

*In Reply:*—We thank Dr. de Saint Maurice *et al.* for their interest in our recent paper on anesthesia-related mortality,<sup>1</sup> in which we presented a comprehensive set of anesthesia safety indicators based on the International Classification of Diseases and Related Health Problems, 10th Revision, codes that are specifically related to anesthesia or anesthetics, and applied these indicators to the United States multiple-cause-of-death data files for the years 1999–2005. In their letter, de Saint Maurice *et al.* raise three issues regarding our methodology.

First, they point out that the International Classification of Diseases codes do not contain detailed information about the “precise” mechanisms of anesthesia-related fatalities, and therefore suggest that it is necessary to rely on an expert panel in determining the role that anesthesia played in a given death. Although information provided by the International Classification of Diseases coding system may not be sufficient to address certain research questions, such as the pathophysiological mechanism of malignant hyperthermia, as the most authoritative disease classification system it does allow a reasonably detailed categorization of the role anesthesia played in the death (table 1 of our article<sup>1</sup>). The expert panel approach, if applied properly, can help enhance the accuracy of data on cause of death and generate valuable information for quality improvement of clinical care. Depending on the purpose of the specific study, an expert panel may not always be necessary, practical, or advisable. One of the caveats in the expert panel approach is the lack of reliability. That is, the degree of agreement among genuine experts on subjective matters, such as the role of anesthesia in a sample of fatalities, may be poor, and thus it is difficult to independently replicate the study results that are based on expert panel reviews.

The second issue raised by de Saint Maurice *et al.* concerns the sensitivity of the anesthesia safety indicators in identifying anesthesia-related deaths. As discussed in our article,<sup>1</sup> we are only able to capture death certificates in which an anesthesia complication or adverse event was listed among the multiple causes of death. It is worth noting that sensitivity and specificity are generally inversely related; an increase in

sensitivity often comes at the expense of specificity. Thus, to include the clinical scenarios suggested by de Saint Maurice *et al.*, such as aspiration during emergency procedures and hemorrhage during surgery, in the anesthesia safety indicators may somewhat reduce false negatives but substantially increase false positives, as many of these events may have little to do with anesthesia or anesthetics. We agree with de Saint Maurice *et al.* that text written on the death certificates might be useful to improve the sensitivity of our method of identifying anesthesia-related deaths, and are actively exploring the feasibility of incorporating these data in our research.

Finally, de Saint Maurice *et al.* comment on the tradeoff between sensitivity and specificity and the practical question of how to assess anesthesia safety under the constraints of imperfect data, inadequate tools, and limited resources. We share their view that, given the constraints facing researchers, the best available option is to monitor the time trends of anesthesia morbidity and mortality using the same indicators and data systems. The anesthesia safety indicators presented in our study of mortality<sup>1</sup> and the forthcoming study of morbidity<sup>2</sup> using well-established national and state health information systems are developed to serve this very purpose.

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(Accepted for publication July 29, 2009.)

## Are Signposts in the Woods Pointing in the Right Direction?

*To the Editor:*—Dr. Eisenach articulately develops a plan for *ANESTHESIOLOGY* to deal with what is arguably the largest case of author misconduct in our specialty’s history.<sup>1</sup> However, I have concern for the statement regarding the lack of interest in publishing confirmatory studies. Is the “bias against confirmatory research” in the best interests of the reader, the journal, or scientific investigation? The Reuben episode is ample evidence that more confirmatory investigations (not less) should be published. Even in the absence of academic fraud, as Ioannidis has documented, data from approximately one-third of “highly cited” publications cannot be supported (or the treatment effect is greatly diminished) by subsequent studies.<sup>2</sup> For example, two large recent investigations have dampened the enthusiasm for the pivotal studies that supported perioperative administration of  $\beta$  blockers and tight control of glucose in the intensive care unit.<sup>3–4</sup>

In essence, by requesting manuscripts reexamining some of Reuben’s hypotheses, the editors are actually seeking confirmatory studies. I realize that *ANESTHESIOLOGY* receives many meritorious studies that because of a number of factors will not achieve priority for publication. Perhaps some of these confirmatory studies (undergoing the same rigorous editorial review as printed articles) could be published in an electronic format so that they will be available to scientists and the

readership. The *New England Journal of Medicine* and *Circulation* are just two examples of high-impact journals that promote “seminal discovery” and publish selected communications in an electronic rather than print format.

The signposts are already in the woods and as skillful explorers we have to read them.

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(Accepted for publication August 10, 2009.)