

had a recent myocardial infarction, and had a significantly higher prevalence of several coexisting conditions. Since all these factors are predictive of higher rates of death and myocardial infarction, we adjusted for them and other factors with the use of both multivariable methods and propensity analyses. Both methods led to the same conclusion. Propensity-score matching, another use of propensity methods, yielded similar relative outcomes.

Also, we do not agree that randomized, controlled trials will “appropriately evaluate the relative merits” of the two treatments. The results of randomized, controlled trials do not apply to many patients because such trials are limited primarily to low-risk patients and because they have artificially higher rates of complete revascularization among patients treated with stents and more frequent patient follow-up than in the real world. These factors all introduce a bias in favor of stenting. In our view, a combination of randomized, controlled trials and observational studies is required to provide a complete picture.

In response to Harjai, we did not think it was appropriate to exclude patients with both drug-eluting stents and bare-metal stents, because stenting was chosen as an option for them, and the comparison was between CABG and stenting.

Excluding them would only have created more dissimilarities between the patients treated with surgery and those treated with PCI.

Ng and Kritharides imply that our comparison is not fair because the patients treated with stents were not as likely to have been effectively (completely) revascularized. We agree that patients with stents in whom complete revascularization is not attempted fare significantly worse than patients in whom complete revascularization is attempted.¹ However, the purpose of our study was to compare the two procedures as they are used in practice, not in some ideal setting that does not reflect what patients can expect to encounter.

We agree with Ng and Kritharides that the use of medical therapy affects outcomes, and differential use according to procedure could be a source of bias. Also, a shorter duration of use of clopidogrel in the early years of drug-eluting stents may have created a bias against stenting.

Edward L. Hannan, Ph.D., M.S.

University at Albany School of Public Health
Rensselaer, NY 12144
elh03@health.state.ny.us

1. Hannan EL, Raczy M, Holmes DR, et al. The impact of completeness of percutaneous coronary intervention revascularization on long-term outcomes in the stent era. *Circulation* 2006; 113:2406-12.

Endovascular vs. Open Repair of Abdominal Aortic Aneurysms

TO THE EDITOR: Schermerhorn and colleagues (Jan. 31 issue)¹ examined the relative effectiveness of endovascular versus open repair of abdominal aortic aneurysms. They used a propensity-score approach to match the open-repair and endovascular-repair groups according to demographic and clinical factors. They argued strongly that unmeasured confounding factors were unlikely to bias their results. Unfortunately, propensity scores do not eliminate bias if there are unmeasured confounders.² The story of the pulmonary-artery catheter provides a cautionary tale. Using a propensity score, investigators found that the use of a pulmonary-artery catheter was associated with a 24% increase in the risk of death as compared with no use of a pulmonary-artery catheter.³ Randomized, controlled trials, however, have not borne out this result.⁴ The discrepancy arose because there were unmeasured confounders in the

observational analysis. In the current study, it is clear that patients in the endovascular-repair group were older and sicker than those in the open-repair group. There is a high likelihood that the propensity score, which is based on administrative data, does not include important confounders and therefore incompletely “controls” for the higher predicted mortality in the endovascular-repair group. Consequently, the analysis probably underestimates the treatment benefit of endovascular repair.

Mark D. Eisner, M.D., M.P.H.

University of California at San Francisco
San Francisco, CA 94143-0111
mark.eisner@ucsf.edu

1. Schermerhorn ML, O'Malley AJ, Jhaveri A, Cotterill P, Pomposelli F, Landon BE. Endovascular vs. open repair of abdominal aortic aneurysms in the Medicare population. *N Engl J Med* 2008;358:464-74.
2. Weitzen S, Lapane KL, Toledano AY, Hume AL, Mor V. Weak-

nesses of goodness-of-fit tests for evaluating propensity score models: the case of the omitted confounder. *Pharmacoepidemiol Drug Saf* 2005;14:227-38.

3. Connors AF Jr, Speroff T, Dawson NV, et al. The effectiveness of right heart catheterization in the initial care of critically ill patients. *JAMA* 1996;276:889-97.

4. Wheeler AP, Bernard GR, Thompson BT, et al. Pulmonary-artery versus central venous catheter to guide treatment of acute lung injury. *N Engl J Med* 2006;354:2213-24.

THE AUTHORS REPLY: With regard to Eisner's comments: we conducted an observational study and used propensity-score methods¹ to create evenly matched cohorts of patients. The propensity-score models controlled for an extensive list of potential confounders, but they were limited to variables that could be obtained from administrative data. Although our results could be biased by unmeasured confounders, the magnitude of the differences we observed makes it unlikely that an unmeasured confounder could have al-

tered our results in favor of open repair. Furthermore, we agree with Eisner that unmeasured confounding is more likely to have led to bias against endovascular repair. Thus, in contrast to the example of the pulmonary-artery catheter, the fact that we found an important difference despite the potential for unmeasured confounders further underscores the importance of our results for clinical practice.

Marc L. Schermerhorn, M.D.

Beth Israel Deaconess Medical Center
Boston, MA 02215
mrscherm@bidmc.harvard.edu

A. James O'Malley, Ph.D.

Bruce E. Landon, M.D., M.B.A.

Harvard Medical School
Boston, MA 02115

1. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika* 1983;70:41-55.

Rituximab in Relapsing–Remitting Multiple Sclerosis

TO THE EDITOR: Hauser et al. (Feb. 14 issue)¹ report positive results of a phase 2 trial of rituximab in relapsing–remitting multiple sclerosis. I wish to draw attention to the Food and Drug Administration (FDA) public health advisory concerning rituximab.² This advisory was recently updated after the reported deaths from progressive multifocal leukoencephalopathy of two patients who were treated with rituximab for systemic lupus erythematosus. Keeping pace with the use of more potent and specific immunosuppressant agents, the incidence of opportunistic infections such as progressive multifocal leukoencephalopathy seems to be increasing. In clinical trials of natalizumab for the treatment of Crohn's disease and multiple sclerosis, progressive multifocal leukoencephalopathy developed in three patients, two of whom died.³ Natalizumab was withdrawn from the market, and after a large postexposure evaluation, it was allowed back on the market with extensive safety instructions. Hence, despite the promising results of the newer generation of immunosuppressive drugs, their safety profiles raise concern. In order to optimize the balance between the risks and benefits of treatment, future trials should both incorporate rigorous safety monitoring and target those patients who have a great risk of disability.

Hans M. Schrijver, M.D.

Westfries Gasthuis
1620 AR Hoorn, the Netherlands
h.schrijver@westfriesgasthuis.nl

1. Hauser SL, Waubant E, Arnold DL, et al. B-cell depletion with rituximab in relapsing–remitting multiple sclerosis. *N Engl J Med* 2008;358:676-88.

2. FDA public health advisory: life-threatening brain infection in patients with systemic lupus erythematosus after Rituxan (rituximab) treatment. (Accessed May 23, 2008, at <http://www.fda.gov/cder/drug/advisory/rituximab.htm>.)

3. Berger JR, Koralnik IJN. Progressive multifocal leukoencephalopathy and natalizumab — unforeseen consequences. *N Engl J Med* 2005;353:414-6.

TO THE EDITOR: The use of rituximab, an anti-CD20 antibody, in the treatment of autoimmune diseases, including multiple sclerosis, is surely promising. In their article, Hauser et al. report that CD19 and CD20 have similar expression profiles, and therefore they monitored CD19 cells in the patients with multiple sclerosis who were treated with rituximab. CD19 and CD20 expression is not the same in different stages of B-cell development and function.¹ CD20– autoreactive B-cell clones could, in some cases, mediate the damage in autoimmune diseases.² Therefore, the monitoring of CD19-expressing and CD20-expressing cells could perhaps improve our understanding of the efficacy of rituximab in patients with