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Recreational use of HIV antiretroviral medication and implications for HIV pre-exposure prophylaxis and treatment

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Abstract

Diversion of antiretroviral therapy (ART) for recreational use is concerning for countries with high HIV prevalence. This paper presents reports of recreational use of ART among adolescents from two HIV prevention studies in South Africa: 1) a cross-sectional survey of N=200 adolescents and 2) a qualitative study of pre-exposure prophylaxis with N=57 adolescents and N=25 clinicians. Among adolescents, 3% used and 14% knew someone who used non-prescribed ART for recreational purposes. Administration included smoking (71%), snorting (15%), injecting (15%), ingesting (15%), and inserting (3%). Participants predicted increased crime as recreational use of ART increased. Future studies should investigate prevalence, composition, and diversion of ART from HIV prevention and treatment.

Keywords

HIV; antiretroviral medication; whoonga; nyaope; medication diversion; South Africa

INTRODUCTION

South Africa has one of the largest HIV treatment programs in the world. With more than four million people on treatment, antiretroviral therapy (ART) is widely accessible (1). In addition to using ART to treat HIV infection, ART is crucial to the implementation of pre-exposure prophylaxis as a relatively new biobehavioral HIV prevention strategy (2). Diversion of ART for recreational use is a concern as South Africa continues to scale-up the national HIV treatment program and implement HIV treatment as prevention. Recreational use of ART may contribute to drug resistance, adherence challenges, diminished supply of lifesaving medications, and increased risk for seroconversion when used as non-prescribed medication for prevention (3–5). Recreational use may also contribute to new forms of substance use and abuse. Yet, the scientific knowledge base on the diversion of ART for recreational use is nascent, especially among adolescents.

Diversion of ART for recreational use is a phenomenon that first gained media and scientific attention in the early 2000s in two sites, the USA and South Africa (6–9). In South Africa, the use of ART as a recreational drug has been called *whoonga* (*wunga* in isiZulu) or *nyaope*. Only a handful of studies have documented recreational use of ART, primarily through qualitative methods (10–13). Prevalence of ART for recreational drug use, as well as patterns and consequences of ART misuse remains largely unknown in the USA and South Africa (11, 13). Nearly all reports of recreational use have been among adults, although we identified one study that reported use among individuals as young as 14 years of age (10).

This paper fills a gap in the literature, providing descriptive data on the emergent phenomenon of recreational use of ART among adolescents. Findings of recreational use of ART were derived from two independent HIV prevention studies. The first study focused on developing a family intervention to prevent adolescent HIV (14). The second study explored the acceptability of pre-exposure prophylaxis (PrEP) for adolescent prevention (15). Data from the two studies in South Africa were synergistic in that both focused on adolescents from the same geographic area with similar demographics. To our knowledge, this paper is one of few to report on prevalence of recreational use of ART among adolescents in a generalized epidemic setting and to characterize the possible negative consequences of diversion of ART for recreational use for the HIV care cascade.

METHODS

The two studies took place in the Cape Town metropolitan area of South Africa from 2015–2017. Quantitative data on recreational use of ART were derived from a baseline survey of N=200 adolescents recruited for a randomized pilot trial of a family intervention targeting prevention of adolescent HIV ([ClinicalTrials.gov #NCT02432352](https://clinicaltrials.gov/ct2/show/study/NCT02432352)). Participants were recruited from a study community that was split into census enumeration areas. These areas were visited in a random sequence. Within each area, each household was visited up to 3 times on random days and times with eligibility screening conducted by the study team using a smartphone programmed with eligibility criteria. Adolescents were included if they met the following criteria: 1) 13–15 years of age; 2) concurred that the adult identified was their parent (or primary caregiver in the parental role); 3) when more than one child in the

family fell within the eligible age range, one child was chosen at random; 4) lived in the household at least 4 days a week; 5) sub threshold depressive symptoms (score 9–15) using the Centre for Epidemiologic Studies Depression scale. Following written informed assent and parental consent, participants completed a survey on smartphones in isiXhosa or English based on participant preference. Interviewers administered items to participants verbally except for a subset of sensitive questions that were captured using audio computer-assisted self-interviewing (ACASI) software to reduce reporting bias; ACASI was used for recreational ART use questions. Interviews lasted approximately 1 hour. We collected sociodemographic characteristics including age, gender, race/ethnicity, and primary language. For recreational use of ART, there are no existing published psychometrically tested measures. As such, we used two questions: “Have you or someone you know ever used ARVs to get high OR another mixture of substances that you suspect may have contained ARVs to get high (this mix is sometimes called *nyaope* or *whoonga*)?” with answer options including the following: 1) you, 2) someone you know, or 3) neither I nor someone I know has done this. Participants could select more than one category of response. We focused on reports of self-use and/or knowledge of use by another. This was followed by the question, “How have you or someone you know used ARVs or mixtures of substances that you suspect may have contained ARVs to get high?” with answer options including the following: 1) smoked, 2) snorted, 3) injected, 4) swallowed, 5) inserted/absorbed, or 5) other. More than one affirmative response was possible. Participants were provided with 50 South African Rand as a stipend for participation. We conducted descriptive statistics to evaluate the prevalence of recreational use of ART and modality of administration with all analyses completed using SPSS Statistics 24 software. All study procedures were approved by an institutional review board and human research ethics committee (Brown University Protocol #1207000666, University of Cape Town Protocol # 072/2013 and 796/2014).

Qualitative data were derived from a study consisting of 10 focus groups and interviews with N=57 adolescents living with and without HIV, and interviews with N=25 clinicians working with adolescents. Adolescents were recruited from HIV treatment clinics and via door-to-door community sampling. Adolescents living with HIV were included if they were: 1) 16–17 years; 2) self-reported HIV-positive status; 3) comfortable discussing HIV status in an adolescent group. Adolescents living without HIV were eligible if they met the following inclusion criteria: 1) 16–17 years of age; and 2) self-reported HIV-negative status. Following written informed parental consent and adolescent assent, focus groups and interviews were conducted in isiXhosa or English based on participant preference. Adolescents received 150 South African Rand for participation. Clinicians were included if they met the following inclusion criteria: 1) 18 years or older; and 2) had 3 or more years of experience providing services to adolescents. An initial seed-pool of participants was generated in consultation with the study team, and these participants referred professional peers to the study. Each clinician received 300 South African Rand for participation. For both participant types, focus groups and interviews lasted approximately 1 hour, were audio-taped, and guided by a semi-structured protocol exploring acceptability of PrEP and anticipated challenges of PrEP implementation. Discussions of recreational use of ART emerged during questions probing for anticipated challenges of PrEP implementation including what community phenomenon might affect PrEP adherence, as well as what sorts of adolescent HIV risk groups clinicians

need to purposively engage in roll-out of PrEP. Thematic analysis of qualitative data was conducted using NVivo (QSR International, 2012). Data were double-coded by two independent coders using open-coding, axial coding, and coding of marginal remarks and comparisons (Strauss & Corbin, 1998). Common words, phrases, sentences, and ideas were clustered to develop a codebook. These pieces of text were compiled under specific codes and these codes were clustered to produce themes. All study procedures were approved by ethical review committees at Brown University (Protocol #1207000666) and University of Cape Town (Protocol #HREC 072/2013).

RESULTS

In the quantitative intervention development study, adolescent participants all identified as Black African with isiXhosa as their primary language, and were 56% female and 43% male. Among adolescents, 3% (n=6) reported recreational use of ART (e.g., *whoonga*). The average age of these adolescents was 14 years (ranging from 13–14 years). Adolescents reported a markedly higher level of use (14.1%) among others that they knew. The demographic details of adolescent participants appears in Table 1. Modalities of reported administration among peers included smoking (71%), snorting (15%), injecting (15%), ingesting (15%), and inserting (3%).

In the qualitative study, the average age of participants was 16 years. Most identified as Black African (97%) with their primary language being isiXhosa (93%), and with 56% female and 43% male. Nearly half (42%) identified as living with HIV. Among the clinicians, the average age was 33 years. Clinicians were a range of racial identities: 48% Black African, 40% White, 4% Coloured, and 8% other. IsiXhosa was the predominate language followed by French or isiZulu 8%, Afrikaans 4% and English 2%. Clinicians were predominately female (96% female, 4% male). Educational attainment among clinicians varied: 48% completed high school, 40% held a masters or doctoral degree or specialized medical training and 12% held a bachelor's degree. The clinicians had a range of specialties: 40% were doctors, 28% were counselors, 16% were clinical staff such as nurses, and 16% were other types of clinical staff such as psychologists.

Recreational use of ART was described by both adolescents and clinicians, providing evidence that ART was being diverted from treatment and prevention. This raises a concern that recreational use of ART may be an emerging substance of abuse among adolescents. Three key themes emerged from qualitative results. One theme was around the phenomenon of recreational use of ART including descriptions of what this emerging substance consists of and how it is administered. Both clinicians and adolescents described ART medication being bought, sold, and stolen in the community for the purpose of recreational use. For example, an adolescent noted:

Some take the ARVs and sell them. They don't take the treatment. Because they want the money. They sell them to those who smoke them. So this pill, also, if it can be 'smoked', it can make a person create his own business.

- Adolescent

Similarly, another adolescent said, “*I have heard that at the clinics, people who work there, the person take the pills and goes to sell them to drug dealers.*” A clinician similarly described, “*You find out friends are stealing the [patients] ARVs and smoke them.*”

While there was consensus on ART being used recreationally, there was little consensus about what *whoonga* was comprised of. Some participants stated that *whoonga* was comprised of ART, with service providers specifying *whoonga* included Efavirenz. Adolescents had a wide variety of answers pertaining to the content, with answers varying from “dagga” (marijuana), “tik” (crystal methamphetamine), “mandrax” (methaqualone) to TV parts. For example, an adolescent said: “*It’s tik. It’s the pill... [it’s] mandrax. Whoonga. All the stuff.*” Participants also described that the main motivation for *whoonga* use was for the drug’s psychotropic effects. Unlike the quantitative data that emerged from the intervention study described previously, all of the participants who discussed *whoonga* use in the qualitative study described *whoonga* as being smoked. For example, an adolescent described, “*They do smoke ARVs. Even this other one [contraceptive implant], they extract it and smoke it. They say the hooligans cut with a blade and take it.*” Of interest is that this particular adolescent describes a possible phenomenon of contraceptive implants being used for recreational substance use, similar to ART.

A second theme was around the consequences of diversion of ART from use as a life-saving medication to recreational drug use. Participants viewed this diversion as a challenge to controlling the HIV epidemic. In regards to community control of the HIV epidemic, participants noted:

The HIV rate increases because the pills are being stolen by the Amaparapas, to smoke them. So HIV increases. [The amaparapas are] those people who are smoking those pills. It’s those taxi guys, the ones who are helping people get into the taxis. They are the Amaparapara.

– Adolescent

Adolescents described a range of concerns with recreational use of ART. For example, adolescents feared that the phenomenon of recreational use of ART would increase crime in their community.

Maybe this drug, perhaps makes the crime rate to go high, in some way. Because some people, there tends to be new pills like this arriving. Some people [think]: ‘Yo! This is another drug that is terrific more so than the one I’m using’ and decides to tag on it. So much that the ones who are smoking the ARVs will stop smoking the ARVs and move on to this new PrEP. They want to see what it could do to them. Perhaps it’ll be even more. Its chemical composition may be higher than that of the ARVs.

- Adolescent

Thus, the recreational use of ART has potentially serious impacts upon crime and safety.

A third and final theme focused on the implications of recreational use of ART on HIV prevention and treatment efforts. For example, clinicians described how concerns about recreational use of ART negatively impacted their excitement about prescribing or

supporting future prescription of HIV treatment as prevention, or PrEP. Clinicians noted that they were less likely to prescribe PrEP to adolescent patients already engaged in substance use - a high risk population that could benefit from PrEP - due to concerns that PrEP would be diverted towards recreational substance use.

So in somebody who was abusing substances and dealing drugs and had conduct or antisocial personality traits, I would worry prescribing to them that they're actually just going to divert the medication for illicit purposes.

- Clinician

Adolescents also feared that this emerging substance use phenomenon would make them targets of crime if they were on ART for treatment or were to use PrEP.

Like, the thugs you see, they want something from you. Then they don't find it. They find these pills. Then they take those pills, [take] them with them to sell them. Others smoke them. So, then it's not good to [take] them with me [when] going to the boyfriend's. I will [take] them at home, then go to my boyfriend's.

- Adolescent

Thus, recreational use of ART has implications for individuals taking ART for treatment while living with HIV as well as for those not living with HIV but who would benefit from taking ART for HIV prevention.

DISCUSSION

Few studies have categorized recreational use of ART among adolescents in generalized epidemic settings or in the context of PrEP implementation. Findings from these two studies document a new emerging substance use phenomenon of recreational use of ART among adolescents and those they know, supporting a broader consensus that recreational use of ART occurs in South Africa. Thus far, our quantitative data reveals relatively low prevalence of recreational ART use. Nonetheless it is concerning given the young age range of participants. Similar to others studies, participants reported recreational ART administration via smoking and ingestion but there were some new modalities of administration that emerged from our data including snorting, injecting, and inserting. Some limitations of our data include the inability to disaggregate whether modalities reported were by adolescents or observed among other users, and lack of information on the demographic characteristics of other users as reported by adolescent participants. Although the prevalence of use by self and others was relatively low in our quantitative adolescent sample, qualitative findings provide a more holistic picture of the range of potential concerns that diversion of ARTs may pose if this emerging phenomenon of substance use grows in size. Specifically, our qualitative findings raise a range of concerns relating to recreational use of ART. There are therapeutic and preventive consequences relating to diversion of ART for recreational drug use including HIV medication resistance and non-adherence. Recreational use of ART also underscored concerns regarding crime and safety. Furthermore, qualitative findings indicated that there were apprehensions regarding whether PrEP would contribute to an emerging epidemic of a new psychoactive substances affecting acceptability and willingness to prescribe PrEP among clinicians, and acceptability among target users such as adolescents.

At the time of both studies, PrEP had not yet been approved for use in South Africa, but now is. The potential for diversion of ART for recreational use may grow as PrEP becomes more widely available for prevention in South Africa. Acceptability and uptake among PrEP prescribers and target users can be managed through careful consideration for formulation and delivery sites. For example, roll-out and messaging about PrEP may need to address concerns regarding community violence and crime, and certain PrEP formulations may be less likely to be diverted such as injectable versions rather than implant or pill versions of PrEP.

CONCLUSIONS

Emergent findings from these adolescent HIV prevention studies focused on a global priority site for HIV prevention, and indicate several new directions for research. First, more studies are needed to characterize the prevalence and administration of recreational use of ART as a substance of abuse. Developing this line of research will contribute to a more robust evidence base on the prevalence of recreational use of ART and administration modalities, especially with younger populations. Second, studies are needed for integrated substance and HIV prevention efforts. This line of research should include efforts to ensure widespread integration of screening of drug use into existing HIV prevention practices. Similarly, research on effective practices for prescription of ART as treatment or prevention is needed to diminish the diversion of ART for recreational drug use, and to limit the negative ramifications that diversion could have for non-adherence and medication resistance among individuals using ART for treatment and prevention. Third, more studies are needed that systematically analyze the composition of emerging new psychoactive substances such as *whoonga*. Determining the composition of *whoonga* has been challenging due to the logistics of systematically and ethically obtaining these samples. Rigorous measurement of composition is also challenging because of the diversity of what *whoonga* actually is, and how those various chemicals might be metabolized in blood, urine, and hair samples. Studies have not yet established the exact composition of this substance but it is thought to be ART alone, or a drug cocktail containing a mix of ART with illicit substances such as heroin (or other opioids), marijuana, methamphetamine, and household products such as detergent, and rat poison. Not all ART has psychotropic effects but qualitative and clinical studies have documented psychotropic effects for Efavirenz, ranging from mania, depression, suicidal thoughts, hallucinations, to psychosis (10, 11, 16, 17). Without further research on composition, we will not be able to determine whether *whoonga* is comprised of certain types of ART, mixed with other psychoactive substances, cut with cheap bulking agents, or a re-labeling of other drugs. Developing new methods for securing and analyzing samples will allow us to better understand the scope of abuse liability – including both the psychoactive effects of ART alone or drug-drug interactions between ART and other drugs or non-traditional substances. Fourth, there is a need for further studies to understand new modalities of recreational use of ART, and the implication for the HIV epidemic. For example, the emergence of injection as a new modality for recreational use of ART may lead to a surge in HIV transmission as well as an increase in blood-borne diseases such as hepatitis which may complicate treatment of HIV. Finally, findings underscore a need to expand studies on possible diversion of ARTs for recreational use among adolescents.

Characterizing the scope and scale of recreational ART use among this younger age group offers many new avenues for prevention with a range of lifelong health benefits.

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Table 1.

Participant demographic characteristics (N=200)

Characteristic	Non use (n=151)*	Use by self, but not others (n=6)	Use by self and others (n=34)
Age, mean (SD), years	14.2 (SD = 0.81)	14.2 years (SD = 0.27)	14.5 years (SD = 0.71)
Gender			
<i>Male</i>	44.9%	50.0%	50.0%
<i>Female</i>	55.1%	50.0%	50.0%

* n=13 refused to answer and n=2 were missing data

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