

Association and Effect of Opioid Abuse—Related Readmission

To the Editor:

Although the medical community is appropriately alarmed and galvanized to action by the current opioid epidemic in our nation, associations can be easily ascribed and portrayed as scientific certainty. In a recent large database study, Gupta *et al.* posited in their title that “Opioid Abuse or Dependence Increases 30-day Readmission Rates after Major Operating Room Procedures.”¹ This title, however, is at odds with more cautiously crafted “association” statements in the abstract conclusion, discussion, and concluding paragraph, which more appropriately describe the retrospective findings.

I applaud the authors for the sheer magnitude of the study and the data describing the presumed inherent risk for this patient cohort. “Adjusted analysis” cannot obfuscate, however, the message apparent from a careful reading of the presented data. I defer to the statistical expertise and skill of the authors, but the presented medical conditions and risks of the opioid abuse/dependence group are significantly different (in exponentially large effect) in 29 of the 32 presented comorbidities spanning every clinically relevant major organ system (table 2). It is not surprising that the odds ratio of the multivariate model (table 4) has several positive predictors of readmission of greater or equal magnitude than opioid abuse/dependence (odds ratio, 1.26), including the following:

- Transfusion: 1.38
- Renal failure: 1.37
- Deep vein thrombosis: 1.34
- Acquired immunodeficiency syndrome: 1.32
- Diabetes mellitus with complications: 1.29
- Peptic ulcer: 1.28
- Liver disease: 1.27
- Fluid/electrolyte disorders: 1.26

Although a couple of these predictors may, in turn, be associated with opioid abuse, several have no plausible explanation for a relationship.

Discussion of the study limitations and concluding that “we describe an association between a history of opioid abuse and increased risk of readmission after perioperative hospitalization” appears to be a fairer reflection of the presented data than the original title, especially when

the magnitude of other, likely independent predictors is considered, even when accounted for as potential confounders. Acknowledgment of the retrospective association appears to be missing from the title, which to the casual reader may be accepted as cause and effect.

Competing Interests

The author declares no competing interests.

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Reference

1. Gupta A, Nizamuddin J, Elmofly D, Nizamuddin SL, Tung A, Minhaj M, Mueller A, Apfelbaum J, Shahul S: Opioid abuse or dependence increases 30-day readmission rates after major operating room procedures: A national readmissions database study. *ANESTHESIOLOGY* 2018; 128:880–90

(Accepted for publication October 2, 2018.)

In Reply:

We thank Dr. Pivalizza for his insightful observations on our article.¹ We agree that our work does not demonstrate a causal relationship between a history of opioid use and postsurgical readmission, and that our title mistakenly suggests that possibility. Because this study was observational, we expected many covariates to be differentially distributed between opioid abuse or dependence and non-opioid abuse or dependence groups. This relationship was indeed evident from table 2,¹ where 29 out of 32 covariates had significant *P* values. However, we did not choose adjustment covariates based upon *P* values. We chose covariates *a priori* because of the possibility that they might confound the association between opioid abuse or dependence or that they were

known surrogate markers for the severity of a patient's postoperative condition (*e.g.*, transfusion).²

As Dr. Pivalizza notes, many comorbidities (*e.g.*, peptic ulcer disease) had no obvious relationship with opioid abuse/dependence and were equally or more strongly associated with readmission. We agree that those comorbidities may themselves predispose to readmission. Even after adjustment for all of these comorbidities, however, the opioid association remained an independent risk factor for readmission. Our data suggest that the relationship between opioid abuse/dependence and readmission is roughly equal in effect to comorbidities such as peptic ulcer or liver disease.

Although the association we found remains significant after our extensive adjustment, we recognize that a retrospective observational trial cannot prove causality. A better title for our paper might be "Opioid Abuse or Dependence Is Associated with Increased Readmission Rates after Major Operating Room Procedures."

Competing Interests

The authors declare no competing interests.

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(Accepted for publication October 2, 2018.)