Contemporary Disengagement from Antiretroviral Therapy in Khayelitsha, South Africa

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Abstract #990

Introduction

Retention in care is an essential component of meeting the third "90" of the UNAIDS "90-90-90" HIV treatment targets: viral suppression. Patients who disengage from care have an increased risk of poor health outcomes, transmitting HIV to others, and developing drug resistance, thereby undermining overall program impact and the public health goal of ending the HIV epidemic.

Site: Khayelitsha township, Cape Town, South Africa (population ~500,000). Data were used from all 13 public sector clinics: three provincially run and ten run by the City of Cape Town. More than 50,000 patients have received ART here since 2001, and the current patients on ART in Khayelitsha constitute 17.5% of the total number of patients on ART in the Western Cape Province.

Previous findings in Khayelitsha: 2009: 65% retention at six years. 2007: 7.6% lost to follow-up (LTFU) at one year. Disengagement from care remains an important challenge, and new estimates are needed.

Objectives

To determine the incidence of and risk factors associated with disengagement from care from 1 Jan 2013- 31 Dec 2014, and outcomes for those who disengaged.

Methods

We conducted a retrospective cohort study of all patients ≥ ten years of age who visited one of the 13 Khayelitsha ART clinics from 1 Jan 2013 – 31 Dec 2014 regardless of the date they initiated ART.

Definitions:

- *Disengagement:* not being seen at a Khayelitsha ART clinic for >180 days. The database was closed on 30 June 2015 to ascertain this outcome for all patients. Excludes silent transfers.
- *Silent transfer*: Not seen in a Khayelitsha clinic for >180 days but seen at an ART or primary care clinic somewhere else in the Western Cape during this time period.

Analysis 1: Cumulative incidence of first disengagement in the study window by time on ART, using flexible parametric survival models (Royston-Parmar), and risk factors for disengagement based on a Cox proportional hazards model. Multiple imputation was conducted to account for missing data.

Analysis 2: For those patients who disengaged, description of outcomes after disengagement using Western Cape Province-wide health databases and the National Death Registry through 30 June 2015.

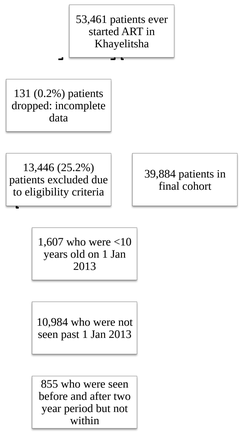


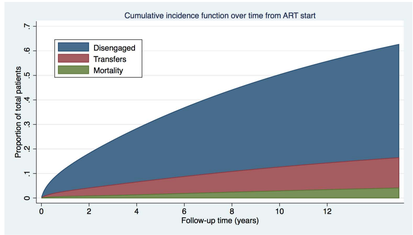
Figure 1. Cohort selection

Results

Table 1. Patient characteristics (Analysis 1)

Patient characteristics (n= 39,884)	
Age at 1 January 2013, years (median, IQR)	34.4 (28.5- 41.0)
Male sex (n, %)	11,687 (29.3%)
Months on ART at 31 Dec 2014 (median, IQR)	33.6 (12.4-63.2)
Median year of starting ART (median, IQR)	2012 (2009-2013)
Baseline CD4 count, cells/uL (median, IQR)	188 (104-280)
Most recent CD4 count as of 31 Dec 2014, cells/uL (median, IQR)	415 (259-593)
Most recent viral load >1000 on ART as of 31 Dec 2014 (n, %)	2,995 (13.5%)
Achieved viral suppression on ART (<400) (n, %)	27,212 (93.9%)
Initiated ART during pregnancy (women only) (n, %)	3,785 (13.5%)
TB treatment at ART initiation (n, %)	8,593 (21.7%)
Ever transferred within Khayelitsha (n, %)	1,686 (4.2%)
Transferred into ART care (n,%)	4,443 (11.1%)
ART club membership (n, %)	6,409 (25.0%)
Most recent ART regimen drug 1 as of 31 Dec 2014 (n, %)	TDF 32,052 (80.4%)
	AZT 5,174 (13.0%)
	d4T 1,924 (4.8%)
Most recent ART regimen drug 3 as of 31 Dec 2014 (n, %)	EFV 32,248 (80.9%)
	NVP 3,600 (9.0%)
	LPV/r 3,470 (8.7%)
Previous gap in care of >180 days prior to study window (n, %)	5,414 (13.6%)
Outcomes as of 31 Dec 2014	
Alive and in care (n, %)	28,069 (70.4%)
Dead (n, %)	592 (1.5%)
Disengagement (n, %)	9,005 (22.6%)
Transfer (n, %)	1,231 (3.1%)
Silent transfer (n, %)	987 (2.5%)

*Percentages reflect proportions of patients with complete data. Completion ranged from 56-100%.



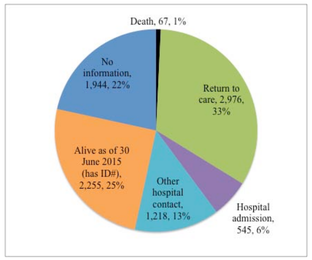
	Estimate at 5 years (95% CI)	Estimate at 10 years (95% CI)
Disengaged	0.251 (0.246-0.255)	0.377 (0.369-0.385)
Transfer	0.061 (0.058-0.063)	0.097 (0.093-0.102)
Dead	0.016 (0.014-0.017)	0.029 (0.026-0.032)

Figure 2. Cumulative incidence (competing risk analysis) of disengagement, transfer (including silent transfers), and mortality, as estimated by a flexible parametric survival model based on time to disengagement from ART start (as early as 2001) during the two-year window of analysis (Analysis 1)

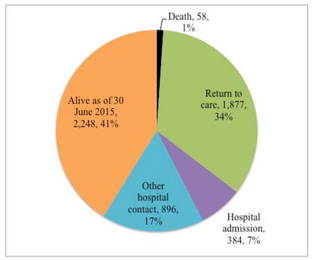
Table 2. Multivariable Cox proportional hazards model for disengagement, with multiple imputation analysis (Analysis 1)

	Multivariable model	n=39,884	Multivariable: Imputed	n=39,884
Variable	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**
Age category				
10-20 yrs	1.39	1.25 - 1.54	1.38	1.24 - 1.54
20-30 yrs	1.44	1.37 - 1.52	1.46	1.38 - 1.54
30-40 yrs	ref	ref	ref	ref
40-50 yrs	0.9	0.85 - 0.96	0.9	0.85 - 0.96
50-60 yrs	0.91	0.83 - 1.01	0.91	0.82 - 1.01
>60 yrs	1.07	0.89 - 1.29	1.08	0.89 - 1.31
Sex / pregnancy				
Non-pregnant women	ref	ref	ref	ref
Pregnant women	1.57	1.47 - 1.68	1.58	1.47 - 1.69
Men	1.14	1.09 - 1.20	1.14	1.08 - 1.20
TB treatment at ART initiation	1.09	1.03 - 1.15	strata	strata
Any transfer	0.76	0.71 - 0.81	strata	strata
Previous gap in care of >180 days	1.61	1.51 - 1.72	strata	strata
Provincial clinic	1.14	1.09 - 1.20	1.06	1.01 - 1.12
Baseline CD4				
>350	ref	ref	ref	ref
200-350	0.62	0.57 - 0.67	0.6	0.56 - 0.65
50-200	0.53	0.49 - 0.57	0.46	0.43 - 0.50
<50	0.49	0.44 - 0.54	0.39	0.35- 0.44
missing	0.77	0.70 - 0.84	-	-
Most recent CD4 as of 31 Dec 2014				
>350	ref	ref	ref	ref
200-350	1.9	1.79 - 2.01	2.03	1.91 - 2.15
50-200	2.64	2.46 - 2.83	3.07	2.84 - 3.31
<50	2.67	2.35 - 3.03	3.34	2.92 - 3.83
missing	1.15	1.07 - 1.23	-	-
Viral load undetectable ever during ART	0.52	0.48 - 0.57	0.58	0.53 - 0.64
missing	1.55	1.42 - 1.69	-	-
ART adherence club membership	0.27	0.24 - 0.30	0.29	0.26 - 0.32
missing	1 (omitted)	omitted	-	-
Most recent ART regimen drug 1 as of 31 Dec 2014				
Other/missing	ref	ref	ref	ref
d4T	1.69	1.54 - 1.85	1.72	1.57 - 1.89
Most recent ART regimen drug 3 as of 31 Dec 2014				
EFV	ref	ref	ref	ref
NVP	1.19	1.09 - 1.30	1.17	1.08 - 1.28
LPV/r	0.78	0.72 - 0.85	0.65	0.60 - 0.71
Other/missing	0.83	0.68 - 1.00	0.21	0.11 - 0.39

Figure 3. Initial outcomes for patients who disengaged, until 30 June 2015 (Analysis 2)



A. All patients who disengaged (n=9,005)



B. Patients who disengaged with national identification numbers, allowing accurate mortality ascertainment (n=5,463)

*Note: "Alive as of 30 June 2015" refers to patients who had valid national identification numbers but were not found in care anywhere in the Western Cape nor were they found to be dead. Therefore, "alive" is the only outcome we could ascertain.

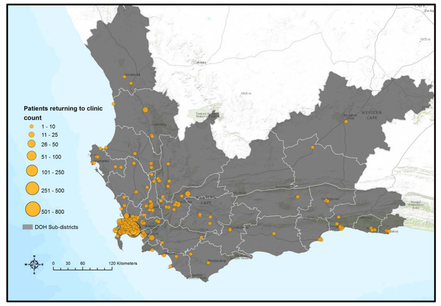


Figure 4. Map of Western Cape Province indicating clinics where silent transfers and patients who disengaged returned to care until 30 June 2015

Key Findings

- Almost one quarter (22.6%) of patients disengaged from ART care at least once from 2013-4, and an additional 987 (2.5%) were "silent transfers" (Table 1). Cumulative incidence of disengagement from care was 25.1% by five years on ART and 37.7% by ten years on ART estimated from time contributed in the study window (Figure 2).
- Key factors associated with disengagement were younger age, male sex, pregnancy at ART start, and lower last CD4 count; protective factors were ART club membership and lower baseline CD4 (Table 2).
- Of those who disengaged, the two most common initial outcomes by 30 June 2015 were return to ART care after 180 days (33%), and being alive but not in care in the Western Cape, as ascertained by a national ID number (25%) (Figure 3A).
- Cumulatively by 30 June 2015, 1,459 patients (16.2%) were hospitalized and 237 (2.6%) died after disengagement.

Limitations

We included only patients from 2013-4, which introduced a survival bias, as those who died or disengaged prior to 2013 were not included. We had a very short period for follow-up, and our results reflect only short-term mortality. Finally, we recognize the non-uniform collection of data, which necessitated dropping particular variables and performing a multiple imputation analysis. This is somewhat mitigated by the large size of the dataset and power of the analysis.

Conclusions and Next Steps

Although the majority of the large proportion of patients who disengaged either subsequently returned to care or remained alive without hospitalization, a challenge to meeting the 90-90-90 HIV treatment targets is developing, testing, and implementing program designs to target mobile populations and retain them in lifelong care. This should be guided by risk factors for disengagement as observed in this and other studies.

Acknowledgments

The authors would like to acknowledge Michael Schomaker at UCT, who was instrumental in completing the multiple imputation analysis, Gerald Friedland, who is SK's thesis advisor at Yale School of Medicine, and the CIDER staff at UCT.

Research reported in this poster was supported by the National Institutes of Health Office of the Director, Fogarty International Center, Office of AIDS Research, National Cancer Center, National Heart, Blood, and Lung Institute, and the NIH Office of Research for Women's Health through the Fogarty Global Health Fellows Program Consortium comprised of the University of North Carolina, John Hopkins, Morehouse and Tulane (R25TW009340). This content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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