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

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

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Questions about these materials may be directed to the Obstetrics & Gynecology editorial office: obgyn@greenjournal.org.
Date: Apr 18, 2019
To: "Kimberly Levinson"
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-517

RE: Manuscript Number ONG-19-517

Lower Genital Tract Dysplasia in Female Solid Organ Transplant Recipients

Dear Dr. Levinson:

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 May 09, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: Introduction

Key to the hypothesis is that the risk of lower genital tract cancers and cervical dysplasia is higher in transplants, coincident with immunosuppression that is needed over the same non-transplant population. I see no general background information on rates in general, or more importantly, in the population under study. That is needed.

Methods

1. The differentiation on the definition of "specimen" is confusing. Pap test (cytologic) specimens are lumped in with the gold standard tissue evidence. Break that out and tell the reader how the cytologic evidence is tabulated separate from the biopsy evidence.

2. Line 193-196 - how was that evidence collected? Chart review, use of codes? This is important for the strength of the evidence to the reader.

3. line 204-207 - perhaps you should have limited the study to a cohort where you had a complete data set? Kidney transplant patients...

Results

4. 250-259 - It is hard to understand how HG dysplasia or cancer detected in n=24 and then you break this down and its seems the incidence was much higher when you break ou the subgroups

Discussion

5. Discuss how this may under report the incidence because lesions may remain occult due to non screening behavior in a post transplant case.

Reviewer #2: This is a very well written study with information that is pertinent to the changing demographics of populations and the accompanying medical issues/treatments they face, as well as the increasing use of immunomodulation and immunotherapies.
I have some minor questions/comments. The patients included had at least one cervical or LGT specimen available in the pathology archive of the authors- I assume this was a pre-transplant specimen? It does not say so but the next sentence notes that patients were excluded if no LGT pathology specimens after transplantation were available, hence my assumption. But it would be better to clearly state it, rather than having the reader assume anything.

I am surprised no discussion was given regarding HPV vaccination status prior to transplantation (whether it be the first transplant or subsequent transplants.) From Table 1, it is clear that a percentage of the population did get vaccinated (about 7-8%) although we do not know when. As the HPV vaccine has been in use for a long time, and given the recent recommendations expanding the age range, further exploration of the role of HPV vaccination pre or post transplantation in possibly impacting the incidence of LGT dysplasia in transplant patients would be quite relevant.

The information on Pap smear history was a bit disappointing; while ~61% of patients had a documented pap prior to transplant, that means 39% did not. This makes the incidence of cervical dysplasia post-transplant hard to interpret. Did the immunosuppression given after transplant allow for the emergence and development of 'new' dysplasia or di it simply allow for the progression of pre-existing cervical dysplasia? This is relevant given that 8 of the 14 women who developed cIN2+ had unknown Pap test results prior to transplantation.

I think a key and fundamental point of the paper is that many clinicians focus on cervical screening post-transplantation but non-cervical LGT dysplasia or cancers must clearly be part of all routine and ongoing surveillance of the genital tract. This paper does add more information to the small amount of data currently available, is clinically relevant, and opens the door for further more in-depth exploration of the issues around LGT dysplasia/cancers and transplant patients, perhaps all immunosuppressed patients.

Reviewer #3: In this manuscript, the authors present a 15-year, retrospective study of female subjects that underwent a solid organ transplant at a large academic medical center. The outcome of interest was lower genital tract (LGT) dysplasia among these women. Similar studies have been done on this general topic. The authors cite this and indicate (twice in the introduction) there is minimal data on non-cervical LGT dysplasia among transplant recipients and thus this study sought to describe the full range of LGT dysplasia in this population. Subjects to be included had to have at least 2 years follow-up and at least 1 cervical OR LGT pathology specimen at the study institution prior to the transplant. Subjects were identified by a pathology archive and chart review was conducted to extract relevant study outcomes. Overall, the study appears to deliver on its objectives. I have the following questions/comments:

1) With respect to the outcome genital warts - was this per the chart report or was this per some ICD diagnosis code? If either, was the diagnosis clinically based or based on a specimen pathology?

2) Line 245 - "age" is cited as protective - please state the direction of age (e.g. younger or older age).

3) Line 245 - its more technically correct to say, "a history of patient-reported normal Pap tests..."

4) Line 318 - With respect the study population size of past investigations, I'm not sure 394 and 262 are different enough to say, the later is "only" relative to the former.

Overall the recommendations of this study - and those like it - are reasonable and pertinent to the general OB/GYN community.

STATISTICAL EDITOR’S COMMENTS:

1. Abstract: The risk estimates should include CIs, eg 47/394 = 11.9%[CI 8.8-15.9%].

2. General: Since the adverse events developed at various time points, it would be informative to include a K-M curve or table to show the time course of cervical dysplasia.

3. Table 2: Should cite in footnote which variables were retained in the final multivariable model and justify their use, since there were only 47 adverse events and therefore the number of adjustors should not exceed 5.

4. lines 373-375, 400-402: The limitations are an important part of the discussion, but whether the true incidence is higher is conjecture. From these data, one can only conclude that point estimate is 11.9%, but the statistical range from these data could be as low as 8.8% or as high as 15.9%

ASSOC EDITOR - GYN:

Please emphasize in the Discussion about the elevated vaginal/vulvar dysplasia rate suggesting that health care providers need to consider this when examining and caring for these patients instead of just focusing on Pap smear screening like the general population.
EDITORIAL OFFICE 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:

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

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. 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, STAR, STROBE, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

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

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 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.

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

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

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

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Original Research articles, 300 words; Reviews, 300 words; Case Reports, 125 words; Current Commentary articles, 250 words; Executive Summaries, Consensus Statements, and Guidelines, 250 words; Clinical Practice and Quality, 300 words; Procedures and Instruments, 200 words. Please provide a word count.

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

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

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

12. 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.

13. The American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found via the Clinical Guidance & Publications page at https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance.

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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 May 09, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

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

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COVER LETTER FOR SUBMISSION OF MANUSCRIPT

May 8, 2019

Dear Editors,

Thank you for your review of our manuscript and the thoughtful comments. We have addressed the comments by the reviewers and editors. Please see our attached response. We followed the STROBE guidelines for this retrospective study, the checklist is included in our submission.

The lead author, Kimberly Levinson, 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.

Thank you again for considering our work. Given the paucity of data on lower genital tract dysplasia (other than cervical dysplasia) in women who have undergone transplantation, we hope this study can help inform clinicians and guide evidence-based screening recommendations for this population.

Sincerely,

Kimberly Levinson, MD

REVIEWER COMMENTS AND RESPONSES
Reviewer #1

Comment 1: Key to the hypothesis is that the risk of lower genital tract cancers and cervical dysplasia is higher in transplants, coincident with immunosuppression that is needed over the same non-transplant population. I see no general background information on rates in general, or more importantly, in the population under study. That is needed.
Response 1: Thank you for this feedback. We added information on the incidence and risk of cervical and non-cervical dysplasia among healthy women to the introduction (Page 4; Line 15-21). Regarding disease rates in transplant recipients, we discuss the increased risk of cancer, CIN, and high-grade CIN in the second paragraph of the introduction (P5; L1-12). Per your suggestion, we also added the incidence rates for all LGT dysplasia and CIN in the transplant
Comment 2: The differentiation on the definition of "specimen" is confusing. Pap test (cytologic) specimens are lumped in with the gold standard tissue evidence. Break that out and tell the reader how the cytologic evidence is tabulated separate from the biopsy evidence.
Response 2: Thank you for this suggestion. We clarified that LGT dysplasia was determined based on gold standard tissue diagnosis (P7; L5-6). We also clarified how cytologic specimens were used separately (P7; L9-11). We kept the definition of specimen the same (P6; L11-14), because we utilized both cytological specimens and tissue specimens to evaluate which patients met inclusion criteria. We have clarified, however, that diagnoses of dysplasia were based on tissue diagnosis rather than cytologic specimens (P7; L5-6).

Comment 3: Line 193-196 - how was that evidence collected? Chart review, use of codes? This is important for the strength of the evidence to the reader.
Response 3: We have clarified that the data was collected through chart review using a standardized extraction form (P6; L20&23).

Comment 4: Line 204-207 - perhaps you should have limited the study to a cohort where you had a complete data set? Kidney transplant patients...
Response 4: Thank you for this comment. We agree that completeness of data is important, and given that kidney transplants were the most common, we did consider limiting our population; however, there are few studies that look at dysplasia outcomes across different organ transplants, and we felt that there were strengths and limitations to each of these strategies (using the larger population with some limitation of data vs. proceeding with a smaller population with a more complete dataset. Ultimately, we felt that given the limited knowledge on lower genital tract dysplasia in all transplant patients, understanding the risk across organ type is important to help guide evidence-based screening for the larger population of transplant patients. We agree that further subset analysis of limited populations is further warranted.

Comment 5: Lines 250-259 - It is hard to understand how HG dysplasia or cancer detected in n=24 and then you break this down and its seems the incidence was much higher when you break you the subgroups
Response 5: We have adjusted the language in this portion of the results. We believe the source of confusion is that although 14 women developed CIN2+ and 13 developed VIN/VAIN/AIN2+, 3 women developed both types of dysplasias (therefore, the total is not 27 but 24 women). Because three women developed both CIN2+ and VIN/VAIN/AIN2+, these three women were counted twice, which makes the incidence look higher when broken into subgroups. We have therefore re-written P10; L12-14 to clarify that 11 developed only CIN2+ or cancer, 10 developed only non-cervical high-grade LGT dysplasia or cancer, and 3 developed both cervical and non-cervical high-grade dysplasia.

Comment 6: Discuss how this may under report the incidence because lesions may remain occult due to non screening behavior in a post transplant case.
Response 6: We agree that this is an important point which may further underrepresent the
incidence of dysplasia in this population. We have added language to further delineate how this may lead to underreporting of the incidence of dysplasia (P16; L5-10).

Reviewer #2

Comment 1: The patients included had at least one cervical or LGT specimen available in the pathology archive of the authors- I assume this was a pre-transplant specimen? It does not say so but the next sentence notes that patients were excluded if no LGT pathology specimens after transplantation were available, hence my assumption. But it would be better to clearly state it, rather than having the reader assume anything.
Response 1: Patients were included if they had one LGT specimen in our pathology archive, regardless of whether it was before or after transplant. We have modified the methods to clarify this point (P6; L11). Some patients did not have pre-transplant specimens [61% had a Pap recorded in our record prior to transplant (P9; L6-7). Patients who had a hysterectomy prior to transplant and had no LGT pathology specimens after transplantation were excluded (P6; L18-20). We have therefore clarified which patients were included and excluded (P8; L20-23).

Comment 2: I am surprised no discussion was given regarding HPV vaccination status prior to transplantation (whether it be the first transplant or subsequent transplants.) From Table 1, it is clear that a percentage of the population did get vaccinated (about 7-8%) although we do not know when. As the HPV vaccine has been in use for a long time, and given the recent recommendations expanding the age range, further exploration of the role of HPV vaccination pre or post transplantation in possibly impacting the incidence of LGT dysplasia in transplant patients would be quite relevant.
Response 2: Thank you for this comment. We also feel that this is an extremely relevant and important topic in the context of this discussion. We unfortunately did not have sufficient data to include HPV vaccination status in this analysis due to inconsistency of documentation on HPV vaccination status in this cohort. Unfortunately, many women had no mention of the HPV vaccine in their record, so vaccination status was unknown for a large percentage of patients. We agree this is an important factor, and we have added this to our discussion at this suggestion (P16; L16-20).

Comment 3: The information on Pap smear history was a bit disappointing; while ~61% of patients had a documented pap prior to transplant, that means 39% did not. This makes the incidence of cervical dysplasia post-transplant hard to interpret. Did the immunosuppression given after transplant allow for the emergence and development of 'new' dysplasia or did it simply allow for the progression of pre-existing cervical dysplasia? This is relevant given that 8 of the 14 women who developed ciN2+ had unknown Pap test results prior to transplantation.
Response 3: We agree that this is an important limitation to our study and we have further expanded our comment on this in the discussion, highlighting the point that given this limitation, it is unclear whether the dysplasias identified are new lesions or progression of prior lesions.
While we cannot determine if dysplasia is “new” or progression of an “old” lesion for those women who did not have documented screening before transplant, a history of abnormal screening was not associated with LGT dysplasia development in our multivariable model. In addition, several women with only normal screening or normal screening immediately prior to transplant went on to develop dysplasia in the first few years after transplant. While further study is necessary in this area, we feel that despite this limitation, this study helps to convey that despite this population’s increased risk for LGT dysplasia, adherence to recommended screening is lower than recommended.

Comment 4: I think a key and fundamental point of the paper is that many clinicians focus on cervical screening post-transplantation but non-cervical LGT dysplasia or cancers must clearly be part of all routine and ongoing surveillance of the genital tract. This paper does add more information to the small amount of data currently available, is clinically relevant, and opens the door for further more in-depth exploration of the issues around LGT dysplasia/cancers and transplant patients, perhaps all immunosuppressed patients.
Response 4: Thank you for this comment. This a major point we are hoping to convey.

Reviewer #3

Comment 1: With respect to the outcome genital warts - was this per the chart report or was this per some ICD diagnosis code? If either, was the diagnosis clinically based or based on a specimen pathology?
Response 1: This outcome was based on either clinician report or pathologic diagnosis. In many cases, genital warts were documented in the chart as present on examination, without histological confirmation. We did not use ICD diagnosis codes to identify patients with warts. We have clarified this in the methods section of the manuscript (P7; L6-7).

Comment 2: Line 245 - "age" is cited as protective - please state the direction of age (e.g. younger or older age).
Response 2: We have indicated that older age is associated with a lower risk of dysplasia (P10; L1-2).

Comment 3: Line 245 - its more technically correct to say, "a history of patient-reported normal Pap tests..."
Response 3: This statement regarding “only normal Pap tests” is based on cytology specimens in our pathology database and medical record, not based on patient report. We have therefore left this language the same. However, this is an important point and we clarified that we determined Pap testing history through review of cytologic specimens (P7; L9-11).

Comment 4: Line 318 - With respect to the study population size of past investigations, I'm not sure 394 and 262 are different enough to say, the latter is "only" relative to the former.
Response 4: We appreciate that the language may imply a vaster differentiation between this and prior studies. We have deleted the word “only” from this sentence (P13; L8).
Statistical Editors Comments

Comment 1: Abstract: The risk estimates should include CIs, eg 47/394 = 11.9\% [CI 8.8-15.9\%].
Response 1: We have added the CIs to the risk estimates (P3; L14-15 & P9; L1-2).

Comment 2: General: Since the adverse events developed at various time points, it would be informative to include a K-M curve or table to show the time course of cervical dysplasia.
Response 2: We appreciate this suggestion, and we have added K-M curves to delineate the time point to development of dysplasia.

Comment 3: Table 2: Should cite in footnote which variables were retained in the final multivariable model and justify their use, since there were only 47 adverse events and therefore the number of adjustors should not exceed 5.
Response 3: Thank you for this comment. In our initial submission, we included more than 5 adjustors in our multivariable model, selected based on their statistical significance in the univariate model. In order to address your point, we made a few changes. To reduce the number of adjustors entering the multivariate analysis, we changed both the variables “indication for kidney transplant” and “organ of first transplant” to single multi-level variables instead of multiple binary variables. This change is reflected in the univariate analysis as well as the multivariate analysis (Table 2). This led to hydroxychloroquine and Black race emerging as statistically significant in the multivariable model. We made these corresponding changes to the results and discussion.

Per your feedback, we also performed a limited multivariable analysis using only 5 adjustors. We included this analysis in Table 2. We have indicated which 5 adjustors in the footnote of Table 2 as well as in the methods. We decided to present both multivariable analyses in the manuscript as the first is underpowered whereas the limited multivariable analysis is better powered but may be more confounded, as we excluded known significant adjustors from the univariate analysis. However, in both models Black race and hydroxychloroquine were statistically significant. These changes are reflected in the methods (P7; L21-23 & P8; L1-6), results (P10; L3-7), discussion (P13; L18-21 & P14; L7-17), and Table 2.

Comment 4: lines 373-375, 400-402: The limitations are an important part of the discussion, but whether the true incidence is higher is conjecture. From these data, one can only conclude that point estimate is 11.9\%, but the statistical range from these data could be as low as 8.8\% or as high as 15.9\%.
Response 4: Thank you for this comment. We have edited the discussion and removed the statement that the true incidence could be higher than 11.9\%. We have revised this statement to reflect that the specific cited limitations could impact the findings, leading to underestimation of the frequency of lower genital tract dysplasia (P16; L7-10).

Assoc Editor Comments
Comment 1: Please emphasize in the Discussion about the elevated vaginal/vulvar dysplasia rate suggesting that health care providers need to consider this when examining and caring for these patients instead of just focusing on Pap smear screening like the general population.
Response 1: Thank you for this suggestion. We have added this and emphasized the elevated rates of non-cervical dysplasia and the need to consider this when screening and caring for these women in the discussion (P17; L18-23).
Dear Dr. Moser,
Thank you again for the comments and edits.
I have included the track change document as well as the responses to the comments here. Please let me know if there are any further questions or issues that I can help to address. Thank you again for your consideration of this manuscript.

Sincerely,

Kimberly Levinson, MD MPH
Assistant Professor
Assistant Fellowship Director
Kelly Gynecologic Oncology Service
Assistant Residency Director
Dept of Gynecology and Obstetrics
Johns Hopkins Hospital

Dear Dr. Levinson,

Thank you for submitting your revised manuscript. It has been reviewed by the editor, and there are a few issues that must be addressed before we can consider your manuscript further:

1. Please note the minor edits and deletions throughout. Please let us know if you disagree with any of these changes.
2. LINE 22: Anne F Rositch will need to complete our electronic Copyright Transfer Agreement, which was sent to them through Editorial Manager.
3. LINE 31: Please add what you are thanking these contributors for.
4. LINE 103: Table 1 says 42 (29-55). Which data are correct?
5. LINE 105: Please be sure this is stated in the body of your paper, tables, or figures. Statements and data that appear in the Abstract must also appear in the body text for consistency.
6. LINE 107: Please be sure this is stated in the body of your paper, tables, or figures. Statements and data that appear in the Abstract must also appear in the body text for consistency.

7. LINE 116: Page 16 says “We found that the median time to develop CIN2+ after first transplant was 3.95 years.” Where is the 3.94 represented other than the abstract?

8. LINE 273: Where is the in-text citation for Table 1? Tables should be cited in order at first mention. Please reorder/renumber your tables if needed.

9. LINE 380: Note query in abstract Results.

10. TABLE 1: Abstract says 41 (29-53)

When revising, use the attached version of the manuscript. Leave the track changes on, and do not use the “Accept all Changes”

Please let me know if you have any questions. Your prompt response to these queries will be appreciated; please respond no later than COB on Wednesday, May 22nd.

Sincerely,
-Daniel Mosier
Looks great!
Thank you.

Kim

Sent from my iPhone

On May 22, 2019, at 11:31 AM, Denise Shields <DShields@greenjournal.org> wrote:

Thank you, Dr. Levinson. We use a hyphen only when it’s a modifier, which is why they aren’t always used in figure 1.

Attached is an edited version of figure 2 for your review.

Dear Denise,

Thank you very much for these revisions.

If agreed on, the only additions that I would suggest are listed below:

Figure 1A they say "high grade" and "low grade" with no hyphens. In Fig 1B and C they use hyphens for high-grade and low-grade. We use hyphens in the text, so we can also add hyphens to 1A

Figure 2B can we add the language high-grade to the y-axis? "Probability of high-grade LGT dysplasia (%)" Currently it says "Probability of LGT dysplasia (%)".

Thank you for your consideration.
Sincerely,

Kimberly Levinson, MD MPH
Dear Dr. Levinson,

The figures in your manuscript have been edited and are attached for your review. Please review the attachments CAREFULLY for any mistakes.

PLEASE NOTE: Any changes to the figures must be made now. Changes made at later stages are expensive and time-consuming and may result in the delay of your article’s publication.

To avoid a delay, I would appreciate a reply no later than Wednesday, 5/22. Thank you for your help.

Best,
Denise

Denise Shields
Senior Manuscript Editor
Obstetrics & Gynecology
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