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

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BACKGROUND

- Cardiovascular disease (CVD) is the leading cause of death among adults in the United States (US)[1]
  - A first fatal or non-fatal myocardial infarction (MI) or stroke occurs in more than 1.2 million people each year[2,3]
  - Over 500,000 people in the US die annually due to coronary heart disease and stroke[2,3]
  - Due to the projected increase in CVD prevalence in the US, direct medical costs associated with CVD are expected to total $749 billion by 2035, and indirect costs are expected to reach $368 billion by 2035[4]
- Aspirin continues to be recommended by multiple clinical guidelines for secondary prevention of cardiovascular (CV) events as part of standard of care[5]
- The American College of Cardiology (ACC) and the American Heart Association (AHA) published new updated primary prevention guidelines in 2019 recommending aspirin for adults aged 40 to 70 years based on patients' totality of evidence for atherosclerotic cardiovascular disease (ASCVD) risk, balanced with their risk of bleed, taking into account factors such as 10-year ASCVD risk estimate, family history of premature MI, and elevation in coronary artery calcium score[6]
- Despite long-standing evidence-based clinical guideline recommendations on the use of aspirin for primary and secondary CV prevention, multiple studies report suboptimal use of aspirin for these indications[7-9]
- A previous budget impact model presented at AMCP Nexus 2017 found that appropriate evidence-based guideline-driven use of aspirin for primary and secondary CV event prevention led to improved patient outcomes and resulted in a total cost savings of nearly $15 million dollars over a 5-year time horizon for a 1 million-member plan[10]

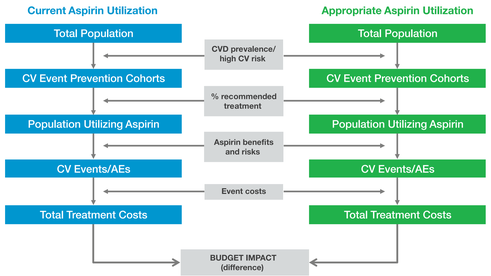
OBJECTIVES

- The objective of this analysis was to update the 2017 budget impact analysis and evaluate the budget impact of appropriate aspirin utilization per 2019 primary prevention guidelines and most recent secondary CVD prevention guidelines compared with current estimated aspirin utilization rates

METHODS

- An economic model measuring total spend for CV events, aspirin therapy, and aspirin-related adverse events (AEs) was developed from the perspective of a US payer (**Figure 1**)
  - The model compares current rates of aspirin utilization to appropriate aspirin utilization rates according to the most recent secondary prevention guidelines and the 2019 ACC/AHA recommendations on primary prevention of CV events
- CV events captured in this model were MI, ischemic stroke, and angina
- To determine the secondary prevention cohort, US census data were used to estimate the distribution of the plan population by age and sex, and then the prevalence of MI, ischemic stroke, and angina were applied[11,12]

Figure 1. Model Overview



Key: AE – adverse event; CV – cardiovascular; CVD – cardiovascular disease.

- The primary prevention cohort was derived by determining the CV risk among the remaining patients (ie, those without CVD), and included patients aged 40 to 69 years with a 10-year CVD risk ≥10% who were candidates for aspirin therapy according to their totality of evidence for ASCVD risk
- In the base case of the primary prevention cohort, 50% of patients aged 40 to 69 years with 10-year ASCVD risk ≥10% were assumed to be candidates for aspirin therapy based on clinician-patient risk discussions. The baseline annual incidence of a secondary CV event was 2.4% for ages <65 years and 3.3% for ages >65, and was based on rates seen in a 5-year longitudinal cohort study[13]
- The model considered recurrent ischemic stroke or MI within 1 year of the incident event in both the primary and secondary prevention cohort[14]
  - Post-MI recurrence risk: 5.6% for males; 7.2% for females
  - Post-ischemic stroke recurrence risk: 8.0% for both males and females
- Aspirin efficacy was based on the Antithrombotic Trialists' Collaboration (ATTC), a meta-analysis of serious vascular events and major bleeds in 6 primary prevention trials and 16 secondary prevention trials comparing long-term aspirin use to a control group (**Table 1a, 1b**)[15]

Table 1a. Aspirin Efficacy for Primary Prevention (Risk Reduction)

Event	Risk Reduction	95% CI
Nonfatal MI	23%	0.77 (95% CI: 0.69, 0.86)
Ischemic stroke	14%	0.86 (95% CI: 0.74, 1.00)
Mortality	3%	0.97 (95% CI: 0.87, 1.09)

Table 1b. Aspirin Efficacy for Secondary Prevention (Risk Reduction)

Event	Risk Reduction	95% CI
Nonfatal MI	31%	0.69 (95% CI: 0.60, 0.80)
Ischemic stroke	22%	0.78 (95% CI: 0.61, 0.99)
Mortality	9%	0.91 (95% CI: 0.82, 1.00)

Key: MI – myocardial infarction.

- Adverse events (AEs) associated with aspirin use included GI bleeds and hemorrhagic stroke[16-18] (**Table 2**)

Table 2. AE Rates for Aspirin and Non-Aspirin Users (Primary and Secondary Prevention)

	Aspirin Users		Non-Aspirin Users	
	Males	Females	Males	Females
GI bleed	0.231%	0.193%	0.138%	0.107%
Hemorrhagic stroke	0.201%	0.201%	0.148%	0.148%

Key: AE – adverse event; GI – gastrointestinal.

- Costs in the model included aspirin pharmacy cost (wholesale acquisition cost), and medical costs associated with ischemic stroke, non-fatal MI, gastrointestinal (GI) bleeds, and hemorrhagic stroke[19,20] (**Table 3**)

Table 3. Cost Inputs

Cost Inputs	Males	Females
Aspirin therapy 81 mg (annual cost)	$17	$17
Aspirin therapy 325 mg (annual cost)	$20	$20
CV event costs		
Nonfatal MI	$24,127	$20,430
Ischemic stroke	$11,540	$10,951
Costs associated with AEs for aspirin		
GI bleed	$10,913	$10,101
Hemorrhagic stroke	$20,548	$17,826

Key: AE – adverse event; CV – cardiovascular; GI – gastrointestinal.

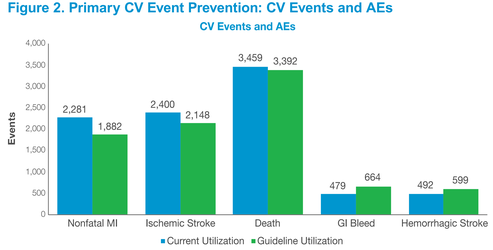
- The budget impact was calculated based on the total costs for patients within the plan assumed to be compliant with physician-recommended aspirin therapy compared to the total costs for the plan if all guideline-recommended patients were taking aspirin
- Current real-world aspirin utilization rates for primary and secondary prevention of CV events were determined based on the National Health and Nutrition Examination Survey (NHANES) 2011–2012 data[7]
  - Primary prevention: 40.9% of high-risk patients eligible for primary CV event prevention were recommended by their physicians to take aspirin, and 79% of these patients were compliant
  - Secondary prevention: 75.9% of patients eligible for secondary CV event prevention were recommended by their physicians to take aspirin, and 89.9% of these patients were compliant

RESULTS

Primary prevention

- In a plan with 1 million members, an estimated 10,139 patients were on low-dose aspirin for primary CV event prevention over a 10-year time horizon, while clinical guidelines recommend that 31,380 patients should be taking aspirin for this indication
- Appropriate aspirin use in this patient population would result in 399 fewer nonfatal MIs, 252 fewer ischemic strokes, 67 fewer deaths, 185 more GI bleeds, and 107 more hemorrhagic strokes (**Figure 2**)
  - By comparison, appropriate aspirin use according to pre-2019 clinical guidelines for primary CV event prevention would have resulted in 367 fewer nonfatal MIs, 232 fewer ischemic strokes, 60 fewer deaths, 169 more GI bleeds, and 98 more hemorrhagic strokes over a 5-year time horizon[10]

Figure 2. Primary CV Event Prevention: CV Events and AEs



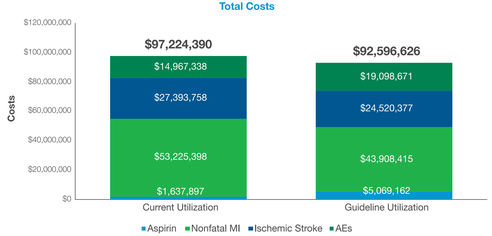
Key: AE – adverse event; CV – cardiovascular; GI – gastrointestinal.

- Evidence-based guideline-driven use of aspirin for primary CV event prevention would result in a cost savings of over $4.6 million over 10 years in a 1 million-member plan (**Figure 3**)
  - By comparison, appropriate aspirin use according to pre-2019 clinical guidelines for primary CV event prevention would have resulted in a cost savings of over $4 million over 5 years in 1-million member plan[10]

Secondary Prevention

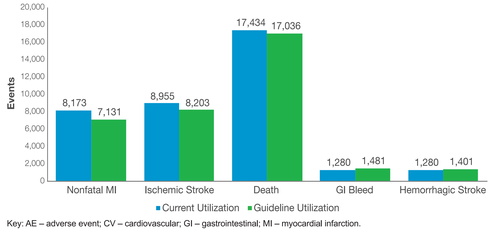
- An estimated 53,345 patients were on aspirin for secondary CV event prevention, while clinical guidelines recommend that 78,179 patients should be on aspirin for this indication
- Appropriate guideline-directed aspirin use for secondary prevention would result in 1,042 fewer nonfatal MIs, 752 fewer ischemic strokes, 398 fewer deaths, 201 more GI bleeds, and 121 more hemorrhagic strokes over 10 years in a 1 million-member plan (**Figure 4**)
  - Similarly, the 2017 budget impact analysis found that appropriate aspirin use for secondary CV event prevention would have resulted in 515 fewer nonfatal MIs, 375 fewer ischemic strokes, 217 fewer deaths, 98 more GI bleeds, and 58 more hemorrhagic strokes over a 5-year time horizon[10]
- Evidence-based guideline-driven use of aspirin for this patient population would result in a cost savings of nearly $23 million over 10 years in a 1 million-member plan (**Figure 5**)
  - Similarly, the 2017 budget impact analysis found that appropriate aspirin use for secondary CV event prevention would have resulted in a total cost savings of nearly $11 million over a 5-year time horizon[10]

Figure 3. Primary CV Event Prevention Total Costs



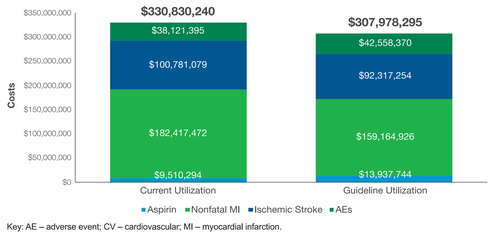
Key: AE – adverse event; CV – cardiovascular; MI – myocardial infarction.

Figure 4. Secondary CV Event Prevention: CV Events and AEs



Key: AE – adverse event; CV – cardiovascular; GI – gastrointestinal; MI – myocardial infarction.

Figure 5. Secondary CV Event Prevention Total Costs



Key: AE – adverse event; CV – cardiovascular; MI – myocardial infarction.

CONCLUSIONS

- Despite updated 2019 guidelines suggesting that fewer patients may be eligible for aspirin therapy for primary CV event prevention, appropriate low-dose aspirin utilization for primary and secondary CV event prevention can still result in improved patient outcomes, with a significant cost savings for a managed care plan
- The use of aspirin for appropriate populations remains suboptimal in clinical practice, in spite of long-standing evidence-based clinical guideline recommendations
- Aspirin use should be considered in all appropriate at-risk adult populations, and patient adherence should be monitored by both providers and payers

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