Aspirin was cost-effective for primary prevention of cardiovascular events in older women at moderate risk

Pignone M, Earnshaw S, Pletcher MJ, Tice JA. **Aspirin for the primary prevention of cardiovascular disease in women: a cost-utility analysis.** Arch Intern Med. 2007;167:290-5.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Cardiology ★★★★★★☆

QUESTION

Is aspirin cost-effective for primary prevention of cardiovascular (CV) events in women?

METHODS

Design: Cost–utility analysis using a Markov model from the perspective of a third-party payer and a lifetime time horizon.

Setting: United States.

Patients: A hypothetical cohort of women assumed to be 65 years of age with moderate 10-year risk for CV events (estimated 7.5% risk for coronary heart disease and 2.8% risk for stroke). Systolic blood pressure was 120 mm Hg; total cholesterol level was 184 mg/dL (4.77 mmol/L); high-density lipoprotein cholesterol level was 40 mg/dL (1.04 mmol/L). They were assumed to be nonsmokers and not to have diabetes or atrial fibrillation.

Intervention: Aspirin or no aspirin.

Outcomes: Cost per quality-adjusted life-year (QALY) gained. Costs were estimated from mixed populations of men and women, derived from published studies and several recent national databases, and expressed in 2005 U.S. dollars with a 3% annual discount rate. Effectiveness estimates were obtained from a meta-analysis of randomized controlled trials (RCTs); clinical probability estimates were derived from National Vital Statistics life tables, Framingham risk equations, population-based studies, and systematic reviews.

MAIN RESULTS

In the base-case analysis, aspirin use in women at moderate risk for CV events led to a cost–utility ratio of $13 300 per QALY gained. The mean cost for women receiving aspirin was greater than for those not receiving aspirin ($3145 vs $3069) for a difference of 0.006 QALYs gained in the aspirin group. One-way sensitivity analysis showed that the model was sensitive to the patient's age, daily pill consumption, risk for CV events, risk reduction with aspirin for ischemic stroke or myocardial infarction, risk reduction with secondary prevention, excess risk for gastrointestinal bleeding or death from gastrointestinal bleeding, and risk for hemorrhagic stroke. Probabilistic sensitivity analysis found that this estimate was most sensitive to the effects of aspirin on rates of myocardial infarction or stroke. For women whose stroke risk was doubled due to hypertension, aspirin was more effective and less costly than no treatment.

CONCLUSION

In older women at moderate risk for cardiovascular disease, aspirin was cost-effective for primary prevention of cardiovascular events.

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COMMENTARY

In 1988, the Physicians' Health Study showed a 44% relative risk reduction in first myocardial infarction (MI) in men taking aspirin. Despite no difference in physiologic response to aspirin by sex, the effectiveness of aspirin in preventing a first MI in women has not been proven by RCTs. In the more recent Women's Health Study (WHS), aspirin led to a nonsignificant reduction in the composite endpoint of major CV events (nonfatal MI, nonfatal stroke, or CV death) but caused a significant decrease in ischemic stroke as well as stroke and MI in the subgroup of women > 65 years of age (1). This was at the expense of increased gastrointestinal bleeding requiring transfusion (relative risk 1.40, 95% CI 1.07 to 1.83) (1).

Pignone and colleagues examined the cost-effectiveness of aspirin for primary prevention of CV events in women. Both benefit and cost-effectiveness, as expected, were highly contingent on the woman's baseline CV risk. In 65-year-old women with a 10% 10-year risk for MI or stroke, the cost-effectiveness of aspirin was estimated at $13 300 per QALY gained. A probabilistic sensitivity analysis to assess the robustness of the results showed a 73% chance that aspirin is beneficial but only a 35% chance of cost-effectiveness at the traditional threshold of < $50 000 per QALY gained.

This analysis highlights the limitations of the underlying data. The WHS is the only large primary prevention trial studying aspirin in women. Many of the women in the WHS were considerably younger (mean age 55 y) than the base-case age of Pignone and colleagues' study, but 10% (n = 4107) were ≥ 65 years. The WHS tested aspirin at a dose of 100 mg every other day. Meta-analysis (mainly secondary prevention) suggests an optimal dose range of 75 to 150 mg/d with less effect at lower doses (2).

According to the American Heart Association and U.S. Preventive Services Task Force recommendations, it is reasonable to limit primary prevention use of aspirin in women to those with ≥ 10% baseline 10-year risk for a first coronary event (vs > 6% in men).

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