

## Aspirin for the Prevention of Cardiovascular Disease and Colorectal Cancer: New Recommendations from the USPSTF

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► See related USPSTF recommendation statement at http://www.aafp.org/afp/2016/1015/od1.html and Putting Prevention into Practice at http://www.aafp.org/afp/2016/1015/p661.html.

In April 2016, the U.S. Preventive Services Task Force (USPSTF) updated its recommendation on the use of aspirin to prevent cardiovascular disease (CVD).¹ Because emerging evidence suggested that aspirin may also be useful for the prevention of cancer, for the first time, the USPSTF developed a recommendation that assessed the use of aspirin for prevention of both CVD and cancer. Despite the seemingly simplistic question, the topic proved to be one of the most complex the USPSTF has undertaken. The recommendation statement1 is based on three comprehensive systematic evidence reviews<sup>2-4</sup> and a modeling analysis that integrated evidence from each of the reviews.<sup>5</sup> The rationale for assessing the potential benefits of aspirin for CVD and cancer is that a patient has a single decision to make: Should I take aspirin? The USPSTF believed that a recommendation evaluating the use of aspirin for CVD or cancer alone would provide an incomplete picture.

The USPSTF recommended the use of aspirin for prevention of CVD based on age, CVD risk, gastrointestinal (GI) bleeding risk, and patient preferences about taking aspirin. The task force recommended aspirin use in persons who are 50 to 59 years of age, have a 10% or greater 10-year cardiovascular risk, are not at increased risk of bleeding, have a life expectancy of at least 10 years, and are willing to take daily low-dose aspirin for at least 10 years. The USPSTF gave this a B recommendation, indicating that the net benefit was judged to be moderate. The USPSTF recommends using the American College of Cardiology/American Heart Association Pooled Cohort Equations risk calculator for estimating 10-year cardiovascular risk (available as an app [ASCVD Risk Estimator] or at http://tools.acc.org/ ASCVD-Risk-Estimator/).1

The task force judged the net benefit from aspirin use in persons 60 to 69 years of age to be less than that of persons 50 to 59 years of age. Therefore, for

persons 60 to 69 years of age (who otherwise meet the criteria for patients 50 to 59 years of age), the decision should be made individually, based on a discussion of benefits, harms, and patient preferences. The USPSTF gave aspirin use in this age group a C recommendation, indicating that the net benefit is likely small, but that benefits nonetheless outweigh harms. Persons 60 to 69 years of age who place a higher value on the potential benefits than the potential harms may choose to initiate low-dose aspirin. In patients younger than 50 years or older than 69 years, the task force found the evidence too sparse to determine whether the benefits of aspirin use for the primary prevention of CVD and colorectal cancer outweigh the harms.

The decision to initiate aspirin should be based on a discussion of potential benefits and harms. Important risk factors for GI bleeding include higher aspirin dose and longer duration of use, history of GI ulcers or upper GI pain, renal failure, severe liver disease, thrombocytopenia, bleeding disorders, and diabetes mellitus.<sup>1,3</sup> Factors that increase the risk of GI bleeding or intracranial hemorrhage include concurrent use of aspirin and anticoagulation or nonsteroidal anti-inflammatory drugs, male sex, older age, smoking, and increased blood pressure.<sup>3</sup> How patients feel about taking medication also matters. Persons who value avoiding long-term medication use may benefit less from taking aspirin.<sup>1,5</sup> Cardiovascular risk is also important: the higher a person's risk of CVD, the more potential benefit aspirin provides. The most favorable balance of benefits and harms occurs in persons who are at substantially elevated CVD risk but are not predisposed to bleeding complications. Finally, although older age increases the risk of cardiovascular events, it also increases the risk of bleeding complications.

What led the USPSTF to make a positive recommendation for aspirin use? The systematic review on which the recommendation is based incorporated new evidence from the past five years, and a meta-analysis of primary prevention trials showed that aspirin reduced the risk of nonfatal myocardial infarction by 22% and nonfatal stroke by 14%.<sup>2</sup> The review of the effect of aspirin on cancer found that aspirin reduced mortality from colorectal cancer by 33% at 20 years and reduced the incidence of colorectal cancer by 40% beginning 10 to 19 years after initiation.<sup>3</sup> Aspirin does have harms, however, increasing the risk of GI bleeding by 58% and the risk of intracranial hemorrhage by 27%.<sup>4</sup> In absolute

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terms, use of aspirin would result in excess GI bleeding at a rate of 1.39 events per 1,000 person-years and hemorrhagic stroke at a rate of 0.32 events per 1,000 person-years.<sup>4</sup> The USPSTF used the modeling study to help account for benefits from aspirin for prevention of CVD and colorectal cancer, as well as the complications from GI bleeding and intracranial hemorrhage.<sup>5</sup>

It may seem counterintuitive that the benefit of aspirin is larger in patients 50 to 59 years of age than in older patients. Although older persons are at higher risk of CVD than younger persons and may have greater potential benefit, they are also at greater risk of bleeding complications. In addition, the benefit from colorectal cancer prevention appears to require aspirin use for five to 10 years and is observed only after 10 to 20 years of aspirin use. Thus, persons 60 to 69 years of age are less likely to benefit from colorectal cancer prevention than younger persons.

Although the USPSTF review was comprehensive and suggests that aspirin has a role in prevention of CVD and colorectal cancer in persons with elevated risk of CVD, many questions remain. Fortunately, a number of ongoing trials and collaborations should provide additional evidence over the next few years to further inform the decision about who should take aspirin, for how long, at what dose, and at what age.<sup>6</sup>

The author was a member of the USPSTF when the recommendation on aspirin was developed. The views expressed are those of the author and do not necessarily reflect the views of the USPSTF, the Department of Veterans Affairs, or the U.S. government.

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