

Perioperative Comparative Effectiveness Research

An Opportunity Calling

IN this issue of ANESTHESIOLOGY, Memtsoudis *et al.*¹ offer compelling evidence that the practice of bilateral total knee arthroplasty—staged within one hospitalization or simultaneous within one anesthetic episode—confers increased risk of in-hospital mortality and morbidity compared with unilateral procedures. One may question why data regarding surgical staging are presented in an anesthesiology journal. This article brings into focus the valuable role anesthesiologists can play in perioperative safety research. More importantly, it reminds us that vital opportunities for perioperative research are within our reach.

The work of Memtsoudis *et al.* highlights the challenge of translating outcomes identified in ideal clinical settings to a broader practice pattern. In the 1990s, some centers began performing bilateral total knee arthroplasty during one operative episode and anesthetic—known as “simultaneous bilateral” total knee arthroplasty—in an attempt to decrease cost, patient inconvenience, total pain and suffering, and the “total duration of anesthesia.”² Although small case series at high-volume centers initially supported this practice,³ larger studies demonstrated that simultaneous procedures were associated with higher mortality and morbidity rates.⁴ The data of Memtsoudis *et al.* advances our knowledge by demonstrating that even staged procedures performed on healthier patients carry a higher risk of in-hospital morbidity or mortality. Their work is a form of comparative effectiveness research (CER), a branch of clinical “research comparing the benefits and harms of different interventions and strategies . . . in ‘real world’ settings.”* Although the data of Memtsoudis *et al.* cannot provide detailed “benefit” information, they do reveal the actual risks of bilateral total knee arthroplasty when it is performed by a broad range of providers and in a broad range of settings.

Comparative effectiveness research has gained increased visibility over the past year because the American Recovery and Reinvestment Act—the \$787 billion

“stimulus package”—allocated an incremental \$1.1 billion of funding to CER. These funds are divided among the National Institutes of Health, Department of Health and Human Services, and Agency for Healthcare Research and Quality. However, CER and its funding are not uniquely American issues. The clinical questions CER hopes to address remain unanswered for patients around the world. To understand what CER is and anesthesiology’s potential role, it is essential to have a basic understanding of the concepts of efficacy, effectiveness, and efficiency. *Efficacy* refers to the potential benefit or risk of a treatment under ideal circumstances in a specific patient population. *Effectiveness* refers to the actual benefit of that treatment in usual care settings in a broad patient population. *Efficiency* incorporates the financial costs and savings of the alternatives. Haynes simplified the concepts more than decade ago as, “Can it work? Does it work? Is it worth it?”⁵

These are not new concepts to anesthesiologists. However, much like the practice of medicine as a whole, many of our clinical decisions are not rooted in large comparative effectiveness trials. Efficacy trials are typically small, early-stage randomized controlled trials of a treatment. They often enroll a specific, high-risk patient population to maximize statistical power and require detailed protocols mandating specific care patterns and ideal use of the studied intervention. An example would be the van den Berghe *et al.*⁶ trial of intensive insulin therapy in surgical intensive care unit patients, which demonstrated a profound mortality and morbidity benefit to targeting blood glucose levels less than 110 mg/dl. This “proof-of-concept” study was then rapidly extrapolated to become a mainstay of critical care protocols. A multicenter study enrolling more than 6,000 heterogeneous patients under typical care settings demonstrated lower mortality using conventional blood glucose targets.⁷ These conflicting results, although initially surprising, have been seen previously in the sagas of perioperative β blockade and aprotinin. Clinical researchers have historically described efficacy *versus* effectiveness as “internal validity” *versus* “generalizability.” However, the current CER focus is more than a semantic change. Previous attempts at evaluating generalizability, such as meta-analyses, used tightly protocolized randomized controlled trial data as the substrate for analysis, rather than real-world care settings. More importantly, the current US healthcare reform debate assumes that providing more effective treatments will decrease overall costs.

On June 30, 2009, the Federal Coordinating Council—a group of officials from the National Institutes of Health, Department of Health and Human Services, and

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* Federal Coordinating Council for Comparative Effectiveness Research Report to the President and the Congress. Available at: <http://www.hhs.gov/recovery/programs/cer/cerannualrpt.pdf>. Accessed August 14, 2009.

other healthcare departments—delivered a report to Congress outlining a CER strategy and specific funding priorities.* The word “anesthesiology” or “anesthesia” cannot be found in this 77-page document. However, “evaluating surgical options” was one of six areas with “high potential impact.”* On the same day, the Institute of Medicine delivered a detailed report outlining the top 100 funding priorities for the \$1.1 billion of funding.† None of the 100 clinical priorities involved the safety of anesthesia, blood products, or different anesthetic options. The “Health Care Delivery System” is the most prominent Institute of Medicine priority for CER, with 23 priority topics. Cardiovascular disease constitutes the second most prominent area, with 8 priority topics. Overall, only 4 topics can be addressed by anesthesiologists as principal investigators: (1) strategies to reduce healthcare-associated infections, (2) opioid and nonopioid pain relievers among subjects with acute and chronic pain, (3) strategies for chronic migraine headaches, and (4) treatment strategies for low back pain.

Anesthesiology’s challenges in obtaining National Institutes of Health funding have been detailed previously.⁸ To maximize our role in CER, we must take several steps. First, although our field is hailed as a patient safety leader, we must recognize that many of our decisions would benefit from increased CER. Hemodynamic management strategies, the use of expensive technology (ultrasound-guided peripheral nerve blockade, video laryngoscopy, and others), neuraxial analgesic options, and even the fundamental choice of anesthetic technique are all based on small efficacy studies, animal models, or anecdote. Comparative effectiveness trials go far beyond comparisons of one medication to another and must become part of the culture of patient safety progress. The American Society of Anesthesiologists Anesthesia Quality Institute⁹ and Committee on Performance and Outcomes Measurement represent initiatives that enable anesthesiologists to engage in CER.

Second, we must actively participate in the perioperative CER opportunities that already exist and have been prioritized for funding. There are 10 priority topics evaluating the effectiveness of surgical *versus* medical options for specific diseases (atrial fibrillation, prostate cancer, low back pain, and others). There are also two topics evaluating open, laparoscopic, and robot-assisted surgical techniques. We are the only perioperative physicians who perform preoperative comorbidity evaluation and optimization, intraoperative management, and postoperative critical care. We must reach across the

drape to our surgeon colleagues and collaborate with them on these CER opportunities. For example, the Agency for Healthcare Research and Quality’s first Recovery Act funding announcement was a \$12 million grant requesting a national registry to evaluate orthopedic devices and medications.‡ One must consider how such a registry could create knowledge if it did not involve anesthesiologists describing the impact of anesthetic technique and postoperative analgesia on long-term outcome. Investigations such as that of Memtsoudis *et al.* reveal the prominent role we can play. Anesthesiologists are already prominent researchers in areas as diverse as perioperative myocardial infarction and critical care quality measures. These achievements must be expanded to include the current CER opportunities.

Finally, we must communicate the scientific controversies of our field to policy developers. The possible impact of anesthesia on neonatal development, cognitive function in the elderly, and cancer progression must be understood by those allocating funding. A recent series of editorials in this journal has demonstrated that management of the perioperative stress response and acute surgical injury could affect long-term outcomes such as stroke, myocardial infarction, chronic pain, and cancer progression.^{10–12} The need for CER in anesthesiology is clear to leaders in our field. However, the large-scale prospective CER necessary to answer these questions *in vivo* will only become a reality if policy makers understand that the historic mortality gains of anesthesia still leave room for progress in morbidity.

Comparative effectiveness research is unlikely to fade away as a public policy fad. Funding for CER will be continued beyond the Recovery Act timeframe and increasing proportions of the federal healthcare research budget will be allocated to it. As anesthesiologists and perioperative medicine physicians, it behooves us to make the most of this opportunity.

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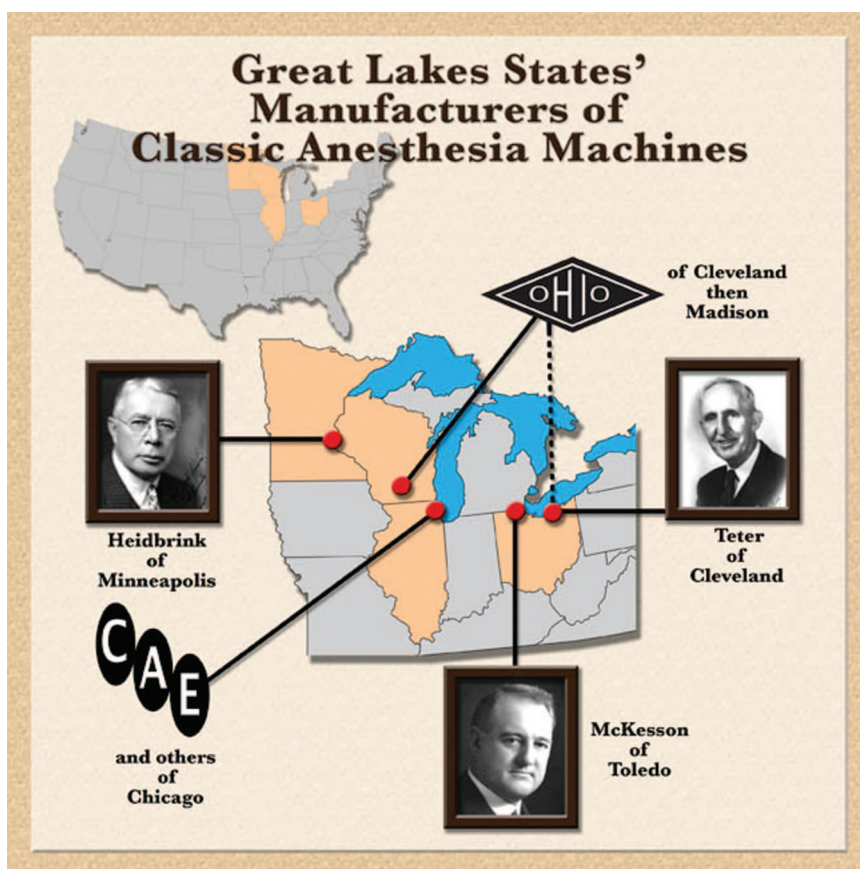
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■ ANESTHESIOLOGY REFLECTIONS

Great Lakers' Anesthesia Machines



Fortunately for American anesthesia, technology for nitrous oxide–oxygen machinery developed in the wake of evolving fossil fuel and steel industries in cities around the nation's Great Lakes. Such “laughing gas machines” were produced by namesake firms founded by Teter of Cleveland, McKesson of Toledo, Heidbrink of Minneapolis, and by at least four Chicago firms. In the wake of machinery pioneered by the Philadelphia firm founded by S. S. White, Cleveland dentist Charles K. Teter (1875–1959) established America's second major line of machines. Another dentist, Jay A. Heidbrink (1875–1957), would eventually merge his namesake machinery into the “Ohio” line of anesthetic apparatus, which sidestepped changing its name to “Minnesota” (for Heidbrink) or to “Wisconsin,” the state to which the company relocated after leaving Cleveland, Ohio. (Copyright © the American Society of Anesthesiologists, Inc. This image appears in color in the *Anesthesiology Reflections* online collection available at www.anesthesiology.org.)

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