Comparative Effectiveness of Aspirin Dosing in Cardiovascular Disease


BACKGROUND

Aspirin is a commonly used medication for the prevention of cardiovascular disease. The American College of Cardiology and the American Heart Association recommend aspirin dosing of 81 mg once daily for primary and secondary prevention. The Food and Drug Administration approved an 81 mg dose for adult patients in 2004. There is uncertainty regarding whether lower-dose aspirin use is superior to standard aspirin dosing for cardiovascular disease prevention.

OBJECTIVE

To determine whether low-dose aspirin is noninferior to standard-dose aspirin for primary and secondary cardiovascular disease prevention.

DESIGN

Randomized, double-blind, placebo-controlled trial in primary prevention and randomized controlled trial in secondary prevention.

PARTICIPANTS

The ADAPTABLE study included 51,452 individuals from 25 diverse adult populations with 14 clinical sites in the United States and 1 in China. The study was conducted from 2016 to 2019.

INTERVENTIONS

The trial randomly assigned patients to receive 81 mg of aspirin or 325 mg of aspirin daily.

OUTCOMES

The primary outcome was cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke over the course of 2 years. Secondary outcomes included major bleeding, major bleeding requiring hospitalization, and strokes or major bleeding.

RESULTS

In the primary outcome analysis, the hazard ratio for cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke between patients assigned to 81 mg of aspirin and those assigned to 325 mg of aspirin was 0.81 (95% confidence interval [CI], 0.73 to 0.91). The inferiority margin for the primary outcome was 1.35, and the study was powered to detect a 15% difference in the primary outcome between the two groups with 80% power. The primary safety outcome was major bleeding, and the hazard ratio for major bleeding was 0.74 (95% CI, 0.62 to 0.88). The study was powered to detect a 25% difference in major bleeding with 80% power. The trial was stopped early after 2 years of follow-up due to the evidence of noninferiority and safety.

CONCLUSIONS

Low-dose aspirin is noninferior to standard-dose aspirin for the prevention of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke and is substantially safer with regard to major bleeding. These results provide evidence to support low-dose aspirin as first-line therapy for cardiovascular disease prevention.