

Literature Review
Cervical Cancer Screening in Sub-Saharan Africa: A review
Rose Academies-Uganda
Andrea Diarte

Abstract:**Cervical Cancer and development**

Cervical cancer is a growing concern for women in developed nations and low and middle-income countries as the incidence increases globally. According to the World Health Organization, Cervical Cancer is the fourth most common cancer for women. To create interventions for cervical cancer prevention, it is important to understand how cervical cancer develops for this will give an additional understanding of times during a women's life where interventions may best be accepted. Cervical cancer is caused by a High-Risk Human Papillomavirus (HR-HPV) infection of the ectocervical mucosa. "Human Papillomavirus (HPV) infections are among the most widespread human viral infections worldwide that can infect the skin and mucous membranes" (Mboumba et al., 2017, pg 613). Human Papillomavirus is transmitted from skin to skin contact and sexual contact, including vaginal, anal, and oral sex. HPV infection is one of the most common sexually transmitted infections with an overall incidence of more than 30 million new cases per year (Mboumba et al., 2017). Studies have found there are more than 170 HPV genotypes, but of those only 15 types are recognized as high-risk HPV which can lead to HPV-caused cancers. In regards to cervical cancer, HPV-16, and HPV-18 globally are the most prevalent type detected causing about 70% of cervical cancers worldwide. After one is infected with HR-HPV there is a silent incubation period for about 10-20 years before the virus begins the process that causes healthy cervical cells to become cancerous cells that will eventually lead to invasive cervical cancer. If cervical cancer is detected early and managed effectively it can be one of the most successfully treated cancers, but if detection is late with this rapidly evolving disease the prognosis can be fatal and lead to inhumane deaths of women globally (World, 2019). This leads to the public health problem of disparities in the prevention, screening, and treatment of women in developed nations versus low and middle-income countries globally.

Background of Cervical Cancer and Screening in Sub-Saharan Africa:

The goal of this paper is to review cervical cancer screening interventions within Sub-Saharan Africa with a focus on Uganda to provide a guide on which are successful, therefore the following discusses the background of cervical cancer in SSA. The World Health Organization, (WHO), stated that cervical will kill more than 443,000 women worldwide by 2030, and more than 98% of these deaths will occur in developing countries with most occurring in Sub-Saharan Africa (Mboumba et al., 2017, pg 615). This prediction by WHO shows the need for extensive prevention and screening interventions to be developed in countries of Sub-Saharan Africa to prevent deaths. A study reviewed current rates of Cervical Cancer in SSA found that Cervical Cancer is the most common cancer and the leading cause of death in women in many countries in SSA, with more than 75,000 new cases and around 50,000 deaths per year (Mboumba et al., 2017). In Uganda, about 6,959 new Cervical Cancer cases are diagnosed annually and over 4,300 women will die each year from this disease. With a high incidence of 56.2 per 100,000, Cervical Cancer ranks as the 1st leading cause of female cancer in Uganda (Bruni L et al., 2021). In comparison developed countries such as the United States have seen a big fall in CC incidence rates since the 1960s due to the implementation of population-wide screening programs. Therefore, the high incidence rates of CC in developing countries in SSA can be attributed to the absence of effective population-level screening programs (Jedy-Agba et al., 2020). Current recommendations for screening practices in low and middle-income countries are given by WHO, which recommends visual inspection of the cervix using acetic acid (VIA) in resource-

constrained settings as the primary approach for screening, or HPV screening when resources allow (Moses et al., 2015). While the WHO has specific recommendations for low and middle-income countries such as those found in Sub-Saharan Africa, there are many barriers to facilitating and uptake of these screening services for women. This paper will review barriers and facilitators that women of Sub-Saharan Africa may face when it comes to screening, to better guide those developing screening programs to address such barriers.

Research Question:

This paper will study and review different cervical cancer screening interventions within Uganda and surrounding low-income countries of Sub-Saharan Africa. The goal of this paper will be to outline interventions that were successful or not in the countries reviewed and to provide a potential guide of where interventions should be targeted in these low-income countries to reduce the incidence and prevalence of cervical cancer depending on the determinants and needs in Uganda and surrounding low-income countries of Sub-Saharan Africa.

Materials and Methods

Search strategy

To obtain the sources necessary to understand the screening practices of cervical cancer in rural villages in Sub-Saharan Africa, searches were conducted through PubMed of the U.S. National Library of Medicine (NLM). The search strategy used for this review was to use the advanced search option in PubMed to search for specific keywords and groupings of keywords to produce vast sources over the topic of interest. Some of the keywords used to start the search were cervical cancer, cervical cancer screening, HPV screening, Uganda, Sub-Saharan Africa, rural villages, Africa, cervical cancer screening practices, perceptions, and cervical cancer screening barriers. After reviewing sources to determine the current common screening practices, the next step was to incorporate the names of the specific practices to obtain more specific sources. These more specific keywords were human papillomavirus (HPV) self-sampling, HR-HPV testing, self-sampling, cervical smear, and visual inspection with acetic acid (VIA) test.

Inclusion and Exclusion Criteria

For studies or sources to be considered in this review they should be focused on the topics of cervical cancer screening and intervention types within the target area of Uganda and Sub-Saharan Africa. The target population for this review is women in Uganda and Sub-Saharan Africa, but sources focused on men's perception of CCS were not excluded due to cultural norms in Africa, and men being a potential barrier to screening services. Sources of any article type were considered as long as they were peer-reviewed and published by a reliable journal. Additional criteria for source selection were studies or sources published after 2000 to the present date.

Study Selection and Data Extraction

With the above-mentioned criteria and guidelines, the search on the PubMed database yielded around 1,200 results. Their titles of articles were scanned for the keywords and comparisons of different intervention practices within studies. If the abstract seemed to match the theme or would yield beneficial results for the review the article was downloaded to be dissected in a literature matrix. After thoroughly reading each article, they were dissected by the following criteria, sample/setting, purpose, methods, results, connection to paper, and limitations. This data

extraction was essential to selecting the final articles that would provide varying evidence and perspectives of different cervical cancer screening practices. At the end of this approach, 10 articles were identified for the analysis of this review.

Methods

Cervical cancer is growing rapidly in incidence within Uganda and Sub-Saharan Africa and is considered a preventable non-communicable disease. To prevent cervical cancer rates in women in SSA there is a need for the implementation of prevention programs that promote primary prevention such as HPV vaccination and secondary prevention such as early diagnosis through screening methods. The following sections of this review will overview the different methods of primary (vaccination) and secondary prevention (screening) for early diagnosis found in the studies selected.

HPV Vaccination

The development of HPV vaccines has been a major breakthrough in the interventions available for the prevention of cervical cancer. The two vaccines available are Gardasil and Monovalent both of which appear to provide full protection against HPV types 16 and 18 which are estimated to cause over 70% of cervical cancer worldwide (Adefuye et al., 2012). The vaccines should be administered before HPV infection which is a largely sexually transmitted infection, therefore should be targeted at children ages 9-12 before the onset of sexual activity which varies from country to country. While HPV vaccination is the ideal primary prevention, developing and low and middle-income countries face barriers to vaccine introduction. The biggest factor is vaccine cost to these low-income countries, there would also be the need to develop new infrastructure for vaccination. Few low-income countries have established adolescent health platforms or school health systems so there would be access to vaccinate children ages 9-12. There would also be the barrier of explaining why children need the vaccination when many adults will not have the HPV vaccine or they will not understand the need or want their child to be vaccinated due to cultural or personal preferences. Besides those barriers, the need for effective infrastructure in these low-income countries is necessary for this vaccine because it requires a cold chain and reliable source of electricity at all times which can be difficult for developing countries (Adefuye et al., 2012). The last barrier posed by the study of Adefuye et al is the need for 3 doses to be completely vaccinated, therefore you must be able to bring these children back for additional doses and there is a high chance for loss to follow up (Adefuye et al., 2012). When looking at the HPV vaccine in Uganda is included in their National Vaccination Program and was introduced in 2015 according to WHO, however, within Uganda 33.6% of women have HPV (Bruni L et al., 2021). The cervical cancer burden in Uganda is high due to the low uptake of the HPV vaccine. A study identifying barriers to HPV vaccination uptake in Uganda found in a cohort of 6,093 girls, 78% of them were not vaccinated due to either individual or community-level barriers (Isabirye, A et al., 2020). While HPV vaccination may be a successful method of primary prevention of cervical cancer in developed countries, there are many barriers to vaccination in low-income countries so it is important to have strong methods of secondary prevention in the form of screening that will be discussed in this paper.

Cytology (cervical smear testing)

The most common screening method for developed countries such as the United States is cytology after performing a Papanicolaou test (pap smear). This method involves a procedure

where a trained medical professional will use a small brush to remove cells from the surface of the cervix and the area around so the cells can be checked under a microscope (cytology) for cervical cancer. This screening method is effective in the U.S. for studies have found that since the introduction of pap smear-based screening, the incidence rate of cervical cancer has dramatically decreased by 50% and 70% respectively among White and African American women (Mboumba et al., 2017). While this method has been successful in developed countries such as the U.S., it has been found unsuitable for Sub-Saharan Africa. For cytology-based screening to be effective, it must be followed up by colposcopy and histological assessment for women with abnormal smears, and once that is complete, surgical treatment for identified precancerous lesions. Therefore, when this method is put in the context of SSA it requires too long wait times for results, resulting in women not obtaining results at all, and the procedures alone are not cost-effective for low and middle-income areas. An additional barrier to this method of screening is the need for adequate health infrastructure and medical personnel to provide such programs, which are often scarce in countries of SSA. Available resources and access are the biggest barriers to why cytology is not a successful screening tool since studies have found that more than 50% of women in most SSA countries live at least more than 10 km from the nearest primary care center, therefore rural populations who are in greatest need would not benefit from such screening methods (Mboumba et al., 2017).

Visual Inspection with Acetic Acid (VIA)

The next method of screening to be reviewed is visual inspection with acetic acid which because of its cost-effectiveness is one of the most widespread in African countries and is recommended by WHO in low-resource countries. While visual inspection with Acetic Acid is the recommended screening method in low and middle-income countries with low resources in comparison to the United States which is a high-income country with plentiful resources this method is not used. The reason for the difference in the screening methods is due to the resource availability in high versus low-income countries. A notable difference in the preferred method of screening methods in the United States versus Sub-Saharan Africa is the time it takes for a patient to receive results. The preferred methods of the United States can take up to 3 weeks to receive results while VIA gives immediate results. Immediate results are necessary in countries where many people do not have insurance or the means to attend the doctor multiple times in such a short time period. Additionally in the U.S. test results can be given via telephone where many people in Sub-Saharan Africa do not have a phone, therefore immediate results are the best way for these women to receive diagnostic health information. The World Health Organization recommends VIA for screening in low-resource countries because it supports the “screen and treat” approach. The screen and treat approach has women screened using the VIA test which gives immediate results, if they are positive they will be treated on the same day with laser or cryotherapy (Corrado et al., 2020). The VIA test's immediate results and immediate treatment address potential barriers of time and loss to follow up after results. While VIA screening is a cost-effective method, a study over nine screening campaigns held in Uganda found that when comparing VIA screening methods to cervical cancer smears (cytology) the VIA test showed 84.2% of false positives, therefore showing low accuracy in finding cervical cancer (Corrado et al., 2020). Low accuracy of the VIA test could be of concern when it comes to the “screen and treat” because it can lead to overtreatment and excessive use of further examinations, especially in countries where resources are limited. However, healthcare workers within SSA have stated that one of the benefits of this method is the ability to teach local healthcare workers the

technique for VIA screening (Chinn et al., 2020). The ability to teach this method to large groups of healthcare workers will allow for screening large groups of women in areas with low resources addressing barriers to care. While VIA testing may be easy to teach masses of health care providers and is the recommended approach by WHO for the ability to treat immediately with quick results, literature found that the low accuracy of this test is concerning and could lead to overtreatment of women who are not positive for cervical cancer. Studies found that a VIA test coupled with an additional test would be the best option to confirm positive tests and prevent overtreatment. However, adding an additional test to confirm this could contribute to loss of follow-up and women not wanting to be screened, to begin with, due to long wait times.

HR-HPV Sampling

Since HPV infection leads to the development of cervical cancer, HPV testing has emerged as an effective screening tool and has even been shown to identify precancerous lesions earlier than cytology. To increase access and address barriers to uncomfortable screening practices, HPV self-sampling has been proposed as an intervention tool to identify precancerous lesions. The literature identified The Advances in Screening and Prevention in Reproductive Cancers (ASPIRE) project which was developed to examine innovations in cancer prevention for women in low and middle-income countries. The ASPIRE team pilot-tested a community-based HPV self-sampling project in Uganda which started with a survey of the women in these communities, this survey found that 80% of women were willing to provide a self-collected specimen for cervical cancer screening (Ogilvie et al., 2013). The ASPIRE project used community outreach workers to approach women in their homes and community gathering locations, invited them to the intervention, and those who agreed were instructed on how to give the cervicovaginal sample and provided it there for the community outreach workers to bring to the hospital within 24 hours (Ogilvie et al., 2013). This approach and method of intervention were found highly acceptable to women in Sub-Saharan Africa, with the present study obtaining self-collected samples from 97.1% of women indicating an opportunity to broaden the scale of these community-based self-sampling programs (Ogilvie et al., 2013). One drawback to this approach is you cannot follow the “screen and treat” approach that is recommended for this population because the results for HPV self-sampling take about 2 weeks to come back, therefore, if the results are positive then the women must be scheduled to come in for treatment. However, in the ASPIRE project, they provided positive HPV results to 85% of women and 26 of those 35 women who required follow-up attended the appointment (Ogilvie et al., 2013). Additional studies have been conducted testing the acceptability of self-collection samples versus hospital collection. For example, a study conducted in a rural district of Nigeria found 95.2% of women found the self-sampling device easy to use and 83.2% reported that they would prefer self-sampling in the future versus a screening in a health facility (Modibbo et al., 2017). A meta-analysis of countries in Sub-Saharan Africa that conducted randomized controlled trials with interventions of HPV self-sampling devices found that the uptake of women using HPV self-sampling as a method of cervical cancer screening was 72% higher than those of women using the standard of care (VIA) (Tesfahunei et al., 2021). The results of current studies on HPV-self sampling show potential for this method to be more accepted among women in SSA and therefore, could increase the number of women being screened and treated before severe cervical cancer develops and a preventable noncommunicable disease takes more lives of these vulnerable women.

Barriers and Facilitators to Screening:

To promote successful cervical cancer screening promotional and education programs it is important to understand the barriers and facilitators of screening in women of Sub-Saharan Africa. Black et al., compiled fourteen studies in a systematic review of the views of 4,386 women to understand the barriers and facilitators they face when it comes to screening for cervical cancer. This review provided a look at important barriers broken up into three categories: individual, sociocultural, and structural factors.

Individual factors identified were: knowledge of CC/CCS, perceived risk and importance of CC/CCS, experiencing CC signs or symptoms, embarrassment, fear of screening procedure, and fear of results/fatalism (Black et al., 2019). Knowledge about the causes of cervical cancer was often cited as the biggest barrier to screening, and often the women who did not know about the causes could not identify any screening method available. Healthcare workers surveyed in these studies hypothesized that low screening uptake could be due to a lack of knowledge, for the review found if a woman had knowledge of at least one screening method they were more likely to have been screened in the past. While a woman's knowledge of what cervical cancer is can increase their likelihood of being screened, a study in Cameroon found 74% of participants had heard of cervical cancer and 43% of those women had undergone screening, however, only 24% of those women were able to identify a risk factor or symptom of cervical cancer (Chinn et al., 2020). This study shows the importance of inclusive education for these women over cervical cancer, which addresses barriers such as knowledge of CC, screening methods, along with signs and symptoms of cervical cancer.

Sociocultural factors identified were: gender power relations, family/spousal support, stigma, personal or family experiences with CC/CCS, recommended screening, and traditional healers (Black et al., 2019). Within the socio-cultural barriers, spousal support is a barrier that is repeated within the literature. Within the cultures of Sub-Saharan Africa, one theme is constant - men are the head of the household and make many decisions for women. Knowing that men's or husbands' approval may be necessary for a woman to be screened for cervical cancer more studies are implementing cervical cancer education classes for men. A physician-led education session on cervical cancer for men in Uganda found that knowledge of HPV and cervical cancer among men was low (Moses et al., 2018). However, after the education session, almost all men who participated were willing to support their partners to attend screenings after the session (Moses et al., 2018). This study in Uganda showed the importance of incorporating men in the education sessions around cervical cancer as a method to address barriers and increase the uptake of screening among women in SSA.

Structural factors identified were: socioeconomic and demographic conditions, access to CCS, limited resources/infrastructure, time constraints, healthcare worker qualities, cost related to CCS, and community outreach services for CCS (Black et al., 2019). This review of barriers begins to give light on areas where screening interventions should target to address specific barriers and how to develop a program that helps women overcome these barriers. Women in these surveys stated that improved knowledge of cervical cancer would help them understand the benefits of screening, therefore it would be important to include comprehensive education over CC in a way that is culturally appropriate and sensitive to other barriers identified (Black et al., 2019). However, education about CC will not be enough for these women to uptake screening, the need for accessible screening and procedures that also limit a women's embarrassment would be beneficial to address barriers identified in this review. To address the barriers of embarrassment and access to screening, many studies have pushed the self-sampling method, however, this intervention is not without barriers itself. Megersa et al., conducted a

study in Ethiopia on barriers to home-based HPV self-sampling in which 47 women participated. This study found that husband disapproval was the main barrier to the acceptance of HPV self-sampling, followed by a lack of knowledge of cervical cancer and screening, and fear of using the self-sampling device (Megersa et al., 2020). While this method may overcome some barriers women face, it shows the importance of future interventions focusing on educating women on cervical cancer and HPV testing, providing clear instructions on collecting self-samples, and including male involvement in the education and screening process since spousal approval is important within Sub-Saharan Africa's culture (Megersa et al., 2020).

Conclusion

The focus of this paper was to review different cervical cancer screening interventions within Uganda as compared with low and middle-income countries of Sub-Saharan Africa. Methods of primary and secondary prevention were examined and the barriers and facilitators women may face with each method. From the reviewed literature there will not be a one size fits all approach to cervical cancer screening. There were pros and cons to each screening method but when choosing an approach it is important to remember the low resource limitation that comes with this type of screening. Improvement in health center infrastructure will be key to improving the number of women who can be screened and get their results back promptly to follow the “screen and treat” approach recommended by WHO. Future program development for cervical cancer screening should include an education component to address barriers so women of Sub-Saharan Africa can be aware of the causes and risks of CC and why it is important to be screened. To address the rising incidence of cervical cancer in Sub-Saharan Africa community-wide screening programs must be developed in these countries. These programs must incorporate education, use screening methods that best address the barriers discussed, and deliver fast results so those testing positive can follow the screen and treat approach and have the best odds of survival.

References

- Adefuye, P. O., Broutet, N. J., de Sanjosé, S., & Denny, L. A. (2013). Trials and projects on cervical cancer and human papillomavirus prevention in sub-Saharan Africa. *Vaccine*, *31 Suppl 5*, F53–F59. <https://doi.org/10.1016/j.vaccine.2012.06.070>
- Black, E., Hyslop, F. & Richmond, R. Barriers and facilitators to uptake of cervical cancer screening among women in Uganda: a systematic review. *BMC Women's Health* *19*, 108 (2019). <https://doi.org/10.1186/s12905-019-0809-z>
- Chinn, Justinea; Tewari, Krishnansu S.b Multimodality screening and prevention of cervical cancer in sub-Saharan Africa: a collaborative model, *Current Opinion in Obstetrics and Gynecology*: February 2020 - Volume 32 - Issue 1 - p 28-35
doi: 10.1097/GCO.0000000000000597
- Corrado, G., Mazzara, C., Certelli, C., Nsubuga, J. B., Zanetto, F., Schurfeld, K., Dell'Antonio, G., Orti, C. D., Savarese, A., & Andriani, M. T. (2021). Screening for cervical cancer in Africa: A proposal of a different combination of VIA test and cervical smear in Uganda. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *152*(1), 68–71. <https://doi.org/10.1002/ijgo.13350>
- Bruni L, Albero G, Serrano B, Mena M, Collado JJ, Gómez D, Muñoz J, Bosch FX, de Sanjosé S. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in Uganda. Summary Report 22 October 2021.
- Isabirye, A., Mbonye, M., Asiimwe, J. B., & Kwagala, B. (2020). Factors associated with HPV vaccination uptake in Uganda: a multi-level analysis. *BMC women's health*, *20*(1), 145. <https://doi.org/10.1186/s12905-020-01014-5>
- Jedy-Agba, E., Joko, W. Y., Liu, B., Buziba, N. G., Borok, M., Korir, A., Masamba, L., Manraj, S. S., Finesse, A., Wabinga, H., Somdyala, N., & Parkin, D. M. (2020). Trends in cervical cancer incidence in sub-Saharan Africa. *British journal of cancer*, *123*(1), 148–154. <https://doi.org/10.1038/s41416-020-0831-9>
- Mboumba Bouassa, R. S., Prazuck, T., Lethu, T., Jenabian, M. A., Meye, J. F., & Bélec, L. (2017). Cervical cancer in sub-Saharan Africa: a preventable noncommunicable disease. *Expert review of anti-infective therapy*, *15*(6), 613–627. <https://doi.org/10.1080/14787210.2017.1322902>
- Megersa, B. S., Bussmann, H., Bärnighausen, T., Muche, A. A., Alemu, K., & Deckert, A. (2020). Community cervical cancer screening: Barriers to successful home-based HPV self-sampling in Dabat district, North Gondar, Ethiopia. A qualitative study. *PloS one*, *15*(12), e0243036. <https://doi.org/10.1371/journal.pone.0243036>

- Modibbo, F., Iregbu, K. C., Okuma, J., Leeman, A., Kasius, A., de Koning, M., Quint, W., & Adebamowo, C. (2017). Randomized trial evaluating self-sampling for HPV DNA based tests for cervical cancer screening in Nigeria. *Infectious agents and cancer*, *12*, 11. <https://doi.org/10.1186/s13027-017-0123-z>
- Moses, E., Pedersen, H. N., Mitchell, S. M., Sekikubo, M., Mwesigwa, D., Singer, J., Biryabarema, C., Byamugisha, J. K., Money, D. M., & Ogilvie, G. S. (2015). Uptake of community-based, self-collected HPV testing vs. visual inspection with acetic acid for cervical cancer screening in Kampala, Uganda: preliminary results of a randomised controlled trial. *Tropical medicine & international health : TM & IH*, *20*(10), 1355–1367. <https://doi.org/10.1111/tmi.12549>
- Moses, E., Pedersen, H. N., Wagner, E. C., Sekikubo, M., Money, D. M., Ogilvie, G. S., & Mitchell-Foster, S. M. (2018). Understanding Men's Perceptions of Human Papillomavirus and Cervical Cancer Screening in Kampala, Uganda. *Journal of global oncology*, *4*, 1–9. <https://doi.org/10.1200/JGO.17.00106>
- Ogilvie, G. S., Mitchell, S., Sekikubo, M., Biryabarema, C., Byamugisha, J., Jeronimo, J., Miller, D., Steinberg, M., & Money, D. M. (2013). Results of a community-based cervical cancer screening pilot project using human papillomavirus self-sampling in Kampala, Uganda. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *122*(2), 118–123. <https://doi.org/10.1016/j.ijgo.2013.03.019>
- Tesfahunei, H. A., Ghebreyesus, M. S., Assefa, D. G., Zeleke, E. D., Acam, J., Joseph, M., Getachew, E., Kajogoo, V. D., Bekele, D., & Manyazewal, T. (2021). Human papillomavirus self-sampling versus standard clinician-sampling for cervical cancer screening in sub-Saharan Africa: a systematic review and meta-analysis of randomized controlled trials. *Infectious agents and cancer*, *16*(1), 43. <https://doi.org/10.1186/s13027-021-00380-5>
- World. (2019, December 2). *Cervical cancer*. Who.int; World Health Organization: WHO. https://www.who.int/health-topics/cervical-cancer#tab=tab_1