The relationship between intimate partner violence, unprotected sex, and detectable plasma viral load in HIV-positive female sex workers in Kenya

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Abstract

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The studies in this dissertation examine the relationship between intimate partner violence (IPV), unprotected sex, and behaviors related to transmission risk in HIV-positive female sex workers, (FSWs) in Kenya. This work includes: 1) prevalence and correlates of IPV in the past year, 2) a prospective study of recent IPV as a risk factor for unprotected sex, and 3) a prospective study of recent IPV as a risk factor for detectable plasma viral load. Findings from our parallel qualitative study of IPV are also included.

Intimate partner violence, including physical, emotional, and sexual violence by an emotional partner, is associated with many negative health outcomes, including HIV. The relationship between IPV and adverse health outcomes in FSWs in Africa is less clear. In HIV-positive FSWs, exposure to IPV may impede the success of new HIV prevention and treatment strategies designed to improve health and reduce secondary HIV transmission risk. We found that 80% of women had 'emotional' partners and that 14.6% reported IPV in the past year (95% confidence interval (CI) 10.9-18.2%). Women's alcohol use problems and partner controlling behaviors were significant correlates of recent IPV. There was a significant positive association between recent IPV and unprotected sex by self-report (adjusted relative risk (aRR) 1.91, 95% CI: 1.32-2.78) and semen biomarker (aRR 1.54, 95% CI: 1.17-2.04). Unexpectedly, recent IPV was associated with significantly lower risk of detectable viral load (aRR 0.21, 95% CI: 0.05-0.86). Our qualitative research suggests that this association was likely due to unmeasured factors including women's resilience, relationship characteristics, and social support. These combined results signal the complexity of the relationship between IPV and HIV treatment outcomes in this population.

Results from this dissertation have the potential to inform new comprehensive HIV treatment and prevention strategies for FSWs that support their health and rights. Empowerment-based behavioral interventions to reduce IPV, high-risk alcohol use, and unprotected sex should be evaluated as HIV prevention strategies. Further research is necessary to identify new intervention targets to improve treatment outcomes and well-being in this key population.

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For Connor, Debbi, John Wilson

and Mary S. Ramsey

Chapter 1: Introduction

Introduction

This dissertation addresses key questions about correlates of intimate partner violence (IPV) and the relationship between IPV, sexual risk behavior, and detectable plasma viral load in high-risk HIV-positive women in Africa, with the goal of informing targeted HIV prevention strategies that improve their quality of life and reduce secondary transmission risk of HIV.

Reducing gender-based violence (GBV) is a core strategy to make progress on achieving an AIDS free generation by 2030 [1]. Intimate partner violence (IPV), which may be defined as any sexual physical or emotional violence or threats of violence by a boyfriend or husband, is the most pervasive form of gender-based violence (GBV), affecting an estimated 36% of women worldwide [2]. According to the ecological framework on violence against women (Figure 1), IPV is thought to arise from a combination of societal, interpersonal, and individual factors, and may be prevented by targeting one or more of these determinants [3].There are several negative mental and physical consequences of IPV, including increased risk of HIV infection [4, 5]. In Africa, women account for 60% of the estimated 27.4 million HIV infections [6]. Exposure to IPV may impede women's ability to use condoms consistently, adhere to anti-retroviral therapy (ART), and benefit fully from HIV care. Many African governments acknowledge the importance of addressing GBV as a problem in its own right, and as a barrier to achieving HIV and reproductive health targets [7]. The Kenyan National AIDS and STD Control Program's (NASCOP) plan to achieve zero new HIV infections by 2030 calls for the rapid identification of evidence-based HIV interventions that protect human rights and reduce GBV in key populations [8]. This may include a combination of community-based primary prevention (e.g. awareness raising about gender equality and rights) and health-sector based secondary prevention (e.g. individual counseling, treatment of injury, and referral for additional care) [7]. Female sex workers (FSWs) are a key population at high risk for HIV acquisition and transmission and in need of effective HIV prevention and treatment strategies tailored to their local context. Women

engaged in sex work are a heterogeneous population in Africa. This definition of 'FSW' encompasses a range of transactional sex behaviors, including exchanging sex for goods or food to full-time commercial sex workers that are based at a bar or brothel. For HIV-positive FSWs, IPV is an under-recognized and potentially important source of violence. Exposure to IPV may result in an increased risk of both unprotected sex and detectable viral load (through poor adherence to ART, which together increase the risk of ongoing HIV transmission. Whether and how to address IPV as part of new comprehensive HIV prevention and treatment strategies tailored to this key population is an open question.[1]

In the Introduction, we provide a brief overview of each research question addressed in this dissertation. We then present, by chapter, study rationale and summary results. The Chapter 4 Addendum presents relevant findings from our parallel qualitative study of IPV. This additional context is key to understanding and interpreting the results from Chapter 4.

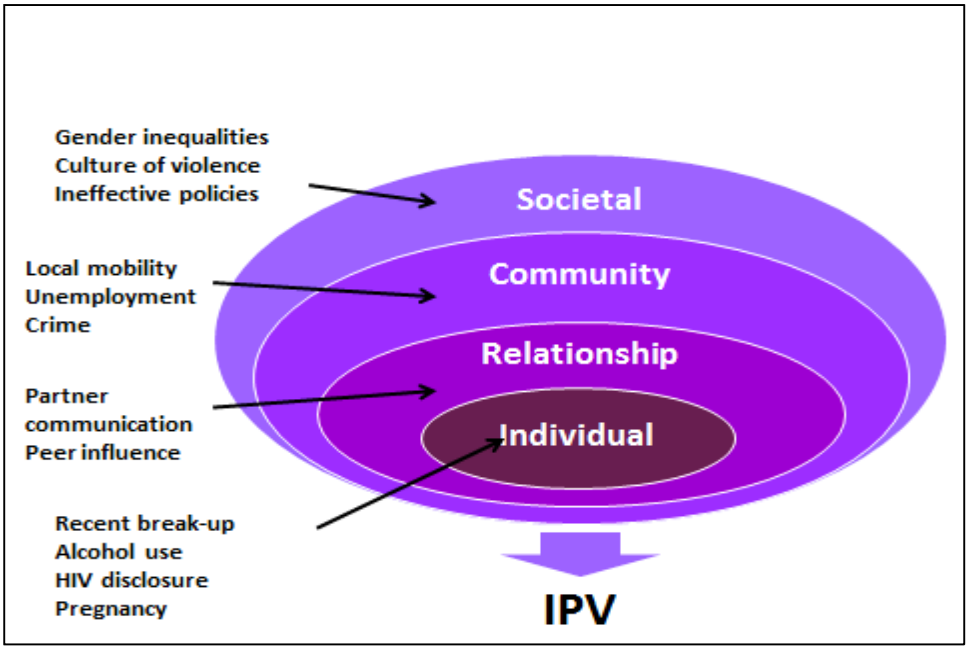

Figure 1. Ecological framework on violence against women, adapted from Heise *1998*

[1] In this dissertation, 'HIV prevention' for HIV-positive individuals refers to prevention of infection to sexual partners and infants.

Intimate partner violence is a problem in high-risk HIV-positive African women

Intimate partner violence is a complex pattern of behavior that can be understood as an extreme expression of gender power inequality in which one member of the partnership exerts disproportionate control over the sexual decisions, material resources, or her freedom of movement. While IPV may arise in any emotional partnership, most research on IPV focuses on violence by men against women. According to the 2008/9 Kenyan Demographic and Health Survey, the estimated prevalence of any IPV in the past year among ever married women was 40.7% [9]. Studies in HIV-negative women have found that IPV is associated with increased risk of adverse health outcomes including unprotected sex, HIV and other sexually transmitted infections, unintended pregnancy, alcohol use problems, and depression [4, 10-13]. Intimate partner violence may continue after women acquire HIV, for example, as a consequence of disclosing HIV status or starting HIV care [14]. However, the problem of IPV in high-risk HIV-positive women has received far less attention. In Kenya for example, FSWs represent 1% of the population and 30% are HIV positive [15]. This population is extremely heterogeneous, and encompasses women who are full time commercial sex workers and women who engage in occasional exchange of sex for money or goods and may not identify as 'sex workers.' Nonetheless, HIV-positive FSWs are particularly marginalized and experience high rates of poverty, stigma, high-risk substance use, and violence [16-18]. Most research and interventions that address violence against FSWs in Africa, including peer-education and advocacy and community mobilization about workplace rights, have focused on violence by clients and police [13, 19]. Emerging evidence suggests that many FSWs have long-term 'emotional partners,' and that violence by intimate partners is common [20]. Understanding the prevalence and correlates of recent IPV in HIV-positive FSWs will be important to help identify potential intervention targets to reduce IPV and its negative health consequences in this key population.

IPV may be an important risk factor for unprotected sex in high-risk HIV-positive women

Intimate partner violence is associated with more sexual risk, including unprotected sex, multiple sex partners, and high-risk male partners (i.e. who have HIV or concurrent sexual partners) [10, 21]. For HIV-positive FSWs, condom use may differ by partner type, and is generally lower with emotional partners [20, 22]. Violence is likely specific to the type of partner and situation. For example, violence by clients may be a single episode of coerced sex or physical violence at the time of the transaction [23]. In contrast, IPV is often recurrent and may not include any overt acts of sexual or physical violence, but only the threat of violence [24]. For high-risk HIV-positive women, IPV may increase their risk of ongoing unprotected sex, which has important implications for sexual risk of HIV transmission, STI acquisition, and unintended pregnancy. Little is known about the relationship between IPV and unprotected sex in high-risk HIV positive women in Africa and further prospective studies will be necessary to address this question.

IPV may be an important risk factor for detectable viral load in high-risk HIV-positive women

Expanded access to ART in Africa since 2004 has dramatically shifted the course of the epidemic. High adherence to ART is essential to achieving viral load suppression and optimizing ART for both treatment and prevention [25, 26]. Trials and demonstration projects are underway to test whether combination prevention packages can reduce HIV incidence at the population level [27, 28]. Combination prevention refers to bundling several evidence-based interventions, including biomedical (e.g. pre-exposure prophylaxis, ART, voluntary male circumcision), behavioral (behavior change communication), and structural (e.g. HIV testing services) approaches. The primary goal of combination prevention is to minimize population-level HIV transmission in a specific setting, though improving individual health outcomes remains important [28]. For FSWs, it is likely that a combination of locally-tailored and acceptable structural, behavioral, and biomedical approaches will be necessary [29]. While HIV-positive

FSWs face many of the same barriers to ART initiation adherence as women in the general population, unique barriers may include concerns about disclosure to clients and emotional partners and prejudice from health care providers. A few studies from high income countries suggest that IPV is associated with poor adherence and unsuppressed viral load [30, 31]. Further prospective studies are needed to clarify whether recent IPV may increase risk of poor adherence and detectable viral load in high-risk HIV-positive women in Africa, and potentially inform the new targeted combination HIV prevention strategies with this population.

We have conducted a series of complementary studies to understand the correlates of IPV in the past year ('recent IPV') and whether recent IPV is a risk factor for unprotected sex and detectable plasma viral load in high-risk HIV-positive women in Mombasa, Kenya. Participants who were enrolled in an ongoing cohort study at our research clinic, located at Ganjoni Health Center. This cohort included data from nearly 400 HIV-positive FSWs, who contributed up to two years of monthly follow-up visits. We used a standardized tool to measure IPV, adapted from the World Health Organization (WHO) survey on violence against women [32]. Biological markers were included to cross-validate our behavioral measures. The cross-sectional analysis allowed us to identify potentially modifiable correlates of recent IPV. Our prospective cohort studies of recent IPV as a risk factor for unprotected sex and detectable plasma viral load provided new understanding of the potential impact of IPV on two core components of secondary prevention in HIV-positive women. Our parallel qualitative study on the beliefs and experiences of women who reported recent IPV, revealed the complexity of these emotional partnerships and has contributed substantially to our interpretation of the quantitative results [33]. Together, these studies have contributed new knowledge to the fields of women's health and HIV prevention. We hope that these results can be used to guide new intervention strategies to reduce unprotected sex, as well as generate new research questions to better understand individual and contextual factors that may support HIV treatment outcomes in this key population.

Chapter 2: Prevalence and correlates of recent IPV in high-risk HIV-positive women

According to the ecological framework on violence against women and research from general-population samples, there are structural, interpersonal, and individual risk factors for experiencing IPV. These include inequitable gender norms [4, 34-36], alcohol use by either partner [13, 37, 38], women having multiple sex partners [39], prior abuse as a child or adult [34, 39], lower education [37], and HIV-positive status [5, 40, 41]. Most studies on IPV in African women have focused on general-population samples or pregnant women. Research on violence against FSWs tends to focus on violence by clients, police or other men rather than emotional partners [13, 22, 42]. One exception was a study in HIV-negative Kenyan women in sex work with alcohol use problems, where 30.2% of women reported physical violence and 44.4% reported sexual violence by a 'non-paying' partner in the past month [22]. Significant correlates of violence by a client or a 'non-paying' partner were the woman's history of child abuse, having more than one sex partner, binge drinking, and supporting dependents [22]. For HIV-positive FSWs, the prevalence and correlates of IPV may be distinct. For example, women's preferences for relationships may change as a result of learning of their HIV status, deciding whether and to whom to disclose their HIV status, and initiating ART [43]. One qualitative study of HIV-positive sex workers in Nairobi, found that many women sought out men for long-term relationships for emotional and financial support and as a way to lower their HIV transmission risk (by reducing the number of sexual partners) [44]. More research on high-risk HIV-positive women, using standardized measures of IPV, will be important to understand and identity potentially modifiable correlates of IPV. In Chapter 2, we present results from a cross-sectional analysis of enrollment data from 357 women. Our results highlight that IPV in the past year is an important problem in high-risk HIV-positive women, and that alcohol use problems and male

partner controlling behaviors may be potentially modifiable intervention targets to reduce IPV in this population.

Chapter 3: The relationship between IPV in the past year and unprotected sex

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Accumulated evidence suggests that IPV is associated with many negative sexual health behaviors and outcomes including unprotected sex, STIs, unintended pregnancy and HIV infection [45-47]. Most research on IPV in Africa has been limited to South Africa and Uganda, and focused on HIV-negative women in the general population [4, 5, 48, 49]. For example, a prospective study of HIV-negative women enrolled in a contraceptive trial in South Africa found that IPV in the past three months was associated with about a 1.5-fold higher risk of not using condoms or diaphragms [50]. A cross-sectional study in HIV-negative FSWs in Kenya found that recent violence by clients or 'non-paying partners' was associated with a higher likelihood of inconsistent condom use [13]. Relationship violence can increase the risk of unprotected sex directly through forced sex, or indirectly, by limiting women's power to negotiate condom use at specific times or throughout the relationship. In addition, high-risk alcohol use may trigger IPV and also be a coping strategy to deal with IPV [38]. We developed a working conceptual model to guide our analysis (Figure 2). From this conceptual model, we developed several directed acyclic graphs (DAG), which show the hypothesized casual relationships between variables measured in this analysis. An example DAG is shown in Figure 3 [51]. Further support for these proposed pathways linking IPV and unprotected sex comes from randomized trials of HIV behavioral interventions for women in South Africa and the US. These trials have shown that empowering women in their romantic relationships and strengthening social ties significantly can reduce unprotected sex [52, 53]. Research on IPV as a risk factor for unprotected sex in HIV-

positive FSWs in Africa is lacking. Prospective studies are needed to understand the relationship between recent IPV and unprotected sex in this key population.

In Chapter 3, we present a prospective cohort study that used data from 390 high-risk HIV-positive women to evaluate the relationship between IPV in the past year and unprotected sex. Outcome measures were unprotected sex by self-report and semen detection by prostate specific antigen test (PSA), a biomarker with high sensitivity to detect semen in vaginal secretions for 24-48 hours after exposure [54]. This study highlights the importance of IPV as a potential intervention target to reduce recurrent violence and unprotected sex in HIV-positive FSWs in Africa.

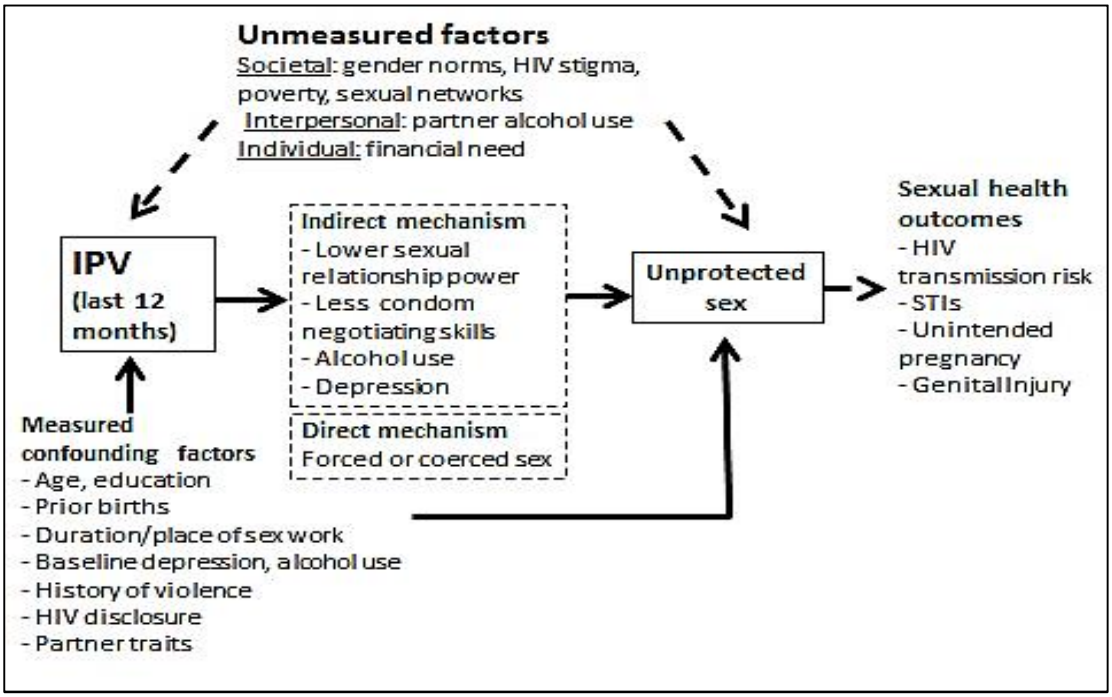

Figure 2. Conceptual model of the relationship between recent IPV and unprotected sex in HIV-positive FSWs

The figure presents a working model of the relationship between recent IPV and unprotected sex in high-risk HIV positive women. It is guided by sociology and feminist theories which posit that IPV can lead to reduced power in the relationship, which results in reduced ability to use condoms. Both IPV and HIV risk behaviors can results from societal and interpersonal factors including inequitable gender norms, which are represented as 'unmeasured factors'. Examples of direct (forced sex) and indirect (low condom negotiation skills) mechanisms through which exposure to IPV may result in higher risk of unprotected sex are shown in boxes with a dashed line.

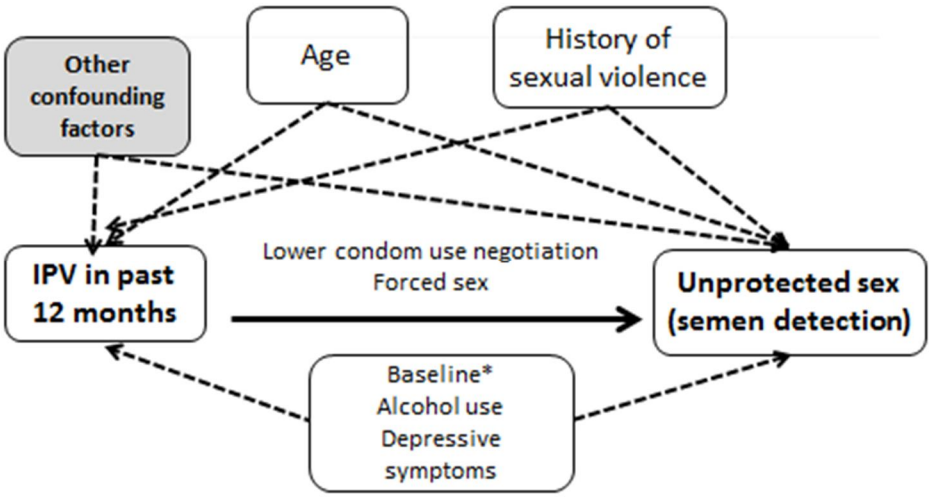

Figure 3. Directed acyclic graph of the hypothesized association between recent IPV and unprotected sex

This simplified DAG shows the hypothesized association between IPV in the past year and unprotected sex in the past week. Age, history of sexual violence by someone other than index partner, and baseline alcohol use were confounding factors that we adjusted for in the multivariate analysis. Only baseline values of alcohol use and depression were considered as possible confounding factors because time varying values could act as confounding factors as well as mediators linking IPV and unprotected sex. The box labeled 'other confounding factors' represent variables that were unmeasured in this study, including alcohol use by the index partner. In a future analysis, we will consider adjusting for alcohol use as a time varying covariate that may also act as mediator, using marginal structural models.

Chapter 4 and Chapter 4 Addendum: The relationship between recent IPV, plasma viral load, and poor adherence; and, relevant findings from our qualitative study

Sustained adherence to ART is essential to achieve undetectable viral load, and reduce the risk of disease progression and secondary transmission [55]. Of the estimated 7.6 million HIV-positive African adults who were taking ART in 2012, 25% were not virally suppressed [6]. Barriers to adherence include transportation cost, HIV stigma, non-disclosure, low social support, poor mental health, alcohol use, and poor memory [56-58]. For FSWs, there are additional structural barriers related to sex work, including detention, migration, and unpredictable work hours [29]. Intimate partner violence may be an important barrier to maintaining optimal adherence and viral suppression in African FSWs. A limited number of studies in HIV-positive women in high-income settings have shown that lifetime or recent IPV was associated with poor ART adherence, not taking ART or poor retention in HIV care [59-61]. For example, a prospective study of ART-eligible women in the US found that lifetime IPV was associated with a 1.7-fold higher risk of not taking ART [59]. Relationship violence may increase the risk of poor adherence directly through partner interference with her care or her disengagement from HIV care [59]. In addition, IPV may lead to poor adherence indirectly through reduced self-efficacy, depression, and substance use [62-64]. The likely mechanism through which exposure to IPV may increase risk of detectable viral load is through poor adherence to ART [65]. Few studies have evaluated whether IPV is a risk factor for detectable plasma viral load. Two cross-sectional studies in the US reported that recent IPV [30, 66] was associated with greater likelihood of detectable viral load, while a prospective study did not find an association [67]. Limitations to the exiting literature on recent IPV, detectable viral load, and poor adherence include a lack of epidemiologic data from Africa, a preponderance of cross-

sectional studies conducted in general-population samples, and the lack of data on high-risk HIV-positive women.

In Chapter 4, we present a prospective study that we conducted to evaluate the association between IPV in the past year and detectable viral load in high-risk HIV-positive women taking ART at our research clinic. We conducted a secondary analysis examining the relationship between recent IPV and poor adherence. A working conceptual model to guide this analysis is shown in Figure 3. An example DAG for this analysis is shown in Figure 4. Our analysis of IPV in the past year as a risk factor for detectable plasma viral load, was conducted in a sub-set of 558 visits contributed by 195 women who had viral load data. Our analysis of recent IPV and poor adherence included 214 women and 3,189 monthly follow-up visits. Contrary to our hypothesis, we found that recent IPV was associated with a significantly lower risk of detectable plasma viral load. We believe that other personal, relationship, and social factors that are associated with reporting IPV likely explain the observed association. Our unexpected results in the IPV and viral load analysis have generated several new hypotheses for future studies in this population, which we describe in the Chapter 4 and Chapter 4 Addendum: Conclusion. In the Chapter 4 Addendum, we present summary results from in-depth interviews with women who had reported experiencing recent IPV at enrollment in the cohort study ('Exploring Women's Lifecourse Events & HIV Transmission Potential: A Qualitative Study'). Findings from our qualitative study revealed the importance of emotional support and love in these partnerships as well as adaptive strategies that women used to stay safe and healthy. Because the findings from the qualitative study are essential for interpreting the quantitative study, we intend to combine these results into a mixed-methods manuscript [33]. In this dissertation, the quantitative and qualitative results are presented separately.

Gender-based violence and HIV are leading health and human rights problems with complex linkages. Reducing the burden of GBV against women and girls is a core strategy to

achieving an AIDS free generation by 2030 and other health and development targets. There is an ongoing need to identify effective primary and secondary prevention strategies for both problems that are locally-relevant and sustainable. Important gaps remain in how best to address IPV and its negative health outcomes in key populations in Africa. Kenya is a country that is well positioned to answer these questions. The country has a robust HIV prevention and care infrastructure, innovative national plans for reducing GBV and HIV, and impetus to translate evidence-based interventions into effective programs. Through this dissertation project, we hope to contribute substantially to the fields of women's health and HIV by highlighting the problem of recent IPV in HIV-positive FSWs women in Africa, identifying modifiable risk factors for IPV, and demonstrating that recent IPV is an important risk factor for unprotected sex. Our unexpected finding demonstrating an inverse association between IPV and detectable plasma viral load suggest that the relationship between IPV and HIV treatment outcomes is more complex. We do not expect that reducing IPV alone would improve the rate of viral load suppression. Future studies are essential to identify other contextual, relationship, and personal factors that improve adherence outcomes and that could be targets for comprehensive, locally-adapted interventions to benefit women's health and reduce secondary transmission risk in this population.

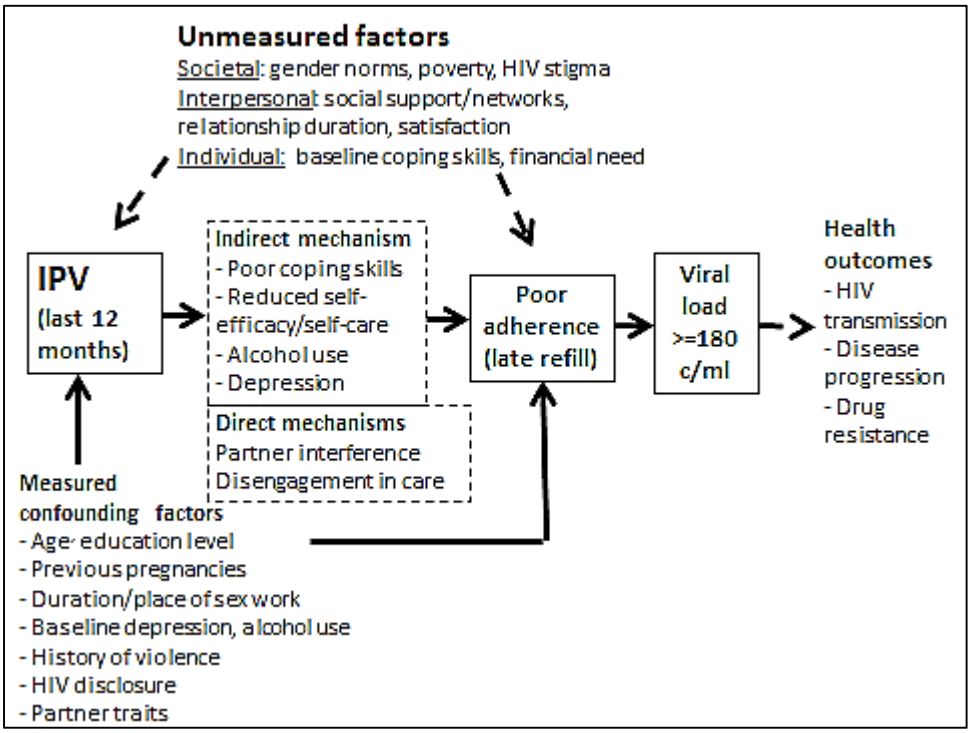

Figure 4. Simplified conceptual model of the relationship between recent IPV and detectable plasma viral load in HIV-positive FSWs

The figure above presents a working model of the relationship between recent IPV and detectable plasma viral load. This model is guided by a mental health and coping model proposed by Sikkema (2010). The primary mechanism through which IPV may result in detectable viral load is through poor adherence. Potential direct and indirect mechanisms through which exposure to IPV may result in poor adherence are shown in boxes with dashed lines. Unmeasured factors are presented at the top of the figure. Coping is presented as an unmeasured factor and a mechanism to distinguish between women's baseline ability to manage life stress and poor coping that may directly result from IPV. Health outcomes of unsuppressed viral load are shown but are not measured in this study.

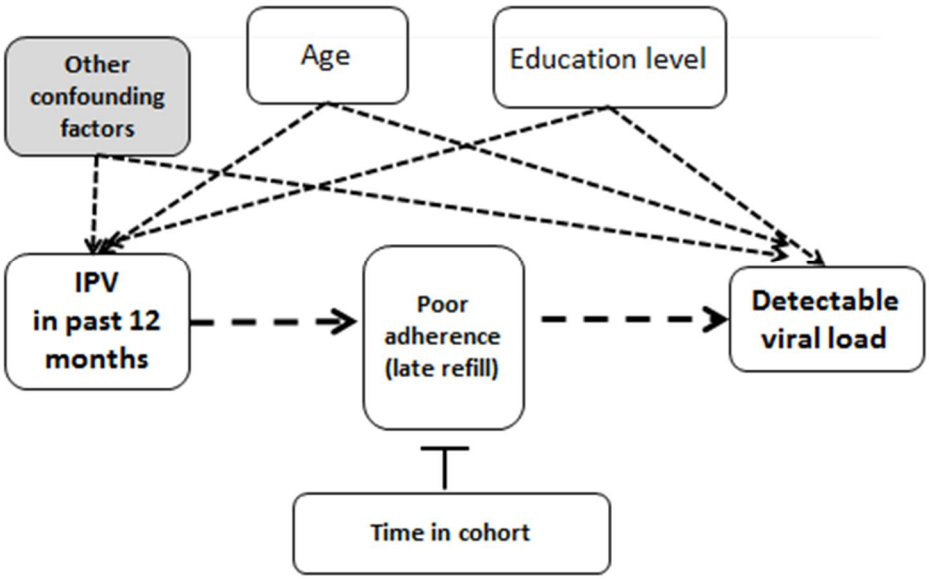

Figure 5. Directed acyclic graph of the association between recent IPV and detectable plasma viral load

The simplified DAG presented above shows the hypothesized association between recent IPV and detectable plasma viral load. Poor adherence is the likely pathway linking IPV to detectable plasma viral load. Age and education level were adjusted for as confounding factors. In exploratory analysis, we also examined whether the primary association differed by time in the cohort. The box labeled 'other confounding factors' represents unmeasured variables, including financial need/socioeconomic status. Time updated values of alcohol use and depressive symptoms were considered as variables on the causal pathway linking IPV and plasma viral load through poor adherence. Future mediation analyses using marginal structural models should be considered that accounts for variables that may act as confounding factors of the association between the mediator and outcome.

CHAPTER 2

Prevalence and correlates of recent IPV in HIV-positive female sex workers in Mombasa, Kenya

Prevalence and correlates of intimate partner violence in HIV-positive female sex workers in Mombasa, Kenya

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Abstract

Objectives: Intimate partner violence (IPV) is common worldwide and associated with unplanned pregnancy, HIV and STI acquisition, depression, and suicide. The objective of this study was to evaluate the prevalence and correlates of IPV in the past year by a regular male partner among high-risk HIV-positive women in Mombasa, Kenya.

Design: Cross-sectional study

Methods: This cross-sectional study included HIV-positive women 16 years or older who reported engaging in transactional sex. We asked 13 questions adapted from the World Health Organization survey on violence against women about any physical, sexual, or emotional violence in the past year by the current or most recent regular partner (index partner). We used standardized instruments to assess socio-demographic, behavioral, and clinical characteristics as possible correlates of IPV. Associations between IPV and these correlates were evaluated using univariate and multivariate logistic regression.

Results: Overall, 286/357 women (80.4%) had an index partner, and 52/357 (14.6%, 95% confidence interval (CI) 10.9% - 18.2%) reported IPV by that partner in the past year. In multivariate analysis, women with severe alcohol problems (adjusted odds ratio (aOR) 4.08, 1.03-16.15) and those experiencing controlling behaviors by the index partner (aOR 4.98, 2.31-10.73) were significantly more likely to report recent IPV.

Conclusions: Intimate partner violence in the past year was common among high-risk HIV-positive women. Interventions targeting risk factors for IPV, including alcohol problems and partner controlling behaviors, could help to reduce recurrent violence and negative health outcomes in this key population.

Key words: Intimate partner violence; HIV-positive women; transactional sex; Africa

Introduction

Intimate partner violence (IPV), defined as any physical, sexual, or emotional violence by a regular partner such as a husband or boyfriend, is the most common form of gender-based violence (GBV) [1, 2]. Intimate partner violence has been associated with numerous negative outcomes including depression [68], unwanted pregnancy [12], sexually transmitted infections (STI) including HIV [4, 5], and suicide [69]. In Africa, the prevalence estimates of IPV in the past year from household surveys of ever married women range from 4-55% [32]. Studies suggest that IPV is particularly common in women who are HIV-positive [5, 14, 70]. Women engaged in sex work are disproportionately affected by HIV, and often have both clients and regular sexual partners [20, 22]. These women may also experience a high frequency of IPV [22, 41, 71, 72].

Studies of IPV among African women have focused on different study populations and used a variety of methods, including different definitions of partner violence as well as different correlates [34, 42, 73]. Inequitable gender norms [4, 34-36], alcohol use by either partner [13, 37, 38], women having multiple sex partners [39], prior abuse as a child or adult [34, 39], lower education level [37], and HIV-positive status [5, 40, 41] have been associated with greater frequency of IPV. The studies on violence among women engaged in transactional sex in Africa typically assess violence by any male perpetrator rather than by a regular partner [13, 22, 42]. In a cross-sectional study of Kenyan women in sex work enrolled in an alcohol use intervention, significant correlates of violence by a client or a 'non-paying' partner were experiencing abuse as a child, having more than one sex partner, binge drinking, and supporting dependents [22]. More research that incorporates standardized measures of IPV will be important to understand the extent of the violence that these women experience from their regular partners. In addition, improved understanding of the correlates of IPV among HIV-positive women in sex work will help to identify potentially modifiable intervention targets that could be included in new comprehensive approaches to HIV care for this key population [74, 75]. To address these knowledge gaps, we conducted a cross-sectional study to evaluate the prevalence and

correlates of IPV in the past year among HIV-positive women engaged in transactional sex in Mombasa, Kenya.

Methods

In this cross-sectional analysis of data from women enrolling in a cohort study at our HIV/STI research clinic, eligible women were laboratory-confirmed HIV-positive, age 16 or older, and reported exchanging sex for cash or in-kind payment. Women completed a standardized face-to-face interview in their preferred language (Kiswahili or English) with a trained Kenyan study nurse to collect data on socio-demographic characteristics, medical histories, sexual behaviors, and exposure to violence. All interviews were conducted in a private room. A study clinician then conducted a physical examination including a speculum-assisted pelvic examination for collection of genital swabs for laboratory testing. Participants received free outpatient care at our research clinic, including comprehensive risk reduction counseling, antiretroviral therapy (ART) according to Kenyan National Guidelines, and STI treatment. Women who reported experiencing violence were offered counseling on site or referral to a local GBV resource center. This study was approved by the ethics committees of the University of Washington and Kenyatta National Hospital. All participants provided written informed consent.

Measures

The main outcome, ‘any IPV’ in the last year, was defined as responding yes to at least one of 13 questions about acts of IPV in the past 12 months committed by a regular partner. Questions were adapted from the WHO survey on violence against women, a tool that has high internal consistency in different cultural settings [32, 76]. All women were asked whether they had a regular partner, such as a boyfriend or husband, whom they did not consider to be a client. If they did not have a regular partner at the time of the interview, they were asked about their most recent regular partner. The current or most recent regular partner was identified as

the ‘index partner.’ Only participants who had an index partner were asked the IPV questions (all women were asked questions about violence by other people). When responding to the IPV questions, women were asked to think about behaviors by that index partner. If a participant reported any lifetime IPV by her index partner, she was then asked whether that act occurred in the past 12 months. Women were also asked about the frequency of each act (‘once,’ ‘a few,’ ‘many times’). There were six questions on physical violence (slapped, pushed, hit, kicked, choked, or threatened with a weapon); four on emotional violence (insulted, belittled, intimidated, threatened to hurt someone you care about); and three on sexual violence (forced sex, coerced sex, or degrading sexual behavior). We measured how closely related these 13 items were in our sample using Cronbach’s alpha. Internal consistency was high (α=0.88). We also created a binary variable for ‘any severe IPV,’ defined as experiencing at least one of the following: hit, kicked, choked, approached with a weapon; and any act of sexual IPV [2, 77]. Women who reported no index partner were classified as having no IPV.

Socio-demographic, behavioral, and clinical characteristics were evaluated as correlates of IPV in the past 12 months. We used the ecological framework of violence against women to guide the analyses, which posits that a combination of individual, interpersonal, and societal factors influence a woman’s risk of IPV [3]. In this analysis, only individual and interpersonal variables were collected. Socio-demographic characteristics included age (continuous); marital status (ever married); years in sex work (<5, 5-9, ≥10); early sexual debut (first sex ≤ 15 years); education level (<8 years versus 8 or more); and workplace (bar, nightclub, home/other). Reproductive characteristics included pregnancy history; desire for (more) children; use of modern contraceptive methods (none/condoms only, short/medium acting, long acting); laboratory-confirmed pregnancy; postpartum status (within nine months of last delivery); and menopause. Post-menopausal status was defined as being 40 years or older, not pregnant, not taking unopposed progesterone contraception, and reporting more than 12 months of amenorrhea since last menstrual period. Partner characteristics were partner types

(casual/client only, regular only, or both a regular partner and casual/client) and regular partner's reaction to a possible pregnancy (excited, neutral, upset). The number of sexual partners in the past week was dichotomized at the median (>1 versus 1 or 0) because the distribution of these data was highly skewed.

We evaluated depressive symptoms, alcohol use, HIV disclosure, and male controlling behaviors with tools used previously in similar populations in Africa [32, 78, 79]. Depressive symptoms in the past two weeks were assessed with the Patient Health Questionnaire-9 (PHQ-9) [79]. Scores ranged from 0 to 27 (Cronbach α=0.88). Both the continuous score and categorical forms were evaluated. We used the standard categories of 0-4 (minimal), 5-9 (mild), 10 or higher (moderate or severe; consistent with a major depressive disorder) [80] . Alcohol use in the past year was evaluated with the Alcohol Use Disorders Identification Test (AUDIT) [81]. Scores ranged from 0-40 and were categorized as non-drinkers (zero), minimal (1-6), moderate (7-15), and severe problem or possible alcohol use disorder (AUD) (≥16) according to WHO recommendations for women (Cronbach α=0.81) [82]. Women were also asked about frequency of drug use in the past month (marijuana, cocaine, and injection drugs). Disclosure of HIV status was assessed by asking whether women had ever shared their results with someone. The presence of controlling behaviors was defined as responding yes to at least one of seven statements about behaviors ever committed by her index partner (e.g. restricts contact with family, suspicious that you are unfaithful, requires permission to get health care). In addition, all women were asked about history of sexual or physical violence since age 15 by any person other than their index partner. Sexual violence was assessed by asking whether women had been forced to have sex or perform a sexual act. Physical violence was assessed by asking women whether they had been beaten or physically mistreated [32]. Prevalent sexually transmitted infection (STI) (*Neisseria gonorrhoeae, Chlamydia trachomatis,* or *Trichomonas vaginalis*) was assessed by nucleic acid amplification testing (APTIMA; Hologic/Gen Probe, San Diego, CA). Baseline CD4 count was dichotomized as <350 versus ≥350 cells/μl. Current

antiretroviral (ART) use was measured by self-report. For women receiving ART through our research clinic, we confirmed that they were taking ART with our pharmacy records.

Statistical analysis

We estimated the prevalence of IPV in the past year and conducted an exploratory analysis of the prevalence and correlates of IPV that included all women in the sample who had IPV data. Prevalence was defined as the number of women reporting IPV in the past year divided by the total number of women in the sample. Univariate logistic regression was used to estimate the association between each correlate and IPV in the past year. Variables associated with any IPV in the past year in univariate analysis ($p<0.1$) were included simultaneously in the multivariate model. Sexual behavior variables (i.e. number of sex acts, abstinence, 100% condom use, and unprotected sex) and STIs were considered outcomes of IPV and were evaluated in a separate analysis. Depressive symptoms and alcohol use problems were considered to be both risk factors for and outcomes of recent IPV [38, 68, 83, 84]. Thus, we decided *a priori* to consider both variables for inclusion in our multivariate models of correlates of IPV [34]. We conducted a sensitivity analyses restricted to the 286 women in the sample who reported an index partner. We also conducted an exploratory analysis with any severe IPV in the past year as the outcome. Model fit was assessed using likelihood ratio tests. Because this analysis was exploratory, we did not adjust the $\alpha=0.05$ level for multiple comparisons. All associations were reported as odds ratios (OR) with 95% confidence intervals (CI). All models used robust standard errors. Analyses were conducted in STATA 13.0 (StataCorp, College Station, TX).

Results

Sample characteristics

Overall, 359 women enrolled between October 2012 and December 2013, of whom, 357 had complete data on the IPV questions. Their baseline characteristics are shown in Table 1. The

median age was 39 years (interquartile range (IQR 33,44). Many had engaged in transactional sex for at least 10 years (173/355, 48.5%). The majority of women (286, 80.1%) reported having a regular partner currently or in the past (index partner). Over one third of women (127, 35.6%) reported ever experiencing physical abuse since age 15 by someone other than the index partner. A lower proportion of women (55/355, 15.4%) reported experiencing any sexual abuse since age 15 by someone other than the index partner. The most common perpetrators of prior physical or sexual violence were former boyfriends, former husbands and strangers. Nearly half of the women reported any alcohol use in the past year (174/357, 48.7%). Among women who were alcohol users, 103/174 (59.1%) reported drinking behavior consistent with minimal alcohol use problems, 57/174 (32.8%) with moderate problems and 14/174 (8.0%) with severe alcohol problems or possible alcohol use disorder. The prevalence of symptoms consistent with mild (scores 5-9; 66/357, 18.5%) and moderate (scores ≥10; 23/357, 6.4%) depression by PHQ-9 in the past two weeks was relatively low. A large proportion of women reported no depressive symptoms (142, 39.6%). Nearly half of the women experienced at least one controlling behavior by the index partner 167 (46.8%). Less than one-third reported more than one sexual partner in the past week (98/356, 27.5%). Self-reported unprotected sex in the past week was low (25/356, 7.0%). Of 228 women who reported taking ART, 116 (50.8%) were receiving ART from our research clinic, while others received their medications elsewhere.

Prevalence of IPV in the past year and ever by the index partner

Fifty two (14.6%, 95% confidence interval (CI) 10.9% - 18.2%) women reported IPV in the past year. Over half of the women (34/52, 65.0%) who reported IPV had experienced severe IPV (9.3%, 6.5% - 12.5%).The most common type of IPV in the past year was physical violence (38, 10.6%), followed by emotional violence (36, 10.1%) and sexual violence (13, 3.6%). Most acts of IPV in the past year occurred ‘once’ (35, 9.8%) followed by ‘many times’ (10, 2.8%) then

'a few times' (7, 2.0%). The prevalence of IPV in the past year restricted to women who reported an index partner was 52/286 (18.2%, 13.7%-22.7%).

Nearly forty percent of women reported ever experiencing IPV by an index partner (137/357, 38.2%, 33.2%-43.3%). About one third of women reported ever experiencing severe IPV by an index partner (108/357, 30.3%, 25.7%-35.2%).

In univariate analysis, having alcohol problems (minimal OR 2.06, 0.99-4.29; moderate OR 3.08, 1.38-6.90; severe OR 7.83, 2.41-25.42), and experiencing controlling behaviors by the index partner (OR 6.05, 2.92-12.51) were associated with a significantly greater likelihood of IPV in the past year (Table 2). Compared to women who reported fewer than five years in sex work, those who reported 10 or more years had a lower likelihood of recent IPV (OR 0.51, 0.24-1.09).

In multivariate analysis, compared to women who did not drink, women with higher alcohol use scores had a greater likelihood of IPV by an index partner in the past year, although only the severe alcohol use category remained statistically significant (≥16 aOR 4.08, 1.03-16.15). The partner's controlling behaviors also remained significantly associated with a greater likelihood of IPV in the past year (aOR 4.98, 2.31-10.73). Results from the sensitivity analyses restricted to women who reported an index partner and the exploratory analysis that used severe IPV in the past year as the outcome were virtually the same as the results in the primary analysis (data not shown).

Discussion

Intimate partner violence by a regular partner during the past year was common in this sample of HIV-positive Kenyan women who engage in transactional sex. Male controlling behaviors and women having more severe alcohol use problems were significantly associated with IPV by the regular partner.

The 15% prevalence of IPV by an index partner in the past year in this study fell within the range of previous studies among African women [9, 13, 14, 32, 45, 71, 85, 86] including those at-risk for HIV acquisition and transmission [87, 88]. We found a lower prevalence of recent IPV compared to prior studies of Kenyan sex workers [22, 83]. Differences in the reported prevalence of IPV are partly due to differences in study instruments, definitions of violence, and prevalence of risk factors for violence across samples [32, 89]. Other studies have included both regular sex partners and clients in the definition of 'intimate partner,' which likely explains the comparably higher prevalence of reported IPV. Both earlier studies included higher proportions of women with alcohol use problems, including one study conducted with women receiving an alcohol use intervention [42, 85]. As a result, those women may have been at higher risk of violence in general. In our sample, most of the women were taking ART and had been counseled that alcohol use can impair adherence, which can decrease medication effectiveness. Our study adds to the limited literature in high-risk HIV-positive women. Specifically, this research focuses attention on the important role of regular partners as perpetrators of violence in women with past or present involvement in transactional sex.

Our finding that alcohol use problems were associated with a greater likelihood of IPV also parallels results from previous studies in Africa [83, 85]. The relationship between alcohol use and IPV is complex and likely bi-directional [38, 83]. Women who consume higher quantities of alcohol may be more likely to get into conflict that culminates in IPV and have regular partners who commit IPV while intoxicated [90]. Alternatively, women may drink to cope with a violent relationship or the stress of sex work [83]. Longitudinal studies are needed to determine the extent to which each of these pathways may contribute to the observed association between IPV and alcohol use [83, 85].

The association between male partner controlling behaviors and experiencing IPV is consistent with other samples of African women [37, 91]. In addition, surveys conducted among

men have found that controlling behaviors are associated with a greater likelihood of male perpetration of IPV [92]. Controlling behaviors like suspiciousness or requiring permission to get health care indicate unequal power dynamics in a relationship [34, 93, 94]. A woman's failure to act within in a designated role may trigger IPV because her partner feels that his power is threatened [35, 94]. In-depth interviews of pregnant women, men, and health care providers in Western Kenya found that one of the triggers of IPV was a woman's failure to consult her husband before getting HIV testing. Men felt that they should have been included in this decision [95]. Similar themes emerged in a qualitative study of South African men [94]. In the South African study, men reported that improved communication and reduced perceptions of sexual entitlement would help them to resolve relationship conflict without resorting to violence.

The strengths of this study include using a standardized instrument to measure IPV. The WHO VAW survey has been used successfully in several recent studies in other populations of women in Africa [4, 77]. Using this tool will enable us to interpret and compare findings across studies. Similarly, we measured potential correlates of IPV, including alcohol use and depressive symptoms, with tools that have been validated in similar populations [41, 79]. We also paid careful attention to the directionality of associations, and aimed only to test variables as correlates of IPV that were plausible risk factors.

This study also had limitations. First, the cross-sectional design limited inferences about temporal sequence or causality. Second, this analysis was exploratory and should be replicated in other samples. Future studies should also evaluate partner characteristics including alcohol use and HIV-status, as well as community-level factors including inequitable gender norms [21, 34, 94, 96]. Third, IPV was measured by self-report, and is subject to underreporting due to recall bias and sensitivity of the topic [97, 98]. We tried to minimize underreporting of IPV by asking behaviorally specific questions, which have been shown to facilitate disclosure [32] as

well as conducting interviews with a trained Kenyan study nurse in a private setting. Fourth, we did not conduct a partner-level analysis to evaluate the frequency of IPV with different partners [22]. Asking about one current or most recent regular partner may underestimate the true prevalence of IPV in this population. In addition, the prevalence and risk factors for IPV may differ by partner type [44, 99]. While results from our sample of HIV-positive women who engage in sex work may not be generalizable to all other populations, our findings are likely applicable to other high-risk African women [10, 50, 84, 100]. Studies from diverse settings and risk groups are important for providing a more comprehensive understanding of IPV among HIV-positive women.

Conclusion

Violence against women engaged in sex work is an important health and human rights problem [1]. There are several important health outcomes at stake, including the risk of injury, depression, post-traumatic stress disorder, unintended pregnancy, STI, and HIV transmission. Our study extends the knowledge about IPV in this key population by highlighting the phenomenon of violence by a regular male partner. Prospective studies are needed to understand the temporal sequence of the relationships between risk factors, IPV and adverse health outcomes [53, 101]. Qualitative studies will help to explain why and how violence occurs in regular partnerships and ways that women cope with violence. Randomized controlled trials will ultimately be essential to establish causal relationships and to demonstrate the efficacy of new interventions to reduce IPV among HIV-positive women.

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Author contribution:

KSW and RSM designed the study. KSW analyzed the data and drafted the manuscript. RSM, LM, RD, JMS, JPH, JS, WJ and AV reviewed drafts of the manuscript. RD, LM, and JS provided oversight of study procedures and data collection at our research clinic.

Table 1.Enrollment characteristics of 357 HIV-positive women who reported current or past engagement in transactional sex

Characteristic	Median (IQR) or n (%)
Socio-demographic characteristics	
Age	39 (33,44)
Highest education level ≥8 years	144 (40.3)
Workplace	
Bar/restaurant	210 (58.8)
Nightclub	83 (23.3)
Home/other	64 (17.9)
Early sexual debut (age 15 or younger)	101 (28.9)
Years in sex work (n=355)	
Less than 5	72 (20.2)
5-9	110 (30.8)
10 or more	173 (48.5)
Ever married	276 (77.3)
Had only a casual partner in the past 3 months	27 (7.6)
Has an index partner	286 (80.1)
Index partner in the past 3 months	160 (44.9)
Index partner in the past 3 months, no casual partner	99 (27.7)
Has both an index and casual partner in the past 3 months	132 (37.0)
Sexual and reproductive health characteristics	
Number of previous pregnancies (n=356)	3 (2,4)
Pregnant by urine hCG test (n=356)	3 (0.8)

Fertility desire (n=355)	87 (24.3)
Postpartum (n=350)	6 (1.7)
In menopause (n=354)	57 (16.0)
Contraceptive use category (n=355)	
None or condoms only	249 (69.8)
DMPA or OCP (short/medium acting hormonal methods)	72 (20.2)
IUD,TL, Norplant, hysterectomy (long acting methods)	34 (9.5)
Partner attitude about pregnancy (n=286)[1]	
Excited	165 (58.3)
Don't care	71 (24.9)
Very upset	47 (16.8)
Depressive symptoms by PHQ-9	
Minimal (0-4)	268 (75.1)
Mild (5-9)	66 (18.5)
Mod/Severe (10 or higher)	23 (6.4)
Alcohol use problems by AUDIT	
Non drinkers	183 (51.0)
Minimal (1-6)	103 (28.9)
Moderate (7-15)	57 (15.9)
Severe (16 or higher)	14 (3.9)
Disclosed HIV status to anyone in the past	228 (68.9)
History of violence and controlling behaviors	
History of sexual abuse since age 15 (n=355)[2]	55 (15.4)
Any sexual abuse in the past 12 months (n=352)[2]	27 (7.6)
History of physical abuse since age 15[2]	127 (35.4)

Any physical abuse in the past 12 months (n=355)[2]	25 (7.0)
Ever had controlling behaviors by the index partner	167 (46.8)
CD4 lymphocyte count <350 cells/µl (n=356)	93 (26.1)
On ART by self-report (n=356)[3]	228 (64.0)
Any GC, CT, or TV by NAAT (n=348)	38 (10.6)

1. Among women who had an index partner
2. Refers to anyone besides the index partner.
3. Of 228 women who reported taking ART at enrollment, 116 (50.9%) were receiving this medication at our clinic and 107 (46.9%) reported getting ART at another clinic (5 missing responses).

AUDIT, Alcohol Use Disorders Identification Test; ART, anti-retroviral therapy; CT, *Chlamydia tracomatis*; DMPA, depot medroxyprogesterone acetate; GC, *Neisseria gonorrhoeae*; hCG, human chorionic gonadotropin; IPV, intimate partner violence; NAAT, nucleic acid amplification test; OCP, oral contraceptive pills; PHQ-9, Patient Health Questionnaire 9; TV, *Trichomonas vaginalis*,

Table 2. Correlates of any IPV in the past 12 months by the index partner

Variable	IPV (n=52)	No IPV(n=305)	OR (95% CI)	p-value	AOR (95% CI)[¥]	p-value
Age	37 (32, 44)	40 (33, 44)	0.98 (0.94-1.00)	0.16	- -	
Early sexual debut (≤15 years)	18 (34.6)	83 (27.2)	1.42 (0.76-2.64)	0.28	- -	
Years in sex work						
<5 (ref)	14 (26.9)	58 (19.1)	1.0		1.0	
5-9	19 (36.5)	91 (30.0)	0.86 (0.40-1.86)	0.71	1.17 (0.51, 2.70)	0.72
10 or more	19 (36.5)	154 (50.8)	0.51 (0.24-1.09)	0.08	0.90 (0.38, 2.11)	0.81
Number of pregnancies (n=356)	3 (2, 4)	2 (2, 4)	1.08 (0.93-1.23)	0.36	- -	
Number of births (n=355)	3 (1, 4)	2 (1, 3)	1.07 (0.90-1.27)	0.43	- -	
Work place						
Bar (ref)	33 (63.5)	177 (58.0)	1.0		- -	
Nightclub	11 (21.2)	72 (23.6)	0.82 (0.39-1.71)	0.60		
Home, Other	8 (15.4)	56 (18.4)	0.73 (0.33-1.76)	0.53		
Ever married	44 (84.6)	232 (76.1)	1.73 (0.78-3.84)	0.18	- -	
8 or more years education	25 (48.1)	119 (39.0)	1.45 (0.80-2.61)	0.22	- -	
Fertility desire (n=355)	13 (25.5)	74 (24.3)	1.06 (0.54-2.11)	0.86	- -	
Contraception (n=355)						
None/condoms (ref)	35 (67.3)	214 (70.6)	1.0			

OCP or DMPA	11 (21.2)	61 (20.1)	1.10 (0.53-2.30)	0.80	- -	
Long acting methods[1]	6 (11.5)	28 (9.2)	1.31 (0.51-3.40)	0.58	- -	
Pregnant (urine bhcg)	2 (3.9)	1 (0.3)	1.68 (0.48-5.90)	0.42	- -	
Post-partum (n=350)	1 (1.9)	5 (1.7)	1.15 (0.13-10.10)	0.90	- -	
Post- menopausal (n=354)	7 (13.7)	50(16.5)	0.81 (0.34-1.89)	0.62	- -	
How would your partner feel if you became pregnant?[2]						
Excited (ref)	33 (66.0)	132 (56.7)	1.0			
Doesn't care	12 (24.0)	59 (25.3)	0.81 (0.39-1.69)	0.58	- -	
Upset	5 (10.0)	42 (17.8)	0.48 (0.17-1.30)	0.15	- -	
>1 sex partner, past 7 days	19 (36.5)	79 (26.0)	1.64 (0.88-3.05)	0.12	- -	
Controlling behaviors by index partner						
	42 (80.8)	125 (41.0)	6.05 (2.92-12.51)	<0.001	4.98 (2.31-10.73)	<0.001
Physical abuse since age 15[3]	24 (46.2)	103 (33.8)	1.68 (0.93-3.05)	0.09	1.45 (0.75-2.82)	0.27
Physical abuse, past year[3] (n=355)	6 (9.6)	20 (6.6)	1.51 (0.54, 4.21)	0.44	- -	
Sexual abuse since age 15[3] (n=355)	7 (13.5)	48 (15.8)	0.83 (0.35-1.94)	0.66	- -	
Sexual abuse, past year[3] (n=352)	5 (9.6)	22 (7.3)	1.34 (0.48, 3.72)	0.57	- -	
Disclosed HIV status	33 (63.5)	195 (64.1)	0.97 (0.53-1.79)	0.93	- -	

Depressive symptoms by PHQ-9 categories						
Min 0-4 (ref)	35 (67.3)	233 (76.4)	1.0			
Mild 5-9	12 (23.1)	54 (17.7)	1.48 (0.72-3.04)	0.29	- -	
Mod/Sev (10 or higher)	5 (9.6)	18 (5.9)	1.85 (0.64-3.51)	0.25		
Alcohol problems by AUDIT						
Non-drinkers (ref)	16 (30.8)	167 (54.8)	1.0		1.0	
Min 1-6	17 (32.7)	86 (28.2)	2.06 (0.99-4.29)	0.05	1.99 (0.91-4.32)	0.09
Mod 7-15	13 (25.0)	44 (14.4)	3.08 (1.38-6.90)	0.006	1.98 (0.81-4.89)	0.14
Sev 16+	6 (11.5)	8 (2.6)	7.83 (2.41-25.42)	0.001	4.08 (1.03-16.15)	0.05
CD4 count <350 cells/µl (n=355)	12 (23.5)	81 (26.6)	0.85 (0.42-1.70)	0.61	- -	
On ART (n=356)	32 (61.5)	196 (64.2)	0.86 (0.58-1.53)	0.61	- -	

ART, anti-retroviral therapy; AUDIT, Alcohol Use Disorders Identification Test; DMPA, depot medroxyprogesterone acetate; hCG, human chorionic gonadotropin; IPV, intimate partner violence; OCP, oral contraceptive pills; OR, Odds Ratio; aOR, adjusted Odds Ratio; PHQ-9, Patient Health Questionnaire 9.

[¥] Multivariate analysis sample was 356.

[1.] Long term methods include Norplant, IUD, tubal ligation, hysterectomy.

[2.] Among 286 women with an index partner.

[3.] Violence by any person besides the index partner.

CHAPTER 3

A prospective study of the relationship between recent IPV and unprotected sex in HIV-positive female sex workers in Mombasa, Kenya

A prospective cohort study of intimate partner violence and unprotected sex in HIV-positive female sex workers in Mombasa, Kenya

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Abstract

We conducted a prospective cohort study to test the hypothesis that recent intimate partner violence (IPV) is associated with unprotected sex in HIV-positive female sex workers (FSWs) in Mombasa, Kenya. Women completed monthly follow-up visits and quarterly examinations. Any IPV in the past year was defined as ≥1 act of physical, sexual, or emotional violence by the current or most recent emotional partner ('index partner'). Unprotected sex in the past week was measured by self-report and prostate specific antigen (PSA) test. Recent IPV was associated with a significantly higher risk of unprotected sex by self-report (adjusted relative risk [aRR] aRR 1.91, 95% CI 1.32, 2.78) and PSA (aRR 1.54, 95% CI 1.17, 2.04) after adjusting for age, baseline alcohol use, and lifetime history of sexual violence by someone besides the index partner. Targeting IPV in new comprehensive HIV prevention strategies is important to reduce risk behavior and improve women's health.

Key words: Intimate partner violence, unprotected sex, semen biomarker, female sex workers, Africa, longitudinal analysis

Introduction

Gender based violence (GBV) is a health and human rights problem, and an important barrier to an effective response to the HIV pandemic [1, 102]. Intimate partner violence (IPV), which can include physical, sexual, and emotional, violence by a regular partner, is the most common form of GBV in women [32]. Negative outcomes associated with IPV include depression [103], substance use disorders [104], sexual risk behaviors [50], unintended pregnancy [12], and HIV infection [4]. A meta-analysis of 79 studies reported a 36% lifetime prevalence of IPV in Africa [2]. According to a national household survey in Kenya, 41% of ever married women reported IPV in the past year [105].

In Africa, female sex workers (FSWs) are a key population that is disproportionately affected by violence and HIV [106-108]. In Kenya, FSWs represent an estimated 1% of the population, of whom 30% are HIV-positive [109]. This population frequently experiences violence by men [13, 22, 106], substance use problems [18], and social stigma [106]. Many FSWs also have regular 'emotional' partners, whom they consider boyfriends or husbands [22, 110]. HIV-positive FSWs may experience IPV as a consequence of HIV status disclosure [111], or initiation of HIV care [112, 113]. For this population, relationship violence may affect their ability to use condoms consistently as well as their ability to benefit fully from comprehensive HIV prevention and care [112]. However, most studies evaluating the association between IPV and sexual risk behavior in women in Africa have been cross-sectional and in HIV-negative women [4, 13, 41]. The few studies on violence and HIV outcomes in women in transactional sex have focused on violence by clients and other men [13, 114, 115]. To address these knowledge gaps, we conducted a prospective study to test the hypothesis that recent IPV would be associated with a higher rate of unprotected sex in high-risk HIV-positive women in Kenya.

Methods

This longitudinal analysis included data from women enrolled in a prospective cohort study in Mombasa, Kenya. Eligible women were age 16 or older and laboratory-confirmed HIV-positive. All participants were FSWs, defined on the basis of reporting exchanging sex for cash or in-kind payment at their screening visit. At enrollment, women completed a standardized face-to-face interview in their preferred language (Kiswahili or English) with a Kenyan study nurse to collect data on health, demographics, sexual risk behaviors, and exposure to violence. A study clinician conducted a physical examination including a speculum-assisted pelvic examination for collection of genital swabs for laboratory testing for sexually transmitted infections (STIs) and the presence of semen. Women returned monthly for behavioral data collection. Physical examinations with specimen collection were conducted quarterly. Participants received free outpatient care at our research clinic, including risk reduction education, antiretroviral therapy (ART) if eligible according to Kenyan National Guidelines, and STI screening and treatment. Women who reported experiencing violence were offered counseling on site or referral for follow-up care. This study was approved by the ethics committees of Kenyatta National Hospital and the University of Washington. All participants provided written informed consent.

Measures

The primary exposure was any IPV in the past 12 months, assessed annually ('recent IPV' hereafter). This variable was defined as responding yes to at least one of 13 questions about acts of IPV in the past 12 months. Questions were adapted from the World Health Organization survey on violence against women, which has high internal consistency [32]. Women were asked whether they had an 'emotional' partner, who they did not consider to be a client or casual partner. If they did not have such a partner at the time of the interview, they were asked about their most recent emotional partner. This man was identified as the index partner. Only participants who were able to identify an index partner were asked the IPV

questions. If a participant reported any lifetime IPV by their index partner, she was then asked whether that act occurred in the past 12 months. There were six questions on physical violence (hit, slapped, kicked, pushed, choked, or threatened with a weapon), four on emotional violence (insulted, belittled, intimidated, or threatened to hurt someone you care about), and three on sexual violence (forced sex, coerced sex, forced to perform degrading sexual behavior). We created a categorical variable for IPV severity (severe, moderate, none). Severe IPV was defined as experiencing being hit, kicked, choked, approached with a weapon plus any act of sexual IPV. Moderate IPV was defined as experiencing any other act of IPV [73]. Women who had no index partner were classified as unexposed to IPV at that visit.

The primary outcome was unprotected sex in the past week, measured monthly. This variable was computed based on responses to four questions about total sex acts and total sex acts with a condom. Women were asked separately about vaginal and anal sex. Unprotected sex was defined as the total number of sex acts exceeding the total sex acts with a condom. Unprotected sex was zero when no sex acts were reported in the past week. The proportion of visits at which women reported no sex in the past week was also evaluated in the full cohort. In the subset of visits where women reported sexual activity in the past week, the total number of sexual partners, total sex acts, and the proportion with 100% condom use were evaluated. The proportion with detection of any STI at quarterly examination visits, defined as presence of *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or *Trichomonas vaginalis* by nucleic acid amplification test (Aptima; Hologic, San Diego, CA), cervical gram stain, or wet preparation were also evaluated.

In addition to the self-reported behavioral outcomes, we evaluated the relationship between IPV in the past year and semen detection in the genital secretions by prostate specific antigen test (PSA) test, a biomarker of unprotected sex collected at quarterly examination visits

(ABACard, West Hills, CA). The PSA is most sensitive for detecting semen within 24-48 hours of unprotected sex [54].

Covariate data were collected at different intervals depending on the measure. Socio-demographic characteristics collected included age (enrollment); marital status (ever married; annually); years in sex work (<5, 5-9, ≥10; enrollment); early sexual debut (first sex ≤ 15 years, enrollment); highest education level (<8 years versus 8 or more; enrollment); and workplace (bar, nightclub, home/other; enrollment). Reproductive characteristics included use of modern contraceptives (no method, condoms only, injectable hormonal contraception, oral contraceptives, intrauterine device, tubal ligation, hysterectomy, or other; monthly); fertility desire (quarterly); laboratory-confirmed pregnancy (quarterly); postpartum status (≤ nine months since last delivery); and post-menopausal status (clinical algorithm; annually). Partner data included questions on any casual partners (quarterly) and an index partner's expected reaction to a future pregnancy (excited, neutral, upset; annually). Controlling behaviors by the index partner were defined as responding yes to at least one of seven statements (e.g. he acts suspicious that you are unfaithful; he requires permission to get health care; annually).

Depressive symptoms, alcohol use, and male controlling behaviors were measured with standardized tools used in similar African populations [79, 116, 117] . Depressive symptoms in the past two weeks were assessed by Patient Health Questionnaire-9 (PHQ-9) (6-monthly) [117]. Scores were categorized as 0-4 (minimal), 5-9 (mild), 10 or higher (moderate or severe; consistent with a major depressive disorder). Alcohol use in the past year was assessed by the Alcohol Use Disorders Identification Test (AUDIT) (annually) [81]. Scores were categorized as non-drinkers (zero), minimal (1-6), moderate (7-15), and severe problem or possible alcohol use disorder (AUD) (≥16). All women were asked about history of sexual or physical violence since age 15 by any person other than their index partner (annually). Exposure to sexual violence was defined as being forced to have sex or perform a sexual act. Physical violence was defined as

beaten or physically mistreated. Disclosure of HIV status was assessed by asking whether women had ever shared their results with someone, and if so, to whom (e.g. sibling, friend, health worker; 6-monthly) [118].

Statistical analysis

Women who enrolled between October 12, 2012 and September 25, 2014 contributed data to this analysis. Follow-up visits were included until administrative censoring (September 30, 2014). Our primary exposure status was carried forward for all visits until the next IPV assessment. This approach is consistent with evidence that recent IPV is a strong predictor of ongoing IPV [24]. Also, exposure to IPV in early adulthood is associated with adverse health outcomes during middle age [119]. We tested this assumption in sensitivity analyses using alternative ways of modeling the exposure window. All covariate values collected less than monthly were imputed forward until the next assessment.

For the primary analysis, we tested the hypothesis that IPV in the past year was associated with increased risk of unprotected sex in the past week. Generalized estimating equations (GEE) with a log link, independence working correlation structure, and robust standard errors were used to generate relative risks (RR) and 95% confidence intervals (CI) [120]. Multivariate models included age (restricted cubic spline) and history of sexual abuse by someone besides the index partner (enrollment value) as *a priori* confounding factors. Additional covariates were considered for inclusion in the adjusted models if they could potentially confound the association between IPV and unprotected sex, based on our causal diagrams [51]. These variables were tested in the regression model in order of decreasing effect size. Covariates that changed the primary effect estimate by ≥10% were retained in the final model [121]. Only enrollment values of depressive symptoms and alcohol use were evaluated in the multivariate models. The time-updated values for these variables were not

used, because both characteristics could also act as steps in the causal pathway linking IPV and unprotected sex [122].

We also tested the hypothesis that IPV in the past year was associated with increased risk of PSA detection in vaginal secretions. This analysis was limited to quarterly examination visits. We used the same adjusted model as the primary analysis, substituting PSA detection as the outcome.

We used a similar model building approach to evaluate IPV as a risk factor for the exploratory outcomes, and adjusted for the same covariates as in the primary analysis. We evaluated the association between recent IPV and self-reported abstinence from sex in the past week. At visits where women reported sexual activity, the association between IPV and total sex partners (binary ≥2 versus <2), total sex acts (binary ≥3 or <3), and proportion of visits with 100% condom use was evaluated. Because continuous measures of total number of sex partners and total sex acts were highly skewed, these values were dichotomized at the median. We also evaluated the association between recent IPV and laboratory-confirmed STI.

Missing data for the exposures, outcomes, and covariates were <2%, so we used complete case analysis. We evaluated loss to follow-up in the cohort, which we defined as the most recent follow-up visit occurring at least six month prior to censoring date [123]. All analyses were conducted in STATA Version 13.0.

Results

Overall, 390 women contributed 4,934 visits and 488 person-years to the analysis. The median number of follow-up visits was 14 (interquartile range [IQR] 5-23). Enrollment characteristics are presented Table 1. Women's median age was 39 years ([IQR] 32-44). Most women worked in bars or restaurants (229, 58.7%). The majority of women had index partners (311/390, 80.0%).

History of physical violence (135/390, 34.6%) and sexual violence (62/389, 15.9%) since age 15 by someone other than the index partner was common.

Longitudinal analysis of recent IPV as a risk factor for unprotected sex

Of 4,934 study visits, women were exposed to IPV in the past year in 863 (17.5%). Any IPV in the past year was associated with a significantly increased risk of self-reported unprotected sex in the past week (146/863, 16.9% vs. 290/4071, 7.1%; RR 2.37, 95% CI 1.65, 3.42) (Table II). This association was attenuated, but remained statistically significant after adjusting for age, lifetime history of sexual violence by someone besides the index partner, and baseline alcohol use (aRR 1.91, 95% CI 1.32, 2.78). The results were similar in sensitivity analyses restricted to visits contributed by women who reported an index partner (aRR 1.63, 95% CI 1.11, 2.38). When the exposure was categorized by severity, there was a suggestion of a higher risk of unprotected sex in visits exposed to higher IPV severity level (severe IPV RR: 3.02, 95% CI 1.15, 6.04; moderate IPV RR: 2.32, 95% CI 1.59, 3.40). These findings were similar in analyses adjusted for potential confounding factors (severe IPV aRR: 2.50, 95% CI 1.35, 4.65; moderate IPV aRR: 1.87, 95% CI 1.27, 2.76).

Recent IPV was associated with a significantly lower proportion of visits where women reported no sex in the past week (aRR 0.67, 95% CI 0.54, 0.83). In a sub-set of visits where women had reported any sex in the past week, recent IPV was associated with a significantly lower proportion of 100% condom use (aRR 0.90, 95% CI 0.82, 0.99).

Longitudinal analysis of recent IPV as a risk factor for semen detection by PSA test

Semen detection by PSA test was more than twice as common as unprotected sex by self-report, occurring at 359 of 2,207 exam visits (16.3%). Notably, PSA was detected in vaginal

secretions at 284/1,993 (14.3 %) of examination visits when no unprotected sex was reported. Positive PSA results were more frequent at visits where women reported IPV compared to visits when no IPV was reported (aRR 1.54, 95% CI 1.17, 2.04).

Differences between women who were retained in follow-up and women who had not returned for a follow-up visit for at least 6 months before the censoring date were assessed. Overall, 105 (26.9%) women were lost to follow-up by this definition. The adjusted association between IPV in the past year and unprotected sex was moderately larger in the group that was lost to follow-up (aRR 2.23, 95% CI 0.82, 6.08) compared to the group that was retained (aRR1.80, 95% CI 1.20, 2.76). Similarly, in women who were lost to follow-up, there was a stronger association between recent IPV and semen detection by PSA test (aRR 2.26, 95% CI 1.28, 4.00) compared to the group that was retained (aRR 1.50, 95% CI 1.11, 2.04). Recent IPV was not associated with a significantly higher risk of loss to follow up (RR 1.13, 95% CI 0.63, 2.02; aRR 1.02, 95% CI 0.56, 1.85).

Discussion

In this prospective analysis of high-risk HIV-positive women, IPV in the past year was associated with a significantly higher risk of unprotected sex by self-report. Recent IPV was also associated with a significantly higher risk of semen detection by PSA test.

These findings complement studies among high-risk, primarily HIV-negative women in Africa [13, 22, 106]. A study conducted among HIV-negative female sex workers recruited from bars and nightclubs in Kenya reported that violence by an ‘emotional partner’ in the last year was associated with a higher frequency of inconsistent condom use in the last three months (no effect estimate reported) [41]. The association between recent IPV and unprotected sex in our sample was modestly higher than the estimate reported in a longitudinal analysis of data from

general-population African women who were HIV-negative and enrolled in a contraceptive trial [50]. Our results differ from two prospective studies in population-based samples of HIV-negative women in South Africa [4] and Uganda [5] , which did not find an association between recent IPV and higher risk of unprotected sex. Our study adds to the literature by demonstrating that recent IPV is an important risk factor for unprotected sex in high-risk HIV-positive women.

There are several mechanistic pathways that may help to explain the relationship between recent IPV and increased risk of unprotected sex. First, IPV can reduce women's power to negotiate condom use [4, 124]. Randomized trials in South Africa have shown that empowering women by strengthening their skills to deescalate relationship conflict can reduce recurrent IPV and unprotected sex [48, 53]. Second, IPV may lead to negative coping strategies such as problem substance use resulting in a reduced ability or motivation to use condoms [106]. Third, condom use tends to be lower with emotional partners than with clients [44, 125]. A qualitative study of HIV positive FSWs in Nairobi revealed that the stronger bonds with emotional partners made it harder for women to insist on using condoms [44] . Finally, IPV may be a marker of relationships with risky men, who have a history of violent behavior or a sense of sexual entitlement, and with whom unprotected sex is more likely to occur [34]. Future research on the psychological and behavioral pathways linking IPV and unprotected sex in high-risk women may help to guide the identification of optimal intervention targets.

This study is one of the first to evaluate the association between IPV and semen detection in vaginal secretions by PSA test. Our finding that recent IPV was associated with a significantly increased risk of positive PSA test supports the results from the primary analysis based on self-reported unprotected sex. We found that 14% of visits at which no unprotected sex was reported had positive PSA results, which was similar to previous studies in high-risk women [126, 127]. Discrepancies between self-reported unprotected sex and PSA test are expected, because they do not measure precisely the same thing [128]. The lower frequency of

self-reported unprotected sex compared to semen detection by PSA was likely due to underreporting [126]. In addition, even when women reported condom use accurately, semen exposure may have occurred due to condom failure or genital exposure before applying or after removing a condom [126]. It is also expected that some self-reported unprotected intercourse may be missed by PSA. Specifically, since PSA is rapidly excreted in 24-48 hours [54], some acts of unprotected sex reported in the past week may have occurred outside the window of detection. These results highlight the value of using both behavioral and biological markers of sexual behavior to gain a more complete understanding of the relationship between IPV and unprotected sex.

This study had several strengths. The longitudinal design with time-updated exposure and outcome measurements permitted evaluation of the temporal sequence between recent IPV and unprotected sex. The inclusion of a semen biomarker for unprotected sex is novel in the field of violence and HIV research, and cross-validated our self-reported measures. We used standardized tools to measure the IPV exposure [32], unprotected sex [129], alcohol use [81], and depressive symptoms [117], which should enhance comparability to other studies using these measures. This attention to methodological considerations is a valuable contribution to the violence and HIV literature. We also examined whether our results were sensitive to loss to follow-up in the cohort. The association between recent IPV and unprotected sex was modestly larger in the visits by women lost to follow-up, suggesting that we may have underestimated the true effect of IPV on unprotected sex. Finally, our study focused on HIV-positive women, all of whom reported engaging in transactional sex at screening. These women represent a key population in Africa, with unique needs for comprehensive HIV prevention and care [112, 130].

This study also had a number of limitations. First, both IPV and sexual behavior are sensitive topics that are subject to underreporting because of social desirability bias. We tried to minimize underreporting of IPV through interviewer training and use of a standardized tool that

included multiple questions about physical, sexual, and emotional IPV [32]. Second, the decision to carry forward IPV exposure status until the next annual visit may have resulted in bias if a woman's true exposure changed between assessments. Notably, incorrect classification of exposure status that changed between assessments (non-differential misclassification), would most likely have led to underestimation of the true association. Third, data were collected on unprotected sex generally, rather than unprotected sex with different types of partners. Unprotected sex may be higher with regular partners than with clients [20, 22]. However, we were unable to determine whether unprotected sex by self-report or semen detection by PSA in vaginal secretions occurred with the index partner, a different regular partner, a casual partner, or a client. Fourth, bias due to unmeasured confounding by partner characteristics, including his HIV status, was possible [34]. Fifth, it is important to consider the extent to which our results can be generalized to other populations. This study sample included HIV-positive FSWs. As such, results may not reflect the association between recent IPV and unprotected sex in women in the general population. However, these results are likely to be relevant to other high-risk women in Africa, and may help to inform targeted HIV prevention strategies for this key population.

Conclusion

Violence against FSWs is a serious problem with important implications for women's health and global HIV prevention [102]. Our study demonstrates that IPV, which by definition was committed by an emotional partner who is not a client, is common in this population of HIV-positive FSWs, and is associated with unprotected sex. These findings underscore the importance of identifying effective strategies that address IPV, with the goals of reducing relationship violence, improving women's quality of life and decreasing sexual transmission of HIV.

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Author contribution:

KSW and RSM designed the study. KSW analyzed the data and drafted the manuscript. RSM, JPH, AV, JMS, RD, KY, JS, BR and WJ reviewed drafts of the manuscript. RD and JS provided oversight of study procedures and data collection at our research clinic.

Table 3. Baseline characteristic of the study sample (N=390)

Characteristic	Median (IQR) or n (%)
Age (years)	39 (32,44)
Years in sex work	9 (5, 15)
Less than 8 years of education	164 (42.1)
Ever married	302 (77.4)
Workplace	
Bar/restaurant	229 (58.7)
Nightclub	94 (24.1)
Home/other	67 (17.2)
Has an index partner[1]	311 (80.0)
Any IPV in the past year	62 (15.9)
Any emotional IPV in the past year	45 (11.5)
Any physical IPV in the past year	44 (11.3)
Any sexual IPV in the past year	15 (3.4)
Any controlling behaviors by the index partner	186 (47.7)
Casual partner in the past 3 months	178 (45.6)
Number of previous live births (n=388)	2 (1,3)
Pregnant by urine β-hcg test (n=389)	1 (0.3)
Fertility desire (n=389)[2]	98 (25.2)
Within 9 months of last delivery	5 (1.3)
Menopausal (n=387)[3]	60 (15.5)
Contraceptive use by method duration (n=389)	
None or condoms only	272 (69.7)
DMPA or OCP	75 (19.3)

IUD,TL, Norplant, hysterectomy, other	42 (10.8)
Partner attitude about pregnancy (n=304)[4]	
Excited	170 (55.9)
Neutral	80 (26.3)
Upset	54 (17.8)
Depressive symptoms by PHQ-9 (n=388)	
Minimal (0-4)	279 (71.5)
Mild (5-9)	84 (21.5)
Mod/Severe (10 or higher)	27 (6.9)
Alcohol use problems by AUDIT	
Non drinkers	194 (49.9)
Minimal (1-6)	113 (29.0)
Moderate (7-15)	69 (17.7)
Severe/possible AUD (16 or higher)	14 (3.6)
Sexual behavior in the past 7 days	
Unprotected sex (n=389)	30 (7.7)
No sex (n=386)	155 (39.7)
100% condom use (n=234)[5]	204 (87.2)
Number of sex acts (n=234)[5]	2 (1,3)
≥2 sexual partners (n=234)	115 (49.2)
Disclosed HIV status to anyone in the past (n=388)	248 (64.0)
Disclosed to a boyfriend[6]	53 (13.6)
Disclosed to a husband[6]	24 (6.2)
Any sexual abuse by someone *other than* the index partner, ever (n=389)	62 (15.9)

Any sexual abuse by someone *other than* the index partner in the past 12 months (n=389)	33 (8.5)
Any physical abuse by someone *other than* the index partner, ever	135 (34.6)
Any physical abuse by someone *other than* the index partner in past 12 months (n=389)	30 (7.7)
CD4 count cells/ml[3] (n=389)	459 (333, 630)
WHO Stage 3 or 4 (n=376)	109 (29.0)
On ART[7] (n=389)	236 (60.5)
Laboratory-confirmed STI (n=383)	51 (13.3)

AUDIT, Alcohol Use Disorders Identification Test; CT, Chlamydia trachomatis; DMPA, Depot Medroxyprogesterone Acetate; IPV, intimate partner violence; IUD, intrauterine device; OCP, oral contraceptive pills; PHQ-9, Patient Health Questionnaire 9; TL, tubal ligation.

1. 'Index' partner refers to a woman's current regular partner who was not a client or casual partner. All IPV questions refer to acts committed by this index partner.
2. Asked of women who were not pregnant at that visit.
3. Menopausal status is defined as being over 40 years and not currently pregnant or on hormonal contraception (i.e. DMPA), who has not had menses for at least 12 months.
4. Asked of women who reported an index partner.
5. Restricted to visits where women reported at least 1 sex act in the past week.
6. This question did not refer specifically to the index partner.
7. ART use was determined by clinic records or, by self-report if the woman had not initiated ART at our research clinic at the time of enrollment. At enrollment, 121/236 (51.3%) who reported taking ART were doing so at our research clinic.

Table 4. Univariate and multivariate associations between IPV in the past year, sexual risk behaviors, and detection of PSA in vaginal secretions

Outcome	Visits IPV exposed	Visits IPV unexposed	RR (95% CI)[¥]	p-value	aRR (95% CI)[§]	p-value
Unprotected sex in the past week	146/863 (16.9)	290/4,071 (7.1)	2.37 (1.65, 3.42)	< 0.001	1.91 (1.32, 2.78)	0.001
Semen detection by PSA[1]	94/387 (24.3)	265/1,837 (14.6)	1.67 (1.26, 2.21)	< 0.001	1.54 (1.17, 2.04)	0.002
% No sex in the past week	270/863 (31.3)	2,174/4,071 (53.4)	0.59 (0.47, 0.74)	< 0.001	0.67 (0.54, 0.83)	< 0.001
100% condom use in the past week[2]	447/593 (75.4)	1,607/1,897 (84.7)	0.89 (0.81, 0.98)	0.02	0.90 (0.82, 0.99)	0.03
≥3 sex acts in the past week [2]	208/593 (35.1)	624/1,897 (32.9)	1.07 (0.82, 1.39)	0.64	1.00 (0.79, 1.26)	0.98
≥2 sexual partners in the past week[2]	233/593 (39.3)	755/1,897 (39.8)	0.99 (0.75, 1.30)	0.93	0.96 (0.76, 1.21)	0.74
Any STI	34/387 (8.8)	57/1,809 (8.7)	1.01 (0.64, 1.60)	0.96	0.88 (0.57, 1.37)	0.57

IPV, intimate partner violence; PSA, prostate specific antigen test; RR, Relative Risk; aRR, adjusted Relative Risk; STI, sexually transmitted infection (positive for *Chlamydia trachomatis, Neisseria gonorrhoeae*; or *Trichomonas vaginalis)*

[¥] RRs estimated using generalized estimating equations with log link, independence correlation structure and robust standard errors.

[§] Multivariate models were adjusted for age (restricted cubic spline), baseline alcohol use level, and lifetime history of sexual violence since age 15 by someone other than the index partner (enrollment value). The adjusted model in the primary analysis included 389 women and 4,933 visits. The adjusted model for the secondary analysis included data from 389 women and 2,206 examination visits.

[1.] Restricted to exam visits when genital samples were collected.

[2.] Restricted to 2,490 visits where women reported being sexually active during the past week.

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CHAPTER 4:

A prospective study of intimate partner violence as a risk factor for detectable plasma viral load in HIV-positive female sex workers in Mombasa, Kenya

A prospective study of intimate partner violence as a risk factor for detectable plasma viral load in HIV-positive female sex workers in Mombasa, Kenya

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Abstract

We conducted a prospective cohort study in Mombasa, Kenya to test the hypothesis that intimate partner violence (IPV) in the last year would be associated with increased risk of detectable plasma viral load in women who were HIV-positive, on antiretroviral therapy (ART), and reported transactional sex. Blood samples for viral load testing were collected every 6 months. Any IPV in the past year was defined as ≥1 act of physical, sexual, or emotional violence by the current or most recent emotional partner (index partner). Late refill in the past month was defined as >48 hours late for a scheduled monthly refill. Unexpectedly, recent IPV was associated with a significantly lower risk of detectable plasma viral load (≥180 copies/milliliter) (adjusted relative risk (aRR) 0.21, 95% CI 0.05- 0.86) after adjusting for age and education. We did not find that IPV was associated with significantly higher risk of late refills (aRR 0.84, 95% CI 0.61-1.14). We believe that the observed association between IPV in the last year and lower risk of detectable viral load is the result of unmeasured factors including women's resilience, nature of her relationship with her partner, and social support. Our results highlight the complexity of the relationship between IPV, ART adherence, and viral load in this population. Further research to explore correlates of viral suppression could reveal new intervention targets to improve ART outcomes and well-being in African women who engage in transactional sex.

Introduction

The goal of ART is to achieve sustained plasma viral load suppression to reduce the risk of drug resistance [131], disease progression [25], and secondary transmission [132]. High adherence (>80%) is essential to optimize ART for treatment and prevention [133]. In Africa, which accounts for an estimated 71.0% of the 35 million HIV infections worldwide, over 7.6 million adults are on ART [6]. However, gaps remain in the 'HIV care cascade' from HIV testing to retention in care [6]. In 2012, one quarter of African adults on ART were not virally suppressed [6].

There are many structural, interpersonal, and individual barriers to adherence, including transportation costs [56], stigma [134], low social support [135], poor mental health [57], and alcohol use [136]. Intimate partner violence (IPV), including by physical, sexual, or emotional violence by a boyfriend or husband is common in African women [2] and is associated with negative outcomes including HIV infection [4, 5], poor self-rated health [84], and psychiatric conditions [64]. Studies conducted primarily in general-population HIV-positive women in high-income settings indicate that IPV may be associated with lower adherence and detectable viral load [61, 66, 84]. However, some studies in these same populations have not found an association between IPV and poor adherence or unsuppressed viral load [63, 67]. Most prior studies of the relationship between IPV and ART adherence and viral load have been cross-sectional. As such, IPV may be a potentially modifiable risk factor for HIV treatment outcomes that could be targeted in future interventions for African women.

Limitations to existing literature on IPV and poor adherence include the lack of epidemiologic studies from Africa, lack of prospective data, and lack of focus on key populations at high risk of HIV transmission, specifically female sex workers (FSWs) [108]. To address these research gaps, we conducted a prospective cohort study to evaluate the association between

recent IPV, detectable viral load, and poor ART adherence in high-risk women in Mombasa, Kenya.

Methods

We conducted a longitudinal analysis of data from women enrolled in an ongoing cohort study. Participants were age 16 or older, laboratory-confirmed HIV-positive, eligible for ART according to Kenyan National Guidelines in 2012 (CD4 ≤350 cells/mm^3 or World Health Organization (WHO) stage 3 or 4 or TB co-infection). All participants were FSWs, defined at their screening visit on the basis of reporting exchanging sex for cash or in-kind payment. Thereafter, women could continue in the cohort regardless of whether they reported ongoing transactional sex. At enrollment, women completed a standardized face-to-face interview in their preferred language (Kiswahili or English) with a trained Kenyan study nurse to collect health and behavioral data. A study clinician conducted a physical examination including a speculum-assisted pelvic examination for collection of genital samples. Women returned for monthly follow-up visits for behavioral data collection and ART refill. Every three months, a genital examination was performed, and CD4 testing was repeated. Blood samples were collected every six months for plasma viral load testing (Hologic/Gen Probe San Diego, CA). Participants received free outpatient care at our research clinic, including risk reduction education, antiretroviral therapy (ART) according to Kenyan National Guidelines, and STI screening and treatment. Women who reported experiencing violence were offered on-site counseling or referral. This study was approved by the ethics committees of Kenyatta National Hospital and the University of Washington. All participants provided written informed consent.

The primary outcome was detectable plasma viral load, defined as HIV ribonucleic acid (HIV RNA) at or above 180 copies per milliliter (c/mL) by Hologic/Gen-Probe second generation assay. This cut-point was higher than the lower limit of detection used for this assay (<30 c/mL)

because some 100 mL samples had to be diluted 6-fold to a final volume of 600 mls before testing. The secondary outcome was late refill in the past month, defined as >48 hours late for a scheduled refill based on our pharmacy data ('late refill', hereafter). Late refill was computed based on the total doses dispensed at the last refill visit and the total days since that visit. If total days without any doses exceeded two, that visit was classified as late refill. We have previously shown that late refill using this definition is a strong predictor of detectable plasma viral load, genotypic resistance to ART, and HIV shedding in the genital secretions in our cohort [137, 138].

We also evaluated adherence in the past 30 days by using a validated single-item self-rating scale [139]. The self-rating scale asked "rate your adherence in the last month" with response categories "very poor, poor, fair, good, very good, and excellent." We created a binary outcome of less than "very good or excellent" which corresponded to <80% adherence in a prior validation study conducted in a clinic sample of HIV-positive adults in the US [139].

The primary exposure was any IPV, defined as responding yes to at least one of 13 questions about acts of IPV in the past 12 months committed by that participant's current or most recent emotional partner (index partner). Questions were adapted from the WHO survey on violence against women, a standardized instrument with good internal consistency [32]. All women were asked whether they had an emotional partner, such as a boyfriend or husband, whom they did not consider to be a client or a casual partner. Any woman without an emotional partner at the time of the interview was asked about her most recent emotional partner. This man was identified as the 'index partner'. Only participants with an index partner were asked the IPV questions at that visit. If a participant reported ever experiencing a specific act of IPV by her index partner, she was then asked whether that act occurred in the past 12 months. There were six questions on physical violence, four on emotional violence, and three on sexual violence [32]. We created a binary variable for 'any severe IPV,' defined as experiencing any type of

sexual IPV or at least one of the following types of physical IPV: hit, kicked, choked, approached with a weapon, based on a prior study that used the WHO tool [73]. Exposure data were updated annually. Women with no index partner were classified as having no IPV at that visit and all subsequent visits until the next annual IPV assessment. All women were asked about history of sexual or physical violence since age 15 by someone other than their index partner (enrollment, annually) [32]. Sexual violence was defined as being forced to have sex or perform a sexual act. Physical violence was defined as beaten or physically mistreated.

Covariate data were collected at different intervals depending on the measure. Socio-demographic characteristics included age (enrollment); marital status (ever married; annually); years in sex work (<5, 5-9, ≥10; enrollment); highest education level (<8 years versus 8 or more; enrollment); and workplace (bar, nightclub, home/other; enrollment). Reproductive characteristics included use of modern contraceptives (none/condoms only, hormonal contraceptive pills, hormonal injections, intrauterine device, tubal ligation, hysterectomy; monthly); fertility desire (quarterly); laboratory-confirmed pregnancy (quarterly); postpartum status (≤ nine months since last birth); post-menopausal status (clinical algorithm; annually). Partner data included questions on any casual partners in the last three months (quarterly) and the index partner's attitude about a future pregnancy (excited, neutral, upset; annually). Controlling behaviors by the index partner were defined as responding yes to at least one of seven statements (e.g. he acts suspicious; he requires permission to get health care; annually) [32].

Depressive symptoms in the past two weeks were assessed by the Patient Health Questionnaire-9 (PHQ-9) (6-monthly) [117]. Scores were categorized as 0-4 (minimal), 5-9 (mild), 10 or higher (moderate or severe; consistent with a major depressive disorder). Alcohol use in the past year was assessed by alcohol use disorders identification test (AUDIT) (annually) [81]. Scores were categorized as non-drinkers (zero), minimal (1-6), moderate (7-15),

and severe problem or possible alcohol use disorder (AUD) (≥16) [81]. Disclosure of HIV status was assessed by asking whether women had ever shared their results with someone, and if so, whom (e.g. sibling, friend, health worker; 6-monthly) [118]. Testing for STIs including *Neisseria gonorrhoeae, Chlamydia trachomatis,* or *Trichomonas vaginalis*, was performed quarterly by nucleic acid amplification test (Aptima; Hologic/Gen Probe, San Diego, CA), cervical gram stain and wet preparation. CD4 testing was performed using an automated method (FACScount, Becton Dickinson, Forest Lakes, NJ).

Statistical analysis

Women who enrolled between October 12, 2012 and September 30, 2014 and were receiving ART at our research clinic contributed data to this analysis. Follow-up visits were included until administrative censoring. Exposure status was carried forward for all visits until the next IPV assessment. This approach aligns with previous studies that suggest that recent IPV is a strong predictor of recurrent IPV [140] and that past exposure to IPV may affect current health outcomes [140]. Covariate values collected less than monthly were filled forward until the next assessment.

For the primary analysis, we tested the hypothesis that IPV in the past year was associated with increased risk of detectable plasma viral load (≥180 copies/ml). This analysis was restricted to visits when women were taking ART at our pharmacy and had viral load data collected. Each woman could contribute multiple outcomes to the analysis. Generalized estimating equations (GEE) with a log link, independence working correlation structure, and robust standard errors were used to generate relative risks (RR) and 95% confidence intervals (CI) [120]. We included age (restricted cubic spline) and education level (<8 years versus 8 or more) as *a priori* confounding factors in our multivariate models. Additional covariates were considered for inclusion in multivariate models if they were plausible confounding factors based

on prior studies and causal diagrams. These included number of births, years in sex work, workplace, AUDIT score (enrollment value), PHQ-9 score (enrollment value), controlling behaviors by the index partner, and HIV status disclosure. Manual forward-stepwise model building was used by entering variables by decreasing effect size with respect to plasma viral load detection. Covariates that changed the primary effect estimate by ≥10% were retained in the final model [121]. We also evaluated whether the associations between IPV in the past year and detectable viral load differed after excluding visits during women's first six months on ART, when viral load may have been detectable, but declining, in response to ART initiation.

Because we hypothesized that IPV in the past year would be associated with detectable plasma viral load because of the effect of IPV on ART adherence, we conducted a separate analysis of the association between IPV in the past year and two measures of adherence, late ART refill (>48 hours) and poor adherence by self-rating scale (<80%). These analyses included the same covariates in the final multivariate model as our primary analysis.

We evaluated whether the association between IPV and detectable plasma viral load differed between women who remained in follow-up compared to those who had not returned for at least 6 months at the time of censoring date [141]. Missing data for viral load was <10% and for all other variables <2%. All analyses were conducted in STATA Version 13.0.

Results

Overall, 214 women contributed 3,189 follow-up visits for inclusion in the analyses. Their baseline characteristics are presented in Table 1. The median age was 40 years (interquartile range (IQR) 36-45)). Median time in transactional sex was 11 years (IQR 8-16). Most women (146, 68.2%) had disclosed their HIV status to another person, most often to a sibling (57, 26.6%), health worker outside our clinic (51, 23.8%), or friend (44, 20.6%). Fewer had ever disclosed to a boyfriend (31, 14.6%) or husband (14, 6.6%). Most women were divorced or

widowed (146, 68.2%), and were in relationships with other men whom they identified as their index partners (164, 76.6%). Median time on ART was 3.8 years (IQR 1.3-6.6).

Longitudinal association between IPV in the past year and detectable plasma viral load

The primary analysis was restricted to 195 women who contributed 558 viral load visits and 189 person-years of follow-up. The women contributed a median of 3 follow-up visits with plasma viral load data to this analysis (IQR 2-4). Twenty-three women (11.8%) were lost to follow-up, defined as the last study visit at least six months from the time of administrative censoring. Of 558 visits included in this analysis, 85 (15.2%) were exposed to IPV in the past year. There were 68 (12.2%) visits with detectable viral load. The median plasma viral load at visits with detectable viral load was 10,799 copies/ml ((IQR) 1,712-91,763).

Unexpectedly, there was a lower prevalence of detectable plasma viral load at visits with IPV in the past year compared to visits where women did not report IPV in the past year (3/85, 3.7% versus 65/473, 13.7%; RR 0.26, 95% CI 0.06-1.10). This association became statistically significant after adjusting for age and education (adjusted RR (aRR) 0.21, 95% CI 0.05-0.86). Results were similar after excluding visits contributed by women who reported that they had no index partner (aRR 0.21, 95% CI 0.05-0.80). Having an index partner (regardless of IPV status) was not significantly associated with detectable viral load (aRR 0.84, 95% CI 0.43-1.64).

Longitudinal association between IPV in the past year and poor ART adherence

A total of 214 women contributed a median of 21 ((IQR) 14-24) monthly follow-up visits to this analysis. Of 3,189 included visits, late ART refill occurred at 560 (17.6%) visits and exposure to IPV in the past year occurred at 517 (16.2%). Reporting IPV in the past 12 months was not associated with significantly increased risk of late refill (81/517, 15.7% verses 479/2,672, 18.0%; RR 0.87, 95% CI 0.65-1.18). The association was similar after adjusting for age and education (aRR 0.84, 95% CI 0.61-1.14) (Table 2). Recent IPV was not associated with a significantly

higher risk of <80% adherence (<"very good/excellent") by self-rating scale (5/530, 1.0% versus 13/2,661, 0.50%; aRR 1.58, 95% CI 0.52-4.74).

Association between ART adherence measures and plasma viral load

Late refill was associated with a significantly higher risk of detectable plasma viral load (RR 95% CI 3.01, 1.67-5.47). Similarly, although <80% adherence by self-rating scale was observed at only 18/3,191 (0.6%) visits, this marker for poor adherence was also associated with a significantly increased risk of detectable plasma viral load (RR 4.32, 95% CI 1.03-18.01).

Discussion

In this prospective cohort study of Kenyan FSWs on ART, we did not find evidence to support our hypothesis that IPV in the past year was associated with a higher risk of detectable plasma viral load. Surprisingly, IPV in the last year was associated with a significantly lower risk of detectable plasma viral load. Recent IPV was not significantly associated with ART adherence measured by refill timing or by self-rating scale.

Our results contrast with studies that have reported that recent IPV was associated with significantly greater likelihood of detectable viral load in women on ART [30, 31, 63, 66]. These studies were conducted in high-income countries with general-population samples of HIV-positive women. For example, a cross-sectional study of HIV-positive women of color in the US reported that lifetime IPV was associated with a 38% lower likelihood of viral load suppression [66]. That study included women who were not engaged in HIV care, and were likely to have a combination of risk factors related to barriers to care engagement and treatment initiation. In our study, all women had initiated ART and many had been on treatment for several years. Furthermore, the cultural, economic, and epidemiologic context of these Kenyan FSWs are likely distinct from those of women in other settings [142].

Overall, we observed a lower proportion of women with poor adherence and detectable viral load compared to studies in US women [30, 59, 84] and to a study of FSWs in Benin [143]. In our population, the 15% prevalence of IPV in the past year was also lower than estimates of 25-50% reported in the US in studies of HIV-positive women of color [30, 63]. These differences could be due to actual differences in risk for IPV or to differences in reporting. Different studies have used a variety of measures for recent IPV and ART adherence, so comparisons between studies should be made with caution. Nonetheless, our finding that IPV was associated with a significantly lower risk of detectable plasma viral load in this population of FSWs is distinctly different from other published studies of this association.

We and others have hypothesized that IPV would be associated with a higher risk of detectable viral load because of detrimental effects of IPV on ART adherence [30, 59, 63, 66, 84]. Specifically, we felt that IPV could lead to poor adherence through psychological and behavioral pathways including stress and depression [63], poor coping [65], and substance use problems [64]. Partners might also interfere with women's ability to take ART on a day-to-day basis or to return to the clinic for medication refills [95]. Given our unexpected findings, we believe these mechanisms may be overly simplistic, and fail to capture key personal or contextual features that have a major impact on adherence.

In an effort to explain the observed association between exposure to IPV in the last year and lower risk of detectable viral load in our population, we have developed a number of new hypotheses that are supported with data from our parallel qualitative study of IPV (Chapter 4 Addendum). One possibility is that the women who reported IPV were also more resilient, defined as the capacity to maintain or regain mental health despite adversity [144]. As such, they may have had better coping skills to handle life stress and be more motivated to stay adherent to ART compared to women who did not report IPV. A cross-sectional study of HIV-positive US women on ART found that higher resilience was associated with a better adherence

in women who had experienced recent IPV, but not in women without recent IPV [145]. In our qualitative study of women who reported IPV, a key theme was women's strong commitment to take their HIV medications regardless of partner violence. A second explanation is that women who were experiencing of IPV had more health needs and were more motivated to get help from our clinic and/or from friends. This additional support helped them to adhere to their HIV medication. A third possible explanation for our observation is that reporting IPV may be a marker for long-term partnerships [44]. Positive features of long-term relationships including emotional bonds, shared resources, and children may have helped to reinforce adherence. In our qualitative study, many women highlighted the importance of love and emotional connections with their regular partners, despite episodes of violence. A fourth explanation for our findings is that the association between IPV and detectable viral load may have been due to chance (type-1 error). We will repeat our analysis using a second batch of plasma viral load data that were collected at different study visits to determine whether these results are reproducible. Given these combined findings, it seems likely that our original hypothesis, that IPV would be associated with poor adherence leading to treatment failure, was incorrect.

We did not find that IPV in the past year was associated with a higher risk of late refill. This result was consistent with studies conducted in HIV-positive women in the US that have not reported an association between recent IPV and poor adherence [63, 146]. It is noteworthy that we did not observe an association between recent IPV and lower risk of poor adherence, given the results of the association between recent IPV and plasma viral load. One reason for this difference in the point estimates could be that late refill is only one predictor of poor adherence, which is a complex phenomenon [147]. Using measures such as plasma drug levels or unannounced pill counts may have given different results. A second possible explanation is that adherence was no longer a strong predictor of viral suppression in women who had developed drug resistance. We do not have drug resistance data to evaluate this possibility directly.

The study had several strengths. The longitudinal design allowed us to better understand the temporal sequence between exposure and outcomes. This is important because starting ART or being on treatment may also trigger episodes of IPV [113]. We used an adapted version of a standardized WHO instrument to measure IPV, which facilitates comparability between studies. Our use of time-updated data on IPV helped to reduce the possibility of incorrectly classifying women's exposure status over time. Finally, we conducted several sensitivity analyses, demonstrating that the observed association between recent IPV and plasma viral load was robust across a range of approaches to measurement and classification of IPV, as well as selection of the analysis population.

Our unexpected findings demonstrate that the major limitation of this study was our lack of data on women's resilience and perceptions about IPV and on relationship context with their index partners, including duration, satisfaction, or perceived support [148]. Fortunately, our parallel qualitative study provides some insight into the relationship dynamics that may help to explain our results (Chapter 4 Addendum) [33]. An additional limitation of this study is the potential for underreporting of IPV, given the sensitivity of discussing this topic. We tried to minimize underreporting by using trained Kenyan study staff to conduct the interviews, and by asking behaviorally specific questions to facilitate disclosure [32]. Finally, our study population consisted of HIV-positive Kenyan women, all of whom reported transactional sex at screening. In addition, all of these women were on ART at our research clinic. Conditions at our research clinic, including no cost medical care, transport reimbursements, and counseling, were such that participants in this study may have been more likely to be adherent. Rather than illustrating generalizability to other populations, we feel that our findings emphasize that the relationship between IPV, ART adherence and viral load and is likely to be closely tied to context. Multiple studies from diverse populations and locations will be essential to inform this field.

Conclusion:

Intimate partner violence is a complex human rights problem that has been associated with many negative physical and psychological health consequences. Achieving a 50% reduction in the global prevalence of GBV in the next 30 years will require sustained commitment to reducing IPV [149]. In this context, expanding targeted screening and evidence-based programs to prevent or reduce IPV and its negative consequences are an essential part of women's health care in general. Our results caution against assertions that addressing IPV alone can be expected to improve viral load suppression in this population of HIV-positive FSWs. Further research on resilience, relationship satisfaction, and social support may reveal novel factors that could be targeted to improve ART outcomes in this key population.

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Table 5. Baseline characteristics of the participants (N=214)[¥]

	IQR or n (%)
Age	40 (36-45)
Highest education (less than 8 years)	89 (41.6)
Years in sex work (n=212)	11 (8-17)
Workplace	
Bar/Restaurant	147 (68.7)
Nightclub	30 (14.0)
Home/Other	37 (17.3)
Ever married	168 (78.5)
Has an index partner[1]	164 (76.6)
Casual partner in the last 3 months	71 (33.2)
Regular partner in the last 3 months (n=210)	103 (48.1)
Ever controlling behaviors by the index partner[2]	88 (41.1)
Number of previous births (n=212)	2 (1-3)
Pregnant by urine β-hcg test (n=211)	1 (0.5)
Fertility desire[3]	44 (20.6)
Within 9 months of last delivery	2 (0.9)
Menopausal[4]	36 (16.8)
Contraceptive use by method duration	
None, condoms only, or other	157 (73.4)
DMPA or OCP	34 (15.9)
IUD,TL, Norplant, hysterectomy	23 (10.8)
Partner attitude about pregnancy (n=160)[3]	
Excited	98 (61.3)
Neutral	36 (22.5)
Upset	26 (16.3)

Depressive symptoms by PHQ-9	
Minimal (0-4)	170 (79.4)
Mild (5-9)	36 (16.8)
Mod/Severe (10 or higher)	8 (3.7)
Alcohol use problems by AUDIT	
Non-drinkers	137 (64.3)
Minimal (1-6)	46 (21.5)
Moderate (7-15)	28 (13.1)
Severe/possible AUD (16 or higher)	3 (1.4)
Unprotected sex[4]	16 (7.5)
No sex[4]	104 (48.6)
100% condom use (n=110)[4,5]	90 (83.3)
Number of sex acts (n=110)[4,5]	2 (1,3)
Has 2 or more sex partners (n=110) [4,5]	36 (32.7)
Disclosed HIV status to anyone in the past	146 (68.2)
Ever disclosed to a boyfriend or husband	43 (20.1)
Ever had sexual violence by another person [6]	29 (13.6)
In the past 12 months [6]	14 (6.7)
Ever had physical violence by another person[6]	77 (36.0)
In the past 12 months[6]	13 (6.1)
CD4 count (n=212)	430 (326-586)
Any GC, CT, or TV by APTIMA (n=208)	14 (6.6)
HIV clinical stage (3 or 4) (n=205)	77 (37.6)
Time on ART (years)[7]	3.8 (1.3- 6.6)

ART, antiretroviral therapy ; AUDIT, Alcohol Use Disorders Identification Test; CT, Chlamydia trachomatis; DMPA, Depot Medroxyprogesterone Acetate; GC, Neisseria gonorrhoeae; IPV, intimate partner violence; IQR, interquartile range; OCP, oral contraceptive pills; PHQ-9, Patient Health Questionnaire 9; TV, Trichomonas vaginalis.

¥ Baseline refers to the visit date on or after initiating ART at our research clinic

[1.] 'Index' partner refers to a woman's current regular partner who was not a client. If she did not have a current regular partner, she was asked to refer to her most recent regular partner. All IPV questions refer to acts committed by this index partner.
[2.] Asked of women who reported an index partner at enrollment.
[3.] Asked of women who were not currently pregnant at that visit and reported an index partner.
[4.] Menopausal status is defined as being over 40 years and not currently pregnant or on hormonal contraception (i.e. DMPA), who has not had menses for at least 12 months.
[5.] Restricted to visits where women reported at least 1 sex act in the past week.
[6.] These questions refer to someone other than the index partner.
[7.] Based on self-report or pharmacy records at enrollment.

Table 6. Univariate and multivariate associations between IPV in the past year and detectable PVL, late ART refill, and self-rated adherence

Outcome	Visits IPV exposed	Visits IPV unexposed	RR (95% CI)[¥]	p-value	aRR (95% CI)[±]	p-value
Detectable plasma viral load[1]	3/85 (3.5)	65/473 (13.7)	0.26 (0.06, 1.10)	0.07	0.21 (0.05, 0.86)	0.03
Late refill (>48 hours)[2]	81/517 (15.7)	479/2,672 (18.0)	0.87 (0.65, 1.18)	0.38	0.84 (0.61, 1.14)	0.26
< 80% by self-rating scale[3]	5/530 (1.0)	13/2,661 (0.50)	1.93 (0.68, 5.47)	0.22	1.58 (0.52, 4.74)	0.42

ART, antiretroviral adherence; IPV, intimate partner violence; PVL, plasma viral load; RR, Relative Risk; aRR, adjusted Relative Risk
1. >=180 viral copies per milliliter. The adjusted model and included 195 women and 558 visits when viral load testing was performed.
2. The adjusted model included 214 women and 3,189 visits when women were taking ART.
3. The adjusted model included 213 women and 3,191 visits when women were taking ART.
¥ RRs estimated using generalized estimating equations with log link, independence correlation structure and robust standard errors.
± Multivariate models adjusted for age (restricted cubic spline) and education (<8 vs. 8 or more years)

CHAPTER 4 Addendum:

Adaptive strategies of HIV-positive female sex workers in Mombasa, Kenya who experience intimate partner violence

Introduction

Violence against FSWs in Africa has gained recent attention in part because violence may increase HIV acquisition and transmission risk and compromise targeted HIV prevention strategies [1, 19]. Most of this work has focused on violence by clients, police and other men. Because new evidence suggests that many FSWs also have emotional partners, and it is important to understand relationship dynamics in these parterships, why IPV may occur in these relationships, and the ways in which experiencing IPV may relate to sexual risk behaviors and ART adherence. Qualitative research from the US suggests that many women who experience IPV choose to remain in violent relationships because of positive features of the relationship, including companionship, affection, financial security, or shared children [148, 150]. Some women may take active steps to change how they interact with their partner to reduce or resolve relationship conflict [151]. In a qualitative study in women in the US who were in abusive relationships and who were on methadone treatment, many women reported that love and companionship were the main reasons to stay with their abusive partners [148]. There is a lack of qualitative research on IPV in high-risk HIV-positive women in African settings, highlighting the need for investigation into their coping in these relationships. The objective of this qualitative study was to explore beliefs, experiences, and adaptive strategies of HIV-positive female sex workers (FSWs) in Mombasa, Kenya who reported experiencing recent IPV.

Methods

We conducted a qualitative study that consisted of 11 in-depth interviews and two focus group discussions (FGD) (6 women per group) to explore beliefs and norms about IPV in high-risk HIV-positive women. All participants in the qualitative study were recruited from the Lifecourse Observational Cohort Study, and reported experiencing IPV at the time of enrollment in that study. Topics covered in the interviews and FGDs included reasons for seeking the partnerships with the violent partner, beliefs about and experiences of IPV, strategies they use

to cope with IPV in their relationships, and the influence of IPV on their condom use and ART adherence. All data collection was performed by a trained Kenyan qualitative researcher. All interviews and FGDs were conducted in Kiswahili and were tape recorded. The audio tapes were later transcribed in Kiswahili and translated into English. Two researchers (GW and KW) developed an initial codebook informed by the topic guide and research aims. The codebook was refined throughout the coding process as the researchers reviewed and discussed the transcripts. The two researchers separately coded and reviewed all transcripts. A behavioral expert (JS) provided an independent review of the initial codes and key themes. In this dissertation, we focus on key themes and illustrative quotes from the in-depth interviews that are most relevant to the interpretation of our results in Chapter 4.

Summary of the qualitative study participants (N=11)

The average age of the women who completed the in-depth interviews was 36 years old, and all of the women had at least one child. All of the women reported having a primary emotional partner whom they referred to as their '*mzee'* ('mm-zay,' meaning 'wise old man' or boyfriend in Kiswahili), who was also the man identified as having committed at least one act of IPV ('index partner'). The averageduration of these relationships was 5 years, with a range of 1 to 10 years. Women described *mzees* as primary sexual partners who were different from former husbands, casual partners, or clients. Some women referred to themselves as the 'woman on the side' (*mpango wa kando* meaning 'side arrangement') if the man was married to another woman. Some participants lived with their *mzees*, while others did not. Some women also had had children with their *mzees.* One woman described this dynamic: *"He is not my husband. He is just someone who helps me. I even had my first child with him. No I don't live with him. It's just helping me out in case of anything. He has his family. It's like I'm the 'mpango wa kando, yeah.'".*

Patterns of IPV and comparison with violence by clients

Women described a variety of experiences of IPV, including insults and belittling comments, arguments, beatings sometimes leading to hospitalization, and sexual coercion. Women described episodes of IPV that were situation specific rather than a constant feature of their relationships. Several women described that they would be beaten when their *mzees* came home drunk or if she did not have money to buy food for the day. Violence was not always unilateral. In some cases, women revealed that they would start arguments, fight back, or 'chase him away,' as illustrated by quotes 10 and 11 (Table 7). These findings highlight the importance of understanding not only whether a specific act of IPV occurred, but the context in which the violence occurred.

Women described help that they sought for IPV. In general, women were reluctant to get help from formal sources, such as police. The most common reasons given were the belief that the police were ineffective or would try to extract bribes from them and that IPV was a domestic problem that should be handled in private. Instead, many women sought help from a sibling or friend. This response is distinct from how women dealt with physical or sexual violence and threats from clients. With clients, women revealed that they were more empowered to refuse a transaction that could be dangerous, fight back, or call on the bar owner for help. As one woman explained about refusing clients who were potentially violent: *"My life is important, my life can't be bought in the shop. Money you can get at any point…"* This contrast in their perceptions and responses to violence by *mzees* compared to clients, suggests that IPV is distinct from non-partner GBV in this population.

Potential explanations for the unexpected association between recent IPV and detectable plasma viral load

In Chapter 4, we propose several possible explanations for the observed association between recent IPV and lower risk of undetectable viral load. Below, we relate these explanations to

relevant themes from the qualitative study (in-depth interviews). A list of key themes with illustrative quotes is presented in Table 7.

One possible explanation is greater resilience in women who reported experiencing IPV compared to those who did not report IPV. Resilience can be defined as being able to regain health despite adversity. This phenomenon is a dynamic process that encompasses positive coping skills, personal attributes like optimism, and contextual factors like social support. Several women described that initiating ART was a life changing decision that strengthened their commitment to do whatever it took to survive, regardless of an abusive partner. This sentiment is illustrated in one woman's quote: "*You know taking medication it's your decision to live. It is not that another person has decided that you live…"* The added stress of IPV may have made them more determined to do what they could, within the scope of their own control, to stay healthy, including adhering to ART. Other positive coping strategies that women cited were reducing their alcohol use, focusing on caring for her children, and keeping busy with housework.

A second possible explanation is that women who were experiencing IPV had more health needs and, therefore, were more motivated to get help. This may have indirectly reinforced their adherence to ART. Some women highlighted the encouragement to persevere and to take their medication that they received from attending support groups at our research clinic. The research clinic is recognized in the FSW community as a safe and non-judgmental space with high quality health care, and is the primary source of health care and psycho-social support for most women in this cohort. Women who reported IPV may have had greater baseline motivation to get help because of life stress, including HIV stigma, and IPV, compared to peers who did not report IPV.

A third possible explanation is that reporting IPV may have been an indicator of longer-term, more committed relationships, that may have helped them stay adherent to ART. All but one of the women said that they planned to remain with their partners primarily out of love,

financial support, and shared dependents. One woman's quote illustrates the importance of love in these relationships: *"I am still with him because I love him, because I wanted a family…"*. The high value that women placed on emotional support despite violence in these relationships is understandable. Many women explained that having a *mzees* enabled them to transition out of sex work to a longer-term romantic partnership. Positive features, including relationship satisfaction may have played an indirect role in reinforcing women's adherence. It is noteworthy that most participants had not disclosed their HIV status to their *mzees*. As such, most men were not actively supporting or interfering with taking their medication. One exception was a woman who had disclosed her HIV status to her *mzee*. She explained that he was, in fact, the one who would remind her to take her medication. These findings suggest that one of our proposed pathways linking IPV and poor adherence, through a partner's direct interference with her ability to take her HIV medication (Figure 4), was not a major theme in this study.

A final theme that emerged from the qualitative study that relates to these explanations is women's empowerment. Empowerment can be defined as increasing one's choices and ability to achieve a desired outcome. While we did not measure empowerment directly in our quantitative analyses, it was a prominent theme in the qualitative study in relation to the actions that women took to stay healthy and safe in their relationships. About half of the women gave specific examples of how they had prevented or de-escalated conflict. Quote 10 in illustrates how one woman was able to convince her *mzee* to stop beating her and to provide her more money for food to improve her health. The second example (Quote 11) is emblematic of several women who were able to insist on condoms with their *mzees* or refuse sex. In these cases, insisting on condom use was not a trigger for IPV. Accordingly, at least in some situations, reduced condom negotiation skills may not be one of the causal pathways linking exposure to IPV with higher rates of unprotected sex, as we had proposed in Chapter 3. These findings highlight the complexity of relationship violence and the importance of understanding acts within context.

In summary, the findings from our qualitative study enhance our interpretation of the results from the study of recent IPV and plasma viral load and illustrate the importance of qualitative research in studies of complex phenomenon such as IPV and HIV transmission risk. Taken together, the results of our multidisciplinary examination of the relationship between IPV and ART adherence call attention to the complexity of IPV in this population and the need to further examine contextual factors, including resilience, relationship satisfaction, and social support, that may be associated with viral suppression.

Table 7. Key themes and illustrative quotes from our parallel qualitative study on IPV

Key Theme	Illustrative quote
Resilience	*You know taking medication it's your decision to live. It is not that another person has decided that you live…* *- Age 39 (1)* *I just give myself strength…yeah sometimes I give myself morale, I don't think, I don't even drink anything…* *- Age 31 (2)* *I even wanted to kill myself (after learning her status), but I said now if I kill myself what about my children? I told myself let me pray to God that I live to look after my children.* *- Age 25 (3)*
Relationship satisfaction and love	*He takes care of me. Especially my children, he pays their school fees, my house rent, and rations. He takes care of me like his wife.* *- Age 40 (4)* *I am still with him because I love him, because I wanted a family* *- Age 38 (5)* *I have chased him away but he won't go (laughs). Yes, now what can I do? (laughs). When I chase him away, he starts saying 'Oh, I love you even with HIV/AIDS'* *He knows everything. He is even the one who reminds me to take my (HIV) medicine. But I think that is (his) fear of testing.* *- Age 32 (6)*

Getting help	*Even the learning I am doing here (at Ganjoni) is for me to help myself not you…For me, my life is important. Now when it gets to the time to swallow medication I won't be worried…* *- Age 39 (8)* *The counseling has helped us a lot…You hear from your peer talk 'ohh so that's what it's like.'…It (a support group) helps sometimes (because) you can have thoughts or have an illness that bothers you or your body feels tired or your body is itching. You can say maybe it's just me who feels like this but when you come there when you ask your peer they tell you they also feel like that, so you say ok maybe that's normal…* *- Age 49 (9)*
Empowerment	*I explained to him that wives should not be beaten and that if he beat me he would be arrested…At the clinic, they said I should eat properly, so if you love me, you should ensure that I eat properly. So these days he leaves me around 200 shillings. These days I cook beef or chicken…* *- Age 32 (10)* *I just see myself leaving him, even at times when he calls me I don't pick up…I will challenge him and talk to him and see what he has to say and if he refuses (to use a condom), then I will leave him..* *- Age 35 (11)*

CHAPTER 5: Conclusion

Chapter 2: Conclusion

We found that IPV in the past year was common in this population of HIV-positive FSWs in Coastal Kenya. Severe alcohol use problems and controlling behaviors by the index partner were associated with a significantly greater likelihood of reporting recent IPV. The prevalence of IPV in the past year was lower than in another study of HIV-negative FSWs in Kenya [22] and in studies of HIV-positive women in the US [30]. This variation between studies is likely due to differences in measurement of IPV, how the questions are administered, and study populations. Importantly, differences in the prevalence of IPV between studies of FSWs in Africa highlight the substantial heterogeneity of this population and the need to understand the local context of risk to inform comprehensive HIV interventions [29]. Our findings also suggest that alcohol use problems and controlling behaviors may be useful intervention targets within a more comprehensive HIV prevention and treatment strategy for this population. One limitation of this cross-sectional study was that we were unable to determine the temporal sequences between correlates and IPV. The relationship between IPV and alcohol use problems is likely bi-directional [38]. Nonetheless, this study suggests that IPV and alcohol use problems are related in this population. From a practical standpoint of delivering a future intervention, an integrated behavioral intervention that targets substance use, sexual risk behavior, and relationship violence, may be more effective than an intervention that focuses only on reducing a single risk factor. This approach is consistent with new research in high-income settings that focuses on the ‘syndemic’ of violence, substance use, and HIV/AIDS in hard-to-reach populations, rather than a single risk behavior [152]. In the Chapter 3 Conclusion, we describe an example of a promising ‘empowerment-based’ behavioral intervention that could be evaluated in this population.

Chapter 3: Conclusion

In this prospective cohort study, we found that IPV in the past year was associated with a significantly higher risk of unprotected sex by self-report and semen detection by PSA test. Reducing unprotected sex is an essential part of reducing the sexual risk of HIV transmission, unwanted pregnancy and STI acquisition. Because IPV is often recurrent, failure to address IPV may result in an excess of unprotected sex and other negative health impacts in HIV-positive FSWs. The combined findings from our observational studies in Chapter 2 and 3 provide further evidence that targeting IPV may strengthen comprehensive HIV treatment and prevention programs for this key population.

Several potentially effective biomedical (e.g. HIV care, including ART), behavioral (e.g. behavior change counseling), and structural (e.g. community-mobilization, stigma reduction) HIV prevention strategies for FSWs exist, although they have not been adequately scaled-up in Africa [29]. Examples of current approaches are presented in Table 8. Community-mobilization and peer-led education about HIV and rights have been shown to improve condom use with clients [107, 153]. It is unclear whether these strategies help women to reduce IPV and its potential negative effects, including unprotected sex. Designated HIV clinics and outreach programs for FSWs have shown to be effective at expanding access to HIV testing and ART, and controlling STIs. However, it is unclear whether and how women's broader psychosocial needs are addressed [154]. In Kenya, despite national guidelines to integrate GBV screening and counseling into HIV prevention and care programs, the health-sector response to GBV remains fragmented, focused on post-rape care, and tailored to women in the general population [155]. The Kenyan government has called for the rapid identification of evidence-

based HIV prevention and treatment interventions for key populations that also address GBV [8]. Integrating a GBV response into HIV prevention and treatment may be a feasible and efficient way to address both problems. New 'combination prevention' strategies for FSWs should build on existing biomedical, behavioral, and structural approaches to optimize individual and population health benefits [28, 29].

One promising behavioral strategy that has been extensively tested in South Africa and the US is a two-session 'woman-focused' behavioral intervention ('Women's Health CoOp, (WHC)) designed for substance-using women [42]. The WHC model has been shown to be efficacious at reducing the prevalence of substance use, unprotected sex, and IPV in trials in South Africa in HIV-negative and HIV-positive women [42, 53, 75]. The focus of the WHC intervention and other 'gender-based HIV prevention' interventions in Africa is empowerment, which means expanding one's ability and choices to achieve desired outcomes [48, 156]. According to this model, lack of empowerment underlies risky sexual behaviors, problem substance use, and relationship violence. The WHC intervention helps women to understand the linkages between lack of power and behavioral risk, develop risk assessments, and set goals, and take steps to reduce risks. The component that addresses IPV is adapted to the woman's situation, and may emphasize skills to improve the quality of the relationship (e.g. communication skills) or how to leave safely. This intervention can be delivered by trained lay health workers in an individual or group-format. Currently, an enhanced version of WHC called 'WHC-Plus' (WHC+) is being evaluated against standard of care in HIV testing and care programs in South Africa [157]. In Kenya, the WHC intervention could be tested in designated HIV clinics and outreach programs for FSWs in Mombasa and Nairobi (i.e. Ganjoni Health Centre and US Government President's Emergency Plan for AIDS Relief (PEPFAR)-funded Sex Worker Outpatient clinics). A potential next step is to conduct a mixed-methods study to adapt and evaluate the feasibility, acceptability, and preliminary effectiveness of the WHC/WHC+

model with Kenyan FSWs who are HIV-positive and HIV-negative. If feasible, acceptable, and effective at reducing IPV, high-risk alcohol use, and unprotected sex, a systematic approach to scaling up the intervention in more clinics could be considered..

Table 8. Examples of potential HIV prevention strategies for HIV-positive FSWs, adapted from Bekker et al., 2015 [29]

Type of intervention	Level	Studies conducted with FSWs	Outcome
Community empowerment: promotion of cohesion and leadership	Structural	Yes	Increased condom use with clients, skills to demand rights in the workplace
Rights-based advocacy	Structural	Yes	Improvements in workplace safety and access to health and legal services
Condom promotion in work venues	Structural	Yes	Increased condom use, skills to negotiate condoms with clients
Addressing GBV, and stigma in the work venue	Structural	Yes	Increased condom use, reduction in GBV, increase in reporting GBV by police and clients
HIV testing, linkage to care	Structural, behavior, biomedical	Yes	Knowledge of HIV status
Sex worker friendly clinics	Behavioral, biomedical	Yes	HIV testing, STI control
Community or health-clinic based peer-education	Behavioral	Yes	Increased condom use, skills to demand rights in the workplace
HIV care, ART	Behavioral, biomedical	Yes	Increased adherence, viral suppression
WHC- Plus	Structural, behavior, biomedical	Enrollment in 14 sites in South Africa is ongoing	Substance use, sexual risk behavior, and, in HIV-positive participants, ART adherence (secondary outcome)

Chapter 4 and Chapter 4 Addendum: Conclusion

Sustained viral suppression is the goal of ART and is essential to reduce the risk of disease progression, drug resistance, and secondary transmission [25]. The prospective cohort study presented in Chapter 4 was designed to understand whether reducing IPV would be a potential

approach to improve viral suppression by improving ART adherence. Our unexpected findings that IPV in the past year was associated with lower risk of detectable plasma viral load reveals a more complex relationship between IPV and HIV treatment outcomes. Our parallel qualitative study helped to contextualize this unexpected result, providing insights into both the positive and negative perceptions that women have about their relationships with their emotional partners who also commit acts of IPV [33]. Further research is needed to identify personal, relational, and social factors that may be associated with improved adherence and viral suppression in this key population. In the following paragraphs, we propose new research directions.

The first area for future research should be on women's *resilience* as a potential predictor of improved adherence and other positive health outcomes in this population [144]. In our qualitative study, women described their strong commitment to taking ART regardless of other stressors in their lives, including, concern for their children, and distress related to HIV stigma. These findings may be interpreted as evidence of resilience. The concept of resilience can be understood as a dynamic process that is a function of personal characteristics and contextual factors, such as optimism and family and friend support. Resilience has been used to explain variation in treatment or risk behaviors in people with histories of trauma or HIV-related stigma [158]. Example questions on a validated resilience scale (Connor and Davidson 2003) include 'when things look hopeless, I don't give up' and 'I know where to turn for help' (response categories range from 'never true' to 'almost always true') [159]. In African settings, there have been a few studies and at least one intervention to promote resilience in children affected by HIV [160, 161]. New studies on the relationship between resilience and HIV treatment outcomes in HIV-positive FSWs would substantially add to this emerging field. Coping is a related construct. Assessing women's positive and negative coping strategies as part of an overall assessment of resilience would enhance our understanding of resilience. Randomized trials in

HIV-positive adults in the US indicate that mental health interventions that target positive coping, social support, and stress reduction can improve adherence [162]. The concepts of resilience and positive coping are 'strengths-based' orientations to health and behavior [144]. A future behavioral intervention that focuses on leveraging women's strengths may be more acceptable to this population than one which emphasizes reducing risk.

A second area of research should examine the relationship context where unequal power and IPV occurs. While all the women included in our qualitative study reported yes to at least one act of IPV on the WHO survey, they revealed a range of beliefs and experiences about this aspect of their relationships. A limitation of the adapted WHO survey is that it only captured acts of IPV committed by the index partner. To gain a better understanding *IPV as a dynamic process* that occurs in the dyad, future studies should measure violence perpetration by both partners, and how IPV relates to relationships initiation, dissolution, and continuity. Other tools, such as the revised Conflicts Tactics Scale which measure these items directly, could be used alongside the adapted WHO survey [163]. Asking about IPV over a shorter recall period (past 3 or 6 months) and including more questions about the index partner, such as his other partners, HIV status, and alcohol use, would also enhance this work. One relevant research question would be the association between relationship change (initiation or dissolution), on ART adherence and viral suppression. Women's experiences are also shaped by their attitudes about gender roles and level of acceptance of IPV. Gender-based HIV prevention interventions in African settings focus on transforming women's and men's attitudes about gender roles and relationships as a way to reduce IPV and HIV risk behavior [164]. Accordingly, another relevant research question would be to examine whether women's level of acceptance of gender inequity and IPV is associated with higher risk of poor adherence or unprotected sex [165]. In the context of longitudinal research, it will be important to determine

an optimal set of questions on IPV timing, patterns, and gender norms to answer a research question while minimizing the data collection burden in this population.

A third area of research should explore the positive features of women's relationships with *mzees*, regardless of IPV status. For example, future studies should measure key domains of these relationships including satisfaction, emotional and financial dependence, alternatives to staying in a relationship, and level of commitment. These relationship factors could be examined as potential risk or protective factors for improved adherence, viral suppression, and other health outcomes in this population. In our qualitative study, an important reason to maintain these relationships, besides the emotional bond, was the financial support. Financial need is an undercurrent in these women's lives that likely influences their partnership choices [44]. Being in a long-term relationship may also be a marker for greater financial stability, which may help to improve ART adherence. Future studies should evaluate women's level of economic empowerment [166], whether it differs by relationship status, and its potential impact on HIV treatment outcomes. More information on relationship factors may help to identify positive features of emotional partnerships that could be targeted in future tailored HIV prevention strategies in this population.

A final contextual factor to examine further in this population is *social support* from family, friends, or *mzees.* Evidence from a randomized trial of a behavioral intervention in HIV-positive African American women found that improving social support along with increasing women's empowerment, can lead to lower rates of unprotected sex (ART adherence was not assessed in that study) [52]. HIV-positive FSWs may limit their HIV status disclosure to minimize further stigma and loss of work. Accordingly, peer networks and other support systems may be highly selective and context-specific. Future studies should identify the women's main sources of social support and social networks that could be leveraged to improve HIV treatment outcomes.

Given the complexity of the constructs that we propose to examine, mixed-methods research is likely the most appropriate design. Rigorous formative research using cognitive interviews and focus groups would be important to ensure that standardized measures of gender norms, IPV, resilience, relationship satisfaction, and social support are appropriately adapted and validated in this population [167].

In summary, our unexpected results in Chapter 4 have generated several new research questions that could move the field forward in our understanding of resilience, relationship dynamics, social support, and HIV treatment outcomes in HIV-positive FSWs in Africa. This work may also inform new integrated theories to guide future studies and interventions. One immediate next step based on this dissertation is to conduct a qualitative study on barriers and facilitators to ART adherence in this population, which will further enhance our understanding of contextual determinants of HIV treatment outcomes in this population. In addition, we will repeat our prospective analysis of the association between recent IPV and detectable plasma viral load in a validation study with a new set of viral load data to test whether our results can be replicated.

The suggested research directions are not exhaustive, and instead stem directly from our findings in Chapter 4. There are likely structural factors, including poverty, laws and norms governing sex work in Kenya, and male partner networks that may impact both IPV and HIV treatment outcomes. Future research on the potential impact of structural factors on poor adherence and detectable plasma viral load should also be explored in this population.

An important overall message from the results from the studies in Chapter 4 is that ***IPV is an important health and human rights problem above and beyond its association with HIV-related outcomes*** [149]. Leveraging HIV prevention and treatment infrastructure to deliver IPV-focused interventions may optimize both strategies in some settings and populations in Africa. Important gaps remain in coverage of GBV/IPV services, especially for marginalized

populations, including FSWs, youth, and men who have sex with men. Kenya is a leader in advancing national guidelines to address GBV and implementing a basic package of screening and referral services in the health sector. Sustained political will, financing, and collaborations between governmental, civil society and academic institutions are critical to expand evidence-based GBV/IPV programs and to ensure that they are implemented effectively and equitably for all people who need them.

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VITA

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