neuraxial blocks, and perhaps additionally more skilled at the management of orthopedic patients. That alone could explain a tiny patient mortality improvement associated with use of neuraxial anesthesia. Conversely, it could be speculated that decreased use of neuraxial anesthesia may be influenced by slower surgeons with reduced surgical skills, causing increased patient surgical stress, blood loss, and sepsis and who may prefer (or their anesthesiologists prefer) general anesthesia.

Based on such factors, we are reluctant to conclude that the use of regional anesthesia *per se* is "superior" to general anesthesia in terms of patient 30-day mortality. Although neither do we dispute the observed difference in the mortality of PATIENTS having regional *versus* general anesthesia nor do we disagree with the importance of this difference, we cannot know whether the choice of anesthetic itself was the causative factor. We conversely observe that, at the least, neither the metanalysis performed by Rodgers *et al.*[5] in 2000 (which was perhaps the "mega-study" for that era) nor the Memtsoudis *et al.*'s study on 382,236 patient records suggest neuraxial blocks are detrimental to the patient.

The Memtsoudis's study it is exceptionally useful for the debate it raises. But as noted by both Memtsoudis *et al.* and Neuman and Brummet[6] in the accompanying editorial, this study is unlikely to be the last word. Further study is clearly needed—but the challenge will be to find improved ways to actually perform (and analyze) such studies.

Robert M. Raw, M.D., Michael M. Todd, M.D., Brad J. Hindman, M.D., Rashmi Mueller, M.D. University of Iowa, Iowa City, Iowa (R.M.R.). rob-raw@uiowa.edu

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(Accepted for publication August 23, 2013.)

In Reply:

I thank Drs. Raw, Todd, Hindman, and Mueller for their interest in our study[1] and their thoughtful comments. The authors raise important points representing different perspectives regarding the use of large databases for research in general and for anesthesia outcomes in particular. Despite the widespread use of administrative databases by various specialties over the last decades, perioperative physicians have only relatively recently been engaged in this type of population-based research. Therefore, traditional approaches to review and interpret studies may seem inadequate for the evaluation of resulting data that often use complex methodologies. However, I believe that it is time for our specialty to embrace these type of studies as many other specialties have done, accepting their strengths AND weaknesses. Although it must be stressed that outcome studies of this kind are not meant to and cannot be the final word on a research question, they do represent population-based observations on issues using information from actual practice that then require further inquiry.

Raw *et al.* discuss the fact that the outcome of mortality may be of limited significance during the career of an individual practitioner. However, viewed through the eyes of a public health researcher, one has to consider that between 1990 and 2004 over 23,000 patients died in the United States alone after hip and knee arthroplasty.[2] At current rates of 1 million joint arthroplasties performed annually, a difference of 0.08% in mortality rate (which is the difference found between cases using neuraxial *vs.* general anesthesia) relates to 800 lives saved if all cases were performed under neuraxial anesthesia *versus* a general approach.

In addition, mortality was only one of the outcomes studied in our analysis, and many other more frequently occurring complications were positively affected in the setting of neuraxial anesthesia. This is important because although individual practitioners may experience very few fatal outcomes during their career, certainly many of us will observe serious complications on many more occasions. It is becoming increasingly clear that although causal relationships cannot be established with database analyses, the association found in our and other studies between outcomes and anesthetic practice needs to be further explored.[1,3]

There is no question that database studies lack the ability to provide explanations of mechanisms associated with observations and are unable to account for many important cofounders. In this context, Raw *et al.* are correct that we cannot establish why neuraxial anesthesia was chosen and it is imperative that readers take this fact into consideration when interpreting the study results. However, these results should be reason for pause and at the very least lead to the rethinking of long-held beliefs, reevaluation of practices, and the generation of hypotheses that should be pursued in a quest for answers regarding potential mechanisms of action. Even if it turns out that, for example, neuraxial anesthesia use by itself is not the reason for better

outcomes, we need to take the association found in our study seriously and identify which factors associated with its use can explain the differences found. To take the view of a patient selecting a hospital for their surgery, one would have to ask if it really matters to them why neuraxial seems to be associated with better outcomes compared with general anesthesia. Patients may not care about mechanisms, and more about associations, even if the performance of neuraxial anesthesia represents a mere marker of a more sophisticated perioperative approach, shorter surgical times, or other beneficial practices.

Finally, although I agree that randomized, controlled studies may not be feasible to pursue questions such as the one evaluated in our study to control for cofounders, other, nontraditional methodologies taking advantage of the naturally occurring variability in practice patterns and ability to collect information on predetermined variables of interest may emerge as preferred tools to determine which interventions work better than others in a real-world setting. For instance, practice-based evidence trials have been highly underutilized in perioperative research and may present opportunities to study questions such as the one regarding the impact of the type of anesthesia on outcomes.[4]

In conclusion, despite their limitations, database studies should be embraced as valuable tools to provide important, but arguably incomplete, information on topics long beyond the reach of traditional research as they have been for decades in other specialties. Anesthesiologists should grasp the opportunities provided by database research and expand their views of outcomes to include the role anesthesia has on the broader medical system and the public's health.

Stavros G. Memtsoudis, M.D., Ph.D., F.C.C.P., Weill Cornell Medical College, Hospital for Special Surgery, New York, New York. memtsoudiss@hss.edu

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(Accepted for publication August 23, 2013.)