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- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*
- Email correspondence between the editorial office and the authors*

*The corresponding author has opted to make this information publicly available.

Personal or nonessential information may be redacted at the editor’s discretion.

Questions about these materials may be directed to the Obstetrics & Gynecology editorial office: obgyn@greenjournal.org.
Date: Nov 30, 2018
To: "Aaron Tanner Poole" [Redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-2053

RE: Manuscript Number ONG-18-2053

Multi-Modal Step-Wise Approach to Reduce Hospital Opioid Use after Cesarean Delivery

Dear Dr. Poole:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Dec 21, 2018, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

REVIEWER #1:

1. Abstract
   a. Line 32. The authors mention a multidisciplinary task force. Please address this more fully in the body of the manuscript. I was not able to locate it.
   b. Might include something about the protocol being applied to those who received neuraxial anesthesia (as others were excluded).
   c. Line 49. Please include the median MME per day before and after the change. This number is relevant (to compare with other publications and to assist providers who may want to implement this protocol).
   d. The last sentence of the manuscript (lines 193-194) might be a nice addition to the abstract conclusion.

2. Introduction. Very well written, excellent background summary.
   a. Lines 72-76 (objective). Nowhere in the objective do the authors explain that QI project was implementation of a specific protocol that shifted administration of post-cesarean opioids from routine/scheduled to prn (limiting opioid use to those with breakthrough pain) in an effort to reduce opioid consumption while maintaining pain relief?
   b. Minor. In line 71, advancing to parenteral administration of what? What do the authors mean by multimodal?

   a. Lines 81-83. Was this the task force?
   b. Lines 86-87. Were the opioids administered as scheduled until discharge, or e.g. for a certain number of days? Did the protocol include tapering them?
   c. Lines 97-98. What happened if the patient experienced breakthrough pain on oral oxycodone?
   d. Lines 113-114. Was a (formal) pain assessment tool used?
   e. Lines 117-118. The power analysis was for 136/arm. But the authors estimated 80 cesareans per month, so 4 months would be more than twice the number needed. Why was this selected?

4. Results.
   a. Lines 144-145. Please include the daily and total MME values for the pre- and post-intervention cohorts in the text of the results and the abstract. The values are useful metrics for readers as they compare their patients’ usage with that of the authors
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   c. Line 155. Please specify the confounding variables for which adjustment was performed.
   d. In table 1, it looks like each of the itemized check-boxes is intended to be checked, with the exception of the left column/ top row/bottom 3 entries (hydrocodone, oxycodone with acetaminophen, and oxycodone without acetaminophen).
Is that the case? In other words, patients should be able to receive all checked items but should only get 1 scheduled opioid at a time. Please clarify this.
e. In table 2, please include a column with p-values.
f. The content of figure 1 is included in the text to the extent that it isn't really needed as a figure.
g. The numerical values are hard to read in the figures. Would consider combining figures 2-4 as a single table.

5. Discussion
a. Please emphasize more fully what the study adds.
b. Lines 160-162. As written, the change in practice was a "multi-modal approach," but was wasn't it a shift from scheduled opioids to opioids only upon request?
c. Line 163-176. Unclear what the authors intend to convey with this paragraph. Would clarify the intended message.

REVIEWER #2:
It is heartening to see that in the face of one of the worst drug epidemics to bedevil the US in a number of decades, obstetricians are using every opportunity to reduce the use of opiates by their patients in the immediate post-operative period. In this paper the authors report on a PI project that appears to have substantially reduced the use of opiates after cesarean section in their institution. The results are so important, that one feels almost churlish pointing out a few peccadilloes. However, the shortcomings noted below should not detract from the important work they have done, nor should it discourage those who want to follow in their footsteps. Specific comments are as follows:

1. The possibility of information bias cannot be dismissed out of hand. The design was before and after. Therefore it is reasonable to assume that in the "after" period, everyone was aware of the focus on reduced use of narcotics. That might have introduced performance or measurement bias by those eliciting and/or recording pain scores.

2. Most of the weaknesses noted by the authors in the discussion are not substantive problems. However, the failure to note the amount of narcotics patients went home with, and the absence of satisfaction scores are serious issues. If patients were dissatisfied with this new approach it might make it difficult to maintain. While I doubt that such is the case, it is important not to rely on pre-hoc assumptions. Similarly, the millions of excess pills that are prescribed on discharge from hospitals annually is not a trivial issue, and an accounting of medications that patients took home is a key outcome that went un-measured.

3. One of the outcomes of interest was length of stay. I did not see a mention of surgical complications among the confounders. Those can clearly influence the length of stay.

4. The power calculation they used to justify their sample size was based on the primarily outcome. Yet the actual number recruited was based on secondary outcomes for which no power considerations were given.

5. In their discussion of potential tools to reduce reliance on opioids they could also mention the use of postoperative neuraxial blocks.

6. Line 86: They use the term, "as scheduled." I assume that means the order was not PRN. What was the amount and interval for dosing?

7. Line 92, what medication and machine setting were used for patient controlled anesthesia?

8. Was any patient education part of the PI initiative?

9. On line 174 the authors quote an ACOG document, without citing it in the text (they do in the reference list). It might add some weight to the comment if they acknowledged the quote's provenance when they cite it.

While the methodology has some flaws, this work demonstrates the utility of a well-designed PI project to improve care in an institution. As such, and given the subject matter, it has a message that should resonate for a broad audience.

REVIEWER #3:
*I would like to congratulate the authors with the impact, that they were able to accomplish at their institution. However this article is a QI project. The current ACOG recommendations and ERAS protocols advocate stepwise multimodal approach to postoperative pain management. This article rather supports the current practice than adding new information.

*For table 2, p value must be provided. Also if available, include variables that could independently require higher doses of opioids, ex. prior/ current substance abuse( methadone users can require up to 70% more opioids), immediate postoperative surgical complications.
*One of the limitations is using median value, which is not an adequate representation of the progression of the pain. Some patients might have experienced more severe pain while others only mild pain, which averaged in the end with the median of the other group. Perhaps using a change in pain scale (ex. delta) can be more objective. Nonetheless, I found interesting that none of the patients the study ever reported a pain scale greater than 5.

STATISTICAL EDITOR’S COMMENTS:

1. line 129: Need to enumerate all missing data.

2. lines 130-132 and 155-158: Were there more than the 7 variables cited in the multivariable adjustment model? If so, should enumerate all. Should contrast the unadjusted with the adjusted ORs, possibly with an additional Table. Should justify the use of the number of variables in the adjusted model for the subsets having either zero MME or ≥ 100 MME. That is, are either models at risk of being over fitted based on the counts of number of patients in the zero or 100+ MME groups vs the number of variables in the aOR models?

3. Table 2: Need units for maternal age.

4. Fig 4: In fig legend, should cite the p-value for the NS difference and was this the overall or were comparisons also done for each day? Could there also be comparisons based on a proportions at a pre-specified pain score, e.g., pain score ≥ 7 for each PO day and was there any evidence of higher pain scores by that criterion for post vs pre implementation protocol? In other words, any evidence of subjective patient worse pain scores after implementation of lower opioid use?

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, as well as subsequent author queries. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
   1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
   2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

2. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained." *The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

3. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), and quality improvement in health care (ie, SQUIRE 2.0). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at http://ong.editorialmanager.com. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, CHEERS, or SQUIRE 2.0 guidelines, as appropriate.

4. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and appendices).
Please limit your Introduction to 250 words and your Discussion to 750 words.

6. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your signature on the journal's author agreement form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

7. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words, written in the present tense and stating the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

8. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Original Research articles, 300 words. Please provide a word count.

9. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

10. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

11. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

12. The American College of Obstetricians and Gynecologists' (College) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite College documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly. If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if a College document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All College documents (eg, Committee Opinions and Practice Bulletins) may be found via the Resources and Publications page at http://www.acog.org/Resources-And-Publications.

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If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at http://ong.editorialmanager.com. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors, that each author has given approval to the final form of the revision, and that the agreement form signed by each author and submitted with the initial version remains valid.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Dec 21, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,
17 Dec 2018

Obstetrics & Gynecology

Dear Obstetrics & Gynecology Editor,

I have enclosed a revised manuscript, “Multi-Modal Step-Wise Approach to Reduce Opioid Use after Cesarean Delivery: a Quality Improvement Project” (ONG-18-2053), which describes our quality improvement project that decreased opioid use in our post-cesarean patients by 75%. This project was previously presented at the American College of Obstetricians and Gynecologist Armed Forces District, September 2018 in Honolulu, HI. I would like to submit this revised manuscript solely to Obstetrics & Gynecology for publication. This manuscript is not under consideration for publication elsewhere and will not be submitted elsewhere until a final decision for publication is made by the editors of Obstetrics and Gynecology.

I affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

The Institutional Review Board (IRB) at our facility waived this quality improvement project for its performance and publication. Tables are original work and no identifiable patient information is included. No funds were dedicated to this Quality Improvement project outside of preexisting institutional resources.

We appreciate your review of our article and feedback from reviewers. We have included all reviewer and editor comments with location of changes in the manuscript. We also changed from original research submission to quality improvement study, following SQUIRE 2.0 guidelines.

OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.

Please see attached transparency letter from the first author. I appreciate your time and consideration.

Very Respectfully,

Aaron T. Poole, MD
Maternal Fetal Medicine
Naval Medical Center Portsmouth, Portsmouth, VA
REVIEWER #1:

1. Abstract
a. Line 32. The authors mention a multidisciplinary task force. Please address this more fully in the body of the manuscript. I was not able to locate it.
   
   Added in methods: “In November of 2017, in response to the growing awareness of opioid over prescription, a multidisciplinary task force was formed to investigate the opioid prescribing administration patterns in post-cesarean patients. The task force included Obstetrics and Gynecology residents, a Nurse Anesthetist, an Anesthesiologist, a Pharmacist, the Perinatal Clinical Nurse Specialist, and the Medical Director of Labor and Delivery”. Line 111-115.

b. Might include something about the protocol being applied to those who received neuraxial anesthesia (as others were excluded).
   
   Added: “The revised order set was implemented for all patients who underwent a cesarean delivery with regional anesthesia.” Line 41-42 of abstract

c. Line 49. Please include the median MME per day before and after the change. This number is relevant (to compare with other publications and to assist providers who may want to implement this protocol).
   
   Added to line 57 of abstract MME per day before and after change.

d. The last sentence of the manuscript (lines 193-194) might be a nice addition to the abstract conclusion.
   
   Added: “By separating acetaminophen from opioid and limiting opioids to breakthrough pain, we were able to have a tier-based approach to pain management.” Line 66-67.

2. Introduction. Very well written, excellent background summary.
   
   a. Lines 72-76 (objective). Nowhere in the objective do the authors explain that QI project was implementation of a specific protocol that shifted administration of post-cesarean opioids from routine/scheduled to prn (limiting opioid use to those with breakthrough pain) in an effort to reduce opioid consumption while maintaining pain relief?

   “Our primary objective was to evaluate if the implementation of a quality improvement program that eliminated the combination of opioids with acetaminophen and shifted the administration of post-cesarean opioids from scheduled to as needed was associated with a reduction in opioid use while maintaining pain relief.” Lines 87-90.

   b. Minor. In line 71, advancing to parenteral administration of what?
   
   Added “before advancing to parenteral administration of ‘opioids’” on line 86
“What do the authors mean by multimodal? –

Explained multimodal on line 71-72 “using two or more methods or medications to manage pain” lines 77-78

   a. Lines 81-83. Was this the task force?
   
   Addressed. Added in methods: “The task force included Obstetrics and Gynecology residents, a Nurse Anesthetist, an Anesthesiologist, a Pharmacist, the Perinatal Clinical Nurse Specialist, and the Medical Director of Labor and Delivery.” Line 115-117

   b. Lines 86-87. Were the opioids administered as scheduled until discharge, or e.g. for a certain number of days? Did the protocol include tapering them?
   
   Added: Opioids were offered at four hour intervals to patients up until the time of discharge, without a routine tampering of quantity prescribed. Line 153-155.

   c. Lines 97-98. What happened if the patient experienced breakthrough pain on oral oxycodone?
   
   Added: For patients who experienced breakthrough pain on oral oxycodone, opioids could be administered intravenously after an exam by a physician. Lines 173-175.

   d. Lines 113-114. Was a (formal) pain assessment tool used?
   
   Added “Pain was determined at routine intervals at the time of vital sign assessment by nursing. The Numeric Pain Rating scale was used, in which the patient selects a number from 0 to 10 that best reflects her pain intensity with 0 representing no pain and 10 representing the worst possible pain.” Line 149-152.

   e. Lines 117-118. The power analysis was for 136/arm. But the authors estimated 80 cesareans per month, so 4 months would be more than twice the number needed. Why was this selected?

   “An initial review prior to the quality improvement project demonstrated an average use of 120 MME during the entire stay after cesarean delivery. It was determined that 136 patients in each arm would need to be included to detect a 20% reduction in MME. With approximately 70 cesarean deliveries per month, 4 total months of data would be required to detect a difference. However, to monitor trends over time and ensure ongoing compliance with the protocol, the time frame was extended to 8 months.” Line 199-204. Also, desired to look at secondary outcome of pain. Clarified why doubled initial power analysis.

4. Results.
a. Lines 144-145. Please include the daily and total MME values for the pre- and post-intervention cohorts in the text of the results and the abstract. The values are useful metrics for readers as they compare their patients' usage with that of the authors.

"There was a 75% reduction in the primary outcome of median morphine milligram equivalents per stay from 120 (90-175.5 interquartile range) preintervention to 30 (5-67.5) postintervention, P<0.001] and a 77.2% reduction in median morphine milligram equivalents per day (50.5 [40.8-60] vs 11.5 [2.1-25.2], P<0.001, see Figure 2).” Added details to results, lines 182-185.

b. Lines 150-154. Some numerical data would be helpful, e.g. acetaminophen consumption.

The median ibuprofen dose per day per patient was similar between both groups (1391 mg/day pre vs 1347mg/day post-implementation; p 0.22). There was also no difference in the percent in the percent of patients receiving ketorolac between the pre- and post-implementation group (Table 3). However, there was an increase in acetaminophen use per day in the post-implementation group (2340mg/day post-implementation vs. 753mg/day pre-implementation; p<0.001). There was no significant difference in postoperative pain scores between the pre- and post-implementation group by postoperative day (see Figure 4). Lines 190-204.

c. Line 155. Please specify the confounding variables for which adjustment was performed.

Added “After controlling for possible cofounders including age, BMI, nulliparity, hours until discharge, TAPS, general anesthesia, diabetes, preeclampsia, multifetal gestation, and repeat cesarean delivery.” Lines 267-269. And 215-216.

d. In table 1, it looks like each of the itemized check-boxes is intended to be checked, with the exception of the left column/ top row/bottom 3 entries (hydrocodone, oxycodone with acetaminophen, and oxycodone without acetaminophen). Is that the case? In other words, patients should be able to receive all checked items but should only get 1 scheduled opioid at a time. Please clarify this.

Changed table 1 to clarify that all patients received ketorolac followed by ibuprofen. Also, preimplementation, the provider could choose one of the three options.

e. In table 2, please include a column with p-values.

Done.

f. The content of figure 1 is included in the text to the extent that it isn't really needed as a figure.

Removed figure.
g. The numerical values are hard to read in the figures. Would consider combining figures 2-4 as a single table.

Changed figures to tables.

5. Discussion
a. Please emphasize more fully what the study adds.
b. Lines 160-162. As written, the change in practice was a "multi-modal approach," but was wasn't it a shift from scheduled opioids to opioids only upon request?
c. Line 163-176. Unclear what the authors intend to convey with this paragraph. Would clarify the intended message.

Discussion reworded to address a, b, c.

REVIEWER #2:

It is heartening to see that in the face of one of the worst drug epidemics to bedevil the US in a number of decades, obstetricians are using every opportunity to reduce the use of opiates by their patients in the immediate post-operative period. In this paper the authors report on a PI project that appears to have substantially reduced the use of opiates after cesarean section in their institution. The results are so important, that one feels almost churlish pointing out a few peccadilloes. However, the shortcomings noted below should not detract from the important work they have done, nor should it discourage those who want to follow in their footsteps.

Specific comments are as follows:

1. The possibility of information bias cannot be dismissed out of hand. The design was before and after. Therefore it is reasonable to assume that in the "after" period, everyone was aware of the focus on reduced use of narcotics. That might have introduced performance or measurement bias by those eliciting and/or recording pain scores.

-Added Additionally, the retrospective design and increasing awareness of narcotic use among nursing and staff may have introduced performance or measurement bias.

2. Most of the weaknesses noted by the authors in the discussion are not substantive problems. However, the failure to note the amount of narcotics patients went home with, and the absence of satisfaction scores are serious issues. If patients were dissatisfied with this new approach it might make it difficult to maintain. While I doubt that such is the case, it is important not to rely on pre-hoc assumptions. Similarly, the millions of excess pills that are prescribed on discharge from hospitals annually is not a trivial issue, and an accounting of medications that patients took home is a key outcome that went un-measured.

- Added preliminary data from ongoing discharge narcotics study

3. One of the outcomes of interest was length of stay. I did not see a mention of surgical complications among the confounders. Those can clearly influence the length of stay.
Added category to table 2 of re-operation or hysterectomy. Low complication rate overall. As we used median length of stay, outliers should not influence outcome. In addition, linear regression controlling for indication for cesarean, blood transfusion, diabetes, age, gestational age at delivery, BMI, preeclampsia, TAPS, and general anesthesia showed no difference between pre and post implementation, P=0.46. (these results not in paper)

4. The power calculation they used to justify their sample size was based on the primarily outcome. Yet the actual number recruited was based on secondary outcomes for which no power considerations were given.

"With approximately 70 cesarean deliveries per month, 4 total months of data would be required to detect a difference. However, to monitor trends over time and ensure ongoing compliance with the protocol, the time frame was extended to 8 months." Clarified that the desire to was to be adequately powered to detect the primary outcome, but also see if process improvement changes were sustained. Line 153-155.

5. In their discussion of potential tools to reduce reliance on opioids they could also mention the use of postoperative neuraxial blocks.

Added info on TAP block to methods (line 145-146), results (line 277-280, table 3), and discussion (line 328-333)

6. Line 86: They use the term, "as scheduled." I assume that means the order was not PRN. What was the amount and interval for dosing?

Reworded “Two tabs of combination opioid medications were scheduled every four hours with a directive that the patient could refuse the medication; routine tapering of the opioids was not performed throughout the patient’s stay.” Line 139-140

7. Line 92, what medication and machine setting were used for patient controlled anesthesia?

“Our standard PCA protocol utilizes hydromorphone, with a loading dose of 0.5mg and a patient request dose of 0.2mg with a lockout of 10 minutes.” Line 148-149. Alaris pump.

8. Was any patient education part of the PI initiative?

Patient awareness of risks of opioid use immediately postpartum and while breastfeeding was addressed with an information handout which was provided to all patients discharged with opioids. This included information regarding goal of opioids to improve function rather than have zero pain, signs of neonatal toxicity, maximum daily dose of opioids while breastfeeding, and how to properly dispose of unused opioids.” Line 121-126
Patients were also informed by nursing of pain goals and use of NSAIDS and acetaminophen prior to opioids.

9. On line 174 the authors quote an ACOG document, without citing it in the text (they do in the reference list). It might add some weight to the comment if they acknowledged the quote's provenance when they cite it.

Done

While the methodology has some flaws, this work demonstrates the utility of a well-designed PI project to improve care in an institution. As such, and given the subject matter, it has a message that should resonate for a broad audience.

REVIEWER #3:

*I would like to congratulate the authors with the impact, that they were able to accomplish at their institution. However this article is a QI project. The current ACOG recommendations and ERAS protocols advocate stepwise multimodal approach to postoperative pain management. This article rather supports the current practice than adding new information.

Switched article format from original research to quality improvement, using SQUIRE guidelines. See attached SQUIRE guideline.

*For table 2, p value must be provided. Also if available, include variables that could independently require higher doses of opioids, ex. prior/ current substance abuse (methadone users can require up to 70% more opioids), immediate postoperative surgical complications.

Added above info to table 2.

*One of the limitations is using median value, which is not an adequate representation of the progression of the pain. Some patients might have experienced more severe pain while others only mild pain, which averaged in the end with the median of the other group. Perhaps using a change in pain scale (ex. delta) can be more objective. Nonetheless I found interesting that none of the patients the study ever reported a pain scale greater than 5.

Figure replaced with Table 5. Included multiple comparisons including median pain score, pain score of 7 or more, and change in pain score compared to postoperative day zero. Cleared up that there were patients with pain scores greater than 5 by reporting proportion greater than or equal to 7.

STATISTICAL EDITOR’S COMMENTS:

1. line 129: Need to enumerate all missing data.

Added info to table 2 regarding missing data.

2. lines 130-132 and 155-158: Were there more than the 7 variables cited in the multivariable
adjustment model? If so, should enumerate all. Should contrast the unadjusted with the adjusted ORs, possibly with an additional Table. Should justify the use of the number of variables in the adjusted model for the subsets having either zero MME or \( \geq 100 \) MME. That is, are either models at risk of being over fitted based on the counts of number of patients in the zero or 100+ MME groups vs the number of variables in the aOR models?

Added table 4. Included all variables in adjusted model. “In order to limit overfitting, only variables with a P value < 0.25 on bivariate analysis were included in the model. Variables in the final model for zero MME included hours from surgery until discharge, nulliparity, chorioamnionitis, TAP block, and preeclampsia with severe features. For \( \geq 100 \) MME per stay, variables included were hours from surgery until discharge, BMI, TAP block, general anesthesia, preeclampsia with severe features, and blood transfusion.” Line 215-236.

3. Table 2: Need units for maternal age.

Completed

4. Fig 4: In fig legend, should cite the p-value for the NS difference and was this the overall or were comparisons also done for each day? Could there also be comparisons based on a proportions at a pre-specified pain score, eg, pain score \( \geq 7 \) for each PO day and was there any evidence of higher pain scores by that criterion for post vs pre implementation protocol? In other words, any evidence of subjective patient worse pain scores after implementation of lower opioid use?

Figure replaced with Table 5. Included multiple comparisons including median pain score, pain score of 7 or more, and change in pain score compared to postoperative day zero. Cleared up that there were patients with pain scores greater than 5 by reporting proportion greater than or equal to 7.
Good Afternoon,

Please attached manuscript with changes.

Very respectfully,
Aaron Poole, MD
Naval Medical Center Portsmouth

Begin forwarded message:

Dear Dr. Poole,

Thank you for submitting your revised manuscript. It has been reviewed by the editor, and there are a few issues that must be addressed before we can consider your manuscript further:

1. Please note the minor edits and deletions throughout. Please let us know if you disagree with any of these changes. done
2. LINE 31: Please make this change throughout: DONE
3. LINE 37: Lines 172-173 refer to the groups as “preimplemenation” and “postimplementation” (per journal style, we drop the hyphen). Did you want to refer to the groups as “intervention” or “implementation”? Please make these consistent. Changed to intervention
4. LINE 42: Table 3 says p=.14. Which is correct? Changed to 0.14
5. LINE 44: Please here and everywhere in manuscript report mg in whole numbers only. Also, everywhere in manuscript please round percentages to whole numbers only. Done
6. Line 188 was changed to “753.4.” Is this correct? Yes, but rounded to 753.
7. LINE45: Please be sure this is stated in the body of your paper. Statements and data that appear in the Abstract must also appear in the body text or tables for consistency. Added to line 199. Also in Table 4.
8. LINE 103: Do you mean "prescribed" or are you actually sending them home with pills. Please clarify throughout. Clarified that all prescriptions are filled and dispensed at hospital prior to discharge.
9. LINE 174: Should the groups be called “intervention” (abstract) or “implementation” (body text). Changed to intervention
10. LINE 190: “.4” was added here. Rounded down per recommendation
11. LINE 205: I do not understand this paragraph-please clarify. Attempted to clarify pain outcomes. Please let me know if more clear.
12. TABLE 2: Here and everywhere please percentages to whole numbers only. Done
13. TABLE 3: Again-Please mg in whole numbers only. Done.
14. The abstract says p=.16. Changed to 0.14 appropriately.
15. TABLE 5: Please move this Table to Appendix and cite accordingly. Moved to appendix and cited as such.

Please let me know if you have any questions. Your prompt response to these queries will be appreciated; please respond no later than COB on Monday, January 7th.

Sincerely,
-Daniel Mosier

---

Daniel Mosier
Editorial Assistant
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On Thu, Jan 3, 2019 at 12:48 PM Daniel Mosier <dmosier@greenjournal.org> wrote:

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13. TABLE 5: Please move this Table to Appendix and cite accordingly

Please let me know if you have any questions. Your prompt response to these queries will be appreciated; please respond no later than COB on **Monday, January 7th**.

Sincerely,

-Daniel Mosier

Daniel Mosier
Editorial Assistant

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