ARRIVE trial of daily aspirin does not show lower risk of first cardiovascular event

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The role of aspirin in preventing a first heart attack or stroke among people at moderate risk of heart disease remains unclear. At the 2018 European Society of Cardiology meeting, J. Michael Gaziano, MD, a preventive cardiologist at Brigham and Women's Hospital, presented findings from ARRIVE, a randomized, controlled clinical trial of the use of daily aspirin to prevent a first cardiovascular event among more than 12,500 participants considered to be at moderate cardiovascular risk. The team's findings are detailed in a paper published simultaneously in *The Lancet*.

"Aspirin did not reduce the occurrence of major cardiovascular events in this study," said Gaziano. "However, there were fewer events than expected, suggesting that this was in fact a low-risk population. This may have been because some participants were taking medications to lower blood pressure and lipids, which protected them from disease. The decision on whether to use aspirin for protection against cardiovascular disease should be made in consultation with a doctor, considering all the potential risks and benefits."

The benefits of taking aspirin to prevent a second or subsequent heart attack or stroke have been well established in previous studies but the effectiveness of taking aspirin to prevent a first cardiovascular event has been unclear, despite 30 years of randomized clinical trials. The Aspirin to Reduce Risk of Initial Vascular Events (ARRIVE) study, sponsored by Bayer, sought to assess both the potential benefits as well as the risks to people at moderate risk of cardiovascular disease who may already be

receiving some protection from modern preventative and therapeutic strategies.

Participants were randomly assigned to receive either daily aspirin tablets (100 mg) or a placebo. A total of 12,546 participants were enrolled from primary care settings in the UK, Poland, Germany, Italy, Ireland, Spain, and the U.S. The primary endpoint was time to first occurrence of a composite of cardiovascular death, heart attack, unstable angina, stroke, and transient ischemic attack.

The rate of such cardiovascular events did not statistically differ between the aspirin group and the placebo group. During the study, 269 patients (4.29 percent) in the aspirin group and 281 patients (4.48 percent) in the placebo group experienced such cardiovascular events.

Overall, these rates were lower than expected. The authors conclude that this may be reflective of contemporary risk-management strategies, such as the use of statins.

Given that aspirin is known to increase patients' risk of gastrointestinal bleeding, ARRIVE excluded patients at high risk of bleeding. It also excluded patients with diabetes. Gastrointestinal bleeding events (mostly mild) occurred in 61 patients in the aspirin group versus 29 in the placebo group. The overall incidence rate of adverse events was similar in both treatment groups.

"The use of aspirin remains a decision that should involve a thoughtful discussion between a clinician and a patient, given the need to weigh cardiovascular and possible cancer prevention benefits against the bleeding risks, patient preferences, cost, and other factors," the authors conclude.

The authors' declaration of interests and the roles of the Executive

Committee and of the sponsor can be found in *The Lancet*. The sponsor was responsible for the conduct of the trial. The independent Executive Committee, of which Gaziano was a member, was responsible for the study protocol, oversight of the study, writing of the report, and the decision to publish the results. All members of the Executive Committee received personal fees from Bayer during the conduct of the study.

More information: J Michael Gaziano et al, Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial, *The Lancet* (2018). DOI: 10.1016/S0140-6736(18)31924-X