidence-based guideline-compliant use of aspirin for secondary cardiovascular event prevention resulted in total cost savings of approximately \$11 million over a 5-year time horizon.

CONCLUSIONS: Appropriate low-dose aspirin use for primary and secondary cardiovascular event prevention can result in improved patient outcomes with significant cost savings for U.S. payers. As a simple and inexpensive prophylactic measure for cardiovascular event prevention, aspirin use should be carefully considered in all appropriate at-risk adult patients.

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What is already known about this subject

- Cardiovascular disease is still the number 1 cause of death in the United States.
- Cardiovascular disease is associated with substantial economic burden; heart conditions and stroke contributed \$116.3 billion and \$17.5 billion in U.S. medical costs, respectively, in 2011.
- Previous studies have demonstrated the health and economic benefits of aspirin use in the prevention of primary and secondary cardiovascular events.

What this study adds

- The appropriate use of low-dose aspirin for the prevention of primary and secondary cardiovascular events can result not only in reduced risk of cardiovascular events but also significant financial savings to U.S. payers.
- This study further validates the link between aspirin's favorable clinical profile and its cost savings to U.S. payers when used in accordance with clinical guidelines.
- Study results support the assertion that aspirin use needs to be more carefully recommended and monitored by health care stakeholders in order to optimize economic and clinical outcomes.

Cardiovascular disease (CVD) is the leading cause of death in adults in the United States,¹ and it constitutes a substantial portion of overall national health expenditures. The American Heart Association (AHA) found that U.S. annual direct health expenditures from heart conditions, hypertension, stroke, and other circulatory disorders over the period of 2012-2013 totaled \$187.7 billion.² Heart conditions alone accounted for \$96.7 billion and were the top diagnosis group in terms of direct health expenditures, followed by trauma-related disorders, mental disorders, and cancer. AHA's 2016 report on projections of CVD prevalence and costs for 2015-2035 found that by 2035, the number of people with CVD is expected to grow to almost 132 million, or 45.1% of the U.S. population.³

Corresponding medical costs of CVD are projected to increase by 135%, from \$318 billion in 2015 to \$749 billion

in 2035, while indirect costs of CVD are projected to increase by 55%, from \$237 billion to \$368 billion over the same period.³ From a humanistic perspective, in 2015, ischemic stroke, hypertensive heart disease, atrial fibrillation, and flutter were estimated to account for over 3.2 million disability-adjusted life-years (DALYs) in the United States, representing a 41% increase from 1990.⁴ These same diseases accounted for approximately 171,000 deaths in 2015, representing a 46% increase from 1990.⁴ Additionally, ischemic heart disease accounted for a staggering 7.7 million DALYs in 2015.⁴ Given that CVD and corresponding cardiovascular events are associated with an outsized economic, morbidity, and mortality burden, it is important to optimize prevention of future cardiovascular events both in patients with no past medical history of cardiovascular events (primary prevention) and in patients who have experienced previous cardiovascular events such as an ischemic stroke or myocardial infarction (MI; secondary prevention). The World Health Organization has said appropriate implementation of interventions to reduce the risk of secondary fatal and nonfatal MIs could prevent nearly one-third of such cardiovascular events.⁵

Aspirin has been commercially available for over a century and has been used as an antiplatelet agent for almost half a century, with major evidence-based clinical guidelines making clear recommendations regarding aspirin use for cardiovascular event prevention.⁶ According to 2002 AHA and 2016 United States Preventive Services Task Force (USPSTF) guidelines for the primary prevention of CVD, aspirin is generally recommended for primary cardiovascular event prevention based on a patient's underlying cardiovascular event risk profile, particularly for those individuals aged 50-69 years with a 10-year risk of coronary heart disease (CHD) of $\geq 10\%$.^{7,8} However, potential cardiovascular benefits must be balanced with potential bleeding risks in order to determine which patients are good candidates for primary prevention with aspirin. For secondary prevention, a multitude of evidence-based guidelines are in agreement that lifelong, low-dose aspirin therapy is warranted following an initial cardiovascular event. Specifically, aspirin for secondary prevention is recommended in AHA guidelines for patients with postcoronary artery bypass graft (CABG), in the American Diabetes Association guidelines for patients with diabetes or atherosclerosis, in American College of Cardiology (ACC)/AHA guidelines for patients with coronary artery disease (CAD), in AHA/ACC guidelines for patients with non-ST-elevation acute coronary syndrome or CABG, in ACC Foundation and AHA guidelines for patients with ST-elevation myocardial infarction, and in AHA/American Stroke Association guidelines for patients after a stroke or transient ischemic attack.⁹⁻¹⁴

Despite widespread recommendations of aspirin for primary and secondary cardiovascular event prevention, aspirin utilization rates have been found to be suboptimal across a number of studies.¹⁵⁻¹⁸ A meta-analysis of 6 trials evaluating

discontinuation of aspirin therapy in CHD (i.e., secondary prevention) patients found that nonadherence or discontinuation of aspirin was associated with a 3-fold increased risk of thrombotic events (odds ratio [OR]=3.1; 95% confidence interval [CI]=1.8-5.6; $P<0.001$) and a 2-fold increased risk of unfavorable CAD-related events (OR=1.8; 95% CI=1.5-2.2; $P<0.001$), demonstrating the deleterious clinical consequences associated with underuse of aspirin.¹⁹

The objective of the present analysis was to evaluate the economic effect of appropriate low-dose aspirin use for primary and secondary cardiovascular event prevention compared with current, suboptimal aspirin utilization rates. It was hypothesized that guideline-recommended use of aspirin for primary and secondary cardiovascular event prevention would result in savings to a hypothetical U.S. payer because of the reduction in downstream cardiovascular events. A budget impact model was created to test this hypothesis.

Methods

Model Overview

An economic model was developed to evaluate the budget impact of appropriate low-dose aspirin use for primary and secondary cardiovascular event prevention from the U.S. payer perspective (Figure 1). The hypothetical plan population consisted of 1 million lives. The model compared current (i.e., real-world) aspirin use versus appropriate guideline-recommended aspirin use in mutually exclusive primary and secondary cardiovascular event prevention cohorts. Current aspirin-use patients were characterized by historical data, and appropriate aspirin use in primary and secondary prevention populations was characterized by evidence-based cardiovascular event prevention guidelines in conjunction with historical data. Current and appropriate aspirin-use rates of cardiovascular events were calculated, and aspirin's effects on the frequency of these events were quantified and applied to both treatment populations. Numbers of significant cardiovascular events and aspirin-related adverse events (AEs) were compared across these 2 utilization-based scenarios in order to understand the clinical effect of appropriate aspirin use. Both pharmacy (i.e., aspirin budget spend) and medical (i.e., cardiovascular events, aspirin-related AEs) cost offsets were compared across current and appropriate-use patients in order to derive the total cardiovascular-related budget spend and, thus, the direct medical cost-related budget impact of maximizing appropriate aspirin use.

Uncertainty in the model was analyzed by a univariate deterministic sensitivity analysis. The model parameters were adjusted up and down one at a time by a set percentage (default 10%) while holding the other parameters constant to assess the influence of each parameter. In addition to the univariate sensitivity analysis, several scenario analyses were performed to test the robustness of the model. The base case of the model

FIGURE 1 Model Overview

AE=adverse event; CVD=cardiovascular disease; MI=myocardial infarction; NHANES=National Health and Nutrition Examination Survey.

uses a 5-year time horizon to examine the long-term implications of appropriate aspirin use. In accordance with the International Society for Pharmacoeconomics and Outcomes Research's Principles of Good Practice for Budget Impact Analysis, discounting was not employed.²⁰ All costs within the analysis were converted to 2016 U.S. dollars using the Consumer Price Index.²¹

Creation of Primary and Secondary Prevention Cohorts.

U.S. Census data were used to determine the age and sex distributions for the entire hypothetical population.²² Patients less than 20 years of age were excluded from the model. After generating age- and sex-related population distributions, the prevalence and risk of CVD were then applied for each respective

patient subgroup defined by age ranges and sex.²³ Using these CVD prevalence and risk data, the secondary cardiovascular event cohort was defined by whether each patient had experienced a previous cardiovascular event and included patients with established CVD (i.e., MI, stroke, or angina). The size of the secondary prevention cohort was derived from the total population expected to have experienced a previous cardiovascular event as reported by CVD prevalence statistics.²⁴ The primary prevention cohort was characterized by determining cardiovascular risk among remaining patients (i.e., those having not previously experienced a cardiovascular event), defined as patients aged 50-69 years without established CVD and a $\geq 10\%$ 10-year risk of CVD. The 10-year risk of CVD was

TABLE 1 10-Year First Cardiovascular Event Risk for the Primary Cardiovascular Prevention Cohort

10-Year Cardiovascular Event Risk, %				
Risk Score	10.0-14.9	15.0-19.9	≥20.0	Totals
Age 50-60 years				
Men	14.5	7.9	2.7	25.1
Women	2.0	0.4	1.1	3.5
Age 60-70 years				
Men	28.9	24.5	23.3	76.7
Women	13.0	4.5	4.6	22.1

based on the 2013 ACC/AHA guideline reporting CVD risk.²³ Ten-year CVD risk was defined as the risk of developing a first cardiovascular event, where first cardiovascular event was defined as nonfatal MI, CHD-related death, or fatal or nonfatal stroke, over a 10-year period among people free from CVD at the beginning of the period.

Determinations of Aspirin Utilization Rates. Current aspirin utilization rates for the primary and secondary prevention cohorts were based on National Health and Nutrition Examination Survey (NHANES) data, where participants who met the primary and secondary prevention cohort definitions were asked whether their provider had instructed them to take aspirin and whether they were currently using aspirin.¹⁵ Appropriate aspirin use for primary and secondary prevention of cardiovascular events was based on current guideline recommendations.^{7-14,25} In accordance with these guidelines, aspirin would be recommended in all patients aged 50-69 years exhibiting a CVD risk $\geq 10\%$ without a history of CVD (i.e., patients within the primary prevention cohort), while all patients in the secondary prevention cohort would bear an indication for aspirin use. The model assumed 100% adherence and compliance for appropriate aspirin use.

Clinical Inputs

Determination of Primary and Secondary Cardiovascular Event Rates. The 10-year risk of a primary cardiovascular event for patients aged 40-79 was derived by applying the age-based risk equations to the NHANES data weighted to a U.S. population consisting of 100,542,000 individuals. Primary cardiovascular events were defined as nonfatal MIs, CHD-related deaths, or fatal or nonfatal strokes. For cardiovascular event calculations, 50% MI and 50% stroke rates were chosen as a default (Table 1).²⁶ The annual incidence of a secondary cardiovascular event was based on a longitudinal cohort study of 12,278 patients in the Kaiser Permanente Northwest CVD registry from 2000 to 2005; incidence rates for patients aged <65 years and ≥ 65 years were assumed to be 2.4% and 3.3%, respectively.²³ Recurrent MI incidence was derived from

a cohort of 387,452 individuals with a primary diagnosis of acute MI between 2004 and 2010 (5.6% for men and 7.2% for women).²⁷ For recurrent stroke, an 8.0% incidence rate was derived from a South Carolina stroke patient cohort.²⁸ The model considered only recurrent cardiovascular events that occur within 1 year of the incident event; thereafter, recurrent risk equals that of a secondary cardiovascular event. Moreover, the model did not allow for new patient entry (i.e., no incident patients were included), and cardiovascular events were assumed to be mutually exclusive; that is, each event was assumed to occur in a unique patient.

Determination of Aspirin's Effectiveness for Primary and Secondary Cardiovascular Event Risk Reduction. The model applied aspirin's conferred relative risk reduction to both utilization scenarios for primary and secondary cardiovascular events and for vascular death. Aspirin effectiveness for primary and secondary prevention was derived from a meta-analysis conducted by the Antithrombotic Trialists' (ATT) Collaboration (Table 2).²⁹ The ATT Collaboration was a meta-analysis of 22 randomized controlled trials comprising 112,000 patients that measured the effects of long-term, regular aspirin use on serious vascular events (i.e., MI, stroke, or vascular death) and major bleeds.

Determination of Baseline and Aspirin-Related AEs. In addition to aspirin-related effectiveness outcomes, the model also measured aspirin safety outcomes. Specifically, the model considered the AEs of gastrointestinal bleeding and hemorrhagic stroke. Risk and rates of gastrointestinal bleeding in men and women were derived from separate studies conducted by Huang et al. (2010, 2011).^{30,31} Furthermore, gastrointestinal bleed rates reported by Huang et al. described episodes in which hospitalization or blood transfusion was necessary; thus, only severe gastrointestinal bleed rates were represented within the model. The risk of hemorrhagic stroke was derived from a pooled estimate from a multitude of clinical trials.³²

All-cause mortality rates in the model were based on those describing the entire U.S. population and were included to capture the number of patients in each prevention cohort who die from both CVD and non-CVD causes.¹ All-cause mortality rates were determined at the 10-year age bracket level, where composite 10-year age brackets were calculated in order to account for both cardiovascular risk and mortality stratified by disparate age groupings.¹

Economic Inputs

Costs for aspirin were derived from Truven Health Analytics' RED BOOK Online.³³ The drug was priced in accordance with the cost of the 325 mg total daily dose (TDD) for the secondary prevention cohort in order to generate a more conservative picture regarding the financial benefits of optimizing aspirin use; this method was employed given that guideline-recommended

Budget Impact of Appropriate Low-Dose Aspirin Use for Primary and Secondary Cardiovascular Event Prevention in the Managed Care Setting

TABLE 2 Aspirin Effectiveness and Safety

Effectiveness/Safety	Event	Relative Risk Reduction, %		Description
Effectiveness (risk reduction)	Nonfatal MI	23 (OR=0.77, 95% CI=0.69-0.86)	31 (OR=0.69, 95% CI=0.60-0.80)	Relative risk reduction for primary and secondary prevention, respectively
	Ischemic stroke	14 (OR=0.86, 95% CI=0.74-1.00)	22 (OR=0.78, 95% CI=0.61-0.99)	
	Mortality	3 (OR=0.97, 95% CI=0.87-1.09)	9 (OR=0.91, 95% CI=0.82-1.00)	
Safety	Gastrointestinal bleed	0.138	0.231	Incidence in male aspirin nonusers and users, respectively
		0.107	0.193	Incidence in female aspirin nonusers and users, respectively
	Hemorrhagic stroke	0.148	0.201	Incidence in aspirin nonusers and users, respectively

CI=confidence interval; MI=myocardial infarction; OR=odds ratio.

doses of aspirin for secondary prevention vary from 81 mg to 325 mg.⁹⁻¹⁴ For the primary prevention cohort, an 81 mg TDD was chosen. Specifically, the annual cost inputs for aspirin were \$17 for an 81 mg TDD and \$20 for a 325 mg TDD. Nonfatal MI costs were derived from National Inpatient Sample (NIS) statistics by mining data for the acute MI principal diagnosis category (cost per episode: \$22,670 in men, \$19,217 in women).³⁴ Ischemic stroke costs were based on NIS statistics given a principal diagnosis category of occlusion or stenosis of precerebral arteries (cost per episode: \$11,317 in men, \$11,125 in women).³⁴ For gastrointestinal bleed costs, the gastrointestinal hemorrhage principal category within NIS data was used (cost per episode: \$10,438 in men, \$9,952 in women).³⁴ Finally, hemorrhagic stroke costs were based on NIS statistics given a principal diagnosis category of acute cerebrovascular disease (cost per episode: \$16,673 in men, \$15,770 in women).³⁴

Both pharmacy (i.e., aspirin budget spend) and medical (i.e., cardiovascular events, aspirin-related AEs) cost offsets were compared across the 2 aspirin utilization scenarios in order to quantify budget spend. Accordingly, costs represented those of aspirin-related care incurred by U.S. payers regardless of whether those costs fall under the medical benefit or pharmacy benefit and absent any patient or provider cost-sharing schemes such as deductibles, copays, or coinsurances.

Results

Base Case Model Outputs

For a plan with 1 million members over a 5-year time horizon, an estimated 18,026 patients were on regular low-dose aspirin for primary prevention, while clinical guidelines recommend that 55,788 patients should have been on aspirin for primary cardiovascular event prevention. This represents a 32.3% appropriate utilization rate, suggesting that approximately 67% of patients in the model were not using aspirin for primary cardiovascular event prevention when clinically indicated. Furthermore, it was found that appropriate aspirin use reduced

the number of nonfatal MIs (-367), ischemic strokes (-232), and deaths (-60) and increased the number of gastrointestinal bleeds (169) and hemorrhagic strokes (98; Figure 2). Given these cumulative cost offsets, evidence-based guideline-compliant use of aspirin for primary prevention resulted in total cost savings of approximately \$4.2 million over the 5-year time horizon (Figure 3).

For secondary cardiovascular event prevention, an estimated 48,663 patients were on regular low-dose aspirin therapy, while guidelines recommend that 71,316 patients should be on aspirin for this indication. This represents a 68.2% appropriate utilization rate. In terms of AE and secondary cardiovascular event rates, appropriate aspirin use reduced the number of nonfatal MIs (-515), ischemic strokes (-375), and deaths (-217), with an increase in the number of gastrointestinal bleeds (98) and hemorrhagic strokes (58; Figure 2). Evidence-based guideline-compliant use of aspirin for secondary cardiovascular event prevention resulted in total cost savings of approximately \$11 million (Figure 3).

Sensitivity Analysis

The univariate deterministic sensitivity analysis reported that the model was most sensitive to the percentage of patients recommended aspirin for secondary cardiovascular event prevention, aspirin compliance for secondary cardiovascular event prevention, and total population size. Other parameters with a large influence on budget impact were cost of MI, effectiveness of aspirin in secondary prevention patients, and incidence of secondary events in patients aged ≥65 years. The parameters with the least influence on budget impact were aspirin's effectiveness on mortality for primary and secondary prevention patients and percentage of women aged 50-59 years with a CVD risk of ≥10%. The univariate sensitivity analysis was robust to changes in the variation percentage as the order of the parameters remained the same at ±30%, with total savings to the plan over 5 years remaining over \$8 million.

Budget Impact of Appropriate Low-Dose Aspirin Use for Primary and Secondary Cardiovascular Event Prevention in the Managed Care Setting

FIGURE 2 Primary and Secondary Cardiovascular Event Prevention: Cardiovascular Events and AEs

AE = adverse event; MI = myocardial infarction.

Scenario Analyses

When the 100% adherence and compliance assumption was reduced to 90% for appropriate aspirin use, the savings for primary prevention and secondary prevention were reduced to nearly \$3.5 million and approximately \$7.5 million, respectively. When the adherence and compliance assumption was reduced to 80%, the savings for primary prevention and secondary prevention were reduced to approximately \$2.9 million and \$4 million, respectively, suggesting significant savings for a health plan even with reduced levels of adherence and compliance. When the annual cost input for 81 mg aspirin was used instead of 325 mg, savings for secondary prevention were slightly higher by approximately \$300,000, representing an additional 3% in cost savings.

In scenario analyses varying multiple model parameters at the same time, the largest impact was seen when increasing by 10% both compliance in the secondary prevention patients and percentage of patients recommended aspirin for secondary prevention under the current aspirin utilization model arm, with savings for the secondary prevention cohort decreasing from nearly \$11 million to just over \$6 million. In a scenario analysis varying the 5 parameters with the largest impact by 10%—aspirin recommended by physician (secondary prevention), aspirin compliance (secondary prevention), the total plan population, the cost of MI, and the aspirin efficacy for nonfatal MI—the total savings for primary and secondary

prevention decreased from over \$15 million to nearly \$7.8 million. The scenario analyses showed the model to be robust to changes in the key model parameters.

Discussion

The results of this budget impact model suggest that aspirin is underused for prevention of primary and secondary cardiovascular events in the United States and that appropriate use of this therapy could result in significant avoidance of additional cardiovascular events and significant financial savings. Specifically, the model estimated that aspirin utilization rates are currently 32.3% and 68.2% for primary and secondary prevention, respectively. As such, it is necessary to allocate resources to minimize the gap between current aspirin utilization rates and appropriate aspirin utilization rates. Given that current use for primary prevention is particularly low from relative and absolute perspectives, it seems prudent to apply substantial effort to increase the frequency of health care providers recommending and monitoring appropriate primary cardiovascular event prevention with aspirin use. Moreover, eliminating the gap between current aspirin utilization rates and appropriate utilization rates would result in cost savings of \$4.2 million and \$11 million for primary and secondary prevention populations, respectively, despite increased incidences of aspirin-related gastrointestinal bleeds and hemorrhagic strokes. The savings realized when the 81 mg aspirin

Budget Impact of Appropriate Low-Dose Aspirin Use for Primary and Secondary Cardiovascular Event Prevention in the Managed Care Setting

FIGURE 3 Primary and Secondary Cardiovascular Event Prevention Total Costs

AE = adverse event; MI = myocardial infarction.

annual cost input was used instead of the 325 mg annual cost input was modest relative to the overall savings in the base case (approximately \$300,000 compared with \$11 million), where the base case model outputs were primarily driven by the 660 fewer cardiovascular events and cardiovascular-related deaths incurred for primary prevention patients and 1,107 fewer such events incurred for secondary prevention patients.

These findings are consistent with the clinical and economic effects noted in recent studies. One study, employing a dynamic microsimulation model that included Americans aged 50 years and older, concluded that if older Americans with elevated risk of CVD take low-dose aspirin every day, the intervention would save 900,000 lives over the next 20 years, improve life expectancy by 0.3%, and save \$692 billion in health care costs by 2036.³⁵ Moreover, a number of cost-effectiveness and cost-utility analyses from the U.S. payer perspective have found that aspirin for primary cardiovascular event prevention is cost-effective.³⁶⁻³⁸ At least 1 aspirin-related public health intervention has been found to be cost-effective as well. Specifically, Michaud et al. (2015) undertook a cost-effectiveness analysis of a statewide campaign to promote aspirin use for primary prevention of CVD events.³⁹ Inputs for the study were derived from real-world aspirin utilization and CVD rates and estimates from the scientific literature. They found that the campaign strategy dominated no intervention, where the campaign conferred health savings of \$28-\$160 per patient and incremental quality-adjusted life-years of 0.001 per patient. These studies reflect our own

in that they support assertions that appropriate aspirin use is beneficial from economic and clinical perspectives.

Most studies of aspirin use for primary and secondary prevention have found aspirin to be underutilized in its intended primary and secondary prevention populations, driven by low prescribing rates and low patient adherence, persistence, and compliance.¹⁵⁻¹⁸ In fact, a study designed to evaluate the temporal changes in primary prevention aspirin use following the release of the 2009 USPSTF recommendations found the recommendations were not associated with an increase in aspirin use.⁴⁰ The data supporting the present model's inputs for current and appropriate aspirin use are consistent with such underuse, and the findings of this analysis emphasize the value of aspirin in the prevention of costly downstream cardiovascular events. Of note, studies have also shown that patients may be regularly taking aspirin for primary prevention when aspirin is not indicated. These cross-sectional studies reported inappropriate use in 13%-18% of patients under examination.^{41,42} Given these results, in conjunction with the present study's results, aspirin use needs to be more prudently recommended and carefully monitored by providers and better tracked by managed care organizations (MCOs) and pharmacy benefit managers to ensure that it is being used appropriately on a patient-by-patient basis.

In 2010, Manson et al. (2010) reported results of an analysis on the budget impact of appropriate aspirin use in distinct primary and secondary prevention CVD populations across 1 million patients over a 10-year time horizon.⁴³ Savings to the

theoretical MCO given full compliance with guidelines totaled \$79.6 million for primary cardiovascular event prevention patients and \$32.2 million for secondary cardiovascular event prevention patients versus \$4.2 million and \$11 million, respectively, in the present analysis.

Differences across these 2 studies can be primarily attributed to assumptions pertaining to overall size of the treated aspirin population. For example, Manson et al. included patients aged ≥ 18 years in the primary prevention cohort (vs. restricting to patients aged 50 years or older, per updated guideline recommendations), and made patients eligible for primary prevention with aspirin if they had a 5-year risk of 3% or higher (vs. a 10-year $\geq 10\%$ risk given guideline recommendations). Moreover, the present analysis uses Healthcare Cost and Utilization Project (HCUP) cost data from 2014 inflated to 2016 dollars, while the previous model uses HCUP cost data from 2005. Despite these differences in inputs and assumptions, both analyses suggested substantial cost savings associated with appropriate aspirin use.

Finally, Zhang et al. (2017) conducted a budget impact analysis of fixed-dose combination (FDC) enteric-coated 325 mg aspirin plus immediate-release omeprazole 40 mg for prevention (i.e., secondary) of cardiovascular events. The FDC was associated with \$81 million to \$190.9 million in savings over 1- and 5-year time horizons, respectively, for a hypothetical plan consisting of 1 million patients.⁴⁴

The findings of the present study can be generalized to those U.S. managed care populations that include patients whose demographics match those of national averages for CVD prevalence and risk, as many inputs for these models are derived for national data sources. In populations with higher levels of CVD and CVD risk, appropriate aspirin use is likely to be associated with cost savings of a larger magnitude.

Additionally, MCOs and other U.S. payers will derive greater or lesser budget spend-related benefits from aspirin-use optimization policies depending on how closely their population's current aspirin utilization rates are to guideline-recommended appropriate utilization rates. Given that appropriate aspirin use is associated with well-evidenced and nontrivial clinical and economic benefits in primary and secondary cardiovascular event prevention, MCO and U.S. payer policies and patient- and provider-targeted incentives should be implemented to promote optimal aspirin use, adherence, persistence, and compliance.

Limitations

Like any economic model, the validity of the model results are a function of the reliability of the model inputs and corresponding assumptions, where not all model inputs may be relevant for all model audiences. Also, the model did not account for patients entering the health plan as new beneficiaries or leaving the plan because of disenrollment. One data-centric limitation

is that current aspirin use was based on patient reports of aspirin recommendation rates contained within NHANES data¹⁵; given that these assumptions are derived from patient-reported data, the true rate of aspirin recommendation rates may be overestimated or underestimated because of patient recall bias. Furthermore, this model's projected effectiveness benefits for aspirin were extrapolated in part from clinical trial efficacy data and not from real-world population estimates. Finally, as aspirin is available over the counter, its use is not precisely captured in claims databases, which limited the robustness of claims data used as inputs to measure aspirin use.

Conclusions

Bridging the gap between current aspirin use and appropriate low-dose aspirin use for primary and secondary cardiovascular event prevention can result in improved patient outcomes with corresponding significant cost savings to U.S. payers. Greater use of 81 mg aspirin is associated with incremental cost savings over the 325 mg TDD because of the lower aspirin price. As a simple and inexpensive prophylactic intervention for cardiovascular event prevention, aspirin use should be carefully considered in all appropriate at-risk adult patients.

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Budget Impact of Appropriate Low-Dose Aspirin Use for Primary and Secondary Cardiovascular Event Prevention in the Managed Care Setting

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Corrections

Glycemic Efficacy, Weight Effects, and Safety of Once-Weekly Glucagon-Like Peptide-1 Receptor Agonists

Handelsman Y, Wyne K, Cannon A, Shannon M, Schneider D, *J Manag Care Spec Pharm.* 2018;24(9-a):S14-S29

In the *JMCP* September 2018 supplement "Once-Weekly GLP-1 Receptor Agonists for the Management of Type 2 Diabetes: A Review of Clinical and Health Economic Data," body weight change data from the AWARD-6 study were presented incorrectly in the article cited above. In Figure 2B on page S20 and related narrative text on page S19, the mean changes in body weight in the AWARD-6 study should have been reported as -3.6 kg with liraglutide and -2.9 kg with dulaglutide 1.5 mg. Readers are encouraged to access the corrected version which is freely available online at: <https://www.jmcp.org/doi/pdf/10.18553/jmcp.2018.24.issue-9-a>.