SEXUAL BEHAVIOR OF HIV-INFECTED PATIENTS RECEIVING ANTIRETROVIRAL THERAPY IN KAMPALA, UGANDA; A PROSPECTIVE COHORT STUDY

by

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Dedication

To my dear wife, Joaniter, and Jonathan Ralph our son, for the Love, encouragement and endurance.

And to Maama, Ndagaano and Taata, Wandera for laying the best foundation for me. May the Almighty God continue to rest you in peace you.

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List of Abbreviations/acronyms

ART- Antiretroviral therapy

HIV- Human immunodeficiency Virus

AIDS- Acquired immunodeficiency syndrome.

CDC- Centers for Disease control and prevention

IDI/IDC- Infectious Diseases Institute/Clinic

P_QOL-Physical health quality of life summary score

OR- Odds Ratio (Crude odds ratio)

AOR- Adjusted odds ratio

CI- Confidence interval

QIC- Quasi-likelihood information criteria

KM- Kaplan- Meier

GEE- Generalized Estimating Equations

Sexual Behavior of HIV-Infected Patients Receiving Antiretroviral Therapy in Kampala, Uganda; a Prospective Cohort Study.

ABSTRACT

By

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Understanding sexual behaviors of persons on ART is critical designing and implementation of positive prevention programs.

559 HIV infected adults were enrolled in clinic based prospective observational study and sexual behaviors ascertained at ART initiation and semi-annually thereafter. Using Logistic regression with generalized estimating equations, factors associated with sexual activity and unprotected sex were examined.

Over the three years of ART, the proportion of sexually active did not change at ~52% ($\chi 2$ Trend, $p=0.94$) while the proportion reporting unprotected sex decreased ($\chi 2$ Trend, $p<0.0001$). Men reported unprotected sex less often than women ($p<0.0001$). In all analyses, having no children and female gender (controlling for other factors) was associated with unprotected sex.

The interventional effects of comprehensive HIV care resulted in marked reductions in unprotected sex over the three years of ART, particularly among men. Strengthening of positive prevention interventions, especially among females are needed in ART programs in this setting.

INTRODUCTION AND SPECIFIC AIMS

Since the first cases of HIV were identified over two decades ago, the prevalence of the disease has continued to rise; an estimated 33.2 million were people living with HIV/AIDS globally by December 2007 of which two thirds were in Sub-Saharan Africa [1,2]. HIV is predominantly transmitted heterosexually from an HIV-infected person and currently there is no effective HIV vaccine; therefore, strengthening of prevention efforts through behavior change remains the practical public health approach to controlling the epidemic.

Sexual transmission of HIV is dependent on a number of other factors but starts with an infected person having (unprotected) sexual intercourse with an uninfected individual. Similarly, several factors interplay in reducing/modifying the probability of transmission from the infected to the uninfected partner, which among others include knowledge of one's HIV status, sexual abstinence or effective condom use, and treatment of ulcerative sexually transmitted infections. Potent antiretroviral therapy (ART) lowers the concentration of HIV in blood and reproductive secretions, essentially making that individual less infectious to the uninfected partner. However, the risk of HIV transmission is not eliminated.

Potent ART for HIV infection has been available in developed countries since 1996, resulting in favorable clinical outcomes of HIV-infected persons

resulting in prolonged and improved quality of life [3,4]. The associated improvements in clinical, immunological and virological parameters may influence the subsequent practice of safer sexual behaviors[5,6]. This may result in the resumption of sexual activity, which in the presence of factors aforementioned could make HIV-infected persons on therapy potential sources of further HIV spread[7]. Therefore, understanding sexual behavior of persons on ART becomes paramount in preventing sexual transmission of HIV from persons aware of their HIV positive status and in care. Studies from western countries regarding sexual behavior demonstrated an increased sexual risk behavior [8,9] and an increased incidence of sexually transmitted infections after initiation of ART[10]. Although other studies from similar settings did not necessarily show increased high-risk sexual behavior, they did show an overall increase in sexual activity after introduction of ART [11-13].

With the current global effort to scale up access to ART in resource-limited settings [14], understanding sexual behaviors among persons on therapy is needed for the planning and implementation of "prevention for positives" programs. Application of the experience from developed world to countries just now scaling up ART, suggests that sexual activity, a natural human behavior among both infected and uninfected individuals, will become an important concern in sub-Saharan Africa ART programs. Currently, there is paucity of information on sexual behavior with ART in Sub-Saharan Africa Uganda inclusive and hence, the specific aims of the proposed research are:

1. To establish the prevalence and predictors of reported sexual activity and unprotected sex in HIV-infected persons at the time of starting ART.
2. To determine factors associated with resumption of sexual intercourse while on ART, in subjects who were abstinent at the time of ART initiation.
3. To examine factors associated with having sexual intercourse and unprotected sex in persons receiving ART for up to three years.

RATIONALE OF THE STUDY

The effect of HIV treatment on sexual behavior may be different in Sub-Saharan Africa from that seen in developed countries because of unique cultural norms regarding sexual behavior, the epidemic in this region is generalized and the fact that ART is started at advanced HIV disease stage with higher HIV RNA concentration, and thus, infectiousness is higher if persons not yet on ART engage in sexual behaviors with high risk of further HIV transmission. There is also a concern that an infected individual receiving ART and engaging in high-risk sex, in the setting of poor ART adherence, may harbor drug-resistant HIV and is at risk of transmitting it.

An increase in sexual risk behavior like unprotected sex among HIV positive population following the introduction of ART may perpetuate the HIV epidemic if not appropriately addressed through prevention interventions[15]. Understanding sexual behavior in persons at risk of potential transmission of HIV sheds light on the gaps in available positive prevention programs in clinical settings and offers a window of opportunity for re-evaluation of these programs thus contributing to HIV prevention efforts.

In order to provide the targeted prevention for positives services, identification of individual factors associated with practicing sexual risk behavior are needed. The simplest approach would need routine clinician inquiry of all patients seen in care. However, such inquiry may not always be feasible with

the burden of disease, work load, clinician-patient ratio most and overburdened health facilities Sub-Saharan Africa[16]. Therefore an understanding of characteristics of persons practicing high sexual risk behaviors is essential in provision of intensive/targeted counseling and prevention education[17].

Of the available studies done in Sub-Saharan Africa, most were cross-sectional; thus, establishing temporality between ART initiation and high-risk sexual behavior is not possible [18,19]. However, there have been a few prospective studies done, but these had a short follow-up duration of 6-12 months after ART initiation [20,21] yet high-risk sexual behavior is likely to vary over the long-term if individuals experience prevention fatigue and burnout[22]. Therefore, data from a prospective study with a longer follow up time is needed to understand the complete sexual behavior changes both in the short and long term while on ART.

Most previous studies were done before free ART had taken root as ART then was accessed mainly through out-of-pocket/private financing. Therefore, findings from such studies may not be generalized to current populations accessing free public-funded health care programs. Studying sexual behavior of persons attending a major public facility providing free antiretroviral drugs to the majority of the population would allow for inferences applicable to the majority of persons attending other free facilities which provide the bulk of HIV treatment in this setting.

There is limited published research of sexual behavior and ART in developing countries with a recent systematic review only using three published articles demonstrating dearth of work, therefore calling for further research to characterize sexual behavior changes in HIV positive persons in the era of ART [23]. Moreover available research from Sub-Saharan Africa has not explored the association of CD4 T cell count and viral load with sexual behavior and unprotected sex.

Therefore, I set out to use already collected data to study reported sexual behavior in persons who were followed up from initiation of ART up to three years of treatment in an urban HIV clinic in Kampala city, Uganda.

BACKGROUND

Burden of HIV

By the end of the year 2007, an estimated 33.2 million people were living with HIV/AIDS, the majority being adults (above 15 years and sexually active) contributing 30.8 million people. A total of 2.5 million people were newly infected with HIV in 2007 alone and in this same year, 2.1 million deaths were attributed to HIV/AIDS[1].

Sub-Saharan Africa is the region most affected by the HIV/AIDS epidemic accounting for about two thirds of the 33.2 million cases of persons living with HIV infection globally and continues to have the highest number of new HIV infections, estimated to have totaled 1.7 million people in 2006 alone. AIDS continues to be the single largest contributor of mortality in 15-35 year old persons[2].

HIV transmission and prevention

HIV is transmitted through unprotected vaginal or anal sexual intercourse with an HIV infected person, from a mother to her baby during pregnancy, childbirth or breastfeeding, sharing of contaminated sharp instruments usually needles by intravenous drug users and through transfusion of contaminated blood and blood products. Sexual exposure accounts for the greatest percentage of all HIV transmissions. The main transmission mode of HIV is the heterosexual route, accounting for approximately 70% of the overall global HIV sexual transmissions.

Sexual transmission of HIV is dependent on a number of factors which include unprotected sexual intercourse with an HIV infected person, presence of HIV in the blood and genital secretions in adequate quantities and other factors such as breach of mechanical barrier through presence of sexually transmitted infections and frequency of exposure. Work done in HIV treatment naive sero-discordant couples showed that HIV transmission was rare at viral loads <1,500 copies/mL from the HIV-infected partner and an increment of 2.5 log10 viral load was associated with a 10-fold rise in risk of transmission [24]. The effect of viral load reduction with ART on sexual transmission of HIV is not well concluded but there are various reports showing significant reductions in likelihood of sexual HIV transmission [25,26].

Various prevention efforts have been put in place to reduce HIV transmission which include promotion of “A”bstinence, “B”eing faithful to one sexual partner and consistent “C”ondom use (the “ABCs”), and these have been widely employed in the general population and targeting mainly HIV negative persons[27].

HIV treatment

HIV treatment with ART is associated with a dramatic reduction in AIDS associated opportunistic infections, gradual clinical improvement and subsequently prolonged and improved survival in persons on therapy[3].

These are mediated through an improvement in pathogen specific immune responses, increase in peripheral circulating CD4+ T cells and reduction of plasma HIV ribonucleic acid (HV RNA; also called “viral load”) to below limits of detection. However, the massive reduction in the plasma viral load is not uniformly seen in other body compartments and most importantly for risk of HIV transmission, including the genital tract [28]. The persistence of HIV in the genital tract poses significant challenges to control of replication and spread of the virus as it has been shown that the genital area may be an area where drug resistant HIV may replicate and therefore more likely to be spread from the host to another individual through sexual intercourse [28].

By August 2006, more than a million people living with HIV in SSA were receiving ART for the treatment of HIV/AIDS and in Uganda, an estimated 96,000 HIV-infected persons were accessing and receiving ART by the end of 2006 which has resulted in dramatic clinical improvement, reduced mortality and prolonged survival.[29]

Role of Continuing Prevention for Positives

Most population-based prevention initiatives were aimed at the general population without putting into consideration one’s HIV status. With prolonged life due to ART, HIV-infected persons are now living a longer and normal life therefore calling for prevention strategies that can be used by these individuals to help them maintain their health and also prevent further spread

of HIV. Such “positive prevention” strategies are designed to offer continued health maintenance of the HIV positive community to increase their ability to protect themselves and the entire population. Positive prevention programs aim to reduce HIV-associated opportunistic illness and improve adherence to treatment medications including antiretroviral drugs thereby reducing possibility of HIV transmission. There are also community benefits from this strategy because of the improved status of its members, there is improved family income, reduced burden to the health system and therefore allowing other community members to engage in productive activities in the time they would have spent taking care of their HIV positive relatives. Comprehensive packages for positive prevention proposed for different settings have been suggested. Broadly they include HIV counseling and testing, HIV status disclosure and partner testing, provision of ART, screening and management of sexually transmitted diseases, provision of family planning services, promoting condom use, access to effective prevention of mother to child services, and family centered approach for HIV counseling, testing, treatment and care.

HIV Treatment and Sexual Behavior

Developed countries

With increased survival following ART, there are a number of published works about changes in sexual behavior including sexually transmitted infections.

Earlier reports suggested that that there was an appreciable increase in the incidence of sexually transmitted diseases, HIV and increments in high risk /unprotected sex [30-33]. Chen and others reported work done in mainly gay community in California that the proportion of MSM reporting any anal sex in the previous 6 months before the interview increased from 67% in 1999 to 74% in 2001. The proportion of respondents reporting any unprotected anal sex increased from 32% to 38%, with a parallel increase from 18% to 23% in the proportion reporting unprotected anal sex with 2 or more partners[30].

Studies from Europe also demonstrated an increase in high risk sexual behaviors and increases in sexually transmitted diseases with therapy [31].

A meta analysis of 25 studies was done in 2004, that included studies done mainly in the United States (64%) and consisting of a majority of subjects who were MSM, assessed sexual behavior and ART between 1996-2000[13]. Sixteen of these studies, assessed the effect of receiving HAART and engaging in unprotected sex and demonstrated no significant association (Odds Ratio(OR) 0.92 95% Confidence Interval(CI) 0.65-1.31). The meta analysis also did not show any significant association between having an undetectable viral load and engaging in sexual risk behavior (OR 0.99; 95% CI 0.82-1.21). Regarding the belief about HAART, viral load and unprotected sexual intercourse, there was a consistent pattern of increased likelihood of engaging in unprotected sexual behavior (OR 1.82; 95 % CI 1.52 -2.17), if the person believed that HAART reduced HIV transmission or the availability of

HAART negated the need for safe sex. These results could not be generalized to sub-Saharan Africa setting because all these studies were from USA and Europe, and were over represented by men who have sex with men.

The increases in sexual activity associated with the advent of ART were attributed to HIV treatment optimism by various studies and personality and personal beliefs about ART and HIV[34-36]. Furthermore, for people taking ART, high adherence to ART was associated with safer sexual behaviors compared to those having low adherence[37]. All these findings may not be the same in developing countries and where the majority of HIV infected persons are women and most of the men are heterosexual. This idea is supported by findings from a study by Elford *et al* from a community of HIV infected persons in London that showed that sexual behaviors of HIV infected persons were different between gay man and heterosexual black African Men and women[38].

Other factors associated with increased unprotected sexual behavior in HIV infected persons include having less HIV/AIDS knowledge[39], beliefs that safer sex decreases sexual pleasure[35], having an HIV positive partner versus uninfected partner[40,41] , living with partner[42], desire for children[43], and non disclosure of HIV status to sexual partner[44]. Important HIV treatment and medical beliefs associated with increased unprotected sexual behavior in HIV

infected persons include having a higher CD4 cell count[5,45-47], longer duration since HIV diagnosis[48], better self reported quality of life, and belief that HIV treatment reduces HIV transmission[49]. Sethi *et al* reported that higher CD4+ cell counts were marginally associated with being sexually active in a cohort of HIV infected intravenous drug users on ART in Baltimore[50].

Developing Countries

Research from Brazil, one of the first developing countries that provided widespread free antiretroviral therapy showed that the proportion of persons receiving ART that reported sexual activity increased from 60% at the start of ART to 78% (p=0.03) at 24 months of therapy and reported use of condoms in all sexual encounters increased from 68% before initiation of ARV to 90% after 6 months (p=0.30), 100% after 12 months (p=0.01) and 85% after 24 months (p=0.15)[51]. In a cross sectional study involving HIV infected persons attending 8 different HIV clinics in Cote d'Ivoire reported that 47% of the subjects reported any sexual activity in the preceding 6 months[18]. Of those patients that reported any sexual activity, 35.3% of them did not use condoms during their most recent intercourse but this proportion was lower among patients on ART compared to those not on ART (p<0.001).

Proportion of those reporting any sexual activity was significantly higher among men and men still reported a statistically significant higher frequency of sexual intercourse than women. Bateganya *et al* in another cross sectional study reported that 48% of 723 respondents reported sexual activity in the

previous six months prior to the interview[19]. However this study did not show any association between receipt of ART and reporting any sexual activity. Subjects on ART were more likely to report condom use than those not on ART (Odds Ratio (OR) 2.82, 95% CI: 1.74- 4.6). Factors associated with sexual activity in this study were male gender (Adjusted Odds Ratio (AOR) 1.86 95% CI 0.32-10.3) and being married (AOR 1.62, 95% CI: 0.34- 7.81). In a prospective cohort study from rural Uganda, Bunnell and colleagues assessed changes in risky sexual behavior over time on ART[21]. At the start of ART, 47% of men and 21% of women reported sexual activity in the preceding 3 months. Factors independently associated with sexual activity at baseline in multivariate analysis included Increasing age (OR=0.96), being married or cohabiting (OR=23.4) compared to widows, having lower plasma viral load (OR=1.9), being a trader (OR=2.4) compared to farmers and reporting >3 lifetime sexual partners (OR=2). There was an overall increase in the desire for sex from 1% at baseline to 19% at 6 months follow up (AOR=22.4, 95% CI: 11.7 – 42.6, p<0.0001) and but the actual proportion of those reporting sex did not change, from 28% at baseline to 31% at 6 months (AOR=1.2 95% CI 1.0–1.5 p=0.07). The odds of any reported unprotected sex were halved over the six months of follow up on ART.

Factors associated with risky sexual activity, Moatti reported in a multivariate analysis, that shorter duration with HIV infection, having only one sexual partner, high alcohol consumption, absence of episodes of acute morbidity, not participating in household's expenditures and not being ARV-treated were

significantly related to a higher likelihood of HIV-related risky sexual behaviors.

Clinical factors like disease stage, including CD4, viral load, and opportunistic illness are likely to impact on sexual behavior. A study from Kenya that assessed women eligible to start ART showed that women with CD4 counts<200 cells/UL were less likely than those who were asymptomatic with CD4>350 cells/UL to report sexual intercourse with in the past week (58 % vs. 26%, p<0.001) [47].

Table 1: Summary of main studies from Sub-Saharan Africa

Author/year	Setting	Population	Design	Main findings
Moatti *et al*., 2003	8 Clinics Cote d'Ivoire	Comparison between persons receiving ART and those not receiving ART 164 ARV treated and 547 ART naïve participants	Cross sectional survey. *Limitation Cannot assess temporality	Patients receiving ART more likely to use condoms ($p<0.001$). Difference in frequency of sexual intercourse between ART and non-ART patients.
Bategenya *et al*. 2005	Clinic in Urban Uganda	Comparison of sexual behavior between ART experienced and ART naïve persons in previous six months. 723 respondents recruited.	Cross sectional study. *Limitation Cannot assess temporality.	ART-experienced respondents more likely to report consistent condom use with regular partners than ART-naïve respondents. Receipt of ART not associated with a significantly higher likelihood of being sexually active nor having multiple sexual partners.
Bunnell *et al*. 2006	Clinic/Community-based HIV care program in Uganda	926 adults followed up from start of ART up to 6 months since ART initiation	Prospective cohort study *Limitation Short follow up duration.	Six months after initiating ART, risky sexual behavior reduced by 70%. Estimated risk of HIV transmission from cohort members declined by 98%, from 45.7 to 0.9 per 1,000 person-years.

Conceptual framework for sexual behavior while on ART

Various studies quoted above that have examined correlates of sexual behavior used more than one of the available behavioral models to try and explain their findings and the observed behavior and have been extensively reviewed by Crepaz *et al* [52]. These constructs include social, psychological and medical factors that influence sexual behavior for persons on ART. Below we construct a model of the factors likely to impact sexual behavior for persons receiving ART.

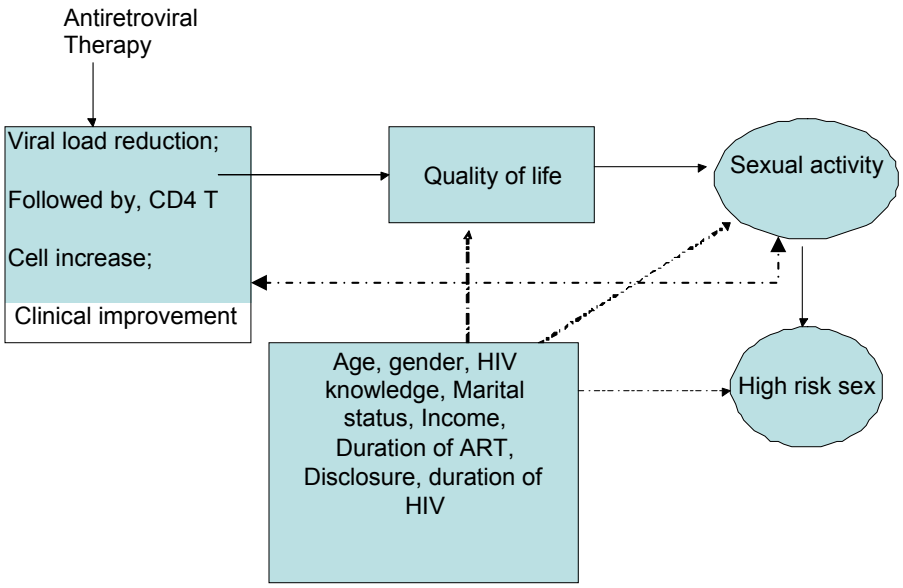


Figure 1: Conceptual Framework of sexual behavior of HIV infected patients on ART

SIGNIFICANCE

Given the rapid expansion of ART programs in developing countries, there is a need to ascertain the relationship between sexual risk behavior and treatment with ART. The effect of HIV treatment on sexual behavior in SSA is likely to be different from that in the developed world because of a number of reasons. These include reduced and late access to care, different cultural norms regarding HIV and sexuality and the fact that ART availability is relatively new in this setting.

Currently, persons initiating ART in Uganda and SSA are mostly at advanced stage of HIV/AIDS with higher viral loads and lower CD4 counts and may be at an increased risk of failing their treatment and developing drug resistant virus than patients who start at a less advanced HIV disease stage since they may take longer to achieve viral suppression. This calls for an understanding the sexual behaviors of persons on ART so as to design interventions to prevent further HIV spread from persons in care to the general population.

There are limited services involving prevention for positives strategies, yet with return of sexual desire, persons on ART are naturally likely to engage in sexual activity therefore positive prevention efforts should address the likelihood of sexual transmission of HIV from infected persons in care. This focused intervention can only be successful after assessment of the burden of the problem through research and identification of a subcategory of persons

that are likely to have the highest risk so to whom this focused intervention was cost effectively offered.

The persons on ART are still potential sources of transmitting HIV to uninfected persons and therefore we need to offer them all the necessary support, education and counseling on risk reduction methods and these can only be implemented well when we have identified the magnitude of the problem and categorized the persons most likely to benefit from the intervention[53]. An appreciable proportion of persons on ART may harbor drug resistant HIV and therefore may transmit drug resistant virus to their partners therefore if they engage in unprotected sexual intercourse[50].

By establishing patterns of sexual habits, health workers was able to provide appropriate messages to patients at time of starting of ART and provision of ongoing counseling, education and support.

The scale up of ART in this setting may lead to complacency on the part of persons on these medications and therefore they may subsequently engage in risky sexual behavior because they no longer consider themselves as infectious and therefore if we are able to establish the trend of sexual behavior then we would be able to know when this break in information occurs and therefore plan on how to address such problems. Auerbach *et al* identify the latter as one of the priority areas among challenges for HIV prevention research that needs to be addressed in the third decade of AIDS[54].

Understanding sexual behavior of persons on antiretroviral medications offers an opportunity of discussing continued disclosure and emphasizing continued prevention therefore establishing these will guide the counseling and education to encourage disclosure. Furthermore, identifying factors associated with sexual risk behavior avails information that may be useful in developing a preliminary prediction rule for possible sexual risk behavior. This would offer clinicians a more efficient and cost effective way of identifying patients at high risk and therefore providing them with extra counseling, education and support.

ART medications have a role in prevention of potential sexual transmission of HIV by a) reducing the HIV RNA load in the blood and genital fluids thus reducing the risk of transmission and b) by use in pre-exposure and or post exposure prophylaxis[55].

As HIV treatments get scaled up widely in Sub Saharan Africa, the relationship between treatment and sexual behavior becomes important aspects to examine for designing and evaluation of treatment and prevention programs in these resource poor settings.

As an implication for prevention of secondary transmission of HIV, sexual behavior data obtained from such studies provides a background to calculate transmission risk estimates in an ART program. These estimates can be used to strengthen prevention for positives in clinical care settings[56]. Sexual behavior is an important parameter needed in tracking determinants of HIV

transmission. Findings from this study will be used to corroborate the need for involving people being seen in HIV primary care in the development and oversight of clinic based programs for prevention with positives programs in the provision of quality care, a sort of mutual obligation.

Work done in an HIV clinic in Baltimore indicated that women were twice as likely as men to report unprotected sex (OR 1.93 95 % CI 1.37-2.73)[50]. Although this study population had other risk behaviors for HIV transmission like IDU, it may point to the vulnerability of women in negotiating for safer sex and therefore in Uganda where women are disproportionately affected by HIV, it is timely to establish sexual behaviors in this setting to aid in positive prevention interventions that are gender orientated.

Despite the increased ART in SSA, there is very limited information on the impact of ART on sexual risk behavior. The studies that have been cross sectional and therefore could not assess the temporal changes in these reported sexual behaviors yet sexual behavior could change over time. There has been only one published longitudinal study which only followed patients for the first six months and since ART is associated with prolonged survival then obviously these patients live longer and therefore continue engaging in sexual activity. Establishing the sexual behavior for a longer time will enable us obtain an answer to the question of whether ART is associated with increased sexual risky behavior and will therefore strengthen the efforts of further HIV prevention especially in the context of provision of antiretroviral

therapy. Secondly the study was done in a rural setting which is likely to have different sexual characteristics than in an urban setting making it hard to generalize the study findings to include urban settings.

To date, there is no study tried to establish changes in reported sexual behavior for a longer duration on ART in sub-Saharan Africa and therefore this study offers an opportunity to examine this trend and therefore inform the wider clinical and public health policy makers in the region on issues related to risky sexual behavior and ultimately strengthen secondary HIV prevention including prevention of spread of drug resistant HIV as has earlier documented in developed countries where new HIV infections in ART naïve patients have been identified as drug resistant HIV. High risk sexual behavior in an HIV infected person places their sexual partner at risk of acquiring HIV and therefore identifying the magnitude of his problem was essential in dissemination of education and counseling to the HIV infected persons and the general population on further strengthen of HIV prevention efforts and encouraging safer sexual practices.

Data on sexual behavioral trends may be used as a proxy evaluation measure of the current prevention efforts and will therefore be beneficial in shaping the prevention efforts and identify strengths and weakness in prevention efforts especially in treatment care centers which is now considered a priority in Africa.

The outcome of this study will also be used by stakeholders in HIV prevention to design secondary transmission/positive prevention strategies to strengthen education, counseling and skills training for HIV positive persons.

Host/Primary Study Background

The study population is part of large cohort of patients involving adults, adolescents and children assembled by the academic alliance for AIDS care in Africa at the adult and pediatric infectious diseases clinics in the national referral and teaching hospital with the main goal of describing various aspects of ART in Uganda. ART is provided according to WHO and the Uganda Ministry of Health guidelines. The first line ART for adults predominantly consists a generic combined formulation of stavudine (d4T), lamivudine (3TC), and nevirapine (NVP)- (Triomune®) or a combined formulation of zidovudine (ZDV) and 3TC (Combivir®) plus efavirenz.

Subjects

657 patients aged above 18 years were consecutively enrolled. Of these, 559 subjects were beginning their first line, 57 subjects were starting 2nd Line ART and the remaining 41 were not yet clinically eligible to receive ART and were receiving only septrin prophylaxis.

Enrolment began April 2004 to June 2005 and thereafter patients followed up every three months with their clinical and laboratory parameters recorded and had their social behavioral characteristics recorded every six months.

Standard medical care for persons on ART in the study population includes monthly visits for clinician evaluations, counseling and to pick up prescriptions. Counseling about contraception, nutrition and sexual risk behavior is done routinely and strengthen further whenever there is any reported non adherence to a previously drawn plan by the patient and their counselor.

On every clinic day, from April 2004 to June 2005, prospective study subjects were conveniently sampled (non probability) from patients attending the AIDC who had completed clinical and counseling preparations to start antiretroviral therapy.

Inclusion Criteria

Subjects were consecutively enrolled if they fulfilled all of the following eligibility criteria: (1) confirmed HIV-1 infection; (2) regular attendance (having attended at least two clinic visits in the past 6 months); (3) stable residence within 20 km radius of Kampala; (4) willingness to be followed and exclusively receive HIV-1 care at IDI for at least two years; and (5) provision of voluntary written informed consent.

Data Collection, Procedures and Measurements

A standardized data collection form is completed for each patient at baseline and every three months for clinical data included both remote and current experience with opportunistic infections and related clinical conditions. At enrolment and every six months a socio-behavioral structured questionnaire

is administered in English or Luganda by a trained nurse counselor and recorded onto a standard study form. Information on loss to follow-up, withdrawals, transfers, and death is recorded for all patients.

Measurements included:

- Complete blood count every 6 months,
- Adherence assessment based on the visual analogue scale .
- CD4+ lymphocyte count every 6 months; measured by FACS Count (Becton Dickinson, San Jose, CA, USA) and since June 2005 by FACS Calibur (Becton Dickinson).
- Plasma HIV-1 RNA level (viral load) every 6 months; determined by the Amplicor HIV-1 Monitor PCR Test version 1.5 (Roche Diagnostics, Indianapolis, IN, USA), lower limit of detection of 400 copies/ml.
- Urine pregnancy test (for females), using Uristix® to determine presence of human chorionic gonadotrophin in Urine.
- Serum syphilis antibody testing is done every six months and annually respectively.

  All laboratory testing is performed at the Makerere University-Johns Hopkins University Core Lab located on site, with adherence to Good Laboratory Practice guidelines, regular proficiency testing and is certified by the College of American Pathologists.

STUDY METHODOLOGY

Study design

To achieve the specific aims, cross-sectional, survival, and longitudinal analyses of secondary data were carried out. The data were previously collected in a clinic-based prospective cohort study of HIV-infected persons commencing antiretroviral therapy at the Adult Infectious Diseases Institute Clinic (IDC) in Kampala City, Uganda.

The primary study enrolled subjects from April 2004 through June 2005. Subjects received HIV care every three months. Study visits were conducted at baseline (i.e., enrolment) and every six months thereafter. Subjects were followed through June 2008. This analysis was carried out between August 2008 and February 2009.

Details of the primary study and data collection methods are detailed in the separate section above.

Study population/Study subjects

Analysis was restricted to only previously ART naive subjects. Data of 559 subjects were eligible for this analysis.

Exclusion:

All data at the three month-visits in between the six month study visits were excluded in these analyses because the laboratory panels and sexual history evaluations were not done at those visits.

All available subjects' enrollment six follow-up monthly data were used.

For details of data collection/Measurements/schedule of evaluation, see the primary study section above.

Outcomes of Interest

The primary outcome was odds of unprotected sex at the last sex. A subject was considered to have had unprotected sex if he or she reported having had sexual intercourse in the preceding six months and also reported not having used a condom the last time they had sexual intercourse.

This was recorded as a dichotomous variable with those who did not report using a condom at the last sexual encounter were recorded as having had unprotected sex and vice versa.

Secondary Outcomes: (a) Odds of having had sexual intercourse at the enrolment visit. (b) Odds of having had sexual intercourse during the three years of ART. (c) Resumption of sexual intercourse among subjects who were not sexually active at enrolment.

All sexual intercourse although not explicitly inquired was presumed to have been heterosexual intercourse and no information was collected on whether the sexual intercourse was vaginal or anal sex.

Predictor/Exposures of Interest

Main predictors included:

a) CD4+ T cell count.
b) Plasma Viral load.
c) Physical health related quality of life (P_QOL) for only the baseline visit. P_QOL was assessed using questions 1-8 in Section B of the questionnaire (see Appendix 1). A summary score was created with higher scores correspond to higher quality of life. The summary score ranged from 20-100.

Other factors /potential confounders and/or effect modifiers included:

Age at enrolment: Was obtained in years since birth. We used only the baseline age because the duration of the overall analysis period of three was not overtly long to create an overall impact on the change in the subject's age. We hypothesize that sexual activity and condom use would decrease with increasing age/age group.

Gender: Gender is thought to influence sexual activity and we hypothesized that men were more likely to report sexual activity and condom use.

Marital status: Reported current relationship as either married/cohabiting versus divorced/widowed/not married at the time of enrolment. We hypothesized that married persons were more likely to report sexual activity. We also hypothesized that married persons were more likely to report unprotected sex than unmarried/divorced/widowed persons.

Spouse/partner HIV status, was obtained from married or cohabiting subjects only. HIV status was dichotomized as either HIV positive or HIV negative/unknown.

Socioeconomic indicators obtained were, employment status, household income and education level. It was hypothesized employed persons were more likely to report sexual activity and condom use that unemployed persons. In the same vein the higher the education and or income the more likely would subjects report sexual activity as well as condom use.

Monthly Household income bracket at enrolment: Categorized as either below 50,000 Uganda shillings, Between 50,000 – 100,000 Uganda shillings and above 100,000 Uganda shillings. These categories were not based on any economic indicators but were developed based on the experience of the researchers with average household incomes of persons in the study's catchment area. At the time of enrolment, the average Uganda shilling: US dollar exchange rate was 2000 USHS per 1 USD (Daily Monitor news paper 15th July 2004). Subjects were at liberty not do disclose household income bracket if they chose not to.

Highest education level attained by enrolment: recorded as no formal education/lower primary (<3 yrs of school), upper primary, secondary and tertiary/university education level.

Baseline employment status, was explored to assess its impact on sexual activity and condom use. This was dichotomized as either employed or unemployed at the time of enrolment.

Number of children in household: This was expected to influence condom use with persons having fewer children more likely to report unprotected sex probably due to the fact that they still wanted children. We chose to use number of children in the household rather than the actual subjects' children because of the extended family nature of households/dwellings in the study setting.

Clinical/Laboratory factors: WHO HIV/AIDS clinical stage, Karnofsky performance score, and ART adherence (by visual analogue scale).

Knowledge/belief about ART and HIV transmission: whether ART on reduces of sexual transmission HIV, whether HIV positive married persons should use condoms. Knowledge/beliefs data was collected/assessed using question 1-5 in Section C (Appendix).

Table 2: Variables schedule of collection

Variable	Baseline/ enrolment	Follow up Month 6/18/30	Follow up Month 12/24/36
Socio-demographics			
Age	X		
Gender	X		
Monthly Income	X		
Housing type	X		
Education level	X		
No. of Children	X		
Disclosure status	X		
Clinical			
Years since HIV diagnosis	X		
History of PMTCT(females only)	X		
WHO HIV clinical stage			
Karnofsky performance score	X	X	X
Spouse HIV status	X	X	X
Quality of life			X
ART adherence(VAS)	X		
	X	X	X
		X	X
HIV knowledge/attitudes	X	X	X
Health related quality of life	X	X	X
Laboratory			
CD4+ T cell count	X	X	X
Plasma HIV Viral load	X	X	X
OUTCOME VARIABLES			
Reported sexual activity within 6 months or less	X	X	X
Condom use at last intercourse			
Reported 2 or more sexual partners	X	X	X
	X	X	X

Data integrity, quality assurance and control

To enhance validity, quality of life was assessed using an instrument adapted from the medical outcomes study form SF-36 and modified culturally appropriateness[57]. Study forms were pre-tested in 25 individuals and were modified accordingly before their large scale application. The interviews were conducted in *Luganda* (the predominantly spoken language in Central Uganda) and English. We are not able to assess how the modification, the language in the interview used affected the various aspects of the questionnaire validity.

Information on sexual behavior was obtained by the nurse counselors who were not involved in clinical care therefore ensuring that the subjects were not inhibited in their responses about sexual behavior. Study interviewers were trained in order to standardize recording and reduce inter-rater variations.

Reliability of physical health quality of life summary score was tested by evaluating correlation coefficients of the different questions assessing quality of life and the total item score i.e. corrected item total correlation.

Study interviewers were trained in order to standardize recording and reduce inter-rater variations. Data was electronically entered into the study database on the day the interview was conducted by professional data entrants of the IDI with daily supervision by a health information specialist to resolve any inconsistencies by consensus in conjunction with the interviewing personnel.

Data Management and Statistical Analysis

Specific data of variables of interest listed in Table 1 were formally obtained from IDI Cohort database. Data was obtained in Microsoft Excel® spreadsheet (Microsoft Corporation) TM and Stata® (Stata Corporation, College Station, TX) file formats. These separate datasets i.e. baseline, follow up, and laboratory results datasets were combined into one main dataset. For all data management and statistical analyses, data was exported to SAS statistical software.

Data with out-of range values/responses were cross checked and confirmed against the primary dataset received. Missing values and unexpected responses was crosschecked against primary dataset received and discrepancies identified were appropriately corrected. Those that were not satisfactorily confirmed were not changed.

Statistical analysis was done using SAS 9.1.3© version statistical software (SAS Institute, Cary North Carolina, USA).

The analysis was organized according to the three specific aims.

For all aims, frequency distributions of variables were examined for distribution characteristics/normality, outliers, missing values and having a general overview of the data.

Graphical displays data were done using histograms for categorical variables and normal distribution curves for continuous variables.

For HIV RNA levels (i.e., viral load), a logarithmic transformations were made to normalize its distribution and valid statistical assumptions.

Similar variables were examined for consistency and expected changes over follow-up time in the entire dataset and plotted using box-whisker plots.

Baseline characteristics of the study population were summarized as proportions for categorical variables and as means and medians where appropriate for continuous variables. These baseline characteristics were compared between males and females and between those with all follow up visits versus those lost to follow-up/without all follow up visits using Pearson chi-square and Fisher exact tests for categorical characteristics and using t-tests or Kruskal–Wallis test for continuous variables. All significance tests were two sided at an alpha = 0.05.

The analytic methods for each specific aim are described below:

Aim 1: To establish the prevalence and factors associated with sexual activity and having unprotected sex in HIV infected persons at time of initiating ART at the adult Infectious Disease Clinic (AIDC) Kampala Uganda.

Sexual activity was defined as heterosexual vaginal sex.

The proportion and 95% confidence interval of a reported sexual behavior outcome was calculated. These included:

a) Proportion reporting sexual activity in the previous six months out of the whole study population.

b) Proportion reporting unprotected at last sexual intercourse out of those reporting sexual activity in last six months.

d) Proportion reporting 2 or more sexual partners in the previous 12 months.

We assessed whether there are any differences in reporting i) sexual activity and ii) unprotected sex, at baseline by the baseline CD4 T cell counts. CD4 T cell counts were dichotomized as either below 100 or above 100 cells /μL. CD4 category was the independent variable and the sexual behavior outcome (dichotomous) was the dependent variable.

All variables listed in the variables table were examined for their association with the outcomes of interest using Chi-square and student-t test where appropriate.

We performed stratified analyses and looking at any differences in the stratum specific associations (odds ratios) between CD4 cell category and the sexual behavior outcome within the strata of the created within the different factors namely Employment category, partner HIV status , gender and quality

of life score. These are the factors we thought and hypothesized to be major confounders or have potential interaction effects. Confounding factors were initially assessed by comparing the crude and the stratum specific odds ratios in the different strata.

Because of very low variability of CD4 cell count at baseline visit, physical health QOL was maintained in all models for sexual activity at the baseline visit. The low variability of CD4 at baseline is due to the fact that all the persons initiating ART were at an advanced disease stage with almost all their CD4 cell counts below 200 cells/μL since this is one of the eligibility criteria for ART receipt.

We assessed for potential interaction by looking out for differences in stratum specific odds ratio of the sexual behavior outcome of interest within the different strata and tested for the statistical significance of this using the Breslow and Day test of homogeneity of the odds ratios. If there was no evidence of interaction, potential confounders were examined by looking at the weighted average odds ratio from the different strata using the Cochran-Mantel-Haenszel procedure relative to the crude odds ratio. This was also repeated using the univariable logistic regression analysis with the dependent variable as i) recent sexual activity and ii) unprotected sex. Potential confounders with probability values of <0.20 in univariable analyses were entered in a multivariable logistic regression model examined for possible retention in multivariable logistic regression models. In the initial multivariable

model, we created interaction terms of the between CD4 cell category and gender, partner HIV status, and employment. These interactions were jointly tested for retention in the model using the chunk test.

The initial multivariable model contained the following independent variables/factors:

CD4 cell count, Physical health quality of life summary score (P_QOL), Age, Gender, Marital status, highest education level attained, number of children in the household, household income and employment status. We created interaction terms between CD4+ T cell count category and gender, marital status, and household income.

A manual backward elimination of the most insignificant parameter from the model, and if its removal did not substantially affect the parameter estimates of the remaining variables then it was dropped. Variables that led to a significant change in the estimate and standard error of the CD4 count parameter relative to the results of the gold standard model were not dropped. This procedure was repeated until no other parameters were eligible for removal.

Final model fit was assessed using the Hosmer-Lemeshow goodness of fit test. All final models assessed for presence of extreme multicollinearity between the variables in the model based on the variance inflation factor of each variable.

Although physical quality of life might be correlated with CD4 cell category we maintained both of them in the model because as anticipated there would be very little variability in the CD4 count especially when CD4 values are below 200 which was almost seen throughout for all the study subjects as this was the cut off for eligibility to receive ART in the setting at the time and so we aimed to also assess the independent contribution of the physical health on recent sexual activity independent of the CD4 cell count.

Aim 2: To determine time to resumption of sexual activity following initiation of ART among persons who were not sexually active at enrolment.

Subjects reporting no sexual activity in the previous six months preceding their enrolment/ART initiation were examined for subsequent report sexual activity within the previous 6 months during follow-up visits after initiating ART.

For this analysis, we included subjects who did report sexual activity in the preceding six months before their enrolment. These subjects were then followed up after for three years after initiation of ART to determine, time to resumption of sex and using their baseline characteristics to establish factors associated with resumption of sexual activity.

A subject was considered to have resumed sexual intercourse if they reported sexual activity on at least one of the follow up visits during the three years of follow up.

Time of resumption was estimated as the midpoint between the last study visit at which sexual activity was denied and the visit on which they reported recent sex.

Using categorized baseline subject characteristics, time (in years) from initiation of ART to reporting resumption of intercourse were analyzed using Kaplan-Meier methods and the survival curves of the strata created by the categorized baseline variables compared using the Log-rank test.

To identify baseline factors that are associated with resumption of sexual intercourse after initiating ART, univariable and multivariable Cox proportional hazards models were used. For multivariate models, covariates from univariable analyses with probability values of <0.20 were retained for multivariable models. We controlled for the reason for previous abstention from intercourse by retaining it in all models.

Variables in the final model were checked for proportionality of hazards using graphical methods by plotting the natural logarithm of negative log of survival by log of time and using product terms of the baseline variables with natural logarithm of time.

Aim 3: To examine factors associated with reported sexual intercourse and unprotected sexual behavior in persons on ART at the AIDC.

Sexual intercourse and unprotected sex at last sex with in the last six months or since the previous study visit was assessed at each follow up visit.

HIV plasma viral load was categorized as either undetectable or detectable viral load defined as by Plasma HIV RNA PCR $\leq$400 c/ml, or >400 c/ml respectively.

CD4+ T cell count at each visit was analyzed as a continuous variable.

CD4 cell count and HIV Viral load were lagged by one visit relative to the outcome (unprotected sex) e.g., the CD4+ T Cell count of visit at 12 months was used as the exposure variable for unprotected sex at 18 months.

Analysis was based on available cases only. There was no imputation done for missing data. Subjects used for this analysis had to have at least 2 visits i.e. at least 1 follow up visit after initiation of ART.

Univariable associations of the factors associated with a given sexual behavior (Recent sexual activity and unprotected sex) outcome after ART initiation, using repeated measures logistic regression models based on generalized estimating equation (GEE) methods, a logit link function, robust variance estimation and an autoregressive (or independent correlation structure for time dependent covariates if inferences were based on the time dependent covariates) was used to obtain unadjusted odds ratios of

association between the given factor and sexual behavior outcome i.e. reporting recent sexual activity, or unprotected sex while on ART. The GEE methods help in accounting for the correlation between the repeated outcomes over time on the same subject although this correlation is not estimated.

To adjust for confounding, factors from the univariate analysis with probability values <0.2 were built into a multivariate repeated measures logistic regression model using marginal GEE methods, a robust estimator of the variance and independence working correlation structure. GEE method is flexible as it accommodates for missing data and varying number of visits per subject implying that each subject's contribution to the overall results is proportional to the number of follow up visits data available. If the main exposure is time dependent, an independent working correlation matrix tends to provide consistently unbiased parameter estimates than another working correlation structure, provided that the mean structure of the model is correctly specified. For comparison purposes, we refit the model using an autoregressive correlation structure was explored.

Data of the final multivariate logistic regression models with GEE extension, was modeled with both first order autoregressive (AR1) and independent working correlation structure. The correlations matrix of the proportions of subjects having unprotected sex on the different visits was closer to the AR (1), but the exposure variables CD4+ T cell count and viral load, together with

a number of other variables were time dependent. For marginal GEE models with time dependent covariates, the independent working correlation structure tends to give unbiased regression estimates[58,59].

Belief about reduced sexual transmission of HIV while on ART was maintained in all models as we had decided *a priori* that this was an important factor to control for in all models. Univariate analyses were re-run after stratifying by gender and marital status.

All factors that fulfilled the above criteria were entered in the initial multivariable models.

Manual backward elimination of the most non statistically significant variables in the multivariable model was done provided removal of the variable from the model did not result in a significant change (10% or more) change in the odds ratio of the variables remaining the model based on in the initial 'gold standard' model. Gender by marital status interaction was created in the multivariable models since there different point estimates for unprotected sex in the stratified analyses. The latter process was repeated until no further variables were eligible for removal from the model. We did not do any likelihood ratio tests since no likelihood is estimated in GEE models. However, our results were comparable to methods were model selection was based on quasi information criteria (QIC). Further analysis was done separately according to marital status, gender and by whether subjects had

all the 6 follow up visits or less than 6. There was no imputation done about missing data for all the above analyses.

ETHICAL ISSUES

The Patients who were enrolled in the prospective cohort were informed of the study and gave voluntary written informed consent to be followed up on the study.

The primary study was approved by the local and national ethics review boards, and this study obtained institutional clearance and ethical review from the scientific review committee of IDI and the institutional review board at Case Western Reserve University respectively. The study was approved by the ethics and research committee of the Makerere University faculty of Medicine and the Uganda National council of Science and technology.

During follow up, patients were continually counseled about nutrition adherence to treatment and further prevention efforts and condoms were availed to all that needed them.

Subjects who subsequently requested withdrawal from the study were allowed to withdraw. The main reason cited for withdrawal was change in the residential location necessitating change to another health facility for continued care.

Data with no subjects identifiable information, labeled only with study identification numbers were obtained and kept on a non shared password locked computer.

There were no direct risks to the study subjects was there was no direct contact with them and all their data was handled above.

The participants whose data were used in this study will be able to benefit not directly but through the information gained that will be used in advancement of counseling and education and care of persons receiving ART.

RESULTS

A total of 657 adults were enrolled in the IDI observational cohort of whom 600 were ARV naive while the remaining 57 subjects were ART experienced and were enrolled at their commencement of second line ART. Subjects who had only previous received single dose nevirapine for Prevention of mother to child transmission of HIV considered ARV naive.

Of the 600 subjects, 41 did not receive ART as they were not eligible based on clinical and laboratory parameters leaving 559 subjects who were previously ART naive and initiated their first line ART under the observation Study.

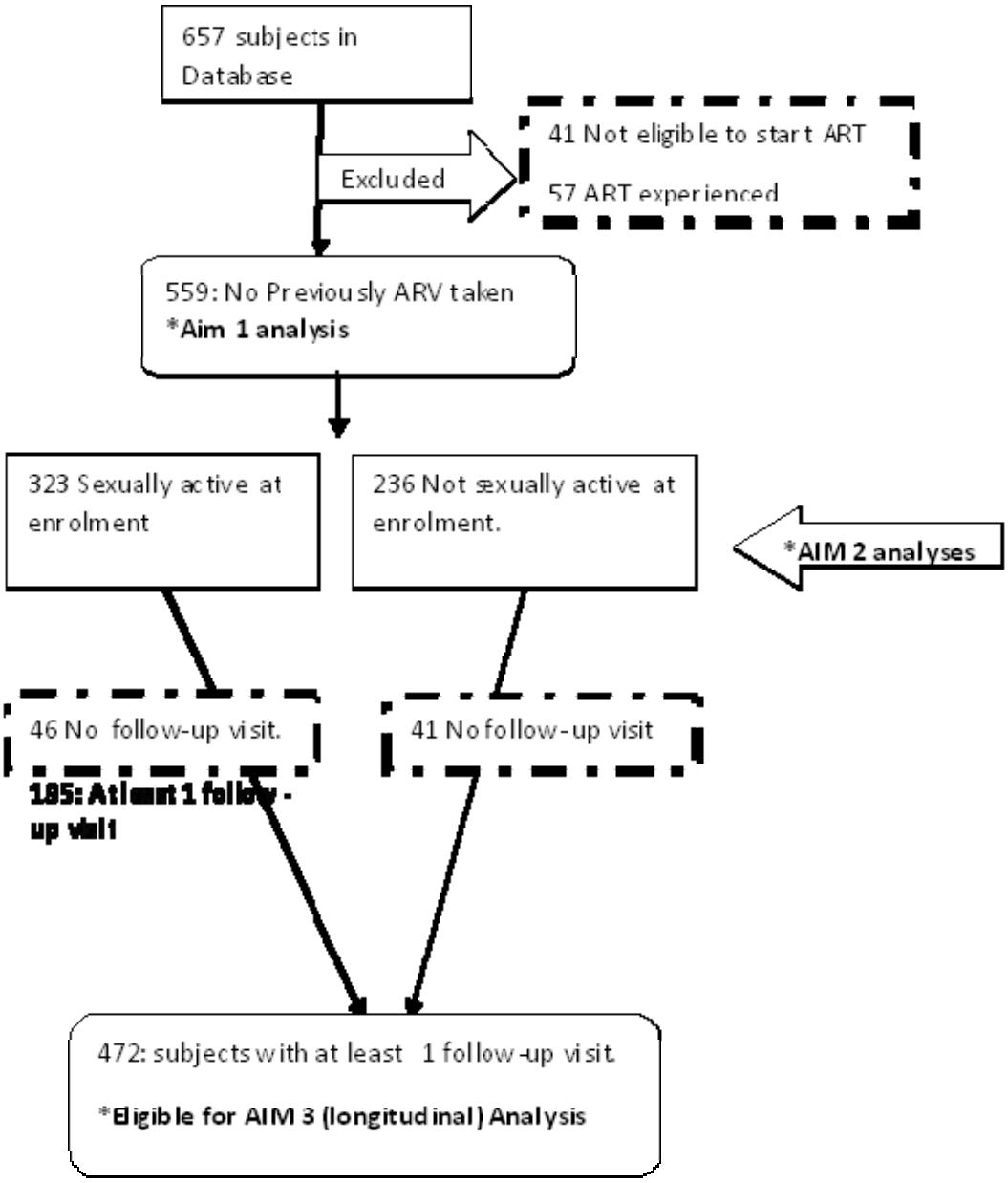
A total 559 subjects who enrolled into the observational ART Cohort study at the adult IDC between April 2004 and June 2005 all met the inclusion criteria and were entered into this study. The overall study flow/schema is shown below.

Specific Aim 1 results

559 subjects were enrolled, of which 385 (69%) were female and the Median (IQR) age at enrolment was 38 (33-44) years. 261 subjects (46.7%) were married/cohabiting at the time of enrolment. The median duration of the marriage/relationship was 9 years (IQR 4-14 years). Among the married/cohabiting persons, only about a third, (78 subjects) reported having a spouse confirmed HIV positive. The remaining 179 subjects, only 16 new

that their spouse was HIV negative, with the majority 163 (63.42%) not knowing their partners HIV sero-status.

Figure 2: Overall study schema



On the socio-economic factors of highest education attained, monthly household income and employment status, most of the subjects were generally in lower social-economic status 48.7% of subjects having no employment at the time of recruitment. This could be attributed to the fact that most of them had been sick for some time and had therefore lost their jobs hence the associated low income too.

The majority of patients had advanced HIV/AIDS with 494 (88.2%) at WHO HIV/AIDS clinical Stage III and IV.

The median baseline CD4 cell count and $\log_{10}$ (plasma HIV RNA copies/ml) was 98 cells/mm^3 (IQR: 21-166), and 5.4 (5.1-5.78) respectively.

Tables 3- 6 show the overall baseline characteristics and a comparison of the baseline characteristics of the study population by their baseline CD4 cell count category as either above or below 100 cells/μL. Subjects with CD4+ T cell count>100 cells/μL were more likely to be older, employed and widowed/divorced. There were no statistically significant differences in the distribution of neither highest education nor gender within in the two CD4 categories. Comparisons of the distribution of other characteristics are listed in the corresponding tables.

Table 3: Baseline Socio-Demographic characteristics of the study subjects

Characteristic	Overall N=559	CD4 Category (cells/μL)* <= 100 N= 293(52.60%)	CD4 Category (cells/μL)* > 100 N= 264(47.40%)	χ2 P-Value
Socio - Demographic Characteristics				
Age in years, Median(IQR)	38(33-44)	36(32-43)	39(34-46)	<0.0001‡
Gender, N(%)				
Male	173	96 (32.8%)	77 (29.2%)	0.3595
Female	386	197 (67.2%)	187 (70.8%)	
Marital status				0.0033
Married /Cohabiting	259(46.34)	153 (52.2%)	105 (39.8%)	
Not married/widowed/divorced	300(53.67)	140 (47.8%)	159 (60.2%)	
Spouse/Partner HIV status (among married/cohabiting)				0.9983
Negative/Unknown	179(69.65)	105 (35.8%)	73 (27.7%)	
Positive	78(30.35)	46 (15.7%)	32 (12.1%)	
Highest Education level				0.9375
No formal education-lower primary	77(13.77)	40 (13.7%)	36 (13.6%)	
Upper primary	180(32.32)	97 (33.1%)	83 (31.4%)	
Secondary level education	232(41.50)	118 (40.3%)	113 (42.8%)	
Technical/University	70(12.52)	38 (13.0%)	32 (12.1%)	
Employment status				0.0037
Not employed	272(48.66)	160 (54.6%)	110 (41.7%)	
employed (Self /casual & or Informal)	142(25.40)	60 (20.5%)	82 (31.1%)	
employed(formal :Private/Government)	145(25.94)	73 (24.9%)	72 (27.3%)	
Monthly Household Income				0.0353
Below 50000 Ushs	194(34.70)	90 (30.7%)	103 (39.0%)	
Between 50000 - 100000 Ushs	95(16.99)	48 (16.4%)	47 (17.8%)	
Above 100K Ushs	86(15.38)	43 (14.7%)	43 (16.3%)	
Declined to answer	184(32.92)	112 (38.2%)	71 (26.9%)	
Number of children in Household				0.5815
0(None)	74(13.24)	41 (14.0%)	32 (12.1%)	
1-2 children	214(38.28)	107 (36.5%)	107 (40.5%)	
3 or more children	271(48.48)	145 (49.5%)	125 (47.3%)	

* 2 subjects had missing CD4 results
‡- Wilcoxon rank sum test

Table 4: Baseline Clinical, Laboratory and quality of Life Characteristics

Characteristic	Overall N=559	CD4 Category (cells/µL)* <= 100 N= 293(52.60%)	CD4 Category (cells/µL)* > 100 N= 264(47.40%)	χ 2 P-Value
Clinical and laboratory				
Log_{10}HIV plasma RNA copies$^{-ml)}$				
Median(IQR)	5.4(5.1-5.8)	5.5(5.2-5.9)	5.4(4.9-5.8)	0.0054‡
HIV plasma RNA PCR (Viral load)				0.0019
<= 38500 copies/ml	41(7.43)	12 (4.2%)	29 (11.1%)	
>38500 copies/ml	511(92.57)	277 (95.8%)	232 (88.9%)	
Body mass index (KG/M^2)	20.0(18.0-22.2)	19.4(17.0-21.5)	20.6(19.0-23.0)	<0.0001‡
Body mass index category(KG/M^2)				<0.0001
</= 18.49	172(30.77)	117 (39.9%)	54 (20.5%)	
18.5-24.99	338(60.47)	158 (53.9%)	179 (67.8%)	
>25.00	49(8.77)	18 (6.1%)	31 (11.7%)	
WHO HIV/AIDS Clinical Stage				<0.0001
Stage I &II	65(11.63)	22 (7.5%)	43 (16.3%)	
Stage III	301(53.85)	145 (49.5%)	156 (59.1%)	
Stage IV	193(34.53)	126 (43.0%)	65 (24.6%)	
Syphillis (*T-Pallidum* Ab test)				0.0516
Positive	49	19 (6.5%)	30 (11.4%)	
Negative	240	137 (46.8%)	103 (39.0%)	
Not done/no results	270	137 (46.8%)	131 (49.6%)	
Years since first HIV test(N=497)				0.012
Less than a year	327(65.79)	186 (71.8%)	140 (59.3%)	
Between 1-5 years	144(29.97)	63 (24.3%)	80 (33.9%)	
Above 5 years	26(5.23)	10 (3.9%)	16 (6.8%)	
Functioning /Quality of life				
Physical health summary score				0.0064
Below Average/ poor(<40)	103(18.43)	67 (22.9%)	35 (13.3%)	
Average score(40-60)	319(57.07)	164 (56.0%)	154 (58.3%)	
Above average (>60)	137(24.51)	62 (21.2%)	75 (28.4%)	
Feeling sad/depressed				0.1794
None	123(22.0)	73 (24.9%)	50 (18.9%)	
Some of the time	394(70.48)	201 (68.6%)	191 (72.3%)	
most of the time	42(7.51)	19 (6.5%)	23 (8.7%)	
Karnofsky score(% score)				<0.0001
<60	73(13.06)	57 (19.5%)	15 (5.7%)	
60-80	311(55.64)	165 (56.3%)	145 (54.9%)	
90-100	175(31.31)	71 (24.2%)	104 (39.4%)	
WHO Performance scale				<0.0001
Asymptomatic,Normal Activity	38(6.80)	17 (5.8%)	21 (8.0%)	
Symptomatic,Normal Activity	367(65.65)	171 (58.4%)	196 (74.2%)	
Bedridden <50% last Month	137(24.51)	91 (31.1%)	44 (16.7%)	
Bedridden >50% last Month	17(3.04)	14 (4.8%)	3 (1.1%)	

* 2 subjects had missing CD4 results ‡- Wilcoxon rank sum test

Table 5 : Baseline HIV related knowledge beliefs and sexual behavior

Characteristic	Overall N=559	CD4 Category (cells/µL)* <= 100 N= 293(52.60%)	CD4 Category (cells/µL)* > 100 N= 264(47.40%)	χ 2 P-Value
Knowledge/beliefs about HIV & ARVs				
Believes that ARVs cure HIV				0.1888
yes	86(15.38)	53 (18.1%)	33 (12.5%)	
no	443(79.25)	225 (76.8%)	216 (81.8%)	
no opinion	30(5.37)	15 (5.1%)	15 (5.7%)	
Can a Healthy looking HIV postive transmit HIV ?				0.8978
Yes	553(98.93)	290 (99.0%)	261 (98.9%)	
No/Do not know	6(1.07)	3 (1.0%)	3 (1.1%)	
ARV treatment reduces of HIV transmission				0.0028
Yes	230(41.14)	139 (47.4%)	91 (34.5%)	
No	297(53.13)	135 (46.1%)	160 (60.6%)	
Do Not know	32(5.72)	19 (6.5%)	13 (4.9%)	
Sexual Behaviour/ practices				
Used Condom at last sex(irrespective of time of last sex)				0.8378
Yes	206(36.85)	109 (37.2%)	96 (36.4%)	
No	353(63.15)	184 (62.8%)	168 (63.6%)	
Report Consistent Condom Use				0.3791
Yes	179(32.14)	99 (33.8%)	80 (30.3%)	
No	380(67.98)	194 (66.2%)	184 (69.7%)	
Had 2 or more sexual partners in last 12 months				0.217
Yes	70(12.52)	32 (10.9%)	38 (14.4%)	
No	489(87.48)	261 (89.1%)	226 (85.6%)	

* 2 subjects had missing CD4 results
‡- Wilcoxon rank sum test

Recent Sexual activity and unprotected sex

A total of 323/559 (57.8% [95%CI 53.7-61.9]), of the study population reported recent sexual activity i.e. within the preceding 6 months prior to ART initiation.

Among the 323 subjects who reported recent sex, 176 (54.5% [95%CI 48.9-60.0]) reported unprotected sex at their last sexual encounter. Apart from the last sexual encounter, the persons reporting unprotected sex at the last

encounter were also more likely to report unprotected sex on other sexual encounters as well compared to those who reported condom at last sexual encounter before the interview (89.29% vs 18.62% p< 0.001).

Multiple sex partners

Seventy (70) subjects, (12.57% of 559) reported two or more sexual partners in the twelve months preceding enrolment/initiation of ART. Those was no difference in the baseline CD4 category between subjects reporting 2 or more sexual partners and those that had only 1 sex partner.

Factors associated with recent sex

Association between the different factors and having recent sex are shown in Tables 7-9.

Most importantly CD4 cell counts showed an association with reporting recent sex in univariable analyses both when modeled as a continuous and categorical variable. Subjects reporting recent sex were more likely to be younger, male, married and with some form of employment.

Duration since testing HIV positive, body mass index category, plasma viral load, physical functioning/quality of life factors and HIV knowledge factors were not associated with reporting recent sex.

Table 6 : Factors associated with reporting recent sex (with in last six months) by patient characteristics.

Characteristic	Overall	Reports Sex in last six months		P-Value
		Yes	No	
	N=559	N=323(57.8%)	N=236(42.2%)	
Demographic				
Age in years, Median(IQR)	38(33-44)	37(32-42)	40(33.5-47.5)	<0.0001*
Age strata(years)				<0.0001
18-28	35(6.26)	19(5.88)	16(6.78)	
28.1-38	274(49.02)	184(56.97)	90(38.14)	
38.1-48	180(32.20)	100(30.96)	80(33.90)	
>48 years	70(12.52)	20(6.19)	50(21.19)	
Gender, N(%)				0.0002
Male	173(30.95)	120(37.15)	53(22.46)	
Female	386(69.05)	203(62.85)	183(77.54)	
Marital status				<0.0001
Married /Cohabiting ,in Monogamous	184(32.92)	161(49.85)	23(9.75)	
Married /Cohabiting ,in Polygamous	75(13.42)	60(18.58)	15(6.36)	
Not married/widowed/divorced	300(53.67)	102(31.58)	198(83.90)	
Spouse/Partner HIV status(if married)				0.8584
Negative/Unknown	179(69.65)	153(69.86)	26(68.42)	
Positive	78(30.35)	66(30.14)	12(31.58)	
Highest Education level				0.114
No formal education-lower primary	77(13.77)	37(11.46)	40(16.95)	
Upper primary	180(32.32)	102(31.58)	78(33.05)	
Secondary level education	232(41.50)	146(45.20)	86(36.44)	
Technical/University	70(12.52)	38(11.76)	32(13.56)	
Employment				0.011
Not employed	272(48.66)	140(43.34)	132(55.93)	
employed (Self /casual & or Informal)	142(25.40)	88(27.24)	54(22.88)	
employed(formal :Private/Government)	145(25.94)	95(29.41)	50(21.19)	
Monthly Household Income				0.0002
Below 50000 Ushs	194(34.70)	97(30.03)	97(41.10)	
Between 50000 - 100000 Ushs	95(16.99)	72(22.29)	23(9.75)	
Above 100K Ushs	86(15.38)	54(16.72)	32(13.56)	
Declined to answer	184(32.92)	100(30.96)	84(35.59)	
Number of children in Household				0.0008
0(None)	74(13.24)	34(10.53)	40(16.95)	
1-2 children	214(38.28)	111(34.37)	103(43.64)	
3 or more children	271(48.48)	178(55.11)	93(39.41)	

Table 7 : Factors associated with reporting recent sex (with in last six months) by patient characteristics. Continued

Characteristic	Overall	Reports Sex in last six months		P-Value
		Yes	No	
	N=559	N=323(57.8%)	N=236(42.2%)	
Clinical and laboratory				
CD4 cell count,Median(IQR) ,Cells/mm^3	98(21-166)	83(15-159)	104(29-173)	0.0479*
CD4 count category(N=557)				0.0376
< 100 cells/mm^3	293(52.60)	182(56.35)	111(47.44)	
> 100 cells/mm^3	264(47.40)	141(43.65)	123(52.65)	
Median Weight,kgs.	54(47-61)	55(48-61)	53(47-60)	0.1490*
$Log_{10(Baseline}$HIV plasma RNA $copies^{-ml)}$, Median(IQR	5.4(5.1-5.78)	5.4(5.1-5.8)	5.5(5.1-5.8)	0.4503*
Baseline HIV plasma RNA				0.7816
<= 38500 copies-ml	41(7.43)	23(7.17)	18(7.79)	
>38500 copies-ml	511(92.57)	298(92.83)	213(92.21)	
Body mass index category(KG/M^2)				0.6071
</= 18.49	172(30.77)	94(29.10)	78(33.05)	
18.5-24.99	338(60.47)	200(61.92)	138(58.47)	
>25.00	49(8.77)	29(8.98)	20(8.47)	
WHO HIV/AIDS Clinical Stage				0.8686
I &II	65(11.63)	39(12.07)	26(11.02)	
III	301(53.85)	175(54.18)	126(53.39)	
IV	193(34.53)	109(33.75)	84(35.59)	
Syphillis test(N=289)				0.0135
Positive	49(16.96)	20(12.20)	29(23.20)	
Negative	240(83.04)	144(87.80)	96(76.80)	
Years since first HIV test(N=497)				0.4645
Less than a year	327(65.79)	193(67.96)	134(62.91)	
Between 1-5 years	144(29.97)	78(27.46)	66(30.99)	
Above 5 years	26(5.23)	13(4.58)	13(6.10)	

Table 8 : Factors associated with reporting recent sex (with in last six months) by patient characteristics. Continued

Characteristic	Overall	Sex in last six months		P-Value
		Yes	No	
	N=559	N=323(57.8%)	N=236(42.2%)	
Functional/Quality of life				
Physical health score median , IQR	50(40-55)	50(40-60)	45(40-55)	0.2163*
Physical health summary score(P_QOL)				0.1468
Below Average/ poor(<40)	103(18.43)	57(17.65)	46(19.49)	
Average score(40-60)	319(57.07)	177(54.8)	142(60.17)	
Above average (>60)	137(24.51)	89(27.55)	48(20.34)	
Feeling sad/depressed				0.593
None	123(22.0)	75(23.22)	48(20.34)	
Some of the time	394(70.48)	226(69.97)	168(71.19)	
most of the time	42(7.51)	22(6.81)	20(8.47)	
Karnofsky score(% score)				0.3412
<60	73(13.06)	40(12.38)	33(13.98)	
60-80	311(55.64)	174(53.87)	137(58.05)	
90-100	175(31.31)	109(33.75)	66(27.97)	
CDC score				0.8431
Working	44(7.87)	24(7.43)	20(8.47)	
Ambulant	329(58.86)	193(59.75)	136(57.63)	
Bedridden	186(33.27)	106(32.82)	80(33.90)	
Knowledge/beliefs about HIV & ARVs				
Believes that ARVs cure HIV				0.8003
yes	86(15.38)	47(14.55)	39(16.53)	
no	443(79.25)	259(80.19)	184(77.97)	
no opinion	30(5.37)	17(5.26)	13(5.51)	
Can a Healthy HIV postive transmit HIV				0.801
Yes	553(98.93)	319(98.76)	234(99.15)	
No/Do not know	6(1.07)	4(1.24)	2(0.85)	
ARV treatment reduces HIV transmission				0.2873
Yes	230(41.14)	139(43.03)	91(38.56)	
No	297(53.13)	163(50.46)	134(56.78)	
Do Not know	32(5.72)	21(6.50)	11(4.66)	
Sexual practices				
Condom at last sex				<0.0001
Yes	206(36.85)	147(54.51)	59(25.00)	
No	353(63.15)	176(54.49)	177(75.00)	
Reports Consistent Condom Use				<0.0001
Yes	179(32.14)	139(43.03)	40(16.95)	
No	380(67.98)	184(56.97)	196(83.05)	
Multiple sexual partners				<0.0001
Yes	70(12.52)	59(18.27)	11(4.66)	
No	489(87.48)	264(81.73)	225(95.34)	

We tested for important plausible interactions by stratifying the association between CD4 cell counts and reporting recent sex by the strata created by gender, employment and the HIV status of the partner in the household. These factors on which we assessed for interaction were hypothesized/ had been previously shown in published work to modify the effect of CD4 cell count on sexual activity and reporting unprotected sex. The odds ratios in the different strata created by the third variable i.e. were homogenous hence we failed to reject the null hypothesis of the test that states that the odds ratios are homogenous in the different strata. The results of the Breslow-Day test of homogeneity of odds ratios and p-values are summarized below.

	Breslow-Day test probability values		
Exposure	**outcome**	**Stratification variable**	**P-Value**
CD4 Cell category	Recent sexual intercourse	Gender	0.738
		Employment	0.1609
		Partner HIV status	0.2479
		Quality of life score	0.738

Without any interaction of interest we proceeded to build a multivariable logistic regression model based on guidelines in methods section.

Although we were primarily interested in looking at the effect of CD4 cell count on sexual activity, we also wanted to look at whether the physical health quality of life was independently associated with sexual activity was therefore left in all models during the model building process.

Below is the summary of the univariable models and only the final multivariable logistic regression model. In univariable analyses, recent sexual activity was most likely in subjects who were male, were employed (versus unemployed), had CD4 cell counts above 100 cells/μL, with household incomes between 50000-10000 Uganda shillings.

In the model building process, after we removed all the interaction terms based on the chunk test, we obtained the gold standard model parameter estimates [60]. The subsequent model building strategy was a backward elimination of the most non significant parameter in model until we achieved the most parsimonious model that still gave us the main exposure (CD4 variable) parameter estimate that is closest (with in 10%) to that we obtained in the gold standard model. The final Model fit was assessed by the Hosmer-Lemeshow goodness of fit test p-value was 0.2062. In the final multivariable model, the association between CD4 cell category and reporting recent sex was not statistically significant (AOR=1.02 95% CI (0.67-1.57) for subjects with CD4 cell counts above versus below 100 cells/μL after adjusting for age, gender marital status, physical health QOL and income. Physical health QOL category was not associated with reporting recent sex.

The adjusted odds ratio of reporting recent sexual activity was, 0.59 95% CI (0.48-0.73) per 10 year increase in age, 2.04 95% CI (1.4-3.0) for male gender, while married/cohabiting subjects had adjusted OR of 11.3 95% CI (7.98-20.3) versus the unmarried/widowed subjects.

Subjects with monthly household income between 50000-100000 Shillings were more likely to report recent sex compared to who declined to answer (AOR=5.59, $p<0.0001$). The other household income categories associations did not attain statistical significance in the multivariable model. The odds of recent sexual activity in the other income categories did not differ from that of subjects who decline to reveal their income. The latter was used as the reference category because they constituted a third of the whole study group and to assess any dose-response relationship.

Table 9 : Univariable and Multivariable Logistic regression analysis results of factors associated with recent sexual activity at ART initiation.

Characteristic	Univariate analysis		Final Multivariate analysis	
	Odds ratio(95% CI)			
	Crude	*pValue*	*Adjusted*	*pValue*
Age in years, (per 10 year incr)	0.59(0.48-0.73)	<0.0001	0.45(0.34-0.60)	<0.0001
Male gender	2.04(1.396-2.984)	0.0002	1.97(1.21-3.23)	0.0069
Married /Cohabiting (Vs.Not married/widowed)	11.289	<0.0001	12.72(7.98-20.30)	<0.0001
Spouse/Partner HIV status(if married)				
Negative/Unknown (Vs HIV Positive)	1.070(0.509-2.248)	0.8584		
Highest Education level				
No formal education-lower primary	0.545(0.324-0.917)	0.0222		
Upper primary	0.770(0.518-1.146)	0.198		
Secondary level education	1			
Technical/University	0.699(0.407-1.201)	0.1949		
Employment				
Not employed	1			
employed (Self /casual & or Informal)	1.537(1.016-2.324)	0.042		
employed(formal :Private/Government)	1.791(1.181-2.718)	0.0061		
Monthly Household Income				
Below 50000 Ushs	0.840(0.561-1.258)	0.3978	1.27(0.76-2.12)	0.3622
Between 50000 - 100000 Ushs	2.630(1.414-4.566)	0.0006	4.59(2.29-9.21)	<0.0001
Above 100K Ushs	1.417(0.839-2.396)	0.1925	1.37(0.69-2.68)	0.3671
Declined to answer	1		1	
Number of children in Household				
0(None)	0.789(0.464-1.340)	0.3802		
1-2 children	1			
3 or more children	1.776(1.230-2.564)	0.0022		
CD4 cell count category				
> 100 cells/mm^3 (Vs less/=100 cells/mm3)	0.699(0.499-0.980)	0.0379	1.02(0.67-1.57)	0.9208
$Log_{10(Baseline}$HIV plasma RNA copies$^{-ml)}$	1.025(0.759-1.384)	0.8737		
Body mass index category(KG/M^2)				
</= 18.49	0.832(0.574-1.204)	0.3289		
18.5-24.99	1			
>25.00	1.00(0.544-1.841)	0.9987		
WHO HIV/AIDS Clinical Stage				
I &II	1.080(0.625-1.865)	0.7825		
III	1			
IV	0.934(0.648-1.346)	0.7153		
Years since first HIV test(N=497)				
Less than a year	1.219(0.821-1.809)	0.3264		
Between 1-5 years	1			
Above 5 years	0.846(0.367-1.952	0.6952		
Physical health summary score				
Below Average/ poor(<40)	0.994(0.636-1.554)	0.9793	1.62(0.90-2.92)	0.1078
Average score(40-60)	1		1	
Above average (>60)	1.488(0.983-2.252	0.0605	1.17(0.70-1.95)	0.5501

Table 9 continued

Characteristic	Univariate analysis Odds ratio(95% CI)		Final Multivariate analysis Odds ratio(95% CI)	
	Crude	*pValue*	*Adjusted*	*pValue*
Feeling sad/depressed				
None	1.162(0.768-1.757)	0.5361		
Some of the time	1			
most of the time	0.818(0.432-1.547)	0.4781		
Karnofsky score(% score)				
<60	0.954(0.572-1.593)	0.8582		
60-80	1			
90-100	1.3(0.890-1.899)	0.1743		
Believes that ARVs cure HIV				
yes	0.856(0.538-1.363)	0.5124		
no	1			
no opinion	0.929(0.440-1.960)	0.8476		
Can a Healthy HIV postive transmit HIV				
Yes	1			
No/Do not know	1.467(0.266-8.077)	0.6597		
ARV treatment reduces HIV transmission				
Yes	1			
No	0.796(0.562-1.129)	0.2015		
Do Not know	1.250(0.575-2.715)	0.5732		
			HLGOF P_value :0.2062	

When analysis was limited to only married/cohabiting subjects, CD4 cell category was still not significantly associated with reporting recent sex (AOR = 0.87, 95% CI 0.42-1.80), for CD4 cell >100 cells/μL versus CD4 cell <=100 cells/μL adjusting forage, HIV status of the spouse, number of children and monthly household income. Age was the only factor that attained statistically significant association with reporting recent sex, with an AOR= 0.64, 95% CI 0.39-1.01, p=0.051 per 10 year age increment. Importantly, although not statistically significant, having an HIV positive spouse versus HIV negative/unknown status, was associated with less odds of reporting recent sex, AOR=0.78; 95% CI 0.35-1.71, p=0.53. Number of children in the household were not associated with recent sex, p=0.70.

Among only the unmarried, factors significantly associated with reporting recent sex were age, AOR = 0.43; 95% CI 0.30-0.61 p<0.0001 per 10 year increase, household income between 50000-100000 shillings, AOR=3.3; 95% CI 1.58-7.05 p=0.0016 versus those earning below 50000 shillings, and being male AOR=2.13; 95%CI 1.16-3.87, p= 0.0147, while having CD4 above 100 cells was not statistically significant in this model (p=0.97). The model in the unmarried was adjusted for Age, CD4 cell category, gender and household income.

Table 10: Multivariable model for recent sex among male subjects

Variable/Characteristic	Adjusted odds ratio	95% Confidence interval	P-value
CD4 cell category (>100 cells/μL Vs <=100 cells/μL)	1.29	0.58-2.88	0.53
Age (Per 10 years increase)	0.54	0.34-0.88	0.013
Married/cohabiting (Vs Unmarried)	10.17	4.33-23.85	<0.0001
Employed (Vs Unemployed)	3.67	1.69-7.98	0.001
Goodness of fit p- value= 0.82	Sensitivity = 57.5 specificity= 86.8		

Gender specific multivariable models:

When we ran separate multivariable models for males and females, still CD4 cell count category was not associated with reporting recent sex in either gender.

Table 11: Multivariate model among female subjects only

Variable /Characteristic	Adjusted odds ratio	95% Confidence interval	P-value
CD4 cell category			
(>100 cells/µL Vs <=100 cells/µL)	0.97	0.58-1.63	0.9133
Age (Per 10 years increase)	0.43	0.30-0.62	<0.0001
Married/cohabiting (Vs Unmarried)	14.45	8.13-25.7	<0.0001
Monthly Household income			
Below 50000 shillings	Ref	Ref	
Between 50000- 100000 Ushs.	5.22	2.30-11.7	<0.0001
Above 100000 shillings	0.41	0.16-1.04	0.0609
Declined to answer	0.95	0.53-1.72	0.9133
Goodness of fit p- value= 0.55	Sensitivity = 72 specificity= 81.5		

Unprotected sex at last sex at the baseline i.e. ART initiation visit

Of the 323 subjects reporting recent sex, 176 (54.5%) reported unprotected sex at their last sexual encounter. Tables 12-14 show distributions of factors associated with reporting unprotected sex in the preceding six months.

Table 12: Factors associated with unprotected sex at ART initiation

Characteristic	Condom use			
	overall =323	no =176(54.49)	yes , =147(45.51)	p-value
Age in years, Median(IQR)	37(32-42)	36(32-41)	37(33-42)	0.2486*
AGE CATEGORY ,years				0.0359
18-28	19(5.88)	16(9.09)	3(2.04)	
28.1-38	184(56.97)	96(54.55)	88(59.86)	
38.1-48	100(30.96)	51(28.98)	49(33.33)	
>48	20(6.19)	13(7.39)	7(4.76)	
Gender				0.0876
Male	120(37.15)	58(32.95)	62(41.18)	
Female	203(62.85)	118(67.05)	85(57.82)	
Marital status				0.1225
Married /Cohabiting ,in Monogamous	161(49.85)	79(44.89)	82(55.78)	
Married /Cohabiting ,in Polygamous	60(18.58)	34(19.32)	26(17.69)	
Not married/widowed/divorced	102(31.58)	63(35.80)	39(26.53)	
Highest Education level				0.9645
No formal education-lower primary	37(11.46)	21(11.93)	16(10.88)	
Upper primary	102(31.58)	57(32.39)	45(31.61)	
Secondary level education	146(45.20)	78(45.32)	68(46.26)	
Technical/University	38(11.76)	20(11.36)	18(12.24)	
Spouse/Partner HIV status(if married) N=219				0.0466
Positive	66(30.14)	27(24.11)	39(36.45)	
Negative/Not Known	153(69.86)	85(75.89)	68(63.55)	
Median Duration with partner ,years (IQR)	8(4-14)	8(4-12)	8(4.5-14)	0.4265*
Number of children in Household				0.0567
0(None)	34(10.53)	23(13.07)	11(7.48)	
1-2 children	111(34.37)	66(37.50)	45(30.61)	
3 or more children	178(55.11)	87(49.43)	91(61.90)	
Employment				0.5078
Not employed	140(43.34)	76(43.18)	64(43.54)	
employed (Self /casual & or Informal)	88(27.24)	52(29.55)	36(24.49)	
employed(formal :Private/Government)	95(29.41)	48(27.27)	47(31.97)	
Monthly Household Income				0.0766
Below 50000 Ushs	97(30.03)	63(35.80)	34(23.13)	
Between 50000 - 100000 Ushs	72(22.29)	33(18.75)	39(26.53)	
Above 100K Ushs	54(16.72)	28(15.91)	26(17.69)	
Declined to answer	100(30.96)	52(29.55)	48(32.65)	

Table 13 : Factors associated with unprotected sex at ART initiation Continued

Characteristic	Condom use			
	overall =323	no =176(54.49)	yes , =147(45.51)	p-value
CD4 cell count,Median(IQR) ,Cells/mm^3	83(15-159)	67.5(12.5-160.5)	100(29-156)	0.3303*
CD4 count category				0.1891
< 100 cells/mm^3	182(56.35)	105(59.66)	77(52.38)	
> 100 cells/mm^3	141(43.65)	71(40.34)	70(47.62)	
Log_{10}HIV plasma RNA $copies^{-ml}$, Median(IQR)	5.4(5.1-5.8)	5.47(5.14-5.79)	5.36(5.02-5.69)	0.0808*
Baseline HIV plasma RNA copies-ml				0.2698
<= 38500	23(7.17)	10(5.71)	13(8.90)	
>38500	298(92.83)	165(94.29)	133(91.10)	
Body mass index category				0.1777
</= 18.49	94(29.10)	58(32.95)	36(24.49)	
18.5-24.99	200(61.92)	101(57.39)	99(67.35)	
>25.00	29(8.98)	17(9.66)	12(8.16)	
CDC score				0.1315
Ambulant	193(59.75)	98(55.68)	95(64.63)	
Bedridden	106(32.82)	61(34.66)	45(30.61)	
WHO Clinical Stage				0.0308
I & II	39(12.07)	17(9.66)	22(14.97)	
III	175(54.18)	89(50.57)	86(58.50)	
IV	109(33.75)	70(39.77)	39(26.53)	
Syphillis *T. Pallidum* Antibody test(N=164)				
Positive	20(12.20)	11(11.58)	9(13.04)	0.7772
Negative	144(87.80)	84(88.42)	60(86.96)	
Karnofsky score(% score)				0.0016
<60	40(12.38)	30(17.05)	10(6.80)	
60-80	174(53.87)	99(56.25)	75(51.02)	
90-100	109(33.75)	47(26.70)	62(42.18)	
WHO Performance scale				0.0823
Asymptomatic,Normal Activity	28(8.67)	11(6.25)	17(11.56)	
Symptomatic,Normal Activity	209(64.71)	110(62.5)	99(67.35)	
Bedridden <50% last Month	74(22.91)	46(26.14)	28(19.05)	
Bedridden >50% last Month	12(3.72)	9(5.11)	3(2.04)	

Table 14 : Factors associated with unprotected sex at ART initiation Continued

Characteristic	Condom use			
	overall =323	no =176(54.49)	yes , =147(45.51)	p-value
Belief that ARVs cure HIV				0.9227
Disagree	259(80.19)	141(80.11)	118(80.27)	
Agree	47(14.55)	25(14.20)	22(14.97)	
Do not Know	17(5.26)	10(5.68)	7(4.76)	
Healthy HIV postive can transmit				0.3338
Yes	319(98.76)	175(99.43)	144(97.96)	
No/Do not know	4(1.24)	1(0.57)	3(2.04)	
ARV treatment reduces HIV transmission				0.5046
Yes	139(43.03)	71(40.34)	68(46.26)	
No	163(50.46)	92(52.27)	71(48.30)	
Do Not know	21(6.50)	13(7.39)	8(5.44)	
Belief about ARV effectiveness in treating HIV				0.1205
effective	288(89.16)	162(92.05)	126(85.71)	
not effective	16(4.95)	5(2.84)	11(7.48)	
no opinion/not sure	19(5.88)	9(5.11)	10(6.80)	
Physical health QOL summary score				0.1205
Below Average/ poor(<40)	57(17.65)	38(21.59)	19(12.93)	
Average score(40-60)	177(54.80)	93(52.84)	84(57.14)	
Above average (>60)	89(27.55)	45(25.57)	44(29.93)	
Feeling sad/depressed				0.2233
No/None of the time	75(23.22)	36(20.45)	39(26.53)	
Some of the time	226(69.97)	125(71.02)	101(68.71)	
most of the time	22(6.81)	15(8.52)	7(4.76)	
Multiple sexual partners				0.0013
Yes	59(18.27)	21(11.93)	38(25.85)	
No	264(81.73)	155(88.07)	109(74.15)	
Previous Consistent Condom Use				<0.0001
Yes	139(43.03)	17(9.66)	122(82.99)	
No	184(56.97)	159(90.34)	25(17.01)	
Years since first HIV test(N=284)				0.8668
Less than a year	193(67.96)	100(67.57)	93(68.38)	
Between 1-5 years	78(27.46)	42(28.38)	36(26.47)	
Above 5 years	13(4.58)	6(4.05)	7(5.15)	

In univariable logistic regression analysis for odds of unprotected sex (Table 15), the association between CD4 cell category (>100 versus <= 100 cells/μL)

and reporting unprotected sex did not reach statistical significance [OR= 0.74; 95% CI 0.48-1.2, p=0.1895].Odds of Unprotected sex were highest among 18-28 year old subjects OR= 4.97, p=0.0123 compared to those between 28-48 years in univariate analysis and this remained high even after controlling for gender, marital status, CD4 and viral loads, and HIV clinical stage. Compared to Married/cohabiting subjects, unmarried/widowed subjects were 1.54 times (p=0.0753) more likely to report unprotected sex and the odds were attenuated in multivariable models that contained age and gender. Model building for multivariable mode was based on guidelines in the methods sections. In final multivariable model, odds of unprotected sex did not differ by CD4 cell count level controlling for age, gender, marital status, viral load, HIV/AIDs clinical stage and reporting multiple sex partners. Unprotected sex was more likely among subjects with HIV/AIDS stage IV versus stage III (AOR= 1.7, p=0.028), aged 18-28 years versus 28.1-48 years, AOR=4.72, p=0.024, and higher $\log_{10}$ plasma viral load, AOR=1.65, p=0.05, per log10. Increase in plasma HIV RNA copies/mL

Table 15 : Logistic regression results of factors associated with the practice of unprotected sex

Characteristic	Univariate analysis Odds ratio(95% CI)		Final Multivariate analysis Odds ratio(95% CI)	
	Crude	*pValue*	*Adjusted*	*pValue*
Age category ,years				
18-28	4.97(1.42-17.45)	0.0123	4.72(1.23-18.09)	0.0236
28.1 - 48	1		1	
>48	1.73(0.67-4.47)	0.2566	2.60(0.93-7.27)	0.0683
CD4 cell count category				
> 100 cells/mm^3 (Vs less/=100)	0.744(0.478-1.157)	0.1895	0.84(0.52-1.38)	0.4951
Log_{10}HIV plasma RNA copies/ml	1.479(0.938-2.331)	0.0918	1.65(1.0-2.71)	
Male gender	0.674(0.428-1.061)	0.0882	0.72(0.43-1.18)	0.1906
CDC score				
Working	0.761(0.472-1.227)	0.2622		
Ambulant	1			
Bedridden	1.791(0.685-4.680)	0.2346		
Marital status:*Not married (Vs Married)*	1.544(0.957-2.492)	0.0753	1.78(1.05-3.02)	0.0326
Highest Education level				
No formal education-lower primary	1.144(0.553-2.368)	0.7165		
Upper primary	1.104(0.664-1.836)	0.7022		
Secondary level education	1			
Technical/University	0.969(0.474-1.980)	0.9304		
overall wellbeing				
Excellent	0.979(0.346-2.771)	0.9674		
Moderate	1			
Poor	1.427(0.605-3.368)	0.417		
Spouse/Partner HIV status(if married) N=219				
Positive	0.554(0.308-0.994)	0.0478		
Negative/Not Known	1			
Median Duration with partner/marriage (per 5 yr increase)	0.971(0.790-1.192)	0.7758		
Belief that ARVs cure HIV				
Disagree	1			
Agree	0.951(0.510-1.773)	0.8744		
Do not Know	1.196(0.441-3.238)	0.7253		
Healthy HIV positive can transmit				
Yes	1			
No/Do not know	0.274(0.028-2.665)	0.2649		
ARV treatment reduces HIV transmission				
Yes	1			
No	1.241(0.788-1.955)	0.3516		
Do Not know	1.556(0.607-3.990)	0.3571		
Belief about ARV effectiveness in treating HIV				
effective	1			
not effective	0.354(0.120-1.044)	0.0598		
no opinion/not sure	0.700(0.276-1.774)	0.4523		

Table 16 : Logistic regression results continued from table 15

Characteristic	Univariate analysis Odds ratio(95% CI)		Final Multivariate analysis Odds ratio(95% CI)	
	Crude	*pValue*	*Adjusted*	*pValue*
Employment				
Not employed	1			
employed (Self /casual & or Informal)	1.216(0.709-2.086)	0.4768		
employed(formal :Private/Government)	0.860(0.510-1.449)	0.5712		
Body mass index category				
</= 18.49	1.579(0.958-2.603)	0.0732		
18.5-24.99	1			
>25.00	1.389(0.631-3.057)	0.4149		
WHO Clinical Stage				
I & II	0.747(0.371-1.502)	0.4126	0.81(0.39-1.67)	0.5583
III	1		1	
IV	1.734(1.061-2.834)	0.028	1.80(1.05-3.07)	0.0325
Karnofsky score(% score)				
<60	2.273(1.046-4.938)	0.0381		
60-80	1			
90-100	0.574(0.354-0.931)	0.0245		
WHO Performance scale				
Asymptomatic,Normal Activity	0.394(0.161-0.961)	0.0407		
Symptomatic,Normal Activity	0.676(0.393-1.164)	0.1578		
Bedridden <50% last Month	1			
Bedridden >50% last Month	1.826(0.456-7.321)	0.3953		
Monthly Household Income				
Below 50000 Ushs	2.190(1.174-4.085)	0.0138		
Between 50000 - 100000 Ushs	1			
Above 100K Ushs	1.273(0.628-2.581)	0.5038		
Declined to answer	1.280(0.698-2.350)	0.4252		
Multiple sexual partners				
Yes	0.389(0.216-0.699)	0.0016	0.33(0.17-0.63)	0.0009
No	1		1	
Years since first HIV test(N=284)				
Less than a year	0.922(0.544-1.562)	0.762		
Between 1-5 years	1			
Above 5 years	0.735(0.226-2.386)	0.608		
Physical health QOL summary score				
Below Average/ poor(<40)	1.81(0.97-3.37)	0.0636		
Average score(40-60)	1			
Above average (>60)	0.92(0.56-1.54)	0.7603		
Number of children in Household				
0(None)	1.425(0.633-3.212)	0.3924		
1-2 children	1			
3 or more children	0.652(0.404-1.053)	0.0803		
Syphilis test(N=164)				
Positive	0.873(0.341-2.238)	0.7773		
Negative	1			
Feeling sad/depressed				
None	0.746(0.442-1.259)	0.2722		
Some of the time	1			
most of the time	1.731(0.68-4.408)	0.2498		
			HLGOF:0.2389	

There was no statistically significant difference in odds of unprotected sex by gender although Males were less likely to have had unprotected sex, AOR=0.72, p=0.191. Subjects who ever reported multiple sex partners were less likely to have had unprotected sex compared to those who reported only one sex partner, AOR=0.33, p=0.0009.

Multiple Sex Partners

Seventy (70) subjects, (12.57% of 559) reported two or more sexual partners in the twelve months preceding enrolment/initiation of ART, while 59 of these subjects reported multiple sex partners in the six months preceding enrolment. Subjects who reported multiple sex partners were less likely to report unprotected sex in the preceding six months, AOR 0.33; 95%CI 0.17-0.63,p=0.0009. We did not have to enable establish whether the multiple sexual partners were causal or regular partners.

Specific Aim 2 Results

For this analysis, we included subjects who did report sexual activity in the preceding six months before their enrolment. These subjects were followed up after for three years after initiation of ART to determine, time to resumption of sex and establish baseline characteristics associated with resumption of sex while on ART.

A total of 236 (42.2%) subjects were eligible for inclusion in this analysis of whom 41/236 (17.4%) subjects did not return for any follow up visit leaving 195 subjects with at least 1 follow up visit and the latter were the effective number used for subsequent analyses. Subjects who did not return for any follow up visit were more likely to have had less favorable clinical characteristics, i.e., a lower Karnofsky scores and CD4 cell counts below 100 cells/μL, (p=0.0002) however they did not differ in any other socio-demographic and behavioral characteristics from those that had at least one follow up visit. This could suggest that those without any follow up visit were more likely to have died after ART initiation given the high mortality rates after ART initiation in subjects with very advanced HIV/AIDS although this data was not available at the time of this analysis.

A subject was considered to have resumed sexual intercourse if they reported sexual activity on at least one of the follow up visits during the three years of follow up.

Table 17: Comparison subjects characteristics by gender

CHARACTERISTIC	GENDER		
	Female	Male	
	N= 183 (77.54%)	N= 53 (22.46%)	p-Value
Age in years, median (IQR)	39(33-47)	42(36-50)	0.1187
Marital status			
Currently Married	25 (13.7%)	13 (24.5%)	0.058
Not married	158 (86.3%)	40 (75.5%)	
Highest Education level			0.0281
No formal education-lower primary	33 (18.0%)	7 (13.2%)	
Technical /University level	19 (10.4%)	13 (24.5%)	
Upper primary-Secondary level	131 (71.6%)	33 (62.3%)	
Employment Status			0.2917
Employed	84 (45.9%)	20 (37.7%)	
Not employed	99 (54.1%)	33 (62.3%)	
Monthly Household Income			0.0233
Below 50000 Ushs	84 (45.9%)	13 (24.5%)	
Between 50000 - 100000 Ushs	12 (6.6%)	9 (17.0%)	
Above 100K Ushs	23 (12.6%)	9 (17.0%)	
Declined to answer	62 (33.9%)	22 (41.5%)	
CD4 cell category/ level			0.3712
<= 100 cells/µL	83 (45.4%)	28 (52.8%)	
> 100 cells/µL	98 (53.6%)	25 (47.2%)	
WHO HIV/AIDS clinical stage			0.4602
Stage I & II	22 (12.0%)	4 (7.5%)	
Stage III & IV	161 (88.0%)	49 (92.5%)	
Physical health QOL summary score			0.232
Below Average/ poor(<40)	34 (18.6%)	12 (22.6%)	
Average score(40-60)	128 (69.9%)	39 (73.6%)	
Above average (>60)	21 (11.5%)	2 (3.8%)	

Table 18 : Comparison previously abstinent subjects characteristics by gender

CHARACTERISTIC	GENDER		
	Female	**Male**	
	N= 183 (77.54%)	N= 53 (22.46%)	p-Value
Body mass index category			0.2481
</= 18.49 (KG/M2)	57 (31.1%)	21 (39.6%)	
> 18.49 (KG/M2)	126 (68.9%)	32 (60.4%)	
Baseline HIV plasma RNA copies-ml			0.7696
<= 38500	15 (8.3%)	3 (5.9%)	
>38500	165 (91.7%)	48 (94.1%)	
Hemoglobin level , Mean (SD),g/DL	11.0(1.9)	12.0(2.3)	0.0063
Karnofsky score(% score)			0.8556
<60	25 (13.7%)	8 (15.1%)	
60-80	108 (59.0%)	29 (54.7%)	
90-100	50 (27.3%)	16 (30.2%)	
Years since first HIV positive test			0.0902
Less than a year	101 (60.1%)	33 (73.3%)	
Between 1-5 years	54 (32.1%)	12 (26.7%)	
Above 5 years	13 (7.7%)	0 (0.0%)	
Number of children in Household			0.0373
0(None)	29 (15.8%)	11 (20.8%)	
1-2 children	88 (48.1%)	15 (28.3%)	
3 or more children	66 (36.1%)	27 (50.9%)	
Reason for prevoius abstention			0.028
No Partner	52 (29.2%)	8 (15.4%)	
My poor health status	28 (15.7%)	16 (30.8%)	
Chose not too	95 (53.4%)	26 (50.0%)	
Other	3 (1.7%)	2 (3.8%)	
Believes that ARVs cure HIV			0.1321
yes	26 (14.2%)	13 (24.5%)	
no	148 (80.9%)	36 (67.9%)	
Do Not know/no opinion	9 (4.9%)	4 (7.5%)	
Believes ARV treatment reduces HIV transmission			0.158
Yes	65 (35.5%)	26 (49.1%)	
No	110 (60.1%)	24 (45.3%)	
Do Not know/no opinion	8 (4.4%)	3 (5.7%)	

Characteristics of the study are shown in tables 17 -18, and are compared between Males and females.

The median (IQR) age and CD4 cell count was 40 (33.5-47.5) years and 104 (29-173) cells/μL, respectively. There were no statistically significant differences in, median ages (P=0.1187), CD4 cell category (p=0.3712) and HIV/AIDS clinical stage (p=0.4602) by gender. Females were more likely to be unmarried/widowed/divorced (p=0.058) than males.

Of the 195 subjects followed up, 81(41.5%) had resumed sexual activity while on ART during the three years of study follow up. Approximately 24% and 35% of the subjects had resumed intercourse by one and two years respectively.

Figure 3 show the KM estimate curve, with cumulative incidence of resumption of sexual activity by 3.03 years in this cohort was 44.9 per 100 population.

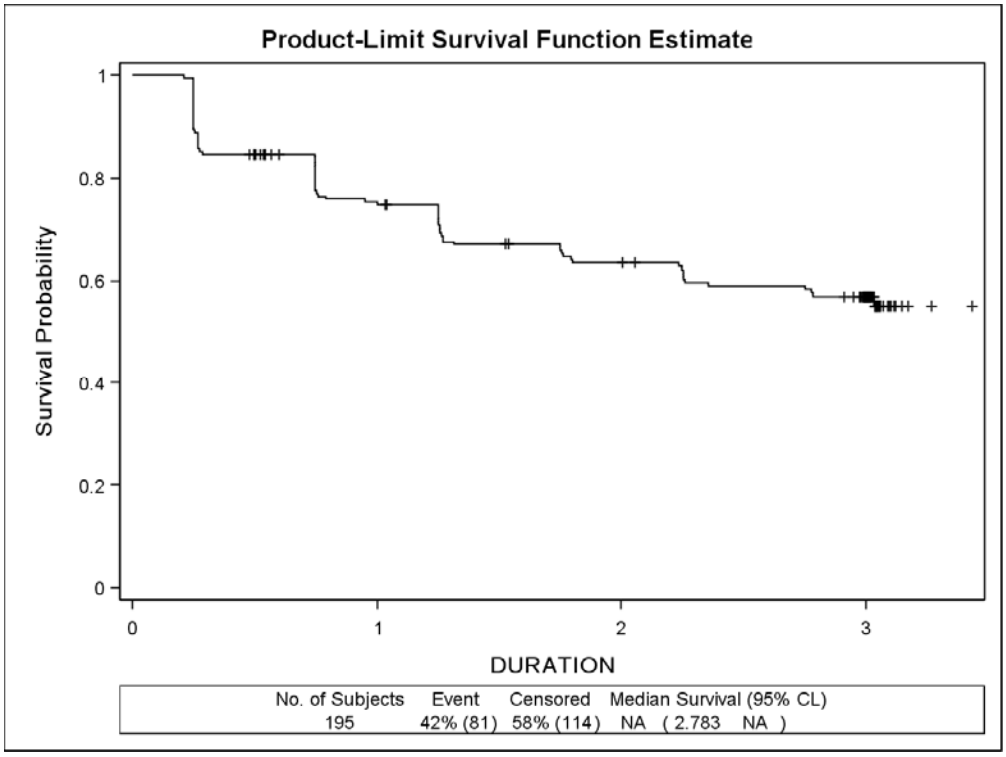


Figure 3: Kaplan Meier curve for time (in years) from ART initiation to resumption of sexual activity in subjects who were not sexually active at ART initiation

Tables 19-20, and figures 4-8 show a comparison of the KM estimates of time to resumption/re-initiation of sexual intercourse by different characteristics and log rank test used was for comparison of the Kaplan-Meier survival curves of the different strata in each characteristic. Males, compared to females (0.0093), subjects who are married/cohabiting (p=0.0007) compared to the single/divorced/widowed, and those having at least upper primary education (p=0.0181) were more likely to re-initiate sexual activity.

Characteristic	Not sexually active at enrolment N=195	Re-initiated sex on follow-up N=81	Log- rank P-Value
Gender			0.0093
Male	43 (22.1%)	25 (30.9%)	
Female	152 (77.9%)	56 (69.1%)	
Age strata (years)			0.0093
18-28	14 (7.2%)	8 (9.9%)	
28.1-38	71 (36.4%)	39 (48.1%)	
38.1-48	67 (34.4%)	24 (29.6%)	
>48 years	43 (22.1%)	10 (12.3%)	
Marital status			0.0007
Currently Married	31 (15.9%)	20 (24.7%)	
Not married	164 (84.1%)	61 (75.3%)	
Highest Education level			0.0181
No formal education-lower primary	32 (16.4%)	7 (8.6%)	
Upper primary-Secondary level	138 (70.8%)	61 (75.3%)	
Technical/University	25 (12.8%)	13 (16.0%)	
Employment Status			0.8020
Employed	90 (46.2%)	38 (46.9%)	
Non employed	105 (53.8%)	43 (53.1%)	
Monthly Household Income			0.0977
Below 50000 Ushs	81 (41.5%)	26 (32.1%)	
Between 50000 - 100000 Ushs	20 (10.3%)	9 (11.1%)	
Above 100K Ushs	27 (13.8%)	13 (16.0%)	
Declined to answer	67 (34.4%)	33 (40.7%)	
CD4 cell category/ level			0.8535
<= 100 cells/ µL	82 (42.1%)	34 (42.0%)	
> 100 cells/µL	113 (57.9%)	47 (58.0%)	
WHO HIV/AIDS clinical stage			0.8061
Stage I & II	24 (12.3%)	11 (13.6%)	
Stage III & IV	171 (87.7%)	70 (86.4%)	
Physical health QOL Summary Score			0.0053
Below Average (<40%)	37 (18.9%)	7 (8.6%)	
Average Score (40-60%)	138 (70.8%)	68(84%)	
Body mass index category			
Above Average (>60%)	20(10.3%)	6(7.4%)	0.4631
</= 18.49 (KG/M2)	57 (29.2%)	26 (32.1%)	
> 18.49 (KG/M2)	138 (70.8%)	55 (67.9%)	

Table 20 : Subjects initiating sexual intercourse and comparison of time to initiation survival curves of intercourse by Log rank test

Characteristic	Not sexually active at enrolment N=195		Re-initiated sex on follow-up N=81		Log- rank P-Value
Baseline HIV plasma RNA copies-ml					0.7689
<= 38500	15	(7.9%)	7	(8.8%)	
>38500	176	(92.1%)	73	(91.3%)	
Hemoglobin level					0.6126
<= 10 g/Dl	41	(21.0%)	18	(22.2%)	
> 10 g/Dl	154	(79.0%)	63	(77.8%)	
Karnofsky score (% score)					0.8653
<60	20	(10.3%)	8	(9.9%)	
60-80	114	(58.5%)	49	(60.5%)	
90-100	61	(31.3%)	24	(29.6%)	
Syphilis test					0.0585
Positive	26	(13.3%)	8	(9.9%)	
Negative	80	(41.0%)	41	(50.6%)	
Not done	89	(45.6%)	32	(39.5%)	
Years since first HIV positive test					0.1768
Less than a year	110	(61.5%)	46	(63.9%)	
Between 1-5 years	59	(33.0%)	25	(34.7%)	
Above 5 years	10	(5.6%)	1	(1.4%)	
Number of children in Household					0.8246
0(None)	31	(15.9%)	12	(14.8%)	
1-2 children	87	(44.6%)	33	(40.7%)	
3 or more children	77	(39.5%)	36	(44.4%)	
Reason for previous abstention					0.3228
No Partner	51	(26.2%)	17	(21.5%)	
My poor health status	35	(17.9%)	17	(21.5%)	
Chose not too	100	(51.3%)	44	(55.7%)	
Other	4	(2.1%)	1	(1.3%)	
Believes that ARVs cure HIV					0.538
yes	32	(16.4%)	10	(12.3%)	
no	152	(77.9%)	65	(80.2%)	
Do Not know/no opinion	11	(5.6%)	6	(7.4%)	
Believes ARV treatment reduces HIV					0.1819
Yes	68	(34.9%)	28	(34.6%)	
No	116	(59.5%)	51	(63.0%)	
Do Not know/no opinion	11	(5.6%)	2	(2.5%)	

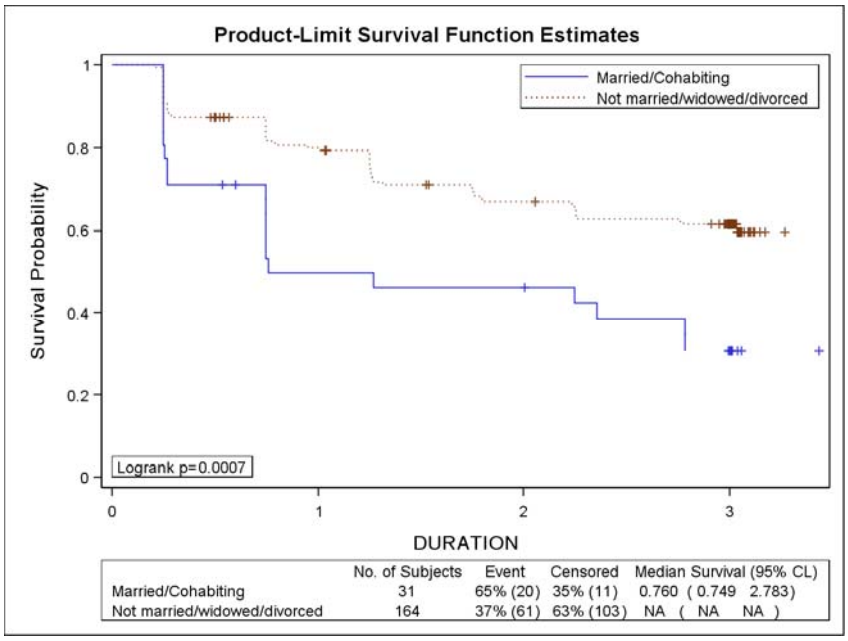


Figure 4 Kaplan Meier curve for time (in years) from ART initiation to resumption of sexual activity by marital status in subjects who were not sexually active at ART initiation.

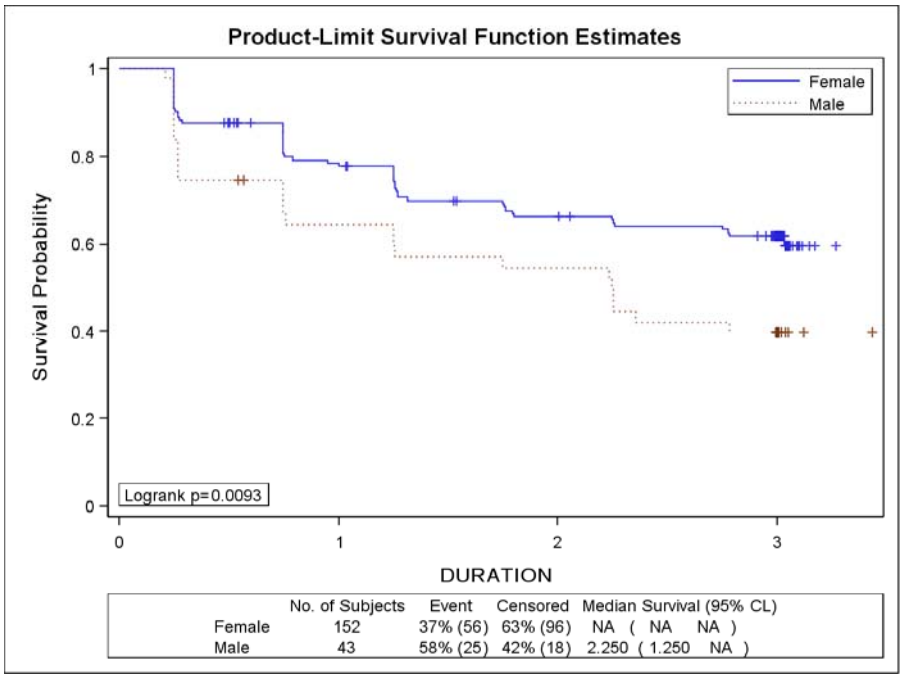


Figure 5: Kaplan Meier curve for time (in years) from ART initiation to resumption of sexual activity by Gender in subjects who were not sexually active at ART initiation

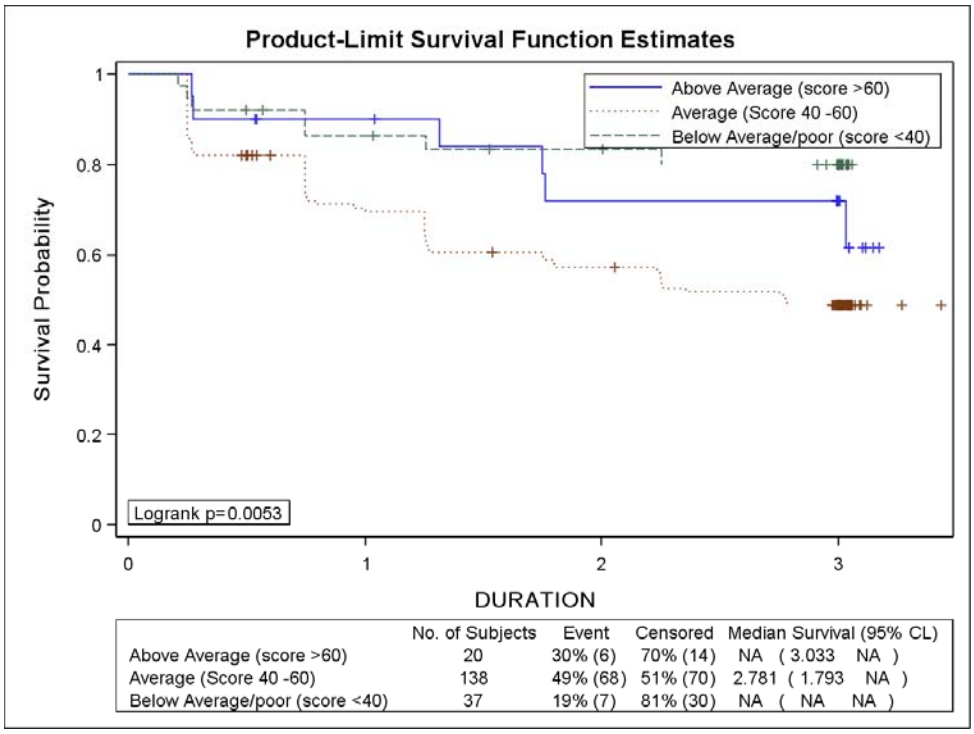


Figure 6 Kaplan Meier curve for time (in years) from ART initiation to resumption of sexual activity by Quality of life category in subjects who were not sexually active at ART Initiation.

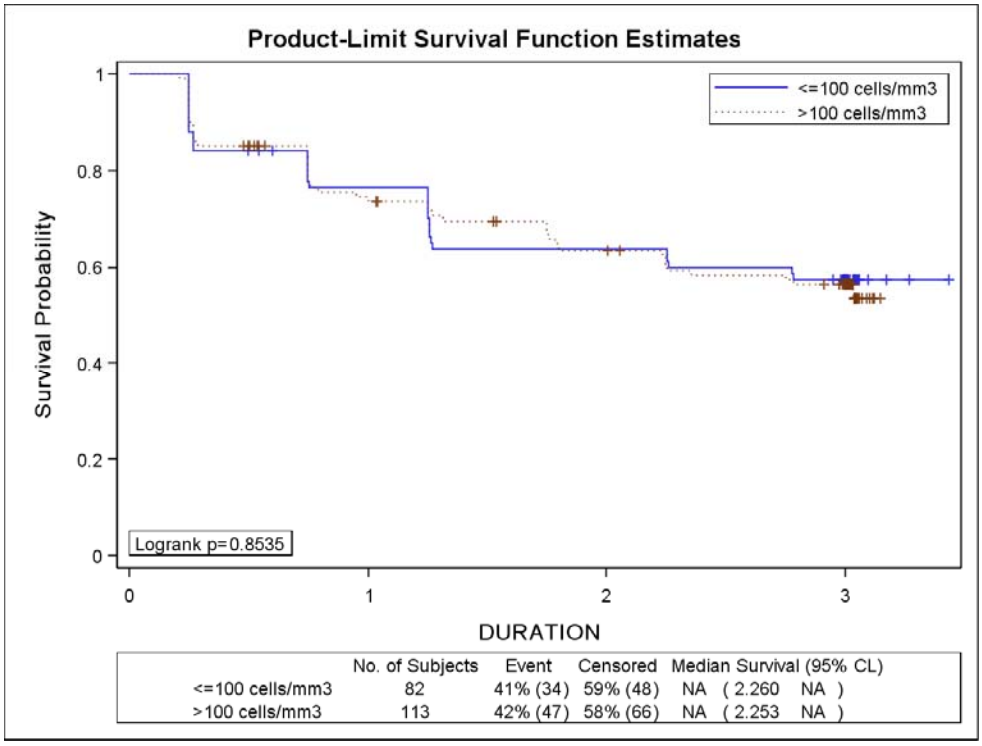


Figure 7 Kaplan Meier curve for time (in years) from ART initiation to resumption of sexual activity by CD4 cell count category in subjects who were not sexually active at ART initiation.

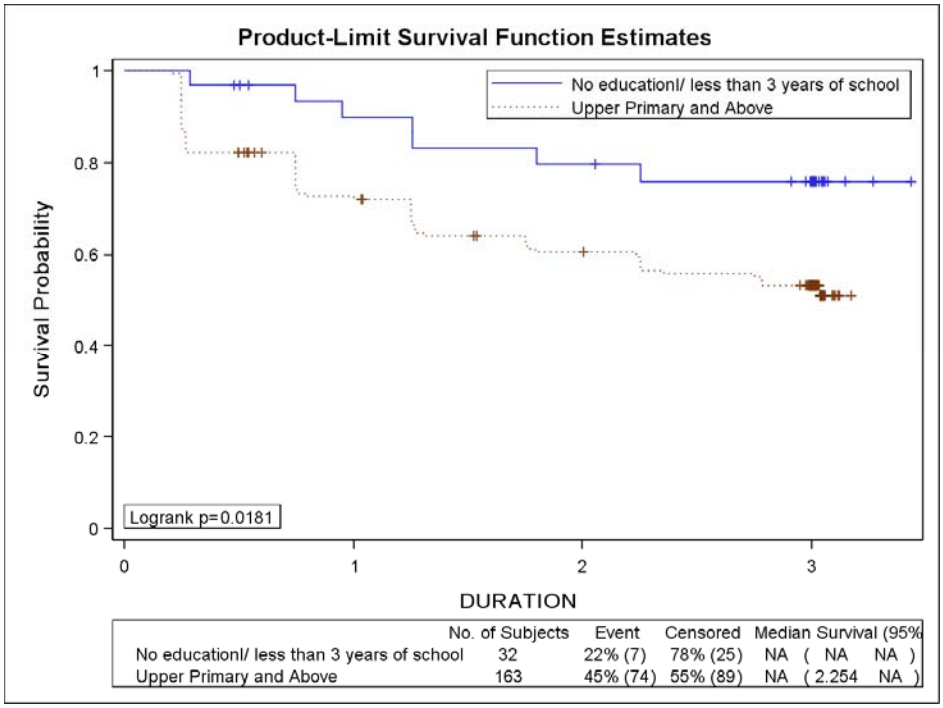


Figure 8 Kaplan Meier curve for time (in years) from ART initiation to resumption of sexual activity by highest Education level in subjects who were not sexually active at ART initiation.

Table 21, summarizes the univariable and final multivariable Cox proportional hazards models of baseline factors associated with resumption of sex intercourse. The Hazard of resumption of sexual intercourse was higher in Males (HR=1.8; 95% CI 1.1-2.9), Married/Cohabiting individuals (HR=2.3; 95% CI 1.4-3.8), while lower hazards were seen in persons with no education (HR= 0.42; 95% CI 0.19-0.89) relative to the rest, those with below average/poor physical health quality of life score (HR=0.33; 95%CI 0.15-0.72) relative to those with average scores, and those with lower monthly household incomes and increasing age. There were no statistically

Table 21: Baseline factors associated with resumption of Sexual Intercourse.

Cox Proportional Hazards model for Baseline Predictors of Resumption of sexual activity.				
	Univariate analysis		Multivariate analysis	
Characteristic	Crude Hazard Ratio(95% CI)	p-Value	Adjusted Hazard Ratio(95% CI)	p-Value
Gender				
Male	1.8(1.1-2.9)	0.0176	1.77(1.08-2.90)	0.0228
Female	1		1	
Age (per 10 years increase)	0.66(0.52-0.84)	0.0009	0.65(0.50-0.84)	0.0011
Marital status				
Currently Married/cohabiting	2.3(1.4-3.8)	0.0013	1.93(1.11-3.36)	0.0207
Not married/widowed/divorced	1		1	
Highest Education level				
No formal education-lower primary	0.41(0.19-0.89)	0.0243	0.46(0.21-1.00)	0.0503
Upper primary and above	1		1	
Monthly Household Income				
Below 50000 Ushs	0.6(0.3-0.9)	0.0211		
Between 50000 - 100000 Ushs	0.9(0.4-1.8)	0.7072		
Above 100K Ushs	1.1(0.6-2.1)	0.8549		
Declined to answer	1			
CD4 cell category/ level				
<= 100 cells/µL	0.96(0.62-1.5)	0.8563		
> 100 cells/µL	1			
WHO HIV/AIDS clinical stage				
Stage I & II	1			
Stage III & IV	0.9(0.5-1.7)	0.8091		
Physical health QOL summary score				
Below Average/ poor(<40)	0.33(0.15-0.72)	0.0051	0.38(0.17-0.85)	0.018
Average score(40-60)	1		1	
Above average (>60)	0.54(0.23-1.24)	0.1441	0.59(0.23-1.49)	0.2613
Body mass index category				
</= 18.49 (KG/M2)	1.2(0.8-2.0)	0.3982		
> 18.49 (KG/M2)	1			
Baseline HIV plasma RNA copies-ml				
<= 38500	1.2(0.5-2.5)	0.7238		
>38500	1			

Table 21 continued

Cox Proportional Hazards model for Baseline Predictors of Resumption of sexual activity.				
	Univariate analysis		Multivariate analysis	
Characteristic	Crude Hazard Ratio(95% CI)	p-Value	Adjusted Hazard Ratio(95% CI)	p-Value
Years since first HIV test				
Less than a year	1			
Between 1-5 years	1.1(0.7-1.8)	0.6588		
Number of children in Household				
0(None)	0.9(0.5-1.7)	0.8452		
1 or more children	1			
Reason for prevoius abstention				
No Partner	0.7(0.4-1.2)	0.2309	0.82(0.46-1.43)	0.4738
My poor health status	1.1(0.6-2.0)	0.6561	1.06(0.59-1.92)	0.8425
All other reasons	1		1	
Believes that ARVs cure HIV				
yes	0.7(0.4-1.3)	0.2824		
No/Do Not know	1			
Believes ARV treatment reduces HIV transmission				
Yes	1.0(0.6-1.6)	0.9633		
No/Do Not know	1			
Employment Status				
Employed	1.1(0.7-1.7)	0.7307		
Non employed	1			

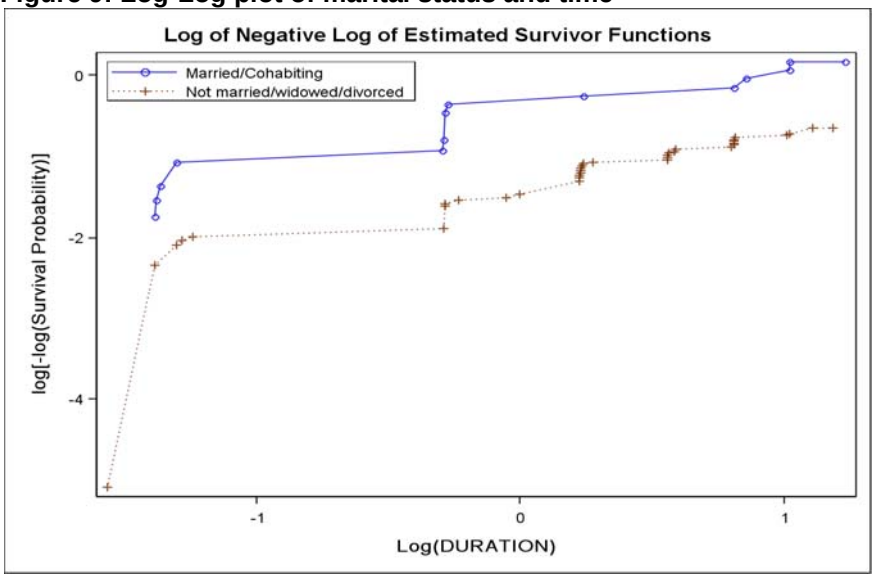
significant differences in the hazard of resumption of sexual intercourse by baseline CD4 cell count level, HIV/AIDS clinical stage, reasons neither for previous abstention nor by level/degree of HIV related knowledge or beliefs.

Baseline factors from the univariable analysis with p-values of less than 0.2 were considered for the multivariable models. The initial multivariable model contained age categories, gender, marital status, highest education attained, house hold income physical quality of life and reasons given for previous abstention from intercourse. The latter was retained in all models because we wanted to control for it in all models. Interaction terms of age category and

gender, gender and marital status were created and tested jointly but they did not improve model fit and were removed from the model. When then modeled age as a continuous variable because the age categories were not showing any particular threshold effects and were most importantly the categories did not satisfy the assumption of proportionality of hazards. All the other variables that had been tested in univariable models were introduced one by one in the model but were all removed because their addition did not provide a better fit for the model based on the Likelihood ratio test. However for reasons given for previous abstention, though did not have any statistically significant parameters in the model, we had chosen *a priori* to control for it in the final model. The final multivariable Cox proportional hazards model shows that the Hazard ratio for resumption of sexual intercourse in men almost twice that in women (p=0.0228) controlling for Age, marital status, quality of life at baseline ,highest education level and reason for abstaining. The hazard of resumption of sexual activity was highest in the married compared to the unmarried, (HR=1.93; 95% CI 1.11-3.36,p=0.0207) controlling for age, education level, gender, physical health quality of life score and reason for abstaining while the lowest hazard was seen in subjects who were in lowest physical health quality of life category (HR=0.38; 95% CI 0.17-0.85) relative to those with average physical health, and among subjects who had lowest education (HR=0.46, p=0.0503).

Proportional Hazards assumption assessment was using graphical log-log plots (Figures 10-11). Proportionality of hazards was also jointly tested for all the variables together in a Cox proportional hazards model by creating interaction terms of the variables with time. Based on both approaches all variable in the final model fulfilled the proportionality of hazards assumption over time.

Figure 9: Log-Log plot of marital status and time



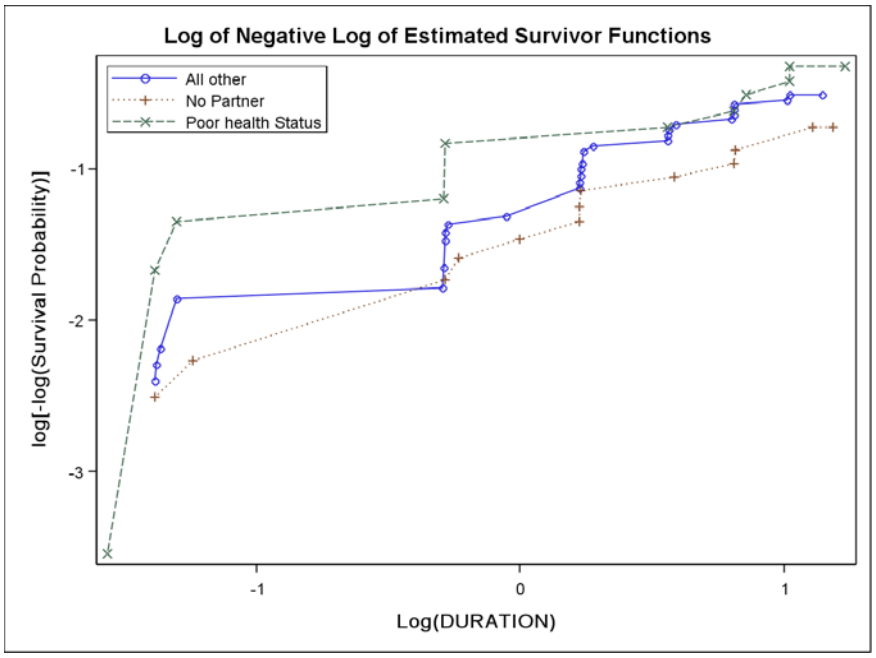


Figure 10 Log-Log plot of reason for previous abstinence and time

Testing for proportionality of hazards, exhibit shown below,

Variable	Parameter Estimate	Standard Error	Chi-Square	Pr > Chi Sq	Hazard Ratio
AGE	-0.47114	0.13791	11.6704	0.0006	0.624
married	0.85486	0.27228	9.8575	0.0017	2.351
Quality of life Score	0.27409	0.22517	1.4817	0.2235	1.315
Abstinence Reason	-0.00578	0.15962	0.0013	0.9711	0.994
Age X time	-0.04447	0.15302	0.0844	0.7714	0.957
Education X time	-0.10784	0.09358	1.328	0.2492	0.898
Quality of life score X time	0.272	0.24924	1.1909	0.2751	1.313
Abstinence reason X time	-0.06622	0.16553	0.16	0.6891	0.936

Linear Hypotheses Testing Results

Label	Wald Chi-Square	DF	Pr > ChiSq
test_proportional	3.1463	4	0.5336

Unprotected sex and multiple sex partners:

Thirty seven percent (30/81) of subjects, who resumed sexual intercourse, reported not using a condom during intercourse while only 3 subjects reported having had sexual intercourse with more than one partner.

Specific Aim 3 results

All the 559 subjects enrolled were eligible for entry in the longitudinal aspect of the analysis. Of the 559 subjects enrolled, 87 (15.56%) subjects did not have any follow-up information leaving 472 subjects with at least 1 follow-up visit. Data of 472 subjects with at least one follow-up visit, contributing a total of 3066 person visits, was used in this longitudinal analysis. A total of 399 (71.38%) subjects had all the 6 follow-up visits from enrollment up to three years.

The chart below shows the distribution of follow up visits.

Total Visits	Number with corresponding total visit	Percent
Baseline(1)	87	15.6
2 visits	23	4
3 visits	15	2.7
4 visits	11	2
5 visits	6	1.1
6 visits	18	3.2
7 visits	399	71.4
	559	**100%**

Study Attrition/ Loss to Follow-Up.

Like in all cohort studies, follow up of enrolled subjects is paramount and could threaten the power and validity of the findings. Analysis of losses to follow up below shows a significant number of subjects lost to follow up at the

initial stages of the study. After the first follow-up visit, there was a significant drop in numbers of subjects subsequently lost to follow-up thereafter.

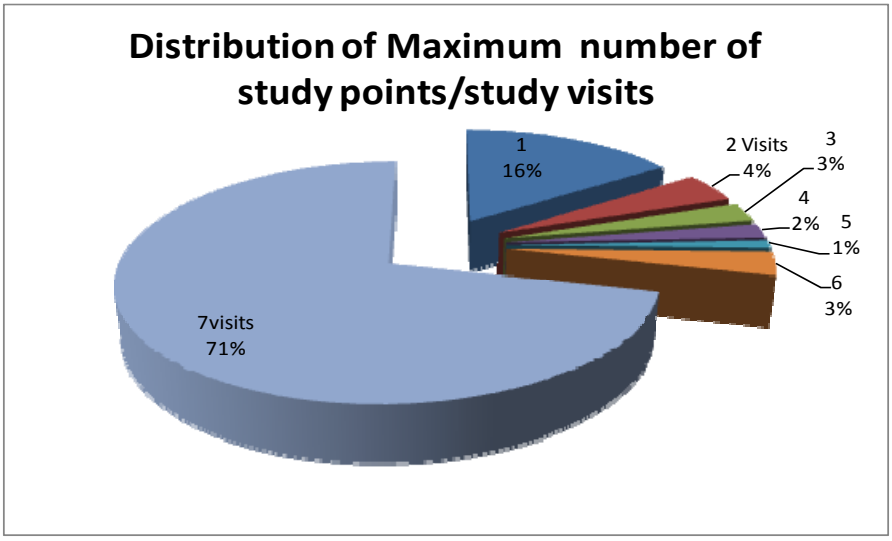


Figure 11 Distribution of maximum visits completed

The reasons for this high numbers of earlier losses to follow up was due to the fact that the cohort consisted of persons with mainly advanced HIV/AIDS and there has reports of mortality after initiation of therapy in advanced HIV have been reported in this setting and although we did have the data of which subjects had died or just did not come back to the clinic, we could infer from the fact the most losses were in subjects with poorer clinical indicators as described in table 22 below suggesting that mortality contributed significantly to early attrition from the study.

Subjects without any follow up visit were more likely to have lower median baseline CD4 cell counts (24 versus 102 cells/mm3, $p<0.0001$), lower

Physical health quality of life (p=0.0007), body mass index less than 18.5 Kg/M2 (p=0.0003), and advanced HIV/AIDS clinical stage (p= 0.0001). However there were no statistically significant differences by gender, marital status, and age, baseline viral loads and all the previously reported sexual behavior and condom use characteristics.

Characteristic/Variable	No follow-up visit	At least 1 Follow-up Visit	P-Value
GENDER			0.8154
Female	61	325	
Male	26	147	
MARITAL STATUS			0.9423
Not married	47	253	
Married/Cohabiting	40	219	
AGE IN Years , MEDIAN(IQR)	37(33-44)	38(33-44)	0.6808 *
CD4 CELL COUNT MEDIAN (IQR) Cells/μL	24(5-107)	102(32-170)	<0.0001*
HIGHESTEDUCATION			0.1695
No formal education-lower primary	17	60	
Upper primary	23	157	
Secondary level and Above	47	255	
Monthly HOUSEHOLD INCOME			0.4677
All above 50000 Ushs	24	157	
Below 50000 Ushs	30	164	
Declined to answer	33	151	
EMPLOYMENT STATUS			0.0065
Employed	33	254	
None/not employed	54	218	
CHILDREN in HOUSEHOLD			0.2305
None	15	59	
At least 1 child	72	413	
HIV/AIDS Clinical Stage			0.0001
Stage I & II	4	61	
Stage III	35	266	
Stage IV	48	145	
BODY MASS INDEX CATEGORY			0.0003
< 18.5 Kg/M^2	41	131	
>/=18.5 Kg/M^2	46	341	
REPORTS RECENT SEX			0.3207
No	41	195	
Yes	46	277	
CONDOM USE AT LAST SEX			0.7975
No	56	297	
Yes	31	175	
REPORTS 2 OR MORE SEX PARTNERS			0.3076
No	79	410	
Yes	8	62	
ART REDUCES HIV TRANSMISSION			0.0518
Yes	44	186	
No	43	286	

Descriptive analysis

Explanatory Factors

During the follow-up period, there was an overall increase in the median CD4 cell counts, physical health quality of life summary score and the majority of subjects had achieved undetectable viral loads by six months after ART initiation and majority retained viral suppression throughout the study period. Below are there graphic displays of the CD4 cell count, physical quality of life summary score and plasma viral load over time.

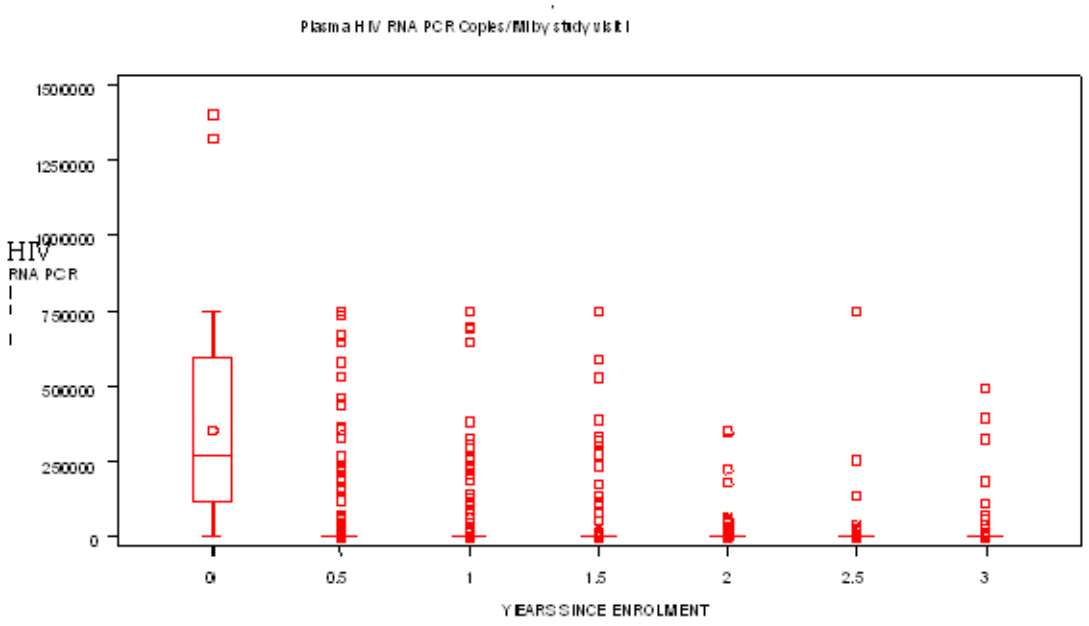
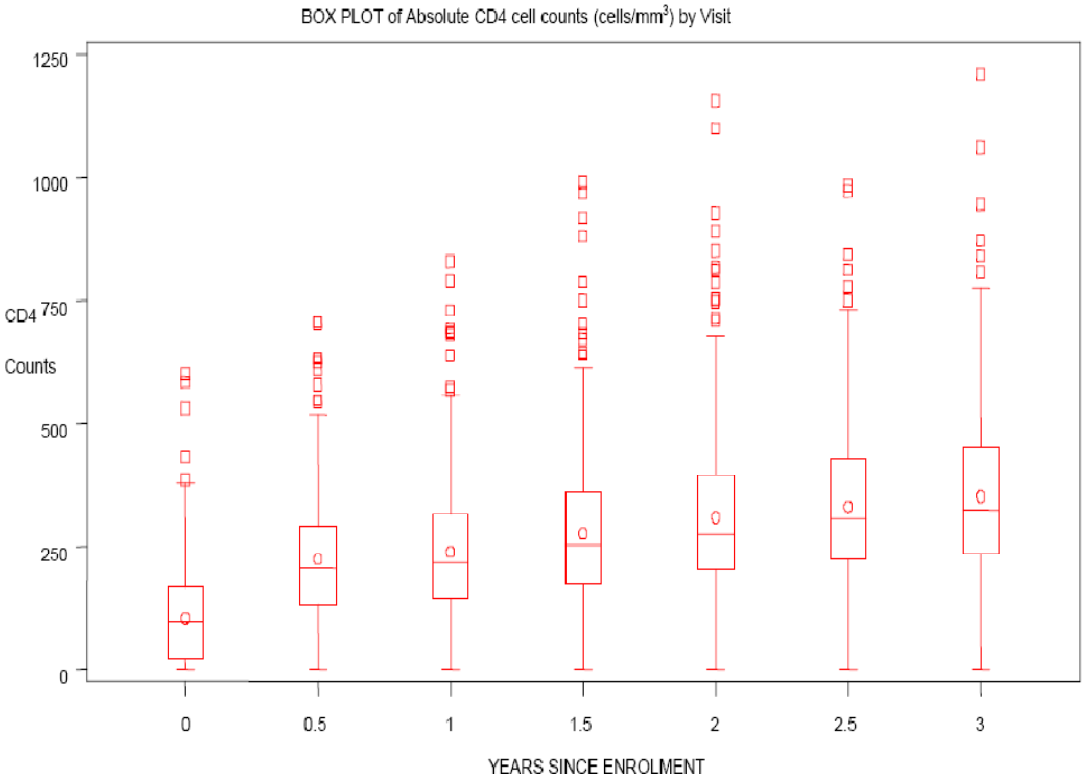
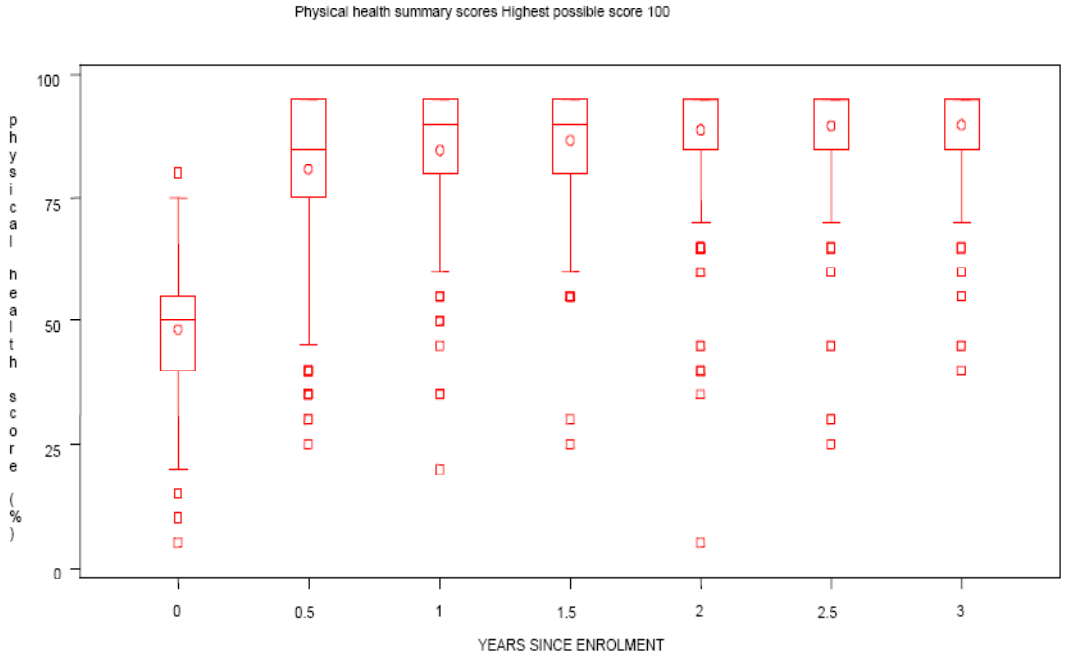
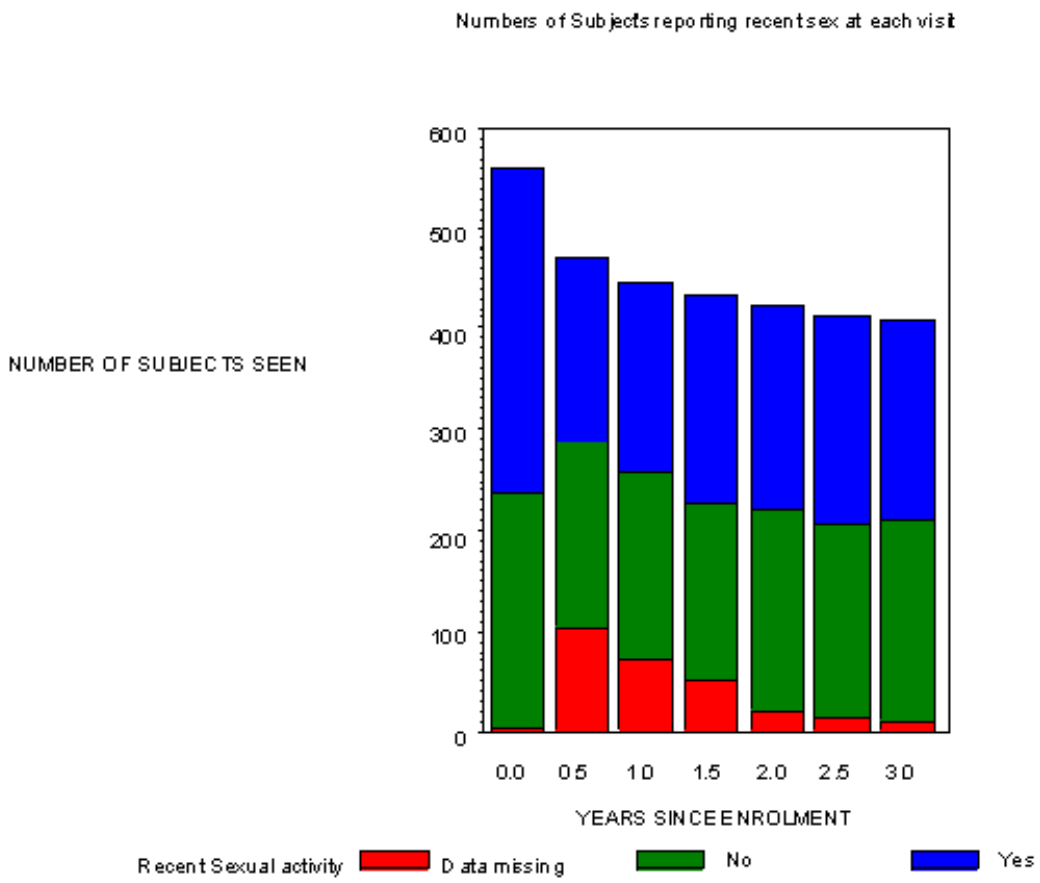


Figure 12: Box whisker plots for plasma Viral load, CD4 cell count, physical health quality of lime score over time


BOX PLOT of Absolute CD4 cell counts (cells/mm3) by Visit
CD4 Counts
1250
1000
750
500
250
0
0
0.5
1
1.5
2
2.5
3
YEARS SINCE ENROLMENT


Physical health summary scores Highest possible score 100
physical health score (%)
100
75
50
25
0
0
0.5
1
1.5
2
2.5
3
YEARS SINCE ENROLMENT



Outcome Variables

Recent Sexual activity :Of the 472 subjects(3066 person visits) with follow-up data, sexual behavior information was present in 2798 (91.3%) person visits while 268 person visits had missing sexual behavior data. Among the 2798 person visits, recent sexual intercourse was reported on 1465 (52.4%) of the visits during the entire study.

There were no drastic changes in the proportion of subjects reporting recent sexual activity over the follow up period(Table 23) with proportions remaining around the lower 50's but there was a statistically significant overall trend

towards reduction in the proportion reporting recent sex over time (p=0.0472). However when the analysis is restricted to periods when patients were on therapy, there is no change in the overall proportions of sexual activity after commencing therapy up to three years(P= 0.9493).

Table 23 Proportion of subjects reporting sexual activity at each visit over during the study period.

REPORTED SEXUAL INTERCOURSE by VISIT								
	Years Since enrolment							Total
Sexual intercourse	0	0.5	1	1.5	2	2.5	3	
No	195	182	187	178	199	192	200	1333
(%)	(41.4)	(49.7)	(49.6)	(46.4)	(49.4)	(48.2)	(50.1)	(47.6)
Yes	276	184	190	206	204	206	199	1465
(%)	(58.6)	(50.3)	(50.4)	(53.6)	(50.6)	(51.8)	(49.9)	(52.3)
Total person visits	471	366	377	384	403	398	399	2798

Sexual intercourse data Missing = 268

Cochran-Armitage Trend Test: Z Statistic=1.9845,

One-sided Pr > Z =0.0236, Two-sided Pr > |Z| =0.0472.

***Unprotected sex while on ART**:* Condom usage at the last sexual encounter was further analyzed among the 1465 person visits where recent sexual intercourse was reported. Unprotected sex at the last sexual encounter was reported was reported in 321/1465 (21.9%) person visits (Table.24). The majority (147/321) of the unprotected sex events were reported at the enrolment visit.

Overall, there was a statistically significant trend of an overall reduction in the proportion of unprotected sex while ART treatment progressed (p < 0.0001).

The lowest proportion, (8.8%) of sexually active subjects, of unprotected sex was reported at 2 years after ART initiation and thereafter there is a slight increase of unprotected sex during the third year of therapy suggesting a curvilinear pattern with the trough at the 2 year visit although this cannot be emphasized because of the small study population in which condom use data was obtained.

Table 24 Proportion of subjects reporting condom use at last recent sexual intercourse at each visit (among those who had sexual intercourse in previous six months)

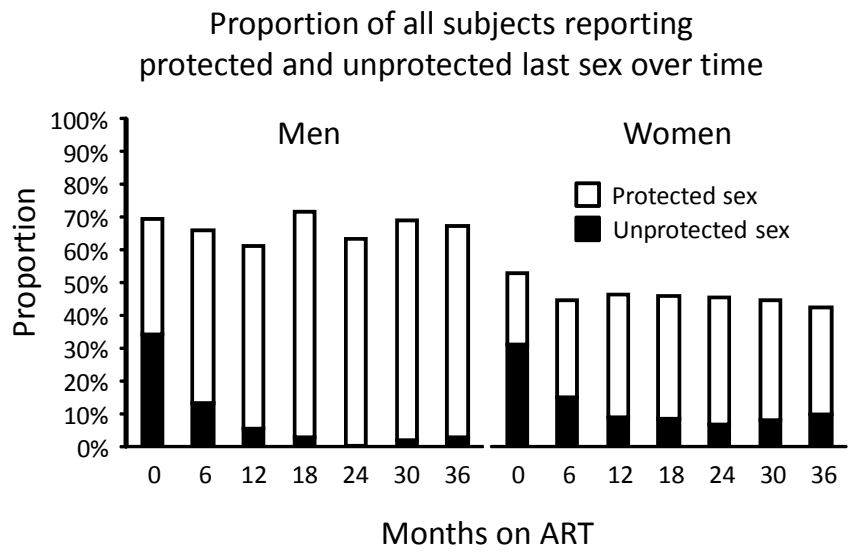
REPORTED CONDOM USE AT LAST SEXUAL INTERCOURSE Among those reporting SEXUAL INTERCOURSE in the interstudy interval								
	Years Since enrolment							Total
Condom use at last sex	0	0.5	1	1.5	2	2.5	3	
No (%)	147 (53.3)	52 (28.3)	28 (14.7)	24 (11.7)	18 (8.8)	23 (11.2)	29 (14.6)	321
Yes (%)	129 (46.7)	132 (71.7)	162 (85.3)	182 (88.4)	186 (91.2)	183 (88.8)	170 (85.4)	1144
Total person visits who had recent sex	276	184	190	206	204	206	199	1465

Cochran-Armitage Trend Test: Statistic (Z) -11.7846

One-sided Pr < Z <.0001, Two-sided Pr > |Z| <.0001

Over the whole study period, the proportion of unprotected sex was higher among females compared to males (Figure 13). There was a reduction in unprotected sex in both males and females over time but significantly less reductions were seen in females than in males.

Figure 13 Proportion of reported unprotected sex by gender



Visit	Men		Women	
	Sexually active (N)	Unprotected Sex (N)	Sexually active (N)	Unprotected Sex (N)
0	119	61	204	85
1	67	54	117	78
2	70	64	120	98
3	87	84	119	98
4	78	78	126	108
5	83	81	123	102
6	83	80	116	90

Factors associated with recent sexual intercourse while on ART

Univariate analysis results (Tables 25-26) show that over the study period, there was no statistically significant association between increasing CD4 T cell count and sexual activity (p=0.7156). The association remained non

significant even when CD4 T cell count was modeled as a categorical variable of < 200, 200-350, and above 350 cells/μL(results not shown).

Table 25 Logistic regression results of Univariate factors associated with reporting recent sexual intercourse while on ART at the IDI clinic in Kampala.

Characteristic/variable	Odds ratio		95% Confidence Limits of OR		*P. Value*
CD4 cell count, Per 100 cell/mm3	0.99		0.91	1.06	0.7156
AGE, Per 10 years	0.62		0.52	0.73	<.0001
Female gender	0.43		0.32	0.59	<.0001
Married	8.06		6.03	10.77	<.0001
Monthly Income, Ref. Below 50000 Ushs					
Declined to answer	1.53		1.09	2.13	0.0128
Above 50000 Ushs	2.58		1.84	3.63	<.0001
Highest Education , Ref Upper primary level					
None/ up to lower primary(3yrs of class)	0.62		0.39	0.97	0.0371
Secondary Level & above	1.07		0.79	1.45	0.6715
Employment, Ref.Employed					
None/not employed	0.67		0.51	0.89	0.0048
Has children, Ref. no children					
1-2 children	1.24		0.81	1.90	0.3307
3 or more children	2.26		1.49	3.44	0.0001
karnofsky score (per 10%)		0.47	1.82	1.52	0.21
Detectable(>400 c/ml) plasma RNA PCR	0.89		0.74	1.08	0.2325
Physical health QOL summary score, Ref >60					
Below Average < 40% Percentile	1.05		0.76	1.45	0.79
Average 40-60 percentile	0.98		0.79	1.20	0.8278

Neither having an undetectable viral load nor higher physical quality of life score was associated with reporting sexual intercourse on the subsequent visit. Notably in univariate analyses, recent sexual intercourse was significantly associated with being married, male, younger ages , being employed and having a relatively higher income.

Table 26: continued from table 25

Characteristic/variable	Odds ratio	95% Confidence Limits of OR		*P. Value*
Spouse HIV status , Ref. Positive				
Negative/unknown	0.96	0.59	1.58	0.8823
Years since HIV diagnosis, Ref. < 1 year				
Between 1-5 years	0.94	0.68	1.30	0.72
Above 5 years	0.71	0.35	1.45	0.346
Can 'healthy looking' person transmit HIV? Ref. Yes				
Do not know/No opinion	0.87	0.65	1.17	0.359
No	0.91	0.54	1.52	0.7164
Should married people use condoms? Ref No				
Yes/Agrees	0.92	0.75	1.12	0.413
ARVs do cure HIV, Ref. Yes				
No	1.09	0.92	1.27	0.3176
No opinion/do not know	0.98	0.75	1.27	0.8726
ARVs effective in treating clinical AIDS, Ref. Yes				
Do not know/No opinion	1.30	0.86	1.98	0.2132
No	1.26	0.74	2.17	0.3966
Is Sexual transmission of HIV reduced by ART?				
No , (reference as yes)	0.98	0.87	1.10	0.7551
Should HIV postive persons abstain from Intercourse				
Yes (No as reference)	0.25	0.20	0.32	<.0001

Belief that HIV postive persons should abstain from sexual intercourse was associated with lower odds of sexual intercourse while on ART. HIV related knowledge and belief factors were not assocatied with recent sexual intercourse.

CD4 T cell count level was still not associated with recent sexual intercourse (p=0.5845) even after controlling for other factors. Sexual intercourse was less likely with increasing age[Adjusted OR= 0.48, 95%CI :0.38-0.61],female gender [Adjusted OR= 0.43, 95%CI:0.29-0.64], among unmarried [Adjusted

OR= 0.16, 95%CI:0.12-0.23] and belief about HIV positive persons abstaining from sexual intercourse.

Earning a monthly income above 50000 Uganda shillings, versus earning less than 50000 shillings was associated with twice the odds of sexual intercourse [Adjusted OR= 2.25,95% CI : 1.49-3.42].

Table 27 GEE results of factors associated with reporting recent sexual intercourse while on ART at the IDI clinic, Kampala – AR(1) Correlation structure.

Final Multivariable model with AR(1) correlation				
Variable /Characteristic		**Adjusted Odds Ratio**	**95% Confidence Limits of OR**	**P- Value**
CD4 cell count	Per 100 cells/μL	1.02	(0.96- 1.09)	0.4438
Age	Per 10 years	0.48	(0.38- 0.61)	<.0001
Female gender	Male reference	0.43	(0.29- 0.64)	<.0001
Not married/widowed/divorced	Married reference	0.16	(0.12- 0.23)	<.0001
Monthly Income	Declined to answer	1.54	(1.02- 2.30)	0.0377
	Above 50000 Ushs	2.25	(1.49- 3.42)	0.0001
	Below 50000 Ushs	1.00	ref	
Highest Education level	No formal education-lower primary	0.58	(0.33- 1.02)	0.0571
	Secondary level education	0.66	(0.46- 0.94)	0.0208
	Upper primary	1.00	ref	
None/not employed	Employed reference	0.83	(0.58- 1.18)	0.2982
Has Children	No children reference	1.42	(0.84- 2.42)	0.1908
Should HIV postive persons abstain from Intercourse	Yes (No as reference)	0.51	(0.43- 0.62)	<.0001

Table 28 GEE results of factors associated with reporting recent sexual intercourse while on ART at the IDI clinic in Kampala- Independent correlation structure.

Final Multivariable model with independent correlation structure				
Variable /Characteristic		**Adjusted Odds Ratio**	**95% Confidence Limits of OR**	**P- Value**
CD4 cell count	Per 100 cells/μL	1.02	(0.94- 1.11)	0.5845
Age	Per 10 years	0.46	(0.36- 0.59)	<.0001
Female gender	Male reference	0.42	(0.28- 0.64)	<.0001
Not married/widowed/divorced	(Married reference)	0.18	(0.12- 0.25)	<.0001
Monthly Income	Declined to answer	1.56	(1.02- 2.38)	0.0391
	Above 50000 Ushs	2.24	(1.44- 3.48)	0.0004
	Below 50000 Ushs	1.00	ref	.
Highest Education level	No formal -lower primary education	0.62	(0.34- 1.15)	0.1313
	Secondary level education	0.65	(0.45- 0.94)	0.0233
	Upper primary	1.00	ref	.
None/not employed	Employed reference	0.85	(0.58- 1.25)	0.4178
Has Children	No children reference	1.57	(0.91- 2.72)	0.1057
Should HIV postive persons abstain from Intercourse	Yes (No as reference)	0.29	(0.23- 0.38)	<.0001

The overall trends of the results above were not altered by controlling for effect of viral load. When analysis was repeated separately for the married and unmarried persons, the overall trends in the results were not altered except that the odds ratio for income was stronger in the married than the unmarried groups and this could be attributed to the differences in the distribution of subjects in the two strata according to income category. The partner/spouse's HIV status was available only among married subjects, and was not associated with sexual intercourse (p=0.5761).

Table 29 Multivariate GEE results of association of both CD4 cell count and HIV plasma Viral

Final Multivariable model with independent correlation structure, and viral load added

Variable /Characteristic		Adjusted Odds Ratio	95% Confidence Limits of OR	P- Value
CD4 cell count	Per 100 cells/μL	1.02	(0.93- 1.12)	0.6487
Age	Per 10 years	0.46	(0.36- 0.59)	<.0001
Female gender	Male reference	0.41	(0.27- 0.63)	<.0001
Not married/widowed/divorced	Married reference	0.18	(0.13- 0.25)	<.0001
Monthly Income	Declined to answer	1.55	(1.01- 2.37)	0.0462
	Above 50000 Ushs	2.20	(1.40- 3.46)	0.0006
	Below 50000 Ushs	1.00	ref	
Highest Education level	No formal -lower primary education	0.62	(0.33- 1.16)	0.1324
	Secondary level education	0.66	(0.45- 0.96)	0.0316
	Upper primary	1.00	ref	
None/not employed	Employed reference	0.88	(0.60- 1.29)	0.5046
Has Children	No children reference	1.58	(0.91- 2.74)	0.101
Should HIV positive persons abstain from Intercourse	Yes (No as reference)	0.29	(0.22- 0.37)	<.0001
Detectable Viral load	<400 c/ml as reference	1.00	(0.75- 1.34)	0.9902

Table 30 Multivariate GEE results of association of CD4 cell count and with reporting recent sexual intercourse while on ART among married subjects only- Among married subjects only.

Among only Married: Final Multivariable model with independent correlation structure

Variable /Characteristic		Adjusted Odds Ratio	95% Confidence Limits of OR	P- Value
CD4 cell count	Per 100 cells/μL	1.01	(0.89- 1.15)	0.8767
Age	Per 10 years	0.46	(0.30- 0.69)	0.0002
Female gender	Male reference	0.45	(0.23- 0.90)	0.0234
Monthly Income	Declined to answer	2.44	(1.30- 4.57)	0.0055
	Above 50000 Ushs	3.28	(1.72- 6.25)	0.0003
	Below 50000 Ushs	1.00	ref	
Highest Education level	No formal -lower primary education	0.43	(0.19- 0.97)	0.0418
	Secondary level education	0.53	(0.30- 0.96)	0.0347
	Upper primary	1.00	ref	
None/not employed	Employed reference	0.96	(0.53- 1.73)	0.8966
Has Children	No children reference	1.54	(0.56- 4.21)	0.402
Should HIV postive persons abstain from Intercourse	Yes (No as reference)	0.31	(0.21- 0.46)	<.0001
HIV Status of Spouse	Negative Versus Positive	1.19	(0.66- 2.16)	0.5671

Table 31 Multivariate logistic regression with GEE extension of results of association of CD4 cell count and with reporting recent sexual intercourse while on ART among unmarried subjects only.

Among only Unmarried: Final Multivariable model with independent correlation structure				
Variable /Characteristic		**Adjusted Odds Ratio**	**95% Confidence Limits of OR**	**P- Value**
CD4 cell count	Per 100 cells/μL	1.03	(0.93- 1.13)	0.6215
Age	Per 10 years	0.46	(0.34- 0.63)	<.0001
Female gender	Male reference	0.40	(0.22- 0.70)	0.0014
Monthly Income	Declined to answer	1.06	(0.59- 1.90)	0.8387
	Above 50000 Ushs	1.72	(0.95- 3.12)	0.0749
	Below 50000 Ushs	1.00	(1.00- 1.00)	
Highest Education level	No formal -lower primary education	0.81	(0.36- 1.84)	0.6141
	Secondary level education	0.76	(0.45- 1.28)	0.2973
	Upper primary	1.00	(1.00- 1.00)	
None/not employed	Employed reference	0.83	(0.50- 1.35)	0.4466
Has Children	No children reference	1.65	(0.85- 3.21)	0.1379
Should HIV postive persons abstain from Intercourse	Yes (No as reference)	0.26	(0.18- 0.37)	<.0001

Factors associated with unprotected sex among persons reporting recent sex

In univariate analyses (Table 32), increasing CD4 cell count was associated with reduced odds of unprotected sex at last sex [OR=0.87, 95% CI: 0.74-1.02].Having viral loads above 400 copies/ml while on ART was not associated with having unprotected sex (P=0.6).

Importantly, among married subjects, having a spouse who was HIV negative/HIV unknown was associated with 77% higher odds of unprotected sex (p=0.0093). Gender and marital status specific associations are shown in tables 33-34.

Table 32 Results of Logistic regression based on GEE methods of univariate factors associated with having unprotected sexual intercourse sex while on ART.

Variable/Characteristic	Odds ratio	95% CI of OR	P-Value
CD4 cell count (Cells/μL), *Per 100 cell increase*	0.87	(0.74- 1.02)	0.0767
Female gender	2.08	(0.36- 0.65)	<.0001
Age in years, Per 10 year increase	0.86	(0.70- 1.06)	0.1596
< 95% Adherence, Ref. 95% and above	4.04	(1.43- 11.39)	0.0082
Virological failure(>400 copies/ml)*Ref. ? 400 c/ml*	1.18	(0.52- 2.65)	0.6925
Physical health summary score, per 33% increase	0.93	(0.88- 0.99)	0.0257
HIV/AIDS Clincal stage, *Ref. Stage III*		ref	
Stage I & II	0.90	(0.59- 1.37)	0.6116
Stage IV	1.42	(1.07- 1.89)	0.0138
Marital Status , *Ref Married*			
Not married/widowed/divorced	1.59	(1.18- 2.13)	0.002
Has at least 1 child, *Ref. no children*	0.40	(0.26- 0.61)	<.0001
Monthly Income, *Ref. Below 50000 Ushs*			
Declined to answer	0.59	(0.41- 0.84)	0.0038
Above 50000 Ushs	0.47	(0.33- 0.66)	<.0001
Not Employment, *Ref.Employed*	1.20	(0.90- 1.60)	0.212
Highest Education , *Ref Upper primary level*			
None/ up to lower primary(3yrs of class)	1.34	(0.82- 2.20)	0.2389
Secondary Level & above	0.96	(0.71- 1.30)	0.778
Spouse HIV status , *Ref. Positive*			
Negative/unknown	1.77	(1.15- 2.71)	0.0093
Years since HIV diagnosis, Ref. 1-5 years			
Above 5 years	0.69	(0.31- 1.53)	0.3614
Less than a year	0.86	(0.62- 1.20)	0.3791
Can 'healthy looking' person transmit HIV? *Ref. Yes*			
Do not know/No opinion	0.44	(0.12- 1.67)	0.228
No	1.12	(0.58- 2.16)	0.7417
Should married people use condoms? *Ref No*			
Yes/Agrees	0.56	(0.40- 0.77)	<0.0001
ARVs do cure HIV, *Ref. Yes*			
No	0.92	(0.67- 1.26)	0.6023
No opinion/do not know	1.10	(0.71- 1.72)	0.669
ARVs effective in treating clinical AIDS, *Ref. Yes*			
Do not know/No opinion	1.91	(0.87- 4.19)	0.1079
No	0.62	(0.28- 1.38)	0.2372
Believes that ART reduces HIV transmission			
No,Ref. Yes	1.10	(0.84- 1.46)	0.4793
Persons on ART should abstain from intercourse			
Yes ,Ref. No	2.24	(1.51- 3.32)	<0.0001

Table 33 Gender specific Univariate GEE results of factors associated with reported unprotected sexual intercourse sex while on ART

Variable	Categorisation/strata	Females			Males		
		Odds ratio	(95% CI OR)	p-Value	Odds ratio	(95% CI OR)	p-Value
Not Married/divorced/widowed	*ref married/cohabiting*	2.17	(1.36- 3.46)	0.0012	0.86	(0.31- 2.39)	0.772
<95% adherence	*ref > 95%*	1.72	(0.42- 7.11)	0.4553	7.08	(1.64- 30.59)	0.009
Not employed	*ref employed*	1.1	(0.69- 1.75)	0.6825	1.07	(0.39- 2.97)	0.894
INCOME	*Declined to answer*	0.66	(0.38- 1.17)	0.1562	0.3	(0.08- 1.12)	0.073
INCOME	*Above 50000 ushs*	0.66	(0.38- 1.17)	0.1576	0.28	(0.09- 0.83)	0.022
INCOME	*Below 50000 Ushs*	1	ref			ref	
Age category	*< 30 years*	1.73	(0.84- 3.56)	0.1358	1.1	(0.11- 10.66)	0.935
Age category	*> 40 years*	1.41	(0.74- 2.69)	0.2965	2.2	(0.79- 6.15)	0.133
Age category	*ref 30-40 years*	1	ref			ref	
Has Children	*ref no children*	0.34	(0.20- 0.58)	<.0001	0.51	(0.10- 2.50)	0.406
CD4 less than 200	*ref above 200*	1.87	(1.26- 2.78)	0.002	2.6	(1.21- 5.58)	0.014
Virological failure[> 400 c/ml)	*ref > 400 c/ml*	1.12	(0.52- 2.39)	0.7761	3.14	(1.16- 8.51)	0.024
Highest education	*No formal education-lower p*	1.71	(0.84- 3.46)	0.1391	1.17	(0.13- 10.69)	0.891
Highest education	*Secondary level and above*	1.17	(0.71- 1.92)	0.5417	1.42	(0.45- 4.49)	0.548
Highest education	*Upper primary*	1	ref			ref	
ARVs reduce HIV transmision	*Yes*	0.69	(0.46- 1.03)	0.0695	1.13	(0.61- 2.10)	0.697
ARVs reduce HIV transmision	*ref No/don't know*	1	ref			ref	
Should HIV+ persons abstain ?	*Yes*	0.66	(0.44- 0.97)	0.0367	0.21	(0.10- 0.45)	<.0001
Should HIV+ persons abstain ?	*ref No/don't know*		ref			ref	
2 or more sex partners	*ref 1 sex partner*	0.56	(0.21- 1.52)	0.2576	0.72	(0.29- 1.80)	0.48
HIV stage	*I & II*	0.92	(0.46- 1.83)	0.8161	1.11	(0.17- 7.39)	0.91
HIV stage	*IV*	1.17	(0.69- 1.99)	0.5658	2.28	(0.89- 5.83)	0.086
HIV stage	*III*	1	ref			ref	
PARTNER HIV STATUS	*Negative*	2.21	(1.08- 4.54)	0.0304	1.21	(0.37- 4.03)	0.752
PARTNER HIV STATUS	*Positive*	1	ref			ref	

Table 34: Univariate GEE results of factors associated with having unprotected sexual intercourse sex while on ART, stratified by Marital status

Variable	Categorisation/strata	Not married/widowed			Married/Cohabiting		
		Odds ratio	(95% CI OR)	p-Value	Odds ratio	(95% CI OR)	p-Value
Female gender		6.46	(2.56- 16.30)	<.0001	2.67	(1.41- 5.05)	0.003
<95% adherence	*ref > 95%*	2.51	(0.57- 11.14)	0.2254	1.98	(0.36- 10.92)	0.431
Not employed	*ref employed*	1.45	(0.75- 2.80)	0.2751	1.26	(0.73- 2.19)	0.412
INCOME	*Declined to answer*	0.7	(0.33- 1.48)	0.3475	0.58	(0.29- 1.18)	0.133
INCOME	*Above 50000 ushs*	0.39	(0.16- 0.95)	0.0371	0.48	(0.25- 0.90)	0.023
INCOME	*Below 50000 Ushs*	1	(1.00- 1.00)	.	1	(1.00- 1.00)	.
Age category	*< 30 years*	1.13	(0.43- 3.00)	0.8036	2.23	(0.84- 5.95)	0.109
Age category	*> 40 years*	0.88	(0.39- 1.99)	0.7569	0.95	(0.52- 1.73)	0.865
Age category	*ref 30-40 years*	1			ref		
Has Children	*ref no children*	0.51	(0.20- 1.27)	0.1483	0.28	(0.15- 0.49)	<.0001
CD4 less than 200	*ref above 200*	2.12	(1.28- 3.50)	0.0033	1.6	(1.01- 2.54)	0.045
Virological failure[> 400 c/ml)	*ref > 400 c/ml*	1.39	(0.64- 3.04)	0.4046	1.14	(0.50- 2.59)	0.763
Highest education	*No formal education-lower p*	0.73	(0.24- 2.18)	0.5714	3.39	(1.45- 7.93)	0.005
Highest education	*Secondary level and above*	0.79	(0.40- 1.59)	0.5129	1.49	(0.82- 2.70)	0.194
Highest education	*Upper primary*	1			ref		
YEARS WITH HIV	*Above 5 years*	0.78	(0.15- 4.01)	0.7704	1.07	(0.39- 2.90)	0.902
YEARS WITH HIV	*Less than a year*	0.48	(0.23- 1.01)	0.0532	0.98	(0.52- 1.83)	0.947
YEARS WITH HIV	*Between 1-5 years*	1	(1.00- 1.00)	.	1	(1.00- 1.00)	.
ARVs reduce HIV transmision	*Yes*	0.47	(0.27- 0.85)	0.0115	0.96	(0.64- 1.42)	0.826
ARVs reduce HIV transmision	*ref No/don't know*	1	(1.00- 1.00)	.	1	(1.00- 1.00)	.
Should HIV+ persons abstain ?	*Yes*	0.58	(0.35- 0.95)	0.0314	0.46	(0.29- 0.74)	0.001
Should HIV+ persons abstain ?	*ref No/don't know*	1			ref		.
2 or more sex partners	*ref 1 sex partner*	0.24	(0.10- 0.56)	<0.0001	0.86	(0.38- 1.97)	0.726

In the final multivariate analyses (Table 35) for factors associated with unprotected sex while on ART, unprotected sex was 26% (p=0.0056) less likely to occur for every additional six months stayed in care controlling for baseline condom use, gender, marital status, having children, knowledge about HIV transmission and belief about abstinence. Subjects who had reported unprotected sex at baseline and those who had no children were more than twice likely to have unprotected sex while on therapy controlling for other factors. Although not statistically significant at α=0.05 level, there was an noteworthy interaction term between gender and marital status in the final model implying that the odds of having unprotected sex in any gender category is dependent on whether the subject's marital status. Compared to married females, the odds ratio for unprotected sex was 0.45 (95% CI: 0.23-0.86, p=0.017) in married male subjects controlling for other factors in the model (table 35). Among females, the odds ratio for unprotected sex was 2.0 (95% CI: 1.18-3.37, p=0.0094) among unmarried/widowed/divorced compared to the married females controlling for other factors. Compared to married females, unmarried males had the lowest odds ratio for unprotected sex (OR=0.33, 95% CI: 0.14 -0.81, p=0.0155) controlling for other factors.

Table 35 Results of multivariate Logistic regression based on GEE methods of factors associated with having unprotected sexual intercourse sex while on ART at the IDI clinic in Kampala – AR (1) correlation structure

Variable/Characteristic	Adjusted Odds Ratio	95% Confidence	P-Value
Visit (Every 6 months)	0.84	(0.74- 0.95)	0.0056
Male Gender	0.45	(0.23- 0.86)	0.0166
Marital Status, Ref Married/Cohabiting			
Not Married/Widowed/Divorced	2.00	(1.18- 3.37)	0.0094
Had Unprotected sex at Baseline visit			
Yes *(Ref. No)*	2.13	(1.34- 3.39)	0.0015
Believes HIV transmission is reduced by ART			
Yes *(Ref. No)*	1.51	(1.03- 2.22)	0.0333
Should HIV+ persons abstain from sex?			
No *(Ref. Yes)*	1.75	(1.17- 2.62)	0.0063
Has Children ?			
None *(Ref. At least 1 child*)	2.65	(1.50- 4.67)	0.0007
GENDER*MARRIED (Male*Not Married)	0.37	(0.12- 1.17)	0.0908

Physical quality of life and having an undetectable viral load were dropped from the final models because they were not statistically significant. There was no association between having virological failure and unprotected sex (p=0.7). The association of CD4 T cell count with unprotected sex was not examined as there were no perceived conceptual relationships between CD4 cell count and unprotected sex.

In order to assess the association of spouse's HIV sero status on condom use, analysis was restricted to only married/cohabiting subjects as spouse's HIV sero status data was only available among married subjects. Among married subjects only, unprotected sex was 77% (p=0.0093) more likely to occur in subjects who had an HIV negative/unknown sero status compared to those that had an HIV positive spouse in univariate analysis. In multivariate analysis, although not statically significant at α=0.05, subjects who had an

HIV negative/ HIV unknown status were 27% (p=0.18) more likely to have unprotected sex compared to those who had a confirmed HIV positive spouse controlling for gender, time on therapy, baseline condom use, having children and belief about abstinence for HIV + persons(table 36).

Table 36: Results of multivariate Logistic regression based on GEE methods of factors associated with having unprotected sexual intercourse modeled separately for) married subjects.

Variable/Characteristic	Adjusted Odds Ratio	95% Confidence Limits of OR	P-Value
Visit (Every 6 months)	0.78	(0.65 -0.93)	0.0048
Male Gender	0.43	(0.22 -0.86)	0.016
Spouse/Partner HIV Sero-Status (Ref. HIV+)			
Negative/Unknown HIV Status	1.27	(0.89 -1.82)	0.1843
Had Unprotected sex at Baseline visit			
Yes *(Ref. No)*	2.76	(1.58 -4.82)	0.0003
Believes HIV transmission is reduced by ART			
Yes *(Ref. No)*	Not significant		
Should HIV+ persons abstain from sex?			
No *(Ref. Yes)*	1.68	(0.99 -2.85)	0.0544
Has Children ?			
None *(Ref. At least 1 child*)	2.59	(1.29 -5.20)	0.0073

Effect of ART

When we compared the proportions of unprotected sex without ART(baseline visit) and after ART initiation(3 year follow up experience), there was a statistically significant difference in the proportions of reported unprotected sex before ART and after starting ART with far less subjects reporting unprotected sex after start of ART [54.7% versus 14.6% P<0.0001].

DISCUSSION

In this study, the majority (88%) of subjects initiating ART at advanced HIV/AIDS clinical stages III and IV of which over a half were sexually active with in the previous six months prior to enrolment. These numbers are comparable to those from an HIV clinic in cape town ,South Africa [61].However they are slightly higher than those reported from other studies from rural Uganda and Kenya [21,62].The higher proportions of sexually active subjects at initiation of ART in this study could be attributed to the differences in the study criteria for defining recent sexual intercourse, and the fact that the mean age of subjects from the latter two studies was higher than in this study. Generally ,sexual activity decreases with age[63].

At ART initiation, neither having a better physical health quality of life nor CD4 T cell counts above 100 cells/µl was associated with higher odds of sexual intercourse. The lack of a difference could be due to the relatively homogenous group of subjects in the lower CD4 levels below any threshold at which dose response observations could be made. This can be seen with the similar odds of sexual behavior in symptomatic subjects with CD4 cell counts below 350 cells/ µl [47]. The odds of recent sexual activity were higher among younger subjects, male and those earning above 50,000 shillings. In multivariate analysis, being married was associated with 12 times the odds of recent sexual activity (p=0.0001). The factors associated with recent sexual activity here are congruent to the similar settings above. It is important to

point out that when analysis was done separately by gender, income higher income was associated higher odds of sexual activity among females but did not reach statistical significance among males. Among males being employed was associated with increased risk for sexual activity. Although higher incomes have been associated with increased sexual activity, this seems to play most importantly among females. This is finding, in conjunction with findings from the Uganda national HIV sero-behavior survey, would imply that women with higher incomes engage in more sexual activity than those with self reported lower incomes[64].

Another important finding was 63.42% of married subjects commencing ART did not know the HIV status of their spouse and we found that knowing the HIV status of the sexual partner was associated with higher odds of unprotected sex. We did not have information on whether the index partner had taken an initiative to disclose her status to the spouse but an extrapolation of the available information suggest that not know the HIV of the spouse among subjects on ART is associated with having unprotected sex.

Regarding subjects who were abstinent at ART initiation, more than a third of those followed up had resumed sexual intercourse by three years of ART initiation. We see that among this sub study population, the same baseline factors that were associated with sexual activity at enrolment still had greater associations with resumption of sexual activity. The hazard for resumption of

sexual activity did not differ between subjects reason for abstinence, prior to ART initiation. The absence of any difference in the hazard could suggest that there are other stronger reasons responsible for the resumption of intercourse. Most importantly we have seen that after ART was initiated, among subjects who were able to survive/stay in the study there are no statistically significant changes in the proportion of subjects reporting recent sexual intercourse over the three year period. This would then be an important positive note to consider in that generally resumption of sexual intercourse reduces after 1 year of therapy. The implication of this is that counseling on sexual behavior may need to be integrated with in care at the earliest opportunity and further strengthened during the Pre-ART initiation counseling and education sessions.

We did not find evidence of factors modifying the effect of CD4 T cell counts on having sexual intercourse based on the test of homogeneity of odds ratio. This could have been due to low power for testing for effect modification or the magnitude of difference in the two strata was not high enough to reach statistical significance although there could have been a difference in the different strata of any of the variables that we tested.

Overall all, in this population, the level of CD4 T cell counts was not associated with engaging in sexual activity whether before ART initiation or over the three years ART initiation. These results are consistent with those from other studies [45,50]. Having a undetectable viral load was also not

associated with engaging in sexual intercourse. It appears that engaging sexual intercourse while on ART was independent of the CD4+ T cell counts viral load level ,suggesting that other non medical factors such as gender($p < 0.0001$),age($p<0.0001$),marital status ($p<0.0001$), monthly income and personal beliefs had more influence in choosing to engage in sexual intercourse. The implications of this is that individual improvements in CD4 T cell counts and Viral load while on ART may not be a good indicator of which subjects are more likely to engage in sexual intercourse. The same factors that affect that influence engaging in sexual intercourse in the general population are the same for HIV infected persons in clinical settings.

In specific aim 2, survival analysis methods were used as the interest was to estimate the risk of resumption of sexual activity following ART initiation given the subjects characteristics. We therefore interpret the estimates from the Cox regression models as (instantaneous) relative risks for resumption of sex. The other advantage of using the hazard ratios compared to the odds ratios is that the odds ratio would overestimate the real relative risk especially since the proportion of the event (sexual intercourse) was high[65]. This could explain why the odds ratios for sexual activity we estimated in aim 3 are consistently above the hazard ratios in AIM 2. However, the other reason why the odds ratio are higher is that in AIM three, our models were logistic regression of recurrent events unlike in AIM 2 where our interest was only on the first report of resumption of sexual activity.

Unprotected sex

CD4 T cell counts and plasma viral load level were not associated with unprotected sex at the baseline visit. Again this could be due to very little variability in the comparison groups in regards to CD4 T cell counts and plasma HIV viral loads. The proportion of subjects reporting unprotected sex had decreased as time on ART progressed. This finding is similar to studies from developing countries demonstrating lower proportions of unprotected sex in subjects on ART both as cross-section and cohort studies [18,19,21,51].To our knowledge, this study is among the first to document a continued reduction in the proportions of unprotected sex up to three years after ART initiation. These reductions could be attributed to the cumulative multitude of the interventions as subjects stay longer in care.

The practice of unprotected sex was less likely to occur among male unmarried subjects, and as well as subjects stayed longer on therapy. Unprotected sex was more likely to occur among unmarried female subjects, subjects who had also reported unprotected sex at the baseline visit, subjects who had no children and those who believed that HIV transmission is reduced by ART as well as those who believed that HIV persons should not abstain from sexual intercourse. Unlike previously stated studies above, here we found that being unmarried/widowed/divorced was associated with higher odds of unprotected sex compared to the married (among females subjects)

due to the fact that a higher proportion of women in study population were unmarried/widowed/divorced (p=0.003) therefore being unmarried in this case might be reflecting more of the burden of unprotected sex among females than the marital category. Secondly this categorization was based on the baseline evaluations so if these subjects later got married they still appeared as unmarried and if most of these switches were the ones almost practicing unprotected sex during the ART period, then this would bias our results hence show that unmarried persons are more likely to have unprotected sex that married subjects. Among male subjects, as expected, married persons were more likely to have unprotected sex than unmarried subjects.

Age was not associated with unprotected sex in our multivariate models, however subjects who had no children were more likely to be younger and we saw that subjects who had no children were more likely to have had unprotected sex. The association of not having children and unprotected sex is based on the premise that subjects who want to have children will most likely have unprotected sex in order to have children. Since the primary data had not collected data on whether subjects wanted to have children we decided to use the number of children as a proxy for desire of children and assumed as we had hypothesized subjects without children would most likely report unprotected sex and this is what the study found suggesting that possibly desire for children and contraceptive services and choices important factors to consider in the counseling for secondary HIV prevention.

Although we did not examine for the association of CD4 cell count and unprotected sex in our final models for unprotected sex in the longitudinal component of the study, it is important to mention that most published studies did not find any associations between CD4 T cell count and unprotected sex [50,66,67] whereas a few found that unprotected sex was associated higher CD4 T cell counts [5,46]. We did not find any statistically significant association between having virological failure and having unprotected sex.

Study Limitations

The clinic provided and encouraged patients to use condoms as it would be unethical not provide these services. Since we only relied on self reported sexual behavior and were unable to verify the information provided, social desirability bias cannot be excluded[68].

We were not able to assess whether the fairly regular study interviewers maintained in the study could have reduced social desirability bias. The sustained difference in the proportions reporting unprotected sex by gender may suggest that bias in the data due to social desirability reporting if any may be constant over time because the difference by gender is constant .Men consistently reported lower proportions of unprotected sex than women. Other possible explanations for the observations could be due to the fact that condom use is primarily controlled by men, males condoms are widely available (female condoms are not widely available and were not provided in the clinic). It is therefore prudent that studies that will enable or improve the

understanding and estimation of social desirability and its mitigation, mainly in resource limited clinical settings be designed. In the same vein it is worth noting that clinics may not be the best place in which such very personal information such as sexual behaviors is divulged and therefore other avenues such as home visits may provide different findings from ours.

We had a predetermined sample size which may have limited the power of the study in identifying variables which may be important predictors of sexual activity/condom use that needed a larger sample size to reach statistical significance.

Another limitation would be the convenient sampling method that was used to enroll study subjects. However we enrolled subjects at all times the clinic was open over a 14 months period which could have reduced the inherent non probability sampling bias, but the resulting selection by indication bias would be limited based on a previous publication showing that the study subjects in this cohort were comparable to those in whole clinic and generally reflected the category of persons accessing ART in Uganda [69,70].

We collected information mainly on last events only which may not be representative of a person's sexual behavioral experience over the inter-study period and provides no information on cumulative risks but this method may yield more accurate response to the event in question and may not be prone to recall bias. Secondly subjects are more likely to remember the last time they had sex – strengthening internal validity our results.

The study did not collect other important variables like alcohol consumption which has been identified in other settings as an important predictor of sexual behavior among HIV infected subjects in Sub-Saharan Africa[71].

Although 559 subjects were enrolled in the study, only 472 returned for follow up evaluations. We showed that subjects not returning for any follow-up were generally sicker than those that returned. This implies that our longitudinal evaluations were done in only subjects who had not been very sick at commencement of ART. However, this initial loss to flow up *per se* may not invalidate our findings as the majority of those without any follow up visits had actually died and therefore not able to experience any of our outcomes of interest. Secondly, among the 472 subjects, there was no evidence to suggest that any differential losses to follow-up thereafter or subsequent systematic missing data in the longitudinal analyses with respect to the subjects' characteristics. We also obtained comparable results in the Sub-group analyses among subjects with all 6 or those with 1-5 follow-up visits.

Despite those limitations, we believe that the three years follow-up, together with free ART and condom distribution (provided by the Global fund and the Presidential emergency program for AIDS relief) provides very relevant information that can be generalized to the majority of HIV treatment centers in Uganda and Sub-Saharan Africa since the study setting, timing, funding and model of ART provision are similar.

CONCLUSIONS AND RECOMMENDATIONS

Approximately (332/559)58% of subjects were sexually active at enrollment, with about 55% of the sexually active subjects reporting unprotected sex at the last sex. At enrollment, factors associated with being sexually active were younger age (18-28 years), male gender, being married and being employed. Unprotected sex was more likely in younger ages, unmarried persons, HIV clinical stage IV and higher baseline $\log_{10}$ HIV plasma Viral load. Baseline CD4 cell count was not associated with unprotected sex.

Among the 195 subjects not sexually active at baseline, 43% of them had resumed sex after initiating ART with 25% resuming by the 1st year and 35% resuming by year two of ART. Subjects who were more likely to resume sex intercourse were younger, male, and with some form of education. Baseline CD4 count did not influence subsequent resumption of intercourse while subjects who had lower quality of life score at baseline were less likely to resume intercourse later. The reason for abstention cited at enrollment did not influence subsequent resumption of intercourse.

Unprotected sex occurred more frequently in unmarried/widowed females than males. Over time on therapy there were there was a 26% reduction in odds of unprotected sex per each additional six months of follow on ART although there were more marked in men than in women.

Factors associated with higher odd of unprotected sex while on ART were being unmarried/widowed, female gender, believing that HIV transmission is

reduced by ART, having had unprotected sex at the baseline evaluation, not believing that HIV positive persons should abstain from intercourse and having no children. We hypothesized that subjects who had no children were not using condoms because they wanted to get children since condoms ould be acting as a contraception tool. Therefore, Innovative prevention messages/tools are needed especially among females for example promotion of female condoms and safer conception counseling until a clinically efficacious microbicide is available.

Generally, the proportion of sexually active subjects remained relatively constant during the three years on ART. Although there were a number of previously abstinent subjects that initiated sex after commencing ART, this number did not significantly alter the overall proportion of sexually active subjects receiving antiretroviral therapy. The overall proportion of subjects reporting unprotected sex at last sexual encounter decreased over time. Although sexually active persons did not reduce significantly, HIV prevention interventions among HIV infected persons in care appeared to be working especially regarding condom use. However, prevention interventions need to be instituted as soon as subjects are in care, not necessarily after ART initiation. The overall reduction in unprotected sex in this study represents an interventional effect of condom distribution and continued interface with health workers and acquisition of more prevention messages. However, we were not able to discern the true reductions in unprotected sex from an augmentation by social desirability bias. Counseling and education on risk reduction to

prevent further HIV transmission needs strengthening among HIV patients in clinical settings with high priority among patients newer in care and among female subjects.

Patients who had taken ART for short periods of time, often had high viral RNA levels, combined with frequent unprotected sex places this population at risk of potential onward transmission of drug- resistant virus. Although virological failure was not associated with unprotected sex, sexual intercourse was reported at 117 person-visits where virological failure was recorded, and of which 11% of those visits, no condom was used representing a potential for transmission of drug resistant HIV strains.

There were very low levels of partners' HIV status awareness yet these subjects had been in care and this was associated higher odds of unprotected sex. This therefore for strengthening of counseling and education on HIV status disclosure as this has a potential of reducing a significant number of new HIV transmissions from occurring especially given that there is a high prevalence of HIV discordance among persons testing for HIV in Uganda[72].

The degree to which individuals may be willing to disclose HIV transmission risk behaviors may vary across gender, and clinical settings. Individual social demographic factors rather than markers of clinical and immunological improvements on ART appeared to influence subsequent sexual intercourse and unprotected sex. This implies that socio-demographic and behavioral factors, rather than the overt clinical factors, need consideration and

incorporation in any prevention for positives programs. Therefore qualitative behavioral and ethnographic studies may provide more insights about the most important factors that have to be considered for screening for, and counseling on high risk sexual behaviors in HIV clinical settings.

APPENDIX

REFERENCES/BIBLIOGRAPHY

1. UNAIDS. AIDS Epidemic Update. 2007 Update UNAIDS, 2007.
2. WHO. Global Burden of Disease(GBD). 2002 Estimates World Health Organisation, 2002.
3. Palella FJ, Jr., Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, Aschman DJ, Holmberg SD. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med 1998;338(13):853-60.
4. Mocroft A, Vella S, Benfield TL, Chiesi A, Miller V, Gargalianos P, d'Arminio Monforte A, Yust I, Bruun JN, Phillips AN, Lundgren JD. Changing patterns of mortality across Europe in patients infected with HIV-1. EuroSIDA Study Group. Lancet 1998;352(9142):1725-30.
5. Dukers NH, Goudsmit J, de Wit JB, Prins M, Weverling GJ, Coutinho RA. Sexual risk behaviour relates to the virological and immunological improvements during highly active antiretroviral therapy in HIV-1 infection. AIDS 2001;15(3):369-78.
6. Dilley JW, Woods WJ, McFarland W. Are advances in treatment changing views about high-risk sex? N Engl J Med 1997;337(7):501-2.
7. Ostrow DE, Fox KJ, Chmiel JS, Silvestre A, Visscher BR, Vanable PA, Jacobson LP, Strathdee SA. Attitudes towards highly active antiretroviral therapy are associated with sexual risk taking among HIV-infected and uninfected homosexual men. AIDS 2002;16(5):775-80.
8. Stolte IG, Dukers NH, Geskus RB, Coutinho RA, de Wit JB. Homosexual men change to risky sex when perceiving less threat of HIV/AIDS since availability

of highly active antiretroviral therapy: a longitudinal study. AIDS 2004;18(2):303-9.

9. Gremy I, Beltzer N. HIV risk and condom use in the adult heterosexual population in France between 1992 and 2001: return to the starting point? AIDS 2004;18(5):805-9.

10. CDC. Increases in unsafe sex and rectal Gonorrrhea among men who have sex with men-San Francisco 1994-97. Morbidity Mortality Weekly Report 1999;48:45-48.

11. Semple SJ, Patterson TL, Grant I. Binge use of methamphetamine among HIV-positive men who have sex with men: pilot data and HIV prevention implications. AIDS Educ Prev 2003;15(2):133-47.

12. Wolf K, Young J, Rickenbach M, Vernazza P, Flepp M, Furrer H, Bernasconi E, Hirschel B, Telenti A, Weber R, Bucher HC. Prevalence of unsafe sexual behavior among HIV-infected individuals: the Swiss HIV Cohort Study. J Acquir Immune Defic Syndr 2003;33(4):494-9.

13. Crepaz N, Hart TA, Marks G. Highly active antiretroviral therapy and sexual risk behavior: a meta-analytic review. JAMA 2004;292(2):224-36.

14. Laurent C, Diakhate N, Gueye NF, Toure MA, Sow PS, Faye MA, Gueye M, Laniece I, Toure Kane C, Liegeois F, Vergne L, Mboup S, Badiane S, Ndoye I, Delaporte E. The Senegalese government's highly active antiretroviral therapy initiative: an 18-month follow-up study. AIDS 2002;16(10):1363-70.

15. Salomon JA, Hogan DR, Stover J, Stanecki KA, Walker N, Ghys PD, Schwartlander B. Integrating HIV prevention and treatment: from slogans to impact. PLoS Med 2005;2(1):e16.

16. Van Damme W, Kober K, Laga M. The real challenges for scaling up ART in sub-Saharan Africa. AIDS 2006;20(5):653-6.

17. WHO/UNAIDS. Antiretroviral Therapy for HIV infection in Adults and Adoloscents Recommendations

for a public health approach. Vol. 2006 Revision Geneva: World Health Organization 2006, 2006.

18. Moatti JP, Prudhomme J, Traore DC, Juillet-Amari A, Akribi HA, Msellati P. Access to antiretroviral treatment and sexual behaviours of HIV-infected patients aware of their serostatus in Cote d'Ivoire. AIDS 2003;17 Suppl 3:S69-77.

19. Bateganya M, Colfax G, Shafer LA, Kityo C, Mugyenyi P, Serwadda D, Mayanja H, Bangsberg D. Antiretroviral therapy and sexual behavior: a comparative study between antiretroviral- naive and -experienced patients at an urban HIV/AIDS care and research center in Kampala, Uganda. AIDS Patient Care STDS 2005;19(11):760-8.

20. Au JT, Kayitenkore K, Shutes E, Karita E, Peters PJ, Tichacek A, Allen SA. Access to adequate nutrition is a major potential obstacle to antiretroviral adherence among HIV-infected individuals in Rwanda. AIDS 2006;20(16):2116-8.

21. Bunnell R, Ekwaru JP, Solberg P, Wamai N, Bikaako-Kajura W, Were W, Coutinho A, Liechty C, Madraa E, Rutherford G, Mermin J. Changes in sexual behavior and risk of HIV transmission after antiretroviral therapy and prevention interventions in rural Uganda. AIDS 2006;20(1):85-92.

22. Chen SY, Weide D, McFarland W. Are the recent increases in sexual risk behavior among older or younger men who have sex with men? Answer: both. AIDS 2003;17(6):942-3.

23. Kennedy C, O'Reilly K, Medley A, Sweat M. The impact of HIV treatment on risk behaviour in developing countries: a systematic review. AIDS Care 2007;19(6):707-20.

24. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, Meehan MO, Lutalo T, Gray RH. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. N Engl J Med 2000;342(13):921-9.

25. Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, VanDyke R, Bey M, Shearer W, Jacobson RL, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. N Engl J Med 1994;331(18):1173-80.

26. Musicco M, Lazzarin A, Nicolosi A, Gasparini M, Costigliola P, Arici C, Saracco A. Antiretroviral treatment of men infected with human immunodeficiency virus type 1 reduces the incidence of heterosexual transmission. Italian Study Group on HIV Heterosexual Transmission. Arch Intern Med 1994;154(17):1971-6.

27. Bunnell R, Mermin J, De Cock KM. HIV prevention for a threatened continent: implementing positive prevention in Africa. JAMA 2006;296(7):855-8.

28. Smith DM, Wong JK, Shao H, Hightower GK, Mai SH, Moreno JM, Ignacio CC, Frost SD, Richman DD, Little SJ. Long-term persistence of transmitted

HIV drug resistance in male genital tract secretions: implications for secondary transmission. J Infect Dis 2007;196(3):356-60.

29. WHO/UNAIDS/UNICEF. Towards Universal Access:Scaling up priority HIV/AIDS interventions in the health sector. Progress report April 2007, 2007.

30. Chen SY, Gibson S, Katz MH, Klausner JD, Dilley JW, Schwarcz SK, Kellogg TA, McFarland W. Continuing increases in sexual risk behavior and sexually transmitted diseases among men who have sex with men: San Francisco, Calif, 1999-2001, USA. Am J Public Health 2002;92(9):1387-8.

31. Dodds JP, Nardone A, Mercey DE, Johnson AM. Increase in high risk sexual behaviour among homosexual men, London 1996-8: cross sectional, questionnaire study. BMJ 2000;320(7248):1510-1.

32. Katz MH, Schwarcz SK, Kellogg TA, Klausner JD, Dilley JW, Gibson S, McFarland W. Impact of highly active antiretroviral treatment on HIV seroincidence among men who have sex with men: San Francisco. Am J Public Health 2002;92(3):388-94.

33. Wolitski RJ, Valdiserri RO, Denning PH, Levine WC. Are we headed for a resurgence of the HIV epidemic among men who have sex with men? Am J Public Health 2001;91(6):883-8.

34. Begley K, Chan DJ, Jeganathan S, Batterham M, Smith DE. Correlates of unprotected anal intercourse in HIV positive men attending an HIV/AIDS clinic in Sydney. Curr HIV Res 2008;6(6):579-84.

35. Hays RB, Paul J, Ekstrand M, Kegeles SM, Stall R, Coates TJ. Actual versus perceived HIV status, sexual behaviors and predictors of unprotected sex among young gay and bisexual men who identify as HIV-negative, HIV-positive and untested. AIDS 1997;11(12):1495-502.

36. Rowniak S. Safe sex fatigue, treatment optimism, and serosorting: new challenges to HIV prevention among men who have sex with men. J Assoc Nurses AIDS Care 2009;20(1):31-8.

37. Diamond C, Richardson JL, Milam J, Stoyanoff S, McCutchan JA, Kemper C, Larsen RA, Hollander H, Weismuller P, Bolan R. Use of and adherence to antiretroviral therapy is associated with decreased sexual risk behavior in HIV clinic patients. J Acquir Immune Defic Syndr 2005;39(2):211-8.

38. Elford J, Ibrahim F, Bukutu C, Anderson J. Sexual behaviour of people living with HIV in London: implications for HIV transmission. AIDS 2007;21 Suppl 1:S63-70.

39. Muller O, Sarangbin S, Ruxrungtham K, Sittitrai W, Phanuphak P. Sexual risk behaviour reduction associated with voluntary HIV counselling and testing in HIV infected patients in Thailand. AIDS Care 1995;7(5):567-72.

40. Sobel E, Shine D, DiPietro D, Rabinowitz M. Condom use among HIV-infected patients in South Bronx, New York. AIDS 1996;10(2):235-6.

41. Wenger NS, Kusseling FS, Beck K, Shapiro MF. Sexual behavior of individuals infected with the human immunodeficiency virus. The need for intervention. Arch Intern Med 1994;154(16):1849-54.

42. Timothy G Heckman JAK, Anton M Somlai. Predictors of Continued High-Risk Sexual Behavior in a Community Sample of Persons Living with HIV/AIDS. AIDS and Behavior 1998; 2 (2):127-135.

43. Kline A, VanLandingham M. HIV-infected women and sexual risk reduction: the relevance of existing models of behavior change. AIDS Educ Prev 1994;6(5):390-402.

44. Timothy Heckman JK, Anton Somlai. Predictors of Continued High-Risk Sexual Behavior in
a Community Sample of Persons Living with HIV/AIDS. AIDS and Behavior 1998; 2 (2):127-135.
45. Wilson TE, Gore ME, Greenblatt R, Cohen M, Minkoff H, Silver S, Robison E, Levine A, Gange SJ. Changes in sexual behavior among HIV-infected women after initiation of HAART. Am J Public Health 2004;94(7):1141-6.
46. Scheer S, Chu PL, Klausner JD, Katz MH, Schwarcz SK. Effect of highly active antiretroviral therapy on diagnoses of sexually transmitted diseases in people with AIDS. Lancet 2001;357(9254):432-5.
47. McClelland RS, Baeten JM, Richardson BA, Lavreys L, Emery S, Mandaliya K, Ndinya-Achola JO, Overbaugh J. A comparison of genital HIV-1 shedding and sexual risk behavior among Kenyan women based on eligibility for initiation of HAART according to WHO guidelines. J Acquir Immune Defic Syndr 2006;41(5):611-5.
48. Rotheram-Borus MJ, Lee M, Zhou S, O'Hara P, Birnbaum JM, Swendeman D, Wright W, Pennbridge J, Wight RG. Variation in health and risk behavior among youth living with HIV. AIDS Educ Prev 2001;13(1):42-54.
49. Hankins C, Gendron S, Tran T, Lamping D, Lapointe N. Sexuality in Montreal women living with HIV. AIDS Care 1997;9(3):261-71.
50. Sethi AK, Celentano DD, Gange SJ, Gallant JE, Vlahov D, Farzadegan H. High-risk behavior and potential transmission of drug-resistant HIV among injection drug users. J Acquir Immune Defic Syndr 2004;35(5):503-10.

51. Barroso PF SM, Cerbino-Neto J, Almeida MH, Littleton M, Harrison LH. Sexual activity after initiation of antiretroviral therapy in Brazil. Abstract no. C10687. . International AIDS Conference. Vol. Jul 7-12; 14, 2002.

52. Crepaz N, Marks G. Towards an understanding of sexual risk behavior in people living with HIV: a review of social, psychological, and medical findings. AIDS 2002;16(2):135-49.

53. Hecht FM. Approaches to HIV Prevention Among Seropositive Patients in the Clinical Care Setting. Topics in HIV Medicine 2001;9(3):12-14.

54. Auerbach JD, Coates TJ. HIV prevention research: accomplishments and challenges for the third decade of AIDS. Am J Public Health 2000;90(7):1029-32.

55. Hosseinipour M, Cohen MS, Vernazza PL, Kashuba AD. Can antiretroviral therapy be used to prevent sexual transmission of human immunodeficiency virus type 1? Clin Infect Dis 2002;34(10):1391-5.

56. Morin SF, Myers JJ, Shade SB, Koester K, Maiorana A, Rose CD. Predicting HIV transmission risk among HIV-infected patients seen in clinical settings. AIDS Behav 2007;11(5 Suppl):S6-16.

57. Rand. Medical Outcomes Study: 36-Item Short Form Survey Instrument. Quality of Life form _SF-36. Vol. 2008 Rand corporation.

58. Pepe MS, Anderson G.L. . A cautionary note on inference for marginal regression

models with longitudinal data and general correlated response data. . Communications

in Statistics, Part B { Simulation and Computation 1994;23(23):939.

59. Diggle PJ, Heagerty, P.J., Liang, K.-Y. and Zeger, S.L. . Analysis of Longitudinal Data 2nd edition. New York: Oxford University Press., 2002.

60. Kleibaum David MK. Logistic regression: A self learning text. New York: Springer, 2002.

61. Eisele TP, Mathews C, Chopra M, Brown L, Silvestre E, Daries V, Kendall C. High levels of risk behavior among people living with HIV Initiating and waiting to start antiretroviral therapy in Cape Town South Africa. AIDS Behav 2008;12(4):570-7.

62. Luchters S, Sarna A, Geibel S, Chersich MF, Munyao P, Kaai S, Mandaliya KN, Shikely KS, Rutenberg N, Temmerman M. Safer sexual behaviors after 12 months of antiretroviral treatment in Mombasa, Kenya: a prospective cohort. AIDS Patient Care STDS 2008;22(7):587-94.

63. Tsitouras PD, Martin CE, Harman SM. Relationship of serum testosterone to sexual activity in healthy elderly men. J Gerontol 1982;37(3):288-93.

64. Bunnell R, Opio A, Musinguzi J, Kirungi W, Ekwaru P, Mishra V, Hladik W, Kafuko J, Madraa E, Mermin J. HIV transmission risk behavior among HIV-infected adults in Uganda: results of a nationally representative survey. AIDS 2008;22(5):617-24.

65. Twisk JW, Smidt N, de Vente W. Applied analysis of recurrent events: a practical overview. J Epidemiol Community Health 2005;59(8):706-10.

66. Cleary PD, Van Devanter N, Steilen M, Stuart A, Shipton-Levy R, McMullen W, Rogers TF, Singer E, Avorn J, Pindyck J. A randomized trial of an education and support program for HIV-infected individuals. AIDS 1995;9(11):1271-8.

67. Dolezal C, Ehrhardt AA, Meyer-Bahlburg HF, Liu X, Exner TM, Rabkin JG, Gorman JM, Marder K, Stern Y. Sexual risk behavior changes among HIV+ and HIV-female injecting drug users over 4 years. Women Health 1998;27(4):1-17.

68. Schroder KE, Carey MP, Vanable PA. Methodological challenges in research on sexual risk behavior: II. Accuracy of self-reports. Ann Behav Med 2003;26(2):104-23.

69. Kamya MR, Mayanja-Kizza H, Kambugu A, Bakeera-Kitaka S, Semitala F, Mwebaze-Songa P, Castelnuovo B, Schaefer P, Spacek LA, Gasasira AF, Katabira E, Colebunders R, Quinn TC, Ronald A, Thomas DL, Kekitiinwa A. Predictors of long-term viral failure among ugandan children and adults treated with antiretroviral therapy. J Acquir Immune Defic Syndr 2007;46(2):187-93.

70. Ahdieh L, Gange SJ, Greenblatt R, Minkoff H, Anastos K, Young M, Nowicki M, Kovacs A, Cohen M, Munoz A. Selection by indication of potent antiretroviral therapy use in a large cohort of women infected with human immunodeficiency virus. Am J Epidemiol 2000;152(10):923-33.

71. Kiene SM, Simbayi LC, Abrams A, Cloete A, Tennen H, Fisher JD. High rates of unprotected sex occurring among HIV-positive individuals in a daily diary study in South Africa: the role of alcohol use. J Acquir Immune Defic Syndr 2008;49(2):219-26.

72. Were WA, Mermin JH, Wamai N, Awor AC, Bechange S, Moss S, Solberg P, Downing RG, Coutinho A, Bunnell RE. Undiagnosed HIV infection and couple HIV discordance among household members of HIV-infected people

receiving antiretroviral therapy in Uganda. J Acquir Immune Defic Syndr 2006;43(1):91-5.