optimal management is not well defined. Continuous treatment with H_2 blockers is the standard recommendation; however, in primary care settings, treatment is often intermittent. This randomized trial compared the use of omeprazole with ranitidine for intermittent treatment of GERD.

Population studied A total of 677 patients were enrolled from 56 European medical centers either following hospital consultation (54%) or directly from general practitioners (46%). These subjects had heartburn that interfered with normal activities for more than 2 days of each of the previous 2 weeks; endoscopy was used to confirm the diagnosis, and patients with severe erosions were excluded. Of those included in the study, 56% were male, and the median age was 47. Most patients were overweight (average body mass index = 27); 27% were smokers; 40% had evidence of *Helicobacter pylori*; and 76% had symptoms for more than 1 year. Thus, the population seems similar to that seen by US family physicians. The major difference is that all subjects had endoscopy-confirmed GERD and may have had more serious disease than is typical in primary care settings in the United States.

Study design and validity This was a randomized double-blind controlled trial. Patients were randomized to receive either ranitidine 150 mg twice daily, omeprazole 10 mg daily, or omeprazole 20 mg daily for 2 weeks. If patients remained symptomatic, the dose was doubled (except for the higher omeprazole dose) for an additional 2 weeks. Patients with no symptoms at 2 weeks or mild or no symptoms at 4 weeks entered the follow-up phase, during which they received treatment only when moderate or severe symptoms recurred. Follow-up rate was 71% over 1 year; intention-to-treat analysis was used, with the Cox proportional hazards statistic used to control for confounding causes.

This trial was of good quality. Weaknesses are relatively minor and include low follow-up rate, limited number of outcomes addressed, lack of information about clinical management including *H pylori* and smoking cessation management, and lack of control of important confounding variables, such as use of alcohol, nonsteroidal anti-inflammatory drugs, or promotility agents. In addition, the design of this trial did not allow a good assessment of the true effectiveness of intermittent therapy, since there was no comparison group receiving continuous therapy.

Outcomes measured The primary outcome was the number of patients successfully completing the study on intermittent treatment. Other outcomes included total time off treatment, number of relapses, and symptom control at 2 weeks. Endoscopic assessment of the effectiveness of therapy was not performed, and other important outcomes, such as patient satisfaction, level of symptoms, functional status (ie, impact on work and family), and cost were not addressed.

Results The groups were similar at baseline. After 2 weeks, 55% of patients taking 20 mg omeprazole were asymptomatic compared with 40% of those taking the 10-mg dose and 26% for ranitidine (P <.001; number needed to treat = 3.5 for 20 mg omeprazole vs 150 mg ranitidine twice daily). At completion, 47% were still receiving intermittent therapy; most patients had no relapses (32%), 1 relapse (24%), or 2 relapses (12%). Long-term outcome was not affected by initial treatment at randomization. Initial endoscopic grade of esophagitis, symptom duration, age, sex, body weight, and presence of *H pylori* did not influence outcomes.

Recommendations for clinical practice **This study provides good evidence that, compared with ranitidine, omeprazole provides faster relief of symptoms but no improvement in long-term success of intermittent treatment for GERD. The data also suggest that an intermittent treatment strategy for GERD may provide adequate symptom control with less medication for about half of patients. The study did not directly compare intermittent therapy with continuous therapy, and further study is necessary to show their equivalence.**

Clinicians choosing an intermittent strategy for treatment of GERD should consider omeprazole 20 mg if rapid reduction of symptoms is necessary, but they should keep in mind that there is little evidence that this agent is superior to ranitidine for long-term outcomes.

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Mediterranean Diet for Heart Disease

de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation 1999; 99:779-85.

Clinical question **Does the Mediterranean diet prevent recurrent myocardial infarction?**

Background The relatively low incidence of coronary heart disease experienced by coastal Mediterranean inhabitants has spurred interest in their dietary intake. The Lyon Diet Heart Study was designed to evaluate the Mediterranean diet as a way to prevent heart attacks in patients with pre-existing heart disease. The diet used in the study consisted of more bread, veg-

etables, and fish; daily fruit; less meat, with red meat replaced by poultry; and butter and cream replaced by a canola-oil–based margarine. The canola-oil–based margarine used in the study was higher in linoleic acid (16.4% vs 8.6%) and alpha-linolenic acid (4.8% vs 0.6%) than olive oil, which is typically used in the Mediterranean diet.

The trial was ended early after finding a 70% reduction in cardiac events with 27 months of follow-up. The report was criticized by some and mostly ignored by the medical community. This final article reports on the results after an average of approximately 4 years of study.

Population studied This study enrolled 605 patients younger than 70 years (mean age 53.5 years, 91% men) who had suffered a first heart attack within 6 months of enrollment. Subjects were recruited from a cardiovascular hospital in France. Patients were excluded if they had overt heart failure, recurrent angina, ventricular arrhythmias, atrioventricular block, or severe uncontrolled hypertension.

Study design and validity This was a 4-year randomized controlled trial comparing the Mediterranean diet with the usual postinfarction diet. The 303 subjects in the control group were prescribed a "prudent Western diet" by their attending physicians. It is unclear how close the control group diet approximates the typical postinfarction diet in the United States and other western countries. Subjects in the treatment group attended a 1-hour class during which a dietitian and cardiologist explained the Mediterranean diet. Both groups returned at 8 weeks and annually for follow-up, but only the treatment group received dietary advice from investigators. Clinical end points were assessed blindly at annual visits. Analysis was by intention to treat. Although the trial was terminated after 2 years and participants were notified of the findings, most continued to follow the diet originally assigned to them.

The investigators did not control for multiple comparisons; it may be that at least some of the differences were due to chance. Another report noted that only 42% of the control group (compared with 92% of the experimental group) changed their diet during the study.[1]

Outcomes measured The primary outcome was the incidence of combined cardiac death and nonfatal heart attack. This outcome plus major secondary end points (including unstable angina, heart failure, stroke, and embolism) constituted composite outcome 2. The preceding outcomes plus minor secondary events, such as recurrent stable angina, surgical intervention for heart disease, and thrombophlebitis, made up composite outcome 3.

Results There were significantly fewer deaths and nonfatal heart attacks in the treatment group, 1.24 per 100 patients per year of follow-up compared with 4.07 in the control group (adjusted risk ratio [ARR] = 0.28; 95% confidence interval [CI], 0.15 - 0.53). Thirty-five patients would have to be treated for 4 years to prevent 1 cardiac death or nonfatal heart attack (number needed to treat [NNT] = 35). For composite outcome 2, the rates were 2.59 compared with 9.03 (ARR = 0.33; 95% CI, 0.21 - 0.52; NNT = 16). For composite outcome 3, the rates were 18.74 compared with 9.63 (ARR = 0.53; 95% CI, 0.38 - 0.74; NNT = 11).

Recommendations for clinical practice **This French study found that the Mediterranean diet is effective in reducing mortality and recurrence of cardiovascular events following a heart attack. The diet, which is high in alpha-linolenic acid, is a significant departure from the step 1 and step 2 diet recommended by the American Heart Association. The dietary manipulations of the Mediterranean diet are simple, but this study should be repeated in other countries before it is used to replace the typical cardiac diet.**

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Amiodarone for the Treatment of Persistent Atrial Fibrillation

Kochiadakis GE, Igoumenidis NE, Solomou MC, et al. Efficacy of amiodarone for the termination of persistent atrial fibrillation. Am J Cardiol 1999; 83:58-61.

Clinical question **Is amiodarone superior to placebo for the restoration of sinus rhythm in patients with persistent atrial fibrillation?**

Background Chemical cardioversion is very effective for the treatment of atrial fibrillation (AF) lasting less than 48 hours. For AF of greater duration, chemical cardioversion has been shown to have limited value. A Class III anti-arrhythmic drug, amiodarone has been shown in previous studies to have potential efficacy in the treatment of AF of longer duration. In most cases, however, amiodarone was only used when AF was refractory to other agents, and no studies used a placebo control group.

Population studied The study included 67 consecutive adult patients (32 men, 35 women) with a mean age of 64 years. All had AF of greater than 48 hours'