

now addressed the need for direct evidence of the effects of aspirin in women.

Ridker and co-workers randomized 39,876 healthy women of at least 45 years of age to receive 100 mg aspirin every other day, or placebo. During an average follow-up period of 10.1 years, fewer major cardiovascular events occurred in the aspirin group than among women receiving placebo, although this difference was not statistically significant. Similarly, no significant differences were observed between the two groups in the risk of death from cardiovascular causes, or the risk of fatal or nonfatal myocardial infarction.

Aspirin was, however, associated with a significant reduction in the risk of stroke (relative risk 0.83 compared with placebo, 95% CI 0.69–0.99,  $P=0.04$ ). This benefit was driven by a 24% reduction in the risk of ischemic stroke; rates of hemorrhagic stroke were similar in the aspirin and placebo groups. Furthermore, a separate analysis of women aged 65 years or older showed significantly lower rates of major cardiovascular events, ischemic stroke, and myocardial infarction in those receiving aspirin compared with placebo.

Unsurprisingly, side effects related to bleeding and ulcers—including gastrointestinal bleeding requiring transfusion—were more frequent among women receiving aspirin than in the placebo group. The investigators recommend, therefore, that the benefits and risks of the use of aspirin in primary prevention in women should be considered on an individual patient basis.

**Original article** Ridker PM *et al.* (2005) A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women. *New Engl J Med* 352: 1293–1304

## Predicting outcome in patients with asymptomatic mitral regurgitation

The timing of surgery in asymptomatic patients with mitral regurgitation is a matter of debate, not least because high-risk subgroups are poorly defined. A new study by Enriquez-Sarano *et al.* has examined the effect of quantitative grading of patients with this condition.

A total of 456 patients with asymptomatic, organic mitral regurgitation and ejection fraction higher than 50% were included in this prospective study. Participants were divided into three groups

according to the effective regurgitant orifice (<20 mm<sup>2</sup>, 20–39 mm<sup>2</sup>, and ≥40 mm<sup>2</sup>). The mean duration of follow-up was 2.7 years for those managed medically, and 5.1 years for those who also underwent surgical treatment.

Age, diabetes and increasing effective regurgitant orifice emerged as independent determinants of survival. Those with an effective regurgitant orifice of 40 mm<sup>2</sup> or above were at almost three times the risk of death compared with those with an orifice of less than 20 mm<sup>2</sup> (adjusted risk ratio 2.90, 95% CI 1.33–6.32,  $P<0.01$ ). In addition, the risk of cardiac events and of death from cardiac causes were each increased more than fivefold in these patients; furthermore, survival was significantly better in those who underwent cardiac surgery than in those who did not (adjusted risk ratio 0.28, 95% 0.14–0.55,  $P<0.01$ ).

The study clearly illustrates the benefits of quantitative grading of patients with mitral regurgitation. Because those with an effective regurgitant orifice of 40 mm<sup>2</sup> or above are at increased risk of cardiac events and death, and appear to benefit considerably from surgery, the authors advise that these patients “should promptly be considered for cardiac surgery”.

**Original article** Enriquez-Sarano M *et al.* (2005) Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *New Engl J Med* 352: 875–883

## High-risk acute coronary syndromes: cost-effectiveness of clopidogrel plus aspirin

Combination therapy with clopidogrel and aspirin has been shown to be more effective than aspirin alone in reducing the risk of myocardial infarction, stroke or cardiovascular death in patients with unstable angina. Information is lacking, however, on the relative cost-effectiveness of these two strategies. Schleinitz *et al.* have addressed this question in their recent cost-utility analysis, using data from the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial.

The investigators used Markov modeling to compare treatment costs and clinical outcomes of clopidogrel plus aspirin versus aspirin alone. The base case was a 64-year-old patient with unstable angina and electrocardiographic changes or non-Q-wave myocardial infarction,