Author’s response to reviews

Title: Knowledge of cervical cancer and HPV vaccine in Bangladeshi women: a population based, cross-sectional study

Authors:

Jessica Islam (islamjy@live.unc.edu)
Fatema Khatun (kfatema@icddrb.org)
Anadil Alam (anadil@icddrb.org)
Farhana Sultana (f.sultana2@student.unimelb.edu.au)
Afsana Bhuiyan (afsana.bhuiyan@icddrb.org)
Nazmul Alam (nazmul@icddrb.org)
Laura Reichenbach (laura.reichenbach@gmail.com)
Lena Marions (lena.marions@ki.se)
Mustafizur Rahman (mustafizur@icddrb.org)
Quamrun Nahar (quamrun@icddrb.org)

Version: 1 Date: 15 May 2017

Author’s response to reviews:

May 14th, 2017

To: The Editor

BMC Women's Health

Re: BMWH-D-16-00145

Manuscript Title: Knowledge of cervical cancer and HPV vaccine in Bangladeshi women: a population based cross-sectional study.
Thank you for your continued interest in our paper and the opportunity to address the reviewer comments and your comments in our manuscript. We have addressed these comments and included tracked changes in the manuscript.

We thank the reviewers for their constructive comments and recognizing that this study provides valuable baseline information for the development of future interventions in Bangladesh. We have responded to each reviewer as follows:

Editor Comments:

1. In accordance with BioMed Central editorial policies, could you please ensure your manuscript reporting adheres to STROBE guidelines (http://www.strobe-statement.org/) for reporting observational research. This is so your methodology can be fully evaluated and utilized. Can you please include a completed STROBE checklist as an additional file when submitting your revised manuscript?

Thank you for your recommendation. We have included a completed STROBE checklist to ensure all elements are covered in our manuscript.

2. Please include a "Consent for publication" section to the Declarations. If your manuscript contains any individual person’s data in any form (including individual details, images or videos), consent to publish must be obtained from that person, or in the case of children, their parent or legal guardian. Please provide details of this consent in this section. If your manuscript does not contain any individual person’s identifiable data or information, please state “Not applicable” under this section.

Thank you for your comment. We have included a “Consent for Publication” section. Our manuscript does not contain any individual person’s identifiable data or information and as such, we have stated “Not applicable” under this section.
Reviewer 1:

This manuscript aimed to assess knowledge of cervical cancer and willingness to receive the HPV vaccine among Bangladeshi women. Given the high global burden of cervical cancer and other HPV related diseases, research that explores current knowledge and awareness about HPV-related morbidity (e.g., cervical cancer) and receptiveness to HPV vaccination is needed. In that light, this study provides valuable baseline information for the development of future interventions in Bangladesh. The manuscript could be strengthened by addressing the comments below.

1) It is unclear how the questions related to knowledge of cervical cancer were operationalized. Were the questions open-ended in the sense that they generated data for which a qualitative analysis would have been appropriate? On the other hand, were the "open ended responses" limited to those listed in Table 2? Please clarify in the methods.

Thank you for your comment and the opportunity to clarify. The survey instrument utilized for this cohort study was structured and a close-ended questionnaire. For each question with possible multiple choice responses, a possible set of options were defined, including an “Other” response in the questionnaire. The “Other” option responses were then recoded.

In response, the methods have been updated to clarify this point as follows (lines 158-164): “In order to assess knowledge, the following questions were asked: 1) From where did you hear about cervical cancer? 2) Do you know how a woman can get this cancer? If yes, how can a woman get this cancer? 3) Do you think cervical cancer can be prevented? If yes, how can it be prevented? Possible responses to all knowledge questions were defined in the questionnaire, including an “Other” option. Participants were able to provide a free response if they chose “Other.” Responses to “Other” were recoded and included in the analysis. Participants were able to provide more than one response for each question.”

2) Lines 121-123: Please explain the rationale for excluding pregnant and post-partum women.

Thank you for your comment. We excluded women who were pregnant and post-partum women as the cervical sampling implements could cause bleeding and interfere with the test results. We have added this to the methods section.
3) Lines 163: Please explain more. Were women ineligible because they were found to have had cervical abnormalities or for some other reason?

We have revised this section for clarity. Please refer to lines 142-147. The revised version reads: “Women who were ever-married, aged 14-64 years and residing in the study area were invited to the study clinics for further assessment by the study physician. Women who were pregnant, post-partum, or with a history of hysterectomy, cervical cancer, uterine prolapse or with major psychological/psychiatric problems were excluded after history taking and/or clinical examination by the study physician. Pregnant women and women who were post-partum were excluded as cervical sampling implements could cause bleeding that could interfere with the HPV test results.”

4) Line 179-180: How was vaccination history determined? If self-reported, please clarify.

Vaccination history was determined based on self-report.

The following update was made to the Results section for clarification (line 224): “Overall, none of the women in this study reported to have previously received the HPV vaccine, based on self-report.”

5) Lines 238-243: This paragraph needs more detail. In the first sentence it is unclear which findings from the population based study relate to the current one. It is also unclear in the second sentence whether the authors are recommending the development of educational programs in general, about HPV, HPV vaccination and/or cervical cancer to improve access to preventive methods. Furthermore, the recommendations made in this paragraph do not acknowledge potential differences in educational programs and differential access to preventive methods for rural vs. urban communities.

Thank you for your feedback. Your feedback has been taken into consideration and the paragraph has been updated to include all factors mentioned. Please refer to lines 293-322 of the manuscript.
6) Tables: Please clarify how variables with small cells (i.e., less than 5 observations) were handled. Typically I would expect to see a Fisher Exact test performed for these comparisons, however it appears that these comparisons were either not calculated or were incorrectly calculated using Chi-square tests.

We agree with your observation. However, tables 3 and 4 have been updated to include results of a logistic regression model to identify predictors of our outcomes of interest.

Reviewer 2:

This is an important and timely manuscript. It highlights the need for increased cervical cancer education and prevention in Bangladesh where cervical cancer is the 2nd most common cancer among women. I have highlighted my primary concerns below. Overall, I think the manuscript is well-written but I did notice a few typos and grammatically incorrect sentences. Please review grammar again.

1) Abstract:

a) What statistical tests were used in this study? Please include in Methods.

Thank you. The following sentence has been added to the Methods section: “Univariate analyses and bivariate analyses using Chi-square and Fisher’s exact test were conducted using the quantitative survey data collected.”

b) Please also report related p-values in results.

Thank you. The relevant p-values have been added to the results section of the abstract.

2) Introduction:

a) Is the HPV vaccine available at all in Bangladesh?

Yes. In 2016, the HPV vaccine was introduced by the Ministry of Health for the first time with the support of the Global Alliance for Vaccines and Immunizations. The following has been added to the introduction to highlight this point: “Data are particularly necessary, as the HPV vaccine has been recently introduced in 2016 for the first time in Bangladesh by the Ministry of Health, with support from the Global Alliance for Vaccines and Immunizations (GAVI).”
b) Has it been available in nearby countries or in the region?

Yes, national HPV vaccine programs have been launched in neighboring countries.

c) How will GAVI possibly assist Bangladesh in the future? How likely is this?

Yes. In 2016, the HPV vaccine was introduced by the Ministry of Health for the first time with the support of the Global Alliance for Vaccines and Immunizations.

d) Is there a national cervical cancer screening program in Bangladesh?

Yes. The program was launched in 2004, however, it is limited to visual inspection with acetic acid and mostly opportunistic with limited coverage. Additionally, lack of colposcopy services and poor access to treatment after screening limits the success of this program.

To avoid confusing the reader, we have moved any discussion of screening programs in Bangladesh to the Discussion section.

e) What other studies have been done in Bangladesh on cervical cancer prevention and HPV vaccination?

To our knowledge, only one other study has assessed knowledge of cervical cancer among Bangladeshi women (Islam, The Oncologist, 2015). However, this assessment was not detailed and did not cover the HPV vaccine, rather only screening.

The following has been added to the introduction to address this point in the page number 4 (line 116-121): “In Bangladesh, one previous report has provided evidence on low knowledge of cervical cancer among, however, the majority (74%) of these data were collected from women residing in rural areas and limited to women above the age of 30 years. Data on knowledge of cervical cancer among a more representative sample, including those who reside in urban areas and younger populations, are needed. Additionally, data on knowledge of HPV and the HPV vaccine among Bangladeshi women are currently non-existent.”

3) Methods:

a) Was IRB approval received?
Thank you for your question. Yes, IRB approval was obtained. The following is our Ethics Statement which is located at the end of our manuscript following BMC Women’s Health formatting guidelines (Lines 403-407): “Informed written consent was taken from women aged 18 – 64 years of age, whereas informed written assent was taken from women aged 14–17 years. For the latter group, the assent form was read out to these women in the presence of their parents/legal guardians. If agreed, the assent form was then signed by the participants in the presence of their parents/guardians. The parents or guardians also signed the same form. The study protocol was approved by the Ethical Review Committee of icddr,b.”

b) Why were only married females included?

The parent study of this assessment investigated HPV prevalence by HPV DNA type through cervical sample collection. As Bangladesh is a majority Muslim country, we limited our assessment to married females to be culturally sensitive to the expectation that only married women are sexually active in Bangladesh.

c) Did participants receive an incentive to complete the interview?

No, an incentive was not provided to complete the interview.

d) How were open ended responses recorded and analyzed?

The survey was a structured, close-ended questionnaire. As such, open-ended responses were not part of this assessment. The Methods section has been updated to clarify this point.

e) Why not include multi-variable analyses? This sample is large enough to carry out more sophisticated models.

Thank you for your comment. We agree that we have the sample size to build more sophisticated predictive models, our outcome of interest would be “ever heard of cervical cancer” or “ever heard of HPV vaccine.” We have updated our analytic approach and Results section to provide results of logistic models to identify predictors of our outcome of interest by urban and rural samples.

f) Were there any hypotheses laid out prior to study implementation?
The parent study of this survey sought to assess HPV infection in the Bangladeshi population and to identify risk factors for HPV infection. As such, sample size for this survey was calculated with this objective in mind. However, prior to data collection, we believed that knowledge of cervical cancer and the HPV vaccine would be low similar to neighboring countries.

4) Results:

a) This section could be better organized to highlight the most important findings.

Thank you for your comment. The Results section was organized to follow the organization of the Tables. However, Table 2 and the text have been reorganized accordingly to highlight main findings first under the Knowledge section of the manuscript.

b) Please refer to tables when providing lists of descriptive and bi-variate results and eliminate this text, only summarize main findings.

Thank you for your comment. The relevant Table has been indicated in parentheses to reference the appropriate data source when summarizing main findings.

c) How were the response rates calculated?

Thank you for your question. Response rates were calculated by study staff after recruitment was completed for each study site. Please refer to lines 200-207.

5) Discussion:

a) What does this study add that is not already known about cervical cancer education in Bangladesh?

Thank you for your question. The following has been added to the Discussion to address the novelty of our study (Lines 293-305): “To our knowledge, only one other study, the Bangladesh Midlife Women’s Health Study (BMWHS) has been previously conducted in Bangladesh to assess women’s knowledge of cervical cancer. However, the focus of the BMWHS’s research question was on cervical cancer screening and there was no assessment of awareness or acceptability of HPV vaccination presented. Eighty-one percent of the study population of BMWHS reported to have ever heard of cervical cancer, which is lower than both our rural
(90%) and urban population’s (93%) awareness. The investigators of this study did not delve further into knowledge of cervical cancer and limited their assessment to five questions which focused on cervical cancer screening. In contrast to our study, the investigators reported that 8.3% of their study population had previously undergone cervical cancer screening. This is particularly interesting as the majority (73%) of their study sample was from rural areas of Bangladesh. In our study, only 3.1% of urban and 0.7% of rural women reported to have ever undergone cervical cancer screening. Data from our study report the first in-depth assessment of knowledge of cervical cancer and the acceptability of the HPV vaccine conducted in Bangladesh. However, findings from our analysis can be compared to other surveys conducted in developing countries, particularly the South-Asian subcontinent.”

b) Highlight the most important findings from this survey and what they add to the current literature.

Thank you for your suggestion. The first paragraph of our Discussion section highlights the study’s most important findings. The following has been updated to address this point (Lines 286-292): “Our study found that while a large majority of participants (~90%) were aware of cervical cancer, less than 10% had in-depth knowledge of the causes of cervical cancer and potential preventive methods against cervical cancer. Additionally, participants reported very limited knowledge of the HPV vaccine, particularly rural women. This is the first population-based study conducted in Bangladesh to demonstrate widespread acceptance of HPV vaccination among ever-married adult Bangladeshi women, for both themselves and for their daughters.”

c) Please discuss in greater detail how this study can help improve the opportunity for women in Bangladesh to receive the HPV vaccine?

Further details on the novelty and public health relevance of this paper have been included in this resubmission to address this point (Pages 10-14).

d) Many questions described in the Methods are open ended where in the discussion, it is reported in the limitations that this was a closed ended survey. Please explain and clarify.

Thank you for your comment and the opportunity to clarify. The survey instrument utilized for this cohort study was structured and a close-ended questionnaire. For each question with possible multiple choice responses, a possible set of options were defined, including an “Other” response in the questionnaire. The “Other” option responses were then recoded.
In response, the methods have been updated to clarify this point as follows (lines 158-164): “In order to assess knowledge, the following questions were asked: 1) From where did you hear about cervical cancer? 2) Do you know how a woman can get this cancer? If yes, how can a woman get this cancer? 3) Do you think cervical cancer can be prevented? If yes, how can it be prevented? Possible responses to all knowledge questions were defined in the questionnaire, including an “Other” option. Participants were able to provide a free response if they chose “Other.” Responses to “Other” were recoded and included in the analysis. Participants were able to provide more than one response for each question.”

We believe we have addressed all the comments from the Reviewers and Editor.

Thank you for your supportive and constructive comments.

Kind regards,