OBSTETRICS & GYNECOLOGY

**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.

**Date:** May 26, 2020
**To:** "Sarah ES Jeney" [redacted]
**From:** "The Green Journal" em@greenjournal.org
**Subject:** Your Submission ONG-20-984

RE: Manuscript Number ONG-20-984

Fecal microbiota transplantation for the treatment of refractory recurrent urinary tract infection

Dear Dr. Jeney:

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).

***Due to the COVID-19 pandemic, your paper will be maintained in active status for 30 days from the date of this letter. If we have not heard from you by Jun 25, 2020, we will assume you wish to withdraw the manuscript from further consideration.***

REVIEWER COMMENTS:

Reviewer #1: Review of Manuscript ONG-20-984 "Fecal microbiota transplantation for the treatment of refractory recurrent urinary tract infection"

Jeney and colleagues have submitted a research letter that evaluates the use of fecal microbiota transplantation, most commonly used for refractory C. difficile infections based on several observations suggesting a reduction in potential uropathogens and thus potential efficacy in the setting of recurrent UTIs. I have the following questions and comments.

Title - Consider noting it is a pilot study?

Précis - No comments seems reasonable.

Abstract - None provided.

Introduction - Does space allow to provide another sentence or so about the prior case report experience?

Methods - Sounds more like a prospective cohort of patients, which is really just a pilot as no information on a formal sample size was provided. Was there a pre-specified number of patients you were hoping to enroll? Line 42 - how was urine collected at these time points - clean catch or catheterized specimen? Line 46 - I believe it is Fisher's exact test and not Fischer. Line 47 - why only a subset? How was this determined? Prior to or following transplant?

Results - Line 54-55 - Is there data comparing the safety/efficacy of directed vs. university-provided or banked specimens? Any other important demographic or medical history information? Lines 58-62 - you present data for 3 and 6 months but don't really comment on the 1-month collection. Is there a reason for this? No differences seen perhaps? Any symptomatic collections needed at the non-specified time points?

Discussion - Limited but seems to address the issues raised.

Tables - None.

Figures - Figure 1 can be deleted or supplementary. This was essentially described in the manuscript. Figure 2 seems more relevant.

Reviewer #2: The aim of this case series was to assess effects of fecal microbiota transplantation for refractory UTI in women. Strengths include the high follow-up rate (10 of 11), evaluation of different aspects of the therapy (treatment success, change in gut microbiome, proportion of drug-resistant bacteria), and recording codes and packages on GitHub. The obvious limitation is small sample of participants and donors. These data can thus be considered preliminary only but are still quite valuable as the results suggest that further study is appropriate.

Comments:
1)The precis conclusion, "Fecal microbiota transplantation for refractory recurrent urinary tract infections in women is safe and may improve antibiotic resistance patterns" does not provide a bottom line of the stated aim of the study: "we hypothesized that FMT may reduce number of symptomatic UTIs in women with refractory by altering the gut microbiome."

Further, it isn't possible to conclude that the procedure (or any procedure) is safe after being used in 11 women. This should be removed from precis and conclusion.

2) Line 40: Please state for how long participants discontinued antibiotic.
3) Line 41: State how the number of symptomatic, culture-proven, antibiotic-treated UTI in the six months prior to FMT was determined (ie, self-report, chart review, other?)
4) Line 46: "Fecal samples were collected for microbiome analysis from donors and a subset of recipients." Please state when fecal samples were collected from recipients and what the N is for the subset. In line 66, you note: "Recipient post-FMT samples (V2-5) do not cluster differently than pre- FMT samples (V1)" which implies that some number of participants feces was tested twice—if that's the case, please add to methods. Please state what the V in V2-5 stands for.
5) Figure: It appears that 4 participants had microbiome testing of feces? Whatever this N is, please state it clearly in results.
6) Line 82: Consider replacing 'this study" with "these pilot data"---the study indeed has limitations as a full-fledged research study, given the small sample size for both participants and donors, but is a great resource as a pilot study.

Reviewer #3: Congratulations to the authors on a well-written research letter addressing the use of FMT to treat rUTI.
I do have a few minor corrections:
Word count is 605 instead of the 600 limits please check.
Results
Line 55 - states "received directed donation and nine received University-provided donation" - if you are able to clarify the difference (either here or in methods)
Conclusion
Line 76 - may try to rewrite the following sentence "4/10 women no longer met criteria for recurrent UTI, while 3/10 women were UTI-free."
Line 83-83 - "Future studies involving FMT via enema or oral capsule with pooled donor stool may offer more robust treatment effect." - rewrite sentence to make the message clearer

ASSOCIATE EDITOR - GYN
Thank you for this Research Letter. We have been experiencing record numbers of submissions and as a result have strict page limit considerations - please keep this in mind as you work through the revisions above. Also, consider which figures might be okay to move to an online-only Appendix. It is likely that some text will be cut from your revised submission and/or figures moved to the appendixes anyway due to our need to not go over our page limit restrictions for the year.

STATISTICAL EDITOR COMMENTS:

How can you make a firm conclusion re: safety based on n =10 patients. For example, if 0 of 10 patients died, the upper bound for 95% CI would be 37% mortality rate. Language in precis needs to change to remove mention of safety.

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. 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.

2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). 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.

3. 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.

4. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Research Letters articles should not exceed 2.5 pages (600 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.

5. 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).

6. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.

7. 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.

8. 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.

9. When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

Figure 2: These four figures will not fit together on a printed page. Please break them into 3 difference figures (C and D may stay together). Please upload higher resolution versions of these figures (eps, tiff, jpeg, etc.). Please cite Figure 2D in the text.

10. 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.

***

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 30 days from the date of this letter. If we have not heard from you by Jun 25, 2020, we will assume you wish to withdraw the manuscript from further consideration.***.

Sincerely,

The Editors of Obstetrics & Gynecology

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

_____

Manuscript Title: A pilot study of fecal microbiota transplantation for the treatment of refractory recurrent urinary tract infection

Dear Reviewers and Editorial Staff,

Thank you for considering our work for publication and for the thoughtful reviews. We would be honored to present our data though this journal. As in the original submission, permission has been granted from the authors listed to be named in this article. Institutional support from the Fry Family Foundation was used for microbiome sequencing and analysis through Zymo Research Corp (Irvine, CA).

The protocol in this trial is the same as was posted in ClinicalTrials.gov (NCT03050515). This study design was presented on February 26th, 2019 at the 1st Annual Urobiome Meeting in La Jolla, CA, and this work has been presented at the combined meeting of the International Urogynecologic Association 44th Annual Meeting and American Urogynecologic Society Pelvic Floor Disorders Week 2019, September 25, 2019, Nashville, TN and the 2nd Annual Urobiome Meeting in La Jolla, CA on March 5th, 2020.

As requested in 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: *Sarah ES Jeney, MD*

This work was originally submitted as Original Research on Feb 4, 2020, and was rejected Mar 18, 2020 with the below revisions and recommendation to resubmit as a Research Letter from the Associate Editor. It was resubmitted as a research letter on Apr 22, 2020, and revisions requested on May 26, 2020. I have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf).

Please see point-by-point responses to Reviewer Comments in blue.

REVIEWER COMMENTS:

Reviewer #1: Review of Manuscript ONG-20-984 "Fecal microbiota transplantation for the treatment of refractory recurrent urinary tract infection"

Jeney and colleagues have submitted a research letter that evaluates the use of fecal microbiota transplantation, most commonly used for refractory C. difficile infections based on several observations suggesting a reduction in potential uropathogens and thus potential efficacy in the setting of recurrent UTIs. I have the following questions and comments.

Title - Consider noting it is a pilot study?
This has been changed

Précis - No comments seems reasonable.

Abstract - None provided.

Introduction - Does space allow to provide another sentence or so about the prior case report experience?
Unfortunately, we are at the allowed word count with this streamlined manuscript. The two published works describing UTI after FMT include a retrospective study by Tariq et al. (2017) of eight women with rUTI who received FMT for recurrent *C. difficile* infection.[1] Median number of UTI in these women

decreased from four in the year prior to FMT to one in the year following FMT, with improved antibiotic susceptibility of uropathogens isolated. In this study, six of eight women no longer met criteria for rUTI in the year following FMT, most of which were via colonoscopy. A 2018 case report by Biehl et al. of a German woman with rUTI post-renal transplantation described complete resolution of UTI post-FMT via one-time oral capsule.[2]

Methods - Sounds more like a prospective cohort of patients, which is really just a pilot as no information on a formal sample size was provided. Was there a pre-specified number of patients you were hoping to enroll?
We planned to and did enroll 12 patients for the study. Sample size calculation was performed off of the effect size seen in Tariq et al (2017) estimating an effect size of 50% reduction in UTI post-FMT. A sample size of 10 participants yielded 82% power to test the hypothesis that participants would have a 50% or greater reduction in number of UTI post-FMT, at a 0.05% significance level, using a 1-sided Fisher's exact test for proportions. Recruitment of 12 participants was planned to account for 15% dropout. On review of the study data, defining the primary outcome as number of UTI pre and post-FMT seemed more appropriate given the overall small sample size. Sample size calculation using the data in this study, an estimated mean of paired differences of -2 UTI with effect size of 1, permits an alpha of 0.05 with 80% power (assuming logistic distribution of the data, as our data was skewed towards zero). This power calculation was performed with statistician consult.

Line 42 - how was urine collected at these time points - clean catch or catheterized specimen?
By protocol, the urines taken for follow-up were permitted to be catheterized or clean-catch samples. Most of these samples were clean catch voided specimens, with the exception of the two patients who were catheter-dependent for neurogenic bladder.

Line 46 - I believe it is Fisher's exact test and not Fischer.
Thank you, this has been changed

Line 47 - why only a subset? How was this determined? Prior to or following transplant?
Funding was only available to perform shogun sequencing and purchase the collection materials for a subset of participants. This was included in the IRB study protocol while we awaiting funding. Funding was secured in the fall of 2018 and all study participants transplanted after that underwent fecal microbiota analysis before and after FMT. The funding covered sample collection devices and nucleotide stabilization media, sequencing services and analysis through Zymo.

Results - Line 54-55 - Is there data comparing the safety/efficacy of directed vs. university-provided or banked specimens?
Only one of the two participants who elected a directed donation completed study protocol, so we feel no conclusion can be drawn regarding comparing directed and anonymous donors in our study. A 2016 abstract from IDWeek by Osman et al examined physician-reported clinical cure and safety data from 2050 patients treated with FMT of pooled stool bank specimens for *C. difficile* infection.[3] Overall clinical cure rate was 84%, with colonoscopy delivery superior to upper endoscopy (clinical cure 86% vs 74%) ($p < 0.01$). 3 Adverse events possibly related to FMT were seen. This data was also published in a 2017 report of non-responders to FMT by the same pooled stool bank, which examined characteristics such as toilet cleaning on *C. difficile* recurrence rates.[4] A 2016 retrospective cohort study of patients who received FMT for *C. difficile* showed no significant difference in the percentage of patients who chose a directed donor among those with and without recurrent CDI, although this study was not powered for this analysis. In this study, 38 of 53 patients without CDI recurrence underwent directed donation vs 7 of 14 patients with CDI recurrence ($p = 0.13$).[5] No safety data by donor type was reported.

Any other important demographic or medical history information?

Unfortunately there is not space in the manuscript to include this relevant information or the antibiotic suppression therapies used by subjects prior to enrollment (inclusion criteria mandated recurrent UTI refractory to at least 6 months of suppressive antibiotic therapy). 9 patients were of non-Hispanic white race, and 1 was Hispanic. 9 were post-menopausal and 1 pre-menopausal. 2 women performed clean intermittent catheterization for neurogenic bladder (one with multi-system atrophy and the other with a history of tethered cord). 1 patient had type 2 diabetes mellitus. Relevant clinical information includes the following information for subjects who underwent microbiome analysis: P7-9 are post-menopausal, and P10 is pre-menopausal; P8, P9 reported taking oral probiotics and P10 a vaginal lactobacillus probiotic suppository; P8 restarted weekly Fosfomycin antibiotic suppression after the one month time point (after V3), P9 underwent suprapubic tube placement after the three month time point (after V4), and P10 restarted methenamine suppressive treatment after the one month time point (after V3).

Lines 58-62 - you present data for 3 and 6 months but don't really comment on the 1-month collection. Is there a reason for this? No differences seen perhaps?
The 3 and 6 month multi-drug resistance data were pre-specified endpoints for the antibiotic resistance data. We analyzed the UTI data at 6-months as it seemed clinically relevant to the use of FMT for treatment of recurrent UTI and also to see which subjects continued to meet criteria for recurrent UTI (using the clinical definition of 2 in 6 months). Additionally, the study design (comparing the number of UTI in 6 months post-FMT to the 6-month pre-FMT) make it difficult to compare the 1-month data as there would be no control. We did not analyze # UTI at one month post-FMT but can if this is requested.

Any symptomatic collections needed at the non-specified time points?
Yes, there were a total of 11 symptomatic collections at non-specified time points.

Discussion - Limited but seems to address the issues raised.

Tables - None.

Figures - Figure 1 can be deleted or supplementary. This was essentially described in the manuscript. Figure 2 seems more relevant.
Respectfully, we believe that Fig 1 provides important visualization of the UTI data that aids in interpretation of the text. This could be suitable for an online only figure. On presentation to the department and at the AUGS/IUGA meeting, this graph was well received in helping to explain the data. However, if it is recommended by the reviewers and editors to remove it as it is extraneous, we are happy to comply.

Reviewer #2: The aim of this case series was to assess effects of fecal microbiota transplantation for refractory UTI in women. Strengths include the high follow-up rate (10 of 11), evaluation of different aspects of the therapy (treatment success, change in gut microbiome, proportion of drug-resistant bacteria), and recording codes and packages on GitHub. The obvious limitation is small sample of participants and donors. These data can thus be considered preliminary only but are still quite valuable as the results suggest that further study is appropriate.

Comments:
1)The precis conclusion, "Fecal microbiota transplantation for refractory recurrent urinary tract infections in women is safe and may improve antibiotic resistance patterns" does not provide a bottom line of the stated aim of the study: "we hypothesized that FMT may reduce number of symptomatic UTIs in women with refractory by altering the gut microbiome."
This has been edited to read: “Fecal microbiota transplantation may reduce episodes of refractory recurrent urinary tract infection by altering gut microbiome.”

Further, it isn't possible to conclude that the procedure (or any procedure) is safe after being used in 11 women. This should be removed from precis and conclusion.
This has been removed from the precis. In the conclusion, we believe it is important to note that there were no serious adverse events related to FMT in our study population as this is the first described case series of the use of FMT for recurrent UTI.

2) Line 40: Please state for how long participants discontinued antibiotic.
This has been added. Participants discontinued antibiotics 48 hours prior to FMT (day FMT -2 was the last dose of antibiotic).

3) Line 41: State how the number of symptomatic, culture-proven, antibiotic-treated UTI in the six months prior to FMT was determined (ie, self-report, chart review, other?)
Chart review (in which patients complained of symptoms of UTI), urine culture review, and medical record confirmation of acute episodic antibiotic treatment were used to determine the pre-FMT UTI number.

4) Line 46: "Fecal samples were collected for microbiome analysis from donors and a subset of recipients." Please state when fecal samples were collected from recipients and what the N is for the subset. In line 66, you note: "Recipient post-FMT samples (V2-5) do not cluster differently than pre-FMT samples (V1)" which implies that some number of participants feces was tested twice—if that's the case, please add to methods. Please state what the V in V2-5 stands for.
This N has been added (n=4). After funding was obtained, the subsequent recipients then collected stool samples at each study visit (pre-FMT, and 1 week, 1 month, 3 and 6 months post-FMT). V stands for visit (V1 is the first visit, V2 the second, etc.). This allowed longitudinal analysis of the recipients post-FMT. This has been clarified in the methods and result section.

5) Figure: It appears that 4 participants had microbiome testing of feces? Whatever this N is, please state it clearly in results.
Please see above, this N has been added (n=4).

6) Line 82: Consider replacing 'this study" with "these pilot data"---the study indeed has limitations as a full-fledged research study, given the small sample size for both participants and donors, but is a great resource as a pilot study.
This has been done, thank you.

Reviewer #3: Congratulations to the authors on a well-written research letter addressing the use of FMT to treat rUTI.
I do have a few minor corrections:
Word count is 605 instead of the 600 limits please check.
Thank you. Excluding Fig 1 legend (which can be on-line) and title headings, we are now within 600 words, including Fig 2 legend.

Results
Line 55 - states "received directed donation and nine received University-provided donation" - if you are able to clarify the difference (either here or in methods)
Two of the individuals preferred to identify their own donor, who was screened, and then that individual provided the stool sample for the FMT. The other women chose to have a University-screened and provided donor who was unknown to them personally.

Conclusion
Line 76 - may try to rewrite the following sentence "4/10 women no longer met criteria for recurrent UTI, while 3/10 women were UTI-free."
This has been changed to “four women no longer met criteria for recurrent UTI, and three had no UTIs.”

Line 83-83 - "Future studies involving FMT via enema or oral capsule with pooled donor stool may offer more robust treatment effect." - rewrite sentence to make the message clearer
Due to word limit restrictions, this sentence has been removed. A better line would say “Future direction of study includes optimal dose, route, and FMT formulation.” Perhaps our treatment lacked efficacy as it was only a one time enema from a single donor and so we would not want this case series to be taken as ‘FMT does not work for rUTI’ if perhaps other dose, route, and formulation (eg pooled donor) stool may have a better treatment effect.

ASSOCIATE EDITOR - GYN
Thank you for this Research Letter. We have been experiencing record numbers of submissions and as a result have strict page limit considerations - please keep this in mind as you work through the revisions above. Also, consider which figures might be okay to move to an online-only Appendix. It is likely that some text will be cut from your revised submission and/or figures moved to the appendixes anyway due to our need to not go over our page limit restrictions for the year.
Figure 1 could be online only, but we feel it is important and useful for the Ob/Gyn journal to include the microbiome images in Fig 2 in the manuscript as that information is novel and is how microbiome data (beta diversity) is best presented.

STATISTICAL EDITOR COMMENTS:

How can you make a firm conclusion re: safety based on n =10 patients. For example, if 0 of 10 patients died, the upper bound for 95% CI would be 37% mortality rate. Language in precis needs to change to remove mention of safety.
This has been removed, thank you.

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. 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.**

2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). 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.

3. 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.

4. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Research Letters articles should not exceed 2.5 pages (600 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.
If necessary, we can move Fig 1 to online-only. Would its legend count towards the word count in this case?

5. 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).

6. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.
FMT for recurrent UTI

7. 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.
Are we permitted to use “UTI” for urinary tract infection after we spell it out as this is a commonly used acronym? Spelling out “urinary tract infection” each time will necessitate much useful information to be cut.

8. 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.
These have been removed.

9. When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your

original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

Figure 2: These four figures will not fit together on a printed page. Please break them into 3 difference figures (C and D may stay together). Please upload higher resolution versions of these figures (eps, tiff, jpeg, etc.). Please cite Figure 2D in the text.
Done thank you.

References for revision comments:


1. Tariq R, Pardi DS, Tosh PK, Walker RC, Razonable RR, Khanna S. Fecal Microbiota Transplantation for Recurrent Clostridium difficile Infection Reduces Recurrent Urinary Tract Infection Frequency. *Clinical Infectious Diseases.* 2017;65(10):1745-1747.
2. Biehl LM, Cruz Aguilar R, Farowski F, et al. Fecal microbiota transplantation in a kidney transplant recipient with recurrent urinary tract infection. *Infection.* 2018;46(6):871-874.
3. Osman MOB, Kelsey; Stoltzner, Zachery; Ling, Kelly; Koelsch, Emily; Dubois, Nancy; Khoiri, Adila; Amaratunga, Kanchana; Smith, Mark; Kassam, Zain. Safety and Efficacy of Fecal Microbiota Transplantation for Recurrent Clostridium difficile Infection From An International Public Stool Bank: Results From a 2050-Patient Multicenter Cohort. *Open Forum Infectious Diseases.* 2016;3(suppl_1).
4. Razik R, Osman M, Lieberman A, Allegretti JR, Kassam Z. Faecal microbiota transplantation for Clostridium difficile infection: a multicentre study of non-responders. *Med J Aust.* 2017;207(4):159-160.
5. Fischer M, Kao D, Kelly C, et al. Fecal Microbiota Transplantation is Safe and Efficacious for Recurrent or Refractory Clostridium difficile Infection in Patients with Inflammatory Bowel Disease. *Inflamm Bowel Dis.* 2016;22(10):2402-2409.


Sincerely,

*Sarah ES Jeney, MD*
June 2, 2020