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Decision - MS#: AA-D-16-00636 "Utilization of Antiemetic Medication as a Marker of Healthcare Disparities in Anesthesia: A Bayesian Hierarchical Model Using the National Anesthesia Clinical Outcomes Registry"

A&A Editorial Office <em@editorialmanager.com>   Wed, May 18, 2016 at 1:14 PM
Reply-To: A&A Editorial Office <editor@anesthesia-analgesia.org>
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CC: editor@anesthesia-analgesia.org, nborkows@uab.edu

May 17 2016 06:05PM

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RE: MS#: AA-D-16-00636 "Utilization of Antiemetic Medication as a Marker of Healthcare Disparities in Anesthesia: A Bayesian Hierarchical Model Using the National Anesthesia Clinical Outcomes Registry"

Dear Dr Andreae:

Thank you for submitting your manuscript "Utilization of Antiemetic Medication as a Marker of Healthcare Disparities in Anesthesia: A Bayesian Hierarchical Model Using the National Anesthesia Clinical Outcomes Registry" to Anesthesia & Analgesia for consideration. Your manuscript has been reviewed by our editorial board and outside experts. Based on their reviews and my own reading of the manuscript, your article is not acceptable for publication in Anesthesia & Analgesia in its present form, but I would be happy to receive a revised version. Please see my comments below and my Quantitative Evaluation Scores at the bottom:

Executive Section Editor Comments to the Author:

This was an interesting paper using a subset of NACOR data. However, as presented in its current form, the manuscript will need considerable modification to make it appropriate for the journal's readership. The paper needs to be reworked to provide the needed explanations and/or revisions to the areas noted by the reviewers below.

If you can address point-by-point the comments of the reviewers (see below), I will be happy to receive a revised version of the manuscript. However, I cannot promise that your revised version of the manuscript would achieve the priority necessary for publication in Anesthesia & Analgesia.

If we do not receive a revised manuscript from you within the 8 weeks, or a letter from you indicating your indication of sending a revised manuscript, I will assume that you have elected to decline to revise your manuscript.

If you choose to revise your manuscript, please submit your revision via Editorial Manager by logging in to your author account and clicking the link "Submissions Needing Revision." Be sure you have pasted your response to the reviewers into the appropriate box on the online submission site.

With all good wishes,

Nancy Borkowski, DBA, CPA, FACHE, FHFMA
Executive Section Editor
Anesthesia & Analgesia

Jean-Francois Pittet, MD
Editor-in-Chief
Anesthesia & Analgesia

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Executive Section Editor Quantitative Evaluation:

1. Novelty of the Topic: 7
2. Significance of Topic: 7
3. Approach to the Topic: 8
4. Interest of the Topic to the Specialty: 7
5. Impact of the Findings on the Specialty: 7

Scale: [1-9]

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Reviewer Comments to the Author:

Reviewer 1: Major Strengths: Strong statistical analyses, large sample size.

Major Weaknesses:
This is a nice paper, but the presentation / writing may be improved. I have lots of comments below, but mostly for the presentation. For example, instead of "alpha" on P10L42, use "type I error rate" or using different terms instead of "yvar" and "xvar" on P11L24.

Specific issues that need to be addressed by author(s):

All thru the paper, instead of "prediction", "association" may be more appropriate. For example, P6L41 - 48. "Our hypothesis is that socioeconomic patient characteristics ARE ASSOCIATED WITH antiemetic utilization…" and on P16L40: "… in Table 3, providing ASSOCIATIONS of ondansetron use by patient insurance status."

Appendix 1: The first paragraph is repeated on Appendix 1. There are also repetitions on the last paragraph.

Appendix 1: "In some models, we included mixed (random) effects…" You can be more specific on Appendix 1. Which models? Once you explain this on Appendix 1, on P12L7, please refer to the Appendix.

Appendix 1: "We present more details on the Bayesian models in the appendix."???

Appendix 1: "We used the default priors as described in the software package(Gabry and Goodrich 2016), i.e. we used uninformative priors for the main effect of insurance status on antiemetic prophylaxis." Please provide the prior distributions you used for each covariate in the Appendix. Then, on P12L21, refer to the Appendix.

Appendix 1 and on P12L26-28: "We performed a sensitivity analysis investigating the appropriateness of our model assumptions." How did you investigate the appropriateness of the model assumptions? Please explain in the Appendix, and refer to appendix on P12L28. Did authors also used sensitivity analysis using different prior distributions and checking the robustness of the results?

It would be also helpful to provide the codes for one of the Bayesian models, including the prior distributions and initial chains, in the Appendix for the interested readers.

P17L24 - 26: I could not find detailed results of several models in the Appendix.

P10L12: instead of "Classical" logistic regression, authors may consider using "frequentist" logistic regression. For the logistic regression model, please also report the c-statistics.

P11L17- 19: please provide a reference for the 20% change on the beta coefficient.

P11L38: why only the interaction of age and gender, but not the other main effects?

P11L59: "divided" instead of "devided"?

P12L14: briefly explain "Rhat."

P14L27: "…antiemetics were utilized in 234453 cases". Numbers are not consistent on Table 1. For example, ondansetron was used on 223,449 cases based on gender and 223,472 based on insurance on Table 1.

P14L37: "antiemetic utilization and insurance status for 173133 anesthesia cases". This number is not consistent to what was presented in Table 1. For example, based on insurance sub-table on Table 1, the sample size is 176,334.

Title of supplemental table 1: "Missing Data Pattern" instead of "Missing Pattern"?

The legend of supplemental table 1 is confusing. "only 128999 have complete information on insurance type and procedure code, a sigificant attrition." Isn't it 116,387 cases have complete information and 128,999 cases have missing information for the insurance type and procedure code?

P14L54: "Anesthesia was provided between 2010 and 2013." Between January 1st 2010 and December 31st 2013?

Table 1: Authors labeled columns as "% cases". Then, provided 0.57 for females and 0.43 for males. It reads like 0.57%, not 57%.

It would be helpful to provide the confidence interval of the OR on Tables 1 and 2.

P15L17: "Most patients were classified as ASA class 1, 2, 3 or 4." Refer to only ASA 2 or 3 instead?

P15L45- 50: Provide OR and the associated CI.

P16L4: "Stratification did change the odds ratios". Maybe provide the initial OR and the lowest OR. Something like: "Stratification did change the odds ratios from XX to as low as YY."

Table 3: Based on the OR and 95% CI for median income, population and case duration, I am assuming authors entered them as continuous variables in the multivariate model. Therefore, the OR provides the one unit increase in duration (1 minute) or income ($1 increase). The OR's may be more meaningful for larger increments, such as 10 minutes for case duration and $1,000 for median income.

On page 15 L45-47, authors presented commercial vs Medicaid; on P16L43, commercial vs Medicaid or medicare and on P17L44, commercial vs medicaid and medicare? Why not to be consistent and provide results comparing only commercial vs medicaid and medicare? On your tables, still present Medicaid and medicare on separate lines, but explain to readers that analyses were provided for commercial vs medicaid and medicare.

Authors have a very large sample size so that their analyses are over powered. Therefore, it is possible to find a clinically meaningless difference as statistically significant. On the very first sentence of discussion, authors mentioned "clinically important association." Please discuss clinically important association in more detail in one of the paragraphs of the discussion section.

Reviewer 2: Major Strengths: The authors present a review of a subset of NACOR data where use of prophylactic antiemetic medications can be linked to indicators of socioeconomic status, principally the payer. Advanced statistical methods are applied, and the methodology could serve as a model for other similar studies. The paper is generally well-written.

Major Weaknesses: Overall, the major problem here is the (final) small sample of NACOR. The authors have done well to describe how the final dataset was obtained and to acknowledge the limitations of their analysis, but the question remains of whether the reader should bother with the paper or not. One way the manuscript might be improved is to provide some sensitivity analysis around the missing data. This could be done by comparing age, sex, case mix or facility type between the final dataset and the excluded cohorts. Comparing demographics between the final dataset and the excluded set of data from comparable facilities (university or large community) would help to demonstrate the representativeness (or not) of the results.

Results of the analysis by median income appear to have disappeared from the results and discussion. What's up there? If not a significant predictor, this should be stated. It would affect how I interpret the results by payer.

Antiemetics might be given as prophylaxis or (in the PACU) as treatment for active vomiting. Could you discriminate between the two? If not, this should be mentioned in the discussion and the implications addressed.

If the answers to the above lead to less confidence in the results, one way to reframe the paper might be around the methodology rather than the results. Something like: 1) we wanted a large dataset to test Bayesian analysis.

2) we found such a set in NACOR -- here's how. 3) Here's the analysis we did. 4) Here's how the analysis came out -- Hey, look there's a difference in prophylaxis based on payer status in this dataset. 5) This interesting finding should be explored further.

Specific issues that need to be addressed by author(s): The paper should be organized in accordance with A&A guidelines: Introduction, Methods, Results, Discussion. Sub-headings are OK, but should fit within these broad areas.

Check the spellchecker! PONV appears to have been globally substituted as PONY.

In the results, the number of groups (or hospitals?) that contributed data is variously described at 3 (in the table), 6 and 7. Which is it?

I recommend stating in the Introduction that guidelines for PONV prophylaxis are well known to anesthesiologists, and are based on assessment of patient risk factors. Those risk factors should be enumerated, and the authors should specifically note that socioeconomic status or payer should NOT influence the decision of what to do.

I recommend spelling out AU rather than abbreviating it. I think this will improve readability.

Medicare and Medicaid should be capitalized throughout.

Thank you for a provocative work!

Reviewer 3: The authors present a manuscript that utilizes a subset of NACOR to try to identify health care disparities in the administration of anesthesia, specifically looking at the relationship between patient zip code and ondansetron administration. While the authors are to be commended for utilizing this unique data source to answer a worthwhile question in anesthesia practice, there are a number of significant issues with the premise of their study.

According to the author's manuscript, this reviewer would fall into Stage I of Don Berwick's model: the data are wrong. Specifically, the authors have ignored almost all of the commonly accepted risk factors for postoperative nausea and vomiting, PONV, which the authors have somewhat inexplicably termed PONY throughout the manuscript. I would encourage the authors to review the work of Apfel and the simplified risk score for PONV, which identified gender, prior history of PONV/motion sickness, smoking and receipt of postoperative opioids as risk factors. Of the 4 elements of risk, the authors have included 1 in their model. The authors state that "antiemetic utilization is relatively independent of patient characteristics." This is not true.

Granted, they are limited by the NACOR dataset not representing these other factors well, but problematically, smoking is associated with both decreased risk of PONV and is also highly associated with low socioeconomic status. So it is entirely possible that the anesthesia providers are acting appropriately in their practice of reducing antiemetics for patients with reduced risk factors for emesis--this is in fact the clinical standard for PONV treatment at my institution, and something I see in clinical practice every day. This is not even mentioned in the

manuscript.

Other significant issues include extrapolation from <1% of the NACOR dataset to the entire speciality, and the fact that the list of antiemetics included in the analysis is incomplete.

Additionally, there are significant typographic errors throughout the document, some of which I have highlighted below.

Major comments:

P17L42 By my calculations, you are looking at less that 1% of the cases available in NACOR, and at a small subset of institutions that you don't quite specify--is it 7, or fewer? I am not sure that it is feasible to draw conclusions on national practice patterns when looking at less than 1% of available data.

P10L24 This is not a complete list of anti-emetics or accepted methods for PONV prophylaxis; suggest repeating the analysis with a comprehensive list, i.e. scopolamine, haloperidol, use of TIVA, avoidance of N2O

P13L28 Insurance status should really be treated as a categorical variable, not an ordinal variable. Patients over the age of 65, for instance, would likely be on Medicare. It doesn't make sense to consider that 'ordered' below private insurance as that's not the case. Similarly, self-pay for non-covered procedures such as breast augmentation could be classified as 'no medical insurance', when in fact they might indicate a patient with a socioeconomic status 'above' private insurance.

Minor comments:

P18L45 lowercase patients

P15L19 You have now mentioned this several times, would just mention it once

P14L50 divided

P14L38 'cut off'

P8L40 Extra '...'

P8L48 'dexamethasone'

P10L22 'Antiemetics'

P10L15 I think you mean American Society of Anesthesiologists Physical Status Classification

P8L50 'et al'

P8L22 'has an accepted'

P6L54 Would capitalize m in medicaid

P13L33 Would capitalize m in medicaid

P13L60 PONV, not PONY. Also, need to define the term before using it.

P22L42 'datasets'

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CHECKLIST FOR REVISED MANUSCRIPTS
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-- Please submit one highlighted version (highlighted font or colored font) of your revised paper showing where changes were made. Please DO NOT use track changes as this will result in your paper being returned to you.
-- Please double space your document and add page numbers in the upper, right corner in header (flush right)
-- Please ensure the title page includes a running head title (to be used in the short table of contents of the journal): It should be no more than 60 characters (including letters and spaces) placed at the bottom of the title page and identified.
-- At first mention of terminology in the abstract, text, each figure legend, and each table, spell out in full and follow immediately with the abbreviation (enclosed within parentheses). Use abbreviations consistently; do not revert to the spelled-out term. Abbreviations can make text very difficult to read, particularly if they are idiosyncratic to the manuscript. Do not create new or unusual abbreviations.
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