Vital status of pre-ART and ART patients defaulting from care in rural Malawi

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Summary

OBJECTIVES   To ascertain the outcome of pre-Antiretroviral therapy (ART) and ART patients defaulting from care and investigate reasons for defaulting.

METHODS   Patients defaulting from HIV care in Chiradzulu between July 2004 and September 2007 were traced at last known home address. Deaths and moves were recorded, and patients found alive were interviewed. Defaulting was defined as missed last appointment by more than 1 month among patients of unknown vital status.

RESULTS   A total of 1637 individuals were traced (54%–88% of eligible), 981 pre-ART and 656 ART patients. Of 694 pre-ART patients found, 49% had died (51% of adults and 38% of children), a median of 47 days after defaulting, and 14% had moved away. Of 451 ART patients found, 54% had died (54% of adults and 50% of children), a median of 52 days after defaulting, and 20% had moved away. Overall, 221 patients were interviewed (90% of those found alive), 42% had worked outside the district in the previous year; 49% of pre-ART and 19% of ART patients had not disclosed their HIV status to other household members. Main reasons for defaulting were stigma (43%), care dissatisfaction (34%), improved health (28%) and for ART discontinuation, poor understanding of disease or treatment (56%) and drug side effects (42%).

CONCLUSION   This study in a rural African HIV programme reveals the dynamics related to health service access and use, and it provides information to correct programme mortality estimates for adults and children.

keywords antiretroviral therapy, HIV, patient dropouts, sub-Saharan Africa

Introduction

Antiretroviral therapy (ART) has been scaled-up in Africa over the past years (UNAIDS & WHO 2003, 2007). At the end of 2007, 30% of the estimated 7 million people in need of treatment were receiving it (WHO *et al.* 2009). Satisfactory immuno-virological response and levels of adherence to ART have been reported in African settings, but evaluations are generally conducted among patients remaining in HIV care (Ferradini *et al.* 2006; Mills *et al.* 2006; Spacek *et al.* 2006; Stringer *et al.* 2006; Toure *et al.* 2008). Nevertheless, high rates of loss to follow-up (LFU) and ART discontinuation can greatly limit the effectiveness of HIV programmes.

A recent meta-analysis summarized information from 17 studies that traced LFU adults receiving ART in resource-limited settings (Brinkhof *et al.* 2009). Combined mortality was estimated at 40% but ranged from 12% to 87% in

African studies. Reasons for defaulting were transfer to another programme, financial difficulty, and improved or poor health. Surprisingly, there are limited or no data on outcomes of pre-ART patients (Bassett *et al.* 2008; Toure *et al.* 2008) or children LFU (Brinkhof *et al.* 2009). To optimize care delivery, prevent treatment discontinuation and monitor HIV programmes over time, it is necessary to ascertainment patients' outcomes and to identify reasons for defaulting (Bisson *et al.* 2008).

In this study, we describe the outcomes and reasons for care discontinuation of pre-ART and ART adults and children who defaulted from HIV care in Chiradzulu, Malawi.

Methods

Since 2001, Médecins Sans Frontières (MSF) has provided free ART to patients infected with HIV in Chiradzulu, a Malawian rural district, with an antenatal HIV prevalence

of 17%–22% (National AIDS Commission 2008). Care is delivered through one district hospital and 10 health centres located 5–40 km from the hospital. Individual and group counselling by community peers and trained advisors are provided at ART start and during follow-up. Clinical visits are scheduled every 6 months for pre-ART, every 2–3 months for ART patients. Generic fixed-dose combinations of two nucleoside-reverse transcriptase inhibitors and nevirapine or efavirenz are prescribed.

Medical information is routinely collected at every consultation on standardized forms and entered in FUCHIA (Epicentre, Paris, France). Data available are age, sex, dates of enrolment, visits and appointments, visit location, clinical stage, height, weight and, when performed, CD4 cell count measurements.

Study design and procedures

As part of an internal audit of programme activities, we conducted a cross-sectional study to ascertain the vital status of defaulting patients. Eligibility criteria for participation were programme enrolment between March 2001 and July 2007, residence in Chiradzulu district, and care discontinuation between July 2004 and September 2007. Patients who missed their appointment by more than 1 month were considered defaulters (programme definition).

All facility records were reviewed to maximize completeness of transfer and death events. Trained interviewers made one to three home visits, recorded patient vital status and reason for non-traceability. For patients found alive, interviewers sought informed verbal consent and offered a return-to-care appointment. For those who died or moved away, family or community leaders were interviewed. Standardized questionnaires translated into Chichewa and back-translated into English were administered. Data collected and entered into Access included date and place of death or move and hospitalization after last recorded clinic visit. To document reasons for care discontinuation the question 'Why did you stop attending the MSF clinic?' followed by a number of dichotomous (yes/no) items were asked. The term *kusalidwa* ('to oppress') was used to ask whether stigma from community or family members was a reason for care discontinuation.

District and traditional authorities were informed and provided guidance to ensure patient confidentiality. The Malawi National Health Sciences Research Committee granted approval for publication of results.

Statistical analysis

Patient characteristics (e.g. traced and untraced individuals) were compared using Student's *t*-tests, Wilcoxon rank-

sum or chi-square tests, as appropriate. All analyses were performed separately for pre-ART and ART patients using STATA 9.0 (StataCorp., College Station, TX, USA). Outcomes were described by age group (children were aged <15 years).

Results

As of July 2007, 19 626 patients were enrolled in the Chiradzulu programme and 11 683 of them had started ART (Figure 1). Between July 2004 and 2007, 3008 patients defaulted from care a median of 14.9 months after enrolment: 1747 pre-ART (1561 adults and 186 children) and 1261 ART patients (1186 adults and 75 children). After excluding 1153 (38.3%) patients with missing address information and 218 (7.2%) who lived outside Chiradzulu, we traced 1637 individuals (54.0%–88.2% of those eligible). Of these, 981 were pre-ART (874 adults and 107 children) and 656 ART patients (624 adults and 32 children).

Patient vital status

We ascertained the vital status of 69.9% of traced patients. Median time since default, 18.9 months [IQR 14.1–26.8] for pre-ART and 23.2 months [IQR 14.4–35.1] for ART patients, was shorter for individuals with ascertained outcome than for other patients (21.7 *vs.* 26.8 months; *P* < 0.001).

Of pre-ART adults traced, 626 (71.6%) were found, 226 (36.1%) were alive (64 of these were receiving care under another identification code), 317 (50.6%) dead and 83 (13.3%) had moved (Figure 2a). Of pre-ART children, 68 (63.6%) were found, 29 (42.7%) were alive, 26 (38.2%) dead and 13 (19.1%) had moved (Figure 2B). Overall, median time between last visit and death was 1.6 months [IQR 0.6–7.1], and 46.8% of those who moved did so within 3 months of last visit. Of ART adults, 429 (68.8%) were found, 111 (25.9%) were alive (63 of these were still receiving care), 233 (54.3%) dead and 85 (19.8%) had moved. Of children traced, 22 (68.8%) were found, 8 (36.4%) were alive, 11 (50.0%) dead and 3 (13.6%) had moved. Overall, median time between last consultation and death was 1.7 months [IQR 0.6–8.0]. More than half of those who moved did so within 3 months of last visit.

Patient characteristics at last medical visit

More than 50% of pre-ART patients discontinued care within a month of programme inclusion. Median age at last visit was 32 years and 61.2% were women (Table 1). Characteristics of traced and untraced patients were
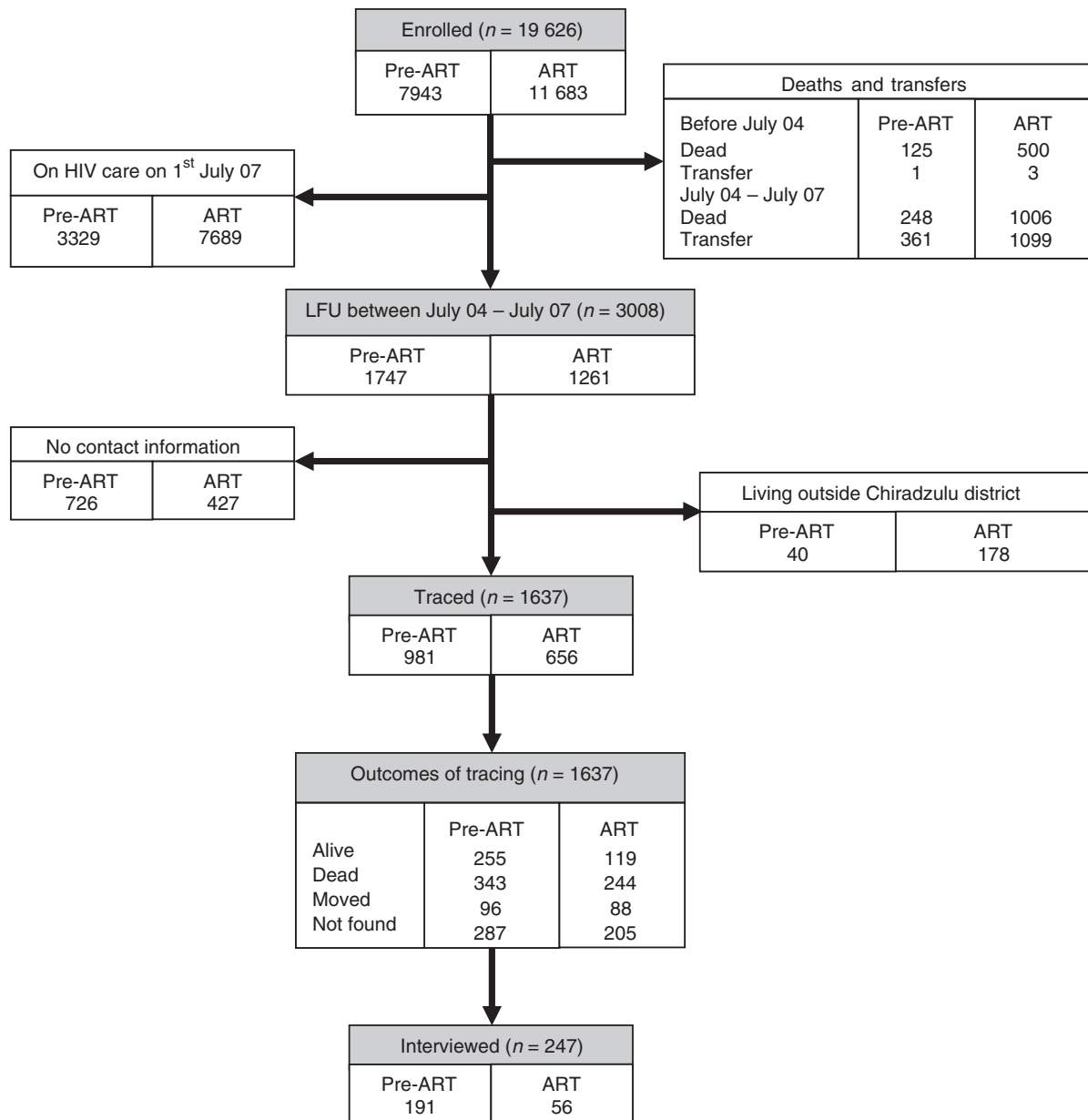
Figure 1 Study profile and outcomes of patients enrolled in the HIV/AIDS care programme of Chiradzulu, Malawi, 2001–2007. Note: LFU before July 2004 were 2132 pre-ART and 125 ART patients.

similar but those traced were more frequently followed in decentralized care (72% *vs.* 54.5%). Patients found dead had lower last recorded median BMI (17.9 and 20.4 kg/m^2) and CD4 cell counts (269 and 426 cells/mm^3) than other patients.

For ART patients, median time on therapy before defaulting was 7.6 months [IQR 1.4–19]. Characteristics at last visit were similar in traced and untraced patients. However, patients traced were receiving therapy for longer (median 10.3 *vs.* 5.8 months) and were more frequently followed in health centres (54.6% and 41.2%, respectively). ART patients found dead had lower recorded BMI (18.4 and 20.6 kg/m^2) and CD4 cell counts (160 and 215 cells/mm^3) than other patients.
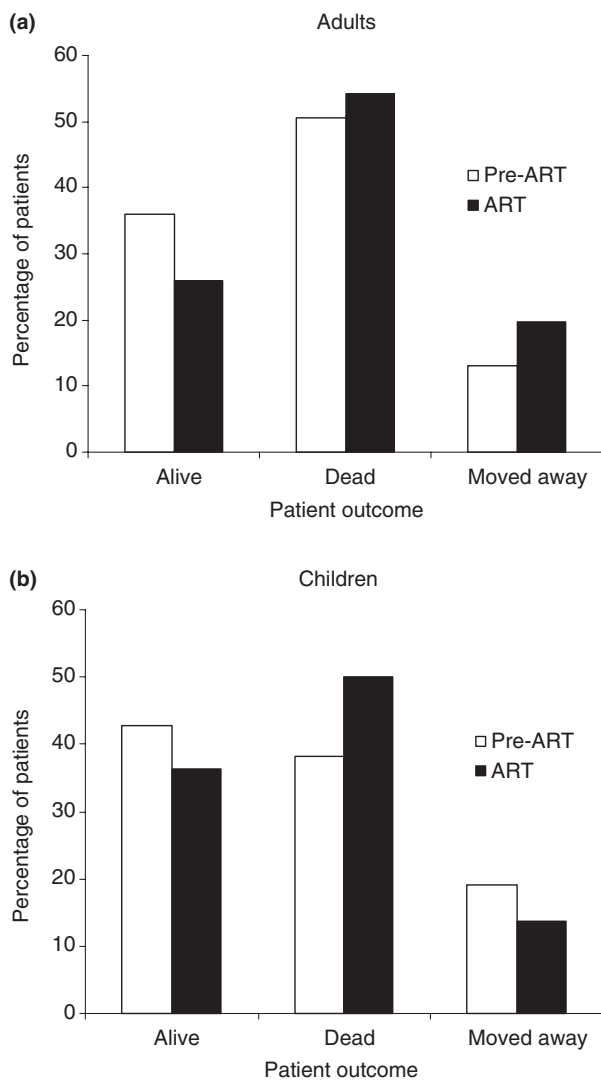
Figure 2 Vital outcomes of pre-ART and ART adults and children traced and found, HIV/AIDS programme of Chiradzulu, Malawi, 2001–2007.

Characteristics of patients interviewed and reasons for defaulting

A total of 172 pre-ART (90.0% of those found alive) and 49 ART (87.5%) patients were interviewed (Table 2). Of pre-ART respondents, 88.4% were adults and 66.3% women. Fifty-one per cent reported to have disclosed their HIV-seropositivity to other household members. Of ART patients, 93.8% were adults and 73.5% women. Eighty-one per cent had disclosed their HIV status to household members, and 68.9% had stopped ART. Reasons for

therapy discontinuation were poor understanding of disease, treatment (56.0%) and side effects (41.7%).

Overall, 41.5% of respondents had worked outside the district in the previous year (Table 2). Forty-four per cent lived more than 2 h from their HIV clinic, and 12.3% had the resources required for travelling. Primary reasons for defaulting were similar in pre-ART and ART patients: stigma (42.5%), dissatisfaction with care or staff behaviour (34.4%), perceived improved health (28.3%) and high transportation cost (18.7%). Of the 161 pre-ART and 37 ART patients who scheduled a return appointment, 71% and 65% sought care, respectively.

Discussion

In this evaluation of patients LFU in an HIV programme of Malawi, 49% of pre-ART and 54% of ART patients had died. Mortality was higher in adults than in children, particularly among pre-ART patients (51% adults compared to 38% in children). Reasons for defaulting were dissatisfaction with care or staff behaviour, stigma and poor understanding of disease and treatment.

We ascertained vital outcomes for 70% of traced patients. Delays between defaulting and survey (75% of patients were traced more than 1 year after their last consultation and many discontinued care before 2006) and seasonal or permanent migration (three of seven individuals reported to have worked outside the district in the previous year and one of six had moved) could explain unsuccessful tracing. In Chiradzulu, the proportion of patients followed under a different identification code (12%) and unrecorded transfers to another programme (8%) were substantial. Better information of patients and strengthening of referral systems could contribute to ensure continuity of care and maximize recording of events. We also found high mortality rates among pre-ART patients defaulting from care, 51% in adults and 38% in children. The observation that 61% of pre-ART patients had no recorded CD4 measurements and almost 50% of dead patients were eligible but not receiving ART, suggests that patients in need of treatment are missed because of poor screening or insufficient education to identify severe disease. The lower mortality rates seen in children should be cautiously interpreted because greater proportions of children than adults were not found (36% compared to 28% of adults) or had moved away (19% compared to 13%). Consistently with results of a recent meta-analysis of sub-Saharan African programmes, where 39%–54% of LFU adults had died (Brinkhof *et al.* 2009), in our programme, half of defaulting ART adults and children had died. Most deaths happened shortly after care discontinuation and therapy initiation when mortality in

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Table 1 Patient characteristics of pre-ART and ART patients at time of defaulting, HIV/AIDS programme of Chiradzulu, Malawi, 2001–2007

	Pre-ART					ART				
	Traced				Not traced	Traced				Not traced
	Found alive N = 255	Found dead N = 343	Moved N = 96	Not found N = 287	N = 726	Found alive N = 119	Found dead N = 244	Moved N = 88	Not found N = 205	N = 424
Socio-demographic factors										
Median age, years [IQR]	29.3 [23.7–36.2]	34.3 [27.9–43.1]	29.1 [22.2–36.1]	30.5 [23.1–37.0]	31.9 [25.1–40.7]	33.0 [27.3–41.3]	35.8 [29.3–44.6]	32.9 [27.6–40.9]	34.1 [28.3–42.2]	34.4 [28.3–42.2]
Females (%)	174 (68.2)	183 (53.4)	65 (67.7)	181 (63.1)	442 (60.9)	83 (68.8)	140 (57.4)	59 (67.1)	131 (63.9)	239 (56.4)
Programme factors										
Median time in programme, months [IQR]	0.9 [0–4.2]	0.5 [0–1.4]	0.9 [0–4.4]	0.5 [0–1.8]	0.9 [0–8.3]	18.2 [10.3–31.7]	4.5 [1.8–12.4]	13.6 [5.1–30.0]	8.9 [2.9–23.4]	12.5 [2.5–26.5]
Year of HIV care enrolment (%)										
2001–2003	15 (5.9)	11 (3.1)	4 (4.2)	12 (4.2)	112 (15.4)	28 (23.5)	34 (13.9)	26 (29.6)	38 (18.5)	129 (30.2)
2004–2005	41 (16.1)	101 (29.5)	24 (25.0)	74 (25.8)	359 (49.5)	47 (39.5)	102 (41.8)	37 (42.1)	105 (51.2)	167 (39.1)
2006	111 (43.5)	103 (37.9)	38 (39.6)	114 (39.7)	170 (23.4)	37 (31.1)	71 (29.1)	20 (22.7)	49 (23.9)	109 (25.5)
2007	88 (34.5)	101 (29.5)	30 (31.2)	87 (30.3)	85 (11.7)	7 (5.9)	37 (15.2)	5 (5.7)	13 (6.4)	22 (5.1)
Decentralized care (%)	199 (78.0)	261 (76.1)	67 (69.8)	179 (62.4)	395 (54.5)	86 (72.2)	145 (59.4)	52 (59.1)	75 (36.6)	176 (41.2)
Clinico-immunological factors										
Median BMI, kg/m² [IQR]*	20.5 [19.3–21.9]	17.9 [16.1–19.7]	20.8 [19.4–22.3]	19.8 [17.9–22.4]	20.2 [17.9–22.2]	20.7 [19.1–22.3]	18.4 [16.2–20.9]	20.6 [18.6–23.0]	20.6 [17.9–22.6]	20.6 [17.9–22.6]
Tuberculosis diagnosis (%)	17 (4.9)	17 (4.9)	4 (4.2)	7 (2.4)	28 (3.9)	2 (1.7)	13 (5.3)	1 (1.4)	9 (4.4)	10 (2.3)
Kaposi's sarcoma (%)	0	9 (2.6)	1 (1.0)	2 (0.7)	11 (1.5)	1 (0.8)	22 (9.0)	2 (2.3)	14 (6.8)	27 (6.3)
Median time on ART, months [IQR]						12.8 [4.1–24.5]	2.4 [0.7–7.6]	11.5 [2.6–21.4]	7.1 [1.4–17.7]	8.9 [1.4–20.5]
Last CD4 cell count, cells/mm³†	N = 129	N = 102	N = 44	N = 109	N = 281	N = 91	N = 121	N = 61	N = 112	N = 234
Median [IQR]	442 [333–581]	269 [117–418]	471 [328–658]	381 [257–543]	416 [295–563]	228 [163–449]	160 [79–263]	191 [126–361]	208 [106–384]	216 [129–396]
<50 (%)	1 (0.8)	8 (7.8)	0	4 (3.7)	8 (2.9)	4 (4.4)	20 (16.5)	4 (6.6)	15 (13.4)	15 (6.4)
50–199 (%)	4 (3.1)	32 (31.4)	5 (11.4)	15 (13.8)	20 (7.1)	31 (34.1)	54 (44.6)	30 (49.2)	37 (33.0)	90 (38.5)
≥200 (%)	124 (96.1)	62 (60.8)	39 (88.6)	90 (82.6)	253 (90.0)	56 (61.5)	47 (38.8)	27 (44.3)	60 (53.6)	129 (55.1)
Median time since last CD4, months [IQR]	1.1 [0.5–3.7]	0.7 [0.5–2.1]	1.1 [0.5–5.9]	1.2 [0.5–2.9]	1.9 [0.5–5.9]	4.8 [2.7–9.1]	3.7 [1.8–7.4]	5.7 [2.5–11.9]	5.2 [2.5–9.1]	5.5 [2.0–10.1]
Median time between last visit and survey, months [IQR]	15.7 [12.3–21.2]	20.7 [14.9–37.1]	17.8 [13.9–26.0]	20.6 [15.5–28.6]	—	12.7 [9.9–37.2]	24.8 [15.4–35.7]	25.6 [16.9–31.9]	26.8 [18.9–37.2]	—

Table 1 (*Continued*)

	Pre-ART						ART					
	Traced				Not traced N = 726		Traced					Not traced N = 424
	Found alive N = 255	Found dead N = 343	Moved N = 96	Not found N = 287			Found alive N = 119	Found dead N = 244	Moved N = 88	Not found N = 205	
Time between last visit & death (%)												
<1 month	–	135 (39.7)	–	–	–		–	93 (38.8)	–	–	–
1–3 months	–	71 (20.9)	–	–	–		–	52 (21.7)	–	–	–
>3 months	–	136 (39.4)	–	–	–		–	244 (39.5)	–	–	–

ART, combined antiretroviral treatment: BMI, body mass index; IQR, interquartile range.
*Among patients aged >18 years.
†Among patients aged >5 years.

ART programmes is also highest (Coetzee *et al.* 2004; Etard *et al.* 2006; Ferradini *et al.* 2006).

Eligibility for study participation was assessed for 62% of LFU patients, and we determined the outcome of 70% of those eligible. Patients not found defaulted longer ago than those found, and as in previous studies (Yu *et al.* 2007; Maskew *et al.* 2007; Ive *et al.* 2005, Dalal *et al.* 2008), missing contact information or patient records were the main reasons for exclusion. Because patients with little family or social support might be less willing to provide their address and those in good health more likely to migrate in search of work, we could have either overestimated or underestimated reported death rates.

The main reason for LFU given by pre-ART and ART patients was stigma, and 50% of pre-ART and 74% of ART patients interviewed had not disclosed their HIV status to household members. Previous research identified fear of rejection and social isolation as reasons for care discontinuation (Maskew *et al.* 2007; Yu *et al.* 2007; Deribe *et al.* 2008) and barriers to treatment adherence (Weiser *et al.* 2003; Mills *et al.* 2006; Yu *et al.* 2007). Our study suggests that developing strategies to empower patients to overcome these difficulties are needed even in HIV highly prevalent areas like Chiradzulu. As in other sub-Saharan contexts (Billy *et al.* 2007; Dalal *et al.* 2008; Ive et al. 2005; Joshi *et al.* 2008; Maskew *et al.* 2007; Muwanga *et al.* 2008; Yu *et al.* 2007), we found that dissatisfaction with care or health personnel behaviour, costly transportation, perceived improved health and drug toxicity were important reasons for therapy discontinuation. Dissatisfaction with health care and poor understanding of treatment commitment and medical follow-up are likely to relate to high work load and task shifting with insufficient training and supervision. Open discussions with personnel, supportive supervision and individual patient counselling during follow-up could help to effectively address these issues. Furthermore, despite decentralization of care provision, many patients needed to walk long distances or use costly transportation in Chiradzulu. Evaluation of strategies such as implementation of longer drug refill periods and task shifting to trained lay care providers for stable patients is therefore needed.

Conclusions

Monitoring and understanding programme retention dynamics is essential for HIV programmes. Long-term success of ART scale-up will require design and regular evaluation of innovative strategies for patient support and education and to improve programme access and quality of care.

Table 2 Reported socio-economic and behavioural characteristics of pre-ART and ART LFU patients interviewed, HIV/AIDS programme of Chiradzulu, Malawi, 2001–2007

	Pre-ART N = 172	ART N = 49	Total N = 221
Socio-economic factors*			
Highest education level† (%)			
No education	23 (15.4)	5 (11.9)	28 (14.7)
Primary school	108 (72.5)	26 (61.9)	134 (70.2)
Secondary school	18 (12.1)	11 (26.2)	29 (15.2)
Missing	–	1	1
Marital status† (%)			
Single	30 (20.3)	16 (38.1)	46 (24.2)
Married	95 (64.2)	14 (33.3)	109 (57.4)
Divorced/separated	13 (8.8)	5 (11.9)	18 (9.5)
Widowed	10 (6.8)	7 (16.7)	17 (8.9)
Missing	1	1	2
Employment† (%)			
Farmer	78 (54.2)	19 (50.0)	97 (53.3)
Housewife	34 (23.6)	8 (21.0)	42 (23.1)
Business	12 (8.3)	6 (15.8)	18 (9.9)
Other	20 (13.9)	5 (13.2)	25 (13.7)
Missing	5	5	10
Cost of travel to HIV care facility (%)			
None	60 (36.8)	14 (32.6)	74 (35.9)
0.01–0.71 USD	47 (28.8)	13 (30.2)	60 (29.1)
≥0.72 USD	56 (34.4)	16 (37.2)	72 (34.9)
Missing	9	6	15
Travel time to HIV clinic (%)			
<1 h	36 (21.8)	12 (28.6)	48 (23.2)
1–2 h	55 (33.3)	14 (33.3)	69 (33.3)
>2 h	74 (44.9)	16 (38.1)	90 (43.5)
Missing	7	7	14
Behavioural characteristics†			
Worked outside district in past year (%)	59 (40.1)	19 (46.4)	78 (41.5)
Disclosed HIV status to people living with (%)	77 (51.3)	34 (80.9)	111 (57.8)
Reasons for defaulting			
Stigma	71 (45.8)	10 (25.0)	81 (42.5)
Transport cost	31 (20.1)	5 (12.8)	36 (18.7)
Unsatisfied with care/staff behaviour	49 (31.6)	18 (45.0)	67 (34.4)
Inconvenient clinic hours	9 (5.9)	3 (7.7)	12 (6.3)
Long waiting time	5 (3.3)	5 (12.8)	10 (5.2)
Perception of health improvement	44 (28.9)	10 (25.6)	54 (28.3)
Poor health	7 (4.6)	3 (7.7)	10 (5.2)
Lack of support by partner†	19 (13.9)	4 (11.1)	23 (13.4)
Use of traditional medicine	14 (9.2)	4 (10.3)	18 (9.4)
Drug toxicity	2 (1.3)	5 (12.8)	7 (3.7)

LFU, loss to follow-up; ART, Antiretroviral therapy.
*178 Pre-ART and 49 ART patients only provided information on reasons for defaulting.
†23 Pre-ART and 6 ART patients aged <15 years were excluded.

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Conflicts of interest

The authors have declared that they have no conflicts of interest.

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