PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The impact of decentralising colposcopy services from tertiary- to primary-level care in inner-city Johannesburg, South Africa: a before and after study
AUTHORS	Maimela, Gloria; Nene, Xolisile; Mvundla, Nontuthuko; Sawry, Shobna; Smith, Trudy; Rees, Helen; Kachingwe, Elizabeth; Chersich, Matthew

VERSION 1 - REVIEW

REVIEWER	Michael L Wilson, MD University of Colorado USA
REVIEW RETURNED	07-Sep-2018

GENERAL COMMENTS	The authors report the findings of a program to decentralize colposcopy services and how that affects access to those services. General comments: the manuscript is generally well-written but the authors could more clearly and concisely state the 1) goals of the study/hypothesis; 2) how the methods and results align with those; and 3) generally streamline the text so that it flows better. In the introduction, the text states that the question is whether decentralizing services improves access. If that is the only goal/hypothesis, then data on HIV status, histologic abnormalities, and so forth are irrelevant. It might be better stated that the questions being asked are whether decentralizing services improve access, what affects (if any) occur on abnormalities detected, the affects (if any) on delays for colposcopy, etc. Specific comments: 1. Tables 1 and 2 appear twice at the end of the manuscript. 2. It isn't clear why the HIV status and ART information are included in the manuscript. In the same way, the median age of patients is reported but it isn't clear why or how it relates to the study hypothesis. 3. There are a few sentences (e.g., page 6, lines 32-34) that seem superfluous as they don't link to anything later in the manuscript. 4. Page 7, lines 51-55: extend what intervention? Further decentralization of services? How do the authors plan to include patients in those activities? 5. Results: this section is very complete but is difficult to follow in places. There is a sense of 'over analysis' at times (see comments above). In addition, the results should open with a statement as to the effect, if any, on access -- which is the hypothesis for the study.

	6. Results: the first paragraph refers to Table 2, the second paragraph to Table 1. Either revise the order of the paragraphs or the tables so that Table 1 is discussed before Table 2. 7. Discussion: this shifts back nicely to the main hypothesis and is a good discussion of the findings and their importance. Suggest revising the Methods (minor revision) and Results (more extensive revision) so that all three sections align in sequence and emphasis.

REVIEWER	Margaret Cruickshank University of Aberdeen UK
REVIEW RETURNED	11-Sep-2018

GENERAL COMMENTS	The issue of provision of colposcopy services is pertinent and topical. With rising numbers of deaths from cervical cancer in LMIC and the introduction of screening in some countries, whether by visual inspection, cytology or HPV testing, there is a growing need for Colposcopic assessment for women not suitable for 'Screen and treat' approach by ablation. Some LMIC may have no colposcopy but as in this paper, there may be colposcopists but located in centres of excellence. Provision, capacity, access and QA are all relevant. The paper is novel in this particular field and will be of interest internationally. The authors provide retrospective observational data from a pre/post study. They have described the limitations to this study design and the available data. They have collected a large data set and conducted suitable analysis. It would have been clearer is a service evaluation at baseline before the service redesign was implemented and if the desired outcomes of the change and primary outcomes of the study were clear. There is little on the training involved or how QA of the service is conducted. Were any of the changes statistically significant? As there are only 2 centres involved, the generalisability is doubtful. Many would use a hub and spoke model so it would help to understand why there was only one outlying service feeding into the tertiary centre. The Sonnex paper (2006) may be quoted accurately but n the UK we have had colposcopy nurses for over 25 years with the training, accreditation and reaccreditation processes and standards the same for nurses as for doctors. They see mainly women referred by the screening programme and are not used just for symptomatic women 9 which was the focus of the Sonnex paper). The conclusion states that quality is maintained but if negative biopsies is a quality indicator then this is not the case. The biopsy rates for no disease will have an impact on the cost and staffing of the colposcopy and pathology services and adverse effects including pain and bleeding for the women. Minor points: Page 6 line 20: visual inspection may be confused with VIA. Colposcopic assessment? More could be made of the benefits of combining additional services such as the HIV testing and treatment. Page 12 line 27 I do not understand 'clear-up referrals.

	There is still problems with waiting times although much improved. What further service changes could be used within constraints of the service? Have they looked at 'Screen and treat'?

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Michael L Wilson, MD

Institution and Country: University of Colorado, USA Please state any competing interests or state 'None declared': None declared.

Please leave your comments for the authors below The authors report the findings of a program to decentralize colposcopy services and how that affects access to those services.

General Comments: the manuscript is generally well-written but the authors could more clearly and concisely state the 1) goals of the study/hypothesis; 2) how the methods and results align with those; and 3) generally streamline the text so that it flows better. In the introduction, the text states that the question is whether decentralizing services improves access. If that is the only goal/hypothesis, then data on HIV status, histologic abnormalities, and so forth are irrelevant. It might be better stated that the questions being asked are whether decentralizing services improve access, what affects (if any) occur on abnormalities detected, the affects (if any) on delays for colposcopy, etc.

Response: The description of the study goals has been revised, as suggested, we outline the primary aims of the study and how these extend to HIV. We have streamlined the text in the introduction to improve the flow, presenting the burden of disease, then screening, then barriers to colposcopy, the decentralization. This structure is then mirrored throughout the paper.

Specific Comments:

Comment: Tables 1 and 2 appear twice at the end of the manuscript.

Response: Duplicate tables have been removed.

Comment: It isn't clear why the HIV status and ART information are included in the manuscript. In the same way, the median age of patients is reported but it isn't clear why or how it relates to the study hypothesis.

Response: HIV is inextricably linked to almost all health conditions and service delivery platforms in the country. With around a quarter of female adults infected with the condition, this is not surprising, and many services, like colposcopy in this case, draw on the considerable health service infrastructure built up around to provide HIV services in the country. Moreover, what we have attempted to emphasize in this study is the need for decentralization of colposcopy services to improve access for HIV-positive women in particular who carry a remarkably high burden of HPV infection and cervical cancer. HIV and ART information is also included to compare the quality and level of integration of colposcopy services at both facilities (HIV testing and ART rates as 'proxies' for this. The rationale for age is to assist in determining the target market for decentralized colposcopy services, as cervical cancer risks and consequently screening guidelines are strongly age dependent. We include this information in the introduction text (the mean age of women at diagnosis of cervical cancer is 52.3 years).

Comment: There are a few sentences (e.g., page 6, lines 32-34) that seem superfluous as they don't link to anything later in the manuscript.

Response: This section explains different procedures that can be done during colposcopy. We removed the text noted by the reviewer on page 6, and cut several other sentences from the methods section.

Comment: Page 7, lines 51-55: extend what intervention? Further decentralization of services? How do the authors plan to include patients in those activities?

Response: We have removed this sentence for several reasons. It stated the obvious, so added little to the paper. Further, we would have had to add additional information about ways of involving patients in expansion for these services. Practically speaking, that would be very difficult as patient groups addressing the topic of cervical cancer, for example, are non existent. We did, however note that patients who we detected as requiring care (e.g. having CIN III on histology, but not having attended care) were identified during the study and contacted.

Comment: Results: this section is very complete but is difficult to follow in places. There is a sense of 'over analysis' at times (see comments above). In addition, the results should open with a statement as to the effect, if any, on access -- which is the hypothesis for the study.

Response: We have changed the flow in the results section, beginning with a statement about the numbers of women accessing colposcopy.

Comment: Results: the first paragraph refers to Table 2, the second paragraph to Table 1. Either revise the order of the paragraphs or the tables so that Table 1 is discussed before Table 2.

Response: As we changed the flow of the results section, the order of tables is now correct.

Comment: Discussion: this shifts back nicely to the main hypothesis and is a good discussion of the findings and their importance. Suggest revising the Methods (minor revision) and Results (more extensive revision) so that all three sections align in sequence and emphasis.

Response: This is a very important comment, we have revised the order of the paragraphs in the results section. The discussion tackles colposcopy access immediately while in the results section we start with patient characteristics which is not directly linked to the hypothesis as per reviewer's comment. This restructuring has helped to improve the paper markedly.

Reviewer: 2

Reviewer Name: Margaret Cruickshank

Institution and Country: University of Aberdeen, UK Please state any competing interests or state 'None declared': none

Please leave your comments for the authors below

General Comment: The issue of provision of colposcopy services is pertinent and topical. With rising numbers of deaths from cervical cancer in LMIC and the introduction of screening in some countries, whether by visual inspection, cytology or HPV testing, there is a growing need for Colposcopic assessment for women not suitable for 'Screen and treat' approach by ablation. Some LMIC may have no colposcopy but as in this paper, there may be colposcopists but located in centres of excellence. Provision, capacity, access and QA are all relevant. The paper is novel in this particular field and will be of interest internationally.

The authors provide retrospective observational data from a pre/post study. They have described the limitations to this study design and the available data. They have collected a large data set and conducted suitable analysis. It would have been clearer is a service evaluation at baseline before the service redesign was implemented and if the desired outcomes of the change and primary outcomes of the study were clear.

Response: An evaluation of the services at the tertiary level facility before the service redesign was conducted (between 2012-2014) before the introduction of colposcopy at the primary healthcare facility. We agree, however, that it would have been useful to have evaluated the access to colposcopy among women attending HCHC before colposcopy begins. That would have allowed us to directly compare access for the target population (women at HCHC), before and after the intervention. We have added this limitation to the paper.

To respond to the second comment, we have included additional sentences at the end of the introduction section to outline the outcomes and aims of the study. That text was not provided in the original submitted paper.

Specific Comments:

Comment: There is little on the training involved or how QA of the service is conducted.

Response: The training provided was at the primary healthcare facility, and there was no formal accreditation to it. Training and support was ongoing, rather than in formal sessions and progress and concerns were reviewed at the monthly meetings between HCHC and CMJAH. Please see an extract of the text from the manuscript:

"Two district medical officers were trained by specialist gynaecology oncologists at CMJAH to provide the service. CMJAH staff provided ongoing support and established referral processes between the two facilities. Monthly meetings were held between staff at the two facilities, where concerns and difficult cases could be discussed."

Comment: Were any of the changes statistically significant?

Response: Many of the changes were significant; we include P values for all the comparisons we were able to make given the available data. Most comparisons had a P value <0.05. Perhaps we do not understand the reviewer's query, and are happy to include additional tests and P values if requested.

Comment: As there are only 2 centres involved, the generalisability is doubtful. Many would use a hub and spoke model so it would help to understand why there was only one outlying service feeding into the tertiary centre.

Response: Yes, unfortunately there are only 2 centres involved in this study. This is because colposcopy services are not generally provided at primary care clinics in SA and this primary care facility was the exception in that a colposcopy machine had been donated by a private sector company because of the burden of high risk Pap Smear cytology results in our setting (linked to a high HIV prevalence) as well as the delay in accessing colposcopy at the tertiary centre. We have included this limitation in the revised paper. The problem is that the Department of Health would not direct resources at this initiative until we had shown it was beneficial and we only had resources for one site. So, practically, we were unfortunately unable to have adopted the approach suggested.

Comment: The Sonnex paper (2006) may be quoted accurately but in the UK we have had colposcopy nurses for over 25 years with the training, accreditation and reaccreditation processes and standards the same for nurses as for doctors. They see mainly women referred by the screening

programme and are not used just for symptomatic women 9 which was the focus of the Sonnex paper).

Response: Many thanks for pointing out this important fact. We have removed the Sonnex reference and added a reference to the UK NHS 2016 guidelines on colposcopy and accreditation, noting the point made by the reviewer.

Comment: The conclusion states that quality is maintained but if negative biopsies is a quality indicator then this is not the case. The biopsy rates for no disease will have an impact on the cost and staffing of the colposcopy and pathology services and adverse effects including pain and bleeding for the women.

Response: Quality is measured by the number of specimen rejections, not negative biopsies. We have shown that specimen rejection rates are similar at both centres (The proportion of invalid specimens was similar across the three groups, ranging from 1.8 to 2.8%). We acknowledge in the paper that this is only a marker or proxy of quality, and that there are many other measures of quality. We have included a sentence in the methods section to note this: 'We used the proportion of invalid specimens as a proxy marker of quality of services'. We have also added this to the study limitations section

Comment: Page 6 line 30: visual inspection may be confused with VIA. Colposcopic assessment?

Response: This has been revised as suggested, thanks for noting this error.

Comment: More could be made of the benefits of combining additional services such as the HIV testing and treatment.

Response: Agreed, we have added this to the text.

Comment: Page 12 line 27 I do not understand 'clear-up referrals.

Response: This has been revised, it now reads: "and future studies might attempt to define criteria for referral".

Comment: What further service changes could be used within constraints of the service? Have they looked at 'Screen and treat'?

Response: There are plans to introduce liquid based cytology, which offers the potential to do HPV screening in South Africa. This, by 2020 may improve access to screening as opposed to cytology-based screening as there is the potential for women to self-collection of samples, which may simplify screening procedures, removing some of the barriers to access in this setting. Screen and treat has also not yet been introduced in South Africa, although Wits RHI will be participating in international pilot studies to show the effectiveness of this modality in improving access to cancer prevention and treatment in SA.

VERSION 2 – REVIEW

REVIEWER	Michael L Wilson Denver Health Denver, Colorado USA University of Colorado Aurora, Colorado USA
REVIEW RETURNED	12-Nov-2018

GENERAL COMMENTS	The revised version of the manuscript reads better and is easier to follow. Thank you for responding to the reviewers' comments/suggestions. As with the second reviewer, likely the main drawback to a study such as this is whether the findings are generalizable. I think they are, because there are organizations that have used a hub-and-spoke model for preventive medicine for many years, especially for TB care, cervical cancer screening, and colorectal cancer screening, all of which rely upon used of an integrated tiered health care and laboratory system. One key point is that services such as this can also be integrated with other health care needs of women -- allowing for leveraging of access and capacity for OB/GYN services.

REVIEWER	Margaret Cruickshank University of Aberdeen UK
REVIEW RETURNED	20-Nov-2018

GENERAL COMMENTS	This paper has improved with the revisions made to understanding delivery and uptake of colposcopy especially on LMIC countries where colposcopy is often only available in specialist centres with limitations of accessibility. This is particularly important as more regions/countries introduce some means of cervical screening. The authors refer to the screening policy but delivery of the programme is not mentioned. It would help to understand the referral populations pre/post if we know something of uptake and delivery of the programme and any differences in the time of the observations. Data is provided which is not directly related to the stated outcomes. I think the results and discussion sections would be clearer if more detailed outcomes and relevance are stated and these sections are structured to reflect there.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Michael L Wilson

Reviewer’s comment: As with the second reviewer, likely the main drawback to a study such as this is whether the findings are generalizable. I think they are, because there are organizations that have used a hub-and-spoke model for preventive medicine for many years, especially for TB care, cervical cancer screening, and colorectal cancer screening, all of which rely upon used of an integrated tiered health care and laboratory system.

Authors’ response:

We have added this useful point about the hub and spoke generalizability, noting that success with this approach for other conditions and in other settings raises the generalizability of the findings and assertions about the validity of the study results.

Reviewer's comment: One key point is that services such as this can also be integrated with other health care needs of women -- allowing for leveraging of access and capacity for OB/GYN services.

Authors' response:

Thanks for this suggestion, we have added a sentence on this: "ART and services such as screening and treatment for sexually transmitted infections could be integrated within colposcopy clinics, reducing the opportunity costs associated with multiple visits to the clinic and lowering the risk of loss to follow up". Most especially we believe that STI screening and treatment should be integrated within the package of interventions provided at colposcopy clinics. At the primary care clinic where colposcopy was done, the services for family planning and STIs are all located in the same place and well linked up.

Reviewer: 2

Reviewer Name: Margaret Cruickshank

This paper has improved with the revisions made to understanding delivery and uptake of colposcopy especially on LMIC countries where colposcopy is often only available in specialist centres with limitations of accessibility. This is particularly important as more regions/countries introduce some means of cervical screening.

Authors' response: Thanks for this comment.

Reviewer's comment: The authors refer to the screening policy but delivery of the programme is not mentioned. It would help to understand the referral populations pre/post if we know something of uptake and delivery of the programme and any differences in the time of the observations.

Authors' response:

We present additional data on the quality of the cervical cancer screening programme in the population. Coverage levels of screening are about 60%, but cervical cancer rates are still very high. This suggests that the gaps in the programme, especially links between Pap smears and treatment, are substantial. Further, we present all data on the patient population that we have. Unfortunately, no additional data on differences in population before and after were available. Such data may have helped us to comment on whether there had been some change in the programme over time.

Reviewer's comment: Data is provided which is not directly related to the stated outcomes. I think the results and discussion sections would be clearer if more detailed outcomes and relevance are stated and these sections are structured to reflect there.

Authors' response:

We have revised the methods and results section, making sure that the structure exactly mirrors each other. We also altered the text in the methods on the outcomes, how they fit together and are relevant to the study question. The order in which variables are presented in the Tables also mirrors the order of the methods and results. Where possible, we also retained the same order in the discussion section.

VERSION 3 – REVIEW

REVIEWER	Margaret Cruickshank University of Aberdeen UK
REVIEW RETURNED	21-Jan-2019

GENERAL COMMENTS	The authors have addressed the comments and feedback from previous review and explain in more detail about cervical screening and uptake. The limitations with potential bias and confounders remain unchanged. There is a message here about decentralising colposcopy services which could be transferable but given the setting generalisability cannot be assumed.

VERSION 3 – AUTHOR RESPONSE

Reviewer: 2

Reviewer Name: Margaret Cruickshank

Reviewer's Comment: The authors have addressed the comments and feedback from previous review and explain in more detail about cervical screening and uptake. The limitations with potential bias and confounders remain unchanged.

There is a message here about decentralising colposcopy services which could be transferable but given the setting generalisability cannot be assumed.

Authors' response:

We have amended the text in both the Strengths and Limitations Section and the Conclusions, to more specifically state that these results could be generalizable only to settings similar to ours.