Challenges for Scaling up ART in a Resource-Limited Setting: A Retrospective Study in Kibera, Kenya

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Objective: To determine levels of dropout and adherence in an antiretroviral treatment (ART) program in sub-Saharan Africa's largest urban informal settlement, Kibera, in Nairobi, Kenya.

Method: Retrospective cohort study.

Results: Of 830 patients that started ART between January 2005 and September 2007, 29% dropped out of the program for more than 90 days at least once after the last prescribed dose. The dropout rate was 23 per 100 person-years, and the probability of retention in the program at 6, 12, and 24 months was 0.83, 0.74, and 0.65, respectively. Twenty-seven percent of patients had an overall mean adherence below 95%. Being a resident of Kibera was significantly associated with 11 times higher risk of dropout.

Conclusion: Despite free drugs and low associated costs, dropout probabilities in this study are higher and adherence to ART is lower compared with other studies from sub-Saharan Africa. Our results illustrate that ART programs in resource-limited settings, such as Kibera, risk low adherence and retention rates when expanding services. Specific and intensified patient support is needed to minimize the risk of dropout and nonadherence causing future significant health threats not only to individuals but also to public health.

Key Words: antiretroviral, adherence, dropout, HIV, Kenya, Kibera, urban informal settlement

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INTRODUCTION

According to the United Nations Population Fund, more than half the world's population today lives in urban areas. In Africa, it is estimated that the urban population will double by 2030[1]; however, health services planning rarely takes informal settlements into consideration despite risks of ill health, including HIV infection rates, being higher than in the general population.[2,3] High unemployment and lack of access to food from subsistence farming leads to undernourishment, poverty, and high mobility. In addition, alcohol abuse, high-risk sexual behavior, and fragmented social networks are common.[4,5]

In sub-Saharan Africa, there are well-described barriers to retention in antiretroviral treatment (ART) programs, such as formal and informal costs, severe poverty, side effects, nondisclosure, long waiting times, alcohol abuse, and use of traditional medicines.[6–8] Factors found to promote adherence are social support and belief in treatment,[6,7] and recent data suggest that adherence levels between 68% and 85% can also be achieved in resource-limited settings.[9,10] The need for high adherence to ART to avoid development of drug resistance is a major concern in sub-Saharan Africa because protease inhibitors and other second-line or third-line HIV regimens are often prohibitively expensive or unavailable.[11]

Rosen et al[12] analyzed 33 patient cohorts from 13 African countries and found that on average, only 60% of patients were retained in ART programs after 2 years from treatment initiation. Loss to follow-up and early death were the major causes of dropout. The authors stressed the importance of early initiation of ART and better tracing systems.[12,13]

However, many of these results were attained in settings that are very different from informal settlements, where less is known of the specific barriers that jeopardize regular drug intake and retention in ART programs. We performed a retrospective cohort study in an ART treatment program in Kibera, in Nairobi, Kenya, sub-Saharan Africa's largest urban informal settlement. Our aim was to determine dropout rates and levels of adherence to ART.

METHODS

Setting and Study Population

The study was conducted at a community-based health clinic run by the African Medical and Research Foundation (AMREF) and Ministry of Medical Services, Kenya. The clinic provides free treatment and care for HIV-infected individuals in Kibera, Kenya, an urban informal settlement with a population of about 1 million. The health clinic offers preventive, diagnostic, and basic health care, including services focusing on immunization, nutrition, and reproductive health. An ART program was started in February 2003 and since then the clinic has provided free voluntary counseling

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and testing, prevention of mother-to-child transmission, and HIV/AIDS treatment, care, and support, including nutritional support and home-based care. Adherence and retention in the ART program is supported by counselors, posttest clubs, treatment literacy training for children and adults, social assessments, and change of pill regimes to fixed doses. Tracing of defaulted patients is done by community health workers with support from the posttest clubs. Patient eligibility to ART was initially based on World Health Organization clinical staging only, but CD4 and viral load testing were later introduced. In 2006, routine use of viral load was discontinued. The clinic faces problems with an increasing workload, increased complexity of ART, and reduced workspace leading to low quality of services and poor data management and record keeping.

In Kenya, 71% of the urban population lives in informal settlements.[14] HIV-related disorders account for over 50% of the disease burden in 2 other informal settlements in Nairobi, comparable to Kibera.[15] The estimated HIV prevalence in Kibera is about 12% compared with the national prevalence of 5.1% (AMREF, Personal oral communication, May 2008).

Ethical approval for the study was obtained from the Kenya Medical Research Institute.

Inclusion Criteria and Data Collection

All patients starting ART who had completed at least their first follow-up visit during the observation time from January 2005 to September 2007 were included in the study. Study patients were followed up on a monthly basis until the end points were reached (dropout or end of observation period). Clinical status at baseline was assessed by the Karnofsky performance scale (Table 1).[16] Data on side effects, regimen switches, and opportunistic infections that should be routinely collected by the clinical officers were not used in the analysis due to a high frequency of missing data.

Definition of Dropout and Adherence

Dropout was defined as a patient who had not showed up 90 days after the last prescribed dose. The follow-up date and number of prescribed doses were retrospectively collected from existing individual patient records. We retrieved each follow-up date, added the number of prescribed daily doses to the last follow-up date, and then added 90 days (Fig. 1). This approach adjusts for differences in the prescribed number of doses.

Adherence was calculated via the continuous single interval measure of medication availability (CSA), that is, the days' supply of drugs divided by the number of days in the interval from the dispensing date up to, but not including, the next dispensing date.[17] We retrospectively collected the *days' supply* from existing routine patient records. The *days in interval* were also obtained from the patient files, using follow-up dates for each patient. If a patient had not returned for a drug refill for more than 90 days after the last prescribed dose, then this particular CSA occasion was excluded, and the patient was classified as a dropout. If a patient reentered the program, they could resume contributing to adherence estimates according to the CSA formula. From the CSA formula, an adherence estimate (a proportion) for each patient and each drug dispensing occasion is derived, taking into account the differences in the number of prescribed doses. This is the recommended refill adherence measurement if a population with high attrition is studied.[18] The mean of all adherence estimates provided the overall adherence for each patient.[18,19]

Most patients at the AMREF clinic are provided with drug supplies for 30 days at a time; some patients up to a maximum of 90 days, depending on the clinician's decision. Hence, well-known patients are occasionally given more medicines and longer intervals between follow-up. Differences in the amount of prescribed doses at the last follow-up were accordingly adjusted for in both the dropout and the adherence calculations.

TABLE 1. Characteristics of Respondents at Screening and Type of HAART Regime at ART Initiation (N = 830)

Characteristics	Respondents, n (%)	Missing data
Sex		1
Male	290 (35)	—
Female	539 (65)	—
Mean age ± SD	35 ± 8	5
Residents of Kibera	644 (79)	15
Patients taken ART before	65 (19)	487
Mean weight at ± SD	57 ± 11	120
Mean hemoglobin ± SD	11 ± 2	206
Mean CD4 ± SD	203 ± 197	223
Mean viral load	5 ± 1	570
Type of HAART regime, %		
NRTI*	99	—
NNRTI†	97	—
Protease inhibitor‡	1	—
Taking TB treatment at screening	33 (4)	—
Karnofsky performance status, %§		
100	16	—
90	76	—
80	7	—
70	2	—
60	0	—
50	0	—

HAART, highly active antiretroviral therapy; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; TB, tuberculosis.

*NRTI: lamivudine, stavudine 30 mg, stavudine 40 mg, zidovudine, didanosine 125 mg, didanosine 200 mg.

†NNRTI: nevirapine 200 mg, efavirenz 600 mg.

‡Protease inhibitor: lopinavir.

§Karnofsky: 100% = normal; no complaints; no evidence of disease, 90% = able to carry on normal activity; minor signs and symptoms of disease, 80% = normal activity with effort; some signs and symptoms of disease, 70% = cares for self; unable to carry on normal activity or do work, 60% = requires occasional assistance, but is able to care for most personal needs, 50% = requires considerable assistance and frequent medical care, 40% = disabled; requires special care and assistance, 30% = severely disabled; hospitalization indicated although death not imminent, 20% = very sick; hospitalization necessary; requires active support treatment, 10% = moribund; fatal processes progressing rapidly, 0% = dead.

Statistical Analysis

SPSS for Windows (version 15.0) was used for statistical analysis. Data are routinely collected at the AMREF clinic by the clinical officer assessing the patient and entered into a Microsoft data entry program by a data clerk. Descriptive

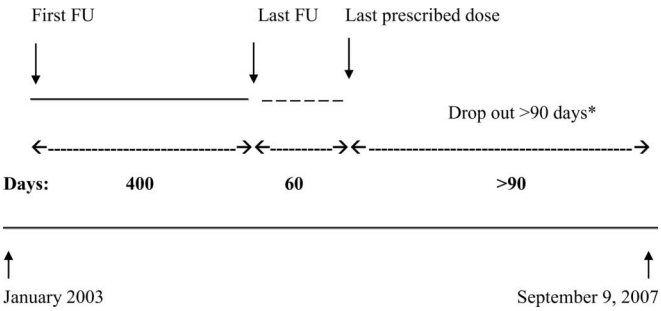

FIGURE 1. An example of patient dropout. A patient was followed for 460 days, including 60 days of ART prescribed at the last follow-up visit. He/she was then lost to follow-up for over 90 days after the last prescribed dose.

statistics were used to describe patient characteristics. Time on ART in days was calculated for all patients. Comparisons of adherent versus nonadherent patients and dropout versus nondropout patients were made using univariate analysis; independent sample *t* test for normally distributed continuous variables was used to compare means. For nonnormally distributed continuous variables, the Mann–Whitney test was used, and χ^2 or Fisher exact tests were used for categorical data. Multivariate logistic regression analysis was used to identify factors associated with dropout and adherence. We included variables with a *P* value <0.1 from the univariate analysis in the logistic regression.[20] The significance level was set to $P < 0.05$. We also performed Kaplan–Meier survival analyses to calculate the probability of dropping out at 6, 12, and 24 months.

RESULTS

Between January 2005 and September 2007, a total of 1674 HIV-positive patients were screened for ART eligibility and 830 patients between 18 and 70 years were started on ART. The sociodemographic and clinical background characteristics of the patients at baseline are presented in Table 1.

Dropout and Adherence Rates

Two hundred forty-four (29%) patients of the 830 patients who were started on ART dropped out of the program for more than 90 days after the last prescribed dose. The corresponding dropout rate was 23 per 100 person-years. For dropout patients, the mean time on ART was 257 days, and for nondropout patients, the mean time on ART was 549 days ($P < 0.01$).

The 830 patients started on ART received a total of 8775 drug prescriptions (mean number of follow-up visits 11 ± 10 SD). Two hundred twenty-one (27%) patients had an overall mean adherence below 95%. Among these, 65 (8% of 830) patients had a mean adherence below 80%.

Seventy (32%) patients with low adherence (overall adherence <95%) while in the program later dropped out for more than 90 days after the last prescribed dose.

Results from univariate analyses of the associations between dropout and clinical and sociodemographic

TABLE 2. Univariate Analysis of Associations With Dropout and Adherence (N = 830)

	Nondropout		Dropout		High Adherence		Low Adherence		
	n	%	n	%	n	%	n	%	N
All % are column %									
Sex†									
Male	208	36.6	82	33.6	220	36	70	32	829
Female	377	64	162	66	388	64	151	68	—
Mean age†	35	—	36	—	35	—	36	—	825
Resident of Kibera*	429	75	215	89	479	80	165	76	815
Earlier ART use	50	18	15	22	43	18	22	20	343
Mean weight at screening*	58	—	55	—	57	—	56	—	710
Mean hemoglobin,	12	—	11	—	11	—	11	—	624
Mean CD4, ART initiation	198	—	216	—	199	—	218	—	607
Mean viral load	5		5		5		5		260
Mean time on ART (days)*	549	—	257	—	484	—	406	—	830
TB treatment at screening	25	4	4	2	36	6	14	7	815
Karnofsky performance status at screening, %*									
100	89	17	26	12	89	16	26	14	737
90	389	76	170	76	411	75	148	78	—
80	29	6	20	9	37	7	12	1	—
70	7	1	6	3	9	2	4	0	—
60	0	0	1	0	1	0	0	0	—

TB, tuberculosis.
*Bold, $P < 0.05$.
†Included in multivariate analysis.

background factors and the association between background factors and low adherence (<95%) are presented in Table 2.

Multivariate Analysis

Complete data were available for 648 patients in the logistic regression model. Sex, age, duration on ART, clinical status on ART initiation, choice of ART regime, concurrent tuberculosis disease, and weight at ART initiation were included in the logistic regression model as independent variables. Residence in Kibera [odds ratio = 11.1, 95% confidence interval (CI): 5.9 to 21.1; $P < 0.001$] was the only factor significantly associated with dropout. In the logistic regression model assessing the association with low adherence, complete data were available for 825 patients, and no factor remained independently associated with adherence.

Survival Analysis

The Kaplan–Meier probability of remaining on care and treatment was 0.83 at 6 months (95% CI 0.81 to 0.84), 0.74 at 12 months (95% CI 0.67 to 0.76), and 0.65 at 24 months (95% CI 0.63 to 0.67) (Fig. 2).

DISCUSSION

The aim of this retrospective study was to determine dropout rates and levels of adherence to ART. We found that a substantial number of patients (29%) dropped out and hence were without treatment for periods that placed them at risk for developing opportunistic infections, deteriorating health, and premature death.[21,22] Kibera residents had 11 times higher risk than non-Kibera residents, of dropping out. The harsh conditions associated with living in an urban slum like Kibera are likely related to this risk elevation and may include underlying causes of dropout such as premature death, competing causes of disease, alcohol or substance abuse, poverty, and high mobility. Kibera residents have usually migrated from the countryside, and the need for traveling may contribute partly to their much higher risk of dropout. One way of handling patients' need to travel is to systematically dispense drugs for longer periods of time, but the disadvantages include drugs being lost or sold and the patient being away from the support structure for a longer period. Scanty evidence exists on possibilities of accessing ART in other geographical areas. Buying ART from a private provider or on the black market is associated with high costs, which likely restricts this possibility for Kibera residents (AMREF, Personal oral communication, September 2008).

We found that a large number of patients receiving ART are at immediate risk of developing drug resistance. Slightly more than a quarter (27%) of patients had an overall adherence below 95%, and 8% of the total had a mean adherence below 80%. The great majority of the patients (99%) were using nucleoside reverse transcriptase inhibitors or nonnucleoside reverse transcriptase inhibitors, requiring high levels of adherence to avoid development of drug resistance.[23,24] In their meta-analysis, Mills et al[25] concluded that among the 12 sub-Saharan ART programs analyzed, 77% of patients reached adequate adherence rates (levels of >95%). The adherence figures from our study are lower than those of the studies presented by Mills et al,[25] which may represent differences due to the demanding circumstances in Kibera.

The dropout rate in this ART program was as high as 23 per 100 person-years, and the probabilities of retention in the

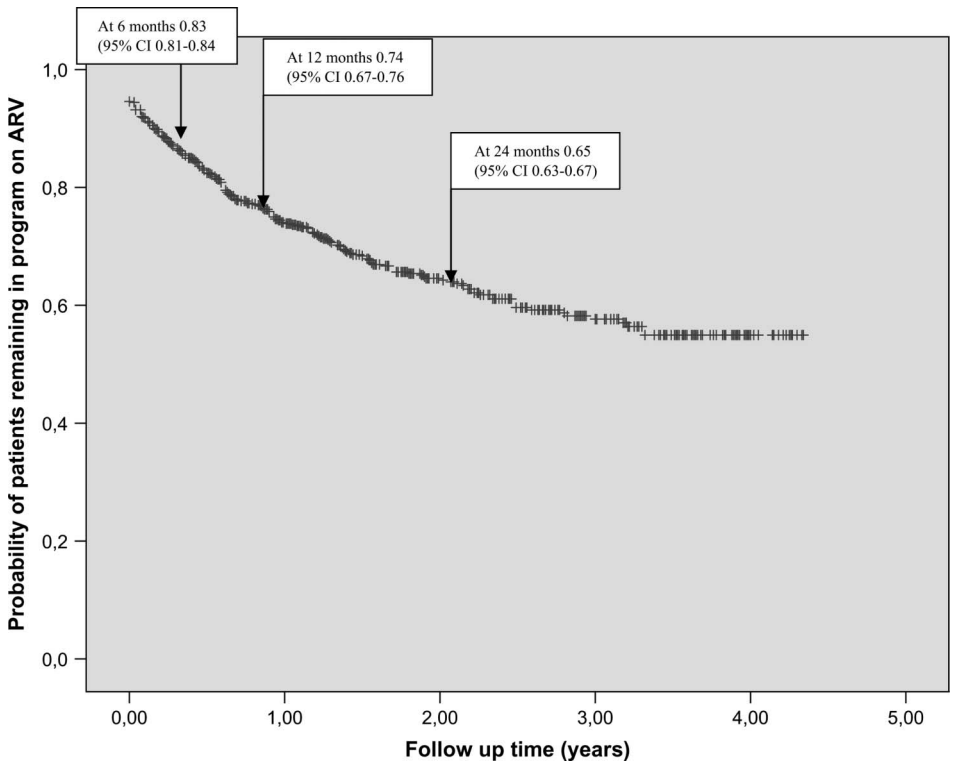

FIGURE 2. Survival analysis.

program at 6, 12, and 24 months were 0.83, 0.74, and 0.65, respectively. In a previous study of dropout in the same ART program in Kibera, Marston et al[26] reported overall higher probabilities of remaining in care: 0.92 at 6 months, 0.87 at 12 months, and 0.85 at 18 months. Their study covered an earlier observation period and a smaller patient cohort (283 patients observed from February 2003 to February 2005 compared with 830 in our study), and they concluded that the response to ART in this setting was similar to that seen in higher income settings. Our study challenges these conclusions by showing a relatively large number of patients with low adherence and high dropout rates. We found that scaling up the ART program by about 300% between 2005 and 2007 has likely posed unmet demands on the program, resulting in low adherence and retention rates.

Good results in terms of reducing dropout have been achieved by educating "adherence support workers"—most often people living with HIV/AIDS—for example, in Zambia, where the loss to follow-up was reduced from 15% to 0% after deploying adherence support workers.[27] To provide training for community members and counseling and support to an ethnically heterogeneous, poor, and challenged patient population such as the one in Kibera requires adequate training of staff. The AMREF clinic is reportedly suffering from a heavy workload and reduced workspace that threatens the quality of services. Data management and record keeping are also poor. We identified a high number of missing data on clinical patient variables, which is partly explained by the high workload of the clinical staff combined with the lack of a user-friendly system for recording adverse events, opportunistic infections, and other clinical events. Without adequate patient monitoring, early warning signs of low adherence or dropout might easily be missed.

Our results feed into the current debate on health system demands and donor-financed scale-up of ART. They illustrate that ART programs in resource-limited settings, such as Kibera, risk low adherence and retention rates when expanding services. To promote a successful outcome, programmatic factors such as well-trained staff, well-functioning routines, and adequate monitoring tools need to be in place. These factors are especially important when expanding a complex treatment to reach a larger patient group in a setting, where the individual's possibilities to adhere and to remain in treatment are threatened by harsh living circumstances.

No significant association was found between low adherence and dropout from the program, and hence, according to our findings, low adherence cannot be used as a warning sign for potential dropout. Still, more than one third of the patients with low adherence levels also had at least 1 dropout episode. This patient group is especially vulnerable, and it is important to study the barriers to successful treatment that could be specific to them.

There are many challenges when measuring dropout rates and adherence. Due to the retrospective nature of this study, we were not able to classify reasons for dropout. We opted for a conservative definition of dropout, using an interval as long as 90 days so as not to overestimate the dropout risk. Various periods from the last visit have been used in previous studies for defining dropout, 30 days being the most common.[28] We used the Measure of Medication Acquisition (CSA) to estimate adherence, which is based on actual prescriptions and days between drug refills.[17,18] The CSA does not give information on actual drug intake but provides convenient, noninvasive, objective, and inexpensive estimates of the highest possible level of drug intake, which will generate a conservative estimate of low adherence.[18]

CONCLUSIONS

The findings from this study indicate that a substantial number of patients drop out of ART treatment despite being provided with ART free of charge at a clinic only a short distance from home. Kibera residents had 11 times higher risk than nonresidents of dropping out from treatment. After 2 years of ART, the probability of remaining in treatment was only 65% in this study population. Treatment interruptions may rapidly lead to deterioration of health and premature death. Dropout probabilities in this study are higher than in an earlier report from the same setting, which suggest problems meeting the high program demands related to scaling up ART in a challenging urban slum context. In addition, more than a fourth (27%) of patients in our study had low ART adherence, below 95%. Adherence rates were lower compared with earlier reports from sub-Saharan Africa. Because these patients almost exclusively use nucleoside reverse transcriptase inhibitors/nonnucleoside reverse transcriptase inhibitors, they face the risk of rapid drug resistance development.

Our results illustrate that ART programs in resource-limited settings, such as Kibera, risk low adherence and retention rates when expanding services. Specific and intensified patient support is needed to minimize the risk of dropout and nonadherence causing future significant health threats not only to individuals but also to the general public.

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