Male, Mobile, and Moneyed: Loss to Follow-up in an Urban African Antiretroviral Treatment Clinic

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Introduction

Retention in an antiretroviral clinic has been identified as a critical component of HIV care. Combination antiretroviral therapy (ART) with three or more antiretroviral drugs reduces both morbidity and mortality from HIV infection (1), but its beneficial effects decline when adherence to treatment regimens is inadequate (2,3). Patients who miss visits or are lost to follow-up (LTFU) from an ART clinic lack continuous access to their medications and are unable to reach optimal adherence levels necessary for viral suppression (4). In some studies LTFU has been aggregated with other negative treatment outcomes, including ART failure (5) and death (6,7), reflecting a common assumption that the majority of LTFU cases represent an influential interruption in care.

LTFU is particularly problematic in sub-Saharan Africa, where there are fewer resources to devote to retention efforts. While funding such as the Presidents Emergency Plan for AIDS Relief (PEPFAR) has increased global access to ART over the past decade (8), growing patient numbers have challenged the ability of many clinics to successfully track and retain individuals who are at risk for LTFU (9,10). Two systematic reviews of ART clinic retention in sub-Saharan Africa indicate that attrition is approximately 20% at six to twelve months after ART initiation, over half of which is attributed to loss to follow-up (LTFU) (11,12).

Few studies have closely examined the timing and reasons for LTFU, and, to our knowledge, none has analyzed the characteristics of those LTFU who transferred their HIV care elsewhere and differentiated them from those who were LTFU without care. This study employed collection of both quantitative and qualitative data to elucidate the correlates and reasons for loss among transfers and LTFU without care from an ART clinic in Nairobi, Kenya.
Methods

This was a prospective study of participants enrolled in a randomized controlled trial that compared adherence to ART between those who received educational counseling and those who carried a pocket alarm device (13). In this study, 400 ART naïve adults who were eligible to initiate fixed-dose combination ART (d4T, 3TC, and nevirapine) at the Coptic Hope Center for Infectious Diseases were randomized into one of four factorial arms: 1) HAART adherence counseling; 2) an electronic reminder alarm; 3) counseling plus the alarm; or 4) neither intervention. Individuals were eligible for the study if they were at least 18 years of age, ART naïve, agreed to home visits by study staff, and planned to stay in Kenya for at least two years. Study participants received their HIV care at the Coptic Hope Center in Nairobi, Kenya (13). Sociodemographic variables, CD4 count, and plasma HIV-1 viral load were collected for all participants at study enrollment as well as addresses, local bus routes, neighborhood landmarks, GPS coordinates, and other contact information in order to facilitate participant tracing.

Participants were followed for 18 months after initiating ART and were scheduled to return monthly to the study pharmacy to pick up antiretroviral medications. Home visits were conducted for those who were more than four weeks late for their monthly pharmacy refill visit and were unresponsive to repeated phone calls. Participants were defined as LTFU if they failed to return to clinic within 60 days of their last visit. Reasons for loss were self-reported or gathered from household members or neighbors.

Baseline characteristics were compared using Mann Whitney U test of medians for continuous variables and Chi-squared test of independence for categorical variables. Fisher’s exact test was used for categorical variables where any cell had a count less than five. Odds ratios were calculated with multivariate logistic regression. All quantitative analyses were
Results

Between May 2006 and September 2008, 400 participants were enrolled and randomized into the adherence trial. Seven participants were excluded from analyses due to incorrect study eligibility or study withdrawal. Among the 393 remaining participants, the median age was 36 years (IQR 31, 42), 66% were female, 67% were employed at baseline, and the median monthly rent was US$27 (IQR 11, 53).

Three hundred and ten participants completed 18 months of follow-up after ART initiation, and 83 participants (21%) never returned to ART clinic (Figure 1). Among the 83 participants who did not return to clinic, 75 (90%) were successfully traced, and 8 (10%) were not located. Among the 75 traced participants, 38 (51%) had died, and 37 (49%) were alive but LTFU. Among these 37 LTFU, 18 (49%) were lost prior to ART initiation, and 19 (51%) were lost after. Among the 38 deaths, 9 (24%) died before ART initiation and 29 (76%) died after (Figure 1). There were no differences in LTFU, mortality, or total study attrition seen by any of the four intervention arms.

Of the 37 LTFU who were traced and alive, 22 (59%) transferred their HIV care elsewhere and 15 (41%) were receiving no HIV care. Among the 22 participants who transferred care, 11 (50%) moved (5 lost or changed jobs, 2 were refugees, 2 moved for family or marriage, and 2 did not give a further explanation); 7 (32%) transferred to an HIV clinic closer to home; and 4 (18%) sought better clinical care elsewhere (Figure 2). Ten (45%) transferred prior to ART initiation and 12 (55%) transferred after. LTFU participants who transferred care had
higher median rent (US$57 vs. 24; p=0.004) and were less likely to use a pit latrine (32% vs. 54%; p=0.04) than those who were retained in care (Table 1).

Among the 15 LTFU who did not receive further HIV care, 11 (73%) moved (4 lost or changed jobs, 2 were refugees, and 5 moved without citing a specific reason); 2 (15%) felt they did not need ART; and 2 (15%) reported being healed by faith (Figure 2). Of the LTFU who were not receiving care, 8 (53%) were lost prior to ART initiation and 7 (47%) were lost after. LTFU participants with no care were more likely to be male (60% vs. 34%; p=0.04) and to have fewer people in their household (median 2 vs. 3; p=0.051) than those who were retained in care (Table 1). Controlling for age, monthly rent, employment and number of people per household, the odds of LTFU with no care were 3.4 for males as compared to females (95% CI: >1.0-11.7; p <0.05).

Discussion

In this study, we comprehensively assessed attrition in an urban ART cohort participating in a randomized trial. We found that the half of all LTFU occurred prior to ART initiation, and that transfer of HIV care comprised the majority of successfully traced LTFU. As such, differentiating between LTFU who did and did not transfer care added important specificity to our definition of LTFU because patients who did not transfer care ART interruption while those who transferred to other ART clinics are expected to continue on ART. Because of our subset definitions, we were able to define characteristics of LTFU individuals who transferred care that distinguished them from those who were retained. Another set of factors characterized LTFU individuals who discontinued care. We found those who transferred care were of higher socioeconomic status (SES) than those retained in care. In contrast, those who were LTFU
without care were more likely to be men. Among all LTFU, with and without transfer, moving one’s home was the most commonly cited reason for loss.

Among LTFU participants alive at tracing in this study, most had successfully enrolled in care elsewhere. These findings are consistent with the proportion of transfer among LTFU patients identified by Gerver et. al. (48%) (14), and are only slightly higher than the proportions of LTFU transfer seen in studies that included mortality in their denominator (15–17). Together with this body of literature, our findings suggest that, without tracing, LTFU is an imprecise criterion that does not exclude successful transfer, in which case ART outcomes would not be compromised. Defining and understanding these subgroups separately is likely to be more effective in improving overall ART clinic retention at a population level. Transfers reported a median monthly rent of nearly 2.5 times that of retained participants and were more likely to use a flush toilet than a pit latrine, indicating a higher SES. This association may explain why initial findings of higher SES among LTFU in this cohort (13) differ from other studies which have associated LTFU with lower values of SES indicators (18–20). To our knowledge, the finding of high SES among transfers has not been previously reported, and may reflect greater financial means to explore multiple clinic options prior to committing to an ART provider, especially in an urban setting such as Nairobi where providers are abundant.

Among LTFU with no subsequent care, male gender was significantly predictive of loss, with men being over 3 times as likely to be lost from care as women. The association between male gender and LTFU is well documented in ART retention literature (19,21–27). Reports from other chronic conditions have found that men are more likely than women to be “unintentionally non-adherent” to their medications (e.g. forgetting to take their medication or carelessness) (28), and are less likely to achieve favorable clinical outcomes(29). Our findings
support the concept that men may have a more difficult time adhering to chronic care treatments than women, and may need targeted maintenance interventions.

We identified several qualitative reasons for LTFU based on home tracing interviews which provide insight into the context in which loss from an ART clinic occurs. Among both transfers and LTFU with no care, moving was the most common reason for loss, the majority of which was due to job loss or change in employment. This reflects the substantial impact of employment on geographic mobility in this urban African population. Nairobi has experienced more in-migration than out-migration since 1969 (30); however, intra-city mobility is more difficult to quantify, particularly among slum settlements which house both short and long-term residents (31). Uneven economic development in resource-limited settings may destabilize populations, promote migration and thereby increase LTFU. High mobility in urban sub-Saharan Africa has also been associated with risky sexual behaviors including earlier initiation (32) and increased partnerships (33,34). Links with social workers and strategies to address mobility and employment may enhance retention efforts and curb HIV morbidity and mortality.

Half of all LTFU occurred before ART initiation. This is consistent with other data indicating that LTFU often occurs prior to ART initiation (18,35) and indicates that the pre-ART period is one in which retention interventions are most necessary.

While other studies in Sub-Saharan Africa have analyzed transfer of care as an outcome alongside retention, mortality, and LTFU (14–17,22,25–27,36–43), ours was unique in determining correlates of LTFUs who did and did not transfer their care elsewhere. Our study also benefited from a high response rate and timely assessment of qualitative reasons for loss. A major strength was the ability to define transfers and those who were truly lost to care and to examine characteristics of individuals in these groups compared to retained participants.
However, these analyses involved relatively small numbers of participants in each sub-group, limiting power to detect differences among them. While our definition of LTFU is consistent with other studies (19,27,39,42), it did not capture potential treatment interruptions within the follow-up period. The scope of the qualitative reasons collected was relatively limited. Primary reasons for LFTU identified by other studies include transport cost (16,36,37,41,44–46); stigma, discrimination, and lack support (16,44–48); and poor patient-provider relationships or clinical outcomes (37,44,48,49), none of which were reported by participants in this study. Our tracing procedures allowed participants and contacts to provide detailed reasons for loss, but we did not probe for more in-depth responses. Without extensive qualitative interview training, interviewers may not have been able to elicit more sensitive reasons such as care-dissatisfaction or stigma. It should be noted that the Coptic Hope Center for Infectious Diseases, with PEPFAR support, provides comprehensive medical care, counseling, nutritional, and social work services in addition to free ART. Thus the comprehensive and high quality care provided at this clinic may not be reflective of underlying LTFU reasons identified by other studies.

This study provides a snapshot of some reasons for transfer and true loss from care from an urban clinic in sub-Saharan Africa. Our findings suggest that interventions focused on men and potential integration of employment counseling or job networks within comprehensive HIV care may be useful to enhance retention in HIV care programs. Finally, it is important for programs to develop strategies to classify clients who have transferred care, to be better able to discern correlates of true loss to care, and to avoid using limited resources to target those who are successfully enrolled in care elsewhere.
Figure 1. Trial profile of ART eligible patients screened and enrolled between May 2006 and September 2008.
Figure 2. Attrition outcomes and reasons for loss

- **Total study attrition**: 83
  - Successfully traced: 75
  - LTFU not located through tracing: 8
  - Died: 38
  - Transferred care: 22
    - Reasons for transferring care:
      - 11 moved:
        - 5 job loss or change
        - 2 refugee
        - 2 family, marriage
        - 2 no reason given
      - 7 to be closer to home
      - 4 better care, drug supply, shorter waiting period
  - No care: 15
    - Reasons for no care:
      - 11 moved:
        - 4 job loss or change
        - 2 refugee
        - 5 no reason given
      - 2 don’t feel need to start ARVs
      - 2 healed by faith
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Retained in Care (N=310) n (%), median (IQR)</th>
<th>Transfer of Care (N=22) n (%), median (IQR)</th>
<th>P-value</th>
<th>No Care (N=15) n (%), median (IQR)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>36 (31, 43)</td>
<td>33.5 (29, 39)</td>
<td>0.12</td>
<td>34 (28, 43)</td>
<td>0.33</td>
</tr>
<tr>
<td>Female</td>
<td>205 (66.1)</td>
<td>18 (81.8)</td>
<td>0.16</td>
<td>6 (40)</td>
<td>0.04</td>
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<tr>
<td>Married</td>
<td>137 (44.2)</td>
<td>7 (31.8)</td>
<td>0.26</td>
<td>7 (46.7)</td>
<td>0.85</td>
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<tr>
<td>Employed</td>
<td>214 (69.3)</td>
<td>16 (72.7)</td>
<td>0.73</td>
<td>8 (57.1)</td>
<td>0.34</td>
</tr>
<tr>
<td>Education level*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; Primary</td>
<td>7 (2.3)</td>
<td>0 (0)</td>
<td>0.52</td>
<td>0 (0)</td>
<td>0.16</td>
</tr>
<tr>
<td>Primary</td>
<td>101 (32.9)</td>
<td>8 (36.4)</td>
<td></td>
<td>9 (60)</td>
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<td>Secondary</td>
<td>124 (40.4)</td>
<td>6 (27.3)</td>
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<td>3 (20)</td>
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<tr>
<td>College</td>
<td>75 (24.4)</td>
<td>8 (36.4)</td>
<td></td>
<td>3 (20)</td>
<td></td>
</tr>
<tr>
<td>(n=307)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number in household</td>
<td></td>
<td></td>
<td>0.46</td>
<td>3 (1, 4)</td>
<td>0.051</td>
</tr>
<tr>
<td>Toilet</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pit latrine</td>
<td>169 (54.5)</td>
<td>7 (31.8)</td>
<td>0.04</td>
<td>9 (60)</td>
<td>0.68</td>
</tr>
<tr>
<td>Flush toilet</td>
<td>141 (45.5)</td>
<td>15 (68.2)</td>
<td></td>
<td>6 (40)</td>
<td></td>
</tr>
<tr>
<td>Share a toilet</td>
<td>170 (54.8)</td>
<td>10 (45.5)</td>
<td>0.39</td>
<td>11 (73.3)</td>
<td>0.16</td>
</tr>
<tr>
<td>Monthly rent (US$)</td>
<td></td>
<td></td>
<td>0.004</td>
<td>33 (20, 73)</td>
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<tr>
<td>(n=265)</td>
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<td></td>
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<tr>
<td>Cost from clinic to house (US$)</td>
<td></td>
<td></td>
<td>0.22</td>
<td>0.7 (0.5, 0.8)</td>
<td>0.65</td>
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<tr>
<td>Distance from clinic to house (Km)</td>
<td></td>
<td></td>
<td>0.15</td>
<td>8.0 (6.5, 10.7)</td>
<td>0.30</td>
</tr>
<tr>
<td>BL VL log10</td>
<td>10.5 (6.8, 15.6)</td>
<td>7.1 (5.6, 12.9)</td>
<td></td>
<td>8.0 (6.5, 10.7)</td>
<td></td>
</tr>
<tr>
<td>(n=307)</td>
<td></td>
<td>(n=13)</td>
<td></td>
<td>(n=12)</td>
<td></td>
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<tr>
<td>CD4 at enrollment (cells/mm³)</td>
<td></td>
<td></td>
<td>0.89</td>
<td>5.4 (4.2, 5.8)</td>
<td>0.13</td>
</tr>
<tr>
<td>(n=308)</td>
<td></td>
<td>(n=21)</td>
<td></td>
<td>(n=14)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.13</td>
<td>164 (63, 201)</td>
<td>0.35</td>
</tr>
</tbody>
</table>

*Test of trend


25. Bajunirwe F, Arts EJ, Tisch DJ, King CH, Debanne SM, Sethi AK. Adherence and treatment response among HIV-1-infected adults receiving antiretroviral therapy in a rural government


