

NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

- 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*

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.

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

Date: Jan 24, 2019

To: "Maureen S. Hamel"

From: "The Green Journal" em@greenjournal.org

Subject: Your Submission ONG-19-22

RE: Manuscript Number ONG-19-22

Randomized controlled trial of intrapartum glucose management in women with gestational diabetes

Dear Dr. Hamel:

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 Feb 14, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: The authors present a paper that will be of significant interest to generalists, laborists and maternal fetal medicine specialists. Many institutions utilize the same protocol for all pregnant diabetics and being able to offer more customized treatment that is both patient centered and cost effective is a step forward. I would ask the authors to consider the following:

- 1. The more liberalized protocol has instructions that that ask use of insulin to be considered. In point of fact, was insulin given the majority of the time? What were the factors individual practitioners did or did not give medication? Did the use or nonuse of medication affect the outcomes? Without clear guidelines, I am of concern that the standardization being desired will not occur.
- 2. Approximately half the patients in each arm were treated with diet alone versus medication. Were there any differences noted between these groups or was the sample size too small to detect any differences?
- 3. Is any information about HGA1C levels available to correlate the outcomes?
- 4. Would urge the authors to continue to follow the children to see if any long term issues are uncovered such as increased rates of diabetes or obesity.

Reviewer #2:

The authors report on a randomized study in which they compared more frequent vs. less frequent monitoring of BG during labor in women with GDM.

The study is well designed and outlined and the results are presented clearly and concisely.

The finding of lack of a difference in clinical outcome in the tight vs. more liberal study arms is of clinical significance.

Reviewer #3: The purpose of this manuscript was to "to compare the effect of two protocols (loose compared to a tight

control) for intrapartum glucose management among women with GDM on neonatal blood glucose concentrations shortly following birth." This was a prospective, randomized trial.

- 1. The authors note that "all neonates of mothers diagnosed with diabetes (including GDM) receive point of care glucose testing." Which Point of Care (POC) device is used to measure glucose at your institution? Was venous, arterial or capillary blood used to perform the neonatal POC glucose test? What is the reliability and precision of their POC testing, especially at lower levels of glucose (<40 mg/dL)? How reliable is their POC glucose testing at neonatal hematocrit levels? How often and what type of quality control/proficiency testing do they perform for their POC glucose monitoring?
- 2. How were the maternal, intrapartum glucose checks performed? Was the glucose measured by a POC device or sent to a central clinical laboratory? Was capillary, venous, or arterial blood used to measure glucose? What was the reliability and precision of the device they used to measure intrapartum glucose levels?
- 3. The authors note that "Data were abstracted from the medical record of all study participants and neonates during the hospitalization and up to 16 weeks postpartum." Who extracted the data from the records? Was the data recorded on a piloted data sheet and transferred to an electronic database? What was done to ensure accuracy of data recording and transfer? What was done if there was missing or incomplete data?
- 4. Line 134: What is "LDR nursing"? Please spell out.
- 5. How did the authors know that none of the subjects diagnosed with gestational diabetes, had pre-gestational diabetes or glucose intolerance? Had they all had pre-gestational testing to rule out glucose intolerance or diabetes?
- 6. Please carefully review references and make sure they all concur with Instructions for Authors for the Green Journal, esp et al.
- 7. In Table 1, row 8 "medical management of GDM". Would the authors consider putting a line right above medical management saying diet management and the 'n'(%)'?
- 8. In Table 2. Did any individuals have to receive 'juice' for hypoglycemia either in the tight or liberalized control group?
- 9. In Figure 1: What is "initiating insulin GTT"? Glucose tolerance test? Insulin drip?
- 10. In the tight control group 12 subjects and in the liberalized control group only 1 subject required intrapartum insulin administration due to hyperglycemia. Of those in both groups who required intrapartum insulin how many were treated for their GDM with insulin or with insulin and metformin? Did any of the subects whose GDM was controlled by diet and exercise alone, require intrapartum insulin in either the tight or liberalized control groups? The authors note that "for women with GDM, our study found no benefit to tight control of glucose in labor and instead supports glucose assessment every 4 hours with intervention only if maternal glucose concentration is <60 or > 120mg/dl." Could this be liberalized even more if the GDM was controlled antepartum by diet and exercise, without the need for insulin?

Reviewer #4: The is an randomized control trial. This article may be cited by meta analysis going forward but does not seem large enough or of a primary outcome sufficient to be frequently cited alone as the primary outcome of this study was the first neonatal blood glucose concentration rather than the more specifically clinically useful outcome of stating the overall number/percentage by treatment group of the number of neonates who experienced hypoglycemia. Possibly this was because a higher number of study participants might have been needed to power such a primary outcome.

This article is correct in stating there are no studies isolated to the outcome of comparing tight control and "less tight" control of glucose in the intrapartum for GDM only patients. However, in review of literature, one can extrapolate that "less tight control" of glucose in the intrapartum is an acceptable treatment for GDM patients based on past studies. From abstract of a cited source on this article (7), there have been recommendations for target intrapartum glucose goals based on pre-gestational diabetes that extend to GDM: "From this review it appears that the maternal glucose should be maintained between 4.0 and 6.0-7.0 mmol/L during labor. Most women with gestational diabetes, especially if they require <1.0 units/kg/d of insulin, can simply be monitored without intravenous insulin." When converted from mmol/L to mg/dL, the range of 4 to 6-7 mmol/L is 72 to 106/126 mg/dL. This study being reviewed confirms the recommendation of the already published review of 19 papers looking at the relationship between intrapartum glucose and effects of neonatal hypoglycemia, and it noted there were 6 studies looking at intrapartum glucose and neonatal hypoglycemia in GDM patients with 3 of 6 of the studies not showing inverse relationship between the two. This seems to go along with the findings of this study being reviewed for publication now, that the range of liberalized control (60-120 mg/dL) is a viable option for intrapartum GDM patients.

Source 8 cited in this study cites a paucity of data in support of tight glycemic control for type 1 and type 2 pregestational diabetes patients which would seem to be extendable to GDM patients based on the study from the cited reference 7 for this study. Additionally, there have been studies such as the study titled Hypoglycemia rates in the first days of life among

term infants born to diabetic mothers by Maayan-Metzget, Lubin, and Kuint in Neonataology in 2009 which looked at pregestational DM and GDM patients and correlated higher risk for hypoglycemia in the neonate to large for gestational age babies and those born to mothers with juvenile onset diabetes. This speaks more to the relationship to longer standing poor or difficult glucose control issues rather than needing tight control in the intrapartum. With respects to this study being reviewed for publication, it would seem more helpful if the data of this study included in Table 1 the antepartum glucose control as poor/fair/good and the average insulin U/kg/day needed to control the patients glucose variation between the two groups.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

lines 181-188: Suggest including a summary of this as a Table.

Table 2 and lines 110-116: Were the frequency of blood glucose measurements for the two cohorts different intra partum and post partum? If so, should cite the number of measurements from which the maternal median plasma glucose or denominator for number of values exceeding upper protocol threshold. That is, the range would be affected by the number of measurements and the likelihood of finding a high value would be a function of how many measurements were taken. Also, were all measurements actually from plasma determinations in lab or were some done via glucometer?

Table 3: Need to clearly separate the primary from the secondary outcomes. Same issue re: number of measurements of glucose for the two cohorts and were all done in lab or some via glucometer?

EDITOR COMMENTS:

- 1. Thank you for your submission to Obstetrics & Gynecology. In addition to the comments from the reviewers above, you are being sent a notated PDF that contains the Editor's specific comments. Please review and consider the comments in this file prior to submitting your revised manuscript. These comments should be included in your point-by-point response cover letter.
- ***The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Randi Zung and she will send it by email rzung@greenjournal.org.***
- why would you schedule these before 36 weeks?
- are women allowed to eat in labor? What IV fluids are used? Do they need to be NPO when they begin induction?
- given concerns about relatively small numbers and potential inclusion in a meta analysis, are you not willing to provide independent patient data in the future for a potential IPD meta analysis? Fine if you are not, but just making sure you had considered this in your decision to not share data.
- When you write that a study occurred between date 1 and date 2, it literally excludes those boundary dates. For instance, "This study was performed between Feb 2018 and Jan 2019" would mean it was performed from March 2018 to Dec 2018. Do you instead mean that the study was performed from date 1 to date 2? If so, please edit.
- Could it be that when you check blood sugars more frequently, as you did with the tight group, that you identify swings in blood sugar that may not be seen if you just check q4 hours? Why did you not check both groups with the same frequency, but liberalize the upper bound for treating in the "loose "control group?
- should be noted as a QA issue for your unit, given this is supposed to occur in 100%
- please provide how many in each group fell below 40 mg/dL.
- The way you state this is a bit of a stretch. Yes, they were closer (53 v 58) but it was above the cut off. Above, I've asked for how many were below 40 in each group. Please provide that.
- Instead of saying "to our knowledge" please state, Based on a pubmed search....from inception..using the terms...... this is the first study of its kind"

- please provide antepartum treatment groups for the patients "Diet only, oral agent or insulin".
- 2. 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.
- 3. 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.

- 4. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Responses to the five bullet points should be provided in a box at the end of the Methods section.
- 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. Provide a short title of no more than 45 characters, including spaces, for use as a running foot.
- 10. 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.

- 11. Abstracts for all randomized, controlled trials should be structured according to the journal's standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf. Please edit your abstract as needed.
- 12. 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.
- 13. 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.
- 14. 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.
- 15. 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.
- 16. Figures 1 and 2 may be resubmitted as-is.
- 17. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at http://links.lww.com/LWW-ES/A48. The cost for publishing an article as open access can be found at http://edmgr.ovid.com/acd/accounts/ifauth.htm.

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

18. 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 Feb 14, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD Editor-in-Chief

2017 IMPACT FACTOR: 4.982

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

In compliance with data protection regulations, please contact the publication office if you would like to have your personal information removed from the database.

Maureen S. Hamel MD
Warren Alpert School of Medicine of Brown University
Women & Infants Hospital
Department of Obstetrics and Gynecology
2645 Railroad Street, Apt 118
Pittsburgh, PA 15222
Email: hamelms2001@gmail.com

Nancy C. Chescheir, MD Editor-in-Chief Obstetrics & Gynecology

Dr. Chescheir,

It is my pleasure to submit a revised version of our original research titled "Randomized controlled trial of intrapartum glucose management in women with gestational diabetes." All authors of the original manuscript have read and approved the revised version of the paper. On the following pages are our responses to the reviewers' comments.

I, Maureen S. Hamel, MD 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.

Thank you very much for your consideration,

Maureen S. Hamel, MD

REVIEWER COMMENTS:

Reviewer #1: The authors present a paper that will be of significant interest to generalists, laborists and maternal fetal medicine specialists. Many institutions utilize the same protocol for all pregnant diabetics and being able to offer more customized treatment that is both patient-centered and cost effective is a step forward. I would ask the authors to consider the following:

1. The more liberalized protocol has instructions that that ask use of insulin to be considered. In point of fact, was insulin given the majority of the time? What were the factors individual practitioners did or did not give medication? Did the use or nonuse of medication affect the outcomes? Without clear guidelines, I am of concern that the standardization being desired will not occur.

Although the liberalized protocol laminated reference card has instructions that read "consider," when the study was carried out and the protocol implemented, the word consider was disregarded and the patients treated according to the liberalized protocol parameter. Figure 1 has been revised to reflect this implementation. In total, 3 patients in the liberalized group had blood glucose values that exceeded the upper protocol threshold, 1 was treated with insulin, the other 2 were not treated. One patient was not treated for unclear reasons, the other delivered before insulin could be administered.

2. Approximately half the patients in each arm were treated with diet alone versus medication. Were there any differences noted between these groups or was the sample size too small to detect any differences?

One third of patients in each arm required treatment with diet alone and two thirds in each arm required medical management. We ran analysis comparing medically managed to diet managed patients and found no differences between these two groups however the study was not powered for this sub-analysis.

3. Is any information about HGA1C levels available to correlate the outcomes?

We have added information about hemoglobin A1c levels to the text of the results section (page 10 lines 193-196 track changes version). Unfortunately, only 40% of patients had hemoglobin A1c values drawn and these were done at the time of GDM diagnosis.

4. Would urge the authors to continue to follow the children to see if any long-term issues are uncovered such as increased rates of diabetes or obesity.

Thank you for this excellent suggestion.

Reviewer #2:

The authors report on a randomized study in which they compared more frequent vs. less frequent monitoring of BG during labor in women with GDM. The study is well designed and outlined; and the results are presented clearly and concisely. The finding of lack of a difference in clinical outcome in the tight vs. more liberal study arms is of clinical significance.

While we did not alter our manuscript based on the remarks of Reviewer #2, we very much appreciate the gracious comments and observations.

Reviewer #3: The purpose of this manuscript was to "to compare the effect of two protocols (loose compared to a tight control) for intrapartum glucose management among women with GDM on neonatal blood glucose concentrations shortly following birth." This was a prospective, randomized trial.

1. The authors note that "all neonates of mothers diagnosed with diabetes (including GDM) receive point of care glucose testing." Which Point of Care (POC) device is used to measure glucose at your institution? Was venous, arterial or capillary blood used to perform the neonatal POC glucose test? What is the reliability and precision of their POC testing, especially at lower levels of glucose (<40 mg/dL)? How reliable is their POC glucose testing at neonatal hematocrit levels? How often and what type of quality control/proficiency testing do they perform for their POC glucose monitoring?

The Nova Biomedical Stat Strip device is used for all point of care glucose measurements at the study institution. Capillary blood obtained via heel stick is used for the neonatal point of care glucose test. The range of detection for this device is 10-600 mg/dL. At a hematocrit of 60% (close to normal neonatal hematocrit), compared to the Yellow Springs Instrument (considered a gold-standard among capillary glucose testing) the coefficient of variation in measurement of the Nova Biomedical Stat Strip device ranges from 4.9 at 21 mg/dL to 2.9 at 537 mg/dL. The maximum coefficient of variation at this hematocrit is 4.5 at 131 mg/dL. Manufacturer specified quality control testing is performed daily and weekly for all devices.

While we have not included this information in the manuscript, if the Editor deems this important, we are happy to include it in the text. Alternatively, we could also include it as supplemental material or an appendix.

2. How were the maternal, intrapartum glucose checks performed? Was the glucose measured by a POC device or sent to a central clinical laboratory? Was capillary, venous, or arterial blood used to measure glucose? What was the reliability and precision of the device they used to measure intrapartum glucose levels?

Maternal intrapartum glucose testing was point of care capillary glucose testing via fingerstick using the Nova Biomedical Stat Strip device. At a hematocrit of 30%, compared to the Yellow Springs Instrument (considered a gold-standard among capillary glucose testing), the coefficient of variation in measurement of the Nova Biomedical Stat Strip device ranges 2.5 at 31 mg/dL to 2.8 at 522 mg/dL for a hematocrit of 30%. The maximum coefficient of variation at this hematocrit is 3.4 at 133 mg/dL.

While we have not included this information in the manuscript, if the Editor deems this important, we are happy to include it in the text. Alternatively, we could also include it as supplemental material or an appendix.

3. The authors note that "Data were abstracted from the medical record of all study participants and neonates during the hospitalization and up to 16 weeks postpartum." Who extracted the data from the records? Was the data recorded on a piloted data sheet and transferred to an electronic database? What was done to ensure accuracy of data recording and transfer? What was done if there was missing or incomplete data?

Data was abstracted from the medical record by the principal investigator, recorded on a piloted data sheet and then transferred to an electronic database. Once data was abstracted, a minimum of 1 week later, the medical record was once again accessed, and spot checks made on 10% of variables to ensure accuracy of data abstraction. Data was transferred to electronic database by the study research assistant. The investigator and assistant met at regular intervals to review missing data points/incomplete date. When appropriate, the medical record was accessed to determine whether data truly were missing/unknown. All variables in the database had a code for "missing/unknown." After all data transferred to the database, spot checks were made on 10% of charts to ensure accurate data transfer.

While we have not included this information in the manuscript, if the Editor deems this important, we are happy to include it in the text. Alternatively, we could also include it as supplemental material or an appendix.

4. Line 134: What is "LDR nursing"? Please spell out.

We have changed "LDR nursing" to labor and delivery room nursing staff (page 8, line 148 track changes version).

5. How did the authors know that none of the subjects diagnosed with gestational diabetes, had pre-gestational diabetes or glucose intolerance? Had they all had pregestational testing to rule out glucose intolerance or diabetes?

At the initial GDM visit, patients had a thorough medical history taken and were considered to be without a "history of pre-gestational diabetes" if they had never received a formal diagnosis prior to pregnancy. Additionally, as an exclusion criterion, any patient with a Hemoglobin A1c of 6.5% or higher was deemed ineligible.

This information has been added to the methods section of the manuscript (page 6 lines 98-103 track changes version).

6. Please carefully review references and make sure they all concur with Instructions for Authors for the Green Journal, esp et al.

Thank you for this suggestion. We have reviewed and revised our references to be sure they concur with the Instructions for Authors.

7. In Table 1, row 8 "medical management of GDM". Would the authors consider putting a line right above medical management saying diet management and the 'n'(%)'?

We have added this line as suggested to table 1 (page 17 track changes version).

8. In Table 2. Did any individuals have to receive 'juice' for hypoglycemia either in the tight or liberalized control group?

At your suggestion we have added "maternal hypoglycemia" to table 2 (page 18). All patients with glucose values < 60 mg/dL received juice. The rate of hypoglycemia did not differ between groups.

9. In Figure 1: What is "initiating insulin GTT"? Glucose tolerance test? Insulin drip?

GTT is insulin drip. Figure 1 has been revised to say insulin drip to avoid confusion.

10. In the tight control group 12 subjects and in the liberalized control group only 1 subject required intrapartum insulin administration due to hyperglycemia. Of those in both groups who required intrapartum insulin how many were treated for their GDM with insulin or with insulin and metformin? Did any of the subjects whose GDM was controlled by diet and exercise alone, require intrapartum insulin in either the tight or liberalized control groups? The authors note that "for women with GDM, our study found no benefit to tight control of glucose in labor and instead supports glucose assessment every 4 hours with intervention only if maternal glucose concentration is <60 or > 120mg/dl." Could this be liberalized even more if the GDM was controlled antepartum by diet and exercise, without the need for insulin?

Among patients in both groups that had maternal hyperglycemia according to protocol:

Hyperglycemia according to Tight control-17 patients
6 managed antepartum with diet
11 managed medically antepartum, with insulin
12 patients treated with insulin intrapartum according to protocol in this group, 5 went untreated

Hyperglycemia according to liberalized control: 3 patients
3 managed medically antepartum, with insulin
1 patient treated with insulin intrapartum according to protocol in this group, 2 went untreated

While it is possible that the findings of our study may be able to be liberalized even further, our study is of too small numbers to substantiate this idea. We hope to conduct an either larger study in the future that likely will be able to answer this question.

While we have not included this information in the manuscript, if the Editor deems this important, we are happy to include it in the text. Alternatively, we could also include it as supplemental material or an appendix.

Reviewer #4: The is a randomized control trial. This article may be cited by metaanalysis going forward but does not seem large enough or of a primary outcome sufficient to be frequently cited alone as the primary outcome of this study was the first neonatal blood glucose concentration rather than the more specifically clinically useful outcome of stating the overall number/percentage by treatment group of the number of neonates who experienced hypoglycemia. Possibly this was because a higher number of study participants might have been needed to power such a primary outcome.

This article is correct in stating there are no studies isolated to the outcome of comparing tight control and "less tight" control of glucose in the intrapartum for GDM only patients. However, in review of literature, one can extrapolate that "less tight control" of glucose in the intrapartum is an acceptable treatment for GDM patients based on past studies. From abstract of a cited source on this article (7), there have been recommendations for target intrapartum glucose goals based on pre-gestational diabetes that extend to GDM: "From this review it appears that the maternal glucose should be maintained between 4.0 and 6.0-7.0 mmol/L during labor. Most women with gestational diabetes, especially if they require <1.0 units/kg/d of insulin, can simply be monitored without intravenous insulin." When converted from mmol/L to mg/dL, the range of 4 to 6-7 mmol/L is 72 to 106/126 mg/dL. This study being reviewed confirms the recommendation of the already published review of 19 papers looking at the relationship between intrapartum glucose and effects of neonatal hypoglycemia, and it noted there were 6 studies looking at intrapartum glucose and neonatal hypoglycemia in GDM patients with 3 of 6 of the studies not showing inverse relationship between the two. This seems to go along with the findings of this study being reviewed for publication now, that the range of liberalized control (60-120 mg/dL) is a viable option for intrapartum GDM patients.

Source 8 cited in this study cites a paucity of data in support of tight glycemic control for type 1 and type 2 pre-gestational diabetes patients which would seem to be extendable to GDM patients based on the study from the cited reference 7 for this study. Additionally, there have been studies such as the study titled Hypoglycemia rates in the first days of life among term infants born to diabetic mothers by Maayan-Metzget, Lubin, and Kuint in Neonataology in 2009 which looked at pregestational DM and GDM patients and correlated higher risk for hypoglycemia in the neonate, too large for gestational age babies and those born to mothers with juvenile onset diabetes. This speaks more to the relationship to longer standing poor or difficult glucose control issues rather than needing tight control in the intrapartum. With respects to this study being reviewed for publication, it would seem more helpful if the data of this study included in Table 1 the antepartum glucose control as poor/fair/good and the average insulin U/kg/day needed to control the patients' glucose variation between the two groups.

Thank you for your gracious comments and review of the literature. At your suggestion, we have added information about hemoglobin A1c levels to the text of the results section (among the patients for which this information was known; page 10 lines 193-196 track changes version)).

Additionally, we also added information regarding units of insulin patients were required antepartum for those managed medically to the results text (page 10 lines 197-201 track changes version).

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

1. lines 181-188: Suggest including a summary of this as a Table.

Thank you for this suggestion, we have added this data to table 3 (page 19 track changes version).

2. Table 2 and lines 110-116: Were the frequency of blood glucose measurements for the two cohorts different intra partum and post-partum? If so, should cite the number of measurements from which the maternal median plasma glucose or denominator for number of values exceeding upper protocol threshold. That is, the range would be affected by the number of measurements and the likelihood of finding a high value would be a function of how many measurements were taken. Also, were all measurements actually from plasma determinations in lab or were some done via glucometer?

As was the nature of the study design, the frequency of blood glucose measurements for the two cohorts were different intrapartum. The tight-control group had blood glucose checked hourly whereas the tight control group had blood glucose checked every four hours. We have altered table 2 to include data regarding the average number of measurements per patient per group (page 18 track changes version). All glucose measurements for mothers and neonates were point of care glucose measurements; none were done in the laboratory setting. This is noted in methods section. (page 7, lines 127-128 and page 8-9 lines 159-162 track changes version).

3. Table 3: Need to clearly separate the primary from the secondary outcomes. Same issue re: number of measurements of glucose for the two cohorts and were all done in lab or some via glucometer?

We have separated the primary and secondary outcomes into a new table, table 4 (page 21 track changes version). The protocol for neonatal glucose measurement was the same for all neonates. Neonates at baseline should have four point of care capillary blood glucose measurements via heel-stick after birth; the only indication for additional

measurements is a measurement indicating hypoglycemia or infant symptomatology concerning providers that the infant may be hypoglycemic. All neonatal blood glucose measurements were point of care measurements; none were done in the laboratory setting. This is reflected in the methods section of the text (page 8-9, lines 159-162 track changes version).

EDITOR COMMENTS:

1. Why would you schedule these before 36 weeks?

At the outpatient clinic, if patients have decided against a trial of labor after cesarean, or have a breech presenting fetus and have declined external cephalic version, an attempt is made to schedule the cesarean by or at the 36-week visit to ensure adequate availability in the operating room schedule.

2. Are women allowed to eat in labor? What IV fluids are used? Do they need to be NPO when they begin induction?

At our hospital women, women are not required to be NPO for labor induction, however at the request of our anesthesia providers, women are not allowed to eat in labor. They are allowed a clear liquid diet. Women with a diagnosis of diabetes in pregnancy (Type I, Type 2 or GDM) are given "diabetic clears." "Diabetic clear" liquids are low-sugar or sugarfree clear liquids. This information has been added to the manuscript (page 8, lines 152-154 track changes version).

While the option of transitioning to D5LR was written into the study's treatment algorithm, no patients in the study received any IV fluid other than lactated ringers.

3. Given concerns about relatively small numbers and potential inclusion in a metaanalysis, are you not willing to provide independent patient data in the future for a potential IPD meta-analysis? Fine if you are not, but just making sure you had considered this in your decision to not share data.

Thank you for pointing this out, when the final version of the manuscript is published we will be willing to share our data.

4. When you write that a study occurred between date 1 and date 2, it literally excludes those boundary dates. For instance, "This study was performed between Feb 2018 and Jan 2019" would mean it was performed from March 2018 to Dec 2018. Do you instead mean that the study was performed from date 1 to date 2? If so, please edit.

Thank you for recognizing this error, we have corrected the text to accurately reflect when the study was performed (page 10, line 187 track changes version).

5. Could it be that when you check blood sugars more frequently, as you did with the tight group, that you identify swings in blood sugar that may not be seen if you just check q4 hours? Why did you not check both groups with the same frequency, but liberalize the upper bound for treating in the "loose "control group?

Excellent observation and it is possible that by checking blood sugars more frequently we were identifying swings in blood glucose levels. To avoid confusion with protocol implementation, we decided to vary both frequency of glucose monitoring and the treatment algorithm.

Additionally, because the tight control protocol mirrors "the standard" care protocol used on the maternal fetal medicine service, we wanted to avoid detecting maternal glucose levels that the providers would usually treat and asking them to not to intervene. We recognize this is a limitation of our protocol.

6. Should be noted as a QA issue for your unit, given this is supposed to occur in 100%

Thank you for this observation. The way the neonatal glucose protocol is written is within two hours of birth, or "as close to that as clinical care allows." Although 100% of neonates did not have blood glucose measured within 2 hours of birth, all neonates in the cohort had blood glucose measured within 2 hours and 30 minutes of birth as noted in the text (page 11 lines 210-215 track changes version; table 3 page 19 track changes version). We feel that our results reflect clinical care in a busy obstetrical unit.

7. Please provide how many in each group fell below 40 mg/dL.

We have added text to the results section (page 11, lines 220-222 track changes version) and this data is included in Table 4 (page 21 track changes version).

8. The way you state this is a bit of a stretch. Yes, they were closer (53 v 58) but it was above the cut off. Above, I've asked for how many were below 40 in each group. Please provide that.

We have added this information as noted above (page 11, lines 220-222 and table 4, page 21 track changes version.)

9. Instead of saying "to our knowledge" please state, Based on a pubmed search....from inception..using the terms...... this is the first study of its kind"

Thank you for suggesting this edit, we have revised the paragraph (page 13, lines 251-253 track changes version).

10. Please provide antepartum treatment groups for the patients "Diet only, oral agent or insulin".

We have edited the table as you suggested (Table 1 page 17 track changes version).

2. 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:

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

3. 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.

4. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Responses to the five bullet points should be provided in a box at the end of the Methods section.

We have amended the box to reflect our plan to share data (page 10, track changes version).

- 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. Provide a short title of no more than 45 characters, including spaces, for use as a running foot.

Randomized trial of intrapartum glucose management

10. 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.

Word count for abstract: 330

- 11. Abstracts for all randomized, controlled trials should be structured according to the journal's standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf. Please edit your abstract as needed.
- 12. 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.
- 13. 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.
- 14. 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.
- 15. 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.
- 16. Figures 1 and 2 may be resubmitted as-is.

Figures 1 and 2 were revised in response to reviewers' comments and due to an error noted during the revision process. Figure 1 had "consider" removed from the liberalized treatment guidelines. Figure 2 had the term "less tight control" in the flow diagram instead of "liberalized control" so this was also fixed.

17. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at http://links.lww.com/LWW-ES/A48. The cost for publishing an article as open access can be found at http://edmgr.ovid.com/acd/accounts/ifauth.htm.

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

18. 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 Feb 14, 2019, we will assume you wish to withdraw the manuscript from further consideration.

From:
To: Randi Zung

Subject: Re: Your Revised Manuscript 19-22R1

Date: Wednesday, March 6, 2019 11:01:30 AM

Attachments: Hamel GDM Intrapartum RCT paper FINALOBGedrev.docx

Hello Randi.

I have made the revisions and my responses are below. We have made the track changes and left those made by the editors, the final revision is attached. Please let me know what else I can do and thank you so much for all of your patience

-Maureen.

1. General: The Manuscript Editor and Dr. Chescheir have made edits to the manuscript using track changes. Please review them to make sure they are correct.

We have reviewed and they are correct

2. Electronic Copyright Transfer Agreement: All co-authors will need to complete our electronic Copyright Transfer Agreement, which was sent to them through Editorial Manager. We still need forms from Lindsey Kanno, Phinnara Has, and Dwight Rouse.

I was told this was completed by all authors, please let me know if this has not occurred.

3. Precis: Please state here that this is for women with gestational diabetes.

This has been corrected page 3 line 40.

4. Line 119: Would you consider changing this to "recorded"?

This has been changed as requested on page 7 line 120.

5. Line 124: I didn't understand your response to my prior question about this. Do you mean that the cesarean delivery was performed prior to 36 weeks or that the date was scheduled prior to 36 weeks? As read, its sounds like you do the cesareans prior to 36 weeks. Could you write it otherwise?

We have revised the sentence to remove the parenthetical in hopes to make this more clear, page 8 line 124.

6. Line 132: I do not feel like you need to provide the information about the type of POC testing equipment or standardization process.

Thank you, please let us know if it should be included as supplemental material

7. Line 193: Do not begin a sentence with a numeral. Either reorganize your sentence to not start with a number OR write out the number in words.

Page 11 line 194 has been revised and we wrote out the number in words.

8. Abstract-Results and Line 200: In both the abstract and the paper, please provide absolute numbers as well as whichever effect size you are reporting + confidence intervals. P values may be omitted for space concerns. By absolute values, I mean something like: "xx (outcome in exposed)/yy (outcome in unexposed) (zz%) (Effect size= ; 95% CI=.). An example might be: Outcome 1 was more common in the exposed than the unexposed 60%/20% (Effect size=3;95% CI 2.6-3.4). Please make sure you include CIs.

Thank you for this suggestion. We have edited the abstract, pages 4-5 lines 63-66 and the paper

page 12 lines 222-225. Please let us know if we you need any additional analyses.

9. Line 206: Can you comment here why fewer patients received the recommended treatment?

We have added text to explain why fewer patients received recommended treatment pages 11-12 lines 208-212

10. Line 234: Please avoid single sentence paragraphs.

We have revised the paragraph beginning on page 13 line 237.

On Wed, Feb 13, 2019 at 9:43 AM Randi Zung < RZung@greenjournal.org > wrote:		
Dear Dr. Hamel:		
Your revised manuscript is being reviewed by the Editors. Before a final decision can be made, we need you to address the following queries. Please make the requested changes to the latest version of your manuscript that is attached to this email. Please track your changes and leave the ones made by the Editorial Office. Please also note your responses to the author queries in your email message back to me.		
1. General: The Manuscript Editor and Dr. Chescheir have made edits to the manuscript using track changes. Please review them to make sure they are correct.		
2. Electronic Copyright Transfer Agreement: All co-authors will need to complete our electronic Copyright Transfer Agreement, which was sent to them through Editorial Manager. We still need forms from Lindsey Kanno, Phinnara Has, and Dwight Rouse.		
3. Precis: Please state here that this is for women with gestational diabetes.		
4. Line 119: Would you consider changing this to "recorded"?		
5. Line 124: I didn't understand your response to my prior question about this. Do you mean that the cesarean delivery was performed prior to 36 weeks or that the date was scheduled prior to 36 weeks? As read, its sounds like you do the cesareans prior to 36 weeks. Could you write it otherwise?		
6. Line 132: I do not feel like you need to provide the information about the type of POC testing equipment or standardization process.		

7. Line 193: Do not begin a sentence with a numeral. Either reorganize your sentence to not start with a number OR write out the number in words.
8. Abstract-Results and Line 200: In both the abstract and the paper, please provide absolute numbers as well as whichever effect size you are reporting + confidence intervals. P values may be omitted for space concerns. By absolute values, I mean something like: "xx (outcome in exposed)/yy (outcome in unexposed) (zz%) (Effect size= ; 95% CI=.). An example might be: Outcome 1 was more common in the exposed than the unexposed 60%/20% (Effect size=3;95% CI 2.6-3.4). Please make sure you include CIs.
9. Line 206: Can you comment here why fewer patients received the recommended treatment?
10. Line 234: Please avoid single sentence paragraphs.
To facilitate the review process, we would appreciate receiving a response within 48 hours. We realize that some people from your author group may be out of the office due to the SMFM meeting, so if that is the case, we are fine with receiving your edited file early next week.
Best,
Randi Zung
Randi Zung (Ms.)
Editorial Administrator Obstetrics & Gynecology
American College of Obstetricians and Gynecologists
409 12th Street, SW
Washington, DC 20024-2188
T: 202-314-2341 F: 202-479-0830
http://www.greenjournal.org

From:
To: Eileen Chang (Temp)

Subject: Re: O&G Figure Revision: 19-22R1

Date: Monday, February 25, 2019 4:27:04 PM

Thanks so much, This looks great!!

I did already receive the "open access" acceptance email. I still have to submit the editorial revisions sent by Randi on 2/13 as I had a specific question from Dr. Cheschier and am awaiting her response (Randi and I have been in correspondence). Once I hear back from her we an make the edits she is asking for and should be good to go!

Appreciate all of your help. Maureen

On Mon, Feb 25, 2019 at 4:21 PM Eileen Chang (Temp) < echang@greenjournal.org> wrote:

Hi Maureen,

Thank you for catching that! I have attached the legend (the edits are crossed out and in blue) for your review. If everything looks good, we would be ready to go ahead and approve your manuscript!

Eileen

From: Maureen S. Hamel

Sent: Monday, February 25, 2019 4:16 PM

To: Eileen Chang (Temp) < <u>echang@greenjournal.org</u>>

Subject: Re: O&G Figure Revision: 19-22R1

Hello Eileen.

Thank you for your email and explanation. The figures look great. I found one additional issue:

For the legend, for part B, it reads " If persistent glucose values >200, consider initiating insulin drop." This should read " If persistent glucose values >200, consider initiating insulin drip."

Thank you

Maureen

On Mon, Feb 25, 2019 at 9:59 AM Eileen Chang (Temp) < echang@greenjournal.org>wrote:

Hello Maureen.

I have attached the edited figures 1 and 2 and the legend for your review.

For figure 2, we capitalized the N in the first box because it represents the total enrolled population. The rest, we left lowercase because they are subgroups of the originally enrolled population. If this is still incorrect, please let us know.

Thank you!

Eileen

From: Maureen S. Hamel

Sent: Wednesday, February 20, 2019 8:59 AM

To: Eileen Chang (Temp) < <u>echang@greenjournal.org</u>>

Subject: Re: O&G Figure Revision: 19-22R1

Good morning Eileen,

Thank you for your email. I did find a few errors

In figure 1 part A: Box #2 should read 121-150 as of right now it reads 212-150

In figure 2, the first box, consented women, the n is capitalized (N=87) however all of the other n in the remaining boxes are lowercase, can we make this n lowercase as well?

In the legends, it reads in two places, "If persistent glucose values > 200, consider initiating insulin drop" it should read "If persistent glucose values >200, consider

i	nitiating insulin drip"
7	Thank you so much
N	Maureen
	On Tue, Feb 19, 2019 at 4:39 PM Eileen Chang (Temp) < echang@greenjournal.org >wrote:
	Good Morning,
	Your figures and legend have been edited and PDFs of the figures 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 made 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 appreciate it if you could reply back no later than the end of Thursday, February 21.
	Best,
	Eileen