

# OBSTETRICS & GYNECOLOGY



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

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

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

Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office:

[obgyn@greenjournal.org](mailto:obgyn@greenjournal.org).

**Date:** Jan 31, 2019  
**To:** "Amy E. Judy" [REDACTED]  
**From:** "The Green Journal" em@greenjournal.org  
**Subject:** Your Submission ONG-18-2366

RE: Manuscript Number ONG-18-2366

Confirming the paradigm shift: systolic hypertension and preeclampsia-related mortality in California

Dear Dr. Judy:

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 21, 2019, we will assume you wish to withdraw the manuscript from further consideration.

#### REVIEWER COMMENTS:

Reviewer #1:

1. Lines 123-131 define HELLP syndrome in your study utilizing platelet count and liver transaminases, but hemolysis is not utilized in the definition. Consider including evidence of hemolysis in the definition of HELLP or referring to the components individually.
2. Labetalol 200mg po was considered a standard antihypertensive treatment in Lines 146-147. Labetalol is not a standard treatment. Consider removing po labetalol from the standard treatment regimens or demonstrate support that it is considered a standard emergency treatment for severe hypertension in pregnancy.
3. The demographic characteristics and perinatal characteristics sections suggest that certain characteristics are more likely to be associated with death by stroke, but the incidence of these characteristics in the general population would affect that relationship. For instance, the statement in lines 181-184 implies that African-American women are less likely than Hispanic women to die from preeclampsia/eclampsia related causes, but this is not supported by the data. This detracts from the more important and clearly stated findings later in the manuscript. Consider rewording to clarify the demographic and perinatal findings or removing the statements entirely.
4. In line 286-287, multiparous patients are identified as being more common than nulliparous patients. The incidence of multiparous vs. nulliparous patients in California Birth Cohort is not defined. A higher incidence of multiparous patients delivering during that time frame might skew the data to appear as if this is a risk factor. Consider including the incidence of multiparous and nulliparous in the California Birth Cohort.
5. Is there a way to use the California Birth Cohort demographics and the mortality characteristics to generate a demographic-related risk? For instance, the data from Table 2 indicates that African-American, non-Hispanic women constitute 4.3% of the California Birth Cohort but represent 11.1 % preeclampsia related deaths. This implies that these women have a higher chance of dying from preeclampsia than others.
6. Your study identifies that more patients who died from stroke had severe systolic hypertension than severe diastolic hypertension. The possibility exists that patients with severe diastolic prevention were treated successfully. Consider acknowledging this possibility.
7. Reference number 5, lines 358-360, Diagnosis and management of preeclampsia and eclampsia. Practice Bulletin No. 33 is no longer in circulation. Consider identifying an alternative reference or removing it.

8. There are many tables and figures. Consider translating Table 1 into the text and simplifying or combining other tables and figures.

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The methods section should start with a clear statement of the type of study.

The inclusion criteria for entry into the study cohort should be clearly stated

The multiple subheadings are not needed - strong topic sentences would serve the purpose of subheadings

## RESULTS

A flow chart of all women who may have met entry criteria (the California cohort) leading down into the comparison groups of this manuscript would help paint a more complete picture of the study population. This helps readers decide how similar the study population is to the population in which the readers work.

The discussion should provide a clear summary statement of the most important findings in your own population then compare and contrast with other publications. The Green Journal Guide to writing can help when writing a discussion. The Guide to Writing is available on the Green Journal website.

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Reviewer #4: This is a retrospective review which describes the clinical characteristics of stroke and opportunities to improve care in a cohort of preeclampsia-related maternal mortalities in California.

This is an excellent manuscript which will be valuable to demonstrate the experience in the United States prior to hypertension protocol implementation.

While well written, consider condensing results section.

## STATISTICAL EDITOR COMMENTS:

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

lines 43-54: Since there were a total of 54 deaths in this series, the proportions should be rounded to nearest integer %, that is, there is no basis to report precision to nearest 0.1%.

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Tables 2, 3, 4: Same issue as in Abstract re: citing %s to nearest 0.1% when basis was small denominator.

Tables 4,5: Need to round % to nearest integer.

Figures 2, 3: Given the small sample sizes, I suspect that none of the differences were statistically significant. Could be place as on-line supplement in the present format or as Table.

#### 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.\*\*\*

- The objective for the abstract should be a simple "to" statement without background. The Journal style doesn't not use the virgule (/) except in numeric expressions. Please edit here and in all instances.

- Frequent seems like the wrong word here as of course it is the rare woman (not rare enough, I agree) who dies of preeclampsia or eclampsia.

- 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.

- most frequent symptom of the stroke? Where you say 66% had a good-to-strong chance, how was that degree determined? Its not mentioned in the methods. Also, on line 53 you nte that 91% had delayed response...is that of the 66%? Since you only have 54 cases overall, instead of just giving percentages please provide the absolute number. as an example Headache occurred in 47/54 (87%).

- your data only looks at the proportion of stroke related deaths in preeclamptic and eclamptic women, not all causes of death so you need to either indicate what percentage of all deaths were related to preeclampsia or eclampsia first to make the statement on line 55 or limit your statement to say Stroke is the major cause of maternal mortality associated with preeclampsia or eclampsia.

- as noted by your reviewers, some disagree with your thesis that there has been any sort of paradigm shift in that they have been aware of the importance of both systolic and diastolic hypertension as risk factors for stroke (and other morbidities). This raises an important question and perhaps some potential to make this more clear. The shift to address systolic as well as diastolic BP really started, as I recall, in the mid-2000 or early 2010's. The time line of your papers goes from 2002-2007 which would have been before this change occurred. For readers trained in the last 10-12 years, however, this shift may not be known to them and for those trained prior to them, they may have been paying attention to systolic BP for 10 years now, so they have forgotten that it was ever not so. As well, part of the emphasis on treating hypertension in pregnancy more aggressively is related to trying to prevent heart failure or cardiomyopathy. so line 75-77 is incomplete.

Can you weave the history of the change from diastolic to both systolic and diastolic BP focus into this and set it into the context of your data?

Otherwise, perhaps a place to focus your introduction would be the safety bundle for hypertension as it specifically addresses the importance of identification of severe ranges of either systolic or diastolic BP and aggressive treatment. This was published in 2017 in several journals, after your time frame for your study. It would seem from reading your abstract that perhaps had that bundle been in place and disseminated/used during this period. that some of these deaths could have been averted.

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- Not clear what you mean in sentence on line 64-66. "Strongly associated with pre-e in nearly 1/2 of cases". Is it weakly associated with preE-E in the other half? Or do you mean ..is associated with preE-E in nearly one half of cases?

- could you say more about the "degree" assessment? What are the ranges for this and how was that determined?

- Please consult the Instructions for Authors regarding the use of abbreviations, and what constitutes an acceptable abbreviation. This is not an acceptable abbreviation. Please spell the words out throughout the manuscript. Please spell out all abbreviations on first use. It is reasonable to not use abbreviations for words that are seldom used in the paper. A lot of non-standard abbreviations make it difficult for the readers.

- Since low platelets are the most common abnormal lab value in preeclampsia (See hypertension monograph 2013, ACOG) wouldn't using this criteria as sole one for diagnosing HELLP likely over-call this disorder.

- clarify if you have data on repeat BP measurements after treatment given and whether repeat doses were given. Or, did you just have this information for initial treatment?

- please condense your results and highlight the key findings and let the tables stand on their own for others. As noted by your reviewers, you have only 33 patients in your study group so non significant differences in your comparisons are likely due to small n. It would be reasonable to make this a descriptive paper primarily, and not worry too much about comparisons.

- Could you start out by saying "From 2002-2007, there were xxx pregnancy-related maternal deaths in California. Of these, 54 were associated with preeclampsia or eclampsia and in 33/54, stroke was identified as the cause of death. Imaging or autopsy or both results were available in 31. Hemorrhagic stroke.....

- we don't use subheadings like this; please eliminate throughout.

- In both the abstract and the paper, please provide absolute numbers as well as which ever 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=. ) Please provide confidence intervals in lieu of P values. 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) Given that about 1/2 of women in the birth cohort are Hispanic, these values don't seem too different to me (line 183.)

- as per one of your reviewers, the 11% may be higher than your birth cohort rate for AA's. (5% ) so African Americans may be disproportionately affected.

- just eyeballing the data in Table 2 it looks like all cause mortality (all three columns) had higher ages than the birth cohort--not just your preeclampsia related deaths.

- as noted near Table 3, why did you not include the California Birth Cohort information for your perinatal characteristics?

- perhaps for brevity, you could organize this chronologically. something like "Stroke occurred antenatally in x/33 (33%), intrapartum in xx/33 (18%) and post partum in 16/33 (46%)." [clarify numbers for missing data]

- please clarify what you mean by symptoms. Symptoms of what? Preeclampsia or eclampsia? Neurologic symptoms? Nausea and vomiting not uncommon in pregnancy and in labor not sure what you mean by "signs and symptoms were not considered to be mutually exclusive". In this paragraph you are reporting only

symptoms, not signs. How could they be mutually exclusive? You could have a headache (symptom) and clonus (sign).

- We do not allow authors to describe variables or outcomes in terms that imply a difference (such as the terms "trend" or "tendency" or "marginally different") unless there is a statistical difference. Please edit here and throughout.

- How did you determine that if in 90% of cases there was a failure to treat adequately, that there was only at 66% chance of altering the outcome? Why isn't it 90%?

- not really large with n=33. This is called a primacy claim (your paper is the first or biggest) and must either be deleted or supported by providing the search terms used, dates, and data bases searched (Medline, Ovid, Pubmed, Google Scholar, etc) in order to substantiate your claim.

- strengths and limitations should be moved to near the end of the discussion. Your first paragraph should give the "bottom line"...in this case something like stroke was underlying cause of death in the majority of deaths associated with preeclampsia or eclampsia and failure to rescue occurred in the majority of the patients. Please see the Guidelines for Writing available on the Editorial Manager website to help you focus your discussion.

What's the most important thing for your readers to get from this work? focus your discussion there. What supports any recommendations in light of other work? There are new practice bulletins on hypertension since you submitted your paper. You may want to include these in your thinking.

- Make this a box instead of a table.

- why not provide birth cohort data here like in table 2?

- Instead of a table here, please include this data in the text.

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. 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. 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).

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

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

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

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

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

12. 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](mailto: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>.

13. Figures 1-3 may be resubmitted as-is.

14. 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/ifaauth.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.

15. 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 21, 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

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

**Reviewer #1:**

1. Lines 123-131 define HELLP syndrome in your study utilizing platelet count and liver transaminases, but hemolysis is not utilized in the definition. Consider including evidence of hemolysis in the definition of HELLP or referring to the components individually.

*The definition of HELLP has been refined as recommended by the Editor. The explanation for not including hemolysis in the definition has been added to the text.*

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*Results section condensed and comparisons clarified.*

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6. Your study identifies that more patients who died from stroke had severe systolic hypertension than severe diastolic hypertension. The possibility exists that patients with

severe diastolic prevention were treated successfully. Consider acknowledging this possibility.

*This possibility is addressed now acknowledged in the Discussion.*

7. Reference number 5, lines 358-360, Diagnosis and management of preeclampsia and eclampsia. Practice Bulletin No. 33 is no longer in circulation. Consider identifying an alternative reference or removing it.

*Retraction of this publication is clarified in the text and reference list. The inclusion of the reference serves a purpose of historical significance.*

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Reviewer #3: The authors present a description of maternal mortality in California. This is a timely subject but there are some major weaknesses with the paper.

This is a descriptive study, the authors should review and use the STROBE guidelines to help with design and dissemination of this study.

*STROBE checklist is included.*

The introduction should clearly state specific aims and objectives of the paper.

*Done.*

The methods section should start with a clear statement of the type of study.

*Done.*

The inclusion criteria for entry into the study cohort should be clearly stated.

*Described in Methods section.*

The multiple subheadings are not needed - strong topic sentences would serve the purpose of subheadings

*All subheadings removed and topic sentences revised.*

## RESULTS

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*Figure 1.*

The discussion should provide a clear summary statement of the most important findings in your own population then compare and contrast with other publications. The Green Journal Guide to writing can help when writing a discussion. The Guide to Writing is available on the Green Journal website.

*Discussion section has been extensively revised.*

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*Tables have been extensively revised. Unnecessary tables, table columns and rows have been removed from the manuscript, and text used preferentially when feasible.*

Reviewer #4: This is a retrospective review which describes the clinical characteristics of stroke and opportunities to improve care in a cohort of preeclampsia-related maternal mortalities in California.

This is an excellent manuscript which will be valuable to demonstrate the experience in the United States prior to hypertension protocol implementation.

While well written, consider condensing results section.

*Results section has been condensed.*

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*Done.*

Figures 2, 3: Given the small sample sizes, I suspect that none of the differences were statistically significant. Could be place as on-line supplement in the present format or as Table.

*We have resubmitted Figures 2 and 3 in current form, as indicated by the Editor.*

EDITOR COMMENTS:

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- The objective for the abstract should be a simple "to" statement without background.

*Done.*

The Journal style doesn't not use the virgule (/) except in numeric expressions. Please edit here and in all instances.

*Done.*

- Frequent seems like the wrong word here as of course it is the rare woman (not rare enough, I agree) who dies of preeclampsia or eclampsia.

*Revised.*

- 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.

*Changes in all instances.*

- most frequent symptom of the stroke? Where you say 66% had a good-to-strong chance, how was that degree determined? Its not mentioned in the methods.

*Clarification provided.*

Also, on line 53 you nte that 91% had delayed response...is that of the 66%? Since you only have 54 cases overall, instead of just giving percentages please provide the absolute number. as an example Headache occurred in 47/54 (87%).

*Done.*

- your data only looks at the proportion of stroke related deaths in preeclamptic and eclamptic women, not all causes of death so you need to either indicate what percentage of all deaths were related to preeclampsia or eclampsia first to make the statement on line 55 or limit your statement to say Stroke is the major cause of maternal mortality associated with preeclampsia or eclampsia.

*Revised as suggested.*

- as noted by your reviewers, some disagree with your thesis that there has been any sort of paradigm shift in that they have been aware of the importance of both systolic and diastolic hypertension as risk factors for stroke (and other morbidities). This raises an important question and perhaps some potential to make this more clear. The shift to address systolic as well as diastolic BP really started, as I recall, in the mid-2000 or early 2010's. The time line of your papers goes from 2002-2007 which would have been before this change occurred. For readers trained in the last 10-12 years, however, this shift may not be known to them and for those trained prior to them, they may have been paying attention to systolic BP for 10 years now, so they have forgotten that it was ever not so. As well, part of the emphasis on treating hypertension in pregnancy more aggressively is related to trying to prevent heart failure or cardiomyopathy. so line 75-77 is incomplete.

*The introduction and discussion sections of the manuscript have been extensively revised with attention to this feedback from the reviewers and the Editor. The manuscript in its current form emphasizes the shift from historic practice to the contemporary emphasis on systolic hypertension, and the temporal relation of these cases to that shift in practice.*

Can you weave the history of the change from diastolic to both systolic and diastolic BP focus into this and set it into the context of your data?

*As above.*

Otherwise, perhaps a place to focus your introduction would be the safety bundle for hypertension as it specifically addresses the importance of identification of severe ranges of either systolic or diastolic BP and aggressive treatment. This was published in 2017 in several journals, after your time frame for your study. It would seem from reading your abstract that perhaps had that bundle been in place and disseminated/used during this period. that some of these deaths could have been averted.

*As above. We have focused on the shift to treatment of systolic hypertension.*

- Not clear what you mean in sentence on line 64-66. "Strongly associated with pre-e in nearly 1/2 of cases". Is it weakly associated with preE-E in the other half? Or do you mean ..is associated with preE-E in nearly one half of cases?

*Revised.*

- could you say more about the "degree" assessment? What are the ranges for this and how was that determined?

*Clarified in text.*

- Please consult the Instructions for Authors regarding the use of abbreviations, and what constitutes an acceptable abbreviation. This is not an acceptable abbreviation. Please spell the words out throughout the manuscript. Please spell out all abbreviations on first use. It is reasonable to not use abbreviations for words that are seldom used in the paper. A lot of non-standard abbreviations make it difficult for the readers.

*Done.*

- Since low platelets are the most common abnormal lab value in preeclampsia (See hypertension monograph 2013, ACOG) wouldn't using this criteria as sole one for diagnosing HELLP likely over-call this disorder.

*Definition of HELLP has been revised as suggested. Text and statistics reflect the new definition.*

- clarify if you have data on repeat BP measurements after treatment given and whether repeat doses were given. Or, did you just have this information for initial treatment?

*Clarified in text.*

- please condense your results and highlight the key findings and let the tables stand on their own for others. As noted by your reviewers, you have only 33 patients in your study group so non significant differences in your comparisons are likely due to small n. It would be reasonable to make this a descriptive paper primarily, and not worry too much about comparisons.

*The results section has been condensed, and tables limited, modified, or eliminated extensively as compared to original submission.*

- Could you start out by saying "From 2002-2007, there were xxx pregnancy-related maternal deaths in California. Of these, 54 were associated with preeclampsia or eclampsia and in 33/54, stroke was identified as the cause of death. Imaging or autopsy or both results were available in 31. Hemorrhagic stroke.....

*Done.*

- we don't use subheadings like this; please eliminate throughout.

*Done.*

- In both the abstract and the paper, please provide absolute numbers as well as which ever 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= . ) Please provide confidence intervals in lieu of P values. 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)

Given that about 1/2 of women in the birth cohort are Hispanic, these values don't seem too different to me (line 183.)

*Done.*

- as per one of your reviewers, the 11% may be higher than your birth cohort rate for AA's. (5% ) so African Americans may be disproportionately affected.

*Results section revised.*

- just eyeballing the data in Table 2 it looks like all cause mortality (all three columns) had higher ages than the birth cohort--not just your preeclampsis related deaths.

*Results section revised.*

- as noted near Table 3, why did you not include the California Birth Cohort information for your perinatal characteristics?

*Added to table (now labeled as table 2).*

- perhaps for brevity, you could organize this chronologically. something like "Stroke occurred antenatally in x/33 (33%), intrapartum in xx/33 (18%) and post partum in 16/33 (46%)." [clarify numbers for missing data]

*Done.*

- please clarify what you mean by symptoms. Symptoms of what? Preeclampsia or eclampsia? Neurologic symptoms? Nausea and vomiting not uncommon in pregnancy and in labor not sure what you mean by "signs and symptoms were not considered to be mutually exclusive". In this paragraph you are reporting only symptoms, not signs. How could they be mutually exclusive? You could have a headache (symptom) and clonus (sign).

*Clarified in text.*

- We do not allow authors to describe variables or outcomes in terms that imply a difference (such as the terms "trend" or "tendency" or "marginally different") unless there is a statistical difference. Please edit here and throughout.

*Done.*

- How did you determine that if in 90% of cases there was a failure to treat adequately, that there was only a 66% chance of altering the outcome? Why isn't it 90%?

*It is possible that the cases in which there was a failure to treat but not a chance to alter the outcome, the sentinel event occurred outside of the hospital. Due to word space*

*constrictions we do not address this point in detail in the current manuscript, favoring other issues of interest. Should the Editor feel that this aspect is crucial to publication, we will gladly address it further.*

- not really large with n=33. This is called a primacy claim (your paper is the first or biggest) and must either be deleted or supported by providing the search terms used, dates, and data bases searched (Medline, Ovid, Pubmed, Google Scholar, etc) in order to substantiate your claim.

*Removed from manuscript.*

- strengths and limitations should be moved to near the end of the discussion. Your first paragraph should give the "bottom line"...in this case something like stroke was underlying cause of death in the majority of deaths associated with preeclampsia or eclampsia and failure to rescue occurred in the majority of the patients. Please see the Guidelines for Writing available on the Editorial Manager website to help you focus your discussion.

What's the most important thing for your readers to get from this work? focus your discussion there. What supports any recommendations in light of other work? There are new practice bulletins on hypertension since you submitted your paper. You may want to include these in your thinking.

*We have incorporated extensive edits to both the introduction and discussion sections to reframe the manuscript, as suggested by the reviewers and the Editor.*

- Make this a box instead of a table.

*Done.*

- why not provide birth cohort data here like in table 2?

*Done.*

- Instead of a table here, please include this data in the text.

*Done.*

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. 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.

*STROBE checklist included in resubmission.*

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.

*Done.*

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.

*Confirmed.*

7. 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).

*Acknowledged.*

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

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

*Confirmed.*

9. Only standard abbreviations and acronyms are allowed. A selected list is available online at <http://edmgr.ovid.com/ong/accounts/abbreviations.pdf>. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be

spelled out the first time they are used in the abstract and again in the body of the manuscript.

*Done.*

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

*Done.*

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

*Done.*

12. 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>.

*We have included as a reference one practice bulletin that has been withdrawn. This practice bulletin is of historical significance which we discuss in the paper, and note in the reference list that the publication is withdrawn.*

13. Figures 1-3 may be resubmitted as-is.

*Resubmitted.*

14. 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/ifaauth.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.

15. 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.

*Addressed.*

**From:** [REDACTED]  
**To:** [Randi Zung](#)  
**Subject:** Re: Your Revised Manuscript 18-2366R1  
**Date:** Monday, March 11, 2019 2:21:08 AM  
**Attachments:** [PreE Stroke Figure 1-3\\_v2.pdf](#)  
[18-2366 ms \(3-6-19v2\)\\_AJ.docx](#)

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Hi Randi,

Thank you greatly for your understanding. Attached please find the revised manuscript with comments/edits addressed and accepted. Additionally my responses to the editors comments are below in blue. Our statistics team noted a typographical error in Figure 1 which I have corrected (upper box n = 3,310,**4**85 rather than n = 3,310,**2**85 as previously shown) and requested that I make a small adjustment to the footnotes of Table 2 (visible with track changes). There are reflected in the attached documents.

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.

[Done.](#)

2. Title: Do you approve the edited title? It seems important to mention stroke, based on your conclusion.

[Proposed title approved.](#)

3. Line 49: Line 246 says 26. Which is correct?

[Lines have been revised to reflect correct statistic - 25/33 \(76%\) in both locations.](#)

4. Line 125 and elsewhere: The Journal style doesn't not use the virgule (/) except in numeric expressions. Please edit here and in all instances. You may use "and" or "or" instead.

[Revised.](#)

5. Line 222: Should this read, "Table 3"? There was no table 5 provided with the article.

[Corrected to read Table 3.](#)

6. Line 301: To be clear, do you mean "appropriate" vis-à-vis standards at the time or standards now?

[Contemporary standards - sentence revised to further clarify timing.](#)

7. Reference 8: Reference 8 was replaced by Committee Opinion No. 767. Please review CO 767 to make sure it supports what you are stating. See <https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions-List>

[New Committee Opinion supports statement as cited.](#)

Please let me know if you require anything further.

Thank you!

Amy

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**From:** Randi Zung <RZung@greenjournal.org>  
**Sent:** Friday, March 8, 2019 9:19 AM  
**To:** Amy Judy  
**Subject:** RE: Your Revised Manuscript 18-2366R1

Hi:

No problem. Our “48 hour” window is just so we process the manuscripts within the same week they are discussed on the Editors’ conference. The Editors did not have any follow up queries about your revision so you are welcome to return your updated file next week.

Thanks,  
Randi

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**From:** Amy Judy [REDACTED]  
**Sent:** Friday, March 8, 2019 11:54 AM  
**To:** Randi Zung <RZung@greenjournal.org>  
**Subject:** Re: Your Revised Manuscript 18-2366R1

Hi Randi,  
I am working on these changes at this very moment and will get them back to you today ASAP.

[REDACTED]  
[REDACTED]

Thank you for your consideration,  
Amy

---

**From:** Randi Zung <[RZung@greenjournal.org](mailto:RZung@greenjournal.org)>  
**Sent:** Wednesday, March 6, 2019 7:54 AM  
**To:** Amy Judy; [REDACTED]  
**Subject:** Your Revised Manuscript 18-2366R1

Dear Dr. Judy:

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. Title: Do you approve the edited title? It seems important to mention stroke, based on your conclusion.
3. Line 49: Line 246 says 26. Which is correct?
4. Line 125 and elsewhere: The Journal style doesn't not use the virgule (/) except in numeric expressions. Please edit here and in all instances. You may use "and" or "or" instead.
5. Line 222: Should this read, "Table 3"? There was no table 5 provided with the article.
6. Line 301: To be clear, do you mean "appropriate" vis-à-vis standards at the time or standards now?
7. Reference 8: Reference 8 was replaced by Committee Opinion No. 767. Please review CO 767 to make sure it supports what you are stating. See <https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions-List>

To facilitate the review process, we would appreciate receiving a response within 48 hours.

Best,  
Randi Zung

— —

**Randi Zung (Ms.)**

Editorial Administrator | *Obstetrics & Gynecology*  
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<http://www.greenjournal.org>

## Eileen Chang (Temp)

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**From:** Amy Judy [REDACTED]  
**Sent:** Tuesday, March 19, 2019 4:49 PM  
**To:** Eileen Chang (Temp)  
**Subject:** Re: O&G Figure Revision

These look great as is! Thank you for your patience.  
Amy

---

**From:** Eileen Chang (Temp) <[echang@greenjournal.org](mailto:echang@greenjournal.org)>  
**Sent:** Tuesday, March 19, 2019 1:41 PM  
**To:** Amy Judy  
**Subject:** RE: O&G Figure Revision

Hi Amy,

Great, thank you! I have attached all the figures and the legend for your final review and approval. Please let me know if these are okay going forward.

Best,  
Eileen

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**From:** Amy Judy [REDACTED]  
**Sent:** Tuesday, March 19, 2019 4:35 PM  
**To:** Eileen Chang (Temp) <[echang@greenjournal.org](mailto:echang@greenjournal.org)>  
**Subject:** Re: O&G Figure Revision

Hi Eileen,  
Thank you so much for clarifying.  
The figure is correct as attached, with the third box reading N=54.  
Thanks,  
Amy

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**From:** Eileen Chang (Temp) <[echang@greenjournal.org](mailto:echang@greenjournal.org)>  
**Sent:** Monday, March 18, 2019 6:13 AM  
**To:** Amy Judy  
**Subject:** RE: O&G Figure Revision

Hi Amy,

Thank you for the clarifications! Attached are all the figures for your review.

For Figure 1, is the third box supposed to read N=45 or N=54? In the edits you sent me it said 54 so I wasn't sure what number I should use there.

Eileen

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**From:** Amy Judy [REDACTED]  
**Sent:** Wednesday, March 13, 2019 4:05 PM  
**To:** Eileen Chang (Temp) <[echang@greenjournal.org](mailto:echang@greenjournal.org)>  
**Subject:** Re: O&G Figure Revision

Thanks Eileen! I don't even notice the formatting changes you have made, so these figures are fine as far as I'm concerned -- with one exception as below:

In **figure 2**, the percentage above the white bar (preE/eclampsia - stroke) for ineffective care should read **76%** (currently reads 79%). I believe that I changed this in the prior version but it doesn't seem to have carried forward. Could we please correct that number?

To answer your questions about the typographical issues that were corrected for Figure 1 -  
In the top box, N=3,310,**4**85

In third box, N=**4**5 (previously 333)

I specified 'typographical' as these don't reflect any recalculation on our end, and are correct where referenced within the manuscript, but somehow were incorrect in the figure.

Thank you!  
Amy

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**From:** Eileen Chang (Temp) <[echang@greenjournal.org](mailto:echang@greenjournal.org)>  
**Sent:** Wednesday, March 13, 2019 11:53 AM  
**To:** Amy Judy  
**Subject:** RE: O&G Figure Revision

Hi Amy,

We have made additional edits to Figure 2 according to our journal's style. I have attached all the figures for another review.

We were also wondering which typographical errors you found in Figure 1 since we were unable to figure out what was changed.

Thank you!

Eileen

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**From:** Amy Judy [REDACTED]  
**Sent:** Tuesday, March 12, 2019 9:35 PM  
**To:** Eileen Chang (Temp) <[echang@greenjournal.org](mailto:echang@greenjournal.org)>  
**Subject:** Re: O&G Figure Revision

Hi Eileen,

We have reviewed the figures and figure legends. There were two typographical errors in Figure 1 which we have corrected. Figure 2 has been edited to include the N in within-figure labels for the two groups. There are no changes to Figure 3, or to the figure legends. The revised PDFs are attached.

Thank you!

Amy

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**From:** Eileen Chang (Temp) <[echang@greenjournal.org](mailto:echang@greenjournal.org)>

**Sent:** Monday, March 11, 2019 10:33 AM

**To:** Amy Judy

**Cc:** [REDACTED]

**Subject:** O&G Figure Revision

Good afternoon,

Your figures and legend have been edited and they have been attached for your review. Please review the attachments 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 a reply no later than Wednesday, 3/13. Thank you for your help.

Best,  
Eileen