Date: Mar 08, 2019
To: "Julia E. Kohn" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-158

RE: Manuscript Number ONG-19-158

Safety and effectiveness of medication abortion provided via telemedicine in four U.S. states

Dear Dr. Kohn:

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 Mar 29, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

Overall: This is an original research report about medication abortion in different regions of the state and when administered via telemedicine or standard. There are some weaknesses. Overall the paper could be shortened by about 50%. There are places where the writing should be more succinct.

Use the Green Journal's writing guide to assist with writing a good discussion. edmgr.ovid.com/ong/accounts/guidetowriting.pdf

1. The abstract should clearly include statements of the study design, primary outcome.

2. Lines 73-76 - very broad objectives, Were you evaluating safety or effectiveness? The paper would be stronger if there was a more specific selected primary objective.

Methods comments:

3. Subheadings shouldn't be necessary

4. Please clearly state the comparison groups - which states in the group of 4 and which states in all the others. Define what telemedicine abortion entails and what standard medical abortion entails.

5. Line 99: How was abortion effectiveness defined?

6. Lines 125-127: This is a major weakness - to state that reaspiration is an outcome but then expect to not have a high follow up rate.

7. Line 211 - this is a high lost to follow up rate for a rare outcome (reaspiration)

8. Line 219 - referred by whom to where?

9. Lines 224-232: This section needs to written more clearly so readers will understand that you were trying to account for the high lost to follow up in a study evaluating a rare outcome.

10. Line 259: Please be clear that this study is about women and not just data. The statement that you found it safe and

effective is far reaching. The opening part of the discussion needs to put in context the locations/states.

11. Lines 255-263: Readers would learn more if there was comparing and contrasting to other areas in medicine that telemedicine is using and comparing the safety of medication abortion to the safety of those other medicine disciplines.

12. Lines 258-263: These statements are too broad. Can you state specifically which states? IF there was such a difference between states should there have been more comparison between states as well as between the main two groups of telemedicine or in person.

13. Table 1: here is too much information. The all column can be removed. The use of standard instead of in-person is confusing and will make it hard for readers not familiar with the details of abortion services to follow the main concepts of the paper.

14. Table 1 - remove the SD/& column - just use the standard N(&) at the top of the columns.

15. Table 1 - is age really normally distributed. For generalizability using categories for age or median and IQR would convey a lot more information.

16. Table 2 - this table must include information about follow up - not the suppositional follow up but true follow up using the standard of care approaches that PPFA has in the MS&G.

Reviewer #2: Thank you for continuing to expand this important body of research. I would love to see prospective data that makes an active attempt to follow up with patients, particularly patients who don't follow up and those who don't have successful procedures. I think these peoples experiences are key in stifling concerns related to the supposed "unknown dangers" of medication abortion.

Reviewer #3: Dr Kohn and colleagues present findings from a retrospective assessment of telemedicine expansion services at 26 health centers in 4 locations across the US. The four states were chosen 2/2 having a complete year of data for evaluation. This included nearly 6000 MAB pts, 12.4% of which received tele-MAB. Provision of telemab was identical for each state.

The outcomes assessed included effectiveness defined as rate of ongoing pregnancy or requiring aspiration, and adverse events. Pts could have been included more than once as each ab episode was the identified unit.

Effectiveness was assessed with bi and multivariate analyses - telemab vs traditional mab.
Sensitivity analysis was performed for missing data using previously published rates. The estimated rate of failure was calculated for the entire population (including those with unknown outcomes) and compared to the population of only those with known outcomes.

Adverse events were captured in the standard PP QI reporting system and captured ectopic, hospitalization, ED or outside visit, transfusion, infection requiring IV Abx, allergy, aspiration if in hospital or ED, and death.

The tele-MAB and traditional MAB groups were different in race/ethnicity, insurance and parity. Tele-mab was also slightly later gestational age, but not clinically significant. 75% of all pts had f/u documentation. F/U did appear to be differential for telemab (less frequently completed f/u) and traditional mab in the overall cohort, but the authors note that it varied by states with some states seeing higher f/u in the telemab group.

The findings note that ongoing pregnancy was identified in 73 (1.6%) with only 2 in the telemab group. 4% underwent aspiration and only 6 (N-188) were telemab patients. Sensitivity analysis attenuated but did not eliminate the significance of the differences.

There were 77 adverse events identified, only 16 of which were determined to be clinically significant. Of the 16, 1 was in the telemab group.

Overall this is a very well written and informative addition to the literature. It was well sourced and will be helpful as more states face increasing restrictions on access. The authors did a good job of identifying their strengths and weaknesses. The conformity of MAB protocol and EMR across states was particularly important. The use of sensitivity analysis was appreciated to address the nearly 25% for whom no outcome data was available.

I have only a few comments and suggestions. It would be nice to see what the f/u protocol was. For example if patients did not return, were they called> sent a letter? None of the above? Also, can you clarify if the expansion of services was

under a research protocol or was the IRB approval simply for the retrospective assessment of what was routinely collected data?

Reviewer #4: This is a well written and carefully conducted study regarding the safety and effectiveness of telemedicine for medication abortion. As the authors note, it adds to a small but important literature on this topic, which was previously limited to a study of such procedures in Iowa. The paper might be strengthened if the following were addressed:

1. There is, obviously, a significant difference in the percentage of patients who were lost to follow up when comparing telemedicine and standard care. While the authors mention this and adjust their analyses to account for this difference, they do not take head on the ways that the telemedicine approach might have prompted this or the degree to which such loss to follow up might be harmful or not. Perhaps, given the statistics, the low follow up numbers are not a concern, but tackling this from an exclusively statistical standpoint leaves one wondering what happened to the nearly 40% of women who did not return within 45 days and how strong these data are as an assurance that this is a reasonably safe approach.

2. I can imagine that lack of continuity (or loss to follow up) is a common critique encountered by those who advocate for or practice telemedicine. How has this been addressed in other contexts where telemedicine is provided? Attending to the broader literature on telemedicine might be useful here.

3. The authors mention that there are inter-state differences in follow up. It might be useful to include a table or graph that displays these data points.

4. The authors bring up in the discussion the problem of abortion deserts and that there are associated burdens and potential harms. This point deserves more attention, perhaps in the discussion section. The laws that have been put in place to restrict abortion access have primarily (if disingenuously) argued that their goal is improved patient safety. Of course, data do not support that contention and the degree to which this study directly contradicts such arguments should be made explicit.

5. It would also be useful for readers to know how widespread the use of telemedicine for abortion is as well as the nature of restrictions on it (e.g., laws in 17? states requiring that providers be in the physical presence of patients when prescribing abortion-inducing drugs) and whether they are based on the absence of safety data.

STATISTICAL EDITOR COMMENTS:

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

Table 1 and lines 152-158: Since the data exists for all women, should statistically compare (1) the complete cohorts for standard and for telemedicine and (2) compare the cohorts of those not lost to follow-up and (3) those lost to follow-up to gain insight as to (1) baseline differences that could potentially confound direct comparison of the standard vs telemedicine groups and (4) differences in those followed-up vs lost to follow-up which potentially could have biased the results. This is important for both cohorts, but especially for the telemedicine cohort, which had ~ 40% loss to follow-up.

Table 2: The counts of adverse events among the telemedicine cohort are too few to allow for adjustment for any covariates. Regarding the statements about Table 1, there may be other covariates that potentially could have confounded the results that might have to be considered.

Table 3: Although these calculations are mathematically correct, there was little power to discern differences, given the small counts and possibly inherent differences in the two cohorts. Should include the incidence (with CIs) for the first row "Any major adverse event or ED visit with treatment". Since there loss of follow-up data, are outcomes for all 5,952 women known, or should the denominators be altered? Perhaps a flow diagram would be informative.

General: The limitations section needs additional discussion re: possible bias due to different cohorts, differential loss of follow-up and low power to discern differences in rare adverse outcomes, not just for States, but for all aggregated data.

EDITOR'S 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 précis is a single sentence of no more than 25 words, written in the present tense and stating the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstracts conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Precis should be the "hook" for people who scan the Table of Contents to see what to read. Don't tell us "findings from the study"...tell us something like "Medication abortion provided via telemedicine is effective" or something like that. The "safety" issue needs to be dealt with as suggested by your reviewers.

- Which telemedicine patients? You state that you did a comparison between "groups" but in your methods section you only describe the telemedicine group. You don't say anything about your "standard" group. You also need to say something about how you did follow up.

- should be a colon.

- This is called a primacy claim: yours is the first, biggest, etc…In order to assert that, you need to provide the search terms used and the data base (s) searched (PubMed, Google Scholar, etc) to substantiate the claim. Otherwise, it needs to be deleted. It wouldn't belong in the abstract anyway, so make sure you address this in the manuscript body.

- As noted in my comments about the abstract, I think I'm missing something here. You don't say anything about the patients who got standard treatment-your comparison group. I am unclear about your description here. You tell us that patients (presumably including the telemedicine cohort) come to a PP health center. If they can do that, why would any of them get telemedicine counseling? Do some of your centers have a provider that can administer the mifepristone but not do the counseling? I thought that mifepristone needs to be administered by a clinician. Please tell us more about which patients got telemedicine (and why) and which got standard.

- by whom?

- were you able to determine any information about patients who may have gone outside of PP health center directly for care?

- In both the abstract and the paper, please provide absolute numbers as well as which ever effect size you are reporting (if appropriate) + Confidence intervals. P values may be omitted for space concerns. We strongly prefer CI's as they give more information about strength of association than do P values. 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).

- Can you please present some data that allows us to assess whether the women for whom there is no follow up are different, based on your available data, than the ones who did get follow up? This is particularly important since your follow up rates were so different between groups.

- In your discussion, I hope you will discuss this difference. Does it make sense that medication abortion would be more effective than standard or is this difference more likely due to lack of ascertainment (missing data) in the telemedicine group? Given the differences in follow up and the biology of this, it seems much more likely that its an ascertainment issue.

- your rates are about double this. Why?

- Again, due to differences in follow up rates, I'm not sure you can draw any strong conclusions from this result in your discussion section.

- please delete these in revision--the tables are not placed in the flow of the paper but are on the same page, placed due to copy editing needs adjacent to where the data are discussed in results. I've also struck through your subheadings, as we don't use those.

- The discussion of safety needs to be softened given statistical editor and other reviewers.

- Your ongoing pregnancy rate that you know about is about 2x higher than published rate. This needs to be addressed.

- please provide CI's.

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. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Materials and Methods section, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB website outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Materials and Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in the manuscript.

5. 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.

6. 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.

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

8. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

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

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

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

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

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

12. Line 61: We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

13. 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.

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/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.

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 Mar 29, 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

_____

April 5, 2019

Dear Editors:

We are pleased to submit the attached revised manuscript for publication in *Obstetrics & Gynecology*. Entitled "Safety and effectiveness of medication abortion provided via telemedicine in four U.S. states," this original research article describes the results an evaluation of medication abortion provided via telemedicine compared to standard medication abortion at Planned Parenthood health centers. While the existing evidence base in the United States is robust, it is limited to the state of Iowa. This study extends the telemedicine for medication abortion delivery model across four geographically-diverse states: Alaska, Idaho, Nevada, and Washington.

This program and its evaluation was funded by a private grant from an anonymous foundation. The funder had no role in the study design, implementation, analysis, manuscript preparation, or the decision to submit for publication. This study was reviewed and approved by the Allendale Investigational Review Board. The authors report no conflicts of interest.

Below you will find a detailed response to the reviewer comments. We thank the reviewers and editors for their thoughtful review and believe that the manuscript is now stronger as a result of their suggestions. We look forward to hearing the results of your review and are available to respond to any questions that the reviewers may have. Thank you in advance.

Sincerely,

Julia E. Kohn, PhD, MPA

[redacted]

Detailed Response to Reviewers:

REVIEWER COMMENTS:

Reviewer #1:

Overall: This is an original research report about medication abortion in different regions of the state and when administered via telemedicine or standard. There are some weaknesses. Overall the paper could be shortened by about 50%. There are places where the writing should be more succinct.

Thank you for your thoughtful and thorough review. While we have made efforts to tighten up the manuscript, the reviewers' requests for additional information about telemedicine and abortion resulted in a manuscript of similar length. We hope that the additional information will be helpful to readers who are less familiar with telemedicine and abortion access more broadly.

Use the Green Journal's writing guide to assist with writing a good discussion.
edmgr.ovid.com/ong/accounts/guidetowriting.pdf

We have revised the Discussion section and incorporated the reviewers' comments and questions.

1. The abstract should clearly include statements of the study design, primary outcome.

We have addressed this in the abstract and in the methods section.

2. Lines 73-76 - very broad objectives, Were you evaluating safety or effectiveness? The paper would be stronger if there was a more specific selected primary objective.

We were assessing outcomes related to both safety and effectiveness, but doing so in comparison to standard medication abortion provided at Planned Parenthood health centers in these same states. We have clarified this language in the abstract, introduction, and methods sections. No single objective or outcome was considered primary for the purposes of this retrospective study.

Methods comments:

3. Subheadings shouldn't be necessary.

These have now been removed.

4. Please clearly state the comparison groups - which states in the group of 4 and which states in all the others. Define what telemedicine abortion entails and what standard medical abortion entails.

We have now clearly outlined what telemedicine abortion entails and clarified that we compared those who received medication abortion via telemedicine versus those who received medication abortion via standard provision in Planned Parenthood health centers in the same four states. (Lines 94-101 and 110-112)

5. Line 99: How was abortion effectiveness defined? Given this question we have now addressed effectiveness earlier in the paper, including listing the effectiveness outcomes (Line 113) and adding "defined as no reported ongoing pregnancy nor receipt of or referral for aspiration abortion" (Line 124).

6. Lines 125-127: This is a major weakness - to state that reaspiration is an outcome but then expect to not have a high follow up rate. We acknowledge that this is a limitation of the retrospective nature of the study. We did not have any set expectations for follow-up rates, nor did we hypothesize that the groups would vary inherently in terms of follow-up. We acknowledge that any study relying on retrospective electronic health record data with no active research follow-up protocol to ascertain study outcomes has limitations.

7. Line 211 - this is a high lost to follow up rate for a rare outcome (reaspiration) We acknowledge that this is a limitation of the study. We have also addressed follow up as a limitation in the discussion.

8. Line 219 - referred by whom to where? This means a patient was referred by Planned Parenthood to an outside provider, such as another local abortion clinic outside of the Planned Parenthood network. The participating health centers documented such referrals in a structured field in the EHR. Self-referrals by the patient are also captured in the chart or in AE reports if the patient or outside provider communicates this to the original clinic site. This is described at Lines 158-160 and now also at 190-192.

9. Lines 224-232: This section needs to written more clearly so readers will understand that you were trying to account for the high lost to follow up in a study evaluating a rare outcome. Thank you for this feedback. We have now addressed this explicitly at Line 247 in addition to the original text in the Methods section (now at Lines 174-177).

10. Line 259: Please be clear that this study is about women and not just data. The statement that you found it safe and effective is far reaching. The opening part of the discussion needs to put in context the locations/states. This has now been changed to "patients". We have also revised this section of the discussion in light of reviewers' feedback.

11. Lines 255-263: Readers would learn more if there was comparing and contrasting to other areas in medicine that telemedicine is using and comparing the safety of medication abortion to the safety of those other medicine disciplines.

We have looked at the literature and did not find comparable examples of studies investigating services like this model that also included a comparison group. Unlike in the present model, it is often follow-up care after an initial in-person procedure or support with chronic conditions that is delivered via telemedicine. In the present study, it is the initial "procedure" itself where telemedicine is utilized. An example we could find – Blozik et al. (2011) investigation of the effectiveness of providing UTI treatment via telemedicine – did not include a direct comparison with similar care provided in person. The authors did state that their findings were consistent with literature published for in-person UTI treatment. Another example we found assessing treatment for minor injuries via telemedicine did include a comparison group and found no significant differences between groups (Benger et al. 2004); however, the primary study outcome was not the effectiveness of the treatment, but the congruence of clinical assessments completed via telemedicine compared to in-person care. A systematic review of telemedicine intervention effectiveness highlighted the need for more large-scale, rigorous research in this area (Ekeland et al.

2010). We agree this would be an interesting area for future research or exploration. See below for cited telemedicine references:

> Blozik, E., Sommer-Meyer, C., Cerezo, M., & von Overbeck, J. (2011). Effectiveness and safety of telemedical management in uncomplicated urinary tract infections. Journal of telemedicine and telecare, 17(2), 78.
>
> Benger, J. R., Noble, S. M., Coast, J., & Kendall, J. M. (2004). The safety and effectiveness of minor injuries telemedicine. Emergency medicine journal, 21(4), 438-445.
>
> Ekeland, A. G., Bowes, A., & Flottorp, S. (2010). Effectiveness of telemedicine: a systematic review of reviews. *International journal of medical informatics*, *79*(11), 736-771.

12. Lines 258-263: These statements are too broad. Can you state specifically which states? IF there was such a difference between states should there have been more comparison between states as well as between the main two groups of telemedicine or in person.

We have tempered these statements and clarified the states. This retrospective study using administrative data did not have specific numeric goals and was not powered to assess differences by state. We have also added an acknowledgement that the lack of sufficient sample sizes to permit state comparisons in the limitations of this study. (Line 300)

13. Table 1: here is too much information. The all column can be removed. The use of standard instead of in-person is confusing and will make it hard for readers not familiar with the details of abortion services to follow the main concepts of the paper.

We have removed the suggested columns in Table 1.

We use the term “standard” medication abortion rather than “in-person” given that even telemedicine patients are technically in a health center at the time of medication abortion, they are just not with the doctor/clinician in person. We therefore think it would be potentially misleading to use in-person and have opted to use “standard” throughout. While neither term is ideal, we want to distinguish this from other forms of telemedicine where patients may receive care in their homes or entirely outside of a clinic setting.

14. Table 1 - remove the SD/& column - just use the standard N(&) at the top of the columns. Revised.

15. Table 1 - is age really normally distributed. For generalizability using categories for age or median and IQR would convey a lot more information. We have revised Table 1 to include a categorical breakdown of patient age in Table 1. Thank you.

16. Table 2 - this table must include information about follow up - not the suppositional follow up but true follow up using the standard of care approaches that PPFA has in the MS&G.

Revised. Thank you. In light of this comment and other reviewers’ feedback, we have revised Table 2 significantly. Table 2 is now broken out into Tables 2a and 2b.

Table 2a, now titled “Observed abortion outcomes among medication abortion patients with follow-up data within 45 days of mifepristone,” shows the study outcomes by group only for those with known outcomes. We have also included a note listing the LTFU values and %s for each group, acknowledging that there was indeed a difference in follow-up between groups.

Table 2b, titled “Estimated abortion outcomes among all medication abortion patients applying published rates to those lost-to-follow-up,” shows the results of our sensitivity analyses applying published rates of ongoing pregnancy and aspiration procedure from Chen et al. (2015). It is our hope that showing these tables side-by-side or in proximity to each other will enable readers to better assess the potential impact of loss-to-follow up on the findings. While the results remain similar in direction and significance, the estimated magnitude of the differences between groups is attenuated.

Reviewer #2:

Reviewer #2: Thank you for continuing to expand this important body of research. I would love to see prospective data that makes an active attempt to follow up with patients, particularly patients who don't follow up and those who don't have successful procedures. I think these peoples experiences are key in stifling concerns related to the supposed "unknown dangers" of medication abortion.

Thank you for taking the time to review. We hope to continue research in this area, including prospective studies of new models of care.

Reviewer #3:

Reviewer #3: Dr Kohn and colleagues present findings from a retrospective assessment of telemedicine expansion services at 26 health centers in 4 locations across the US. The four states were chosen 2/2 having a complete year of data for evaluation. This included nearly 6000 MAB pts, 12.4% of which received tele-MAB. Provision of telemab was identical for each state.

The outcomes assessed included effectiveness defined as rate of ongoing pregnancy or requiring aspiration, and adverse events. Pts could have been included more than once as each ab episode was the identified unit.

Effectiveness was assessed with bi and multivariate analyses - telemab vs traditional mab.

Sensitivity analysis was performed for missing data using previously published rates. The estimated rate of failure was calculated for the entire population (including those with unknown outcomes) and compared to the population of only those with known outcomes.

Adverse events were captured in the standard PP QI reporting system and captured ectopic, hospitalization, ED or outside visit, transfusion, infection requiring IV Abx, allergy, aspiration if in hospital or ED, and death.

The tele-MAB and traditional MAB groups were different in race/ethnicity, insurance and parity. Tele-mab was also slightly later gestational age, but not clinically significant. 75% of all pts had f/u documentation. F/U did appear to be differential for telemab (less frequently completed f/u) and traditional mab in the overall cohort, but the authors note that it varied by states with some states seeing higher f/u in the telemab group.

The findings note that ongoing pregnancy was identified in 73 (1.6%) with only 2 in the telemab group. 4% underwent aspiration and only 6 (N-188) were telemab patients. Sensitivity analysis attenuated but did not eliminate the significance of the differences.

There were 77 adverse events identified, only 16 of which were determined to be clinically significant. Of the 16, 1 was in the telemab group.

Overall this is a very well written and informative addition to the literature. It was well sourced and will be helpful as more states face increasing restrictions on access. The authors did a good job of identifying their strengths and weaknesses. The conformity of MAB protocol and EMR across states was particularly important. The use of sensitivity analysis was appreciated to address the nearly 25% for whom no outcome data was available.

I have only a few comments and suggestions. It would be nice to see what the f/u protocol was. For example if patients did not return, were they called> sent a letter? None of the above? Also, can you clarify if the expansion of services was under a research protocol or was the IRB approval simply for the retrospective assessment of what was routinely collected data?

First, thank you for your thoughtful and thorough review. In terms of follow-up protocol, Planned Parenthood affiliates must follow standard protocols of a minimum of one attempt (via letter or HIPAA compliant secure messaging system) to contact patients following medication abortion if they do not complete follow-up. These were part of standard of care, not study procedures. No additional active follow-up was conducted for research purposes. (This is acknowledged at Line 313)

The implementation of telemedicine for medication abortion was a service expansion, not itself part of a research protocol. Participating affiliates chose to offer this service and received operational and technology support to do so. The research, and IRB approval for such, was for retrospective analyses of administrative data/records collected during routine care. We have added the following sentence to the Methods section for clarity at Line 116: “This retrospective analysis of routinely-collected administrative data study was reviewed and approved by the Allendale Investigational Review Board.”

Reviewer #4:

Reviewer #4: This is a well written and carefully conducted study regarding the safety and effectiveness of telemedicine for medication abortion. As the authors note, it adds to a small but important literature on this topic, which was previously limited to a study of such procedures in Iowa. The paper might be strengthened if the following were addressed:

1. There is, obviously, a significant difference in the percentage of patients who were lost to follow up when comparing telemedicine and standard care. While the authors mention this and adjust their analyses to account for this difference, they do not take head on the ways that the telemedicine approach might have prompted this or the degree to which such loss to follow up might be harmful or not. Perhaps, given the statistics, the low follow up numbers are not a concern, but tackling this from an exclusively statistical standpoint leaves one wondering what happened to the nearly 40% of women who did not return within 45 days and how strong these data are as an assurance that this is a reasonably safe approach.

First, thank you for your thoughtful and thorough review. Though the follow-up rates in this study were higher than typical for medication abortion generally (for example, see discussion by Grossman et al. 2004), this point is well taken. We have now added the following text at Lines 291-294: "It is possible, however, that meeting with a clinician remotely rather than in person may reduce one's likelihood to return for a follow-up visit. Nevertheless, there is no biologically plausible reason that medication abortion would be appreciably different with respect to safety or effectiveness given an identical medication regimen."

> (Grossman, D., Ellertson, C., Grimes, D. A., & Walker, D. (2004). Routine follow-up visits after first-trimester induced abortion. Obstetrics & Gynecology, 103(4), 738-745.)

2. I can imagine that lack of continuity (or loss to follow up) is a common critique encountered by those who advocate for or practice telemedicine. How has this been addressed in other contexts where telemedicine is provided? Attending to the broader literature on telemedicine might be useful here. We have not found examples in the literature of studies specifically exploring continuity of care in the telemedicine context. Interestingly, most references to this concept in the telemedicine literature hypothesize that telemedicine would actually promote better continuity of care, especially given that telemedicine is often used specifically for follow-up care. For example, telemedicine can enable patients to connect with specialist providers via telemedicine that may be too far away to visit in-person for care following a procedure. (See also response to Reviewer #1 above regarding broader telemedicine literature.)

3. The authors mention that there are inter-state differences in follow up. It might be useful to include a table or graph that displays these data points. Thank you for this suggestion. Unfortunately, when we break down the numbers by both service type and by state, the numbers become rather small within cells and therefore do not add much clarity or meaningful information to the reader.

4. The authors bring up in the discussion the problem of abortion deserts and that there are associated burdens and potential harms. This point deserves more attention, perhaps in the discussion section. The laws that have been put in place to restrict abortion access have primarily (if disingenuously) argued that their goal is improved patient safety. Of course, data do not support that contention and the degree to which this study directly contradicts such arguments should be made explicit.

Thank you for this suggestion. We have added the following sentence to the Discussion at Line 338: "To the extent that state bans on telemedicine for abortion rest upon arguments of improved patient safety, the findings of this and previous studies do not support such contentions."

5. It would also be useful for readers to know how widespread the use of telemedicine for abortion is as well as the nature of restrictions on it (e.g., laws in 17? states requiring that providers be in the physical presence of patients when prescribing abortion-inducing drugs) and whether they are based on the absence of safety data.

Unfortunately, we cannot speak to the use of telemedicine for medication abortion outside of the Planned Parenthood network as we are not privy to information about other providers' practices. Indeed 17 states require that the clinician providing a medication abortion be physically present during the procedure, thereby prohibiting the use of telemedicine to prescribe medication for abortion remotely, despite absence

of data to support these bans. The only studies of this in the U.S. — the previous study in Iowa and the present study — do not provide any evidence to support such bans.

STATISTICAL EDITOR COMMENTS:

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

Table 1 and lines 152-158: Since the data exists for all women, should statistically compare (1) the complete cohorts for standard and for telemedicine and (2) compare the cohorts of those not lost to follow-up and (3) those lost to follow-up to gain insight as to (1) baseline differences that could potentially confound direct comparison of the standard vs telemedicine groups and (4) differences in those followed-up vs lost to follow-up which potentially could have biased the results. This is important for both cohorts, but especially for the telemedicine cohort, which had ~ 40% loss to follow-up.

First, thank you for your thorough review. We ran additional multivariable regression models adjusting for all covariates that were associated with loss-to-follow-up (e.g. insurance, race/ethnicity, and parity). For the aspiration outcome, the effect of telemedicine was slightly attenuated (AOR=0.33, 95% CI 0.2, 0.54). For the ongoing pregnancy outcome, the effect of telemedicine was comparable (AOR=0.22, 95% CI 0.12, 0.41). In both models, no covariates excepting gestational age (which we had chosen to adjust for a priori) were significantly associated with the effectiveness outcomes.

To address this comment, we added the following text at Lines 255-258: “We also ran additional multivariable models adjusting for covariates found to be associated with loss-to-follow-up in bivariate models (e.g. insurance, race/ethnicity, and parity); none, excepting gestational age, was significantly associated with the effectiveness outcomes (results not shown).”

Table 2: The counts of adverse events among the telemedicine cohort are too few to allow for adjustment for any covariates. Regarding the statements about Table 1, there may be other covariates that potentially could have confounded the results that might have to be considered.

Please see the response to the previous comment above. The only covariate we adjusted for (in Table 2) was gestational age, which was determined a priori based on the literature. We cannot account for any unobserved variables as this study relied on existing data collected during routine clinical charting.

Table 3: Although these calculations are mathematically correct, there was little power to discern differences, given the small counts and possibly inherent differences in the two cohorts. Should include the incidence (with CIs) for the first row "Any major adverse event or ED visit with treatment". Since there loss of follow-up data, are outcomes for all 5,952 women known, or should the denominators be altered? Perhaps a flow diagram would be informative.

This point is well taken. While we conducted Fisher’s exact tests, the outcomes are rare and therefore absolute values will always be quite small. This retrospective study did not have any particular target numbers and was not adequately powered to detect differences in these rare outcomes. Nevertheless, we think it is useful to present this information to readers. We have removed the p values from the Table.

Regarding the denominator, we used the full sample of 5952 medication abortion patients as all of these had an opportunity to have an adverse event reported. Whether or not a patient returns to a PP health center, if she or an outside provider communicates with the health center about an adverse event occurrence, this is captured here. Therefore, we included the full sample. For example, a patient may never return to the PP health center (i.e. have no EHR follow-up data) but may present to an emergency department and notify the PP health center to make them aware of this, in which case an AE report is submitted by the PP health center to PPFA. The same is true if an external provider contacts a PP health center with information about a patient. So we have used the full universe of patients for the AE analysis.

As suggested, we have added 95% CIs to the first line, which is in essence a “roll up” category of all adverse events. Per your suggestion, we limited this to the first row only, rather than attempting to include CIs for every row and cluttering up the table despite very low numbers. We also removed the p values.

Furthermore, in light of this comment and other reviewers’ feedback, we have revised Table 2 significantly. Table 2 is now broken out into Tables 2a and 2b.

Table 2a, now titled “Observed abortion outcomes among medication abortion patients with follow-up data within 45 days of mifepristone,” shows the study outcomes by group only for those with known outcomes. We have also included a note listing the LTFU values and %s for each group, acknowledging that there was indeed a difference in follow-up between groups.

Table 2b, titled “Estimated abortion outcomes among all medication abortion patients applying published rates to those lost-to-follow-up,” shows the results of our sensitivity analyses applying published rates of ongoing pregnancy and aspiration procedure from Chen et al. (2015). It is our hope that showing these tables side-by-side or in proximity to each other will enable readers to better assess the potential impact of loss-to-follow up on the findings. While the results remain similar in direction and significance, the estimated magnitude of the differences between groups is attenuated.

General: The limitations section needs additional discussion re: possible bias due to different cohorts, differential loss of follow-up and low power to discern differences in rare adverse outcomes, not just for States, but for all aggregated data. We have attempted to address this, both in the limitations in the discussion section and throughout the manuscript. Thank you.

EDITOR'S COMMENTS:

- The précis is a single sentence of no more than 25 words, written in the present tense and stating the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstracts conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Precis should be the "hook" for people who scan the Table of Contents to see what to read. Don't tell us "findings from the study"...tell us something like "Medication abortion provided via telemedicine is effective" or something like that. The "safety" issue needs to be dealt with as suggested by your reviewers.

Thank you. This has now been revised.

- Which telemedicine patients? You state that you did a comparison between "groups" but in your methods section you only describe the telemedicine group. You don't say anything about your "standard" group. You also need to say something about how you did follow up.

We have added clarification to the abstract to read “Telemedicine patients visited a health center and met with a clinician via secure videoconference platform. Standard patients visited a health center and met with a clinician in-person.” (Lines 13–15) We have also added additional clarification on this to the Methods section to ensure that readers understand the telemedicine model and the comparison groups.

- should be a colon.

Revised.

- This is called a primacy claim: yours is the first, biggest, etc…In order to assert that, you need to provide the search terms used and the data base (s) searched (PubMed, Google Scholar, etc) to substantiate the claim. Otherwise, it needs to be deleted. It wouldn’t belong in the abstract anyway, so make sure you address this in the manuscript body.

We have deleted the primacy claim as it is not necessary to the article.

- As noted in my comments about the abstract, I think I'm missing something here. You don't say anything about the patients who got standard treatment-your comparison group. I am unclear about your description here. You tell us that patients (presumably including the telemedicine cohort) come to a PP health center. If they can do that, why would any of them get telemedicine counseling? Do some of your centers have a provider that can administer the mifepristone but not do the counseling? I thought that mifepristone needs to be administered by a clinician. Please tell us more about which patients got telemedicine (and why) and which got standard.

It is clear from this reviewer’s comment that we did not adequately explain the service model. In addition to the abstract, we have now done so in both the Introduction and Methods sections. Please see additional explanation below to ensure that we have adequately answered your questions:

In this telemedicine for medication abortion model, all patients visit a PP health center and are counseled and receive ultrasound from onsite clinical support staff or nurses. The only difference is that, when patients are ready for and consent to the medication abortion, the telemedicine patients meet with a clinician via videoconference to review the medications, view the lot number, answer any questions, and observe the patient taking the mifepristone. The standard patients meet with an onsite clinician in person and follow similar procedures. This is referred to as site-to-site telemedicine given that patients are still in a physical health center site, but meet “virtually” with the clinician.

A number of states have physician-only laws for abortion that require a patient to be seen by a physician, rather than an advanced practice clinician (i.e., NP, PA, CNM). Many remote health centers are unable to consistently staff remote locations with physicians, often requiring physicians to travel many hours to offer medication abortion only a few days a month, reducing access in outlying areas. Telemedicine enables them to visit a health center closer to home — and sooner — by meeting with the physician via telemedicine while receiving onsite counseling and support from trained clinical support staff or nurses. We have added this information to the text.

- by whom?

This sentence has been clarified to read: “During the video consultation the patient takes the mifepristone in view of the on-screen clinician.” (Line 97)

- were you able to determine any information about patients who may have gone outside of PP health center directly for care?

We were able to include information on any adverse events treated outside of Planned Parenthood if they were reported to the original health center (either by the patient, a hospital, or other provider). We have clarified this in the section on AEs at Lines 190-192 with the following text: “If patients seek care at a hospital or other provider this information is captured and reported if Planned Parenthood is notified by the patient or outside provider.”

- In both the abstract and the paper, please provide absolute numbers as well as which ever effect size you are reporting (if appropriate) + Confidence intervals. P values may be omitted for space concerns. We strongly prefer CI's as they give more information about strength of association than do P values. 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).

We have followed this example in both the abstract and text. Of course in the case of adjusted ORs, rather than RRs, the calculations will not work out exactly if replicated manually.

- Can you please present some data that allows us to assess whether the women for whom there is no follow up are different, based on your available data, than the ones who did get follow up? This is particularly important since your follow up rates were so different between groups.

Please see response above to Statistical Editor. We ran additional multivariable regression models adjusting for all covariates that were associated with loss-to-follow-up (e.g. insurance, race/ethnicity, and parity). For the aspiration outcome, the effect of telemedicine was slightly attenuated (AOR=0.33, 95% CI 0.2, 0.54). For the ongoing pregnancy outcome, the effect of telemedicine was comparable (AOR=0.22, 95% CI 0.12, 0.41). In both models, no covariates excepting gestational age (which we had chosen to adjust for a priori) were significantly associated with the effectiveness outcomes.

To address this comment, we added the following text at Lines 255-258: “We also ran additional multivariable models adjusting for covariates found to be associated with loss-to-follow-up in bivariate models (e.g. insurance, race/ethnicity, and parity); none, excepting gestational age, was significantly associated with the effectiveness outcomes (results not shown).”

- In your discussion, I hope you will discuss this difference. Does it make sense that medication abortion would be more effective than standard or is this difference more likely due to lack of ascertainment (missing data) in the telemedicine group? Given the differences in follow up and the biology of this, it seems much more likely that its an ascertainment issue.

Thank you for this comment, which was similar to that of Reviewer #4. We have added the following text at Lines 291-294: “It is possible, however, that meeting with a clinician remotely rather than in person

may reduce one's likelihood to return for a follow-up visit. Nevertheless, there is no biologically plausible reason that medication abortion would be appreciably different with respect to safety or effectiveness given an identical medication regimen."

- your rates are about double this. Why?

It is true that the rates of ongoing pregnancy observed in this study were higher than those reported elsewhere. Given the nature of the study design, which was purely retrospective, the rates cited in the literature are helpful guideposts but admittedly not the same as those observed in naturalistic settings with standard of care follow-up. Given this, we chose not to speculate as to the reasons for any differences. (Chen et al. 2015 report a range of ongoing pregnancy rates from 0–2.6%.)

- Again, due to differences in follow up rates, I'm not sure you can draw any strong conclusions from this result in your discussion section.

While we have left this result in the Results section to provide the results of our sensitivity analyses, we have now more fully addressed the limitations in the Discussion section.

- please delete these in revision--the tables are not placed in the flow of the paper but are on the same page, placed due to copy editing needs adjacent to where the data are discussed in results. I've also struck through your subheadings, as we don't use those.

Removed. Thank you.

- The discussion of safety needs to be softened given statistical editor and other reviewers.

We have tempered these statements to be clear that they are in comparison to standard provision of medication abortion. Thank you.

- Your ongoing pregnancy rate that you know about is about 2x higher than published rate. This needs to be addressed.

It is true that the rates of ongoing pregnancy observed in this study were higher than those reported elsewhere. Given the nature of the study design, which was retrospective, the rates cited in the literature are helpful guideposts but admittedly not the same as those observed in naturalistic settings with standard of care follow-up. Given this, we chose not to speculate as to the reasons for any differences. (Chen et al. 2015 report a range of ongoing pregnancy rates from 0–2.6%.)

- please provide CI's.

As suggested by the statistical editor, we have added 95% CIs to the first line, which is in essence a "roll up" category of all adverse events. Per their suggestion, we limited this to the first row only, rather than attempting to include CIs for every row and cluttering up the table despite very low numbers.

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. We choose to opt-in.

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.

Agreed.

4. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Materials and Methods section, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB website outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Materials and Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in the manuscript.

This is provided at Line 117.

5. 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 https://urldefense.proofpoint.com/v2/url?u=http-3A__ong.editorialmanager.com&d=DwIGaQ&c=M9Y9dUXA_fD4PBleyTV_Lw&r=yXBvtbxT90bYzeyD7E67K9VQ2oOczpANXnPKG3iWna0&m=cJjNYH9ui0BuRxZs8o53zlzjUgBCeGK_3Hg9hm5awAw&s=0hre-OjscoW3hqnrR_j4Gtavrm-gqKlYOjYIJjIE0TI&e=. 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.

We have now included a TREND (Transparent Reporting of Evaluations with Non-Randomized Designs) Statement checklist, which we believe is most appropriate for the present study.

6. 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://urldefense.proofpoint.com/v2/url?u=https-3A__www.acog.org_About-2DACOG_ACOG-2DDepartments_Patient-2DSafety-2Dand-2DQuality-2DImprovement_reVITALize&d=DwIGaQ&c=M9Y9dUXA_fD4PBleyTV_Lw&r=yXBvtbxT90bYzeyD7E67K9VQ2oOczpANXnPKG3iWna0&m=cJjNYH9ui0BuRxZs8o53zlzjUgBCeGK_3Hg9hm5awAw&s=CRmZdfwboUJCVUGR8-RKBJcaTxJwTW_0z9M0H0wvNlc&e=. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

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

We confirm that our manuscript is well within these limits (~3300 words, 20 pages).

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.

Confirmed.

* 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).

N/A

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

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

The abstract is 300 words without headings.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at https://urldefense.proofpoint.com/v2/url?u=http-3A__edmgr.ovid.com_ong_accounts_abbreviations.pdf&d=DwIGaQ&c=M9Y9dUXA_fD4PBleyTV_Lw&r=yXBvtbxT90bYzeyD7E67K9VQ2oOczpANXnPKG3iWna0&m=cJjNYH9ui0BuRxZs8o53zlzjUgBCeGK_3Hg9hm5awAw&s=hUFqguYjZw6e6BP7aDKgngpE1Ikv8a3aVDJGguOx_Ck&e=. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement. Now only used to express mathematical calculations per editor's example.

12. Line 61: We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit. Removed.

13. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: https://urldefense.proofpoint.com/v2/url?u=http-3A__edmgr.ovid.com_ong_accounts_table-5Fchecklist.pdf&d=DwIGaQ&c=M9Y9dUXA_fD4PBleyTV_Lw&r=yXBvtbxT90bYzeyD7E67K9VQ2oOczpANXnPKG3iWna0&m=cJjNYH9ui0BuRxZs8o53zlzjUgBCeGK_3Hg9hm5awAw&s=IITw0pBfkydr4h91IT557EIZELQrw4OU3aSKWpmzhZc&e=.

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 https://urldefense.proofpoint.com/v2/url?u=http-3A__links.lww.com_LWW-2DES_A48&d=DwIGaQ&c=M9Y9dUXA_fD4PBleyTV_Lw&r=yXBvtbxT90bYzeyD7E67K9VQ2oOcz

pANXnPKG3iWna0&m=cJjNYH9ui0BuRxZs8o53zlzjUgBCeGK_3Hg9hm5awAw&s=j4xxA6eHZFV0xTi16_YxU8slCi4Pby0-5HLmfBQQ2U8&e=. The cost for publishing an article as open access can be found at https://urldefense.proofpoint.com/v2/url?u=http-3A__edmgr.ovid.com_acd_accounts_ifauth.htm&d=DwIGaQ&c=M9Y9dUXA_fD4PBleyTV_Lw&r=yXBvtbxT90bYzeyD7E67K9VQ2oOczpANXnPKG3iWna0&m=cJjNYH9ui0BuRxZs8o53zlzjUgBCeGK_3Hg9hm5awAw&s=ItMgbV9ri6WerBde0BwcI9kw5sj2zRl-9n38Hp3On7g&e=.

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 https://urldefense.proofpoint.com/v2/url?u=http-3A__ong.editorialmanager.com&d=DwIGaQ&c=M9Y9dUXA_fD4PBleyTV_Lw&r=yXBvtbxT90bYzeyD7E67K9VQ2oOczpANXnPKG3iWna0&m=cJjNYH9ui0BuRxZs8o53zlzjUgBCeGK_3Hg9hm5awAw&s=0hre-OjscoW3hqnrR_j4Gtavrm-gqKlYOjYIJjIE0TI&e=. 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.

From: [redacted]
To: Randi Zung
Subject: Re: Your Revised Manuscript 19-158R1
Date: Friday, April 26, 2019 1:20:59 PM
Attachments: Transparency Declaration_SIGNED_KOHN.pdf
19-158R1 ms (4-23-19v2) (2)_REVISED_KOHN_R2.docx

Dear Editors:

Thank you for the opportunity to submit the attached revised manuscript. We have made edits and revisions using track changes in the attached Word document. Below you will find our point-by-point response to the additional questions and comments. Also attached please find my signed transparency statement.

Finally, one of our co-authors, Daniel Grossman, would like to disclose one potential conflict of interest that was inadvertently left out of the initial submission. He would like to add that: "Daniel Grossman has received consulting payments from Planned Parenthood Federation of America for work related to telemedicine for medication abortion." Dr. Grossman has also completed and submitted the copyright transfer agreement separately as requested.

Please let me know if you require any additional information. We look forward to the results of your review.

Sincerely,
Julia Kohn

REVIEWER QUERIES AND AUTHOR RESPONSES (in blue):

Dear Dr. Kohn:
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.
We have reviewed and either made or amended changes as appropriate using track changes.
2. Title: "Via" was changed to "through," since it's journal style to use "via" only as it pertains to travel.
Thank you.
3. Transparency Declaration: Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained." *The manuscript's guarantor. Please provide a signed version of this statement. A blank copy is attached.
Completed. Please see attached signed agreement.
4. Daniel Grossman will need to complete our electronic Copyright Transfer Agreement, which was sent to him through Editorial Manager. Please have him check for an email from EM@greenjournal.org.
This has been completed and submitted independently by Dr. Grossman earlier this week.
5. Funding: Please provide the name of the anonymous funder. The editor prefers that this information is disclosed. The problem of an anonymous funder is the concern for Conflicts of interests. Not knowing

who the funder
The name of the funder, The Susan T. Buffett Foundation, has now been added to the title page with permission from the Foundation.
6. Precis and elsewhere: Please change the title and precis (and elsewhere if necessary) to reflect that given your large loss to follow up in the telemedicine group that your “safety” assessment is quite compromised and should be removed as a primary focus of your study.
We have now changed the title, précis, abstract, and other language throughout the manuscript to refer broadly to outcomes of medication abortion, and specifically to those outcomes measured in this study, rather than speaking about safety and effectiveness generally.

7. Abstract-Methods: The methods should be something like (assuming this is true): “This is retrospective cohort study of consecutive women treated at Planned Parenthood Clinics at 26 health centers in Alaska, Idaho, Nevada and Washington from April 2017 to March 2018. All women had on-site ultrasound, lab testing, education, counseling, and informed consent, prior to meeting with the clinician. At centers without a clinician present able to meet requirements for observed dosing with mifipristone, telemedicine was used for this treatment step. Otherwise, the on-site clinicians provided this care. Study outcomes included occurrence of ongoing pregnancy, receipt or referral for an aspiration procedure, and clinical-significant adverse events. To compare outcomes between telemedicine and standard group, we performed logistic regression accounting for gestational age and health center clustering.”
Please insert this into the manuscript if you agree. Please also review your body text to make similar wording changes as needed.

The language proposed here is not exactly accurate. We have incorporated and amended this suggested language to ensure accuracy both in the abstract and in the manuscript body. Please see the revised manuscript for slightly revised final text.

The abstract Methods section now reads:
“In this retrospective cohort study, we analyzed electronic health records for patients receiving telemedicine versus standard medication abortion at 26 health centers in Alaska, Idaho, Nevada, and Washington from April 2017–March 2018. All patients had on-site ultrasound, lab testing, counseling, and informed consent before meeting with the clinician. Telemedicine patients met with a clinician by secure videoconference platform; standard patients met with a clinician in-person. We also reviewed adverse event reports submitted during this period. Study outcomes included ongoing pregnancy, receipt of or referral for aspiration procedure, and clinically-significant adverse events. To compare outcomes between the telemedicine and standard groups, we performed logistic regression accounting for gestational age and health center clustering.”

8. Abstract-Results: Please provide a statistical assessment of differences or lack thereof (Confidence intervals) for data in the abstract. In this instance re EGA you could however just say” The mean gestational age for the two groups were similar (50.4 days telemedicine and 48.9 days for standard care).
Completed. The sentence now reads: “The mean gestational age was 50.4 days for telemedicine patients vs. 48.9 days for standard patients (PR=1.02; 95% CI 1.00–1.03).”

9. Line 63: Please make it clear here that there were differences in follow up: perhaps something like: “Follow up at the health center within 45 days of the abortion was less for telemedicine patients (60.2%) compared to standard patients (76.8) (OR, 95% CI).
Completed. The sentence now reads: “We had outcome data for 4,456 (74.9%) patients; follow up within 45 days of abortion was lower among telemedicine patients (60.2%) than standard patients (76.9%) (PR=0.83; 95% CI 0.78–0.88).”

10. Line 66: Please clarify: Are “Reaspiration” patients a subset of “ongoing pregnancy” patients? IN other words, were there 8 patients for whom the MAB was unsuccessful in the telemedicine group (2 ongoing and 6 reaspiration) or did you have 6 ongoing pregnancies, of whom 2 continued the pregnancies?
We identified 2 ongoing pregnancies in the telemedicine group, and 71 in the standard group. These are not mutually exclusive categories. Women can be counted in both groups, including aspirations performed to resolve ongoing pregnancies as well as aspiration for other reasons such as uterine debris. We have left this as-is for the abstract due to space limitations but have clarified this in the manuscript text in the Results section.
11. Line 73: As noted in my original comments, please remove the references to safety. You have too much missing data to address this. Safety needs to be taken out of title, precis and highly tempered in the conclusions of the abstract and paper.
Completed.

12. Line 98: Can you clarify that this is related to being administered the mifepristone?
This is not specific to mifepristone. This is about state-specific laws and regulations about who can provide abortions generally, whether medical or surgical. We added “whether by medication or aspiration” to the sentence in parentheses to clarify.

13. Line 121: Could you please state that this occurs at Planned Parenthood with telemedicine options do not have physicians or other clinicians who can legally administer the mifepristone in the state? Maybe say something like the following (assuming its true).
As part of medical abortion, patients are prescribed both misoprostol and mifepristone. The Food and Drug Administration requires that mifepristone be physically handed the pill(s) by a clinician allowed by the individually state law. Some states require a physician to serve this role, while others allow advanced practice providers such as nurse practitioners and physician assistants to do this. Patients seeking a medical abortion attend a Planned Parenthood health sent and receive in-person care from staff at the health center including ultrasound, lab testing, education, counseling, and informed consent, prior to meeting with the clinician. At those health centers with an available approved clinician, patients physically see the clinician. This group is considered the standard group. At those centers without an approved clinician physically present, the patient meets with a clinician virtually and on video takes the mifepristone in view of the on-screen clinician.”

The language proposed here is not entirely accurate. Whether a doctor or advanced practice clinician can provide abortion is not related to the FDA or regulation of mifespristone specifically, but rather to state laws and regulations related to abortion provision more broadly (surgical or medical) as discussed above. Therefore, we prefer not to conflate these issues here and inadvertently confuse readers.

We have amended the suggested language somewhat to ensure accuracy both in the abstract and in the manuscript body. Please see the revised manuscript for revised final text.

The text now reads:
“Medication abortion involves the provision of two medications: mifepristone and misoprostol. Currently, the U.S. Food and Drug Administration requires that mifepristone be provided only in clinics, hospitals, or medical offices under the supervision of a certified prescriber. At Planned Parenthood, patients seeking medication abortion visit a health center and receive in-person care from staff including ultrasound, lab testing, education, counseling, and informed consent prior to meeting with the clinician. At health centers with an available clinician able to provide medication abortion, patients meet with the clinician in-person. We refer to this as standard medication abortion. At participating health centers without an available clinician able to provide medication abortion on-site, the patient meets with a clinician virtually using a secure videoconference platform and takes the mifepristone in view of the on-screen clinician. We refer to this as telemedicine medication abortion. For both groups misoprostol, taken up to 48 hours later, is either dispensed at the health center or prescribed along with other auxiliary medications.”

14. Line 146: Please define “ongoing pregnancy” vis-à-vis my comments above.
Completed.
15. Line 189: Is there any reason to believe that individual patients may be resistant to medications used for medication abortions such that a failed medication abortion in the same patient in 2 instances are not independent occurrences?
We do have any reason to suspect this.
16. Line 243 and Lines 248-256: In both the abstract and the paper, please provide absolute numbers as well as whichever effect size you are reporting (if appropriate) + Confidence intervals. P values may be omitted for space concerns. We strongly prefer CI's as they give more information about strength of association than do P values. 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).”
We have removed all p values from the manuscript and tables. We have revised the abstract and manuscript text to conform with the above example and have also added an additional column to Table 1 to display prevalence ratios and corresponding CIs for differences in patient characteristics between groups. While this may be more information than the reader needs, we provided it here for your review and defer to the editors on whether to include this.

17. Line 268: Given that your rates of ongoing pregnancies were twice as high as published rates, do you think it’s reasonable to use the published rates for your loss to follow up estimates? This needs to be addressed in your discussion.
We do think it is reasonable to use this rate for the purposes of this sensitivity analysis. The systematic review by Chen et al. (2015) cites varying observed ongoing pregnancy rates ranging from 0–2.6%. The overall rate and the rates we observed in both groups fall squarely within that range. We chose to use the overall rate of 0.8% cited by Chen for the sensitivity analysis as the purpose of this additional analysis was not to try to estimate with precision the actual ongoing pregnancy rates (which is outside the scope of our study design), but to illustrate the potential effects of loss-to-follow-up on the differences between groups.

We have also added the ranges from the Chen et al. systematic review to the Methods section of the paper when discussing the sensitivity analysis in case this is helpful to readers.

18. Line 324: Can you tell us the minimum? I recall, it’s at least 1. Please include that here.
We have now clarified that: “At least one contact attempt for medication abortion patients is required of all Planned Parenthood health centers for patients who do not follow up.”
19. Table 4: Does the data in the first line need to be boldface? If so, please add a note to the footnote to indicate the reason.
No. This was simply to indicate that this is a “roll-up” category of all of the event types listed below it. We have now removed the boldface formatting.

On Tue, Apr 23, 2019 at 2:06 PM Randi Zung <RZung@greenjournal.org> wrote:

> Dear Dr. Kohn:
>
> 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: “Via” was changed to “through,” since it’s journal style to use “via” only as it pertains to travel.

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

Please provide a signed version of this statement. A blank copy is attached.

4. Daniel Grossman will need to complete our electronic Copyright Transfer Agreement, which was sent to him through Editorial Manager. Please have him check for an email from EM@greenjournal.org.

5. Funding: Please provide the name of the anonymous funder. The editor prefers that this information is disclosed. The problem of an anonymous funder is the concern for Conflicts of interests. Not knowing who the funder

6. Precis and elsewhere: Please change the title and precis (and elsewhere if necessary) to reflect that given your large loss to follow up in the telemedicine group that your “safety” assessment is quite compromised and should be removed as a primary focus of your study.

7. Abstract-Methods: The methods should be something like (assuming this is true): “This is retrospective cohort study of consecutive women treated at Planned Parenthood Clinics at 26 health centers in Alaska, Idaho, Nevada and Washington from April 2017 to March 2018. All women had on-site ultrasound, lab testing, education, counseling, and informed consent, prior to meeting with the clinician. At centers without a clinician present able to meet requirements for observed dosing with mifipristone, telemedicine was used for this treatment step. Otherwise, the on-site clinicians provided this care. Study outcomes included occurrence of ongoing pregnancy, receipt or referral for an aspiration procedure, and clinical-significant adverse events. To compare outcomes between telemedicine and standard group, we performed logistic regression accounting for gestational age and health center clustering.”

Please insert this into the manuscript if you agree. Please also review your body text to make similar wording changes as needed.

8. Abstract-Results: Please provide a statistical assessment of differences or lack thereof (Confidence intervals) for data in the abstract. In this instance re EGA you could however just say" The mean gestational ag for the two groups were similar (50.4 days telemedicine and 48.9 days for standard care).

9. Line 63: Please make it clear here that there were differences in follow up: perhaps something like: "Follow up at the health center within 45 days of the abortion was less for telemedicine patients (60.2%) compared to standard patients (76.8) (OR, 95% CI).

10. Line 66: Please clarify: Are "Reaspiration" patients a subset of "ongoing pregnancy" patients? IN other words, were there 8 patients for whom the MAB was unsuccessful in the telemedicine group (2 ongoing and 6 reaspiration) or did you have 6 ongoing pregnancies, of whom 2 continued the pregnancies?

11. Line 73: As noted in my original comments, please remove the references to safety. You have too much missing data to address this. Safety needs to be taken out of title, precis and highly tempered in the conclusions of the abstract and paper.

12. Line 98: Can you clarify that this is related to being administered the mifepristone?

13. Line 121: Could you please state that this occurs at Planned Parenthood with telemedicine options do not have physicians or other clinicians who can legally administer the mifepristone in the state? Maybe say something like the following (assuming its true).

As part of medical abortion, patients are prescribed both misoprostol and mifepristone. The Food and Drug Administration requires that mifepristone be physically handed the pill(s) by a clinician allowed by the individually state law. Some states require a physician to serve this role, while others allow advanced practice providers such as nurse practitioners and physician assistants to do this. Patients seeking a medical abortion attend a Planned Parenthood health sent and receive in-person care from staff at the health center including ultrasound, lab testing, education, counseling, and informed consent, prior to meeting with the clinician. At those health centers with an available approved clinician, patients physically see the clinician. This group is considered the standard group. At those centers without an approved clinician physically present, the patient meets with a clinician virtually and on video takes the mifepristone in view of the on-screen clinician."

14. Line 146: Please define "ongoing pregnancy" vis-à-vis my comments above.

15. Line 189: Is there any reason to believe that individual patients may be resistant to medications used for medication abortions such that a failed medication abortion in the same patient in 2 instances are not independent occurrences?

16. Line 243 and Lines 248-256: In both the abstract and the paper, please provide absolute numbers as well as whichever effect size you are reporting (if appropriate) + Confidence intervals. P values may be omitted for space concerns. We strongly prefer CI's as they give more information about strength of association than do P values. 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)."

Don't just give the p values.

17. Line 268: Given that your rates of ongoing pregnancies were twice as high as published rates, do you think it's reasonable to use the published rates for your loss to follow up estimates? This needs to be addressed in your discussion.

18. Line 324: Can you tell us the minimum? I recall, it's at least 1. Please include that here.

19. Table 4: Does the data in the first line need to be boldface? If so, please add a note to the footnote to indicate the reason.

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

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

--

Julia Kohn, PhD, MPA

[redacted]

This e-mail is for the sole use of the intended recipient(s) and contains information which is confidential and/or legally privileged. If you are not the intended recipient, you are hereby notified that any disclosure, copying, distribution, or taking of any action in reliance on the contents of this e-mail information is strictly prohibited. If you have received this e-mail in error, please immediately notify the sender by reply e-mail and destroy all copies of the original message.