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Recreational ART use among individuals living with HIV/AIDS in South Africa: Examining longitudinal ART initiation and viral suppression

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ABSTRACT

Background: South Africa has the highest number of people living with HIV (PLWH) and one of the largest antiretroviral therapy (ART) programs globally. High rates of substance use comorbidity exist, including speculation of recreational ART use (i.e., mixing ART with other illicit drugs). Recreational ART use may affect viral load among PLWH due to ART nonadherence and/or viral resistance; however, prior quantitative research has not examined rates of recreational ART use, nor associations with HIV treatment outcomes longitudinally.

Methods: Data were drawn from a prospective, observational cohort study (n = 500) of ART-eligible adults recruited from two HIV voluntary counseling and testing centers in Cape Town, and Johannesburg, South Africa. Multiple logistic regression models assessed recreational ART use as a predictor of ART initiation over six months and viral load suppression over nine months, above and beyond other substance use (binge drinking and illicit drug use).

Results: Approximately 5% (n = 24) reported recreational ART use, which was less frequent in Cape Town compared to Johannesburg (AOR = 0.025; 95%CI: 0.003-0.19; p < 0.001). Recreational ART use was not significantly associated with ART initiation or viral suppression. Other substance use, but not recreational ART use, was significantly associated with lower odds of ART initiation (AOR = 0.54; 95%CI: 0.33-0.87; p = .01) and viral suppression (AOR = 0.47; 95%CI: 0.25-0.89; p = .02).

Conclusions: Recreational ART use was infrequent and not uniquely associated with ART initiation or viral suppression. Findings suggest that comorbid use of other substances is ultimately what may make recreational ART use problematic for ongoing engagement in care and viral suppression.

1. Introduction

South Africa has the highest number of people living with HIV (PLWH) in the world, with an estimated 7.1 million PLWH (Joint United Nations Programme on HIV/AIDS (UNAIDS, 2017). Of the 7.1 million PLWH in South Africa, approximately 56% are on antiretroviral therapy (ART), making South Africa home to one of the largest ART programs in the world. However, South Africa also has one of the

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highest unmet needs, with over three million PLWH in South Africa not utilizing ART, thus also making South Africa home to the largest number of PLWH not on ART in the world (Joint United Nations Programme on HIV/AIDS (UNAIDS, 2017).

High rates of substance use in South Africa have been shown to compromise efforts to achieve successful HIV treatment and prevention outcomes (Cook et al., 2001; Kader et al., 2014; Kalichman et al., 2007; Patterson et al., 2005). An estimated 13–37% of HIV clinic-attending patients in peri-urban areas of Cape Town present with substance use (Kader et al., 2014), which is concerning as problematic substance use is associated with worse ART adherence, lower rates of viral suppression, and HIV transmission risk (Cook et al., 2001; Kader et al., 2014; Kalichman et al., 2007; Patterson et al., 2005). In Cape Town, there have been very high rates of methamphetamine ("tik") use (Plüddemann et al., 2012). In other areas (e.g., Johannesburg), there have been high rates of other illicit substance use, including heroin use (Burnhams, 2017; Plüddemann et al., 2012). South Africa also has one of the highest global rates of per capita alcohol consumption (Shield et al., 2013).

In addition to the aforementioned substances, there is qualitative evidence that individuals in Western Cape, KwaZulu-Natal, and Gauteng provinces of South Africa may use ART recreationally to get high, either by smoking efavirenz or by smoking whoonga and nyaope, a drug "cocktail" rumored to be a mixture of antiretroviral medication and illicit drugs such as heroin, methamphetamine, and/or cannabis (Grelotti et al., 2014; Larkan et al., 2010; Rough et al., 2014). Efavirenz is a non-nucleoside reverse transcriptase inhibitor which is combined with other antiretroviral medications for use in the treatment of HIV, and it has been prescribed as part of first-line therapy in South Africa since 2013. Efavirenz, like lysergic acid diethylamide (LSD), has activity at the 5HT-2A receptor (Cavalcante et al., 2017; Dalwadi et al., 2018; Gatch et al., 2013; Möller et al., 2018). In support of its LSD-like psychoactivity, it has been reported that efavirenz has been smoked in South Africa for its "hallucinogenic and relaxing effect" (Marwaha, 2008). Despite media attention to whoonga and nyaope (i.e., names used in different regional contexts to describe the same street drug), whoonga and nyaope may only rarely contain ART, and whether whoonga or nyaope actually contain ART has been the source of some debate (Cullihan, 2011). However, it has been suggested that the use of these recreational drugs may lead to a variety of individual- and community-level consequences, including poor adherence to ART, decreased ART supplies at clinics, increased stigma for people living with HIV (Grelotti et al., 2013) and increased violence towards HIV patients and healthcare providers by people trying to obtain the drugs (Grelotti et al., 2013; Rough et al., 2014; Tsuyuki et al., 2015).

Prior qualitative research has pointed to individuals stealing ART from PLWH and then selling these pills in the community (Rough et al., 2014) and engaging in other forms of illegal distribution (Grelotti et al., 2014). As such, recreational ART use is not limited to PLWH or individuals prescribed ART. However, among PLWH on ART, recreational ART use may lead to poor viral load outcomes due to developing ART resistance and/or poor ART adherence and treatment response as a consequence of use (Grelotti et al., 2013).

Despite qualitative research (Chinouya et al., 2014; Grelotti et al., 2014; Rough et al., 2014) and case studies (Larkan et al., 2010) indicating that recreational ART use may be a large problem in South Africa, there has been minimal quantitative evidence of recreational ART use. To our knowledge, few prior studies have examined recreational ART use quantitatively, and none have examined longitudinal associations with HIV treatment outcomes, while also accounting for other forms substance use, including binge drinking and other illicit drug use. Given the magnitude of the HIV epidemic in South Africa (Joint United Nations Programme on HIV/AIDS (UNAIDS, 2017), recreational ART use that may contribute to poor viral load outcomes would have enormous public health implications; recreational ART use may affect viral load outcomes via direct mechanisms (i.e., viral resistance from inconsistent patterns of ART exposure) or indirect mechanisms (i.e., lower ART adherence as a result of intoxication due to recreational ART use and/or other co-occurring substance use). Further, understanding recreational ART use not only has significance for South Africa but also for countries all over the world, including the United States, where recreational ART use has also been documented (Davis et al., 2014).

Therefore, the overall aims of this study were to (1) quantitatively describe rates of recreational ART use among a sample of ART-naïve, treatment eligible PLWH; (2) assess factors associated with recreational ART use; and (3) assess longitudinally whether recreational ART use was associated with lower odds of initiation of ART over six months and viral suppression over nine months among those who initiate ART, above and beyond other substance use (binge drinking and other illicit substance use). We hypothesized that compared to individuals who did not report recreational ART use, individuals who used ART recreationally would be less likely to initiate treatment and achieve viral suppression due to potential direct (i.e., viral resistance) and/or indirect mechanisms (i.e., lower ART adherence in the context of diversion or the effects of substance use on adherence).

2. Methods

2.1. Participants

Participants were enrolled at HIV testing centers from two peri-urban areas in South Africa: a public health clinic in Soweto (outside of Johannesburg) and a community health center in Gugulethu (outside of Cape Town). These clinics were chosen to reflect patterns of HIV prevalence in urban South Africa, with an overall HIV prevalence of close to 20% (Shisana et al., 2014). Together, the study clinics provide rapid HIV tests to over 500 people over the age of 18 each month, as well as family planning, tuberculosis screening, and tests for sexually transmitted infections. Trained lay counselors provide additional social support to patients. During the period of this study, patients who received a positive HIV test result would return a week later for their CD4 cell count, and if eligible, were referred for treatment. After referral, social workers provide information regarding ART initiation.

2.2. Procedures

Data for this study came from a prospective, observational cohort study over a nine-month follow up period. At baseline, trained multilingual interviewers administered in-person surveys to collect information on eligible individuals' intention to start treatment, as well as clinical characteristics and psychosocial factors. Follow up assessments were conducted at three- and six-months over the phone, including repeated assessment of substance use, recreational ART use, and other relevant psychosocial factors. Viral load was assessed over a nine-month period following baseline.

In total, 500 ART-eligible adults (18 years or older) were recruited between July 2014 and July 2015 (200 from Soweto, 300 from Gugulethu) when they returned for their CD4 test results. Due to treatment guidelines shifting in South Africa during the study, ART eligibility changed from CD4 ≤ 350 cells/mm^3 before Jan 1, 2015, to CD4 ≤ 500 cells/mm3 after Jan 1, 2015. In South Africa, all patients are offered the same, "first-line" efavirenz (EFV)-based regimen, and only the 600 mg dose of EFV is available. Since 2015, first-line treatment in South Africa has been offered as a single medication (TDF/FTC/EFV). For individuals enrolled in this study prior to 2015, they also would have been offered an EFV-based regimen, but as separate medications (EFV, TDF, 3TC). Regardless of the timing, all participants in this study would have been offered the only available option, an EFV-based regimen (600 mg). The only situation in which someone would not have been offered an EFV-based regimen, which is quite rare, is if someone had a strong clinical contraindication (e.g., due to

hypersensitivity or renal dysfunction, which is uncommon). Pregnant women and children were excluded from the study because they would qualify for intensive adherence support.

Ethics review and approval were granted by the human subjects committees at Partners Healthcare (Boston, Massachusetts), the University of Witwatersrand Ethics Committee (Johannesburg, South Africa), and the University of Cape Town Faculty of Health Science Research Ethics Committee. All enrolled participants provided written informed consent. Study data were collected and managed using a secure, web-based Research Electronic Data Capture (REDCap) tools managed by Partners Healthcare.

2.3. Assessments

Viral load and ART initiation were the main outcomes in this study. These were measured as: 1) treatment initiation within six months of HIV testing; and 2) viral suppression (< 50 copies/mL) within nine months (among those who initiated ART). These outcomes were ascertained through accessing routine laboratory data collected in South Africa's National Health Laboratory Service (NHLS). NHLS provides laboratory testing services for all public-sector clinics throughout South Africa, including all laboratory testing required for ART monitoring in South Africa. Data regarding viral load were directly entered into NHLS by clinical providers, and ART initiation was imputed based on a measure of creatinine, performed prior to initiation of Tenofovir, part of a standard first-line ART regimen in South Africa. As noted above, all PLWH in South Africa are offered the same, "first-line" treatment, which is an efavirenz (EFV) and Tenofovir-based regimen. ART workup blood tests as recorded in NHLS have been previously validated as an accurate measure to impute dates of treatment initiation among South African PLWH who are receiving public-sector HIV care (Fox et al., 2018, 2013; Maskew et al., 2017). We chose these two outcomes based on clinical relevance and timing of viral load measurements performed in South Africa during this timeframe.

CD4 count was primarily obtained via blood draw and sent to NHLS for processing. A small number of participants in Cape Town received immediate CD4 testing using Alere Pima™and then verified through NHLS.

Demographic and clinical characteristics assessed included age, gender, prior HIV testing history and results, prior TB diagnosis, depression (PHQ-9; Kroenke et al., 2001, dichotomized using the median response for the PHQ-9 questionnaire).

Recreational ART use was measured using two dichotomous self-report questions at baseline, three-month, and six-month follow ups that were developed based on our team's prior qualitative research on recreational ART use in South Africa (Rough et al., 2014); questions included: "Have you ever used antiretrovirals recreationally or for the way they made you feel?" and "Have you ever used whoonga or nyaope?" A binary variable was created in which recreational ART use was defined as individuals who responded "yes" to either or both of these questions at any point over the study period. Individuals who responded "no" to both questions at all study time points were categorized as not having used ART recreationally (see Supplementary Table 1).

Other substance use was assessed using a substance use frequency questionnaire from the AIDS Clinical Trials Group Adherence/Quality of Life/Psychosocial Interview (Outcomes Committee of AIDS Clinical Trials Group, 2006) at baseline, three-month and six-month follow ups. Specifically, participants were asked about illicit drug use and binge drinking alcohol (separately by substance) over the past 30 days. First, they were asked if they used intravenous drugs in the past 30 days, and if they used any of the following: marijuana, cocaine, heroin, crystal-meth, solvents, glues, and thinners. Then, for the substance used most, they were asked to report how often they used it in the past 30 days (daily, nearly every day, 3 or 4 times a week, once or twice a week, 2 or 3 times a month, or once a month). For binge drinking, participants were asked how often they had 5+ serial alcoholic drinks within 2–4 hours in the last 30 days (daily, nearly every day, 3 or 4 times a week, once or twice a week, 2 or 3 times a month, or once a month). If individuals reported any illicit drug use or binge drinking at least once or twice per week, they were classified as "yes" for "other substance use."

2.4. Statistical analysis

Results for univariate statistics are presented stratified by recreational ART use. Bivariate associations between recreational ART use and other independent variables were tested using Wald statistics from multiple logistic regression models, including unadjusted and adjusted for age and gender with recreational ART use as the outcome variable. We used multiple logistic regression to model the association between recreational ART use and both HIV care outcomes (ART initiation, viral load) separately, presenting both unadjusted and models adjusted for other substance use and potential confounding variables. Results are presented as odds ratios with 95% confidence intervals and p-values. For all analyses, we adjusted for a priori selected covariates that have been shown to be related to substance use and HIV care outcomes in prior research, including depression, CD4 count, age, and gender. Despite there being a strong association between study site and recreational ART use, we did not include study site as a confounding variable in our analysis due to high collinearity between study site and recreational ART Use.

3. Results

Table 1 depicts demographic and clinical characteristics in the total sample and by recreational ART use category. In the full cohort (n = 500), 4.8% (n = 24) were in the recreational ART use group. Among those who reported using ART recreationally, 22/24 (91.7%) responded "yes" to the question "have you ever used antiretrovirals recreationally or for the way they made you feel?" while the remaining two people responded "yes" to the question "Have you ever used whoonga or nyaope?" One person responded "yes" to both questions. Only two individuals reported recreational ART use at baseline (2/24; 8.3% of the recreational ART use group), whereas the other 22 participants first reported recreational ART use at the three-month follow up (n = 8; 33.3%) or six-month follow up (n = 14; 63.6%). See Supplementary Table 1 for more detail.

Among individuals who reported recreational ART use, 87.5% (21/24) reported no other illicit drug use. When examining "other substance use" (i.e., including binge drinking as well as illicit drug use), 70.8% (17/24) of individuals with recreational ART use reported no other substance use. In the full cohort, 17.2% (n = 86) of participants reported either binge drinking at least once or twice per week or other illicit drug use. Individuals who reported recreational ART use were 54.2% female (vs. 63.0% in the overall sample); 12 (50.0%) of participants reporting recreational ART use reported living in a house, with 5 (20.8%) reporting living in a shack and 7 (29.2%) reporting living in a bathroom. Table 2 presents multivariable logistic regression results comparing individuals based on recreational ART use, adjusting for age and gender. Recreational ART use differed by site such that individuals in Gugulethu vs. Soweto were less likely to report recreational ART use (AOR = 0.025; 95%CI: 0.003–0.19; p < 0.001). As shown in Table 2, there was no statistically significant association between recreational ART use and other substance use (OR = 2.07; 95%CI: 0.83–5.12; p = .12).

Table 1
Descriptive characteristics of recreational ART use.

	Total (N = 500)		Recreational ART use (N = 24)		No recreational ART use (N = 476)	
	N	%	N	%	N	%
Age (mean, SD)	35.73	9.11	38.91	9.24	35.58	9.08
Baseline CD4 (mean, SD)	241.89	133.91	235.17	129.65	242.23	134.24
Female	313	62.6	13	54.2	300	63.0
Prior TB diagnosis	63	12.6	3	12.5	60	12.6
Prior HIV test	309	61.8	15	62.5	294	61.8
Of those with previous HIV test, previous positive result	169	55.4	10	66.7	159	54.8
Binge drinking (i.e., in the last 30 days, frequency of 5+ serial drinks within 2-4 hrs)*						
Daily	2	0.4	1	4.5	1	0.2
Nearly every day	2	0.4	.	.	2	0.4
3 or 4 times/week	18	3.7	.	.	18	3.9
Once or twice per week	44	9.0	4	18.2	40	8.6
2 to 3 times/month	103	21.1	1	4.5	102	21.9
Once a month	64	13.1	2	9.1	62	13.3
Never	254	52.1	14	64.6	240	51.6
Count of number of types of illicit drugs used						
0	484	96.8	21	87.5	463	97.3
1	16	3.2	3	12.5	13	2.7
Other substance use (illicit drug use and binge drinking)	86	17.2	7	29.2	79	16.6
Married/Cohabiting	112	22.4	6	25.0	106	22.3
Depression (Severe/Moderate)	187	37.4	12	50.0	175	36.8
Location						
Soweto	200	40.0	23	95.8	177	37.2
Gugulethu	300	60.0	1	4.2	299	62.8
ART Initiation at 6 months	308	61.6	13	54.2	295	62.0
Viral load suppressed at 9 months	125	25.0	4	16.7	121	25.4

* $n = 487$ due to missing data.

Table 3 presents multivariable logistic regression results for odds of ART initiation within six months and odds of viral suppression at nine months. Of the full cohort, 94.6% (n = 473) were successfully identified in the NHLS system and thus would have information available if still engaged in public sector HIV care in South Africa at any point during the study period. Based on NHLS records in the total sample, 61.6% (n = 308) initiated ART within six months. Among those who initiated ART, n = 125 (25% of the total cohort) had a suppressed viral load within nine months (Katz et al., in press). Regarding predictors of ART initiation, recreational ART use was not significantly associated with ART initiation at six months (AOR = 0.68; 95%CI: 0.29–1.60; p = .39). However, other substance use was associated with 46% lower odds of ART initiation (AOR = 0.54; 95%CI: 0.33-0.87; p = .01), and an additional year of age was associated with 3% increased odds of ART initiation (AOR = 1.03; 95%CI: 1.01–1.05; p = 0.01).

Regarding viral suppression outcomes (also depicted in Table 3), recreational ART use was not significantly associated with viral load suppression at nine months (AOR = 0.58; 95%CI: 0.19–1.78; p = .41). However, other substance use was associated with 53% lower odds of viral suppression (AOR = 0.47; 95%CI: 0.25–0.89; p = .02), and an additional year of age was associated with 2% increased odds of viral suppression (AOR = 1.02; 95%CI: 1.00–1.05; $p < 0.05$).

As a sensitivity analysis, we restricted our definition of recreational ART use to include only the participants who responded yes to the question “have you ever used antiretroviral recreationally or for the way they made you feel?” (i.e., excluding the two participants who only reported whoonga or nyaope use and not recreational ART use), which did not change our viral load analysis results (see Supplementary Table 2).

Table 2
Bivariate associations between predictors and recreational ART use (multiple logistic regression, unadjusted and adjusted for age and sex).

	Unadjusted			Adjusted for age and sex		
	OR	95% CI	p-value	AOR	95% CI	p-value
Age (1 year increase)	1.04	0.99-1.08	0.10	1.04	0.99-1.08	0.12
Baseline CD4						
< 250	1.59	0.51-4.93	0.42	1.45	0.46-4.54	0.52
250-350	1.00	–		1.00	–	
> 350	1.43	0.40-5.22	0.58	1.33	0.36-4.89	0.66
Female	0.69	0.30-1.58	0.38	0.74	0.32-1.70	0.48
Prior TB diagnosis	1.01	0.29-3.49	0.99	1.09	0.31-3.77	0.90
Prior HIV test	1.03	0.44-2.41	0.94	1.14	0.48-2.67	0.77
In the last 30 days, frequency of 5+ serial drinks within 2-4 hrs at least weekly (Ever v Never)*	0.61	0.25-1.48	0.27	0.60	0.24-1.48	0.27
ART non-initiation at baseline	0.60	0.079-4.61	0.63	0.60	0.079-4.64	0.63
Other substance use	2.07	0.83-5.12	0.12	2.15	0.85-5.46	0.11
Married/Cohabiting	1.16	0.45-3.01	0.75	0.98	0.37-2.62	0.97
Depression (Severe/Moderate)	1.72	0.76-3.91	0.20	1.85	0.81-4.24	0.15
Gugulethu v. Soweto	0.026	0.003-0.192	0.0004	0.025	0.003-0.19	0.0003

* $n = 487$ due to missing data.

Table 3
Multiple logistic regression model for odds of ART initiation within 6 months and odds of viral load suppression within 9 months.

Factor	ART Initiation (6 months)			Viral Load Suppression (9 months)		
	AOR	95% CI	p-value	AOR	95% CI	p-value
Recreational ART use	0.68	(0.29-1.60)	0.39	0.58	(0.19-1.78)	0.41
Other substance use	0.54	(0.33-0.87)	0.01	0.47	(0.25-0.89)	0.020
CD4 0-250 vs 251-350	1.14	(0.73-1.81)	0.55	0.64	(0.38-1.08)	0.094
CD4 351+ vs 251-350	1.48	(0.87-2.53)	0.15	1.07	(0.60-1.90)	0.81
Age	1.03	(1.01-1.05)	0.01	1.02	(1.00-1.05)	0.047
Female v. male	0.85	(0.58-1.26)	0.42	0.79	(0.51-1.21)	0.27
Depression (Severe/Moderate vs Mild)	1.13	(0.77-1.66)	0.54	1.12	(0.73-1.73)	0.61

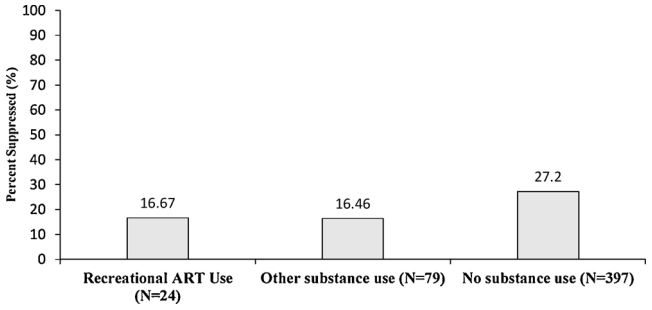

Fig. 1. Viral load suppression at 9 months stratified by type of substance use. Note. Chi-squared test for independence between groups: $p = 0.082$, between other substance use and no substance use categories: $p = 0.045$.

Fig. 1 presents viral suppression at nine months by substance use category (recreational ART use; n = 24), other substance use (illicit drug use and binge drinking; n = 79), and no reported substance use (n = 397). Viral suppression was similar across substance use groups (approximately 16% had viral suppression in each group) vs. 27.2% in the no substance use category. Viral suppression was significantly higher among those who did not report any substance use compared to those who reported other substance use (chi-squared p = 0.045), although there was not a statistically significant difference in viral suppression by nine months between the substance use groups (chi-squared p = .082). Overall during the study period, 61.6% (n = 308) of the total sample initiated ART, including 54.2% (n = 13) in the recreational ART use group and 62.0% (n = 295) in the no recreational ART use group.

4. Discussion

This study identified recreational ART use among ART naïve, treatment eligible PLWH, which was not significantly associated with ART initiation at six months, nor viral suppression at nine months among those who initiated ART. Overall in this sample, less than two-thirds (62%) of ART-eligible individuals initiated ART within six months, and of those, only one-quarter had a documented suppressed viral load within nine months (Katz et al., in press). Other substance use (binge drinking or non-ART illicit drug use), but not recreational ART use, was significantly associated with a lower odds of ART initiation within six months and viral suppression at nine months. Findings suggest that comorbid use of other substances is ultimately what may make recreational ART use problematic for ongoing engagement in care and viral suppression, as we did not find unique associations of recreational ART use with ART initiation or viral suppression.

Approximately 5% of the sample (n = 24 of 500) self-reported recreational ART use, which is likely an underestimate given social desirability biases that may contribute to lower likelihood of reporting substance use in HIV care in sub-Saharan Africa (Hahn et al., 2010; Magidson et al., 2018; Vu et al., 2011), and in South Africa specifically (Magidson et al., in press; Myers et al., 2018). Although there is more data to support the stigma and social desirability biases for other substance use (vs. recreational ART use specifically) in South Africa (Magidson et al., in press; Myers et al., 2018), there is qualitative research unique to recreational ART use in Durban, South Africa that demonstrated high rates of stigma towards individuals with recreational ART use (Grelotti et al., 2014). Indeed, prior research has shown that recreational use of ART may put an even stronger stigma on HIV-positive persons and their communities (Larkan et al., 2010) and may promote crime both involving and victimizing HIV patients (Chinouya et al., 2014; Rough et al., 2014). Despite the potential for under-reporting of recreational ART use in our sample, these findings are an important contribution to the literature given the lack of prior quantitative research on recreational ART use.

The majority of our sample who did self-report recreational ART use was almost exclusively in Soweto (vs. Cape Town), possibly indicating a geographic distribution to its use. Although there has not been extensive epidemiological work to understand patterns of recreational ART use across South Africa, and the first report of recreational ART use that we are aware of was from the Western Cape (Larkan et al., 2010), the majority of research on this topic to date has been identified in Gauteng and KwaZulu-Natal provinces (Grelotti et al., 2013; Rough et al., 2014). This may explain the small sample of recreational ART use identified overall, and especially in Cape Town. Future work is needed to understand geographic patterns of use, and recreational ART use should be tracked nationally in case it spreads in other areas.

In addition to a small sample size of individuals who reported recreational ART use, a few other limitations are noteworthy when interpreting these results. First, we relied on a self-report assessment of recreational ART use that only included two dichotomized questions. Given the lack of prior quantitative research in this area, we were not aware of any prior validated measures of recreational ART use, and we used our prior qualitative work in this area to guide our assessment (Rough et al., 2014). Future work is needed to develop and validate a measure of recreational ART use that should be guided by existing qualitative research capturing the phenomenon of recreational ART use. Additionally, we assessed lifetime recreational ART use at all time points to maximize sample size and given concerns about under-reporting; thus, we cannot make precise conclusions about the timing of recreational ART use and its relationship to viral load suppression. Finally, we used NHLS to obtain viral load and ART initiation outcomes in line with prior work that has demonstrated NHLS to be a reliable and valid source of HIV clinical information for clinical research (Fox et al., 2018, ; Maskew et al., 2017). Given our reliance on NHLS, we only have viral load data for individuals who initiated ART, and we also did not have information available on viral resistance or specific ART regimens. Although we can assume that the vast majority of patients who initiated ART were offered an EFV-based regimen (600 mg) given current practice guidelines to prescribe the same “first-line treatment” in South Africa, specific ART regimens were not accessible from NHLS for this study.

5. Conclusions

Despite the noted limitations, we believe this study offers important data to build on prior research on recreational ART use that at least in South Africa has largely relied on qualitative analysis, case reports, and media reports. Recreational ART use was infrequent and not uniquely associated with ART initiation or viral suppression. Rather, comorbid use of other substances is ultimately what may make recreational ART use problematic for ongoing engagement in care and viral suppression. Findings confirm prior work that has well-established substance use as an important predictor of HIV care outcomes in South Africa (Kader et al., 2014; Kalichman et al., 2007); given its often chronic and relapsing nature, problematic substance use can interfere with HIV care engagement throughout the continuum of care. More broadly, findings point to the need to integrate substance use screening and treatment into HIV care in South Africa, which is a timely concern and in line with national and international priorities that stress the need for integrated care models and task sharing for substance use in HIV care in South Africa (National Department of Health, 2014; World Health Organization (WHO, 2008, 2016). We hope this work leads to future epidemiological research to understand the prevalence of recreational ART use in South Africa using objective assessment of recreational ART use and its association with viral resistance.

Contributors

JFM, HSI, and ITK conceptualized the manuscript. HSI was responsible for data analysis, with input from JFM and ITK. JFM wrote the first draft of the manuscript, with contributions from KSR, HSI, and ITK. All authors provided a critical review of the manuscript and contributed to its intellectual content. All authors additionally reviewed and approved the final manuscript.

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Conflict of interest

No conflict declared.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2019.02.009.

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