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Competing Interests

The authors declare no competing interests.

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Opiates and IV Acetaminophen

To the Editor:

I read with keen interest the article by Wasserman *et al.*,¹ “Impact of Intravenous Acetaminophen on

Perioperative Opioid Utilization and Outcomes in Open Colectomies,” in the July issue of *ANESTHESIOLOGY*. Using billing codes to determine opiate use in 602 disparate hospitals in various states without knowing precisely what protocols are used renders the conclusion that IV acetaminophen has no important impact on postoperative opioid use in question. Hospitals with excellent compliance with Enhanced Recovery After Surgery Group protocols obtain decreases in opiate use. However, compliance with Enhanced Recovery After Surgery protocols is highly variable from hospital to hospital, let alone from practitioner to practitioner. For instance, some physicians routinely give patients an opiate patient-controlled analgesia in addition to IV acetaminophen as part of a multimodal protocol when they assume a patient is going to have very high demands *versus* oral for those they assume will not. If nursing staff receive scheduled orders for non-steroidal antiinflammatory drugs or IV acetaminophen but do not deliver them in a timely fashion, the patient may get behind in pain control, thus necessitating rescue opiate. In states with high rates of chronic opiate users, the results will skew to no impact for IV acetaminophen. For that matter, if a patient is given an opiate patient-controlled analgesia but does not use it, the billing codes will still reflect opiate given, when in fact, the patient may not have used it. In hospitals where thoracic epidurals are not routinely used, or if individual patients decline or cannot receive thoracic epidural, opiates become the mainstay treatment for severe pain. Patients who are content with oral acetaminophen are more likely to have either high pain tolerance or negative personal convictions about taking opiates. Those with low tolerance or already taking chronic opiates will likely require potent opiates postoperatively.

Without actually examining doses and types of opiates used, analysis of impact is specious. A person receiving one hydrocodone or a small dose of meperidine for postoperative shivering will display an opiate given, but that cannot be compared with a patient who requires a patient-controlled analgesia. Respiratory events are common after open colectomies in the elderly and in those who smoke and may not always relate to opiates. Ileus is associated with longer surgical or anesthesia times, lack of low thoracic epidural use, prolonged use of nasogastric tubes, and extensive bowel manipulation, not just opiate use.² Giving a single dose of IV acetaminophen and expecting a miraculous change in opiate use is unsophisticated at best. IV acetaminophen is a tool like any other in our armamentarium. If we use a tool ineffectively, then we are the problem—not the tool. Avoiding opiates altogether with a robust Enhanced Recovery After Surgery program including IV acetaminophen for 24 h has shown large effects on outcomes.³ Finally, one has to examine the motivation of Premier Healthcare Solutions, Inc., because their motto is to provide “better care and outcomes at a lower cost.” If the driving desire to

lower costs means accessing the databases of 602 of their 3,750 hospitals with a majority lacking a robust Enhanced Recovery After Surgery service, that too, could skew the results.

A better study would be a randomized, double-blinded one in which the only variable would be the use of IV acetaminophen *versus* oral acetaminophen for 24 h in a cohort of patients that did not include chronic opiate users and in which the multimodal regimen was standardized rather than determined by individual predilections. Ultimately, anesthesiologists typically have limited control over pain management of patients and infrequently beyond the first postoperative day. It is impossible to create a major impact on an inflammatory process that will extend well beyond the first 24 h.⁴ Consequently, until we have complete ownership of perioperative pain management well beyond the immediate postoperative period using all available modalities, we will have minimal impact, IV acetaminophen or not.

Competing Interests

The author declares no competing interests.

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When Large Administrative Databases Provide Less Relevant Information than Randomized Studies

To the Editor:

We read with interest the retrospective study conducted by Wasserman *et al.*,¹ based on a national administrative database assessing the impact of intravenous acetaminophen on perioperative opioid utilization and outcomes in patients undergoing open colectomies.

Research based on administrative data sets can provide information of major importance for clinical practice, but the interpretation of results is difficult, and causal inference is circumscribed by intrinsic methodologic limitations. In this study,¹ we observed three main limitations with potential impact on result interpretation: (1) the validity of main outcome data (morphine consumption) is questionable compared with monitored clinical studies, (2) the doses of acetaminophen administered in the treated group were heterogeneous, and (3) the estimation of treatment effect is likely to be biased by uncontrolled confounding factors. The sensitivity analysis provided by the authors is not enough to provide an unbiased estimation of treatment effect. To minimize bias, a propensity score analysis² or another sophisticated multivariable matching process³ should have been performed, because the patients who received acetaminophen differed markedly from those who did not. Despite the large sample size ($n = 181,640$),¹ we believe that the average treatment effect estimation is not robust enough to support any practice recommendations based on this study. Therefore, the amount of new information is relatively limited.

Although we thank the authors for not stating recommendations based on their results, we respectfully disagree with their conclusions: “Important next steps include validation of these results with alternative data and identifying patients and administration schedules (*e.g.*, routine IV acetaminophen every 6 h, dosing for 48 h) most likely to result in benefit.”¹ The largest randomized control trial ($n = 550$ patients) evaluating the treatment effect of a homogeneous and appropriate dose of acetaminophen demonstrated a reduction in morphine requirements greater than the threshold prespecified by Wasserman *et al.*¹ (-31% ; $P < 0.001$) and was not cited.⁴ Citing appropriate references allows readers to understand new results and interpret them while taking into account results obtained using a high level of evidence-based studies. Such an approach in the