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Clinical importance of cervical cancer prevention and education in Zambia and Sub-Saharan Africa

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BOSTON UNIVERSITY
SCHOOL OF MEDICINE

Thesis

**CLINICAL IMPORTANCE OF CERVICAL CANCER PREVENTION AND
EDUCATION IN ZAMBIA AND SUB- SAHARAN AFRICA**

by

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B.S., Boston University, 2011

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CLINICAL IMPORTANCE OF CERVICAL CANCER PREVENTION AND EDUCATION IN ZAMBIA AND SUB- SAHARAN AFRICA

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ABSTRACT

Introduction: Cervical cancer exists as the second most common cancer among women world wide, and in numerous countries is the leading type of female cancer. Specifically, Zambia has one of the highest mortality rates and cervical cancer incidence rates. The goal of this study is to analyze the published literature on preventative techniques for cervical cancer in resource-deprived areas of sub-Saharan Africa by focusing on the correlation between the Human Papilloma Virus (HPV), Acquired Immunodeficiency Syndrome (AIDS), and cervical cancer; the accuracy and feasibility of “screen and treat” clinics; and socio-economic and geographical barriers.

Results: Correlations exists between the prevalence of HIV, HPV, and cervical cancer in sub-Saharan Africa, and a clear association exists between HPV and cervical cancer. The deliverance of HPV vaccines as well as educational programs has helped to improve this medical problem. Main screening methods for cervical cancer include the Pap smear, naked eye visual inspection of the cervix after the application of either diluted acetic acid (VIA), Lugol’s iodine (VILI),

or with a magnifying device (VIAM), colposcopy, and tests for HPV markers. Studies indicate that the VILI screening test has the highest level of sensitivity with the LEEP method also of importance. The procedure is relatively low cost and is easy to implement when excising lesions. Major risk factors and determinants of cervical cancer can help to explain the underlying barriers of access to care. Women's misconceptions regarding cervical cancer, gender inequality in African nations, socio-economic status, and foreign aid all play major roles the cervical cancer screening process. A lack of proper education, especially among women in sub-Sahara Africa, has led to misconceptions about the causes of cervical cancer. Studies have found that some women associated cervical cancer with prostitution, a Satanic curse, and other bad behavior. Gender inequality also plays a significant role since the Zambia government had reported that a husband would have absolute rights over children and reproductive rights over his wife once he had made payments for a bride. Geographical barriers also exist as the terrain in Zambia is swamp-like and heavy flooding throughout the year is common. After flooding occurs, communities become physically separated. Furthermore, there are correlations between high incidence rates of cervical cancer and high poverty as it has been shown that the largest number of people living on less than \$1.25 dollars per day is that of sub-Saharan Africa.

Discussion: Studies have indicated that virtually all of cases of cervical cancer are caused by HPV, implying that HPV testing and detection would largely

prevent the progression of lesions. Ultimately, this would reduce the high incidence rate of cervical cancer in Zambia and in other Sub-Saharan African countries. In areas where cytology programs are either non-existent or not efficient, HPV testing approaches should be evaluated and implemented, and they should be based off of the HIV/AIDS infrastructure that has already been established. In regards to the screening approaches, VIAM and VIA are the only two tests that are also practical, affordable, and available. Affordability is the major concern when implementing screening programs in sub-Saharan Africa; for this reason, either VIAM and VIA would arguably be the best options as long as they were effective. VIA would be considered the most appropriate method in terms of screening procedures as the method has the advantage of giving immediate results that can be applied to large populations. Lastly, the lack of proper education, including sex education, has in part led to drastic misconceptions about the causes of cervical cancer. Women hold negative beliefs about cervical cancer since they associate it with being unclean and view it as a reflection of bad behavior. Geographical barriers also play a role; the physical inaccessibility of the clinic discourages women to come to the clinic for screenings. Home visits by physicians and/or the utilization of community health workers may help to eliminate this particular barrier of access. This strategy would be especially beneficial to residents of rural areas since they are more likely to live farther away from institutionalized clinics and screen and treat facilities and are also more likely to be in a state of extreme poverty.

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ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
ART	anti-retroviral therapy
CDC	Center for Disease Control and Prevention
CIN	cervical intraepithelial neoplasia
FDA	Food and Drug Administration
HC2	Hybrid Capture-2 assay
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
ICC	invasive cervical cancer
LEEP	loop electrosurgical excision procedure
PAP	Papanicolaou
STD	sexually transmitted disease
VIA	visual inspection of the cervix after application of diluted acetic acid
VIAM	visual inspection of the cervix after application of diluted acetic acid with a magnifying glass
VILI	visual inspection of the cervix after application of Lugol's iodine
WHO	World Health Organization

INTRODUCTION

Cervical Cancer

Cervical cancer exists as the second most common cancer among women world wide, and in numerous countries is the leading type of female cancer (24). As seen in Figure 3, cervical cancer is most prevalent on the South American continent as well as the western and southeastern portions of Africa (24). Worldwide, an estimated 500,000 women are diagnosed with cervical cancer, and over half of the women diagnosed die from the cancer; additionally, nearly 80% of these women live in resource-deprived countries (12). More specifically, Zambia has one of the highest mortality rates and cervical cancer incidence rates world-wide (12). Anatomically, the cervix of the female provides an opening that allows for communication between the vagina and uterus, and the outer surface of the cervix is the region in which squamous epithelium develop during the early stages of cervical cancer (28). Sexual contact is one of the most widespread methods of transmission of cervical cancer (25). Human Papilloma Virus, HPV, is one of the most common causes of sexually transmitted diseases worldwide in both men and women. It is associated with a variety of clinical conditions that range from innocuous lesions to cancer and was originally linked to cervical cancer in the early 1980's by Hrold zur Hausen (1). Since his demonstration was published, the link between HPV and cervical cancer has become well

established. The degree of association has been found to be greater than the association between smoking and lung cancer (1).

Transmission of HPV occurs mainly through skin-to-skin contact and is heavily influenced by sexual activity. Along with sexual activity, age is an extremely important determinant of risk of HPV infection since the greatest risk coincides with greatest metaplastic activity within the cervix.

“Most cervical cancers arise at the squamocolumnar junction between the columnar epithelium of the endocervix and the squamous epithelium of the ectocervix” (1)

The greatest changes occur at puberty and when a woman becomes pregnant. Therefore, HPV infection is typically most common when a woman is sexually active, between the ages of 18 and 30. However, cervical cancer seems to be most prevalent in the age group of 35 years and older, suggesting that the infection occurs at a young age and progresses slowly to cancer. The clinical manifestation of HPV can lead to one of three possible fates, including anogenital warts, latent or inactive infection in which symptoms are usually not noticeable or active infection, which is associated with high-risk developments (1).

In terms of scientific pathology, the microbiological pathway of HPV development can be seen in Figure 1. Ultimately, the HPV oncogenes E6 and E7 have a high affinity for p53 and pRB. Binding disrupts the normal function of the proteins and can lead to continuous proliferation of the virus. The viral infection can lead to malignancy and cervical cancer since more DNA becomes damaged

and cannot be repaired. More specifically, the high risk- HPV types disrupt normal cell protein functions including gene expression (1).

Several types of malignant cervical tumors exist, the most common being squamous cell carcinoma. The carcinomas are scientifically classified into grades or stages depending on the severity and spread of the cancer. For instance, grade 1 carcinomas include squamous cells with keratin, little pleomorphism, and low mitotic rate and grade 2 tumors are a bit more developed and contain greater nuclear pleomorphism, high mitotic rate. Grade 3 is considered to have very severe nuclear atypia and very little squamous differentiation. Figure 2 below exemplifies a more severe cervical adenomcarcinoma.

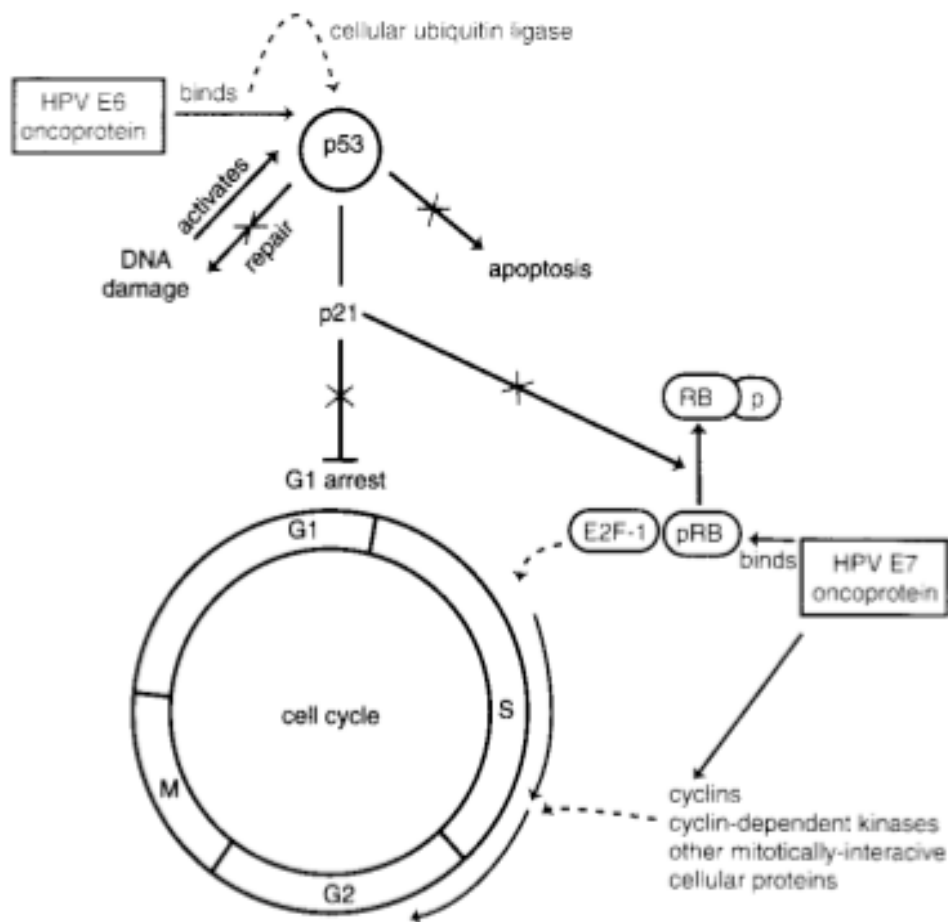


Figure 1: Pathogenesis of HPV. The E6 and E7 genes commonly bind to p53 and pRB proteins. This leads to altered regulation, function and ultimately oncogenic transformation. Figure taken from Burd, 2006 (1).

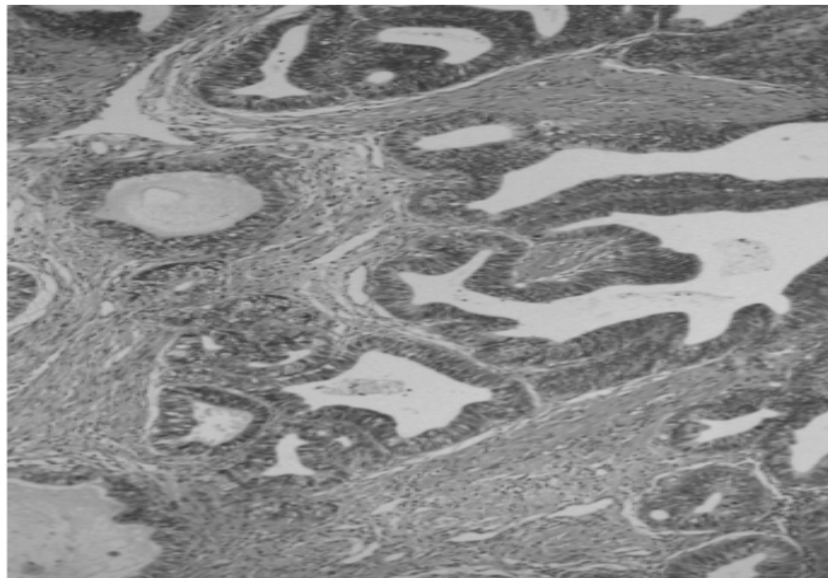


Figure 2 Invasive Endocervical Adenocarcinoma. The development and progression of a invasive cervical cancer is depicted in the figure above. Figure taken from Silverberg, 2003 (2).

When abnormal cervical changes are observed, a colposcopy is performed and cervical tissue samples are examined microscopically (27). The cancer progresses slowly and begins as precancerous dysplasia; if detected early enough by a Pap (Papanicolaou) smear test, the condition is 100% treatable (27). Women who are younger than 35 years old have a lower chance of survival if their stage of cervical cancer is II or above (2). The most invasive type of carcinoma develops from an intraepithelial neoplasm, forming from within the tissues of the cervical ectopy (3). Cervical carcinomas spread from the cervical stroma into the parametrial tissues, the uterus, vagina, and can spread to the bladder as they progress in the later stages of the disease (3). If left untreated, cervical cancer will result in death.

Regional Discrepancies

Cervix exams and cervical cancer screenings exist as critical elements in cancer prevention. Zambia, Ethiopia, and Malawi are amongst the top nations in terms of the percentage of women who have never had a pelvic exam (Figure 3) (25). Within a cohort of individuals in Tanzania, for example, only 22.6% of the women had ever obtained cervical cancer screening (29). Reasons for such low rates are primarily due to level of education, preconceived notions regarding cervical cancer, the spouse's opinion and approval to get screened, and the location in which the screening or exam is being conducted (26). The majority of the studies that have been conducted highlight the extremely elevated rates of cervical cancer and the factors that have led to such unfortunate circumstances. Screening via the Pap test and other tests can potentially provide 100% remission. Furthermore, Pfaendler discusses the clinical significance of the loop electrosurgical excision procedure (LEEP) and how it can be managed locally and performed safely with low rates of complications when treating cervical cancer abroad (12). Cervical cancer has been a leading concern in African nations, but promising solutions do exist. The needle for access to care and resources needs to be moved.

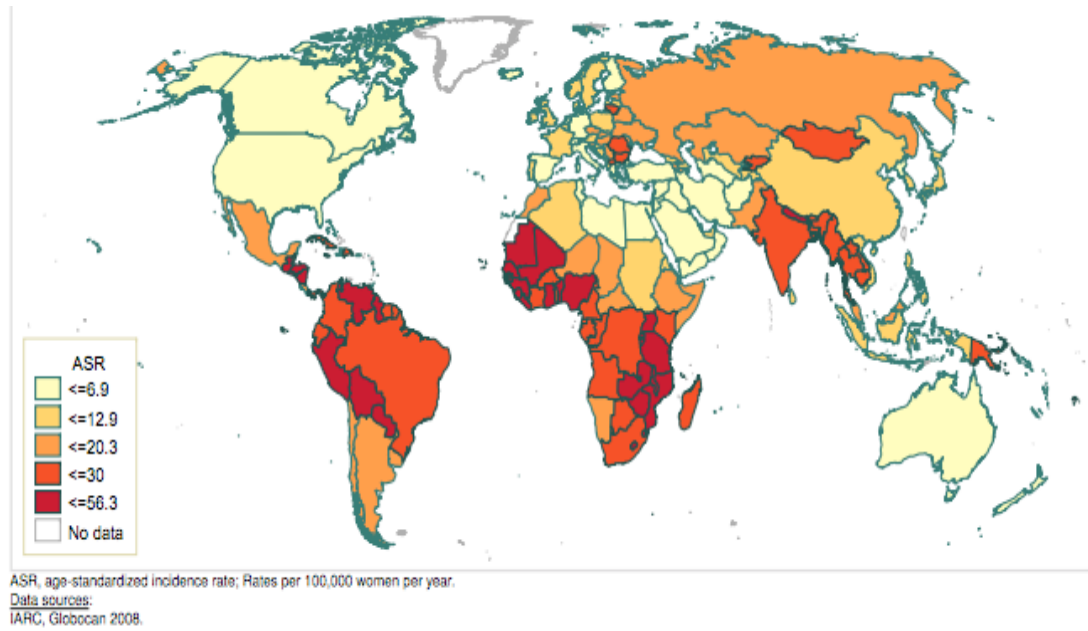


Figure 3: Incidence Rates of Cervical Cancer World-Wide. Figure taken from World Health Organization, 2009 (24).

STUDY OBJECTIVES

As shown in previous studies, it is evident that cervical cancer screening via Pap smears and various other screening methods tremendously aid in the prevention of cervical cancer. The disparity in the accessibility of care and screening between women residing in the U.S. and in third world nations is quite alarming. Lack of proper resources, inadequate education and infrastructure, misconception about cervical cancer, and numerous other factors contribute to the high prevalence of cervical cancer.

The goal of this study is to analyze the published literature on preventative techniques for cervical cancer in resource deprived nations that have barriers to healthcare. Specifically,

- (1) The correlation between the Human Papilloma Virus (HPV), Acquired Immunodeficiency Syndrome (AIDS), and cervical cancer will be analyzed as well as the implications for prevention.
- (2) The accuracy and feasibility of “screen and treat” programs and different types of screening procedures from studies conducted in the U.S. and worldwide will be examined.
- (3) Barriers such as the level of education, women’s’ misconceptions about cervical cancer, gender inequality, resource deprived settings, lack of professional medical training, and foreign aid and funding will be considered.

We hope the findings from this study will bring conclusive information about more sound and organized methods for cervical cancer prevention in not only Zambia but in similar resource-deprived nations. A proposal will be made in regards to broadening the scope in order to target Human Immunodeficiency Virus (HIV), HPV and cervical cancer simultaneously, to using the most feasible type of screening test, and to finding solutions for the barriers previously stated. Such solutions are vital for the health and well being of individuals in dire need of medical attention.

PUBLISHED STUDIES

The Correlation Between The Human Papilloma Virus (HPV), Acquired Immunodeficiency Syndrome (AIDS), And Cervical Cancer

A significant correlation and causal relationship between HPV and cervical cancer has been determined by several studies. Similarly, the prevalence of AIDS has been shown to be indicative of higher risk for the development of cervical cancer especially in Sub-Sahara Africa. The most frequently reported risk factors for HPV and AIDS have included a high number of sexual partners, early age at first intercourse, or any previous sexually transmitted disease (STD) (5). The deliverance of HPV vaccines as well as educational programs has helped to improve this medical problem. According to Bosch, epidemiological evidence gathered from a large and consistent body of studies have supported without doubt the clear association between HPV and cervical cancer (5). This can be seen through case control studies and prevalence surveys which show that in 90-100% of cases, HPV DNA has been found in adequate specimens of cervical cancer, and this is in comparison with a prevalence of 5-20% in cervical specimens from women identified as controls in epidemiological studies (5). Nearly all of the cervical cancer cases had detectable traces of HPV, indicating a strong correlation between HPV and cervical cancer. Among the 50 countries that were observed during the study, striking consistency exists, further supporting the existence of a meaningful correlation. The correlations were

based upon epidemiological factors including strength of association, consistency, and specificity, which asserts that a cause should lead to a single effect rather than multiple effects (5). The specificity in this case was very high, further supporting the evidence that HPV infection leads to cervical cancer.

The human immunodeficiency virus, HIV, can lead to acquired immunodeficiency syndrome, more commonly known as AIDS. HIV affects and slowly destroys the CD4 cells of the immune system. It can be transmitted through vaginal or anal sex or by sharing needles or drug injection materials with someone who is already infected with HIV (32). The number of new HIV infections, especially among women, in the United States is decreasing primarily due to antiretroviral therapy and an increased level of awareness and preventative measures; however, Black and African American women are disproportionately affected by HIV in the U.S. and in Sub-Saharan Africa (32). HIV is of particular interest when analyzing HPV and cervical cancer trends because a great amount of co-prevalence exists between the two viruses. According to a comprehensive review in 2009, areas of Sub-Saharan Africa that have the highest HIV prevalence rates also have extremely high incidences of cervical cancer, as can be seen by Figure 4 (7). The dark red areas indicate areas with an HIV prevalence of 20-28% and cervical cancer incidences of the same percentage (7). While the prevalence is not exact, patterns in specific areas can be seen, indicating some level of correlation. Whether or not the HIV epidemic has affected the incidence of invasive cervical cancer on a grand scale (ICC) in Sub-

Sahara Africa remains unclear; however, according to Louie, the ICC incidence rates have not been reduced significantly between the 1960's and the 1990s, demonstrating that great need for continued research (Figure 4) (7)

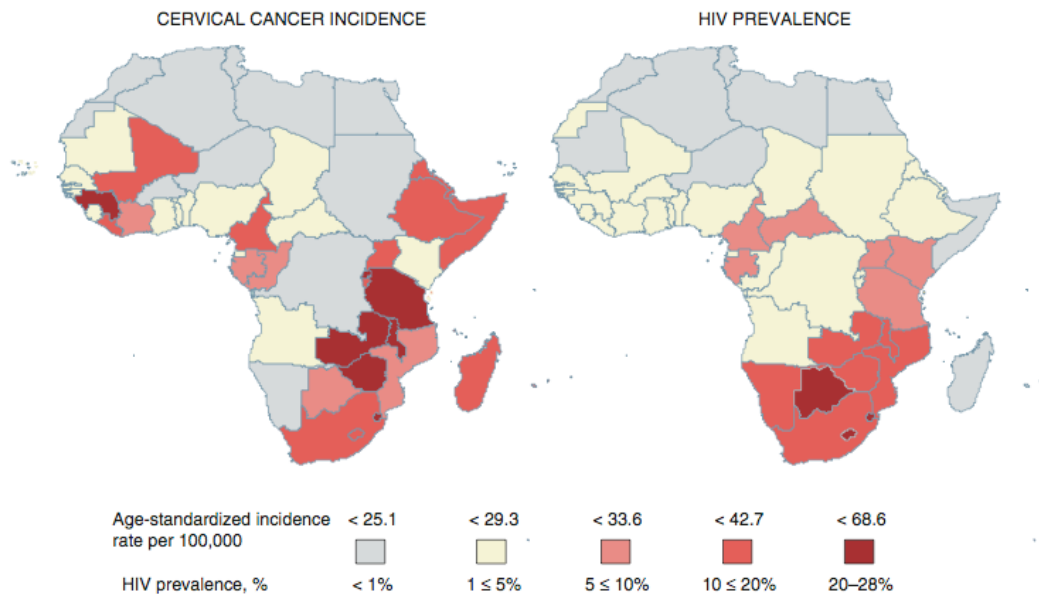


Figure 4: World Incidence of Cervical Cancer and HIV. Shown are the rates of cervical cancer and HIV world-wide per 100,000. Figure taken from Louie, 2009 (7).

Contrarily, epidemiological studies have consistently shown that women who are HIV- infected are at a much higher risk of becoming infected with HPV than are HIV-negative women (7). Furthermore, it has been shown that HIV-positive women with ICC are more likely to have more multiple infections than that of HIV- negative women (7). Pfaendler discusses the importance of a study conducted in Zambia, which helps to support the claim that HIV-infected women

are at a higher risk of becoming infected with HPV. The main cohort enrolled included HIV infected women, and it was demonstrated that co-infection with HPV and HIV results in increased rates of cervical intraepithelial neoplasia (CIN) which in turn is the precursor to cervical cancer (12). All such findings reveal that HIV positive women are at higher risk for developing HPV, and ultimately for developing cervical cancer (12). Reasons for such risks are not conclusive. Studies have proposed that the high prevalence of communicable diseases sexually transmitted infections, and sexual behaviors may have an influence upon the immune status of women with cervical cancer (ref). In an effort to reduce the risky behaviors, Pfaendler's study included an HIV peer education program implemented in Zambia. The *Educator Program* consisted of five major components. Peer educators in the area were trained on how to deliver messages in the community regarding the importance of cervical cancer screening, especially among HIV-infected women. The peer educators were also given daily cervical cancer preventions talks in the HIV care and treatment clinics in which cervical cancer prevention services were being offered. Furthermore, the peer educators assisted HIV- positive women to getting to the HPV screening clinics (12). Lastly, the staff members within the HIV- care clinics strongly encouraged HIV-infected women to be screened, and the nurses educated patients about the potentially deadly risks of cervical cancer (12). The *Peer Education* system helped Zambian women understand the severity of cervical cancer as well as the importance of getting screened.

Overall, the correlation between HIV, HPV and cervical cancer is very apparent, and important measures including the use of anti-retroviral therapy (ART), measuring viral load, and the use of HPV vaccines may help to decrease the prevalence of cervical cancer, especially among HIV-positive women. According to Louie, after the use of ART, the immune system is better able to control and recover from HIV- related opportunistic infections, including Kaposi's sarcoma and possibly HPV (7). An important measurement that may help to distinguish clinically relevant infections from those that are less severe is determining the viral load. This was found by Bosch's study that

“confirmed that high viral load predicted cervical lesions and... the reduction of viral load or clearance of viral DNA in repeated visits [and] predicts regression of CIN lesions to normalcy” (5).

In essence, high viral load was indicative of more severe and progressive forms of cervical cancer. Lastly, the use of HPV vaccines is arguably the soundest method to decrease the prevalence of cervical cancer, especially among HIV-infected women. The data suggests that HPV vaccines that contain the HPV16/18 can potentially prevent invasive cervical cancer cases among HIV-positive women (5). Therefore, HPV vaccinations are of paramount importance.

HPV Vaccines

Two main HPV vaccines for women, Cervarix and Gardasil, are licensed by the Food and Drug Administration, according to the Center for Disease Control and Prevention (CDC) (31). Cervarix is a bivalent HPV vaccine and prevents the formation of HPV type 16 and 18, which cause approximately 70% of cervical cancers (GlaxoSmithKline, USA) (38). Gardasil is a quadrivalent vaccine which prevents HPV types 16,18, 6, and 11 (Merck Sharp & Dohme) (39). HPV types 6 and 11 are known to lead to about 90% of genital warts (31). The vaccines are intended as a preventative measure and will not treat any already existing HPV-related disease. Both Cervarix and Gardasil are generally administered in early adolescence as part of a 3 dose regiment (31). Ultimately, the vaccinations are recommended for protection against and prevention of cervical cancers as well as precancers in young women. Only the quadrivalent HPV vaccine is recommended for use of men (31). It is recommended that young men and women receive the vaccinations before the onset of sexual activity since they may become exposed to HPV during sexual activity (31). While the HPV vaccine can prevent severe cases of cervical cancer, the vaccine is incredibly expensive. The three-dose vaccine is about 360 U.S. dollars (7). Because of the high price, it would especially be difficult to implement vaccination services in developing countries including those in Sub-Sahara Africa. Nearly 80% of cervical cancer cases occur in developing countries, and cost barriers need to be overcome in order to initiate the introduction of vaccines (7). Vaccines

would be targeted towards women who have not been diagnosed with HPV or cervical cancer. However, since many women in Sub-Sahara Africa already suffer from HPV and varying degrees of cervical cancer, screen and treat programs may be a more suitable approach to improving their health.

The Accuracy And Feasibility Of “Screen And Treat” Programs And Different Types Of Screening Procedures From Studies Conducted In The U.S. And Worldwide

Some of the main types of screening methods for cervical cancer include a Pap smear, naked eye visual inspection of the cervix after the application of either diluted acetic acid (VIA), Lugol’s iodine (VILI), or with a magnifying device (VIAM), HPV testing with the high risk probe of the Hybrid Capture-2 assay (HC2), colposcopy, and tests for HPV markers (8). A Pap smear is a screening procedure in which the cells within the cervix are examined. A speculum is placed into the vagina, allowing it to open slightly. Cells are then gently scraped from the cervix and examined microscopically for any traces of cervical cancer or HPV (33). Figure 5 below depicts a Pap smear with abnormal squamous cells (1).

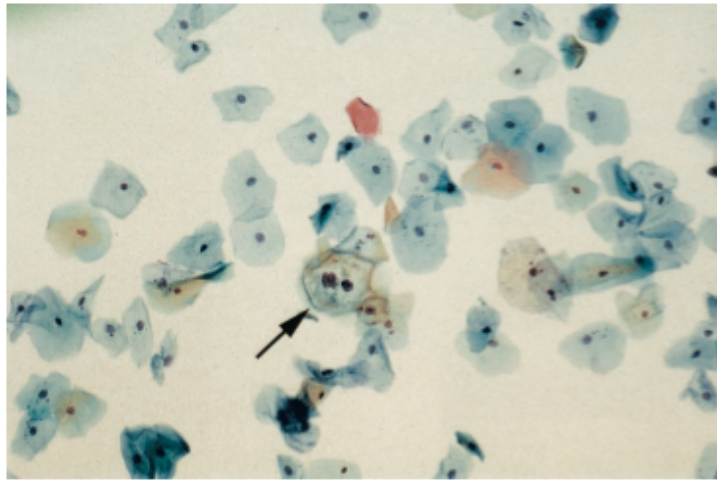


Figure 5: Abnormal Pap Smear . Thin Prep Pap Smear indicating abnormal squamous cells due to HPV. Figure taken from Burd, 2006 (1).

Visual inspection of the cervix may entail either swabbing the cervix with acetic acid, which is the VIA method, or using magnification to inspect the cervix, which is termed VIAM (9). Similarly, Lugol's iodine can be applied to the cervix to test for cervical cancer. Cervical tissue that may be cancerous does not stain upon application of Lugol's iodine and thus can be identified since it is more pale (9). Molecular HPV DNA tests can also be used as screening measures and help to detect the presence of the HPV virus prior to developing cancer (9).

Cervicography, which entails taking pictures of the cervix and submitting them for examination by a physician, also exists as a viable option of screening (9). All of the screening methods have been shown to be safe and almost all are available

in low-resource settings. Table 1 below indicates whether each test is effective, practical, affordable, and available.

Table 1 Cervical Cancer Screening Approaches. Various screening approaches and their effectiveness in low-resource settings are depicted. Figure taken from Abwao, 1988 (9).

Proposed Approaches to Cervical Cancer Screening in Low-Resource Settings					
Approach	Effective	Safe	Practical	Affordable	Available
VIAM	?	Yes	Yes	Yes	Yes
VIA	?	Yes	Yes	Yes	Yes
Automated Pap Screening	Yes?	Yes	?	No	No
HPV Screening	?	Yes	?	?	Yes
Cervicography	Yes?	Yes	?	?	Yes

Some tests are more reliable than others since they vary in degrees of sensitivity and specificity. Sensitivity and specificity are epidemiological terms that determine the accuracy of screening measures. Sensitivity indicates the proportion of positive screening tests that are actually positive, while specificity indicates the proportion of negative screening tests that are actually in fact negative (35). An increase in sensitivity of a screening methods will lead to a decrease in specificity, and vice versa (35). Concerns have been raised in regards to poor sensitivity, which can lead to over-looking cancers, and poor

specificity, which can lead to over-treatment. It has been determined that no HPV or cervical cancer screening method exists that would be able to attain high levels of both sensitivity and specificity (9). The level of accuracy, cost, and overall feasibility of each type of screening test varies to some extent. (9). Arbyn conducted a pooled analysis of five cervical cancer-screening tests in order to compare the accuracies of each. The tests were assessed in eleven different studies in India and Africa, and over 58,000 women were tests (8). Arbyn's findings for the five different types of screening tests, as well as their specificity and sensitivity, are summarized in Table 2. According to the data, the screening test with the highest level of sensitivity, with 95% of a confidence interval, was that of the VILI (8).

Table 2: Sensitivity and Specificity of Various Cervical Cancer Screening Tests, VIA, VILI, VIAM, Pap Smear, and HC2 shown depending on their sensitivity and specificity levels.
Table taken from Arbyn, 2008 (8) .

Test	Outcome	Test Cutoff	Sensitivity			Specificity		
			Min	Max	Pooled (95% CI)	Min	Max	Pooled (95% CI)
VIA	CIN 1+	AW lesions or growth	0.425	0.900	0.618 (0.523–0.713)	0.752	0.951	0.865 (0.828–0.901)
	CIN2+		0.650	0.911	0.792 (0.733–0.850)	0.742	0.945	0.847 (0.807–0.888)
	CIN3+		0.583	0.946	0.829 (0.771–0.887)	0.738	0.943	0.842 (0.800–0.883)
VILI	Cancer	Non iodine uptake yellow areas or growth	0.667	1.000	0.887 (0.831–0.943)	0.731	0.941	0.836 (0.793–0.880)
	CIN 1+		0.503	0.941	0.737 (0.630–0.845)	0.741	0.928	0.866 (0.834–0.898)
	CIN2+		0.741	0.980	0.912 (0.878–0.946)	0.730	0.916	0.845 (0.813–0.878)
VIAM	CIN3+	AW lesions or growth	0.729	1.000	0.938 (0.906–0.971)	0.726	0.914	0.838 (0.805–0.871)
	Cancer		0.667	1.000	0.957 (0.918–0.997)	0.719	0.911	0.832 (0.798–0.865)
	CIN1+		0.425	0.684	0.585 (0.432–0.739)	0.864	0.901	0.881 (0.858–0.904)
Pap smear	CIN2+	ASCUS+	0.646	0.732	0.670 (0.618–0.722)	0.833	0.893	0.862 (0.824–0.900)
	CIN3+		0.657	0.744	0.682 (0.618–0.747)	0.828	0.891	0.859 (0.820–0.898)
	Cancer		0.763	1.000	0.826 (0.677–0.976)	0.824	0.889	0.855 (0.815–0.896)
HC2	CIN1+	LSIL+	0.230	0.655	0.343 (0.153–0.532)	0.866	0.987	0.946 (0.915–0.977)
	CIN2+		0.333	0.819	0.570 (0.376–0.763)	0.865	0.985	0.928 (0.887–0.968)
	CIN3+		0.356	0.964	0.630 (0.379–0.882)	0.863	0.982	0.923 (0.881–0.966)
	Cancer	HSIL+	0.400	1.000	0.725 (0.549–0.900)	0.857	0.977	0.918 (0.875–0.962)
	CIN1+		0.172	0.633	0.306 (0.112–0.499)	0.929	0.993	0.967 (0.948–0.985)
	CIN2+		0.238	0.779	0.512 (0.300–0.724)	0.886	0.991	0.949 (0.921–0.977)
	CIN3+	RLU>1	0.267	0.893	0.561 (0.327–0.796)	0.873	0.988	0.945 (0.916–0.975)
	Cancer		0.200	1.000	0.651 (0.432–0.871)	0.865	0.983	0.941 (0.910–0.971)
	CIN2+		0.175	0.617	0.426 (0.265–0.586)	0.977	0.997	0.993 (0.988–0.997)
	CIN3+		0.222	0.768	0.516 (0.320–0.711)	0.975	0.997	0.990 (0.984–0.995)
	Cancer		0.200	1.000	0.651 (0.432–0.871)	0.973	0.995	0.985 (0.978–0.993)
	CIN1+		0.215	0.337	0.266 (0.215–0.316)	0.922	0.951	0.940 (0.929–0.951)
	CIN2+		0.484	0.677	0.619 (0.562–0.677)	0.916	0.946	0.936 (0.924–0.948)
	CIN3+		0.623	0.735	0.684 (0.615–0.754)	0.914	0.944	0.934 (0.922–0.946)
	Cancer		0.615	0.857	0.721 (0.603–0.838)	0.911	0.940	0.930 (0.918–0.942)

VIA, visual inspection after application of acetic acid; VILI, visual inspection after application of lugol's iodine; VIAM, visual inspection after application of acetic acid and using a magnifying loupe; HC2, Hybrid-Capture 2 assay; CIN, cervical intra-epithelial neoplasia; AW lesion, aceto-white lesion; ASCUS+, atypical squamous cells of unspecified significance; LSIL, low grade squamous intraepithelial lesion; HSIL, high-grade intraepithelial lesion; RLU, relative light units.

A similar study was conducted in Lusaka, Zambia in 2006 and 2007; Zambian physicians and nurses were trained to not only perform VIA, but also to conduct punch biopsies on women who had been diagnosed with cervical cancer (12). The method of LEEP, which stands for loop electrosurgical excision procedure, is one of the major types of treatment services offered in developing countries (12). The procedure is relatively low cost, has a high success rate, and is easy to implement. The procedure entails the use of a thin wire loop that functions as a surgical knife. The loop is placed within the cervix, and an electric current passes through the loop; this process cuts a fairly thin layer of the cervix in an effort to excise and remove the cancerous cells (Figure 6) (36).

The study conducted in Lusaka, Zambia utilized LEEP, the VIA screen, and preventative services in 13 clinics within the region. A very high amount of women were diagnosed with cervical cancer. More specifically, 155 of the women who had undergone evaluation had CIN I, 144 had CIN II and III, and 149 had invasive cancer (12). LEEP was performed on almost all of the women. The physician training process for LEEP was therefore vital. The major steps of the training are depicted in Figure 6, and, overall, it was fairly simple. Four physicians were able to complete the procedure with a high level of skill after completing the training (12). LEEP has shown to be very effective in treatment, and the entire training for nurses and physicians was thoroughly completed within four weeks (12). Other screening methods have been shown to be very effective, as well, but their success also depends upon the patient population,

community, and terrain of the area in which the screenings will be conducted (7). In order to be successful, screening program should be accessible to patients, and referral services should be made available.

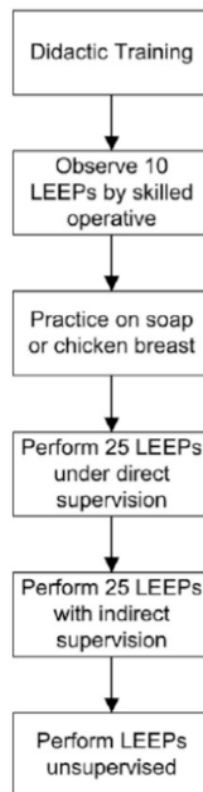


Figure 6: LEEP Training Process. Overview of the training process for LEEP for physicians, which involves didactic training, direct supervision, indirect supervision, and unsupervised steps. Figure taken from Louie, 2009 (7)

Louie asserts that it would be wise to develop screen and treat programs as opposed to a three visit strategy in an effort to avoid loss to follow up (7). Furthermore, it was determined that screening with either one or two visits during

“a lifetime using visual inspection or HPV DNA test coupled with immediate cryotherapy for screen women aged 35 years or older has the potential to reduce the risk of cancer by 25-35% compared with no screening” (7).

The model that had been used for this study was cost-effective and had been conducted in five developing countries in Sub-Saharan Africa.

While screen and treat programs are very promising for developing nations with high rates of cervical cancer, several barriers to access exist as well as limitations within the screening programs. Poor staffing and training, lack of on-site equipment, and lack of health education among community members are just a few of the barriers for success in Sub-Saharan Africa. In a study conducted in the Kabalo district of Zambia, it was found that mainly male workers run the clinic, which can deter potential female patients from coming to the clinic. A strong association was found between a female's attitudes towards male workers as well as the use of services that are conducted predominantly by males (13). Such a gender bias in the work place led to a barrier of access to the clinic for some females. The facilities in Kabalo are also very poorly staffed. It was found that of the fourteen clinics, two have clinical officers and only one clinic as a trained midwife (13). In order to cater to the entire patient population that needs care, many more officers and clinicians are needed. Sustaining the clinic by preventing high physician turn over also exists as a barrier for the screening clinics (12). In addition to the lack of proper staff in screening and prevention clinics, the lack of equipment poses a barrier to healthcare. A study conducted in

2006 in Africa found that a lack of vaginal instruments and medical supplies, inability to conduct blood transfusions, and inability to treat shock with fluids, all prevented the clinics from operating at an acceptable rate (10). Additionally, water shortages within the hospital, waste disposal and sanitation issues, as well as the difficulties with timely delivery of medical supplies negatively affected the efficiency and effectiveness of clinics (12). Barriers exist on the patient side of care, as well. Reasons for patients not being present for evaluations and screenings included: fear of the procedure itself, travel costs in order to get to the hospital or clinic, difficulty in getting to the clinic by other means such as walking or transportation, and difficulty getting partner or family support for treatment (12). Lack of HPV and cervical cancer education among women also exist as a barrier to care. A study conducted in 2006 in Kinshasa of the Democratic Republic of Congo found that the majority of women who enrolled in a health education session had never used any sexual contraceptives and only 3% of the women who had used a contraceptive had used one that was medically approved (10). Such low use of contraceptives indicates that educational programs regarding healthy sexual practices should be implemented in these areas. Of the women who visited the clinic, only 5% had received some form of health education, which may imply that among those who did not visit the clinic, even a lower percentage had received health education (10). Many women in Sub-Saharan Africa, and more specifically in Zambia, are becoming more aware of HIV and risk factors associated with it. For this reason, it is important to link HIV education

to HPV and cervical cancer education. Individuals who are HIV positive are more prone to developing HPV and cervical cancer, as well (12). Screen and treat programs and other screening measures have the potential to prevent and eradicate most cervical cancers, but severe barriers limit their success.

Barriers Such As The Level Of Education, Women's' Misconceptions About Cervical Cancer, Gender Inequality, Resource Deprived Settings, And Foreign aid

Akinyemiju conducted a study in 2012 to analyze data from the World Health Survey of 2003. He wanted to assess the determinants, specifically socio-economic and health access, of cervical cancer screening and prevention in low-income countries, including African countries (15). It was found that an alarmingly low percentage, 4.1%, of women between the ages of 18 to 69 had received cervical cancer screening (15). Figure 7 below shows the breakdown of pelvic and mammography exams among different low-income nations. As can be seen, countries of sub-Saharan Africa, including Kenya, Malawi, and Ghana, have much lower rates of pelvic examinations as compared to other low-income countries.

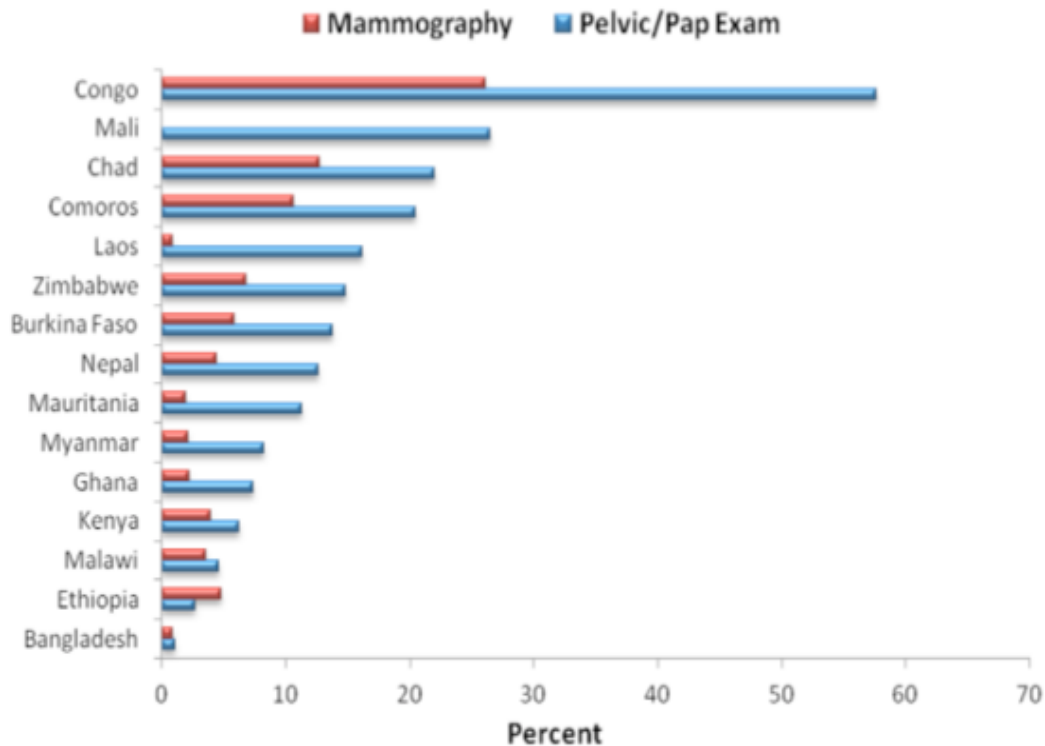


Figure 7: Percentage of Mammograms and Pelvic Exams by Country .

Comparison between the percentage of women in various countries who obtain mammograms and pelvic exams; Low-income countries, specifically, are being assessed. Figure taken from Akinyemiju , 2012 (15)

The survey also captured a wealth of information regarding the demographics, health status, access to health services, and risk factors that may increase the likelihood of women developing cervical cancer. The risk factors and determinants can help to explain the underlying barriers of access to care. For example, factors may increase the likelihood of not obtaining a pelvic exam include (i) being older than 60 years, (ii) having less than a secondary education, and (iii) not having seen a nurse or midwife at the last health center visit (15). In addition to the level of education of women in African countries, other stagnant

barriers to health care access also exist. Women's misconceptions regarding cervical cancer, gender norms and inequality in African nations, as well as socio-economic status and foreign aid all play major roles in the successful implementation of the cervical cancer screening process. Barriers need to be eliminated, or, at the very least, drastically reduced in order to allow for proper development of cancer screen and treat clinics.

Correlations between low literacy and education levels in low-income countries and not receiving a pelvic exam exist. According to the World Survey of 2003, 70.7% of women who had only completed a primary school level of education did not receive a pelvic exam, compared to 24.9% of women who had completed a secondary level of education (15). While there is a distinction between overall education level and education regarding the importance of obtaining a pelvic exam, the trends are still meaningful. According to the United States Department of Education, "low literacy is an important but frequently overlooked factor that influences preventative health and cancer screening behavior" (16). In 2002, the Department conducted the National Adult Literacy Survey, in which it was found that a higher level of knowledge, specifically 9th grade or above was in fact independently associated with accurate knowledge regarding the Pap test (16). Additionally, a higher proportion of women who had a more adequate level of literacy indicated they would seek medical care about any abnormalities compared to that of women who had lower levels of literacy (16). Even though this information was gathered in the United States, similar data

has been found in African countries. In essence, the education and literacy rates of women play a role in their ability and willingness to obtain pelvic exams and cervical cancer screening.

A lack of proper education, especially among women in Sub-Saharan Africa, has led to misconceptions about the causes of cervical cancer. The misconceptions exist as barriers to healthcare. In 2009, a community-based rapid assessment was conducted in Zambia in an effort to understand the common myths and causes of cervical cancers. Peer educators led the assessments and asked unscreened women two questions during home visits. The questions included what the women thought causes cervical cancer and why they had not been screened (23). Some of the responses have been documented in Table 3.

Table 3: Questions and Answers form 2009 Study by Chirwa Addressing Knowledge of Cervical Cancer and Screening. Table taken from Chirwa, 2009 (23).

‘What do you think causes cervical cancer?’

1. If you are found to have cancer of the cervix, that means you were a prostitute.
2. People think that cervical cancer is not from sex but from a Satanic curse.
3. Having sex with a married woman's husband can give you cervical cancer.
4. When one has cervical cancer that means she was bewitched so I don't want to know if I have it.
5. Putting herbs in private parts can cause cancer of the cervix.
6. A dirty womb causes cancer so you have to wash yourself out every day.
7. The family planning medicines that they give out at the clinic cause cancer.
8. If you are found with cervical cancer you will die so I don't want to know.
9. Some people think that it's a family disease.
10. Eating bad food causes cancer of the cervix.

‘Why haven't you been screened for cervical cancer?’

1. The nurses who do the screening are Satanists and may take our children.
2. The instruments they use are painful.
3. We are afraid to be cut by the nurses.
4. After screening you have long periods and discharge.
5. There is no privacy and I'm just scared to be screened by people who know me.
6. I'm worried about how clean the instruments are and I am scared of being infected with HIV or any other disease.
7. People think that if you have cancer, they say you have HIV.
8. When someone is found with cervical cancer, they think that the womb will be removed.
9. Screening destroys the ability of a woman to have a baby.
10. Screening enlarges the vagina and reduces sexual enjoyment for men and women.

As can be seen by Table 3, many unscreened women's' interpretations of cervical cancer are inaccurate and may can be classified as socially constructed (23). Fear of the screening process, misunderstanding of the causes of cervical cancer, and social stigma around cervical cancer are all barriers to the acceptance and use of screen and treat programs. The peer educators sought to convey the importance of obtaining a screening since cervical cancer can be prevented and potentially cured if it is detected early enough (23).

Socially constructed gender norms and gender inequality in African countries also exist as barriers for women to obtain pelvic exams and cervical cancer screenings. The World Bank published a Health, Nutrition, and Population Discussion paper in 2000 that outlined women's health issues, and the findings can be applied broadly to women from all nearly all countries (11). The paper states that women's health is determined by various factors including individual behavior, biological factors, social and cultural influences, and nutrition (11). Biologically, women are at higher risk for contracting sexually transmitted infections and HIV as compared to men. Additionally, women in Sub-Saharan African countries are subject to increased risks related to pregnancy, and it has been estimated that one out of seven women will die due to pregnancy-related complications. Figure 8 below summarizes the main lifetime health problems categorized by age groups for women (11). Reproductive health problems continue to be the worst among the poorer nations; most of the issues relate to reproductive health, including HPV and cervical cancer, can be prevented or

treated in a cost-effective manner (11). The low socio-economic status of women in low-income countries, unequal power in sexual relationships, and biological predispositions of women make them more vulnerable to unwanted pregnancies, STIs, and other unwanted medical conditions, such as HPV and cervical cancer (11). In some cultures of Sub-Sahara Africa, including in Zambia, some women are discouraged from seeing male health providers (13). Since the majority of health care providers are male, this poses yet another barrier to access to care.



Figure 8: Lifetime Health Problems of Women. The lifetime health problems of women world wide are being depicted within certain categories and stages of life. Figure taken from National Institute of Health, 2013 (33)

Social gender inequality exists to a great degree in African countries. According to the Social Institutions and Gender Index, a high level of sexual violence towards women exists in Zambia. Based on the 2007 Demographic Health Survey, 64% of women reported that they had been victims of sexual violence either by their husband, partner, boyfriend and even relative (34). The apparent disparity in gender norms and rights can be seen by Zambian government reports. In 2010, the Zambian government had reported that a husband would have absolute rights over children and reproductive rights over his wife once he had made payments for a bride (34). Furthermore, while polygamy is not legally permitted in Zambia, it is unofficially accepted in society (34). Efforts have been made to decrease and prevent acts of sexual violence in the country. However, it has been reported that women often are “pressured by law enforcement into withdrawing complaints” (34). Gender inequality and sexual abuse can lead to higher cases of STIs, HIV, and HPV, and decrease the likelihood that women will seek medical attention and obtain pelvic exams.

Geographical barriers to HPV clinics and resource deprived settings exist as a prominent problem, especially in the Kabalo District of Zambia. Between 1998 and 2000, a cross sectional study regarding women’s health services was conducted in the Kabalo district and it was found that several geographical barriers prevented women from seeking care (13). Most of the terrain in the region is swamp-like and heavy flooding throughout the year is common. After flooding occurs, communities on either side of the flood plains become

geographically separated, making clinic visits to either side very difficult (13).

Lack of proper resources and methods of transportation also discouraged women from seeking care at the clinic in Kabalo. According to a survey conducted by Stekelenburg and colleagues, 76% of respondents stated that they had to walk to the clinic, and 50% of those who had to walk, had to walk for at least two hours in order to reach the clinic (13). Therefore, access to the clinic required a great deal of physical effort, and many women felt discouraged to seek care at an institution because of this barrier. The perceived quality of care also influenced women's decision to travel to the clinic; if their perception of the clinic was poor, then they were less likely to make the effort to seek care (13).

The high level of poverty and resource deprivation in Sub-Saharan Africa also largely impacts the accessibility of screen and treat clinics for HPV and cervical cancer. Table 4 below outlines the percentage rates of poverty in Zambia from 1991 to 1998 (18). Low poverty rates contribute to the inability of some women to seek care. According to Stekenberg, the cost of services plays a large role in the decision-making process of going to the clinic. For the majority of women, the fees were not affordable and they did not seek and receive the care that they needed (13). Over two thirds of Zambian families have a monthly income under 500,000 Zambian Kwacha, which is equivalent to \$100 U.S. dollars (12). Such an amount is not sufficient for a healthy lifestyle, let alone payments for clinical visits. According to Pfaendler's study, roughly 75% of Zambian women were familiar with the term "cervical cancer." However, the greatest barrier to care is

that facilities for early detection and treatment for cervical cancer in Sub-Saharan African settings does not exist for most women (12). Zambia is of particular interest because it has the second highest incidence rate of cervical cancer world wide, at 1,839 per 100,000 people. It ranks second to Guinea (19).

Year	Zambia		Rural		Urban	
	Overall Poverty %	Extreme Poverty %	Overall Poverty %	Extreme Poverty %	Overall Poverty %	Extreme Poverty %
1991	69.7	58.2	88	80.6	48.6	32.3
1993	73.8	60.6	92.2	83.5	44.9	24.4
1996	69.2	53.2	82.8	68.4	46	27.3
1998	72.9	57.9	83.1	70.9	56	36.2

Source: Zambia PRSP (2002)

Table 4: Poverty Levels in Zambia. Rural and urban overall and extreme poverty levels (%) are shown between the years of 1991 and 1998. Table taken from Pitamber, 2006 (18),

As can be seen by Table 5 and Figure 9, there are correlations between high incidence rates of cervical cancer and high poverty.

Table 5: Countries with Highest Mortality Rates and Highest Incidence Rates of Cervical Cancer. Top 25 countries with the highest mortality and cervical cancer rates are indicated. Table taken from Singh, 2012 (Source 19)

Guinea	1,736	56.3	Guinea	1,217	41.7
Zambia	1,839	52.8	Comoros	76	39.1
Comoros	110	51.7	Zambia	1,276	38.6
Tanzania	6,241	50.9	Malawi	1,621	38.3
Malawi	2,316	50.8	Tanzania	4,355	37.5
Mozambique	3,690	50.6	Burundi	900	37.2
Swaziland	198	50.0	Uganda	2,464	34.9
Burundi	1,270	49.1	Mozambique	2,356	34.5
Uganda	3,577	47.5	Zimbabwe	1,286	33.4
Zimbabwe	1,855	47.4	Sierra Leone	466	33.0
Jamaica	624	45.7	Swaziland	116	31.4
Guyana	161	44.7	Liberia	341	31.2
Sierra Leone	670	41.9	Mali	1,010	28.4
Liberia	487	41.8	Ghana	2,006	27.6
Nicaragua	869	39.9	Guinea-Bissau	130	26.0
Ghana	3,038	39.5	Mauritania	244	25.5
Honduras	1,014	37.8	Senegal	795	25.5
Mali	1,491	37.7	Rwanda	678	25.4
El Salvador	1,145	37.2	Gambia	133	24.4
Bolivia	1,422	36.4	Benin	616	24.4
Mauritania	364	35.1	Nigeria	9,659	22.9
Guinea-Bissau	185	35.1	Lesotho	178	22.7
Benin	925	35.0	Angola	1,008	21.9
Lesotho	279	35.0	Togo	417	21.8
Paraguay	864	35.0	Burkina Faso	838	21.5

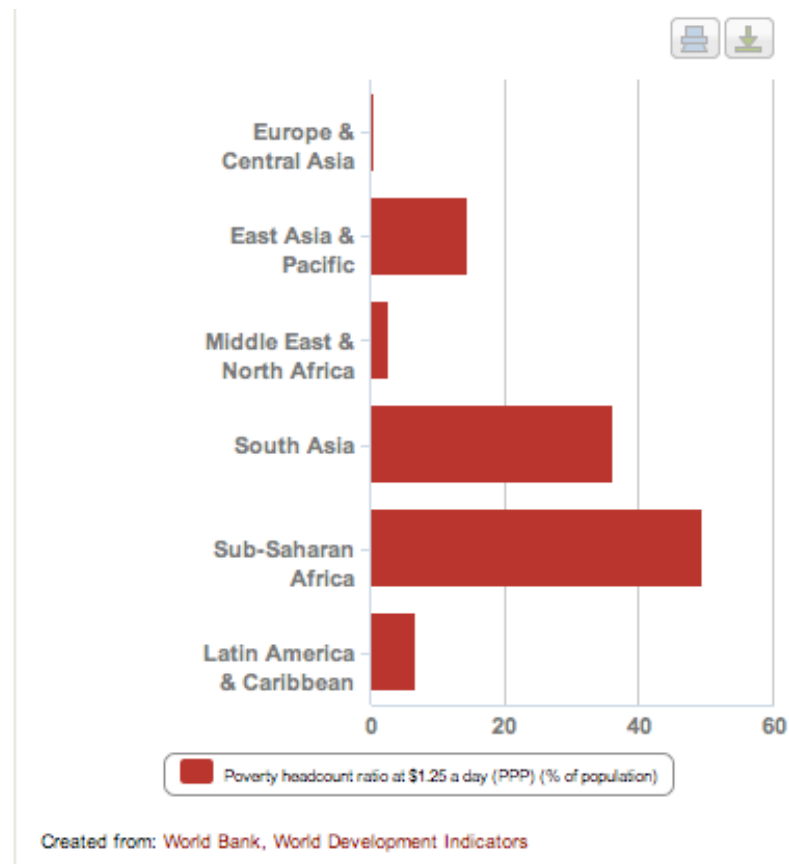


Figure 9: The Number of People Living on Less Than \$1.25 per Day World-wide. Shown are the areas where poverty is rampant and Sub-Saharan Africa is the highest. Figure taken from World Bank, 2013 (37).

Foreign aid has successfully helped with improving the issues of HIV/AIDS, malaria, and tuberculosis. However, Macgrath asserts that cancer care requires a more individualistic approach, and successful cancer treatment would involve a team of skilled experts (6). Cancer treatment is also very difficult because of its high cost. Low-income nations, including Zambia, have assigned a low priority to

cancer control, resulting in an unfortunate situation in which poor access to care results in patients having more severe cases of the disease; since the disease is more severe, this leads to increased costs and toxicity of treatments which leads to lower survival rates overall (6). In an effort to make clinical services affordable and accessible, the Zambian government introduced free health care in rural areas in 2006, which was made feasible by the British charity, Oxfam (14). While the barriers of lack of education, misconceptions regarding causes of cervical cancer, gender inequality, and resource deprivation exist, foreign aid helps relieve mainly the barrier of resource deprivation.

DISCUSSION

Correlation between the Human Papilloma Virus, Human Immunodeficiency Syndrome, and Cervical Cancer

Numerous studies have indicated the strong association between HPV and cervical cancer. According to Rudlowski, specific types of HPV (high-risk HPVs, and lower extent low-risk HPVs) have been detected in a transcriptionally active form in about 95% of cervical cancer biopsies (4). Since even low-risk HPVs are detected in cervical cancer biopsies, early detection of HPV would be extremely beneficial to women who have any range of risk HPVs in an effort to prevent the development of cervical cancer. Other studies have indicated that virtually 100% of cases of cervical cancer are caused by HPV, implying that HPV testing and detection would largely prevent the progression of lesions (17). Ultimately, this would reduce the high incidence rate of cervical cancer in Zambia and in other Sub-Saharan African countries and likely eradicate it in the US. In areas where cytology programs are either non-existent or not efficient, HPV testing approaches should be evaluated and implemented (5). The high prevalence of HIV is correlated with HPV in part because of the similarity in transmission; both HIV and HPV are sexually transmitted viruses. HIV is also associated with more severe classes of HPV including those associated with cervical neoplasia and invasive cancer (20). AIDS also disproportionally affects women, making them more vulnerable to sexually transmitted diseases as well as HPV (18). Because

of the high prevalence and awareness of HIV in Sub-Saharan Africa, many AIDS relief and Global Funds Programs currently exists updating healthcare infrastructures in some areas of sub-Saharan Africa (20). The HIV/AIDS infrastructure that has already been established in developing countries can be used as a sound basis for the further development of HPV and cervical cancer prevention and treatment. Existing awareness of HIV among sub-Saharan Africa communities can aid in the push for awareness of HPV and its health implications. This would be especially important in Zambia since it has one of the world's highest incident rates (20). Furthermore, since HIV- infected women are at greater risk for becoming infected with HPV, the impact of ART on HPV should be evaluated since ART is being used to treat HIV (7). Additionally, education linking HIV to HPV and further cervical cancer education is a crucial element of preventative measures (12). While HIV treatment is largely accepted in sub-Saharan Africa, the acceptability of HPV vaccinations and cervical cancer screenings will require persistent efforts by community health workers, physicians, and the government. Other vaccine deployment considerations include channels of vaccine deliveries, strategies, etc. many of which can be modeled after HIV programs that have already been established (7). By collaborating with other HIV care and treatment leadership teams, the organizational history of the HIV treatment and care program can be determined, and suitable infrastructure can successfully be applied to new HPV treatment and care programs (20). However, adjustments would need to be made since cancer

prevention is much more costly, as compared to HIV care, and requires a more individualistic approach depending on the patient's particular medical case (20).

The Accuracy and Feasibility of “Screen and Treat” Programs

While all screening methods are viable options, some approaches may be more feasible and less costly than others. According to Table 1, the methodological approaches of VIAM, VIA, Pap Screening, HPV screening, and Cervicography are all safe (9). However, VIAM and VIA are the only two that are also practical, affordable, and available. Affordability is the major concern when implementing screening programs in sub-Saharan Africa; for this reason, either VIAM and VIA would arguably be the best options as long as they were effective. Table 2 depicts the specificity and sensitivity of the VIA, VILI, VIAM, Pap Smear and HC2 methods (8). According to the data, the VILI approach had the highest pooled level of sensitivity while the Pap smear had the highest pooled level of specificity; the VIA approach had high levels of both measures (8). Both measures of sensitivity and specificity are important indicators of the accuracy of screening tests, and one is usually sacrificed for the other (35). In another study conducted by the International Agency for Research on Cancer, it was shown that up to 90% of the cancerous lesions can be identified by the VIA method however they went on to state that the specificity, or reduction of over-treatment, was more valuable than the sensitivity especially in light of limited resources to pay for screening tests (9). A sensitivity level between 70% and 80% and a

specificity level of 90% to 95% was considered reasonable (9). Based on these values, the VIA would be considered the most appropriate method in terms of screening procedures (9). The VIA method has the advantage of giving immediate results that can be applied to large populations (20). Various studies have also validated the efficacy, acceptability, and overall cost-effectiveness of the VIA screening approach (20). Lifetime costs associated with different screening approaches vary depending on the country (22). Screening tests are most cost-effective when the linkage between screening and treatment is enhanced, which is the case for VIA screening approach (22). Screen and treat methods that consist of only one visit, are more preferable than methods that require multiple visits since follow-up may pose a problem for multiple visit procedures (7). While VIA is arguably the best screening method, the LEEP has been shown to effectively remove cancerous lesions, and can be implemented into screen and treat programs (12). As can be seen by Figure 6, LEEP involves didactic training, observations of LEEP conducted by skilled personnel, extensive practice, and performance of LEEP with supervision by skilled personnel will lead to the eventual practice without supervision (7). The overall process is thorough, precise, and easy to implement. Physicians are carefully observed and supervised as to ensure proper technique and quality of care for the patients (7). Therefore, it can be easily implemented into screen and treat programs if proper staff and equipment are also provided. However, several issues regarding the screen and treat programs exist, according to various studies, and the issues

need to be addressed in order to increase the efficacy of the clinical programs. It was found that healthcare facilities in the Kabalo District of Zambia are severely under-staffed and face a high turn over rate (12). Increasing the number of staff members, properly training them, and providing incentives to continue working in the clinic for long periods of time would help to reduce this issue (13). The lack of adequate medical supplies may also be a contributing factor to the issue of a high turn over rate (10). Physicians may feel unprepared or incompetent to perform surgeries and screenings without the proper equipment. Furthermore, water shortages and waste disposal issues within the clinic can reduce the perception of quality of care for patients, thereby discouraging patients from going to the clinic (12). Sanitation issues within clinics also discourage physicians from working in such locations. The demographic composition of the staff in clinics can also discourage women from attending appointments. Specifically, in some regions of Zambia, women are discouraged to seek care from male physicians (13); cultural customs such as these detract a large number of women from seeking care when they need it. Training and hiring more female physicians and staff members in clinics can help to eliminate this particular issue. Addressing and improving the limitations of screen and treat clinics may help to increase the number of women who actually seek care at the clinics.

Barriers of Lack of Education, Women's' Misconceptions About Cervical Cancer, Gender Inequality, Resource Deprived Settings, and Foreign Aid and Funding

The fundamental barriers of a lack of education, culturally produced gender inequalities and misconceptions about cervical cancer, and lack of proper resources exist as root causes for such high incidence rates of cervical cancer in Zambia and other countries of sub-Saharan Africa. In a study conducted by Sangwa Lugoma, it was found that only three percent of a group of women in Africa had used a contraceptive that was medically approved (10). Such a low percentage reflects the unavailability of proper resources and contraceptives, as well as a lack of education regarding sexual practices. Since the education levels and literacy rates of women affect their willingness and ability to seek HPV and cervical cancer screenings, more attention and financial aid needs to be given to the education sector of Zambia and other countries of sub-Saharan Africa. Currently, the education sector of Zambia is very weak as children often have to travel long distances to reach the school, often have to care for family members in addition to the fact that they tend to work in order to contribute to household income (18). The low enrollments and high dropout rates are seen especially among young females. The lack of proper education in some areas, including sex education, has in part led to drastic misconceptions about the causes of cervical cancer (23). Table 3 depicts Zambian women's responses to the questions of what they think causes cervical cancer and why they have not been screened;

their responses are far from remotely accurate. Based upon the responses, it seems as though cervical cancer is a condition that is greatly stigmatized within Zambian societies (23). Women hold negative beliefs and attitudes regarding cervical cancer, and they associate it with being unclean as well as a reflection of bad behavior. In general, cervical cancer is stigmatized beyond its true medical condition, and this is partially a result due to a lack of proper education for women in the region. More recently, in a study conducted in 2012, it was found that levels of knowledge regarding HPV vaccines were very low, due to lack of public education (21). Overall, there is a great need for increased sex education and basic medical education regarding infections in sub-Saharan Africa. Improving school infrastructure would also be needed in order for the education to occur.

According to the World Bank, women's health is determined by various factors and they are more vulnerable than men at each stage of their life, especially in their reproductive years (11). Figure 8 outlines the major biological and social predispositions of women. Gender violence is especially of concern in Zambia and other African countries. Reports from the Social Institutions and Gender Index conclude that an alarming high percentage of Zambian women have been victims of sexual assault (34). Sexual assault may entail having unprotected sex, which is a major risk factor for being infected with HPV and developing cervical cancer. Since sexual assault is quite high, individuals may have many sexual encounters or sexual partners, which is also a major risk

factor for HPV and cervical cancer. Traditionally, Zambian men have “reproductive rights over [their] wives” and culturally have “control” over their wives’ behaviors (34). If a woman’s husband does not want her to get screened for HPV or cervical cancer, she is much less willing and able to go to the clinic. Therefore, both sexual violence and gender inequality may be contributing to high incidence rates of HPV and cervical cancer despite the existence of screen and treat programs.

Geographical barriers, resource deprivation, and overall extreme poverty can prevent women from going to screen and treat clinics. The terrain in Zambia and other areas in sub-Saharan Africa can become quite difficult to travel through during flood seasons due to geographical separations that are created due to the floods (13). Roughly half of the women in one study reported that they had to walk, indicating that the clinic was not located in an area that was largely accessible. The physical inaccessibility of the clinic discouraged women, who were willing, to come to the clinic for screenings. Since not all clinics can be comfortably reached, home visits by physicians and/or the utilization of community health workers may help to eliminate this particular barrier of access. This strategy would be especially beneficial to residents of rural areas since they are more likely to live farther away from institutionalized clinics and screen and treat facilities and are also more likely to be in a state of extreme poverty (18).

The cost associated with healthcare and screenings also affects women’s decision about whether or not to seek care. Table 4 depicts the statistics

regarding poverty rates in Zambia during the 1990's (18). Zambia is a low-income country and healthcare fees are not affordable for most women and families. Because most families have very low incomes, they tend to use their income on basic necessities, including food, water, and shelter; this leaves healthcare as a lower priority since not getting screening for HPV and cervical cancer does not seem life-threatening. Not having enough food or water is more life threatening, and obtaining food and water persists as a high priority item for almost all people (6). The longer patients wait to seek care, the more severe their condition becomes, and the care to treat the condition becomes more costly (6). Cervical cancer care and treatment is especially costly, and many women of sub-Saharan Africa do not get screened for HPV well in advance, resulting in high incidence rates of cervical cancer. Table 13 and Figure 9 relay the correlation between age-adjusted cervical cancer incidence rates and poverty. According to Table 5, a significant majority of countries with high rates of cervical cancer are located in sub-Saharan African (19). Similarly, Figure 9 illustrates that the region with the highest percentage of people living on less than \$1.25 per day is that of sub-Saharan Africa (37). While these data cannot provide conclusions about a cause and effect relationship, it does imply a correlation between high poverty levels and vulnerability to cervical cancer.

Foreign aid has improved the barrier of resource deprivation to a large degree. Contributions made by charities, such as OxFam, and by non-profit organizations, such as Partners in Health, have led to the development of sound

infrastructures for hospitals and clinics in Zambia, Malawi, and other parts of sub-Saharan Africa. Large donations by health organizations have also helped to create more screen and treat programs in the region, thereby helping to reduce the incidence rates of cervical cancer (14). The implementation of free health care in rural areas by the Zambian government had a direct positive impact to the residents of rural areas, especially women (14). However, the social conditions that involve gender inequality, sexual violence, lack of health education, and continued misconceptions of cervical cancer still need to be more directly addressed and improved.

CONCLUSION

The major aims of this literature-based review were to understand the reasons for high incidence rates of cervical cancer in Sub-Saharan Africa and to provide meaningful proposals for healthcare access improvement in the region, and more specifically preventative techniques. The main focus within Sub-Saharan Africa was on the country of Zambia, since it has one of the highest incidence rates of cervical cancer in the world. The pathology of cervical cancer and HPV were both discussed, as well as the method of transmission of HPV via sexual activity. The importance of cervical cancer screening and treatment was also heavily discussed. Three main points of interest were analyzed, including: the correlation between the prevalence of HIV, HPV and cervical cancer, the accuracy and feasibility of screen and treat programs, and lastly, barriers such as a low level of education, women's misconceptions about cervical cancer, gender inequality, resource deprivation, and foreign aid.

A strong correlation and causal relationship was found between HPV and the development of cervical cancer. HIV/AIDS was shown to be a high risk factor for becoming infected with HPV since both can be transmitted via sexual contact. The majority of Zambian residents and other residents of sub-Saharan Africa were well informed and knowledgeable about HIV. However, a very few percentage of residents were aware of HPV and cervical cancer. For this reason, it is proposed that cervical cancer and HPV screening programs be modeled

after HIV preventative programs since the infrastructure has already been established, and this would ensure the optimization of resources and additional efficiencies for both of programs (20). HPV vaccinations are also relevant to the screening program since they were found to potentially decrease the number of invasive cervical cancer cases among HIV positive women. Overall, much collaboration between successfully running HIV programs and newly developing HPV and cervical cancer programs needs to occur.

The accuracy and feasibility of several different types of HPV screening methods were discussed. The screening methods included: VIA, VILI, VIAM, HC2, Pap Smears, and Cervicography. The methods were analyzed based on specificity, sensitivity, overall affordability, and feasibility according to research studies conducted. It was determined that the VIA approach was the best method to use in Zambia. Therefore, it is proposed that HPV and cervical cancer screen and treat programs implement the VIA method rather than other methods mentioned. Furthermore, LEEP was found to be an important and cost-effective method for treating cervical cancer. The development of LEEP in clinics and screen and treat programs would involve training of physicians and staff members in a step-wise process. LEEP has been shown to effectively remove cancerous lesions. It is proposed that LEEP be implemented into cervical cancer care treatment programs together with the VIA approach. Both will ultimately help to lower the high incidence rates of HPV and cervical cancer in Zambia and sub-Saharan Africa.

Various educational, social, geographical, and economical barriers were also considered in an effort to understand the underlying causes of high cervical cancer incidence rates. In Zambia and other surrounding countries, it was found that a lack of education, especially among young women exists. Because of this, young women have inaccurate and negative misconceptions regarding the causes of cervical cancer. The misconceptions contribute to their unwillingness and, in some cases, fear of getting screened or treated, which ultimately results in higher rates of cervical cancer incidence and more severe cases. Sexual violence, which is highly prevalent in Zambia, leads to unwanted sex and higher rates of STI, HIV, and HPV. It was also found that gender inequality also contribute to women's inability to seek care at screening and treatment clinics. It is proposed that educational infrastructures need to be improved and the Zambian government and culture needs to encourage women to be educated, especially about their own health. Other barriers of access to care that were determined include geographical barriers that make transportation difficult, high poverty rates, and resource deprivation. Appropriate funding and foreign aid can diminish nearly all barriers. It is proposed that the Zambian government and other countries of sub-Saharan Africa utilize and train their own nurses and physicians when developing the screen and treat programs. Emphasis needs to be placed upon program infrastructure, increasing resources, providing and

encouraging young women to attain a high level of education, especially sex education, and severely discouraging the practice of sexual violence and unprotected sex within Zambia and other regions of sub-Saharan Africa.

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VITA

