Author's response to reviews

Title: Predictors of default from follow-up care in a cervical cancer screening program using direct visual inspection in south-western Nigeria.

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Author's response to reviews: see over
Dear Editor,

**Re-Submission of Peer reviewed Manuscript. MS4636980771029047**

**Cervical cancer screening using direct visual inspection: Default from follow up care and its predictors in south western Nigeria**

I am pleased to re-submit the revised manuscript of our original research article now titled “Predictors of default from follow-up care in a cervical cancer screening program using direct visual inspection in south-western Nigeria.” by Ezechi Oliver Chukwujekwu, Odbert Pettersson Karen, Titilola A Gbajabiamila, Ifeoma Eugenia Idigbe Olutunmike Kuyoro, Ujah Innocent Achaya Otobo, Ostergren Per-Olof according to the comments and recommendation of the two reviewers.

We have addressed all the issues raised the reviewers.

Please see a point by point response to the concerns below.

A clean copy of the revised manuscript is hereby uploaded

Thank you for your consideration

Dr. Oliver Ezechi
Corresponding authors
Point by Point response to reviewer’s comments and Report

Title: Cervical cancer screening using direct visual inspection: Default from follow up care and its predictors in southwestern Nigerian.

Reviewer 1 : Julie Quinlivan

Version : 1
Date: 27 December 2013

Summary

This paper addresses an important clinical issue and adds to the data supporting an argument to see and treat to prevent cervical cancer. I suggest the following changes as MINOR ESSENTIAL REVISIONS:

Introduction

(1) The authors should include hard data on default rates at other centres to set the scene for the high default observed in the study in the introduction. For example, insert a sentence like the following into the introduction: Default rates in programs designed to identify cervical cancer at a premalignant phase are usually very high, ranging from 5 to 20% in developed and 20 to 41% in developing countries (ref 1-3 below plus existing refs 24 and 34 from manuscript).

Supporting references:


PLUS Your ref 24 and 34.

This sets the scene for the very high default subsequently identified in the study population, which is the highest yet observed.

Author response: Comments taken. See Page 4, 3rd paragraph, last sentence. The suggested sentence “Default rates in programs designed to identify cervical cancer at precancerous stages are usually very high, ranging from 5-20% in high income countries and 20-41% in low income countries and references (24,29-32) incorporated.

Methods

(2) NIMR is expressed as initials and subsequently written out in full. The paper needs to be checked to ensure the first time it is mentioned it is stated in full with (NIMR) in brackets and thereafter may be referred to by the initials only.

Author response: Correction effected. See page 5, line 1, The first time NIMR appeared is written in full followed by abbreviation. “Nigerian Institute of Medical Research (NIMR)”

(3) Briefly describe the education women received before the screening test. This needs a full paragraph as it ties into the final recommendations that the education phase of the program is strengthened.
Author response: Accepted and effected. See Page 6, 4th paragraph. The following inserted
“Before the screening, participants were introduced to cervical cancer and its premalignant
lesions, its causes, burden and strategies for prevention. This was followed by what screening
entails and various method of screening including the follow up requirement until a definitive
diagnosis is made. The prognosis of advanced disease and cost implication were emphasized
visa viz early diagnosis. Finally the reliability of the DVI, who will conduct the test and the
study specific follows up plan and schedules were explained. Participants were also giving
chance to seek clarification and ask questions. The points highlighted above were again
reinforced during the individual consenting process.

(4) Default from follow up. In the text it states women who did not attend the initial
appointment were contacted and a second made. They were classified as defaulting if they
missed the second appointment. However, the variable definition just states “women who
screened positive and failed to keep the follow up appointment.” Please clarify if defaulters
missed two or only a single appointment and make the two statements consistent.

Author Response. The two statements reconciled. The correct variable definition is “Default
from follow-up: Women who screened positive but failed to keep the rescheduled second
appointment or could not be reached “. Correction effected in the text. See variable definition
on page 9, last paragraph

Results
(5) Grammar – wrong who’s in sentence beginning Women who’s communities were more than 10 km from the clinic (OR: 3.6, CI:1.5 – 9.1),

Author response: Noted and correction effected. See page 13, 1st paragraph, 2nd sentence. The sentence now reads “Women who resides more than 10 km from the clinic (OR: 3.6, CI:1.5 – 9.1),”

Discussion

(6) Expand by a sentence or two why the observed default is higher than observed at other centres within Africa. Are there unique cultural or social factors at play?

(7) This needs to include discussion of non demographic variables found to be associated with default in this setting like domestic violence and unstable housing (Quinlivan JA, Collier RR, Petersen RW. Prevalence and associations of domestic violence at an Australian colposcopy clinic. J Low Genit Tract Dis. 2012 Oct;16(4):372-6. doi: 10.1097/LGT.0b013e3182480c2e.)

Author response (Comments 6 and 7): Suggestions accepted and effected. See Page 13-14 i.e. first and second paragraph of discussion. Inserted paragraphs read “The default rate in this study is much higher than rates reported from other low income countries and may be due to differing sociocultural, environmental and health system issues (5,18,23). In Nigeria women are culturally expected to be subservient to their spouse and thus needs their permission to honour invitations including hospital visits (23,35). In addition, a large percentage of women, especially in rural areas, are not gainfully employed depending on their spouse for their daily sustenance. Their spouses even provide transportation fees and thus need his concurrence to
attend clinic for follow up. Poor public transportation and health systems are other challenges confronting the women and making it difficult to honour such invitations (18,23). A large percentage of Nigerian women prefer to present in private health facilities because of the long waiting time and poor quality of services in public facilities (36,37). The cost of transportation, although not very high, is also out of reach for poor peasants in the rural communities (36). In the end, the choice made by women stand between keeping an appointment for a “disease they are not aware off” and “disobeying” their spouses with its possible consequences including violence (32, 38). The women are also mindful of the fact that in a country with a poor health system including its extensive waiting time, keeping appointments do not equate to finding solution to their “health challenge”. Furthermore the encroachment of religious institutions i.e. churches and mosques in health care without providing health infrastructure like the traditional mission hospitals do, could have contributed to the high default rate (35). In our previous study regarding willingness to screen for cervical cancer, the second most common reason for refusal of the test was related to client’s religious belief and teaching (23). Some clients further believed that they could not have cervical cancer because of their religious belief. It may therefore be correct to assume that some participants in this study with similar belief may have defaulted.
(8) Given the final recommendations, a paragraph should be devoted to the ‘see and treat’ programs in operation in other countries that have been associated with improved outcomes. This could then lead into the final recommendations listed.

Author response: Suggestion accepted and effected. A paragraph on “see and treat strategy” has been added. See page 13, last paragraph. It reads ”Cervical cancer prevention programmes adopting a “see and treat” strategy might best suit the women in the setting described above. Several studies in sub Saharan African evaluating the “see and treat” strategy reported very good outcome with significant reduction in default rate (39-43). The reduction in default rate was attributed to the reduction in number of visits, reduced service and transportation costs as well as reduction in man hours of work (39-41).”

**Reviewer 2: Monjurul Hoque**

**Version: 1**

**Date: 6 January December 2014**

Re: Cervical cancer screening using direct visual inspection: Default from follow up care and its predictors in Southwestern Nigerian.

It is an important public health issue. Any attempt to improve the screening services would positively improve life expectancy of women. Identifying the predictors of non-adherence to national and or local programme is thus of paramount importance.

The manuscript is well written. However, the following shortfalls should be dealt with before acceptance.

The title can be changed to make it more catchy/ attractive to readers.
Author response: Suggested and effected. See title page. Title redrafted to read “Predictors of default from follow-up care in a cervical cancer screening program using direct visual inspection in south-western Nigeria”.

Text

The first sentence of introduction is incomplete.

Author response: Noted and corrected. See page 3. It now read “Every year half a million women are diagnosed with cervical cancer and another 250,000 reported dead from the disease, which makes cancer of the cervix the second most common female cancer globally (1-3).”

Methods

What were the HIV and anti-retroviral treatment status of the sample? Was there any effect on non-adherence to cervical cancer screening? One might argue the relationship thus it would be appreciated to indicate.

Author response: The HIV prevalence in Nigeria and Lagos is relatively low. Only 40, out of the 629 that accepted to be screened for HIV tested positive. Of the 40 HIV positive only 7 were eligible for enrollment into the study. They were all antiretroviral drug naïve as they were yet to enroll into HIV programme at the time of the study. The number is very small to make any statistically significant deduction. See table 2. Two sentences were added to result
section, first paragraph to catch this. It read “Forty (6.4%) of the 629 women that accepted to be screened for HIV tested positive. Of the forty, only seven screened positive to DVI.”

The standard DVI or the practice on DVI should be explained in the method section for the understanding of the general readers.

Author response: Suggestion accepted and effected. See page 7-8. The following section were added

“Clinical Procedures

After signing the Informed Consent Form, information on sociodemographic characteristics, sexual and reproductive history was collected using the study case record form. All participants were subjected to a thorough pelvic examination with subsequent collection of the Pap smear, a sample for microbiological examination (when indicated) and Direct Visual Inspection (DVI) using either Acetic Acid (VIA) or Lugol’s Iodine (VILI). Physicians and midwives, who received training on the study procedures, performed the examinations. The women were placed in the modified lithotomy position and the cervix was exposed with the help of a Cusco’s bivalve speculum and examined. The cervical scraping was obtained by placing the Ayres spatula at the cervical os and rotated gently by 360° twice. A Smear was prepared by spreading the specimen uniformly across a pre-labeled glass slide, which was immediately fixed using a commercial fixator containing 95% ethyl alcohol. After collecting the cervical smear, the same examiner performed VIA or VILI depending on a predetermined group allocation.
It is not understood from the manuscript that the process of data collection from the defaulters. How the pattern of and reasons for default were measured? Was it a questionnaire survey or Focus group discussion?

Author response: Quantitative method was used. Study specific Case record form was used to collect all study related information. Clarified. See page 9, 3\textsuperscript{rd} paragraph. It now reads:

“\textbf{Data Collection}

Participants who did not keep their appointments were contacted on the phone or visited at home and rescheduled for another appointment at a mutually acceptable convenient time. Participants who missed the rescheduled appointment were interviewed to obtain quantitative data on reason(s) for default using study case record forms.”

How did the authors determine the sample size? Was the sample adequate to test the hypothesis?

Author response. The concern is noted and addressed as sample size determination subsection has been added. See page 9, 2\textsuperscript{nd} paragraph. The subsection read;

“\textbf{Sample size determination}

The sample size for this study was based on a reference of VIA positive rate obtained in Sagamu Nigeria during the WHO demonstration project in six African countries (WHO) of 5.7\% (33). The study sample size was calculated according to the following formula: \( N = \)
$Z_\alpha^2 P (1-P)/d^2$, where $Z_\alpha$ is the Z statistic for a 95% confidence level, $N$ is the sample size, $p$ is the VIA positive rate, and $d$ is the precision (34). Based on this calculation, following up 72 DVI positive women aged 18 years and above was considered sufficient to identify defaulters. The sample size was however increased by 25% in anticipation of non-acceptance to be followed up after testing positive to DVI. A final minimum sample size of 90 was obtained.”

The type of study (study design) is unknown from the method section.

Author response: Study design subsection added. See page 6, 3rd paragraph. It read “Study design: Prospective study design”

There is no mention of time when this research was started and finished (data collection and or field work).

Author response: Though the time for the larger study was stated originally, it has been clarified to be more specific. See page 6, 4th paragraph. It now reads:

“Study Population: Adult women of known HIV status aged 18 years and above who screened positive or inconclusive to direct visual inspection of cervix during community outreach cervical cancer screening programme and consented to be part of the study were enrolled into the study. Enrolment for this specific study commenced on the 2nd October 2011 and follow up completed on the 17th December 2011.”
What happened to those who had migrated in or out of the area?

Author response: The study period for this specific study was short and thus we did not notice any migration. However the women that could not be reach may fall within this category, but there is no objective way to certain this in our setting.

One would like to know the standard education (?) was given to women before screening proper.

Author response: Standard education given before the screen is now added. See Page 6, 4th paragraph. Author response: Accepted and effected. See Page 6, 4th paragraph. The following inserted “Before the screening, participants were introduced to cervical cancer and its premalignant lesions, its causes, burden and strategies for prevention. This was followed by what screening entails and various method of screening including the follow up requirement until a definitive diagnosis is made. The prognosis of advanced disease and cost implication were emphasized visa viz early diagnosis. Finally the reliability of the DVI, who will conduct the test and the study specific follows up plan and schedules were explained. Participants were also giving chance to seek clarification and ask questions. The points highlighted above were again reinforced during the individual consenting process.

It is also important for readers to know what the national and or local strategy is regarding cervical cancer screening in Nigeria.

Author response. This was addressed in the background section. See page 4, 2nd paragraph, which reads “In Nigeria, cervical cancer screening services using visual inspection is not yet
institutionalized despite its adoption by the Nigerian government as the prevention and control strategy of choice [12,22,23]. The cervical cancer screening is largely opportunistic during gynaecological consultations and uncoordinated outreach programmes often performed by nurses and medical officers (12,20). Moreover women found positive at the outreach programmes are referred for confirmation at a tertiary facility several kilometers away [20,24]. There is consequently a risk of drop-out in such a system, as the women have to make multiple visits for confirmation of screening result and treatment [23-27].’’

**Results**

Well written results but it is not clear how the pattern and reasons for default were determined.

Author response: Effectuated, see page 9, 3rd paragraph, now reading

‘‘**Data Collection**’’

Participants who did not keep their appointments were contacted on the phone or visited at home and rescheduled for another appointment at a mutually acceptable convenient time.

Participants who missed the rescheduled appointment were interviewed to obtain quantitative data on reason(s) for default using study case record forms.’’

The title of table 2 is incomplete.

Authors response: Now completed, reading: ‘‘Association between default from follow-up care after screening positive to precancerous lesion of the cervix and sociodemographic and reproductive characteristics of the participants (n=108).’’
In “Table 2” the comparison of Crude OR for two groups is not part of the study objective. However, it would probably be better to show the level of significance for the same (difference).

Author response: Please recall that it was clearly stated in the last paragraph of the background section that “The overall aim of this study was to investigate the magnitude of default and factors associated with default from follow-up care after screening positive to cervical precancerous lesion using direct visual inspection.” Our opinion is that odd ratio and the 95% CI better express the “strength” of association between outcome variable and exposure variable, hence the reason the choice over p value. Nevertheless, we have added columns to show the level of significance of the difference between exposure variables. See table 2.

Figure 1 is also confusing. What is DIA.

Author response: Correction effected, it is DVI and not DIA. See fig 1.

What is the type of study?

Author response: Addressed under method section above. See page 8 paragraph 3 of this document (above), i.e. response on study design.

Discussion
This part is well written too. The words “in other” after “see and treat strategy” should probably be “in order”.

Author response: Correction effected. See page 16, 1st paragraph. It now reads “several countries in sub Saharan African and Southeast Asia have adopted the “see and treat strategy” in order to ensure prompt treatment and consequently prevention of default”

Conclusions

Most of the conclusions are not derived from the findings of the study namely no’s 1, 2, 4 & 5. Thus there is a need to rewrite the conclusion

Author response: The last section of the manuscript incorporated conclusion and recommendations, see page 17. The conclusion which stated “The findings from this study contributed to the growing body of evidence indicating that the current strategy of opportunistic testing and outreach cervical cancer screening programme is associated with high rates of default. The multiple visits associated with this strategy and cost implication makes it burdensome and unattractive to poorly educated women residing several kilometers from the few hospitals offering unaffordable cervical cancer services.”

The issues itemized are recommendation to address the study conclusions.