

detection in randomized controlled trials, and instead they advocate large (expensive) prospective, observational cohort experimental designs. A 3,988-patient prospective cohort trial, published after our editorial, reinforces the evidence finding no indication of persistent cognitive decline or incident dementia attributable to surgery.<sup>17</sup> In fact, its only significant finding was that patients with exposure to surgery and general anesthesia had a decreased risk of dementia.<sup>17</sup>

### Competing Interests

The authors declare no competing interests.

**Michael S. Avidan, M.B.B.Ch., F.C.A.S.A., Alex S. Evers, M.D.** Washington University School of Medicine, St. Louis, Missouri (M.S.A.). avidanm@anest.wustl.edu

### References

1. Avidan MS, Evers AS: The fallacy of persistent postoperative cognitive decline. *ANESTHESIOLOGY* 2016; 124:255–8
2. Doja A, Roberts W: Immunizations and autism: A review of the literature. *Can J Neurol Sci* 2006; 33:341–6
3. Taylor LE, Swerdfeger AL, Eslick GD: Vaccines are not associated with autism: An evidence-based meta-analysis of case-control and cohort studies. *Vaccine* 2014; 32:3623–9
4. Newman MF, Kirchner JL, Phillips-Bute B, Gaver V, Grocott H, Jones RH, Mark DB, Reves JG, Blumenthal JA; Neurological Outcome Research Group and the Cardiothoracic Anesthesiology Research Endeavors Investigators: Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. *N Engl J Med* 2001; 344:395–402
5. McDonagh DL, Mathew JP, White WD, Phillips-Bute B, Laskowitz DT, Podgoreanu MV, Newman MF; Neurologic Outcome Research Group: Cognitive function after major noncardiac surgery, apolipoprotein E4 genotype, and biomarkers of brain injury. *ANESTHESIOLOGY* 2010; 112:852–9
6. Kühberger A, Fritz A, Lermer E, Scherndl T: The significance fallacy in inferential statistics. *BMC Res Notes* 2015; 8:84
7. Seitz DP, Shah PS, Herrmann N, Beyene J, Siddiqui N: Exposure to general anesthesia and risk of Alzheimer's disease: A systematic review and meta-analysis. *BMC Geriatr* 2011; 11:83
8. Goodman SN, Berlin JA: The use of predicted confidence intervals when planning experiments and the misuse of power when interpreting results. *Ann Intern Med* 1994; 121:200–6
9. Button KS, Ioannidis JP, Mokrysz C, Nosek BA, Flint J, Robinson ES, Munafò MR: Power failure: Why small sample size undermines the reliability of neuroscience. *Nat Rev Neurosci* 2013; 14:365–76
10. Dokkedal U, Hansen TG, Rasmussen LS, Mengel-From J, Christensen K: Cognitive functioning after surgery in middle-aged and elderly Danish twins. *ANESTHESIOLOGY* 2016; 124:312–21
11. Ahmed N: 23 years of the discovery of *Helicobacter pylori*: Is the debate over? *Ann Clin Microbiol Antimicrob* 2005; 4:17
12. Bedford PD: Adverse cerebral effects of anaesthesia on old people. *Lancet* 1955; 269:259–63
13. Sauër AM, Nathoe HM, Hendrikse J, Peelen LM, Regieli J, Veldhuijzen DS, Kalkman CJ, Grobbee DE, Doevendans PA, van Dijk D; Octopus Study Group: Cognitive outcomes 7.5 years after angioplasty compared with off-pump coronary bypass surgery. *Ann Thorac Surg* 2013; 96:1294–300
14. Hlatky MA, Bacon C, Boothroyd D, Mahanna E, Reves JG, Newman MF, Johnstone I, Winston C, Brooks MM, Rosen AD, Mark DB, Pitt B, Rogers W, Ryan T, Wiens R, Blumenthal JA: Cognitive function 5 years after randomization to coronary angioplasty or coronary artery bypass graft surgery. *Circulation* 1997; 96(9 suppl):II–11
15. Währborg P, Booth JE, Clayton T, Nugara F, Pepper J, Weintraub WS, Sigwart U, Stables RH; SoS Neuropsychology Substudy Investigators: Neuropsychological outcome after percutaneous coronary intervention or coronary artery bypass grafting: Results from the Stent or Surgery (SoS) Trial. *Circulation* 2004; 110:3411–7
16. Cormack F, Shipolini A, Awad WI, Richardson C, McCormack DJ, Colleoni L, Underwood M, Baldeweg T, Hogan AM: A meta-analysis of cognitive outcome following coronary artery bypass graft surgery. *Neurosci Biobehav Rev* 2012; 36:2118–29
17. Aiello Bowles EJ, Larson EB, Pong RP, Walker RL, Anderson ML, Yu O, Gray SL, Crane PK, Dublin S: Anesthesia exposure and risk of dementia and Alzheimer's disease: A prospective study. *J Am Geriatr Soc* 2016; 64:602–77

(Accepted for publication April 20, 2016.)

## Evaluation of Perioperative Medication Errors

### To the Editor:

The recent article by Nanji *et al.*<sup>1</sup> concerning errors related to anesthetic drug administration is interesting and raises a number of provocative questions. However, we are concerned that the manner in which the data are presented and interpreted may lead readers to conclusions that may not be warranted.

Nanji *et al.* have utilized a very broad definition of drug administration error. For example, “significant hypotension (mean arterial pressure < 55 mmHg) that is not treated”<sup>1</sup> is listed as a drug error in table 2. We would argue that depending upon the circumstances, this is not an error of drug administration (it may be an error in anesthetic management) and may not be an error at all. We would also argue that an unattended syringe of hydromorphone (table 5) is not a drug administration error, although it may be a violation of a hospital policy for handling controlled substances. The authors have given other examples of their definitions of drug administration error but have not provided a complete list of all drug error definitions or a list of the errors observed in this study. Thus, it is difficult to know what was actually measured. This is important because their reported rate of error is at least an order of magnitude greater than reported by other investigators.

Nanji *et al.* have also utilized a very broad definition of adverse drug events. We would argue that the example of adverse drug events listed in table 2, “a patient with > 4/10 pain on emergence that is not treated until after arriving in the recovery room,”<sup>1</sup> is not an adverse drug event. It has to do with the strategy for perioperative pain management rather than drug administration *per se*.

Webster *et al.*<sup>2</sup> performed a key study of anesthetic drug administration error using prospective facilitated incident

monitoring (self-reporting) by anesthesiologists in New Zealand. We replicated this study at the University of Washington Medical Center, Seattle, Washington, using similar methodology and obtained similar results,<sup>3</sup> as did Zhang *et al.*<sup>4</sup> in a study of over 24,000 anesthetics in China. The rate of drug administration error in the study by Webster *et al.* was 0.75% of anesthetics; it is important to note that the rate of error was expressed as the percentage of patients who were subject to at least one error (the rate “per anesthetic”), not as a fraction of the total drugs administered. It is also important to note that Webster *et al.* were concerned with actual performance errors of drug administration that reached the patient, such as administering the wrong drug, not process errors such as errors in labeling or record keeping.

Nanji *et al.* state that the rate of error determined by Webster *et al.* (as confirmed by us in the United States and Zhang *et al.* in China) is “markedly lower than the rates that we found, which may be due to provider reluctance to self-report errors or failure of providers to recognize errors they have made.”<sup>1</sup>

If we examine table 5, we find a classification of errors as defined by Nanji *et al.* These include five types of errors that did not reach patients—labeling errors (37 to 24% of total errors), documentation errors (26 to 17%), monitoring errors (10 to 6.5%), wrong timing (5 to 3.3%), and other (2 to 1.3%). These errors account for 52% (80/153) of the total errors. Webster *et al.* did not classify any of these error types to be drug administration performance errors (such as giving the wrong drug), and these error types were not reported in their study.

In order to compare the results of Webster *et al.* to that of Nanji *et al.*, we should first subtract the 80 errors that are not directly related to the performance of drug administration, leaving 73 errors directly related to drug administration (error rate,  $73/3297 = 0.022$  or 2.2%). The rate of errors per anesthetic (Nanji *et al.* did not specify the number of patients effected by errors, but an assumption of no more than one error per patient is a reasonable approximation) would be  $73/277 = 0.26$ , *i.e.*, 26% of anesthetics would have been affected by an error. This is 35 times greater than the rate reported by Webster *et al.*, which was 0.75% of anesthetics. How are we to explain this enormous difference in results? Nanji *et al.* suggest that this is due to dramatic underreporting of errors in studies where providers report their own errors.

However, Merry *et al.*<sup>5</sup> (the same group in New Zealand who reported the study by Webster *et al.*) also performed a direct observation study. In that study, the rate of drug administration error was 0.32% of drugs administered (table 2), or 3.2% of anesthetics ( $0.0032 \times 5084 = 16$ ;  $16/509 = 0.032$ ). Thus, the rate of drug administration error (comparing apples to apples, using the error classification of Merry *et al.*) is about 10 times higher in the Nanji *et al.*'s direct observation study than in the Merry *et al.*'s direct observation study.

We agree that self-reporting underestimates the rate of error. However, comparing the direct observation data from the study by Merry *et al.* to the self-reporting data from the study by Webster *et al.* (both from New Zealand), the magnitude of the difference is about 4- to 5-fold (3.2 *vs.* 0.75%), not 35-fold as when comparing the study by Nanji *et al.* to the study by Webster *et al.* (26 *vs.* 0.75%). Moreover, Nanji *et al.* found a rate of error about 10 times greater than Merry *et al.* when both used direct observation.

We would speculate that the higher rates found by Nanji *et al.* have to do with what appears to be overly broad definitions of error; however, it is impossible to know from their article because the actual drug error data are not provided. We believe that this is important, and that Nanji *et al.* should provide their actual data so that readers are able to make their own interpretations of what constitutes a drug administration error and what does not.

Also, we were disappointed that Nanji *et al.* did not provide data describing their use of the Codonics Safe Label System (Codonics Inc., USA) to produce syringe labels or their use of the MetaVision anesthesia information system (iMDSOFT, USA) to scan bar codes on syringes before administration, since there is some evidence that proper labeling and scanning bar codes may reduce drug administration errors. Without having more information, it is not possible to know whether these technologies had a significant impact on the errors that they have reported. Simply having these systems in place does not ensure that they are properly used, as reported previously by our group<sup>6</sup> and by Merry *et al.*<sup>5</sup> The fact that 24% of the errors reported in table 5 involved labeling suggests that Nanji *et al.* are not obtaining the full potential benefits of the Codonics Safe Label System. Clearly, education, a culture of safety, and the details of the implementation are all important when it comes to technology that is employed to mitigate medical errors.

## Competing Interests

The authors declare no competing interests.

**T. Andrew Bowdle, M.D., Ph.D., F.A.S.E., Srdjan Jelacic, M.D., Bala Nair, Ph.D.** University of Washington, Seattle, Washington (T.A.B.). bowdle@u.washington.edu

## References

1. Nanji KC, Patel A, Shaikh S, Seger DL, Bates DW: Evaluation of perioperative medication errors and adverse drug events. *ANESTHESIOLOGY* 2016; 124:25–34
2. Webster CS, Merry AF, Larsson L, McGrath KA, Weller J: The frequency and nature of drug administration error during anaesthesia. *Anaesth Intensive Care* 2001; 29:494–500
3. Bowdle A, Kruger C, Grieve R, Emmens D, Merry A: Anesthesia drug administration errors in a university hospital. *ANESTHESIOLOGY* 2003; 99:A1358
4. Zhang Y, Dong YJ, Webster CS, Ding XD, Liu XY, Chen WM, Meng LX, Wu XY, Wang DN: The frequency and nature of drug administration error during anaesthesia in a Chinese hospital. *Acta Anaesthesiol Scand* 2013; 57:158–64

5. Merry AF, Webster CS, Hannam J, Mitchell SJ, Henderson R, Reid P, Edwards KE, Jardim A, Pak N, Cooper J, Hopley L, Frampton C, Short TG: Multimodal system designed to reduce errors in recording and administration of drugs in anaesthesia: Prospective randomised clinical evaluation. *BMJ* 2011; 343:d5543
6. Jelacic S, Bowdle A, Nair BG, Kusulos D, Bower L, Togashi K: A system for anesthesia drug administration using barcode technology: The Codonics Safe Label System and Smart Anesthesia Manager. *Anesth Analg* 2015; 121:410–21

(Accepted for publication April 20, 2016.)

## Adverse Drug Events Link to Severity of the Event Data Needed

### To the Editor:

Although thought provoking and likely to lead to significant research in the future, the data presented by Nanji *et al.*<sup>1</sup> are not sufficient to support a conclusion that medication errors (MEs) occurring during the course of anesthesia lead to *meaningful* harm. A primary concern is the tenuous link between MEs and adverse drug events (ADEs). Forty of 91 actual ADEs were not related to MEs and were considered “nonpreventable.” No tabulation of the harm caused by these events is given, and it is possible that most of the significant and life-threatening outcomes fell into this category. Of the remaining 51 ADEs, the Naranjo algorithm determined that only about half were “probably” related to the ME, and the other half were considered “possibly” or “doubtfully” due to the error. Thus, MEs may have caused or contributed to less than a third of the ADEs. The overall rate of 28 of 3,671 (0.8%) is considerably smaller than the undifferentiated error rate of 193 of 3,671 (5.3%) and ADE rate of 91 of 3,671 (2.5%) offered by the authors.

A more critical look at the data is necessary to avoid the impression that MEs during anesthesia are a source of

**Table 1.** Occurrence of Adverse Drug Events *versus* the Severity of the Event

Severity	Preventable ADE (Yes ME)		Nonpreventable ADE (No ME)
	ADE Probably Related to ME	ADE Possibly or Doubtfully Related to ME	
Life threatening			
Significant			
Serious			

ADE = adverse drug event; ME = medication error.

significant patient harm and to provide a proper baseline rate for future studies that attempt to lower the rate of ADE during anesthesia by behavioral or technical means. (One can imagine the results of this study being used to promote new barcode/syringe labeling systems, for example.)

What is needed for clarity is a table that gives counts (not percentages) of ADE distributed across the categories of severity. Then the reader can see if the data support the implied conclusion that preventable MEs actually caused significant harm. The authors may wish also to explain why the severity scale starts at “serious,” rather than some lesser degree of harm. In table 1, we present a suggested format for a table to be published as part of the authors’ response.

### Competing Interests

The authors declare no competing interests.

**James W. Ibinson, M.D., Ph.D., Charles W. Buffington, M.D.** University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania (J.W.I.). [ibinsonjw@upmc.edu](mailto:ibinsonjw@upmc.edu)

### Reference

1. Nanji KC, Patel A, Shaikh S, Seger DL, Bates DW: Evaluation of perioperative medication errors and adverse drug events. *ANESTHESIOLOGY* 2016; 124:25–34

(Accepted for publication April 20, 2016.)

## Counting Errors: Medication or Medical?

### To the Editor:

We congratulate Nanji *et al.*<sup>1</sup> for their recent prospective, observational study defining the frequency of medication errors (MEs) and potential adverse drug events (ADEs) in the operating rooms of the Massachusetts General Hospital, Boston, Massachusetts. We read this article with great interest, considering the sensational headlines it has generated in the mainstream media because the incidence of MEs was much higher than previously described. We must take this information seriously and identify methods for reducing MEs and ADEs; however, because of the effort and resources required to address such issues, we must also question the validity and consistency of these data and the conclusions they have generated.

To examine the accuracy of the measured ME rate, we must begin by examining the definition of ME used by Nanji *et al.* While adopting the definition to the perioperative setting, the author combined a commonly used definition for ME with one that is taken from an article on *medical* errors not MEs.<sup>2</sup>