Risk and protective factors for *whoonga* use among adolescents in South Africa

Teresa DeAtley[a,*], Catherine Mathews[b], Dan J. Stein[b], David Grelotti[c], Larry K. Brown[d,e], Danielle Giovenco[f], Millicent Atujuna[g], William Beardslee[h], Caroline Kuo[a,b,e]

[a] Brown University School of Public Health, Department of Behavioral and Social Sciences Brown University School of Public Health, 121 S Main St, Providence, Rhode Island 02903, USA
[b] University of Cape Town, Department of Psychiatry and Mental Health & South African Medical Research Council, Unit on Risk & Resilience in Mental Disorders, Groote Schuur Hospital, Anzio Road, Observatory, Cape Town 7925, South Africa
[c] University of California San Diego, Department of Psychiatry, 220 Dickinson Street, Suite B, San Diego, CA 92103, USA
[d] Alpert Medical School of Brown University, Department of Psychiatry and Human Behavior, 222 Richmond St, Providence, Rhode Island 02903, USA
[e] Providence/Boston Center for AIDS Research, 164 Summit Avenue CFAR Building, Room 134, Providence, Rhode Island 02906, USA
[f] University of North Carolina at Chapel Hill, Department of Epidemiology, 135 Dauer Drive, 2101 McGavran-Greenberg Hall, CB #7435, Chapel Hill, NC 27599-7435, USA
[g] Desmond Tutu HIV Foundation, P.O. Box 13801, Mowbray, 7705 Cape Town, South Africa
[h] Boston Children's Hospital & Judge Baker Children's Center & Harvard Medical School, Department of Psychiatry, 53 Parker Hill Ave, Roxbury Crossing, MA 02120, USA

ABSTRACT

Background: Antiretroviral therapy (ART) is publicly available in South Africa
in response to the urgent need to address HIV and AIDS. Off-label use of ARV medication alone or in combination with other substances is known as "*whoonga*" and "*nyaope*" in South Africa. Diversion of ARVs for whoonga use is not well understood, especially among adolescents. This secondary analysis explores risk and protective factors for adolescent *whoonga* use in a community-based HIV endemic setting.
Methods: Data on *whoonga* use were derived from a baseline survey of N = 200 adolescents recruited for participation in a randomized controlled trail to reduce adolescent HIV risk behaviors and depression. Risk and protective factors for adolescent *whoonga* use were explored using an ecological systems framework using one-way ANOVAs, chi-squared tests and hierarchical regression.
Results: Individual level factors increased the odds of *whoonga* use or known use such as child age OR:1.22 (95% CI, 1.03–1.43), hazardous drug use OR:1.62 (95% CI, 1.02–2.59), and hazardous alcohol OR:1.80 (95% CI, 1.05–3.09). Food insecurity appears to have a slightly protective effect on the odds of *whoonga* use or reports of use among people adolescents knew OR:0.649 (95% CI, 0.541–0.779).
Conclusions: Larger epidemiological studies should expand the surveillance of hazardous alcohol use and illicit drug use, specifically for recreational use of prescription medication. Granular data is warranted to characterize the patters of use, especially among highly vulnerable populations. Future surveillance studies that explore these multi-level relationships are warranted to further understand this phenomenon among teens in South Africa.

1. Introduction

South Africa has the largest country population of individuals living with HIV (UNAIDS, 2014). Antiretroviral therapy (ART) medication is widely available through large public sector roll out (Jain & Zorzi, 2017; Chin, Sangmanee, & Piergallini, 2015). ART was initially being used for treatment but now is increasingly being used as pre-exposure prophylaxis (PrEP) for HIV prevention. In parallel with efforts to increase the availability of HIV prescription medication in South Africa for treatment and prevention, there has been an emergence of a new substance use phenomenon with a drug known as *whoonga* (or *wunga/*

nyaope). Diversion of ART for recreational use has also been documented in the United States (Eban, 2005; Grelotti, Closson, & Mimiaga, 2013).

There is limited consensus on the chemical composition of *whoonga*. The chemical composition is likely to vary by context and change over time. It is thought that *whoonga* contains ART medication mixed with detergent, rat poison, marijuana, and/or methamphetamine. While not all ART has neuropsychiatric effects, efavirenz has documented neuropsychiatric effects including hallucinations, psychosis and mania (Grelotti et al., 2014; Mimiaga et al., 2015; Rough et al., 2014), likely a result of agonism of the 5-HT(2A) receptor, the serotonin receptor

implicated in mediating the psychoactive effects of lysergic acid diethylamine (LSD) (Gatch et al., 2013).

Diversion of ART for recreational substance use is especially concerning for adolescents. The 2011 Youth Risk Behavior Survey reported that adolescent illicit drug use was highest for cannabis/daga (12.5%) followed by prescription drugs (11.5%) and inhalants (11.5%). Mandrax, heroin, club drugs, tik and *whoonga* self-reported ever use ranged from 4.5 to 5.5% (Reddy, 2013). Early experimentation with drugs can intensify use and place adolescents at increased risk for substance use dependence in adulthood (Grant & Dawson, 1998; Van Ryzin & Dishion, 2014; Wang et al., 2014).

Of the reports, we identified on this emergent phenomenon, only one reported *whoonga* use among adolescents (Grelotti et al., 2014). Much remains unknown on the patterns and risk factors for *whoonga* among adolescents (Rough et al., 2014). In this paper, we report on one of few studies to examine this phenomenon in a community-based sample of adolescents from a community with high prevalence of HIV. We utilized ecological systems theory to understand how multiple environments influence adolescent *whoonga* use (Bronfenbrenner, 1979) and to examine risk and protective factors in three levels of the adolescent ecosystem, 1) individual, 2) interpersonal, and 3) community. This approach has been previously used to understand adolescent substance use among Zambian street youth (Tyler et al., 2016).

2. Methods

This paper utilizes data from *Our Family Our Future,* a pilot randomized controlled trial (RCT) designed to explore the acceptability and feasibility of an intervention to reduce adolescent HIV risk behaviors and depression. Data on *whoonga* use were derived from the baseline survey of N = 200 adolescents recruited for participation in the RCT.

The RCT took place during 2015–2017 in a community in Cape Town, South Africa. An institutional review board approved all study protocols. Adolescents were recruited house-to-house within randomly selected enumeration areas. Adolescents were eligible to participate if they were between the ages of 13–15 years, lived in the household at least four days a week, confirmed that the adult was either a primary caregiver or parent, and met a threshold for elevated depressive symptoms. Parent or guardian and adolescents provided written informed consent. Adolescents completed a survey in English or isiXhosa using smartphones. Surveys occurred in participant's homes. Interviewers administered non-sensitive behavioral questions by reading questions and answer options off a smartphone and entering answers. Sensitive questions including questions on recreational ARV use were administered through Audio Computer-Assisted Self-Interviewing (ACASI). In this process participants were given headphones attached to a smartphone. Participants were provided pre-recorded audio of questions and answer options and provided their answers in complete privacy.

2.1. Measures & analysis

Since *whoonga* is an emergent drug phenomenon there were no previously validated measures to pull from. *Whoonga* use was captured using the following question: "Have you or someone you know ever used antiretroviral medication (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*)?" Response options were: 1) you, 2) someone you know or 3) neither I nor someone I know has done this.

In addition to *whoonga* use, administration modality was captured using the following question: "How have you or someone you know used ARVs or mixtures of substances that you suspect may have contained ARVS to get high?" Possible response options were: 1) smoked, 2) snorted, 3) injected, 4) inserted/absorbed, and 5) swallowed.

Risk and protective factors were organized into three levels using

the ecological systems theory framework informed by current scientific evidence base on adolescent substance abuse and analyzed using hierarchical regression.

2.1.1. Individual level measures

2.1.1.1. The Alcohol Use Disorders Identification test (AUDIT-C). The AUDIT-C is a 3-item version of the full AUDIT scale (Bush, Kivlahan, McDonell, Fihn, & Bradley, 1998). Studies have found high comparability between the AUDIT-C and the full AUDIT (Reinert & Allen, 2007). AUDIT-C identifies frequency and quantity of hazardous drinking. A cutoff score of three or more drinks for girls and four or more drinks for boys was used per standardized scoring convention for the scale (Morojele et al., 2016).

2.1.1.2. Drug use Disorders Identification test (DUDIT). The 11-item DUDIT) was used to assess current substance use among adolescents. This scale focused on frequency of drug use, physical and psychological problems and symptoms of dependency (Berman, Bergman, Palmstierna, & Schlyter, 2005; The Drug Use Disorders Identification Test Manual). We followed the standard scoring which identifies men with drug-related problems at a cut-off score of 6 or more and women with at a cut-off score of 2 points or more. In our sample, these scores were dichotomized for hazardous drug use yes or no, following previous studies (The Drug Use Disorders Identification Test Manual). This scale has been validated for use among adolescents (Matuszka et al., 2014).

2.1.2. Relational level measure

2.1.2.1. Parent monitoring questionnaire (PMQ). The PMQ is a 15-item questionnaire that assesses three sources of parental knowledge about adolescents' routine activities (child disclosure, parental solicitation, and parental control) (Kerr and Stattin, 2000). Of the three subscales, the PMQ disclosure subscale was included into our hierarchical regression based on Table 1.

2.1.2.2. The Parent Adolescent Communication Scale (PACS). The PACS (Olson, 1985) is at 20-item questionnaire that assesses communication quality between adolescents and parents. In this study, the adolescent filled out the questionnaire in relation to one parent or guardian. This scale has two subscales which were usesdin this study, Open Family Communication (OFC) and Problems in Family Communication (PFC). Following the existing scoring approach, raw scores were used in our aalysis because of our inclusion of the subscales (Houck, Rodrigue, & Lobato, 2007). Of the two subscales, the OFC subscale was included in our hierarchical regression (Table 1).

Table 1
Anova and chi-squared test for associations.

DV	IV	P-value
Baseline Child Whoonga use	Child age	**0.007***
	AUDIT-C	**0.000***
	DUDIT	**0.000***
	CESDD	0.100
	CONDUCT	0.255
	Parental Monitoring subscale	0.469
	Parental Monitoring Solicitation subscale	0.280
	Parental Monitoring Control subscale	0.899
	Parental Monitoring Disclosure subscale	**0.028***
	Connor Davidson-Resilience Scale	0.728
	Parent Adolescent Communication Scale – Problems	0.302
	Parent Adolescent Communication Scale – Openness	**0.019***
	Any lifetime sex	**0.000***
	Exposure to community violence	0.320
	Food Insecurity Index	**0.000***

*p value less than 0.05.

2.1.2.3. Lifetime sex exposure. Adolescents were asked to self-report sexual history including oral, anal and vaginal sex (if applicable). A composite measure was created using these three questions and a summary frequency was derived for each individual. These questions were derived from questions used by the Adolescent Medicine Trials Network for HIV/AIDS Interventions (National Institutes of Health Office of AIDS Research, 2019).

2.1.3. Community level measure

2.1.3.1. Food Insecurity index. A food insecurity index was created using the following four questions. An aggregate sum of all questions was derived, summary scores ranged from 0 to 4 for each parent. Respondents were categorized as low (summary value of 0), moderate (summary values of 1, 2, or 3) or high (summary value of 4) on the food insecurity scale.

2.2. Analysis

We tested every scale or index using one-way ANOVAs and chi-squared tests for association to describe the relationship with baseline adolescent *whoonga* use as an outcome (with the three levels as described above). Based on the results in Table 1, the following six measures were included in our hierarchical regression, child age, AUDIT-C, DUDIT, Parental Monitoring Disclosure Subscale, Parent Adolescent Communication, Open Family Communication subscale, any lifetime sex and the Food Security Index based on a p-value cut-off of less than 0.05 for statistical significance. Hierarchical variables were coded to align to the ecosystem model. All beta coefficients and 95% confidence intervals were exponentiated so that results could be reported in odds.

3. Results

3.1. Patterns of whoonga use

Adolescent participants were an average age of 14.1 years. All identified as Black African with isiXhosa as their primary language. There were 56% females and 43% males in our sample. Three percent of adolescents (n = 6) reported use of off-label ART for recreational use. Adolescent's reports of *whoonga* use among others were notable higher (14.1%). Among those who reported recreational ART use, either themselves or by others, it was most commonly smoked (71%) followed by snorting (15%), injecting (15%), ingesting (15%), and inserting (3%).

3.2. Hierarchical regression

Results from the hierarchical regression models are shown in Table 2. The R-squared value did improve as levels of the ecological systems theory were added but we were less concerned with model fit, as this analysis is exploratory. A number of meaningful relationships held between the tests for association and hierarchical regression models. Namely, child age, hazardous drug use, hazardous alcohol use and food insecurity.

Individual level factors increased the odds of *whoonga* use such child age, hazardous drug use, and hazardous alcohol. The reported odds of self-reported *whoonga* use or known use were OR:1.22 (95% CI, 1.03–1.43) among adolescents that were older. The odds of *whoonga* use were OR: 1.80 (95% CI, 1.05–3.09) higher among adolescents that reported hazardous alcohol use and were OR:1.62 (95% CI, 1.02–2.59) higher among adolescents that reported hazardous drug use. Food insecurity appears to have a slightly protective effect on *whoonga* use or reports of use among people adolescents knew OR: 0.649 (95% CI, 0.541–0.779). Ideally, in other studies we could see if these relationships are more pronounced and if the directionality holds within a data set with a larger sample of *whoonga* users.

4. Discussion

Our findings highlight that there are multilevel factors that influence *whoonga* use among adolescents in South Africa. Individual level risk behaviors such as drug and alcohol use slightly increased the odds of *whoonga* use or reports of use among people adolescents knew. This makes sense as risk for behaviors like substance use or other illicit drug use may be associated with more risk for *whoonga* use which adolescents tend to experiment with growing age. These factors may be suited as targets for future intervention should these relationships be found more pronounced in larger surveillance studies. Food insecurity as a protective factor for *whoonga* is difficult to interpret and would need to be explored further; it is possible that this may relate to poverty, and the lack of disposable income to purchase *whoonga*.

With more people starting treatment for HIV and the introduction of PrEP using emtricitabine-tenofovir disoproxil fumarate, the undeniable growth in ART use highlights the urgency to determine the magnitude of the public health problem posed by *whoonga*. Should this drug phenomenon continue to emerge, it may gain traction given the widespread availability of ARVs in South Africa. Future surveillance studies are needed to track *whoonga* use. Specifically, we need to more effectively characterize this emerging illicit drug phenomenon by developing psychometrically validated measures to capture frequency of use and administration modality. Second, we need to develop methods to

Table 2
Hierarchical Regression for Adolescent Whoonga use.

Variables	Model 1				Model 2				Model 3			
	β	95% CI		P value	β	95% CI		P value	β	95% CI		P value
Individual Level		Low	High			Low	High			Low	High	
Child Age	1.19	1.01	1.40	**0.039***	1.12	1.01	1.42	**0.037***	1.22	1.03	1.43	**0.019***
AUDIT-C	1.87	1.06	3.27	**0.029***	1.77	1.01	3.11	**0.046***	1.80	1.05	3.09	**0.032***
DUDIT	1.70	1.07	2.70	**0.025***	1.61	0.99	2.63	0.053	1.62	1.02	2.58	**0.040***
Relational level												
PMQ (Disclosure subscale)					0.999	0.980	1.02	0.935	0.999	0.981	1.02	0.999
PACS (Openness subscale)					0.805	0.660	0.982	**0.032***	0.842	0.696	2.76	0.075
Any lifetime sex					0.997	0.966	1.03	0.874	0.997	0.967	1.03	0.838
Community Level												
Food Insecurity									0.649	0.541	0.779	**0.000***
Adjusted R squared		0.105				0.131				0.226		

*p value less than 0.05.

examine the chemical composition of *whoonga*. Third, this phenomenon needs to be tracked starting early in the life course of adolescence to determine if and how it may affect an ART referral, use and adherence, and to support prevention efforts for substance use. Use of ART as a lifesaving drug should not waver. However, our results indicate that further study of this emerging substance of abuse is vital as countries transition for the use of ART for treatment to ART for prevention in regards to drug supply as well as risk for drug resistance.

These findings have a few notable limitations. This sample may be less representative of the overall adolescent population in South Africa given the elevated levels of depression that adolescents were recruited in this study. Overall, our sample size for *whoonga* use was small, as such our R-squared measures should only be interpreted as pseudo R-squared. Nonetheless, we feel this data is of value in identifying emergent trends in adolescent substance use.

5. Conclusion

Larger epidemiologic studies should expand upon the surveillance of substance use, specifically for recreational use of prescription medication. Granular data is warranted to characterize the patters of use, especially among highly vulnerable populations like adolescents. Expanding surveillance on this category of drug will allow us to track patterns of use for *whoonga* and other meaningful proxies that may not typically be captured in surveillance studies beyond food insecurity and hazardous drinking such as social/familial support. Surveillance studies that are powered to further explore these multi-level relationships are warranted to further understand this phenomenon among adolescents in South Africa.

6. Role of funding sources

7. Contributors

Teresa DeAtley was the lead writer on this publication and was responsible for the analysis. Dr. Caroline Kuo is the senior author and supervised all steps of the analysis and writing. Drs. Catherine Mathews, Dan J. Stein, David Grelotti, Larry K. Brown, Millicent Atujuna, William Beardslee and Ms. Danielle Giovenco, were coauthors that provided meaningful input and revisions throughout the publication preparation.

CRediT authorship contribution statement

Teresa DeAtley: Formal analysis, Conceptualization, Methodology, Writing - original draft. **Catherine Mathews:** Writing - review & editing. **Dan J. Stein:** Writing - review & editing. **David Grelotti:** Writing - review & editing. **Larry K. Brown:** Writing - review & editing. **Danielle Giovenco:** Writing - review & editing. **Millicent Atujuna:** Writing - review & editing. **William Beardslee:** Writing - review & editing. **Caroline Kuo:** Funding acquisition, Conceptualization, Methodology, Supervision, Writing - review & editing, Resources, Validation.

Declaration of Competing Interest

The authors declare that there are no conflicts of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.abrep.2020.100277.

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