

Aspirin for Primary Prevention: A Challenging Decision

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Aspirin for primary prevention of cardiovascular disease (CVD) remains a challenging issue for clinicians, patients, and health policy makers. Even with the availability of multiple randomized trials and several high-quality systematic reviews and meta-analyses, significant debate remains about which patients, if any, should be offered aspirin for primary prevention.^{1–5} The main US guideline-issuing organizations, including the US Preventive Services Task Force and the American Heart Association, have made recommendations in favor of aspirin use for primary prevention in people with increased CVD risk who are not at high risk for aspirin's adverse effects.^{6,7} Others have recommended against aspirin use for most patients without a prior history of CVD events.⁸ Recently, the US Food and Drug Administration issued a statement reaffirming that “[it] has reviewed the available data and does not believe the evidence supports the general use of aspirin for primary prevention of a heart attack or stroke.”⁹

Much of the debate about aspirin's use for primary prevention centers on 2 key issues: (1) how to integrate information on potential benefits derived from multiple trials that were performed in heterogeneous populations, that used a range of doses of aspirin, and that were conducted in the context of differing availability of other effective interventions, such as statins; and (2) how to assess whether the potential benefits outweigh the known harms of aspirin, including gastrointestinal bleeding and, less commonly but more seriously, hemorrhagic stroke. Most analyses accept the general concept that aspirin will be more clearly indicated for people at higher CVD risk because even a modest reduction in

relative risk of CVD events would offer net benefit after taking into account aspirin's effects on bleeding.

The potential stakes of the aspirin decision are enormous. Decisions about aspirin for primary prevention could apply to the more than 100 million US adults aged 40 to 75 years. CVD remains a leading cause of morbidity and mortality in this age group and results in more than \$200 billion in direct and indirect care costs.¹⁰ Cost-effectiveness analyses have suggested that aspirin, if modestly effective for CVD prevention, could extend lives and reduce health care costs, particularly in higher-risk patients.^{11,12} An analysis by the Prevention Priorities Project ranks aspirin near the top of all preventive services in terms of cost-effectiveness and ability to reduce burden of suffering.¹³ Alternatively, if the downsides of aspirin exceed its benefits (overall or in people below a certain level of CVD risk), widespread use could cause large amounts of morbidity and deflect health resources from better uses.

Given the importance of this issue and its controversy, it is surprising that only a modest number of previous studies have examined the frequency of aspirin use for primary prevention and the factors affecting such use.^{14–16} In general, these analyses have found limited use of aspirin among people without known CVD. Physician recommendation appears to be a strong influence on usage, and some analyses have also noted higher rates of aspirin use among people with CVD risk factors, including older age, male sex, hypertension, smoking, and high cholesterol. Such analyses have often relied on self-report or crude measures of the presence or absence of risk factors rather than on actual measures of lipids or blood pressure; as such, investigators have not been able to perform analyses based on actual global CVD risk.

Within this context, the analysis by Mainous and colleagues offers new insight into recent patterns of aspirin use in the United States.¹⁷ Using information from the National Health and Nutrition Examination Survey (NHANES) from 2011 to 2012, they were able to make nationally representative estimates of aspirin use for primary prevention for adults aged 40 and older. They found, based on a sample of 3079 adult respondents, that 31.2% had received a physician recommendation to take aspirin and that 77.4% of those were actually taking aspirin.

More important, NHANES also collected sufficient data to allow analysis by CVD risk level. Mainous and colleagues

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divided respondents into 2 groups: Those at 10% or lower risk of a CHD event over 10 years based on a Framingham risk score were considered “low risk,” whereas those at higher than 10% risk were considered “high risk.” Most respondents (77.5%) fell into the low-risk group; of these, only 26.0% had received a physician recommendation. In contrast, 40.9% of those at higher risk had been recommended to take aspirin. Self-reported adherence to provider recommendation was high (more than 75%) in both groups. Factors associated with aspirin recommendation included older age, having health insurance, and having a regular source of care. For the full sample in multivariate analysis, risk status (ie, higher than 10% risk versus 10% or lower risk) was only marginally associated with a recommendation for aspirin (odds ratio 1.26, 95% CI 0.99 to 1.60).

The findings of Mainous and colleagues suggest that recommendations about aspirin use for primary prevention continue to vary considerably and do not necessarily reflect a clear risk-based approach, at least based on the thresholds examined. Given the lack of consensus in the recommendations about who should be offered aspirin, this is not surprising.

Several limitations preclude a deeper understanding of decision making about aspirin in this sample. First, the investigators did not have access to information about some elements of medical history (eg, prior gastrointestinal bleeding) or current medication use that would help define each person’s bleeding risk and potentially affect net benefit determination. Similarly, we do not know whether the risk of adverse effects was discussed; prior work suggests that such information often is not discussed in encounters about preventive care.¹⁸ Second, the decision to create only 2 risk groups makes it unclear whether aspirin use in the lower risk group is in a range of risk that would be a “close call” (in which case patient preference-based decision making is indicated) or whether they are at such low risk that aspirin use represents “overuse” that should be actively discouraged. Finally, we do not know whether the respondents’ use (or nonuse) was informed and preference concordant; such information is necessary to evaluate the quality of decision making overall.¹⁹

Despite these limitations, the analysis by Mainous and colleagues presents the most up-to-date analysis of aspirin use for primary prevention and suggests, at least indirectly, the need for better decision-making processes. Given the uncertainty about aspirin’s effects and the differences in how people may assess the beneficial and adverse consequences of aspirin use, providers and patients should routinely discuss aspirin use within the context of an overall strategy for CVD prevention that is tailored to the patient’s CVD risk. Such discussions should include (quantitative) information on the potential benefits (prevention of CVD events) and harms

(mainly gastrointestinal bleeding) of aspirin. Patients should be offered the opportunity to express their values and preferences about the potential outcomes, and a mutual decision should be reached with the understanding that it can, and should be, revisited periodically. Decision aids are available to assist with such discussions and have been shown to be effective in helping patients reach informed decisions.²⁰

Disclosures

Dr Pignone is a member of the US Preventive Services Task Force. The opinions expressed here are his and do not necessarily reflect the views of the task force.

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