Gender Based Violence and HIV Risk: Mediating Pathways and Strategies for Prevention

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Abstract

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The studies within this dissertation address gender-based violence (GBV) and its relationship with risk factors for HIV acquisition in African women. Women exposed to GBV have a higher risk of HIV infection, but the mechanisms for this association are not well understood, and the mechanisms may differ according to the patterns of violence experienced. Therefore, a full assessment of pathways to HIV risk requires meaningful GBV classifications that consider variations in GBV type, frequency, and severity. This work: 1) characterizes the patterns of GBV experienced by female sex workers, 2) describes the association of those GBV patterns with mental health and sexual risk behavior, and 3) examines the relationship between GBV and adherence to pre-exposure prophylaxis (PrEP) among HIV-uninfected women in HIV serodiscordant couples.

Using latent class analysis, we identified 4 GBV patterns in female sex workers, labeled Low (21% prevalence), Sexual (23%), Physical/Moderate Emotional (18%), and Severe (39%). Compared to women with Low GBV, those with Severe GBV had higher symptom scores for depression, posttraumatic stress disorder (PTSD), and alcohol abuse, and higher numbers of sex partners. Women with Sexual GBV had higher symptom scores for alcohol abuse only, but there were no differences in sexual risk behavior. Women with Physical/Moderate Emotional GBV had higher numbers of sex partners and a higher prevalence of unprotected sex, but no differences in mental health symptoms. Among women in HIV serodiscordant couples, those with recent GBV had lower PrEP adherence than women with no GBV, and the effect increased with increasing number of violent episodes.

This research has contributed to HIV prevention in high-risk African women by providing a more nuanced understanding of how the relationship between GBV and on HIV risk varies by GBV type, frequency, and severity. It also provides new data on the impact of GBV on PrEP adherence, which has not been previously studied. Prevention programs for women should screen for violence and address these multiple pathways to effectively reduce HIV incidence in this vulnerable population.

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Chapter 1: Introduction

Introduction

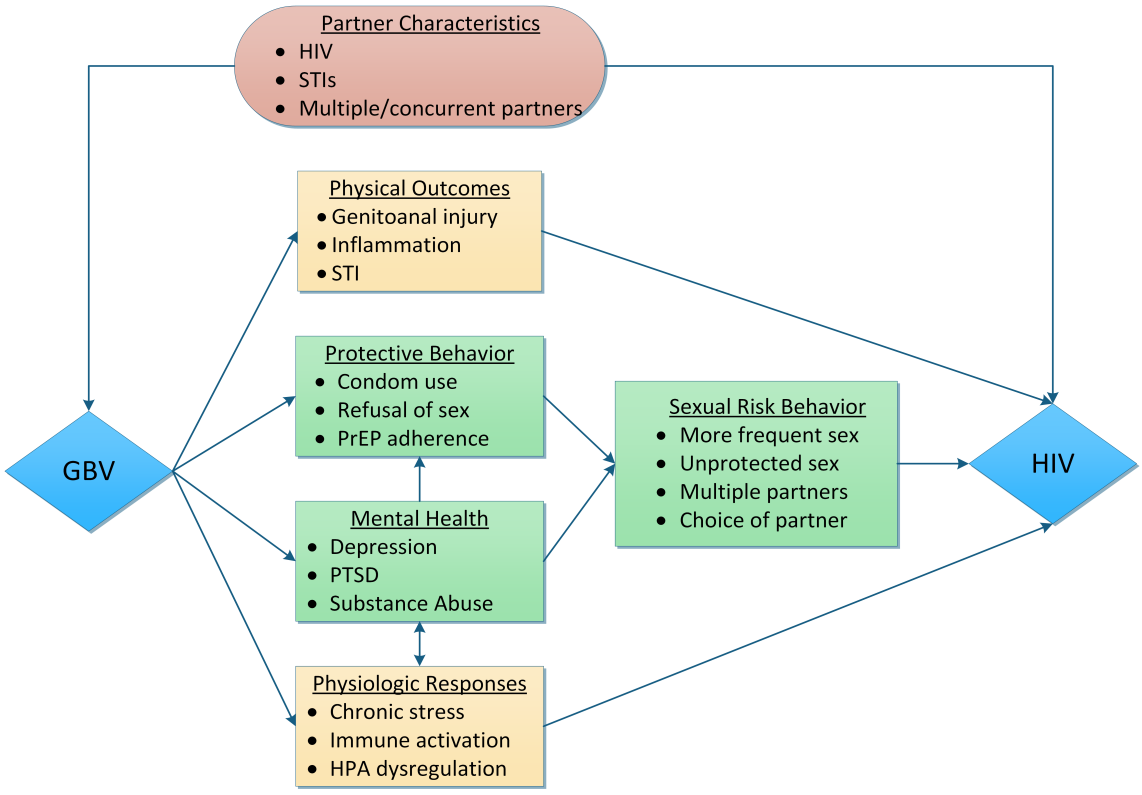
This dissertation addresses the relationship between gender-based violence (GBV) and several mediating factors thought to increase HIV acquisition risk among African women, including poor mental health, high-risk sexual behavior, and low adherence to prevention methods (hereafter referred to as "HIV risk factors"). Despite enormous progress in testing and treatment over the last 15 years, there are still 2.1 million new HIV infections each year [1]. Nearly 70% of these infections occur in sub-Saharan Africa, and in that region, women experience more than half of all new adult infections [1]. Two groups of women at particularly high risk of HIV acquisition are female sex workers (FSWs), for whom the odds of HIV infection are 12 times higher than in the general population [2], and women in stable HIV serodiscordant couples (i.e., couples in which the male partner is HIV-infected and the woman is HIV-uninfected). Modeling studies estimate that 30%-60% of new HIV infections in sub-Saharan Africa occur within HIV serodiscordant couples, with equal numbers of male-to-female as female-to-male infections [3,4].

Women's increased vulnerability to HIV arises from a complex interaction between biological factors and social and structural factors, including mucosal vulnerability, low access to information and prevention services, stigma and discrimination around HIV and sex work, and gender inequality [5]. As a manifestation of gender inequality, GBV may play a particularly important role. The World Health Organization estimates that 35% of women worldwide have experienced some form of GBV in their lifetime, including physical or sexual intimate partner violence or non-partner sexual violence [6]. Prospective studies have shown that GBV increases the relative risk of HIV acquisition by up to 50% [7,8] and may be responsible for 12%-25% of new HIV infections among African women [7–9]. Effect sizes are generally similar for physical, sexual and verbal or emotional violence; increase with frequency and severity of violence; and persist for more than one year after the last violent episode [7]. This long duration of effect has also been shown for other health consequences of GBV, including depression, anxiety, and

PTSD, and suggests that interventions need to address both GBV prevention and HIV prevention among women already exposed to violence [10,11].

To develop more effective HIV prevention interventions, we need to understand the pathways through which violence increases HIV risk. Published evidence supports involvement of physical, behavioral, and psychological pathways, as illustrated in Figure 1 (adapted from Stockman *et al.* [12]). Perpetrators of GBV are themselves more likely to engage in high-risk behavior and to be infected with HIV or other sexually transmitted infections (STIs), increasing the risk of transmission to their victims [13,14]. In addition, sexual violence can cause genitoanal injury, inflammation, or STIs, directly increasing the per-act probability of HIV transmission [15–17]. However, evidence suggests that GBV-associated HIV risk is not primarily driven by the physical effects of sexual assault, as other forms of GBV are associated with similar increases in risk [7,18,19].

Figure 1: Causal pathways between gender-based violence and HIV risk. *GBV: gender-based violence; PTSD: post-traumatic stress disorder; STI: sexually transmitted infection; PrEP: pre-exposure prophylaxis*



This dissertation focuses on behavioral and psychological HIV risk factors that are potential intervention targets for women who have already experienced GBV. A large body of literature relates GBV to high-risk sexual behavior. Due to fear of further violence from their partners, women who experience GBV may have limited ability to adopt HIV risk reduction behaviors [18,20–22]. They use condoms less frequently, and have less power in relationships to determine the timing and frequency of sex [8,19,23,24]. Women who experience GBV are also more likely to report multiple partnerships and sex under the influence of alcohol or drugs [7,19,25]. However, interventions to prevent GBV have not consistently led to changes in women's sexual risk behavior [26–28].

These interventions may be unsuccessful because they do not address the mental health sequelae of GBV. Experience of GBV increases women's risk of posttraumatic stress disorder (PTSD), depression, and substance abuse [10,29–32]. Symptoms of these mental health conditions, such as low self-esteem or hyperarousal, may increase women's high-risk sexual behaviors and reduce their ability to change these behaviors [12,33–37]. Poor mental health may also affect HIV risk through other mechanisms. For example, PTSD, depression, and substance abuse can alter cortisol levels, which may cause physiological changes that increase HIV risk, such as HSV-2 reactivation or the activation of a Th-1 type pro-inflammatory immune response [38–43].

GBV may also influence women's adoption of novel HIV prevention methods such as pre-exposure prophylaxis (PrEP), the use of antiretroviral drugs in HIV-uninfected persons to prevent HIV acquisition [44–47]. Because of increased HIV risk, women exposed to GBV are a potential target population for PrEP [7,48,49]. However, high adherence levels are required for PrEP efficacy, particularly in women [50,51]. Women exposed to GBV have lower adherence to a variety of medication regimens [18,52] and may be at particular risk of poor PrEP adherence [53]. If demonstrated empirically, this association would provide evidence of another behavioral pathway from GBV to HIV risk.

A full assessment of pathway roles and importance requires meaningful classifications of GBV exposure. GBV can vary widely with respect to perpetrator, type of act, severity, duration, timing, and frequency [54]. It is typically dichotomized into “ever” or “never” in analyses, but this approach fails to capture the comprehensive experiences of individual women who may be subjected to multiple, overlapping types of violence [30,55]. New approaches use latent class models to identify subgroups of women who experience similar *patterns* of exposure [30,55–57], identified by variables such as violence type, severity, duration, or frequency. Different patterns of GBV experiences may have different psychological or behavioral consequences and thus may affect HIV risk through different mechanisms. Although several studies in Europe and North America have used these approaches [30,56–58], they have not been implemented in African settings or among high-risk populations such as female sex workers (FSWs) or HIV serodiscordant couples. GBV patterns and their effects on HIV risk factors may differ in these women due to their unique risk profiles. In particular, FSWs experience violence more frequently and from multiple perpetrators, including clients, intimate partners, and strangers or acquaintances [59], so the impact on HIV risk may be magnified.

In this dissertation, we sought to evaluate behavioral and psychological HIV risk factors to identify potential mechanisms for the association between GBV and HIV acquisition in FSWs and HIV-uninfected women in HIV serodiscordant couples in Africa. In Aim 1, we developed a pattern-based exposure classification derived from a comprehensive evaluation of GBV experiences among FSWs in Mombasa, Kenya, and tested the association of these patterns with mental health. We hypothesized that women exposed to patterns of intense GBV (characterized by type, severity, and frequency) would have higher symptoms scores for depression, PTSD, alcohol abuse, and drug abuse. In Aim 2, we evaluated whether the same GBV patterns were associated with high-risk sexual behavior among the Mombasa FSWs. Here, our hypothesis was that women exposed to patterns of intense GBV would have higher numbers of sex partners and a higher prevalence of recent unprotected sex. In Aim 3, we

conducted a prospective cohort study to test whether recent and/or past exposure to GBV was associated with adherence to PrEP among HIV-uninfected women in HIV serodiscordant relationships in Kenya and Uganda. We hypothesized that GBV exposure would be associated with lower PrEP adherence.

Our findings will provide new evidence on the effect of GBV on behavioral and psychological HIV risk factors in African women. By focusing our work on two populations at high risk of HIV and GBV, we ensure that our findings are applicable to those in the greatest need of prevention strategies. Different interventions may be indicated according to the HIV risk factors found to be associated with specific patterns of GBV. For example, experience of severe violence, regardless of perpetrator, may be more strongly associated with substance abuse, while experience of intimate partner violence may increase the risk of unprotected sex, directly increasing HIV risk. Negative findings will help redirect interventions away from pathways that are not likely to reduce risk. Improved understanding of these pathways will therefore inform the development of effective, targeted interventions to reduce HIV risk through interruption of the pathways leading from GBV to HIV acquisition.

Chapter 2: Patterns of Gender-Based Violence and Associations with Mental Health among Female Sex Workers in Mombasa Kenya: A Latent Class Analysis

Patterns of Gender-Based Violence and Associations with Mental Health among Female Sex Workers in Mombasa, Kenya: A Latent Class Analysis

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Abstract:

Introduction: Gender-based violence (GBV) is common among female sex workers (FSW) and is associated with poor mental health, including depression, post-traumatic stress disorder (PTSD), and substance abuse. Prior studies have focused on GBV of one type (e.g. physical or sexual) or from one perpetrator (e.g. clients or intimate partners), but most women experience overlapping types of violence from multiple perpetrators, with varying frequency and severity. To better understand the mental health sequelae of GBV, exposure classifications should consider women's comprehensive experiences.

Methods: We used a person-centered approach to identify GBV patterns among FSWs in Mombasa, Kenya and examined their associations with mental health outcomes. In a cross-sectional study (n=283), we used an adaptation of the WHO Violence Against Women Instrument to assess the frequency and severity of specific acts of physical, sexual, and emotional violence from multiple perpetrators. Standardized instruments were used to measure depression (PHQ-9), PTSD (PCL-C), alcohol abuse (AUDIT) and drug abuse (DAST-10). We used latent class analysis to describe GBV patterns and tested the relationship between the patterns and mental health symptom scores with bivariable and multivariable linear regression models.

Results: Lifetime prevalence of GBV was 87%. We identified 4 latent classes of GBV patterns, labeled as Low (21% prevalence), Sexual (23%), Physical/Moderate Emotional (18%), and Severe (39%). In adjusted models, women with Severe GBV had significantly higher symptom scores than women with Low GBV for depression (beta =1.5, 95% CI: 0.02-3.1), PTSD (beta = 3.7, 95% CI: 0.6-6.8), and alcohol abuse (beta= 3.9, 95% CI: 1.8-6.0). Women with Sexual GBV had significantly higher symptom scores for alcohol abuse only (beta = 3.7, 95% CI: 0.5-6.9). Symptom scores were not higher for any mental health outcome among women with Physical/Moderate Emotional GBV.

Conclusions: The lifetime prevalence of GBV was extremely high in this sample of Kenyan FSW. A person-oriented approach revealed 4 GBV patterns associated with distinct mental health outcomes. Interventions that address women's comprehensive experiences of GBV may be more effective in preventing GBV recurrence and improving mental health.

Introduction

Gender-based violence (GBV) is a global public health problem, and female sex workers (FSWs) are disproportionately affected [60,61]. Prevalence estimates vary widely depending on geographic location, work environment, and types of violence included. In particular, estimates depend on whether GBV assessment includes physical and emotional violence in addition to sexual violence, and whether violence from intimate partners is included along with "workplace" violence from clients, pimps, and police. Among African FSWs, prevalence is as high as 49% for lifetime experience of forced sex [62–65] and 82% for lifetime experience of client-perpetrated GBV of any type (physical, sexual, emotional, or financial) [65]; estimates of intimate partner violence in the past year alone range from 15%-55% [59,66].

Gender-based violence has been associated with numerous health consequences, including homicide, suicide, injury, poor reproductive and perinatal health, HIV and other sexually transmitted infections, and mental health disorders such as depression, posttraumatic stress disorder (PTSD), and substance abuse [6]. Most research has focused on the consequences of intimate partner violence in the general population [67], but health consequences may be more common or more severe for FSWs, who experience GBV more frequently and from multiple types of perpetrators. High levels of stigma and discrimination against FSWs also impede access to health services to treat GBV-related outcomes [68]. Though studies of African FSWs have recently begun to report associations with HIV/STI risk factors [e.g. 3,4,15,16], the data are still sparse for mental health outcomes. History of any physical or sexual violence, workplace violence, and intimate partner violence have been associated with alcohol abuse and drug abuse [64,66,71–73], and one study showed that women with a history of client-perpetrated forced sex were twice as likely to report depression symptoms [63]. We did not find any studies addressing the relationship between violence and PTSD among African FSW, but studies in other settings suggest that sexual assault and workplace rape are associated with PTSD diagnosis and symptom severity [74,75].

A common limitation of many published studies is their classification of GBV exposure. Gender-based violence is a heterogeneous phenomenon, and its effects vary according to the type (e.g. physical, sexual or emotional), severity, frequency, and duration of violence, as well as the relationship to the perpetrator [54]. When research studies measure multiple types of violence, they typically group them into a dichotomous measure of any versus no GBV. Though this approach is analytically straightforward, it fails to account for the diversity of women's experiences. Studies that do examine the effects of specific GBV types or perpetrators often exclude other categories of violence entirely (e.g., they measure rape from clients, but not physical violence or intimate partner violence). Most survivors experience multiple, overlapping types of GBV, from multiple perpetrators, and this focus on individual dimensions does not capture the cumulative effects of their experience [54,76].

An alternative approach is to use "person-centered" methods, such as latent class or cluster analysis, to identify subgroups of women who experience similar patterns of GBV. This method presents a parsimonious way of classifying GBV exposure while still capturing multiple dimensions of women's experiences. In European and North American studies in the general population, person-centered approaches have shown that specific GBV patterns are more strongly associated with poor mental health [30,56]. However, these relationships have not been characterized in FSWs living in resource-limited settings. In the present study, we used latent class analysis to identify common patterns of GBV among FSWs in Mombasa, Kenya and determined the associations between the GBV patterns and mental health symptoms, including depression, PTSD, alcohol abuse, and drug abuse.

Methods

We conducted a cross-sectional study among participants from the Mombasa Cohort, a prospective cohort study of risk factors for HIV acquisition and transmission among FSWs in Mombasa, Kenya. The cohort was initiated in 1993 and detailed procedures have been

published [77]. Eligibility criteria include age 16–60 years, residing within 1-day commuting distance to the clinic, self-identifying as exchanging sex for payment in cash or in kind, and able to provide informed consent. To participate in the sub-study, women also had to be HIV-uninfected; not currently menstruating, pregnant, or <6 weeks post-partum; and able to provide separate written informed consent for the additional study procedures. Trained counselors conducted standardized face-to-face interviews with participants in a private setting in their preferred language (English or Kiswahili). Women who reported violence or screened positive for depression, PTSD, or substance abuse were offered counseling on site or referral to other facilities. The study was approved by ethics committees at Kenyatta National Hospital and the University of Washington.

Measures

Exposure to GBV was assessed using a modified version of the World Health Organization Violence Against Women Instrument (VAWI) [78]. Women were asked if they had ever experienced specific acts of physical, emotional, or sexual violence from any sexual partners, including regular partners such as husbands or long-term boyfriends, casual partners, or clients. These acts are listed in the Table S1 of the Supplemental Materials. To improve reporting accuracy [12], we added behaviorally-specific questions on sexual coercion from the Sexual Experiences Survey [79,80]. For each act that a woman experienced, we asked about the timing (past 12 months, >12 months ago), frequency (one, few, many times), and her relationship to the perpetrator. To assess violence from non-partners (e.g., strangers or acquaintances with whom the participant had not engaged in a consensual sexual relationship), we asked if the participant had ever been beaten/ physically mistreated or forced to have sex by anyone other than a husband, boyfriend, or client. Because we were unable to determine whether physical non-partner violence was gender-based, we focused our analysis and interpretation on sexual non-partner violence.

Mental health symptoms were assessed with the following tools, which have been used successfully in multiple studies in African populations [81–87]:

- The Patient Health Questionnaire-9 (PHQ-9) evaluates depression symptoms in the past 2 weeks. It comprises 9 questions rated on a 4-point Likert scale, which are summed for a total score from 0–27. Scores ≥10 represent moderate to severe depression [88].
- The PTSD Checklist - Civilian version (PCL-C) measures PTSD symptoms in the past month. There are 17 items rated on a 5-point Likert scale and summed for a total score of 17–85 points [89]. We used a threshold of ≥30 points to indicate a positive screen for PTSD, consistent with previous studies in similar populations [83,84].
- The Alcohol Use Disorders Identification Test (AUDIT) is a 10-item survey on drinking behavior and alcohol-related problems in the past year. Responses are scored from 0 to 4 and summed for a total score from 0–40. A score of ≥16 indicates harmful drinking [90].
- The 10-item Drug Abuse Screening Test (DAST) consists of 10 ‘Yes/No’ questions, with a total score ranging from 0–10. A cut-off of ≥3 identifies harmful use of substances other than alcohol [91,92].

Data on socio-demographic characteristics, sex work history, and financial hardship were collected at enrollment into the Mombasa Cohort or at the SV Study visit [93,94]. We used additional questions from the VAWI and other published studies to assess experiences of controlling behaviors or financial abuse (Table S1) and direct consequences of partner violence including physical injuries; fear of sexual partners; and loss of relationship, home, children, employment, or other economic support [19,78,95].

Statistical Analysis

We identified patterns of GBV using latent class analysis (LCA), a multivariate person-centered method that assumes an unobserved categorical variable that divides a population into a small number of mutually exclusive and exhaustive latent classes [96]. Characteristics of, and membership in, each class are modeled with a set of measured items called indicators. Results of the analysis include the number of latent classes, class prevalence, the class-specific probability of each indicator, and the posterior probability of membership in each class for each individual. The last outcome can be used to classify individuals by their GBV patterns, based on the class with the highest probability of membership, while accounting for the uncertainty of membership (i.e., measurement error).

We condensed the act-specific GBV data into a smaller number of indicator variables to avoid issues with sparse data that arise when the number of possible response patterns is large relative to the sample size [97]. Because there are limited data on violence patterns in FSW or on which characteristics of GBV are associated with mental health, we developed 2 sets of indicator variables *a priori* to represent different dimensions of GBV. Both sets referred to lifetime experience of GBV. The first set focused on relationship to perpetrator, frequency, and severity of violence. These indicators did not yield meaningful patterns in this sample and were not explored further (see Appendix). The results reported here reflect the second indicator set, which describes type, severity, and frequency of violence and is based on a previous study of GBV among women in the general population [55]. There were 4 polytomous indicators (Table 1): The indicator for physical partner violence focused on severity (none, moderate, or severe) because the prevalence of moderate physical GBV was low, and most severe physical GBV was experienced "many" times (58%). The indicator for sexual partner violence described frequency only (none, 1-2 acts, few acts or many acts), because we considered all sexual GBV to be severe. The indicator for emotional partner violence described both frequency and severity (none, moderate acts few times, moderate acts many times, or severe acts any number of

times). The indicator for non-partner violence was limited to type (none, physical only, or sexual [with or without physical]) because we did not collect data on severity of non-partner violence, and most women reported that this type of violence had occurred once only.

We fit models with 1–5 classes and selected the best-fitting model based on measures of absolute fit (G^2 likelihood ratio statistic); relative fit, including the Akaike information criteria (AIC), Bayesian information criteria (BIC), consistent AIC (CAIC) and adjusted BIC (aBIC); entropy (a summary measure of measurement error in class assignment); parsimony; class size; and the scientific interpretation of the classes. Each model was run with 1000 random starting values to ensure model identification. From a theoretical perspective, it was important to ensure that the final model included one class of women with little or no experience of GBV, to provide an appropriate reference class for our subsequent analyses [98]. Therefore, we used parameter restrictions to fix the probability of any physical, sexual, and emotional partner violence and any non-partner sexual violence to 5% in one class. Previous studies have restricted one class to no violence at all [99,100]. Our approach is similar but allows for measurement error in violence reporting. A sensitivity analysis suggested that class characteristics and membership did not shift substantially when the fixed value for the probability of any physical, sexual, and emotional partner violence and any non-partner sexual violence was varied from 1%-10%.

Women were assigned to classes based on the highest posterior probability of class membership. We used bivariable statistics to describe correlates of class membership and compare additional GBV characteristics across classes. We examined between-class differences in mental health symptom scores using bivariable and multivariable linear regression models, with separate models for each outcome. The multivariable analysis considered potential confounding by the following variables, which were selected using causal diagrams: age (continuous), education (<8, 8–11, or ≥12 years), income (quartiles), household size (1, 2-3, or ≥4 persons), charge for sex (in kind, ≤500 Kenyan Shillings [KSh], or >500 KSh), age at first sex

(≤15 or >15 years), years enrolled in Mombasa Cohort (<1, 1–4, 5–9, ≥10 years), years as FSW before cohort enrollment (<1, 1–4, 5–9, ≥10 years), any sex work in past 8 weeks (yes/no), nationality (Kenyan or non-Kenyan), number of live births (0 or ≥1), primary occupation (unemployed, sex work, other formal, or other informal), workplace (bar/restaurant, nightclub, or home/other), and 3 measures of financial security: feels financial future is certain (certain, uncertain, or very uncertain), ran out of money for basic needs in past year (never, once/twice, or few/many times), and needed to borrow money to survive financially in past year (never, once/twice, or few/many times). Variables were retained in the model if they resulted in meaningful changes (>10%) to the effect estimates. To account for uncertainty in GBV class assignment resulting from the latent class model, we used the modified BCH approach, developed by Bolck, Croon, and Hagenaars and revised by Vermunt and colleagues [101–103]. This approach creates an expanded dataset with one record for each latent class for each subject and assigns a set of weights based on classification errors calculated from the model. Subsequent regression analyses are conducted using survey data analysis methods with linearized (robust) standard errors to account for the weights and for multiple records per subject [104].

Latent class analyses were conducted in Stata 14.1 using the Stata LCA Plugin [105]. The BCH weights were obtained by replicating the LCA in MPlus 7.4 with the *save=bchweights* command [106], and then exported into Stata to conduct the regression analyses with the *svy:* prefix command to account for the weighting.

Results

Participant Characteristics

The study enrolled 283 women with median age of 33.5 years (interquartile range [IQR] 27.2–40.6 years). They had a median of 8 years of education (IQR 7–12 years) and had participated in the Mombasa Cohort for a median of 3 years (IQR 1.2–9.8 years). Nearly all

(93%) had worked as an FSW in the past 2 months, but only 31% considered sex work their primary occupation. Most (88%) worked in bars, restaurants, or nightclubs, while the rest worked at home or in other settings. Median weekly income was 2000 KSh (IQR 1000–5000), about US$20. Participants experienced substantial financial insecurity: 70% had run out of money for basic needs in the past year and 80% reported that their financial future was uncertain or very uncertain.

GBV Prevalence

Lifetime prevalence of physical, sexual, or emotional partner GBV was 87%, and past year prevalence was 40%. Violence from regular partners was most common (59%), followed by clients (25%) and casual partners (19%). The indicator variables in Table 1 summarized lifetime GBV experiences. Lifetime prevalence of physical partner violence was 63%, with 16% reporting moderate only (slap or push) and 47% reporting severe physical violence (hit, kick, choke, or use a weapon). For lifetime sexual GBV, 15% of women experienced 1–2 acts, 9% few acts, and 21% many acts. Prevalence of lifetime emotional partner violence was 60%, including 12% for moderate acts once or few times, 14% moderate acts many times, and 34.6% any severe act. Additionally, 56% of women reported any lifetime experience of non-partner violence: 30% with physical non-partner violence only, and 26% with non-partner sexual violence. Most women (85%) had experienced these non-partner acts once only.

Latent Class Model

Fit statistics for each latent class model are shown in Table 2. The 4-class model was selected based on 1) clear, interpretable classes; 2) minimum AIC; 3) relatively small BIC, CAIC, and aBIC; and 4) adequate identification. The best-fitting 4-class model had a G^2 value of 121.33 and was reached in 70% of model runs. The next best-fitting model had a G^2 value of 122.05 and was reached in 5% of model runs. Each latent class corresponds to a pattern of

GBV experiences. The first class, labeled *Low GBV,* included women with little to no GBV and comprised 21% of the population (Table 3). By design (due to parameter restrictions), women in this class had a 5% probability of any physical, sexual, or emotional partner violence, and a 5% probability of non-partner sexual violence. The other 3 classes arose from natural clustering in the remaining data. The second class included 23% of the population and was labeled *Sexual GBV*. Women in this class had a 59% probability of sexual partner violence and a 49% probability of non-partner sexual violence, substantially higher than in the overall cohort. The third class, labeled *Physical/Moderate Emotional GBV,* had 18% prevalence. Eighty-five percent (85%) of women in this class experienced physical violence, evenly split between moderate and severe. There was a 62% probability of moderate emotional violence few or many times, but no severe emotional violence. The last class was characterized by severe violence of all types, and was labeled *Severe GBV.* This was the largest class, at 39% of the population. The probability of severe physical and emotional partner violence was 80%–90%, and the probability of sexual violence was >50% from partners and 35% from non-partners. The classes were similar on most measures of socio-demographic characteristics, sex work history, and financial security (Table 4). Only income was significantly associated with class membership, with women in the *Sexual GBV* class less likely to have weekly income above 2000 KSh than women in the other classes (29% vs. 47%–56%, p=0.016).

Associations between GBV Latent Classes and Mental Health

Table 5 shows the associations between the classes and mental health outcomes: depression, PTSD, alcohol abuse, and drug abuse. Median symptom scores were low for all outcomes, especially for drug abuse, which was infrequently reported in this population. However, substantial proportions of women had scores above the relevant thresholds in the *Severe* and *Sexual GBV* classes, e.g. 15% for depression in the *Sexual GBV* class and 22% for PTSD in the *Severe GBV* class. In the adjusted BCH-weighted linear regressions, women in the

Severe GBV class had significantly higher symptom scores than women in the *Low GBV* class for depression (beta =1.5, 95% confidence interval [CI]: 0.02–3.1), PTSD (beta = 3.7, 95% CI: 0.6–6.8), and alcohol abuse (beta= 3.9, 95% CI: 1.8–6.0). Women in the *Sexual GBV* class had significantly higher symptom scores for alcohol abuse (beta = 3.7, 95% CI: 0.5–6.9). The *Sexual GBV* class also had higher symptom scores for depression, but the adjusted estimate was not statistically significant (beta =2.1, 95% CI: -0.5–4.7). Women in the *Physical/Moderate Emotional GBV* class did not have higher symptom scores for any mental health outcome, and there were no associations between GBV patterns and DAST scores.

We further explored the construct validity of the classes by examining variation in other forms of abuse, relationship to perpetrators, and consequences of GBV (Supplemental Table S2). The following variables showed statistically significant differences between the classes, with proportions increasing between the *Low, Sexual, Physical/Moderate Emotional,* and *Severe GBV* classes: controlling behaviors, fear of sexual partners, relationship dissolution, loss of residence, and moderate or severe injury. The prevalence of GBV from regular partners followed the same trend (5% in the *Low GBV* class, 50% *Sexual*, 70% *Physical/Moderate Emotional*, 86% *Severe*, $p<0.001$), but there were no class differences in the prevalence of GBV from casual partners or clients. Financial abuse varied in a similar manner and the differences were also statistically significant, but the prevalence was higher in the *Sexual GBV* class than in the *Physical/Moderate Emotional GBV* class.

Discussion

This study identified 4 latent classes that represent distinct patterns of GBV among FSWs, with distinct mental health profiles. Women with severe GBV had higher symptom scores for PTSD, depression, and alcohol abuse. Sexual GBV was associated with alcohol abuse, and we observed a non-significant trend towards higher depressive symptoms. There were no associations between physical and moderate emotional GBV and any mental health symptoms.

These findings build on previous studies showing that violence affects the mental health of women in general and of FSW specifically [10,72,75,107–109]. The use of a person-oriented perspective provides insight into overarching patterns of GBV instead of separate experiences of sexual or physical violence from intimate partners or clients. By considering women's holistic experiences, we gained a better understanding of the extent of GBV exposure, and identified a subset of women with the highest burden of mental health symptoms. The more widespread application of a person-oriented approach may help to explain differences in mental health and conflicting findings about the relationship between GBV and mental health across multiple studies. For example, a study that found no association between forced sex and depression among Nepalese FSW would be consistent with our study findings if the exposed women experienced predominantly sexual GBV, but inconsistent if they had also experienced severe physical and emotional GBV [109].

A previous study, from which we adapted our indicator variables, used LCA to classify intimate partner violence (IPV) among women from the general population in Peru, Brazil, Namibia, and Ethiopia [55]. Each site had a class of extreme, systematic IPV, a class of sexual-dominant IPV, and a class of less severe IPV with or without emotional IPV. Our LCA revealed the same patterns, despite incorporating violence from other perpetrators, but the prevalence of the most severe class was substantially higher in our cohort (40% versus 13%-25% across 6 sites). Two LCA studies of IPV patterns in the US and Canada also identified a severe abuse class, but had no class of sexual-dominant IPV. Instead, intermediate IPV classes consisted of ordered levels of physical and emotional violence [58,99]. In each of these studies, GBV patterns were associated with different mental health profiles: In Brazil and Peru, the odds of suicidal thoughts were 4.4-fold higher in the sexual-dominant IPV class, 5.2-fold higher in the less severe IPV class, and 8.1-fold higher in the systematic IPV class, compared to women with no IPV [55]. In the United States, all 3 IPV classes were associated with depression, sedative use, and antidepressant use, but only women in the two most severe classes had a higher

probability of daily drinking and prescription pain pill use [99]. In the Canadian study, the prevalence of self-reported depression or anxiety attacks increased linearly with increasing severity of IPV experiences, but feelings of shame, guilt, and low self-esteem were only significantly higher in the systemic abuse class [58].

The high prevalence of any GBV and severe GBV in this study population emphasizes the need for violence prevention and mental health services. In addition to being a human rights and public health concern in its own right, experience of GBV is associated with higher HIV incidence [7,19], and poor mental health may be mediator of this relationship. Depression, PTSD, and alcohol use are all associated with high-risk sexual behaviors [12,33–37] and with physiological responses, such as HSV-2 reactivation and pro-inflammatory immune activation, which may increase susceptibility to HIV [38–43]. Studies have also suggested that violence, alcohol use, and depression influence the success of HIV prevention interventions, including adherence to PrEP and reduction of sexual risk behavior [37,110,111]. This highlights the importance of addressing mental health and GBV as part of a comprehensive HIV prevention package for FSWs.

Recognition of distinct GBV patterns and related variation in mental health outcomes may allow for more targeted and appropriate interventions for GBV and mental health. For example, small-group participatory interventions could group women with similar violence patterns to facilitate social support and sharing of prevention and coping strategies. Intervention content or intensity could also be tailored based on GBV patterns: Women with severe GBV and worse mental health may need more comprehensive, frequent, or long-lasting interventions. For women with physical and moderate emotional GBV, who had few mental health symptoms, more intensive interventions may have a negative impact by stigmatizing participants or placing an undue burden on their time. The appropriateness of intervention structure may impact participant retention and efficiency, in terms of financial costs and staff time [112]. Ultimately, these factors could increase program effectiveness and have a greater public health impact.

This study had several strengths. We used validated instruments for GBV and mental health assessments, including an act-specific measurement of GBV that provided multiple opportunities for disclosure and did not require women to identify as battered or abused. In addition, we were able to control for several important confounders, including financial insecurity, which is a strong predictor of GBV and poor mental health [113,114]. Our novel use of parameter restrictions to ensure a low-violence class is another study strength. Latent class analysis is usually conducted in an "exploratory manner", without any parameter restrictions, to describe natural clustering in the data. However, the exploratory approach does not ensure the existence of a no-violence class, which is necessary as a reference group when the latent classes are to be used as an exposure variable in additional analyses. To address this, some latent class analyses of GBV have created a no-violence class based on observed response patterns, where women reporting no violence have 100% probability of membership in this class, and women reporting any violence have 0% probability [55,99,100]. This approach does ensure an appropriate reference group, but the no-violence class is now directly observed rather than latent, so there is no allowance for measurement error. More precisely, there is zero probability that any participant who reports any experience of GBV could truly be a member of the no-violence class. In our analysis, we allowed a 5% probability of each type of GBV in the reference class. This ensured that the class was predominantly composed of women reporting no GBV while allowing a small possibility of measurement error in violence reporting.

There are several limitations that should be noted. First, despite the use of validated tools, GBV and mental health symptoms may have been underreported due to the sensitive nature of these subjects. Second, participation in the Cohort may have given women social support or access to health care that reduced the risk or sequelae of GBV, and this could limit the generalizability of our findings. Third, due to the cross-sectional study design, we cannot establish the direction of the association between GBV and mental health. Fourth, our small sample size reduced statistical power to detect a larger number of GBV patterns or associations

between classes and mental health outcomes. The small sample size also prevented us from including indicators of perpetrator type, controlling behaviors, or financial abuse in the LCA, due to issues with model identification. Our first analysis did not identify clustering by perpetrator type, and the distribution of violence from clients and casual partners was similar in the current analysis, so there may have been little gained by including indicators of perpetrator type in the LCA. However, controlling behaviors and financial abuse were strongly correlated with GBV patterns in our sample, and inclusion of these indicators in future analyses may improve class definitions.

Conclusion

Gender-based violence is endemic among FSWs and is associated with significant health effects, including depression, PTSD, and alcohol abuse, as well as poor reproductive health outcomes and increased HIV/STI risk. Using a person-oriented approach, we found that many FSWs in our sample experienced frequent and severe violence from multiple perpetrators, and there was a clear difference in mental health outcomes between women with different GBV patterns. Interventions that address women's comprehensive experiences of GBV may be more effective in preventing GBV recurrence and improving mental health. Programs to reduce violence and protect women’s rights in workplaces, communities, and relationships are essential to improving the mental health and quality of life of FSWs.

Table 1: GBV indicator variables

	N	%
Total	283	100%
Physical partner violence*		
None	106	37.5
Moderate (slap or push)	45	15.9
Severe (hit, kick, choke, weapon)	132	46.6
Sexual partner violence*		
None	159	56.2
Once or twice	41	14.5
Few times	25	8.8
Many times	58	20.5
Emotional partner violence*		
None	112	39.6
Moderate (insult or belittle), once/few times	33	11.7
Moderate (insult or belittle), many times	40	14.1
Severe (scare or threaten), any frequency	98	34.6
Non-partner violence*		
None	124	43.8
Physical only	84	29.7
Sexual	74	26.2

* Partner violence refers to violence from any consensual sexual partner, including regular partners, casual partners, and clients. Non-partner violence refers to violence from strangers or acquaintances with whom the participant has not initiated a sexual relationship.

Table 2: Latent class model statistics

Model	DF	LL	G^2	AIC	BIC	CAIC	aBIC	Entropy	% Solution
1-class	137	-2202.8	2184.7	2196.7	2218.6	2224.6	2199.5	1.00	100
2-class	126	-1216.3	211.7	245.7	307.7	324.7	253.8	0.79	100
3-class	115	-1183	145.1	201.1	303.2	331.2	214.4	0.71	100
4-class	104	-1171	121.3	199.3	341.5	380.5	217.8	0.72	68
5-class	93	-1161	101.1	201.1	383.3	433.3	224.8	0.71	40*

* Not identified

Table 3: Class indicators and descriptions

	Class membership & item response probabilities			
	Low	**Sexual**	**Physical/ Moderate Emotional**	**Severe**
Estimated prevalence	20.9%	23.0%	17.5%	38.6%
Women in study sample assigned to class, n (%)	60 (21.2%)	52 (18.4%)	61 (21.6%)	110 (38.9%)
Distribution within classes:				
No physical	**95.0%**	**50.8%**	14.8%	8.7%
Moderate physical	3.3%	27.1%	42.4%	4.0%
Severe physical	1.7%	22.1%	42.8%	**87.3%**
No sexual	**95.0%**	41.3%	**80.3%**	34.0%
Sexual 1-2 times	2.1%	22.5%	19.7%	13.6%
Sexual, few times	0.9%	21.0%	0.0%	9.7%
Sexual, many times	1.9%	15.1%	0.0%	42.7**%**
No emotional	**95.0%**	**60.4%**	36.2%	0.0%
Moderate emotional, few times	0.0%	10.7%	39.4%	6.0%
Moderate emotional, many times	0.0%	23.6%	22.5%	12.4%
Severe emotional	5.0%	5.3%	1.9%	**81.6%**
No non-partner violence	**75.4%**	9.8%	**67.6%**	37.3%
Physical non-partner violence only	19.6%	41.5%	32.4%	27.4%
Sexual non-partner violence	5.0%	48.7%	0.0%	35.3%

Note: To aid with interpretation of the class characteristics, probabilities over 50% are highlighted in bold-text, and gray shading shows probabilities <50% which are important for class interpretation either individually or in groups.

Table 4: Correlates of GBV classes as determined by modal class assignment

	Low N (%)	Sexual N (%)	Physical/ Moderate Emotional N (%)	High N (%)	p value
Total	60	52	61	110	
Age (Mean, SD)	34.7 (10.7)	34.5 (8.9)	35.0 (10.0)	34.9 (8.9)	0.99[a]
Kenyan	57 (96.6%)	47 (90.4%)	55 (90.2%)	102 (92.7%)	0.48[b]
Income >2000 KSh/wk	33 (55.0%)	15 (28.9%)	34 (55.7%)	52 (47.3%)	0.016
Education ≥12 yrs	24 (40.0%)	15 (28.9%)	14 (23.0%)	29 (26.4%)	0.17
Any live births	51 (85.0%)	43 (82.7%)	57 (93.4%)	103 (93.6%)	0.07
Reports "regular" (intimate) partner	23 (38.3%)	22 (42.3%)	30 (49.2%)	47 (42.7%)	0.68
Sex Work History					
Sex work in past 2 months	56 (93.3%)	49 (94.3%)	57 (93.4%)	101 (92.7%)	>0.99[b]
Workplace					0.70
Bar/Restaurant	27 (45.7%)	30 (57.7%)	25 (41.0%)	51 (46.4%)	
Nightclub	24 (40.7%)	16 (30.7%)	28 (45.9%)	47 (42.7%)	
Home/Other	8 (13.6%)	6 (11.5%)	8 (13.1%)	12 (10.9%)	
Charge for sex					0.13
Living expenses only	12 (20.3%)	6 (11.5%)	11 (18.0%)	20 (18.2%)	
≤500 KSh	19 (32.2%)	23 (44.2%)	34 (55.7%)	43 (39.1%)	
>500 KSh	28 (47.5%)	23 (44.2%)	16 (26.2%)	47 (42.7%)	
>1 year since cohort enrollment	13 (22.0%)	9 (17.3%)	11 (18.0%)	26 (23.6%)	0.74
>1 year as FSW before enrollment	39 (66.1%)	38 (73.2%)	43 (70.5%)	80 (72.7%)	0.81
Financial Security, past year					
Believes financial future is certain	15 (25.0%)	9 (17.3%)	15 (24.6%)	19 (17.3%)	0.49
Ran out of money for basic needs	35 (58.3%)	38 (73.0%)	39 (63.9%)	82 (74.6%)	0.12
Had to borrow money to survive financially	29 (48.3%)	27 (51.9%)	25 (41.0%)	57 (51.8%)	0.55

All p-values are based on chi-squared statistics except for [a]ANOVA and [b] Fisher's exact tests

Table 5: Associations between GBV classes and mental health outcomes

Outcome / Class	Based on modal class assignment		BCH-Weighted Linear Regression			
			Crude		Adjusted	
Depression: PHQ-9 Score	Mean (SD)	Moderate/ Severe Depression N (%)	β (95% CI)	p	β (95% CI)	p
Low	2.6 (4.3)	4 (6.8%)	reference		reference	
Sexual	4.6 (5.4)	8 (15.4%)	2.7 (0.3–5.2)	0.03	2.1 (-0.5–4.7)	0.11
Physical/ Moderate Emotional	2.6 (3.5)	4 (6.6%)	-0.5 (-2.4–1.5)	0.64	-0.6 (-2.2–1.1)	0.51
Severe	4.1 (4.5)	14 (12.7%)	1.8 (0.2–3.4)	0.03	1.5 (0.0–3.1)	0.047
PTSD: PCL-C Score	Mean (SD)	PTSD Screen+ N (%)	β (95% CI)	p	β (95% CI)	p
Low	20.8 (6.9)	5 (8.3%)	reference		reference	
Sexual	22.9 (9.1)	8 (15.4%)	2.8 (-1.2–6.9)	0.17	2.0 (-2.5–6.5)	0.38
Physical/ Moderate Emotional	21.3 (7.9)	9 (14.8%)	0.1 (-3.6–3.8)	0.95	-0.7 (-4.7–3.3)	0.74
Severe	24.6 (11.2)	24 (21.8%)	4.4 (1.2–7.6)	0.007	3.7 (0.6–6.8)	0.02
Alcohol Abuse: AUDIT Score	Mean (SD)	Harmful Drinking N (%)	β (95% CI)	p	β (95% CI)	p
Low	4.7 (5.2)	3 (5.0%)	reference		reference	
Sexual	6.8 (7.9)	7 (13.5%)	2.8 (-0.6–6.2)	0.10	3.7 (0.5–6.9)	0.02
Physical/ Moderate Emotional	5.6 (5.3)	3 (4.9%)	0.7 (-1.9–3.3)	0.59	1.4 (-1.1–4.0)	0.27
Severe	7.7 (7.6)	20 (18.2%)	3.5 (1.2–5.7)	0.003	3.9 (1.8–6.0)	<0.001
Drug Abuse: DAST Score	Mean (SD)	Moderate - Severe Abuse N (%)	β (95% CI)	p	β (95% CI)	p
Low	0.3 (0.8)	3 (5.0%)	reference		reference	
Sexual	0.5 (1.2)	5 (9.6%)	0.3 (-0.3–0.8)	0.32	0.1 (-0.5–0.7)	0.68
Physical/ Moderate Emotional	0.5 (1.2)	3 (4.9%)	0.2 (-0.3–0.7)	0.39	0.1 (-0.4–0.6)	0.67
Severe	0.6 (1.4)	8 (7.3%)	0.4 (-0.0–0.8)	0.07	0.24 (-0.2–0.7)	0.25

PHQ-9 model is adjusted for education, income, workplace, and borrowing money. Moderate/severe depression is score ≥10.

PCLC model is adjusted for education, income, charge for sex, years in cohort, occupation, and borrowing money. PTSD screen + is score≥30.

AUDIT model is adjusted for age, income, and charge for sex. Harmful drinking is score ≥16.

DAST model is adjusted for age at first sex, years as FSW before cohort enrollment, and nationality. Moderate to severe abuse is score ≥3.

Supplemental materials:

Table S1: Questionnaire wording for specific acts of GBV, controlling behaviors, and financial abuse. *For each act that a woman experienced, we asked about the timing (past 12 months, >12 months ago), frequency (one, few, many times), and her relationship to the perpetrator (regular/intimate partners, casual partners, clients).*

The next questions are about things that happen to many women and that a sexual partner may have done to you. Has a partner ever:
Physical violence: Moderate
Slapped you or thrown something at you that could hurt you?
Pushed or shoved you or pulled your hair?
Physical violence: Severe
Hit you with his fist or with something else that could hurt? Kicked you, dragged you, or beaten you up?
Choked or burnt you on purpose?
Threatened to use or actually used a gun, knife, or other weapon against you?
Emotional violence: Moderate
Insulted you or made you feel bad about yourself?
Belittled or humiliated you in front of other people?
Emotional violence: Severe
Done things to scare or intimidate you on purpose, e.g. by the way he looked at you, by yelling or smashing things? Threatened to hurt you or someone you care about?
Sexual violence:
Physically forced you to do something sexual when you did not want to, for example by holding you down, or hurting you in some way? Remember to include husbands and other intimate partners.
Forced you to do something sexual by threatening to physically harm you?
Forced you to do something sexual by giving you drugs or alcohol so that you could not consent or stop what was happening?
Forced you to do something sexual by pressuring you without threats of physical harm? This could include telling threatening to end the relationship, threatening to spread rumors, telling lies, insulting or criticizing you, making promises you knew were untrue, showing displeasure, getting angry without using physical force, or continually verbally pressuring you after you said you didn't want to.
Did he force you to do something sexual that you found degrading or humiliating?
If a woman replied "Yes" to an act of sexual violence, she was also asked:
Were you forced to have oral sex? Were you forced to have vaginal intercourse? Were you forced to have anal intercourse?
Controlling behaviors:*
Tried to keep you from seeing your friends?
Tried to restrict contact with your family of birth?
Insisted on knowing where you are at all times?
Ignored you and treats you indifferently?
Gotten angry if you speak with another man?
Was often suspicious that you are unfaithful?
Expected you to ask his permission before seeking health care for yourself?
Financial abuse:
Taken your earnings or pay packet from you?
Tried to prevent you from going to work, selling, or making money in any way?
Failed to provide money that was expected, to run the house or look after the children, but had money for other things?

* In the analysis we used a narrow definition of controlling behaviors, including whether a partner keeps her from seeing her friends, restricts contact with family of birth, ignores her or treats her indifferently, and expects her to ask permission to seek healthcare. Questions on whether a partner insists on knowing where she is at all times, gets angry if she speaks with another man, and is often suspicious that she is unfaithful were excluded because they were highly prevalent in this population (>60%) and could be attributable to jealousy arising from the participant's engagement in sex work.

Table S2: Across-class comparison of additional GBV characteristics and consequences not included in the latent class indicators

	Low N (%)	Sexual N (%)	Physical/ Moderate Emotional N (%)	Severe N (%)	p value
Total	**60**	**52**	**61**	**110**	
Additional GBV History:					
First sex ≤15 years	12 (21.1%)	16 (30.8%)	18 (29.5%)	33 (30.0%)	0.61
Violence in past 12 months^	7 (11.7%)	25 (48.1%)	50 (48.1%)	55 (50.0%)	0.52
Controlling behaviors**	21 (35.0%)	29 (55.8%)	45 (73.8%)	93 (84.6%)	<0.001
Financial abuse	15 (25.0%)	29 (55.8%)	28 (45.9%)	85 (77.3%)	<0.001
Regular partner GBV^	3 (5.0%)	26 (50.0%)	43 (70.5%)	95 (86.4%)	<0.001
Casual partner GBV^	4 (6.7%)	11 (21.2%)	17 (27.9%)	22 (20.0%)	0.48
Client GBV^	3 (5.0%)	16 (30.8%)	15 (24.6%)	36 (32.7%)	0.53
Consequences (Among women who reported violence from partners)#:					
N	10 (16.7%)	42 (80.8%)	61 (100.0%)	110 (100.0%)	
Fears sexual partners	3 (30.0%)	28 (66.7%)	44 (72.1%)	85 (77.3%)	0.01
Relationship ended	6 (60.0%)	28 (66.7%)	45 (73.8%)	101 (91.8%)	<0.001
Forced to leave home	4 (40.0%)	18 (42.9%)	34 (55.7%)	92 (83.6%)	<0.001
Lost custody of children	2 (20.0%)	4 (9.5%)	8 (13.1%)	12 (10.9%)	0.79
Lost job	0 (0.0%)	1 (2.4%)	4 (6.6%)	17 (15.5%)	0.06[a]
Lost economic support	0 (0.0%)	7 (16.7%)	6 (9.8%)	18 (16.4%)	0.41[a]
Moderate injury (e.g. sprain, bruise, physical pain)	1 (10.0%)	21 (50.0%)	40 (65.6%)	97 (88.2%)	<0.001
Severe injury (e.g. broken bone, unconscious, requires medical care or hospitalization)	1 (10.0%)	4 (9.5%)	10 (16.4%)	63 (57.3%)	<0.001

All p-values are based on chi-squared statistics except for [a]Fisher's exact tests

^ P values are for the comparison excluding the low violence class since that class was fixed to have a low prevalence of violence

Excludes 60 women who did not report partner violence (50 from the *Low GBV* class and 10 with non-partner violence only from the *Sexual GBV* class).

** Including the following variables: whether a partner keeps her from seeing her friends, restricts contact with family of birth, ignores her or treats her indifferently, and expects her to ask permission to seek healthcare. Questions on whether a partner insists on knowing where she is at all times, gets angry if she speaks with another man, and is often suspicious that she is unfaithful were excluded because they were highly prevalent in this population (>60%) and could be attributable to jealousy arising from the participant's engagement in sex work

Chapter 3: Patterns of Gender-Based Violence and Associations with Sexual Risk Behavior and Incidence of Sexually Transmitted Infections among Female Sex Workers in Mombasa, Kenya

Patterns of Gender-Based Violence and Associations with Sexual Risk Behavior and Incidence of Sexually Transmitted Infections among Female Sex Workers in Mombasa, Kenya

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Abstract:

Background: Gender-based violence (GBV) is common among female sex workers (FSWs) and is associated with high-risk sexual behavior and incidence of HIV and other sexually transmitted infections (STIs). Characterizing women's overall experiences of GBV may contribute to a better understanding of the impact of GBV on HIV risk.

Methods: We examined the association between GBV patterns and sexual behavior in 283 FSWs. Patterns of GBV were identified with latent class analysis based on physical, sexual, or emotional GBV from multiple perpetrators. Cross-sectional outcomes were self-reports of the number of partners and of any unprotected sex in the past week, prostate-specific antigen (PSA) detection in vaginal secretions, and a combined indicator of unprotected sex based on self-report or PSA detection. We also measured HIV/STI incidence over 12 months following the GBV assessment. Each association was modeled separately with Poisson regression.

Results: Lifetime prevalence of GBV was 87%. We identified 4 GBV patterns, labeled Low (21% prevalence), Sexual (23%), Physical/Moderate Emotional (18%), and Severe (39%). Compared to the Low GBV class, women with Severe GBV had more sex partners (adjusted risk ratio [aRR] 3.78, 95% CI 1.95-7.32, $p<0.001$), but similar prevalence of unprotected sex. Physical/Moderate Emotional GBV was associated with more sex partners (aRR 5.05, 95% CI 1.85-13.75, $p=0.002$) and a higher prevalence of any unprotected sex with the combined self-report/PSA detection outcome (aRR 2.01, 95% CI 1.02-4.33, $p=0.045$), but not with either measure individually. There were no significant differences in HIV/STI incidence, and women with Sexual GBV did not have higher sexual risk by any measure.

Conclusions: The prevalence of GBV was extremely high in this sample of Kenyan FSWs. Sexual risk behavior differed by patterns of GBV experience. HIV prevention programs should incorporate detailed GBV screening and target multiple risk behaviors.

Introduction

Since the beginning of the HIV epidemic, female sex workers (FSWs) have faced a disproportionate burden of disease. In a 2012 meta-analysis, the odds of HIV infection in FSWs were over 13 times higher than in the general population, and pooled HIV prevalence was 37% in sub-Saharan Africa, the epicenter of the epidemic [2]. Increased vulnerability to HIV is due to a constellation of behavioral and structural factors, including multiple partnerships, inconsistent condom use, high levels of stigma and discrimination, lack of legal protections, and reduced access to health services [70]. The HIV epidemic also overlaps with an epidemic of gender-based violence (GBV) among FSWs, driven by many of the same structural factors [59,63,65,69,109,115–117]. Longitudinal studies in the general population have linked GBV to incident HIV and other sexually transmitted infections (STIs) [7,8,118]. Though studies among FSWs are predominantly cross-sectional, the majority show similar associations with prevalent disease or symptoms [63,69,117,119–122]. Violence may increase HIV/STI risk through biologic pathways, including genitoanal injury and inflammation; behavioral mechanisms such as unprotected vaginal sex, anal sex, and increased numbers of sex partners; and partner characteristics, including an increased prevalence of HIV and STIs among perpetrators [8,12,123,124]. A recent modeling study in Kenya and Ukraine estimated an intervention that reduced physical and sexual GBV to near-zero levels would lead to a 25% reduction in incident HIV infections among FSWs. In Kenya, this translated to approximately 20,000 infections averted among FSWs and an additional 45,000–53,000 infections averted in the general adult population in a 5-year period [9]. This substantial impact highlights the need for programming to reduce GBV and related HIV/STI risk in this population.

Existing studies of GBV in FSWs have used inconsistent and limited definitions of violence. Literature from the general population shows that physical, sexual, and emotional GBV each increase HIV risk, and that there is a dose-response effect based on GBV severity and frequency [7,19,125]. In addition, GBV can impact HIV risk long after the violence has ended,

with higher incidence among women experiencing GBV more than 1 year ago than in the past year [7,11]. Effects of violence may vary by perpetrators as well, including clients, police, pimps, and intimate partners [115,126,127]. Yet most assessments of violence among FSWs address only a subset of violent experiences, such as lifetime history of forced sex, any physical or sexual violence due to sex work in the past week, or client-perpetrated violence in the past 6 months [63,121,128]. In particular, few studies address emotional violence or violence from intimate partners [59,122,127,129]. When studies use limited definitions, women experiencing other forms of GBV are characterized as "unexposed", which can lead to an attenuation of the true effect of violence on HIV risk [55,98]. Furthermore, most studies dichotomize violence exposure into any versus none, ignoring gradients of severity and frequency. Although there are advantages to understanding the effects of specific GBV types or perpetrators [54,76], most women experience multiple, overlapping types of violence [7,78,111,130], which may have a cumulative effect on HIV risk. Narrow definitions of GBV fail to capture the entirety of women's experiences and may underestimate the prevalence and consequences of violence.

An alternative approach is to use person-centered methods to describe the patterns of GBV that women sustain from multiple partners throughout the life course. Studies in Europe and North America have used latent class models to identify subgroups of women experiencing similar GBV patterns, and have shown that specific patterns predict different mental health [58,99] and substance use outcomes [99]. However, GBV patterns have not been studied in FSWs. Characterizing women's overall experiences will contribute to a better understanding of the cumulative impact of GBV on HIV risk. In addition, if specific patterns are associated with distinct HIV risk behaviors, or a greater degree of overall risk, this approach may be useful to tailor interventions to maximize effectiveness [112]. In the current study, we used latent class analysis to characterize GBV patterns among FSWs in Mombasa, Kenya, and to determine whether the patterns were associated with multiple sexual risk behavior outcomes, including the number of sex partners, unprotected sex, and HIV/STI incidence.

Methods

The Sexual Violence Study (SV Study) was a cross-sectional study conducted among participants from the Mombasa Cohort, a prospective cohort study of risk factors for HIV acquisition and transmission among FSWs in Mombasa, Kenya. The cohort was initiated in 1993 and detailed procedures have been published [77]. Eligibility criteria include age 16–60 years, residence within 1-day commuting distance to the clinic, self-identifying as exchanging sex for payment in cash or in kind, and able to provide informed consent. To participate in the SV Study, women also had to be HIV-uninfected; not currently menstruating, pregnant, or <6 weeks post-partum; and able to provide separate written informed consent for the additional study procedures. Trained counselors conducted standardized face-to-face interviews with participants in a private setting in their preferred language (English or Kiswahili). Women who reported violence were offered counseling on site or referral to other facilities. The study was approved by ethics committees at Kenyatta National Hospital and the University of Washington.

Measures

Exposure to GBV was assessed using a modified version of the World Health Organization Violence Against Women Instrument (VAWI) [78], described in Chapter 2. Women were asked if they had ever experienced specific acts of physical, emotional, or sexual violence from any sex partners, including intimate partners, clients, and casual partners, and about the frequency and perpetrator of each reported act. We assessed physical and sexual violence from non-partners (e.g. strangers or acquaintances), but our analysis and interpretation focused on sexual non-partner violence because we were unable to determine whether physical non-partner violence was gender-based or had other causes.

Sexual risk behavior was assessed by self-report and with biological measures. At the SV Study visit, participants reported the number of sex partners in the past 3 months, the total

number of vaginal sex acts in the past week, the number of vaginal sex acts with a condom in the past week. We created a binary measure of any unprotected sex in the past week based on whether the total number of vaginal sex acts exceeded the number of vaginal sex acts with a condom. We did not include anal sex as an outcome because no participants reported this behavior in the past week at the time of data collection.

A vaginal swab was collected at the SV Study visit and tested for the presence of prostate-specific antigen (PSA), a biomarker for unprotected sex, using the ABAcard rapid test (Abacus Diagnostics, West Hills, CA). This test can detect PSA within 24–48 hours after unprotected sex, but sensitivity is low after 24 hours [131,132]. HIV and STI testing was conducted prospectively as part of routine Mombasa Cohort procedures. Endocervical swabs were tested quarterly for gonorrhea, chlamydia, and trichomoniasis by Aptima nucleic acid amplification tests (Hologic, San Diego, CA). HIV screening was performed monthly using the Determine HIV 1/2 rapid test (Alere International Ltd, Ireland). All positive screening tests were confirmed with Uni-gold HIV rapid test (Trinity Biotech, Ireland). Discordant rapid tests were resolved with the Vironostika HIV-1 Uni-Form II Ag/Ab ELISA (bioMérieux, Marcy l'Etoile, France).

Data on potential confounders, including socio-demographic characteristics, sex work history, and financial hardship [93,94] were collected in face-to-face interviews at enrollment into the Mombasa Cohort or at the SV Study visit. We asked detailed partnership characteristics for each of the last 5 sex partners in the 3 months before the SV Study visit, and data were summarized to characterize the proportion of women reporting at least one partner with a given characteristic, such as heavy drinking or known HIV status, and the proportion of total partners reported to provide money, goods, or rent in exchange for sex. Participants reporting >5 sex partners (37.8%) had incomplete data on partnership characteristics.

Statistical Analysis

In the study in Chapter 2, we used latent class analysis (LCA) to identify patterns of GBV in the SV Study participants. LCA is a multivariate person-centered method that assumes an unobserved categorical variable that divides a population into a small number of mutually exclusive and exhaustive latent classes [96]. Participants are assigned to the class for which they have the highest posterior probability of membership. We identified 4 latent classes that represented 4 distinct patterns of GBV.

The current study examined the association of the GBV patterns with sexual risk behavior outcomes. Each outcome was modeled separately with bivariable and multivariable regression models. The multivariable analysis considered potential confounding by the following variables, selected based on causal diagrams: age in years (continuous), education (<8, 8–11, or ≥12 years), nationality (Kenyan or non-Kenyan), number of live births (0 or ≥1), income in Kenyan Shillings (KSh, quartiles), household size (1, 2–3, or ≥4 persons), charge for sex (in kind, ≤500KSh, or >500 KSh), age at first sex (≤15 or >15 years), years enrolled in Mombasa Cohort (<1, 1–4, 5–9, ≥10 years), years as FSW before cohort enrollment (<1, 1–4, 5–9, ≥10 years), any sex work in past 8 weeks (yes/no), primary occupation (unemployed, sex work, other formal, other informal), workplace (bar/restaurant, nightclub, or home/other), contraceptive method (any modern method or none/condoms only), and 3 measures of financial security: feels financial future is certain (certain, uncertain, or very uncertain), ran out of money for basic needs in past year (never, once/twice, or few/many times), and needed to borrow money to survive financially in past year (never, once/twice, or few/many times). Variables were retained in the model if they resulted in meaningful changes (>10%) to the effect estimates. We using the BCH weighting procedure to account for uncertainty in GBV class assignment resulting from the latent class model [44–47]. This procedure creates an expanded dataset with one record for each latent class for each subject and assigns a set of weights based on the classification errors. Subsequent regression analyses are conducted using survey data analysis methods

with linearized (robust) standard errors to account for the weights and for multiple records per subject [104].

We used Poisson regression to estimate the relative difference in the number of sex partners in the past 3 months for each GBV pattern, compared to the reference class of little or no GBV. The distribution of sex partners was highly right-skewed, but all reports of ≥100 sex partners (n=16) were verified with participants to rule out data entry errors. The primary analysis excluded 6 outliers reporting ≥200 sex partners but included all other participants. A sensitivity analysis examined the effect of excluding additional outliers.

Three binary measures of unprotected sex were considered: self-report of unprotected sex in the past week, detection of PSA as a biomarker of unprotected sex in the past 24–48 hours, and a combined measure of any unprotected sex by PSA or self-report. The combined measure serves to partially correct for the low sensitivity of the self-reported measure by reclassifying women with biological evidence of underreporting. Although the self-reported measure of unprotected sex was collected monthly as part of the Mombasa Cohort procedures, PSA testing was only conducted at the SV Study visit, and we limited analysis of all unprotected sex measures to data from that visit to maximize the comparability of the results. Because unprotected sex was not rare (i.e. <10% prevalence), Poisson models were used to estimate the relative prevalence of each outcome. The robust standard errors used for survey data analysis ensure accurate inference with this approach [133].

The last outcome was the incidence of HIV/STIs in the one year following the SV Study visit, including gonorrhea, chlamydia, trichomoniasis, or HIV. We used Poisson models to calculate incidence rate ratios, with an exposure term for time at risk. A woman could have multiple incident infections, but consecutive infections with the same STI without an intermittent negative test result were considered persistent and were counted only at first detection. The estimated date of infection was calculated as the midpoint between the last negative test and first positive test, and time between infection and diagnosis was excluded from the analysis.

Because patterns of GBV can change over time, follow-up time was restricted to 1 year from SV Study enrollment. Participants were also censored after HIV seroconversion, because HIV infection may alter the risk of STI acquisition [134,135]. We conducted a descriptive analysis to compare incidence rates for HIV alone across the GBV patterns, but hypothesis testing was not performed due to the small number of events.

Latent class analyses were conducted in Stata 14.1 using the Stata LCA Plugin [105]. The BCH weights were obtained by replicating the LCA in MPlus 7.4 with the *save=bchweights* command [106], and then exported into Stata to conduct the regression analyses with the *svy:* prefix command to account for the weighting.

Results

Participant Characteristics

The SV Study enrolled 283 women. Descriptive statistics for the sample are shown in Table 6. Median age was 33.5 years (interquartile range [IQR] 27.2–40.6 years). Participants had a median of 8 years of education (IQR 7–12 years) and had enrolled in the Mombasa Cohort a median of 3.1 years ago (IQR 1.2–9.8 years). Forty-three percent (43%) reported a regular partner (e.g., husband or cohabiting partner) as one of her last 5 sex partners in the past 3 months. Median weekly income was 2000 KSh (IQR 1000–5000 KSh), about US$20. Participants experienced substantial financial insecurity: 70% had run out of money for basic needs in the past year and 80% reported that their financial future was uncertain or very uncertain. Over 88% of the last 5 partners provided financial support (i.e. money, goods or rent), regardless of partnership type. The use of effective contraceptive methods was low (39%) and 80% of women had at least one sex partner with HIV-positive or unknown status.

Prevalence and Patterns of GBV

Lifetime prevalence of physical, sexual, or emotional partner violence was 87%, and past year prevalence was 40%. GBV from intimate partners was most common (59%), followed by clients (25%) and casual partners (19%). The latent class model described 4 GBV patterns, as detailed in Chapter 2. The first class, labeled *Low GBV*, included women with little to no GBV and comprised 21% of the population (Table 7). We imposed parameter restrictions to ensure that women in this class had a low (5%) probability of each type of violence. The other 3 classes arose from natural clustering in the remaining data. The second class included 23% of the population and was characterized by predominately sexual GBV from partners or non-partners (labeled *Sexual GBV*). The third class, with 18% prevalence, was labeled *Physical/Moderate Emotional GBV* and was described by moderate or severe physical partner violence and moderate emotional partner violence. The last class, *Severe GBV*, was characterized by severe violence of all types, and was the largest class at 39% of the population. Based on the probability for membership in each latent class, 60 women were assigned to the *Low GBV* Class, 52 women to the *Sexual GBV* class, 61 women to the *Physical/Moderate Emotional GBV* class, and 110 to the *Severe GBV* class.

Associations between GBV Latent Classes and Sexual Risk Behavior

Table 8 shows the findings for the number of sex partners and unprotected sex. The median number of sex partners in the past 3 months was low, ranging from 2.5 to 4 partners across the classes. However, there was a wide range, and substantial numbers of women reported ≥10 partners in the *Severe* class (28%) and in the *Physical/Moderate Emotional* class (38%). In adjusted models, women in the *Severe* class had nearly 4 times as many partners as women in the *Low GBV* class (adjusted risk ratio [aRR] 3.78, 95% CI 1.95–7.32, p<0.001) and women in the *Physical/Moderate Emotional* class had 5 times as many partners (aRR 5.05, 95% confidence interval [CI] 1.85–13.75, p=0.002). The findings were highly sensitive to outliers

in the number of partners (Table S3, Supplementary Materials): For the *Severe GBV* class, the association remained statistically significant even when the analysis was restricted to women reporting <25 partners, excluding 17% of participants in this class, but the effect size was substantially attenuated (aRR 1.53, 95% CI 1.10–2.14, p=0.01). For the *Physical/Moderate Emotional GBV* class, the effect was no longer significant when the analysis was restricted to women reporting <100 partners, excluding 10% of participants in this class (aRR 2.12, 95% CI 0.98–4.61, p=0.06), and disappeared all together for participants with <25 partners, excluding 21% of women in the class (aRR = 0.98, 95% CI 0.50–1.91, p=0.95).

The proportion of women with recent unprotected sex was similar by the self-report and PSA measures (12%–27% across the classes), but there was little overlap in the two measures, so the proportion with unprotected sex by the combined measure was substantially higher (25%–46%). In the entire sample, 54 (18.1%) women had unprotected sex in the past week by self-report, 56 (19.8%) had a positive PSA test, and 97(34.3%) had unprotected sex by either measure (Table S4). Table S5 shows agreement between the PSA and self-report measures by GBV class. The self-report, PSA, and combined endpoints were consistent in showing that women in the *Physical/Moderate Emotional GBV* class had the highest prevalence of unprotected sex. The adjusted prevalence ratio (PR) for the *Physical/Moderate Emotional* class was significantly higher with the combined outcome (aPR 2.01, 95% CI 1.02-4.33, p=0.045) but not with either of the individual outcomes (aPR for self-report 2.43, 95% CI 0.74-8.03, p=0.14; aPR for PSA 1.39, 95% CI 0.52-3.69, p=0.51). There were no significant differences in unprotected sex by any measure when comparing the *Severe* or *Sexual GBV* classes to the *Low GBV* class (Table 8).

Twenty percent of women (57/283) had no gonorrhea, chlamydia, or trichomoniasis testing after the SV Study visit and were excluded from the HIV/STI incidence analysis. An additional 65 women (23%) did not complete the full year of follow-up. The STI/HIV incidence rate ranged from 19.2 per 100 person years (PY) in the *Low GBV* class to 33.7 per 100 PY in

the *Physical/Moderate Emotional* class (Table 9). The differences in HIV/STI incidence across the classes were not statistically significant, but incidence was highest among women in the *Severe* and *Physical/Moderate Emotional* classes. Eighty-nine percent (89%) of women had at least one HIV test after the SV Study visit, and were included in the analysis of HIV alone; 71% were followed for 1 year. There were 6 HIV infections, with an overall incidence rate of 2.9 per 100 PY (95% CI 1.31–6.47, Table 10). Incidence was 4.6 per 100 PY in the *Low GBV* class (95% CI 1.14–18.23), 2.6 per 100 PY in the *Sexual GBV* class (95% CI 0.36–18.24), and 7.6 per 100 PY in the *Physical/Moderate Emotional GBV* class (95% CI 2.45–23.56). No incident HIV infections were observed in the *Severe GBV* class.

Discussion

In this study of Kenyan FSWs, we identified 4 latent classes describing distinct GBV patterns, and these patterns were associated with different profiles of sexual risk behavior. Women with the severe GBV pattern had significantly higher numbers of sex partners in the past 3 months, but their prevalence of unprotected sex was similar to women with little or no history of GBV. The physical/moderate emotional GBV pattern was associated with a higher prevalence of unprotected sex, as measured by the combined outcome of self-report or PSA detection, and with a significantly higher number of sex partners. Incidence of HIV and other STIs was also higher among women with these two patterns, though the confidence intervals were wide due to the small number of infections, and the trends were not statistically significant. Women with the sexual GBV pattern did not have indication of higher sexual risk by any measure.

Most research in FSWs has focused on sexual violence from clients or in the workplace, but our findings underscore the importance of also measuring physical and emotional violence and violence from intimate and casual partners. With a more comprehensive definition, the lifetime prevalence of GBV was 87% in this cohort, and half of GBV experiences included

severe physical, sexual, and emotional violence. There was also a high prevalence of unprotected sex (34% with the combined outcome of either self-report or PSA detection) and high HIV/STI incidence, highlighting the urgent need for programs to address GBV and HIV-related risks among FSWs.

Our conclusions on the association between physical and moderate emotional GBV and increased sexual risk behavior should be interpreted with caution. The association with the number of sex partners was significant in our primary analysis, but the result was primarily driven by a small proportion of women (10%) in this group who had ≥100 sex partners. These reports were verified by the participants but may still be subject to recall bias. Women with this GBV pattern also had a significantly higher prevalence of unprotected sex with the combined outcome of self-report or PSA detection, but the associations were not significant when either measure was considered individually. Our sample size may have been too small to detect differences of the magnitude that we observed. The physical/moderate emotional GBV pattern had the largest effect sizes consistently across every outcome, lending confidence to the conclusion that it is truly associated with an elevated HIV/STI risk profile. Additional research in a larger sample is needed to confirm these findings. Such research should also investigate potential mechanisms for the associations. Of note, this pattern was not associated with mental health symptoms in the previous study (Chapter 2), and the associations with sexual behavior persisted after adjustment for measures of financial need and security. Other mechanisms could include internalized stigma or low self-esteem, fear of further violence, or the influence of pimps or venue owners over work conditions.

Because different GBV patterns are associated with different sexual risk behaviors, prevention interventions may be most effective by addressing a wide range of HIV risk factors. In doing so, they must also acknowledge the broader context of HIV risk. For example, although a higher number of sex partners increases the risk of HIV acquisition, sex partners are a source of income for FSWs, and they may not be willing or able to reduce partner numbers.

Women in the study described significant financial vulnerability, and nearly all partners of all types provided financial support. A high number of sex partners may be necessary for financial survival, and a better approach may be to increase consistent condom use or provide access to other methods of HIV protection, such as pre-exposure prophylaxis (PrEP), for financially vulnerable women. However, the number of partners may not be driven only by financial considerations. In this study, the number of partners was higher among women with severe or physical and moderate emotional GBV, even after adjustment for several markers of income, financial need, and occupation. PTSD, depression, and alcohol abuse have been associated with higher numbers of sex partners in previous studies [136–140], and in Chapter 2 we showed that women with severe GBV had higher symptom scores for each of these outcomes. Combination HIV prevention programs that address mental health, condom negotiation, and financial need for FSWs may be better suited to reduce sexual risk than programs that directly advocate for partner reduction [141]. Though PrEP may be an important component of such packages, there are currently no data available on PrEP use among FSWs, and concerns have been raised about adherence, stigma, and reduced ability to insist on condom use [141]. Several PrEP demonstration projects are currently being conducted with FSWs to address these issues and evaluate delivery options [142].

The discrepancy that we observed between self-reported unprotected sex and PSA detection demonstrates the challenge of measuring unprotected sex in research studies. Although PSA testing is highly accurate immediately after intercourse, its sensitivity drops to 29% within 24 hours [131]. It is well documented that self-reported measures underestimate the prevalence of unprotected sex [122,143–145], but there is little evidence of over-reporting (i.e. reporting unprotected sex when it hasn't occurred) [146]. For the misclassification of unprotected sex to bias our findings, the accuracy of the measurement tools would have to differ among women with different GBV patterns [147]. Although recent violence could conceivably influence reporting of unprotected sex or attendance at the clinic within 24 hours of unprotected

sex, our patterns were based on lifetime GBV history. Less than 10% of women in any class had experienced violence in the past week, suggesting that any differential measurement error that did occur due to recent GBV would have a small effect, and among women with positive PSA tests, there was no evidence of that the prevalence of self-reported unprotected sex differed by GBV pattern. As mentioned above, the lack of association with the individual outcome measures may be due to low power, or there may be no true effect. The combined outcome increases power by increasing the number of women with the outcome from 18% to 34%. Since both measures are highly specific, there is minimal risk of increasing the number of false positive reports with the combined measure. However, the significant association that we observed with the combined measure could be due to chance (i.e., a type 1 error).

This study had several strengths. We used a validated act-specific measurement of GBV that provided multiple opportunities for disclosure and did not require women to identify as battered or abused. We used biological markers of unprotected sex to help address the limitations of self-reported behavior, and prospective data on HIV and STI infections in the year following GBV assessment. In addition, a previous study in this cohort found that self-reported sexual behavior was highly correlated with biological outcomes, including detection of sperm in genital secretions and pregnancy [148], indicating reasonable validity in this population.

There were also important limitations. First, due to a small sample size divided into 4 exposure groups, we had low power to detect differences in sexual risk behavior between the GBV classes. This was compounded by the need to account for uncertainty in latent class assignment, which increased the variability of our estimates [149]. Second, the cross-sectional study design prevents us from establishing the direction of the association between GBV and the number of sex partners or measures of unprotected sex. Third, because most women had participated in the Mombasa Cohort for a number of years, they may have benefitted from social support or access to health care that reduced sexual risk behavior and/or GBV risk, and this could limit the generalizability of our findings. Fourth, there were high rates of loss to follow-up

in our HIV/STI incidence measures: 20% of women had no follow-up testing and an additional 23% were followed for <1 year. We have previously shown that women in this cohort who become lost to follow-up have lower HIV risk behaviors, but that this did not bias estimates of HIV risk [150]. If the same is true for our present analysis, the estimates of incidence may be biased upward, but the measures of association between GBV class and HIV/STI incidence would be valid. Finally, despite the strengths of our measurement tools, there is still a risk of underreporting of GBV and sexual behavior due to the sensitive nature of these subjects.

Conclusion

Female sex workers are burdened by overlapping epidemics of gender-based violence and HIV. This study contributes to the body of evidence that GBV is associated with high-risk sexual behavior, and extends it in two ways. By employing a more comprehensive tool for GBV measurement, we show that FSWs experience a substantial burden of physical, sexual, and emotional violence from multiple perpetrator types. With a person-oriented analysis, we show that different patterns of GBV experience are associated with different behavioral risk factors. There is an urgent need for programs to reduce the risk of GBV, HIV, and other STIs among FSWs. To be most effective, these interventions a should address a wide range of structural and behavioral factors, including violence prevention and safety strategies, mental health, consistent condom use, PrEP, legal rights and protections, stigma and discrimination, and financial well-being. Given the complex web of risk factors and mechanisms for HIV risk, a multi-faceted approach is essential to reduce the burden of violence and HIV in this population.

Table 6: Sample Characteristics (N=283)

	Median (IQR) or n (%)	
Age, years	33.5	27.2–40.6
Education, years	8	7–12
Years in Mombasa Cohort	3.1	1.2–9.8
Years in sex work before cohort entry	2	0–5
Monthly income, Kenyan Shillings	2000	1000–5000
Charge for sex, Kenyan Shillings	500	200–1000
Kenyan	261	92.6%
First sex ≤15 years of age	79	28.2%
≥1 sex partner, past 3 months	264	93.3%
Use of any highly-effective contraceptive method*	109	38.5%
Among the last 5 sex partners in the past 3 months:		
≥1 intimate partner	122	43.1%
≥1 partner who is wealthy	66	23.3%
≥1 partner who gets drunk ≥ few times/week	108	38.2%
≥1 partner with HIV-positive or unknown status	226	79.9%
Primary Occupation		
Unemployed	42	14.8%
Sex work	89	31.5%
Other formal	45	15.9%
Other informal	107	37.8%
Workplace		
Bar/restaurant	133	47.2%
Nightclub	115	40.8%
Other	34	12.1%
Believes financial future is uncertain or very uncertain	225	79.5%
Ran out of money for basic needs, past 12 months		
Never	89	31.5%
Once or twice	110	38.9%
Few or many times	84	29.7%
Of the last 5 sex partners in the past 3 months, proportion who gave money, goods, and/or rent in exchange for sex:	n/N**	%
Regular partners	122/134	91.0%
Casual partners	128/145	88.3%
Clients	587/598	82.2%

Abbreviations: *IQR* interquartile range; *HIV* human immunodeficiency virus
Missing data: 1 observation missing for age, education, years in Mombasa Cohort, years in sex work before cohort entry, charge for sex, and workplace. 3 observations missing for age at first sex.

* Includes any hormonal method (oral contraceptives, injectables, implants), intrauterine device (IUD), tubal ligation, or hysterectomy.

** Shows the number of each partner type who gave money, goods, and/or rent over the total number of each partner type reported.

Table 7: Class indicators and descriptions (replicated from Chapter 2)

	Class membership & item response probabilities			
	Low	**Sexual**	**Physical & Moderate Emotional**	**Severe**
Estimated prevalence	20.9%	23.0%	17.5%	38.6%
Women in study sample assigned to class, n (%)	60 (21.2%)	52 (18.4%)	61 (21.6%)	110 (38.9%)
Distribution within classes:				
No physical	**95.0%**	**50.8%**	14.8%	8.7%
Moderate physical	3.3%	27.1%	42.4%	4.0%
Severe physical	1.7%	22.1%	42.8%	**87.3%**
No sexual	**95.0%**	41.3%	**80.3%**	34.0%
Sexual 1-2 times	2.1%	22.5%	19.7%	13.6%
Sexual, few times	0.9%	21.0%	0.0%	9.7%
Sexual, many times	1.9%	15.1%	0.0%	42.7**%**
No emotional	**95.0%**	**60.4%**	36.2%	0.0%
Moderate emotional, few times	0.0%	10.7%	39.4%	6.0%
Moderate emotional, many times	0.0%	23.6%	22.5%	12.4%
Severe emotional	5.0%	5.3%	1.9%	**81.6%**
No non-partner violence	**75.4%**	9.8%	**67.6%**	37.3%
Physical non-partner violence only	19.6%	41.5%	32.4%	27.4%
Sexual non-partner violence	5.0%	48.7%	0.0%	35.3%

Note: To aid with interpretation of the class characteristics, probabilities over 50% are highlighted in bold-text, and gray shading shows probabilities <50% which are important for class interpretation either individually or in groups.

Table 8: Associations between GBV class and sexual risk behavior

Outcome / Class		BCH-Weighted Poisson Regression			
		Crude		Adjusted	
*Number of sex partners, past 3 months**	Median (IQR)	Relative Increase (95% CI)	P	Relative Increase (95% CI)	P
Low	2.5 (1–9)	reference		reference	
Sexual	3 (2–9)	1.01 (0.40–2.52)	0.99	1.49 (0.52–4.29)	0.46
Physical/Moderate Emotional	3 (1–20)	3.54 (1.43–8.77)	0.006	5.05 (1.85–13.75)	0.002
Severe	4 (1–15)	3.03 (1.53–6.00)	0.002	3.78 (1.95–7.32)	<0.001
*Any unprotected sex, past week^*	N (%)	Prevalence Ratio (95% CI)	P	Prevalence Ratio (95% CI)	P
Low	7 (11.7%)	reference		reference	
Sexual	10 (19.2%)	2.09 (0.54–8.12)	0.29	1.73 (0.45–6.62)	0.42
Physical/Moderate Emotional	17 (27.9%)	3.37 (1.01–11.28)	0.049	2.43 (0.74–8.03)	0.14
Severe	20 (18.2%)	1.89 (0.60–5.97)	0.28	1.62 (0.52–5.04)	0.40
Positive PSA test[#]	N (%)	Prevalence Ratio (95% CI)	P	Prevalence Ratio (95% CI)	P
Low	11 (18.3%)	reference		reference	
Sexual	10 (18.2%)	1.08 (0.37–3.12)	0.89	0.67 (0.22–2.00)	0.47
Physical/Moderate Emotional	16 (26.2%)	1.66 (0.68–4.10)	0.27	1.39 (0.52–3.69)	0.51
Severe	19 (17.3%)	0.96 (0.42–2.19)	0.92	0.81 (0.35–1.87)	0.62
Combined outcome: Any unprotected sex by PSA or self-report[†]	N (%)	Prevalence Ratio (95% CI)	P	Prevalence Ratio (95% CI)	P
Low	15 (25%)	reference		reference	
Sexual	19 (36.5%)	1.71 (0.76–3.87)	0.19	1.44 (0.64–3.21)	0.38
Physical/Moderate Emotional	28 (45.9%)	2.31 (1.11–4.81)	0.03	2.01 (1.02–4.33)	0.045
Severe	35 (31.8%)	1.42 (0.71–2.82)	0.32	1.33 (0.69–2.59)	0.39

Abbreviations: IQR interquartile range; *CI* confidence interval; *PSA* prostate-specific antigen

* Model for number of sex partners adjusts for age, nationality, income, household size, charge for sex, years in cohort, age at first sex, occupation, having a current intimate partner, and running out of money to survive in the past 3 months. Excludes 3 observations with missing data

^ Model for self-reported unprotected sex adjusts for education, years in cohort, and having a current intimate partner. Excludes 1 observation with missing data

[#] Model for PSA adjusts for age, occupation, having a partner who drinks, having a partner who is wealthy, and having an intimate partner. Excludes 1 observation with missing data

[†] Model for combined outcome adjusts for income and charge for sex. Excludes 1 observation for missing data.

Table 9: Associations between GBV class and HIV/STI incidence* (n=226)

Class:	Cases	PY at risk	Incidence per 100 PY	Crude IRR (95% CI)	P	Adjusted IRR (95% CI)	P
Low	8	41.52	19.27	reference		reference	
Sexual	9	35.13	24.62	1.49 (0.42–5.26)	0.54	1.41 (0.35–5.69)	0.63
Physical/Moderate Emotional	12	35.40	33.90	2.18 (0.63–7.57)	0.22	2.03 (0.56–7.44)	0.28
Severe	22	76.29	28.84	1.66 (0.58–4.73)	0.34	1.57 (0.51–4.90)	0.43

Abbreviations*: CI* confidence interval; *STI* sexually transmitted infection; *HIV* human immunodeficiency virus; *PY* person-years

* Includes chlamydia, gonorrhea, trichomoniasis, and HIV.

Model for STI incidence adjusts for age, household size, and having a partner who drinks to get drunk at least a few times/week.

Table 10: HIV incidence by GBV class (n=253)

Class	Cases	Person-years at risk (PY)	Incidence per 100 PY	95% Confidence Interval
Low	2	43.85	4.56	1.14–18.23
Sexual	1	38.92	2.57	0.36–18.24
Physical/Moderate Emotional	3	39.48	7.60	2.45–23.56
Severe	0	84.28	0.00	.
Total	6	206.54	2.91	1.31 - 6.47

Supplementary tables

Table S3: Sensitivity analysis of the effect of outliers on the association between class and number of sex partners

Subset	Class	Adjusted RR*	95% CI		P	Excluded n (%)
Entire Sample	Low	reference				0 (0.0%)
	Severe	7.18	2.11	24.48	0.002	0 (0.0%)
	Sexual	11.69	1.04	131.85	0.047	0 (0.0%)
	Phys/mod emot	7.80	2.07	29.38	0.003	0 (0.0%)
<200 partners	Low	reference				0 (0.0%)
	Severe	3.78	1.95	7.32	<0.001	2 (1.8%)
	Sexual	1.49	0.52	4.29	0.461	2 (3.8%)
	Phys/mod emot	5.05	1.85	13.75	0.002	2 (3.3%)
<100 partners	Low	reference				0 (0.0%)
	Severe	2.06	1.29	3.28	0.002	8 (7.3%)
	Sexual	1.88	0.81	4.38	0.141	2 (3.8%)
	Phys/mod emot	2.12	0.98	4.61	0.057	6 (9.8%)
<50 partners	Low	reference				2 (3.3%)
	Severe	1.82	1.22	2.71	0.003	14 (12.7%)
	Sexual	1.25	0.62	2.54	0.534	4 (7.7%)
	Phys/mod emot	1.78	0.90	3.53	0.095	8 (13.1%)
<25 partners	Low	reference				3 (5.0%)
	Severe	1.53	1.10	2.14	0.013	19 (17.3%)
	Sexual	1.15	0.67	1.98	0.614	5 (9.6%)
	Phys/mod emot	0.98	0.50	1.91	0.954	13 (21.3%)

***** Adjusted for age, nationality, income, household size, charge for sex, years in cohort, age at first sex, occupation, having a current intimate partner, and running out of money to survive in past 12 months.

Table S4: Concordance of unprotected sex measured by self-report for past 7 days and PSA for past 24-48 hours

	Self-report of unprotected sex, past 7 days		
PSA Results	**No**	**Yes**	**Total**
Negative	186 (65.7%)	41 (14.5%)	227 (80.2%)
Positive	43 (15.2%)	13 (4.6%)	56 (19.8%)
Total	229 (80.9%)	54 (18.1%)	283 (100%)

Table S5: Proportion of women with positive PSA test in each GBV class who reported unprotected sex in the past week

Class	Total with positive PSA	Self- reported unprotected sex n (%)	P (Fisher's exact test)
Low	11	3 (27.3%)	0.736
Severe	19	4 (21.1%)	
Sexual	10	1 (10.0%)	
Physical/Moderate Emotional	16	5 (31.3%)	
Total	56	13 (23.2%)	

Chapter 4: Intimate partner violence and adherence to HIV pre-exposure prophylaxis (PrEP) in African women in HIV serodiscordant relationships: A prospective cohort study

Intimate partner violence and adherence to HIV pre-exposure prophylaxis (PrEP) in African women in HIV serodiscordant relationships: A prospective cohort study.

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Abstract

Background: Intimate partner violence (IPV) is associated with higher HIV incidence, reduced condom use, and poor adherence to antiretroviral therapy and other medications. IPV may also affect adherence to pre-exposure prophylaxis (PrEP).

Methods: We analyzed data from 1785 HIV-uninfected women enrolled in a clinical trial of PrEP among African HIV-serodiscordant couples. Experience of verbal, physical, or economic IPV was assessed at monthly visits by face-to-face interviews. Low PrEP adherence was defined as clinic-based pill count coverage <80% or plasma tenofovir levels <40 ng/mL. The association between IPV and low adherence was analyzed using generalized estimating equations, adjusting for potential confounders. In-depth interview transcripts were examined to explain how IPV could impact adherence.

Results: 16% of women reported IPV during a median of 34.8 months of follow-up (IQR 27.0 - 35.0). Overall, 7% of visits had pill count coverage <80% and 32% had plasma tenofovir <40 ng/mL. Women reporting IPV in the past 3 months had increased risk of low adherence by pill count (adjusted RR 1.49, 95% CI 1.17-1.89) and by plasma tenofovir (adjusted RR 1.51, 95% CI 1.06-2.15). Verbal, economic, and physical IPV were all associated with low adherence. However, the impact of IPV diminished and was not statistically significant 3 months after the reported exposure. In qualitative interviews, women identified several ways in which IPV affected adherence, including stress and forgetting, leaving home without pills, and partners throwing pills away.

Conclusion: Women who reported recent IPV in the Partners PrEP Study were at increased risk of low PrEP adherence. Strategies to mitigate PrEP non-adherence in the context of IPV should be evaluated.

Introduction

Randomized trials have demonstrated that oral antiretroviral pre-exposure prophylaxis (PrEP) is effective for HIV prevention in several populations, including heterosexual men and women [44,46], men who have sex with men [45,151,152], and injection drug users [47]. Based on these data, the World Health Organization (WHO) recommends PrEP as part of a comprehensive HIV prevention package for people at substantial risk of HIV infection [153]. Several PrEP demonstration projects are testing strategies to maximize population impact and cost-effectiveness [154,155].

One population eligible for PrEP targeting is sexually active women in sub-Saharan Africa [156]. In this region, women have considerably higher incidence of HIV than men, particularly at young ages [1]. Intimate partner violence (IPV) is also common, with lifetime prevalence estimates ranging from 36-71% [78]. IPV is associated with an increased risk of HIV infection [12,24,157–162], with two prospective studies showing that HIV incidence is approximately 50% higher among women who have experienced IPV than women with no IPV history [7,8]. In the study by Kouyoumdjian *et al.*, the effect size was similar for physical, sexual, and verbal IPV; increased with IPV frequency and severity; and persisted for more than one year after the last violent episode [7]. In the context of violent relationships, individual-level biomedical interventions such as PrEP may be more effective for HIV prevention than behavioral interventions requiring cooperation of both partners [7,48]. However, for PrEP to prevent HIV infection, consistently high adherence is necessary during periods of potential exposure [50,163,164]. Women who experience IPV have lower adherence to several medication regimens, including antiretroviral therapy for HIV treatment and methadone treatment for drug addiction [52,165–167]; IPV may also be a barrier to PrEP adherence [53].

With programs or demonstration projects beginning to offer PrEP to women, including women who experience IPV, it is important to understand whether adherence levels will be high

enough for PrEP to be effective. If IPV is associated with low PrEP adherence, additional, targeted adherence support may be required for IPV survivors. We conducted a prospective cohort study to examine whether recent and/or past exposure to IPV is associated with low PrEP adherence among HIV-uninfected women participating in a clinical trial of PrEP.

Methods

Study Population

The population for this analysis was all HIV-uninfected women participating in the Partners PrEP Study, a phase 3, randomized, double-blind, placebo-controlled clinical trial that demonstrated the efficacy of daily oral PrEP among HIV-uninfected members of HIV serodiscordant couples. The design, procedures, and outcomes of the trial are described elsewhere [44,168]. Briefly, from 2008–2012, 4747 couples were randomized and followed at 9 research sites in Kenya and Uganda. HIV-uninfected partners were randomly assigned to once-daily tenofovir disoproxil fumarate (TDF), emtricitabine (FTC)/TDF, or placebo, and followed monthly for 12–48 months. All couples received a package of HIV prevention services, including risk-reduction counseling, couples' counseling, and condoms. The study protocol was approved by the University of Washington Human Subjects Review Committee and ethics review committees at each of the study sites. All participants provided written informed consent in English or their local language.

Data Collection

Experience of IPV was assessed monthly by asking whether the participant had been verbally, physically, or economically abused by her partner since the last study visit. Participants were asked in the context of a risk-reduction counseling session, in local languages, and in a manner considered culturally appropriate for each study site [169]. Although the wording of the question varied and was context specific, all interviewers were experienced in couples'

counseling and were trained through multiple role-plays to assess and document IPV on case report forms according to standard protocols. If the participant reported IPV, the type (verbal, physical, or economic), frequency, and consequences (e.g., relationship breakup, income loss) were documented on a structured questionnaire.

PrEP adherence was measured by clinic-based pill counts and plasma tenofovir concentrations. For all HIV-uninfected participants, pill counts were conducted on returned, unused medication tablets each month at the study clinic. Plasma samples were collected and stored at visit months 1, 3, and quarterly thereafter, plus at any visit where a participant tested positive for HIV. Plasma tenofovir concentrations were measured in a subset of participants only, using ultra-performance liquid chromatography-mass spectrometry assay methods.[170] Of the 1297 plasma tenofovir measurements, 606 (47%) were from 113 randomly sampled women, and 691 (53%) were from 302 women purposively selected for other secondary analyses [168,170–173].

Demographic characteristics were collected separately from the participant and her partner at enrollment, including age, income, education, weekly alcohol intake, marital status, relationship duration, and how long the couple had known they were serodiscordant. Data on sexual behavior, including coital frequency, condom use, and outside partnerships, were collected by interviewer-administered questionnaires at monthly intervals for the participant and quarterly intervals for her partner. We relied on participant reports for dyad-level data such as relationship duration and coital frequency, and on partner reports for his individual-level data, including demographic characteristics and outside partnerships. Monthly HIV testing and annual STI testing were conducted using methods described previously [174].

Data Analysis

At each study visit, women were categorized as having no IPV reported to date in the study, IPV reported in the past 3 months, or IPV reported in the study and >3 months ago. This approach enabled us to distinguish between an acute effect of recent IPV on PrEP adherence, compared to a more long-lasting effect.

Pill count coverage was defined as the percentage of days between study visits when a pill was available to be taken, calculated as (number of pills dispensed – number of pills counted) / number of days between study visits. Coverage was dichotomized into high (≥ 80%) or low (<80%), consistent with other HIV prevention studies [110,175] and with recent pharmacodynamic modeling suggesting that 6 of 7 doses per week of oral FTC/TDF PrEP may be required to protect female genital tissue from HIV infection [51]. Although clinic-based pill counts are an imperfect measure of adherence, they were strongly correlated with other objective measures of adherence in the Partners PrEP Study [110,170]. Visits were excluded if the participant was not taking study drug for a protocol-defined reason, such as pregnancy, breastfeeding, seroconversion, or toxicity concerns. Missed visits were included, because one possible consequence of IPV could be failure to attend clinic visits, and adherence was set to zero when the number of days since the last visit exceeded the number of pills dispensed. About 2% (1400/59,806) of eligible follow-up visits were missed.

Plasma tenofovir adherence was dichotomized at 40 ng/mL. This concentration is based on the lower 95% confidence interval 24 hours after dose for directly observed daily dosing at steady state, but is also consistent with a single dose taken in the last 24 hours [176–179]. We selected this threshold because it is more sensitive to occasional missed doses than a threshold of detectable vs. non-detectable, and because data suggest that near-daily dosing may be

necessary to achieve adequate vaginal concentrations of activated intracellular metabolites of tenofovir diphosphate and FTC triphosphate required for effective protection from HIV [51,180].

We evaluated the associations between IPV and each PrEP adherence measure using univariate and multivariable (adjusted) generalized estimating equation (GEE) Poisson models with an exchangeable correlation matrix and robust standard errors, to account for repeated measures for each participant [133,181]. Multivariable models adjusted *a priori* for age, study site, and time in study. We also evaluated the following covariates as potential confounders and retained them in the model if they resulted in meaningful changes (>10%) to the estimated risk ratios: baseline covariates of partnership duration, years in the known HIV serodiscordant partnership, age difference with HIV-infected partner, income, education, alcohol intake; and time-varying covariates of HIV-infected partner's report of outside sexual partners, and participant's reports of outside sexual partners and any sex with their HIV-infected partner. Because changes in the participant's sexual behavior could be either a cause or a consequence of IPV, the last two time-varying covariates were lagged by 3 months to ensure that they preceded both the exposure and the outcome. Because the amount of missing data was small (<5% of visits), we conducted complete case analyses. Risk estimates did not change under different assumptions about the values of missing data. In sensitivity analyses, we excluded participants with pill count coverage >103%, indicating that fewer pills were returned than would be expected based on the number of days since the last visit. Previous studies suggest that coverage above that threshold may indicate lower adherence [170,182]. To maximize statistical power, we included measurements from both randomly sampled and purposefully sampled participants in our plasma tenofovir analysis. We also restricted the analysis to randomly sampled participants to assess the potential for selection bias.

Additional analyses examined the effects of type of IPV (physical, verbal, or economic) and frequency of physical and verbal IPV on PrEP adherence measured by pill count coverage.

The comparison group for each of these analyses was women who reported no IPV to date in the study. We used a Cox proportional hazards model to determine whether IPV was associated with higher HIV incidence in this cohort. The adjusted hazard ratios (aHRs) controlled for study arm and did not change with adjustment for age, marital/cohabiting status, number of children, any sex or unprotected sex in past month, male partner viral load and circumcision status, HSV-2 status at enrollment, or DMPA use.

Qualitative data

As part of an ancillary adherence sub-study, in-depth qualitative interviews were conducted with 88 HIV-uninfected participants (40 female and 48 male) at a single study site in Uganda. Methods and other findings from these interviews are described elsewhere [183,184]. Participants were purposively sampled based on adherence levels, as estimated from unannounced home-based pill counts conducted as part of the sub-study procedures. The study enrolled all 58 participants at the site whose adherence dropped below 80% at some point during the sub-study ("low adherers"), and a sample of 30 participants with 100% adherence throughout the sub-study ("perfect adherers"). Women in the qualitative sample were older than in the overall study (median age 36 years, IQR 29.5–40.5), had fewer years of schooling (median 3, IQR 0–5), and were more likely to earn an income (97.5%). They were similar to the overall sample on marital status, relationship duration, and number of children. The interview addressed participants' experiences of taking PrEP, accounts of missed doses and lapses in adherence, and strategies for sustaining adherence. Interviews were conducted a minimum of 3 months and median of 21 months after enrollment (IQR 16–24 months). Data were analyzed using an inductive process to understand social influences that appeared to impact adherence. For this analysis, we reviewed the 7 transcripts that contained references to IPV, including 4 low adherers and 3 perfect adherers. Relevant content was organized to reveal patterns in the data.

The ancillary adherence sub-study was approved by the Partners Health Care Human Research Committee, the University of Washington Human Subjects Review Committee, and the Uganda National Council on Science and Technology. Separate written consent was obtained from all participants for this sub-study.

Results

Participant characteristics

Characteristics of the 1785 HIV-uninfected female participants are shown in Table 11. Mean age was 33.2 years, participants had completed an average of 5.6 years of school, and 69.6% had earned an income in the past 3 months. The vast majority of participants were married (99.2%), with a mean relationship duration of 12.9 years, and had mutually-disclosed HIV serodiscordant status for a mean of 1.4 years.

Prevalence and correlates of IPV

Over the course of the study, 288 women (16.1%) reported IPV at 437 visits (0.7% of 60,191 total visits). Of these women, 198 (68.8%) reported IPV at 1 study visit, 19.8% at 2 visits, 6.6% at 3 visits, and 4.9% at ≥4 visits. Most women reported multiple types of IPV (Figure 2A). Verbal IPV was the most common, reported at 376 visits, followed by physical IPV (235 visits) and economic IPV (212 visits). At 53% of visits with verbal IPV, women reported 1-2 incidents since the last monthly study visit. Three to 5 incidents were reported at 31% of visits, and ≥6 incidents at 15%. At the majority of visits with physical IPV (86%), women reported 1-2 incidents since the last visit, with 13% reporting 3-5 incidents and 3% reporting ≥6 incidents (Figure 2B). The most common consequences of IPV were change of residence, relationship loss, and income/property loss. Missed doses of study drug and missed study visits were also reported,

though these were not predetermined response categories and were mentioned infrequently (Figure 2C).

Women who reported IPV were similar to women who reported no IPV on most demographic, relationship, and behavioral characteristics (Table 11). Baseline characteristics associated with subsequent reporting of IPV included having younger partners (mean 38.2 versus 39.4 years), having mutually-disclosed HIV serodiscordant status for slightly longer (1.6 versus 1.3 years), and reporting any income (78.1% versus 67.9%). Seventy-five percent of women who reported IPV were from Uganda (versus Kenya), compared to 65.9% of women who did not report IPV in the study. At visits with IPV, women were less likely to report sexual activity with their study partners than at visits with no IPV (68.7% versus 81.1%), more likely to report unprotected sex (22.4% versus 12.3%), and more likely to have partners who reported an outside sexual partner (19.8% versus 14.8%).

Adherence to PrEP and association with IPV

Pill count coverage was high among most women, regardless of reported IPV (mean 95.3%, standard deviation [SD] 19.8%, Table 12); the proportion of visits with pill count coverage <80% was 7.0%. Among visits with plasma tenofovir measurements, 32.0% had concentrations <40 ng/mL.

Table 13 presents crude and adjusted risk ratios (aRRs) for the association of IPV with PrEP adherence. After adjusting for age, study site, time on study, and male partner reports of outside sex partners, women were 50% more likely to have low PrEP adherence at visits with IPV in the past 3 months, compared to visits with no IPV to date in the study. This association was consistent regardless of whether adherence was measured by pill count (aRR 1.49, 95% confidence interval [CI] 1.17-1.89, p=0.001) or by plasma tenofovir (aRR 1.51, 95% CI 1.06-2.15, p=0.02). Adherence at visits >3 months after reported IPV was similar to adherence at visits with no IPV to date in the study (aRR for pill count: 1.08, 95% CI 0.86-1.36, p=0.5, aRR for

plasma tenofovir: 0.95, 95% CI 0.73-1.24, p=0.7). There was no evidence of effect modification by time on study, or by country for recent IPV; for IPV occurring in the study >3 months ago, lower adherence persisted in Kenya but not in Uganda (p-interaction =0.02) in the pill count analysis but not in the plasma tenofovir analysis.

The association between IPV in the past 3 months and low adherence was similar in women who reported sex in the past month (aRR: 1.53, 95% CI 1.11-2.10, p=0.009) and women reported no sex in the past month (aRR 1.44, 95% CI 1.04-1.99, p=0.03). Risk estimates did not substantially change when pill count analyses excluded participants with coverage >103%, when tenofovir analyses were restricted to the randomly sampled cohorts, or when adjusting for other potential confounding factors listed in the Methods.

When different types of IPV were considered separately, effect sizes for pill count coverage were similar for recent (past 3 month) verbal IPV (aRR 1.65, 95% CI 1.17-2.33, p=0.005) and recent economic IPV (aRR 1.48, 95% CI 1.14-1.92, p=0.003). The effect of recent physical IPV was not statistically significant (aRR = 1.27, 95% CI 0.89-1.82, p=0.2). However, the frequency of IPV since the last study visit was higher for verbal IPV (mean 4.1 episodes, SD 6.9) than for physical IPV (mean 1.7 episodes, SD 2.1), and the risk of low adherence increased significantly with increasing frequency of recent physical IPV (aRR = 1.09 for each additional episode of IPV within the reporting period, 95% CI 1.04-1.14, p<0.001) and recent verbal IPV (aRR = 1.02 for each additional episode, 95% CI 1.02-1.03, p<0.001). Type and frequency of IPV reported in the study and >3 months ago were not associated with adherence.

IPV and HIV incidence

There were 48 HIV seroconversions among women with no IPV to date in the study, 9 among women with IPV during the study and >3 months ago, and 2 among women with IPV in the past 3 months, resulting in HIV incidence rates of 1.2, 1.3, and 2.2 per 100 person-years, respectively. The associations between IPV and HIV incidence were not statistically significant

(aHR for IPV in the past 3 months: 1.54, 95% CI 0.37-6.51, p=0.6; aHR for IPV > 3 months ago: 1.26, 95% CI 0.55-2.90, p=0.6).

Participant reports on IPV and PrEP use

Although the in-depth interviews did not specifically ask about IPV, seven women raised the topic when describing adherence challenges and strategies. Three patterns of how IPV interfered with adherence were evident in the transcripts (Table 14). Some women explained how violence and discord in the home made it difficult to remember to take the pills (Table 14A). Others described running away during violent episodes, either because they feared for their safety or because they were chased away by their partners; they did not take their pills with them when leaving the house, so these episodes could result in missed doses (Table 14B). In two cases, women's partners threatened to take or throw away their pills, either as a form of punishment or because they blamed relationship discord on the pills themselves (Table 14C). Some women also described ways to surmount these challenges, and maintained high adherence despite experiences of IPV. Two women reported sending their children to retrieve their pills after they had run away from the house, and another was able to replace pills her husband had thrown away by explaining her situation to the study staff (Table 14D).

Discussion

Overall, adherence to PrEP was high among women in the Partners PrEP Study, regardless of IPV history. However, women who reported IPV in the past 3 months had an increased risk of low PrEP adherence. The association did not persist for more than 3 months after the violence occurred, suggesting that among this group of women, the effects of IPV on adherence were acute and time-limited. Qualitative findings suggested several pathways through which IPV may cause short-term adherence lapses, including stress, being forced to

leave the home, or a partner trying to take pills away from the participant; some women also developed strategies to maintain high adherence during IPV episodes.

This is the first study to examine the association between IPV and PrEP adherence. IPV was associated with lower condom and diaphragm use in one prospective study [18] and with lower ART uptake, self-reported adherence, and viral suppression in a meta-analysis [165]. Other studies have described the importance of partner support and disclosure of product use for good adherence in PrEP and microbicide trials [184–190], and the role of violence as a barrier to disclosure [188,190]. Since couples enrolled in the Partners PrEP Study together, our findings suggest that IPV impacts adherence even when women are using PrEP with their partner's knowledge and consent. It will be important for PrEP demonstration projects targeting high-risk women to collect data on this risk factor going forward.

At 16%, the period prevalence of IPV during this study was similar to that reported in another study of HIV serodiscordant couples using the same instrument [169], but lower than national Demographic and Health Survey estimates of spousal violence in the past 12 months: 41% in Kenya and 45% in Uganda [191,192]. Our study population consisted of women in stable, long-term relationships who were willing to be tested for HIV with their partners and enroll in a couples-based prevention study. Women with these characteristics may be less likely to experience IPV than women in the general population or those participating in other PrEP trials. Several qualitative studies have noted the predominance of violence in the lives of PrEP and microbicide study participants in some geographies, such as for some women in South Africa where the majority of VOICE and FEM-PrEP participants resided [193,194]. Our estimates of the impact of IPV on PrEP adherence may be based on more moderate or infrequent IPV, and the effect may be stronger or more persistent in other populations. However, women reporting IPV in our study population reported higher risk sexual behavior, such as unprotected sex and having a partner who reported outside partners, relationship loss,

change of residence, and property loss, suggesting that they experienced meaningful consequences of IPV.

Strengths of this study include a large sample size, prospective study design, and integration of quantitative and qualitative methods. Our findings were robust to different measures of PrEP adherence, adjustment for multiple potential confounding factors, and several sensitivity analyses to address misclassification, missing data, and selection bias. The association between recent IPV and PrEP adherence persisted when we restricted the analysis to women reporting sexual activity with their study partners, suggesting that IPV increases the risk of low adherence during periods in which women are at risk for HIV acquisition. Although the study was not powered to test for an association between IPV and HIV incidence, the hazard ratio point estimates are consistent with previous estimates of a 50% increase in HIV incidence associated with IPV [7,8,169].

An important limitation to our study is that classification of IPV was based on self-report and may be under-reported. Our measurement tool did not ask about sexual IPV, violence severity, history of IPV before enrollment, or specific violent acts such as hitting, slapping, or threatening. Women may not have disclosed IPV if they did not consider specific acts to be abusive or if they did not feel comfortable discussing IPV with the study staff. In addition, IPV was assessed in the context of a counseling session rather than with a standardized question. This approach may have increased disclosure of IPV, but IPV assessment may have differed between sites. We cannot distinguish whether differences in reported IPV and its effects represent true differences in the rate of IPV by site or country, differences in participant willingness to report IPV, or differences in IPV ascertainment by study interviewers. If the degree of under-reporting is the same among women with low versus high PrEP adherence, this would likely underestimate the risk of low adherence associated with IPV. Although the proportion of visits with low adherence was higher when measured by plasma tenofovir levels than by pill-count coverage, the risk estimates for IPV and PrEP adherence were consistent

between adherence measures, increasing our confidence in the results. Although the qualitative interviews were conducted at only one study site, a review of the narrative descriptions of IPV episodes and consequences on study case report forms suggest that the mechanisms described were relevant to other sites in Uganda and to Kenya as well.

In sub-Saharan Africa, targeting PrEP to high-risk women may be a cost-efficient approach to reducing HIV incidence [195–197], but high adherence levels are required during periods of risk. Demonstration projects are ongoing to evaluate the feasibility of this approach and to identify strategies for implementation [198–200]. Given the high prevalence of IPV in this region, and its impact on HIV risk, IPV should be considered when identifying high-risk women. In our cohort, the vast majority of women were able to take PrEP consistently, regardless of IPV history, but IPV in the short-term was associated with lower adherence in some subjects. Efforts to target PrEP towards women with IPV should recognize the risk of low adherence, and interventions should be evaluated to promote PrEP adherence in the context of violence. A potential intervention could integrate lessons from successful PrEP adherence programs [201] and from interventions to improve ART adherence among HIV infected women with histories of abuse [202], and could include motivational interviewing and problem-solving approaches to help women identify ways that IPV impacts their adherence and develop approaches to prevent violence or avoid lapses in adherence associated with IPV [201,202]. Individual or group counseling approaches should be evaluated; group counseling may involve a social support network that could increase self-efficacy for adherence [203]. Some women in our study reported strategies to maintain adherence in the face of IPV, and lessons from these examples of resilience could help in developing successful interventions. Such interventions could increase the prevention benefit of PrEP by promoting effective use in a population at high risk of HIV.

Table 11: Participant characteristics at baseline and during follow-up.

Enrollment (Mean (SD) or N(%))	N	Total (N=1785)	Any IPV in study (N=288)	No IPV in study (N=1497)	*P*^
Demographic and Relationship Characteristics					
Age (years)	1785	33.2 (7.5)	32.6 (7.2)	33.4 (7.6)	0.08
Partner age (years)	1785	39.2 (8.1)	38.2 (8.2)	39.4 (8.0)	0.03
Age difference (participant age - partner age)	1785	6.0 (6.0)	5.7 (6.3)	6.0 (5.9)	0.4
Ugandan (vs. Kenyan)	1785	1203 (67.4%)	216 (75.0%)	987 (65.9%)	0.003
Years of school	1785	5.6 (3.8)	5.4 (3.7)	5.6 (3.8)	0.4
Any income	1785	1242 (69.6%)	255 (78.1%)	1017 (67.9%)	0.001
Married	1785	1770 (99.2%)	286 (99.3%)	1484 (99.1%)	0.8
Partnership duration (years)	1711	12.9 (8.3)	12.2 (7.7)	13.0 (8.4)	0.1
Years known discordant	1781	1.4 (1.7)	1.6 (1.6)	1.3 (1.7)	0.02
Number of children	1785	3.9 (2.2)	3.8 (2.2)	3.9 (2.2)	0.6
Behavioral Characteristics					
Number of drinks per week	1785	0.2 (0.9)	0.3 (0.8)	0.2 (0.9)	0.3
Number of sex acts with study partner, past month	1785	5.5 (5.0)	6.0 (6.2)	5.4 (4.7)	0.1
Unprotected sex with study partner, past month	1785	406 (22.8%)	69 (24.0%)	337 (22.5%)	0.6
Sex with outside partner, past month	1785	8 (0.5%)	0 (0.0%)	8 (0.5%)	0.2
Male partner reports outside partner, past month	1785	264 (14.8%)	44 (15.3%)	220 (14.7%)	0.8
Any STI diagnosis*	1636	221 (13.5%)	32 (12.2%)	189 (13.8%)	0.5
Follow-Up (per person)	**N**	**Total (N=1785)**	**Any IPV in study (N=288)**	**No IPV in study (N=1497)**	
Number of visits	1785	33.7 (9.4)	35.7 (8.4)	33.3 (9.6)	<0.001
Duration of follow-up (months)	1785	31.2 (8.3)	33.0 (7.4)	30.9 (9.5)	<0.001
Number of visits reporting IPV:	288				
1		--	198 (68.8%)	--	--
2		--	57 (19.8%)	--	--
3		--	19 (6.6%)	--	--
4 or more		--	14 (4.9%)	--	--
Ever pregnant	1785	397 (22.2%)	57 (19.8%)	340 (22.7%)	0.3
Any STI diagnosis*	1781	258 (14.5%)	51 (17.7%)	207 (13.9%)	0.09
HIV seroconversion	1781	57 (3.2%)	9 (3.1%)	48 (3.2%)	0.9
Follow-Up (per visit)	**N**	**Total (N = 58,406 visits)**	**Any IPV† (N = 419 visits)**	**No IPV (N = 57,987 visits)**	
Number of sex acts with study partner, past month	57,439	3.7 (4.1)	3.5 (5.3)	3.7 (4.1)	0.4
Any sex with study partner, past month	57,439	46,538 (81.0%)	288 (68.7%)	46,250 (81.1%)	<0.001
Number of unprotected sex acts, past month	57,439	0.5 (1.9)	1.0 (3.7)	0.4 (1.8)	0.001
Any unprotected sex with study partner, past month	57,439	7,111 (12.4%)	94 (22.4%)	7,017 (12.3%)	<0.001
Outside sexual partner, past month	58,384	1,329 (2.3%)	13 (3.1%)	1,316 (2.3%)	0.3
Male partner reports outside partner, past month	55,310	8,069 (14.8%)	79 (19.8%)	7,990 (14.8%)	0.005

* Any positive test result for chlamydia, gonorrhea, syphilis, or trichomonas. At enrollment, 149 women were missing 1 or more STI tests at enrollment and had no positive tests

† IPV was reported at 437 total visits, of which 18 were enrollment visits and 419 were follow-up visits.

^ P values are based on t-tests with unequal variance for continuous variables and Pearson's chi-squared tests for categorical variables

Table 12: Summary of adherence by measure and IPV status

	Adherence Measure				
	Pill count coverage			Plasma tenofovir levels	
	Number of Visits	Mean (SD)	<80% N (%)	Number of Visits	<40 ng/mL N (%)
IPV in study, ≤ 3 months ago	1,100	95.5% (18.7%)	88 (8.0%)	38	16 (42.1%)
IPV in study, >3 months ago	5,471	94.8% (21.5%)	433 (7.9%)	142	40 (35.2%)
No IPV to date in study	43,562	95.5% (19.6%)	2,962 (6.9%)	1117	349 (31.2%)
Total	50,165	95.3% (19.8%)	3,510 (7.0%)	1297	415 (32.0%)

Table 13: Effect of IPV exposure on each PrEP adherence outcome: bivariable and multivariable results

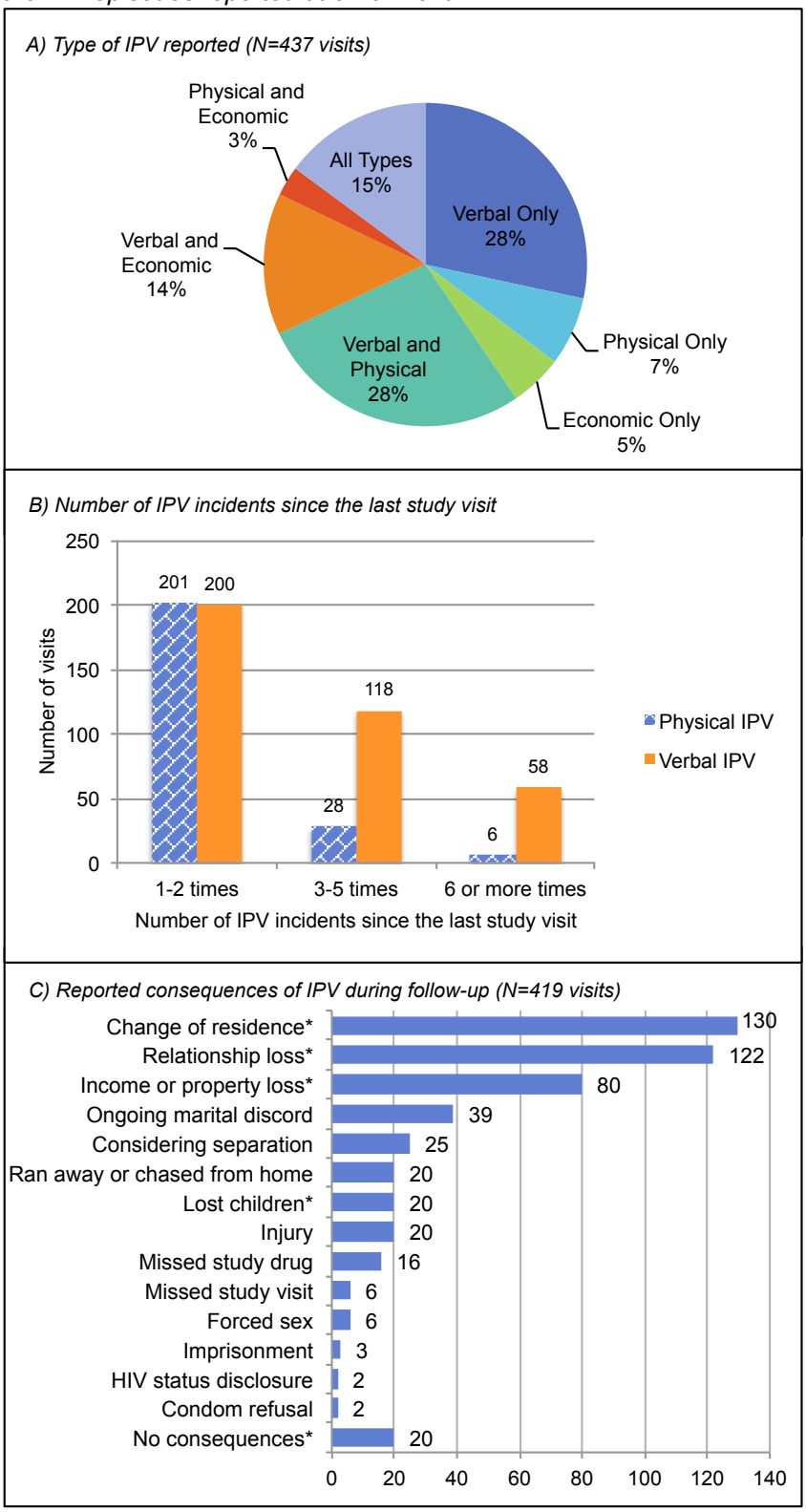
	Pill count coverage <80%				Tenofovir <40 ng/mL			
	Risk ratio (95% CI)	p	Adjusted* risk ratio (95% CI)	p	Risk ratio (95% CI)	p	Adjusted* risk ratio (95% CI)	p
IPV in study, ≤ 3 months ago	1.28 (1.03−1.59)	0.03	1.49 (1.17–1.89)	0.001	1.41 (1.01–1.99)	0.05	1.51 (1.06–2.15)	0.02
IPV in study, >3 months ago	1.27 (1.05−1.54)	0.02	1.08 (0.86–1.36)	0.5	1.15 (0.91–1.45)	0.3	0.95 (0.73–1.24)	0.7
No IPV to date in study	1.00	--	1.00	--	1.00	--	1.00	--

* Adjusted for age (years), study site, time on study (days), and whether male partner reports outside sex partner

Table 14: Excerpts from qualitative interviews on how IPV impacts PrEP adherence

Pattern	*Example*
A) Stress	Now when you don't have peace or you have slept outside, can't the day end when you are embroiled in quarrels and forget about the drugs? *(participant QLA028)*
	If the family is not fine and there is no co-operation between you and your husband, that eventually affects the way one swallows his/her medicine. But if the home is okay and there is peace, even the children will be allowed to remind you. *(participant QLA055)*
B) Leaving home without study drug	Of course I go without drugs. Now if we fight and I run away, can I go with the drugs? Or I just run for safety and look for refuge somewhere? *(participant QLA 028)*
	The whole of December and November, I was in serious problems; I could not remember to swallow medicine... he would chase me out of the house and I would not get a chance to take my medicine with me. He would chase me and I spend the nights in the middle of nowhere; sometimes in church or in the bush…it was hard for me to remember to swallow medicine. Our relationship was not good; it was a very difficult moment in our relationship. *(participant QLA 055)*
	We fought, my husband and I, so I ran away to my parents' home. In the process, I left the bottles behind. *(participant QPA 002)*
	It's hard for me to remember each and every day I missed. But one common reason that has led me to miss my medicine on several occasions is..; My husband likes taking alcohol. And when he drinks, he becomes violent. There are times when he chase me and I run out of the house. Sometimes, that happens before I swallow the medicine and you find that I don't have a chance to go back. *(participant QLA 053)*
C) Partner throws away or threatens to take study drugs	…there is some problem that happened where we quarreled at home and he threw away my drugs …He was telling me that; "let me throw away these pills and we will remain the same because it seems they are the ones making you behave like that. He had taken some alcohol which was forcing him to behave like that. *(participant QPA 020)*
	He was saying that since I refused to use condoms, he would also swallow my drugs... We quarreled over it, he chased me and I slept in the kitchen, from there I never looked back, I went back to my parents…*(participant QPA 016)*
D) Resilience	When my child brought me what to put on in the morning, he also carried my drug bottles along. The man was busy staging a roadblock carrying a panga that I should not dare step in the house looking for clothes, while the children bypassed him and entered the bedroom where they picked clothes and drugs and brought them to me. So ever since I started taking the drugs, I have never stopped or missed taking them. *(participant QPA 016)*
	It is my son who sneaked the bottles out of the house and brought them to me. My husband had actually locked everything in the bedroom. So I told my son to devise all means possible to get for me my pill bottles. *(participant QPA 002)*
	… he threw away my drugs, but I gathered them again and when the study staff came to visit us, I explained to them. They told me to come to the clinic the following day and get more drug. *(participant QPA 020)*

Figure 2: Descriptive statistics for IPV exposure during the study. *A) Type of IPV reported at each study visit in which any IPV was reported. B) Number of IPV episodes reported since the last study visit. Data were not collected on frequency of economic IPV. C) Reported consequences of IPV. Consequences marked with an asterisk (*) were explicitly listed as response options, while those without the asterisk were described by participants in the open-ended "other" category. Note: participants were only asked to describe IPV consequences during follow-up visits. Data are missing for the IPV episodes reported at enrollment*



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Chapter 5: Discussion

Discussion

The studies presented in this dissertation contribute to understanding the mechanisms through which GBV may increase HIV risk, and advance the methodological approaches to the classification of GBV exposure for future research studies. By elucidating the heterogeneous nature of GBV experiences and the associations with multiple HIV risk factors, our results can inform new approaches to improve the effectiveness of GBV and HIV prevention programs.

Chapters 2 and 3: Interpretations and Implications for HIV Prevention in FSWs

The work presented in Chapters 2 and 3 suggests that FSWs in Mombasa bear a heavy burden of GBV, that their experiences fall into several distinct patterns, and that these GBV patterns are associated with different adverse outcomes. Women in the *Severe GBV* class had higher symptom scores for depression, PTSD, and alcohol abuse, and they reported higher numbers of sex partners in the past 3 months. Women in the *Sexual GBV* class had higher symptom scores for alcohol use, but they did not have higher sexual risk behavior than women in the *Low GBV* class. In contrast, women in the *Physical and Moderate Emotional GBV* class reported higher numbers of sex partners in the past 3 months and were more likely to have had unprotected sex in the past week, but their mental health symptoms did not differ from women with *Low GBV*. Reports of sexual risk behavior were consistent with estimated HIV/STI incidence: lowest in the *Low GBV* class and increasing from the *Sexual GBV* class, to the *Severe GBV* class, and then the *Physical and Moderate Emotional GBV* class.

The high prevalence of physical and sexual GBV that we observed is consistent with findings from FSWs around the world [63,65,69,73,109,115,121,125,204], and calls attention to the need for structural interventions to provide social and legal protections for sex workers. Several studies have described associations between GBV and mental health or sexual risk behavior in FSWs, but ours is the first to look at these associations according to patterns of violent experiences. This difference in exposure classification provides unique insights, but

makes it challenging to compare our results to previous studies. Generally, we found significant associations between at least one GBV pattern and each outcome, with the exceptions of drug abuse and HIV/STI incidence. Overall these results are consistent with previous studies showing that GBV is associated with depression, PTSD, alcohol abuse, the number of sex partners, and unprotected sex [59,66,69,75,109]. Drug abuse was rare in this study population (<7%), and despite high HIV/STI incidence, the actual number of infections was small (<25 in each group), so we lacked statistical power to identify associations with these outcomes. Our findings that *Severe* and *Sexual GBV* were not associated with unprotected sex and that *Sexual* GBV was not associated with the number of sex partners were unexpected, given that many previous studies have found associations between sexual violence and sexual risk behavior [69,71,127]. However, a closer inspection shows that the published studies are inconsistent in their measures of violence type, perpetrator, and time frame, choice of sexual behavior timeframe and outcome, and, not surprisingly, in their results (Table 15). This highlights the need for researchers to come to a consensus on the best practices for measurement of both GBV and sexual behavior, to allow valid comparison of findings in the future.

A smaller body of work has examined GBV patterns in the general population and has shown that such patterns explain variance in mental health and sexual risk behavior outcomes. For example, in one study, membership in the "interpersonal conflict" and "physical aggression" classes was associated with depression, sedative use, and recreational drug use, while the "systematic abuse" class was associated with depression, alcohol use, sedative use, and prescription drug use [99]. In another study, "emotional only" violence was associated with suicidal thoughts and poor general health status, but not with whether the last pregnancy was unwanted. In contrast, "sexual dominant" violence was associated with last pregnancy unwanted, but not poor general health status [55]. An analysis of patterns of community violence, child abuse, and IPV found that all types of violence were associated with a higher lifetime number of sex partners, but only multiple victimization with all 3 violence types was

associated with the number of recent partners, and only women with exposure to predominantly community violence were more likely to never use condoms in the past 3 months [57]. Our study extends this literature by examining patterns of GBV in an FSW population. Again, however, comparison of findings is hampered by the different measures employed in each study.

Our findings support our overarching hypothesis that women with different GBV experiences have different potential pathways for HIV risk. This implies that to effectively address HIV and other health consequences of GBV among FSWs, programs should address a broad range of risk factors. A narrow focus on consistent condom use, for example, will only address the needs of some women, while others may need assistance with alcohol abuse, depression, and/or reducing the number of sex partners. Although it was not directly explored in this dissertation, financial need played an important role in GBV, mental health, and sexual risk behavior; for example, measures of income, charge for sex, or financial insecurity were important confounding factors in each analysis. Similarly, stigma and discrimination against FSW, which were not measured in this study, increase the risk for violence against FSWs, directly impact mental health, and make it difficult for women to adopt or adhere to safer sex practices. Therefore, efforts to address these factors are an essential part of any GBV or HIV prevention program for this population [141].

The findings also suggest that a one-size-fits-all approach to HIV prevention may not be appropriate for GBV survivors, and there may be benefits to tailoring interventions based on GBV experiences. This is not to advocate that interventions should be limited to a specific set of risk factors for women with each GBV pattern. Our findings are not conclusive enough to promote such an approach, and it may be ethically indefensible to exclude some services all together. However, as discussed in Chapter 2, our findings do suggest that women with different patterns might benefit from emphasis on certain topics, or from different lengths or frequencies of intervention sessions. For example, women in the *Sexual GBV* class could be offered an intervention focused on alcohol abuse and strategies to prevent or diffuse threats of sexual

violence, with more limited discussion of partner reduction or unprotected sex. Women in the *Physical and Moderate Emotional* class could be offered an intervention that aims to improve condom negotiation skills in the context of violent relationships, without devoting substantial time to mental health issues. By targeting issues that are more salient to particular groups of women, this approach may improve intervention uptake and retention, and ultimately effectiveness [112]. Alternatively, in interventions that work with small groups of women in a participatory manner [27,205,206], the formation of groups of women with similar violence patterns may increase intervention efficacy if women can share effective strategies to address their common experiences.

Examination of GBV patterns may be important for intervention evaluation as well as design. Evaluations may show that an intervention worked well for women with some GBV patterns and poorly for other patterns, or may explain why an intervention worked well in one study setting and poorly in another [96]. For example, an intervention to increase condom use may not show efficacy in a women with predominately sexual GBV, but may be highly effective in women with the physical and moderate emotional GBV pattern, for whom baseline risk of unprotected sex is higher.

Clearly, attempts to use GBV patterns to develop or evaluate interventions may be premature if they are based on this study alone. As noted above, this is the first study to examine GBV patterns in FSWs, and our sample of women participating in an ongoing cohort study may not be generalizable to the overall population of FSWs in Mombasa or more broadly. In addition, this was a cross-sectional study with a relatively small sample size, so our results lacked precision. Additional work should seek to replicate the GBV patterns identified and their associations with the various health outcomes. This is discussed in more detail below.

Chapter 4: Interpretations and Implications for Women in HIV Serodiscordant Couples

In Chapter 4, we found that among HIV-uninfected women in HIV serodiscordant couples, any report of IPV in the past 3 months was associated with a 50% increase in low adherence. Verbal, physical and economic IPV were each associated with low adherence, and the effect size increased with each additional IPV episode reported. This appeared to be a short-term effect, and possible reasons included stress and being forced to leave home during violent episodes.

This published work was the first study to measure the association between GBV and PrEP adherence. The findings are consistent with other studies showing that violence is correlated with poor adherence to antiretroviral therapy for treatment and for prevention of mother to child transmission, and with poor adherence to other HIV prevention modalities such as condoms and diaphragms [18,165,207]. Although PrEP may not be a feasible HIV prevention strategy for women in relationships with frequent or severe violence, most women in the Partners PrEP Study reported only IPV at only one visit over a median of 35 months, and many women maintained high adherence despite experiencing violence. Combined with fact that the observed impact of IPV on adherence was short-lived, these factors suggest that PrEP may be a promising prevention tool for many women who face overlapping risk from both violence and a known HIV-infected partner. At the same time, there may be scenarios in which frequent or severe IPV precludes effective PrEP adherence for an extended period of time, or where PrEP use may make it more difficult for women to insist on condom use with violent partners. In these cases, the risks of PrEP may outweigh the benefits. As PrEP is rolled out to women in programs and demonstration projects in sub-Saharan Africa, it will be important to screen for IPV and to develop counseling messages that address GBV and its impact on adherence. At present, there are few evidence-based PrEP adherence support interventions [201]. As interventions are developed, they should include explicit considerations of violence and use a client-centered approach to develop strategies for remaining adherent during periods of violence.

The findings and projected implications of this study only strictly apply to HIV-uninfected women in HIV serodiscordant couples, and their experiences of violence and PrEP use may differ from that of women in the general population or in other high-risk groups, such as female sex workers or young women and adolescent girls. Although there is ongoing concern that women in HIV serodiscordant couples may be at increased risk of violence, relationship discord, and abandonment [208–210], most studies suggest that violence is rare, and that the risks are highest when the woman is HIV-infected or when the violence was extant prior to the couple's HIV diagnosis [169,208,211,212]. The rate of IPV was low in our study, compared with DHS data from Kenya and Uganda [191,192], but this may be attributable to the fact that serodiscordant couples who are experiencing violence or relationship dissolution are less likely to enroll in a study together. Women in HIV serodiscordant couples may also differ from women in the general population in their motivation to adhere to PrEP, due to their known risk and the promise of PrEP as a potential solution to the dilemma posed by discordance [184]. Lastly, because HIV-infected men in the Partners PrEP Study were aware of and supportive of their partner's PrEP use [184,213], IPV may have had a smaller impact on adherence than in partnerships where PrEP use is covert or not actively supported by the male partner. The effects of IPV on PrEP adherence may differ for women in HIV serodiscordant couples who are not enrolled in a trial with their HIV-infected partner, and for other groups of women such as female sex workers and young women who are not in known HIV serodiscordant relationships.

Methodological Contributions

A methodological strength of this dissertation is classification of GBV by frequency and/or severity in all 3 chapters. In both variable-oriented and person-oriented approaches, more detailed measurement and classification of GBV can provide important insights for our understanding of the impact of GBV and for evaluation of interventions. Very few studies consider GBV frequency or severity [55,127,214]; The more common approach is to

dichotomize exposure into any versus none. In doing so, we risk underestimating the strength of the effect for the women with higher levels of exposure, and we may miss opportunities to mitigate violence when it cannot be eliminated all together. For example, a GBV prevention intervention may result in reductions in violence severity or frequency, perhaps shifting from a "severe" GBV pattern to a more moderate pattern, even if the proportion of women experiencing any GBV does not change. This impact would not be captured with a binary outcome but could have a meaningful impact on women's health and well-being.

Our use of latent class analysis to identify GBV patterns addresses another important methodological issue in the study of violence and HIV risk. As described throughout this dissertation, the vast majority of studies on GBV and health consequences employ a variable-oriented approach, as we did in Chapter 4 for the study on IPV and PrEP adherence. With this approach, the relationship between each aspect of GBV and the health consequence is studied separately: for example, we conducted 3 analyses to examine the associations between any IPV, physical IPV, and verbal IPV with PrEP adherence. This approach is valuable for understanding overall trends, directionality, and aggregate relationships, but it does a poor job of capturing heterogeneity, clustering, or interaction. As described by Nurius and Macy [76]:

> *Within this field of study [IPV], ordinary least squares statistical models of the relationships between the dependent and independent variable(s) are often not sufficient approximations of phenomena (e.g., there may be different trends or trajectories for different groups, or the trends may be nonlinear), interactions are more common than rare, distinct subgroups challenge the validity of summary statistics, and variables often have more salient meaning as parts of constellations and patterns than by themselves alone.*

To examine interactions and clustering with a variable-oriented approach, we typically rely on subgroup analyses or statistical interaction terms. However, when a large number of subgroups are under consideration, such as when we consider type, frequency, and severity

together, this approach raises problems with multiple comparisons and increased Type I error rates. Small sample sizes within each subgroup can reduce statistical power and result in inconclusive results for some comparisons. Additionally, there may be important higher-order interactions between the subgroup variables that cannot be examined due to small cell sizes [96]. Furthermore, it is unlikely that each combination of the variables under consideration represents individuals in the target population, making the interpretation of the results more challenging. (For example, there may be few or no women who experience physical GBV without emotional GBV.)

In contrast, a person-oriented approach, such as the latent class analysis used in Chapters 2 and 3, enables the identification of a small number of representative classes that describe patterns that commonly occur in the population. Practically speaking, this reduces the number of subgroups to a manageable number. In our study, it was more realistic to examine 4 latent classes than up to 72 subgroups defined by 4 types of violence and 3–4 frequency and severity levels within each violence type. More importantly, this approach allowed us to identify women at elevated risk for specific health outcomes by virtue of the holistic or comprehensive experiences of GBV that they have endured. For example, in Chapter 2, a variable-oriented analysis may have shown that physical, sexual, and emotional GBV were all associated with PTSD, but the person-oriented approach shows us that the risk is only substantially higher among women who have severe or frequent experiences of all 3 violence types together.

Gaps and Future Directions

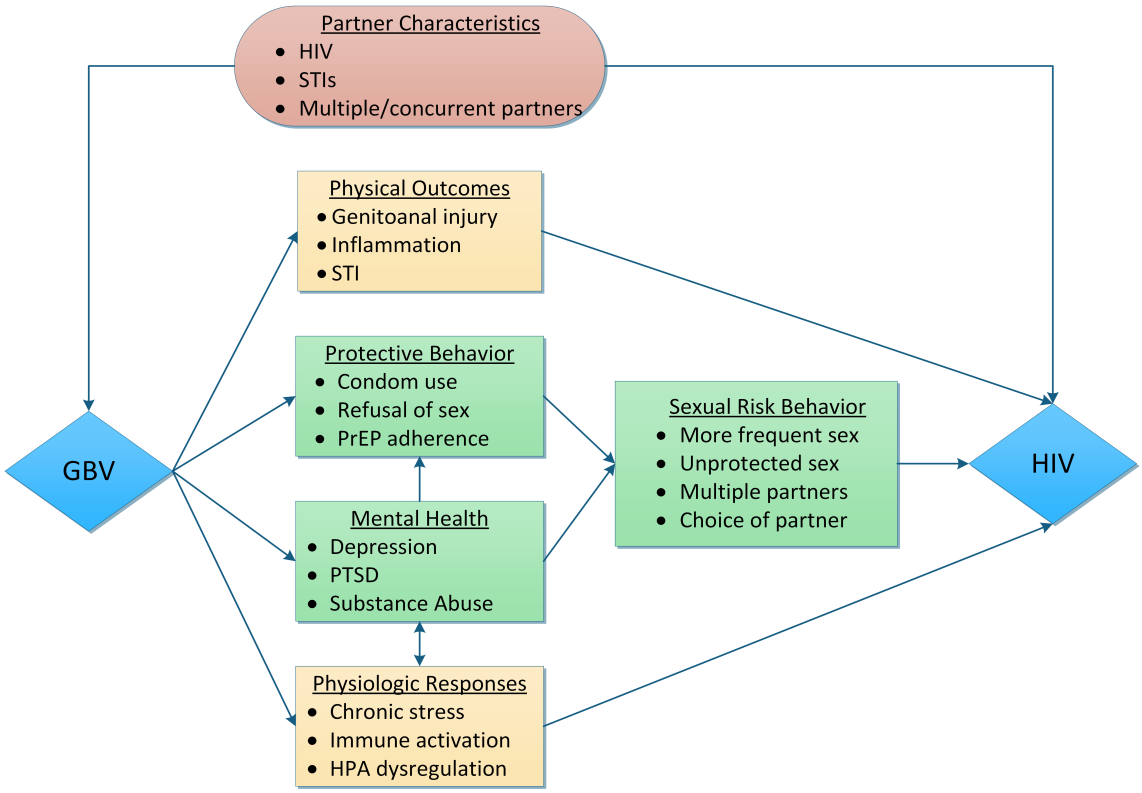
Returning to the conceptual diagram from Chapter 1 (Figure 3), these studies provide valuable data supporting the pathways from GBV to HIV risk through protective behavior, mental health, and sexual risk behavior. However, many gaps remain in our understanding of these dynamics. Below I outline 5 areas for future research: additional dimensions of GBV,

additional pathways from GBV to HIV risk, replication and generalizability, expansion to other high-risk populations, and intervention development.

1. Additional Dimensions of GBV

First, there are many dimensions of GBV that we were not able to explore. We were not able to discern patterns of GBV based on relationship to perpetrator in our sample of FSWs. Although this suggests that violent experiences may not cluster by perpetrator type, it does not mean that the effects of violence on HIV risk factors do not vary by perpetrator type. As shown in Table 15, for example, studies suggest that effects of violence from intimate partners may differ from effects of violence from clients [115,117,125,127,204]. Similarly, sexual risk behavior differs by partnership type, with condom use being less common in intimate partnerships than with clients [117,125,127,129,204,215,216].

Figure 3: Causal pathways between gender-based violence and HIV risk. *GBV: gender-based violence; PTSD: post-traumatic stress disorder; STI: sexually transmitted infection; PrEP: pre-exposure prophylaxis*



We also were not able to address the interactions between GBV and controlling behaviors or economic abuse in the latent class analysis. One study in the general population suggested that controlling behaviors may be more important than IPV alone in driving HIV risk [98], and in Chapter 4, we showed that economic IPV had a significant impact on PrEP adherence. In Chapters 2 and 3, we conceptualized these factors as co-occurring with GBV but did not seek to evaluate them separately, partly because our sample size was not large enough to include them as indicator variables in the latent class analysis. The prevalence of controlling behaviors and economic abuse were both strongly correlated with class membership (see Table S2 in Chapter 2), suggesting that the classes captured patterns of these variables to at least some extent. However, future work should give further consideration to the role of these factors in HIV risk.

2. Additional Pathways from GBV to HIV Risk

This dissertation addresses only a subset of the pathways outlined in the conceptual model (Figure 3). Our studies were designed to be complementary to the parent Sexual Violence (SV) Study, and results from that study will improve our understanding of potential mechanisms of GBV's impact on HIV risk through injury, inflammation, chronic stress, and immune activation. The SV Study will focus on the effects of sexual GBV on genital outcomes (e.g., injury and local inflammation), but will also examine the effects of other dimensions GBV on variables that represent systemic effects, such as hair cortisol and immune activation.

The SV Study also collected rich data on partner characteristics, although they were limited to the 5 most recent partners from the past 3 months. Absence of data on client characteristics is a common limitation in studies of GBV and/or HIV risk among FSWs [126,217], so it would be worthwhile to evaluate whether the variables we have measured are predictive of future violence, sexual behavior, or HIV/STI incidence in this or other cohorts.

Finally, a complete picture of these pathways should include the personal and societal factors that promote resilience among women exposed to violence. Resilience was not included

in our conceptual diagram, but multiple studies indicate that individual women react differently to specific acts and cumulative experiences of violence [218–220]. A better understanding of psychological and community resources that minimize negative effects may be inform intervention development [221,222].

3. Replication and Generalizability

As noted above and in Chapters 2 and 3, this is the first time GBV patterns have been described among FSWs, and only one previous study has characterized such patterns among African women [55]. Furthermore, our study had a small sample size, which could have limited statistical power to detect a larger number of patterns or clustering by perpetrator type. Future work should aim to characterize GBV patterns in other, larger groups of FSWs to determine whether the patterns we identified and their associations with different HIV risk factors are replicable. Replication in different settings will also address concerns about the generalizability of our study population. It was previously demonstrated that ongoing participation in the Mombasa Cohort was associated with a reduction in inconsistent condom use and in partner numbers [223]. Repeated counseling may also improve mental health or connect participants to resources to prevent GBV. The associations between GBV and HIV risk factors may therefore differ for FSWs who are not enrolled in the Cohort. In addition, future studies should be prospective to a) establish a temporal relationship between GBV and HIV risk factors, b) understand the duration of changes in HIV risk factors that may be attributable to GBV, c) examine how changes in GBV patterns affect risk factors over time, and d) evaluate whether HIV risk is best predicted by current GBV exposure or by cumulative GBV history, as suggested by this and other studies [7,10].

4. Other High-Risk Populations

Another area for future research is extension to other high-risk populations, particularly young women and adolescent girls, aged approximately 15-24 years. In sub-Saharan Africa, about 25% of all new HIV infections occur among women in this age group [1]; incidence rates

from recent multi-country HIV prevention trials are as high as 6%-8% per year, and >10% per year in KwaZulu-Natal, South Africa [224–226]. Young age is also a risk factor for GBV [192,227,228]. Pre-exposure prophylaxis is a promising strategy to reduce HIV risk in young women, but we need to understand the degree to which violence impacts adherence in this population, and conversely, how use of HIV prevention methods may increase the risk of violence [190,229]. Additionally, studies of GBV patterns and associated HIV risk factors in this population may help build our understanding of why HIV incidence is so high and how social and structural interventions may reduce risk. There is also a need to understand how GBV and PrEP adherence are associated in FSWs, given that rates of violence are extraordinarily high, and that the impact of client-perpetrated violence may differ from that of IPV.

5. Intervention Development

Our ultimate goal should be to use the results from these observational studies to develop interventions for GBV and HIV prevention. A number of interventions for FSWs have successfully used individual- and community-level empowerment approaches to reduce both GBV and HIV risk [117,230,231], and there are also promising examples for women in the general population [205,206]. Opportunities to build on these interventions could include better integration of components to address mental health and substance abuse, exploration of tailored interventions for women with different GBV patterns, and the inclusion of PrEP to mitigate HIV risk that persists after the violence has ended. Another important intervention approach is to screen for GBV in HIV prevention programs, particularly PrEP delivery programs, and provide supplemental counseling and safety planning to help women maintain prevention behaviors in the context of violence. An example of this approach is the CHARISMA project, which is developing a screening tool to assess the level of male partner support and experiences of GBV among women accessing the dapivirine vaginal ring for HIV prevention [232]. A clinic-based intervention will provide counseling on how to safely disclose product use, maintain high adherence, or gain partner support, depending on the participant's needs and

wishes, while a parallel community engagement component will aim to challenge gender norms and misconceptions about HIV prevention in general and the ring specifically. Additional studies should seek to develop PrEP adherence support interventions for GBV-exposed women in other settings. For women in serodiscordant couples, a brief safety planning intervention may help women avoid short-term adherence lapses that result directly from violence. Women with more severe or persistent GBV may require additional resources to promote uptake and maintenance of HIV prevention strategies including PrEP [49].

Conclusions

This dissertation has contributed to our understanding of HIV prevention in African women by illustrating that gender-based violence can increase HIV risk through the pathways of poor mental health, increased sexual risk behavior, and reduced PrEP adherence. It also adds a more nuanced understanding of how the specific effects on HIV risk will vary by GBV type, frequency, and severity. Prevention programs for women must screen for violence and address these multiple pathways in order to effectively reduce HIV incidence in this vulnerable population.

Table 15: Summary of previous studies on GBV and sexual risk behavior. A check mark (✔) indicates that a significant association was detected; an "x" indicates that there was no significant association. Blank cells indicate that the association was not examined.

Types of violence	Author (Ref)	Perpetrator	Violence timeframe	Sexual behavior timeframe	Number of clients	Number of non-paying partners	Number of partners, type unspecified	Unprotected sex with client	Unprotected sex with intimate partner	Unprotected sex, partner type unspecified
Sexual	Wirtz [69]	Any	Lifetime	Past 30 days				✔		
	Chersich [71]	Client	Past year	Past week			✔			
	El Bassel [125]	Client	Lifetime	Current/usual	x			x	x	
	Deering [127]	Client	Past year	Current/usual				✔		
	Deering [127]	Intimate	Past year	Current/usual					x	
Physical	Platt [233]	Client	Past year	Past week	x					
	El Bassel [125]	Client	Lifetime	Current/usual	✔			x	x	
	Deering [127]	Client	Past 6 mos.	Current/usual				✔		
	Deering [127]	Intimate	Past 6 mos.	Current/usual					x	
Physical and/or sexual	Berger [73]	Any	Lifetime	Past 6 mos.						
	Pack [204]	Any	Past month	Last sex				x	✔	
	Beattie [117]	Any	Past year	Last sex				✔	x	
	Decker [121]	Any	Past week	Past 5 sex acts						x
	Luchters [59]	Intimate	Past year	Past week			✔			✔
	Argento [234]	Intimate	Past 6 mos.	Past 6 mos.					✔	
Physical and sexual	El Bassel [125]	Client	Lifetime	Current/usual	✔			x	x	
Physical, sexual and/ or emotional	Wilson [122]	Intimate	Past year	Past week						✔

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Appendix: Latent class analyses of gender-based violence using indicators of violence perpetrator and frequency/severity

This appendix describes the methods and statistical analyses that were conducted with the primary indicator set for the latent class analysis on gender based violence among female sex workers in the Mombasa Cohort, as referenced in Chapter 2. The purpose is to justify the decision to forgo further analyses with this indicator set and use another set instead. Below we describe the characteristics of the indicator set and the justification for its selection as the first set to use in the latent class analyses. Then we describe the analytical steps that we took to conduct the latent class analyses with this indicator set, the challenges that arose, and how we addressed these challenges. Lastly, we describe the additional steps that could be taken, the reasons that we believe it is not worthwhile to pursue those steps, and why we chose instead to move on to another indicator set.

Primary indicator set: Description and Justification

The objective of the latent class analysis was to identify patterns of gender-based violence (GBV) exposure experienced by study participants (HIV-uninfected female sex workers) and to assign each participant to a GBV class based on the patterns of violence that she had experienced.

The first step of the analysis was to define indicator variables representing the most important characteristics of the hypothesized latent classes. These indicator variables condensed the variables that categorized each reported GBV act by type (physical, sexual or emotional), perpetrator, frequency, severity, and timing/duration. Because little is known about violence patterns in African FSW or about which characteristics of GBV have the most impact on mental health and sexual behavior, we proposed to develop 3 sets of indicators variables *a priori:* a primary set and two alternative sets, which highlighted different dimensions of GBV. The purpose of the alternative sets was to provide other options should the primary set fail to

identify meaningful GBV patterns or subgroups in the study sample.

The primary indicator set focused on relationship to perpetrator, frequency, and severity of violence. Examining the effects of women's relationship to GBV perpetrators was a priority since this is one of the richest and most unique aspects of the Sexual Violence (SV Study) data, and this aspect of GBV has not been widely addressed in quantitative studies of HIV risk. In several studies, increasing frequency and severity of GBV were associated with higher risk of HIV infection [7,19]. In contrast, effect size did not vary according to the type of violence that women experience [7,18,19]. Studies are also consistent in the finding that the effects of violence are long-lasting, suggesting that violence does not have to be recent to affect risk [7,11,235]. Therefore this indicator set did not focus on violence type or timing/duration.

We created 4 indicators, one for each perpetrator type: regular partner, casual partner, client, and non-partner. For the regular partner, casual partner, and client indicators, women were categorized by the most frequent and most severe violence that they reported from that perpetrator type. The baseline category grouped together women with no GBV and women with experience of one moderate act only, based on evidence that experience of a single moderate act does not increase HIV risk.[7,19] Classification of physical violence severity was based on the WHO Violence Against Women Survey methodology. Moderate physical violence was defined as pushing or slapping. Severe physical violence consisted of hitting, kicking, choking, threatening to use a weapon or actually using a weapon.[78] The WHO Survey does not provide guidance on classifying the severity of sexual or emotional violence. Since we adapted the sexual violence section to include questions from the Sexual Experiences Survey,[79] we followed their methodology and distinguished "coercion" (being pressured without threats of physical harm) from "rape or attempted rape" (being forced by physical harm, threats of physical harm, or the use of drugs or alcohol).[80] We considered coercion and being forced to do something degrading to be moderate and rape or attempted rape as severe. Of 12 emotional violence scales included in a recent CDC compendium, only the revised Conflict Tactics Scale

(CTS-2) scores emotional violence by severity level.[236] We felt that of the 4 emotional violence acts measured in the WHO Survey, “insulting” and “belittling” were qualitatively different from “scaring you on purpose” or “threatening to hurt you or someone you care about”, and this distinction was consistent with the CTS-2 scoring method.[237] Therefore, we categorized the first set of items as moderate, and the second set of items as severe.

For regular partners, we distinguished between moderate violence a few times, moderate violence many times, and severe violence any number of times. Since violence from clients and causal partners was less common, we combined the two moderate violence categories to compare moderate violence a few or many times to severe violence any number of times. The indicators and their frequency in the study sample are shown in Table S 6.

Table S 6: Primary Set of Indicator Variables for Latent Class Analysis (N=283)

Indicator: Regular partner violence		
Categories:	*Count*	*Percent*
No violence or any moderate acts once only	125	44.2
Any moderate act a few times	10	3.5
Any moderate act many times	15	5.3
Any severe act at least once	133	47.0
Indicator: Casual partner violence		
Categories:	*Count*	*Percent*
No violence or any moderate acts once only	233	82.3
Any moderate act a few or many times	14	5.0
Any severe act at least once	36	12.7
Indicator: Client violence		
Categories	*Count*	*Percent*
No violence or any moderate acts once only	230	81.3
Any moderate act a few or many times	11	3.9
Any severe act at least once	42	14.8
Indicator: Non-partner violence		
Categories	*Count*	*Percent*
None	124	43.8
Physical only	85	30.0
Sexual (with or without physical)	74	26.2

For non-partner violence, the indicator categories were none, physical only, or sexual violence (with or without physical). The different categorization is due to the fact that there were no severity measures for non-partner violence and that the vast majority of women experienced

one episode only. In addition, non-partner physical violence could include violence from neighbors, co-workers, and family members as well as violence from strangers, police, and teachers, suggesting that not all of it was "gender-based." In contrast, all sexual violence from non-partners could be considered gender-based. We did not exclude non-partner physical violence with no sexual violence, because we did not want to equate women who experienced it with women who experienced no violence, but we kept it as a separate category to reflect our uncertainty about its underlying causes.

[Note: The non-partner violence category also included violence that women reported was perpetrated by "other" partners, who were not regular, casual or client. This decision was based on a review of the episodes of other-partner GBV reported in our dataset. Other partner sexual violence was coded as non-partner sexual violence and severe other partner physical violence as non-partner physical violence. Of 28 acts of violence reported by "other" partners, 18 were sexual and 2 were severe physical and were re-coded as non-partner violence. Six moderate emotional or physical acts occurring once only were excluded but would have be categorized as "none or once only" regardless. Two episodes of moderate emotional violence from other partners few or many times were not included in the analysis. This approached minimized the misclassification without creating an extra indicator variable.]

Revision of the Primary Indicator Set

We conducted 2-class and 3-class simple, unrestricted latent class analyses with the primary indicator set. Each model was re-estimated from 500 different sets of random start values in an effort to find the global maximum of the likelihood function rather than one or more local maxima. Both models were unidentified, meaning that multiple, distinct solutions were equally likely given the data. This was likely to due to the small sample size and sparse cells in the contingency table, given the small cell counts in Table S 6 for indicators such as "regular partner violence: any moderate acts few times" (3.5%), and "client violence: any moderate acts a few or many times" (3.9%).

To address this issue, we revised the indicator variables to reduce the number of categories. We observed that of all women reporting violence, the large majority reported severe acts, and that the low frequencies of moderate violence were the primary reason for sparseness. However, we did not want to collapse the indicators over all levels of violence severity, because then we would be left with dichotomous indicators of violence for each partner type, and we did not believe that dimension of violence was of enough interest on its own to warrant the latent class analysis. Therefore we moved the focus from severity to frequency. For each perpetrator type, we created categories of none or one moderate act only, one severe act or few acts (of any severity), and many acts (of any severity).

In addition, we revisited the categorization of sexual violence to consider all acts of sexual violence as severe. This decision was not intended to address the issue of sparse cells, but came from a reconsideration of the consequences of grouping women who experienced one act of sexual coercion or one degrading act with women who experienced no violence. Few women moved indicator levels as a result of this change in the regular partner violence (n=1) or casual partner violence (n=2) indicators, but 10 women moved from the "no/one moderate" category of client violence to the "one severe/few" category. The resulting indicator set & frequency table is shown in Table S 7.

Latent Class Models with Revised Primary Indicator Sets

We then ran 2-, 3-, 4- and 5-class latent class models with the revised indicator sets, with 1000 sets of random start values to try to ensure we were finding the global maximum. The revision improved model identification; the 2 and 3-class models showed good identification, with 63% and 74% of the 1000 runs converging on the best-fitting solution.[1] The 4-class model was under-identified: the maximum likelihood solution was the modal solution, but only 24% of random starts converged to this solution. Several other solutions fit the data nearly as well. The

[1] The fact that a model is not 100% identified suggests that some iterations converged at local maxima on the likelihood function rather than the global maximum. This is not problematic as long as a substantial plurality of models reaches the global maximum.

5-class model was unidentified: only 12% of random starts converged on the ML solution, while >30% converged on two separate solutions with lower likelihood values.

Table S 7: **Revised Primary Indicator Set (N=283)**

Indicator: Regular Partner Violence		
Categories	*Count*	*Percent*
No violence or any moderate act once only	125	44.2
Any severe act once only or any act few times	40	14.1
Any act many times	118	41.7
Indicator: Casual Partner Violence		
Categories	*Count*	*Percent*
No violence or any moderate act once only	232	82.0
Any severe act once only or any act few times	29	10.3
Any act many times	22	7.8
Indicator: Client Violence		
Categories	*Count*	*Percent*
No violence or any moderate act once only	219	77.4
Any severe act once only or any acts few times	39	13.8
Any act many times	25	8.8
Indicator: Non-partner Violence		
Categories	*Count*	*Percent*
None	124	44.0
Physical only	84	29.8
Sexual (with or without physical)	74	26.2

The results above could have provided a feasible model solution with a choice of a 2-class or 3-class model to carry forward into subsequent analyses. However, none of the models resulted in a class characterized by low levels of violence. For example, in the 3-class model, there was a 62% probability of casual partner violence (many acts) in Class 1, a 77% probability of non-partner sexual violence in Class 2, and a 55% probability of regular partner violence in Class 3 (many or few acts). From an epidemiological perspective, it is necessary to have a low-violence class to serve as the unexposed or reference group.

To create a low-violence class, we used parameter restrictions. The advantage of parameter restrictions is that they give the researcher more control over the model structure. In addition, we reduce the number of parameters that the model has to estimate, and this should

reduce problems with model identification. Parameter restrictions can take 2 forms: equality constraints and fixed values. With equality constraints, we assign certain conditional item response probabilities to be equal to each other, without specifying what the actual values should be. For example, we can specify that in a certain class (arbitrarily, Class 1), the probability of "No violence or any moderate act once only" (hereafter, "low violence") should be the same for each indicator. With fixed parameters, we assign specific values to certain conditional item response probabilities - for example, that the probability of low violence in Class 1 should be 90% for each indicator. The fixed parameter approach provides more control but can substantially reduce model fit. The equality constraints provide less control, but model fit is likely to be better.

We started with equality constraints, constraining the parameters for Class 1 to have the same probability of low violence for all 4 indicators, and the same probability of "few" or "many" acts of violence for all 4 indicators. We expected that this would result in a high probability of no violence and a low probability of few or many acts of violence in that class. No constraints were placed on the parameters of the other class(es). This approach was successful for the 2-class model, which was well-identified and had a class with 81% probability of low violence for each perpetrator type, 12% probability of "few" violent acts, and 5% probability of many violent acts. In the 3-class model, however, we saw a class with 52% probability of low violence, a 10% probability of few violent acts, and a 39% probability of many violent acts. This represented poor item separation within the class and was not a good model solution.

Next we tried the fixed parameters approach. A 3-class model with 80% probability of low violence, 10% probability of violence “few” times, and 10% probability of violence “many” times for Class 1 was not identified. We tried another set of restrictions, considering the sample distribution of violence for each indicator in determining the fixed values for the conditional item response probabilities. For example, the overall prevalence of regular partner violence was much higher (56%) than the prevalence of casual partner violence (18%), so the probability of

regular partner violence within the low violence class would also be higher, allowing for measurement error. These "more informed" fixed parameters for Class 1 had the following values:

1. Regular partner violence: 80% low violence, 15% few, 5% many
2. Casual partner and client violence: 95% low violence, 2.5% few, 2.5% many
3. Non-partner violence: 80% low violence 10% few, 10% many

We ran 2-, 3- and 4- class models with these parameter restrictions, each with 1000 random starts. This model was 100% identified for the 2-class model, but the 3-class model was still unidentified, with 2 equally likely but substantively different solutions. The solution with the highest likelihood had an extremely small low violence class (0.7% of the sample). Furthermore, when we assigned women to latent classes based on the highest posterior probability of class membership, the latent class characterized by low violence did not include any of the women who actually experienced no violence during the study. This is because another latent class was much larger (65% of the sample) and still had a high probability of no violence, and the combination of these factors skewed the posterior probability towards the larger class. The modal solution, which was the solution for 48.5% of the random starts, had a better distribution of the class prevalence parameters and classified all women without violence into class 1, but had substantially worse fit based on log likelihood and other statistics.

The 4-class model was identified (66% of random starts converging on the maximum likelihood solution), and had a solution that looked promising in terms of the class distribution and item response probabilities. However, when we assigned classes based on the highest posterior probability of class membership, one latent class had only one person, and the latent class characterized by low violence did not include any of the women who experienced no violence during the study. (Again, this is because the largest class had a much higher prevalence and still had a high enough probability of no violence that the combination of these factors skewed the posterior probability slightly towards the largest class.) Women with low

violence had a 51% probability of belonging to the largest class (Class 4, 64% of the population), characterized by moderate violence, and a 49% probability of belonging to the class characterized by no violence (Class 1, 13% of the population). Therefore, these parameter restrictions still failed to separate out a low violence class to serve as a reference group in subsequent analyses.

Possible Next Steps:

At this point, we considered the following options as next steps:

1) *Further adjusting the parameter restrictions to improve identification and posterior class assignment.* This could have resulted in a working low violence class and better model identification, but we risked overfitting the model, reducing our ability to replicate the results in other samples.
2) *Combining partnership types.* Combining casual partners with either clients or regular partners would have reduced the number of indicators and improve model fit. However, casual partners differed substantively from clients and regular partners on a number of characteristics, including relationship duration, condom use, frequency of sex, payment for sex, and knowledge of HIV status. Therefore, combining them would complicate the interpretation of the results. After much debate, we decided to try combining casual partners with clients. With a 3-class model, both unrestricted and fixed parameter models were still unidentified, so this did not improve our results. We did not explore this option further.
3) *Further exploration of equality constraints across classes*. Conceptualizing equality constraints across classes was difficult because we did not have a strong hypothesis about how the classes would be characterized (except for the low violence class). We could have used the results from the models we had seen so far to give us an idea of what we might expect, but this also posed a risk of overfitting the data.

4) *Adding a Bayesian Prior.* Conceptually, what we tried to do above was to apply a prior belief in a low violence class to inform the results of the latent class analysis. This is consistent with a Bayesian approach using a prior that includes a low violence class. This could be implemented by specifying that in a certain class, the probability of the low violence response pattern (low violence from all 4 perpetrator types) is 100%. A similar approach was described in a 2004 paper in *American Statistician* to address the problem of "label switching" in Bayesian latent class models [238]. However, it cannot be implemented in any standard software. Furthermore, this experimental methodology has not been validated, so the results would be difficult to interpret.

Although we could have continued to analyze this indicator set using steps 3 and 4 outlined above, we would still have been working with the same data and likelihood function, so it isn't clear that they would have produced better results. Furthermore, aside from the complications with model identification and the establishment of a low violence class, this indicator set was not showing evidence of multidimensional clustering in the data. The indicator level for "any severe act once only or any act few times" did not contribute to the characterization of the latent classes, because none of the classes had a high probability of few violent acts from any partner type. Therefore, the classes were primarily characterized by perpetrator type, rather than perpetrator type and frequency and severity. These one-dimensional classes were not particularly informative from a scientific perspective.
Table S8 shows the results of the 4-class model with parameter restrictions based on the prevalence of violence in the study sample, discussed above. The findings are typical of the many of the model results for this set of indicators.

The indicator level for "any severe act once only or any act few times" did not contribute to the characterization of the latent classes, because none of the classes had a high probability of few violent acts from any partner type. Therefore, the classes were primarily characterized

by perpetrator type, rather than perpetrator type and frequency and severity. These one-dimensional classes were not particularly informative from a scientific perspective.

Table S8: Class prevalence and conditional item response probabilities for 4-class model with fixed parameters

		Class 1*	Class 2	Class 3	Class 4
Class prevalence		0.132	0.074	0.159	0.635
Item Response probabilities (conditional on class membership)	**Regular partner violence**				
	No violence or any moderate act once only	0.80	1.00	0.193	0.362
	Any severe act once only or any act few times	0.05	0.00	0.115	0.186
	Any act many times	0.15	0.00	0.692	0.452
	Casual partner violence				
	No violence or any moderate act once only	0.950	0.00	0.879	0.876
	Any severe act once only or any act few times	0.025	0.279	0.123	0.091
	Any act many times	0.025	0.721	0.00	0.033
	Client violence				
	No violence or any moderate act once only	0.950	0.684	0.577	0.799
	Any severe act once only or any act few times	0.025	0.087	0.000	0.201
	Any act many times	0.025	0.229	0.423	0.000
	Non-partner violence				
	None	0.80	0.422	0.000	0.474
	Physical only	0.10	0.414	0.423	0.345
	Sexual (with or without physical)	0.10	0.164	0.780	0.180

* Fixed parameters

Conclusions

Based on the challenges with identification, difficulties in defining a low violence referent class, and evidence that categorizing violence by frequency did not contribute to defining or characterizing latent classes, we concluded that this indicator set had not successfully identified meaningful GBV patterns or subgroups in the study sample. Therefore we stopped work with this indicator set and moved to an alternate set of indicators based on type, severity and frequency of violence, without consideration of perpetrator type. This set was based directly on previous work and had been shown to capture meaningful patterns of GBV in African women in the general (non-FSW) population [55]. Although studies are consistent in finding that sexual, verbal/emotional, and physical violence all increase HIV risk, combining types of violence within

indicators may be problematic because severity and frequency could have different implications for different types of violence. For example, experiencing one episode of rape may not have the same effect as being punched one time, and moderate physical violence may be more or less harmful than moderate emotional violence. Therefore examining each violence type separately may be more important for identifying latent classes. We moved forward with the second indicator set because it provided another opportunity to look at frequency and severity of GBV, which have been associated with HIV risk in empirical studies, and because it would be interesting to compare the GBV patterns that emerged with this indicator set in a population of FSW to the patterns that emerged in the general population in the previous study.

CURRICULUM VITA

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Education

Doctor of Philosophy, Epidemiology 2016
University of Washington, Seattle, WA
Dissertation: Gender-based violence and HIV risk: mediating pathways and strategies for prevention

Master of Public Health, Global Health 2005
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Thesis: Qualitative evaluation of a pregnancy and HIV prevention program for secondary school students in rural KwaZulu/Natal, South Africa

Bachelor of Arts, Human Biology, *magna cum laude* 2001
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Professional Experience

Predoctoral Research Associate
University of Washington, Seattle, WA 2012 – 2016
Research Areas:

- Intimate partner violence, male partner involvement, and adherence to oral pre-exposure prophylaxis and microbicides in African women
- Systematic review of the cost-effectiveness of partner notification services for sexually transmitted infections in the United States and Europe
- Mathematical modeling of the impact of antiretroviral treatment as prevention on HIV incidence in South Africa and Uganda.
- Hormonal contraception and STI incidence in African women
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Predoctoral Teaching Associate, Introduction to Epidemiology 2015
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Research Manager
Center for Infectious Disease Research in Zambia (CIDRZ), Lusaka, Zambia 2008 – 2012
University of North Carolina Chapel Hill (2012)
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- Managed implementation of 8 research studies focused on biomedical HIV prevention methods for women and tuberculosis/HIV co-infection
- Mentored, supervised and trained 5 Study Coordinators, 2 interns, and other study staff
- Contributed to study design, grant writing, protocol development, data analysis, and results dissemination, in collaboration with study Principal Investigators

Research Coordinator
Zambia-Emory HIV Research Project, Lusaka, Zambia
Emory University 2005 – 2008

- Managed regulatory, training & administrative operations; developed site standard operating procedure (SOP) system, oversaw staff development program, and managed over $2 million in operating funds from CDC, NIH and USAID.
- Study Coordinator for International AIDS Vaccine Initiative (IAVI) studies, including a phase 2 vaccine trial;
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Teaching Assistant, Proposal Development 2005
Emory University, Atlanta, GA

- Graduate level 2-credit course on writing research proposals

Research Assistant & Group Facilitator
Atlanta Intervention Network, Atlanta, GA 2004 – 2005

- Implemented a clinical trial of a computer-based domestic violence prevention intervention
- Co-facilitator of weekly group sessions for 6-25 male domestic violence offenders

Research Intern
Medical Research Council of South Africa, Hlabisa, South Africa 2004

- Qualitative evaluation of a school-based HIV and pregnancy prevention education program, including design, training, and analysis of 40 in-depth interviews with program participants

Research Assistant
Brown University, Providence, RI 2001 – 2003

- Field director for epidemiologic studies on genetic susceptibility to diabetes and overweight in Samoa and American Samoa

Research Intern
Aaron Diamond AIDS Research Center, New York, NY 1997

- Conducted bench work on frequency and geographic distribution of the CCR5Δ32 mutation

Awards and Honors

CROI Young Investigator Scholarship 2016
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Achievement Rewards for College Scientists (ARCS) Foundation Fellowship 2012
University of Washington Top Scholar Award 2012
Population Fellows Graduate Applied Project Mini-Grant 2004
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Peer Reviewed Publications

Manuscripts

1. Roberts ST, Haberer J, Celum C, Mugo N, Ware N, Cohen CR, Tappero JW, Kiarie J, Ronald A, Mujugira A, Tumwesigye E, Were E, Irungu E, Baeten JM. Intimate partner violence and adherence to HIV pre-exposure prophylaxis (PrEP) in African women in HIV serodiscordant relationships: A prospective cohort study. J Acquir Immune Defic Syndr. 2016 May 26. [Epub ahead of print].

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Presentations and Abstracts

1. Roberts ST, DA Katz, MR Golden, TR Bell, RV Barnabas RV. "Population-Level Effectiveness and Cost-Effectiveness of Enhanced Partner Services for Curable Sexually Transmitted Infections: a Systematic Review." Poster presentation at the 17th IUSTI World Congress, Marrakech, Morocco, May 9-12, 2016: Abstract 0259.
2. Roberts ST, AS Khanna, RV Barnabas, SM Goodreau, JM Baeten, C Celum, S Cassels. "Targeting Serodiscordant Couples Within Home HIV Testing Campaigns: A Modeling Study." Poster presentation at the 2016 Conference on Retroviruses and Opportunistic Infections, Boston, MA, February 22-25, 2016: Abstract 1063.
3. Roberts ST, R Deya, J Ngina, L Masese, SM Graham. "Gender-based Violence Among Female Sex Workers in Mombasa, Kenya: Prevalence, Patterns, and Associations with Substance Abuse." Poster presentation at the Sexual Violence Research Forum 2015, Stellenbosch, South Africa, September 15-17 2015. Abstract Number SVF 290.
4. Roberts ST, C Celum, N Mugo, J Haberer, CR Cohen, E Irungu, J Kiarie, E Were, JM Baeten. "Intimate Partner Violence is Associated with Low PrEP Adherence in African Women." Poster presentation at the 2015 Conference on Retroviruses and Opportunistic Infections, Seattle, WA, February 23-26, 2015: Abstract 980.
5. Khanna, A, ST Roberts, S Cassels, J Baeten, P Murnane, C Celum, R Barnabas. "Lifelong antiretroviral therapy for prevention of mother to child transmission of HIV has potential to decrease adult HIV incidence due to sexual transmission." Oral presentation at the 4th International HIV Treatment as Prevention Workshop, Vancouver, Canada, April 1-4, 2014: Abstract 6014.
6. Heffron R, K Ngure, N Mugo, C Celum, K Curran, A Kurth, S Roberts, J Baeten. "Preferred PrEP Dosing Regimens and Sex Planning among Kenyan HIV-1 Serodiscordant Couples." Poster presentation at the 2013 Conference on Retroviruses and Opportunistic Infections (CROI), Atlanta, GA, March 3-5, 2013: Abstract 1003.
7. Henostroza G, J Harris, M Siyambango, K Kaunda, K Maggard, S Roberts, A Mwinga, S Reid. "High Prevalence of Tuberculosis among Zambian HIV Care Enrollees: Urgent Need for Enhanced Screening Approach." Oral presentation at the 43rd Union World Conference on Lung Health, Kuala Lumpur, Malaysia, November 13-17, 2012: Abstract OP-110-15.
8. Harris J, M Siyambango, C Moyo, A Kruuner, K Maggard, S Roberts, N Kapata, S Reid. "Role of Physical Exam as an Adjunct to World Health Organization Symptom Screening in HIV-Infected Persons." Oral presentation at the 43rd Union World Conference on Lung Health, Kuala Lumpur, Malaysia, November 13-17, 2012: Abstract OP-113-15.
9. Luhanga D, J Morse, J Harris, S Roberts, G Henostroza, N Kapata, S Reid, N Kancheya. "Pulmonary Tuberculosis Screening in Antenatal Clinics in Lusaka, Zambia." Poster presentation at the 43rd Union World Conference on Lung Health, Kuala Lumpur, Malaysia, November 13-17, 2012: Abstract PC-642-17.
10. Maggard, K, S Hatwiinda, W Phiri, J Morse, E Turnbull, S Topp, S Roberts, G Samungole, N Kapata, C Chileshe, J Harris, S Reid, G Henostroza. "Inmate Peer Educators are Essential to Prison-Based HIV Testing and TB Screening in Zambia." Poster presentation at the XIX International AIDS Conference, Washington, DC, July 22-27, 2012: Abstract THPDE0305.
11. Roberts, ST, C Kelly, C Reid, MB Guffey. "Predictors of Pregnancy Among HPTN 035 Participants in Lusaka, Zambia." Oral presentation at the Microbicides 2010 Conference, Pittsburgh, PA, May 22-25, 2010: Abstract 6.
12. Zulu DT, C Reid, ST Roberts, MB Guffey. "Improving Participant Retention Interventions During Back-to-Back Microbicide Trials in Lusaka, Zambia." Poster presented at the Microbicides 2010 Conference, Pittsburgh, PA, May 22-25, 2010: Abstract 301.

13. Phiri W, C Reid, ST Roberts, MB Guffey. "Cost-Effectiveness of Prescreening VCT During HPTN 035." Poster presented at the Microbicides 2010 Conference, Pittsburgh, PA, May 22-25, 2010: Abstract 163.
14. Milambo E, C Namakobo, V Munamunungu, F Madyabi, ST Roberts, C Reid, MB Guffey. "Improvement of Quality Assurance/Quality Control During Back-to-Back Microbicide Trials in Lusaka, Zambia". Poster presented at the Microbicides 2010 Conference, Pittsburgh, PA, May 22-25, 2010: Abstract 282.
15. Gorbach, PM, JA Borgerding, G Ramjee, T Tembo, N Kumwenda, P Musara, S Roberts, L Maslanowski. "Effects of partnership change on gel adherence in HPTN 035." Poster presented at the Microbicides 2010 Conference, Pittsburgh, PA, May 22-25, 2010: Abstract 415.
16. Richardson B, G Ramjee, C Kelly, L Maslankowski, T Fleming, B Makanani, N Mkandawire, P Musara, S Roberts, A Coletti, L Soto-Torres, SA Karim. "Appropriateness of Hydroxyethylcellulose gel as a placebo control in vaginal microbicide trials: A comparison of the two control arms of HPTN 035." Oral presentation at the Microbicides 2010 Conference, Pittsburgh, PA, May 22-25, 2010: Abstract 195.
17. Roberts, ST and the Rwanda-Zambia HIV Research Group. "Predictors of Decision to Test at Three Couples' VCT Centers in Lusaka, Zambia." Poster presented at the International AIDS Conference, Toronto, Canada, August 2006: Abstract WEPE0435.
18. McGarvey ST, ST Roberts, P Turituri, J Tufa, R Deka, DE Weeks. "Pedigree Structure in a Genetic Epidemiology Study of Adiposity in Samoans: Preliminary Report." American Journal of Human Biology 15 (2), 2003: 274.
19. Roberts ST, ST McGarvey, N Tu'u'au-Potoi. "Changes in Blood Pressure of Samoan Children and Adolescents." American Journal of Human Biology 14(1), 2002: 120.

Research Support

Ongoing:

NIH 1 F31 MH107258 (Roberts, PI) 06/16/2015 – 06/16/2017

Gender-Based Violence and HIV Risk: Mediating Pathways and Prevention Strategies

A Ruth L. Kirschstein National Research Service Award (NRSA) Individual Predoctoral Fellowship to support doctoral dissertation research on the effects of different patterns of gender-based violence on HIV risk factors in African women, including mental health, sexual behavior, and adherence to pre-exposure prophylaxis.

Completed:

NIH 5 T32 AI007140 (Lukehart, PI) 09/16/2014 – 06/15/2015

STD and AIDS Research Training Grant

This training program, now in its 35th year, has trained nearly 200 postdoctoral and predoctoral fellows in STD and HIV/AIDS research, nearly 90% of whom have continued in academia, public health or government, or in other biomedical research venues.

Role: Trainee

FHI FCO 887 (J. Stringer, PI) 10/2010 – 07/2012

HIV Prevention Trials Network (HPTN) 063: Preparing for International Prevention Trials Involving HIV-Infected Individuals in Care Settings (NIH Passthrough)

Preparatory research to design a behavioral intervention to decrease sexual transmission risk behavior in HIV-infected persons in care and to determine whether a similar intervention structure can be used across various sexual risk groups and cultural settings.

Role: Investigator of Record

CDRF- ZAB1-22027-LU-10 (Kancheya, PI) 11/2010 – 07/2012
Pilot evaluation of Pulmonary Tuberculosis Screening in Antenatal Clinics in Lusaka, Zambia
Pilot study of tuberculosis (TB) screening services within antenatal clinics in one district in Lusaka.
Role: Co-Investigator

CDC-U2GPS001421-01 (Chi, PI) 08/2011 – 07/2012
Expansion of ART, TB, and VCT programs in Zambia
Expansion of TB screening and treatment services within HIV care and treatment programs across three provinces of Zambia. Included funding for research to identify optimal screening algorithms for TB in HIV clinics and to determine TB incidence and prevalence in this setting.
Role: Co-Investigator

NIH/University of Bern 5 U01 AI069924-04 (Henostroza, PI) 11/2010 – 07/2012
IeDEA: International Epidemiological Databases to Evaluate AIDS: Malaria Research Preparedness (Malaria Diagnostics and Case Tracking in Zambia)
A grant to build capacity for potential sites for future malaria vaccine trials. Objectives were to develop diagnostic capacity for malaria in two rural Zambian clinics and to implement GPS surveillance of malaria cases in one clinic catchment area.
Role: Co-Investigator

NIH 5U01-AI069455-04 (Stringer, PI) 07/2008 – 07/2012
NIH/NIAID, Centre for Infectious Diseases Research in Zambia HIV/AIDS Clinical Trials Unit

- *MTN 020: A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Phase 3 Safety and Effectiveness Trial of a Vaginal Matrix Ring Containing Dapivirine for the Prevention of HIV-1 Infection in Women* (pre-implementation only)
- *Validation of Laboratory Reference Ranges and HIV Finger Stick Testing in Lusaka, Zambia*
- *MTN 015: An Observational Cohort Study of Women following HIV-1 Seroconversion in Microbicide Trials*
- *MTN 003: Phase 2B Safety and Effectiveness Study of Tenofovir 1% Gel, Tenofovir Disoproxil Fumarate Tablet and Emtricitabine/Tenofovir Disoproxil Fumarate Tablet for the Prevention of HIV Infection in Women* (pre-implementation only)

A U01 grant to establish an adult and pediatric HIV/AIDS prevention, therapeutics, and microbicide clinical trials unit at CIDRZ and replace the separate network grants from HPTN and ACTG.
Roles: MTN Project Coordinator, Study Coordinator, Co-Investigator