patients with obstructive sleep apnea undergoing non-cardiac surgery. Chest 2012; 141:436–41

3. Weingarten TN, Flores AS, McKenzie JA, Nguyen LT, Robinson WB, Kinney TM, Siems BT, Wenzel PJ, Sarr MG, Marienau MS, Schroeder DR, Olson EJ, Morgenthaler TI, Warner DO, Sprung J: Obstructive sleep apnoea and perioperative complications in bariatric patients. Br J Anaesth 2011; 106:131–9
4. Bryson GL, Gomez CP, Jee RM, Blackburn J, Taljaard M, Forster AJ: Unplanned admission after day surgery: A historical cohort study in patients with obstructive sleep apnea. Can J Anaesth 2012; 59:842–51

(Accepted for publication February 14, 2015.)

In Reply:

We appreciate Dr. Kaw's interest in our article,[1] but we believe our interpretation of the data respected the study's limitations, offering valid new insight on postoperative outcomes in patients with obstructive sleep apnea (OSA). We will respond in turn to the four issues raised by Dr. Kaw.

1. Although the patients with undiagnosed OSA (UOSA) in our study definitely did not have access to perioperative continuous positive airway pressure (CPAP), Dr. Kaw has correctly noted that even if CPAP was prescribed, it is unknown whether each patient with diagnosed OSA (DOSA) in our study used it perioperatively. We chose not to substitute procedure codes for noninvasive ventilation as a surrogate for perioperative CPAP use in these patients because this code definition has poor sensitivity based on the exceedingly low rates in another administrative database study[2] and our own unpublished results (unpublished rate of procedure codes for noninvasive ventilation in surgical admissions for patients with OSA, from queries of our own database[1] by Thomas C. Mutter, M.D., F.R.C.P.C., M.Sc., Assistant Professor, Department of Anesthesia, University of Manitoba, Winnipeg, Manitoba, Canada, in 2012). Due to these and other limitations documented in the Discussion, we carefully interpreted our finding as an *association* between *polysomnography diagnosis of OSA with prescription of CPAP* and reduced risk of cardiovascular complications. Nowhere do we propose an absence of effect of CPAP on respiratory complications, and we devote the fifth last paragraph of the Discussion to hypothesizing why such a risk reduction was not detected in our study. Furthermore, in the last three paragraphs of the article, based on our results and others', we discussed how CPAP could have a causal role in reducing cardiovascular complications. However, consistent with the aforementioned limitations, we also indicated that large clinical studies are ultimately needed to test these hypotheses.
2. We did not attempt to find controls from within the polysomnography database as it represents a referral population distinct from the typical surgical patient, and there were only approximately 100 database patients without OSA or another sleep disorder; too few for matching on surgical risk, which was integral to our analysis (see Materials and Methods). To be clear, the general population controls in our study were screened to be at low risk of having UOSA or DOSA (see Materials and Methods and Supplementary Digital Content 2), but Dr. Kaw has correctly noted that false negatives from this screening could result in a misclassification bias. As reviewed in the fourth paragraph of the Discussion, this misclassification would not affect relationships between the UOSA and DOSA groups but would bias estimates of risk for OSA *versus* non-OSA controls toward a nil effect. In a worst case scenario, if our control group had the prevalence of OSA in the general population (20 to 25%), the true risk estimates would be modestly higher than we estimated. It is uncertain whether the mild and moderate OSA estimates would become statistically or clinically significant.

   Nevertheless, due to this potential bias and the wide CIs for risk estimates in less severe OSA, we did not conclude that only severe OSA is associated with increased risk. Instead, due to the significant relationships between risk and OSA severity, we suggested that patients with severe OSA are at *greatest risk*. Finally, the novel finding of a relationship between OSA severity and postoperative complications in this study is surely a matter of statistical power. The three studies cited by Dr. Kaw are at least 10 times smaller than our study and the largest (n = 1,547) only included low-risk ambulatory surgeries, whereas we included almost all surgeries.
3. Our matching strategy and justification for not matching on comorbidities (using propensity-based methods) are extensively documented in the Study Design and Analysis sections of the article. We chose instead to adjust for comorbidities at the analysis stage. This enabled us for the first time to estimate the importance of OSA relative to age, type of surgery, comorbidities, and other factors in predicting postoperative complications. These models were robust through multiple sensitivity analyses (see Supplemental Digital Content 8), and we believe that any unmeasured confounders are unlikely to significantly alter our interpretation of the data as presented in the article. It is also unlikely that the models were overfitted as (1) we did not observe large changes in regression coefficient estimates when adding or deleting predictor variables from the final models, (2) multiple sensitivity analyses did not change the results, (3) we arrived at the same models through backwards and forwards regression, and (4) whether OSA variables were added first or last. Nevertheless, due to the limitations of administrative data, we believe that even though the models can inform clinical practice, they should not be directly applied to it.
4. We agree with Dr. Kaw that caution is necessary in assigning clinical meaning to administrative data, and we accordingly recognized this methodologic challenge in the discussion. To enhance the construct validity of our outcomes, we chose International Classification Disease

code definitions that had been previously validated against chart review when possible (see Supplementary Digital Content 5). Although heterogeneous, these outcomes were selected because they were of interest in other studies of patients with OSA. Furthermore, the significant 28-day mortality rates after both respiratory and cardiovascular complications (26 and 18%) testify to their clinical significance, even if their exact clinical meaning is uncertain.

The sensitivity and specificity of administrative data to clinical events vary by diagnosis.[3] We can only hypothesize that a diagnosis of cardiac arrest and shock was the most frequently documented cardiovascular complication in both patients with OSA and their controls because it was more consistently detected and/or documented in the discharge abstract than acute coronary syndrome or atrial fibrillation, particularly, at the time the data were collected (1987–2008). Differences in the availability of cardiac troponin assays, the use of postoperative telemetry, and the range of included surgeries may explain the different rates of these complications between our study and another administrative database.[2] Finally, the biologic plausibility of increased risk of cardiac arrest in patients with untreated OSA that Dr. Kaw is seeking can be found in the third last paragraph of the article.

In summary, by linking polysomnography and administrative data, we created a large, unique database of postoperative outcomes in patients with OSA, from a time before routine preoperative screening and intensive postoperative monitoring. We carefully planned our study to address the limitations of administrative data and maximize its clinical applicability. It addressed important research questions that have eluded previous clinical studies for lack of statistical power[4] and previous large administrative database studies for lack of polysomnography data.[2] The results were cautiously interpreted within the limitations of the data and can help strengthen and refine current guidelines,[5] with the goal of improving postoperative outcomes for patients with OSA.

Competing Interests

Dr. Kryger is a volunteer board member with the National Sleep Foundation (Arlington, Virginia). He has received research grants from Respironics, Inc. (Murrysville, Pennsylvania), ResMed Corp. (San Diego, California), and Dymedix Diagnostics Inc. (Shoreview, Minnesota) that were not used to fund this research. Since this research has been completed, he has received consultancy fees from Inspire Medical Systems Inc. (Maple Grove, Minnesota), Ventus Medical Inc. (Belmont, California), Dymedix, Medtronic (Minneapolis, Minnesota), and Merck & Co., Inc. (Whitehouse Station, New Jersey). The other authors declare no competing interests.

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References

1. Mutter TC, Chateau D, Moffatt M, Ramsey C, Roos LL, Kryger M: A matched cohort study of postoperative outcomes in obstructive sleep apnea: Could preoperative diagnosis and treatment prevent complications? Anesthesiology 2014; 121:707–18
2. Memtsoudis SG, Stundner O, Rasul R, Chiu YL, Sun X, Ramachandran SK, Kaw R, Fleischut P, Mazumdar M: The impact of sleep apnea on postoperative utilization of resources and adverse outcomes. Anesth Analg 2014; 118:407–18
3. Quan H, Li B, Saunders LD, Parsons GA, Nilsson CI, Alibhai A, Ghali WA; IMECCHI Investigators: Assessing validity of ICD-9-CM and ICD-10 administrative data in recording clinical conditions in a unique dually coded database. Health Serv Res 2008; 43:1424–41
4. Kaw R, Chung F, Pasupuleti V, Mehta J, Gay PC, Hernandez AV: Meta-analysis of the association between obstructive sleep apnoea and postoperative outcome. Br J Anaesth 2012; 109:897–906
5. American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea: Practice guidelines for the perioperative management of patients with obstructive sleep apnea: An updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Anesthesiology 2014; 120: 268–86

(Accepted for publication February 14, 2015.)

Neostigmine: You Can't Have It Both Ways

To the Editor:

We read the recent study by Sasaki *et al.*[1] with interest but were confused by its clinical take-home message (or lack thereof). This article represents the logical extension of previous work by Eikermann and coworkers, which states that "… neostigmine and qualitative neuromuscular transmission monitoring did not mitigate the increased risk of postoperative respiratory complications linked to the use of non-depolarizing neuromuscular blocking agents. Furthermore, neostigmine may [adversely] affect postoperative respiratory function…"[2,3] In their current study, the authors conclude "Neostigmine reversal … was associated with increased atelectasis. High-dose neostigmine or unwarranted use of neostigmine may translate to increased postoperative respiratory morbidity." We find the authors' discussion highly unbalanced. They spend considerable time reviewing the well-known limitations of neostigmine as an antagonist of moderate to deep neuromuscular block but essentially ignored the clinical reality that for those clinicians who do not have access to sugammadex, neostigmine represents a valuable and necessary addition to our armamentarium.