Author’s response to reviews

Title: Current patient perspectives of vulvovaginal candidiasis: incidence, symptoms, management and post-treatment outcomes

Authors:

Junko Yano (jyano@lsuhsc.edu)

Jack Sobel (JSobel@med.wayne.edu)

Paul Nyirjesy (paul.nyirjesy@drexelmed.edu)

Ryan Sobel (rsobel69@gmail.com)

Valerie Williams (vwil10@lsuhsc.edu)

Qingzhao Yu (qyu@lsuhsc.edu)

Mairi Noverr (mnover@lsuhsc.edu)

Paul Fidel, Jr. (pfidel@lsuhsc.edu)

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Author’s response to reviews:

To the Editor:

Thank you for the comments and the opportunity to revise our manuscript. We are extremely disappointed that the review process took so long that a decision on the manuscript could not be reached for close to 7 months since the original submission. We have worked to submit the revision as quick as possible and are hopeful that the revised manuscript can be accepted now in a timely manner and soon published in BMC Women’s Health. We also appreciate reviewers’ comments and suggestions on clarifying the study design and including information about clinical observations. I have included our responses to each comment individually, addressing issues/clarifications and describing the changes we have made in the revised manuscript.

Editor/Reviewer comments: The original comments were copied verbatim and the respective responses follow immediately.

Editor’s comments

1. Please provide email addresses of all authors on the title page.
Response: We have provided the e-mail addresses for all authors on the title page.

2. Please move the Declarations section to before the References.

Response: The Declarations have been relocated to before the References.

3. Please include a summary of the informed consent procedure in the Ethics approval and consent to participate statement.

Response: There was no informed consent procedure in this study. There was a ‘waiver of informed consent’ since the survey was anonymous with no risk to the subjects. We have included a statement to this effect in the Declarations section.

4. Please consider the STROBE guidelines for reporting observational studies (http://www.equator-network.org/reporting-guidelines/strobe/) and the CHERRIES guidelines for reporting internet surveys (http://www.equator-network.org/reporting-guidelines/improving-the-quality-of-web-surveys-the-checklist-for-reporting-results-of-internet-e-surveys-cherries/). Please ensure that your manuscript includes all relevant information described in these guidelines and please include a completed checklist for one of these guidelines as an additional file.

Response: We have followed both guidelines where applicable. A checklist for the CHERRIES guidelines been submitted as supplementary material.

5. Please include a brief Conclusions section after the Discussion section.

Response: We have added a Conclusions section after the Discussion.

6. Please remove the figure numbers from the figure files.

Response: The figure numbers have been removed from the figure files.

Reviewer #1 (Comments for the Author):

1. The study subjects were wary (from who sought gynecologic care in university-affiliated Obstetrics and Gynecology clinics at the time of visit with a health care provider to via group encounters such as meetings, classes, community activities).
Response: We recognize that the recruitment procedure to identify potential participants was conducted in a variety of settings. As a result, we feel that this strengthens the study by representing a broader subject pool. We acknowledge this diversity in subject enrollment in the Discussion.

2. The diagnosis of VVC was not accurate.

Response: The Reviewer is correct that the VVC diagnosis in this study may not have been always entirely accurate. In fact, the questionnaire was administered by an open survey method in which no formal screening for VVC was provided. Responses were collected on a self-reporting basis and analyzed as aggregate information with no identifiers. We realize that this method of inquiry may affect the true accuracy of the VVC diagnosis but feel the benefits of the broad anonymous inquiry survey outweigh any possible diagnostic inaccuracy. We have added a statement regarding this issue in the Discussion.

3. Clinical features of VVC symptomatology and risk factors associated with disease and cure rates following treatment will not accurate.

Response: As mentioned above, the survey method of inquiry leaves the possibility open for inaccuracies. We have added a statement regarding this issue in the Discussion.

4. A smaller study sample.

Response: We recognize that the sample size of this study was relatively small and acknowledged this in the Discussion. However, we feel confident that our data was adequate showing strong significance levels and similar trends to past less formal studies. We have addressed this issue in the Discussion.

Reviewer #2 (Comments for the Author):

1. you could add the some days before published article of Denning DW, Kneale M, Sobel JD and Rautemaa-Richardson: Global burden of recurrent vulvovaginal candidiasis: a systematic review. Lancet Infect Dis 2018, in the references and add a short sentence in the introduction or discussion to the global burden of this disease.

Response: The review article by Denning, et al. had just been published shortly after we submitted the original manuscript, and the pre-published information we had available at the time of submission was scant. We have now included the reference and added supportive statements regarding the global burden of RVVC.
2. You mention the clinical outcomes of VVC/RVVC: relief rate considerably lower in women with OTC treatment (15.6% no-relief treatment by a physician vs. 42.6% no-relief by treatment of the patient). You mention, that the diagnosis could be incorrect. Denning et al. (2018) (see above) pronounce this fact clearer and mention also “vulvar vestibulitis” as cause for burning...". Farmer et al. (Farmer et al.: Repeated vulvovaginal fungal infections cause persistent pain in a mouse model of vulvodynia. Sci Transl Med 2011; 3: 101ra91) showed, that Candida albicans can trigger persistent pain/burning and so cause vestibulodynia, which is often (in my personal experience mostly!) misdiagnosed as Candida vulvovaginitis. It is probable, that a high amount of the no-relief cases are misdiagnosed by patients, but also physicians, and indeed vestibulodynia, but also possible, that both (recurrent) Candida vulvovaginitis in the beginning and later vestibulodynia exist together.

Response: We have also included the references suggested to support the misdiagnosis as an explanation for the lower relief rate for women choosing OTC drugs for treatment and the possibility of a similar scenario (albeit fewer) for physician diagnosis. Statements regarding these citations have been included in the Discussion.