

The Role of Aspirin in the Prevention of Cardiovascular Disease

Sunitha V. Ittaman, MD; Jeffrey J. VanWormer, PhD; and Shereif H. Rezkalla, MD

Aspirin therapy is well-accepted as an agent for the secondary prevention of cardiovascular events and current guidelines also define a role for aspirin in primary prevention. In this review, we describe the seminal trials of aspirin use in the context of current guidelines, discuss factors that may influence the effectiveness of aspirin therapy for cardiovascular disease prevention, and briefly examine patterns of use. The body of evidence supports a role for aspirin in both secondary and primary prevention of cardiovascular events in selected population groups, but practice patterns may be suboptimal. As a simple and inexpensive prophylactic measure for cardiovascular disease, aspirin use should be carefully considered in all at-risk adult patients, and further measures, including patient education, are necessary to ensure its proper use.

Keywords: Non-steroidal anti-inflammatory agents; Aspirin/history/therapeutic use; Cardiovascular diseases/drug therapy; Coronary artery disease

Aspirin is the most widely used drug in medicine. In 2007, the Agency for Healthcare Research and Quality (AHRQ) reported that nearly 20% of adults in the United States reported taking aspirin daily or every other day, with this number increasing to nearly 50% in those aged 65 and older.¹ Aspirin is also one of the oldest drugs in use, with a history dating back to the period of Hippocrates and Galen, when the bark of the willow tree was famous for its analgesic and anti-inflammatory properties. Records show its widespread use by ancient Mesopotamian, Greek, and Chinese civilizations. In 1758, in the first recorded clinical trial in history, Reverend Edward Stone of the Royal Society of London demonstrated the efficacy of ground, dried bark from the English willow tree for treating the symptoms of malaria. However, aspirin as we know it today was not introduced for public use until 1904, following a series of attempts at extraction and purification of salicylic acid from willow bark and subsequent modification to acetylsalicylic acid to reduce the unpleasant side effects.² In addition to its

anti-inflammatory properties, aspirin was also observed to increase bleeding time, and later studies demonstrated the utility of aspirin as an anti-thrombotic agent.³

It was not until 1971 that aspirin's exact pharmacological mechanism of action of irreversible cyclooxygenase (COX) inhibition and related suppression of prostaglandin production was discovered. Later studies demonstrated that the antithrombotic effects of aspirin were the result of acetylation of COX in platelets.³ Low-dose aspirin regimens (≥ 30 mg/day) can effectively suppress platelet aggregation without affecting important endothelial cell functions.⁴ In contrast, inhibition of inflammatory cell function requires higher, more frequent dosing.² The major drawback to continuous aspirin use is the risk of major gastrointestinal, and more rarely, intracranial bleeding, that can occur at any dose. Other side effects, such as hypertension and gastrointestinal or renal toxicity, are usually dose-related.

Corresponding Author: Shereif Rezkalla, MD, FACP; Department of Cardiology; Marshfield Clinic; 1000 N Oak Ave; Marshfield, WI 54449; Tel: (715) 387-5845; Fax: (715) 389-5757; Email: rezkalla.shereif@marshfieldclinic.org

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Table 1. Summary of trials evaluating aspirin for primary prevention of serious cardiovascular events.

Trial	BDT ¹⁶	PHS ¹⁷	TPT ¹⁸	HOT ¹⁹	PPP ²⁰	WHS ²¹	POPADAD ²²	JPAD ²³	AAA ²⁴
Country	United Kingdom	Unites States	United Kingdom	Multinational	Italy	United Stated	Scotland	Japan	United Kingdom
Year	1988	1989	1998	1998	2001	2005	2008	2008	2010
Study design	Randomized, open label	Randomized, double blind, placebo controlled	Factorial, double blind, placebo controlled	Factorial, double blind, placebo controlled	Randomized, open label, 2x2 factorial	Randomized, double blind, placebo controlled	Randomized, double blind, placebo controlled	Randomized, open label	Randomized, double blind, placebo controlled
Number of patients	5,139	22,071	5,085	18,790	4,495	39,876	1,276	2,539	3,350
Number of women	0	0	0	8,883	2,583	39,876	713	1,153	2,412
Aspirin dose	500 mg/day	325 mg every other day	75 mg/day	75 mg/day	100 mg/day	100 mg every other day	100 mg/day	81 or 100 mg/day	100 mg/day
Duration of therapy	5.8 years	5 years	6.8 years	3.8 years	3.6 years	10.1 years	6.7 years	4.4 years	8.2 years
Risk in aspirin group									
Any CV event	NS	NR	NR	RR=0.85 (95% CI 0.73-0.99)	RR=0.77 (95% CI 0.62-0.95)	RR=0.91 (95% CI 0.80-1.03)	HR=0.98 (95% CI 0.76-1.26)	HR=0.80 (95% CI 0.58-1.10)	HR = 1.03 (95% CI 0.87-1.27)
MI	NS	RR=0.56 (95% CI 0.45-0.70)	20% reduction (95% CI 1-35)	RR=0.64 (95% CI 0.49-0.85)	RR=0.69 (95% CI 0.38-1.23)	RR=1.02 (95% CI 0.84-1.25)	NS	HR=0.81 (95% CI 0.49-1.33)	NS
Stroke	NS	RR=1.22 (95% CI 0.93-1.60)	3% reduction (95% CI -45-35)	RR=0.88 (955 CI 0.78-1.24)	RR=0.67 (95% CI 0.36-1.27)	RR=0.83 (95% CI 0.69-0.99)	NS	HR=0.84 (95% CI 0.53-1.32)	NS
CV-specific mortality 6% decrease		RR=0.96 (95% CI 0.60-1.54)	NR	RR=0.95 (95% CI 0.75-1.20)	RR=0.56 (95% CI 0.31-0.99)	RR=0.95 (95% CI 0.74-1.22)	HR=1.23 (95% CI 0.79-1.93)	HR=0.10 (95% CI 0.01-0.79)	NR
All-cause mortality	NS	RR=0.95 (95% CI 0.79-1.15)	6% increase (95% CI -28-12)	RR=0.93 (95% CI 0.79-1.09)	RR=0.81 (95% CI 0.58-1.13)	RR=0.95 (95% CI 0.85-1.06)	HR=0.93 (95% CI 0.71-1.24)	HR=0.90 (95% CI 0.57-1.14)	HR=0.95 (95% CI 0.77-1.16)

BDT, British Doctors' Trial; PHS, Physicians' health Study; TPT, thrombosis prevention trial; HOT, hypertension optimal treatment; PPP, Primary Prevention Project; WHS, Women's Health Study; POPADAD, Prevention of Progression of Arterial Disease and Diabetes; JPAD, Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes; AAA, Aspirin for Asymptomatic Atherosclerosis; CV, cardiovascular; MI, myocardial infarction; NS, not significant; NR, not reported; RR, relative risk; HR, hazard ratio; CI, confidence interval

The use of a low-dose aspirin regimen as an anti-thrombotic measure has become increasingly common. However, recent evidence suggests discrepancies exist between clinical guidelines for the use of aspirin therapy for primary and secondary cardiovascular disease (CVD) prevention and actual patient use patterns.^{5,6} Here we review and describe the literature to support the use of aspirin for primary and secondary CVD prevention, as well as the role of clinical guidelines in patient and physician practices.

Aspirin in Secondary Prevention

Patients who suffer from one or more CVD events, such as myocardial infarction (MI) or ischemic stroke, are at very high risk for another CVD event. While rescue procedures, such as percutaneous coronary intervention (PCI), are aimed at stabilizing acute events, aspirin therapy may actually serve to prevent subsequent CVD events. The role of aspirin in reducing CVD mortality and repeat events after acute MI was first demonstrated in the second International Study of Infarct Survival (ISIS-2) trial.⁷ In this study, 17,187 patients from 417 hospitals were enrolled within 24 hours after onset of suspected acute MI and randomized to receive: (i) a 1-hour intravenous infusion of 1.5 MU of streptokinase; (ii) one month of 160 mg/day enteric-coated aspirin; (iii) both treatments; or (iv) neither. Aspirin use resulted in a significant

reduction in non-fatal reinfarction, stroke, 5-week vascular mortality, and all-cause mortality.⁷ Although other, smaller trials showed similar benefits for patients with a history of previous MI, the ISIS-2 trial was the first to provide evidence of a direct effect of aspirin on acute MI, demonstrating that one month of low-dose aspirin started immediately after MI in 1000 patients would prevent 25 deaths and 10 to 15 nonfatal infarcts and strokes. Additional mortality benefits were observed with longer duration of aspirin therapy.⁷

Since the ISIS-2 trial, many other groups have demonstrated similar results when aspirin is used for secondary prevention of CVD events. In 2002, the Antithrombotic Trialists' Collaboration analyzed 16 trials of long-term aspirin use with doses ranging from 50 – 1500 mg/day for secondary prevention of CVD events, including over 17,000 subjects and 3,306 serious vascular events.⁸ In these trials, aspirin use resulted in significant reductions in serious vascular events including stroke and coronary events in both men and women and low dose regimens (75 – 100 mg/day) were found to be as effective as higher doses.⁸ Aspirin use as a secondary prevention measure for serious CVD events is well-accepted and recommended by several major organizations.⁹⁻¹³

Aspirin in Primary Prevention

Secondary prevention following a serious CVD event is necessitated by the high risk for a repeat event. However, initial CVD events can be fatal or disabling, making primary prevention an important consideration as well.¹⁴ The notion that aspirin could be used for primary CVD prevention existed before its well-established use for secondary prevention. More than half a century ago, Dr. Lawrence Craven introduced the concept of aspirin therapy for primary prevention of MI and frequently recommended aspirin therapy to his patients.³ Dr. Craven worked as a general practitioner at the Glendale Memorial Hospital in California and was fascinated by the etiology of MI. Noting an increased risk of bleeding in patients who received aspirin gums for pain relief after tonsillectomy, Craven hypothesized that aspirin's antithrombotic properties would be beneficial for preventing MI. Craven conducted informal clinical trials of aspirin for prevention of MI with positive outcomes and ultimately recommended aspirin for primary CVD prevention in males aged 45–65 years. It is interesting to note that Craven's recommendations are remarkably similar to the present guidelines for the use of aspirin in primary CVD prevention. Since Craven's early descriptions, several major trials have examined the use of aspirin for primary prevention, as outlined in table 1. The role of aspirin for primary CVD prevention remains controversial, however, particularly in Europe, due largely to the potential for major bleeding as an adverse effect.¹⁵

In the last 30 years, nine major trials have examined the benefit of aspirin for primary CVD prevention, including the British Doctors' Trial,¹⁶ Physicians' Health Study,¹⁷ Thrombosis Prevention Trial,¹⁸ Hypertension Optimal Treatment,¹⁹ Primary Prevention Projects,²⁰ Women's Health Study,²¹ Prevention of Progression of Arterial Disease and Diabetes,²² Japanese Primary Prevention of Atherosclerosis,²³ and Aspirin for Asymptomatic Atherosclerosis²⁴ trials (table 1). Trial results were published between 1988 and 2010 and included a mix of healthy subjects and subjects with elevated CVD risk based on signs of underlying atherosclerotic disease or the presence of diabetes mellitus. Aspirin doses ranged from 50 mg to 650 mg per day, with all trials after 1998 prescribing 100 mg or less. Trial results were mixed to some degree, but the preponderance of evidence suggested that aspirin could decrease CVD risk,^{19,20} including MI¹⁷⁻¹⁹ and stroke.²¹ When cardiovascular and all-cause mortality was assessed, no statistically significant effect on all-cause mortality was observed, but the Primary Prevention Project and Japanese Primary Prevention of Atherosclerosis trials noted a significant reduction in cardiovascular-specific mortality secondary to regular aspirin use of 100 mg/day.^{20,23}

Several meta-analyses have been conducted to evaluate the collective outcomes of the studies described above. Three recent meta-analyses examined the effects of aspirin on risk of any serious cardiovascular event, myocardial infarction, stroke, cardiovascular-specific mortality, and all-cause

mortality in the more than 100,000 subjects included in the nine major trials described above. Bartolucci et al,²⁵ Berger et al,²⁶ and Seshasai et al²⁷ found a significant decrease in the risk of serious cardiovascular events, including nonfatal myocardial infarction, stroke, or cardiovascular death, with use of aspirin. Odds ratios (ORs) ranged from 0.85 (95% CI 0.79–0.92) to 0.90 (95% CI 0.85–0.96). Seshasai et al²⁷ also demonstrated an overall reduction in all-cause mortality (OR=0.84, 95% CI 0.88–1.00), but this was not observed in the other two meta-analyses.^{25,26} Despite the apparent benefits of aspirin therapy for primary CVD prevention, some meta-analyses suggest that the benefits may be outweighed by the risk of major bleeding.^{26,27,28}

Several groups have investigated possible solutions for maintaining the benefits of aspirin therapy while reducing the risk for bleeding. In a 2009 meta-analysis, the Antithrombotic Trialists' Collaboration examined six primary prevention trials including over 95,000 subjects.²⁸ Interestingly and unfortunately, the main risk factors for CVD were similar to those for major bleeding.²⁸ To ameliorate the risk of gastrointestinal bleeding, several groups demonstrated the utility of co-administration of a proton-pump inhibitor,²⁹⁻³¹ which was later recommended concurrent with aspirin in those at high-risk for ulcer bleeding.^{32,33} Others hypothesized that aspirin could be replaced with another anti-thrombotic agent to reduce CVD risk while eliminating the bleeding risk. However, in two prospective clinical trials, Chan et al³⁴ and Lai et al³⁵ demonstrated that the combination of aspirin and esomeprazole was superior to clopidogrel for the prevention of recurrent ulcer bleeding. Despite its inferiority as an agent for prevention of CVD, clopidogrel can be considered in eligible patients with a mild intolerance to aspirin.

A recent study by Brighton et al³⁶ showed no reduction in recurrent thromboembolic events with aspirin use of 100 mg/day, but there was a clear reduction in the occurrence of other serious cardiovascular events by 34% ($P = 0.01$) compared to the placebo group. In addition, no differences in bleeding or other serious adverse events were observed.³⁶ Despite the relatively small reduction in mortality demonstrated in trials of aspirin for primary CVD prevention, there is a clear reduction in the risk of incident CVD events and several organizations, including the American Heart Association (AHA), the American College of Chest Physicians, the U.S. Preventative Task Force (USPSTF), and the European Society of Cardiology (ESC), have concluded that aspirin is beneficial and safe for primary CVD prevention when used properly.¹⁵ Considering the conflicting data, physicians must be cognizant of their role in assessing the potential for benefit and subsequent risk of bleeding in individual patients prior to making recommendations.

Aspirin and Gender Differences

Well known differences exist in the epidemiology of vascular events in men and women. Men are more prone to stroke and MI, yet women are more likely to die from these events than

men.¹² Similarly, meta-analysis results suggest that there are also gender differences in the effects of aspirin on CVD, whereby risk of MI appears to be reduced in men and risk of stroke appears to be reduced in women.^{28,37} Current guidelines for the use of aspirin for CVD prevention take these differences into consideration. Aspirin use in males is primarily intended for the prevention of coronary artery disease, while in females, prevention of stroke is the main target.¹² The reason for differences in the effect of aspirin therapy by gender is currently unknown, but evidence suggests that there may be some biological basis for these differences. For example, baseline platelet reactivity is greater in women than in men, with higher residual reactivity following aspirin treatment in women.³⁸ As such, physicians should also be sure to consider gender-specific risks, benefits, and guidelines for aspirin therapy prior to making patient recommendations.

Aspirin and Diabetes

Much of the ongoing controversy regarding the utility of aspirin for prevention of cardiovascular disease surrounds use in patients with diabetes. Individuals with diabetes have a 2–4 fold increased risk for serious cardiovascular events as a result of increased coronary thrombus formation, increased platelet reactivity, and worsened endothelial dysfunction.³⁹ Few of the early studies on aspirin focused specifically on patients with diabetes. The Early Treatment Diabetic Retinopathy Study included patients with type 1 and 2 diabetes mellitus and some degree of retinopathy.⁴⁰ Cardiovascular outcomes were compared in patients given 650 mg of aspirin daily versus placebo as a secondary study outcome. A significant reduction in fatal and nonfatal MI was observed in the aspirin group.⁴¹ Based on these findings, and findings from the above-mentioned trials, in 2007, the AHA and American Diabetes Association issued joint guidelines recommending aspirin as a primary prevention strategy in patients with diabetes at increased cardiovascular risk, including those over age 40 or with other risk factors such as family history of cardiovascular disease, hypertension, smoking, dyslipidemia, or albuminuria.⁴² However, later studies that focused on patients with diabetes exclusively, including the Prevention of Progression of Arterial Disease and Diabetes²² and Japanese Primary Prevention of Atherosclerosis With Aspirin for Diabetes²³ studies, provided limited evidence for heart health benefits with aspirin use in patients with diabetes and no history of CVD. A 2010 meta-analysis by Zhang et al⁴³ focused on the benefits and risks of aspirin therapy in patients with diabetes in seven trials involving 11,618 patients with diabetes and found no significant reduction in either serious cardiovascular events or all-cause mortality. However, sex-specific effects on MI and stroke were observed, consistent with previous studies. The meta-analysis authors hypothesize that the more neutral role of aspirin in this population may be the result of side effects, such as gastrointestinal bleeding and aspirin resistance.⁴³ In light of these findings, the American Diabetes Association now recommends that low-dose aspirin be

prescribed primarily for men over age 50 and women over age 60 who have diabetes and at least moderate CVD risk or who have had a previous MI or stroke.³⁹ Given these guidelines and the findings described above, it is important for physicians to remember that, despite the increased risk for CVD in patients with diabetes, simply having diabetes does not qualify a patient for aspirin therapy. Physicians must still perform a proper cardiovascular and bleeding risk assessment before making patient recommendations.

Ongoing Aspirin Trials

Despite the widespread use of aspirin for CVD prevention and the recommendation for such treatment by many prominent medical organizations, regional controversies regarding aspirin use remain.¹⁵ For example, the Canadian Cardiovascular Society (CVS) maintains that the number of primary serious cardiovascular events prevented is offset by the risk of bleeding.¹⁰ An additional concern of the CVS is the age of the primary prevention trials, which occurred before the widespread use of other prevention therapies such as statins.^{10,17} As such, additional studies are currently ongoing including the Aspirin in Reducing Events in the Elderly (ASPREE) study,⁴⁴ Aspirin and Simvastatin Combination for CV Events Prevention Trial in Diabetes (ACCEPT-D),⁴⁵ and A Study of Cardiovascular Events in Diabetes (ASCEND).⁴⁶ The ASPREE trial is being conducted jointly in the United States and Australia to compare use of low-dose aspirin to a placebo control in patients age 65 and older over a period of 5 years.⁴⁴ The ACCEPT-D trial is an Italian, open-label, primary prevention study comparing use of 100 mg aspirin to no aspirin in patients over 50 years of age with diabetes and on simvastatin.⁴⁵ The ASCEND trial is being conducted in the United Kingdom to compare use of 100 mg aspirin/omega-3 fatty acid versus placebo control in men and women over age 40 with type 1 or 2 diabetes mellitus and no prior cardiovascular events.⁴⁶ Most recently, the Aspirin to Reduce Risk of Initial Vascular Events trial began and is designed to examine the efficacy of low-dose aspirin for the prevention of several vascular events including fatal and nonfatal MI, stroke, and sudden cardiac death in men over age 50 and women over age 60 with no known congestive heart disease, but at moderate CVD risk.⁴⁷ Physicians should be mindful of these ongoing trials and be ready to adapt practices if necessary pending outcomes, especially in patients on or who may benefit from combination therapy with aspirin and statins.

Current Guidelines for Aspirin Use

Nearly all major heart health organizations have made recommendations regarding aspirin use for CVD prevention, including the AHA/American Stroke Association,^{9,14,48} American College of Chest Physicians (ACCP),¹³ USPSTF,¹² CVS,¹⁰ and ESC.¹¹ Organizational guidelines are in relative agreement for secondary prevention with life-long, low-dose aspirin therapy recommended following a CVD event.⁹⁻¹³ As previously intimated, however, the guidelines for primary CVD prevention are more variable (table 2). With the exception of the CVS, aspirin is generally recommended for

Table 2. Recommendations for low-dose aspirin therapy.

Organization	Primary Prevention	Secondary Prevention
American Heart Association/American Stroke Association ^{9,14,48}	Recommended for persons whose cardiovascular risk is sufficiently high for the benefits to outweigh the risks associated with treatment (10-year risk of cardiovascular events greater than 6 – 10%).	Heart attack and stroke survivors are recommended to regularly take low-dose aspirin for secondary prevention.
American College of Chest Physicians ¹³	Recommended in all patients \geq 50 years of age.	Recommend use of low-dose aspirin or clopidogrel for all patients with established cardiovascular disease.
U.S. Preventive Services Task Force ¹²	Recommended for men ages 45 – 79 when potential benefit due to reduction in myocardial infarction outweighs potential harm due to increased bleeding. Recommended for women ages 55 – 79 when potential benefit due to reduction in ischemic strokes outweighs the potential harm due to increased bleeding.	Same as primary prevention.
Canadian Cardiovascular Society ¹⁰	Use not recommended in men or women without evidence of manifest vascular disease.	Recommend indefinite therapy with low-dose aspirin for all patients following a serious cardiovascular event.
European Society of Cardiology ¹¹	Recommended when the 10-year risk of cardiovascular mortality is markedly increased and blood pressure is controlled.	Recommend life-long, low-dose aspirin therapy in all patients with established cardiovascular disease, including those with diabetes, unless contraindicated.

primary CVD prevention based on a given patient's underlying CVD risk profile. Difficulties arise when defining CVD risk, as many scoring systems and other metrics have been developed, but their availability and ease of use varies in different settings.^{15,49} For example, the AHA guidelines are based on the Framingham Risk Score,⁵⁰ while the ESC uses the Systematic Coronary Risk Evaluation model for cardiovascular disease mortality.⁵¹ The USPSTF recently performed a systematic review of CVD risk assessment tools and found that patient characteristics, such as comorbid diabetes mellitus, also affect the validity of scoring systems.⁴⁹ In contrast, the ACCP makes no stipulations regarding CVD risk, stating only that low dose aspirin therapy is recommended for persons \geq 50 years of age without symptomatic CVD, while recognizing that those who are averse to taking medication for a prolonged period of time for only small benefit are unlikely to use aspirin prophylactically.¹³

Despite certain inconsistencies, all guidelines are clear that aspirin is inappropriate for patients with aspirin intolerance and those at increased risk of gastrointestinal bleeding or hemorrhagic stroke, which is usually evident from a previous history of such conditions. These aspirin contraindications are relatively uncommon, however, and the benefits of CVD risk

reduction typically outweigh the bleeding risks for most patients at high CVD risk. Note that aspirin doses of 75 mg to 162 mg per day are typically better tolerated and are as effective as higher doses in conferring cardiovascular protection.¹⁴

Extensive review of the literature revealed a strong favor toward the use of low dose aspirin therapy for the primary prevention of CVD. While guidelines are somewhat controversial, several resources exist to help physicians make decisions with their patients. For example, the USPSTF guidelines provide a table that can help physicians assess risk versus benefit associated with aspirin use in primary prevention.¹² Of note, a recent study showing evidence of a reduction in colon cancer mortality in patients attributable to low dose aspirin therapy is likely to result in additional all-cause mortality benefits and to make a positive impact on patient and provider attitudes regarding aspirin use.⁵²

Aspirin and Patient Use Patterns: Are We Using it the Right Way?

Aspirin has been commercially available for over a century and used for antithrombotic purposes nearly as long. Despite clinical guidelines governing the use of aspirin for primary

and secondary CVD prevention, evidence suggests that aspirin use remains suboptimal. In a meta-analysis of two studies examining use of low-dose aspirin therapy for secondary prevention, adherence was found to be approximately 65% (95% CI 53–77).⁵ Efforts to increase adherence to aspirin therapy for secondary prevention may therefore be worthwhile. Aspirin use patterns for primary CVD prevention may be even more troublesome. A recent study by VanWormer et al⁶ suggests that, across the population of Wisconsin adults without CVD or diabetes, aspirin is simultaneously underused by those at high CVD risk and overused by those at low CVD risk (per USPSTF guidelines). Specifically, among those clinically indicated for aspirin therapy, only 31% reported using aspirin regularly, whereas among those not clinically indicated for aspirin therapy, 18% reported regular aspirin use. These findings suggest that providers need to play a bigger role in educating patients, perhaps by becoming more aware of the evidence base themselves. Development of clinician-led programs to ensure that patients undergo regular screening for aspirin use may be not only beneficial to patient practices,⁶ but may also be relatively easy to implement in the era of widely-used electronic medical records (EMRs). Prompting in the EMR may remind physicians that low-dose aspirin is recommended for primary CVD prevention,^{12,14,48} but that individual risk factors as well as the risks and benefits associated with aspirin use should be considered on a case-by-case basis. In each case, patient education regarding both the potential benefits and harms of aspirin therapy should be given equal attention.

Conclusion

The benefit of low-dose aspirin therapy for the secondary prevention of serious cardiovascular events is clear, but the use of aspirin for the primary prevention of CVD remains challenging due to mixed findings on mortality benefit.¹⁰ Based on the available evidence, the USPSTF and AHA have put forth recommendations for the use of aspirin therapy in primary prevention with clearly delineated populations expected to benefit from use.^{12,14,48} Despite the availability of evidence-based guidelines for aspirin therapy in both primary and secondary prevention populations (table 2), aspirin therapy is both underused^{5,6} and overused⁶ for reasons not yet understood. These could be related to patient beliefs⁵³ or clinician preferences. Therefore, more research is needed in this area to optimize aspirin use in the groups most likely to benefit. Several trials are currently ongoing and may shed additional light on lingering concerns regarding the precise efficacy of aspirin therapy. In the interim, primary care physicians are urged to categorize their patients based on individual risk factors and to assess the risks and benefits associated with aspirin use on a case-by-case basis.⁶ The ability to prevent serious cardiovascular events and their associated sequelae with a single, inexpensive pill makes low-dose aspirin therapy worth considering.

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Author Affiliations

*Sunitha V. Ittaman, MD**; *Jeffrey J. VanWormer, PhD†*; *Shereif H. Rezkalla, MD‡*

**Department of Internal Medicine, Marshfield Clinic, Marshfield, WI USA*

†Epidemiology Research Center, Marshfield Clinic Research Foundation, Marshfield, WI USA

‡Department of Cardiology, Marshfield Clinic, Marshfield, WI USA