

## Using Database Research to Affect the Science and Art of Medicine

**I**N the current issue of ANESTHESIOLOGY, Turan *et al.*<sup>1</sup> report on research employing a massive healthcare database to determine the effects of prolonged corticosteroid use on intraoperative blood replacement in noncardiac surgical patients. Database research is a growing trend in medicine, influenced by the rich collections of computerized data that are part and parcel of efforts to better record and access patient- and healthcare-delivery information. Low funding rates for competitive grants and the stigma attached to research funding from the pharmaceutical and device industries<sup>2</sup> are steering investigators away from high-budget prospective studies. Collectively, these factors will continue to move creative, energetic researchers toward database research to address the science and art of contemporary medicine.

For database research to function optimally, it must have several critical elements: (1) the parent database must contain meticulously collected and recorded data, (2) the database should be exposed to periodic audits or other quality-assurance exercises, (3) the research should begin with an evidence-based hypothesis, (4) the numbers should provide adequate statistical power, and (5) if possible, a given research project should contain secondary information that validates the credibility of the research. Using these criteria, the research of Turan *et al.*<sup>1</sup> scores well.

As reviewed by Turan *et al.*,<sup>1</sup> there is some evidence in the literature that corticosteroids *per se* affect the underpinnings of blood coagulation; however, the nature of these alterations make it difficult to predict the direction and magnitude on clinical hemostasis. Offsetting any uncertainty is an appreciation that patients with prolonged corticosteroid excess (*e.g.*, Cushing syndrome) have a propensity to bruise.<sup>3</sup> Turan *et al.*<sup>1</sup> addressed the hypothesis that long-term steroid use will affect intraoperative blood transfusion by probing the massive 363,897-patient American College of Surgeons National Surgical Quality Improvement Program database. After applying exclusion criteria to eliminate patients who would unduly confound data interpretation (*e.g.*, those having disseminated cancer, perioperative infections, known bleeding disorders), the researchers were left with 296,059 patients (or 81% of the original). Thereafter, the investigators identified 7,760 patients who were taking steroids preoperatively for any reason, and they offered a detailed de-

scription of baseline patient characteristics and a cursory calculation of the transfusion requirements compared with 288,299 patients who were not taking steroids. However, the forte of the Turan *et al.*<sup>1</sup> research was that the investigators were able to use sophisticated patient-matching techniques to pair 6,350 steroid users with the same number of highly comparable patients not taking steroids. The quality of patient matching (quantified in tables 1 and 2) and the approach to data analysis are exemplary. Based on their research, Turan *et al.*<sup>1</sup> were able to determine, perhaps better than any other researchers to date, that long-term corticosteroid use, *per se*, has no meaningful independent effect on intraoperative blood transfusion in noncardiac surgical patients. By using blood transfusion records as an endpoint for bleeding tendency, the authors removed some of the errors inherent to assessing blood loss. If there were clinical shortcomings linking blood loss and blood replacement (*e.g.*, undertransfusion or overtransfusion), Turan *et al.*<sup>1</sup> did not report whether these correlated with adverse cardiovascular and neurologic outcomes.

Lest readers have concerns that, by matching patients so rigorously between the steroid and nonsteroid groups, the authors abolished the potential for identifying *any* corticosteroid effect, the Turin *et al.*<sup>1</sup> research had positive results as well: steroid users were more likely to experience 30-day postoperative systemic infections and postoperative wound infections. Such findings increase the believability of the overall study results.

One of the peculiarities of the Turin *et al.*<sup>1</sup> research is that by highly focusing the research on the isolated effects of steroids, independent of confounding baseline disease states, the research improved its scientific authority but may have diminished its relevance to practicing anesthesiologists. Specifically, anesthesiologists are probably less interested in knowing whether steroids *per se* enhance bleeding than in being able to answer the question, "If I have a patient whose disease state warrants the long-term use of steroids, will that patient experience increased perioperative blood loss and, if so, how should I better prepare for monitoring and replacing that blood loss?" Here, there is an amusing relationship be-

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tween art, science, and economics. Anesthesiologists can use scientific knowledge about steroids, coexisting disease, and blood loss to better plan the ordering of blood and the insertion of venous, arterial, and urinary catheters to collectively assess vascular volume status and treat it. And—as a result of this artistry—clinicians' choices can feedback to affect science (*e.g.*, more catheters equate to higher infection rates<sup>4</sup>) and healthcare costs (*e.g.*, excessive ordering of blood wastes money). These clinically relevant issues can be addressed in more detail simply by using the same database and methods employed by Turan *et al.*<sup>1</sup> but directing the research differently. In doing so, the results can have an important impact on daily medical practice.

Contemporary concepts of the quality of evidence provided by scientific research espouse that—among the many options—prospective randomized trials provide the highest levels of evidence, followed by database analyses, case series, and case reports. Nonrandomized trials and meta-analyses fit in here as well, though their quality can be highly variable based on the components that go into the research (“junk in, junk out”). The prospective randomized trial has rightfully gained its place at the head of the rankings, as this genre is associated with the greatest advances in clinical research, and its prominence has moved medical reporting away from the anecdotal and toward more substantial scientific foundations over the past half century. Further, the codification of research methods and the continuously improving statistical analyses that are critical to prospective randomized trials have had a positive trickle-down effect on other research forms.

Unfortunately, this same hierarchy linking research form to quality of evidence does not always correlate with the research's clinical utility. As Sirven<sup>5</sup> has recently written, prospective randomized trials sometimes address such narrowly focused issues, and the patients may be so highly selected, that the results—although having considerable scientific credibility—may provide little value in guiding daily clinical practices. In such instances, scientific methods alleged to be inferior (*e.g.*, case series) may produce more clinically relevant information. And even within the realm of database research, the clinical utility of the findings can be highly variable, depending on the study design paradigms. In some instances, database research results can provide near-definitive results that are unlikely to be further investigated and improved upon through prospective studies.<sup>6–9</sup> In other instances, the database research results may best be viewed as provocative and hypothesis-generating,<sup>10,11</sup> requiring additional research for definitive answers.

While the Turan *et al.*<sup>1</sup> research took advantage of immense statistical power to rule out a specific effect of *steroid use* on operative blood use, they did not offer a comment on *the interaction of medical conditions treated with long-term steroid use* on blood utilization. Indeed, others have addressed this issue. As reviewed by Turan *et al.*,<sup>1</sup> Bruewer *et al.*<sup>12</sup> retrospectively evaluated the influence on intraoperative blood transfusion of high-dose, low-dose, and no corticosteroid use in patients with Crohn's disease. Although this re-

search identified a corticosteroid-associated effect, it was unable to determine whether steroid dose, the severity of Crohn's disease, or some interaction between the two dictated transfusion requirement. Despite this limitation, practicing anesthesiologists would nevertheless view the findings as valuable in planning anesthesiology care. Such subgroup analysis is also possible using the database and statistical methods employed by Turan *et al.*,<sup>1</sup> and there is some evidence in their data that subgroup analysis would produce positive findings (*i.e.*, erythrocyte transfusion occurred in 7.3% of 7,760 steroid users but only 3.5% of 288,299 non-steroid users). However, such an approach to subgroup analysis of the Turan *et al.*<sup>1</sup> data would involve fragmentation of their database and data mining, both considered pejorative terms. While this direction for future research would diminish the scientific quality of the findings, it might concomitantly enhance the clinical relevance of the research. Positive findings could translate into improved resource utilization, better-targeted patient care, and perhaps improved outcomes in subsets of patients in a manner that cannot be addressed by the design of the present research.<sup>1</sup>

An interesting message provided by the Turan *et al.*<sup>1</sup> research is that the power of scientific methods does not necessarily correlate with an ability to deliver the most useful clinical information. The investigators' exemplary research methods provide important insights into the role of steroids in affecting operative blood loss in noncardiac surgical patients. Practicing anesthesiologists will appreciate this information but will also want more specific information on steroid-disease interactions and how those affect blood utilization. Resolution of these differences will likely involve scientific methods that are less impressive than those used by Turan *et al.*<sup>1</sup> In this and other instances, it is possible to develop evidence-related improvements in the art of clinical practice through less powerful scientific means.

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## ANESTHESIOLOGY REFLECTIONS

### *The Waters-Morton House by Vandam*



After William T. G. Morton's birthplace had burned to the ground, the 8-yr-old boy's father bought a replacement house in 1827 in Charlton Center, Massachusetts, from the estate of a successful tanner named Israel Waters. Nineteen years later, the younger Morton would publicly demonstrate surgical anesthesia in Boston. The second Morton home, the Waters-Morton House, was memorialized in watercolor (see above) by a retired Editor of *ANESTHESIOLOGY*, Leroy D. Vandam, M.D. (1914-2004). To benefit the Wood Library-Museum, Professor Vandam signed 100 prints of this work, only a few of which remain available for sale. (Copyright © the American Society of Anesthesiologists, Inc. This image appears in color in the *Anesthesiology Reflections* online collection available at [www.anesthesiology.org](http://www.anesthesiology.org).)

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