

University of California
Los Angeles

**Behavior Change and Other Factors Related to HIV Transmission
among Female Sero-converters in Microbicide Trials**

A dissertation submitted in partial satisfaction of the requirement for the degree Doctor
of Philosophy in Epidemiology

by

Jennie Lee McKenney

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Abstract of the Dissertation

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HIV/AIDS continues to be a major public health problem throughout the world. In 2011, 23.5 million people were living with HIV/AIDS worldwide, with the greatest burden of disease in Africa, representing 2/3 of the total HIV/AIDS population. Specifically, sub-Saharan Africa bears the highest burden of the disease, with 22.9 million people living with HIV/AIDS (PLWHA), 60% of the total infections worldwide. Furthermore, within this region, women are disproportionately affected, accounting for 58% of people living with HIV/AIDS.¹ With the continued high prevalence and incidence of HIV among women, despite an increase in prevention interventions, including pre-exposure prophylaxis (PrEP), suggests behavior change still plays a key role in transmission. This dissertation aims to seek to understand high-risk sexual behaviors and other factors associated with an increased risk of secondary transmission among women in order to inform the implementation of new HIV prevention strategies and reduce the burden of HIV. Chapter 1 is a brief introduction into HIV and the high-risk sexual behaviors that affect its transmission. Chapter 2 is based on data from a cohort study of recently seroconverted women from the Microbicide Trials Network (MTN) and demonstrated that depression plays a significant role in the acquisition of STIs. Chapter 3 is based on data from a cohort

study of recently sero-converted women from the MTN and demonstrated that there are several factors that influence disclosure and timing of disclosure of HIV status. Chapter 4 is based on data from a cohort study of recently sero-converted women from the MTN and demonstrated that high-risk sexual behaviors are still frequent among HIV-infected women, and that ART may modify the risk of high-risk sexual behaviors. Finally, Chapter 5 is a brief discussion of results as well as their implications for future research.

This dissertation of Jennie Lee McKenney is approved.

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2015

To my amazing family. You are the source of my strength; thank you for your support, honesty, and love.

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Chapter 1. Introduction and Background

1.1 Introduction

In 2012, sub-Saharan Africa had over 23 million people living with HIV/AIDS. Furthermore, within this region, women are disproportionately affected, accounting for 58% of people living with HIV/AIDS¹. Although incidence rates within southern Africa have decreased more than 25% since 2001, prevalence and incidence are still among the highest in the world, despite an increase in coverage of HIV treatment.¹ Poor treatment retention, coupled with high-risk sexual behaviors most likely account for the high rates of incidence and prevalence within this region.²⁻⁵ On average, only 64% of people who initiate antiretroviral treatment remain on treatment after 3 years.² Moreover, a cohort study that examined factors associated with an increase incidence of HIV infection in South Africa, found that, despite efforts to prevent sexual behaviors, participants still reported high-risk sexual behaviors, such as multiple sex partners.⁶ Thus, the continued high prevalence and incidence of HIV among women in southern Africa, suggests behavior change still plays a key role in transmission.

A number of studies have assessed behavior change longitudinally however, only a limited number have focused on African women, and even fewer have examined women who have recently sero-converted.⁷⁻¹⁰ One longitudinal study conducted among recently sero-converted women at three southern African sites examined sexual behaviors and found that women practice less high-risk sexual behaviors after sero-conversion.⁹ However, the study failed to examine several factors that affect behavior change, including disclosure of HIV status to husband and/or partner, depression, and the husband's and/or partner's HIV status. Additionally, the study only enrolled women from three study sites: Harare, Zimbabwe, and Durban and Johannesburg, South Africa, limiting the generalizability of the study results.

Therefore, a better understanding of sexual risk behaviors and factors associated with these behaviors among women over time is needed to inform the development of behavioral interventions. To address these gaps in knowledge, the proposed dissertation project will use longitudinal data collected from within the Microbicide Trials Network (MTN): a cohort study entitled: An Observational Cohort Study of Women following HIV-1 Sero-conversion in Microbicide Trials (MTN-015). Further, data will be used to identify predictors of disclosure of HIV status, an important component in HIV prevention, to help identify women who are less likely to disclose their HIV status and are therefore, at higher risk for transmitting HIV. Finally, the data will be used to investigate the effects of depression, a prevalent psychiatric condition among HIV-positive individuals, on the prevalence of sexually transmitted infections (STIs), which have shown to increase the risk HIV transmission. The proposed research project will also extend earlier applications of the Social Action Theory, which posits that self-protective behaviors are regulated by both individual and social-contextual factors, to guide in the analysis of both sexual behavior changes and predictors of disclosure. Thus, the proposed project seeks to understand behavioral change and factors associated with an increased risk of transmission among women who sero-converted in a microbicide trial in order to inform the implementation of new HIV prevention strategies and reduce the burden of HIV within southern Africa.

1.2 Epidemiology of HIV Infection Worldwide and in Southern Africa

In 2012, there was an estimated 35.3 million PLWHA and 2.3 million incident cases of HIV worldwide.^{1, 11} Since 2001, there has been nearly a 33% decline in the rate of new infections, a reflection of the global effort to prevent HIV/AIDS. Further, there has been a decrease in the amount of death due to AIDS, estimated to be 1.6 million in 2012.¹¹

However, sub-Saharan Africa, represents the majority of the global HIV burden, with nearly two-thirds of PLWHA residing in the region.^{1, 11} In 2012, sub-Saharan Africa had over 23 million

PLWHA.² HIV within the region has become a generalized epidemic as it's localized around adults between the ages of 15-59 and among populations at high-risk.¹² Moreover, women in the region are disproportionately affected by HIV infection, accounting for 58% of all people living with HIV in sub-Saharan Africa in 2011.¹

HIV has several modes of transmission including sexual, perinatal, and parenteral however, sexual transmission is the most common globally.¹¹ Within sub-Saharan Africa specifically, unprotected heterosexual sex is the most common mode of transmission.¹¹ Sexual transmission is fueled by high-risk sexual behaviors such as inconsistent condom use, and multiple sexual partners.¹¹ Moreover, there are several factors that increase the risk of transmission including co-infection with an STI, abuse, and depression.¹² Parenteral transmission is most common among injection drug users (IDU).¹¹ Among IDU globally, the burden of HIV remains high, and in some countries accounts for almost 40% of new infections.¹¹ Finally, perinatal transmission represents transmission that occurs from mother to child either during pregnancy, labor and delivery, or breastfeeding. There has been significant decline (51%) in the rate of mother to child transmission since 2001, a reflection of the scale up of antiretroviral treatment (ART) in general and specifically among pregnant women.¹¹

Although there is no cure for HIV/AIDS, ARTs have been shown to be effective at increase time to AIDS diagnosis, and decreasing poor health outcomes.¹³ There has been a substantial increase in the number of PLWHA on ART care globally.¹³ Specifically, in sub-Saharan Africa 4 million PLWHA had initiated ART by 2009.¹³ However, retention to care remains a problem specifically in some African countries.¹³ A review of ART programs in sub-Saharan Africa found that only 64% of people who initiate ART continue in care after 3 years.¹³ Therefore, prevention efforts should also focus on reducing sexual behaviors that increase the risk of HIV transmission. Engaging in sexual behaviors such as multiple sex partners,

inconsistent or no condom use, sexual positioning (anal vs. vaginal) have shown to increase the probability of transmission of HIV.^{14, 15}

1.3 Condom Use

Condom use has shown to reduce the risk of STI/HIV transmission when used consistently and correctly.¹⁶⁻¹⁹ Among discordant partners, in which one partner is HIV positive and the other is not, studies have shown the rate of HIV transmission was 80% when condoms were used consistently compared to when condoms were not used at all.¹⁷ In a study conducted in Lusaka, Zambia, the risk of HIV sero-conversion was approximately 5 times lower among sero-discordant partners that used condoms consistently compared to those who used condoms inconsistently.²⁰ Moreover, inconsistent condom use has shown to increase risk of HIV transmission, with the risk even greater among sero-discordant partnerships^{7,18} Inconsistent condom use has also been shown to be correlated with other high-risk sexual behaviors, further increasing the risk of HIV transmission.¹¹⁷

However, the challenge with condoms is obtaining consistent use within populations; especially in countries that associate condom use with promiscuity, unfaithfulness, and distrust, as they do in most African communities.¹⁶ Despite numerous behavioral interventions within schools and communities in Africa, studies still show that consistent condom use is low.¹⁶ In the 2007 Demographic Health Survey (DHS), only 18.8% of women reported any condom use, while 28.4% reported using a condom during their last intercourse.¹⁶

1.4 Multiple Sexual Partners

Prevalence of concurrent sexual partnerships is the highest in Sub-Saharan Africa where, on average, both men and women report having at least two ongoing sexual relationships in a year.^{3,4} Having concurrent sexual partners has been shown to increase the probability of HIV transmission by increasing the probability of sexual contact with an HIV-infected individual.^{3,4}

Mathematical modeling of HIV transmission in populations in which concurrent partnerships is the norm, compared to populations in which serial monogamy was the norm, found that the rate of HIV transmission was 10 times greater in populations with concurrent partnerships.⁴

A potential confounder in the relationship between multiple partners and an increase risk of HIV transmission is condom use. Studies have shown that condoms are less consistently used in concurrent partnerships compared to casual relationships.³ Moreover, consistent condom use has been shown to be associated with a reduction in risk of HIV transmission.¹⁶⁻¹⁹ In a study conducted among recent sero-converters in Uganda, the odds of HIV transmission among participants with sexual partners outside of marriage, whom they did not use a condom with, was three times that compared to participants that did not report having sexual partners outside the marriage.²¹

1.5 Unprotected Receptive Anal Intercourse

The prevalence of anal intercourse (AI) in Africa has shown to be as high as 20%.²² However, the prevalence ranges between countries and populations of people. For instance, among female sex workers in Sub-Saharan Africa, the prevalence of AI is as high as 43%.²² However, among the general population of Kenya, the prevalence of AI is shown be much lower, at 2%.²²

Compared with unprotected receptive vaginal intercourse (URVI), the risk of HIV transmission is higher among unprotected receptive anal intercourse (URAI); due to the lack of barriers in the rectal mucosal and the amount of trauma in the rectal mucosal surface leading to inflammation.²² Studies have shown the risk of HIV transmission during URAI is 1.4 times that compared to URVI.²² Further increasing the risk for HIV transmission is the correlation between AI and coerced or forced sex.²² During coerced or forced URAI, there is greater trauma to the

rectal mucosa, leading to increased inflammation, resulting in an increase in the number of immune cells- the target cells of HIV.²² Mathematical modeling conducted by Baggely *et al.* demonstrated that women exposed to one act of forced URAI have a three-fold increase in risk of HIV transmission. Moreover, models have shown women exposed to consistent forced URAI (1 act per week) with a sero-discordant partner have a cumulative risk of HIV transmission of 67%.²²

1.6 Patterns in Sexual Risk Behaviors among Women who Recently Sero-converted

With the continued high prevalence and incidence of HIV among women¹, despite an increase in prevention interventions, including pre-exposure prophylaxis (PrEP),²³ suggests behavior change still plays a key role in transmission. Sexual behaviors are particularly important among recently infected individuals, whose viral loads are high and are often highly infectious.²¹⁻²⁶ Studies among sero-discordant couples have estimated the risk of HIV infection to be seven times higher during the first five months after sero-conversion compared to later stages of infection.²⁶

While numerous cross-sectional studies have examined sexual behaviors among those both at high-risk for HIV infection and HIV positive individuals, factors that influence behavior change vary over time.^{7,27-29} Therefore, in order to capture its time varying nature, behavior change and its influencing factors should be assessed longitudinally.⁸ Moreover, assessing behavior change immediately after sero-conversion, as well as months following sero-conversion, allows us to examine both the immediate effects of HIV infection on behavior change, as well as the effects that occur over time.

A number of studies have assessed behavior change longitudinally however, only a limited number have focused on African women, and even fewer have examined women who have recently sero-converted.^{8, 9, 30} The Women's Interagency HIV Study (WIHS) is a cohort study

conducted in the United States that has enrolled both HIV-infected and high-risk women since 1994.³¹ Several studies conducted within this cohort have shown that sexual behavior change does occur among HIV-infected women. For example, women reported more consistent condom use after learning that they were HIV positive.³² However, the WIHS study did not collect data on the timing of sero-conversion thus, and its immediate effects could not be examined. Another limitation of WIHS is that it did not collect data on participants' sexual behavior before sero-conversion, therefore comparisons can only be made to HIV negative women. These groups may be different with respect to key factors that affect behavior change.

Additionally, a study by Venkatesh et al, examined sexual behaviors longitudinally among recently sero-converted women at three southern African sites.⁹ However, the study failed to examine several factors that affect behavior change, including disclosure of HIV status to husband and/or partner, depression, husband's and/or partner's HIV status, the use of ARTs by the study participant, husband, and/or partner. Additionally, the study only enrolled women from three study sites: Harare, Zimbabwe, and Durban and Johannesburg, South Africa, limiting the generalizability of the study results.

Thus, more research is needed to thoroughly examine behavior change and the factors that affect it over time.

1.7 Impact of Co-Infection with an STI on the Transmission of HIV

In 2008, there was an estimated 9.1 million people infected with at least one STI and 92.6 million new cases of STIs in Africa.³³ There is substantial biological evidence that supports the relationship between co-infection with an STI and an increase in HIV transmission.^{7,34} STIs cause a disruption in the mucosal surface of the genital tract, causing inflammation of the region, resulting in an influx of immune cells, the target cells of HIV.^{7,34} Ulcerative STIs are associated with bleeding, especially during sex, which may also increase HIV transmission.^{7,34}

Further, STIs have been shown to effect immune function, such as altered cytokine production.^{7,34}

Along with substantial biological evidence, there have been numerous observational studies examining the relationship between STI co-infection and transmission of HIV, all of which have shown a positive association.³⁴ A meta-analysis of 31 cohort studies showed a four-fold increase in the risk of HIV transmission when co-infected with any STI and 2 to 3 fold-increase in risk when stratified by ulcerative and non-ulcerated STIs, respectively.³⁴ Observational studies examining the association between co-infection of STI and genital tract viral shedding have demonstrated a 2 to 3-fold increase in viral shedding.³⁴ Moreover, studies have shown that co-infection with an STI increases the infectiousness of HIV to levels almost as high as during acute infection.^{3,7}

Despite overwhelming evidence from observational studies, there are few randomized control trials (RCTs) that substantiate the association between STI co-infection and higher risk of HIV transmission.³⁴ In total there have been 9 RCTs that have examined STI case management as a method to prevent HIV transmission; only 1 has shown an effect.³⁴

The Mwanza trial, a cluster randomized trial, examined the effect of syndromic management of STIs at government health centers in the Mwanza region of Tanzania.³⁴ The trial estimated that 9% of women were infected with active syphilis, 75% had HSV-2 infection, 27% were infected with *Trichomonas vaginalis*, and 8% were infected with either chlamydia or gonorrhea.³⁵ Data from this trial showed that improved case management of STIs reduced the incidence of HIV infection by as much as 40%.³⁶

There are several possible explanations for the discrepancy in results seen between observational studies and RCTs. One such explanation is the effects of improved case management in RCTs may be masked due to interventions given to the control group.³⁴ Due to

ethical reasons; all control groups in the 9 RCTs received some type of intervention, which could make the control group more similar to the exposed group, driving the measure of association toward null.³⁴

1.8 Impact of Disclosure on Transmission of HIV

Rates of disclosure vary by population however, in general, low rates of disclosure are reported throughout Africa.^{37,38} In Tanzania, rates of disclosure are estimated to be 64% among HIV positive women.³⁸ Similar percentages of disclosure among women are seen in Kenya.³⁸ There are many factors that can influence disclosure of HIV status including fear of rejection from partners, family, and friends, divorce, and being accused of infidelity.^{30, 37-39} However, there are also several benefits to disclosure of HIV status including, an increase in support, access to HIV treatment, and an increase in HIV testing among sexual partners.⁴⁰ Moreover, disclosure of HIV status can affect the transmission of HIV by declining the amount of high-risk sexual behaviors and is especially important in sero-discordant partnerships.³⁹ Models have shown that disclosure of HIV status can reduce HIV transmission by more than 41%.³⁰

1.9 Patterns of Disclosure among Women who Recently Sero-converted

Disclosure to partners, particularly among sero-discordant partnerships, has shown to decrease the probability of HIV transmission.³⁹ Disclosure is especially important among recently infected individuals, whose viral loads are high and are often highly infectious.⁴¹⁻⁴³ There have been numerous studies that have examined the relationship between demographic characteristics, partnership dynamics, and disclosure.^{30,37,40,44} These studies have shown that marital status, duration of relationship, occupation, monthly income, and education are all positively associated with disclosure status.^{30,37,40,44}

However, time affects disclosure, in that an individual's decision to disclosure may change over the course of their diagnosis.³⁷ Further, factors that influence disclosure vary over time.

Therefore, in order to capture its time varying nature, disclosure and its influencing factors should be assessed longitudinally.

There have been a few studies that examine predictors of disclosure longitudinally among both men and women.^{37, 40} However, to my knowledge there have not been multi-country longitudinal studies that assessed predictors of disclosure among recently sero-converted women in Africa. Because factors that affect disclosure may be gender and region-specific,^{30,37,39,44} research is needed to identify patterns of disclosure within this group.

One longitudinal study, conducted among HIV-infected pregnant women, found that 'immediate' disclosure was positively associated with high income and marriage and negatively associated with a history of violence.³⁷ Further, 'delayed' disclosure was positively associated with a history of violence and an internalized stigma associated with diagnosis.³⁷ However, the study had several limitations. The study classified women as disclosing immediately if they disclosed their HIV status as of the baseline questionnaire and delayed disclosing if they disclosed their HIV status by the end of the 3 months of follow-up. The conservative time periods for classification of outcome could have led to misclassification. Similarly, women who did not disclose their HIV status in this study could have done so at a later time however, the length of the study was not adequate enough to include these women. Moreover, 3 months may be insufficient to truly capture time varying predictors of disclosure especially, delayed disclosure.

Therefore, more research is needed to thoroughly examine predictors of disclosure and the factors that affect it over time.

1.10 Impact of Depression on HIV Transmission

The association between psychiatric disorders among HIV-infected individuals has been well documented.⁴²⁻⁴⁷ Psychiatric disorders most likely occur within this population because of

the direct result of stress resulting in HIV diagnosis, coupled with lack of social support due to delayed disclosure.⁴²⁻⁴⁸ Thus, the prevalence of psychiatric disorders among HIV-infected individuals is high compared to the HIV-negative population.⁴⁵⁻⁵⁰ Among the psychiatric disorders prevalent among HIV-infected individuals are mood disorders, anxiety disorders, major depression, posttraumatic stress disorder (PTSD), and alcohol and substance abuse.⁴⁵⁻⁵⁰

Depression is one of the most common psychiatric complications associated with HIV diagnosis worldwide.⁴⁵⁻⁵⁰ Specifically, in Africa, studies have shown a wide range (3-54%) in the prevalence of depression, depending on both the country and population under study.⁴⁹ In Uganda, a study of HIV-infected men and women found the prevalence of depression to be 47%.⁴⁷⁻⁵⁰ However, in two other studies conducted in Uganda, one among men and women attending HIV clinics and another among women participating in a cohort study, the prevalence of depression was lower- 8.1% and 23.7%, respectively.⁴⁹⁻⁵⁰ Moreover, depression is more prevalent in women, especially in Africa, due to gender inequalities within relationships.⁵⁰ Women are less likely to hold power within their relationships, leading to an increase risk in interpersonal violence- a predictor of depression.⁵⁰ A cross sectional study of HIV-infected men and women in Uganda found that women had 2 times the odds of depression compared to men.⁴⁹ Further, in a study conducted among HIV-infected women in Uganda, women who reported moderate to high relationship power had .44 times the odds of depression compared to women with low relationship power.⁵⁰

Depression has also been associated with an increase in both primary and secondary HIV transmission, as well as faster disease progression.⁴⁸ Biological mechanisms have been hypothesized to link depression with an increase risk of HIV transmission. Among them, is the idea that depression stimulates the release of neurotransmitters that in turn, decrease the immune system's ability to fight infection, leading to an increase in susceptibility of infection.⁴⁷

However, additional studies on the biological mechanisms are needed to substantiate any hypothesis.

Co-existence of depression with HIV leads to interference with health seeking behaviors, such as treatment and treatment retention, and is associated with delayed disclosure of HIV status.^{45, 48, 49} Further, due to low self-esteem, depression is associated with sexual risk behaviors that increase the risk of HIV transmission. Specifically, studies have demonstrated depression is associated with an earlier sexual debut and inconsistent condom use.^{47,51} A study conducted in Cape Town, South Africa, found that women who were depressed had 1.53 times the risk of engaging in unprotected sex compared to women who were not depressed.⁵¹

1.11 Impact of Interpersonal Violence (IPV) on HIV Transmission

IPV, which includes physical, sexual, and mental abuse, is prevalent among women globally.⁵²⁻⁵⁴ The World Health Organization's study of Women's Health and Domestic Violence in 10 countries, demonstrated that the prevalence of IPV is as high as 28%.⁵³ IPV is especially prevalent among HIV-infected women in Africa, where a woman's power within a relationship is likely lower.⁵²⁻⁵⁴ Moreover, IPV is prevalent among individuals with depression, as it is a predictor for depression.^{52, 54}

Several studies have shown an association between IPV and an increase risk for HIV transmission among women.⁵²⁻⁵⁵ Women who are subject to IPV are at an increased risk of HIV transmission, regardless of their sexual behaviors.^{52,54} This is because men, who perpetuate violence, are themselves at higher risk for HIV infection due to high-risk sexual behaviors, such as inconsistent condom use and multiple sex partners.^{52,54} Thus, women who experience IPV have a higher probability of coming into contact with an HIV-infected partner. In a cross sectional study of women in Rwanda, women who reported experiencing IPV had a 3-4-fold increase in odds of testing positive for HIV, compared to women who did not report experiencing

IPV.⁵² Further, IPV can lead to conditions within the genital tract that facilitate HIV transmission.^{52,54} Forced sexual activity can lead to damage of the genital mucosa, resulting in inflammation and recruitment of immune cells, the target of HIV.^{52,54} Finally, women who experience IPV are less likely to seek testing and disclose their HIV status, for fear of abuse and social abandonment.^{52,54,55}

1.12 Impact of PrEP on HIV Transmission

PrEP, or pre-exposure prophylaxis, is the use of antiretroviral medications by HIV-negative individuals before exposure to reduce their risk of infection.¹⁴ PrEP can be both oral, in the form of tablets or topical, in the form of microbicides.¹⁴ Specifically, microbicides are products used in the vagina or rectum to reduce the risk of HIV transmission.¹⁴ Vaginal microbicides come in many forms including gels, films, sponges, and rings.¹⁴ PrEP effectiveness is dependent on adherence and has shown a range from 21-73%.¹⁴ There have been several clinical trials examining the efficacy of microbicides with mixed results. Table 1.1 lists the results of several such RCTs. Specifically, CAPRISA, a RCT testing the efficacy of Tenofovir gel in reducing the risk of vaginal HIV transmission, demonstrated a 39% efficacy.¹⁴ However, other RCTs, such as VOICE, have not been able to replicate such findings.¹⁴

Table 1.1 Microbicide trials and results

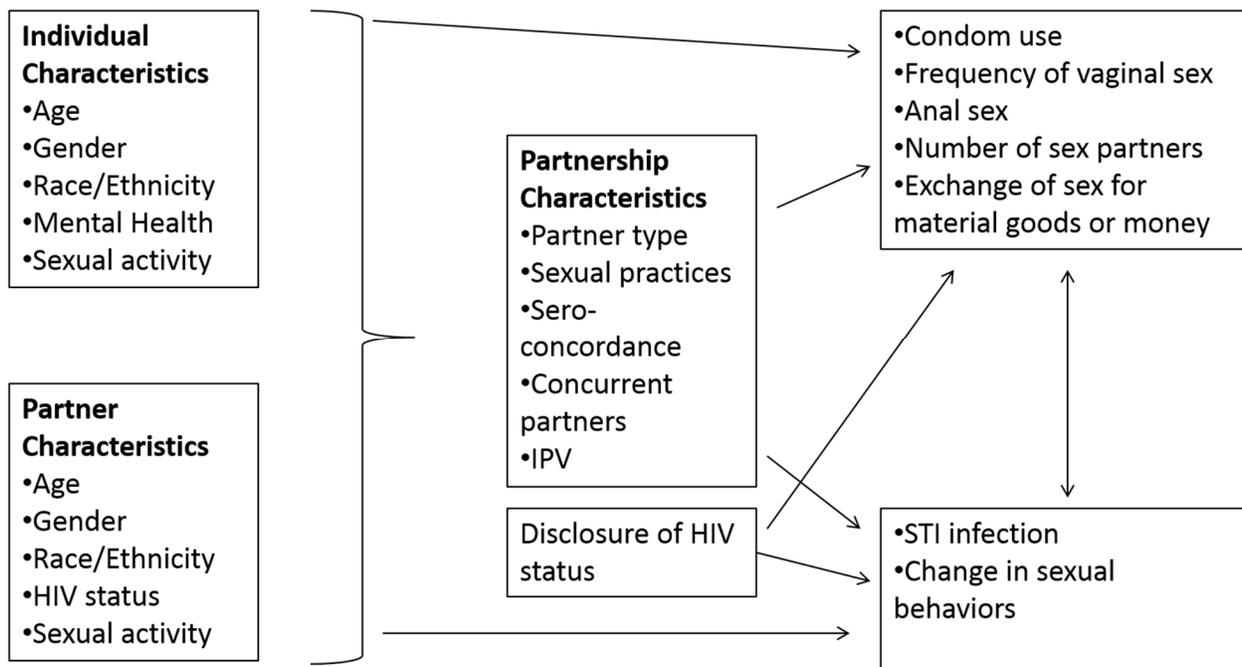
Study ID	Status	Phase	Type of prevention	Component	Results
MDP301	Complete	III	Gel, vaginal	PRO 2000/5 gel 0.5% and 2%	Not efficacious
CONRAD	Terminated	III	Gel, vaginal	Cellulose, sulfate gel (6%)	No protection, possible enhancement
Population Council #332	Completed	III	Gel, vaginal	Carraguard (PC-515)	No protection
CAPRISA 004	Completed	II	Gel, vaginal	Tenofovir 1% gel	39% efficacy
VOICE	Completed	II	Gel, vaginal and ART oral	Tenofovir 1% gel vaginal gel, emtricitabine/tenofovir disoproxil fumarate	Vaginal and oral Tenofovir arms halted. No efficacy.
HPTN 035	Completed	IIb	Gel, vaginal	BufferGel and 0.5% PRO2000/5	No protection

Table adapted from Demberg T, Robert-Guroff M.¹¹

1.13 Conceptual Model

The conceptual model shown in Figure 1 was adapted from a model developed by Gorbach and Holmes⁵³ to explain how individual and partner characteristics affect sexual risk behaviors and the incidence of sexually transmitted infections including HIV (STI/HIV). Further, this model reflects key elements of the Social Action Theory⁵⁷ as both personal and situational factors interact to affect the self-protective behavior of condom use within partnerships. Thus, this model will guide all of the analyses described below to achieve each of the specific aims.

Figure 1.1 Conceptual model of individual and partnership characteristics, disclosure, and sexual behavior change



1.14 MTN-015: *Microbicide Trials Network cohort study entitled: An Observational Cohort Study of Women following HIV-1 Seroconversion in Microbicide Trials*

Longitudinal data collected from a clinical trial conducted among high-risk women enrolled in MTN-015 since August 2008, will be used to examine changes in condom use over time, identify predictors of disclosure of HIV status, and investigate the effect of depression on the prevalence of STIs. MTN-015 is designed to follow women who recently seroconverted in a parent MTN microbicide trials (HPTN 0135, MTN-003, and MTN-020) and the primary research aim was to compare plasma RNA HIV-1 level in women 12 months after sero-conversion compared to control participants. A breakdown of MTN-015 enrollment can be seen in Figure 1.2 MTN-015 was conducted by MTN investigator Dr. Riddler and investigators from all sites, the scientific leadership groups in the MTN, as well as community partners at the following sites: Bothas Hill Clinical Research Site, CAPRISA Aurum CRS, CAPRISA eThekweni CRS, Chatsworth CRS, Isipingo CRS, Kamwala Health Centre, Makerere University, Overport CRS, Seke South Clinical Research Site, Soweto MTN CRS, Spilhaus Clinical Research Site, Tongaat CRS, Umkomaas Clinical Research Site, UNC Lilongwe CRS, Verulam CRS, Wits Reproductive Health and HIV Institute, Zengeza 3 Clinic.

Efforts were made by MTN-015 study staff to recruit all women who seroconvert during a MTN microbicide trial. Women who seroconverted prior to the start of MTN-015 were contacted retrospectively by study staff. Women who seroconverted after the start of MTN-015 were contact prospectively by study staff at the time at which they were identified as seroconverted. The following eligibility criteria were then used to screen women who expressed interest in participating: HIV-1 sero-conversion during participation in a MTN clinical trial, able and willing to provide written consent to participate in the study, and does not have a condition deemed by the investigator that could prevent informed consent, make participation in the study harmful, or interfere with the study objectives. There were several components to the screening/enrollment

visit such as behavioral component in which participants were administered the behavioral baseline and ART adherence questionnaires, STI risk reduction and contraceptive counseling, HIV secondary prevention counseling, and provision of condoms. Moreover, extensive biological samples were taken. As the study is ongoing a final study size number has not been determined, to date there have been a total of 355 women enrolled in MTN-015 across 15 sites. Enrollment as of May 27, 2013 by country, for MTN-003 participants only is shown in Table 1.2.

MTN-015 questionnaires were administered using face-to-face interviewing based on two different schedules based on if antiretroviral treatment (ART) was initiated at the time of enrollment. Questionnaires were administered to participants who had not initiated ART at the time of enrollment at baseline and months 1, 3 and 6, and every 6 months thereafter. Questionnaires were administered to participants who have initiated ART at the time of enrollment at baseline, week 2, and months 1, 3, and 6 and every 6 months thereafter. Study questionnaires for MTN-015 collected information on demographics (baseline only), microbicide trial participation (baseline only), sexual behavior, partnership types and dynamics, disclosure of HIV status, depression, social harms, and ART adherence (participants who initiated ART before enrollment only) at baseline and months 3, 6, and 12. For all participants, interim visits were performed for any reason including but not limited to: administration, clinical (STI symptoms), and psychosocial. All data collected from interim visits will be reported on applicable CRFs.

Participants in MTN-015 were also underwent extensive biological and clinical testing however, for the purposes of this proposal, only STI information will be used. STI testing was conducted at each scheduled follow-up. Blood was taken for syphilis serology, vaginal fluid was used to test for trichomonas, and urine was taken for SDA to test for both chlamydia and gonorrhea.

Figure 1.2 MTN-015 enrollment from parent microbicide trials

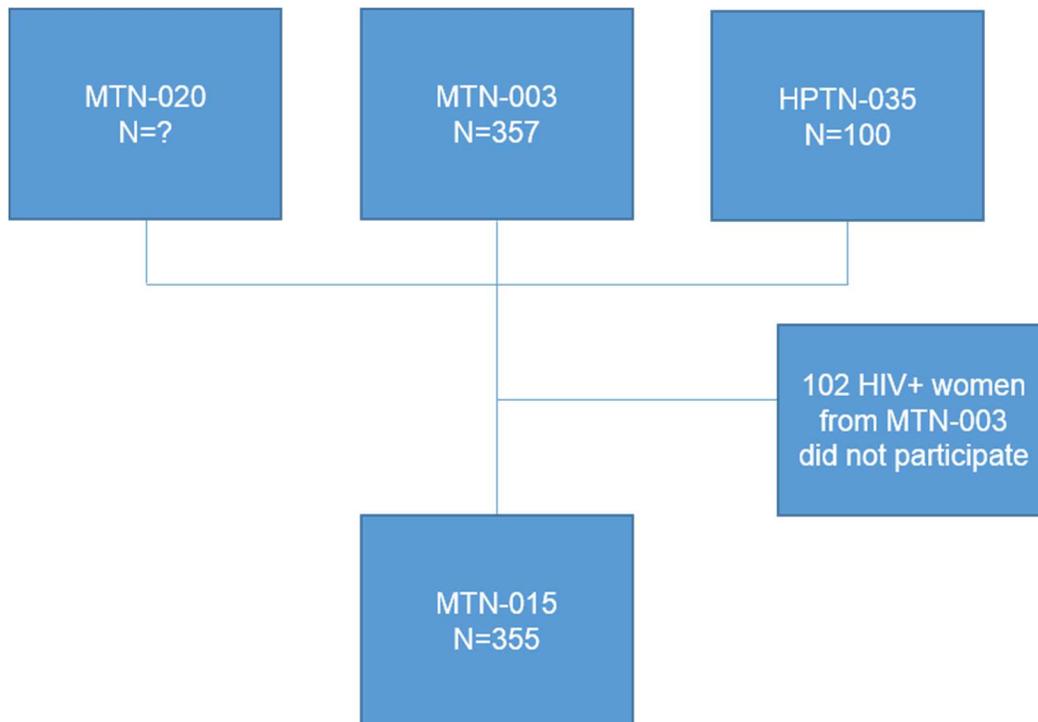


Table 1.2 MTN-015 enrollment by country

	All sites N	Zimbabwe N (%)	South Africa N (%)	Uganda N (%)
Total Eligible	357	7 (1.96%)	339 (94.96%)	11 (3.08%)
Total Enrolled	255	7 (2.73%)	237 (92.91%)	11 (4.30%)

1.15 Reference

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Chapter 2: Depression, sexual behaviors, and risk of sexually transmitted infections among recently HIV-infected women in Africa

2.1 Abstract

Background: Prevalence of depression in Sub-Saharan Africa ranges from 10-20% and is especially high among women living with HIV. Depression among people living with HIV has been associated with negative outcomes including higher prevalence of risky behaviors that may result in an increase in acquisition of sexually transmitted infections (STIs). There is cross-sectional evidence of an association between depression and HIV acquisition, but the relationship with STI has not been assessed longitudinally for those recently HIV infected.

Methods: We examined data from 254 women participating in the MTN-015 study, an observational study of women who sero-converted to HIV during a MTN microbicide trial. Data were collected from August 2008 and women were eligible for inclusion in this analysis if they did not have delayed enrollment into MTN-015 and had follow-up data. All women completed face-to-face interviews, were assessed clinically and tested at enrollment, yearly and when clinically indicated for STIs including gonorrhea (GC) and chlamydia (CT) using nucleic acid amplification tests. Depression was assessed using an abbreviated Hopkins Symptom Checklist. Other factors of interest included demographics and sexual risk behaviors such as socioeconomic status (SES) condom use, intimate partner violence (IPV). Factors associated with GC/CT acquisition were analyzed using regression analysis using generalized estimating equations. Odds ratios (OR) for acquisition of GC/CT after enrollment were estimated for variables listed above and age, sought medical care after sero-conversion, condom use at last sex, and interpersonal violence (IPV).

Results: Among the 254 women, the median time of follow-up for women was 1.4 years. At enrollment the mean age was 24 and almost all reported last sex with a main partner- 99%. The

baseline prevalence of major depression (case cutoff score of 2.4) was 16%, IPV 18%, condom use 85%. In the first year of observation, there were a total of 125 cases of STIs, of which 68 cases (54%) were from women infected with multiple STIs over the year of follow-up. The OR for STI among those depressed was 2.67 (C: 1.17-6.08) after controlling for several factors. Moreover, the magnitude of the OR increased (OR: 4.14, CI: 1.54-11.11) when the analysis was restricted to just women ≤ 25 , after controlling for several factors.

Conclusions: Among women recently infected with HIV, depression plays a significant role in STI acquisition; especially among those ≤ 25 years of age. Efforts are needed to manage depression among women living with HIV/AIDS to help reduce risky sexual behaviors, increase and maintain health seeking behaviors, and reduce the risk STI co-infection and its potentially harmful reproductive health sequelae.

2.2 Introduction

HIV/AIDS continues to be a major public health problem throughout the world. In 2011, 23.5 million people were living with HIV/AIDS worldwide, with the greatest burden of disease in Africa, representing 2/3 of the total HIV/AIDS population, despite a decrease in incidence of nearly 25% since 2001.¹ In 2011, an estimated 1.8 million new cases were reported in southern Africa, highlighting the fact that HIV/AIDS continues to be a major public health problem within this region.¹ Furthermore, within this region, women are disproportionately affected, accounting for 58% of people living with HIV/AIDS.¹ Among women with HIV/AIDS, sexually transmitted infections (STIs) continue to be a major problem.² Co-infection of HIV and STIs has several important implications, as co-infection increases genital viral load, thus increasing infectiousness.³⁻⁹ Also, STIs may be a marker for risky sexual behaviors, such as unprotected sex.^{3,4} Despite this important association, there is limited epidemiological information on STIs among those infected with HIV in Africa especially among women.² A review of studies

conducted in Africa found the prevalence of confirmed STIs to be 16.3% among people infected with HIV/AIDS, and the highest prevalence was among those recently infected with HIV.²

The association between mental health among HIV-infected individuals has been well documented.¹⁰⁻¹⁵ One of the reasons psychiatric disorders are common among this population is the result of the stress associated with an HIV diagnosis.¹⁰⁻¹⁶ Thus, the prevalence of psychiatric disorders among HIV-infected individuals is high compared to the HIV-negative population.¹⁰⁻¹⁶ One of the most common neuropsychiatric disorders among those with HIV/AIDS is depression.¹⁰⁻¹⁵ In Sub-Saharan Africa the prevalence of major depression ranges from 10-20%, and the prevalence of minor depression ranges from 20-30%.¹⁷ Several studies have shown women infected with HIV/AIDS are at an increased risk of depression compared to men infected with HIV/AIDS.¹⁵ Differences in risk may be reflective of gender inequalities both outside and within relationships.¹⁴⁻¹⁵ Outside of relationships, women are more likely to report traumatic life experiences within the region, and thus score higher on depression and stress scales.¹⁸⁻²⁰ Within relationships, women are less likely to hold power, leading to an increase risk in interpersonal violence, a predictor of depression.¹⁵

Depression among people living with HIV/AIDS has several important public health implications. Depression has been linked to an acceleration of HIV disease progression, and poor outcomes.¹³⁻¹⁴ Evidence suggests that those with depression may practice riskier sexual behaviors, such as unprotected sex and sex with multiple partners, and as a result, they are more likely to acquire and transmit STIs.^{12,16} Moreover, treatment for depression has been shown to be effective at increasing adherence to antiretroviral treatment, likely decreasing disease progression and improving outcomes.²¹ Despite the large amount of evidence that suggests an association between HIV infection and depression, little research has focused on the relationship between STIs and depression longitudinally among those recently infected with HIV; specifically assessing if the presence of depression increases the risk of STIs among those

HIV-infected.²²⁻²³ The association, if present, could lead to targeted behavioral interventions as well as both pharmacological interventions and psychotherapeutic treatment among HIV-infected women with STIs.

2.3 Methods

We utilized data on recently HIV-infected women who sero-converted during VOICE: a Microbicide Trials Network (MTN) phase 2B randomized control trial entitled: Phase 2B Safety and Effectiveness Study of Tenofovir 1% Gel, Tenofovir Disoproxil Fumarate tablet and Emtricitabine/Tenofovir Disoproxil Fumarate Tablet for the Prevention of HIV Infection in Women (MTN-003).²⁴ These women were subsequently enrolled in the MTN cohort study entitled: An Observational Cohort Study of Women following HIV-1 Sero-conversion in Microbicide Trials (MTN-015).²⁵ MTN-015 is a longitudinal study aimed to follow women who recently sero-converted in a parent MTN microbicide trial (HPTN 0135, MTN-003, and MTN-020) across 15 different study sites in Zimbabwe, South Africa and Uganda, since August 2008. The primary research aim of the study was to compare plasma RNA HIV-1 levels in women 12 months after sero-conversion to controls. For the purpose of this analysis women who sero-converted in HPTN- 035 were not included given the delayed time to enrollment since sero-conversion. Additionally, there were no sero-converters in MTN-020, and therefore these women were not included in this analysis. A total of 357 recently sero-converted women from VOICE were eligible for MTN 015, with 255 (71.2%) enrolling. Only data on 254 of the women were used in this analysis, as one woman did not have adequate follow-up data. Data for this analysis was censored on October 31, 2013.

MTN-015

MTN-015 questionnaires were administered using face-to-face interviews on two different schedules based on if antiretroviral treatment (ART) was initiated at the time of

enrollment or during follow-up. For participants who had not initiated ART at the time of enrollment, visits occurred at baseline and at months 1, 3, 6, and every 6 months thereafter; while follow-ups occurred at baseline, week 2, and months 1, 3, 6, and every 6 months after for participants who had initiated ART at the time of enrollment. For participants who initiated ART during follow-up, their follow-up schedule switched from the non-ART schedule to the ART schedule after ART initiation. Participants also underwent extensive biological and clinical testing, including STI testing.²⁵

Sexually Transmitted Infections

STI testing was conducted annually, but participants were permitted to schedule interim visits if needed for symptoms of STIs among other concerns, the results of which were included in our final dataset. Urine was taken for strand displacement amplification (SDA) to test for both chlamydia and gonorrhea. For the purposes of our analyses, study participants categorized as having an STI were infected with either chlamydia or gonorrhea, or both.

Depression

Depression and anxiety were measured using a subset of the Hopkins Symptom Checklist (HSCL-25), a 10 item index of anxiety and a 15 item index for depression.¹³ Validation studies of HSCL-25 conducted by Kaaya et al. determined that a subset of only 8 of those questions, along with adjusting the “caseness” cutoff score to 1.06 or greater yielded highly sensitive and specific results in identifying depression and anxiety validated by clinical exam.²² Thus, MTN-015 and subsequently this study as well, used the 8 item index to assess anxiety and depression. However, after evaluation of the cutoff score of 1.06, it was determined that the score was too liberal in the identification of anxiety and depression, as 78% percent of the study population was deemed depressed based on this cutoff. Based on recent publications, depression among those with HIV/AIDS in Africa should be between 10-20% for

major depression and 20-30% for mild depression.¹⁷ Based on this *a priori* information, a cutoff score of 2.4 was used in this analysis, as it yielded a depression prevalence of 17% which was well within the prevalence range for major depression. However, a sensitivity analysis was conducted to determine the effects of the results when the cutoff score was varied.

Demographic and Behavioral Characteristics

Behavioral questionnaires were administered as face-to-face interviews at baseline and at month 3, no matter the participant's ART schedule. Participants were asked a series of demographic questions, including their age, their education level, and whether they own their own home. We considered owning a home as a proxy for socioeconomic status (SES). Women were asked a series of questions about sexual health behaviors, including their partnership status. Women were asked to provide their partners age, the length of their relationship, and if their husband and/or partner has more than one wife or sexual partner. Women were asked about the number of condoms they used in the past week and whether or not they used a condom at last sex, the latter was used in this analysis as a measure of condom use. Women were asked if they had history of interpersonal violence (IPV) with their partner or husband and also if they experienced violence from their partner after they disclosed their HIV status. Finally, women were asked a series of questions related to their health care post HIV diagnosis, such as have you seen a healthcare provider/doctor/nurse for HIV care, have you seen a traditional healer for HIV care or treatment, etc. We combined all health seeking behaviors post diagnosis into one variable.

2.4 Analysis

Data were analyzed using SAS 9.4 (SAS Institute, Cary, NC, USA). Study population baseline characteristics were assessed using Chi-square (X^2) and Student's T test. Univariate and multivariable analyses were conducted to examine correlates of STIs. Variables of

significance in the univariate analysis ($p\text{-value} \leq 0.05$) and/or variables that are known to be associated with STI acquisition were included in the final model. Multivariable analysis was conducted using generalized estimating equations (GEE) through the genmod procedure. GEE is an extension of linear model theory and is most appropriate when dealing with longitudinal data that is correlated.²⁶ Failure to account for correlation may lead to incorrect estimation of the model parameters.²⁶ Using the logit function and assuming a binomial distribution odds ratios were estimated to examine repeated binary measures. Odds ratios are preferred for binary measures because they are not bound by the means of the data.²⁶ The correlation structure assumed for this analysis was a first-order autoregressive correlation structure (AR-1), which is appropriate when measurements closer together in time are more correlated than measurements further apart in time and when subjects are assessed at the same time intervals, as is the case with this study.²⁷⁻³² Moreover, use of AR-1 correlation structure is consistent with other analyses on longitudinal data analysis.²⁷⁻³² MTN-015 protocols and study material was reviewed by each site's IRB/EC. Further, for this study, approval was given by the University of California, Los Angeles IRB.

2.5 Results

Study Population

The median follow-up time for participants was 1.4 years. The majority of participants (93.3%) were from South African study sites. The median age of the participants was 24 years (range 18-40). Additional demographic and behavioral characteristics for both those with major depression and those without are shown in Table 2.1.

Using a caseness cutoff score of 2.4, the prevalence of major depression at baseline was 17.3%. The median age among both those with major depression and those without was 24. Compared to women with major depression, a higher proportion of women without major

depression reported using a condom at last sex (67.4% and 89.1%, respectively, p-value: 0.003) and more likely to disclose their HIV status to both their partner (33.3% and 42.7%, respectively, p-value: 0.04). Additionally, a higher percentage of women without major depression completed secondary education when compared to women with depression (52.6% and 43.2% respectively) and owned their own home (73.9%, 62.8%, respectively), however these differences were not statistically significant (p-value: > 0.05).

Incidence of STIs

The incidence rate for STIs was 1.49 STIs per person-year. Among women diagnosed with an STI during follow-up, the majority of women (64.8%) were only infected with one STI. The median age of women with an STI was 24, while the median age was 25 for those women without an STI. Women with and without an STI reported similar percentages at baseline of behaviors of condom use (86.3%-infected with STI, 86.6%-not infected with STI) and disclosure of HIV status (disclosed to both partner and other: 36.5%- infected with STI, 34.5%- not infected with STI), however, a higher percentage of women without an STI reported seeking medical care when compared with women with an STI (29.6%, 13.0%, respectively).

Characteristics of women with multiple STIs

Of the 125 cases of STIs, 68 cases (54.4%) were from women infected at more than one time point over follow-up. The majority of women with multiple STIs were infected only twice over the course of the follow-up (91.2%). Women with multiple infections were more likely to be younger, less educated, and not have their own source of income compared to women infected with just 1 STI or not infected with any STIs. Women not infected with an STI were more likely than those infected with either one STI or two STIs to use a condom at last sex (87.4%, 84.5%, 75.9%, respectively) (Table 2.2). They were also less likely to experience interpersonal violence (IPV) (16.3%, 18.6%, 23.3%, respectively). Table 2.2 describes additional behavioral

characteristics of women infected with multiple STIs compared to women with one STI, and no STIs during follow-up

Correlates of STI acquisition

Results from the multivariable analysis of all women are presented in Table 2.3. Women who were depressed had almost 2-fold odds of acquiring an STI during the year of follow-up compared to women who were not depressed when adjusted for other covariates. To examine age as a modifier on the association between depression and STI acquisition, we conducted a separate analysis among women less than 25 years of age (n=156) (Table 2.4). After adjusting for confounders, among depressed women less than 25 years of age, the odds of acquiring an STI during the year of follow-up was 4 times the odds among non-depressed women (Odds Ratio(aOR)= 4.14 Confidence Interval (CI):1.54-11.11). The risk of STI acquisition varied significantly by condom use (OR= 0.43, CI: 0.20-0.91) and seeking medical care after sero-conversion (OR= 0.56, CI: 0.34-0.94). However, when examining the association of depression and STI acquisition among women 26 years of age or older, the relationship did not hold. Specifically, the magnitude of the associations decreased dramatically, especially for depression, and the significance of the associations between STI acquisition and the correlates was no longer present (Table 2.5) In addition, we conducted a sensitivity analysis using different cutoffs for depression (Table 2.6). From this analysis we see that similar results to our analysis hold at a range of major depression prevalences (15-24%).

2.6 Discussion

Our longitudinal analysis of 254 recently sero-converted women revealed a prevalence of 17.25% for major depression when the case cutoff score was set at 2.4, and an incidence rate of 1.49 STI cases per person-year. Multivariable analyses indicated major depression and age were significant correlates for STI acquisition for the entire cohort of women, and when the

analysis was restricted to those 25 years of age or younger the effects of major depression increased. Condom use and seeking medical care after sero-conversion were significantly associated with STI acquisition in the age-restricted analysis

Depression is associated with accelerated HIV disease progression likely due to impaired immune functions and interference with health-seeking behaviors.¹³⁻¹⁴ Our findings suggest that major depression is also associated with an increased risk of STI acquisition. The magnitude of odds increased substantially when the analysis was restricted to women 25 years of age or less. This may be partly explained by the fact that this age group is more likely to practice riskier sexual behaviors, such as multiple sex partners, and inconsistent condom use, compared to their older counterparts; highlighting the importance of targeted prevention programs.³³⁻³⁷ Moreover, these results highlight the importance of STI risk reduction counseling among those depressed not only to reduce the number of STI among this population, but also the risk of secondary HIV transmission. Co-infection with an STI often leads to dramatic increases in HIV viral loads almost as high as during acute infection and a 2 to 3-fold increase genital tract viral shedding, increasing the risk of secondary HIV transmission.¹³⁻¹⁴

Those with depression are more likely to practice riskier sexual behaviors, in particular inconsistent condom use.^{12,16} Condom use has shown to reduce the risk of STI/HIV transmission when used consistently and correctly.³⁷⁻⁴³ Despite numerous behavioral interventions within schools and communities throughout Africa, the prevalence of consistent condom use is still low.^{40,44} In 2007, the South African Demographic Health Survey (DHS) reported only 18.8% of women reported any condom use, while 28.4% reported condom use during last intercourse.^{40,45} Participants received risk reduction counseling during VOICE and condoms were made available. The results from our study reflect the benefits of these risk reduction efforts- women who reported using a condom at last sex had 0.43 times the odds of

acquiring an STI during follow-up compared to women who reported not using a condom at last sex.

A potential confounder in the relationship between condom use and STI acquisition that could also be affecting the results is IPV.⁴⁶⁻⁴⁹ IPV may lead to an increase in inconsistent condom use among this population.⁴⁶⁻⁴⁹ IPV, which includes physical, sexual, and mental abuse, is prevalent among women globally, especially in Africa, where a woman's power within a relationship is likely lower.⁴⁶⁻⁴⁹ Women who are subject to IPV are at an increased risk of STIs, regardless of their sexual behaviors, because men, who perpetuate the violence, are themselves at high-risk for STIs due to high-risk sexual behaviors, such as inconsistent condom use and multiple sexual partners.⁴⁶⁻⁴⁹ This study supports the relationship between IPV and condom use in relation to STI incidence. Although the prevalence of condom use was high for our study (86%), among women who reported condom use at last sex there was a statistically significant difference (p-value 0.0006) between those that reported experiencing IPV (14.4%) and those that have not (35.1%). Thus, reducing the rate of risky sexual behaviors, such as inconsistent condom use, requires targeting not only those depressed, but those that have experienced violence.

There are several limitations with this study. Behavioral questionnaires were administered using face-to-face interviews. The questionnaires contained sensitive and highly stigmatized information about sexual behaviors and past history of violence. These questions are more likely to be accurately reported when administered through computer-assisted self-interviewing (CASI) or audio-computer-assisted self-interview (ACASI).⁵⁰ It is likely then that many behaviors were therefore under reported, leading to non-differential misclassification of exposures. It is likely that our results include misclassification of depression. A "caseness" cutoff score greater than the one used in validation studies was used in this study. The validated cutoff score yielded a prevalence of depression of over 80%- greater than what was

reported in other studies; highlighting the fact that this cutoff score may be too sensitive in detecting depression, especially major depression. Therefore, the cutoff was increased so that the prevalence of major depression was within range of other studies in the region. Using a greater cutoff score may result in missing cases of depression, potentially biasing the results of the study. Finally, women were enrolled from among those participating in a clinical trial. Some of the women enrolled may have been recruited from an STI clinic where they may have been seeking services because they perceived themselves at high-risk of infection. Additionally, because women were participants of a clinical trial, they may have had a clear or perceived level of risk for infection. Therefore, the results may not be generalizable to all HIV-infected women.

Nevertheless our results highlight several key factors that need to be addressed in future interventions in order to reduce both primary and secondary HIV transmission and STI acquisition. Targeted interventions especially to younger women, including pharmacological interventions and psychotherapeutic treatment such as individual or group therapy and/or social support groups, has the potential to reduce STI acquisition/transmission and possible HIV transmission as well.^{21,51,52} The limited availability of antidepressants in Africa coupled with their cost, might make psychotherapeutic treatment the more practical option. Group therapy has been successfully implemented in southwestern Uganda.⁵¹ Finally, targeting specialized risk reduction counseling to women who have experience interpersonal violence will be key in reducing risky sexual behaviors that perpetuate the HIV epidemic.

Table 2.1 Baseline demographic and behavioral characteristics of those depressed (using a depression cutoff of 2.4) and not depressed

Baseline characteristic	Total Cohort N (%) N= 254	Depressed N (%) N= 44	Non-depressed N (%) N= 210
Average age (range)	24 (18-40)	23.46 (18-33)	24.47 (18-40)
Average number of children (range)	1 (0-6)	1.30 (0-6)	1.32 (0-5)
Live with partner [†]	32 (13.6)	7 (17.5)	25 (12.8)
Own their own home [†]	183 (72.1)	27 (62.8)	156 (73.9)
Education [†]			
Less than primary school	10 (4.31)	4 (9.1)	6 (3.3)
Primary school completed	7 (2.75)	2 (4.6)	5 (2.4)
Secondary not completed	107 (42.0)	19 (43.2)	88 (41.7)
Secondary completed and higher	130 (51.0)	19 (43.2)	111 (52.6)
Average number of partners in the past 3 months (range)	1 (0-6)	1.05 (0-3)	0.96 (0-6)
Sought medical care after sero-conversion [†]	66 (25.9)	9 (20.5)	57 (27.0)
Condom use at last sex [†]	216 (85.4)	29 (67.4)	187 (89.1)
Experienced interpersonal violence in the past year [†]	45 (17.7)	9 (20.5)	36 (17.1)
Disclosure [†]			
Both partner and other	102 (41.1)	14 (33.3)	88 (42.7)
Partner only	55 (22.2)	8 (19.1)	47 (22.8)
Other only	36 (14.5)	12 (28.6)	24 (11.7)
No one	55 (22.2)	8 (19.1)	47 (22.8)
Partner HIV status [†]			
Concordant	215 (84.7)	38 (86.4)	177 (84.4)
Discordant	39 (15.3)	6 (13.6)	33 (15.6)

[†] Significant X² value

Table 2.2 Behaviors among those infected with multiple STIs over follow-up

Baseline characteristic	Women with 2 or more STIs %	Women with 1 STI %	Women with no STIs %
Average number of partners in the past 3 months (range)	0.97 (0-2)	1.00 (0-3)	0.97 (0-6)
Sought medical care after sero-conversion	23.3	25.4	26.5
Condom use at last sex	75.9	84.5	87.4
Experienced interpersonal violence in the past year	23.3	18.6	16.3
Disclosure			
Both partner and other	27.6	49.1	40.7
Partner only	27.6	21.1	21.6
Other only	20.7	12.3	14.2
No one	24.1	17.5	23.5
Partner HIV status			
Concordant	80.0	81.4	86.8
Discordant	20.0	18.6	13.3

Table 2.3 Association between depression and other co-factors and the odds of acquiring an STI among all women using a depression cutoff of 2.4 (prevalence of depression = 17.25%) over follow-up

	Unadjusted OR	Confidence Interval	Adjusted* OR	Confidence Interval
Time**	1.00	0.99-1.00	1.00	1.00-1.002
Age	1.05	1.03-1.08	1.07	1.03-1.12
SES***	1.72	1.32-2.26	1.63	1.10-2.44
Depression	2.05	0.95-4.43	2.67	1.17-6.08
Condom use at last sex	1.00	0.60-1.67	0.67	0.38-1.19
IPV	0.80	0.40-1.58	1.46	0.72-2.98
Sought medical care after sero-conversion	0.36	0.26-0.51	0.74	0.48-1.27

*Additionally adjusted for education, and study site **Days since enrollment ***Own their own home

Table 2.4 Association between depression and other co-factors and the odds of acquiring an STI among women 25 years of age or younger over follow-up

	Unadjusted OR	Confidence Interval	Adjusted* OR	Confidence Interval
Time**	1.00	0.99-1.00	1.00	1.00-1.002
Age	1.11	1.03-1.19	1.14	1.04-1.26
Low SES***	1.73	1.23-2.42	1.83	1.12-2.96
Depression	2.75	1.08-7.02	4.14	1.54-11.11
Condom use	0.70	0.35-1.38	0.43	0.20-0.91
Did not experience interpersonal violence	0.95	0.43-2.07	0.25	0.61-1.20
Sought medical care after sero--conversion	0.32	0.21-0.47	0.56	0.34-0.94

*Additionally adjusted for education, and study site **Days since enrollment ***Did not own their own home

Table 2.5 Association between depression and other co-factors and the odds of acquiring an STI among women 26 years of age or older over follow-up

	Unadjusted OR	Confidence Interval	Adjusted* OR	Confidence Interval
Time**	1.00	0.99-1.00	1.00	1.00-1.002
Age	0.98	0.96-0.99	1.18	1.05-1.33
Low SES***	0.88	0.79-0.99	1.42	0.69-2.92
Depression	0.98	0.74-1.30	1.01	0.25-4.12
Condom use	0.93	0.80-1.08	1.45	0.60-3.48
Did not experience interpersonal violence	1.48	0.93-1.41	0.35	0.08-1.60
Sought medical care after sero--conversion	1.19	1.04-1.35	1.16	0.55-2.45

*Additionally adjusted for education, and study site **Days since enrollment ***Did not own their own home

Table 2.6 Association between depression and other co-factors and the odds of acquiring an STI among all women when depression prevalence varies over follow-up

Depression prevalence	13.94% Cut-off- 2.7	15.69% Cut-off- 2.6	17.25% Cut-off- 2.4	24.31% Cut-off- 2.2	31.76% Cut-off- 1.9	38.04% Cut-off- 1.7
Independent variable	Adjusted* OR (CI)					
Time**	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)
Age	1.07 (1.03-1.11)	1.07 (1.03-1.12)	1.07 (1.03-1.12)	1.07 (1.03-1.11)	1.07 (1.03-1.11)	1.07 (1.03-1.11)
SES***	1.65 (1.11-2.44)	1.65 (1.11-2.45)	1.63 (1.10-1.12)	1.66 (1.11-2.48)	1.68 (1.25-2.50)	1.66 (1.12-2.47)
Depression	2.53 (1.00-6.37)	2.79 (1.15-6.74)	2.67 (1.17-6.08)	2.06 (1.05-4.03)	1.47 (0.83-2.59)	1.37 (0.79-2.32)
Condom use	0.70 (0.40-1.23)	0.68 (0.39-1.20)	0.67 (0.38-1.19)	0.70 (0.40-1.24)	0.72 (0.41-1.27)	0.74 (0.42-1.28)
Interpersonal violence	1.48 (0.73-3.00)	1.44 (0.71-2.94)	1.46 (0.72-2.98)	1.39 (0.67-2.87)	1.49 (0.73-3.03)	1.48 (0.73-3.03)
Sought medical care after sero-conversion	0.74 (0.49-1.13)	0.74 (0.49-1.13)	0.74 (0.48-1.27)	0.74 (0.49-1.13)	0.75 (0.49-1.13)	0.75 (0.50-1.14)

*Additionally adjusted for education, and study site **Days since enrollment ***Own their own home

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Chapter 3: Correlates of Disclosure of HIV status among Recently Sero-converted Women in Africa

3.1 Abstract

Background: Prevalence of disclosure of HIV-sero-status varies greatly by population, however, in general, rates of disclosure throughout Africa are low ranging from 16-86%. Disclosure has been shown to decrease of HIV transmission and is particularly important in sero-discordant partnerships. Numerous cross-sectional studies have examined correlates of disclosure, however inferences are limited by the time-varying nature of disclosure.

Methods: We examined data from 254 women participating in the MTN-015 study, an observational study of women who sero-converted to HIV during a MTN microbicide trial. Data were collected from August 2008 and women were eligible for inclusion in this analysis if they did not have delayed enrollment into MTN-015 and had follow-up data. All women completed face-to-face interviews, were assessed clinically and tested at enrollment, yearly and when clinically indicated for STIs including gonorrhea (GC) and chlamydia (CT) using nucleic acid amplification tests, and trichomonas using vaginal swabs. Depression was assessed using an abbreviated Hopkins Symptom Checklist. Other factors of interest included demographics and sexual risk behaviors such as socioeconomic status (SES) condom use, intimate partner violence (IPV). Odds ratios (OR) for disclosure were estimated for variables listed above in addition to age, sought medical care after sero-conversion, condom use at last sex,.

Results: Among the 254 women, the median time of follow-up for women was 1.4 years. At enrollment the mean age was 24 and almost all reported last sex with a main partner- 99%. The baseline prevalence of major depression (case cutoff score of 2.4) was 16%, IPV 18%, condom use 85%,and disclosure 77%, with the majority (41%) of those women disclosing to their partner and someone other than their partner. Correlates with a positive association with

disclosure included having an STI (OR: 1.56 CI 1.06-6.79) and depression (OR: 2.69 CI: 1.39-5.19); while negative correlates included not seeking medical care (OR: 0.59 CI: 0.39-0.88), did not report a condom at last sex (OR: 0.47 CI: 0.27-0.84), and lower education (OR: 0.39 CI: 0.15-0.97). Correlates of immediate disclosure included reporting condom use at last sex (OR: 1.60 CI: 1.02- 13.87), number of children (OR: 2.44 CI: 1.31- 4.55), and having an STI (OR: 0.33 CI: 0.14-0.80).

Conclusion: Among women recently infected with HIV, there are several factors that influence disclosure and in particular immediate disclosure. Targeted behavioral interventions that emphasize not only safe sex practices, but also the importance of disclosure of HIV status are needed for those at high-risk and also those that have recently sero-converted to help reduce behaviors that perpetuate the HIV epidemic.

3.2 Introduction

In 2011, 23.5 million people were living with HIV/AIDS (PLWHA) worldwide, with an estimated 1.8 million new cases reported in southern Africa.¹ In this region, women are disproportionately affected, accounting for 58% of PLWHA, a percent that has increased in the last 10 years.^{1,2} The high prevalence among women in this region is likely due to gender inequalities both outside and within relationships.^{3,4}

While HIV incidence rates in southern Africa have decreased more than 25% since 2001, and the percentage of individuals accessing HIV treatment has increased, prevalence and incidence are still among the highest in the world.¹ Poor treatment retention coupled with high-risk behaviors, most likely account for the high rates of incidence and prevalence within this region.⁵⁻⁸ Despite numerous prevention efforts targeted at decreasing high-risk behaviors, such as multiple sex partners, an alarmingly large number of people still report these behaviors, putting them at higher risk of acquiring HIV and other STIs, but also transmitting them to others.⁹

The continued high prevalence and incidence of HIV among women in southern Africa suggests behavior change still plays a key role in transmission.

One behavior in particular that has shown to decrease the probability of HIV transmission is disclosure of HIV status, especially disclosure to sexual partners.¹⁰⁻¹³ Disclosure is particularly important in sero-discordant partnerships, where one partner is HIV-positive and the other is negative. Models have shown that disclosure of HIV status can reduce HIV transmission by more than 41%.¹⁴ Disclosure may reduce HIV transmission in one of two ways: after disclosing HIV status to a sexual partner, the partner may decline to continue engaging in sexual activity, or they may agree to have only protected sex.¹⁰ Therefore, disclosure reduces risky sexual behaviors, and the probability of HIV transmission.¹⁰ Disclosure also has the potential to increase access to HIV treatment, HIV testing among sexual partners, and social support, a key factor in reducing depression among this population, and thus, increase treatment retention and further reduce high-risk behaviors.¹⁰⁻¹⁴

Prevalence of disclosure varies greatly by population, however, in general, rates of disclosure throughout Africa are low. A review of 17 studies conducted in low-resource settings (15 within Africa) estimated the prevalence of disclosure as low as 16% to 86%.¹⁵ Specifically, a cross-sectional study conducted in Kenya reported a prevalence of disclosure of 32%.¹⁵ Additionally, the majority (76%) of the women who did not disclose their HIV status had no plans for disclosure.¹⁵

Within many parts of the world, especially in southern Africa, HIV is still a highly stigmatized disease.^{12, 16, 17} Some PLWHA have reported being more fearful of the social backlash than the actual disease.¹² There are many barriers that likely account for the low prevalence of disclosure throughout Africa. Among the most reported factors influencing disclosure are fear of rejection from partners, family, and friends, abandonment/divorce, abuse,

and accusations of infidelity.¹⁰⁻¹³ These fears continue to disproportionately affect women in the region due to gender inequalities.^{12,18}

Disclosure is also influenced by time, in that an individual's decision to disclose may change over time, rendering cross-sectional studies inadequate.¹² Longitudinal studies are needed to increase our understanding of factors associated with disclosure and timing of disclosure. By identifying predictors of disclosure, specifically related to timing, targeted risk reduction interventions can be developed, reducing HIV transmission and incidence.

3.3 Methods

We utilized data on recently HIV-infected women who sero-converted during VOICE: a Microbicide Trials Network (MTN) phase 2B randomized control trial entitled: Phase 2B Safety and Effectiveness Study of Tenofovir 1% Gel, Tenofovir Disoproxil Fumarate tablet and Emtricitabine/Tenofovir Disoproxil Fumarate Tablet for the Prevention of HIV Infection in Women (MTN-003).¹⁹ These women were subsequently enrolled in the MTN cohort study entitled: An Observational Cohort Study of Women following HIV-1 Sero-conversion in Microbicide Trials (MTN-015).²⁰ MTN-015 is a longitudinal study aimed to follow women who recently sero-converted in a parent MTN microbicide trial (HPTN 0135, MTN-003, and MTN-020) across 15 different study sites in Zimbabwe, South Africa and Uganda, since August 2008. The primary research aim of the study was to compare plasma RNA HIV-1 levels in women 12 months after sero-conversion to controls. For the purpose of this analysis women who sero-converted in HPTN- 035 were not included given the delayed time to enrollment since sero-conversion. Additionally, there were no sero-converters in MTN-020, and therefore these women were not included in this analysis. A total of 357 recently sero-converted women from VOICE were eligible for MTN 015, with 255 (71.2%) enrolling. Only data on 254 of the women

were used in this analysis, as one woman did not have adequate follow-up data. Data for this analysis was censored on October 31, 2013.

MTN-015

MTN-015 questionnaires were administered using face-to-face interviews on two different schedules based on if antiretroviral treatment (ART) was initiated at the time of enrollment or during follow-up. For participants who had not initiated ART at the time of enrollment, visits occurred at baseline and at months 1, 3, 6, and every 6 months thereafter; while follow-ups occurred at baseline, week 2, and months 1, 3, 6, and every 6 months after for participants who had initiated ART at the time of enrollment. For participants who initiated ART during follow-up, their follow-up schedule switched from the non-ART schedule to the ART schedule after ART initiation. Participants also underwent extensive biological and clinical testing, including STI testing.²⁰

Sexually Transmitted Infections

STI testing was conducted annually, but participants were permitted to schedule interim visits if needed for symptoms of STIs and other concerns, the results of which were included in our final dataset. Vaginal fluid was used to test for trichomonas, and urine was taken for strand displacement amplification (SDA) to test for both chlamydia and gonorrhea. For the purposes of our analyses, study participants categorized as having an STI were infected with either chlamydia, gonorrhea, or trichomonas.

Disclosure

Disclosure information was collected as part of the behavioral questionnaires. Behavioral questionnaires were administered as face-to-face interviews at baseline, month 3, 12, and 24, no matter the participant's ART schedule. Participants are first presented with a list

of people (husband, partner, mother, sister, son, etc.) and asked to check everyone to whom they have disclosed to since they were diagnosed (at baseline visit) or since your last interview (at follow-up visits). For the purposes of this analysis, disclosure was first assessed as a categorical variable- disclosed to sexual partner (husband or partner) only, other only, both sexual partner and other, and no one. Disclosure was then collapsed and assessed as a dichotomous variable- yes/no.

Participants were also asked about the timing of their disclosure to their partner and/or husband. Women who reported disclosing to their partner were subsequently asked when they disclosed to their partner: immediately after diagnosis, within a month, more than 1 month but less than a year, a year or more, or don't remember. The same question regarding timing of disclosure was asked to participants who reported disclosing to their husband. For the purposes of this analysis, data on timing of disclosure to both partner and husband were collapsed into one variable. Additionally, timing of disclosure was collapsed into 3 categories- within a month of diagnosis, more than a month but less than a year, and more than a year. Women who reported not remembering the timing of disclosure were excluded in the analysis examining timing of disclosure. There were a total of 8 women who reported not remembering, and thus excluded.

Depression

Depression and anxiety were measured using a subset of the Hopkins Symptom Checklist (HSCL-25), a 10 item index of anxiety and a 15 item index for depression.²¹ Validation studies of HSCL-25 conducted by Kaaya et al. determined that a subset of only 8 of those questions, along with adjusting the "caseness" cutoff score to 1.06 or greater yielded highly sensitive and specific results in identifying depression and anxiety validated by clinical exam.²² Thus, MTN-015 and subsequently this study as well, used the 8 item index to assess anxiety

and depression. However, after evaluation of the cutoff score of 1.06, it was determined that the score was too liberal in the identification of anxiety and depression, as 78% percent of the study population was deemed depressed based on this cutoff. Based on recent publications, depression among PLWHA in Africa should be between 10-20% for major depression and 20-30% for mild depression.²³ Based on this a priori information, a cutoff score of 2.4 was used in this analysis, as it yielded a depression prevalence of 17% which was well within the prevalence range for major depression.

Demographic and Behavioral Characteristics

Participants were asked a series of demographic questions, including their age, their education level, and whether they own their own home on baseline questionnaires. We considered owning a home as a proxy for socioeconomic status (SES). Women were asked a series of questions about sexual health behaviors, including their partnership status, on all behavioral questionnaires (baseline and month 3, 12, and 24). Women were asked to provide their partners age, as well as their partner's age in comparison to theirs, and if their husband and/or partner has more than one wife or sexual partner. Women were asked whether or not they used a condom at last sex, the latter was used in this analysis as a measure of condom use, and if they had history of interpersonal violence (IPV). Finally, women were asked a series of questions related to their health care post HIV diagnosis, such as have you seen a healthcare provider/doctor/nurse for HIV care, have you seen a traditional healer for HIV care or treatment, etc. We combined all health seeking behaviors post diagnosis into one variable.

3.4 Analysis

Data were analyzed using SAS 9.4 (SAS Institute, Cary, NC, USA). Study population baseline characteristics were assessed using Chi-square (X^2) and Student's T test. Univariate and multivariable analyses were conducted to examine correlates of disclosure and timing of

disclosure. Variables of significance ($p\text{-value} \leq 0.05$) in univariate analyses and/or variables that are known to be associated with disclosure were included in the final model. Multivariable analysis was conducted using generalized estimating equations (GEE) through the genmod procedure. GEE is an extension of linear model theory and is most appropriate when dealing with longitudinal data that is correlated.²⁴ Failure to account for correlation may lead to incorrect estimation of the model parameters.²⁴ Using the logit function and assuming a binomial distribution odds ratios were estimated to examine repeated binary measures. Odds ratios are preferred for binary measures because they are not bound by the means of the data.²⁴ Using the logit function and assuming a binomial distribution, risk ratios were estimated to examine repeated binary measures. The correlation structure assumed for this analysis was a first-order autoregressive correlation structure (AR-1), which is appropriate when measurements closer together in time are more correlated than measurements further apart in time and when subjects are assessed at the same time intervals, as is the case with this study.²⁵⁻³⁰ Moreover, use of AR-1 correlation structure is consistent with other analyses on longitudinal data analysis.²⁵⁻³⁰ MTN-015 protocols and study material was reviewed by each site's IRB/EC. Further, for this study, approval was given by the University of California, Los Angeles IRB.

3.5 Results

Study Population

The median follow-up time for participants was 1.4 years. The majority of participants (93.3%) were from South African study sites. The median age of participants was 24 years (range 18-40). At baseline, the majority of participants (85.1%) reported their partner providing them with money or material support from their partner, owning their own home (72.1%), not living with their partner (86.4%), and completing secondary education (45.5%). With respect to behavioral characteristics, the majority of participants reported using a condom at last sex

(85.4%), were in a concordant partnership (84.7%), and did not have an STI (58.1%) (Table 3.1).

Disclosure

At baseline, the majority of participants (77.8%) had disclosed their HIV status to someone, while 22.2% did not disclose. Among those disclosing, 41.1% of women informed both their sexual partner and someone other than their sexual partner, 22.2% reported to just their partner, 14.52% reported to someone other than their sexual partner. Among those who reported disclosing their HIV status to their partner, the majority reported disclosing their HIV status immediately (58.3%) (Figure 3.1).

Characteristics by disclosure

The median age among women who disclosed was 23 (range 18-36), which did not differ statistically from those who did not disclose (24, range 18-40) (p-value: 0.50). At baseline, among women with depression there was no difference in the percent of women reporting disclosure than not reporting disclosure (17.6%- disclose, 14.6% did not disclose, p-value: 0.60). Similarly, among those reporting IPV there was no significant difference among women reporting disclosure (16.1%- disclose, 23.6%- did not disclose, p-value: 0.19). Similarly, there was no significant difference in the median number of men women reported having sex with in the past 3 months among women who disclosed compared to women who did not disclose (p-value: 0.06). However, among those women completing secondary education or higher a higher proportion reported disclosing their HIV status (53.4%- disclose, 45.5%- did not disclose, p-value: 0.01). Additionally, more women who reported using a condom at last sex disclosed their HIV status than did not disclose (88.1%- disclose, 74.1%- did not disclose, p-value: 0.01); and among those who sought medical care after their diagnosis, a higher percent disclosed

(71.5%-disclose, 85.5%-did not disclose, p-value: 0.04). Table 3.1 describes additional demographic and behavioral characteristics based on disclosure.

Correlates of Disclosure

After controlling for age, women were more likely to disclose their HIV status if they had at least 1 STI (Odds Ratio (OR): 1.56 Confidence Interval (CI): 1.06-2.30) and were depressed (OR: 2.69 CI: 1.39-5.19) (Table 3.2). On the other hand, women were less likely to disclose their HIV status if they did not seek medical care after their HIV diagnosis (OR: 0.59 CI: 0.39-0.88), if they did not use a condom at last sex (OR: 0.47 CI: 0.27-0.84), and had not completed primary schooling/had no schooling (OR: 0.38 CI: 0.15-0.97).

We examined correlates of timing of disclosure among women who reported their HIV status to a sexual partner (Table 3.3). After controlling for confounders, women were more likely to immediately disclose (within 1 month of diagnosis) to their sexual partner if they used a condom at last sex (OR: 3.76 CI: 1.02- 13.87) and had more children increased (OR: 2.44 CI: 1.31- 4.55). However, women were less likely to immediately disclose to their sexual partner if they had an STI (OR: 0.33 CI: 0.14-0.80).

3.6 Discussion

Our longitudinal analysis of 254 recently sero-converted women revealed a high percentage reported having disclosed their HIV status over the course of follow-up (89%). Multivariate analyses indicated that having an STI and depression were all positive correlates of disclosure; while not seeking medical care after diagnosis, not using a condom at last sex, and lower education were negative correlates of disclosure. Additionally, among women who disclosed to their sexual partner, parity and condom use at last sex were positive correlates of immediate disclosure.

Numerous prevention efforts targeted at decreasing high-risk behaviors have taken place not only among those who are HIV-infected, but also among those at high-risk for HIV infection.^{1,9} One such risk reduction behavior is disclosure. Disclosure has been shown to be more common among those who practice low-risk behaviors and results in a decrease in the probability of HIV transmission.^{2,15,31} Our findings support this claim, as women who reported using a condom at last sex were more likely to disclose their HIV status. Moreover, we saw that women who sought medical care after diagnosis were more likely to disclose their HIV status, indicating that those who disclose have more concern regarding their overall behaviors and well-being, compared to women who don't disclose. These results highlight the importance of risk reduction counseling among both high-risk and recently sero-converted populations that practice risky sexual behaviors in order to reduce the risk of primary and secondary HIV transmission, respectively.

Among the most reported factors influencing disclosure are fear of rejection from partners, family, and friends, abandonment/divorce, abuse, and accusations of infidelity.¹⁰⁻¹³ These fears disproportionately affect women in the region due to gender inequalities both outside and within relationships.^{12,18} In particular, women have less power to negotiate condom use and often suffer from abuse.^{32,33} Women dependent on their sexual partner are more likely to exhibit fear of disclosure, as they depend on their partner for housing and/or financial support.^{2,10,12,13,15,18} A woman's education has been shown to be directly related to her power in a relationship. Thus, women with higher education, who potentially have more personal power over their lives and are less dependent on others should participate in less risky sexual behaviors and exhibit a higher frequency of disclosure.^{2,10,12,13,15,18} We examined education as a correlate of disclosure and found that compared to women with higher education (completed secondary school or higher), women that did not completed primary schooling/had no schooling were less likely to disclose (OR: 0.39 CI: 0.15-0.97). This suggests that education not only

plays a critical role in reducing high-risk sexual behaviors such as condom use, but also disclosure. It also suggests that in fact education may result in women being more empowered to discuss their HIV status with others and feel less vulnerable about acknowledging they are positive.

Another factor that is likely to influence disclosure is depression, a condition that affects a large proportion of the HIV-infected population.³³⁻³⁸ Depression has been associated with delayed disclosure, a relationship that is likely confounded by a woman's exposure to IPV.³³⁻³⁸ Results from our study contradict this claim, and instead indicate that women who are depressed are more likely to disclose their HIV status (OR: 1.56 CI: 1.06-6.79). However, depression with respect to disclosure should be thought of as a double-edged sword, in that those who are depressed are less likely to disclose their HIV status, isolating them from any potential social support and thus, increasing depression.^{13, 14, 39, 40} On the other hand, disclosure followed by an adverse reaction from a partner or family member, such as abuse or abandonment, can lead to depression.^{13,14,39,40} Also given that our measure of depression captured women with severe depression and other studies may have used a broader definition that included those with mild depression, severely depressed women may be reaching out to seek help and support for their HIV, a different response than for women with mild depression. Thus, the results of our analysis in comparison to other study findings highlight the temporal ambiguity of depression and disclosure and suggest that the relationship warrants further investigation that considers the level of depression.

There are several limitations with this study. Behavioral questionnaires were administered using face-to-face interviews. The questionnaires contained sensitive and highly stigmatized information about sexual behaviors and past history of violence. These questions are more likely to be accurately reported when administered through computer-assisted self-interviewing (CASI) or audio-computer-assisted self-interview (ACASI).⁴¹ Therefore, it is likely

then that many behaviors were under reported, leading to non-differential misclassification of exposures. For the current trial that is enrolling this cohort, ACASI has been implemented and will be used to administer this questionnaire for women who seroconvert in MTN trials in the future. Additionally, there was a discrepancy in recall periods for disclosure and depression that may have led to temporal ambiguity between the outcome (disclosure) and the predictor (depression). The recall period for depression was in the past month, while the recall period for disclosure was since you were diagnosed (taken at baseline) or since your last interview (taken at follow-up), which could have been as short as 3 months, or as long as 12 months. Due to the discrepancy in recall periods, we may be capturing women who disclosed their HIV status and subsequently became depressed due to an unfavorable reaction associated with their disclosure. Finally, women were enrolled from among those participating in a clinical trial. Some of the women enrolled may have been recruited from an STI clinic where they may have been seeking services because they perceived themselves at high-risk of infection. Additionally, because women were participants of a clinical trial, they may have had a clear or perceived level of risk for infection. Therefore, the results may not be generalizable to all HIV-infected women.

Nevertheless our results highlight several key factors that need to be addressed in future interventions in order to reduce both primary and secondary HIV transmission. Current international guidelines and protocols for HIV testing encourage disclosure as a risk reduction technique.^{2,15, 42} Targeting risk reduction interventions as well as counseling to women who practice high-risk sexual behaviors is needed to eliminate behaviors that perpetuate the HIV epidemic. Further, risk reduction interventions and counseling for those who recently seroconverted need to promote disclosure not only as a risk reduction technique, but also to increase social support. Social support is crucial among this population and has been shown to be beneficial with respect to adherence to antiretroviral treatment (ARTs) and decreasing

depression.^{12, 16, 39, 42} Additionally, support groups or group therapy for those who do not have support are needed to facilitate disclosure among those who haven't disclosed as well as provide support to those who have disclosed, and as a result of their disclosure, experienced abandonment or abuse. Finally, future studies should be conducted to help tease apart the complex relationship between depression and disclosure, improving the measurement of depression, findings from which may further help target interventions and support.

Figure 3.1 Frequency of disclosure at baseline among women who recently sero-converted

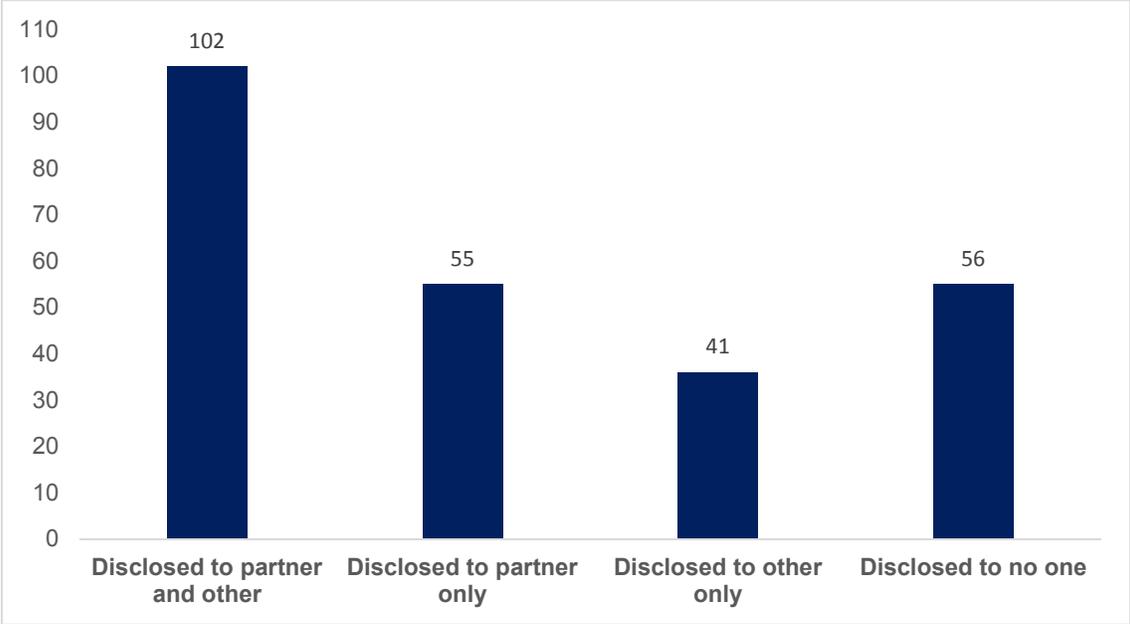


Table 3.1 Baseline demographic and behavioral characteristics overall and by disclosure

Baseline characteristic	Total Population N (%) N= 25	Disclosed N (%) N= 198	Did not Disclose N (%) N= 56
Median age (range)	24 (18-40)	23 (18-36)	24 (18-40)
Median number of children (range)	1 (0-6)	1 (0-6)	1 (0-4)
Live with partner	32 (13.6)	21 (11.5)	7 (15.2)
Own their own home	183 (72.1)	140 (72.5)	40 (72.3)
Education [†]			
Primary school completed or less	17 (7.1)	8 (4.1)	7 (12.7)
Secondary not completed	107 (42.0)	82 (42.5)	23 (41.8)
Secondary completed and higher	130 (51.0)	103 (53.4)	25 (45.5)
Partner provides support	200 (85.1)	155 (85.2)	38 (82.6)
Median number of partners in the past 3 months (range)	1 (0-6)	1 (0-6)	1 (0-3)
Sought medical care after sero-conversion [†]	66 (25.9)	138 (71.5)	47 (85.5)
Condom use at last sex [†]	216 (85.4)	170 (88.1)	40 (74.1)
Experienced interpersonal violence in the past year	45 (17.7)	31 (16.1)	13 (23.6)
Depressed	44 (17.3)	34 (17.6)	8 (14.6)
STIs			
None	147 (58.1)	108 (56.5)	35 (63.6)
1	66 (26.1)	53 (27.8)	11 (20.0)
2+	40 (15.8)	30 (15.7)	9 (16.4)
Partner HIV status			
Concordant	215 (84.7)	162 (83.9)	47 (85.5)
Discordant	39 (15.3)	31 (16.10)	8 (14.5)

[†]Significant X²value

Table 3.2 Correlates of disclosure among all women over follow-up

	Unadjusted OR	Confidence Interval	Adjusted* OR	Confidence Interval
Co-infected with an STI	1.09	1.01-1.18	1.56	1.06-2.30
Primary school not complete or no schooling	0.80	0.64-1.02	0.38	0.15-0.97
Primary school completed, secondary not complete	1.03	0.77-1.57	1.02	0.68-1.53
Depression	1.16	1.03-1.30	2.69	1.39-5.19
No condom use at last sex	0.85	0.75-0.96	0.47	0.27-0.84
Did not seek medical care after sero-conversion	0.92	0.86-0.99	0.59	0.39-0.88

*Additionally adjusted for age and IPV

Table 3.3 Correlates of immediate disclosure among women who disclosed to their husband or partner over follow-up

	Unadjusted OR	Confidence Interval	Adjusted* OR	Confidence Interval
Parity	1.07	1.03-1.12	2.44	1.31-4.55
Co-infected with 1 STI	0.87	0.77-0.97	0.33	0.14-0.80
Co-infected with 2 or more STIs	0.95	0.83-1.08	0.31	0.10-0.95
Partner support	1.19	0.99-1.44	2.43	0.85-6.99
Depression	1.07	0.97-1.18	3.11	0.85-11.40
Condom use at last sex	1.08	0.91-1.28	3.76	1.01-13.87
Discordant partnership	0.90	0.98-1.02	0.53	0.20-1.40

*Additionally adjusted for age and IPV

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Chapter 4: Correlates of Continued High-Risk Sexual Behaviors among Recently Sero-converted Women in Africa

4.1 Abstract

Background: HIV/AIDS continues to be a major public health problem throughout the world. Sub-Saharan Africa, bears the highest burden of the disease, with 22.9 million people living with HIV/AIDS, 60% of the total infections worldwide. Within this region, women are disproportionately affected, accounting for 58% of people living with HIV/AIDS. Despite numerous prevention efforts targeted at decreasing high-risk behaviors, an alarmingly large number of people still report these behaviors post sero-conversion, increasing the risk of transmission to others. More data are needed to understand risky sexual behaviors after sero-conversion to help targeted secondary prevention efforts.

Methods: We examined data from 254 women participating in the MTN-015 study, an observational study of women who sero-converted to HIV during a MTN microbicide trial. Data were collected from August 2008 and women were eligible for inclusion in this analysis if they did not have delayed enrollment into MTN-015 and had follow-up data. All women completed face-to-face interviews, were assessed clinically and tested at enrollment, yearly and when clinically indicated for STIs including gonorrhea (GC) and chlamydia (CT) using nucleic acid amplification tests, and trichomonas using vaginal swabs. Depression was assessed using an abbreviated Hopkins Symptom Checklist. Other factors of interest included demographics and sexual risk behaviors such as socioeconomic status (SES) condom use, intimate partner violence (IPV). Odds ratios (OR) for disclosure were estimated for variables listed above in addition to age, sought medical care after sero-conversion, condom use at last sex,.

Results: Among the 254 women, the median time of follow-up for women was 1.4 years. At enrollment the mean age was 24 and almost all reported last sex with a main partner- 99%. The

baseline prevalence of major depression (case cutoff score of 2.4) was 16%, IPV 18%, condom use 85%, and disclosure 77%. After controlling for confounders, women had a higher odds of not using a condom if they were older (OR: 0.90, CI: 0.84-0.97), and if they were depressed (OR: 0.19 CI: 0.09-0.40).

Conclusions: High-risk sexual behaviors are still prevalent among women recently infected with HIV. Moreover, several factors are shown to influence these behaviors. Behavioral interventions aimed at recently HIV-infected women are needed to reduce behaviors that may perpetuate the HIV epidemic.

4.2 Introduction

After more than three decades since AIDS was first described, HIV/AIDS continues to be a major public health problem throughout the world. Africa, and in particular, sub-Saharan Africa, bears the highest burden of the disease, with 22.9 million people living with HIV/AIDS (PLWHA), 60% of the total infections worldwide.¹⁻³ Within this region, women are disproportionately affected, accounting for 58% of PLWHA.^{4,5} The high prevalence among women in this region is likely due to gender inequalities both outside and within relationships.^{6,7} As a result, women often hold less power within sexual partnerships, increasing risky sexual behaviors that perpetuate the epidemic.^{8,9} With the continued high prevalence and incidence of HIV among women^{4,5}, despite an increase in prevention interventions, including pre-exposure prophylaxis (PrEP)¹⁰, suggests behavior change still plays a key role in transmission. Sexual behaviors are particularly important among recently sero-converts, as they have high viral loads and often highly infectious.¹¹⁻¹³

Despite numerous prevention efforts targeted at decreasing high-risk behaviors, such as multiple sexual partners and inconsistent condom use, an alarmingly large number of people still report these behaviors, putting them at higher risk of acquiring HIV and other STIs, but also

transmitting them to others.¹⁴ One behavior shown to be related to HIV transmission is condom use. Condom use has shown to reduce the risk of STI/HIV transmission when used consistently and correctly.¹⁵⁻¹⁸ Among discordant partners, in which one partner is HIV infected and the other is not, studies have shown the risk of HIV sero-conversion was approximately 5 times lower among partners that used condoms consistently compared to those who used condoms inconsistently.¹⁶ Further, among discordant partners that report consistent condom use, the HIV infection rate is reported to be less than 1%, compared with 10-14.5% among those who report inconsistent condom use.¹⁷ Inconsistent condom use has been shown to be correlated with other high-risk sexual behaviors, further increasing the risk of HIV transmission.^{15-17,19-24}

Despite the evidence that consistent condom use reduces HIV transmission, there is considerable challenge in obtaining consistent use within populations; especially in countries that associate condom use with promiscuity, unfaithfulness, and distrust, as they do in most African communities.¹⁵ Despite numerous behavioral interventions within schools and communities in Africa, studies show that consistent condom use is still low.¹⁵ In the 2007 Demographic Health Survey (DHS) conducted in South Africa, only 18.8% of women reported any condom use, while 28.4% reported using a condom during their last intercourse.¹⁵

Despite the numerous studies demonstrating an association between high-risk sexual behaviors and transmission of HIV, more data are needed to understand risky sexual behaviors after sero-conversion to help targeted secondary prevention efforts. Specifically, examining behaviors immediately after sero-conversion, where viral loads are highest and individuals are highly infectious,¹¹⁻¹³ as well as women's behaviors, due to the female driven HIV epidemic in southern Africa.⁴⁻⁵

4.3 Methods

We utilized data on recently HIV-infected women who sero-converted during VOICE: a Microbicide Trials Network (MTN) phase 2B randomized control trial entitled: Phase 2B Safety and Effectiveness Study of Tenofovir 1% Gel, Tenofovir Disoproxil Fumarate tablet and Emtricitabine/Tenofovir Disoproxil Fumarate Tablet for the Prevention of HIV Infection in Women (MTN-003).²⁵ These women were subsequently enrolled in the MTN cohort study entitled: An Observational Cohort Study of Women following HIV-1 Sero-conversion in Microbicide Trials (MTN-015).²⁶ MTN-015 is a longitudinal study aimed to follow women who recently sero-converted in a parent MTN microbicide trial (HPTN 0135, MTN-003, and MTN-020) across 15 different study sites in Zimbabwe, South Africa and Uganda, since August 2008. The primary research aim of the study was to compare plasma RNA HIV-1 levels in women 12 months after sero-conversion to controls. For the purpose of this analysis women who sero-converted in HPTN- 035 were not included given the delayed time to enrollment since sero-conversion. Additionally, there were no sero-converters in MTN-020, and therefore these women were not included in this analysis. A total of 357 recently sero-converted women from VOICE were eligible for MTN 015, with 255 (71.2%) enrolling. Only data on 254 of the women were used in this analysis, as one woman did not have adequate follow-up data. Data for this analysis was censored on October 31, 2013.

MTN-015

MTN-015 questionnaires were administered using face-to-face interviews on two different schedules based on if antiretroviral treatment (ART) was initiated at the time of enrollment or during follow-up. For participants who had not initiated ART at the time of enrollment, visits occurred at baseline and at months 1, 3, 6, and every 6 months thereafter; while follow-ups occurred at baseline, week 2, and months 1, 3, 6, and every 6 months after for

participants who had initiated ART at the time of enrollment. For participants who initiated ART during follow-up, their follow-up schedule switched from the non-ART schedule to the ART schedule after ART initiation. Participants also underwent extensive biological and clinical testing, including STI testing.²⁶

Sexually Transmitted Infections

STI testing was conducted annually, but participants were permitted to schedule interim visits if needed for symptoms of STIs and other concerns, the results of which were included in our final dataset. Blood was taken for syphilis serology, vaginal fluid was used to test for trichomonas, and urine was taken for strand displacement amplification (SDA) to test for both chlamydia and gonorrhea. For the purposes of our analyses, study participants categorized as having an STI were infected with either chlamydia, gonorrhea, or trichomonas.

Condom Use

Condom use information was collected on behavioral questionnaires. Behavioral questionnaires were administered as face-to-face interviews at baseline, month 3 and 12, and 24, no matter the participant's ART schedule. Participants were asked if a condom was used the last time they had vaginal sex. To measure predictors of condom use after sero-conversion, condom used was assessed as a dichotomous variable and correlates of condom use were assessed at each time interval over follow-up. In order to examine the changes in condom use after sero-conversion, condom use at baseline was compared to each follow-up visit in which condom use was assessed.

Depression

Depression and anxiety were measured using a subset of the Hopkins Symptom Checklist (HSCL-25), a 10 item index of anxiety and a 15 item index for depression.²⁷ Validation

studies of HSCL-25 conducted by Kaaya et al. determined that a subset of only 8 of those questions, along with adjusting the “caseness” cutoff score to 1.06 or greater yielded highly sensitive and specific results in identifying depression and anxiety validated by clinical exam.²⁸ Thus, MTN-015 and subsequently this study as well, used the 8 item index to assess anxiety and depression. However, after evaluation of the cutoff score of 1.06, it was determined that the score was too liberal in the identification of anxiety and depression, as 78% percent of the study population was deemed depressed based on this cutoff. Based on recent publications, depression among those with HIV/AIDS in Africa should be between 10-20% for major depression and 20-30% for mild depression.²⁹ Based on this *a priori* information, a cutoff score of 2.4 was used in this analysis, as it yielded a depression prevalence of 17% which was well within the prevalence range for major depression.

Demographic and Behavioral Characteristics

At baseline participants were asked a series of demographic questions, including their age, their education level, and whether they own their own home, on baseline questionnaires. We considered owning a home as a proxy for socioeconomic status (SES).

Women were asked a series of questions about sexual health behaviors, including their partnership status, on behavioral questionnaires (baseline and month 3, 12, and 24). Women were asked to provide their partners age, as well as their partner’s age in comparison to theirs, and if their husband and/or partner has more than one wife or sexual partner. Women were asked if they had history of interpersonal violence (IPV) and a series of questions related to their health care post HIV diagnosis, such as have you seen a healthcare provider/doctor/nurse for HIV care, have you seen a traditional healer for HIV care or treatment, etc. We combined all health seeking behaviors post diagnosis into one variable. Finally, women were asked about their disclosure of their HIV status with respect to their husband and/or partner, as well others

(family, community, etc.). For the purpose of these analyses, disclosure was collapsed and assessed as a dichotomous variable- yes/no.

4.4 Analysis

Data were analyzed using SAS 9.4 (SAS Institute, Cary, NC, USA). Study population baseline characteristics were assessed using Chi-square (X^2) and Student's T test. Univariate and multivariable analyses were conducted to examine correlates of condom use. Variables of significance (p -value < 0.05) in univariate analyses and/or variables that are known to be associated with condom use were included in the final model. Multivariable analysis was conducted using generalized estimating equations (GEE) through the genmod procedure. GEE is an extension of linear model theory and is most appropriate when dealing with longitudinal data that is correlated.³⁰ Failure to account for correlation may lead to incorrect estimation of the model parameters.³⁰ Using the logit function and assuming a binomial distribution odds ratios were estimated to examine repeated binary measures. Odds ratios are preferred for binary measures because they are not bound by the means of the data.³⁰ Using the logit function and assuming a binomial distribution risk ratios were estimated to examine repeated binary measures. The correlation structure assumed for this analysis was a first-order autoregressive correlation structure (AR-1), which is appropriate when measurements closer together in time are more correlated than measurements further apart in time and when subjects are assessed at the same time intervals, as is the case with this study.³¹⁻³⁴ Moreover, use of AR-1 correlation structure is consistent with other analyses on longitudinal data analysis.³¹⁻³⁴ MTN-015 protocols and study material was reviewed by each site's IRB/EC. Further, for this study, approval was given by the University of California, Los Angeles IRB.

4.5 Results

Study Population

The median follow-up time for participants was 1.4 years. The majority of participants (93.3%) were from South African study sites. The median age of participants was 24 years (range 18-40). At baseline, the majority of participants (85.1%) reported being provided with money or material support from their partner, owning their own home (72.1%), not living with their partner (86.4%), and completing secondary education (45.5%). With respect to behavioral characteristics, the majority were in a concordant partnership (84.7%), did not have an STI (58.1%), and disclosed their HIV status to someone (77.8%) (Table 4.1).

Characteristics of Condom Use

At baseline, the majority (85.4%) of participants reported using a condom at last sex. The median age among women who used a condom at last sex was 23 (range 18-40), which was statistically different from those who did not use a condom at last sex (median age 25 (range 18-39), p-value: 0.001). Women who reported using a condom at last sex, a lower proportion reported experiencing IPV compared to women who did not use a condom, compared to those that did (14.4%, 35.1% respectively, p-value: 0.002). Similarly, women who reported using a condom at last sex, a lower proportion were not depressed compared to women who did not use a condom (13.4%, 37.8%, respectively, p-value: 0.0003). Additionally, a higher proportion of women who used a condom at last sex owned their own home compared to women who did not use a condom, however, this difference was only trending towards significance (74.1%, 59.5%, respectively, p-value: 0.06).

Correlates of Condom use over follow-up

After controlling for SES, IPV, and whether a woman reports exchange sex for money, shelter, drugs, or goods, women were less likely to use a condom at last sex if they were older (Odds Risk (OR): 0.90, Confidence Interval (CI): 0.84-0.97) and if they were depressed (OR: 0.19 CI: 0.09-0.40). Additionally, women were less likely to report condom use at last sex if they did not disclosed their HIV status to someone-either partner or someone other than their partner (OR: 0.45, CI: 0.26-0.78) and if they were in a concordant partnership (OR: 0.36, CI: 0.14-0.97). Finally, after assessing for modification of the association between correlates of condom use at last sex, we saw a statistically significant interaction between ART and STIs (p-value: 0.04). Therefore, condom use varied depending on if a woman was on ART and whether or not she was co-infected with an STI. Specifically, women on ART and not co-infected with an STI were more likely to use a condom at last sex compared to those not on ART and not co-infected with an STI (OR: 2.55, CI: 1.00-6.63) (Table 4.2).

Changes in Condom use

After controlling for SES, IPV, and whether a woman reported exchanging sex for money, shelter, drugs, or goods, women after sero-conversion were more likely to adopt condom use (a change from reporting no condom at last sex to reporting condom use at last sex) if they had disclosed their HIV status to someone (OR: 2.79, CI: 1.51-5.16). On the other hand, women were less likely to adopt condom use (change from reporting no condom at last sex to reporting condom use at last sex) if they were depressed (OR: 0.62, CI: 0.40-0.96) (Table 4.3).

4.6 Discussion

Our longitudinal analysis of 254 recently sero-converted women indicated that being younger and depressed negatively affected women's ability to change their behavior to reduce transmission risk by using condoms after sero-conversion, while women in discordant partnerships who had disclosed their HIV status were more likely to make changes in their condom use. We also found that women who represented a higher risk behavior profile (reporting multiple sexual partners, depression and co-infection with an STI) did manage to make positive changes in practice of transmission risk by adopting condom use.

Despite numerous studies that have shown the benefits of condom use with respect to HIV transmission, and multiple interventions throughout communities in Africa, inconsistent condom use continues to be a problem among HIV-infected women.¹⁴ While, our findings support this claim by showing condom use remains uneven after sero-conversion yet our results also suggest that condom use among HIV-infected women after sero-conversion is correlated with disclosure. Disclosure reduces the probability of HIV transmission by decreasing the frequency of high-risk sexual behaviors, as well as increasing access to HIV treatment, and social support.³⁵⁻³⁹ The latter is key among HIV-infected women, who, due to social, cultural, and political gender-inequalities that plague Africa, often suffer from abuse.^{38,39} Therefore, increasing social support within this population is key in reducing the prevalence of depression, thus further reducing high-risk sexual behaviors.^{7,15} These results highlight the importance of targeted interventions that promote disclosure, in order to reduce high-risk sexual behaviors and ultimately, the rate of secondary HIV transmission.

Depression is one of the most common neuropsychiatric disorders among those living with HIV/AIDS, and disproportionately affects women.^{6,9,27,42-44} Depression has been linked to an acceleration of HIV disease progression, and poor outcomes.^{6,9} Moreover, evidence

suggests that those with depression may practice riskier sexual behaviors, and as a result, increase the risk of secondary HIV transmission. Results from our study support this claim, as depression was associated with both inconsistent condom use and multiple sexual partnerships among HIV-infected women. Our results with respect to changes in condom use after sero-conversion further support this claim, as women with depression were less likely to change their condom use (no condom at last sex to condom use at last sex). These results emphasize the need for targeted pharmacological interventions and psychotherapeutic treatment such as individual or group therapy and/or social support groups, among HIV-infected women to reduce the prevalence of depression and thus, decrease the risk of secondary HIV transmission.⁴⁵⁻⁴⁷

As the number of PWLHA on ART increases (in 2009 there were an estimated 4 million PLWHA on ART in sub-Saharan Africa), research demonstrating the benefits of ART are numerous.⁴⁸⁻⁵⁰ Effective ART improves health outcomes, such as increasing time to AIDS diagnosis, as well as decreasing the probability of secondary transmission.⁴⁸⁻⁵⁰ However, some research have shown unintentional consequences of ART initiation, such as sexual disinhibition.⁴⁸ HIV-infected individuals on ART may perceive themselves no longer infectious to sexual partners and as a result, increase the frequency of unprotected sex.⁴⁸ However, this theory is misleading, as studies have shown HIV shedding in the genital tract among those with low viral loads.⁴⁸ We examined modification of ART through an interaction term and found that ART modifies the effect that co-infection of STI has on condom use. Specifically, women on ART and not co-infected with an STI were more likely to use a condom at last sex compared with non-ART users who were not co-infected with an STI. These women may represent a healthier group of women, who have safer sexual practices compared to those not on ART. While this result does not support the theory that ART may cause sexual disinhibition, it does highlight the importance of continued risk reduction counseling among HIV-infected women.

Further, additional studies are needed to better understand the relationship between ART initiation and its effect on high-risk sexual behaviors.

There are several limitations with this study. Measurements of condom use taken prior to sero-conversion were not available. Therefore, comparisons could not be made between condom use reported prior sero-conversion to condom use post sero-conversion, and any changes between these two time points would have been missed. Additionally, behavioral questionnaires were administered using face-to-face interviews. The questionnaires contained sensitive and highly stigmatized information about sexual behaviors and past history of violence. These questions are more likely to be accurately reported when administered through computer-assisted self-interviewing (CASI) or audio-computer-assisted self-interview (ACASI).⁵¹ Therefore, it is likely that many behaviors were underreported, leading to non-differential misclassification of both outcomes and exposures. Finally, women were enrolled from among those participating in a clinical trial. Women may have been recruited from an STI clinic where they may have been seeking services because they perceived themselves at higher risk of infection. Additionally, because women were participants of a clinical trial, they may have had a clear or perceived level of risk for infection. Therefore, the results may not be generalizable to all HIV-infected women.

Nevertheless our results highlight several key factors that need to be addressed in future interventions targeted at reducing secondary HIV transmission. The sexual behaviors of women not only affect the risk of transmission to their sexual partners, but also increase the risk of perinatal transmission, should they become pregnant. Therefore, targeted risk reduction interventions along with counseling are needed to reduce practice of behaviors that perpetuate the HIV epidemic. Finally, targeted pharmacological interventions and psychotherapeutic treatment such as therapy and/or social support groups, to recently sero-converted women

should be implemented to decrease the prevalence of depression, and in turn, high-risk sexual behaviors that contribute to ongoing transmission of HIV.⁴⁵⁻⁴⁷

Table 4.1. Baseline demographic and behavioral characteristics overall and by condom use at last sex

Baseline characteristic	Total Population N (%) N= 254	Used a condom N (%) N= 216	Did not Use a condom N (%) N= 38
Median age (range) [†]	24 (18-40)	23 (18-40)	25 (18-39)
Median number of children (range)	1 (0-6)	1 (0-5)	2 (0-6)
Live with partner	32 (13.6)	25 (12.4)	6 (19.4)
Own their own home [†]	183 (72.1)	160 (74.1)	22 (59.5)
Education [†]			
Primary school completed or less	17 (7.1)	14 (7.0)	3 (8.1)
Secondary not completed	107 (42.0)	88 (40.7)	17 (46.0)
Secondary completed and higher	130 (51.0)	113 (52.3)	17 (46.0)
Partner provides support	200 (85.1)	171 (84.7)	27 (87.1)
Median number of partners in the past 3 months (range)	1 (0-6)	1 (0-3)	1 (0-6)
Sought medical care after sero-conversion	66 (25.9)	55 (25.5)	11 (29.7)
Received money, goods, drugs, or shelter for sex	7 (3.0)	4 (2.0)	2 (6.7)
Experienced interpersonal violence in the past year [†]	45 (17.7)	31 (14.4)	13 (35.1)
Depressed	44 (17.3)	29 (13.4)	14 (37.8)
Disclosed HIV status [†]	193 (77.8)	170 (81.0)	23 (62.2)
STIs			
None	147 (58.1)	128 (59.5)	19 (52.8)
1	66 (26.1)	55 (25.6)	10 (27.8)
2+	40 (15.8)	32 (14.9)	7 (19.4)
Partner HIV status			
Concordant	215 (84.7)	179 (82.9)	35 (94.6)
Discordant	39 (15.3)	37 (17.3)	2 (5.4)

[†]Significant X² value

Table 4.2 Predictors of condom use at last sex over follow-up, among women who recently sero-converted

	Unadjusted OR (Confidence Interval)	Adjusted* OR (Confidence Interval)	Adjusted* OR† (Confidence Interval)
Age	0.48 (0.30-0.80)	0.90 (0.84-0.96)	0.90 (0.84-0.97)
Did not disclosure of HIV status	0.47 (0.30-0.77)	0.45 (0.78-3.86)	0.45 (0.26-0.78)
Depression	0.49 (0.15-1.62)	0.20 (0.09-0.42)	0.19 (0.09-0.40)
Concordant partnership	0.37 (0.15-0.92)	0.36 (0.14-0.94)	0.36 0.14-0.97)
ART use	1.48 (0.79-2.79)	1.45 (0.74-2.96)	2.55 (0.98-6.63)
Co-infection with an STI	0.78 (0.49-1.25)	0.60 (0.35-1.00)	0.78 (0.43-1.42)
ART users, not co-infected with STI	—	—	2.56 (1.00-6.63)
ART users, co-infected with STI	—	—	0.50 (0.23-1.33)
Non-ART users, co-infected with STI	—	—	0.78 (0.43-1.42)
Non-ART users, not co-infected with STI	—	—	—

*Additionally adjusted for SES, IPV, education, and whether a women exchange sex for money, shelter, drugs, or goods.

† Model including statistical interaction between STI and ART use.

Table 4.3 Adoption of condom use after sero-conversion among women who recently sero-converted

	Adjusted* OR	Confidence Interval
Age	0.98	0.89-1.08
Depression	0.62	0.40-0.96
Disclosure of HIV status	2.79	1.51-5.16
Primary school completed	1.87	0.39-8.94
Secondary school or higher completed	3.06	0.95-15.17

*Additionally adjusted for SES, IPV, education, and whether a women exchange sex for money, shelter, drugs, or goods.

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Chapter 5: Conclusions and Implications of Research

5.1 Conclusions

Globally, HIV continues to be a major public health problem, and in particular sub-Saharan Africa, where 23 million people were living with HIV/AIDS in 2012.^{1,2} Although rates of HIV within the region have decreased, they are still among the highest in the world, despite an increase in ART coverage, the advent of PrEP and PEP.³⁻⁶ This suggests that high-risk sexual behaviors still play a key role in transmission.

There are many behaviors associated with increased probability of HIV transmission, including inconsistent condom use and multiple sexual partners.^{7, 8} HIV infection rate among discordant partners who report consistent condom use has been shown to be less than 1%, compared with 10-14.5% among those who report inconsistent condom use.⁹ Additionally, there are a number of non-behavioral factors that contribute to HIV transmission. For instance, depression, one of the most common neuropsychiatric disorders among people living with HIV/AIDS (PLWHA), has been linked with an accelerated disease progression and a higher frequency of high-risk sexual behaviors.¹⁰⁻¹⁵ Further, disclosure of HIV status is associated with HIV transmission, in that those who disclose have a lower frequency of high-risk behaviors, such as inconsistent condom use.^{9,10,16-19} Moreover, disclosure is linked with an increase in social support, which has numerous benefits including, better retention of HIV care and lower risk of depression.¹⁶⁻²⁰ Finally, co-infection of an STI has been linked with a higher probability of HIV transmission, as those co-infected have a higher genital viral load, increasing infectiousness.^{4,21-25} Moreover, co-infection may be a marker for high-risk sexual behaviors, such as inconsistent condom use.^{4,21}

Our analyses indicated that depression plays a large role in behaviors post sero-conversion. Depression was shown to increase the risk of STI acquisition, as well as predicting condom use at last sex and change in condom use after sero-conversion. Indicating that depressed HIV-infected women are at a high-risk of secondary HIV transmission. Our results

also indicated that there were several factors that influenced whether a women disclosed her HIV status, including condom use at last sex and a woman's education. Highlighting the fact that those who practice high-risk sexual behaviors may be less likely to disclose their HIV status, increasing the risk of secondary transmission. Finally, our results indicated that there were several factors that influenced condom use. In particular, ART use was shown to modify the relationship between co-infection with an STI and condom use at last sex. Supporting one theory, that ARTs may cause disinhibition. Specifically, HIV-infected individuals on ART may perceive themselves no longer infectious to sexual partners and as a result, increase the frequency of unprotected sex.²⁷

High-risk sexual behaviors and factors related to an increase in HIV transmission among those infected with HIV must be addressed in order to reduce secondary HIV transmission. Specifically, addressing the problem of depression among PLWHA. Targeted pharmacological interventions and psychotherapeutic treatment among PLWHA are needed to help reduce the prevalence of depression.^{13,14} However, the limited availability of antidepressants in Africa coupled with their cost, might make psychotherapeutic treatment the more practical option.^{13,14}

Additionally, targeting specialized risk reduction counseling to core groups of women, immediately after sero-conversion and well into their disease are needed to reduce high-risk sexual behaviors. Specifically targeting women who are depressed, less educated, practice high-risk behaviors prior to sero-conversion, and those that have experienced IPV is key to reduce high-risk sexual behaviors that perpetuate the epidemic.

Finally, risk reduction interventions need to emphasize the importance of disclosure not only as a risk reduction technique, but also as a means to increase social support.^{18,28-30} Social support is critical for retention of HIV care, decreasing depression, and other factors related to HIV transmission.^{18,28-30} Moreover, interventions need to incorporate a form of support, such as

support groups, for those who don't have it, as well as for women who suffer from abuse as a result of their HIV diagnosis.^{18,28-30}

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