have dropped out early, making the treatment group's outcome look better than it actually was.

Results. More patients in the group receiving minocycline had improvement in joint swelling (54% vs 39%, $P=.023$) and joint tenderness (56% vs 41% $P=.021$). There was no difference between groups in the degree of morning stiffness. Patients in the treatment group had a greater increase in grip strength than did those in the control group as well as greater improvement in physiologic measures, such as IgM rheumatoid factor, platelet count, and erythrocyte sedimentation rate. There was no significant difference, however, between the treatment and control groups with regard to global patient-oriented outcomes of overall disease activity as assessed by the patient, overall disease activity as assessed by the physician, and functional status.

Recommendations for clinical practice. Minocycline appears to have a physiologic effect on rheumatoid arthritis, and there is evidence that it may help reduce joint swelling and tenderness in some patients. However, there is no evidence that this treatment has a significant effect on overall disease activity or functional status. Given the low toxicity of minocycline in patients who are not and do not plan to become pregnant, it seems appropriate to consider a 1-year trial of minocycline in patients with active rheumatoid arthritis. Given the variable efficacy of the therapy, it is important to assess the patient's response carefully and objectively and at regular intervals.

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SIMVASTATIN DECREASES MORTALITY

TITLE: Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S)
AUTHORS: Scandinavian Simvastatin Survival Study Group
JOURNAL: *Lancet*
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Clinical question. Can long-term treatment of hypercholesterolemia with simvastatin (Zocor) decrease all-cause mortality in patients with known coronary heart disease (CHD)?

Background. There is ample documentation that high serum cholesterol is associated with coronary heart disease (CHD). Evidence also suggests that lowering cholesterol decreases the risk of patients experiencing, or dying from, a coronary event. No current clinical trials have convincingly shown, however, that cholesterol-lowering strategies actually prolong life in patients with CHD.

Population studied. The study included 4444 patients aged 35 to 70 years with a history of angina pectoris or acute myocardial infarction (MI), who were recruited from 94 centers in Scandinavia. Patients were excluded from the study if they had congestive heart failure, atrial fibrillation, unstable or Prinzmetal angina, or if they had experienced an MI during the preceding 6 months.

Study design and validity. Patients with fasting cholesterol levels between 5.5 and 8.0 mmol/L (212 and 310 mg/dL) were randomized to receive simvastatin 20 mg or placebo. The dose was increased as necessary to decrease the cholesterol to <5.2 mmol/L (200 mg/dL). Double-blinding was preserved by allowing a study supervisor to monitor cholesterol determinations and provide dosing instructions to the clinician. Patients continued on therapy for a median follow-up of 5.4 years. The study was stopped earlier than scheduled when the difference between the two groups became statistically significant. In general, studies may be stopped by an external monitoring committee when treatment is proven so helpful that it would be unethical to deny it to the control group, or when an intervention is so harmful that it would be unethical to continue giving it to the treatment group. Use of such a "stopping rule" is becoming common in large trials.

Outcomes measured. The primary endpoint of the study was mortality related to any cause. Secondary endpoints included the incidence of major coronary events (coronary deaths and silent or nonfatal MI), revascularization procedures, noncoronary deaths, and hospital admissions for acute coronary events. Intention-to-treat analysis was used for all outcomes: results were reported for all patients, even those who did not complete the intervention. This is important because if the intervention had been either unpleasant or harmful, patients might have dropped out early, making the group's outcome look better than it actually was.

Results. There was a statistically significant decrease in total mortality in the treated group as compared with the placebo group (8% vs 12%, $P<.001$). Coronary-related deaths were also reduced in the simvastatin-treated group (relative risk = 0.58), and, unlike other studies of cholesterol therapy, there was no increase in the number of deaths from noncardiovascular causes. Simvastatin did not increase the number of violent deaths (suicide and trauma-related) as has been seen in some other studies.

Simvastatin also affected the other outcomes evaluated in this study, significantly decreasing the risk of a coronary event (relative risk = 0.73) and the likelihood of undergoing coronary artery bypass surgery or angioplasty. There was no significant effect on non-MI acute CHD events. The drug was judged to be well tolerated, based on the similarity of adverse effects and the rate of patients discontinuing therapy between the two groups. Subgroup analysis revealed that elderly patients (>60 years) benefited to the same extent as younger patients, although mortality in women (as a group) was not decreased.

To help interpret these results, a useful measure of clinical significance (not reported in the study) is the "number needed to treat" (NNT), which is the number of patients who would have to be treated for one of them to achieve the goal of therapy. Calculating the NNT for this trial reveals that about 135 people would have required treatment for 1 year, or 25 patients for 5 years, for one death to be prevented. By comparison, only 81 people would need to be treated with a beta-blocker for 1 year following an MI to prevent one death.[1]

Recommendation for clinical practice. This trial provides the first evidence that patients with documented CHD are less likely to die if treated with a cholesterol-lowering agent. Therefore, physicians should recommend simvastatin to their hyperlipidemic patients with CHD. Three cautions, however, are warranted.

First, simvastatin is the only agent that has been convincingly shown to decrease all-cause mortality. A meta-analysis that combined the results of previous cholesterol-lowering trials has shown that only patients at highest risk benefit from therapy, and that patients at low risk may actually be harmed.[2] As a result, it is risky to extend the results of this trial to include other drugs. Second, all patients in this study already had evidence of CHD. Patients without CHD are at much lower risk of cholesterol-related mortality. Using lipid-lowering agents to treat these patients may not be beneficial and may actually be harmful. Finally, no significant benefit to patients occurred for the first several years of therapy, which underscores the importance of continuous treatment.

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EFFECT OF EPIDURAL ANESTHESIA ON LABOR

TITLE: The effect of epidural anesthesia on the length of labor
AUTHORS: Johnson S, Rosenfeld JA
JOURNAL: *The Journal of Family Practice*
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Clinical question. Does the use of epidural anesthesia increase the length of the second stage of labor?

Background. Several studies have shown that women who receive epidural anesthesia have a longer second stage of labor than women who do not. Because these trials were not randomized, however, the observed difference in the duration of labor may be related to factors other than the epidural anesthesia itself. That is, women who elected to receive epidural anesthesia or whose physician recommended it may have been different in some other way (such as having a greater incidence of cephalopelvic disproportion), which also may have affected the duration of the second stage of labor. In the state of Tennessee, a change in the state's insurance program for the indigent resulted in a sudden decrease in the use of epidural anesthesia among patients at a family practice clinic, setting the stage for the "natural experiment" observed by the authors.

Population studied. The study included all women under the care of residents and faculty of the Bristol Family Practice Residency in Bristol, Tennessee, over a 1-year period from July 1, 1993, to June 30, 1994. Women who had a precipitous delivery for which the length of the second stage could not be accurately measured and women whose infants were delivered by cesarean section were excluded from measurement of the second stage of labor.

Study design and validity. This was a nonrandomized (or quasi-experimental) trial that used a pretest-posttest design. That is, the length of the second stage of labor and other outcome variables were measured in a sample of patients for a 6-month period, known as the pretest period. Then, after the insurance coverage for this group of