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## High level of HIV drug resistance and virological nonsuppression among female sex workers in Ethiopia: a nationwide cross-sectional study

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## Abstract

**Objective:** To determine viral load non-suppression (VLN) rates, HIV drug resistance (HIVDR) prevalence and associated factors among female sex workers (FSWs) in Ethiopia.

**Methods:** A cross-sectional biobehavioural survey was conducted among FSWs in 11 cities in Ethiopia in 2014. Whole blood was collected and HIVDR genotyping was done. Logistic regression analysis was used to identify factors associated with VLN and HIVDR.

**Results:** Among 4900 participants, 1172 (23.9%) were HIV-positive, and 1154 (98.5%) had a VL result. Participants were categorized into ART (n=239) and ART-naïve (n=915) groups based on self-report. From the 521 specimens (ART, 59; ART-naïve, 462) with VL 1000 copies/mL, genotyping was successful for 420 (80.6%), and 92 (21.9%) had drug resistance mutations (DRMs). Pre-treatment drug resistance (PDR) was detected in (63/381) 16.5% ART-

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DA, PB, and PM were responsible for the overall study design. DA, YK, AR, JH, CZ, PM, and TB were responsible for overall project coordination. AR, JC, JH, and CZ coordinated the laboratory tests. DA and MD performed database entry and data cleaning and analysis. DA and PM performed the resistance testing and sequencing analyses. DA, PM, MD and PB interpreted the results. DA, MD, and PM wrote the manuscript. All authors revised the manuscript, provided important intellectual content and approved the manuscript.

Transparency declaration

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naïve participants. Nucleoside, non-nucleoside reverse transcriptase inhibitors (NRTIs, NNRTI), and dual-class DRMs were detected in 40 (10.5%), 55 (14.4%), and 35 (9.2%) of the participants, respectively. Among 239 on ART, 59 (24.7%) had VLN. Genotyping was successfully performed for 39 (66.1%). DRMs were detected in 29 (74.4%). All 29 had NNRTI, 23 (79.3%) had NRTI or dual-class DRMs. VLN was associated with age 35 years, CD4+ T-cell count <350 cells/mm<sup>3</sup> and being forced into selling sex. PDR and acquired drug resistance was associated with CD4+ T-cell count <350 cells/mm<sup>3</sup> (p<0.001).

**Conclusions:** The high VLN and HIVDR rates among FSWs underscores the need for targeted interventions to improve ART access and virological monitoring to maximize the benefit of ART and limit the spread of HIV and HIVDR.

#### Keywords

Female sex worker; HIV drug resistance; pre-treatment drug resistance; acquired drug resistance; virologic failure; Ethiopia

#### Introduction

Female sex workers (FSWs) are at high risk of HIV infection and transmission and bear a disproportionately large burden of the disease<sup>1–4</sup>. As in many low- and middle-income countries (LMIC), Ethiopia has a generalized HIV epidemic primarily through heterosexual transmission. Since the beginning of the epidemic, FSWs have had high risk of HIV infection and were considered key drivers of HIV transmission<sup>5–8</sup>. According to the 2014 at-risk population survey (MARPS), HIV prevalence among FSWs in Ethiopia was 24%, more than five times the prevalence of HIV in the general female population of reproductive age<sup>9</sup>.

In Ethiopia, antiretroviral therapy (ART) was rolled-out free of charge in 2005 and since then, ART has been scaled up to provide access to all HIV-infected individuals<sup>10</sup>. In 2019, 473,261 people living with HIV were receiving ART in Ethiopia (75% coverage). Ethiopia has also implemented the test-treat recommendation since 2017. Accordingly, every person tested positive for HIV will start treatment irrespective of his/her immunological and virological status<sup>11</sup>. However, with rapid scale up of ART an increased trends in emergency and transmission of HIV drug resistance (HIVDR) particularly to non-nucleoside reverse transcriptase inhibitors (NNRTI) have been reported from several low-middle-income countries<sup>12</sup>.

Despite advances in expanding access to HIV treatment and prevention, Ethiopia has limited access to regular virologic monitoring and HIVDR testing, delaying identification of patients with treatment failure and increasing the risk of drug-resistance mutations (DRMs) and onward transmission of HIVDR<sup>12,13</sup>. This may be more pronounced among FSWs who are highly mobile, are hard to reach, have low access to antiretroviral therapy (ART), adherence support, and viral load (VL) monitoring, and have low care retention rates<sup>3,14</sup>. Moreover, FSWs are frequently exposed to violence, and women who report violence have poor ART adherence and viral suppression<sup>15,16</sup>. Addressing these barriers has the potential to reduce HIV infection and improve HIV treatment outcome<sup>17</sup>.

Data about ART uptake and treatment outcomes among FSWs in Ethiopia and other LMICs are limited. Given the potential risk of transmission to the general population, monitoring risk behaviour and testing for viral load non-suppression (VLN; VL 1000 copies/mL) and HIVDR among FSWs can help inform prevention strategies to decrease HIVDR rates and onward transmission. Although FSWs are known to be at high risk of HIV infection and play an important role in HIV transmission dynamics, there is a lack of data on VLN and HIVDR among FSWs in Ethiopia. This study describes the prevalence of VLN, HIVDR mutations, and associated factors among FSWs in Ethiopia.

## Methods

This study was part of a larger cross-sectional study that assessed HIV prevalence and related risk factors among FSWs in Ethiopia in 2014. Data were collected via respondentdriven sampling in 11 cities (Addis Ababa, Mekele, Bahir Dar, Adama, Dire Dawa, Gambela, Hawassa, Metema, Kombolcha, Semera, and Shashamene) (Figure 1). We defined FSWs as women who engage in sexual activity with the precondition of financial or in-kind benefits. The inclusion criteria for the study were women receiving money or other benefits for sex with four or more people within the last 30 days, aged 15 years, recruited by a peer, and providing consent for the interview and blood tests. The study methods have previously been described<sup>16</sup>. For this study only women aged 18 were included. Briefly, six seed FSWs were selected to use coupons to recruit peers in each town. Eligible FSWs who provided informed consent participated in a face-to-face interview with nurses using a structured questionnaire in a private room. After completing the interview, participants provided blood specimens for HIV, CD4<sup>+</sup> T-cell counts, VL, and HIVDR testing and were given three coupons to recruit their peers into the study.

During the survey, sociodemographic characteristics and bio-behavioural data were collected. Awareness of HIV status and prior ART exposure were used to classify study participants. Participants who reported they were currently receiving ART were in the ART group, whereas those who reported not receiving ART (either ongoing or previous treatment including antiretroviral for prevention of mother-to-child HIV transmission) were categorized as ART-naïve group. This categorization also was used to classify pre-treatment drug resistance (PDR) in ART-naïve participants and acquired HIVDR (ADR) in the ART group.

Participants were screened for HIV at the collection site via point-of-care rapid testing, which is used for HIV diagnosis in Ethiopia<sup>10</sup>. CD4+ T cell counts were obtained in nearby health facilities using the FACSCalibur and FACSCount systems (Becton Dickinson, San Jose, CA USA) according to the manufacturer's recommendations. Plasma was separated from whole blood and transported to the Ethiopian Public Health Institute (EPHI), where HIV-1 VL was determined using Abbott RealTime HIV-1 assay (Abbott Molecular Inc., Des Plaines, IL USA). Using 1000 copies/mL as VL suppression threshold based on WHO recommendation<sup>18</sup>, all samples with VL 1000 copies/mL were shipped to the International Laboratory Branch of the Division of Global HIV & Tuberculosis, Center for Global Health, CDC (Atlanta, GA) for HIVDR genotyping (for details, see the supplementary information).

#### **HIV-1** genotyping

Genotyping was performed using the ABI HIV-1 Genotyping Kit (Thermo Fisher Scientific, Waltham, MA USA)<sup>19</sup>. Briefly, a 1084 base-pair fragment of HIV-1 pol (corresponding to the position 2243-3326 of HXB2; Genbank Accession Number: K03455) comprising amino acids 6–99 of the protease and 1–251 of the reverse transcriptase was generated by reverse transcriptase polymerase chain reaction (PCR) and nested PCR. The purified PCR fragments were then sequenced and analysed on the ABI Prism 3730 Genetic Analyzer (Applied Biosystems, Foster City, CA USA). Sequence assembly and editing were performed using the RECall V 2.0 HIV-1 sequencing analysis tool (University of British Columbia, Vancouver, Canada)<sup>20</sup>. Sequence quality control was performed using the online Quality Control program of the Los Alamos HIV sequence database (https://www.hiv.lanl.gov/).

#### Drug resistance mutations analysis

Surveillance drug resistance mutations (SDRMs) were examined according to the Stanford Genotypic Resistance calibrated population resistance tool, version 6.0 (https://hivdb.stanford.edu/cpr). PDR levels were classified (low, <5%; moderate, 5%–15%; or high, >15%) using the World Health Organization (WHO) threshold survey protocol<sup>21</sup>. ADR was analysed using the Stanford HIVdb program. Genotypic susceptibility scores 60 for each NNRTI and/or NRTI were considered a high level of resistance<sup>22</sup>.

#### Statistical analysis

Statistical analysis was performed using SPSS, version 20 (Chicago, IL USA). We used logistic regression analysis to identify potential risk factors for VLN and for PDR and ADR mutations. We used a multivariable model to assess biologically plausible interactions. Variables considered were age, education status, income from selling sex, khat chewing, heavy episodic drinking, sex-selling venues, frequency of sexual encounters per month, violence, being forced to sell sex, CD4<sup>+</sup> T-cell counts, vaginal discharge, and genital ulcers. In the model, we included a binary response, indicating detection of any VLN, PDR, and ADR mutations from each participant as an outcome. We analysed all variables separately and entered those associated (p<0.2) with the outcomes into the multivariable model. Odds ratios (crude and adjusted OR) with 95% confidence intervals (CI) were obtained using logistic regression analysis. P-values 0.05 were considered statistically significant. Although the data were collected using RDS sampling, our study focuses on a segment of samples (i.e., participants with VL 1000 copies/mL) to extrapolate the HIVDR (ADR and PDR) prevalence among FSWs, sample RDS weighting was not included in our analysis.

#### **Ethical considerations**

The protocol was cleared by the Scientific and Ethical Research Office of EPHI, and the Ethiopian Science and Technology Ministry Ethical Committee Institutional Review Boards (NHSBS-Round 1). This project was reviewed in accordance with CDC human research protection procedures (CDC-IRB #6343.0) and was determined to be research, but CDC investigators did not interact with human subjects or have access to identifiable data or specimens for research purposes. Individual written informed consent was obtained from each participant.

## Results

Figure 2 summarizes how participants were selected for HIVDR genotyping using the HIV test, VL and the genotyping results. Of 4900 participants, 1172 (23.9%) were HIV-positive; of these, 1154 (98.5%) had VL results and were grouped based on self-report in the ART-naïve or ART groups. The threshold for VL suppression was 1000 copies/mL per WHO recommendations<sup>18</sup>. Among 915 participants in the ART-naïve group, 453 had VL <1000 copies/mL, indicating they may have been exposed to ART but did not report it. The 521 samples (ART group, 59; ART-naïve group, 462) with VL 1000 copies/mL were subjected for HIVDR genotyping. The genotyping success rates were 82.5% for the ART-naïve group (381/462) and 66.1% (39/59) for the ART group, respectively. Overall HIVDR prevalence rates were 16.5% (63/381) for the ART-naïve group and 74.4% (29/39) for the ART group.

We also calculated the ART uptake of participants (proportion of FSWs who tested HIV positive and were receiving ART). Self-report of ART uptake was 20.7% (239/1154). However, including participants with VL <1000 copies/mL but who self-reported being ART naïve, ART uptake was 60.0% (692/1154).

#### Prevalence of pretreatment drug resistance

In the ART-naïve group, 462 participants had VL 1000 copies/mL, and 381 had genotyping results that were included in the PDR analysis. Median age was 25 years (interquartile range [IQR], 22–29 years). Median HIV VL and CD4<sup>+</sup> T-cell count were 28,823 copies/mL (IQR, 7,809–122,812 copies/mL) and 421 cells/mm<sup>3</sup> (IQR, 251–606 cells/mm<sup>3</sup>), respectively.

Sixty-three (16.5% [95% CI: 12.8%–20.3%]) of the genotyped specimens were associated with at least one major DRM. The highest prevalence of PDR was found against NNRTIS (55/381 [14.4%]), and five DRMs (K103N, Y181C, G190A/E/S, K101E/P, and V106M) accounted for most (90.0%) of the NNRTI PDR mutations (Table 1).

NRTI PDR mutations were detected in 10.5% (40/381) of the specimens, and 9.2% (35/381) had dual-class (NRTI and NNRTI) DRMs. The most prevalent NRTI DRMs were M184V and thymidine-analogue mutations (TAMs; M41L, D67G/N, K70R, L210W, T215F/Y, and K219E/Q), accounting for 58.7% (37/63) and 27.0% (17/63) of the NRTI PDR, respectively. PI PDR mutations were detected in 0.8% (3/381) of the specimens (Table 1). According to the WHO classification of HIVDR prevalence, the overall PDR level among our participants was high (15%) but was moderate for NNRTIs and NRTIs and was low for PIs.

#### Prevalence and patterns of acquired drug resistance

Among 239 participants receiving ART, 59 (24.7%) had VL 1000 copies/mL. Median CD4<sup>+</sup> T-cell count and VL were 384 cells/mm<sup>3</sup> (IQR, 163–568 cells/mm<sup>3</sup>) and 10,225 copies/mL (IQR, 2,802–95,220 copies/mL), respectively. Genotyping was successful for 39 (66.1%) of the specimens. Twenty-nine (74.4% [95% CI: 60.7%–88.1%]) of the genotyped specimens had at least one major DRM. All 29 specimens had NNRTI DRMs, 23 (79.3%) had NRTI DRMs, and none had PI DRMs (Table 2). The most prevalent NNRTI DRMs were K103N, Y181C, and G190A. The most frequent NRTI DRMs were M184V (20 [69.0%]) and TAMs (18 [62.1%]; Table 2).

Dual-class resistance was present in 79.3% (23/29) of the specimens. Overall, the mean numbers of NRTI and NNRTI DRMs detected per specimen were 3.4 and 4.7, respectively. Four of the sequences had only one mutation (all NNRTI DRMs), three sequences had two mutations, and 22 (76.0%) of the sequences had 3 mutations.

Genotypic susceptibility scores of individual antiretroviral drugs indicated that many of the specimens had high levels of resistance to several of the most used first-line ART drugs in Ethiopia. Most (69.0%) specimens showed high-level resistance to lamivudine and tenofovir, nevirapine (100%), efavirenz (86.2%), and rilpivirine (51.7%; Supplementary Table 1).

#### Factors associated with VLN and HIVDR

In both bivariate and multivariate analysis, VLN was significantly associated with being forced into selling sex (p<0.036), age 35 years (p<0.037), and low CD4<sup>+</sup> T-cell counts (<350 cells/mm<sup>3</sup> (p<0.001; Table 3). In bivariate analysis, PDR was significantly associated with low CD4 counts (p<0.001) and ever giving birth (p<0.03). However, in multivariate analysis, only low CD4 counts remained significantly associated with PDR (p<0.001). Moreover, low CD4 counts were significantly associated with ADR in both bivariate and multivariate analysis (p<0.001).

## Discussion

To our knowledge, this is the first national study that comprehensively describes the level of VLN and HIVDR among FSWs in Ethiopia. Overall, our results showed a high prevalence of HIVDR (PDR, 16.5%; ADR, 74.4%), poor ART uptake (20.7%), and high VLN (24.7%) with multiple DRMs among participants, which indicates high risk of HIVDR transmission to the general population.

We found high prevalence of PDR, particularly toward NNRTIs. This level is higher than the PDR level reported among the general population in Ethiopia  $(4\%-6\%)^{10,23-29}$ . Consistent with our findings, other studies have reported high PDR levels (10%-48%) among FSWs in different countries, including those in sub-Saharan Africa<sup>28,30-34</sup>. Moreover, previous studies also have shown a higher PDR rate among communities and groups with high-risk behaviours<sup>29,35</sup>. This highlights the vulnerability of FSWs to HIVDR and the risk of onward transmission to the general population.

After 10 years of ART roll-out in Ethiopia, the prevalence of NNRTI PDR in our study is above the WHO-recommended levels to replace NNRTIs with dolutegravir in first-line regimens<sup>36</sup>. Similar findings have been reported in other LMICs, which depend on standardized first-line ART<sup>37,38</sup>. The high NNRTI DRM prevalence might in part be due to the low genetic barrier of these drugs and their wide use for prevention of mother-to-child HIV transmission and as part of the standard first-line ART regimen<sup>12,39</sup>.

In our study, K103N, Y181C, G190A/E/S, K101E/P, and V106M accounted for the vast majority of the NNRTI PDR mutations. Strains with K103N and other NNRTI mutations have a fitness similar to wild-type virus, and the mutation can persist for years in HIV-positive individuals<sup>39–41</sup>. It is therefore likely that the high prevalence of these mutations is

The most common NRTI PDR mutations detected in our study were M184V, K65R, and TAMs. However, both M184V and K65R revert to wild-type relatively quickly in the absence of ART<sup>42,43</sup> and would be expected to be found at low frequencies among individuals with PDR. Nevertheless, M184V is one of the most detected PDR mutations in most countries, including sub-Saharan African countries<sup>38</sup>.

We found that FSWs had poor ART uptake. Only one in five HIV-positive participants were receiving ART, which is consistent with results of other studies in sub-Saharan Africa, showing generally poor ART uptake among FSWs (range, 26%–38%)<sup>44–47</sup>. However, in our study, more than half of participants with self-reported ART-naïve status had VL<1000 copies/mL, indicating they may have been exposed to ART but did not disclose this history<sup>48–51</sup>. A recent report from Ethiopia also showed that only 26% of HIV-positive FSWs were receiving ART<sup>52</sup>. Consistent with our results, several studies in sub-Saharan Africa have shown high levels of VLN among FSWs<sup>28,53–56</sup>. This might be due to multiple barriers, such as stigma related to HIV and sex work or high mobility, that prevent FSWs from accessing the HIV care continuum (20). Moreover, FSWs are frequently exposed to violence, and women who report violence have poor ART adherence and viral suppression<sup>15,16</sup>.

Improving access to ART for FSWs and not only will improve the survival and health of this population but also will reduce the risk of HIV transmission to their clients and could lower HIV transmission at the general population level<sup>4,57–59</sup>. Our findings highlight the importance of identifying potential factors that prevent FSWs from accessing HIV treatment services. Improving ART uptake could help improve outcomes for clients in national HIV control programs<sup>57,58</sup>. Furthermore, targeting scaleup of viral load monitoring among FSWs could help ensure timely therapy changes for those with virologic failure, according to the national treatment guidelines<sup>60</sup>.

In our study, a high proportion of FSWs with VLN carried dual-class DRMs with high genotypic susceptibility scores to several commonly used first-line ART drugs. Consistent with our study, other studies have reported high DRM frequency with a complex pattern in patients with prolonged use of failing regimens in the absence of VL monitoring<sup>61,62</sup>. Besides the resultant limitations in the choice of effective treatment regimens for patients with VLN, the high prevalence of HIVDR detected among participants in our study highlights the potential risk of HIVDR transmission to the general population. Furthermore, when individuals carrying multiple DRMs are switched to second-line therapy, there is a risk of introducing a functional monotherapy, which may be associated with substantial risk of subsequent virologic failure and emergence of HIVDR.

Among FSW receiving ART with VL 1000 copies/mL, 26% had no HIVDR mutations, which suggests that non-adherence could be the possible cause for the detected virologic failure. This shows the importance of strengthening adherence among FSWs and of using

HIVDR testing before treatment switches to reduce the cost associated with prematurely switching to costly second-line regimens.

We found that older participants aged 35 years experienced higher prevalence of VLN compared to younger participants aged 18–24 years. This finding contrasts with those of a study in Uganda, where young (18–24 years) FSWs experienced higher prevalence of virological failure than older (>35 years) FSWs<sup>28</sup>. This difference might in part be due to the difference in the research design of the studies. The study in Uganda was conducted among FSWs with virological failure identified during follow-up, whereas our study collected lifetime ART status, and the older participants in our study might be more likely to have treatment failure due to prolonged ART exposure compared to younger participants. The longer the duration of ART treatment, the higher the odds of developing drug resistance leading to treatment failure<sup>65</sup>.

Moreover, participants who reported being forced into sex work had higher prevalence of VLN. Women and girls forced into sex work are especially vulnerable because they cannot control their environment<sup>16</sup>. This may increase the risk of substance use as a coping mechanism, which can decrease the efficacy of ART (including poor adherence), potentially leading to treatment failure<sup>66</sup>. Our results showed that low CD4<sup>+</sup> T-cell count (<350 cells/mm<sup>3</sup>) was associated with VLN and DRMs among ART-experienced participants, suggesting disease progression among those with VLN and ADR and underlining the importance of DRM monitoring to improve individual outcomes.

Our study has several limitations. One limitation of our study and similar studies is that the duration of HIV infection before sampling is unknown. Because our classification of ART status among participants was based on self-report, there is a risk of misclassification if participants did not disclose previous ART exposure for fear of discrimination, which has been documented in other studies<sup>50,51,67</sup>. We used 1000 copies/mL as the cut-off for VLN, however, other studies have shown the development of HIVDR among patients with low-level viremia<sup>68</sup>. The overall genotyping success rate was 80.6%, which might have affected the overall study results. Although the data used in our analysis was collected using RDS sampling, our study only focused on a segment of the samples (i.e., participants with VL 1000 copies/mL) to extrapolate the HIVDR prevalence among FSW, therefore, weighting was not included in the data analysis. We also did not collect information about ART regimens, ART duration, or ART adherence, which could affect the level of ADR. Finally, some of the ART-experienced participants with VLN might have been infected with a DRM virus.

## Conclusions

The suboptimal ART uptake and high VLN and HIVDR levels detected among FSWs underscore the importance of programmatic intervention to improve ART access and routine virological monitoring among this population to maximize the benefit of ART and limit the spread of HIV, HIVDR and disease progression. Our findings also demonstrate the need for implementation of HIVDR genotyping to optimize selection of regimen and transition to dolutegravir-based first-line ART in Ethiopia.

## **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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#### References

- Baral S, Beyrer C, Muessig K, et al. Burden of HIV among female sex workers in low-income and middle-income countries: a systematic review and meta-analysis. The Lancet Infectious Diseases. 2012;12(7):538–549. doi:10.1016/s1473-3099(12)70066-x [PubMed: 22424777]
- Shannon K, Crago AL, Baral SD, et al. The global response and unmet actions for HIV and sex workers. Lancet. Aug 25 2018;392(10148):698–710. doi:10.1016/S0140-6736(18)31439-9 [PubMed: 30037733]
- Doshi RH, Sande E, Ogwal M, et al. Progress toward UNAIDS 90-90-90 targets: A respondentdriven survey among female sex workers in Kampala, Uganda. PLoS One. 2018;13(9):e0201352. doi:10.1371/journal.pone.0201352 [PubMed: 30231030]
- Prüss-Ustün A, Wolf J, Driscoll T, Degenhardt L, Neira M, Calleja JM. HIV due to female sex work: regional and global estimates. PLoS One. 2013;8(5):e63476. doi:10.1371/journal.pone.0063476 [PubMed: 23717432]
- Aklilu M, Messele T, Tsegaye A, et al. Factors associated with HIV-1 infection among sex workers of Addis Ababa, Ethiopia. Aids. Jan 5 2001;15(1):87–96. doi:10.1097/00002030-200101050-00013 [PubMed: 11192872]
- Mehret MKL, Shanko B, Belete F. Sexual behaviours and some social features off female sex workers in the city of Addis Ababa. Ethiopian Journal of Health Development 1990;4 (2): 133–13
- Mehret MKL, Zewdie D. Ayehunie S, Shanko B, Gizaw G, et al. HIV-1 infection and some related risk factors among female sex workers in Addis Ababa. Ethiopian Journal of Health Development 1990;4: 171–176
- 8. Mehret MKL, Zewdie D. et al. HIV-1 infection and related risk factors among female sex workers in urban areas of Ethiopia. Ethiopian Journal of Health Development. 1990;4 (2, Suppl.):163–70
- 9. EPHI. Ethiopian national key population HIV bio-behavioral surveillance Round I, 2013 Report: EPHI; 2014. 2014;
- Arimide DA, Abebe A, Kebede Y, et al. HIV-genetic diversity and drug resistance transmission clusters in Gondar, Northern Ethiopia, 2003–2013. PLoS One. 2018;13(10):e0205446. doi:10.1371/journal.pone.0205446 [PubMed: 30304061]
- Tesfaye B, Ermias D, Moges S, Astatkie A. Effect of the Test and Treat Strategy on Mortality Among HIV-Positive Adult Clients on Antiretroviral Treatment in Public Hospitals of Addis Ababa, Ethiopia. HIV AIDS (Auckl). 2021;13:349–360. doi:10.2147/hiv.S303557 [PubMed: 33833584]
- Gupta RK, Jordan MR, Sultan BJ, et al. Global trends in antiretroviral resistance in treatmentnaive individuals with HIV after rollout of antiretroviral treatment in resource-limited settings: a global collaborative study and meta-regression analysis. Lancet. Oct 6 2012;380(9849):1250–8. doi:10.1016/s0140-6736(12)61038-1 [PubMed: 22828485]
- 13. Kityo C, Thompson J, Nankya I, et al. HIV Drug Resistance Mutations in Non-B Subtypes After Prolonged Virological Failure on NNRTI-Based First-Line Regimens in Sub-Saharan Africa.

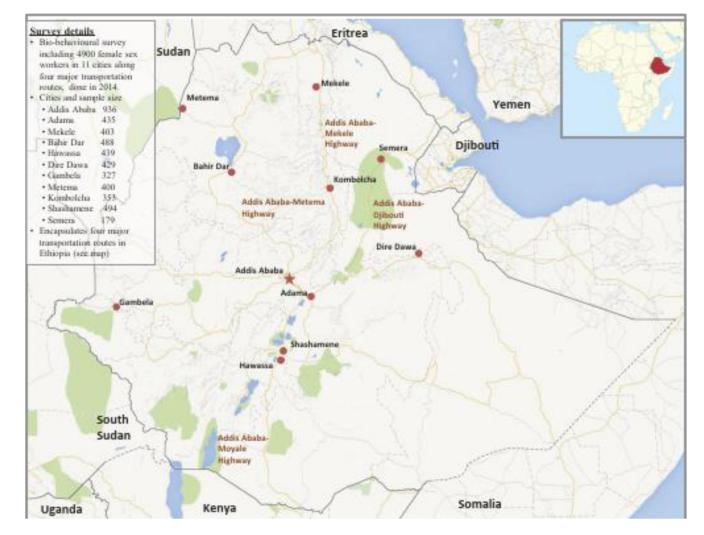
J Acquir Immune Defic Syndr. Jun 1 2017;75(2):e45–e54. doi:10.1097/qai.00000000001285 [PubMed: 28129253]

- Van Blerk L AIDS, mobility and commercial sex in Ethiopia: Implications for policy. AIDS Care. Jan 2007;19(1):79–86. doi:10.1080/09540120600805091 [PubMed: 17129861]
- Hatcher AM, Smout EM, Turan JM, Christofides N, Stockl H. Intimate partner violence and engagement in HIV care and treatment among women: a systematic review and meta-analysis. Aids. Oct 23 2015;29(16):2183–94. doi:10.1097/qad.00000000000842 [PubMed: 26353027]
- Amogne MD, Balcha TT, Agardh A. Prevalence and correlates of physical violence and rape among female sex workers in Ethiopia: a cross-sectional study with respondent-driven sampling from 11 major towns. BMJ Open. Jul 30 2019;9(7):e028247. doi:10.1136/bmjopen-2018-028247
- Decker MR, Wirtz AL, Pretorius C, et al. Estimating the impact of reducing violence against female sex workers on HIV epidemics in Kenya and Ukraine: a policy modeling exercise. Am J Reprod Immunol. Feb 2013;69 Suppl 1:122–32. doi:10.1111/aji.12063 [PubMed: 23387931]
- WHO. World Health Organization Global Strategy for the Surveillance and Monitoring of HIV Drug Resistance WHO press: Geneva, Switzerland. 2012;
- Rosemary A, Chika O, Jonathan O, et al. Genotyping performance evaluation of commercially available HIV-1 drug resistance test. PLoS One. 2018;13(6):e0198246. doi:10.1371/ journal.pone.0198246 [PubMed: 29953436]
- Woods CK, Brumme CJ, Liu TF, et al. Automating HIV drug resistance genotyping with RECall, a freely accessible sequence analysis tool. J Clin Microbiol. Jun 2012;50(6):1936–42. doi:10.1128/ jcm.06689-11 [PubMed: 22403431]
- Bennett DE, Myatt M, Bertagnolio S, Sutherland D, Gilks CF. Recommendations for surveillance of transmitted HIV drug resistance in countries scaling up antiretroviral treatment. Antivir Ther. 2008;13 Suppl 2:25–36. [PubMed: 18575189]
- Liu TF, Shafer RW. Web resources for HIV type 1 genotypic-resistance test interpretation. Clin Infect Dis. Jun 1 2006;42(11):1608–18. doi:10.1086/503914 [PubMed: 16652319]
- 23. Kassu A, Fujino M, Matsuda M, Nishizawa M, Ota F, Sugiura W. Molecular epidemiology of HIV type 1 in treatment-naive patients in north Ethiopia. AIDS Res Hum Retroviruses. Apr 2007;23(4):564–8. doi:10.1089/aid.2006.0270 [PubMed: 17451346]
- Mulu A, Lange T, Liebert UG, Maier M. Clade homogeneity and Pol gene polymorphisms in chronically HIV-1 infected antiretroviral treatment naive patients after the roll out of ART in Ethiopia. BMC Infect Dis. Mar 22 2014;14:158. doi:10.1186/1471-2334-14-158 [PubMed: 24655349]
- Huruy K, Maier M, Mulu A, Liebert UG. Limited increase in primary HIV-1C drug resistance mutations in treatment naive individuals in Ethiopia. Journal of medical virology. Jun 2015;87(6):978–84. doi:10.1002/jmv.24110 [PubMed: 25649964]
- 26. Abdissa A, Yilma D, Fonager J, et al. Drug resistance in HIV patients with virological failure or slow virological response to antiretroviral therapy in Ethiopia. BMC Infect Dis. Apr 4 2014;14:181. doi:10.1186/1471-2334-14-181 [PubMed: 24708645]
- 27. Telele NF, Kalu AW, Gebre-Selassie S, et al. Pretreatment drug resistance in a large countrywide Ethiopian HIV-1C cohort: a comparison of Sanger and high-throughput sequencing. Scientific reports. May 15 2018;8(1):7556. doi:10.1038/s41598-018-25888-6 [PubMed: 29765082]
- 28. Namale G, Kamacooko O, Bagiire D, et al. Sustained virological response and drug resistance among female sex workers living with HIV on antiretroviral therapy in Kampala, Uganda: a crosssectional study. Sex Transm Infect. Sep 2019;95(6):405–411. doi:10.1136/sextrans-2018-053854 [PubMed: 31266818]
- Chen I, Connor MB, Clarke W, et al. Antiretroviral Drug Use and HIV Drug Resistance Among HIV-Infected Black Men Who Have Sex With Men: HIV Prevention Trials Network 061. J Acquir Immune Defic Syndr. Aug 1 2015;69(4):446–52. doi:10.1097/qai.000000000000633 [PubMed: 25861015]
- Coetzee J, Hunt G, Jaffer M, et al. HIV-1 viraemia and drug resistance amongst female sex workers in Soweto, South Africa: A cross sectional study. PLoS One. 2017;12(12):e0188606. doi:10.1371/ journal.pone.0188606 [PubMed: 29244809]

- 31. da Costa LM, Frade PCR, Blandtt LDS, et al. HIV-1 Genetic Diversity and Transmitted Drug Resistance Mutations in Female Sex Workers from a Brazilian Municipality in the Amazon Region. AIDS Res Hum Retroviruses. Feb 2020;36(2):99–100. doi:10.1089/AID.2019.0243 [PubMed: 31724429]
- 32. Diallo M, Behanzin L, Guedou FA, et al. HIV treatment response among female sex workers participating in a treatment as prevention demonstration project in Cotonou, Benin. PLoS One. 2020;15(1):e0227184. doi:10.1371/journal.pone.0227184 [PubMed: 31971957]
- Carobene M, Bolcic F, Farias MS, Quarleri J, Avila MM. HIV, HBV, and HCV molecular epidemiology among trans (transvestites, transsexuals, and transgender) sex workers in Argentina. Journal of medical virology. Jan 2014;86(1):64–70. doi:10.1002/jmv.23805 [PubMed: 24123155]
- 34. Sampathkumar R, Shadabi E, La D, et al. Naturally occurring protease inhibitor resistance mutations and their frequencies in HIV proviral sequences of drug-naïve sex workers in Nairobi, Kenya. Retrovirology. 2014/01/07 2014;11(1):P133. doi:10.1186/1742-4690-11-S1-P133
- Weinstock HS, Zaidi I, Heneine W, et al. The epidemiology of antiretroviral drug resistance among drug-naive HIV-1-infected persons in 10 US cities. J Infect Dis. Jun 15 2004;189(12):2174–80. doi:10.1086/420789 [PubMed: 15181563]
- WHO. Guidelines on the public health response to pretreatment HIV drug resistance. Geneva, Switzerland. 2017:http://apps.who.int/iris/bitstream/10665/255880/1/9789241550055-eng.pdf.
- Chimukangara B, Lessells RJ, Rhee SY, et al. Trends in Pretreatment HIV-1 Drug Resistance in Antiretroviral Therapy-naive Adults in South Africa, 2000–2016: A Pooled Sequence Analysis. EClinicalMedicine. Mar 2019;9:26–34. doi:10.1016/j.eclinm.2019.03.006 [PubMed: 31143879]
- Rhee SY, Blanco JL, Jordan MR, et al. Geographic and temporal trends in the molecular epidemiology and genetic mechanisms of transmitted HIV-1 drug resistance: an individualpatient- and sequence-level meta-analysis. PLoS Med. Apr 2015;12(4):e1001810. doi:10.1371/ journal.pmed.1001810 [PubMed: 25849352]
- Clutter DS, Jordan MR, Bertagnolio S, Shafer RW. HIV-1 drug resistance and resistance testing. Infection, genetics and evolution : journal of molecular epidemiology and evolutionary genetics in infectious diseases. Dec 2016;46:292–307. doi:10.1016/j.meegid.2016.08.031
- Castro H, Pillay D, Cane P, et al. Persistence of HIV-1 transmitted drug resistance mutations. The Journal of infectious diseases. Nov 01 2013;208(9):1459–63. doi:10.1093/infdis/jit345 [PubMed: 23904291]
- 41. Kuhnert D, Kouyos R, Shirreff G, et al. Quantifying the fitness cost of HIV-1 drug resistance mutations through phylodynamics. PLoS Pathog. Feb 2018;14(2):e1006895. doi:10.1371/ journal.ppat.1006895 [PubMed: 29462208]
- Castro H, Pillay D, Cane P, et al. Persistence of HIV-1 transmitted drug resistance mutations. J Infect Dis. Nov 1 2013;208(9):1459–63. doi:10.1093/infdis/jit345 [PubMed: 23904291]
- Wertheim JO, Oster AM, Johnson JA, et al. Transmission fitness of drug-resistant HIV revealed in a surveillance system transmission network. Virus Evol. Jan 2017;3(1):vex008. doi:10.1093/ve/ vex008 [PubMed: 28458918]
- 44. Lancaster KE, Cernigliaro D, Zulliger R, Fleming PF. HIV care and treatment experiences among female sex workers living with HIV in sub-Saharan Africa: A systematic review. Afr J AIDS Res. Dec 2016;15(4):377–386. doi:10.2989/16085906.2016.1255652 [PubMed: 27974017]
- 45. Mountain E, Mishra S, Vickerman P, Pickles M, Gilks C, Boily MC. Antiretroviral therapy uptake, attrition, adherence and outcomes among HIV-infected female sex workers: a systematic review and meta-analysis. PLoS One. 2014;9(9):e105645. doi:10.1371/journal.pone.0105645 [PubMed: 25265158]
- 46. Holland CE, Papworth E, Billong SC, et al. Antiretroviral treatment coverage for men who have sex with men and female sex workers living with HIV in Cameroon. J Acquir Immune Defic Syndr. Mar 1 2015;68 Suppl 2:S232–40. doi:10.1097/qai.00000000000443 [PubMed: 25723989]
- Cowan FM, Mtetwa S, Davey C, et al. Engagement with HIV prevention treatment and care among female sex workers in Zimbabwe: a respondent driven sampling survey. PLoS One. 2013;8(10):e77080. doi:10.1371/journal.pone.0077080 [PubMed: 24143203]

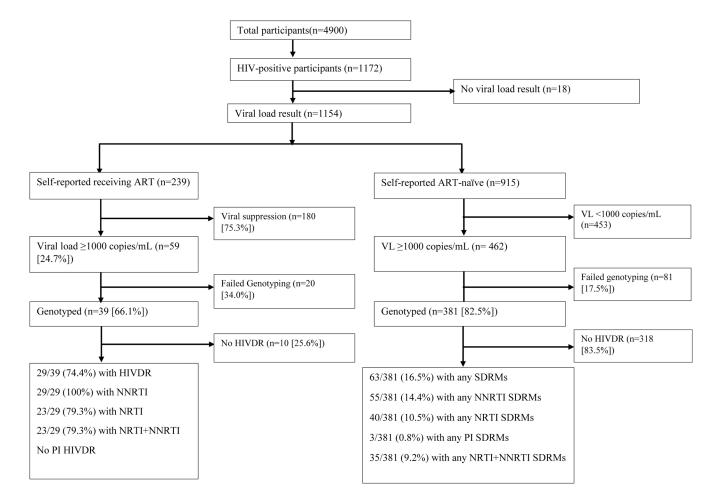
- 48. Huerga H, Shiferie F, Grebe E, et al. A comparison of self-report and antiretroviral detection to inform estimates of antiretroviral therapy coverage, viral load suppression and HIV incidence in Kwazulu-Natal, South Africa. BMC Infect Dis. Sep 29 2017;17(1):653. doi:10.1186/ s12879-017-2740-y [PubMed: 28969607]
- Fogel JM, Wang L, Parsons TL, et al. Undisclosed antiretroviral drug use in a multinational clinical trial (HIV Prevention Trials Network 052). J Infect Dis. Nov 15 2013;208(10):1624–8. doi:10.1093/infdis/jit390 [PubMed: 23908493]
- 50. Moyo S, Gaseitsiwe S, Powis KM, et al. Undisclosed antiretroviral drug use in Botswana: implication for national estimates. AIDS. Jul 17 2018;32(11):1543–1546. doi:10.1097/ QAD.000000000001862 [PubMed: 29762166]
- 51. Kim AA, Mukui I, Young PW, et al. Undisclosed HIV infection and antiretroviral therapy use in the Kenya AIDS indicator survey 2012: relevance to national targets for HIV diagnosis and treatment. Aids. Nov 13 2016;30(17):2685–2695. doi:10.1097/qad.000000000001227 [PubMed: 27782965]
- 52. PSI. Community HIV Care and Treatment for Female Sex Workers in Ethiopia: Successful Servic Provision through Drop- in Centers (THPEE774), 2016 https://www.psi.org/publication/community-hiv-care-and-treatment-for-female-sex-workersin-ethiopia-successful-service-provision-through-drop-in-centers-thpee774 Assessed October 2020.
- Mountain E, Pickles M, Mishra S, Vickerman P, Alary M, Boily MC. The HIV care cascade and antiretroviral therapy in female sex workers: implications for HIV prevention. Expert Rev Anti Infect Ther. Oct 2014;12(10):1203–19. doi:10.1586/14787210.2014.948422 [PubMed: 25174997]
- 54. Cowan FM, Davey CB, Fearon E, et al. The HIV Care Cascade Among Female Sex Workers in Zimbabwe: Results of a Population-Based Survey From the Sisters Antiretroviral Therapy Programme for Prevention of HIV, an Integrated Response (SAPPH-IRe) Trial. J Acquir Immune Defic Syndr. Apr 1 2017;74(4):375–382. doi:10.1097/qai.00000000001255 [PubMed: 27930599]
- 55. Lancaster KE, Powers KA, Lungu T, et al. The HIV Care Continuum among Female Sex Workers: A Key Population in Lilongwe, Malawi. PLoS One. 2016;11(1):e0147662. doi:10.1371/ journal.pone.0147662 [PubMed: 26808043]
- 56. Lindman J, Djalo MA, Biai A, et al. The HIV care continuum and HIV-1 drug resistance among female sex workers: a key population in Guinea-Bissau. AIDS Res Ther. Jun 12 2020;17(1):33. doi:10.1186/s12981-020-00290-3 [PubMed: 32532294]
- 57. Delva W, Eaton JW, Meng F, et al. HIV treatment as prevention: optimising the impact of expanded HIV treatment programmes. PLoS Med. 2012;9(7):e1001258. doi:10.1371/journal.pmed.1001258 [PubMed: 22802738]
- Alary M, Lowndes CM, Van de Perre P, et al. Scale-up of combination prevention and antiretroviral therapy for female sex workers in West Africa: time for action. AIDS. 2013;27(9):1369–1374. doi:10.1097/QAD.0b013e32835fd7bd [PubMed: 23945501]
- Moses S, Ramesh BM, Nagelkerke NJ, et al. Impact of an intensive HIV prevention programme for female sex workers on HIV prevalence among antenatal clinic attenders in Karnataka state, south India: an ecological analysis. Aids. Dec 2008;22 Suppl 5:S101–8. doi:10.1097/01.aids.0000343768.85325.92 [PubMed: 19098470]
- 60. MOH E. National guideline for comprehensive HIV prevention, care, and treatment 2017;
- Etta EM, Mavhandu L, Manhaeve C, et al. High level of HIV-1 drug resistance mutations in patients with unsuppressed viral loads in rural northern South Africa. AIDS Res Ther. Jul 27 2017;14(1):36. doi:10.1186/s12981-017-0161-z [PubMed: 28750647]
- 62. Gupta RK, Hill A, Sawyer AW, et al. Virological monitoring and resistance to first-line highly active antiretroviral therapy in adults infected with HIV-1 treated under WHO guidelines: a systematic review and meta-analysis. Lancet Infect Dis. Jul 2009;9(7):409–17. doi:10.1016/s1473-3099(09)70136-7 [PubMed: 19555900]
- 63. Kwon EH, Musema GMA, Boelter J, et al. HIV-1 subtypes and drug resistance mutations among female sex workers varied in different cities and regions of the Democratic Republic of Congo. PLoS One. 2020;15(2):e0228670. doi:10.1371/journal.pone.0228670 [PubMed: 32045455]

- 64. Barth RE, van der Loeff MF, Schuurman R, Hoepelman AI, Wensing AM. Virological follow-up of adult patients in antiretroviral treatment programmes in sub-Saharan Africa: a systematic review. Lancet Infect Dis. Mar 2010;10(3):155–66. doi:10.1016/s1473-3099(09)70328-7 [PubMed: 20185094]
- 65. Feleke R, Geda B, Teji Roba K, Weldegebreal F. Magnitude of antiretroviral treatment failure and associated factors among adult HIV-positive patients in Harar public hospitals, Eastern Ethiopia. SAGE Open Med. 2020;8:2050312120906076. doi:10.1177/2050312120906076
- 66. Gupta J, Raj A, Decker MR, Reed E, Silverman JG. HIV vulnerabilities of sex-trafficked Indian women and girls. Int J Gynaecol Obstet. Oct 2009;107(1):30–4. doi:10.1016/j.ijgo.2009.06.009 [PubMed: 19625022]
- 67. Kahle EM, Kashuba A, Baeten JM, et al. Unreported antiretroviral use by HIV-1-infected participants enrolling in a prospective research study. J Acquir Immune Defic Syndr. Feb 1 2014;65(2):e90–4. doi:10.1097/QAI.0b013e3182a2db02 [PubMed: 24442233]
- von Braun A, Sekaggya-Wiltshire C, Bachmann N, et al. HIV-1 Drug Resistance Among Ugandan Adults Attending an Urban Out-Patient Clinic. J Acquir Immune Defic Syndr. Aug 15 2018;78(5):566–573. doi:10.1097/QAI.000000000001717 [PubMed: 29771783]



#### Figure 1.

Map of the cities in Ethiopia included in the 2014 study of HIV drug resistance among female sex workers. Details of the study are shown in the box. This figure was modified from Google Maps (https://www.google.com/maps/place/Ethiopia).



#### Figure 2.

Flow chart of selection of female sex workers who participated in a biobehavioural survey and genotypic analysis of drug-resistant HIV in Ethiopia (2014)

#### Table 1.

Frequency of pre-treatment drug-resistance mutations detected among female sex workers (n=63) in Ethiopia (2014)

NNRTI SDRMs	N (%) <sup>1</sup>	NRTI SDRMs	N (%) <sup>1</sup>	PI SDRMs	N (%) <sup>1</sup>
K103N/S	30 (47.6)	M184V/I	37 (58.7)	L23I	1 (1.6)
Y181C	17 (27.0)	K65R	10 (15.9)	M46I	1 (1.6)
G190A/E/S	14 (22.2)	T215F/Y	8 (12.7)	185V	1 (1.6)
K101E/P	8 (12.7)	Y115F	3 (4.8)		
V106M	8 (12.7)	L210W	3 (4.8)		
Y188H	3 (4.8)	M41L	2 (3.2)		
M230L	3 (4.8)	K70R	2 (3.2)		
L100I	1 (1.6)	L74V/I	2 (3.2)		
V179F	1 (1.6)	D67N	1 (1.6)		
Р225Н	1 (1.6)	T69D	1 (1.6)		
		K219R/Q	1 (1.6)		

Abbreviations: SDRM, surveillance drug-resistance mutation included in the WHO 2009 SDRM list; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitors

 $^{I}$ To calculate the percentages of each SDRM, we used 63 as the denominator, corresponding to the number of specimens with a PDR in the study.

#### Table 2.

Type and frequency of acquired drug resistance mutations detected among female sex workers with viral load non-suppression (n=29) in Ethiopia (2014)

NNRTI DRMs	N (%)	NRTI DRMs	N (%)
K103N/s	18 (62.1)	M184IV	20 (69.0)
Y181C	10 (34.5)	K65R	6 (20.7)
G190A/E/S	7 (24.1)	K70R/E	6 (20.7)
H221HY	6 (20.7)	T215F/Y	5 (17.2)
A98G	5 (17.2)	K219Q	4 (13.8)
K101E/P	5 (17.2)	A62V	3 (10.3)
V106M	4 (13.8)	Y115F	3 (10.3)
V108I	4 (13.8)	D67N	2 (6.9)
L100I	3 (10.3)	M41L	1 (3.4)
E138A	2 (6.9)	L74V/I	1 (3.4)
V179D	2 (6.9)		
P225H	2 (6.9)		
F227FL	1 (3.4)		
M230L	1 (3.4)		
K238T	1 (3.4)		

Abbreviations: NNRTI; non-nucleoside reverse transcriptase inhibitor; NRTI; nucleoside reverse transcriptase inhibitor; DRM, drug resistance mutation

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Table 3.

Bivariate and multivariate analyses for factors associated with virologic failure and HIV drug resistance among female sex workers in Ethiopia (2014)

Arimide et al.

	VLN			PDR			ADR		
	z	OR (95% CI)	aOR (95% CI)	z	OR (95% CI)	aOR (95% CI)	z	OR (95% CI)	aOR (95% CI)
Age, years									
18–24	30	Ref		163	Ref		128	ref	
25–34	139	2.36 (0.77–7.21)	3.02 (0.83–11.06)	175	1.57 (0.87–2.85) ¥	1.47 (0.74–2.92)	392	1.78 (0.51–6.18)	
35	70	2.25 (0.69–7.33) ¥	$4.09\ (1.04 - 16.1)^{*}$	42	$1.84 (0.77 - 4.39)^{rac{4}{2}}$	1.69 (0.65–4.41)	141	3.2 (0.86–11.83)	
Income (monthly; currency in USD)									
<\$100)	169	Ref		230	Ref		432	ref	
\$100	70	1.20 (0.64–2.27)		149	1.19 (0.69–2.06)		229	0.53 (0.19–1.46)	
Level of education									
No education	89	Ref		128	Ref		241	ref	
Primary 1st cycle (grade 1–4)	32	0.68 (0.23–2.01)		63	0.49 (0.20–1.20)		66	0.24 (0.03–1.92)	
Primary 2nd cycle (grade 5-8)	96	1.37 (0.70–2.70)		139	0.70 (0.37–1.32)		250	1.36 (0.59–3.18)	
Secondary and above	22	2.55 (0.95–6.86)		50	$0.86\ (0.37{-}1.20)$		71	0.98 (0.19-4.94)	
Ever given birth									
No	52	Ref		130	Ref		194	ref	
Yes	187	1.12 (0.54–2.31)		250	$2.02 \ (1.07 - 3.82)^{*}$	1.56 (0.76–3.20)	467	1.37 (0.49–3.83)	
Number sexual partners /month									
4-10	114	ref		164	Ref		267	ref	
11	125	$1.76(0.96–3.21)^{ mu}$	1.82 (0.89, 3.73)	216	1.02 (0.59–1.75)		394	$1.99 (0.88 - 4.51)^{rac{F}{2}}$	1.85 (0.71–4.83)
Sex selling venue									
Street	23	Ref		89	Ref		152	ref	
Local drinking houses	86	1.26 (0.38–4.16)		83	1.74 (0.80–3.79)		196	0.93 (0.23–3.73)	
Spa/massage/beauty salon/own house	31	1.39 (0.35–5.44)		23	1.23 (0.36-4.20)		56	0.79 (0.14-4.38)	
Red light houses	33	1.52 (0.40–5.81)		33	1.30 (0.45–3.76)		78	1.01 (0.20-5.08)	
Bar/hotel	49	1.90 (0.55–6.59)		136	1.01 (0.47–2.15)		140	1.09 (0.24-4.84)	
Other	17	4.22 (1.00–17.80)		16	0.39 (0.05–3.21)		39	2.11 (0.35–12.59)	

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N         OR (95% CI)         aOR (95% CI)           Heavy episodic drinking in the past month $1.62 (.052 + .05)$ $aOR (.95% CI)$ No         72         Ref $1.62 (.052 + .26)$ Yes         32 $1.62 (0.62 - 4.26)$ $1.62 (.052 + .26)$ Frequency of khat chewing per week $1.68 Ref$ $1.62 (.0.62 - 4.26)$ Never $1.68 Ref$ $1.61 (.0.43 - 3.17)$ Less than once $2.3 1.17 (.0.433.17)$ $1.17 (.0.433.17)$ Less than once $2.3 1.17 (.0.433.17)$ $1.12 days$ Jest than once $2.3 1.05 (.0.153.22)$ $1.46 (.0.663.22)$ On ope to the past 12 months $1.46 (.0.663.22)$ $1.46 (.0.663.22)$ No $2.09 Ref$ $1.13 (.0.47 - 2.69)$ $1.13 (.0.47 - 2.69)$ Mo $1.13 (.0.47 - 2.69)$ $1.13 (.0.47 - 2.69)$	95% CJ) N 172 172 168 168 51 40 24 97 313	OR (95% CI) aO Ref Ref 0.60 (0.29–1.23) 0.60 (0.29–1.23) 0.40 (0.15–1.08) 0.40 (0.15–1.08) 0.30 (0.09–1.02) 0.52 (0.15–1.86) 0.52 (0.15–1.86) 0.72 (0.38–1.39) 0.72 (0.38–1.39) 0.74 (0.35–1.59)	aOR (95% CI)	N         OR (95% CI)           260         ref           261         ref           347         ref           77         1.08 (0.29-4.02)           349         1.76 (0.34-9.03)           30         0           33         0           36         0.74 (0.20-2.66)           158         0.74 (0.20-2.66)           16         0.52 (0.19-2.39)	aOR (95% CI)
sodic drinking in the past month       72       Ref         72       Ref         73       1.62 (0.62-4.26)         74       Ref         75       1.62 (0.62-4.26)         76       Ref         77       1.62 (0.62-4.26)         78       Ref         79       1.62 (0.62-4.26)         70       0.95 (0.19-4.74)         70       0.95 (0.19-4.74)         71       1.65 (0.15-8.73)         72       1.65 (0.15-8.73)         73       1.65 (0.15-8.73)         74       1.65 (0.15-8.73)         75       1.66 (0.66-3.22)         75       1.66 (0.66-3.22)         76       1.13 (0.47-2.69)         77       1.13 (0.47-2.69)         76       1.13 (0.47-2.69)         76       1.13 (0.47-2.69)         77       1.13 (0.47-2.69)         76       1.13 (0.47-2.69)         77       1.13 (0.47-2.69)         78       1.13 (0.47-2.69)	172 103 168 51 40 24 97 97 813	Ref 0.60 (0.29–1.23) Ref 0.40 (0.15–1.08) 0.30 (0.09–1.02) 0.52 (0.15–1.86) 0.52 (0.15–1.86) 0.72 (0.38–1.39) 0.72 (0.38–1.39) Ref Ref			
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32 $1.62 (0.62 - 4.26)$ of khat chewing per week $1.62 (0.62 - 4.26)$ $1.68$ Ref $1.68$ Ref $1.68$ Ref $1.68$ $1.17 (0.43 - 3.17)$ $1.61 - 4.74$ $1.17 (0.43 - 3.17)$ $1.61 - 6.62$ $1.17 (0.43 - 3.17)$ $1.61 - 6.62$ $1.17 (0.43 - 3.17)$ $1.61 - 6.62$ $1.61 (0.66 - 3.22)$ $1.61 - 6.62$ $1.61 (0.66 - 3.22)$ $1.61 - 6.62$ $1.61 (0.66 - 3.22)$ $1.61 - 6.62$ $1.13 (0.47 - 2.69)$ $1.13 - 6.91$ $1.13 (0.47 - 2.69)$ $1.13 - 6.91$ $1.13 (0.47 - 2.69)$ $1.13 - 6.91$ $1.13 (0.47 - 2.69)$ $1.13 - 6.91$ $1.13 (0.47 - 2.69)$ $1.13 - 6.91$ $1.13 - 6.99$ $1.13 - 6.91$ $1.13 - 6.99$ $1.13 - 6.90$ $1.11 - 6.99$	103 168 51 40 24 97 97 813	0.60 (0.29–1.23) Ref 0.40 (0.15–1.08) 0.30 (0.09–1.02) 0.52 (0.15–1.86) 0.52 (0.15–1.86) 0.72 (0.38–1.39) 0.72 (0.38–1.39) Ref Ref			
of khat chewing per week       168       Ref         168       Ref         0nce       23       1.17 (0.43–3.17)         0nce       23       1.17 (0.43–3.17)         0nce       23       1.65 (0.19–4.74)         17       3       1.65 (0.15–8.73)         17       3       1.65 (0.15–8.73)         17       3       1.66 (0.66–3.22)         17       36       1.46 (0.66–3.22)         17       36       1.46 (0.66–3.22)         17       36       1.46 (0.66–3.22)         17       209       Ref         18       30       1.13 (0.47–2.69)         19       113 (0.47–2.69)       30         10       113 (0.47–2.69)       30         10       113 (0.47–2.69)       30         10       113 (0.47–2.69)       30         10       113 (0.47–2.69)       30         11       113 (0.47–2.69)       30         11       113 (0.47–2.69)       30         11       113 (0.47–2.69)       30         11       113 (0.47–2.69)       30	168 51 40 24 97 313	Ref 0.40 (0.15–1.08) 0.30 (0.09–1.02) 0.52 (0.15–1.86) 0.72 (0.38–1.39) 0.74 (0.35–1.59) 0.74 (0.35–1.59)			
168Refonce23 $1.17 (0.43-3.17)$ once23 $1.17 (0.43-3.17)$ $9$ $0.95 (0.19-4.74)$ $3$ $1.65 (0.15-8.73)$ $3$ $1.65 (0.15-8.73)$ $3$ $1.65 (0.15-8.73)$ $3$ $1.66 (0.66-3.22)$ $20$ $1.46 (0.66-3.22)$ $20$ $1.46 (0.66-3.22)$ $20$ $1.13 (0.47-2.69)$ $20$ $1.13 (0.47-2.69)$ $0$ selling sex $213$ $213$ $Ref$ $213$ $Ref$	168 51 40 24 97 97 813	Ref 0.40 (0.15–1.08) 0.30 (0.09–1.02) 0.52 (0.15–1.86) 0.72 (0.38–1.39) 0.72 (0.38–1.39) Ref Ref			
once         23         1.17 (0.43-3.17)           9         0.95 (0.19-4.74)           3         1.65 (0.15-8.73)           3         1.65 (0.15-8.73)           3         1.65 (0.15-8.73)           3         1.65 (0.15-8.73)           3         1.65 (0.15-8.73)           3         1.65 (0.15-8.73)           3         1.65 (0.15-8.73)           3         1.46 (0.66-3.22)           9         8           9         1.46 (0.66-3.22)           9         8           9         1.46 (0.66-3.22)           9         8           9         8           9         1.46 (0.66-3.22)           9         8           9         1.13 (0.47-2.69)           9         1.13 (0.47-2.69)           9         8           9         1.13 (0.47-2.69)           9         8           9         1.13 (0.47-2.69)           9         8           9         8           9         1.13 (0.47-2.69)	51 40 24 97 313 67	0.40 (0.15–1.08) 0.30 (0.09–1.02) 0.52 (0.15–1.86) 0.72 (0.38–1.39) Ref Ref 0.74 (0.35–1.59)			
9     0.95 (0.19-4.74)       3     1.65 (0.15-8.73)       3     1.65 (0.15-8.73)       36     1.46 (0.66-3.22)       4     1.46 (0.66-3.22)       5     1.46 (0.66-3.22)       5     1.46 (0.66-3.22)       5     1.46 (0.66-3.22)       5     1.46 (0.66-3.22)       6     1.46 (0.66-3.22)       7     209     Ref       9     Ref       9     1.13 (0.47-2.69)       9     1.13 (0.47-2.69)       9     Selling sex       10     1.13 (0.47-2.69)       11     1.13 (0.47-2.69)	40 24 97 313 67	0.30 (0.09–1.02) 0.52 (0.15–1.86) 0.72 (0.38–1.39) Ref Ref 0.74 (0.35–1.59)			
days       3 $1.65 (0.15-8.73)$ days       36 $1.65 (0.15-8.73)$ days       36 $1.46 (0.66-3.22)$ sically beaten in the past 12 months       2 $209$ sically beaten in the past 12 months       2 $209$ days       209       Ref         and the past 12 months       30 $1.13 (0.47-2.69)$ ed into selling sex       2 $213 (0.47-2.69)$ ed into selling sex       2 $213 (0.47-2.69)$ ed into selling sex       2 $213 (0.47-2.69)$	24 97 313 67	0.52 (0.15–1.86) 0.72 (0.38–1.39) Ref 0.74 (0.35–1.59)			
days       36 $1.46 (0.66-3.22)$ dialy beaten in the past 12 months $209$ Ref $209$ Ref $1.13 (0.47-2.69)$ ed into selling sex $213$ Ref $213$ Ref $213$ $213$ Ref $213$	97 313 67	0.72 (0.38–1.39) Ref 0.74 (0.35–1.59)			
sically beaten in the past 12 months 209 Ref 209 Ref 30 1.13 (0.47–2.69) ed into selling sex 213 Ref 2	313 67	Ref 0.74 (0.35–1.59)		6	
209     Ref       30     1.13 (0.47-2.69)       ed into selling sex     213       213     Ref       26     3.03 (1.31-6.99)*	313 67	Ref 0.74 (0.35–1.59)		6	
30 1.13 (0.47–2.69) ed into selling sex 213 Ref 26 3.03 (1.31–6.99)*	67	0.74 (0.35–1.59)			
ed into selling sex 213 Ref 26 3.03 (1.31–6.99)*					
213 Ref 26 3.03 (1.31–6.99)*					
26 3.03 (1.31–6.99)*	326	Ref		581 ref	
	2.79 (1.07–7.27)* 54	0.59 (0.24–1.44)		80 3.77 (1.37–10.36)*	6)* 3.21 (0.99–10.38)
Unusual vaginal discharge in the past 12 months					
No 194 Ref	311	Ref		583 ref	
Yes 45 1.14 (0.54–2.38)	69	1.36 (0.70–2.64)		78 0.71 (0.23–2.19)	(
Genital ulcer in the past 12 months					
No 215 Ref	335	Ref		260 ref	
Yes 24 1.02 (0.38–2.70)	45	1.30 (0.59–2.86)		158 0.32 (0.04–2.51)	
CD4 count (cell/mm <sup>3</sup> )					
Lower (<350) 48 4.19 (2.11–8.32)* 4.67 (2.23	4.67 (2.23–9.77)* 129	3.44 (1.90–6.23) <sup>*</sup> 3.2	3.24 (1.78–5.89)*	124 6.51(2.77–15.32)*	2)* 7.25 (2.95–17.83)*
Higher ( 350) 172 Ref	215	Ref		491 ref	

 ${}^{*}_{{
m P}}$  0.05;  ${}^{*}_{{
m P}}$  < 0.2;

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