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

References

1. Kheterpal S, Shanks A, Tremper KK: Impact of a novel multiparameter decision support system on intraoperative processes of care and postoperative outcomes. ANESTHESIOLOGY 2018; 128:272–82
2. Stephens-Davidowitz S: Everybody lies: Big data, new data, and what the internet can tell us about who we really are. New York, HarperCollins, 2017
3. Houle ME, Kriegel HP, Kröger P, Schubert E, Zimek A: Can shared-neighbor distances defeat the curse of dimensionality? Sci Stat Database Manag 2010; 6187:482–500
4. Beyer K, Goldstein J, Ramakrishnan R, Shaft U: When is "nearest neighbor" meaningful? Database Theory ICDT 1999, Lecture notes in Computer Science, vol 1540. Edited by Berri C, Buneman P. Berlin, Springer, 1999, pp 217–35
5. Torjesen, I: Drug development: The journey of a medicine from lab to shelf. The Pharmaceutical Journal 2015. Available at: http://www.pharmaceutical-journal.com/publications/tomorrows-pharmacist/drug-development-the-journey-of-amedicine-from-lab-to-shelf/20068196.article. Accessed April 11, 2018

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.

We also share Doctoral Candidate Patel's interest in the complexity of data elements and factors involved in clinical research. We struggle, however, to identify a specific way forward offered by Patel *et al.*, or any recommendation underlying their correspondence. The "curse of dimensionality" is not unique to the study of decision support systems or healthcare research in general. Nor is pharmaceutical research, and the billions of dollars expended each year on unsuccessful drug targets, an appropriate model for future work. In fact, much of current drug development involves the use of hypothesis-generating phenome-wide or genome-wide association studies that provide hundreds of candidate targets for a given disease state; these potential targets are then evaluated at scale using computational, theoretical models. Although increased sample size and data breadth may address some issues with analyses of multifactorial clinical outcomes, data heterogeneity and quality issues often arise in concert. Increased sample size may have allowed adequate power to detect a difference in infrequent outcomes such as stage 2 acute kidney injury.

In summary, we concur that new data types and approaches are needed to advance the science of decision support system evaluation. Although our current analysis demonstrated process of care impact, it could not evaluate the impact on many crucial clinical outcomes inconsistently recorded in the electronic health record, such as surgical site infection, pulmonary complications, delirium, or patient satisfaction. Finally, the positive impact upon process of care measures and some resource outcomes should offer encouragement to clinicians and researchers seeking to advance care for their patients. Changing clinician behavior remains a goal almost as elusive as improving clinical outcomes.

Competing Interests

Dr. Tremper is the founder of, and has an equity interest in, AlertWatch (Ann Arbor, Michigan), the company that developed the decision support system being evaluated.

Sachin Kheterpal, M.D., M.B.A., Kevin K. Tremper, Ph.D., M.D. University of Michigan Medical School, Ann Arbor, Michigan (S.K.). sachinkh@med.umich.edu

References

1. Kheterpal S, Shanks A, Tremper KK: Impact of a novel multiparameter decision support system on intraoperative processes of care and postoperative outcomes. ANESTHESIOLOGY 2018; 128:272–82
2. Ayanian JZ, Markel H: Donabedian's lasting framework for health care quality. N Engl J Med 2016; 375:205–7
3. Angus DC: Fusing randomized trials with big data: The key to self-learning health care systems? JAMA 2015; 314:767–8
4. Multicenter Perioperative Outcomes Group Clinical Trials Network. Available at: https://mpog.org/ctn. Accessed May 30, 2018

(Accepted for publication June 8, 2018.)