patients redeveloped pain following readministration of the drug therapy. After discontinuation of the drug treatment, some patients experienced immediate improvement while the majority had more gradual improvement.

The FDA received 6 US SAE reports of severe bone, joint, or muscle pain for risedronate sodium (Actonel; Procter & Gamble Pharmaceuticals, Cincinnati, Ohio), a less widely used bisphosphonate, between initial marketing in September 1998 and June 2003. The data suggest a possible class effect.

The clinical trials leading to FDA approval of alendronate and risedronate were reviewed and did not show meaningful differences between drug and placebo for SAE reports of severe bone, joint, and/or muscle pain. However, differences in reported adverse events are sometimes seen for marketplace experience compared with pre-approved clinical trials.

Underreporting of pain is probably considerable because of its subjective nature and because physicians may attribute pain to osteoporosis. Serious or severe bone, joint, and/or muscle pain that begins shortly after bisphosphonate use should be reported to physicians for consideration of discontinuing drug therapy.

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Resistance to Use of Perioperative β-Blockers: A No-Man’s Land

Siddiqui et al reported underutilization of perioperative β-blockers. We wish to confirm and extend their observation by demonstrating resistance to change.

We prospectively monitored the perioperative use of β-blockers, before and after an intervention among the medical staff, as a project of safety and quality at Hadassah University Hospital (a leading academic center in Jerusalem, Israel), following a recent recommendation by the Agency of Healthcare Research and Quality.

At baseline, over a period of 6 weeks, 602 patients underwent a noncardiac operation in general surgery, neurosurgery, urology, orthopedics, or gynecology. Of 75 patients who met criteria for β-blocker use, none received this treatment (18 had known coronary artery disease [CAD] and 57 had at least 2 CAD risk factors). In 43 patients receiving β-blockers before surgery, the treatment was maintained.

An intervention included presentations of current evidence and local use at several departmental meetings of surgery and anesthesiology. An institutional protocol for perioperative β-blocker use was developed in agreement with senior cardiologists, anesthesiologists, and surgeons and approved by department heads. In 2 departments, we attempted academic detailing by a visiting nurse who reminded physicians about the protocol and suggested use of β-blocker for patients meeting the criteria. After the intervention, there was no change at all. Over a period of 6 weeks, 475 patients underwent noncardiac operations, 72 patients met criteria for β-blocker use, and none received treatment (18 had known CAD and 54 had at least 2 CAD risk factors).

During the same period and using a similar intervention, we observed a significant increase in the use of low-molecular-weight heparin for postoperative thromboprophylaxis. We were surprised by the resistance to change with regard to the use of perioperative β-blockers: although the medical staff knew and generally accepted the recommendations, they did not get implemented. Only a few physicians might have been aware of an emerging controversy regarding the use of perioperative β-blockers.

In addition to the explanations suggested by Siddiqui et al., we suggest another reason for this inertia: the surgeon thinks this is a problem for cardiologists or internists (who do not see most of the patients) or for anesthesiologists (who see the patients too late). For this no-man’s land problem, we need perhaps a system solution, such as a computer-based reminder.

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An Alternative View of Current Evidence in Support of Perioperative β-Blockers

We read with interest the studies by Siddiqui et al. and Lindenauer et al. Each report has, as its raison d’être, the supposition that perioperative β-blockade is the standard of care for the prevention of postoperative cardiac complications. Furthermore, both studies presume that physicians who do not prescribe β-blockers are not practicing good perioperative medicine. We wish to express the contrarian view that the evidence supporting the recommendation for perioperative β-blockade is insufficient and that a vast amount of research is still required in the field of perioperative risk reduction.

Two meta-analyses have pooled the data from randomized controlled studies of perioperative β-blockade. Although both groups of reviewers found statistically significant reductions in myocardial infarction (MI), the pooled effect estimates were heavily weighted by 2 studies. One study was an interim analysis of an un-
blinded trial of highly selected, high-risk vascular patients. In the second study, the in-hospital incidence of MI was actually higher in the group receiving atenolol. The analysis of the 2-year follow-up in the second study demonstrated benefits with atenolol; however, this long-term effect could be explained by a higher incidence of chronic use of β-blockers in patients randomized to atenolol, and the authors had excluded all patients who died in-hospital in their long-term analysis. When the data from these 2 studies were removed, the pooled-effect estimate no longer demonstrated a significant benefit with β-blockade. We believe that the current evidence is very encouraging but is a long way from being sufficient to make definitive guidelines.

Thus, we agree with Auerbach and Goldman who state the following in their meta-analysis:

Studies often included patients who were selected and not consecutively recruited, making generalizability of their results difficult. . . . There is little direct evidence describing the impact of β-blockers in average patients, such as those who have stable coronary disease and are undergoing elective surgery. . . . [W]ider use of this therapy will be better supported if findings from existing studies are replicated in large randomized trials.

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**Are β-Blockers Useful to Protect High-Risk Patients Scheduled for Open Cholecystectomy?**

We read with great interest the article by Siddiqui et al regarding the underutilization of β-blockers during the perioperative period. The authors have evaluated the frequency of perioperative use of β-blockers in patients scheduled for open cholecystectomy. They found that 70% of patients eligible for β-blockers did not receive these medications during the perioperative period. While there is no doubt about the interest of β-blockade in reducing perioperative cardiac events in high-risk patients scheduled for major noncardiac surgery, the advantage of β-blockers remains controversial in patients scheduled for intermediate or low-risk surgery. Morbidity and mortality after open cholecystectomy have been studied extensively. One relatively recent study with more than 40000 patients showed a low risk of cardiac morbidity and mortality (<1%) after this procedure.

The American College of Cardiology/American Heart Association has recently stated that the randomized trials evaluating medical therapy in noncardiac surgery do not provide enough data to draw recommendations. Therefore, the class I recommendations for perioperative medical therapy concerned only patients undergoing vascular surgery with symptomatic arrhythmias, hypertension, or angina or who were considered high-risk patients owing to the finding of ischemia on preoperative testing. The benefit of β-blockade in patients with CAD have been demonstrated in large randomized controlled trials (RCTs) and meta-analysis of large RCTs in comparison with small RCTs and meta-analysis of small RCTs, which evaluated the benefit of perioperative β-blockers in patients undergoing noncardiac surgery. Moreover, most of the studies were performed in patients scheduled for thoracic and vascular surgery. Consequently, the efficacy of perioperative β-blocker use is doubtful and needs to be studied more in intermediate-risk patients scheduled for intermediate- or low-risk surgery. Therefore, the underutilization of β-blockers in patients scheduled for open cholecystectomy is not only due to the absence of concordance of physicians with guidelines but also because physicians are uncertain about the benefit of perioperative use of β-blockers specifically aimed to protect patients during low- or intermediate-risk surgery. Finally, did the consultant indicate β-blockade to protect the patient specifically for the perioperative period or for the long run?

**In reply**

Our study identified perioperative underutilization of β-blockers in patients with risk for CAD despite their use having been incorporated in the American College of Physicians (ACP) practice guidelines. Beattie et al and Marret and Albaladejo raise the question of benefit of perioperative β-block-