



Published in final edited form as:

Lancet Infect Dis. 2013 January ; 13(1): 10–12. doi:10.1016/S1473-3099(12)70294-3.

Pretreatment HIV antiretroviral exposure as a result of the recreational use of antiretroviral medication

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The international community has overcome many obstacles in making HIV antiretroviral (ARV) medication available globally, but ARV resistance in treatment-naïve individuals remains an implementation challenge. The subject of many recent reports,¹⁻³ worries about that pretreatment ARV resistance is related to treatment failure and that further increases in the rates of pretreatment ARV resistance might “jeopardise the global HIV response”.^{1,2} Largely attributed to transmitted resistance, pretreatment ARV exposure such as inadequate treatment outside of sanctioned care networks is believed to be a contributing factor.³ While investigating HIV-risk behaviour in South Africa,⁴ we learned of a preventable form of pretreatment ARV exposure that has gone largely unreported and may accelerate rates of pretreatment ARV resistance: the recreational use of ARVs referred to by our informants as “whoonga”.

Whereas whoonga has received significant media attention since 2010, the first and only report in the medical literature documenting the recreational use of ARVs appeared years earlier from the United States. In discussions with HIV-infected individuals in Miami about prescription drug diversion, Inciardi and colleagues learned that some individuals abuse efavirenz for its “intoxicating” effects and use ritonavir to enhance the effects of illicit drugs such as methamphetamine and 3,4-methylenedioxymethamphetamine (MDMA/ecstasy).⁵ Claims about the psychoactive effects of these ARVs are supported by scientific case reports.^{6,7}

Similar ARV abuse patterns in South Africa have been reported in the social science literature and news media. Larkan and colleagues provide an account of individuals smoking efavirenz in Western Cape and summarise media reports that ARVs are combined with illicit drugs such as opiates, methamphetamine, and/or marijuana to make drug cocktails.⁸ Whoonga, believed to be one such cocktail, brought media attention to the problem of recreational ARV use in Kwazulu-Natal because of its addictive potential, its association with criminal activity, and the challenge it posed to ARV rollout.⁹ Even local experts who

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Authors' contributions: We declare that we have no conflicts of interest. We thank Jennifer Mitty for her helpful comments on an earlier draft.

maintain that whoonga is heroin and does not contain ARVs acknowledge that a number of South African drug abusers use ARVs recreationally.¹⁰

Although essentially a substance abuse problem, the implications for HIV treatment are broad. For example, diversion of ARVs, in addition to impacting adherence, reduces ARV supply and limits access to treatment. Criminal behaviour related to diversion of ARVs endangers patients and healthcare providers while deterring others from seeking care. Finally, the recreational use of ARVs further stigmatises HIV-infected patients and their communities and may undermine donor willingness to fund ARV treatment.⁸

In addition to these impacts, when untreated HIV-infected individuals are exposed to ARVs recreationally, they are at risk for acquiring resistance.⁸ Mutations conferring resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs) such as efavirenz are among the most common in individuals with pretreatment ARV resistance.¹⁻³ Interestingly, serum concentrations of ARVs including efavirenz have been detected in some HIV-infected individuals with pretreatment ARV resistance who deny prior history of ARV treatment.³ To help explain some of these findings, researchers may wish to inquire specifically about recreational ARV use or use of drug cocktails when assessing pretreatment ARV exposure.

Expanding pretreatment ARV resistance screening will help to minimize the risk that this form of pretreatment ARV exposure poses; however, a comprehensive strategy to investigate this problem also involves expanding substance abuse research. Existing substance abuse surveillance methods have not reported on the phenomenon,^{11,12} and they may need to be improved if we are to understand the extent of pretreatment ARV exposure from recreational ARV use. Systematic research is also needed to explore the chemical makeup of South African street drugs, the abuse liability of ARVs, and the bioavailability and likelihood of developing resistance when ARVs are smoked or otherwise administered inappropriately.

Given the high prevalence and complex medical, psychosocial, and political context of HIV in southern Africa, it is important that treatment strategies adapt to emerging issues like recreational ARV use. We may decrease the recreational use of ARVs, decrease drug diversion, and improve adherence to HIV treatment if we avoid ARVs used recreationally when developing ARV treatment guidelines or distribute ARVs to patients in a way that minimizes the potential for misuse. The recreational use of ARVs also serves as a reminder that ARV treatment is not synonymous with HIV treatment and demonstrates the importance of access to effective community-based mental health and substance abuse services.

Acknowledgements

Role of funding sources: The authors receive salary support from the National Institute of Health. No funding source provided payment to write this manuscript or submit it for publication. As corresponding author, Dr. Grelotti had final responsibility for the decision to submit this manuscript for publication.

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