

Letter to the Editors

RE: Severe mental illness at ART initiation is associated with worse retention in care among HIV-infected Ugandan adults by JM Nachega *et al.* (2013), *TMIH* 18, pp 53–57

Dear Sirs,

We thank Shailendra Kapoor for his commentary on our publication titled ‘Severe mental illness at antiretroviral therapy (ART) initiation is associated with worse retention in HIV care among Ugandan adults’ (Nachega *et al.* 2013). The primary goal of that work was to investigate the association of severe mental illness (SMI) with retention in HIV care. The substantial amount of research findings that point to an association between efavirenz use and psychiatric symptoms (Kenedi & Goforth 2011), and the report by Kapoor compelled us to carry out additional analyses to determine whether efavirenz use had any effect on our previously observed association between severe mental illness (SMI) and retention in HIV care.

Only 7.8% of our study sample used efavirenz. Bivariate analysis indicates that HIV-positive individuals with an SMI diagnosis were significantly less likely to be initiated on an efavirenz-based ART regimen (Odds ratio = 0.15, 95% CI 0.05–0.50, $P = 0.002$). To determine whether efavirenz use modified the association between SMI and retention in HIV care, we conducted multivariate Cox hierarchical proportional hazards regression analyses (Table 1). Interestingly, we found that efavirenz use modified the association between SMI and retention in HIV care. Specifically, as shown in Table 1, among people not taking efavirenz, SMI was weakly associated with interruption of continuous HIV care (adjusted hazard ratio, aHR 1.38, 95% CI 1.08–1.77), but among people taking efavirenz, SMI was

associated with a sixfold higher risk of interruption of care (aHR 6.98, 95% CI 1.55–31.37, p for interaction = 0.006).

While these observational results cannot demonstrate causality, we postulate that, in people with pre-existing SMI, efavirenz could lead to or exacerbate primary psychiatric symptoms leading to relapses, readmissions on psychiatric wards or alternative sources of care which would result in interruption of continuous HIV care. The current standard of care for first-line treatment of HIV in most ART delivery programmes in Africa – and that recommended by the World Health Organization (WHO) – is efavirenz-based ART (WHO HIV Treatment Guidelines 2013). For patients with a history of psychosis or who develop psychosis symptoms, alternative ART regimens (e.g. nevirapine-based ART) are recommended.

Also, our results underscore the need for targeted education and close clinical monitoring of patients on efavirenz to allow appropriate management in the event of occurrence of psychosis or aggravation of pre-existent psychiatric symptoms. More research in sub-Saharan Africa is urgently needed to gain better insight into the effects of ART regimens on mental health of HIV-positive individuals, particularly in the light of the mounting evidence that some ART regimens are associated with psychiatric symptoms (De la Garza *et al.* 2001; Foster *et al.* 2003; Poulsen & Lublin 2003) which in turn are associated with poor HIV treatment outcomes (Nakimuli-Mpungu *et al.* 2012).

Table 1 Multivariate Cox proportional hazards analysis of the association of SMI with retention in HIV care by Efavirenz use

Characteristic	Efavirenz users ($N = 60$)		Non-efavirenz users ($N = 713$)	
	HR (95% CI)	P -value	HR (95% CI)	P -value
Severe mental illness	6.98 (1.55–31.37)	0.011	1.38 (1.08–1.77)	0.010
Age, years	1.04 (0.97–1.11)	0.287	0.98 (0.97–0.99)	0.045
Female gender	.94 (0.52–1.68)	0.823	0.98 (0.88–1.09)	0.773
CD4 count < 200 cells/ μ l	1.66 (0.60–4.57)	0.329	1.42 (1.11–1.83)	0.005
Wasting syndrome	0.57 (0.19–1.64)	0.293	1.46 (1.16–1.82)	0.001

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References

- De la Garza CL, Paoletti-Duarte S, Garcia-Martin C & Gutierrez-Casares JR (2001) Efavirenz-induced psychosis. *AIDS* **15**, 1911–1912.
- Foster R, Olajide D & Everall IP (2003) Antiretroviral therapy-induced psychosis: case report and brief review of the literature. *HIV Medicine* **4**, 139–144.
- Kenedi CA & Goforth HW (2011) A systematic review of the psychiatric side-effects of efavirenz. *AIDS and Behavior* **15**, 1803–1818.
- Nachega JB, Mutamba B, Basangwa D *et al.* (2013) Severe mental illness at ART initiation is associated with worse retention in care among HIV-infected Ugandan adults. *Tropical Medicine & International Health* **18**, 53–57.
- Nakimuli-Mpungu E, Bass JK, Alexandre P *et al.* (2012) Depression, alcohol use and adherence to antiretroviral therapy in sub-Saharan Africa: a systematic review. *AIDS and Behavior* **16**, 2101–2118.
- Poulsen HD & Lublin HK (2003) Efavirenz-induced psychosis leading up to involuntary detention. *AIDS* **17**, 451–453.
- WHO (2013) Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. <http://www.who.int/hiv/pub/guidelines/arv2013/download/en/index.html>