

Aspirin Use to Prevent Cardiovascular Disease and Colorectal Cancer

Interim Guidance from the Kaiser Permanente National Integrated Cardiovascular Health (ICVH) Work Group

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Three randomized clinical trials (ARRIVE¹, ASCEND², and ASPREE³) recently published results on aspirin use in patients without known Atherosclerotic Cardiovascular Disease (ASCVD). The studies looked at benefits including cardiovascular event prevention, and risks including serious bleeding events. Overall the studies suggest that aspirin lacks net benefit (total benefits minus total harms) beyond age 70, and there is low net benefit in younger adults. USPSTF 2016 aspirin recommendations point to highest net benefit for aspirin in adults age 50-59 (lower bleeding risk than older patients) with 10-year ASCVD risk* $\geq 10\%$.

The National Kaiser Permanente Aspirin recommendations will be formally updated following a comprehensive review of the literature (to include these three studies) and inter-regional vetting with clinical leads and National Guideline Directors (NGD). This ICVH interim guidance document is intended to provide guidance pending release of the updated aspirin recommendations over the next several months using the National Guideline Program process.

ICVH clinical leads recommend the following as **interim guidance** on this topic:

- **In adults aged 50-59 years with 10-year ASCVD risk $\geq 10\%$, *consider* aspirin 81 mg daily.**
- **There is no recommendation for or against aspirin therapy in adults aged < 50 or ≥ 60 years.**
- Exclude adults with increased risk of bleeding. This includes those with a history of gastrointestinal (GI) bleeding, GI ulcers, intracranial bleed, bleeding disorders, renal failure, severe liver disease, thrombocytopenia, or using NSAIDs daily, or other medicine to prevent blood clots.

The recommendations above reflect a change from *initiate* to *consider* in adults aged 50-59 years with 10-year ASCVD risk $\geq 10\%$ and the inclusion of those ≥ 60 years of age for no recommendation for or against.

*10-year ASCVD Risk is risk of fatal or nonfatal myocardial infarctions or strokes. Kaiser Permanente ASCVD Risk Estimator (KAISER PERMANENTEARE) of 10% correlates approximately with ACC/AHA ASCVD Risk of 16% at the population level.

ARRIVE, ASCEND and ASPREE Trials Overview:

The ARRIVE Trial

The Aspirin to Reduce Risk of Initial Vascular Events (ARRIVE) trial randomized over 12,000 moderate cardiovascular risk patients who were over 55 years of age (males) or 60 years of age (females) to 100 mg aspirin or placebo. The primary efficacy endpoint was a composite outcome consisting of time to first occurrence of confirmed myocardial infarction, stroke, cardiovascular death, unstable angina, or transient ischemic attack. There was no difference in CV events between groups. There were significantly higher rates of gastrointestinal bleeding among patients taking aspirin (0.97%) compared to the placebo group (0.47%).

The ASCEND Trial

The A Study of Cardiovascular Events in Diabetes (ASCEND) trial randomized over 15,000 men and women with diabetes who were over 40 years of age to 100 mg aspirin or placebo. The primary efficacy outcome was the first serious vascular event, defined as a composite of nonfatal myocardial infarction,

nonfatal stroke (excluding confirmed intracranial hemorrhage) or transient ischemic attack, or death from any vascular cause (excluding confirmed intracranial hemorrhage). The number of serious vascular events was lower in the aspirin group compared to the placebo group (8.5% vs. 9.6%; rate ratio, 0.88; P = 0.01). There was a higher incidence of major bleeding the aspirin group compared to the placebo group (4.1% vs. 3.2%; rate ratio, 1.29; P = 0.003).

The ASPREE Trial

The Aspirin in Reducing Events in the Elderly (ASPREE) trial randomized over 19,000 men and women from Australia and the United States who were 70 years of age or older (or ≥ 65 years of age among blacks and Hispanics in the United States) to 100 mg aspirin or placebo. The primary outcome was a composite of death, dementia, or persistent physical disability. Secondary outcomes included major hemorrhage and cardiovascular disease (defined as fatal coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal stroke, or hospitalization for heart failure). The rate of cardiovascular disease was 10.7 events per 1000 person-years in the aspirin group vs. 11.3 events per 1000 person-years in the placebo group (hazard ratio, 0.95; 95% confidence interval [CI], 0.83 to 1.08). The rate of major hemorrhage was 8.6 events per 1000 person-years and 6.2 events per 1000 person-years, respectively (hazard ratio, 1.38; 95% CI, 1.18 to 1.62; P<0.001).

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3. McNeil JJ, Wolfe R, Woods RL, et al. Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly.