

surgery centers may be looking to shrink their preoperative clinics and replace in-person evaluations with phone calls or less for all but the sickest, we need to avoid missing both a need and an opportunity. Anesthesiologists should endeavor to both improve patient care and enhance their value to their patients and their institutions by meeting this important patient need.

### Competing Interests

Dr. Kharasch is the Editor-in-Chief of ANESTHESIOLOGY, and his institution receives salary support from the American Society of Anesthesiologists (Schaumburg, Illinois) for this position. Dr. Avram is the Assistant Editor-in-Chief of ANESTHESIOLOGY, and his institution receives salary support from the American Society of Anesthesiologists for this position. Dr. Avram also has a financial relationship with the Department of Anesthesiology, North Shore University Evanston Hospital (Evanston, Illinois) for research consultation. Dr. Clark is a consultant for Teikoku Pharma USA (San Jose, California).

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## Implications of Practice Variability: Comment

To the Editor:

I read with interest the Editorial by Sessler<sup>1</sup> on the implications of practice variability. There is considerable interpatient variability in the response to surgical stress,

hemodynamic perturbations, anesthetics, fluids, vasopressors, inotropic therapy, extracorporeal-circulation, hemotherapy, ischemia-reperfusion, and others, and also considerable interindividual variation in the incidence and severity of the perioperative complications. Although personalized or precision medicine is gaining implementation generally in disease prevention and treatment, the potential of precision perioperative medicine remains to be fully explored and implemented, such as in hemodynamic optimization, anesthetic regimens, pharmacologic therapy, pain management, mechanical ventilation, and other organ protective strategies.<sup>2</sup> The guideline- and protocol-based perioperative approach constitutes the antithesis of precision medicine in perioperative practice. Nevertheless, the proponents of precision perioperative medicine embrace the notion that most of the standardized therapies are designed for an average patient and are insensitive to the wide heterogeneity wherein different subsets of patients respond differently to an allocated treatment. In addition, they cite an assortment of confounding factors ranging from Hawthorne effect to the impact of a heightened vigilance in modulating the outcomes under evaluation while adhering to a protocol. Moreover, the lack of firm evidence on the results of protocolized interventions, such as early goal-directed therapy in sepsis, accentuates the debate furthermore.<sup>3</sup> Interestingly, the theory of refuting a free pass to the clinical pathways on evidence to preclude the extrapolation of the same to procedures and populations they were never investigated upon begets the need of a robust context-appropriate evidence.<sup>1</sup> As precision medicine evolves across diverse clinical settings, the lack of acknowledgment to this evolving paradigm shift under the preconceived notion that the standardized approach is sacrosanct in perioperative practice is a disfavor to the speciality when the impetus to execute precision medicine in other clinical fields is captivating society.

### Competing Interests

The author declares no competing interests.

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## Implications of Practice Variability: Comment

To the Editor:

If Charles Dickens were alive today, he might be convinced to pen an epic about the current state of perioperative medicine instead of a nineteenth-century 7-yr-old orphan. But just as Pip painfully learned how readily *Great Expectations* can evaporate, we believe anesthesiology must avoid a similarly painful downfall by immediately adopting vigorous testing procedures to the great expectations of enhanced recovery after surgery (ERAS) programs. ERAS requires the same scientific inquiry, systematic collection and analysis of quality outcome data, and statistical validation—quite simply EVIDENCE—that are required of pharmaceutical medications and medical devices.

Thus, we applaud Dr. Sessler's editorial "Implications of Practice Variability" in the February issue of *ANESTHESIOLOGY*,<sup>1</sup> in which he opines that the rampant proliferation of perioperative protocols, pathways, and ERAS guidelines vastly exceeds the sustaining scientific evidence. But we humbly suggest that Dr. Sessler's editorial may not have gone far enough in raising the alarm about instituting new, obligatory clinical pathways as "best practices" when the published evidence for such interventions is either absent, contradictory, or statistically inadequate. Moreover, of greatest concern is the common practice whereby medical centers and ERAS committees invoke new clinical pathways, but omit the commensurate requirement for concurrent, parallel, and meaningful (*i.e.*, more than just hospital discharge) patient data to provide definitive answers to whether these protocols indeed improve patient value as well as hospital efficiency. We posit that the future of ERAS must embrace three key concepts.

### Differentiating Proven from Unproven

Let's be clear—the general concept for the standardization of patient care for particular perioperative interventions is prudent, efficient, cost-effective, and—most critically—proven to work with selective and usually simple practice modifications. Thus, interventions such as practicing minimally invasive surgery, avoidance of nasogastric tubes, adoption of updated *non per os* and antibiotic guidelines, early perioperative oral intake, and early ambulation are prime examples that are proven to improve patient outcomes. But in many institutions, current ERAS protocols have quickly morphed from relatively simple interventions to multipage, detailed clinical mandates that dictate everything from type (and doses) of "approved" anesthetic drugs (inhalation anesthesia *vs.* total intravenous anesthesia), content and rate of fluid infusions, types of monitoring (BIS, FloTrac, *etc.*), and perhaps even the exact vasopressor for the treatment of hypotension. Such mandates clearly increase the cost, complexity, and preparation time for intraoperative care. But there is an alarming paucity of data for the majority of these trendy components of recent ERAS pathways. For example, although specific drugs such as infusions of lidocaine, magnesium, and ketamine are often promoted during major spine surgery, they have never, to our knowledge, been proven to be more efficacious than traditional anesthetic regimens. Indeed, a current randomized, controlled trial in patients having multilevel spine surgery with a protocol consisting of preoperative oral gabapentin and acetaminophen with intraoperative infusions of lidocaine and ketamine was stopped early because of futility—lacking evidence of efficacy!<sup>2</sup>

### Length of Stay—the Right Metric?

Originally, outcome reports from the early ERAS literature focused on the reduction of postoperative complications. More recently, length of stay has emerged as the "gold standard" for tracking protocol efficacy. Although there is no question that length of stay equates with reduction of required hospital resources—pleasing hospital administrators with cost savings—it is not clear that length of stay as a stand-alone metric is necessarily in the patient's best interest. As pointed out by Memtsoudis and Kehlet in their 2019 editorial,<sup>3</sup> a decreased length of stay may be associated with increased postdischarge spending. Furthermore, many of these postdischarge costs are *de facto* shifted to an alternative facility, such as a rehabilitation hospital, or the invisible but very real costs to the patient's caregivers (friends, family, neighbors) at home.

Moreover, although ERAS pathways are clearly linked to a reduced length of stay, we challenge clinicians and administrators to avoid the statistical trap of *associating* events (easy to do and easy to analyze) compared with designing and implementing valid inferential outcome studies proving *cause-and-effect* (hard to do and more complex to analyze).<sup>4</sup> Lastly, it is our impression that some of the length of stay improvement with ERAS could be due to setting new patient expectations during the preoperative anesthesia and

surgical visits. Indeed, one must consider either a placebo or even a Hawthorne effect as confounders.

### Generalizing the Academic Medical Center ERAS Experience

The bulk of the ERAS literature has come out of major academic medical centers, and we challenge investigators to expand and test whether and how these protocols are applicable to community and even small critical-access rural hospitals. In that process, we must recognize a number of barriers to generalized adoption of ERAS, including the following:

- **Cost.** Additional resources are needed to initiate and maintain protocols, rewrite standard order sets in your electronic medical record, provide sufficient monitors for protocol-driven algorithms, and hire data collection and analytic personnel to continually monitor quality outcomes within the institution.
- **Robust informatics.** Measuring pathway improvements is vital to both intelligently modify the protocols for maximum benefit as well as sustain support from hospital leadership. This requires both a sophisticated functional data system as well as skilled informatics practitioners to analyze the outcomes. At the University of Minnesota, more than \$150,000 per year is spent tracking these quality metrics (personal communication, Richard C. Prielipp, M.D., Department of Anesthesiology, University of Minnesota, Minneapolis, Minnesota; verbal communication as of June 2020).
- **A new team culture.** Although a local champion is key to initiating an ERAS pathway, the long-term success requires sustained collaboration of anesthesia, surgery, nursing, and hospital administration. Any breakdown in this network exposes impediments to sustained compliance.

### Summary

We applaud Sessler and Memtsoudis for sounding the alarm about the unbridled enthusiasm for ERAS protocols.<sup>1,3,4</sup> As Sessler opined: “There is no basis for giving clinical pathways a ‘free pass’ on evidence.”<sup>1</sup> Indeed, we applaud *ANESTHESIOLOGY* for increasing the volume of the alarm bell with publications like the randomized, controlled trial by Maheshwari *et al.*<sup>2</sup> Publication of such “negative” trials<sup>4</sup> is vital to separating valid ERAS elements from unnecessary or perhaps even detrimental components of proposed pathways. “Great expectations” for ERAS may indeed prove to be true, but in 2020 we still don’t know whether the reality equates to the hype. Regardless, it is time to put the evidence in ERAS.<sup>1,5</sup>

### Competing Interests

Dr. Prielipp is a member of the Board of Directors of the Anesthesia Patient Safety Foundation (APSF; Rochester, Minnesota) and serves on the speakers’ bureau for Merck Co., Inc. (Kenilworth, New Jersey). Dr. Rice declares no competing interests.

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## Impact of Closed-loop Anesthesia on Cognitive Function: Comment

To the Editor:

Joosten *et al.* are to be congratulated on their deployment of technically complex closed-loop systems to support patients during anesthesia and surgery.<sup>1</sup> The possibility of experiencing impaired neurocognitive function in association with a surgical episode is a concern to patients and those who care for them. It makes sense to establish whether changes in clinical technologies might diminish or abolish these unwelcome syndromes.