Author’s response to reviews

Title: Cervical precancerous changes and selected cervical microbial infections among women attending Family Health Option Clinic in Thika, Kiambu County, Kenya, 2014: A cross sectional study

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Author’s response to reviews:

1. TITLE: The title can be shortened by removing the clinic name which is long

The clinic name was dropped. See line 2-3.

2. Abstract:
- Line 32: specify the type of clinic the women were attending. Leaving it open implies a general clinic which does not sit in well with the first statement under results - '97.5% of the women had cervical inflammation.'

The women were attending reproductive health screening clinic. Revised See line 28
- Under methods, specify how cervical inflammation was determined as this is a key finding

Cervical Inflammation was determined by Pap smear screening test and High Vaginal Swab wet preparation microscopy. See line 29-31. Both tests are used for the diagnosis. Presence of more than 10 white blood cells under microscopic high-power field examination of High vaginal swab was classified as cervical inflammation. See line 90 – 92.
3. Introduction

- This statement is incorrect: "In Kenya, cervical cancer is the leading cause of morbidity and mortality among women (Bruni et al., 2014)"

Cervical cancer is the leading cancer among women. Revised, see line 53 – 54.

- The introduction should also state the burden of cervical cancer in Kenya as well as the prevalence of the microbial infections of interest

An estimated 4802 women are diagnosed with cervical cancer annually of which 51% (2451) die from the disease (Bruni et al., 2014). Cervical microbial infections have not been quantified. Revised, see line 57 – 58.

- Other important areas to cover would be the recommended age and frequency for cervical cancer screening and the reasons why coverage is so poor.

Revised, see line 59 – 60.

4. Methodology:

- Line 66: Delete 'prospective'

Deleted, see line 68

- Yeast cell infection was the most common among microbial infections. Candida often causes vulvovaginitis but it is also normal flora in the female genital tract. How did you differentiate normal flora from infection? How did you pick out inflammation caused by Candida?

Diagnosis was made if pseudohyphae or hyphae or yeast buds were present in the Pap smear or Gram stained specimen. See line 83 – 85, 89 -90.

- Did you collect any data on antimicrobial use prior to the visit?
All those who had taken antibiotics 72 hours before study enrollment were excluded from study participation. See line 77 – 78.

- Was culture done for the HVS especially for Neisseria gonorrhea and Actinomyces?

Culture was not done. Our diagnosis was based on Pap smear and HVS wet mount and Gram staining techniques. This was part of our limitation – not using culture and molecular techniques for identification of microbes. The study however demonstrate the use of multiple laboratory techniques which could be used extensively in low-income settings to give an in depth picture of the cervix.

- Briefly describe how data was stored rather than stating that 'data was stored properly'

Data was store in filing cabinet and computer. See line 265 – 267

- The statement that 'There was no risk involved in Pap smear and HVS specimen collection' is incorrect

Revised, see line 267 – 269.

- In this section (methodology), you should state how you arrived at your sample size.

We used a prevalence of 50% estimated by Fisher and Van Belle (2004) as no previous study had been done in the area. See line 72 – 74.

- For the each of the various statistical techniques mentioned, give examples of the variables tested revised, see line 100 – 102.

5. Results:

- This section should be organized better by reporting related data together: e.g. you could have a section on participant characteristics, a section on risk factors for cervical cancer and infection, a section on cervical cancer, on infections, etc.
Revised, see lines 105, 117 and 135.

- Data reported on line 126/127 is misinterpreted: "The odds (OR: 1.11, 95% CI: 0.23-5.23) of cervical precancerous changes in women who were married was one time higher that of non-married women."

Revised, see line 129. There is no difference in both groups.

- What was the basis (standard) for the sensitivity reported in line 138? '… HVS wet preparation had the 'highest sensitivity' to inflammatory changes and their causes.'

Revised, see line 141 - 142. We meant the number identified as positive for inflammation and their cause. We cannot term it as sensitivity as we are not checking against a gold standard.

- What was the basis (comparator) for the odds given in line 141? "Use of IUCDs (OR: 2.47, 95% CI 1.3-4.6) was associated with having cervical inflammation."

Revised, comparator was non-IUCDs users. Women who opted for other modes of contraception see line 143 – 145.

6. Discussion

- The first paragraph in this section should report the two or three key findings of the study not just CIN

Revised, see line 148 - 151.

- When the data being discussed is derived from a small sample, it is more accurate to report the absolute numbers, not just the percentage e.g. 2 out of 10 rather than 20%

- Specify the country in line 170: 'This is important in a country where 157 60% of cancer victims are below 70'
Revised, the country is Kenya. see line 163.

- When you cite studies for comparison, it is more informative to state the population where the study was conducted rather than the full name of the research centre or site. E.g. 'A study in women seeking care at a reproductive health clinic in Pakistan,' rather than, 'A study done at Nishtar Hospital Multan and Multan Institute of Nuclear Medicine & Radiotherapy (MINAR) in Pakistan.' Make your sentences short, concise and unambiguous.

Revised, see line 154, 158 and 159.

- Line 178: "not having a previous Pap smear test was not significantly associated with cervical precancerous changes in our study." Did you have enough numbers to make this conclusion?

This conclusion was based on our study findings. This may change in different study design and study population. It cannot be generalized since this was a hospital based study among women seeking health services from private practitioners.

- Line 196 "This higher prevalence of inflammatory changes in a population which has high literacy level and majority working women could be due to more liberal sexual behavior in this group." Specify which population you're referring to avoid ambiguity. Is there evidence that higher literacy levels lead to high risk sexual behavior? Please cite the evidence here.

Revised, see line 203 – 204.

7. Conclusion

- 231 'Yeast cell was the predominant microbial organism detected with most causes of inflammation remaining non-specific.' What does non-specific mean in this statement, undiagnosed?

Non-specific inflammation meant that pus cells were identified without evidence of accompanying cause of inflammation with the various test employed in this study. Revised, see line 238.
8. References:

- Use a uniform referencing style. E.g. line 181 has numbering while the rest are authors' names. Several references are mentioned in a sentence but not cited at the end of the sentence as should be. Check the referencing requirements for authors for BMC or any other journal that you chose to publish in

- National Guidelines for Prevention and Management of Cervical, Breast and Prostate Cancer (NGPMCBPC), 2012. Insert the authors/publishers of this reference e.g. Ministry of Health Revised, see line 313 – 315.

9. General

- The correct name of the study site (Family Health Options Kenya) should be used consistently. The acronym (FHOK) would be best given the long name rather than using different versions of the same name.

There are many grammatical errors that suggest that the manuscript was put together hurriedly. The authors should take time to revise the manuscript in order to improve readability. Examples are listed below (not exhaustive)

- Line 47: should read as 'scale up' not 'scaled up'

  Revised, see line 43

- 56: Delete "have been documented to…"

  Revised, see line 51

- 57-58: Grammar

  Revised, see line 52 - 53

- 69 Delete 'vastly'
Revised, see line 70 - 71.
- 86 Univariate analyses were "determined"

Revised, see line 96.
- 108 Use 'parous' instead of 'had given birth'

Revised, see line 110
- 139 Delete: 'as their preferred mode of contraception'

Revised, see line 143
- 164 Use the correct name for CDC

Revised, see line 170 – 171.
- 166 should read 30-39 years

Revised, see line 172
- 171 change 'can' to 'may',

Revised, see line 177
- 172 What is "invase"?

Revised, see line 178. It should read, ‘invasive’ nature
- 190 replace "in the present study" with 'in this study"
- 216 "This can be attributed to the fact that all IUCD users had a history of a previous Pap tests and therefore might have been treated previously." This explanation is unlikely unless the participants were having pap smears within short intervals of each other (e.g. within months) or had one very recently.

It is not possible to currently determine the exact time of the participants’ previous Pap smear.

- 218 Use the correct term for "polymorphs"

Revised, see line 224–225.

For the 'Availability of data and materials' section, please provide information about where the data supporting your findings can be found. We encourage authors to deposit their datasets in publicly available repositories (where available and appropriate), or to be presented within the manuscript and/or additional supporting files. Please note that identifying/confidential patient data should not be shared. Authors who do not wish to share their data must confirm this under this sub-heading and also provide their reasons. For further guidance on how to format this section, please refer to BioMed Central's editorial policies page (see links below).

See line 276 – 278.