

## Nitrous Oxide–related Postoperative Nausea and Vomiting Depends on Duration of Exposure: More Questions than Answers

*To the Editor:*

We have read the recent article by Peyton and Wu<sup>1</sup> with great interest, which suggested nitrous oxide–related postoperative nausea and vomiting (PONV) was correlated with the length of time exposed to nitrous oxide. Their excellent meta-analysis on this important subject deserves applause. However, we would like to add some comments to emphasize a few important issues.

First, the concentrations of inhaled nitrous oxide were ignored in the current analysis, which may have a confounding influence on the relationship between the incidence of PONV and duration of exposure to nitrous oxide besides patient sex, age, and duration of anesthesia. In fact, several studies included in this meta-analysis observed different concentrations of inhaled nitrous oxide and showed that nitrous oxide increased the incidence of PONV in a dose-dependent manner.<sup>2–4</sup> Both duration of exposure to nitrous oxide and concentrations of inspired nitrous oxide may be significant covariates in the incidence of PONV. Therefore, it is necessary to rule out the influence of concentrations of inhaled nitrous oxide on PONV when determining whether duration of exposure to nitrous oxide was related to the incidence of PONV.

Second, the authors stratified studies based on duration of anesthesia and suggested that the effect of duration of anesthesia on nitrous oxide–induced PONV may instead simply reflect the invasiveness and magnitude of the surgery. However, the type of surgery *per se* may also be a confounding covariate. In this meta-analysis, more than one-third of the studies involved gynecologic surgery with or without laparoscopy, including a large sample study<sup>5</sup> in which up to 45.1% was gynecologic surgery. Duration of anesthesia in this type of surgery was usually no more than 1 to 2 h, while nongynecologic surgeries in remaining studies were almost more than 1 to 2 h except orthopedic surgery in two studies and day case/ambulatory surgery laparoscopy in one study less than 1 h. That is to say, a big difference exists in the types of surgery among groups stratified by duration of anesthesia. Although whether the type of surgery identified as a risk factor of PONV is still somewhat controversial, increased incidence of PONV has been demonstrated in the gynecologic, laparoscopic, and middle-ear surgeries.<sup>6–8</sup> Thus, the heterogeneity of the type of surgery may have tempered their conclusion.

Though this meta-analysis brings us closer to draw overall conclusion, it may only be regarded as an interim analysis toward reaching a final answer. Further studies are still needed to clarify the relationship between duration of exposure to nitrous oxide and the incidence of PONV.

### Competing Interests

The authors declare no competing interests.

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### References

1. Peyton PJ, Wu CY: Nitrous oxide-related postoperative nausea and vomiting depends on duration of exposure. *ANESTHESIOLOGY* 2014; 120:1137–45
2. Mraovic B, Simurina T, Sonicki Z, Skitarelic N, Gan TJ: The dose-response of nitrous oxide in postoperative nausea in patients undergoing gynecologic laparoscopic surgery: A preliminary study. *Anesth Analg* 2008; 107:818–23
3. Lonie DS, Harper NJ: Nitrous oxide anaesthesia and vomiting. The effect of nitrous oxide anaesthesia on the incidence of vomiting following gynaecological laparoscopy. *Anaesthesia* 1986; 41:703–7
4. Felts JA, Poler SM, Spitznagel EL: Nitrous oxide, nausea, and vomiting after outpatient gynecologic surgery. *J Clin Anesth* 1990; 2:168–71
5. Apfel CC, Korttila K, Abdalla M, Kerger H, Turan A, Vedder I, Zernak C, Danner K, Jokela R, Pocock SJ, Trenkler S, Kredel M, Biedler A, Sessler DI, Roewer N; IMPACT Investigators: A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. *N Engl J Med* 2004; 350:2441–51
6. Watcha MF, White PF: Postoperative nausea and vomiting. Its etiology, treatment, and prevention. *ANESTHESIOLOGY* 1992; 77:162–84
7. D'souza N, Swami M, Bhagwat S: Comparative study of dexamethasone and ondansetron for prophylaxis of postoperative nausea and vomiting in laparoscopic gynecologic surgery. *Int J Gynaecol Obstet* 2011; 113:124–7
8. Gan TJ: Risk factors for postoperative nausea and vomiting. *Anesth Analg* 2006; 102:1884–98

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## Questioning a Relationship between Nitrous Oxide Duration of Exposure and Postoperative Nausea and Vomiting

*To the Editor:*

Peyton and Wu<sup>1</sup> have recently published a systematic review with meta-analysis that identified a relationship between the risk of postoperative nausea and vomiting within the first 24 h and the duration of the intraoperative exposure to nitrous oxide. Using data from over 10,000 patients in 29 randomized controlled trials of nitrous oxide administration (Peyton and Wu<sup>1</sup>; table 1),

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