

OBSTETRICS & GYNECOLOGY



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Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office:
obgyn@greenjournal.org.

Date: Jul 18, 2018
To: "Jennifer S. Smith" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-1116

RE: Manuscript Number ONG-18-1116

Using Home Self-Collection with Mailed Return to Detect Human Papillomavirus and Sexually Transmitted Infections

Dear Dr. Smith:

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 Aug 08, 2018, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:
Comments to Author

Manuscript #: ONG-18-1116

Title: Using Home Self-Collection with Mailed Return to Detect Human Papillomavirus and Sexually Transmitted Infections

Overview:

This manuscript reviews the North Carolina experience with self-collected vs provider-collected vaginal/cervical specimen in detection of hrHPV, CT, GC, TV, and MG. The authors found equivalent results for three different sample groups: self-collected at home; self-collected in the clinic; and provider collected samples. This presents a viable option for screening of low-income patients, with limited access to health care, a population at high risk for premalignant and malignant cervical disease.

My recommended edits follow.

Abstract:

1. Line 58. How was "underscreened" defined?
2. Lines 59-62. This sentence is confusing and needs to be revised for clarity.
3. Line 74. How do you define "infrequently screened women?" How did you select such patients as you indicated you recruited them from a low-income, infrequently screened population in North Carolina? Was this population from the University of North Carolina or actually from the state? How did you assure they were infrequently screened?

Materials and Methods:

4. Lines 124-125. Most resources define "low-income" as those earning < twice (<200%) the federal poverty level. Why did you chose 250% and what impact did this have on the results?
5. Line 161. What was the interval between the self-test and the specimen collected in the office?
6. Line 165. The clinician does not perform the testing. Perhaps it would be better to state "clinician-collected HPV and

cytology..." or just "HPV and cytology..."

Results:

7. Lines 264-265. To what do you ascribe these discrepancies? It would be helpful to suggest an explanation.

Reviewer #2:

1. Lines 73-75: You conclude that mail-based, at-home self-collection for high risk HPV and sexually transmitted infection was valid and well-accepted in infrequently screened women, and that high risk HPV self-collection could be an effective way to increase cervical cancer screening rates in higher-risk populations. In a period of 33 months of direct outreach by study personnel and collaborators, and with an incentive of \$35 for returning the sample and coming to clinic plus \$10 for completing a survey, only 284 women were recruited who were eligible for the study. Of these, 80% returned the sample, and 70% also came to clinic. So, of these 284 women, only 193 were eligible for the study. You seem to have had a fairly aggressive outreach and advertising campaign by study personnel and collaborators, referral from the United Way social assistance hotline, posters and flyers distributed in a variety of locations likely to reach low-income women, and screening for eligibility by phone by a call center run by the American Sexual Health Association. In your study it seems that it took a significant amount of manpower and some expense over 33 months, to reach a relatively small number of women. Therefore, although you might conclude that at home self-collection was relatively well accepted by the women who ultimately participated in your study, it would be a great leap to conclude that performing self-collection would be well accepted in the overall population of infrequently screened women.

2. Lines 193-196: You indicate that women who did not attend an in-clinic appointment received at-home self-collection results from study staff by phone or letter, along with information to schedule a clinic appointment with a local clinic offering low-cost cervical cancer screening. Do you know what percent of the women who did not attend their in-clinic appointment, but who required further evaluation for abnormal cytology or treatment for a sexually transmitted infection, did not receive the required care?

3. It would be useful to have a table of the number of women who your study identified as having high risk HPV, abnormal cytology, or other sexually transmitted infections, for whom you are not certain they had treatment to completion or further evaluation as indicated.

4. In this 33 month period, 11 women were referred for colposcopy. Of these 11, 3 were lost to follow-up. By what means did you attempt to track down the three women who required colposcopy but did not receive it?

5. Of the 8 women who had colposcopy, six were ultimately referred for treatment for biopsy-confirmed CIN2+ by LEEP or cold-knife cone. One did not complete treatment. Please indicate why that was.

6. You indicate that for high-risk HPV detection, agreement was good between self-home and clinician samples ($\kappa = .66$) and moderate between self-clinic and clinician samples ($\kappa = .56$). Are either of these agreement rates really good enough (especially since your numbers are relatively small)?

7. Lines 353-360: You state that the use of mailed self-collection in under-screened US women allows for the assessment of a self-collection screening strategy that may be more cost-effective and scalable than approaches based on face-to-face distribution and personal instruction, and that mail-based self-collection could be critically useful as a primary screening option for infrequently screened women. Over a 33 month period, despite extensive outreach and resources, in an underserved population of women, only 5 women were identified and treated for CIN 2+ lesions. In addition, you have not addressed in the manuscript the total number of women who had abnormal findings on at-home self-testing but for whom you do not know whether they received appropriate further evaluation/treatment. I am not certain that these results really demonstrate the cost-effectiveness and effectiveness of this type of program.

Reviewer #3: Nicely constructed research design with the three arms for detecting hrHPV.

1. Your first sentence in the abstract presents a very hypothetical scenario that self collection 'may' improve access to cervical cancer screening. You do allude in lines 87 and 88 to various factors but the sentence remains a wish rather than a documented fact. Perhaps references to other papers may help validate that statement.

2. In your introduction you infer that in 2018 there will be 4170 deaths due to cervical cancer but your reference (1) is from 2010.

3. You mention an estimated 56% incidence of cervical cancer due to insufficient screening but your reference (2) is from 2005.

4. A lot has changed with the advent of the HPV vaccine and thus the old data is rapidly becoming inaccurate. It would improve the acceptability of this paper if more modern data was included.

5. You do acknowledge that the numbers involved are small and larger numbers would improve the sensitivity and

specificity.

But the case for self-collection is rapidly evolving and may well be the future.

STATISTICAL EDITOR'S COMMENTS:

1. lines 198-206 and Table 2: The counts for N positive are generally quite small and the CIs should be calculated using an appropriate method, such as binomial or Poisson. The CI for $0/189 = (0, 0.019)$, ie, not zero.
2. Table 3: Although the values for Kappa are generally favorable, as can be seen from the CIs, the estimates for kappa are not precise, owing to the relatively small number of positives and the smaller number of discordant results.
3. Table 4: Again, owing to the small counts for abnormal, the CIs are very wide. Comparisons among groups (home, clinic self, clinician) are likely NS different, but there is insufficient power to generalize those inferences.

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. Based on the forms that have been submitted, the only author who qualifies for authorship is Marcia M. Hobbs. On the third page of the agreement form, under the section labeled "Authorship," items #2-4, in addition to #1a or 1b, must be checked in order to qualify for authorship. The other contributors should be moved to the acknowledgments, or he/she could resubmit a revised author agreement form if he/she filled it out erroneously the first time. All updated and missing forms should be uploaded with the revision in Editorial Manager.
 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."
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- 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. 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 will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at <http://links.lww.com/AOG/A515>, and the gynecology data definitions are available at <http://links.lww.com/AOG/A935>.
 5. 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 appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.

6. Titles in Obstetrics & Gynecology are limited to 100 characters (including spaces). Do not structure the title as a declarative statement or a question. Introductory phrases such as "A study of..." or "Comprehensive investigations into..." or "A discussion of..." should be avoided in titles. Abbreviations, jargon, trade names, formulas, and obsolete terminology also should not be used in the title. Titles should include "A Randomized Controlled Trial," "A Meta-Analysis," or "A Systematic Review," as appropriate, in a subtitle. Otherwise, do not specify the type of manuscript in the title.
7. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with the following guidelines:

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* 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 signature on the journal's author agreement 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. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words, written in the present tense and stating the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

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

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13. Our readers are clinicians and a detailed review of the literature is not necessary. Please shorten the Discussion and focus on how your results affect or change actual patient care. Do not repeat the Results in the Discussion section.

14. 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.

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, that each author has given approval to the final form of the revision, and that the agreement form signed by each author and submitted with the initial version remains valid.

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 Aug 08, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

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