Author’s response to reviews

Title: SELF-SAMPLING FOR HUMAN PAPILLOMAVIRUS DNA DETECTION: A PRELIMINARY STUDY OF COMPLIANCE AND FEASIBILITY IN BOLIVIA

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The authors' response letter has been included as a supplementary file. Please find here bellow the same text:

Reference: BMWH-D-17-00032R1
(Self-sampling for human papillomavirus DNA detection: a preliminary study of compliance and feasibility in Bolivia)

September, the 22th 2017

Dear Mrs. Olaitan,

We thank you for your letter and your editorial comments on our manuscript.

Please find hereunder our point-by-point responses to the issues raised by the reviewers. The line number and the page number are indicated in agreement with our revised manuscript file containing track changes.

In regard to reviewer #1 comments:

1. “- Abstract: Conclusion part

Instead of saying "Furthermore, Bolivian women showed willingness to accept self-sampling for cervical cancer prevention"…better to replace by preferred self-sampling…because this is your study result.”

- We agree, this is now modified and improved as suggested, in line 45 page 2 –line 47 page 3

“Furthermore, most Bolivian women preferred self-sampling over clinician-sampling for cervical cancer screening”

2. “- Introduction: The incidence and mortality rates in Bolivia are the highest in Latin America: What is the cause for mortality…mention it.”

- We agree, this is now mentioned line 51 page 5

“The incidence and mortality rates of cervical cancer in Bolivia are the highest…”

3. “- What is the protocol for sample taking, smearing on slides (how many times), handling, transport and patient preparation before taking self-samples …..please describe in detail.”

- This is now described in details in Material and methods from line 110 till 135 page 7-8

“The recruitment was done through women’s organizations in all areas of the study. The leader of the organization called a meeting and all women who were interested to participate in the study signed an inform consent. No previous cytological results were required to be included in
this study. In brief, participants received written and verbal instructions, illustrated by images and video, explaining how to perform self-sampling with both devices. Self-sampling with the cotton swab was performed first to avoid cell depletion with the vaginal tampon. Briefly, women were asked to hold the cotton swab by the end of the handle, to introduce it deep (approximately 6 cm) inside the vaginal tract until bottom was reached, to rotate the swab 3 times, to take it out and then to smear the cells once over the glass slide. Each slide should be put inside a small cardboard box specifically designed for it. The box was then transported in a zippered storage bag to the laboratory. To perform self-sampling with tampon, women were instructed to introduce it deep (around 6 cm) inside the vagina, until bottom was reached, for at least 30 seconds, then to remove it and to place it in a Falcon tube containing 15 ml of Easyfix® solution. After self-sampling, women were asked to complete a questionnaire to evaluate their experience with self-sampling and their preference for a device.”

4. “- Did you take samples from the same patients to compare self Vs Physician …? Because it has different clinical implication. If not it is difficult to make a conclusion.”

Yes, two kind of samples (self-sampling and physician sampling) were taken from the same patients. This is now better explained in the Material and Methods, lines 129-135 page 8

“Finally, hr-HPV detection was compared between self- and physician-collected samples. Both samples were collected from 201 women. Each woman was asked to perform first self-sampling with cotton swab and to smear cervical cells from the swab on glass slide, as previously described. After self-sampling, a vaginal speculum was inserted and a physician obtained a regular cervical smear on a glass slide using cervical brush.”

5. “- How much of the cotton tip inside the vagina? (Considering individual variation) It will affect your result because if it inserted deep you may samples from cervix.”

This is now described in details, see remark 3 for the same reviewer.

6. “You should specify the time for how long the tampon will stay in the vagina (instead of saying few seconds)”

This is now described in details in Material and Methods, see remark 3 for the same reviewer, but also in the Discussion, line 251-252, page 14.

“…i.e. in our study women introduced the vaginal tampons only for a 30 seconds…”

7. “Write/document for how long cell suspension incubated. (Instead of saying overnight)”

This is now done in Material and Methods, page 146, page 8
“The cell suspension was incubated for 16 - 20 h. at 56°C and then incubated at 100°C for 10 min for proteinase K inactivation.”

In regard to reviewer #2 comments:

1. « A question still remains though regarding the commitment of these women to self-sampling and their ability or will to perform it in a proper manner. »

The women are willing to commit self-sampling as reported in the text (see the chapter in Results « Assessment of women’s preference for a self-sampling device”, discussion lines 261-263 and conclusion) and shown in Table 2 and 3, but their ability or will to perform it should be further investigated in the future as reported in the conclusion. This is now better emphasized lines 291-292 page 16.

« Nevertheless, further studies should be performed to prove that our self-sampling method has a sufficient clinical sensitivity for detection of precancerous lesions (CIN2+) and to verify that self-sampling could improve cervical cancer screening coverage in the Bolivian population.»

2. “Page 6, line 29: replace 'and' with 'an'”.
Done, line 87 page 6

“….and could represent an interesting option to economically”

3. “Page 7, line 56: sentence needs alterations, it makes no sense»
This sentence was totally modified as it was in a rewritten chapter (see point 3 reviewer 1)

4. “Page 8, line 2: replace 's' with 'as' »
This sentence was totally modified as it was in a rewritten chapter (see point 3 reviewer 1)

We thank you for your editorial work and the reviewers for their critical comments. We believe that we correctly respond to these comments and thank reviewers for their very important suggestion to better present our results. We hope that our manuscript is now acceptable for publication in BMC Women’s Health.

Yours sincerely,

V. Fontaine