
Article:
Namale, Gertrude, Kamacooko, Onesmus, Bagiire, Daniel et al. (12 more authors) (2019) Sustained virological response and drug resistance among female sex workers living with HIV on antiretroviral therapy in Kampala, Uganda:a cross-sectional study. Sexually Transmitted Infections. pp. 405-411. ISSN 1368-4973

https://doi.org/10.1136/sextrans-2018-053854

OPEN ACCESS

ORIGINAL ARTICLE

Sustained virological response and drug resistance among female sex workers living with HIV on antiretroviral therapy in Kampala, Uganda: a cross-sectional study

Gertrude Namale,[1] Onesmus Kamacooko,[1] Daniel Bagiire,[1] Yunia Mayanja,[1] Andrew Abaasa,[1] William Kilembe,[2] Matt Price,[3,4] Deogratius Ssemwanga,[1] Sandra Lunkuse,[1] Maria Nanyonjo,[1] William Ssenyonga,[1] Philippe Mayaud,[1,5] Rob Newton,[1,6] Pontiano Kaleebu,[1] Janet Seeley[1,5]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/sextrans-2018-053854).

[1]MRC/UVRI and LSHTM Uganda Research Unit, Kampala, Uganda
[2]Rwanda Zambia HIV Research Group, Emory University, Lusaka, Zambia
[3]Medical Affairs, International AIDS Vaccine Initiative, New York City, New York, USA
[4]University of California, San Francisco, California, USA
[5]London School of Hygiene and Tropical Medicine, London, UK
[6]University of York, York, UK

Correspondence to
Dr Gertrude Namale, MRC/UVRI and LSHTM Uganda Research Unit, Kampala 256, Uganda; gertrude.namale@mrcuganda.org

Received 11 October 2018
Revised 27 March 2019
Accepted 10 April 2019

Check for updates

To cite: Namale G, Kamacooko O, Bagiire D, *et al*. *Sex Transm Infect* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/sextrans-2018-053854

ABSTRACT

Objectives We assessed the prevalence and risk factors associated with virological failure among female sex workers living with HIV on antiretroviral therapy (ART) in Kampala, Uganda.

Methods We conducted a cross-sectional study between January 2015 and December 2016 using routinely collected data at a research clinic providing services to women at high risk of STIs including HIV. Plasma samples were tested for viral load from HIV-seropositive women aged ≥18 years who had been on ART for at least 6 months and had received adherence counselling. Samples from women with virological failure (≥1000 copies/mL) were tested for HIV drug resistance by population-based sequencing. We used logistic regression to identify factors associated with virological failure.

Results Of 584 women, 432 (74%) with a mean age of 32 (SD 6.5) were assessed, and 38 (9%) were found to have virological failure. HIV resistance testing was available for 78% (28/38), of whom 82.1% (23/28) had at least one major drug resistance mutation (DRM), most frequently M184V (70%, 16/23) and K103N (65%, 15/23). In multivariable analysis, virological failure was associated with participant age 18–24 (adjusted OR (aOR)=5.3, 95% CI 1.6 to 17.9), self-reported ART non-adherence (aOR=2.6, 95% CI 1.2 to 5.8) and baseline CD4+ T-cell count ≤350 cells/mm^3 (aOR=3.1, 95% CI 1.4 to 7.0).

Conclusions A relatively low prevalence of virological failure but high rate of DRM was found in this population at high risk of transmission. Younger age, self-reported ART non-adherence and low CD4+ T-cell count on ART initiation were associated with increased risk of virological failure.

INTRODUCTION

With the new focus of ending the AIDS epidemic by 2030 and the declaration of the United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 targets, virological suppression is now a global public health priority.[1] In 2017, only 52% of adults in sub-Saharan Africa (SSA) who were living with HIV and on antiretroviral therapy (ART) had achieved virological suppression.[2] High HIV prevalence in SSA particularly among key populations including female sex workers (FSWs) poses a major challenge to achieving the targets.[3] The critical factors for improving health outcomes of people living with HIV and stopping onward transmission are early ART initiation accompanied by sustained virological suppression.[4] In Uganda, the HIV prevalence among FSWs ranges between 33% and 37% compared with 9.5% among the general female population.[5–7]

Reports show that an estimated 16% of new infections in Uganda may be attributed to FSWs and their clients.[8] Due to various social issues, stigma and discrimination, and criminalisation of sex work, FSWs are usually hard to reach, creating challenges in providing appropriate HIV care services, including early HIV testing, ART initiation, adherence support and HIV plasma viral load (VL) monitoring.[9] Very good adherence to medication is required to prevent the development of antiretroviral drug resistance, an important goal in preserving the benefits of ART at the individual and population level.[10]

Previous research has shown that HIV drug resistance poses a threat to future ART success, particularly in countries where documented HIV prevalence in key populations is high.[7] In South Africa, 73.7% of FSWs and in Rwanda 77.1% of FSWs with virological failure had at least one major drug resistance mutation (DRM) to either nucleoside reverse transcriptase inhibitors (NRTIs) or non-nucleoside reverse transcriptase inhibitors (NNRTIs). The lamivudine (3TC, an NRTI drug) mutation M184V and the efavirenz (EFV) and nevirapine (NVP) (two NNRTI drugs) mutations K103N and 181C are frequently observed in cases of virological failure.[11 12] Yet combinations of tenofovir (TDF) 3TC and EFV/NVP are extensively used as a first-line regimen in limited resource settings.[13] The accumulation of mutations against drugs from different drug classes and the presence of broad cross-resistance mutations will jeopardise the effectiveness of ART care.

Despite the growing focus on the HIV treatment cascade, there is little information about the continuum of care from diagnosis to virological suppression among FSWs in SSA. Available data on factors associated with VL among FSWs have been from developed countries[14 15] and have shown that virological suppression is associated with older age, higher CD4+ T-cell counts and good adherence. Furthermore, virological suppression has been shown to reduce morbidity and mortality and improve overall quality of life as well as economic productivity.[16]

In 2014, Uganda adopted VL testing guidelines[17] as a gold standard for monitoring the individual response to ART. However, little is known about virological suppression and associated factors among FSWs on ART. An understanding of these factors is important to guide sustainable long-term strategies for ART adherence programmes in this population. In this paper, we assess factors associated with virological failure among HIV-positive FSWs on ART in Kampala, Uganda.

METHODS

Study design, population and setting

From January 2015 to December 2016, we enrolled FSWs living with HIV on ART into a cross-sectional study to test for VL. The FSWs were recruited from a cohort of women at high risk of HIV infection attending the Good Health for Women Project (GHWP) clinic. The FSWs coming to the clinic are mobilised from 'sex work hotspots'. We defined female sex work as having sex with men in exchange for money, favours or other goods either regularly or casually. The GHWP clinic is in a periurban suburb in the south of Kampala, the capital city of Uganda. The clinic was established in 2008 to study the epidemiology of HIV and STIs and to implement HIV/STI prevention among FSWs. HIV prevalence in the cohort is 37%[7] and the ART acceptance rate within 1 month is 28%.[18]

Eligibility criteria

The eligibility criteria for participation in the study included (1) being an FSW aged ≥18 years old living with HIV, (2) having documented evidence of being on ART for ≥6 months and (3) having had VL tested at ≥6 months of being on ART. We excluded participants who were not on ART, those enrolled within 6 months of starting ART and those who did not have data on VL and selected covariates.

The GHWP ART programme and procedures

The GHWP clinic was accredited by the Ministry of Health (MoH) in Uganda to provide ART in January 2013. From January 2013 to July 2014, FSWs living with HIV were initiated on ART using CD4+ T-cell counts (≤350 cells/mm^3) and WHO staging criteria. In August 2014, the GHWP clinic started rolling out the new test and start ART guidelines,[17] with all FSWs living with HIV being initiated on ART irrespective of CD4 T-cell counts as long as they were willing and ready to start treatment. In the same year, in pursuit of meeting the 90-90-90 targets, the GHWP clinic, in collaboration with the MoH and the Central Public Health Laboratories, initiated VL monitoring and testing. A VL test is done every 6–12 months for all patients on ART as follows: (1) after 6 months on ART if newly initiated; (2) if VL <1000 copies/mL, VL is repeated at 12 months, then every 12 months thereafter; (3) if VL >1000 copies/mL, three intensive adherence counselling (IAC) sessions are done 1 month apart and VL is repeated on third IAC session; (4) if VL >1000 copies/mL, at third IAC session, patients are switched to second-line ART or to third-line if already on second line.[19]

The initial ART prescriptions were for 2 weeks, then 1 month, followed by an evaluation to check for any ART reactions, and then three monthly refills. First-line ART regimens combined two NRTIs (TDF or zidovudine and lamivudine or emtricitabine) and one NNRTI (NVP or EFV). Second-line regimens combined two NRTIs not used in the first-line regimen with a boosted protease inhibitor (PI) (ritonavir-boosted lopinavir). Second-line regimens were given to women who failed to respond to a first-line regimen. IAC was done routinely for women identified with virological failure to enhance ART adherence. For those who missed appointments, active tracking by the field team and peer educators was done through phone calls, SMS (short message service) reminders, biweekly peer support group sessions and home visiting, and updating clients' contact details at each clinic visit.

Laboratory procedures

As part of routine clinical care, blood samples were collected to assess HIV VL and CD4+ T-cell counts. Baseline CD4+ T-cell counts on ART initiation and VL were done at least 6 months after ART initiation. VL testing was performed on plasma using an Abbott RealTime HIV-1 PCR assay (Abbott Park, Illinois, USA), whereas CD4+ T-cell counts were performed on whole blood using Multiset Trucount tube-lyse no-wash method (Becton, Dickinson and Company, San Jose, California, USA). Samples from patients with virological failure (≥1000 copies/mL) were retrieved and submitted for drug resistance testing at the Medical Research Council/Uganda Virus Research Institute laboratory in Entebbe, Uganda. Briefly, viral RNA was extracted from 140 μL of plasma using the QIAamp Viral RNA Mini Kit (Qiagen), and the entire protease (codons 1–99) and amino terminus of reverse transcriptase (codons 1–320) were amplified and sequenced using the ABI 3500 machine (Applied Biosystems).[20] Sequences were base-called using Sequencher V.5.2.4 and DRM was analysed using the Stanford HIVdb program (https://hivdb.stanford.edu/hivdb/by-mutations),[21] using the 2009 WHO mutation list. Basic phylogenies were performed to determine sequence relatedness and to rule out sample contaminations. Viral sequences are available in GenBank (accession numbers MH166811–MH166838).

Data collection and study measures

Counsellors collected data on sociodemographic characteristics, sexual behaviour and relevant ART care history. Data on initial WHO staging, place of ART initiation, ART treatment regimen given and ART duration were abstracted from the MoH ART card and the ART register. Laboratory tests abstracted included baseline CD4+ T-cell counts on ART initiation and absolute VL at least 6 months after initiating ART.

VL was categorised as virology failure (≥1000 copies/mL) and virological suppression (<1000 copies/mL).[10 19] The primary outcome of this study was virological failure assessed at least 6 months after initiating ART. Sociodemographic measures included age, marital status, education level, alcohol use, sexual partner violence in the last 3 months and main source of income. Alcohol use was assessed using a standardised WHO Alcohol Use Disorders Identification Test.[22] Alcohol use was classified into three categories: harmless or low risk drinkers, score 1–7; harmful or high-risk drinkers, score 8–19; and alcohol-dependent, score 20+. The main source of income was categorised as sex work alone or sex work and other sources of income (working in the bar, salon, nightclub and karaoke). Sexual behaviour characteristics included the number of lifetime sexual

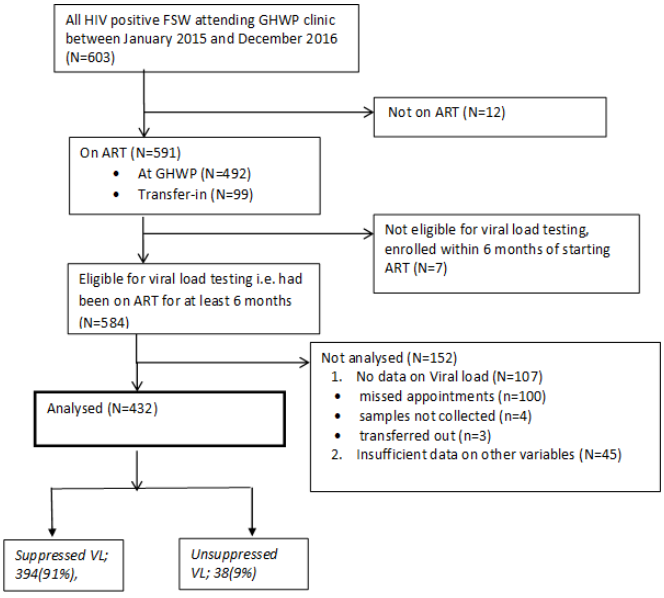

Figure 1 Recruitment profile of female sex workers (FSWs) living with HIV on antiretroviral therapy (ART) at Good Health for Women Project (GHWP) clinic in Kampala, Uganda (2015–2016). VL, viral load.

partners and condom use at last sexual intercourse with paying clients and other partners. Clinical characteristics included baseline CD4+ T-cell counts, VL at least ≥6 months after ART initiation and adherence level using self-report to prescribed ART doses. Adherence was assessed using a self-reported adherence method[23] where women were asked how many doses they had missed in the previous 7 days. The overall individual self-reported adherence was estimated by aggregating the self-reported number of missed doses during the 7 days prior to each clinic visit divided by the total number of doses expected for all the visits attended (aggregated over 7-day periods) expressed as a percentage. Non-adherence was defined as taking <95% of the prescribed doses in the 7 days prior to all visits completed.[19]

Statistical analyses

Data were double-entered in Microsoft Access, cleaned and exported to STATA V.14.0 for analysis. We resolved discrepancies by checking the source documents for clarification. Categorical demographic and clinical characteristics were summarised by counts and percentages. Continuous variables were summarised by means and SD or medians and IQRs. The proportion with virological failure was analysed by the different demographic and clinical characteristics. Factors for which the association attained statistical significance on log likelihood ratio test (LRT) of p<0.20 were selected for the multivariable logistic regression model. Logistic regression models were fitted to identify factors associated with virological failure at unadjusted analysis. Factors were retained in the final multivariable logistics regression model if their inclusion did not make the fit of the model significantly worse at the 5% level on an LRT.

Sensitivity analyses

We conducted sensitivity analyses to address the issue of missing data on selected covariates. Participants who had VL results but with insufficient data on some covariates were imputed using multivariate imputation by *chained equations* approach. A sample of missing values were created, conditional on the distribution of the remaining predictors in the multivariable model. We assumed that the data were missing at random and carried out 10 rounds of multiple imputations; the final data for analysis after imputation were combined using Rubin's rule.[24] We compared the results from the complete case analysis and those from the imputation model.

RESULTS

Recruitment profile

During the study period, 603 FSWs living with HIV attended the GHWP clinic (figure 1); of these, 171 (28%) were excluded from analysis due to ineligibility: 12 (2%) were ART-naive, 7 (1%) had been on ART for <6 months, 107 (18%) had no VL results (missed appointments (n=100), transferred (n=3), sample not collected (n=4)), and 45 (7%) had insufficient data on study independent variables. Of the 45 who had insufficient data, 5 (11%) had virological failure. Thus 432 FSWs were included in the analysis (figure 1).

Participant characteristics

The mean age of the FSWs included in the analysis was 32.5 years (SD±6.5). About half of the FSWs (55%) were aged 25–34 years, 58% had attained at least primary education, and 66% were divorced or separated. About a third had experienced physical sexual partner violence in the previous 3 months, 47% reported sex work as their main source of income, and 14% of FSWs were alcohol-dependent (table 1).

Eighty per cent reported to have had at least 50 lifetime sexual partners, 60% reported using condoms during the last sexual intercourse, and 60% reported consistent condom use. Two-thirds initiated ART at WHO stage I and 9% at stages III and IV. Participants' median duration on ART was 2.3 years (IQR, 1.8–3.2) and the median CD4+ T-cell count at baseline was 395 cells/mm^3 (IQR, 248–597 cells/mm^3). The majority (98%) were on first-line ART regimen and 83% were >95% adherent to their ART treatment. Virological suppression was achieved by 394 FSWs (91%) (table 1).

Drug resistance mutations

Of the 38 (9%) FSWs who had virological failure, plasma samples of 28 (74%) were successfully sequenced, and 23 of 28 (82%) had at least one major surveillance drug resistance mutations (SDRM). Of the FSWs with at least one major DRM, 21 of 23 (91%) were on first-line regimen. All had an NNRTI DRM, 16 (70%) had both NRTI and NNRTI DRM, while 1 patient had DRM to all ART drug classes (NRTI: TDF or zidovudine and lamivudine or emtricitabine; NNRTI: NVP and EFV; and PI: ritonavir-boosted lopinavir). The predominant mutations were M184V16 (70%) and K103N 15 (65%). The median duration on ART among those with DRM was 3.4 years (IQR, 2.3–6.2). We observed a high frequency of thymidine analogue mutation (15, 65%) (see table 2).

Virological failure and associated factors

The proportion of FSWs with virological failure increased with decreasing age, 18% (18–24 years) vs 6% (>35 years), and was higher among non-adherent participants (16%) compared with those adherent to ART (7%) (table 3). More FSWs with no education had virological failure (15%) compared with FSWs with secondary level and above (12%). Compared with FSWs with CD4 ≤350 cells/mm^3, those with CD4 >350 cells/mm^3 had a lower proportion of virological failure, that is, 6% vs 13%. Additionally, the proportion with virological failure was higher among transfer-in patients (16%) compared with those

Table 1 Characteristics of FSWs living with HIV who remained on ART for at least 6 months in Kampala, Uganda

Variable	Category	Included in the analysis (n=432), n (col %)
Sociodemographic characteristics		
Age category		
	35–54	151 (35)
	25–34	237 (55)
	18–24	44 (10)
Level of education		
	No education	40 (9)
	Primary	251 (58)
	Secondary and above	141 (33)
Religion		
	Christian	333 (77)
	Muslim	99 (23)
Marital status		
	Married	19 (4)
	Widowed	47 (11)
	Divorced/Separated	288 (67)
	Never married	78 (18)
Source of income		
	Other in addition to sex work	227 (53)
	Sex work only	205 (47)
Violence experience in the last 3 months		
	Yes	148 (34)
	No	284 (66)
Alcohol use		
	Low risk	188 (44)
	Harmful/High risk	182 (42)
	Alcohol-dependent	62 (14)
Sexual behavioural characteristics		
Condom use at last sexual intercourse		
	Yes	259 (60)
	No	173 (40)
Lifetime sexual partners		
	<50	77 (18)
	≥50	345 (80)
	Missing	10 (2)
Participants' clinical characteristics		
Baseline CD4+ T-cell counts		
	≤350	187 (43)
	>350	245 (57)
WHO stage		
	Stage I	265 (61)
	Stage II	82 (19)
	Stages III and IV	37 (9)
	Missing	48 (11)
Place of ART initiation		
	Clinic-initiated	374 (87)
	Transfer-in	58 (13)
ART regimen		
	First-line	
	AZT-3TC-EFV	5 (1)
	AZT-3TC-NVP	17 (4)
	TDF-3TC-EFV	378 (88)
	TDF-3TC-NVP	22 (5)
	Second-line	3 (1)
	TDF-3TC-LPV/r	6 (1)
	TDF-3TC-ATV/r	1 (0)
	AZT-3TC-ATV/r	
Adherence status		
	Adherent	359 (83)
	Non-adherent	73 (17)
Duration on ART (years)	Median (IQR)	2.3 (1.8–3.2)
Baseline CD4+ T-cell count	Median (IQR)	395 (248–597)
Criteria for ART initiation		
	CD4 ≤350 cells/mm^3	171 (40)
	Test and treat	261 (60)

ART, antiretroviral therapy; ATV/r, Atazanavir/Ritonavir; AZT, zidovudine; EFV, efavirenz; FSWs, female sex workers; LPV/r, Lopinavir/Ritonavir; NVP, nevirapine; 3TC, lamivudine; TDF, tenofovir.

who initiated ART at GHWP (8%), with borderline statistical significance. The proportions of virological failure did not differ within the categories of the other FSW characteristics.

In adjusted (multivariable) analysis, virological failure was independently associated with participant age 18–24 (adjusted OR (aOR)=5.3, 95% CI 1.6 to 17.9), non-adherence (aOR=2.6, 95% CI 1.2 to 5.8) and low baseline CD4+ T-cell counts (≤350 cells/mm^3) (aOR=3.1, 95% CI 1.4 to 7.0) (table 3).

Table 2 Type and frequency of drug resistance mutations detected in 23 samples of HIV-positive FSWs with virological failure who remained on ART for at least 6 months

Mutations	n (%)
Resistance category (n=28)	
Sequences with any SDRM	23 (82.1)
PR sequences with any PI SDRM	1 (3.6)
RT sequences with any NRTI SDRM	16 (57.1)
RT sequences with any NNRTI SDRM	23 (82.1)
RT sequences with any NRTI + any NNRTI SDRM	16 (57.1)
PRRT sequences with any NRTI + any NNRTI + PI SDRM	1 (3.6)
NRTI-related mutations (n=23)	
M184V	16 (70)
T215Y	6 (26)
K65R	3 (13)
L74V	3 (13)
M41L	3 (13)
D67N	2 (9)
K219Q	2 (9)
L210W	1 (4)
K70R	1 (4)
NNRTI-related mutations (n=23)	
K103N	15 (65)
G190A	7 (30)
P225H	6 (26)
K101E	5 (22)
Y181C	4 (17)
V106M	1 (4)
V179F	1 (4)
L100I	1 (4)
PI-related mutations (n=23)	
M46L	1 (4)

ART, antiretroviral therapy; FSWs, female sex workers; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PR, Protease; PRRT, Protease and Reverse Transcriptase; RT, Reverse Transcriptase; SDRM, surveillance drug resistance mutation.

Table 3 Characteristics of HIV-positive FSWs and association with virological failure in Kampala, Uganda (n=432)

Variable	Suppressed, n (col %)	Not suppressed, n (col %)	OR (95% CI)	LRT p value	aOR (95% CI)
Age category, years				0.064	
35–54	142 (36)	9 (24)	1		1
25–34	216 (55)	21 (55)	1.5 (0.7 to 3.4)		1.9 (0.8 to 4.7)
18–24	36 (9)	8 (21)	**3.5 (1.3 to 9.7)**		**5.3 (1.6 to 17.9)**
Level of education				0.048	
No education*	34 (9)	6 (16)	1		1
Primary	236 (60)	15 (39)	0.4 (0.1 to 1.0)		0.4 (0.1 to 1.1)
Secondary and above	124 (31)	17 (45)	0.8 (0.3 to 2.1)		0.9 (0.3 to 2.5)
Religion					
Christian*	304 (77)	29 (76)	1		
Muslim	90 (23)	9 (24)	0.9 (0.4 to 2.1)		
Source of income				0.091	
Others in addition to sex work	212 (54)	15 (39)	1		1
Sex work only	182 (46)	23 (61)	1.8 (0.9 to 3.5)		1.6 (0.8 to 3.4)
Marital status					
Never married	69 (18)	9 (24)	1	0.361	
Married	325 (82)	29 (76)	0.7 (0.3 to 1.5)		
Physical violence with sexual partners in the past 3 months					
No*	137 (37)	11 (29)	1	0.464	
Yes	257 (65)	27 (71)	0.8 (0.4 to 1.6)		
Alcohol use					
Harmful/High risk	338 (86)	32 (84)	1		
Alcohol-dependent	56 (14)	6 (16)	1.1 (0.5 to 2.8)		
Condom use at last sexual intercourse					
Yes*	236 (60)	23 (61)	1	0.94	
No	158 (40)	15 (39)	1.0 (0.5 to 1.9)		
Baseline CD4+ T-cell counts					
>350 cells/mm^3	231 (59)	14 (37)	1	0.01	1
≤350 cells/mm^3	163 (41)	24 (63)	**2.4 (1.2 to 4.8)**		**3.1 (1.4 to 7.0)**
Place of ART initiation				0.072	
Clinic-initiated*	345 (88)	29 (76)	1		1
Transfer-in	49 (12)	9 (24)	**2.2 (1.0 to 4.9)**		1.7 (0.5 to 5.9)
Adherence status				0.019	
Adherent*	333 (85)	26 (69)	**1**		**1**
Non-adherent	61 (15)	12 (31)	**2.5 (1.2 to 5.3)**		**2.6 (1.2 to 5.8)**
Duration of ART (in years), median (IQR)	2.3 (1.8–3.1)	2.7 (2.2–3.8)	**1.2 (1.0 to 1.4)**	0.071	1.1 (0.8 to 1.4)

For the values in bold; Statistically significant(p<0.05) ; For Multivariate analysis, we retained variables with LRTp-value less than 0.20 and common confounders (age).
*Reference category.
aOR, adjusted OR.ART, antiretroviral therapy; FSWs, female sex workers; LRT, likelihood ratio test;

Sensitivity analysis results

A sensitivity analysis by imputing data for participants missing other covariates but having VL data was conducted, and the results were similar to when they were excluded.

DISCUSSION

We found that the proportion of FSWs with virological failure was relatively low. These encouraging results are almost similar to the results from another study in Malawi among FSWs[25] and those from the Ugandan general population,[26] although this was lower than the virological results of a study among Zimbabwean FSWs.[27] The high level of virological suppression in this population highlights good progress as we move towards reaching the 90-90-90 target introduced by UNAIDS in 2014.[1] Our study was conducted in a clinical research setting with free care, with IAC and active follow-up of participants. Thus, this may explain the relatively high levels of adherence observed in this study, which may have contributed to the lower virological failure, even though some reporting bias may have occurred. One study in Benin among a cohort of FSWs found that higher VL was attributed to lower reported adherence.[28] Good adherence with the goal of virological suppression is critical to improving health outcomes and onward transmission.[29]

We found that FSWs with virological failure had high rates of DRM. Our findings were within similar ranges to those from Uganda[30] in the general population and South Africa among FSWs.[11] It is possible that this high level of drug resistance could have been a result of non-adherence. Poor adherence has been shown to be a major cause of virological failure with a potential risk of drug resistance (W1). However, due to relatively short average ART time, we cannot exclude that some of these mutations were already present at baseline. However, given the multiple sexual relationships and inconsistent condom use in this population, our major concern is that there may be some

alarming rates of DRM being transmitted between clients or regular partners and FSWs. This highlights the importance of monitoring of VL and drug resistance within FSW programmes and the urgent need to understand the DRM transmission dynamics and the outcomes.

Furthermore, consistent with findings from Rwanda,[12] the most predominant mutations observed in this study were M184V for NRTI and K103N for NNRTIs. This finding reflects high-level resistance to lamivudine, NVP and EFV, which are the backbone ART drugs in this setting. The combination of TDF+3TC+EFV/NVP/dolutegravir is extensively used as a first-line regimen which greatly limits treatment choices in our ART programme.

Young age was independently associated with virological failure in our study. This is consistent with other studies (27, W2) conducted among FSWs in SSA. These findings have also been demonstrated in Uganda in the general population.[26] In Uganda, young people face numerous challenges, including social, economic, cultural and treatment-related challenges, which may contribute to the higher rates of non-adherence (W3). However, our results contradict with the results from a study in Canada among FSWs which did not find an association with age (W4). This difference in findings could be related to the diversity in the age ranges used in that study and the sociocultural factors that vary across populations.

We demonstrated that having virological failure was significantly associated with non-adherence and low CD4+ T-cell counts. This is consistent with the results from Burkina Faso, where FSWs with reported lower adherence had lower CD4 gains, higher virological failure and a higher mortality rate compared with the general population (W2). Research from our cohort has shown that these FSWs are often exposed to high levels of alcohol use and partner violence, which impact on their ability to adhere to treatment (W5). A systematic review among FSWs also reported that not being at home to take pills and potential loss of clients if seen taking ART during work hours were factors that prevented them from adhering to treatment (W6). It is therefore important that HIV interventions and ART programmes for FSWs try to address the structural and social barriers to HIV treatment that FSWs face.

Our study had some limitations. First, 18% of FSWs had no VL test results mainly due to missed clinic appointments. This could have reduced the power to detect more associations with virological suppression. We observed significant differences between the women with VL data and those without, suggesting that there may be a selection bias; it is not known whether those who missed appointments are at risk of not being suppressed virally. Second, while we observed that 98% of FSWs living with HIV more than 6 months postreferral and linkage into ART care were on ART, our study was designed to report virological suppression. We did not assess the HIV test status of FSWs and thus do not have adequate data on the full HIV treatment cascade to characterise the 90-90-90 targets. Third, our findings may not represent virological suppression rates of FSWs in other clinic settings in Kampala because the study was conducted in only one clinic and may not be generalisable to places with limited access to HIV care services. Lastly, because we do not have SDRM data on those with virological failure, we were unable to compare control by mutation status.

In summary, we found a relatively low prevalence of virological failure among FSWs, but this is accompanied by a high proportion of DRMs among women with virological failure. Younger age, non-adherence and low CD4+ T-cell counts (≤350 cells/mm^3) at baseline assessment were associated with an increased risk of virological failure at 6 months.

Key messages

- Given the high virological suppression in this population, strategies that enhance the 90-90-90 targets among female sex workers (FSWs) are needed to maximise the benefits of antiretroviral therapy.
- Considering the significant association between young age and virological failure, interventions targeting young FSWs to improve virological suppression should be developed.
- Given the high rate of drug resistance mutation (DRM), there is a need for research to monitor the transmission dynamics of DRM and its impact on treatment success among FSWs.

Handling editor Jackie A Cassell

Contributors GN conceived and designed the study. AA, OK and DB performed the statistical analysis. GN wrote the manuscript. PK, MP, WK, AA, JS, RN, YM, DS, DB, OK, WS, SL and MN oversaw the overall execution of the manuscript writing. MP, WK, AA, JS, PM and RN oversaw the critical revisions of the manuscript. All authors read and approved the final manuscript.

Funding We would like to thank the UK Medical Research Council (MRC) and the UK Department for International Development (DFID) under the MRC/DFID Concordat agreement, which is also part of the EDCTP2 programme supported by the European Union, for funding. The clinic services and ART programme were supported by PEPFAR. This work was partially funded by IAVI with the generous support of USAID and other donors; a full list of IAVI donors is available at www.iavi.org. The content of this manuscript is the responsibility of the authors and does not necessarily reflect the views of USAID or the US Government. We also thank the University of California, San Francisco's International Traineeships in AIDS Prevention Studies (ITAPS), US NIMH, R25MH064712, for support.

Competing interests None declared.

Patient consent for publication Obtained.

Ethics approval Ethical approval was obtained from the Uganda Virus Research Institute Research and Ethics Committee and the Uganda National Council for Science and Technology (reference number HS364). Written informed consent was obtained from participants and confidentiality was maintained throughout the study period.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement The data collected in this study are suitable for sharing and the procedures for accessing it are contained in the data sharing policy accessible from the Medical Research Council website (https://www.mrcuganda.org/publications/data-sharing-policy).

REFERENCES

1 HIV/AIDS JUNPo, HIV/Aids JUNPo. 90-90-90: an ambitious treatment target to help end the AIDS epidemic. Geneva UNAIDS; 2014.
2 UNAIDS. UNAIDS data 2018;2018.
3 Doshi RH, Sande E, Ogwal M, *et al*. Progress toward UNAIDS 90-90-90 targets: a respondent-driven survey among female sex workers in Kampala, Uganda. *PLoS One* 2018;13:e0201352.
4 Organization WH. *Technical and Operational Considerations for implementing HIV viral load testing*. Geneva, Switzerland: WHO, 2014.
5 Makerere University SoPH, Kampala, Uganda. The Crane survey report: high risk group surveys conducted in 2008/9, Kampala, Uganda, 2010. Available: https://sites.google.com/site/cranesurvey/downloads
6 Uganda A. Indicator survey 2011. demographic and health surveys, ICF international. 2012.
7 Vandepitte J, Bukenya J, Weiss HA, *et al*. HIV and other sexually transmitted infections in a cohort of women involved in high-risk sexual behavior in Kampala, Uganda. *Sex Transm Dis* 2011;38:1–23.
8 Commission UA. *HIV and AIDS Uganda country progress report 2013*. Kampala: Uganda AIDS Commission, 2014.

9 Scorgie F, Nakato D, Akoth DO. I expect to be abused and I have fear": sex workers' experiences of human rights violations and barriers to accessing healthcare in four African countries Final report African Sex Workers Alliance; 2011.
10 Organization WH. *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach*. World Health Organization, 2016.
11 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:e0188606.
12 Ndahimana Jean d'Amour, Riedel DJ, Mwumvaneza M, *et al*. Drug resistance mutations after the first 12 months on antiretroviral therapy and determinants of virological failure in Rwanda. *Trop Med Int Health* 2016;21:928–35.
13 Renaud-Théry F, Nguimfack BD, Vitoria M, *et al*. Use of antiretroviral therapy in resource-limited countries in 2006: distribution and uptake of first- and second-line regimens. *AIDS* 2007;21 Suppl 4:S89–S95.
14 Duff P, Goldenberg S, Deering K, *et al*. Barriers to viral suppression among female sex workers: role of structural and intimate partner dynamics. *J Acquir Immune Defic Syndr* 2016;73:83–90.
15 Ti L, Milloy M-J, Shannon K, *et al*. Suboptimal plasma HIV-1 RNA suppression and adherence among sex workers who use illicit drugs in a Canadian setting: an observational cohort study. *Sex Transm Infect* 2014;90:418–22.
16 Tomita A, Garrett N, Werner L, *et al*. Health-related quality of life dynamics of HIV-positive South African women up to art initiation: evidence from the CAPRISA 002 acute infection cohort study. *AIDS Behav* 2014;18:1114–23.
17 GOU. Addendum to the National antiretroviral treatment guidelines 2013.
18 Mayanja Y, Kamacooko O, Bagiire D, *et al*. 'Test and treat' among women at high risk for HIV-infection in Kampala, Uganda: antiretroviral therapy initiation and associated factors. *AIDS Behav* 2018;22:1053–61.
19 GOU. Consolidated guidelines for prevention and treatment of HIV in Uganda 2016.
20 Kaleebu P, Kirungi W, Watera C, *et al*. Virological response and antiretroviral drug resistance emerging during antiretroviral therapy at three treatment centers in Uganda. *PLoS One* 2015;10:e0145536.
21 Liu TF, Shafer RW. Web resources for HIV type 1 genotypic-resistance test interpretation. *Clin Infect Dis* 2006;42:1608–18.
22 WHO. Alcohol use disorders identification test (audit) 2001.
23 Farmer KC. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clin Ther* 1999;21:1074–90.
24 Rubin DB. *Statistical analysis with missing data*. Wiley, 1987.
25 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:e0147662.
26 Bulage L, Ssewanyana I, Nankabirwa V, *et al*. Factors associated with virological non-suppression among HIV-positive patients on antiretroviral therapy in Uganda, August 2014–July 2015. *BMC Infect Dis* 2017;17.
27 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* 2017;74:375–82.
28 Diabaté S, Zannou DM, Geraldo N, *et al*. Antiretroviral therapy among HIV-1 infected female sex workers in Benin: a comparative study with patients from the general population. *World J AIDS* 2011;01:94–9.
29 Cohen MS, Chen YQ, McCauley M, *et al*. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med Overseas Ed* 2011;365:493–505.
30 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* 2018;78:566–73.