

# OBSTETRICS & GYNECOLOGY



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- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)\*

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

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

**Date:** Sep 20, 2019  
**To:** "Stephanie Marie Glass Clark" [REDACTED]  
**From:** "The Green Journal" em@greenjournal.org  
**Subject:** Your Submission ONG-19-1588

RE: Manuscript Number ONG-19-1588

Effect of surgery for stress incontinence on female sexual function: A secondary analysis

Dear Dr. Glass Clark:

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 Oct 11, 2019, we will assume you wish to withdraw the manuscript from further consideration.

#### REVIEWER COMMENTS:

Reviewer #1: This is a well done secondary analysis of a large sample size examining sexual function as an important element to overall quality of life for women after surgery for urinary stress incontinence. This is a topic that is understudied and important in comprehensive patient care.

1. Is it potentially a problem to have a statistically significant difference in baseline pelvic organ prolapse types between groups when POP itself can affect sexual function? Is adjusting for POP enough to limit this confounding effect?
2. The PISQ-12 seems to assume the participant is heterosexual. Was sexuality questioned in this study to confirm that the tool would be appropriate? If not, this is a limitation that should be discussed. While I agree with what you have stated in your discussion regarding its limitations, I wonder if it also meant that some eligible participants were not included because of the heteronormative questions.
3. Follow-up rate for 12 and 24 months is a strength worth highlighting as much longitudinal data in sexual function and quality of life in general is challenging to capture due to loss to follow-up over time.

Reviewer #2: This is a secondary analysis of 2 randomized controlled trials evaluating sexual function after surgery for stress urinary incontinence. The study is well done, well written, and a comprehensive evaluation of the subject.

1. Methods: It is still unclear to me in the methods from Table 1 and Figure 1 because the numbers don't match, whether or not subjects had to be sexually active at each time point baseline, 12 months, and 24 months, or only at least 1 of those times. Line 118 states they needed to report sexual activity at ANY of the study visits. Figure 1 implies that they had to be sexually active at each time point.
2. Results/Discussion: The PISQ-12 total score ranges from 0-48? The mean change from baseline to 24 months ranges from 3.4-5.1 depending on the surgery, also reflected in Figure 2...how do we know that this is a clinically meaningful improvement as you state in the Discussion? I would be more tempered and state that sexual function didn't worsen, was likely the same overall, but did improve in some specific areas e.g. those questions having to do with incontinence and sex.
3. Table 2: Please clarify what types of prior incontinence surgery and treatment participants experienced before the trial. Also what types of concomitant surgeries were performed?

#### 4. Table 2. Subjective failure seems quite high--are these 4 treatments really that effective?

Reviewer #3: Well written secondary analysis of two multi-centered randomized trials. The TOMUS study has already been published, including the sexual function outcomes in 2012 and before this the Sister study in the early 2000s.

Strengths: A significant strength is the number of women followed following anti-incontinence procedure for up to 24 months. This highlights that anti-incontinence procedures improve incontinence related issues with sexual activity over time and that there does not appear to be a significant difference between the type of anti-incontinence procedure. An advanced secondary analysis of two well done and previously published multi-centered randomized trials.

Limitations: secondary analysis of two multi-centered randomized trials in which the sexual outcomes data has already been published. The combination of the two data sets and republishing does not add anything significantly new to the literature, though the advanced analytic evaluation is unique.

A major issue of this data is that inclusion criteria was quite generous- only requiring the patient to mark they were sexually active at a single time point (6 months prior to baseline visit, 12 or 24 months) and then only filling out the PISQ-12 once (minimal as it was a secondary outcome to begin with). In the women without PISQ-12 data, it is inappropriate to conclude anything substantial from the fact that women were reporting sexual activity. Going forward, I recommend assessing sexual activity at each time point as it is a fluid measure and may change significantly over the course of 24 months.

#### STATISTICAL EDITOR COMMENTS:

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

Table 1: Need to explain the differences in denominators for each surgical cohort, comparing baseline, 12 and 24 months post-op. If the differences from baseline to 12 months (eg, 32, 33, 74, 66) do represent significant differences from baseline. The corresponding differences from baseline to 24 months were not statistically different. If these changes represent differential loss to follow-up or differential loss due to sexual inactivity or a combination of those, then that could have introduced bias.

lines 180-182: How many of the women in each surgical cohort answered the survey questions at baseline, 12 months and 24 months? How many answered for all 3 times? The wording "at either ..." leaves open the potential for significant missing data or selective missing data by time point or by surgical cohort that could have biased the results. Need to give a complete enumeration of the completion rates.

lines 190-203: These statements need corroboration by how complete and uniform across surgical cohorts the answers to scores were.

It would also be important to determine whether completing the answers was associated with any of the baseline differences noted in Table 2, for example, by race or ethnic group, prolapse stage, concomitant surgery.

Table 4: In addition to the issues regarding completion rates at baseline, 12 and 24 months, were there differential rates of answering Q1-Q12 by time, surgical group or demographic factors which might have biased the results?

Table 5: Same question as in Table 4.

Fig 2: The error bars of 1 SD should be changed to 95% CIs and a concise explanation of the statistical significance of serial and across surgical cohort differences.

#### EDITOR COMMENTS:

1. Thank you for your submission to Obstetrics & Gynecology. In addition to the comments from the reviewers above, you are being sent a notated PDF that contains the Editor's specific comments. Please review and consider the comments in this file prior to submitting your revised manuscript. These comments should be included in your point-by-point response cover letter.

\*\*\*The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Randi Zung and she will send it by email - rzung@greenjournal.org.\*\*\*

In general, it is not at all clear to us what data you have at the different time points and how you handled missing data. The answers to these questions, raised most clearly by the statistical editor and mentioned by some of the peer reviewers, are critical in or consideration of moving the paper forward. If you cannot address these issues adequately, unfortunately we would not move the paper forward.

#### PDF Comments:

- We no longer require that authors adhere to the Green Journal format with the first submission of their papers. However, any revisions must do so. I strongly encourage you to read the instructions for authors (the general bits as well as those specific to the feature-type you are submitting). The instructions provide guidance regarding formatting, word and reference limits, authorship issues, and other things. Adherence to these requirements with your revision will avoid delays during the revision process, as well as avoid re-revisions on your part in order to comply with the formatting.
- what were the years these original studies were done?
- this should be a colon ":" instead of an m-dash.
- While P values are a central part of inference testing in statistics, when cited alone, often the strength of the conclusion can be misunderstood. Whenever possible, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone. This is true for the abstract as well as the text.
- what does PISQ measure?
- Instead of a dash, please put these in parentheses
- It is an idiosyncratic fact that at the Journal we tend to avoid the use of the word impact to imply the result of a change, preferring to limit "impact" to mean a physical blow.
- Is this a planned 2nd analysis? In your revision, please spell out the names of the trials throughout as the abbreviations won't be allowed.
- please provide the years of the studies. Also, how did you get the data?
- please state why it was exempted?
- age of 21 years
- there should be a hyphen with stress-predominant
- For clarity, women who reported NO sexual activity at -6 months through +24 months were excluded? I can see that this would exclude non-partnered women but might it not have excluded women with partners who avoided sex at all time points? This part of the methods is where all of the reviewers, including the statistical editor have major issues with the paper. To be clear, to be included women had to report sexual activity OR complete a short form, alternatively, they had to report any sexual activity AND complete a short form. Are both correct? How was sexual activity reported and recorded? Also, the issue of needing to enumerate exactly what data you have and what time points cannot be understated. From the way this reads at present, a participant could be included if they completed a short form at on visit so there could be a great deal of missing data.
- marital or partnered status?
- no retreatment for stress incontinence (behaviorial, pharmacologic or surgical).
- most readers will not be familiar with the PISQ12 questionnaire. Can you include the questions or a link to the form if you cannot reproduce the questionnaire?
- what do you mean by "condition specific sexual function"? What condition?
- ok, so here is some explanation of the PISQ-12. It needs to be put closer to when you first mention it.
- why was this limitation placed? What if due to embarrassment, etc, the woman did not have sex before she had surgery and then, after surgery, things were so much better she began having sex again? This exclusion would underestimate

possible benefits sexually of the surgery.

- why did you consider this clinically meaningful
- avoid single sentence paragraphs
- how did you handle missing data?
- no clue what these p values are referring to. What comparisons are being made? Can you provide an assessment of sexual function in women who had prolapse surgery at the same time as well as those that did not? What about hysterectomy? Did you control for that?
- Sentence starting line 208 is incomplete.
- differences between what groups?
- between what groups? Please articulate important differences here and don't just refer to the table for key points you are trying to make.
- I'm flummoxed by what you mean by "groups". Are these different surgical approaches or are the different time frames (12 and 24 months after surgery), for instance
- nor do they seem to improve after an initial gain
- Important limitation is the low degree of diversity in race among the participants.

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. 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:

- A. OPT-IN: Yes, please publish my point-by-point response letter.
- B. OPT-OUT: No, please do not publish my point-by-point response letter.

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.

Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

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

\*The manuscript's guarantor.

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

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. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%).

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](http://edmgr.ovid.com/ong/accounts/table_checklist.pdf).

#### 14. Figures

Figure 1: Please upload as a figure file to Editorial Manager.

Figure 2: Please upload as a figure file to Editorial Manager. Please upload the original figure file, we find that images pasted in Word often lose resolution.

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

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a

publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

16. If you choose to revise your manuscript, please submit your revision through Editorial Manager at <http://ong.editorialmanager.com>. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:

- \* A confirmation that you have read the Instructions for Authors (<http://edmgr.ovid.com/ong/accounts/authors.pdf>), and
- \* A point-by-point response to each of the received comments in this letter.

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 Oct 11, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD  
Editor-in-Chief

2018 IMPACT FACTOR: 4.965  
2018 IMPACT FACTOR RANKING: 7th out of 83 ob/gyn journals

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In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: <https://www.editorialmanager.com/ong/login.asp?a=r>). Please contact the publication office if you have any questions.

To the Editors of *Obstetrics & Gynecology*:

Thank you for your consideration of the following manuscript and the attached revisions. The authors intend to solely submit this manuscript to *Obstetrics & Gynecology*. This manuscript is not currently in consideration at any alternate journal and we have no intention of submitting elsewhere unless not selected for publication in this journal. I agree to full transparency regarding this study and manuscript with any forthcoming discussions of publication. This study was classified as exempt by the Virginia Commonwealth University Institutional Review Board (IRB HM20012510).

Please see the following pages for point-by-point responses to each reviewer and editors and attached is the amended manuscript with tracked changes. This letter also serves as confirmation that I have read the Instructions for Authors.

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. Signed by Stephanie Glass Clark.

Thank you again for your consideration,

Stephanie Glass Clark, M.D.

*Reviewer #1: This is a well done secondary analysis of a large sample size examining sexual function as an important element to overall quality of life for women after surgery for urinary*



*stress incontinence. This is a topic that is under-studied and important in comprehensive patient care.*

*Is it potentially a problem to have a statistically significant difference in baseline pelvic organ prolapse types between groups when POP itself can affect sexual function? Is adjusting for POP enough to limit this confounding effect?*

Thank you for this point. In the overall analysis, we feel that to adjust for prolapse as a confounding variable is sufficient in the generalized linear regression model. When looking at prolapse specific sexual function (Table 4, Q8) there was a statistically significant difference observed between surgical groups at baseline and 24 months, and the groups with higher stages of prolapse at baseline showed greater increase/improvement in prolapse specific sexual function. However, this difference is less than 0.5 and is likely not clinically meaningful.

*The PISQ-12 seems to assume the participant is heterosexual. Was sexuality questioned in this study to confirm that the tool would be appropriate? If not, this is a limitation that should be discussed. While I agree with what you have stated in your discussion regarding its limitations, I wonder if it also meant that some eligible participants were not included because of the heteronormative questions.*

This is a very important point and is a limitation of the study. We have added a response to this in the full text, see lines 280-283:

“Additionally, it limits partner-related problems to erectile dysfunction and premature ejaculation; some eligible participants may be excluded secondary to sexual preferences given the assumptions inherent to the questionnaire that the partner is male. This limits our ability to evaluate important aspects of sexual function for our patients like self-stimulation, same sex partners and sexual activity beyond vaginal penetration.”

*Follow-up rate for 12 and 24 months is a strength worth highlighting as much longitudinal data in sexual function and quality of life in general is challenging to capture due to loss to follow-up over time.*

We agree. In the strengths section, we have added emphasis to this point, see lines 274-275:

“The study is also strengthened by the number of subjects with responses out to 24 months, which is reflective of more stable, long-term quality of life metrics.”

*Reviewer #2: This is a secondary analysis of 2 randomized controlled trials evaluating sexual function after surgery for stress urinary incontinence. The study is well done, well written, and a comprehensive evaluation of the subject.*

*Methods: It is still unclear to me in the methods from Table 1 and Figure 1 because the*

numbers don't match, whether or not subjects had to be sexually active at each time point baseline, 12 months, and 24 months, or only at least 1 of those times. Line 118 states they needed to report sexual activity at ANY of the study visits. Figure 1 implies that they had to be sexually active at each time point.

Thank you for this point. In this study, subjects were included in the study if they had completed the PISQ-12 questionnaire at any study visit (BL, 12, 24 mo). We have amended Figure 1 to clarify this:

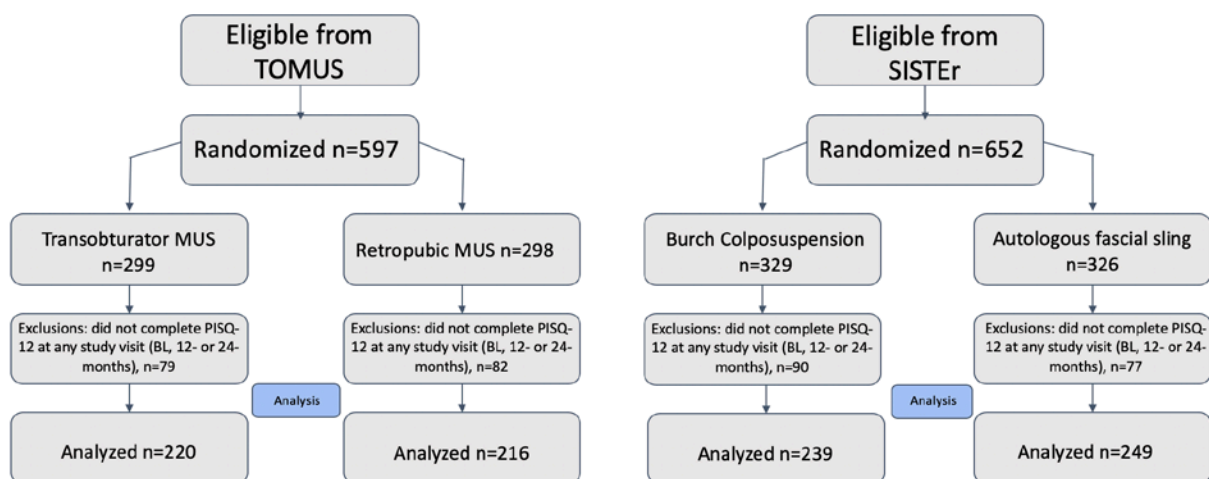


Table 1 does not include every subject from the original studies, as some subjects did not respond to the questionnaire. We included subjects with sexual inactivity for Table 1 only if they responded to the pre-PISQ-12 question asking if they had been sexually active in the preceding 6 months. If yes, they went on to answer the full PISQ-12 survey, and if no they did not have responses to the PISQ-12 and were excluded from the remaining analyses evaluating sexual function.

*Results/Discussion: The PISQ-12 total score ranges from 0-48? The mean change from baseline to 24 months ranges from 3.4-5.1 depending on the surgery, also reflected in Figure 2...how do we know that this is a clinically meaningful improvement as you state in the Discussion? I would be more tempered and state that sexual function didn't worsen, was likely the same overall, but did improve in some specific areas e.g. those questions having to do with incontinence and sex.*

We thank the reviewer for this observation. As there is no published minimal important difference for the PISQ-12, we used one-half the baseline standard deviation as a proxy to determine clinical significance. See lines 137-139 and 220-224.

(137-139) There is no minimum important difference (MID) established for the PISQ-12, thus we used one-half the baseline standard deviation to determine clinical significance.

(220-224) There is no published minimally important difference (MID) for the PISQ-12 so we conservatively estimated the MID as half the standard deviation of the baseline score.<sup>15</sup> The standard deviation of PISQ-12 at baseline is 7.08 for all surgical treatment groups. The mean scores for each treatment improved beyond this estimate for MID regardless of treatment type (**Table 3**).

*Table 2: Please clarify what types of prior incontinence surgery and treatment participants experienced before the trial. Also what types of concomitant surgeries were performed?*

Unfortunately, we do not have access to the types of prior incontinence surgery or treatments in order to comment in this paper, only that there were or were not prior surgeries performed for incontinence.

While we have access to the types of concomitant procedures performed for the TOMUS trial, the data we acquired from the NIDDK Central Repository for SISTER did not include the concomitant surgeries within the dataset. Therefore we included only those who had concomitant surgery or not.

*Table 2. Subjective failure seems quite high--are these 4 treatments really that effective?*

We agree, these rates are high, but they corroborate those published in the literature. This deserves further research in our field, particularly as we shift our focus in the field of urogynecology to patient centered outcomes and our emphasis being placed on subjective rather than objective outcomes. These were both very well done, multi-center randomized controlled trials. We have not focused on the failure rates in this study as this was outside the scope of our clinical question and the focus of the original studies.

*Reviewer #3: Well written secondary analysis of two multi-centered randomized trials. The TOMUS study has already been published, including the sexual function outcomes in 2012 and before this the Sister study in the early 2000s.*

*Strengths: A significant strength is the number of women followed following anti-incontinence procedure for up to 24 months. This highlights that anti-incontinence procedures improve incontinence related issues with sexual activity over time and that there does not appear to be a significant difference between the type of anti-incontinence procedure. An advanced secondary analysis of two well done and previously published multi-centered randomized trials.*

*Limitations: secondary analysis of two multi-centered randomized trials in which the sexual outcomes data has already been published. The combination of the two data sets and republishing does not add anything significantly new to the literature, though the advanced analytic evaluation is unique.*

*A major issue of this data is that inclusion criteria was quite generous- only requiring the patient to mark they were sexually active at a single time point (6 months prior to baseline visit, 12 or 24 months) and then only filling out the PISQ-12 once (minimal as it was a secondary outcome to begin with). In the women without PISQ-12 data, it is inappropriate to conclude anything substantial from the fact that women were reporting sexual activity. Going forward, I recommend assessing sexual activity at each time point as it is a fluid measure and may change significantly over the course of 24 months.*

We want to thank the reviewer for these comments. In subjects with data available at each study time point, we included their data in the analysis. We did not want to exclude patients who became sexually active or stopped reporting sexual activity during the study period.

#### STATISTICAL EDITOR COMMENTS:

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

*Table 1: Need to explain the differences in denominators for each surgical cohort, comparing baseline, 12 and 24 months post-op. If the differences from baseline to 12 months (eg, 32, 33, 74, 66) do represent significant differences from baseline. The corresponding differences from baseline to 24 months were not statistically different. If these changes represent differential loss to follow-up or differential loss due to sexual inactivity or a combination of those, then that could have introduced bias.*

This is annual loss of follow up seen in the study. We are attempting to show in this table that the proportion of patients who are sexually inactive is not different at each time point.

The difference in loss to follow up is a limitation of combining two trials where one study had a stronger retention rate of subjects. However, the numbers of women who are sexually inactive is not different between groups at any time period, which is our point of emphasis. Unfortunately, this is a potential bias in this secondary analysis.

*lines 180-182: How many of the women in each surgical cohort answered the survey questions at baseline, 12 months and 24 months? How many answered for all 3 times? The wording "at either ..." leaves open the potential for significant missing data or selective missing data by time point or by surgical cohort that could have biased the results. Need to give a complete enumeration of the completion rates.*

This is an excellent point. We have queried the data to obtain those numbers and have included them here in Table 3. Each surgical cohort subject number at each time point is included in the final table. The total numbers at each time point does not match the total number included in the analysis for the flow chart in Figure 1; this is due to the fact that subjects could become sexually active postoperatively and were included in the analysis at the time point where survey data was captured.

We have removed the fourth line, showing the “mean change in PISQ-12 score” as it was confusing given it was

Table 3. Mean Change in Sexual Function over 2-year postoperative period					
Measure of Sexual Function	Transobturator sling	Retropubic sling	Burch procedure	Fascial sling	p- value
Baseline PISQ-12	32.6 (31.6-33.5), 204	33.1 (32.1-34.0), 201	31.9 (31.0-32.8), 220	31.4 (30.4-32.3), 225	0.07
PISQ-12 at 12-months	37.7 (36.8-38.5), 167	37.8 (37.0-38.6), 169	36.9 (36.1-37.8), 166	37.1 (36.2-38.0), 179	0.42
PISQ-12 at 24-months	37.7 (36.7-38.7), 144	37.1 (36.1-38.0), 148	36.7 (35.8-37.6), 154	37.4 (36.5-38.3), 167	0.50
PISQ-12 Change, Baseline to 24-months	4.7 (3.7-5.7), 135	3.4 (2.5-4.4), 138	4.3 (3.3-5.2), 142	5.1 (4.2-6.0), 142	0.08
<i>*shown are means, 95% confidence intervals, n</i>					

*lines 190-203: These statements need corroboration by how complete and uniform across surgical cohorts the answers to scores were.*

Table 3 includes 95% confidence intervals which speaks to the range of scores at each time point for each surgical cohort. We have amended the table to include the subject numbers at each time point to address completeness of the cohort.

*It would also be important to determine whether completing the answers was associated with any of the baseline differences noted in Table 2, for example, by race or ethnic group, prolapse stage, concomitant surgery.*

At baseline, there is a significant association with missing data for PISQ-12 and prolapse, but not seen for any other observed baseline differences (race/ethnicity, number of prolapse, concomitant surgeries). This is not surprising as people with prolapse may be avoidant of sexual activity.

No other baseline differences were associated with completing the PISQ-12 survey.

There is no difference in rates of missing PISQ-12 data at any time point by surgical group.

*Table 4: In addition to the issues regarding completion rates at baseline, 12 and 24 months, were there differential rates of answering Q1-Q12 by time, surgical group or demographic factors which might have biased the results?*

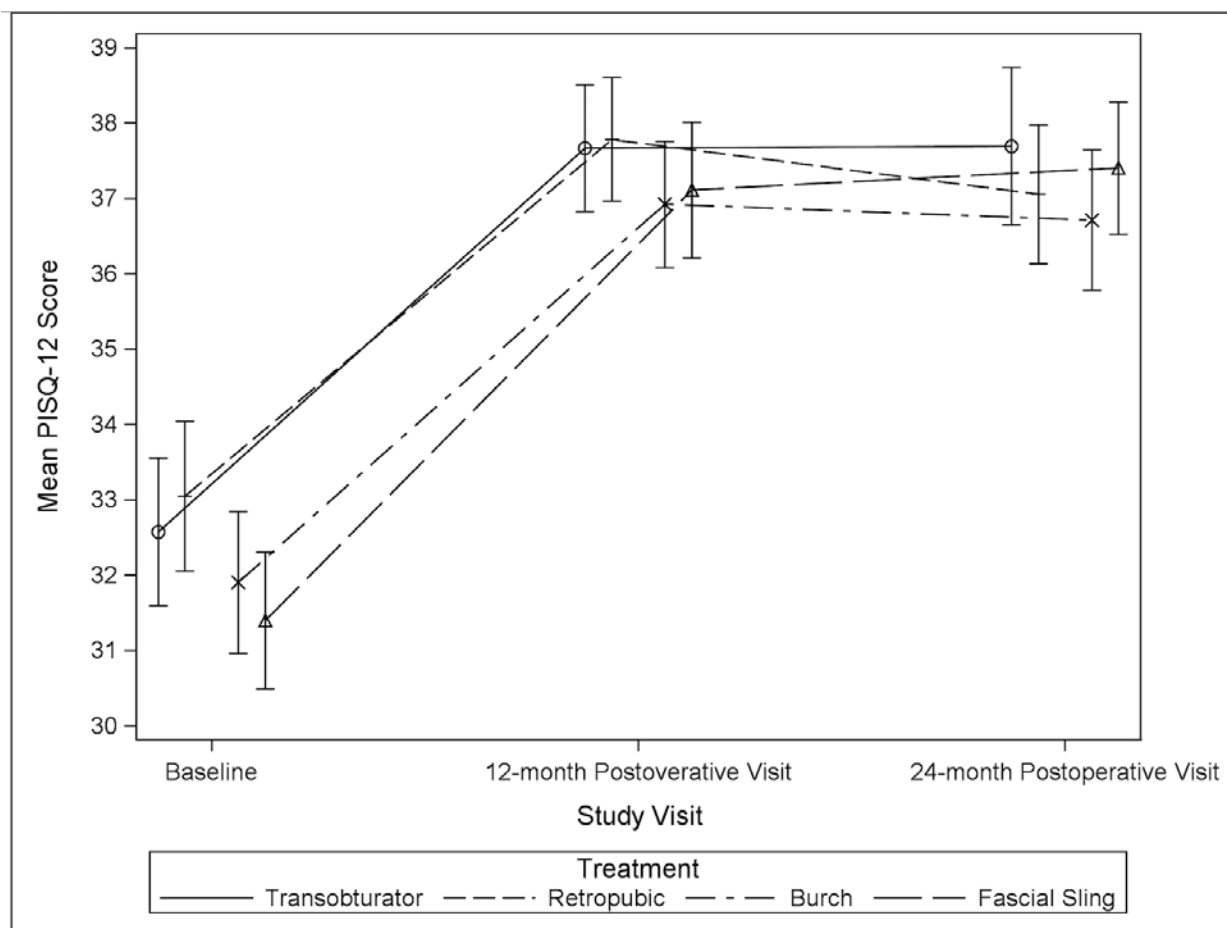
There were no significant differences in completion rates for individual questions as a factor of time, surgical group or baseline demographic differences except for prolapse stage. As expected, given there was a difference in completion rates for baseline PISQ-12 based on prolapse, the completion rates of the majority of individual questions were different as a factor of prolapse stage as well.

*Table 5: Same question as in Table 4.*

Each domain showed significant differences in completion rates as a factor of prolapse stage, as above for each individual question. No differences were observed based for time or surgical group or other baseline differences.

*Fig 2: The error bars of 1 SD should be changed to 95% CIs and a concise explanation of the statistical significance of serial and across surgical cohort differences.*

This figure has been updated in the text with the following caption:



**Figure 2.** PISQ-12 Scores at Study Visits by SUI Treatment Group. Shown are mean PISQ-12 score at each included study visit (baseline, 12-month postoperative, 24-month postoperative). Error bars correspond to 95% Confidence Intervals. Graph shows the improvement in mean sexual function, as measured by PISQ-12, over the study period and the maintenance of the improvement from 12 to 24 months.

#### PDF Editor Comments:

*We no longer require that authors adhere to the Green Journal format with the first submission of their papers. However, any revisions must do so. I strongly encourage you to read the instructions for authors (the general bits as well as those specific to the feature-type you are submitting). The instructions provide guidance regarding formatting, word and reference limits, authorship issues, and other things. Adherence to these requirements with your revision will avoid delays during the revision process, as well as avoid re-revisions on your part in order to*

*comply with the formatting.*

We have reviewed the guidelines carefully and hope we have made the necessary changes to the manuscript.

*what were the years these original studies were done?*

The SISTER study was conducted from February 2002 through June 2006. The TOMUS study was conducted from April 2006 through June 2010. We have added this to the main text of the document, see lines 110-112:

“The Stress Incontinence Surgical Treatment Efficacy Trial study was conducted from February 2002 through June 2006. The Trial of Mid-Urethral Slings study was conducted from April 2006 through June 2010.”

*this should be a colon ":" instead of an m-dash.*

This has been corrected in the manuscript. See line 54.

*While P values are a central part of inference testing in statistics, when cited alone, often the strength of the conclusion can be misunderstood. Whenever possible, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone. This is true for the abstract as well as the text.*

*What does PISQ measure?*

PISQ-12 is a validated questionnaire measuring condition-specific sexual function in the setting of incontinence or prolapse. This is mentioned in brief in the abstract in lines 49-51:

“Sexual function (assessed by the short version of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12)) was compared between groups at baseline, 12- and 24-months.”

*Instead of a dash, please put these in parentheses*

This is corrected, see lines 93-94.



*It is an idiosyncratic fact that at the Journal we tend to avoid the use of the word impact to imply the result of a change, preferring to limit "impact" to mean a physical blow.*

We have altered the terminology to reflect this, see lines 97-99:

While the four surgical approaches are all effective for resolving symptoms of SUI, there may be important differences between them regarding their effect on sexual function.

*Is this a planned 2nd analysis? In your revision, please spell out the names of the trials throughout as the abbreviations won't be allowed.*

This is not a planned secondary analysis. This is a combined secondary analysis of the two studies performed by an independent group of researchers.

I have put the full names of the trials throughout the manuscript.

*Please provide the years of the studies. Also, how did you get the data?*

I have listed the years of the studies in the methods section, see line

We obtained the data by accessing the Central Repository for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). This is now included in the Methods section as well as in the acknowledgments, see lines 112-114:

The data was obtained by accessing the Central Repository for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

*Please state why it was exempted?*

This study was exempt as both trials are now publicly available. This has been added to lines 114-116:

"This study was classified as exempt by the Virginia Commonwealth University Institutional Review Board (IRB HM20012510) as these are both publicly available datasets."

*Age of 21 years*

This has been corrected.

*There should be a hyphen with stress-predominant*

Thank you for this point. This has been amended.

*For clarity, women who reported NO sexual activity at -6 months through +24 months were excluded? I can see that this would exclude non-partnered women but might it not have excluded women with partners who avoided sex at all time points? This part of the methods is where all of the reviewers, including the statistical editor have major issues with the paper. To be clear, to be included women had to report sexual activity OR complete a short form , alternatively, they had to report any sexual activity AND complete a short form. Are both correct? How was sexual activity reported and recorded? Also, the issue of needing to enumerate exactly what data you have and what time points cannot be understated. From the way this reads at present, a participant could be included if they completed a short form at on visit so there could be a great deal of missing data.*

Women who reported no sexual activity during the entirety of the study period (-6 months through +24 months) were excluded from analysis; these are the 325 women excluded for our analysis from the original 1249 women in both trials combined. To be included in the analysis, women needed to report sexual activity and complete the PISQ-12 questionnaire at any study visit to be included. This means that women who only completed the PISQ-12 at one visit would be included in the mean data presented at each time point. We analyzed in this fashion so we could include the greatest number of subjects at each time point for greater generalizability.

This is a limitation of our study, to be sure. We are limited by the data that was collected and we have limited the scope of our study to only address sexually active women. The point is not taken lightly that we have excluded subjects with valuable information to learn regarding female sexuality. However the reasons for sexual inactivity or to not responding to the questionnaire are beyond the scope of our research question.

*marital or partnered status?*

This is an excellent point. Partnered status. Both the line 134 and table 2 have been updated to reflect this change.

*No retreatment for stress incontinence (behavioral, pharmacologic or surgical).*

This is now corrected in the manuscript.

*Most readers will not be familiar with the PISQ12 questionnaire. Can you include the questions*

*or a link to the form if you cannot reproduce the questionnaire?*

Table 4 includes all of the questions to the PISQ-12 questionnaire. We have additionally cited the paper by Rogers RG in the references which also has the questionnaire.

*What do you mean by "condition specific sexual function"? What condition?*

This is a sexual function questionnaire that focuses on sexual function in the setting of pelvic organ prolapse and urinary incontinence. It addresses specific questions women with these conditions may have issues with, as they relate to sexual function.

*Ok, so here is some explanation of the PISQ-12. It needs to be put closer to when you first mention it.*

I have moved the description to closer to the first mention of PISQ-12.

*Why was this limitation placed? What if due to embarrassment, etc, the woman did not have sex before she had surgery and then, after surgery, things were so much better she began having sex again? This exclusion would underestimate possible benefits sexually of the surgery.*

We measured sexual function by means for the surgical treatment groups. We excluded patients who were not sexually active and thus did not complete the PISQ-12 questionnaire. There very well could be women who were abstinent prior to surgery and then resumed sexual activity following surgery. We believe we have captured those women by allowing subjects who completed only one questionnaire at any time point to be represented in this study.

Areas for further research would include more patient centered questionnaires that measure sexual activity on the spectrum of activity that we as practitioners hear from our patients every day – self stimulation, same sex partnerships, etc – that this questionnaire does not address.

We have tried to address this limitation of our study in our discussion. See lines 280-285:

“Additionally, it limits partner-related problems to erectile dysfunction and premature ejaculation; some eligible participants may be excluded secondary to sexual preferences given the assumptions inherent to the questionnaire that the partner is male. This does limit our ability to evaluate important aspects of sexual function for our patients like self-stimulation, same sex partners and sexual activity beyond vaginal penetration.”

*Why did you consider this clinically meaningful*

Based on the article by Norman GR, Sloan JA, Wyrich KW, this is a excellent estimate for the minimum important difference when evaluating health-related quality of life instruments. As there is no MID for this questionnaire, we used a known quantitative method to estimate a clinical improvement for subjects.

*Avoid single sentence paragraphs*

This has been corrected.

*- how did you handle missing data?*

We recognize the potential biasing impact of missing data on the study results, especially in these studies as participants who were not sexually active had 'missing' PISQ-12 scores. In the worst case scenario, participants could have had differing rates of not being sexually active over the different treatment regimens, which would led to very different conclusions. However, we investigated this and found no differences in this rate between the treatment groups at any of the time points (second sentence in Results, see lines 214-216).

This does limit the generalizability of our results to participants who were sexually active, as we allude to in the second to last paragraph in the Discussion. As such, the biggest potential for the biasing influence of missing data comes from participant retention in the trial. The linear mixed effect model that was used has been shown to produce unbiased estimates when accounting for the variables related to the missing data. We adjusted for a wide array of variables and performed analysis with and without adjusting for any variables and came to the same conclusions. Thus, we are confident that the missing information present in these studies will have limited impact on our results.

*No clue what these p values are referring to. What comparisons are being made? Can you provide an assessment of sexual function in women who had prolapse surgery at the same time as well as those that did not? What about hysterectomy? Did you control for that?*

Thank you for this point. We have edited this paragraph to better explain this point, see lines 243-247:

"We found that postoperative objective failure and subjective failure are significantly associated with lower PISQ-12 scores in a generalized linear regression, controlling for baseline differences ( $p < 0.01$ ,  $p < 0.01$ ). Concomitant prolapse repair surgery is significantly associated with higher PISQ-12 scores when controlling for baseline characteristic differences ( $p < 0.01$ ). "

Because of the limitations within our dataset, we cannot specifically control for subjects who had specific prolapse repairs or a concomitant hysterectomy.

- Sentence starting line 208 is incomplete.

This has been amended.

*Differences between what groups? between what groups? Please articulate important differences here and don't just refer to the table for key points you are trying to make.*

Treatment groups where the treatment refers to route of anti-incontinence surgery (Burch colpopsuspension, rectus fascia pubovaginal sling, transobturator midurethral sling, retropubic midurethral sling)

*I'm flummoxed by what you mean by "groups". Are these different surgical approaches or are the different time frames (12 and 24 months after surgery), for instance*

We have made changes to this paragraph to better demonstrate that we intend to highlight the differences between surgical treatment groups are statistically different but are not clinically meaningful differences. See lines 243-251:

"While the differences in sexual function domains and individual condition-specific questions show statistically significant differences, they are all less than 0.4 points different in mean scores between surgical treatment groups which is lower than the baseline standard deviation for all questions/domains and therefore unlikely clinically meaningful (**Table 4, Table 5**). The greatest improvement from baseline to postoperatively in sexual function postoperatively was seen in the specific questions 6 and 7 "are you incontinent of urine with sexual activity" or "does fear of incontinence restrict your sexual activity?", and noted in the physical domain, although improvements in all three domains were apparent in these data."

*Nor do they seem to improve after an initial gain*

This is a correct statement. We would love to acquire more long-term data to evaluate this further. Did the subjects peak at 12 months or is the slope of the improvement just less than immediately postoperatively.

*Important limitation is the low degree of diversity in race among the participants.*

This is an excellent and unfortunate point. This is a limitation across a significant amount of urogynecologic literature and is an active area of focus for the specialty. I have added this point to the discussion, see lines 276-277:

The generalizability of this study is limited by the low degree of diversity among subjects in these trials.

**Date:** Oct 22, 2019  
**To:** "Stephanie Marie Glass Clark" stephanie.glass3@gmail.com  
**From:** "The Green Journal" em@greenjournal.org  
**Subject:** Your Submission ONG-19-1588R1

RE: Manuscript Number ONG-19-1588R1

Effect of surgery for stress incontinence on female sexual function: A secondary analysis

Dear Dr. Glass Clark:

Your revised manuscript has been reviewed by the Statistical Editor. He has the following comments that need to be addressed before we can consider your submission further:

First, I want to thank the Authors for providing more information to the reader re: the follow-up counts at 12 and 24 months, which added more transparency to the analyses. However, it also pointed out limitations to generalizing the results of the analysis and will require further statement of limitations. That is no fault of the Authors, but is a limitation imposed by loss to follow-up in long term studies.

Specifically, in Fig 1, as compared to the potentially eligible subsets of 299,298,329 and 326, some women did not complete any PISQ-12 questionnaires, resulting in a loss of from 24-28% of their initial counts, leaving 220,216,239 and 249 available for analysis. That needs to be acknowledged as a potential limitation, although all response rates were > 70%.

Next, in Table 3, the number of respondents is shown for the 4 subsets at baseline, 12 months, 24 months and change from baseline to 24 months. Of the 220,216,239 and 249 available for analysis, the response rate at baseline varied from 90-93%, then 70-78% by 12 months, then 64-69% by 24 months and for those with both baseline and 24 months responses for comparison, the rates were 57-64%. IN other words, even though Table 3 showed no difference in mean scores or difference in scores, by 24 months and for the baseline to 24 month survey, the respondents may represent a biased sample and cannot be generalized. Could instead show baseline, 12 month and change from baseline to 12 months in PISQ-12 scores.

The next version of your submission will be due October 29, 2019.

Sincerely,

Nancy C. Chescheir, MD  
Editor-in-Chief

2018 IMPACT FACTOR: 4.965  
2018 IMPACT FACTOR RANKING: 7th out of 83 ob/gyn journals

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In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: <https://www.editorialmanager.com/ong/login.asp?a=r>). Please contact the publication office if you have any questions.

To the Editors of *Obstetrics & Gynecology*:

Thank you for your consideration of the following manuscript and the attached revisions. The authors intend to solely submit this manuscript to *Obstetrics & Gynecology*. This manuscript is not currently in consideration at any alternate journal and we have no intention of submitting elsewhere unless not selected for publication in this journal. I agree to full transparency regarding this study and manuscript with any forthcoming discussions of publication. This study was classified as exempt by the Virginia Commonwealth University Institutional Review Board (IRB HM20012510).

Please see the following pages for point-by-point responses to each reviewer and editors and attached is the amended manuscript with tracked changes. I have included the second set of comments from the statistical editor in this point-by-point response at the end of this document. This letter also serves as confirmation that I have read the Instructions for Authors.

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. Signed by Stephanie Glass Clark.

Thank you again for your consideration,

Stephanie Glass Clark, M.D.

*Reviewer #1: This is a well done secondary analysis of a large sample size examining sexual function as an important element to overall quality of life for women after surgery for urinary stress incontinence. This is a topic that is under-studied and important in comprehensive patient care.*

*Is it potentially a problem to have a statistically significant difference in baseline pelvic organ prolapse types between groups when POP itself can affect sexual function? Is adjusting for POP enough to limit this confounding effect?*

Thank you for this point. In the overall analysis, we feel that to adjust for prolapse as a confounding variable is sufficient in the generalized linear regression model. When looking at prolapse specific sexual function (Table 4, Q8) there was a statistically significant difference observed between surgical groups at baseline and 24 months, and the groups with higher stages of prolapse at baseline showed greater increase/improvement in prolapse specific sexual function. However, this difference is less than 0.5 and is likely not clinically meaningful.

*The PISQ-12 seems to assume the participant is heterosexual. Was sexuality questioned in this study to confirm that the tool would be appropriate? If not, this is a limitation that should be discussed. While I agree with what you have stated in your discussion regarding its limitations, I wonder if it also meant that some eligible participants were not included because of the heteronormative questions.*

This is a very important point and is a limitation of the study. We have added a response to this in the full text, see lines 280-283:

“Additionally, it limits partner-related problems to erectile dysfunction and premature ejaculation; some eligible participants may be excluded secondary to sexual preferences given the assumptions inherent to the questionnaire that the partner is male. This limits our ability to evaluate important aspects of sexual function for our patients like self-stimulation, same sex partners and sexual activity beyond vaginal penetration.”

*Follow-up rate for 12 and 24 months is a strength worth highlighting as much longitudinal data in sexual function and quality of life in general is challenging to capture due to loss to follow-up over time.*

We agree. In the strengths section, we have added emphasis to this point, see lines 274-275:

“The study is also strengthened by the number of subjects with responses out to 24 months, which is reflective of more stable, long-term quality of life metrics.”

*Reviewer #2: This is a secondary analysis of 2 randomized controlled trials evaluating sexual function after surgery for stress urinary incontinence. The study is well done, well written, and a comprehensive evaluation of the subject.*



*Methods: It is still unclear to me in the methods from Table 1 and Figure 1 because the numbers don't match, whether or not subjects had to be sexually active at each time point baseline, 12 months, and 24 months, or only at least 1 of those times. Line 118 states they needed to report sexual activity at ANY of the study visits. Figure 1 implies that they had to be sexually active at each time point.*

Thank you for this point. In this study, subjects were included in the study if they had completed the PISQ-12 questionnaire at any study visit (BL, 12, 24 mo). We have amended Figure 1 to clarify this:

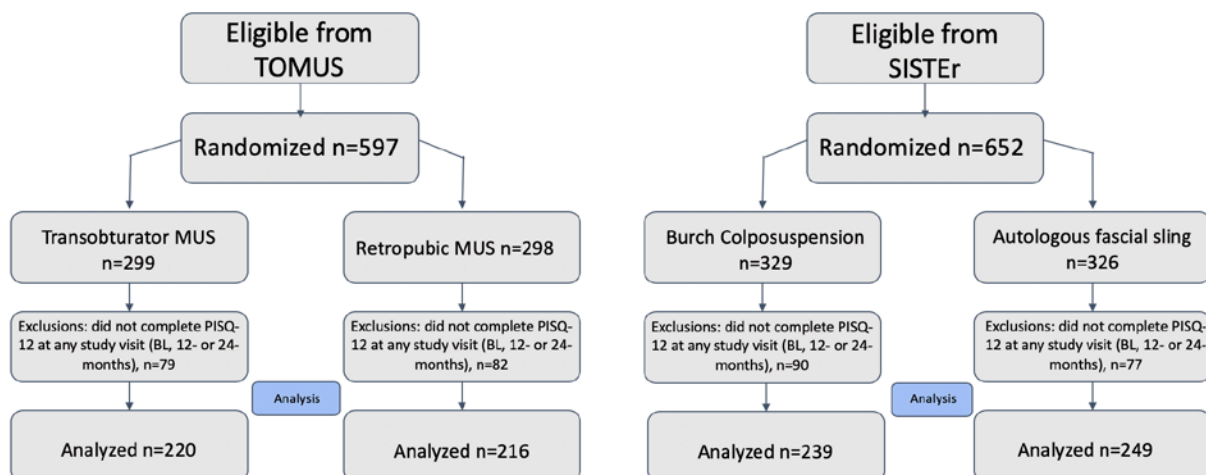


Table 1 does not include every subject from the original studies, as some subjects did not respond to the questionnaire. We included subjects with sexual inactivity for Table 1 only if they responded to the pre-PISQ-12 question asking if they had been sexually active in the preceding 6 months. If yes, they went on to answer the full PISQ-12 survey, and if no they did not have responses to the PISQ-12 and were excluded from the remaining analyses evaluating sexual function.

*Results/Discussion: The PISQ-12 total score ranges from 0-48? The mean change from baseline to 24 months ranges from 3.4-5.1 depending on the surgery, also reflected in Figure 2...how do we know that this is a clinically meaningful improvement as you state in the Discussion? I would be more tempered and state that sexual function didn't worsen, was likely the same overall, but did improve in some specific areas e.g. those questions having to do with incontinence and sex.*

We thank the reviewer for this observation. As there is no published minimal important difference for the PISQ-12, we used one-half the baseline standard deviation as a proxy to determine clinical significance. See lines 137-139 and 220-224.

(137-139) There is no minimum important difference (MID) established for the PISQ-12, thus we used one-half the baseline standard deviation to determine clinical significance.

(220-224) There is no published minimally important difference (MID) for the PISQ-12 so we conservatively estimated the MID as half the standard deviation of the baseline score.<sup>15</sup> The standard deviation of PISQ-12 at baseline is 7.08 for all surgical treatment groups. The mean scores for each treatment improved beyond this estimate for MID regardless of treatment type (**Table 3**).

*Table 2: Please clarify what types of prior incontinence surgery and treatment participants experienced before the trial. Also what types of concomitant surgeries were performed?*

Unfortunately, we do not have access to the types of prior incontinence surgery or treatments in order to comment in this paper, only that there were or were not prior surgeries performed for incontinence.

While we have access to the types of concomitant procedures performed for the TOMUS trial, the data we acquired from the NIDDK Central Repository for SISTEr did not include the concomitant surgeries within the dataset. Therefore we included only those who had concomitant surgery or not.

*Table 2. Subjective failure seems quite high--are these 4 treatments really that effective?*

We agree, these rates are high, but they corroborate those published in the literature. This deserves further research in our field, particularly as we shift our focus in the field of urogynecology to patient centered outcomes and our emphasis being placed on subjective rather than objective outcomes. These were both very well done, multi-center randomized controlled trials. We have not focused on the failure rates in this study as this was outside the scope of our clinical question and the focus of the original studies.

*Reviewer #3: Well written secondary analysis of two multi-centered randomized trials. The TOMUS study has already been published, including the sexual function outcomes in 2012 and before this the Sister study in the early 2000s.*

*Strengths: A significant strength is the number of women followed following anti-incontinence procedure for up to 24 months. This highlights that anti-incontinence procedures improve incontinence related issues with sexual activity over time and that there does not appear to be a significant difference between the type of anti-incontinence procedure. An advanced secondary analysis of two well done and previously published multi-centered randomized trials.*

*Limitations: secondary analysis of two multi-centered randomized trials in which the sexual outcomes data has already been published. The combination of the two data sets and*

*republishing does not add anything significantly new to the literature, though the advanced analytic evaluation is unique.*

*A major issue of this data is that inclusion criteria was quite generous- only requiring the patient to mark they were sexually active at a single time point (6 months prior to baseline visit, 12 or 24 months) and then only filling out the PISQ-12 once (minimal as it was a secondary outcome to begin with). In the women without PISQ-12 data, it is inappropriate to conclude anything substantial from the fact that women were reporting sexual activity. Going forward, I recommend assessing sexual activity at each time point as it is a fluid measure and may change significantly over the course of 24 months.*

We want to thank the reviewer for these comments. In subjects with data available at each study time point, we included their data in the analysis. We did not want to exclude patients who became sexually active or stopped reporting sexual activity during the study period.

#### STATISTICAL EDITOR COMMENTS:

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

*Table 1: Need to explain the differences in denominators for each surgical cohort, comparing baseline, 12 and 24 months post-op. If the differences from baseline to 12 months (eg, 32, 33, 74, 66) do represent significant differences from baseline. The corresponding differences from baseline to 24 months were not statistically different. If these changes represent differential loss to follow-up or differential loss due to sexual inactivity or a combination of those, then that could have introduced bias.*

This is annual loss of follow up seen in the study. We are attempting to show in this table that the proportion of patients who are sexually inactive is not different at each time point.

The difference in loss to follow up is a limitation of combining two trials where one study had a stronger retention rate of subjects. However, the numbers of women who are sexually inactive is not different between groups at any time period, which is our point of emphasis. Unfortunately, this is a potential bias in this secondary analysis.

*lines 180-182: How many of the women in each surgical cohort answered the survey questions at baseline, 12 months and 24 months? How many answered for all 3 times? The wording "at either ..." leaves open the potential for significant missing data or selective missing data by time point or by surgical cohort that could have biased the results. Need to give a complete enumeration of the completion rates.*

This is an excellent point. We have queried the data to obtain those numbers and have included them here in Table 3. Each surgical cohort subject number at each time point is included in the final table. The total numbers at each time point does not match the total number included in the analysis for the flow chart in Figure 1; this is due to the fact that subjects could become sexually active postoperatively and were included in the analysis at the time point where survey data was captured.

We have removed the fourth line, showing the “mean change in PISQ-12 score” as it was confusing given it was

Table 3. Mean Change in Sexual Function over 2-year postoperative period					
Measure of Sexual Function	Transobturator sling	Retropubic sling	Burch procedure	Fascial sling	p- value
Baseline PISQ-12	32.6 (31.6-33.5), 204	33.1 (32.1-34.0), 201	31.9 (31.0-32.8), 220	31.4 (30.4-32.3), 225	0.07
PISQ-12 at 12-months	37.7 (36.8-38.5), 167	37.8 (37.0-38.6), 169	36.9 (36.1-37.8), 166	37.1 (36.2-38.0), 179	0.42
PISQ-12 at 24-months	37.7 (36.7-38.7), 144	37.1 (36.1-38.0), 148	36.7 (35.8-37.6), 154	37.4 (36.5-38.3), 167	0.50
PISQ-12 Change, Baseline to 24-months	4.7 (3.7-5.7), 135	3.4 (2.5-4.4), 138	4.3 (3.3-5.2), 142	5.1 (4.2-6.0), 142	0.08
<i>*shown are means, 95% confidence intervals, n</i>					

*lines 190-203: These statements need corroboration by how complete and uniform across surgical cohorts the answers to scores were.*

Table 3 includes 95% confidence intervals which speaks to the range of scores at each time point for each surgical cohort. We have amended the table to include the subject numbers at each time point to address completeness of the cohort.

*It would also be important to determine whether completing the answers was associated with any of the baseline differences noted in Table 2, for example, by race or ethnic group, prolapse stage, concomitant surgery.*

At baseline, there is a significant association with missing data for PISQ-12 and prolapse, but not seen for any other observed baseline differences (race/ethnicity, number of prolapse,

concomitant surgeries). This is not surprising as people with prolapse may be avoidant of sexual activity.

No other baseline differences were associated with completing the PISQ-12 survey.

There is no difference in rates of missing PISQ-12 data at any time point by surgical group.

*Table 4: In addition to the issues regarding completion rates at baseline, 12 and 24 months, were there differential rates of answering Q1-Q12 by time, surgical group or demographic factors which might have biased the results?*

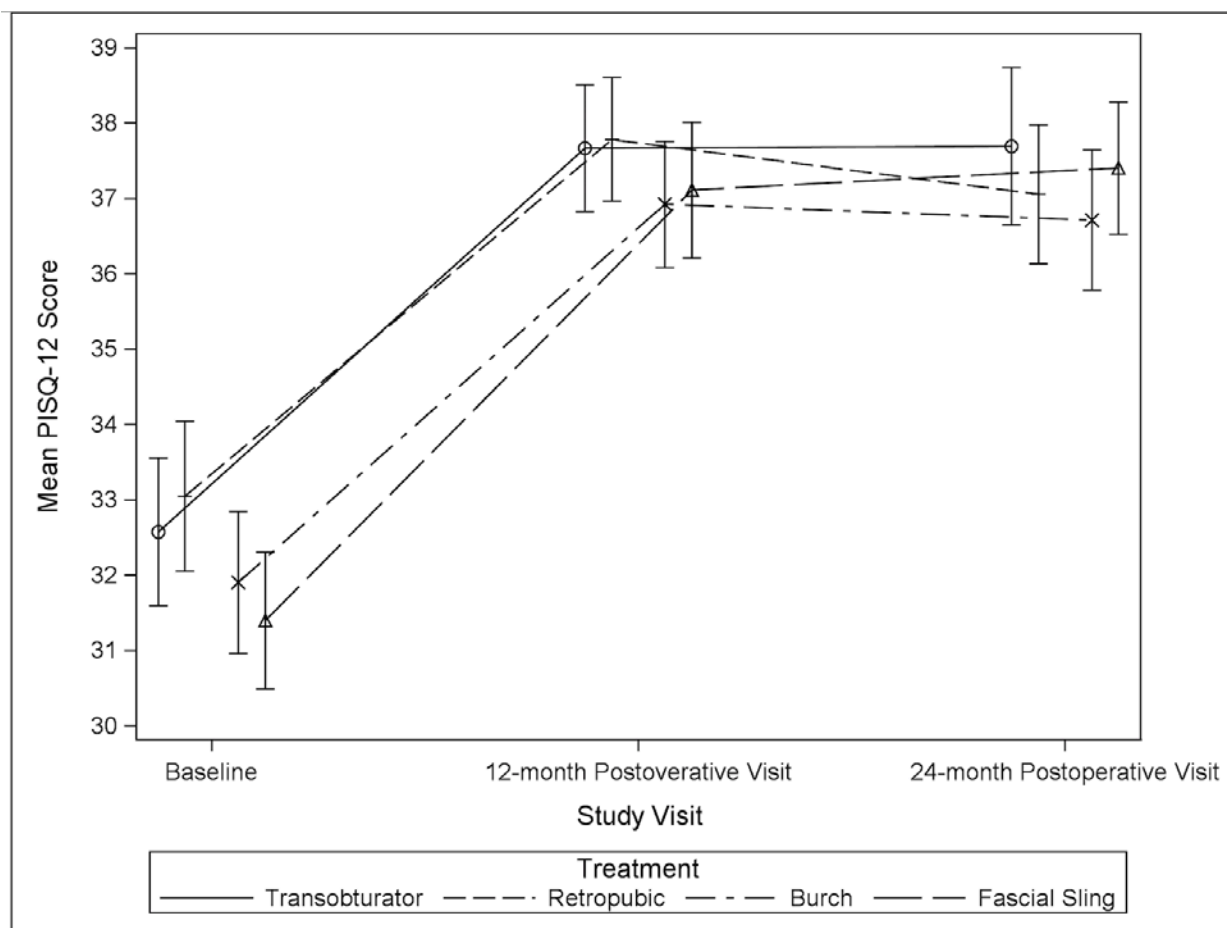
There were no significant differences in completion rates for individual questions as a factor of time, surgical group or baseline demographic differences except for prolapse stage. As expected, given there was a difference in completion rates for baseline PISQ-12 based on prolapse, the completion rates of the majority of individual questions were different as a factor of prolapse stage as well.

*Table 5: Same question as in Table 4.*

Each domain showed significant differences in completion rates as a factor of prolapse stage, as above for each individual question. No differences were observed based for time or surgical group or other baseline differences.

*Fig 2: The error bars of 1 SD should be changed to 95% CIs and a concise explanation of the statistical significance of serial and across surgical cohort differences.*

This figure has been updated in the text with the following caption:



**Figure 2.** PISQ-12 Scores at Study Visits by SUI Treatment Group. Shown are mean PISQ-12 score at each included study visit (baseline, 12-month postoperative, 24-month postoperative). Error bars correspond to 95% Confidence Intervals. Graph shows the improvement in mean sexual function, as measured by PISQ-12, over the study period and the maintenance of the improvement from 12 to 24 months.

#### PDF Editor Comments:

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*comply with the formatting.*

We have reviewed the guidelines carefully and hope we have made the necessary changes to the manuscript.

*what were the years these original studies were done?*

The SISTER study was conducted from February 2002 through June 2006. The TOMUS study was conducted from April 2006 through June 2010. We have added this to the main text of the document, see lines 110-112:

“The Stress Incontinence Surgical Treatment Efficacy Trial study was conducted from February 2002 through June 2006. The Trial of Mid-Urethral Slings study was conducted from April 2006 through June 2010.”

*this should be a colon ":" instead of an m-dash.*

This has been corrected in the manuscript. See line 54.

*While P values are a central part of inference testing in statistics, when cited alone, often the strength of the conclusion can be misunderstood. Whenever possible, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone. This is true for the abstract as well as the text.*

*What does PISQ measure?*

PISQ-12 is a validated questionnaire measuring condition-specific sexual function in the setting of incontinence or prolapse. This is mentioned in brief in the abstract in lines 49-51:

“Sexual function (assessed by the short version of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12)) was compared between groups at baseline, 12- and 24-months.”

*Instead of a dash, please put these in parentheses*

This is corrected, see lines 93-94.

*It is an idiosyncratic fact that at the Journal we tend to avoid the use of the word impact to imply the result of a change, preferring to limit "impact" to mean a physical blow.*

We have altered the terminology to reflect this, see lines 97-99:

While the four surgical approaches are all effective for resolving symptoms of SUI, there may be important differences between them regarding their effect on sexual function.

*Is this a planned 2nd analysis? In your revision, please spell out the names of the trials throughout as the abbreviations won't be allowed.*

This is not a planned secondary analysis. This is a combined secondary analysis of the two studies performed by an independent group of researchers.

I have put the full names of the trials throughout the manuscript.

*Please provide the years of the studies. Also, how did you get the data?*

I have listed the years of the studies in the methods section, see line

We obtained the data by accessing the Central Repository for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). This is now included in the Methods section as well as in the acknowledgments, see lines 112-114:

The data was obtained by accessing the Central Repository for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

*Please state why it was exempted?*

This study was exempt as both trials are now publicly available. This has been added to lines 114-116:

"This study was classified as exempt by the Virginia Commonwealth University Institutional Review Board (IRB HM20012510) as these are both publicly available datasets."

*Age of 21 years*

This has been corrected.



*There should be a hyphen with stress-predominant*

Thank you for this point. This has been amended.

*For clarity, women who reported NO sexual activity at -6 months through +24 months were excluded? I can see that this would exclude non-partnered women but might it not have excluded women with partners who avoided sex at all time points? This part of the methods is where all of the reviewers, including the statistical editor have major issues with the paper. To be clear, to be included women had to report sexual activity OR complete a short form , alternatively, they had to report any sexual activity AND complete a short form. Are both correct? How was sexual activity reported and recorded? Also, the issue of needing to enumerate exactly what data you have and what time points cannot be understated. From the way this reads at present, a participant could be included if they completed a short form at on visit so there could be a great deal of missing data.*

Women who reported no sexual activity during the entirety of the study period (-6 months through +24 months) were excluded from analysis; these are the 325 women excluded for our analysis from the original 1249 women in both trials combined. To be included in the analysis, women needed to report sexual activity and complete the PISQ-12 questionnaire at any study visit to be included. This means that women who only completed the PISQ-12 at one visit would be included in the mean data presented at each time point. We analyzed in this fashion so we could include the greatest number of subjects at each time point for greater generalizability.

This is a limitation of our study, to be sure. We are limited by the data that was collected and we have limited the scope of our study to only address sexually active women. The point is not taken lightly that we have excluded subjects with valuable information to learn regarding female sexuality. However the reasons for sexual inactivity or to not responding to the questionnaire are beyond the scope of our research question.

*marital or partnered status?*

This is an excellent point. Partnered status. Both the line 134 and table 2 have been updated to reflect this change.

*No retreatment for stress incontinence (behavioral, pharmacologic or surgical).*

This is now corrected in the manuscript.

*Most readers will not be familiar with the PISQ12 questionnaire. Can you include the questions*

*or a link to the form if you cannot reproduce the questionnaire?*

Table 4 includes all of the questions to the PISQ-12 questionnaire. We have additionally cited the paper by Rogers RG in the references which also has the questionnaire.

*What do you mean by "condition specific sexual function"? What condition?*

This is a sexual function questionnaire that focuses on sexual function in the setting of pelvic organ prolapse and urinary incontinence. It addresses specific questions women with these conditions may have issues with, as they relate to sexual function.

*Ok, so here is some explanation of the PISQ-12. It needs to be put closer to when you first mention it.*

I have moved the description to closer to the first mention of PISQ-12.

*Why was this limitation placed? What if due to embarrassment, etc, the woman did not have sex before she had surgery and then, after surgery, things were so much better she began having sex again? This exclusion would underestimate possible benefits sexually of the surgery.*

We measured sexual function by means for the surgical treatment groups. We excluded patients who were not sexually active and thus did not complete the PISQ-12 questionnaire. There very well could be women who were abstinent prior to surgery and then resumed sexual activity following surgery. We believe we have captured those women by allowing subjects who completed only one questionnaire at any time point to be represented in this study.

Areas for further research would include more patient centered questionnaires that measure sexual activity on the spectrum of activity that we as practitioners hear from our patients every day – self stimulation, same sex partnerships, etc – that this questionnaire does not address.

We have tried to address this limitation of our study in our discussion. See lines 280-285:

“Additionally, it limits partner-related problems to erectile dysfunction and premature ejaculation; some eligible participants may be excluded secondary to sexual preferences given the assumptions inherent to the questionnaire that the partner is male. This does limit our ability to evaluate important aspects of sexual function for our patients like self-stimulation, same sex partners and sexual activity beyond vaginal penetration.”

*Why did you consider this clinically meaningful*

Based on the article by Norman GR, Sloan JA, Wyrich KW, this is a excellent estimate for the minimum important difference when evaluating health-related quality of life instruments. As there is no MID for this questionnaire, we used a known quantitative method to estimate a clinical improvement for subjects.

*Avoid single sentence paragraphs*

This has been corrected.

*- how did you handle missing data?*

We recognize the potential biasing impact of missing data on the study results, especially in these studies as participants who were not sexually active had 'missing' PISQ-12 scores. In the worst case scenario, participants could have had differing rates of not being sexually active over the different treatment regimens, which would led to very different conclusions. However, we investigated this and found no differences in this rate between the treatment groups at any of the time points (second sentence in Results, see lines 214-216).

This does limit the generalizability of our results to participants who were sexually active, as we allude to in the second to last paragraph in the Discussion. As such, the biggest potential for the biasing influence of missing data comes from participant retention in the trial. The linear mixed effect model that was used has been shown to produce unbiased estimates when accounting for the variables related to the missing data. We adjusted for a wide array of variables and performed analysis with and without adjusting for any variables and came to the same conclusions. Thus, we are confident that the missing information present in these studies will have limited impact on our results.

*No clue what these p values are referring to. What comparisons are being made? Can you provide an assessment of sexual function in women who had prolapse surgery at the same time as well as those that did not? What about hysterectomy? Did you control for that?*

Thank you for this point. We have edited this paragraph to better explain this point, see lines 243-247:

"We found that postoperative objective failure and subjective failure are significantly associated with lower PISQ-12 scores in a generalized linear regression, controlling for baseline differences ( $p < 0.01$ ,  $p < 0.01$ ). Concomitant prolapse repair surgery is significantly associated with higher PISQ-12 scores when controlling for baseline characteristic differences ( $p < 0.01$ ). "

Because of the limitations within our dataset, we cannot specifically control for subjects who had specific prolapse repairs or a concomitant hysterectomy.

- Sentence starting line 208 is incomplete.

This has been amended.

*Differences between what groups? between what groups? Please articulate important differences here and don't just refer to the table for key points you are trying to make.*

Treatment groups where the treatment refers to route of anti-incontinence surgery (Burch colpopsuspension, rectus fascia pubovaginal sling, transobturator midurethral sling, retropubic midurethral sling)

*I'm flummoxed by what you mean by "groups". Are these different surgical approaches or are the different time frames (12 and 24 months after surgery), for instance*

We have made changes to this paragraph to better demonstrate that we intend to highlight the differences between surgical treatment groups are statistically different but are not clinically meaningful differences. See lines 243-251:

"While the differences in sexual function domains and individual condition-specific questions show statistically significant differences, they are all less than 0.4 points different in mean scores between surgical treatment groups which is lower than the baseline standard deviation for all questions/domains and therefore unlikely clinically meaningful (**Table 4, Table 5**). The greatest improvement from baseline to postoperatively in sexual function postoperatively was seen in the specific questions 6 and 7 "are you incontinent of urine with sexual activity" or "does fear of incontinence restrict your sexual activity?", and noted in the physical domain, although improvements in all three domains were apparent in these data."

*Nor do they seem to improve after an initial gain*

This is a correct statement. We would love to acquire more long-term data to evaluate this further. Did the subjects peak at 12 months or is the slope of the improvement just less than immediately postoperatively.

*Important limitation is the low degree of diversity in race among the participants.*

This is an excellent and unfortunate point. This is a limitation across a significant amount of urogynecologic literature and is an active area of focus for the specialty. I have added this point to the discussion, see lines 276-277:

The generalizability of this study is limited by the low degree of diversity among subjects in these trials.

From Oct 22, 2019:

*First, I want to thank the Authors for providing more information to the reader re: the follow-up counts at 12 and 24 months, which added more transparency to the analyses. However, it also pointed out limitations to generalizing the results of the analysis and will require further statement of limitations. That is no fault of the Authors, but is a limitation imposed by loss to follow-up in long term studies.*

*Specifically, in Fig 1, as compared to the potentially eligible subsets of 299,298,329 and 326, some women did not complete any PISQ-12 questionnaires, resulting in a loss of from 24-28% of their initial counts, leaving 220,216,239 and 249 available for analysis. That needs to be acknowledged as a potential limitation, although all response rates were > 70%.*

We acknowledge these response rates as a potential limitation of the study and agree with acknowledging in the manuscript. We have added additional verbiage to this effect, see lines 292-293:

“Additionally, the study is limited by the decreasing response rates and loss to follow up for subjects over the 24 month study period.”

*Next, in Table 3, the number of respondents is shown for the 4 subsets at baseline, 12 months, 24 months and change from baseline to 24 months. Of the 220,216,239 and 249 available for analysis, the response rate at baseline varied from 90-93%, then 70-78% by 12 months, then 64-69% by 24 months and for those with both baseline and 24 months responses for comparison, the rates were 57-64%. IN other words, even though Table 3 showed no difference in mean scores or difference in scores, by 24 months and for the baseline to 24 month survey, the respondents may represent a biased sample and cannot be generalized. Could instead show baseline, 12 month and change from baseline to 12 months in PISQ-12 scores.*

We appreciate this point made by the statistical editor, though we wanted to include the maximum subjects at each time point, which is why we included all subjects at each time point who completed the PISQ-12. We are interested in the longer-term follow up at 24 months as the primary objective of this study, and would not wish to change our analysis post hoc to a 12 month comparison. We have acknowledged the limitation with the following lines, 293-294:

“This has a potential to bias our results and overestimate improvement in sexual function over the study period.”