

Predictors of late presentation of cervical cancer in HIV-positive Ugandan women

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BACKGROUND

Cervical cancer is one of the leading causes of cancer deaths in women globally and 80% of these deaths occur in developing countries.^{1, 2} Cervical cancer is the most common cause of cancer deaths among women in Uganda and the rest of sub-Saharan Africa.³ Importantly, over 90% of patients with cervical cancer in Uganda present with late stage disease, contributing to Uganda's poor 5-year cervical cancer survival of less than 20%.^{4, 5}

HIV infection is associated with an increased risk of persistent infection with oncogenic human papillomavirus and progression of precancerous intraepithelial cervical lesions to invasive cervical cancer.^{6, 7} Of the 1.2 million people living with HIV in Uganda over 50% are women,^{8, 9} representing a large group at high risk of developing cervical cancer.

Studies have shown that screening is an effective strategy to prevent and reduce mortality of cervical cancer.^{10, 11} Most current HIV care guidelines in high income countries such as the US and Canada recommend that HIV-positive women are screened for cervical cancer as part of their baseline evaluation, again at six months, and yearly thereafter for those with normal results.^{6, 12-15} Though 80% of the global cervical cancer burden is carried by sub-Saharan Africa, screening for cervical cancer at least once is done for less than 5% of women in the region.^{16, 17}

The current HIV programs funded by PEPFAR (Presidential Emergency Fund for AIDS Relief), the Global Fund for AIDS, TB and Malaria, other international agencies, and non-governmental organizations have led to infrastructure improvement and expansion in the region.¹² These programs could be leveraged to improve cervical cancer survival by integrating prevention and screening strategies in routine HIV care. Moreover, more than half of those receiving care in these programs are women.

According to current WHO and most local guidelines, HIV-infected women are seen at 3-6 month intervals by a healthcare provider. The 'bundling' of non-communicable disease care with HIV treatment could afford unique opportunities for health promotion. This will take advantage of the personnel, physical infrastructure and care delivery systems already in place. Studies in sub-Saharan Africa have demonstrated cumulative increase in cervical cancer screening in both HIV positive and negative women as a result of integration of the intervention in HIV care.¹⁸⁻²⁰

One potential pitfall to integrating cervical cancer screening into HIV care delivery programs is the lack of a relationship between CD4 T-cell count and incidence of cervical cancer²¹. Unlike most other HIV-associated malignancies, cervical cancer incidence is not inversely proportional to CD4 T-cell count in HIV-infected

individuals. Due to the overwhelming burden of HIV disease in many sub-Saharan African countries, taken with the limited resources for HIV care, women with high CD4 T-cell counts are seen less regularly by HIV clinics in the region, often being told to return when their T-cell counts approach the level where treatment for their HIV disease is indicated or opportunistic infections are more common (below 350 cells / mm³). In this study we hypothesize that since HIV-positive patients with high CD4+ are not seen in care as frequently as those with low CD4+ who may be on ART, they present with more advanced cervical cancer. We also aim to identify other discrete factors associated with late stage cervical cancer presentation.

In the pathogenesis of cervical cancer, cervical intraepithelial neoplasia (CIN) precedes invasive carcinoma. This precancerous condition has three stages- CIN 1, CIN2 and CIN 3. It can take up to 10-12 years for CIN1 (the most common and most benign form of cervical intraepithelial neoplasia) to progress to invasive carcinoma. However, 90% of CIN 1 and 50% of CIN 2 will resolve spontaneously within two years, but 2% of women with CIN 3 have invasive carcinoma at the time and 20% would progress to invasive carcinoma without treatment²²⁻²⁶ This (CIN 3) is actually considered stage 0 invasive carcinoma of the cervix. This progression history provides opportunity to prevent the invasive carcinoma through screening since CIN 1-3 (which is not cancer) can be cured.^{22, 23}

According to the International Federation of Gynecology and Obstetrics (FIGO) staging system, invasive carcinoma of the cervix has stages I, II, III and IV. These are each further sub-staged into; Stage I-IA1, IA2, IB1 and IB2, stage II-IIA1, IIA2 and IIB, Stage IIIA and IIIB and stage IVA and IVB. All Stage I cervical cancer is limited to the cervix and therefore potentially surgically curable, stage II is beyond the cervix but not extending to the pelvic wall, stage III extends to the pelvic wall, and stage IV has distant metastases.^{24, 25}

This is the staging system used in Uganda and therefore cervical cancer staging in this study is based on the same system.

In cervical cancer prognosis, stage is the most important determinant of survival. The global overall 5-year survival rate (all stages put together) is 72% but it can be 92% for early stage cervical cancer (stage I-IIA).²⁶ The global average survival rates with treatment at each are; 80-90% for stage I, 50-65% for stage II, 25- 35% for stage III and 15% or less for stage IV. While stages I to IIA are considered early stage cervical cancer, in this study we categorized stage I and all of stage II as early stage cervical cancer since at this stage the cancer has not spread to the pelvic wall²⁴ and staging may not be accurate enough to differentiate between stage IIA and IIB in 100% of patients.

METHODS

Study design, sites, setting and population

This was a cross-sectional study in which both quantitative and qualitative data were collected during June and July 2012. To collect quantitative data, cervical cancer patients were identified at the gynaecological oncology ward of Mulago Hospital, Uganda's largest national referral hospital and the teaching hospital for Makerere University College of in Kampala. All women presenting to the gyaenecological oncology ward on days during which the study was being conducted were consecutively approached for participation in the study. Inclusion criteria included; age ≥ 18 years, laboratory confirmed HIV positive status, histopathological diagnosis of cervical cancer, and availability of staging of the cervical cancer. Women who were not able to complete study procedures were excluded.

Qualitative data were collected using Focus Group Discussions (FGDs) with HIV care clinic staff of Mulago Hospital Communicable Disease Clinic (CDC), The AIDS Support Organization (TASO), and Mildmay Centre Uganda. Staff that formed the FGDs were selected with the help of the clinic managers who were contacted two weeks before and requested to identify the most appropriate date to hold the FGD at their clinic. They were also requested to identify 1 or 2 staff in each category of doctors, nurses, counselors, laboratory personnel and pharmacy personnel who fulfilled the inclusion criteria of age ≥ 18 years and having worked with the clinic for not less than one year. Staff who could not participate in a FGD for at least one hour were excluded.

Data collection methods

Quantitative data collection

A standard data abstraction form was developed prior to study initiation and used uniformly to review participants' medical records. Cervical cancer stage was abstracted from the participants' hospital charts as documented by the attending physician. After the abstraction, participants were interviewed using a standard questionnaire which was pilot tested prior to enrollment of the first participant. After the interview, a blood sample was obtained for CD4 T-cell count testing.

Qualitative data collection

Three focus group discussions (FGDs) with 7-10 participants each were held, one in each of the three HIV clinics. The FGD participants included doctors, nurses, counselors, social workers, laboratory staff, pharmacy

staff and managers. The participants were purposefully recruited with the help of the clinic management. The FGDs took place in a room within the clinic facility and guide questions were used to keep the discussion focused. Some of the questions included: What can you tell me about cervical cancer risk of the HIV positive women you care for? What do you think the HIV positive women who attend your clinic know about their cervical cancer risk? What do you think about making cervical cancer awareness and screening part of routine HIV care? The FGDs were recorded using a voice recorder and notes of non-verbal expression were written. Each FDG lasted about one and a half hours.

Data management and analysis

Quantitative data

Quantitative data was entered and cleaned using Epidata 3.1 database, exported to Stata 12 statistical software and analyzed for summary statistics, proportions in percentages and associations. The probability value and correlation were used as statistical inferential tests.

Stage was defined using FIGO staging system. While stages I to IIA are considered early stage cervical cancer, in this study we categorized stage I and all of stage II as early stage cervical cancer since at this stage the cancer has not spread to the pelvic wall²⁴ and staging may not be accurate enough to differentiate between stage IIA and IIB in 100% of patients.

Qualitative data

The recordings of FGDs were transcribed verbatim and summarized. The texts were analyzed using manifest content analysis technique, themes teased out and merged and conclusions made.

Quality control

All study staff were trained on study procedures. Completed study questionnaires were double entered and data discrepancies were reconciled prior to analysis.

Ethical and legal considerations

The study was approved by Institutional Review Boards (IRBs) of University of Washington and Mulago Hospital, Uganda National Council for Science and Technology (UNCST) and the Ugandan President's Office. Permission was also granted by the study site authorities and informed consent was obtained from every participant prior to the study procedures.

RESULTS

Demographic characteristics

We approached 45 women for participation in the study of whom 40 (88.9%) met the criteria for inclusion and completed the study procedures. Characteristics of the 40 women who participated are summarized in **Table 1**. Mean age of the women was 40 (range 25 - 68). All of them had given birth, and over half (52.5%) had given birth five or more times. Eighty percent (32) were married and 20% (12) had either separated or divorced. All of them had received a form of formal education with 65% having attended primary school and 35% secondary school. Regarding their religious affiliation, 45% were Roman Catholic, 27.5% were Anglican and 27.5% belonged to other religions.

Cervical cancer stage

Cervical cancer distribution by stage is shown in **Figure 1**. Majority of the women who participated had cervical cancer stage II (40%) and 4.4% had stage IV. On categorizing stage I and II as early stage and stage III and IV as late stage, 53.3% and 35.6% had early and late stage cervical cancer respectively.

Lifestyle

Sexual behavior

The lowest age of sexual debut was 14 years, and half (50%) of the women had experienced their sexual debut at 16 years or younger. Ninety percent (36/40) of the women had had more than one sexual partner in their life time.

HIV history

Seventeen (42.5%) participants had tested HIV positive for time more than five years before the study and 12 (30%) had done so 5 years or less. Thirty three (82.5%) were referred to an HIV clinic when they initially tested HIV positive and 37 (92.5%) of the women were enrolled in HIV care. Of these, 15 (40.5%) had been enrolled in HIV care for over 5 years, 12 (32.4%) for 5 years or less and 10 (27%) could not remember for how long they had been enrolled in HIV care. Thirty (75%) were taking Highly Antiretroviral drugs (HAART) at the time of the study. Twelve (30%) had been changed from one combination of ARVs to another; 3 for treatment failure, 3 for lack of drugs and others for different reasons.

CD4+ T-cell count

Median CD4 T-cell count was 324 cell/mm³ and range was 30 to 685. Distribution according to selected categories of levels of immunity is shown in **Figure 4**. Seventeen 17 (37.8%) of the participants had 200 to < 3500 cell/mm³, 8 (17.8%) had < 200 and 5 (11.1%) > 500.

Cervical Cancer History

All participants knew that they were being treated for cervical cancer on the gynecological oncology ward at the time of the study. Regarding the symptoms experienced at the beginning of the illness, majority of the women (82.5%), had experienced vaginal bleeding at the beginning of the illness, 28 (70%) had experienced vaginal discharge, 12 (30%); weight loss, 10 (25%); pain during vaginal intercourse and 3 (7.5%) had noticed genital swellings (warts) as the first symptom of the illness. Nine (22.5%) suspected it was cancer when they first noticed symptoms. Four (10%) of the women who participated in the study had been with symptoms for over 6 months before they visited a health facility, and 2 (5%) sought care within the first week of noticing symptoms. Seventeen (42.5%) did between one week and one month of noticing symptoms and 13 (32.5%) sought care between one month and six months. Twenty four (60%) of the women who participated in the study had their cervical cancer diagnosis made in Mulago hospital-the study site and only 2 (5%) were diagnosed in HIV care but up to 10 (25%) had been referred from HIV care.

Bivariate Analysis

We evaluated predictors of late stage cervical cancer including demographic characteristics, sexual behaviors, HIV history and CD4+ T-cell count as shown in **Tables 2, 3, 4 and 5** respectively. We found most of these variables were not associated with late stage cervical cancer in bivariate analysis, except for age at sexual debut and lifetime sexual partners. Greater likelihood of presenting with late stage cervical cancer was associated with having first vaginal sexual intercourse at the age of sixteen or below (OR = 0.273, p = 0.043) and having two or more sexual partners in a woman's life time (OR=1.800, p=0.045). Importantly, CD4+ T-cell count was not associated with late stage cervical cancer (**Figure 4**).

Results from Focus Group Discussions

Data from all the three FGDs showed that HIV care personnel in the three HIV clinics know that HIV-positive women are at high risk for cervical cancer. The HIV care personnel who participated in FGDs also said that this high risk is because the HIV disease compromises the immunity of these women. It was also reported

that many HIV-positive women have more than one sexual partner and some do not practice safe sex. The HIV care personnel also said that to some of the women, being HIV-positive is a disincentive to have cervical cancer screening. “Some say, ‘I already have HIV, I do not want to be told that I have cancer also.’”

Regarding whether HIV-positive women receiving care know that they are at high risk for cervical cancer it was very clear from the FGD participants that many of these women do not know that they are at high risk. During one FGD, a participant said, “Most of these HIV-positive women live in the dark; they don’t know much about cervical cancer.” It also came out of the FGDs that some women have wrong information which is passed one from fellow women during peer to peer information sharing. These are usually women who have had cervical cancer screening done for them but do not know why they had to have certain procedures like cervical biopsy done. When they share their experience, they share it as though every woman who goes for cervical cancer screening must have the same procedures done not knowing that it is what the examiner finds on examination that guides what procedures are done. Such information sharing can lead to misinformation among some HIV-positive women. Another reason why these women do not know about their cervical cancer risk is that some care providers in HIV clinics do not give out this information, though they know that cervical cancer is one of the conditions these women are likely to present with because the guidelines by which they work do not include anything concerning cancer of the cervix neither awareness nor screening. During one of the FGDs in one of the clinics where cervical cancer screening is currently being offered, it was said that cervical cancer education by the health personnel takes place early in the morning before some clients come to the clinic. This means that because some women who are HIV positive though enrolled in care, miss awareness and probably screening because they live far from their HIV care clinics or they for some other reasons the service is offered at a time they cannot be available to access the service.

It also came out of all three FGDs that cervical cancer screening should be made routine for all HIV positive women. One participant went on to say, “It is possible to screen all women attending our clinic routinely but a lot needs to be done for the intervention to succeed. Some barriers must be addressed!” However, during another FGD in an HIV clinic in a government facility, one participant also said, “...without monetary incentives staff in our HIV clinic will do cervical cancer screening if there is a policy in place and the procedures are included in HIV care guidelines but if funds can be found, the staff will be glad to receive an incentive.”

The barriers to cervical cancer screening identified by the FGDs are;

1. Absence of policy regarding cervical cancer in HIV-positive women in Uganda and HIV care practice guidelines which are silent about the issue. One of the participants said, “though we are a non-governmental organization we implement government policy” Two of the FGDs in the NGO clinics clearly said that without a government policy in place even though they are not funded by government, they may never do cervical cancer screening because their funders base their funding on what government policy requires. Indeed one participant said, “without a policy in place omission is not a crime”. Meaning that even though they know it is important to screen the HIV-positive women they care for, they do not make much effort because it is not something they judge their service by.
2. Inadequate manpower: This was mainly emphasized during the FGD in the HIV clinic in the government hospital. Participants said, “We are already over burdened by the number of patients, adding more tasks to staff may compromise HIV care.” “The system may crush” one participant added.
3. Inadequate training of HIV care providers to competently screen for cervical cancer. One participant, a manager who is also a medical doctor further said that though medical workers acquire a number of different procedural skills during their pre-service training, there is always a need for in-service training to implement some policies. He went on to say, "for example none of us here is trained, yet we care for over 100,000 clients a year majority of whom are women. Imagine how many we would be reaching out to!" This was during a FGD in an HIV clinic that does not offer cervical cancer screening.
4. Insufficient funds: All FGDs raised this as a major potential barrier. This was raised during the FGDs in the HIV clinic in a government hospital and the non-government HIV clinic which does not offer cervical cancer screening. The participants in the HIV clinic in a government hospital said we do not have money to procure sundries, speculums, acetic acid or pap kits and other supplies that are specific to cervical cancer awareness and screening. “I am not sure government will avail these funds”, said one participant during the FGD in the clinic in a government hospital. “I have not seen anyone else using government money to screen except Mulago Hospital and Uganda Cancer Institute. We will need to convince funders to fund the service”, said a manager in the non-government HIV clinic which does not offer the service.
5. The FGDs also raised another category of challenges which we called implementation challenges. These are to do with utilization of the available infrastructural space, patient scheduling and team formation in a way that will ensure the intervention does not negatively impact on the already on-going services and it is sustainable.

Listening to the FGDs, it was clear that HIV clinic personnel knew what their roles would be in the implementation process of cervical cancer screening in routine HIV care and were indeed ready to perform them. However, some indicated that it is after training that every cadre would be clearly sure of his or her roles and that the specifics of the intervention would define ‘what is done by who’ much more clearly. In one of the FGDs, a laboratory technician said, “If staining of pap smears will need to be done in the laboratory, I’m ready to do it as long as the supplies to use are available.” A nurse also said, “This integration should not involve only a few people, everyone should participate.” A manager who is also a doctor said, “Involving everyone in the clinic will protect the intervention from failing in case someone happens not to be available.”

A participant-an expert patient counselor said, “it is better when the service is provided in the same room as the rest of the services, such that when a client goes in a room to be seen by a clinician cervical cancer screening is also done there. This will increase acceptability and uptake because if the service is provided in a separate room, some clients may hesitate to go in for it for fear of being stigmatized by their fellow clients who will see them entering the room. A female doctor participant agreed saying, “‘One Room for All’ would be a good idea!” Discussions of this kind of detail show that even at the time of this research, HIV care providers already had a fair idea of what needs to be done to ensure that the integration of cervical cancer awareness and screening in HIV care is a success.

In order to have a sense of how HIV care providers view the concept of integrating interventions targeting non-communicable diseases in HIV care, we brought up the idea for discussion in all the FGDs. The discussion guide question was, “**What are your views about integration of interventions targeting other chronic non-communicable diseases in routine HIV care?**” All the data shows the HIV care personnel consider it good but are not sure how feasible it is given the limited resources in terms of manpower, technical knowhow, funds and all that may be needed to implement the interventions. One of the examples given is the need to integrate HIV care guidelines to include these interventions. Participants also raised a concern of a possibility ‘over integrating’ to include specialized services which may not be sustainable because of lack of specialized personnel or even the necessary resources. They said that moreover many HIV care programs are donor funded and they have to adhere to what they agree upon with the funders or else risk losing the funding. Other potential barriers to integrating interventions targeting other non-communicable diseases identified in FGDs were similar to those identifies for cervical cancer awareness and screening intervention.

Other views regarding integration of cervical cancer awareness and screening in routine HIV care raised by HIV care personnel in the FGDs include;

1. Ministry of health should take the lead by developing a policy and ensuring that all HIV-positive women are given cervical cancer prevention and screening services,
2. The knowledge gaps both among care providers and patients in HIV care should be addressed as priority in the integration process.
3. Aggressive advocacy as is done for malaria through media and other means can increase political will and improve the odds for the intervention to succeed and be sustainable.

DISCUSSION

Forty percent of patients in this study had late cervical cancer (FIGO stage III and IV). This percentage is much lower than what has been reported by other studies in sub-Saharan Africa involving general cervical cancer patients which have reported more than 70%.^{27, 28} A similar study done in Sudan on a cancer registry data of general cervical cancer women reported up to 72% to have late stage (FIGO stage III and IV) and another one in Nigeria reported even a much higher proportion (86%).^{29, 30} A lower proportion (47.3%) of late stage cervical cancer was reported by study in Tanzania.³¹ The fact that our cohort had less than half late stage disease may be because over 90% of these patients were enrolled in HIV care which gave them an opportunity to be in contact with health care providers and could have facilitated earlier diagnosis. Although only 5% were diagnosed in HIV clinics and 59.5% were diagnosed in Mulago hospital (the study site), regular interaction with health care providers in HIV clinics could have encouraged the patients to present their complaints earlier than if they were not enrolled in any care as is the case for many HIV-negative women.

Early age at first sexual debut (≤ 16 years of age) and multiple life time sexual partners (≥ 2) were associated with late stage cervical cancer. These are well known risk factors for cervical cancer in the general population. This may mean that women who are at risk of suffering from cervical cancer in a setting of limited access to early identification services are also at risk of presenting with late stage disease. These findings are consistent with results from other studies.^{32, 33} This means that without an effective prevention program that can reduce the population's exposure to risky behaviors screening for early identification is necessary to reduce late stage presentation which ultimately improves survival. Multiple births, low average monthly household income and low education level also seem to increase the likelihood that an HIV-positive woman in this study presents with late stage cervical cancer. This agrees with findings reported by other studies.³⁴⁻³⁶

HIV history including being on HAART and CD4+ T-cell count was not associated with late stage cervical cancer at presentation as shown by **Table 4, 5** and **Figure 4**. This is consistent with several other

studies.^{34,35} This poses a challenge of selecting who of the HIV-positive women should be prioritized to be screened. Implying that all HIV-positive women need to be empowered with information regarding their cervical cancer risk and screened if effective control of cervical cancer among this high risk population is to be realized.

Another likely contributor to late stage cervical cancer presentation is lack of cancer awareness among HIV-positive women. From the FGD results, a majority of the HIV positive women have no access to information about cervical cancer because though over 92.5% are enrolled in care. There is no cervical cancer awareness and some HIV care clinics. The FGD findings also show that even in the clinics where the service is available not every enrolled client accesses it. Up to 10% of the patients in this study had symptoms for over six months before seeking hospital care despite 55% of them living within 5 km from a health facility. This finding could be because they did not know that the symptoms could be of cancer of the cervix. The FGD participant also pointed out that these women are living in the dark. These findings are consistent with findings in earlier studies in Nigeria and Sudan.^{36,37}

Lack of policy and HIV care guidelines that include cervical cancer awareness and or screening in the care process likely contributes to presentation with late stage cervical cancer among HIV-positive women. As data from the FGDs showed, without a policy in place, omission is not a crime. This occurs despite the fact that in the era of Highly Active Antiretroviral Therapy (HAART), cervical cancer screening of HIV-positive women is highly recommended and is done in many other countries.^{38,39} This gap stands in the way of the HIV care programs that are donor funded because they cannot solicit for funds for a service that is not supported by policy and their care guidelines.⁴⁰ According to one of the FGD participants, we know cervical cancer is one of the conditions these women are likely to present with but we do not look for it because it is not part of our care protocols and we have an excess work load.

Most of the other barriers including insufficient funds, insufficient infrastructure and insufficient personnel raised by HIV care providers in this study can be dealt with when a policy is in place. Moreover, many developing countries have HAART policies in place but do not have enough funds to provide the treatment to all who need it in their countries. However policies provide a platform for advocates to lobby government and donors to support such services.^{41,42} For instance, Uganda has managed to bring down the HIV prevalence from over 15% to 6.5% national average with a national HIV program that depends almost entirely on donor funds^{43,44} In addition to this, cost effective approaches to cervical cancer screening are now available and Uganda could take advantage of these reasonably cheap to formulate a policy and guidelines.⁴⁵

Limitation

A major limitation in this study is a small sample size. The study lacks power to assess associations between some factors such as demographic characteristic and HIV history with late stage cervical cancer at presentation.

Conclusions

Majority of the HIV-positive women who participated in this study presented with late stage cervical cancer. The results also suggest that HIV-positive women who have experience their first vaginal sexual intercourse at a young age and those who have multiple sexual partners are likely to present with late stage cervical cancer.

They also suggest that being enrolled in HIV care, being on HAART and CD4+ T-cell count may have an influence on cervical cancer stage at presentation. There is lack of cervical cancer awareness among HIV-positive women and many do not know that they are at high risk of suffering from the cancer.

Importantly, absence of policy and HIV care guidelines that include cervical screening may be a major reason why the intervention has not be considered by many HIV care programs in Uganda. Staffs in HIV care understand that HIV-positive women are at high risk for cervical cancer and may provide cervical cancer screening without monetary incentives if the policy is in place and HIV care guidelines include cervical cancer screening procedures.

Recommendations

We recommend collection of more data in this study so that other predictors of late stage cervical cancer can be assessed. Cervical cancer awareness programs should also be designed and implemented through mass media, schools, hospitals and importantly HIV clinics. The Ugandan ministry of health should consider developing a policy on cervical cancer screening and integrating Uganda national HIV care guidelines to include the intervention. A feasibility study may be done to predict the success of the intervention.

TABLES AND FIGURES

Table 1: Participants' characteristics

Characteristic	Total % (N=40)
Age	
Median (range)	40 (25 – 68)
Religion	
Anglican	27.5
Roman Catholic	45.0
Others Religions	27.5
Education level	
At most primary school	65.0
At least secondary school	35.0
Household average monthly income	
Less than 150,000	62.5
Greater than 150,000	37.5
Distance from Health facility	
<5km	55.0
>5km	45.0
Marital status	
Separated/widowed/Divorced	20.0
Married	80.0
Number of child births	
1 – 4	47.5
5+	52.5

Table 2: Relationship of predictors and cervical cancer stage

Background characteristic	Early % (n=24)	Late % (n=16)	Total % (n=40)	p-value	Corr.	Odds ratio
Age						
Below 40 years	45.8	37.5	42.5	0.557	0.144	
40 – 49 years	37.5	31.2	35.0			
50 and above years	16.7	31.2	22.5			
Religion						
Anglican	20.8	37.5	27.5	0.506	-0.138	
Roman Catholic	50.0	37.5	45.0			
Others	29.2	25.0	27.5			
Education level						
Primary school	66.7	62.5	65.0	0.787	0.043	1.20
Secondary school	33.3	37.5	35.0			
Average monthly household income						
Less than 150,000	62.5	62.5	62.5	1.00	0.000	1.000
Greater than 150,000	37.5	37.5	37.5			
Distance from nearest health facility						
<5km	58.3	50.0	55.0	0.604	0.082	1.400
>5km	41.7	50.0	45.0			
Marital status						
Separated/widowed/Divorced	16.7	25.0	20.0	0.519	-0.102	0.600
Married	83.3	75.0	80.0			

	Early	Late	Total	p-value	Corr.	Odds ratio
	%	%	%			
Background characteristic	(n=24)	(n=16)	(n=40)			
Number of child births						
1 – 4	45.8	50.0	47.5	0.796	-0.041	0.846
5+	54.2	50.0	52.5			

Table 3: Sexual behaviors and Stage of cervical cancer

Characteristics (Predictors)	Early (I and II) n=24 (60%)	Late (III and IV) n=16 (40%)	Total % (n=40)	p-value	Corr.	Odds ratio
Age at sexual debut						
16 or less	37.5	68.8	50.0	0.043	-0.306	0.273
17 or above	62.5	31.2	50.0			
Number of lifetime sexual partners						
Only 1 partner	16.7	0.0	10.0	0.045	0.272	1.800
More than 1 partner	83.3	100.0	90.0			

Table 4: HIV history variables and cervical cancer stage

Characteristics (Predictors)	Early (I and II) % n=24	Late (III and IV) % n=16	Total % (n=40)	p-value	Corr.	Odds ratio
Period knowing HIV-positive status						
5 or less years	29.2	31.2	30.0	0.858	0.027	
Above 5 years	45.8	37.5	42.5			
Don't know	25.0	31.2	27.5			
Referred to HIV care after testing HIV positive						
Yes	87.5	75.0	82.5	0.308	0.161	2.333
No	12.5	25.0	17.5			
Enrolled in HIV care						
Yes	95.8	87.5	92.5	0.327	0.155	3.286
No	4.2	12.5	7.5			
Years enrolled in HIV care						
5 years and below	33.3	25.0	30.0	0.463	0.168	
6 – 26 years	41.7	31.2	37.5			
Don't know	25.0	43.8	32.5			
On HAART						
Yes	79.2	68.8	75.0	0.456	0.118	1.727
No	20.8	31.2	25.0			

Table 5: Relationship between CD4+ T-Cell count and cervical cancer stage

CD4 count (Cells/mm ³)	Early % (n=24)	Late % (n=16)	Total % (n=40)	p-value	Corr.
50 to < 200	12.5	20.0	15.4	0.562	-0.108
200 to < 350	37.5	46.7	41.0		
350 to < 500	41.7	20.0	33.3		
≥ 500	8.3	13.3	10.3		

Figure 1: Cervical cancer stage distribution

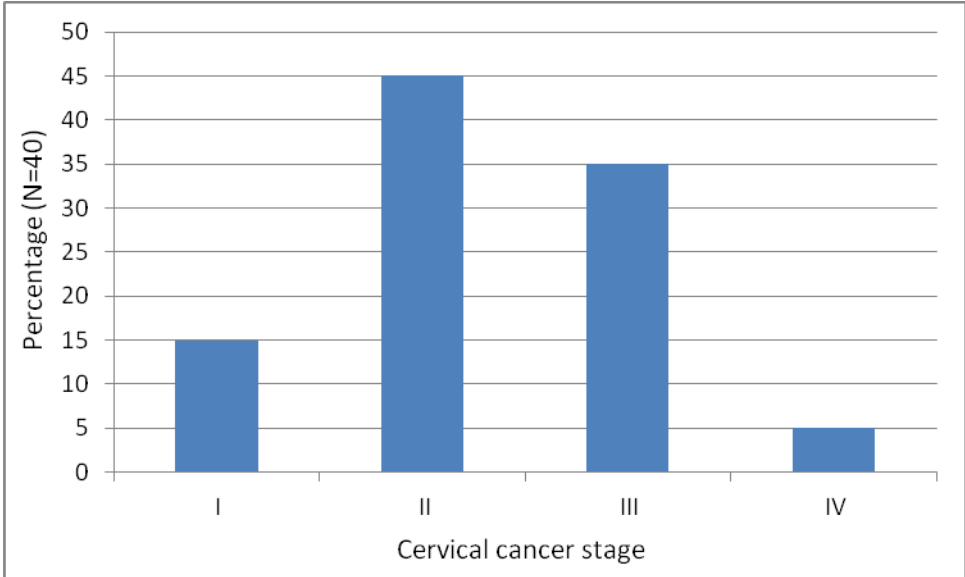


Figure 2: Age at sexual debut Vs cervical cancer stage

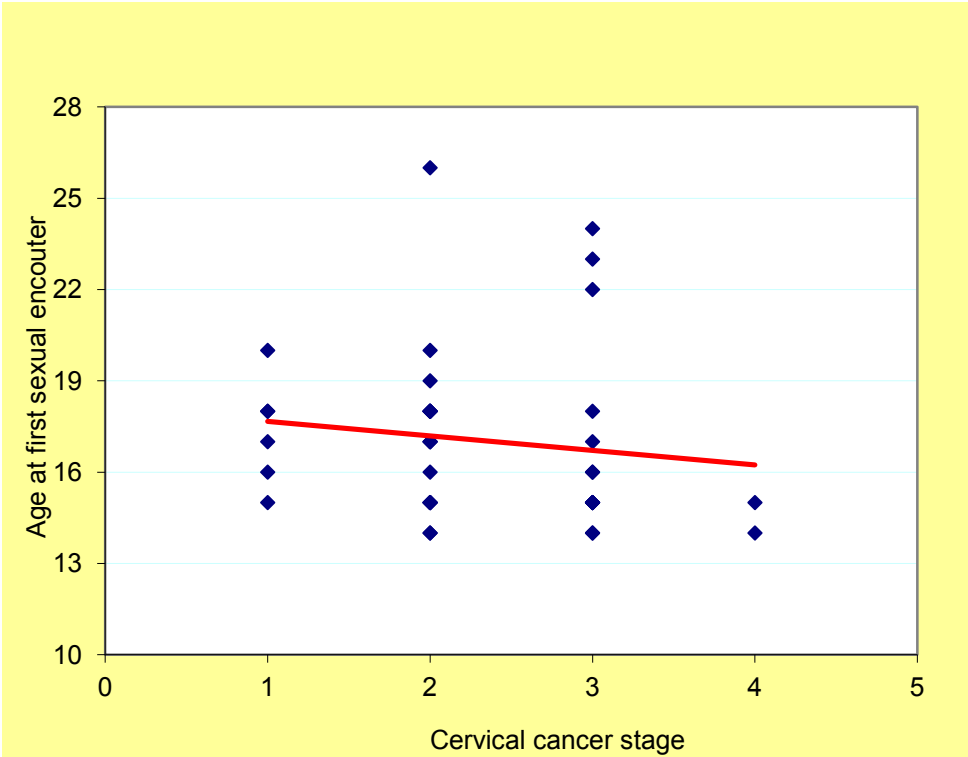


Figure 3: Distribution of CD4 counts by categories

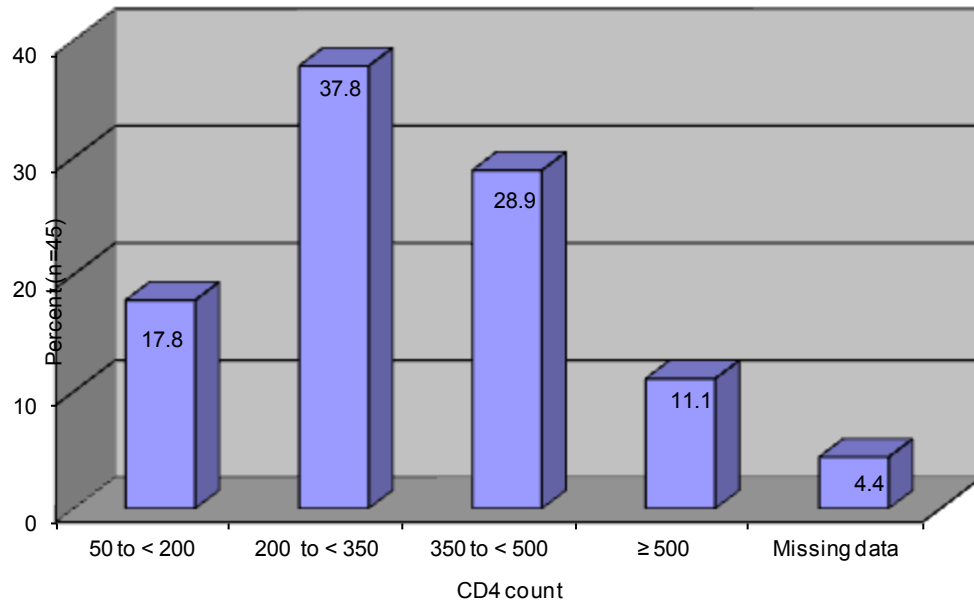
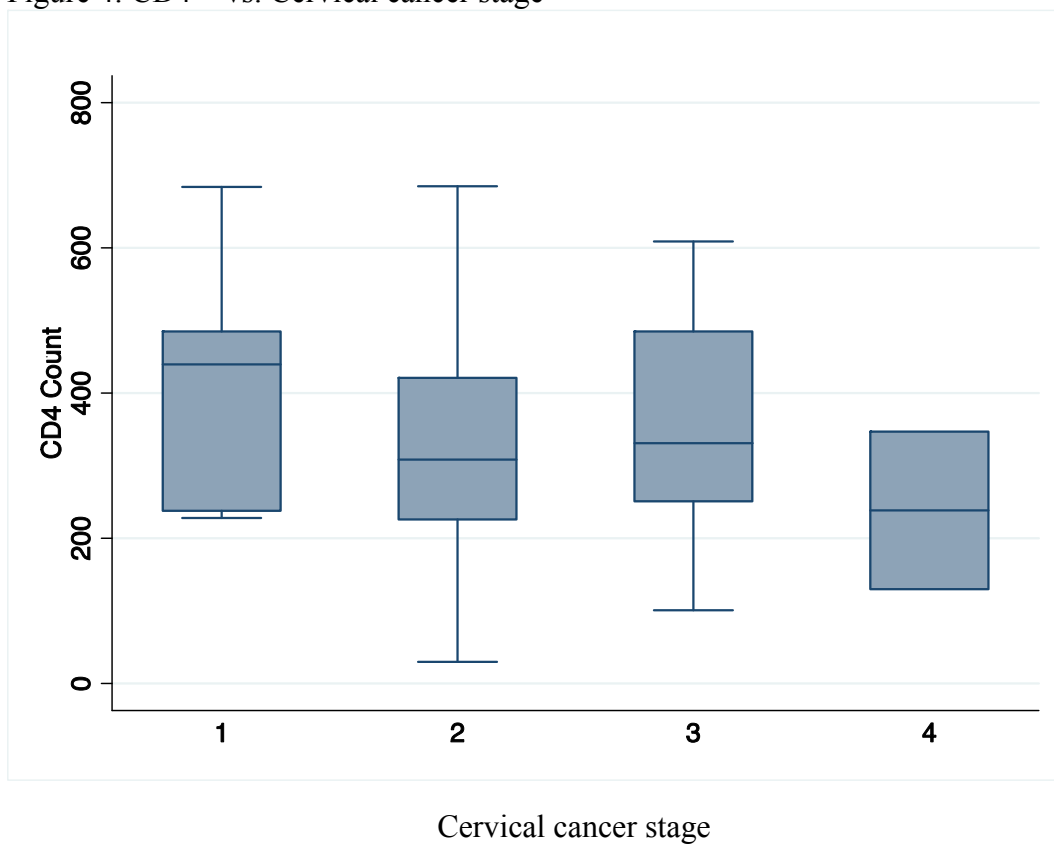


Figure 4: CD4+ vs. Cervical cancer stage



LIST OF REFERENCES/BIBLIOGRAPHY

1. Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. 2010; 19(8): 1893-907.
2. Shanta V, Krishnamurthi S, Gajalakshmi CK, Swaminathan R, Ravichandran K. Epidemiology of cancer of the cervix: global and national perspective. *Journal of the Indian Medical Association*. 2000; 98(2): 49-52.
3. Gondos A, Brenner H, Wabinga H, Parkin DM. Cancer survival in Kampala, Uganda. *British Journal of Cancer*. 2005; 92(9): 1808-12.
4. Gondos A, Brenner H, Wabinga H, Parkin DM. Cancer survival in Kampala, Uganda. *British journal of cancer*. 2005; 92(9): 1808-12.
5. Wabinga H, Parkin DM, Namboozee S, Amero J. Cancer survival in Kampala, Uganda, 1993-1997. *IARC scientific publications*. 2011; (162): 243-7.
6. Ahr A, Rody A, Cimposiau C, Faul-Burber C, Kissler S, Kaufmann M, et al. [Cervical cancer screening of HIV-positive women: is a prolongation of the screening interval meaningful?]. *Zentralbl Gynakol*. 2006; 128(5): 242-5.
7. Zhang YX, Xiong Y, Gui XE, Rong YP, Cai HB, Ma L. [Analysis of cervical HPV infection in HIV positive Chinese women]. *Zhonghua fu chan ke za zhi*. 2012; 47(3): 185-90.
8. Hladik W, Musinguzi J, Kirungi W, Opio A, Stover J, Kaharuza F, et al. The estimated burden of HIV/AIDS in Uganda, 2005-2010. *Aids*. 2008; 22(4): 503.
9. Mermin J, Musinguzi J, Opio A, Kirungi W, Ekwaru JP, Hladik W, et al. Risk factors for recent HIV infection in Uganda. *JAMA: The Journal of the American Medical Association*. 2008; 300(5): 540-9.
10. Peto J, Gilham C, Fletcher O, Matthews FE. The cervical cancer epidemic that screening has prevented in the UK. *The Lancet*. 2004; 364(9430): 249-56.
11. Sankaranarayanan R, Esmey PO, Rajkumar R, Muwonge R, Swaminathan R, Shanthakumari S, et al. Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. *The Lancet*. 2007; 370(9585): 398-406.
12. Franceschi S, Jaffe H. Cervical cancer screening of women living with HIV infection: a must in the era of antiretroviral therapy. *Clin Infect Dis*. 2007; 45(4): 510-3.
13. Bardaro L. Cervical cancer screening issues for HIV positive women: a physician's perspective. *BETA*. 1996: 35-8.
14. Oster AM, Sullivan PS, Blair JM. Prevalence of cervical cancer screening of HIV-infected women in the United States. *J Acquir Immune Defic Syndr*. 2009; 51(4): 430-6.
15. Heard I. Cervical disease and cancer in HIV positive women. Recommendations for screening and diagnosis. *Med Wieku Rozwoj*. 2003; 7(4 Pt 1): 479-85.
16. Somdyala NIM, Bradshaw D, Gelderblom WCA, Parkin DM. Cancer incidence in a rural population of South Africa, 1998-2002. *International Journal of Cancer*. 2010; 127(10): 2420-9.
17. Anorlu RI. Cervical cancer: the sub-Saharan African perspective. *Reprod Health Matters*. 2008; 16(32): 41-9.
18. Mwanahamuntu MH, Sahasrabudde VV, Pfaendler KS, Mudenda V, Hicks ML, Vermund SH, et al. Implementation of 'see-and-treat' cervical cancer prevention services linked to HIV care in Zambia. *Aids*. 2009: 1.
19. Ward J, Donnelly N, Holt P. Impact in general practice of the policies of the organised approach to preventing cancer of the cervix. *Aust N Z J Public Health*. 1998; 22(3 Suppl): 336-41.

20. Walker JJ, Brewster D, Gould A, Raab GM. Trends in incidence of and mortality from invasive cancer of the uterine cervix in Scotland (1975-1994). *Public Health*. 1998; 112(6): 373-8.
21. Biggar RJ, Chaturvedi AK, Goedert JJ, Engels EA. AIDS-Related Cancer and Severity of Immunosuppression in Persons With AIDS. *J Natl Cancer Inst*. 2007; 99(12): 962-72.
22. Jones RW. The natural history of cervical and vulvar intraepithelial neoplasia. *American journal of obstetrics and gynecology*. 2010; 202(3): e12-3.
23. Cantor SB, Atkinson EN, Cardenas-Turanzas M, Benedet JL, Follen M, MacAulay C. Natural history of cervical intraepithelial neoplasia: a meta-analysis. *Acta cytologica*. 2005; 49(4): 405-15.
24. Pecorelli S, Odicino F. Cervical cancer staging. *The Cancer Journal*. 2003; 9(5): 390.
25. Petignat P, Loubeyre P. Should we modify the current FIGO staging system for early-stage cervical cancer? Expert review of anticancer therapy. 2008; 8(7): 1015-7.
26. Eggen T, Arnes M, Moe B, Straume B, Orbo A. Prognosis of early cervical cancer (FIGO Stages IA2, IB, and IIA) in northern Norway predicted by malignancy grading score and objective morphometric image analysis. *International journal of gynecological pathology : official journal of the International Society of Gynecological Pathologists*. 2007; 26(4): 447-56.
27. Udigwe GO, Ogabido CA. A clinico-pathological study of cervical carcinoma in South Eastern Nigeria; a five-year retrospective study. *Nigerian journal of clinical practice*. 2008; 11(3): 202-5.
28. Adewuyi SA, Shittu SO, Rafindadi AH. Sociodemographic and clinicopathologic characterization of cervical cancers in northern Nigeria. *European journal of gynaecological oncology*. 2008; 29(1): 61-4.
29. Ibrahim A, Rasch V, Pukkala E, Aro AR. Predictors of cervical cancer being at an advanced stage at diagnosis in Sudan. *International Journal of Women's Health*. 2011; 3: 385.
30. Umezulike AC, Tabansi SN, Ewunonu HA, Nwana EJ. Epidemiological characteristics of carcinoma of the cervix in the Federal capital Territory of Nigeria. *Nigerian journal of clinical practice*. 2007; 10(2): 143-6.
31. Matovelo D, Magoma M, Rambau P, Massinde A, Masalu N. HIV serostatus and tumor differentiation among patients with cervical cancer at Bugando Medical Centre. *BMC Research Notes*. 2012; 5(1): 406.
32. Mandelblatt J, Andrews H, Kerner J, Zauber A, Burnett W. Determinants of late stage diagnosis of breast and cervical cancer: the impact of age, race, social class, and hospital type. *Am J Public Health*. 1991; 81(5): 646-9.
33. Ferrante JM, Gonzalez EC, Roetzheim RG, Pal N, Woodard L. Clinical and demographic predictors of late-stage cervical cancer. *Arch Fam Med*. 2000; 9(5): 439-45.
34. Biggar RJ, Chaturvedi AK, Goedert JJ, Engels EA. AIDS-related cancer and severity of immunosuppression in persons with AIDS. *J Natl Cancer Inst*. 2007; 99(12): 962-72.
35. Nkoua-Mbon JB, Kocko I, Ampion EE. [Cervical cancer associated with HIV in young Congolese women. Preliminary study]. *Cancer Radiother*. 2004; 8(4): 277-8.
36. Massad LS, Evans CT, Weber KM, Goderre JL, Hessol NA, Henry D, et al. Changes in knowledge of cervical cancer prevention and human papillomavirus among women with human immunodeficiency virus. *Obstetrics & Gynecology*. 2010; 116(4): 941.
37. Rabiou KA, Akinbami AA, Adewunmi AA, Akinola OI, Wright KO. The need to incorporate routine cervical cancer counselling and screening in the management of HIV positive women in Nigeria. *Asian Pacific journal of cancer prevention : APJCP*. 2011; 12(5): 1211-4.
38. Leece P, Kendall C, Touchie C, Pottie K, Angel JB, Jaffey J. Cervical cancer screening among HIV-positive women. *Canadian Family Physician*. 2010; 56(12): e425-e31.
39. Franceschi S, Jaffe H. Cervical cancer screening of women living with HIV infection: a must in the era of antiretroviral therapy. *Clinical infectious diseases*. 2007; 45(4): 510.

40. Goldie SJ, Kuhn L, Denny L, Pollack A, Wright TC. Policy analysis of cervical cancer screening strategies in low-resource settings. *JAMA: The Journal of the American Medical Association*. 2001; 285(24): 3107-15.
41. Balakrishnan P, Solomon S, Kumarasamy N, Mayer KH. Low-cost monitoring of HIV infected individuals on highly active antiretroviral therapy (HAART) in developing countries. *Indian J Med Res*. 2005; 121(4): 345-55.
42. Bogaards JA, Goudsmit J. Meeting the immense need for HAART in resource-poor settings. *Journal of Antimicrobial Chemotherapy*. 2003; 52(5): 743-6.
43. Green EC, Halperin DT, Nantulya V, Hogle JA. Uganda's HIV prevention success: the role of sexual behavior change and the national response. *AIDS and Behavior*. 2006; 10(4): 335-46.
44. Gray RH, Serwadda D, Kigozi G, Nalugoda F, Wawer MJ. Uganda's HIV prevention success: The role of sexual behavior change and the national response. Commentary on Green et al.(2006). *AIDS and Behavior*. 2006; 10(4): 347-50.
45. Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, Gordillo-Tobar A, Levin C, Mahé C, et al. Cost-effectiveness of cervical-cancer screening in five developing countries. *New England Journal of Medicine*. 2005; 353(20): 2158-68.