Missed Study Visits and Subsequent HIV Incidence Among Women in a Predominantly Sex Worker Cohort Attending a Dedicated Clinic Service in Kampala, Uganda

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Background: There is limited evidence on the relationship between sustained exposure of female sex workers (FSWs) to targeted HIV programmes and HIV incidence. We investigate the relationship between the number of missed study visits (MSVs) within each episode of 2 consecutively attended visits (MSVs) and subsequent HIV risk in a predominantly FSW cohort.

Methods: Women at high risk of HIV are invited to attend an ongoing dedicated clinic offering a combination HIV prevention intervention in Kampala, Uganda. Study visits are scheduled once every 3 months. The analysis included HIV-seronegative women with ≥1 follow-up visit from enrollment (between April 2008 and May 2017) to August 2017. Cox regression models were fitted for characteristics on sociodemographic, reproductive, behavioral, and sexually transmitted infections (through clinical examination and serological testing for syphilis).

Findings: Among 2206 participants, HIV incidence was 3.1/100 (170/5540) person-years [95% confidence interval (CI): 2.6 to 3.5]. Incidence increased from 2.6/100 person-years (95% CI: 2.1 to 3.2) in episodes without a MSV to 3.0/100 (95% CI: 2.2 to 4.1) for 1–2 MSVs and 4.3/100 (95% CI: 3.3 to 5.6) for ≥3 MSVs. Relative to episodes without a MSV, the hazard ratios (adjusted for confounding variables) were 1.40 (95% CI: 0.93 to 2.12) for 1–2 MSVs and 2.00 (95% CI: 1.35 to 2.95) for ≥3 MSVs (P-trend = 0.001).

Conclusion: Missing study visits was associated with increased subsequent HIV risk. Although several factors may underlie this association, the finding suggests effectiveness of targeted combination HIV prevention. But exposure to targeted interventions needs to be monitored, facilitated, and sustained in FSWs.

Key Words: HIV, HIV incidence, missed study visits, female sex workers, sub-Saharan Africa

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INTRODUCTION

Combination of HIV-prevention programmes targeting sex workers is cost-effective, especially in settings with high HIV incidence and prevalence among sex workers. However, when HIV prevention in sex work is not sustained in these settings, there can be rapid HIV acquisition and onward HIV transmission beyond female sex workers (FSWs) and their clients to the wider population. In Uganda, a systematic review of epidemiological data among FSWs showed an estimated HIV prevalence in the range of 32–52%, which is 4–7 times that in adult women in the general population. Although there is sufficient evidence that supports effectiveness of multicomponent-targeted HIV interventions for FSWs, sustaining exposure to these interventions remains a major challenge.

The WHO recommends routinely offering evidence-based comprehensive HIV-prevention services to key populations such as FSWs, which includes HIV counseling and testing (HCT), and diagnosis and treatment of sexually transmitted infections (STIs). This regular exposure to services is likely to reinforce behavioral messages, to facilitate community empowerment, and to detect and treat STIs early among FSWs. Furthermore, regular exposure to HCT can facilitate earlier initiation of antiretroviral therapy (ART) during the acute and early infectious phases of HIV.
Notwithstanding the limited coverage for FSW-targeted services across Africa, several factors exist at multiple levels that facilitate or deter FSWs from using services. The most commonly identified contextual factors are stigma, discrimination, and criminalization and their associated consequences. However, other contextual factors such as the high mobility among sex workers have been identified to delay the utilization of services. These contextual factors typically act through the individual factors such as perceptions of HIV risk and importance of services as well as behavioral (sexual and substance abuse), reproductive, and biological characteristics. At the same time, these key determinants of service utilization are also important risk factors for HIV infection among FSWs.

Although there is growing interest in improving service utilization among FSWs, it remains unclear how recent levels of service attendance are associated with subsequent HIV risk. Using the proportions of study visits completed, research has linked reduced incidence of HIV and other STIs among FSWs to amount of exposure to targeted HIV interventions such as peer-mediated HIV education, condom promotion, risk-reduction interventions, and presumptive treatment for STIs. However, assessment of the HIV risk associated with previous recent levels of service attendance may offer better evidence for risk associated with intervention exposure because an individual’s level of attendance can vary over time and for different reasons. If we understand this relationship better, we could then inform the design and scale-up of appropriate interventions in sex work.

In a Kenyan FSW cohort with monthly clinic visits followed for a median of 16.2 months, a time-varying preceding gap in clinic attendance of 60 days was associated with reduced HIV risk. But this variable of preceding gap in clinic attendance in this study was only considered as a confounding variable and, thus, warrants further investigation as a main exposure of interest. As a main exposure, a different approach that considers the conceptual interrelationships with potential confounders and their relationship with HIV risk should be applied. Furthermore, instead of assigning the date of seroconversion as midpoint between the last-negative and first-positive test dates, we assigned a random date in this interval, thereby reducing the artificial clustering of seroconversion times in the middle of observation periods with missed scheduled testing.

Therefore, the aim of this study was to examine the association between the number of missed study visits (MSVs) within episodes of 2 consecutively attended visits and subsequent HIV risk in a predominantly FSW cohort attending a dedicated clinic in Kampala, Uganda.

**METHODS**

**Study Population**

Between March 2008 and May 2009 (cohort-1), the Good Health for Women Project (GHWP) enrolled women acknowledging being FSWs or working in entertainment facilities such as bars, night clubs, or lodges (women at high risk of HIV infection) in Kampala, Uganda. Participants were scheduled to attend the study clinic once every 3 months, which is consistent with the Uganda Ministry of Health guidelines for HCT of key populations. From January 2013 (cohort-2), more participants were continuously enrolled into GHWP alongside cohort-1 participants.

**FIGURE 1.** Conceptual framework linking factors leading to MSVs and subsequent HIV incidence used to fit the Cox regression model within the GHWP. IEC, information education communication; SRH, sexual and reproductive health.
The procedures for recruiting, screening, enrolling, and following up of cohort-1 participants have been described in detail elsewhere. But, identical procedures were followed for cohort-2. Briefly, outreach workers visited and assessed study eligibility for women at high risk of HIV infection who had been recruited by peer educators or contacted through evening community-outreach HCT sessions. Women were eligible if they were involved in commercial sex (self-identified FSWs or received money, goods, or other favors in exchange for sex) or employed in entertainment facilities within mapped sex work hotspots (clusters of bars, night clubs, lodges, and guest houses providing rooms for sex work or street spots frequented by sex workers). Those who were eligible were invited to attend the study clinic for rescreening and study enrollment.

**Targeted Intervention**

The GHWP intervention follows the WHO standard framework for HIV prevention in FSWs; aiming at reducing condomless sex, decreasing HIV transmission efficiency, and empowering FSWs. This intervention integrates sex worker–friendly HIV services with other sexual and reproductive health services and offers free general health care for participants and their children aged 5 years younger. Table 1 shows the detailed components of the intervention broadly classified as structural, behavioral, and biomedical.

At each visit, HIV-preventive behaviors were promoted to each participant, but the content of the counseling sessions was dependent on each participant’s behavioral responses, outcomes of clinical examinations, and serological test results. Low-risk participants were encouraged to maintain behavior, whereas those with risky behaviors were supported to acknowledge the behavior and its possible consequences. In addition, high-risk participants were encouraged to take immediate steps to reduce the risk associated with behaviors such as harmful alcohol use or inconsistent condom use. Depending on their identified needs, participants were also counseled on a wide range of other physical and psychosocial issues including their general health, family, spiritual needs, and employment.

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**TABLE 1. HIV-Prevention Intervention Available at the GHWP by the Type of Intervention**

| Type of Intervention | Components | Delivery |
|----------------------|------------|---------|
| **Behavioral**       | Condom promotion, demonstration, and free condom distribution | Each visit |
|                      | Sexual counseling | Each visit |
|                      | Excessive alcohol use counseling including the AUDIT* questionnaire as part of the motivational interviewing | Each visit |
|                      | Knowledge of HIV status through HIV testing | Each visit and at moonlight outreaches to sex work hotspots |
|                      | If diagnosed with HIV, offered positive prevention strategies, treatment adherence counseling, and HIV care | Each visit and at ART refill visits |
|                      | Information sharing and health education | Each visit and at the group meetings held fortnightly for participants with upcoming visits |
|                      | General counseling services | Each visit |
| **Biomedical**       | Syndromic management of sexually transmitted infections | Each visit |
|                      | Referrals to other collaborating service providers for participants in need of postexposure prophylaxis | As needed |
|                      | Antiretroviral therapy (ART) if diagnosed with HIV | As needed |
| **Structural**       | Access to a free sex worker–friendly dedicated clinic | As needed |
|                      | Sexual and reproductive health services including antenatal care and contraceptive provision | Every visit and as needed |
|                      | Free general health care and their children aged <5 years old | As needed |
|                      | Support by peer support network | As needed |
|                      | Outreach HIV counseling and testing, and supply of condoms and health information at the sex work hotspots | Two nights a week, with a team that includes peer educators, venue managers, and study staff |
|                      | Community mobilization involving police, venue managers and owners, and local authorities | Quarterly meetings |
|                      | Protection services and referrals to community-based organizations in case of gender-based violence | As needed |

*Alcohol Use Disorders Identification Test (AUDIT) was initiated in April 2012, but there was ongoing risk-reduction counseling.

†ART became available at the clinic in January 2013 (eligibility: CD4 cell counts <350 cells/μl, and from August 2014, for all diagnosed with HIV regardless of CD4 cell count), but before that participants with CD4 cell count below 250 cells/μl were referred to HIV care providers.
To ensure high retention, group meetings were held every 14 days at the study clinic with women who had scheduled visits within the following month. Participants with 2 or more consecutive MSVs were contacted by phone or traced in the community (either at their workplace or home) through a peer leader or the local council member of the respective area and then invited to attend the clinic at an appointed time.

Data
At the clinic, trained nurse-counselors used structured questionnaires to collect data on sociodemographics, sexual behavior, reproductive health, and substance abuse (alcohol use and illicit drug use). Data were collected only at enrollment for age, education level, source of income (sex work alone or sex work and other jobs), place of client recruitment (street, bar, club or restaurant, and several avenues), and number of children. However, data collected at enrollment and follow-up visits included marital status and behavioral variables such as alcohol use, illicit drug use, number of sexual partners, number of paying sexual partners, frequency of condom use with clients, report of any paid sex in the last month, and contraceptive use and pregnancy. Pregnancy was determined using human chorionic gonadotropin urine sample tests or visible pregnancy.

A participant had an STI if he/she had an active syphilis infection (rapid plasma reagin titers $\geq 1:8$) and positive Treponema pallidum hemagglutination assay based on serology tests conducted at 6-month intervals or had any of the STI symptoms of abnormal vaginal discharge, genital ulcer disease syndrome, or pelvic inflammatory disease. Between 2008 and 2010, endocervical and vaginal swabs were also used to detect Neisseria gonorrhoeae, Chlamydia trachomatis, Mycoplasma genitalium, and bacterial vaginosis.

Outcome Variable
The primary outcome was HIV seroconversion, which was defined as a negative test result at a given visit attended followed by a positive result at the subsequent visit. Testing for HIV followed the Uganda MoH algorithm for HIV testing. According to this algorithm, HIV screening was performed using Determine HIV-1/2 (Abbott Diagnostics, Maidenhead, United Kingdom). Before 2013, reactive results were confirmed using 2 enzyme immunoassay tests for HIV screening (Vironostika Uniform II plus O, Murex HIV 1.2.0) and then a Western Blot Test. But from 2013, confirmation was done using Stat-Pak dipstick HIV-1/2 (Chembio Diagnostics), and discordant samples were further tested with the Uni-Gold HIV-2 (Trinity Biotech, Ireland). Participants were included in this analysis if they tested HIV-negative at enrollment and had at least one follow-up visit by 29th August 2017 (administrative censoring date). The total person-years (pyr) for each participant were calculated from their enrollment date to the earliest of (1) estimated date of seroconversion for seroconverters or (2) last known HIV-negative test date for nonseroconverters. The approach for estimating the date of seroconversion is described under the statistical analysis section.

Exposure Variable
The number of MSVs within each participant’s episodes of 2 consecutively attended visits was used to define the exposure of interest. This exposure variable is a proxy for the extent of exposure to and engagement with the combined components of the HIV intervention offered at the clinic. We classified a scheduled study visit as missed if the participant did not attend the study clinic within 14 days before and 76 days after the scheduled visit date. At each follow-up visit, the number of scheduled visits that the participant consecutively missed since the previous visit attended was calculated, resulting in a time-varying exposure variable. However, because the exposure variable is likely to have sparse data for higher numbers of MSVs, we categorized the counts of MSV into 3 levels: (1) no missed visit, (2) 1–2 MSV, and (3) $\geq$ 3 MSV.

Statistical Analysis
The total person-years of observation for each participant were split according to their number of episodes of attendance represented by the time period between 2 consecutively attended visits. Each episode was then assigned an appropriate category for the 3-level MSV variable defined previously. There would be increased uncertainty for the date of seroconversion during episodes with MSVs while estimating the person-years for seroconverters. To address this potential concern, the date of seroconversion was assigned as a random date from a uniform distribution bounded by the last-negative and first-positive test dates. In addition, the variability due to assigning a random date was accounted for by multiple imputations (200 imputations). For each set of imputed seroconversion dates, the HIV incidence rates and crude and adjusted hazard ratios (aHR) were calculated and combined using Rubin’s rules.30

To facilitate identifying potential confounders for the association between MSV and HIV incidence, we examined factors associated with MSV using repeated-measures ordered logistic regression. In this model, the three-level MSV variable was fitted as the outcome. Within-woman clustering due to repeated measures was accounted for using the random-effects model. We also examined factors associated with HIV infection.

All models included an indicator variable for cohort (1 or 2) and age group a priori. The incidence analysis was performed in 3 stages: first, the association between MSV and HIV seroconversion was examined using Cox regression models that included the cohort indicator and age. Second, sociodemographic, behavioral, reproductive health, and STIs characteristics were added individually to the base model to assess whether the crude association persisted. Third, the final model was adjusted for variables that were likely confounders of the MSV and HIV seroconversion relationship (ie, at least a 10% change in the log-transformed MSV effects). As a sensitivity analysis, results from the final model were
| Characteristic                          | Follow-up Status, n (%) | P     |
|----------------------------------------|-------------------------|-------|
| Number enrolled                        | 2206 878                | <0.001|
| Sociodemographic                       |                         |       |
| Age in years                           |                         | <0.001|
| 24                                     | 891 (41.0) 459 (54.1)   |       |
| 25–34                                  | 985 (45.3) 321 (37.8)   |       |
| 35+                                    | 299 (13.7) 69 (8.1)     |       |
| Missing                                | 31 29                   |       |
| Highest education level                |                         | 0.94  |
| Less than primary                      | 863 (41.3) 328 (42.0)   |       |
| Completed primary to incomplete O level| 889 (42.6) 330 (42.3)   |       |
| Completed secondary ordinary level above| 336 (16.1) 123 (15.7)  |       |
| Missing                                | 118 97                  |       |
| Marital status                         |                         | 0.01  |
| Widowed/divorced                       | 1381 (63.2) 484 (57.1)  |       |
| Currently married                      | 148 (6.8) 67 (7.9)      |       |
| Never married                          | 654 (30.0) 296 (34.9)   |       |
| Missing                                | 23 31                   |       |
| No. of children                        |                         | <0.001|
| None                                   | 297 (13.7) 187 (22.4)   |       |
| One                                    | 542 (25.1) 239 (28.7)   |       |
| At least 2                             | 1322 (61.2) 407 (48.9)  |       |
| Missing                                | 45 45                   |       |
| Source of income                       |                         | 0.01  |
| Sex work alone                         | 1227 (56.5) 523 (62.1)  |       |
| Sex work and other job                 | 844 (38.8) 276 (32.8)   |       |
| No sex work                            | 102 (4.7) 43 (5.1)      |       |
| Missing                                | 33 36                   |       |
| Where paying clients are recruited by participants| |<0.001|
| Bar, club, or restaurant               | 1040 (50.9) 356 (45.4)  |       |
| Street                                 | 472 (23.1) 291 (37.1)   |       |
| Several avenues                        | 532 (26.0) 138 (17.6)   |       |
| Missing                                | 162 93                  |       |
| Reproductive health                    |                         | 0.02  |
| Pregnancy status                       |                         |       |
| Not pregnant                           | 2048 (94.8) 812 (96.9)  |       |
| Pregnant                               | 112 (5.2) 26 (3.1)      |       |
| Missing                                | 46 40                   |       |
| Current contraceptive use              |                         | <0.001|
| None or other                          | 1285 (61.7) 531 (68.9)  |       |
| Oral cc                                | 170 (8.2) 34 (4.4)      |       |
| Inject                                 | 514 (24.7) 180 (23.3)   |       |
| Pregnant                               | 112 (5.4) 26 (3.4)      |       |
| Missing                                | 125 107                 |       |
| Behavioral characteristics             |                         | <0.001|
| Frequency of paid sex in the past 12 months | 275 (12.6) 125 (14.6) |       |

*STI variable was a composite variable combining data on STI symptoms from clinical examination and test results for STI for syphilis.
compared with those where analyses were restricted to women with at least 6 months of observation time. This is because HIV incidence peaked within the first 6 months, yet participants were less likely to miss scheduled visits during this period than later periods. After performing an interaction of MSV with the cohort indicator variable in the final model adjusted for other confounders, results were also compared for the 2 cohorts.

Figure 1 shows the relationship between MSV and subsequent HIV risk and the relationships across factors controlled for in the regression model. Although behavioral factors and detection of STIs can influence attendance at the study clinic, attendance can also influence reported behavioral and STI outcomes. As a result, the Cox regression model adjusted for time-dependent variables at the preceding visits. Ordered categorical variables in the model were assessed for extralinear variability using likelihood ratio tests by comparing models with variables as categorical versus a linear fit. Analyses were performed using STATA 14 (StataCorp, College Station, TX).

RESULTS

Cohort Characteristics

Of the 3084 HIV-negative women enrolled at the clinic, 2206 (71.5%) attended ≥1 follow-up visit after enrollment: 93.5% (605/647) in cohort-1 and 65.9% (1601/2437) in cohort-2. Between the first enrollment (April 2008) and end of follow-up (Aug 2017), a total of 24,476 visits (cohort-1: 12,786, cohort-2: 11,690) had been scheduled by the last visit of each participant with ≥1 follow-up visit. Of these, 17,486 (71.4%) scheduled visits (cohort-1: 9,462, cohort-2: 8024) were attended. The median number of visits attended per participant was 15 [interquartile range (IQR): 8–22] in cohort-1 and 4 (IQR: 2–6) in cohort-2.

Table 2 compares enrollment characteristics for HIV-negative women with and without a follow-up visit. In the multivariable analysis (see Table 1, Supplemental Digital Content, http://links.lww.com/QAI/B362), the factors associated with having no follow-up include younger age, fewer children, street-based recruitment of clients, not on oral contraceptives, less frequent paid sex, and consistently using condoms with clients in the last month.

HIV Incidence

Among women with ≥1 follow-up visit, we observed 5540 person-years and 170 (7.7%) seroconversions, giving an incidence rate of 3.1/100 person-years [95% confidence interval (CI): 2.6 to 3.5]. Overall incidence was similar in the 2 cohorts (cohort-1: 93 seroconversions; incidence = 3.1/100 person-years; cohort-2: 77 seroconversions; incidence = 3.0/100 person-years). HIV incidence declined after enrollment, from 3.6/100 person-years within the first year, 2.8/100 person-years in the second year, and 2.5/100 person-years beyond 2 years of follow-up.

Figure 2 shows that episodes of 2 consecutively attended visits during which HIV was diagnosed are longer (have their distribution more skewed to the right) than those with HIV-negative test results at both attended visits. After restricting to episodes with ≥3 MSV, the median number of MSV within each participant’s period of 2 consecutively attended visits was 4 MSVs (IQR: 3–6), whereas one person had the longest episode of 30 missed visits (Fig. 2). In examining the potential confounders for the association of MSV and HIV seroconversion (see Table 2, Supplemental Digital Content, http://links.lww.com/QAI/B362), there was evidence that the odds of being in higher categories of MSV than in lower categories were independently associated with: enrollment in cohort-2, longer follow-up, incomplete ordinary secondary education level, street-based recruitment of clients, being pregnant, reporting no paid sex within the last month, alcohol consumption, illicit drug use in past 3 months, and having no STI at the previous visit.

The number of MSVs seems to be positively correlated with HIV incidence. HIV incidence was 2.6/100 person-years (95% CI: 2.1 to 3.2) during episodes without missed visits, 3.0/100 person-years (95% CI: 2.2 to 4.1) in episodes with 1–2 MSV, and 4.3/100 person-years (95% CI: 3.3 to 5.6) in episodes with ≥3 MSV (P value for trend = 0.003; Table 3).

In this multivariable model, episodes with 1–2 MSV were associated with 40% higher risk of HIV infection (aHR = 1.40, 95% CI: 0.93 to 2.12) than episodes without a MSV, but the evidence for this association was weak. However, episodes with ≥3 MSV had twice the risk of HIV infection (aHR = 2.00, 95% CI: 1.35 to 2.95) compared with that in episodes without a MSV. Furthermore, there was strong evidence in favor of the risk of HIV infection increasing with the increasing number of MSV within episodes; P value for trend = 0.001 and P-value for extralinear variability = 0.91.

The evidence for the association between MSV and increased HIV incidence remained when analyses were restricted to follow-up of >6 months [P value for trend <0.001; aHR = 1.61 (95% CI: 1.00 to 2.58) for 1–2 MSV, and aHR = 2.05 (95% CI: 1.31 to 3.22) for ≥3 MSV]. But the estimated effect for the 1–2 MSV category was stronger in this restricted analysis. Although there was no evidence that the effect of MSV differed by cohort (P value for interaction = 0.24), the results are also shown by cohort in Table 3, Supplemental Digital Content, http://links.lww.com/QAI/B362.

Other factors independently associated with increased risk of HIV incidence included the following: not having a stable sexual partner, recruiting clients from the street, not being pregnant, and inconsistent condom use with clients.

DISCUSSION

Our findings demonstrate the importance of ensuring sustained exposure to combined HIV-prevention
interventions targeting women at high-risk of HIV infection in the prevention of HIV. Sustained exposure is not only likely to reinforce prevention interventions but also facilitate earlier initiation of ART among those recently infected with HIV. Participants attending the clinic had access to a range of services including HIV and other sexual health and reproductive services. At every visit, participants attended counseling sessions where they were encouraged to modify or maintain behaviors depending on their interview responses, results from clinical examinations, and serological test. Participants diagnosed with STIs were additionally given treatment. Therefore, MSV within episodes of consecutive attendances was a proxy for recent degree of exposure to combined HIV-prevention interventions.

Compared with episodes without MSV, those with 1–2 MSV had 40% higher risk of HIV infection, whereas those with ≥3 MSV had twice the risk. This dose–response relationship further supports the effectiveness of combination HIV-prevention interventions among FSWs for improved HIV-related outcomes such as consistent condom use with clients, earlier treatment of STIs, and consequently, lower HIV infection. However, this effectiveness is dependent on good program adherence.

In addition, our findings are consistent with studies that have suggested a link between the amount of exposure to HIV interventions and improved HIV-related outcomes. Most notable is a study in Côte d'Ivoire that conducted health talks, provided condoms, treated STIs at monthly clinic visits, and serological tests every 6 months. In this study, HIV incidence was 4.6/100 person-years for women who attended 4 of the 5 scheduled visits before their last assessment and 13.0/100 person-years among those who attended fewer visits. But a time-varying preceding gap in clinic attendance of ≥60 days was associated with reduced HIV risk in a Kenyan FSW cohort with monthly clinic visits. Although the authors did not offer a reason for this association, it is likely that participants who missed the monthly visits may have had low-risk perception and, therefore, saw no need to regularly attend visits. In addition, the variable indicating a preceding gap was correctly analyzed as a confounder, but where it is the main exposure of interest, the time-varying variables in that analysis represent potential mediating factors. Thus, these mediating factors underestimate the overall effect of the preceding gap.

In our study, the mechanisms through which MSV within episodes of consecutive visit attendances influence HIV infection may be explained by interconnected factors operating at the structural, behavioral, and biomedical levels.

**Structural Factors**

HIV determinants such as high mobility, economic difficulties, and risky work environments of FSWs may underlie the risk associated with MSV. Although the ability to take risks (being a more risky individual) could influence an individual to be mobile in search of work; mobility itself can affect the risk of HIV if there is risk of HIV associated with the new environment/place (ie, the new place has high HIV prevalence, low condom use, and low ART coverage or adherence). A previous qualitative study in this cohort reported that participants commonly moved to fishing communities for extended periods in search of clients. These communities have been linked with high HIV prevalence and incidence, yet the fishermen usually preferred condomless sex, thus increasing HIV vulnerabilities for the mobile participants.

Other findings in this cohort are a signal to the potential economic pressures facing participants to not only deter them from accessing the much-needed clinic services but also affecting their ability to refuse sex with a client paying more for noncondom use. For example, when transport refund for participants was stopped in January 2013, the rate of MSV among those attending each visit increased substantially from 10% to 30%. Furthermore, some 5% of participants reported lack of transport as a cause for missing 2 or more visits.
| Characteristic                                           | New HIV Cases/pyr (Rate/100 pyr) | Crude Hazard Ratio (95% CI) | P      | Adjusted Hazard Ratio (95% CI) | P      |
|---------------------------------------------------------|---------------------------------|-----------------------------|--------|-------------------------------|--------|
| Overall (both cohort)                                   | 170/5540 (3.1)                  |                             |        |                               |        |
| No. of visits missed between attendances                |                                 |                             |        |                               |        |
| No missed visit                                         | 81/3106 (2.6)                   | 1                           | 0.003* | 1                             | 0.001* |
| One/2 missed visit(s)                                   | 38/1250 (3.0)                   | 1.18 (0.80 to 1.74)         | 0.03   | 1.40 (0.93 to 2.12)           | 0.04   |
| At least 3 missed visits                                | 51/1180 (4.3)                   | 1.77 (1.23 to 2.54)         | 0.004  | 2.00 (1.35 to 2.95)           | 0.007  |
| Sociodemographic                                        |                                 |                             |        |                               |        |
| Cohort of enrollment                                    |                                 |                             |        |                               |        |
| Cohort-1                                                | 93/3003 (3.1)                   | 1                           | 0.45   |                               | 0.43   |
| Cohort-2                                                | 77/2537 (3.0)                   | 0.87 (0.61 to 1.24)         | 0.85   | (0.56 to 1.27)                |        |
| Calendar period†                                        |                                 |                             |        |                               |        |
| Jan 2013–Dec 2014                                       | 46/1394 (3.3)                   | 1                           | 0.16   |                               |        |
| Jan 2015–Aug 2017                                       | 65/2138 (3.0)                   | 0.99 (0.64 to 1.55)         | 0.86   | (0.60 to 1.24)                | 0.80   |
| Apr 2008–Dec 2012                                       | 59/2007 (2.9)                   | 1.09 (0.70 to 1.70)         | 0.80   | (0.48 to 1.33)                |        |
| Age in years                                            |                                 |                             |        |                               |        |
| <25                                                     | 53/1562 (3.4)                   | 1                           | 0.49   |                               | 0.37   |
| 25–34                                                   | 92/2955 (3.1)                   | 0.96 (0.68 to 1.35)         | 0.86   | (0.60 to 1.24)                |        |
| At least 35                                             | 25/994 (2.5)                    | 0.76 (0.46 to 1.24)         | 0.80   | (0.48 to 1.33)                |        |
| With a stable sexual partner§                           |                                 |                             |        |                               |        |
| Yes                                                     | 113/3959 (2.9)                  | 1                           | 0.01   |                               | 0.003  |
| No                                                      | 57/1211 (4.7)                   | 1.55 (1.13 to 2.14)         | 1.75   | (1.23 to 2.50)                |        |
| Highest education level at enrollment                   |                                 |                             |        |                               |        |
| Incomplete primary level                                | 74/2361 (3.1)                   | 1                           | 0.03   |                               | 0.24   |
| Completed primary to incomplete O level                  | 70/2267 (3.1)                   | 0.97 (0.70 to 1.35)         | 1.06   | (0.76 to 1.49)                |        |
| Completed secondary O level above                       | 25/792 (3.2)                    | 1.00 (0.63 to 1.57)         | 1.20   | (0.75 to 1.92)                |        |
| Marital status§                                         |                                 |                             |        |                               |        |
| Widowed/divorced                                        | 112/3325 (3.4)                  | 1                           | 0.33   |                               |        |
| Currently married                                       | 28/1150 (2.4)                   | 0.77 (0.50 to 1.17)         | 0.81   | (0.54 to 1.22)                |        |
| Never married                                           | 30/1044 (2.9)                   | 0.81 (0.51 to 1.30)         | 0.81   | (0.54 to 1.22)                |        |
| No. of children§                                        |                                 |                             |        |                               |        |
| None                                                    | 21/583 (3.6)                    | 1                           | 0.41   |                               |        |
| One                                                     | 42/1247 (3.4)                   | 0.94 (0.56 to 1.59)         | 0.81   | (0.51 to 1.30)                |        |
| At least 2                                               | 107/3665 (2.9)                  | 0.81 (0.51 to 1.30)         | 0.81   | (0.51 to 1.30)                |        |
| Source of income§                                       |                                 |                             |        |                               |        |
| Sex work alone                                          | 74/2241 (3.3)                   | 1                           | 0.13   |                               |        |
| Sex work and other job                                  | 73/2416 (3.0)                   | 0.94 (0.68 to 1.31)         | 0.89   | (0.54 to 1.45)                |        |
| No sex work                                             | 23/851 (2.7)                    | 0.89 (0.54 to 1.45)         | 0.89   | (0.54 to 1.45)                |        |
| Recruitment of clients§                                 |                                 |                             |        |                               |        |
| Bar, club, or restaurant                                | 76/2717 (2.8)                   | 1                           | 0.01   |                               | 0.004  |
| Street                                                  | 46/888 (5.2)                    | 1.78 (1.23 to 2.57)         | 1.89   | (1.27 to 2.80)                |        |
| Several avenues                                         | 48/1634 (2.9)                   | 1.07 (0.75 to 1.54)         | 0.98   | (0.68 to 1.42)                |        |
| Reproductive health                                     |                                 |                             |        |                               |        |
| Current contraceptive use§                              |                                 |                             |        |                               |        |
| None or other                                           | 100/3160 (3.2)                  | 1                           | 0.001  |                               | <0.001 |
| Oral cc                                                 | 12/526 (2.3)                    | 0.73 (0.40 to 1.33)         | 0.70   | (0.38 to 1.28)                |        |
| Inject                                                  | 56/1378 (4.1)                   | 1.29 (0.93 to 1.80)         | 1.35   | (0.96 to 1.88)                |        |
| Pregnant                                                | 2/397 (0.5)                     | 0.16 (0.04 to 0.66)         | 0.13   | (0.03 to 0.55)                |        |
| Behavioral characteristics§                             |                                 |                             |        |                               |        |
| No. of sexual partners§                                  |                                 |                             |        |                               |        |
| <5                                                      | 77/2765 (2.8)                   | 1                           | 0.30   |                               |        |
| 5–19                                                    | 32/1119 (2.9)                   | 0.97 (0.64 to 1.49)         | 0.97   | (0.64 to 1.49)                |        |
| At least 20 or cannot remember                         | 61/1543 (4.0)                   | 1.29 (0.90 to 1.84)         | 0.97   | (0.64 to 1.49)                |        |
The social components of targeted HIV interventions such as peer outreach are not only critical in facilitating clinic attendance but are also associated with increased consistent condom use among FSWs. Some of the participants with MSV might also have had limited engagement with peer educators as well as with outreach services, particularly participants working in isolation such as street or phone-based FSWs. Yet, our findings show that street-based FSWs were more likely to miss study visits and to acquire HIV infection than those who recruit clients from facilities such as bars or clubs. Among other reasons, street-based FSWs in this cohort as in other studies report a particularly higher risk of sexual or physical violence and exploitation by clients and law enforcers than venue-based FSWs. Consequently, they are likely to be at a greater risk of STIs and HIV than those based in facilities. Furthermore, participants starting out in sex work are usually young and without social support networks to help them manage daily risks, including getting support for attending clinic visits. These young participants are likely to be more isolated, more stigmatized, and to be highly vulnerable. Therefore, targeted programmes should work with potentially isolated groups of women at high risk of HIV (such as the highly mobile or young women) to develop better delivery models for services, which models could include scaling-up and intensifying mobile night clinics and intensifying peer outreach.

**Behavioral Factors**

Regular attendance of a dedicated clinic creates opportunities for reinforcing individual behavioral change messages among women at high risk of HIV. HIV prevention behavior can be achieved and sustained when participants are continually provided with appropriate information, are motivated to act, and enabled to obtain behavioral skills. These are key elements of the information–motivational–behavioral skill model that has been proposed for ART adherence but can also be applied for behavioral change among women at high risk of HIV. Our study, trained counselors provide information on HIV prevention to participants through interactive sessions. Similar interactive sessions have been credited by FSWs in Zimbabwe for improving awareness of self-care as well as prevention and treatment of HIV and STIs.

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**TABLE 3. (Continued) Association of HIV Seroconversion With the Number of Missed Visits Between Consecutively Attended Visits Based on the Cox Regression Model**

| Characteristic                                      | New HIV Cases/pyr (Rate/100 pyr) | Crude Hazard Ratio (95% CI) | P    | Adjusted Hazard Ratio (95% CI) | P    |
|----------------------------------------------------|----------------------------------|-----------------------------|------|------------------------------|------|
| No. of men the participant had paid sex within the last month§ |                                  |                              |      |                              |      |
| <5                                                 | 79/2816 (2.8)                    | 1                           | 0.14 | 1                            | 0.29 |
| 5–19                                               | 27/1089 (2.5)                    | 0.84 (0.54 to 1.32)         | 0.70 | (0.43 to 1.14)               |      |
| At least 20 or cannot remember                     | 60/1522 (3.9)                    | 1.29 (0.90 to 1.85)         | 0.96 | (0.62 to 1.47)               |      |
| Condom use frequency with paid sex in the last month§ |                                  |                              |      |                              |      |
| Inconsistent                                       | 72/1616 (4.5)                    | 1                           | 0.01 | 1                            | 0.002|
| Consistent (always)                                | 55/2223 (2.5)                    | 0.84 (0.40 to 0.80)         | 0.51 | (0.35 to 0.74)               |      |
| No paid sex                                        | 43/1601 (2.7)                    | 0.64 (0.43 to 0.96)         | 0.76 | (0.48 to 1.20)               |      |
| Alcohol consumption frequency§                     |                                  |                              |      |                              |      |
| Nondrinker                                         | 49/1870 (2.6)                    | 1                           | 0.30 | 1                            | 0.41 |
| Non-daily drinker                                  | 68/2202 (3.1)                    | 1.17 (0.81 to 1.70)         | 1.17 | (0.79 to 1.73)               |      |
| Daily drinker                                      | 53/1418 (3.7)                    | 1.37 (0.92 to 2.04)         | 1.34 | (0.87 to 2.07)               |      |
| Binge drinking in past 3 months§                   |                                  |                              |      |                              |      |
| Nondrinker                                         | 48/1847 (2.6)                    | 1                           | 0.21 |                              |      |
| No binging                                         | 58/1617 (3.6)                    | 1.41 (0.95 to 2.07)         | 1.41 | (0.95 to 2.07)               |      |
| Binged                                             | 64/2039 (3.1)                    | 1.14 (0.78 to 1.67)         | 1.14 | (0.78 to 1.67)               |      |
| Illicit drug use in the past 3 months§             |                                  |                              |      |                              |      |
| No                                                 | 122/3949 (3.1)                   | 1                           | 0.34 |                              |      |
| Yes                                                | 48/1260 (3.8)                    | 1.18 (0.84 to 1.66)         | 1.18 | (0.84 to 1.66)               |      |
| Sexually transmitted infections (STIs)§‡          |                                  |                              |      |                              |      |
| No STI                                             | 109/4033 (2.7)                   | 1                           | 0.01 | 1                            | 0.12 |
| With STI                                           | 61/1471 (4.1)                    | 1.49 (1.09 to 2.05)         | 1.31 | (0.93 to 1.85)               |      |

Adjusted for: cohort of enrollment, age at follow-up in years, having a stable sexual partner (both married and unmarried), highest education level at enrollment, where clients are recruited from, current contraceptive use, condom use frequency with paid sex in the last month at follow-up, alcohol consumption frequency at follow-up, and presence of a sexually transmitted infection at follow-up.

*Test for linear trend. Pyr—person-years of observation.

The calendar period of January 2013–December 2014 was common to both cohorts (cohort-1 and cohort-2) because cohort-2 was initiated in January 2013 and was, therefore, used as the reference category.

†STI variable was a composite variable combining data on STI symptoms from clinical examination and test results for STI for syphilis.

‡Data collected at enrollment and follow-up study visits.
ongoing risk-reduction counseling sessions in our study, participants are motivated to improve or maintain healthy behaviors. This motivation may not only facilitate the adoption of healthy behaviors but also influence participants to regularly attend the clinic. Attending follow-up visits at the clinic was associated with higher parity, being on oral contraceptives, and having had an STI at the previous visit, which factors also reflect some underlying motivations related with the services offered at the clinic. According to the information–motivational–behavioral model, ongoing information on HIV prevention and motivation to stay healthy would act through acquired behavioral skills such as correct use of condoms to influence HIV incidence.

Therefore, participants who miss study visits are likely to also miss opportunities for reinforcing HIV risk-reduction behaviors. In addition, the HIV risk associated with MSV may increase where the participant’s decision to attend the clinic is influenced by new intimate relationships. When participants start new intimate relationships, they might be afraid to associate with the clinic and they could be stopped by spouses from attending the dedicated clinic. In participants who missed ≥2 consecutive visits, 10% reported the reason as being in a new stable relationship or being stopped by a spouse. In this cohort as elsewhere, it is not uncommon for some of these new relationships to involve paying clients who transitioned into regular partnerships. These partnerships have not only been associated with limited condom use which is usually seen as a sign of mistrust within intimate relationships across Africa but also with high HIV burdens.

Biomedical Factors

Regular attendance of a dedicated clinic enables timely access to biomedical interventions for prevention, treatment, and care. For example, 18% of all syndrome-based STIs might not have been detected if FSWs had not attended the clinic in a large study in Southern India on the impact of peer outreach on clinic utilization reported. Similarly, the clinical examination at our study clinic is likely to facilitate earlier diagnosis and treatment of STIs for those regularly attending the clinic. As a result, earlier treatment would reduce the efficiency of STIs for HIV transmission.

Despite the substantial decline in HIV incidence after enrollment that was recently observed in this cohort, the incidence remained high and persisted over time. HIV incidence also remained high during episodes with no MSV, although it was substantially lower in these episodes compared with those with at least 3 MSV. This persistently high HIV incidence despite combined HIV-prevention efforts may suggest presence of potential barriers in HIV control among women at high risk of HIV in this cohort. Among other factors, HIV control may be hindered by common barriers reported across studies in Africa such as accepting offers of sex without condoms for more money, hazardous alcohol use, and sexual and physical violence among women at high risk of HIV. To further interrupt the spread of HIV through sex work, there is a need to strengthen targeted HIV-prevention efforts by integrating promising direct biomedical interventions such as pre-exposure prophylaxis, strengthening risk-reduction interventions for substance abuse, and perhaps implementing mental health interventions. These individual-level interventions should be further supported by structural interventions such as community empowerment that ensure targeted services are supplied and delivered to all women at high risk of HIV. Community empowerment conceptualized as an active involvement of sex workers, and the community in targeted activities could also reduce on the interconnected HIV risk factors for social stigmas, discrimination, and violence. More importantly, there is need to monitor and strengthen regular engagement between women at high risk of HIV and service providers including their attendance at clinic services in the design and implementation of HIV-prevention interventions. Intensified peer outreach is associated with improved clinic utilization among FSWs and may be particularly important among isolated groups such as street-based FSWs.

We note some key limitations. The measurement of MSV and seroconversion within the same episode could lead to some misclassification for the timing of seroconversions in the episodes with MSV if seroconversion occurred earlier before the missed visits. However, we assigned the timing of seroconversion as a random date rather than the commonly used midpoint to reduce on the potential for overestimation of HIV risk during episodes with MSVs. Also, the number of events per predictor variable (EPV) in the multivariable model was relatively low (8.5) compared with the recommended minimum EPV of 10. Although this low EPV can affect model-based inferences, the strong evidence for the association between MSV and HIV incidence in both the simple and multivariable models suggests that our conclusions could be valid. Similarly, data on some important risk factors such as duration of sex work were not collected, meaning this association could be confounded. Furthermore, the study did not fully record reasons for MSV and on a longitudinal basis, which would have facilitated better understanding of what underlies the HIV risk associated with MSV.

In conclusion, the need for scaling-up targeted combination HIV-prevention and treatment interventions for FSWs has been emphasized, but this study stresses the importance of monitoring, facilitating, and sustaining exposure to these services once women at high risk of HIV have been linked to services. Sustained exposure reinforces HIV prevention and facilitates earlier initiation of ART among those recently infected with HIV. Therefore, HIV programmes should include moving a wider scope of services to HIV-vulnerable women who are unable or unwilling to attend clinic services, particularly those working outside of established venues such as street-based FSWs.

REFERENCES

1. Rinaldi G, Kiadaliri AA, Haghparast-Bidgoli H. Cost effectiveness of HIV and sexual reproductive health interventions targeting sex workers: a systematic review. Cost Eff Resour Alloc. 2018;16:63.
2. Vassall A, Pickles M, Chandrashekar S, et al. Cost-effectiveness of HIV prevention for high-risk groups at scale: an economic evaluation of the Avahan programme in south India. Lancet Glob Health. 2014;2: e531–e540.
47. Li Q, Li X, Stanton B. Alcohol use among female sex workers and male clients: an integrative review of global literature. *Alcohol Alcohol.* 2010; 45:188–199.

48. Shahmanesh M, Wayal S, Cowan F, et al. Suicidal behavior among female sex workers in Goa, India: the silent epidemic. *Am J Public Health.* 2009;99:1239–1246.

49. Moore L, Chersich MF, Steen R, et al. Community empowerment and involvement of female sex workers in targeted sexual and reproductive health interventions in Africa: a systematic review. *Global Health.* 2014;10:47.

50. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. *Am J Epidemiol.* 2007;165:710–718.