In Reply:

We appreciate the message from Drs. Klein, Yentis, and Clyburn in response to our Editorial in Anesthesiology[1] and our Letter to the Editor in *Anaesthesia.*[2] Clearly all correspondents are dedicated to scientific integrity in research.

Competing Interests

Dr. Kharasch is Editor-in-Chief and Dr. Houle is Statistical Editor for Anesthesiology.

Evan D. Kharasch, M.D., Ph.D., Timothy T. Houle, Ph.D. Duke University, Durham, North Carolina (E.D.K.). editorial-office@asahq.org

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Michael M. Todd, M.D., served as Handling Editor for this letter.

Clinical Decision Support Tools Need to Improve More Than Just Process Outcomes

To the Editor:

We read with great interest the recent article by Kheterpal *et al.*[1] We would contend that this article highlights an issue common in studies of clinical decision support—namely, that they improve process outcomes but have little demonstrable ability to improve clinically relevant outcomes.[2] To date, there have been few studies correlating clinical decision support to improved patient outcomes in the perioperative literature.[3,4] Given the amount of time and energy investigators devote to designing and implementing clinical decision support, this is, to be blunt, frustrating. Even more so because clinical decision support tools offer a means for using informatics expertise to implement an intervention that has significant face validity. That is, they offer providers timely and relevant information that highlights opportunities for making clinical interventions that they otherwise may have failed to recognize, thereby improving outcomes.

Why, then, the disconnect—inadequate validation and flawed study design, as Dr. Sessler asserts in his editorial?[5] Small effect size? We would contend that it is more likely indicative of a need to perform multicenter validation of clinical decision support tools. As the authors have shown previously, clinical decision support tools may vary in their effectiveness across institutions.[6] We propose that future studies of clinical decision support tools would be best structured as multicenter studies and, where possible, should be designed to demonstrate the intervention's impact on patient outcomes, rather than just process change—the field is ready for that critical next step.

Research Support

Competing Interests

Dr. Freundlich has received grant support from Medtronic (Boulder, Colorado) for work unrelated to the content of this letter. The remaining authors declare no competing interests.

Robert E. Freundlich, M.D., M.S., Jonathan P. Wanderer, M.D., M.Phil., Jesse M. Ehrenfeld, M.D., M.P.H. Vanderbilt University Medical Center, Nashville, Tennessee (R.E.F.). Robert.e.freundlich@vanderbilt.edu

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The Curse of Dimensionality

"Remember that all models are wrong; the practical question is how wrong do they have to be not to be useful." —George E. P. Box

To the Editor:

In a recent article, Kheterpal *et al.*[1] analyzed the impact of a real-time intraoperative decision support system. Borrowing tactics from the aviation industry, the authors hypothesized that "decision support systems, which integrate across disparate data sources, devices, and contexts, to highlight and recommend specific interventions" might lead to better postoperative outcomes. For now, the authors showed that these systems did improve process measures, but the clinical outcomes were lacking. These results are not surprising.

In the field of data science, researchers understand that the "curse of dimensionality" is lurking behind every hypothesis.[2] Here, the introduction of additional dimensions waters down the "relative contrast" of each data point and they become clustered together. One is no longer looking at data points on an *x,y* plane and one cannot differentiate the "distance," or significance, of each point.[3] As a result, one may observe a statistical significance when analyzing the data in its entirety, but in reality, it may only be in a subset of data points. Further, the aggregation of large amounts of data may inadvertently create a collection of irrelevant, correlated, or redundant data, interfering with any subsequent analyses.[3] For example, heart rate and blood pressure are commonly inversely related and correlated to a different degree depending on the scenario. The variation in correlation forces the researcher to account for these differences when analyzing the data. Finally, when patterns are uncovered with insufficient data, the model may have statistical significance, but the overall utility/effect size may not justify the means.[4]

When pharmaceutical companies identify potential new drugs, they circumvent the issue of dimensionality by first taking time to research and identify specific targets (the variable), compare "the target" against several thousand compounds, and then take time to understand why each compound was effective before moving forward to further testing.[5] By contrast, this study was based on previous observational studies that found associations between intraoperative physiologic management and postoperative outcomes in four dimensions out of numerous variables.[1] In contrast to pharmaceutical companies, not taking the time to fully understand why each "target" was effective can lead to unexpected results. For instance, it would be interesting to understand how one or two extra minutes of hypotension can increase the risk of myocardial injury or renal injury, especially when this scenario is compared with the intensive care unit setting where the response to hypotension is often more delayed.

Ultimately, we are not saying that AlertWatch is ineffective at what it does or how it helps anesthesiologists. This use of airplane technology has some applicability in our practice, but the intervention made to improve patient outcomes needs to reflect the patient's physiologic complexity. The problem with adding dimensions is that it results in an exponential increase in data needed to make accurate generalizations. In other words, as we add more dimensions to analyze a system, we are increasing the chances that a pattern is found, but we may find it more difficult to demonstrate effectiveness—the crux of "the curse dimensionality."[3] The key is to understand the difference between the models and reality and to harness and continually refine the opportunities afforded by large databases.

Competing Interests

The authors declare no competing interests.

Niketu P. Patel, B.A., Elie Sarraf, M.D., C.M., Mitchell H. Tsai, M.D., M.M.M. University of Vermont Larner College of Medicine, Burlington, Vermont (N.P.P.). niketu.patel@med.uvm.edu

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In Reply:

We thank our colleagues for their interest in the published work[1] and their thoughtful comments. The study of clinical decision support, process of care measures, and clinical outcomes is a complex area that demands increased attention from the peer-reviewed literature, academic institutions, and industry.

We concur with Dr. Freundlich *et al.* that multicenter studies of clinical decision support are necessary to advance the field. To maximize generalizability and reproducibility, multicenter research is a natural step in the evolution of evidence-based practice change. Donabedian's classic "structure-process-outcomes" framework clearly identifies that the context within which care is delivered must be incorporated into clinical and health services research.[2] A decision support system that is associated with clinical impact in one health system or structure of care may demonstrate no value in another setting, or *vice versa*. Multicenter pragmatic clinical trials and Randomized, Embedded, Multifactorial, Adaptive Platform (also known as "REMAP") trial designs are potential cost-effective avenues to study clinical decision support.[3] With support from a multitude of national and international anesthesiology organizations, the Multicenter Perioperative Outcomes Group, on behalf of its more than 40 contributing member organizations, has invested in the Initiative for Multicenter Perioperative Clinical Trials (IMPACT).[4] We look forward to working with centers and investigators from around the world that wish to use this infrastructure for pragmatic perioperative trials.