Date: Jan 04, 2019
To: "Elizabeth E. Krans" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-2311

RE: Manuscript Number ONG-18-2311

Medication-assisted treatment utilization among pregnant women with opioid use disorder in Pennsylvania Medicaid, 2009-2015

Dear Dr. Krans:

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 Jan 24, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: The authors are to be congratulated for conducting this study of medication-assisted treatment in pregnant women with an opioid use disorder in Pennsylvania. The authors document the use of opioid treatment and counseling over a time period from 2009-2015. The paper is clear and well written.

Specific comments are as follows:

1. The abstract is concise

2. The authors introduce importance of the topic and rationale for MAT. The data are intended to show opportunities for expansion of treatment throughout Pennsylvania.

3. The methods are fairly clear and complete. Could the authors please state how they can assure that the patients studied did not have a past history of opioid use that is no longer under treatment? There are other codes in addition to the 304 series that could have been used. This could explain partially the underutilization of services including counseling.

4. The presentation of the results is clear emphasizing the overall increase in pharmacotherapy and the increased utilization of buprenorphine with decreased of methadone. I was surprised that there were no significant differences in the behavioral therapy visits. Would the authors offer an interpretation?

5. The discussion is appropriate for the results and includes the importance of increased utilization of buprenorphine in urban areas. The authors also highlight challenges in the care of teen and minorities.

Reviewer #2: This is a rerospective cohort study of Pennsylvania medicaid administrative data from 2009-2015 with the objective of determining temporal trends in medication-assisted treatment utilization among pregnant women with opiod use disorder. Authors do provide 3 specific areas of evaluation for this objective. A limitation of this study is authors relied on diagnostic codes for data and it is possible data was missing from this data base. Authors do meet their objectives. Study would be stronger if it provided correlation with availability of services to these individuals and regions and other contributing factors to results. Limitations acknowledged by authors are significant.

1. Line 52-53 - objective as stated in abstract is vague

2. Line 75-76 - please quantify "quadrupled"

3. Line 79 - please state which government agencies and professional organizations besides ACOG

4. Line 86-88 - what % of pregnant women with substance abuse disorder get admited to treatment facilities?

5. Line 90-94 - references here please

6. Line 128-134 - Please clarify this section. Does data base confirm the pregnancies included were all term births (authors assuming 280 days prior date of conception)? Why were preterm births excluded or are authors assuming live births were all term in data base?

7. Line 142-147 - were these co-morbidities the only ones identified in the data base or were other co-morbidities not included in study?

8. Line 157-159 - why wasn't a category for both methadone and buprenorphine created?

9. Line 207-210 - please clarify this sentence as the % do not add up to 100% and it is confusing as written

10. Line 257-258 - how do these findings correlate with access to MAT and behavioral health counseling services for pregnant women (availability of counselors, MAT services, transportation, child care and other social factors limiting patient's ability to access, especially in rural areas)?

11. Line 275 - please describe superior neonatal outcomes here

12. Line 281-282 - please describe these additional barriers

13. Line 282 -284 - is this true in all states? Pregnant women in Pennsylvania are considered capable of making their own medical decisions, so why would they not have access to MAT? please explain.

14. Line 290-301 - is this cultural, lack of access to services, or what other factors contribute to the racial-ethinic disparities?

15. Line 304-308 - is this in PA or the entire country? Please specify.

16. Line 308-310 - what are the statistics for availability of providers in rural PA? How does that correlate with study findings for MAT and behavioral health counseling in those areas?

17. Line 326-331- do other states' medicaid programs provide the full range of services for treatment that PA does? If not, then these results would not be generalizable to those states.

Reviewer #3: This is a retrospective cohort study using the Medicaid database in Pennsylvania. It is a well modeled study that provides valuable information about trends in medication assisted treatment (MAT) throughout the state. It is likely to be reflective of trends throughout the country. Outcome data is mostly maternal. It would have been interesting to see neonatal abstinence syndrome data which should have been available in the database, as well.

The authors appear to avoid speculation and the table and graphs support the manuscript. The references appear pertinent, but number 6 appears somewhat outdated. The observation that around 40% of counties in the United States do not have a substance abuse provider is of great concern and may account for many of the observations in this manuscript. Serving this population can be demanding and not particularly gratifying for the healthcare provider.

STATISTICAL EDITOR'S COMMENTS:

1. General and Fig 1: The years in this report (2009-2015) span the passage of the Affordable Care Act and presumably, an effect on Medicaid eligibility/coverage in Pennsylvania. To what extent is the decrease in "no pharmacotherapy" and the increase in buprenorphine or methadone a result of greater availability of care? And to what extent are the geographic changes a reflection of changes in availability?

2. Table 1: Need to clarify the format x(y) in the Table. Mostly, it appears to be n(%), but the first row is apparently mean(SD) for age.

3. Figs 1, 2: Need to define the error bars. Do they represent SD, CIs? Should include as a footnote to figures or in the legends that the prevalences are adjusted and refer to methods section for list of all variables included in the the multivariable model.

4. Should include as supplemental material the crude Prevalences, then the multivariable adjusted prevalences.

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. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

Any author agreement forms previously submitted will be superseded by the eCTA. During the resubmission process, you are welcome to remove these PDFs from EM. However, if you prefer, we can remove them for you after submission.

3. 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.

4. 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), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). 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, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

5. 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 has adopted the use of the reVITALize definitions. Please access the obstetric and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

6. 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 26 typed, double-spaced pages (6,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

7. Titles in Obstetrics & Gynecology are limited to 100 characters (including spaces). Do not structure the title as a declarative statement or a question. Introductory phrases such as "A study of..." or "Comprehensive investigations into..." or "A discussion of..." should be avoided in titles. Abbreviations, jargon, trade names, formulas, and obsolete terminology also should not be used in the title. Titles should include "A Randomized Controlled Trial," "A Meta-Analysis," or "A Systematic Review," as appropriate, in a subtitle. Otherwise, do not specify the type of manuscript in the title.

8. Specific rules govern the use of acknowledgments in the journal. Please note 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 response in the journal's electronic author 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).

9. 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.

10. 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.

11. 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.

12. 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.

13. The American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG 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 (exceptions could include manuscripts that address items of historical interest). 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 an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found via the Clinical Guidance & Publications page at https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance.

14. The Journal's Production Editor had the following to say about the figures in your manuscript:

"Figures 1–2: Please upload high resolution versions (eps, tiff, jpeg). Items pasted into Word often do not reproduce well. Figure 3: Please upload high resolution versions (eps, tiff, jpeg). Items pasted into Word often do not reproduce well. Additionally, the journal aims to avoid the use of patterns, so please replace the patterns with a solid color. Finally, please include the percentages below the figures. These will be added back per journal style."

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

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If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

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promptly.

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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 and that each author has given approval to the final form of the revision.

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 Jan 24, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2017 IMPACT FACTOR: 4.982
2017 IMPACT FACTOR RANKING: 5th out of 82 ob/gyn journals

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University of Pittsburgh

SCHOOL OF MEDICINE
Department of Obstetrics, Gynecology and Reproductive Sciences

January 29th, 2019

Obstetrics & Gynecology
409 12th Street, SW
Washington, DC 20024-2188

RE: Manuscript Number ONG-18-2311

Dear Editors,

Enclosed please find our revised original research manuscript for consideration for publication in *Obstetrics & Gynecology* entitled: "**Medication-assisted treatment utilization among pregnant women with opioid use disorder."** The authors thank the reviewers for their thoughtful comments and suggestions following the review of this manuscript. We have included detailed response to each of the reviewer's comments below. Page and line numbers for reviewer reference refer to the clean copy of the revision.

As the lead author, 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. All authors have made a substantial contribution to this work and have met criteria for authorship. This study was approved by the University of Pittsburgh Institutional Review Board (PRO16120171). Neither the manuscript nor the data it contains have been previously published and are not currently under consideration for publication elsewhere.

Disclosures: Research reported in this publication was supported by the National Institute on Drug Abuse under Award Number K23DA038789 (Krans) and R01DA045675 (Krans and Jarlenski). This research was also supported by an inter-governmental agreement between the University of Pittsburgh and the Pennsylvania Department of Human Services.

Other disclosures: Elizabeth E. Krans is an investigator on grants to Magee-Womens Research Institute from the National Institutes of Health, Gilead and Merck outside of the submitted work. The other authors did not report any potential conflicts of interest. Thank you for your consideration of our manuscript.

Sincerely,

Elizabeth E. Krans, MD, MSc

[redacted]

REVIEWER COMMENTS:

REVIEWER #1: The authors are to be congratulated for conducting this study of medication-assisted treatment in pregnant women with an opioid use disorder in Pennsylvania. The authors document the use of opioid treatment and counseling over a time period from 2009-2015. The paper is clear and well written. Specific comments are as follows:

Comment 1: The abstract is concise.

Response to Comment 1: Thank you.

Comment 2: The authors introduce importance of the topic and rationale for MAT. The data are intended to show opportunities for expansion of treatment throughout Pennsylvania.

Response to Comment 2: Thank you.

Comment 3: The methods are fairly clear and complete. Could the authors please state how they can assure that the patients studied did not have a past history of opioid use that is no longer under treatment? There are other codes in addition to the 304 series that could have been used. This could explain partially the underutilization of services including counseling.

Response to Comment 3: Thank you for this important question. Our cohort was created using the complete set of codes in the 304 series which includes codes for "opioid type dependence." However, while we also included codes from the 305 series for "opioid abuse," we did not include the code 305.53 "opioid abuse, in remission" to account for the concern the reviewer raised that some pregnant women may be in remission and no longer require MAT. We have revised the list of codes we used to reflect our exclusion of women with a diagnosis of 305.53.

We identified Medicaid-enrolled women ages 15-44 years who had a live birth from January 1, 2009-September 30, 2015 and who had an International Classification of Diseases, Ninth Revision (ICD-9) diagnosis of OUD (304.0X, 304.7X, 305.50, 305.51, 305.52) during their pregnancy. (Page 7, Lines 125-128)

Comment 4: The presentation of the results is clear emphasizing the overall increase in pharmacotherapy and the increased utilization of buprenorphine with decreased of methadone. I was surprised that there were no significant differences in the behavioral therapy visits. Would the authors offer an interpretation?

Response to Comment 4: Thank you for this question. We have clarified this in the Results section of the manuscript. We did not find a significant difference over time in the number of visits among women who used methadone, buprenorphine or who had no pharmacotherapy. However, in the last 2 years of our analysis, we did find a significant difference in the number of visits by opioid pharmacotherapy type. In 2014 and 2015, pregnant women who received methadone had significantly more visits compared to those who received buprenorphine and those with no pharmacotherapy. We have included the revised section of the manuscript below.

Between 2010 and 2015, an increase in the adjusted number of behavioral health visits occurred among women who received methadone during pregnancy, 5.7 (95% CI: 4.3-7.1) versus 6.4 (95% CI: 4.9-7.9) visits, although the increase was not statistically significant. There were no significant changes over time in the adjusted number of behavioral health visits during

pregnancy among women using buprenorphine (3.1 versus 3.4 visits) and among women with no observed opioid pharmacotherapy use (3.6 versus 4.0 visits). However, we did find significant variability in the number of counseling visits during pregnancy by opioid pharmacotherapy type. In 2014 and 2015, pregnant women who received methadone had significantly more counseling visits compared to women who received buprenorphine and women who did not receive pharmacotherapy. (Page 12, Lines 238-247)

Comment 5: The discussion is appropriate for the results and includes the importance of increased utilization of buprenorphine in urban areas. The authors also highlight challenges in the care of teen and minorities.

Response to Comment 5: Thank you.

REVIEWER #2:

Comment 1: This is a retrospective cohort study of Pennsylvania Medicaid administrative data from 2009-2015 with the objective of determining temporal trends in medication-assisted treatment utilization among pregnant women with opioid use disorder. Authors do provide 3 specific areas of evaluation for this objective. A limitation of this study is authors relied on diagnostic codes for data and it is possible data was missing from this data base. Authors do meet their objectives. Study would be stronger if it provided correlation with availability of services to these individuals and regions and other contributing factors to results. Limitations acknowledged by authors are significant.

Comment 1: Line 52-53 - objective as stated in abstract is vague.

Response to Comment 1: Thank you for this comment. We revised our objective to be more specific.

To determine temporal trends in medication-assisted treatment (MAT) utilization among pregnant women with opioid use disorder. (Page 4, Lines 51-52)

Comment 3: Line 75-76 - please quantify "quadrupled"

Response to Comment 3: Thank you for this clarification. We have revised this sentence to quantify quadrupled.

Over the past 15 years, the prevalence of opioid use disorder among pregnant women has increased 333%, from 1.5 to 6.5 per 1,000 hospital births per year, resulting in increased treatment needs during pregnancy (Page 5, Lines 74-76).

Comment 4: Line 79 - please state which government agencies and professional organizations besides ACOG

Response to Comment 4: Thank you for this clarification. We have added the referenced professional organizations and government agencies.

A consensus of government agencies and professional organizations, including the American College of Obstetrics and Gynecology (ACOG), the American Society of Addiction Medicine and the Substance Abuse and Mental Health Services Administration (SAMHSA), endorse the

effectiveness of MAT for pregnant women, which improves maternal health outcomes by providing a stable opioid dosing regimen, reducing illicit drug use, and decreasing behaviors that increase the risk for HIV and HCV infection (Page 5, Lines 78-84).

Comment 5: Line 86-88 - what % of pregnant women with substance abuse disorder get admitted to treatment facilities?

Response to Comment 5: Thank you for this important question. The current data available for pregnant women receiving substance use treatment is derived from publicly available datasets like the Evaluations of the Treatment Episodes Data Set (TEDS). The TEDS sample is composed of pregnant women who have already made contact with the treatment system and not the total number of pregnant women with a substance use disorder in the general population. After a review of the available literature, we were unable to find any information regarding number of pregnant women with a substance use disorder in the general population who were admitted to treatment facilities. Thus, this remains an important research question for future research.

Comment 6: Line 90-94 - references here please.

Response to Comment 6: Thank you. We have added the appropriate references to this sentence.

While previous research highlights significant unmet treatment need, prior analyses are limited to publicly funded treatment programs, have not investigated differences in opioid pharmacotherapy type (methadone versus buprenorphine), and have not evaluated the utilization of behavioral health counseling, an important component of comprehensive substance use treatment.[7,8] (Pages 5-6, Lines 91-95)

Comment 7: Line 128-134 - Please clarify this section. Does data base confirm the pregnancies included were all term births (authors assuming 280 days prior date of conception)? Why were preterm births excluded or are authors assuming live births were all term in data base?

Response to Comment 7: Thank you for this question. Preterm births were not excluded from our analysis. Live births were identified using the date of delivery and a look-back period from the date of delivery to quantify the pregnancy period using an algorithm validated by the National Committee for Quality Assurance.[16] Using this method, we calculated 280 days prior to the date of delivery to approximate the date of conception. If a birth was preterm, this approach would have included a small preconception period for some women in our analysis. Our approach is the most common, validated approach used in the analysis of large administrative datasets. We have revised the language in our methods section to more clearly describe this process.

Live births were identified using the date of delivery in inpatient data. The pregnancy period was approximated using an algorithm validated by the National Committee for Quality Assurance.[16] Using this method, we calculated 280 days prior to the date of delivery to approximate the date of conception. Because we focused on pregnancies that resulted in a preterm or term live birth, if a woman had an interpregnancy interval of less than 24 weeks (<168 days), the later pregnancy was excluded from the analysis. (Page 7, Lines 130-135)

Comment 8: Line 142-147 - were these co-morbidities the only ones identified in the data base or were other co-morbidities not included in study?

[redacted]

Response to Comment 8: Thank you for this question. Our dataset includes a census of hospital, pharmaceutical, and provider data for all individuals enrolled in Pennsylvania Medicaid and includes both physical health and behavioral health diagnoses. Therefore, due to the large number of co-morbidities available for study, we selected a subset of co-morbidities that are commonly associated with substance use (i.e. hepatitis C virus, HIV, psychiatric disorder, alcohol, tobacco, polysubstance use), high prevalence co-morbidities commonly evaluated in pregnant women (i.e. asthma, chronic hypertension, thyroid disorder, diabetes) and commonly evaluated pregnancy-associated co-morbidities (i.e. gestational hypertensive disorders, gestational diabetes mellitus).

Comment 9: Line 157-159 - why wasn't a category for both methadone and buprenorphine created?

Response to Comment 9: Thank you for this question. We observed claims for both methadone and buprenorphine in only a very small proportion of pregnancies (n=365, 2.9%). Due to the significant discrepancy in sample sizes between a combined category and our buprenorphine and methadone groups, we categorized these pregnancies in the any buprenorphine group. We chose to create an "any buprenorphine" and a "methadone only" group because pregnant women using buprenorphine are clinically more likely to switch to methadone than the likelihood of women who use methadone switching to buprenorphine. We have revised our methods section to describe this rationale.

We created 3 mutually exclusive opioid pharmacotherapy utilization groups: methadone only, any buprenorphine, and no pharmacotherapy observed. In a small number of pregnancies (n=365, 2.9%) we observed claims for both buprenorphine and methadone. Because of the extremely small sample size of the combined group, we categorized these pregnancies in the "any buprenorphine group." We chose to create an "any buprenorphine" and a "methadone only" group because women are clinically more likely to switch from buprenorphine to methadone than methadone to buprenorphine during pregnancy. (Page 8, Lines 157-163)

Comment 10: Line 207-210 - please clarify this sentence as the % do not add up to 100% and it is confusing as written.

Response to Comment 10: Thank you for this observation. The revised the numbers now add up to 100%.

The majority of behavioral health claims (59.8%) were associated with drug and alcohol diagnoses with the remaining claims associated with psychiatric disorder diagnoses (7.9%), both drug and alcohol and psychiatric disorder diagnoses (13.2%), and a mix of other pregnancy-related diagnoses codes (19.2%). (Page 11, Lines 210-213)

Comment 11: Line 257-258 - how do these findings correlate with access to MAT and behavioral health counseling services for pregnant women (availability of counselors, MAT services, transportation, child care and other social factors limiting patient's ability to access, especially in rural areas)?

Response to Comment 11: Thank you for this important question. The objective of our current analysis was to first describe temporal trends in MAT use which has not been done at the population-level. We agree with the reviewer that the next critical step is to begin the process of

identifying factors that correlate with disparities in MAT use. To begin this process for this analysis, we evaluated the important correlation between geographic region (rural vs. urban) MAT use patterns. Future research efforts are necessary to individual (i.e. child care, transportation) and system-level factors (availability of counselors) that could be contributing to the rural vs. urban disparities we found but were outside of the scope of our current analysis.

Comment 12: Line 275 - please describe superior neonatal outcomes here.

Response to Comment 12: Thank you for this clarification. We have now described the specific neonatal outcomes.

Further, randomized clinical trials have established buprenorphine's safety in pregnancy and demonstrated superior neonatal outcomes including a shorter treatment duration for NAS and a shorter neonatal length of stay compared to methadone.[22-24] *(Page 14, Lines 282-285)*

Comment 13: Line 281-282 - please describe these additional barriers.

Response to Comment 13: Thank you for this clarification. The additional barriers mentioned for adolescents are described in the subsequent sentences and include age restrictions and the need for parental consent.

In the United States, buprenorphine/naltrexone is only approved for persons age 16 years or older, while persons younger than 18 years must fail two attempts at detoxification and provide a written consent from a parent prior to the initiation of methadone.[24] *(Page 14, Lines 291-293)*

Comment 14: Line 282 -284 - is this true in all states? Pregnant women in Pennsylvania are considered capable of making their own medical decisions, so why would they not have access to MAT? please explain.

Response to Comment 14: Thank you for this question. All 50 states have statutes that allow for the emancipation of minors due to pregnancy and specify that pregnant adolescents can make their own decisions *regarding their pregnancy* including decisions about prenatal care. However, there is no formal guidance about whether or not this emancipation applies to MAT. We could not find any other published data regarding MAT use among pregnant adolescents or provider-willingness to provide MAT services to pregnant adolescents. Because the use of MAT among non-pregnant adolescents is a developing area of clinical practice and emerging area of research, many providers may be resistant to providing MAT services to adolescents even during pregnancy. We have added the following sentence to our discussion section to address this important issue.

While pregnant adolescents are emancipated to make their own decisions regarding their pregnancy, many providers may not extend this autonomy to MAT and provider willingness to provide MAT services to pregnant adolescents remains largely unknown. (Page 14, Lines 294-296)

Comment 15: Line 290-301 - is this cultural, lack of access to services, or what other factors contribute to the racial-ethnic disparities?

Response to Comment 15: Thank you for this important question. We were interested to see possible racial-ethnic disparities in pharmacotherapy use in our analysis. Further evaluations are

warranted which utilize the Institute of Medicine definition of racial-ethnic disparities in health care that account for criminal history, socioeconomic status and other individual-level factors that may contribute to this finding. While a formal racial-ethnic disparities analysis was outside of the scope of our objective, we described the importance of future research efforts to explore this finding in our discussion.

Previous evaluations of racial and ethnic substance use treatment disparities in the adult, non-pregnant population have been mixed. In an analysis of the National Survey on Drug Use and Health, unadjusted differences in racial-ethnic substance use treatment receipt did not persist after adjustment for criminal history and socioeconomic factors.[29] Likewise, racial-ethnic disparities in treatment completion using the TEDS-D data set were also largely explained by differences in socioeconomic status.[30] Further evaluations are warranted to explain differential racial-ethnic opioid pharmacotherapy use rates among pregnant women.(Page 15, Lines 306-313)

Comment 16: Line 304-308 - is this in PA or the entire country? Please specify.

Response to Comment 16: Thank you for this question. NAS has disproportionately increased in rural geographic areas across the United States. We have revised this sentence accordingly.

Rural-urban disparities in pharmacotherapy use is of significant concern as the prevalence of maternal opioid use and neonatal abstinence syndrome (NAS) have disproportionately increased in rural geographic areas across the United States and over 80% of pregnant women living in rural areas experience barriers to substance use treatment services.[31,32] (Page 15, Lines 316-320)

Comment 17: Line 308-310 - what are the statistics for availability of providers in rural PA? How does that correlate with study findings for MAT and behavioral health counseling in those areas?

Response to Comment 17: Thank you for this important question. The Substance Abuse and Mental Health Services Administration (SAMHSA) keeps administrative data on substance use providers across the United States including Pennsylvania. However, to determine the specific influence of the geographic availability of Medicaid-billing providers in PA on MAT use, the SAMHSA provider file will need to be linked to our Medicaid provider files which was outside of the scope of our current analysis. However, this remains an important research question and we hope our analysis highlights the importance of evaluating this correlation in the future.

Comment 18: Line 326-331- do other states' Medicaid programs provide the full range of services for treatment that PA does? If not, then these results would not be generalizable to those states.

Response to Comment 18: Thank you for this important point. We have revised the limitations section to reflect the fact that our results would not be generalizable to states whose Medicaid programs do not provide the full range of services.

While Pennsylvania Medicaid provides reimbursement for all components of MAT including methadone, buprenorphine and behavioral health counseling, our results may not be generalizable to states whose Medicaid programs do not cover the full range of treatment

services. Methadone is not included on Medicaid preferred drug lists in 20 states while Medicaid covers buprenorphine in all 50 states.[42] *(Page 16-17, Lines 344-349)*

REVIEWER #3:

Comment 1: This is a retrospective cohort study using the Medicaid database in Pennsylvania. It is a well modeled study that provides valuable information about trends in medication assisted treatment (MAT) throughout the state. It is likely to be reflective of trends throughout the country. Outcome data is mostly maternal. It would have been interesting to see neonatal abstinence syndrome data which should have been available in the database, as well.

Response to Comment 1: Thank you for this important question regarding the relationship between trends in MAT use and neonatal abstinence syndrome. Unfortunately, Pennsylvania Medicaid has not yet linked maternal-infant dyad records, so we were unable to include neonatal outcome data in our analysis.

Comment 2: The authors appear to avoid speculation and the table and graphs support the manuscript. The references appear pertinent, but number 6 appears somewhat outdated. The observation that around 40% of counties in the United States do not have a substance abuse provider is of great concern and may account for many of the observations in this manuscript. Serving this population can be demanding and not particularly gratifying for the healthcare provider.

Response to Comment 2: Thank you for this comment. Reference 6 was one of the original references to identify fetal stress associated with withdrawal. However, reference 7 is a more updated evaluation of fetal stress associated with withdrawal and is from 2017. Therefore, reference 6 was removed and reference 7 was retained.

STATISTICAL EDITOR'S COMMENTS:

Comment 1: General and Fig 1: The years in this report (2009-2015) span the passage of the Affordable Care Act and presumably, an effect on Medicaid eligibility/coverage in Pennsylvania. To what extent is the decrease in "no pharmacotherapy" and the increase in buprenorphine or methadone a result of greater availability of care? And to what extent are the geographic changes a reflection of changes in availability?

Response to Comment 1: Thank you for this important question. On January 1st, 2015, Pennsylvania expanded its Medicaid coverage under the ACA to all *non-pregnant* persons with household income up to 138% percent of the federal poverty level (FPL). Importantly, prior to the ACA, all states were already required to provide Medicaid coverage for pregnant women with incomes up to 133% of the FPL. Thus, the impact of the ACA on pregnant women was to extend their ability to receive Medicaid services before and after (> 60 days postpartum) pregnancy. Thus, Medicaid expansion in Pennsylvania did not have a significant impact on the availability of MAT during pregnancy.

Comment 2: Table 1: Need to clarify the format x(y) in the Table. Mostly, it appears to be n (%), but the first row is apparently mean (SD) for age.

Response to Comment 2: Thank you for this correction. The first row is mean (SD) and this has been added to the table. We have also provided a footnote for Table 1 that states, "n (%) unless otherwise specified."

Comment 3: Figs 1, 2: Need to define the error bars. Do they represent SD, CIs? Should include as a footnote to figures or in the legends that the prevalences are adjusted and refer to methods section for list of all variables included in the multivariable model.

Response to Comment 3: Thank you for this clarification. A footnote has been added to the figure legends.

Figure 1*. Opioid pharmacotherapy utilization among Medicaid-enrolled pregnant women with opioid use disorder, 2009-2015*

Footnote for Figure 1 *- Error bars represent 95% confidence intervals; prevalences are adjusted; refer to the methods section for the list of all variables included in the multivariable model and Supplemental Table A for crude and adjusted prevalences*

Figure 2*. Behavioral health counseling utilization by opioid pharmacotherapy type among Medicaid-enrolled pregnant women with opioid use disorder, 2009-2015*

Footnote for Figure 2 *- Error bars represent 95% confidence intervals; predicted number of visit counts are adjusted; refer to the methods section for the list of all variables included in the multivariable model and Supplemental Table B for crude and adjusted counts (Page 24, Lines 500-509)*

Comment 4: Should include as supplemental material the crude prevalences, then the multivariable adjusted prevalences.

Response to Comment 4: Thank you. The crude and adjusted prevalences of Figures 1 and 2 with associated confidence intervals have been included as Supplemental Tables A and B.

Crude and adjusted prevalences and counts for Figures 1 and 2 are described in Supplemental Tables A and B. (Page 12, Lines 247-248)

EDITORIAL OFFICE COMMENTS:

Comment 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:

Response to Comment 1: OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.

Comment 2: As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author

agreement forms. When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

Any author agreement forms previously submitted will be superseded by the eCTA. During the resubmission process, you are welcome to remove these PDFs from EM. However, if you prefer, we can remove them for you after submission.

Response to Comment 2: Thank you.

Comment 3: 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.

Response to Comment 3: Thank you. This statement is now included in our cover letter.

Comment 4: 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), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). 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, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

Response to Comment 4: Thank you. We have uploaded the STROBE checklist for observational studies.

Comment 5: 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 has adopted the use of the reVITALize definitions. Please access the obstetric and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-

Safety-and-Quality-Improvement/reVITALize. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

Response to Comment 5: Thank you. Our manuscript is complaint with reVITALize definitions.

= Comment 6: 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 26 typed, double-spaced pages (6,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

Response to Comment 6: Thank you, our revised manuscript does not exceed 26 typed, double-spaced pages.

Comment 7: Titles in Obstetrics & Gynecology are limited to 100 characters (including spaces). Do not structure the title as a declarative statement or a question. Introductory phrases such as "A study of..." or "Comprehensive investigations into..." or "A discussion of..." should be avoided in titles. Abbreviations, jargon, trade names, formulas, and obsolete terminology also should not be used in the title. Titles should include "A Randomized Controlled Trial," "A Meta-Analysis," or "A Systematic Review," as appropriate, in a subtitle. Otherwise, do not specify the type of manuscript in the title.

Response to Comment 7: Thank you. Our title character count is now compliant with journal guidelines.

Comment 8: Specific rules govern the use of acknowledgments in the journal. Please note 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 response in the journal's electronic author 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).

Response to Comment 8: Thank you. Funding and financial support have been noted.

Comment 9: 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.

Response to Comment 9: Thank you. The abstract is 249 words.

Comment 10: 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.

Response to Comment 10: Only standard abbreviations and acronyms have been used.

Comment 11: 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.

Response to Comment 11: The virgule symbol (/) in sentences with words has been removed.

Comment 12: 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.

Response to Comment 12: Table 1 now conforms to journal style.

Comment 13: The American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG 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 (exceptions could include manuscripts that address items of historical interest). 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 an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found via the Clinical Guidance & Publications page at https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance.

Response to Comment 13: ACOG documents cited in our manuscript are still current and available.

The Journal's Production Editor had the following to say about the figures in your manuscript:

PRODUCTION EDITOR COMMENTS:

Comment 1: "Figures 1–2: Please upload high resolution versions (eps, tiff, jpeg). Items pasted into Word often do not reproduce well.

Response to Comment 1: Figures 1-2 have been uploaded as high-resolution tiff images.

[redacted]

Comment 2: Figure 3: Please upload high resolution versions (eps, tiff, jpeg). Items pasted into Word often do not reproduce well. Additionally, the journal aims to avoid the use of patterns, so please replace the patterns with a solid color. Finally, please include the percentages below the figures. These will be added back per journal style."

Response to Comment 2: Figure 3A-C have been uploaded as high-resolution tiff images. We have also replaced patterns with a solid color. As each of the images are meant to all be part of a Figure 3, we have labeled them Figures 3A-C.

[redacted]

Daniel Mosier

From: Krans, Elizabeth [redacted]
Sent: Monday, February 4, 2019 3:01 PM
To: Daniel Mosier
Subject: RE: Manuscript Revisions: ONG-18-2311
Attachments: 18-2311R1 ms (2-1-19v2) (002) - EEK comments.docx; Krans_Appendixes - EEK comments.docx

Hi Daniel,

I have attached comments to the manuscript version that you send via track changes and via comments (see attached ☺).

I also have my responses to your specific questions below:

1. Please note the minor edits and deletions throughout. Please let us know if you disagree with any of these changes.
   Thanks! I have responded in the manuscript.

2. LINE 36: Drs. Kim and Kelley will need to complete our electronic Copyright Transfer Agreement, which was sent to them through Editorial Manager.
   We emailed them to complete this on Friday, 2/1. Please let me know if you still have not heard from them yet.

3. LINE 65: Please round one of these percentages so that they total 100%
   I rounded the methadone percentage from 28.7% to 28.8% so that they now total 100%. **I have also made this change to Table 1.**

4. LINE 70: Please quantitate in some way
   This has now been quantified.

5. LINE 71: Please be sure these data stated in the body of your paper, tables, or figures. Statements and data that appear in the Abstract must also appear in the body text for consistency.
   We added this sentence to the body of the manuscript.

6. LINE 77: Please shorten this introduction by 1/3
   I have attempted to do this! ☺

7. LINE 233: Please review the Appendixes PDF file we created and let us know if you would like to make any edits.
   I have attached the Appendices and made a few edits in the document.

8. Please review the order of your references and citations to those references to ensure that they are accurately numbered (based on their order of appearance within the manuscript text).

   These have been reviewed and are correct.

Please let me know if you have any questions or need anything else!

Liz Krans

From: Daniel Mosier <dmosier@greenjournal.org>
Sent: Friday, February 01, 2019 10:27 AM
To: Krans, Elizabeth [redacted]
Subject: Manuscript Revisions: ONG-18-2311

Dear Dr. Krans,

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.
2. LINE 36: Drs. Kim and Kelley will need to complete our electronic Copyright Transfer Agreement, which was sent to them through Editorial Manager.
3. LINE 65: Please round one of these percentages so that they total 100%
4. LINE 70: Please quantitate in some way
5. LINE 71: Please be sure these data stated in the body of your paper, tables, or figures. Statements and data that appear in the Abstract must also appear in the body text for consistency.
6. LINE 77: Please shorten this introduction by 1/3
7. LINE 233: Please review the Appendixes PDF file we created and let us know if you would like to make any edits.
8. Please review the order of your references and citations to those references to ensure that they are accurately numbered (based on their order of appearance within the manuscript text).

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 **Tuesday, February 5th**.

Daniel Mosier
Editorial Assistant
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From: [redacted]
To: Stephanie Casway
Cc: Daniel Mosier
Subject: RE: O&G Figure Revision: 18-2311
Date: Thursday, January 31, 2019 2:31:24 PM

Thanks Stephanie,

For Figure 3A-C (the one with the 3 maps), the regions #'s are correct, but they are not in numeric order – do you think we could list them in numeric order – i.e. Region 1, 2, 3, 4, 5 – for all 3 maps?

Let me know if that doesn't make sense – thanks!

Liz Krans

From: Stephanie Casway <SCasway@greenjournal.org>
Sent: Thursday, January 31, 2019 8:12 AM
To: Krans, Elizabeth [redacted]
Cc: Daniel Mosier <dmosier@greenjournal.org>
Subject: O&G Figure Revision: 18-2311

Good Morning Dr. Krans,

Your figures and legend have been edited, and PDFs of the figures and legend are attached for your review. Please review the figures CAREFULLY for any mistakes.

PLEASE NOTE: Any changes to the figures must be made now. Changes at later stages are expensive and time-consuming and may result in the delay of your article's publication.

To avoid a delay, I would be grateful to receive a reply no later than Friday, 2/1. Thank you for your help.

Note that I will be leaving for maternity leave tomorrow, so please copy Daniel Mosier on your reply.

Best wishes,

Stephanie Casway, MA
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