

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Cervical cancer screening Uptake and correlates among HIV-infected women: a cross-sectional survey in Côte d'Ivoire, West Africa
<b>AUTHORS</b>	Tchounga, Boris; Boni, Simon Pierre; Koffi, Jean Jacques; Horo, Apollinaire; Tanon, Aristophane; Messou, Eugène; Koulé, Serge-Olivier; Adoubi, Innocent; Ekouevi, Didier; Jaquet, Antoine

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Heather L. White Population Services International Washington, DC USA
<b>REVIEW RETURNED</b>	18-Apr-2019

<b>GENERAL COMMENTS</b>	<p>I have specific questions and suggestions related to how education level was defined in the study, in my notes on the manuscript attached below. While the level of English is generally sufficient, there are several linguistic edits that need to be made so that meanings are clear to readers.</p> <p>The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.</p>
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<b>REVIEWER</b>	Qiao Wang University of California Irvine, USA
<b>REVIEW RETURNED</b>	24-Apr-2019

<b>GENERAL COMMENTS</b>	<p>Summary: The paper entitled "Cervical cancer screening Uptake and correlates among HIV-infected women on antiretroviral treatment: a cross-sectional survey in Côte d'Ivoire, West Africa" by Tchounga et al. describes the prevalence of cervical cancer screening uptake among women with HIV in Côte d'Ivoire.</p> <p>Introduction:</p> <ul style="list-style-type: none"><li>- Second paragraph, "In addition, a two-fold increase in the risk of death...", please specify that this increase of risk of death was due to CC.</li><li>- Last paragraph, "This study aimed at estimating the uptake of CC screening and correlates among WLHIV...", should be specified as correlates of CC screening.</li><li>- It would be useful to describe the current state of cervical cancer screening in Cote d'Ivoire. What is the screening coverage among</li></ul>
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	<p>eligible women? Among HIV-positive women? Are women starting ART screened for cervical cancer? What type of screening and treatment is generally conducted (VIA, pap, HPV DNA)?</p> <ul style="list-style-type: none"> <li>- Overall writing style needs to be improved.</li> </ul> <p>Methods:</p> <ul style="list-style-type: none"> <li>- Was number of lifetime sexual partners collected? This could affect the decision of women taking up screening.</li> <li>- The statistical method used in this study for the specified outcome (CC screening uptake) is inappropriate. The authors should consider using a log binomial regression or Poisson regression (both with robust standard errors) instead of multivariate logistic regression, since this is a cross-sectional study and the outcome variable is not rare in your sample. Also, analysis should be based on those who have heard of CC (N=1913)</li> <li>- Please clarify the definition of outcome variable in this section (e.g. at least one CC screening over what period of time was considered "Yes" and otherwise "No")</li> <li>- Each predictor variables and how they are categorized should be clearly defined in this section. For example, why was age cutoff 45 instead of 42 (median age)?</li> <li>- Have the authors considered or looked at CD4 count in relation to the outcome? is it possible for healthcare providers to recommend screening based on CD4 cell counts?</li> <li>- Abbreviation should be used throughout the manuscript for consistency (e.g. WLHIV)</li> <li>- Why was a significance level of <math>\leq 0.25</math> used in univariate analysis? This cutoff seems arbitrary and should be avoided (consider choosing variables based on a priori knowledge regardless of statistical significance)</li> <li>- According to recent statistical guidelines and American Statistical Association, no alpha cutoff was recommended for statistical significance. see: Wasserstein RL and Lazar NA. The ASA's Statement on p-Values: Context, Process, and Purpose. The American Statistician 2016; 70: 129-133. Greenland S, Senn SJ, Rothman KJ, et al. Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations. Eur J Epidemiol 2016; 31: 337-350.</li> <li>- Describe what method is used to estimate the 95% CI for CC screening coverage</li> </ul> <p>Results:</p> <ul style="list-style-type: none"> <li>- How many participant were eligible and how many refused to participate in the study?</li> <li>- "screening and HPV vaccine were identified as preventive methods by 939 (90.4%) and 423 (29.7%) participants". Please</li> </ul>
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	<p>specify the denominator for these numbers, the percentage does not make sense (e.g. 939 out of 1,450 is not 90.4%).</p> <ul style="list-style-type: none"> <li>- Please pay attention to specifying the denominators in this section. For example, among those who have ever been screened, "The main screening methods were VIA for 1,050 (88.4%) participants and Pap smear for 120 (10.1%) participants". It makes the text and percentages easier to follow for readers.</li> <li>- it looks like not 100% of the participants were on ART. Wording of sample population should be changed in the conclusion section and abstract (e.g. among WLHIV, not WLHIV on ART).</li> </ul> <p>Discussion:</p> <ul style="list-style-type: none"> <li>- Spell out abbreviation for MOH</li> <li>- "The aim was to integrate CC screening in HIV clinics and improve access to screening for women living with HIV, highly exposed to cervical cancer", should be highly exposed to the risk of cervical cancer.</li> <li>- "They also have to attend screening unit one year after treatment for a control." This sentence needs clarification.</li> <li>- Last paragraph, the authors wrote " using a daily-repeated systematic random selection procedure over a period of three months." But in strength and limitation section the authors said "over a period of four months". These information are inconsistent.</li> <li>- The authors need to describe the limitations of the study. For example, a main limitation for cross-sectional study is that the temporal relationship between exposure and outcome cannot be ascertained. Did participants get CC screening first before knowledge of HIV as a risk factor? Also, bias from self-reported questionnaire is possible.</li> <li>- Discussion needs to improve writing style/mispelling</li> </ul> <p>Conclusion:</p> <ul style="list-style-type: none"> <li>- "which remains a cancer defining AIDS that is..." should be AIDS-defining cancer.</li> <li>- "which remains a cancer defining AIDS that is poorly prevented by antiretroviral treatments." This statement is incorrect. There is evidence to suggest that ART reduces cervical lesions and cervical cancer. See: Kelly H1, Weiss HA2, Benavente Y3, de Sanjose S4, Mayaud P5; ART and HPV Review Group. Association of antiretroviral therapy with high-risk human papillomavirus, cervical intraepithelial neoplasia, and invasive cervical cancer in women living with HIV: a systematic review and meta-analysis. Lancet HIV. 2018 Jan;5(1):e45-e58.</li> </ul>
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## VERSION 1 – AUTHOR RESPONSE

Reviewer1: Heather L. White

Summary: I have specific questions and suggestions related to how education level was defined in the study, in my notes on the manuscript attached below. While the level of English is generally sufficient, there are several linguistic edits that need to be made so that meanings are clear to readers.

Page 1: lines 7 to 10: insert semi Colum after Koffi, Messou and Jaquet

Page 1: line 19: put capital letter for obstetrics

Page 2 line 12: remove the bulk on Cross

Authors: we thank the reviewer for these remarks that have been taken into account in the revised version of the manuscript.

Abstract

Page 2, line 15: More details here to offer on the outpatient settings; urban, peri urban, public/private sector, other?

Authors: we thank the reviewer for this comment, we have added more details on the outpatient's settings in the revised version of the manuscript as follow.

Settings: Outpatient setting in the four highest volume urban HIV clinics of government's or NGO's sector in Côte d'Ivoire.
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Page 2, line 38: Language not entirely clear here; self-perceived? Meaning that the woman understood the information presented to her?

Authors: we thank the reviewer for this comment, the correct word is self-perceived, to explain that the participant declare that the information was clear and they understood it very well. We have updated the revised version of the manuscript to make this sentence clearer by writing self-perceived instead of self-considered where appropriate.

Page 2, line 41: So, being told that screening was available and being offered screening were considered independent variables? Really high aOR and worth highlighting as a finding.

Authors: we thank the reviewer for this comment, in our context, where cervical cancer is a priority for the national cancer control program, there are lot of awareness activities conducted by local NGOs affiliated to the NCCP. Most of these awareness activities are in the community, in churches and mosques as well as in markets and also in the hospitals, but it is not always clear if these messages are clearly understood by the participants. This is why we made the difference between being informed that CC screening exist, and being proposed the screening. In our analyses, being informed that CC screening exist in the hospital and being proposed the screening in the same hospitals were not different, and we just present being proposed the screening. We however agree with the reviewer that this was less highlighted in the text, and we added one sentence in the revised version of the manuscript to highlight the importance of being offered the screening in the usual health facility.

The positive effect of this service integration is emphasized in our study by the association between screening uptake and the offer of cervical cancer screening "onsite", in the HIV clinic were the participant is usually followed. This underlines the importance of scaling up the cervical cancer screening in all HIV clincs, as WLHIV will be more willing to accept the screening when proposed in the health facility they usually attend. Indeed, half of the screened women declared having accept the screening because it was advised by the healthcare worker at the HIV clinic [27].
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## Strengths and limitations

Page3, line 14: Not sure I understand what is being articulated as a strength here? That you're able to capture a wide variety of patients who've been on ART for many months?

Authors: we thank the reviewer for this question, we were trying to explain that by using this sampling method and the enrollment within four months, we were able to capture a wide variety of women including those who received ART every three months and who could be excluded with a shorter recruitment period. We tried to simplify this sentence to make it easier to understand.

The methodological approach used in this study allowed the enrolment of a quite representative sample of WLHIV visiting the participating HIV clinics.

Page3, line 18: insert comma

Authors: we thank the reviewer for this comment, the comma has been added in the revised version of the manuscript.

## Introduction

Page 4, line 11: should be plural

Page 4, line 20: insert comma

Authors: we thank the reviewer for these suggestions. We have taken them into account in the revised version of the manuscript.

Page 4, line 21: UNAIDS reference cites women risk up to 5-fold higher for

Authors: we thank the reviewer for this comment, we agree that UNAIDS reference cites women risk up to 5-fold higher for invasive cervical cancer. We have added this precision of UNAIDS in the revised version of the manuscript.

Page 4, line 37: suggest 'has been' instead of 'was'; may also consider citing doi: 10.1002/ijgo.12194. as an example of integrated CC/SRH services within programs in SSA region

Authors: we thank the reviewer for these suggestions. We made change suggested by the reviewer and added the citation from White and Coll. in the revised version of the manuscript.

Page 4, line 43: You may be able to find region-specific or country-specific estimates through IARC's HPV Information Centre data. May be worth pointing out that these data generally do not exist given insufficient surveillance/data capture mechanisms, both for general population, and for WLHIV in particular.

Authors: we thank the reviewer for this comment, we agree that some data exist and may be found in the UNAIDS country reports and IARC estimates. We amend the sentence minimize the idea of scarcity of data.

Cervical cancer screening uptake among women in developed settings is relatively high, 79.4% in Brazil [14], 60% in United States [15], and 89.1% in France [16], mainly with Pap smears. In developing countries, recent studies conducted in Ethiopia and Uganda revealed a low cervical cancer screening uptake of 23.5% and 30.3%, respectively [17,18] and emphasized the importance of sociodemographic factors and attitude of healthcare providers on the decision of beneficiaries to attend cervical cancer screening units [18,19].

Page 4, line 46: emphasized the importance?

Authors: we thank the reviewer for this suggestion, we have changed 'pointed out the role' and replaced it by "emphasized the importance" in the revised version of the manuscript, to make the sentence clearer.

Page 4, line 51: language not clear; Cdi has the highest HIV prevalence in the region, correct? The way the sentence reads, it sounds as though it's the fourth-highest in the region.

Authors: we thank the reviewer for this comment. Indeed, it was not clear. We modify the sentence to clarify that Côte d'Ivoire have the highest HIV prevalence among women in West Africa.

In West Africa, Cote d'Ivoire has the highest HIV prevalence among women (4.1%) [20]. Cervical cancer is the second most common cancer among women accounting for 28.6% of all women's cancers and the leading cause of cancer deaths with 22.2% of all cancer related deaths [2]. The national guidelines on cervical cancer screening in the country are aligned with WHO guidelines for low- and middle-income countries, and recommend the screen-and-treat approach based preferentially on visual inspection with acetic acid or pap smear and cryotherapy or electrocoagulation, respectively. This recommendation targets women between 25 and 55 years old in the general population, and those diagnosed with HIV who should be systematically offered a screening per year once linked to HIV care [21].

Page 4, line 52: change verb tense to plural

Authors: we thank the reviewer for this comment, we modify the sentence to make it clearer and change the verb in the revise version of the manuscript.

Method

Page 5, line 9: On what basis did you select clinics for the study?

Authors: we thank the reviewer for this comment, the clinics were selected based on the volume of their active file. We selected the four HIV clinic with the largest active file of WLHIV. This precision has been added in the revised version of the manuscript.

Page 5, line 36: suggest 'number of screenings conducted'

Authors: we thank the reviewer for this suggestion. We modify the text accordingly in the revised version of the manuscript.

Page 5, line 48: Not sure why you didn't categorize as a continuous variable and create cut-offs based on years of education. Based on the definition presented, a woman who has completed secondary education would be considered 'less educated', correct?

Authors: we thank the reviewer for this comment, we agree that it would have been helpful to categorize as continuous variable and create cut-offs based on years of education. But it was very difficult to create this cut-off, and to categorize as continuous since it induces lot of proxies and estimates of the number of years. We collected aggregated data on educational level with four classic modalities (no formal, primary, secondary and university. And the number of years of education is not always correlated to the educational level, as one person can stay three or four year in the same class. Assuming that the level of language of health care workers in town is usually high, we were trying to show that the awareness messages are well understood by women with very university level. We are not suggesting that women or people with secondary educational level are less educated. We change the denomination of the categories in the revised version of the manuscript to avoid confusing ideas or stigmatization on WLHIV. It is now below university level / university level.

Page 5, line 48-2: suggest 'dichotomous'

Authors: we thank the reviewer for this suggestion, we made the change accordingly in the revised version of the manuscript.

Page 5, line 15: How did you define 'knowledge of cervical cancer'?

Authors: we thank the reviewer for this comment, we have changed the term knowledge on cervical cancer by awareness of cervical cancer and we have clarified the signification in the revised version of the manuscript.

variable related to awareness of cervical cancer (having heard about cervical cancer, being aware of the relationship with HIV, being aware of the cervical cancer prevention by screening, having been proposed the screening).

Page 6, line 7: suggest use of acronyms here

Authors: we thank the reviewer for this suggestion, we have modified the text accordingly in the revised version of the manuscript.

Page 6, line 10: suggest analyses

Authors: we thank the reviewer for this suggestion, we have modified the text accordingly in the revised version of the manuscript.

Page 6, line 19: use acronym that you've already defined. What language did you conduct the study in? Was this an inclusion/exclusion criterion?

Authors: we thank the reviewer for this suggestion, the study questionnaire was in French, but the participant have the possibility to ask a translator and a witness to assist in case she was not able to read or understand French. No, it was not an inclusion / exclusion criterion. We amend the text to use the acronym WLHIV consistently.

Page 6, line 20: Suggest alternate language such as, 'insights generated from this panel of women...'

Authors: we thank the reviewer for this comment, we have updated the text of the revised manuscript to take into account this suggestion.

Additional 'insights generated from this panel of women were taken into account in the final version of the questionnaire.

Page 6, line 30: country's national. Should the name of this body be capitalized?

Authors: we thank the reviewer for this comment, we have provided the full original name of this country's national body and the acronym in the revised version of the manuscript.

Ethical approval was obtained from the "Comité National d'Ethique des Sciences de la Vie et de la Santé (CNESVS)", that is the National Ethic Committee for life Science and Health, the country's national IRB. The registry number of our study is "IORG00075". Each participant was given comprehensive information on the protocol of the study and had to provide a written consent before being enrolled.

## Results

Page 7, line 11: correct typo. Needs a comma

Authors: we thank the reviewer for this observation, we have added a coma consistently in the revised version of the manuscript.

Page 7, line 12: suggest HIV-related

Authors: we thank the reviewer for this suggestion, we added HIV related characteristics in the revised version of the manuscript.

Page 7, line 28: Suggest restructuring this sentence to active voice: A total of XXX (%) of patients stated that the information provided about CC was understandable and clear.

Authors: we thank the reviewer for this suggestion that we have taken into account by restructuring the sentence into active voice as follow:

Among the 1,913 participant who ever heard about cervical cancer, 1,167 (61.0%) stated that the information provided about cervical cancer was understandable and clear.

Page 7, line 32: Suggest recognized or 'known to be'

Authors: we thank the reviewer for these suggestions, we have used "recognized" in the revised version of the manuscript.

Page 8, Table 1, line 16: Were there other sources of information among these women that were also common?

Authors: we thank the reviewer for this comment, women were also informed via the mass media (TV, radio internet) and during awareness campaigns organized in churches, mosques, markets, stadium and other public places. The aim of this question was to show that women were effectively informed in the hospitals by healthcare workers, since patients usually have more confidence in healthcare workers. We modified the shorten title of the variable in the table to reflect that in the revised version of the manuscript.

Page 8, Table 1, line 21: Do not see where details associated with asterisk are located?

Authors: we thank the reviewer for this comment, it was a mistake, we removed the asterisks in the Table 1, in the revised version of the manuscript.

Page 8, Table 1, line 28: Is this ANY information related to CC, or only referring to the sources mentioned here, i.e., media and/or HIV clinic?

Authors: we thank the reviewer for this comment, it is any information related to cervical cancer, but in our studies, the most important sources of information were media and healthcare workers, the other sources are minor and are known to provide very basic information and advise women to go to the hospital for more information and being screened.

Page 8, Table 1, line 35: disease? I believe a word is missing here?

Authors: we thank the reviewer for this comment, the word disease was missing. We added it in the revised version of the manuscript.

Page 8, Table 1, line 40: No need to label this footnote since you have

Page 8, Table 1, line 47: Not clear what this refers to?

Authors: we thank the reviewer for this comment, the signs have been removed in the revised version of the manuscript.

Page 9, line 11: Why did some women not get results?

Authors: we thank the reviewer for this comment, few women did not get the results either because the VIA was non conclusive and they were referred to a gynecologist for diagnosis confirmation. If the women did not see the gynecologist, they will not know the final result of their screening.

Page 9, line 13: advice

Page 9, line 21: no need to capitalize negligence

Authors: we thank the reviewer for these remarks, we have corrected “advice” and removed the capital N on negligence in the revised version of the manuscript.

Page 9, line 22: It would be very useful to also provide data on the % of women with positive results and who were treated. I understand that this paper is about screening coverage, but from a public health perspective, screening alone does not confer health impact.

Authors: we thank the reviewer for this comment, we agree that providing data on treatment would have been very useful. However, this study is a cross-sectional one based on declarative information. It would have been very difficult to present declarative data on the result of a cervical cancer screening and access to treatment. To describe the cervical cancer screening cascade, we need to access screening record sheet of each participant, stored in the screening units, unfortunately the study was not design for that. However, the National cancer control program in Côte d’Ivoire has adopted the screen and treat approach, consisting in a systematic treatment of eligible pre-cancerous lesions by cryotherapy.

Page 9, line 33: This is a strange sentence; see my earlier note.

Authors: we thank the reviewer for this remark, we have change to use self-perceived consistently in the revised version of the manuscript.

Page 10, Table 2, line 3: Uptake? Didn't all of these women have access to screening by participating in the study?

Authors: we thank the reviewer for this comment, the correct word is indeed uptake, all of these women have access to screening. We change this in the revised version of the manuscript.

## Discussion

Page 11, line 5: restate N here

Page 11, line 9: Suggest 'the majority'

Authors: we thank the reviewer for these remarks and suggestion that we have taken into account in the revised version of the manuscript.

Page 11, line 22: Do you mean 3 out of 5 or 60% of women?

Authors: we thank the reviewer for this suggestion, we chose to use 3 out of five in the revised version of the manuscript.

Page 11, line 27: Were these populations comparable?

Authors: we thank the reviewer for this question, the population of these three studies were comparable since all the studies were dealing with adult WLHIV, who attend the HIV clinic or the health facility participating to the study, for their routine HIV follow up visit or antiretroviral drug refill, in sub-Saharan African countries.

Page 11, line 35: susceptible

Page 11, line 37: outlying areas?

Authors: we thank the reviewer for these suggestions that have been taken into account in the revised version of the manuscript.

Page 11, line 40: Again, making the comment that providing data on treatment uptake would also be compelling to report, if available, from a public health impact perspective.

Authors: we thank the reviewer for this comment and we agree that it would be very useful in a public health perspective to present data on treatment. However, we were unable with this design to present such data here.

Page 11, line 43: May want to also reference PEPFAR's recent investment for CCSPT in PEPFAR-supported ART clinics in high HIV burden countries: <https://www.pepfar.gov/press/releases/281984.htm>

Authors: we thank the reviewer for this suggestion, we have appreciated this reference and added it in the revised version of the manuscript.

Page 11, line 50: Can also cite results from this study which showed similar results: doi: 10.1186/s12889-016-3450-x

<https://www.usaid.gov/what-we-do/global-health/hiv-and-aids/information-center/hiv-and-aids-research-corner/cervical-cancer-screening-zambia>

Authors: we thank the reviewer for this suggestion, we appreciated the citation suggested and have added it in the revised version of the manuscript.

Page 12, line 6: or poorly disseminated?

Page 12, line 9: remove 's'

Page 12, line 12: make plural

Authors: we thank the reviewer for this remarks that have been taken into account in the revised version of the manuscript.

Page 12, line 14: Are there review articles to cite on this topic?

Authors: we thank the reviewer for this comment, there are two recent systematic reviews treating the barriers to utilization of cervical cancer screening. These two reviews have been cited in the revised version of the manuscript.

Barriers to utilisation of cervical cancer screening in Sub Sahara Africa: a systematic review.  
Lim JN<sup>1</sup>, Ojo AA<sup>2</sup>

Integrated Review of Barriers to Cervical Cancer Screening in Sub-Saharan Africa.  
McFarland DM<sup>1</sup>, Gueldner SM<sup>2</sup>, Mogobe KD<sup>3</sup>.

Page 12, line 23: Could also cite the need for patient-centered communications

Authors: we thank the reviewer for this suggestion, we have added the need for patient-centered communications among the element influencing patient's decision to take utilize cervical cancer screening, in the revised version of the manuscript.

Page 12, line 23: remove 's'

Authors: we thank the reviewer for this remark that have been taken into account in the revised version of the manuscript.

Page 12, line 28: You touch on an important topic here; that is, the importance of the providers' influence in her decision-making for screening, your most significant cofactor. Suggest you highlight this finding more clearly and provide context with other studies/findings.

Authors: we thank the reviewer for this very helpful comment, we have highlighted this finding more clearly and provide context with other studies findings in the revised version of the manuscript.

In addition to participant-related barriers, providers-related barriers such as lack of knowledge and failure to inform or encourage women to be screened were reported as important factors influencing cervical cancer screening uptake in other SSA countries [33]. In our study the role of health care providers appeared to be central in the decision of WLHIV to get screened as highlighted by the strong association between screening uptake and proposition of screening in the usual HIV clinic of the participants. This idea is supported by the association reported between screening uptake and receiving clear and understood information on cervical cancer screening from health care providers. Thus, the high rate of cervical cancer screening uptake reported in this study compared to other SSA countries could be explained by the influence of health care providers, mostly psychosocial agent who are in charge of linkage and retention of WLHIV and who are trained to inform WLHIV and refer them to screening unit. However qualitative studies are needed to deeply explore the provider's related barriers for screening uptake among the 40% of WLHIV who have never been screened in the participating HIV clinics.

Page 12, line 55: WLHIV?

Page 13, line 3: use acronym

Authors: we thank the reviewer for these remarks, we have used WLHIV consistently along the text in the revised version of the manuscript.

Conclusion

Page 13, line 26: an AIDS-defining illness

Authors: we thank the reviewer for this suggestion, we have used AIDS-defining illness in the revised version of the manuscript.

Figure and legend caption

Page 13, line 39: Is there a reason that the figure does not show the number of women interviewed? Hard to tell the significance of the table without knowing the denominator.

Authors: we thank the reviewer for this comment, we have added the denominator in the Figure one to make it easier to understand.

References

Page 15, line 3: References are not uniform and still have some French language embedded. Need careful review.

Authors: we thank the reviewer for this remark, we have made a careful review of the reference section, to make it more uniform, in the revised version of the manuscript.

Reviewer2 : Qiao W ang

Summary: The paper entitled "Cervical cancer screening Uptake and correlates among HIV-infected women on antiretroviral treatment: a cross-sectional survey in Côte d'Ivoire, W est Africa" by Tchounga et al. describes the prevalence of cervical cancer screening uptake among women with HIV in Côte d'Ivoire.

Introduction:

1- Second paragraph, "In addition, a two-fold increase in the risk of death...", please specify that this increase of risk of death was due to CC.

Authors: We thank the reviewer for this comment and we have added the precision that risk of death was due to CC in the text of the revised version of the manuscript.

In addition, a two-fold increase in the risk of death due to cervical cancer was reported in WLHIV compared to their HIV-negative counterparts [9].

2- Last paragraph, "This study aimed at estimating the uptake of CC screening and correlates among WLHIV...", should be specified as correlates of CC screening.

Authors: We thank the reviewer for this comment, we have updated this section to specify that it was the correlates of CC screening, in the revised version of the manuscript.

3- It would be useful to describe the current state of cervical cancer screening in Cote d'Ivoire. What is the screening coverage among eligible women? Among HIV-positive women? Are women starting ART screened for cervical cancer? What type of screening and treatment is generally conducted (VIA, pap, HPV DNA)?

Authors: We thank the reviewer for this suggestion, we have updated the intro section by adding a paragraph on the current state of cervical cancer in Côte d'Ivoire, specifying the cervical cancer screening policy and program outcomes:

Cervical cancer is the second most common cancer among women accounting for 28.6% of all women's cancers and the leading cause of cancer deaths with 22.2% of all cancer related deaths [2]. The national guidelines on cervical cancer screening in the country are aligned with WHO guidelines for low- and middle-income countries, and recommend the screen-and-treat approach based preferentially on visual inspection with acetic acid or pap smear and cryotherapy or electrocoagulation, respectively. This recommendation targets women between 25 and 55 years old in the general population, and those diagnosed with HIV who should be systematically offered a screening per year once linked to HIV care [21]. These guidelines relied on the screening program that was piloted in HIV clinics from 2008 to 2012 before being scaled up in all the government health facilities and at national level. However, data on the national coverage of cervical cancer screening among women in Côte d'Ivoire are currently not available. The only data available on the coverage of cervical cancer screening among WLHIV is the 10% UNAIDS estimates based on the data from 2011-12 Demographic and Health Survey [22].

4- Overall writing style needs to be improved.

Authors: we thank the reviewer for this comment, we have tried our best to improve the writing style. The paper was reviewed by a native English speaker.

Methods:

5- Was number of lifetime sexual partners collected? This could affect the decision of women taking up screening.

Authors: we thank the reviewer for this question, unfortunately, we did not collect the number of lifetime sexual partners, as the study was focus on the screening uptake and knowledge. In addition, this declarative variable is hardly reliable given the high risk of information (memory) bias.

6 -The statistical method used in this study for the specified outcome (CC screening uptake) is inappropriate. The authors should consider using a log binomial regression or Poisson regression (both with robust standard errors) instead of multivariate logistic regression, since this is a cross-sectional study and the outcome variable is not rare in your sample.

Authors: We thank the reviewer for this interesting comment. Based on the frequency of our measured outcome, we surely agree that our measure of association reported as Odd ratio differs significantly from the relative risk that could be reported through prevalence ratio. Indeed, the modified Poisson or Log binomial regression would have been more appropriate to provide risk estimates. However, our main objective was to identify association between our covariates and the measure of cervical cancer screening uptake. Therefore, we have chosen to provide estimates through Odds ratio as logistic regression, that remains an applicable model in this particular situation (Cook, TD. ACAD EMERG MED, 2002). To prevent any misinterpretation of our results we have reviewed the manuscript and ensured that measured Odds ratio were not interpreted as "measures of risk".

7- Also, analysis should be based on those who have heard of CC (N=1913)

Authors: We thank the reviewer for this suggestion. However, we feel that excluding from the present analysis those who never heard about cervical cancer screening may be interpreted as excluding women unable to understand awareness messages, meaning those with lower education level. In addition, previous reports describing cervical cancer screening coverage did not apply such exclusion criteria in their denominator. Therefore, in order to enable comparability with previous reports we believe that all solicited WLHIV should be kept in the analysis.

8- Please clarify the definition of outcome variable in this section (e.g. at least one CC screening over what period of time was considered "Yes" and otherwise "No").

Authors: We thank the reviewer for this suggestion, the definition of the outcome variable has been clarified as "the uptake of at least one cervical cancer screening in lifetime" in the revised version of the manuscript (page 6, line 31-32).

To perform the logistic regression analysis, we defined the uptake of cervical cancer screening using the dichotomic variable "at least one lifetime cervical cancer screening" (yes/no) as the dependent variable.

9- Each predictor variables and how they are categorized should be clearly defined in this section. For example, why was age cutoff 45 instead of 42 (median age)?

Authors: We thank the reviewer for this comment, we have now clearly defined predictor variables used in the subsequent analysis, in the revised version of the manuscript (page 6/7, line 26-34/ 1-11).

Independent variables where demographic characteristics, HIV follow up characteristics and variable related to awareness of cervical cancer (having heard about cervical cancer, being aware of the relationship with HIV, being aware of the cervical cancer prevention by screening, having been proposed the screening). The educational level was categorized in three modalities: "No formal education or primary level" for women with no formal or primary education level, "secondary level" for women who attend at least one class in secondary school and "university level" for those with university education level. Age of participants was categorized into two modalities (<45 / ≥45) based on previous reports. The marital status was dichotomized as living alone (single, divorced, widowed) or living with a partner (married or engaged with a life partner). To characterize information of cervical cancer, we combine two variables (having heard about cervical cancer and source of information) to create a new variable indicating if the participants has been informed in the HIV clinic or elsewhere "information on cervical cancer". The time since first positive HIV serology was categorized into three modalities (1-4; 5-9; ≥10 years). We also created a variable to assess the influence of the place and the category of person who proposed the screening, this variable "proposition of screening" has two modalities for participants who had ever been proposed a screening (proposed elsewhere/ proposed in the HIV clinic). The clinical stage was dichotomized into I-II/A-B for the participants with the corresponding WHO or CDC clinical stage in their medical records, and III-IV/C for those with advanced stage disease.

10 - Have the authors considered or looked at CD4 count in relation to the outcome? is it possible for healthcare providers to recommend screening based on CD4 cell counts?

Authors: We thank the reviewer for this interesting question, CD4 count measures (last known measure and first measure at entry into HIV care) were available. Given the absence of association with our measured outcome, CD4 count were not presented as covariates in the present analysis. Based on current national as well as international guidelines, cervical cancer screening should be recommended regardless of immunological status. One hypothesis could be that women with a severe HIV disease might be less likely to attend screening due to their physical condition but in this case, the clinical status of women should be associated with screening uptake.

11 - Abbreviation should be used throughout the manuscript for consistency (e.g. WLHIV)

Authors: We thank the reviewer for this suggestion, the abbreviations are now consistently used throughout the text in the revised version of the manuscript.

12 - Why was a significance level of  $\leq 0.25$  used in univariate analysis? This cutoff seems arbitrary and should be avoided (consider choosing variables based on a priori knowledge regardless of statistical significance)

Authors: We thank the reviewer for this comment, we acknowledge that the use of a 0.25 cutoff to select a univariate analysis factors eligible to be included in a multivariable analysis is somehow arbitrary. We have now revised our way of including variable in our first multivariable model based on "a priori" knowledge and hypothesis rather than using this 0.25 threshold.

13 - According to recent statistical guidelines and American Statistical Association, no alpha cutoff was recommended for statistical significance. see: Wasserstein RL and Lazar NA. The ASA's Statement on p-Values: Context, Process, and Purpose. The American Statistician 2016; 70: 129-133. Greenland S, Senn SJ, Rothman KJ, et al. Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations. Eur J Epidemiol 2016; 31: 337-350.

Authors: We thank the reviewer for highlighting this important issue as there is growing concerns on relying the dogmatic statistical significance based on a 0.05 p-value and its subsequent misinterpretations. While we agree with this statement, there are also major challenges to disseminate alternative approaches to replace this historic and widely used "statistical significance". In an effort to "move towards a World Beyond  $p < 0.05$ " we have deleted this specific statement from the method section and tried to reframe the discussion avoiding the term statistical significance throughout the manuscript.

14 - Describe what method is used to estimate the 95% CI for CC screening coverage

Authors: We thank the reviewer for this suggestion, the method used to estimate the 95% CI for CC screening coverage has been described in the revised version of the manuscript.

The 95% confidence interval of the proportion of WLHIV covered by cervical cancer screening was estimated using the following formula:  $p \pm Z \cdot \sqrt{p(1-p)/n}$  where  $n$ =sample size,  $p$ =ratio of the number of WLHIV covered by cervical cancer screening in the sample to the sample size and the Z-value=1.96 for 95% confidence.

Results:

15 - How many participants were eligible and how many refused to participate in the study?

Authors: We thank the reviewer for this question, almost all the patients who were selected through the systematic random procedure and offer to participate to the survey agreed. The initial projection was to enrolled a maximum of 500 women in each HIV clinic, but at the end of the study period we registered 1921 persons selected for the survey, among which only eight (0.04%) refused to participate. This was highlighted in the revised version of the manuscript page 8, line 3-5.

During the study period, 1,921 women attending their usual HIV clinic for routine follow-up visit where selected and proposed the study, among which eight (0.04%) refused to participate because of lack of time.

16 - "screening and HPV vaccine were identified as preventive methods by 939 (90.4%) and 423 (29.7%) participants". Please specify the denominator for these numbers, the percentage does not make sense (e.g. 939 out of 1,450 is not 90.4%).

Authors: We thank the reviewer for this remark, there was a mistake when reporting the data in the table formatted for the submission. The number and percentage have been carefully checked and corrected in the revised version of the manuscript.

17 - Please pay attention to specifying the denominators in this section. For example, among those who have ever been screened, "The main screening methods were VIA for 1,050 (88.4%) participants and Pap smear for 120 (10.1%) participants". It makes the text and percentages easier to follow for readers.

Authors: We thank the reviewer for this suggestion, we have specified the denominator for most of the percentages in the results section and updated the revised version of the manuscript accordingly.

18 - it looks like not 100% of the participants were on ART. Wording of sample population should be changed in the conclusion section and abstract (e.g. among WLHIV, not WLHIV on ART).

Authors: We thank the reviewer for this comment, we have changed the language in the conclusion and abstract sections of the revised version of the manuscript, to refer now to WLHIV not WLHIV on ART. We also updated the title to reflect that.

Discussion:

19 - Spell out abbreviation for MOH

Authors: We thank the reviewer for this suggestion that has been taken into account in the revised version of the manuscript. MOH stands for Ministry of Health.

20 - "The aim was to integrate CC screening in HIV clinics and improve access to screening for women living with HIV, highly exposed to cervical cancer", should be highly exposed to the risk of cervical cancer.

Authors: We thank the reviewer for this suggestion, we have modified the sentence in the revised version of the manuscript page 13, line 19-21.

The aim was to integrate cervical cancer screening in HIV clinics and improve access to screening for women living with HIV, highly susceptible to cervical cancer.

21 - "They also have to attend screening unit one year after treatment for a control." This sentence needs clarification.

Authors: We thank the reviewer for this comment, we have now clarified the sentence in the revised version of the manuscript page 15, line 4-6.

In case of precancerous lesions eligible for treatment, they will have to attend the screening unit one year after treatment for a follow up visit with the aim of checking recurrence [29].

22 - Last paragraph, the authors wrote " using a daily-repeated systematic random selection procedure over a period of three months." But in strength and limitation section the authors said "over a period of four months". These information are inconsistent.

Authors: We thank the reviewer for this remark. The study period was four months and has now been consistently specified in the revised version of the manuscript.

23 - The authors need to describe the limitations of the study. For example, a main limitation for cross-sectional study is that the temporal relationship between exposure and outcome cannot be ascertained. Did participants get CC screening first before knowledge of HIV as a risk factor? Also, bias from self-reported questionnaire is possible.

Authors: We thank the reviewer for this suggestion, we agree that a cross-sectional and declarative survey may have endogen bias that should be taken into account such as memory bias or social desirability bias. This suggestion was taken into account in the revised version of the manuscript page 14, line 22 -26.

The cross-sectional design of the study did not allow us to draw any causal relationship between the uptake of cervical cancer screening and the reported associated factors. Although the questionnaire was administered during face-to-face interviews by previously trained monitors, we cannot exclude bias related to the declarative nature of the collected information, such as memory bias or social desirability bias. However, the survey was conducted in the four largest HIV clinics in the country, using a daily-repeated systematic random selection procedure over a four-month period. This enabled to take into account the heterogeneity of the population attending these HIV clinics and helped mitigate the risk of selection bias.

23 - Discussion needs to improve writing style/misspelling

Authors: We thank the reviewer for this remark, we have tried our best to improve writing style/misspelling in the revised version of the manuscript.

Conclusion:

24 - "which remains a cancer defining AIDS that is..." should be AIDS-defining cancer.

Authors: We thank the reviewer for this suggestion, that have been taken into account, who now wrote AIDS-defining-cancer in the revised version of the manuscript page 14, line 31.

25 - "which remains a cancer defining AIDS that is poorly prevented by antiretroviral treatments." This statement is incorrect. There is evidence to suggest that ART reduces cervical lesions and cervical cancer. See: Kelly H1, W eiss HA2, Benavente Y3, de Sanjose S4, Mayaud P5; ART and HPV Review Group. Association of antiretroviral therapy with high-risk human papillomavirus, cervical intraepithelial neoplasia, and invasive cervical cancer in women living with HIV: a systematic review and meta-analysis. Lancet HIV. 2018 Jan;5(1):e45-e58.

Authors: We agree that recent findings have reported a lower incidence of ICC in women on ART compared to untreated women living with HIV. However, the magnitude of this association is far beyond to the two other AIDS defining malignancies, namely Kaposi Sarcoma and Non Hodgkin Lymphoma. To specify this particular point the sentence was reformulated as follows in the revised version of the manuscript page 14, line 30-32:

Nevertheless, efforts are still needed to provide universal access to cervical cancer screening, which remains an AIDS-defining cancer poorly prevented by antiretroviral treatments compared to Kaposi Sarcoma or Non-Hodgkin Lymphomas. Promoting cervical cancer screening among socio-economically disadvantaged WLHIV by addressing client barriers still need to be prioritized.

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Qiao Wang University of California Irvine
<b>REVIEW RETURNED</b>	18-Jun-2019

<b>GENERAL COMMENTS</b>	The authors have addressed majority of my comments satisfactorily, just one remain: if authors insist on using logistic modeling (even though interpretations in the text are appropriate), please address in the discussion section that the effect measures or strength of the association are inflated or overestimated by this method.
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**VERSION 2 – AUTHOR RESPONSE**

Reviewer2 : Qiao Wang

The authors have addressed majority of my comments satisfactorily, just one remain:

if authors insist on using logistic modeling (even though interpretations in the text are appropriate), please address in the discussion section that the effect measures or strength of the association are inflated or overestimated by this method.

Authors: We thank the reviewer for this comment, we have updated the discussion section of the revised manuscript to underline the effect of the analysis method on the estimates of the measure of association.

Given the relatively high prevalence of cervical cancer screening uptake, measures of association reported between this outcome and its correlates through Odd ratio have likely overestimated relative risks usually reported through prevalence ratio. While alternative modeling approaches such as a Log binomial regression would have been more appropriate to provide risk estimates. However, as our main objective was to identify association between our covariates and the measure of cervical cancer screening uptake, a logistic regression model remains an adapted approach in this situation.