aini et al used a Markov model to estimate the effectiveness and cost-effectiveness of routinely adding a PPI for older adults with coronary heart disease who are taking ASA for secondary prevention. They assumed that PPI use would reduce the incidence of UGIB by 66%, based on the results of 2 previous small randomized trials in higher-risk Asian patients who received a prescription PPI to prevent recurrent ulcer-related bleeding. They also assumed that the PPI would have no major adverse effects itself and would have an annual cost of $250. They did not examine changes in quality of life, based on the assumption that any decrement in quality of life from UGIB would be short-lived. They also did not incorporate any adverse effects associated with taking an additional pill daily, which can have important effects when considering preventive therapies, or any benefits from reduction in dyspepsia.

Based on their assumptions, they found that routine PPI use would reduce the lifetime risk of UGIB from 9.5% to 3.1% and death from UGIB from 1.4% to 0.4%. The cost per life-year gained was approximately $40,000 for patients starting treatment at age 65 years, suggesting reasonable cost-effectiveness, comparable with many commonly accepted health care interventions. Patient age, the effectiveness of PPI for reducing UGIB, and the cost of the PPI each had important effects on the cost per life-year gained, with younger age, lower effectiveness, and higher costs associated with less favorable cost-effectiveness ratios.

Based on these modeling results, should prophylactic therapy with PPI be adopted as standard practice in average-risk US adults older than 65 years taking ASA for secondary prevention? Several factors suggest that recommending such a change in practice may be premature. First, it is possible that the actual efficacy when using PPI to prevent UGIB in patients without a history of ulcer-related bleeding may be lower than that observed in the 2 small trials in higher-risk patients. If the true efficacy is 33% or less, the cost per life-year gained of PPI prophylaxis becomes high (over $75,000). Second, the previous trials used prescription PPIs (esomeprazole magnesium, 20 mg twice daily, or lansoprazole, 30 mg/d). Achieving cost-effectiveness ratios under $50,000 per life-year gained in the current US environment would require use of generic omeprazole magnesium, which has not been evaluated itself for preventive efficacy. Finally, we need greater confidence about the risk of adverse effects of PPI from fractures, pneumonia, or other unrecognized conditions.

Despite the uncertainty around these key elements, the model by Saini et al suggests that there is potential benefit from PPI prophylaxis and compels further study. Ideally, we would like to have evidence from a well-designed randomized trial of low-cost omeprazole in average-risk patients that would have sufficient power to detect a 33% or greater reduction in the incidence of UGIB and would allow us to estimate the frequency of important adverse effects. Such a trial would require several thousand participants in each group to be followed over 5 years or more in order to have enough outcomes to reach definitive conclusions and thus would be costly. However, given the high costs and morbidity from UGIB and the increasing elderly population, it would provide important guidance for the management of patients with cardiovascular disease who require antiplatelet agents. Until better evidence is available, physicians and their patients should use PPI medications to prevent recurrent bleeding in patients with previous UGIB, but physicians should not prescribe them routinely for patients at average risk.

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Additional Information: Dr Pignone has planned to conduct additional modeling research on the use of PPI prophylaxis for patients taking ASA for primary prevention with 2 of the coauthors of the article by Saini et al.