Reviewer's report

Title: Symptomatic presentation with cervical cancer in Uganda: a qualitative study assessing the pathways to diagnosis in a low-income country

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Reviewer: Anita Lim

Reviewer's report:

Mwaka et al have conducted an interview-based study assessing the symptomatic presentation of women with cervical cancer in Uganda. Their manuscript provides data in an area where very little evidence exists, thus it is likely to be of interest to readers. However, it requires a substantial amount of work. My primary recommendations for improving this manuscript are to clarify the methods of analysis, and to standardise and clarify the language and the definitions used.

Major compulsory revisions

1. Content analysis technique: Content analysis technique involves systematically analysing text (in this instance, interview transcripts) and organising words into smaller categories based on explicit rules of coding. It’s not clear that this was the method used. Rather, it appears from the text that a thematic analysis was conducted. Could the authors please confirm if content analysis was used?

2. Definitions: Some of the terms and key timepoints need to be defined more clearly:
   • How was date of diagnosis defined? Was it self-reported by the women or is this from the medical records (eg date of first histology showing cervical cancer)
   • Line 217: It is not clear to me how “time to diagnosis” was calculated. Could the authors please clarify exactly how patient recall and medical records were used to derive this interval. There is a definition in the results (line 259) - this should be copied into the methods and clarified.
   • Time to diagnosis is referred to inconsistently in the text as “time to diagnosis”, “Total time to diagnosis” particularly in Table 2 “Total diagnostic interval”, “TTD”, TTI” are used. This needs to be clearly defined as a single term in the methods then made consistent throughout the manuscript.

3. Participant with CIN3 It is unclear why the authors have included a participant who did not have invasive cervical cancer in the study - CIN3 (P8). Could they please either provide justification for including this participant or remove from the results.

4. Quotations: The use of quotations in some instances requires revisiting as they do not support or match the manuscript text well.
   Eg.1 Lines 309-312: the manuscript text refers to symptom attribution being
influenced by their healthcare professionals’ diagnoses and how received no or a benign diagnosis made them cease taking their symptoms seriously, but the quotation on lines 314-315 refers only to how when she went to hospital she was “not given much attention”. Are there any quotations that could be provided which exemplify how an alternate diagnosis was given and changed how the respondent changed their symptom attribution?

Eg. 2 Lines 430-431: manuscript text refers to how respondents promptly sought help when “severe pain became a dominant feature of their illness” but the quotation on lines 433-437 does not mention severe pain, only pain.

Eg 3 Lines 461-465 describe how women with prolonged time to diagnosis were treated for other conditions but the quotation on lines 467-469 only describe how she went to numerous clinics, there is no mention of being treated for other conditions.

5. Definition of “open-ended question”: Line 181 states that all interviews were started with an open-ended question but text they have quoted as the first question describes an open question followed by a series of close-ended questions. Either they have started with an open question and the closed questions were used once participants had answered the first, or the first question was very long and was not really open-ended. Could they please clarify this point?

“Please tell me about the illness you have which is now known to be cervical cancer; what were the first symptoms, when did the first symptoms start, what did you think was causing the problem and what have you done about the symptoms since onset up to the time you came to this hospital?”

6. Back translation It is standard practice for studies using translated interviews to back translate into the original source language to ensure there has not been loss of meaning. It seems that this was not done. Loss of meaning in qualitative studies using translated interview data is a particular problem that should be discussed as a limitation. Closely related to this is the fact that the quotations used to exemplify the results are sometimes difficult to follow because they are translated into unusual English. It perhaps would have been better to use professional translators rather than the researchers themselves:

Lines 273-275 “I could bleed after meeting a man in bed. I used not to have the pain. When I did not meet the man . . . no blood would come”

7. Tables: Table 1 needs work:

• The respondent details are not aligned within each row of data and therefore Table 1 is very difficult to read.

• Add a footnote to describe why letters a, b, c are repeated within a respondent (presumably because the symptoms started at the same time?)

• Label column 2 “age at diagnosis” if this is correct

• Label column 5 “FIGO stage” if this is correct

• Standardise language used for symptoms. I assume these are not verbatim as most women would not refer to “postcoital bleeding” but rather “bleeding after
sex” – “postcoital bleeding” vs “post-coital PV bleeding”, “Painless PV bleeding” vs “PV bleeding” (does the latter infer “painful PV bleeding”?)

- The term “PV bleeding” is unclear. Suggest use 3 categories for abnormal vaginal bleeding “postcoital bleeding”, “intermenstrual bleeding” and “postmenopausal bleeding”

- Table 2 also needs work as it is difficult to follow and interpret. Is it intended to show how the attribution of first symptom relates to total diagnostic interval? If so, this is not clear at the moment.

- Suggest grouping of first attribution into more sensible categories:
  - Genital infections (include STD and candida)
  - Menstrual problems (include menstrual abnormalities and menopause onset)
  - Suggest ordering groups in the table going from less serious to serious eg genital infections should come before menstrual problems, serious illness and cervical cancer.

- Clarify what “challenged on cause” means

- Clarify what “serious illness” means or change to “other serious illness”, as HIV and cervical cancer are both serious!

- Columns 2 and 3 are mislabelled

- Make language consistent in title and table “Total diagnostic interval (TTI)” “TDD”

- Include column 2 units “(months)”

8. References: Some of the references are incorrect/inappropriate and need to either be replaced with a reference that supports the statements made in the text or the text needs to be amended:

Ref 25 – This reference is to support the statement on line 512-514 that the symptoms of cervical cancer also occur very commonly with sexually transmitted diseases however, the reference is a paper about gonorrhoeal infections which states that over 95% of females with gonorrhoea are asymptomatic. This would be better replaced with a reference for Chlamydia which is a common cause of postcoital bleeding and vaginal discharge.

Ref 28 – (lines 516-518) this reference is a paper about anticipated help-seeking for symptoms of lung, breast or colorectal cancer and uses data from the UK general population. The paper DOES NOT provide any evidence for associations between prompt symptom recognition and earlier diagnosis of these cancers.

Ref 34 – (lines 545-546) – again this reference is for a paper which analysed anticipated help-seeking. Participants from the general population were either asked to name symptoms of cancer that they knew about or to select them from a list. The paper does not assess whether symptoms awareness campaigns can help people recognise cancer symptoms as due to cancer or not. Ref 33 is a review article and it would be preferable if original research was cited.

Minor essential revisions
Terminology: The terminology is inconsistent and in some cases non-standard. The following are some examples:

- Lines 39 and 271 “unprovoked vaginal bleeding”. This needs to be tidied up.
- Lines 78, 341, 430 – “biomedical care” is not standard terminology, suggest change to “medical care”
- Lines 270, 277 – “painless vaginal bleeding” – this is not standard, normally abnormal vaginal bleeding would be classified as either postcoital bleeding, intermenstrual bleeding, postmenopausal bleeding or menorrhagia.
- Line 271 – “intermittent bleeding” – do the authors mean “intermenstrual bleeding”
- Line 318 – “family planning medicines” – normally referred to as “contraceptives”

1. Methods: The methods in the abstract and main text have not mentioned the type of interview used, ie semi-structured interview. This should be added to both.

2. Cancer stage: Stage of cervical cancer is important because there are inferences drawn between this and delayed diagnosis. Could the authors please confirm if the staging reported is FIGO stage, and if so, could they mention this in the text and in Table 1 and 2. Could they also add FIGO stage to the participant details included with each quotation, as I feel this would be of interest to readers when considering delays in diagnosis.

3. Summary statistics: It is standard to present medians with the associated interquartile ranges (not the range). Suggest the authors include these with the medians reported on lines 254, 259 and 849.

4. There are a number of minor (mostly typographical) errors in the manuscript which need correcting:

   - Line 632 – “lower levels in Uganda” – please clarify, lower levels of what?
   - Line 628 – “compare the intervals with cancer stage and differentiations at diagnosis...” unclear what “differentiations” means in this context.
   - Line 94 – “health seeking” should be “help-seeking” or “healthcare seeking”
   - Line 186 – “probes” should this be “prompts”?
   - Lines 242-246 – sentences from “All study respondents...” to “.....about the research” are unnecessary. I suggest you remove these.
   - Line 309 – “Symptom attribution was also influenced by their healthcare professionals’ diagnoses”. It’s not clear from the data that a diagnosis was always given. Would it be more accurate to say “diagnosis or advice”?
   - Line 451 – “cessation of menstruation” – I think what is meant here is “the menopause” – the former could apply to the end of any period.
   - Line 563 – some of the symptoms listed in line 562 are not life threatening (eg “foul smelling vaginal discharge”), suggest change “cause reasonable threat to life” to cause reasonable perceived threat to life.”
Line 567 – add FIGO stage 2B to the participant details.

Line 593 – add space between “symptoms.It”

Line 602 “There is evidence” not “There are evidences” – also, add space between full stop and “There”

Line 638 – “revealing symptoms” change to “disclosing symptoms”

Line 870 – Missing total diagnostic interval unit “months”

Discretionary revisions

1. There is no real mention of cervical screening. It may be worthwhile adding in a sentence into the introduction about how most women in low income countries are diagnosed via symptomatic presentation because organised screening is inadequate. I feel this would give some context to the manuscript.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests