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LETTERS

Inappropriate Analogy

I read with shock and distaste the opening of the Research News article about the Keck telescope that begins, "In the pages of *Mademoiselle* and *Cosmo*, there's an eternal debate about whether bigger really is better" (15 Apr., p. 346). A sophomoric sexual reference attributed to women's magazines is hardly an appropriate lead-in to a *Science* article, especially when more amusing and less offensive "bigger is better" analogies exist. Respect for your female and male readers should preclude the publication of such a comment. This type of writing degrades the journal.

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Response: The News department regrets the tone of the offending sentences in the article. Those sentences were inappropriate, and the News department takes responsibility for them. In the future we will redouble our efforts to be sure it doesn't happen again.

—John Benditt, Features Editor

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Black Rhino Conservation

Our recent Policy Forum (4 Mar., p. 1241) about the efficacy of different black rhino conservation strategies may have had an unfortunate result, the premature termination of our research project in Namibia. We had little choice but to leave the country when our research permits were not renewed. This occurred after publication of our Policy Forum, which did not unequivocally support "official" policy.

Our study was designed to evaluate biological consequences of dehorning rhinos as a conservation measure. It was officially approved by Namibia's Ministry of Wildlife, Conservation, and Tourism (MWCT). After 3 years, our findings regarding dehorning were mixed, news apparently not well received by MWCT officials in light of their decision to continue to dehorn rhinos and to support legalized horn trade.

Namibia, as an independent country, should of course be free to manage their resources any way that they so please. The choice to accept or discard information is ultimately theirs alone. But they have much to lose. There will now be no way to validate declarations about the success or failure of different programs, including dehorning. Without research by independent scientists, it will be difficult to know whether assertions of management successes are credible. The MWCT is no longer free from conflicts of interest. As they pointed out to us, some of our results could be used by detractors of the dehorning tactic and possibly hundreds of thousands of international dollars would be lost.

Clearly, the unenviable dilemma is whether to make no waves and continue one's work or, at some risk, to attempt to notify local officials, drawing attention to results that do not wholeheartedly embrace a host country's official policy. It would be impossible for any field study of rhino conservation, no matter how long, to remove unequivocally *all* possible competing explanations. Because many countries are now trying to assess management strategies for rhinos and to implement sanctions against those using rhino horn, we felt a responsibility to release scientific results quickly so as to enable informed decision-making.

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Outcomes Research

We read Christopher Anderson's review of outcomes research with a curious sense of déjà vu (News & Comment, 25 Feb., p. 1080). The alleged inadequacies of nonrandomized studies of human health have provoked spirited exchanges in *Science* and elsewhere (*1*). These debates have centered on traditional epidemiologic studies of disease causation in which, for ethical reasons, randomization is prohibited and nonrandomized studies must be used.

For assessing new therapies, however, randomization *is* often ethically acceptable and has traditionally been the method of choice. Randomization greatly enhances one's ability to make unbiased comparisons

between treatments within studies and to draw statistical inferences about a therapy's efficacy. It does not necessarily ensure, however, that a study's results apply to all patients with the condition under study because, unlike laboratory rats, people can refuse to participate in studies. The reasons for refusal may limit a trial's generalizability to others. Nonparticipation is not merely a theoretical concern. In a recent randomized controlled trial of stopping antiepileptic drugs in patients with epilepsy in remission, nearly half of the eligible patients refused to participate (*2*). Funding was withdrawn for another trial of epilepsy surgery after an insufficient number of patients were willing to have the decision of whether to have part of their brains surgically removed decided at random (*3*).

The personal preferences that play a role in deciding which treatment is best for an individual and those that distinguish individuals who are willing to have such decisions made at random from those who are not are critical to the complete assessment of a therapy's risks and benefits. Randomization does not excuse investigators from considering such nonrandom issues. Each individual's decision represents an attempt to maximize the likelihood of obtaining the best possible outcome for himself or herself. What is best for one person may not be best for another. Traditional measures of morbidity and mortality are often insufficient for fully assessing the benefits and risks of many treatments.

Quality of life and self-reported measures of well-being are increasingly recognized as equally valid and important measures of a therapy's success. Recently, research efforts, some funded through the Agency for Health Care Policy and Research (AHCPR), have been devoted to the development of valid, reliable measures of the quality of life. Yet only passing mention of this fundamental thrust of outcomes research was made in Anderson's article.

Because personal factors influence who participates, randomized controlled trials cannot always provide many important answers needed for rational decision-making. Outcomes research is a developing field with the potential for providing some of these answers. We can draw on the considerable strengths and sophistication of traditional epidemiology to improve nonrandomized studies of treatments. Admittedly, this involves challenging, thought-intensive processes as well as special methodologic approaches developed by epidemiologists in studies of disease causation. Our goals should be to develop the field of outcomes research so that it complements experimental clinical science and to improve the ability of both randomized and nonrandomized studies to measure those outcomes most relevant to individual patients.

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Anderson's article takes too limited a view of outcomes research and its accomplishments. Outcomes research is not a single methodology based on analysis of claims data; rather, it is a strategy that uses a variety of methods and approaches, including randomized clinical trials (RCTs), to reduce scientific uncertainties about the outcomes of medical care. This approach is a pragmatic one, seeking efficiency in the solution of complex evaluation problems.

Randomized trials cannot be conducted to solve every question about treatment effectiveness in medicine. The tools for resolving uncertainty under the umbrella of "outcomes research" include decision analysis; structured reviews of the literature, including meta-analyses; retrospective analyses of existing databases and medical records using case-control or cohort designs; and prospective clinical trials based on randomized and nonrandomized (preference) design.

Outcomes researchers are particularly interested in the outcomes of treatment that most matter to patients, with less emphasis on intermediate physiological or "proxy" outcomes. Focus groups with patients can help identify all relevant outcomes that matter to patients, allowing construction of measures, particularly of functioning and health status, to better achieve these outcomes. For many medical problems, multiple treatment options exist, with different trade-offs between therapeutic effects and side effects, or even quantity and quality of life. Individual patients can and should weigh these factors differently in arriving at an optimal treatment decision.

Since 1987, our Patient Outcomes Research Team (PORT), funded by AHCPR, has applied the spectrum of methods described above in its ongoing investigation of

the treatment of benign prostatic hyperplasia (BPH), a common cause of morbidity among older men. PORT work clarified that the main effect of surgery for this condition was improvement in symptoms and quality of life and that, in fact, surgery had a large therapeutic effect on symptoms and health status.

A significant conclusion of the PORT research agenda—that rational decision-making depends on active patient involvement in the choice of treatment (shared decision-making)—is a major feature of the recent national guideline on BPH issued by AHCPR.

PORT research has had a significant impact on patient choice: when shared decision-making has been adopted, patients have expressed a more conservative pattern of treatment preference, even in HMOs where surgery rates were already lower than average, suggesting that patients may prefer less surgery than the amount now prescribed in the United States.

Before the paper by John Concato and Alvan Feinstein (*1*) reporting the association between transurethral resection of the prostate (TURP) and higher mortality rate referred to in Anderson's article was published, we had already completed a review of individual records (using essentially the same methods as Concato and Feinstein) that did not alter the results of the claims data studies (the broad confidence interval around the relative risk in the small Concato and Feinstein study is, in fact, still consistent with the elevated relative risks in the 1.3 to 1.5 range seen in the claims databases). A small RCT showing an excess mortality after TURP compared with open prostatectomy came to our attention. We concluded that the hypothesis should be tested by a large RCT.

The neglect of RCTs in the treatment of BPH has not been because of an unwillingness of PORT or leading urologists to organize the necessary studies. Even though the American Urological Association has invested more than a million dollars demonstrating the feasibility of a clinical trial network, the necessary federal support for clinical trials has not been forthcoming. Congress should put RCTs on the agenda for the AHCPR.

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