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Using the side door: non-linear patterns within the HIV treatment cascade in Zambia

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BACKGROUND

The HIV care and treatment cascade has typically been understood to consist of a linear process starting with HIV testing and counseling, linkage to pre-antiretroviral therapy (ART) care, and ultimately linkage to ART.

Using modeled projections, investigators have noted potential gaps in the care and treatment cascade.[1] Although many patients are recorded as presenting late in their illness, there are high rates of loss to follow-up earlier in the cascade. There appears to be a high likelihood that some individuals are re-presenting to care after dropping out at an earlier stage of the cascade – a phenomenon dubbed the "side door" to the care and treatment cascade. The side door is an entry point for those who may have been previously tested or in care and treatment who have dropped out for some period of time, and who may be re-presenting lower down in the cascade, likely in a sicker state.

Although numerous studies have assessed the characteristics of those patients becoming lost to follow-up, very little is known globally or in Zambia about patients who re-present for care through a side-door. Our objective was to empirically evaluate the frequency and characteristics of this phenomenon, the predictors of re-presentation, and the clinical effects of this gap in care among patients on ART in a large ART program in Zambia.

METHODS

Our analysis cohort comprised treatment-naïve, HIV-infected adults (≥15 years) initiating ART across 18 Lusaka sites Jan. 2002 – Feb. 2008, and included follow-up for their first 3 years on ART.

Individuals were divided into 3 groups based on their outcomes at 3 years post-ART initiation, including those:
1) remaining on treatment,
2) >60 days late for a scheduled visit but not returning, and
3) >60 days late for a scheduled visit but "re-presented" into care.

The frequency of re-presentation for those in the re-presentation group (group 3) was enumerated, and baseline characteristics were compared between the 3 groups.

A multivariable logistic model was constructed among those LTFU (groups 2 and 3), with a dependent variable of re-presentation/ continued loss and covariates including baseline characteristics.

Among those patients re-presenting after first loss, clinical status (based on body mass index (BMI), hemoglobin (Hb), CD4 cell count, WHO stage, active tuberculosis (TB) and pregnancy) was ascertained within a window of up to 240 days prior to classification as lost to follow-up, and within 60 days of re-presentation. Clinical status was compared prior to loss and at re-presentation.

RESULTS

48,126 patients were included in the analysis, with median age 34 (IQR29, 41), 61% women, and median CD4 at initiation of 132 (IQR 66, 205). Among those who were >60 days late for a scheduled visit (n=28,417), 65.4% never returned, 27.8% had one re-presentation episode, 5.3% had two re-presentation episodes, and 1.3% had three representation episodes (Figure 1).

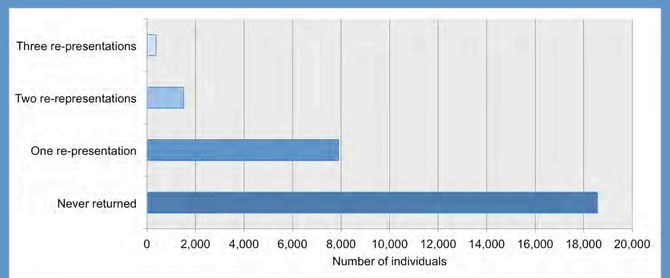


Figure 1. Number of re-presentations among those individuals >60 days late for a scheduled visit

The period of loss between **first loss** and re-presentation ranged from 1 day after being classified as lost to follow-up, and 1019 days (Figure 2). The average period of loss before first representation was 105 days (SD 161), and the median period of loss was 35 days (IQR 10,124).

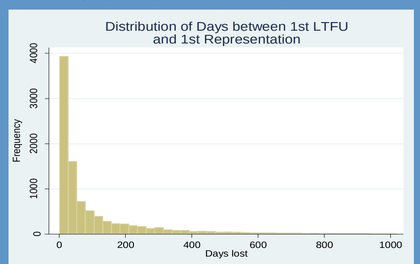


Figure 2. Distribution of days between first loss to follow-up and re-presentation

Re-presenting patients were less likely to have Hemoglobin <8 g/dL, CD4<200 cells/mm^3, and WHO Stage 3/4 at baseline ART initiation (Table 1).

Table 1. Characteristics of ART patients remaining in care, lost and re-presenting, and lost and not returning during first 3 years on ART*

	Lost and re-presenting	*Remaining on ART*	*p-value†*	*Lost and not returning*	*p-value†*
n	9,846	19,709		18,571	
Demographic characteristics					
Age (*median, IQR*)	34 (29,40)	35 (30,41)	<0.01	34 (29,41)	0.19
Female (%)	59.00	64.21	<0.01	57.98	0.10
Clinical characteristics					
BMI<16 (%)	7.25	6.39	0.01	12.27	<0.01
Hemoglobin <8g/dL (%)	8.72	7.15	<0.01	12.29	<0.01
CD4 cell count <200/mm^3 (%)	70.11	74.11	<0.01	74.01	<0.01
WHO Stage (% Stage 3 or 4)	67.5	66.0	0.01	72.5	<0.01
Active tuberculosis (%)	13.3	13.5	0.58	13.6	0.41
Pregnant (%)	4.9	6.8	0.10	5.1	0.82

Among those classified as lost to follow-up (>60 days late for their last scheduled visit), predictors for re-presentation in a multivariable logistic regression model included higher baseline CD4 cell count, higher baseline BMI, and higher baseline hemoglobin, lower baseline WHO stage and active TB (Table 2).

Table 2. Predictors of first re-presentation within first 3 years on ART

Characteristic	*OR*	*95% CI*		*P-value*
Age, continuous	0.99	0.99	1.00	<0.01
Sex				
Male	--	--	--	--
Female	1.02	0.96	1.08	0.62
Baseline BMI				
≥16.00	1.64	1.47	1.82	<0.01
<16.00	--	--	--	--
Baseline Hemoglobin				
≥8	1.30	1.18	1.43	<0.01
<8	--	--	--	--
Baseline CD4 count				
<200	0.92	0.85	0.99	0.02
200-350	--	--	--	--
>350	1.03	0.90	1.18	0.65
Baseline WHO Stage				
Stage 1 or 2	1.22	1.14	1.30	<0.01
Stage 3 or 4	--	--	--	--
Active TB, baseline				
No	--	--	--	--
Yes	1.12	1.02	1.22	0.01

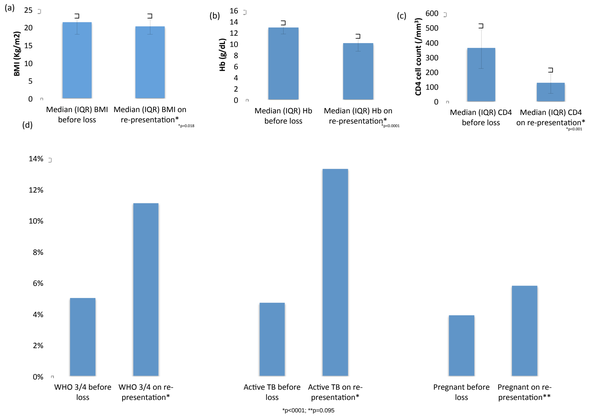


Figure 3. We compared the clinical characteristics of individuals prior to loss, with their clinical characteristics on re-presentation, including (a) BMI, (b) Hemoglobin, (c) CD4 cell count, and (d) proportion with WHO Stage II/IV, active TB and pregnancy.

CONCLUSION

Re-presentation after initial loss to follow-up is common in an urban HIV treatment cohort in Zambia and is generally more likely in healthier individuals. Exiting and re-entering the care cascade appears to be associated with significant declines in clinical wellbeing.

This is one of the first empiric characterizations of this important phenomenon in ongoing HIV care and treatment efforts, and one that should be considered in the design of future interventions for program retention and monitoring.

REFERENCES

1. Hallett TB, Eaton JW. A side door into care cascade for HIV-infected patients? *J Acquir Immune Defic Syndr* 2013;63:S228-S232.

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