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

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

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

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

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

obgyn@greenjournal.org.
RE: Manuscript Number ONG-19-780

Antibiotic Prophylaxis During Catheter-managed Postoperative Urinary Retention A Randomized Controlled Trial

Dear Dr. Lavelle:

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 referees 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 Jun 06, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: COMMENTS FOR THE AUTHORS:

Dear Dr. Lavelle et al,

Congratulations on an interesting manuscript investigating whether nitrofurantoin affects the incidence of culture-proven UTI in women with catheter-managed postoperative urinary retention after pelvic reconstructive surgery.

Comments:

1. The manuscript is overall well written with few grammatical errors throughout.

2. Lines 1-2: Suggest including in the title the type of surgery performed, i.e.: "Antibiotic Prophylaxis During Catheter-managed Postoperative Urinary Retention after Pelvic Reconstructive Surgery: A Randomized Controlled Trial"

3. Line 95: Which five sites were included for this multi-centered trial? This should be included in the Materials and Methods.

4. Line 99: What specific procedures were performed for pelvic organ prolapse and/or urinary incontinence? This is not mentioned at all in the manuscript. Was cystoscopy routinely performed on all procedures? If so, were the number of times cystoscopy was performed recorded due to transurethral manipulation, which could potentially contribute to the incidence of UTI? (ie. Inserting the cystoscope multiple times vs. one time).

5. How long were patients taking nitrofurantoin for duration of catheter use? What is the protocol per site for management of postoperative urinary retention and were protocols all the same?

6. Lines 130-132: Up to what time point was collected for collection of data regarding adverse events, UTI’s, etc? This was not mentioned.

7. Materials and methods: what size catheters were used and were they all the same for all patients?

8. Line 212: How do you know that constipation was not a side effect from surgery?

9. Lines 246-249: Patients may have over-reported UTI symptoms also due to the fact that they had pelvic reconstructive surgery and would that inflate the percentage of UTI symptoms and result in over-testing with urine cultures and therefore a higher detection of UTI?
10. Given the older patient population, could patients have asymptomatic bacteruria preoperatively that was undetected? Were preoperative urine cultures obtained?

Reviewer #2:

Line 76: I suggest Reference 4 rather than Reference 5 is the relevant reference for association between prolonged catheterization and UTI.

Lines 189 - 191: Was there any difference between type of surgery and percentage of indwelling catheter? Does the median number of catheter days include both indwelling and CISC patients? If not, what was the difference in duration between the two groups? Also, why was median used rather than mean?

Lines 195, 196: Of the patients who had more than 1 culture positive test, were the organisms the same in all cultures, and did they prove resistant to nitrofurantoin?

Lines 198, 218: 26 women met the primary outcome of UTI, but there were 27 positive cultures. Please explain. Was there any analysis comparing number of days of catheterization and incidence of culture-proven UTI?

Table 1 Baseline Characteristics

Numbers do not correspond with text. Headings in Table 1 indicate 77 patients were included in each group. The text states that 77 patients were randomized to each arm, but only 75 were included in the treated group and 76 in the placebo group. Table 1 shows each group contained 77 patients. However, the text reports 75 patients were in the treated group, and 76 in the placebo group:

- Menopausal Status: Treated: 77 patients, Placebo: 78 patients
  Total percentage: 100% 80.3%
  The placebo percentage appears to be a typographical error. The value for the premenopause cohort should be 23%.

- Pre-operative POP-Q: Treated: 75 patients, Placebo: 77 patients
  Total percentage: 97% 100%
  In the treated group, assuming 75 patients, the percentages for stage II and III should be 36 and 53 respectively.

- Indication for Surgery: Treated: 75 patients, Placebo: 76 patients
  Total percentage: 100% 95.1%
  In the placebo group, assuming 76 patients, 25% underwent incontinence surgery.

I also noted that in the text (lines 189-190), 101% of patients had an indication for surgery.

- Catheter Type: Treated: 77 patients, Placebo: 76 patients

Reviewer #3: Prospective, randomized, double blind placebo controlled study with the objective of evaluating if nitrofurantoin is more effective than placebo in decreasing the incidence and symptoms and culture confirmed UTI in women with acute urinary retention following prolapse or incontinence surgery. Authors do meet this objective, showing no difference between placebo and nitrofurantoin.

Line 77 and 78 - which types of prophylactic antibiotics?

Line 78-80 - please provide a brief summary of this evidence

Line 122-123 - were patients educated on UTI symptoms to report?

Line 134 - what or where is the data coordinating center

Line 115-153 - please provide brief details about these guidelines

Line 264 - please quantify the reduced incidence
STATISTICAL EDITOR COMMENTS:

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

lines 101-102: Would have been preferable to eliminate variable of indwelling vs intermittent cath, since was by surgeon preference and not randomly assigned. Or, could have increased sample size to test each cath method, rather than aggregating the methods. Need to acknowledge that there was insufficient power to conclude separate NS effects for nitrofurantoin in both intermittent and indwelling cath subsets, but only powered for aggregated methods.

Table 2: Should clearly demarcate/label the primary outcome (ITT) from the subsets. Low power to discern differences for the subsets by catheter type.

Table 4: Why are the serious adverse events statistically different at p < .001? Looks NS.

Fig 1: Should extend the flow diagram to show the number in each treatment arm with symptoms, then number of those who tested (+) for ≥ 1000 cfu/mL.

EDITOR COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, as well as subsequent author queries. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

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

B. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

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

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

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

*The manuscript's guarantor.

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

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

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.
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, tables, boxes, figure legends, and print appendixes) but exclude references.

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).

Please list the 2018 AUGS meeting on the title page. We need the city/state and dates of the meeting.

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.

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

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.

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.

Abstract-Results and Results Sections: Please express outcome data as both absolute and relative effects since information presented this way is much more useful for clinicians. In both the Abstract and the Results section of the manuscript, please give actual numbers and percentages in addition to odds ratios (OR) or relative risk (RR). If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh).

Your revised manuscript must include relative risk and 95% confidence intervals. As written, your study is only powered to predict large differences.

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.

Figure 1: Please double-check the arithmetic in your flow diagram.

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/acid/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.

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 Jun 06, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

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

In compliance with data protection regulations, 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.
June 4, 2019

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

Dear Dr. Chescheir,

Thank you very much for your review of our manuscript. The comments from the reviewers and editors are reproduced in entirety below. Our response to each comment is immediately below the comment and demarcated by the bullet point ●. The location of added or edited text is listed by line number in the tracked changes document, and edited text is reproduced in this letter.

Thank you again for your time and consideration.

Erin Seifert Lavelle, MD

REVIEWER COMMENTS:

Reviewer #1:

1. The manuscript is overall well written with few grammatical errors throughout.
   ● We have made our best effort to find and address any grammatical errors identified

2. Lines 1-2: Suggest including in the title the type of surgery performed, i.e.: "Antibiotic Prophylaxis During Catheter-managed Postoperative Urinary Retention after Pelvic Reconstructive Surgery: A Randomized Controlled Trial"
   ● Agree the more specific title is more descriptive and reflects our original title. Please note this exceeds journals length limit and can be edited as requested or suggested.
   ● Line 1
   ● Antibiotic Prophylaxis During Catheter-managed Postoperative Urinary Retention after Pelvic Reconstructive Surgery: A Randomized Controlled Trial

3. Line 95: Which five sites were included for this multi-centered trial? This should be included in the Materials and Methods.
   ● Edited line 121
   ● Patients were recruited from the University of Pittsburgh, MedStar Washington Hospital Center, Washington University, University of Texas Southwestern, and the University of Iowa.
4. Line 99: What specific procedures were performed for pelvic organ prolapse and/or urinary incontinence? This is not mentioned at all in the manuscript. Was cystoscopy routinely performed on all procedures? If so, were the number of times cystoscopy was performed recorded due to transurethral manipulation, which could potentially contribute to the incidence of UTI? (ie. Inserting the cystoscope multiple times vs. one time).

- Edited line 125
- Reconstructive surgery was considered any procedure performed for correction of urinary incontinence or pelvic organ prolapse of any compartment, and intraoperative cystoscopy was performed at surgeon discretion. Sacral neuromodulation procedures and intradetrusor BOTOX® (onabotulinumtoxinA) injections were excluded.

5. How long were patients taking nitrofurantoin for duration of catheter use? What is the protocol per site for management of postoperative urinary retention and were protocols all the same?

- Specified line 141
- Participants were allocated 1:1 to extended release nitrofurantoin 100mg or an identical-appearing placebo capsule, taken once daily during catheter use.
- Edited line 158
- Catheter use was discontinued when adequate bladder emptying was documented by assessment of post void residual volume, either by straight catheterization, bladder scan, or repeat of void trial.

6. Lines 130-132: Up to what time point was collected for collection of data regarding adverse events, UTI's, etc? This was not mentioned.

- Edited line 150
- Women were instructed to seek care for urinary tract infection symptoms only from their study physician team during the six week postoperative study period.
- Specified line 174
- The primary outcome was incidence of symptomatic urinary tract infection confirmed with a positive urine culture within six weeks of surgery.
- Edited line 186
- Secondary outcomes included the frequency of urine cultures with nitrofurantoin-resistant or intermediate sensitivity isolates, and frequency of adverse symptoms possibly related to daily nitrofurantoin exposure as endorsed by daily diary within six weeks of surgery including nausea, vomiting, headache, flatulence, diarrhea, dyspepsia, abdominal pain, constipation, emesis, dizziness, drowsiness, amblyopia, pruritis,
urticaria, hair loss, fever, chills, malaise, and acute pulmonary, dermatologic, or hepatic reaction.

7. Materials and methods: what size catheters were used and were they all the same for all patients?
   - Unfortunately this was not prespecified or recorded

8. Line 212: How do you know that constipation was not a side effect from surgery?
   - We agree that constipation is a common occurrence after pelvic reconstructive surgery. As patients were randomized, we believe the impact of surgery on constipation was equivalent between groups, and noted the difference between treatment arms in line 256 and Table 2.

9. Lines 246-249: Patients may have over-reported UTI symptoms also due to the fact that they had pelvic reconstructive surgery and would that inflate the percentage of UTI symptoms and result in over-testing with urine cultures and therefore a higher detection of UTI?
   - We agree there may be a detection bias both related to the patient’s knowledge of the primary outcome, as well as the patient awareness of UTI risk after pelvic surgery in clinical practice. The high rate of UTI-type symptoms, prophylactic antibiotic prescriptions, and empiric treatment is what inspired this study.

10. Given the older patient population, could patients have asymptomatic bacteruria preoperatively that was undetected? Were preoperative urine cultures obtained?
    - Important question, we did not have the resources to pay for study tests and do not have baseline culture or microbiome data
    - Edited line 369
    - We encourage future research evaluating the perioperative urinary microbiome, and potential impact of surgery and prophylactic antibiotics.

Reviewer #2:

Line 76: I suggest Reference 4 rather than Reference 5 is the relevant reference for association between prolonged catheterization and UTI.

    - Edited citation line 99
Was there any difference between type of surgery and percentage of indwelling catheter?

- There was no difference between indication for surgery – POP vs UI – but the author team decided not to present this data as the included procedures are too heterogeneous for meaningful comparison. The volume of each procedure performed is too small for a statistically powered comparison. We could include if preferred by the editorial team. Data below for review.

<table>
<thead>
<tr>
<th>Procedure type</th>
<th>n=38</th>
<th>n=31</th>
<th>0.73</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolapse only</td>
<td>6 (15.8)</td>
<td>4 (12.9)</td>
<td></td>
</tr>
<tr>
<td>Incontinence only</td>
<td>3 (25.0)</td>
<td>2 (10.5)</td>
<td>0.35</td>
</tr>
<tr>
<td>Combined prolapse and incontinence procedure</td>
<td>4 (16.0)</td>
<td>7 (26.9)</td>
<td>0.50</td>
</tr>
</tbody>
</table>

Does the median number of catheter days include both indwelling and CISC patients? If not, what was the difference in duration between the two groups?

- Edited line 246
- Fifty-eight percent of patients were discharged with an indwelling catheter, and 42% performed clean intermittent self-catheterization, with no difference between study groups (Table 1). Median duration of catheter use was four days (interquartile range 3, 7) and not statistically different between for self-catheterization and indwelling catheter patients.

Also, why was median used rather than mean?

- This was a non-normally distributed variable, skewed by the small number of outliers with prolonged catheterization

Lines 195,196: Of the patients who had more than 1 culture positive test, were the organisms the same in all cultures, and did they prove resistant to nitrofurantoin?

- Paragraph added line 397
- There were two women with multiple urinary tract infections during the study period, both in the placebo group. One patient had two cultures positive for pansensitive E. coli 12 days apart, followed by a culture growing Enterobacter four weeks later. The other patient was treated for Enterobacter cystitis with nitrofurantoin based on sensitivities,
and grew nitrofurantoin-resistant Enterobacter in a subsequent culture three weeks later.

Lines 198,218: 26 women met the primary outcome of UTI, but there were 27 positive cultures. Please explain.

- Because many patients had multiple symptomatic episodes, some had more than one positive urine culture although were only counted once in the primary outcome, and others were treated empirically, this becomes confusing. We have attempted to address this in multiple areas.
- Outlined in updated flow diagram
- Measurement of primary outcome clarified line 180
- Any woman diagnosed with urinary tract infection one or more times during the study period, by culture or empiric treatment, is included in the primary outcome. After a patient was diagnosed with urinary tract infection either by culture or empiric treatment, they were considered to have met the primary outcome. Any additional symptom and culture data were collected, however women experiencing more than one episode of urinary tract infection were counted only once in the primary outcome.
- Line 287 edited
- There were a total of 27 positive urine cultures during the study period.

Was there any analysis comparing number of days of catheterization and incidence of culture-proven UTI?

- Risk factors for UTI including duration of catheterization was not performed as a part of this analysis but is an interesting question that we would like to consider in future work. Further analysis could be performed for this manuscript if preferred by the editors.

Table 1 Baseline Characteristics. Numbers do not correspond with text. Headings in Table 1 indicate 77 patients were included in each group. The text states that 77 patients were randomized to each arm, but only 75 were included in the treated group and 76 in the placebo group. Table 1 shows each group contained 77 patients. However, the text reports 75 patients were in the treated group, and 76 in the placebo group:

- Baseline characteristics are now reported in Table 1 for only patients included in the primary analysis, and not the entire randomized population. Headings edited to reflect this, and totals confirmed.

I also noted that in the text (lines 189-190), 101% of patients had an indication for surgery

- Rounding error, edited line 243
Reviewer #3:

Prospective, randomized, double blind placebo controlled study with the objective of evaluating if nitrofurantoin is more effective than placebo in decreasing the incidence and symptoms and culture confirmed UTI in women with acute urinary retention following prolapse or incontinence surgery. Authors do meet this objective, showing no difference between placebo and nitrofurantoin.

Line 77 and 78 - which types of prophylactic antibiotics? Line 78-80 - please provide a brief summary of this evidence

- We did not cite or specify as this is from our collective clinical experience and we are unaware of any publications detailing choice of postoperative prophylactic antibiotics among urogynecologic providers.

Line 122-123 - were patients educated on UTI symptoms to report?

- There was not a standardized script or list of symptoms which mandated report. Patients were asked to report any symptoms they felt warranted attention to their study providers, consistent with the realities of clinical practice.

Line 134 - what or where is the data coordinating center

- Edited line 169
- The University of Pittsburgh served as the data coordinating center.

Line 115-153 - please provide brief details about these guidelines

- Paragraph edited lines 193-202

Adverse events and serious adverse events were recorded and graded according to Clavien-Dindo Classification and Food and Drug administration guidelines (19-21). Adverse events of Dindo grade II (those requiring pharmacological treatment with drugs, blood transfusions and total parenteral nutrition) or higher were recorded. In addition, any other event occurring during the study period that warranted reporting in the opinion of the site primary investigator were recorded. An event was considered "serious" if, in the view of either the investigator or data safety monitoring board, it resulted in death, life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or congenital anomaly/birth defect.
The Statistical Editor makes the following points that need to be addressed:

lines 101-102: Would have been preferable to eliminate variable of indwelling vs intermittent cath, since was by surgeon preference and not randomly assigned. Or, could have increased sample size to test each cath method, rather than aggregating the methods. Need to acknowledge that there was insufficient power to conclude separate NS effects for nitrofurantoin in both intermittent and indwelling cath subsets, but only powered for aggregated methods.

- We recognize this limitation and considered this as we designed the trial. As a fellow initiated study, dependent on participation on supervising attending surgeons, we elected to leave route of catheterization to surgeon preference to maximize participation while allowing supervising physician autonomy. In addition, Cochrane Review data suggests that there is no difference in UTI rate between indwelling and intermittent catheterization in the short term (15 days or less) supporting the use of the combined inclusion.

- Edited line 315

Table 2: Should clearly demarcate/label the primary outcome (ITT) from the subsets. Low power to discern differences for the subsets by catheter type.

- Edited, footnote added to table

Table 4: Why are the serious adverse events statistically different at p < .001? Looks NS.

- Apologies, updated with accurate p value

Fig 1: Should extend the flow diagram to show the number in each treatment arm with symptoms, then number of those who tested (+) for ≥ 1000 cfu/mL.

Edited, Figure 1
Figure 1. Study enrollment, randomization, and primary outcome

510 Women screened for eligibility

285 Excluded
  118 Exclusion criteria
  167 Declined participation

225 Consented

71 Passed voiding trial

154 Randomized

77 Randomized to nitrofurantoin

1 Withdrawn at patient request
1 Ineligible after randomization

75 Included in primary analysis

20 Women reported symptoms
22 Total episodes
21 Cultures obtained

13 Included in primary outcome
12 Diagnosed by culture
1 Treated empirically

77 Randomized to placebo

1 Withdrawn at patient request

76 Included in primary analysis

22 Women reported symptoms
33 Total episodes
31 Cultures obtained

13 Included in primary outcome
11 Diagnosed by culture
2 Treated empirically
EDITOR COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, as well as subsequent author queries. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

A. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
   - We opt in

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

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

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

   If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.
   - Cover letter updated and uploaded
4. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Responses to the five bullet points should be provided in a box at the end of the Methods section.

- Added line 219

| The authors do not have plans to share individual deidentified participant data. The authors do not have plans to make additional, related documents available (eg, study protocol, statistical analysis plan, etc.) but can do so by request. As there are no plans to share patient data, what data, when the data will become available and for how long, and by what access criteria data it would be shared have not been specified |

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

- Reviewed, no use of these defined terms noted to be problematic

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 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, tables, boxes, figure legends, and print appendixes) but exclude references.

- Word count added line 34, Abstract 300 words including headings
7. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

* All financial support of the study must be acknowledged.

* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.

* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.

* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

Please list the 2018 AUGS meeting on the title page. We need the city/state and dates of the meeting.

- Line 26
- This research was supported by grant funding from the Society of Gynecologic Surgeons and American Urogynecologic Society Fellows Pelvic Research Network

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

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

- Revised abstract line 40

9. Abstracts for all randomized, controlled trials should be structured according to the journal's standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample
abstract that is located online here:

- Revised abstract line 40

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.

- Removed

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.

- Removed

12. Abstract-Results and Results Sections: Please express outcome data as both absolute and relative effects since information presented this way is much more useful for clinicians. In both the Abstract and the Results section of the manuscript, please give actual numbers and percentages in addition to odds ratios (OR) or relative risk (RR). If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh).

Your revised manuscript must include relative risk and 95% confidence intervals. As written, your study is only powered to predict large differences.

- These are now included in the abstract and results section in text for primary and secondary outcomes.

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.

- Reviewed and modified as needed

14. Figure 1: Please double-check the arithmetic in your flow diagram.

- We checked this again and could not any discrepancies
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/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.

- Noted

16. 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.