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The relationship between adherence to clinic appointments and year-one mortality for newly enrolled HIV infected patients at a regional referral hospital in Western Kenya, January 2011–December 2012

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Abstract

This retrospective cohort analysis was conducted to describe the association between adherence to clinic appointments and mortality, one year after enrollment into HIV care. We examined appointment-adherence for newly enrolled patients between January 2011 and December 2012 at a regional referral hospital in western Kenya. The outcomes of interest were patient default, risk factors for repeat default, and year-one risk of death. Of 582 enrolled patients, 258 (44%) were defaulters. GEE revealed that once having been defaulters, patients were significantly more likely to repeatedly default (OR 1.4; 95% CI 1.12–1.77), especially the unemployed (OR 1.43; 95% CI 1.07–1.91), smokers (OR 2.22; 95% CI 1.31–3.76), and those with no known disclosure (OR 2.17; 95% CI 1.42–3.3). Nineteen patients (3%) died during the follow-up period. Cox proportional hazards revealed that the risk of death was significantly higher among defaulters (HR 3.12; 95% CI 1.2–8.0) and increased proportionally to the rate of patient default; HR was 4.05 (95% CI1.38–11.81) and 4.98 (95% CI 1.45–17.09) for a cumulative of 4–60 and ≥60 days elapsed between all scheduled and actual clinic appointment dates, respectively. Risk factors for repeat default suggest a need to deliver targeted adherence programs.

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Disclosure statement

No potential conflict of interest was reported by the authors.

Keywords

Compliance; HIV/AIDS; outcome; adherence; survival

HIV infection is an incurable illness that requires long-term engagement with health-care providers (Bofill, Waldrop-Valverde, Metsch, Pereyra, & Kolber, 2011; National AIDS and STI Control Program, 2011). Appointments at HIV Comprehensive Care Clinics (CCC) in Kenya are scheduled to coincide with prescription refills, adherence support, and timely delivery of required interventions (National AIDS and STI Control Program, 2011). Repeatedly missing appointments has been shown to lead to non-adherence to medication, faster disease progression, and treatment failure (Alamo et al., 2012; Fong, Cheng, Vujovic, & Hoy, 2013). Adherence to scheduled clinic visits can be used as an objective proxy for adherence to medication between clinic visits (National AIDS and STI Control Program, 2011; Park et al., 2007). We have examined the effect of adherence to clinic appointments on year-one mortality rates for newly diagnosed HIV-infected patients at a regional referral hospital in western Kenya.

Methods

Study design, setting, and population

A retrospective medical records review was conducted at the Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH), Kisumu, western Kenya for all patients aged ≥ 15 years (defined as adults by Kenya's HIV program) (Ministry of Health National AIDS and STI Control Program (NASCOP), 2014) enrolled between January 2011 and December 2012. Patients who transferred-in from other facilities were excluded.

Data collection

Clinicians entered data into structured forms during clinic visits per routine guidelines (Swash, 2001); forms were scanned and uploaded into clinic databases from which demographic, clinical (WHO stage and CD4 (Cluster of Differentiation 4) T cell counts), and psychosocial information (alcohol consumption, cigarette-smoking, and drug-abuse), clinic visits, and year-one patient outcomes were extracted. Patient disclosure status was described as "disclosed to family only" (reported disclosing positive HIV status to family member only), "disclosed to friends only" (reported disclosing to nonfamily), "disclosed to family and friends only" (disclosed to both family and non-family), "non-specific disclosure" (person disclosed to unidentified) or "no known disclosure" (no disclosure reported).

Scheduling of clinic appointments

At first clinical visit, all patients received a clinical assessment; baseline laboratory tests investigations, initiation of daily cotrimoxazole preventative therapy, appropriate treatment of opportunistic infections (OIs), and adherence counseling. Patients were scheduled to return two weeks later for review of test results and if ART eligible, initiated on ART within two weeks and provided preparatory adherence counseling. Patients were scheduled to return two weeks after ART initiation for initial ART monitoring. Patients were scheduled to

return monthly or quarterly for assessment of their physical condition, adherence assessment and counseling, and ART monitoring and, if necessary, changes. Those not yet on ART were re-assessed through CD4 testing every six months. The total number of visits was 8–12 in the first year, though may exceed 12 when warranted by the patient's medical condition. At enrollment, patients were invited to participate in a support group consisting of patients of similar characteristics that regularly met to receive moral support and information from peers (National AIDS and STI Control Program, 2011).

Definitions

A patient was considered a defaulter if still absent three days after missing a scheduled clinic appointment. Defaulters were described as "one-time defaulters" if they missed only one clinic appointment during the 12-month follow-up period, and as "repeat defaulters" if they missed more than one clinic appointment during the same period. Defaulter status was also described in terms of number of appointments missed, proportions of appointments missed during the 12-month follow-up period, and the cumulative number of days that elapsed between the appointment and actual visit date for all defaulted visits.

HIV program case definitions were used to describe patient outcomes as alive/active in care, dead, lost to follow-up (LTFU) or transferred. Patient tracing was done to determine true patient outcomes and avoid misclassification (National AIDS and STI Control Program, 2011).

Data analysis

Patients' age groups were dichotomized at 24 years based on the United Nations definition of young persons as those aged 15–24 years (United Nations, 2015). Chi-square statistics were used to describe patient characteristics by defaulter status. Alternating logistic regression (Generalized Estimating Equations, GEE) was used to describe factors associated with patient default over time. Cox proportional hazards were used to estimate hazard ratios associated with mortality at 12 months of follow-up. CD4 count averages were computed at each CD4 test period to visualize CD4 trends over time.

Patients with unknown outcomes (transfers out and lost to follow-up) were excluded from risk of death analyses. The total duration on care for all patients was computed from enrollment to outcome date in person-years in order to account for the time in follow-up for each patient (Bruce, Pope, & Stanistreet, 2007). Complete case analysis was adopted for missingness in the data since this was completely at random (Little, 1998). Analysis was conducted using Statistical Analysis Software (SAS) version 9.2 (SAS Institute Inc., 2012).

Ethical approval

Approval was granted by the Kenya Medical Research Institute Ethical Review Committee (SSC. No. 1525) and the US Centers for Disease Control IRB.

Results

Study cohort

Of the 1129 enrolled patients, 582 met the criteria for inclusion in the analysis (Figure 1). Patient characteristics are summarized in Table 1.

Characteristics of defaulters

Compared to non-defaulters, defaulters were significantly more likely to have attained secondary or a higher level of education (11% vs. 5%), be smokers (6% vs. 3%), and were less likely to have disclosed to both family and friends (53% vs. 60%).

Once having been a defaulter one time, a patient was significantly more likely to default at future visits (OR 1.4; 95% CI 1.12–1.77) especially the unemployed (OR 1.43; 95% CI 1.07–1.91), smokers (OR 2.22; 95% CI 1.31–3.76), and whose disclosure status was "non-specific" compared to those who disclosed to both family and friends (OR 2.17; 95% CI 1.42–3.3, $p = .0003$). The clinical status of patients and alcohol consumption were not associated with one-time or repeated default (Table 1). A total of 4079 appointments were scheduled for the 582 patients during the follow-up period; 367 (9%) were not kept by the defaulters during the study period.

Clinical progression

The mean increase in CD4 count at month six of follow-up was higher among the non-defaulters compared to defaulters; however, this was not statistically significant (161.1 [114.7–207.6] and 118.9 [44.4–193.4]). Further comparison beyond this was limited by limitedCD4 counts data.

Twelve-month patient mortality

Defaulters experienced significantly higher proportions of deaths compared to non-defaulters (6% vs. 2%); this difference was not significant between one-time and repeat defaulters (6% vs. 5%). A higher rate of transfers out was observed among non-defaulters and a higher rate of LTFU patients among defaulters (Figure 1).

Overall, the risk of death was significantly higher among defaulters compared to non-defaulters (HR 3.09; 95% CI 1.11–8.62), among members of support groups (HR 3.12; 95% CI 1.11–9.09) and among those who had been on ART for a shorter duration (HR 4.55; 95% CI 1.51–13.77) (data not shown).

Impact of default on year-one patient mortality

The overall mortality rate was 6.3 per 100 person years; this was lower among non-defaulters and increased significantly with the rate of patient default ($p < .005$) (Table 2).

Discussion

As supported by other literature, defaulters were more likely to have poorer patient outcomes. This could be attributed to missed doses of ART medication, missed opportunity

for clinical intervention, and the increased possibility of repeat default or stopping clinic attendance as suggested by higher rates of LTFU among defaulters (National AIDS and STI Control Program, 2011; Walburn, Swindells, Fisher, High, & Islam, 2012).

The default rate observed was higher than seen in urban Nairobi's Kibera slums where only one-third of patients defaulted over a three-year period (Unge et al., 2010). JOOTRH being a referral facility may have influenced this default trend. Although close to half of the patients were defaulters, they only accounted for 9% of the missed scheduled appointments. As observed in the published literature, this could be explained by the number of scheduled appointments at HIV clinics (an average of 10 annual visits), which were all kept by the non-defaulting patients and defaulters only missing a proportion of their scheduled appointments (Kunutsor et al., 2010).

An examination of patient scheduling may explain why patients with a higher level of education were more likely to default for one visit but not multiple appointments (Collazos, Asensi, Carton, & Ibarra, 2009; Lacy, Paulman, & Reuter, 2004).

The unemployed, smokers, and those with non-specific disclosure status were more likely to default multiple times verses a single time. Limited financial resources among unemployed may suggest an inability to afford transport to clinic appointments or even limited access to the food to take with ART (Bonolo et al., 2005; Falagas, Zarkadoulia, Pliatsika, & Panos, 2008). Smokers are likely to engage in other forms of drug-abuse and may have lower levels of conscientiousness (Bonolo et al., 2005; Terracciano & Costa Jr, 2004). No specific substance-use questionnaire is in place at JOOTRH, which might explain limited data on drug-abuse and hence no relationship with default (Fagan et al., 2013; World Bank, 2014). Non-specific disclosure status may mean non-disclosure of HIV status which may imply lack of family support and other behaviors related to denial of HIV status (Bofill et al., 2011). It may be that sicker patients are more likely to attend support groups, explaining their higher mortality (Shacham et al., 2008).

Our analysis was limited by missing data on TB diagnosis and other opportunistic infections, causes of death, true outcomes of untraceable patients, and a short duration of follow-up. Nonetheless, finding strategies to avoid patient default from clinic appointments may be critically important. We propose that, stable patients should have additional drug delivery options made available to facilitate medication-adherence and that HIV programs deliver targeted adherence programs that address income-related barriers, promote disclosure, discourage smoking, and educate patients on appointment-scheduling (National AIDS and STI Control Program, 2011; Unge et al., 2010; Walburn et al., 2012). Encouraging early diagnosis of HIV infection and ART uptake mean little, if patients inconsistently engage in care.

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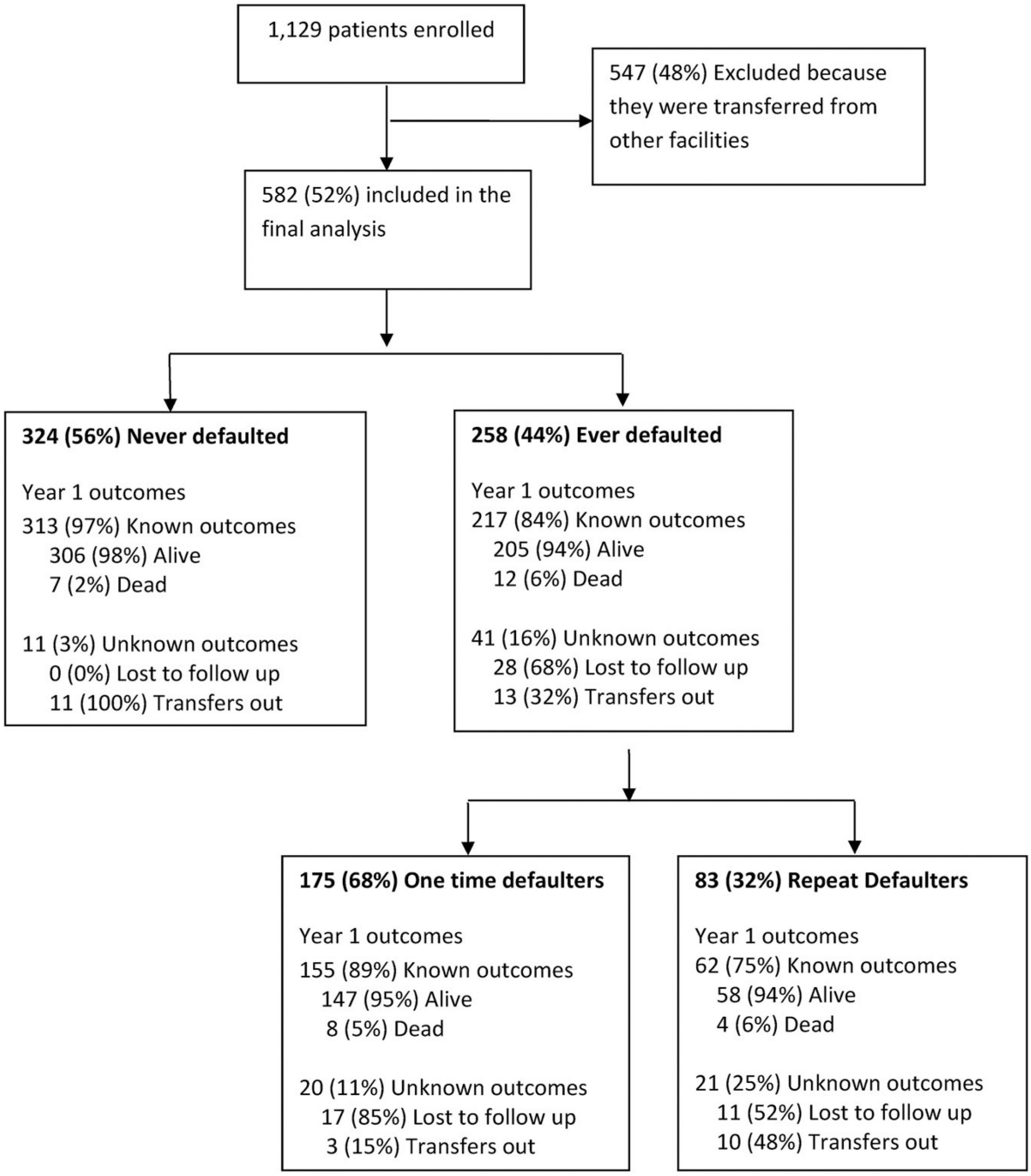

Figure 1.
Year-one patient retention rates at the Jaramogi Oginga Odinga Teaching and Referral Hospital for patients enrolled between 2011 and 2012.

Table 1

Baseline demographic, clinical and psychosocial characteristics of HIV-infected adult patients [*] and factors associated with rate of defaulting clinic appointment repeatedly among HIV-infected adult patients enrolled in a referral hospital in western Kenya, 2011–2012[#].

Characteristic	Total = 582, *N* (column %)	Defaulter, *N* (column %)	GEE model	
			Univariate analysis [OR (95%CI); *p*-value]	Multivariate analysis [OR (95%CI); *p*-value]
Age group	*N* = 582			
< 24 years	66 (11)	32 (12)	1.34 (0.91–1.95); .13	
>= 24 years	516 (89)	226 (88)	Reference	
Gender	*N* = 582			
Male	235 (40)	107 (41)	Reference	
Female	347 (60)	151 (59)	1.00 (0.78–1.28); .99	
Marital status	*N* = 550			
Not married	228 (41)	102 (42)	1.05 (0.81–1.37); .69	
Married	322 (59)	142 (58)	Reference	
Employed	*N* = 518			
Yes	289 (56)	125 (55)	Reference	Reference
No	229 (44)	102 (45)	1.33 (1.03–1.73); .03	1.62 (1.03–2.56); .04
Education level	*N* = 582			
Primary or less	538 (92)	230 (89) [*]	1.59 (1.12–2.26); .01	1.86 (0.91–3.82); .09
Above primary	44 (8)	28 (11)	Reference	Reference
Entry point	*N* = 572			
Within facility	385 (67)	164 (65)	Reference	
Outside facility	187 (33)	89 (35)	1.01 (0.78–1.30); .95	
WHO stage	*N* = 573			
Stage I & II	329 (57)	147 (59)	Reference	Reference
Stage III & IV	244 (43)	104 (41)	1.26 (0.98–1.62); .07	1.22 (0.82–1.81); .33
CD4 category [¶]	*N* = 564			
< 350 cells/mm^3	422 (75)	184 (74)	0.74 (0.49–1.11); .14	
>= 350 cells/mm^3	142 (25)	66 (26)	Reference;	
Member of a support group [¥]	*N* = 577			
Yes	76 (13)	32 (11)	Reference	
No	501 (87)	225 (89)	0.93 (0.62–1.41); .75	
Disclosure [ǂ]	*N* = 582			
Yes	510 (88)	227 (88)	Reference;	
No	72 (12)	31 (12)	1.05 (0.71–1.54); .81	
Disclosed to who	*N* = 510			
Family only	94 (18)	37 (16) [*]	1.38 (0.96–1.99); .08	1.13 (0.50–2.53); .77
Friends only	26 (5)	11 (5)	1.51 (0.76–2.97); .24	0.96 (0.29–3.20); .96

Characteristic	Total = 582, *N* (column %)	Defaulter, *N* (column %)	GEE model	
			Univariate analysis [OR (95%CI); *p*-value]	Multivariate analysis [OR (95%CI); *p*-value]
Family & friends	288 (57)	120 (53)	Reference	Reference
Not specified	102 (20)	59 (26)	1.90 (1.41–2.57); <.01	2.30 (1.45–3.65); <.01
Smoking	*N* = 582			
Yes	24 (4)	16 (6) *	1.91 (1.09–3.35); .02	3.15(1.60–6.21); <.01
No	558 (96)	242 (94)	Reference	Reference
Alcohol	*N* = 582			
Yes	62 (11)	30 (11)	1.16 (0.77–1.75); .47	
No	520 (89)	228 (89)	Reference	

*Chi-square statistics used to compare characteristics of defaulters to non-defaulters.

#Alternating logistic regression used to determine risk factors for repeat default among HIV-infected patients.

¶CD4 counts within one month of enrollment were available for 564 patients (314 non-defaulters, 250 defaulters).

¥Enrollment in a support group within one month of enrollment in care.

ǂDisclosure status within one month of enrollment in care.

#Education level strongly correlated to “disclosed to who” (correlation = −.04, $p = .018$) hence not significant in the multivariate model. We conducted multicolinearity test after we found it was significant in the univariate analysis and not in the multivariate analysis.

Table 2

Impact of adherence to clinic appointments on year-one mortality among newly enrolled HIV-infected patients at JOOTRH, 2011–2012[*] (*N* = 530)[#].

	Number of patients	Number Of deaths	Total duration of follow-up in years	Occurrence rate of event per 100 person years (95% CI)	Unadjusted HR (95% CI)	*p*-value
Total	530	19	302.3	6.3 (3.6–9.6)		
Cumulative elapsed time (days)						
None	313	7	218.2	3.2 (1.3–6.5)	Reference	–
4–60 days	177	7	63.7	11.0 (4.5–21.2)	4.50 (1.53–13.20)	.006
60+ days	40	5	20.5	24.4 (8.2–47.2)	6.75 (1.96–23.18)	.002
Number of defaulted appointments						
Zero	313	7	218.2	3.2 (1.3–6.5)	Reference	–
One	155	8	50.1	16.0 (7.2–29.1)	6.74 (2.38–19.13)	.0003
Two or more	62	4	34.1	11.7 (3.3–27.4)	3.21 (0.82–12.57)	.094
Proportion of appointments missed						
Zero	313	7	218.2	3.2 (1.3–6.5)	Reference	–
0–25%	165	7	59.9	11.7 (4.7–22.6)	4.14 (1.35–12.65)	.013
>25%	52	5	24.3	20.6 (7.1–42.2)	7.13 (2.24–22.70)	.001

[*] *N* = 530, excludes patients lost to follow-up or transferred out.

[#] Incidence rates of death among each group were computed as the ratio between number of deaths and total follow-up time among patients in each group.