A retrospective notes-based review of patients lost to follow-up from anti-retroviral therapy at Mulanje Mission Hospital, Malawi

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Abstract

Aim
To analyse patients with HIV who were lost to follow-up from anti-retroviral therapy (ART) at Mulanje Mission Hospital (MMH), Malawi.

Methods
All patients on adult antiretroviral combinations at MMH, who were classified as lost to follow-up (LTFU) according to the national guidelines (patients missing a scheduled follow-up visit by more than two months) over a 12-month period, were included in the study and compared against a control group who had never been lost. Variables compared were gender, age, months on ART, time of year, WHO clinical stage, ART regimen, reported side effects, number of doses missed in the previous 12 months, whether the patient has been followed up in the community and if so, the length of time elapsed before follow-up.

Results
In all, 136 patients had been LTFU over the previous 12 months at MMH. Of these, 43 had incomplete or missing ART cards, resulting in 93 LTFU patient’s data that could be analysed. Patients were more likely to get LTFU if they were men (p=0.03), who had been on anti-retroviral therapy for a short duration (p=0.06) and the proportion of patients who missed more than 4 doses in the previous 12 months was higher among LTFU patients (p=0.05). Only 34.4% of those LTFU had been traced in the community at the time of analysis. Of those traced, 27% had moved to another area, 5.5% had died, 5.5% had the wrong documentation and 62% gave no reason as to why they had missed appointments.

Conclusion
This study in MMH has highlighted the importance and feasibility of comprehensive facility-level data-collection, both to identify local patient populations at risk of becoming lost to follow-up and to assess the follow-up measures in place to bring these lost to follow-up patients back into the programme. Even in the short time and with the small sample that was collected, there was evidence that patients most likely to get LTFU in MMH were young men, who had been on anti-retroviral therapy for a short duration and had missed over 4 doses in the last 12 months.

Introduction
More than three decades after the first cases of Human Immunodeficiency Virus (HIV) infections were recognized, the epidemic in sub-Saharan Africa (SSA) has claimed the lives of over 36 million people, and is still one of the world’s most important public health issues¹. However, in recent years, significant advances have been made to address the epidemic, in line with the political intent of Millennium Development Goal 6, which was first to halve then begin to reverse the spread of HIV by 2015². Key to this success has been the expansion of antiretroviral therapy (ART), which has led to a 30-fold increase in ART coverage in SSA over the last decade³.

For patients accessing ART, Acquired Immune Deficiency Syndrome (AIDS) has been transformed from a life-limiting condition, with a median survival of one year from diagnosis, into a chronic disease⁴, one which requires lifelong management⁵. However, the long-term retention of patients on ART has, itself, become a major challenge in SSA. In 2010, a systematic review of 39 papers found that 30% of patients were no longer taking their ARTs two years after starting treatment⁶. In the same review, it was noted that there was a paucity of data as to why patients become lost to follow-up (LTFU) in SSA⁶. This study will examine the current prevalence and reasons for patients becoming LTFU in resource-poor settings. The particular focus is on Mulanje Mission Hospital (MMH) in Malawi, serving one of the poorest regions of a nation with the lowest Gross Domestic Product (GDP) per capita in the world⁷.

Definitions
Throughout the literature, there is no universal definition for patients who are not retained in ART programmes. The World Health Organization (WHO) defines retention as “patients known to be alive and receiving highly active ART (HAART) at the end of a follow-up period.” This vague definition, which does not prescribe a specific follow-up period, has led to a wide disparity of retention periods being used in the studies: 30 days⁸, 3 months⁴, 6 months⁵ and 1 year⁹ are all quoted. Further confusion arises from the term ‘LTFU’ being used interchangeably with ‘attrition’ and ‘defaulting’ across studies⁴. In this report, LTFU has been utilized instead of
Prevalence of patients LTFU from ART in SSA

The largest systematic review, which aimed to quantify the number of patients retained on ART in SSA (using 39 cohort studies with a total of 226,307 patients), found that retention was 70.2% after 24 months. Although this study brought substantial benefits, it did not stratify the data for the three distinct cohorts of patients who were not retained in care. One study which looked at samples of patients not retained in ART across 13 countries in SSA, including Malawi, found that 36% were LTFU, 40% had died, and 4% were retained in care despite stopping ART. In 2008, a more detailed single-cohort study in South Africa found that 31% of its non-retained patients had died, 25% had transferred to another facility and 44% were LTFU.45

Despite differences in the absolute proportions across the different studies, the recurring finding is that patients LTFU make up the biggest share of patients not retained in ART programmes.15

Reasons for patients LTFU in SSA

Adherence to drug programmes is affected by the complex interplay of self-care, community factors, care delivery and the drug itself. Despite a paucity of qualitative research in developing countries, many reasons have been identified or hypothesized for the significant proportion of patients LTFU in ART programmes. Several papers have identified financial constraints as a major cause of LTFU in SSA.49 One study in Malawi found that 24% of patients originally recorded as LTFU, re-enrolled at the same site after ARTs were offered free of charge. However, the variation in adherence rates in different areas of the country, irrespective of free access, suggests that other barriers to treatment are involved.49

A qualitative study in Malawi’s southern region of Chiradzulu found that fear and stigma were the main reasons LTFU.50,51 Of the 221 patients interviewed, 74% of ART patients had not disclosed their HIV status to household members.51 In addition, the only published systematic review examining the concerns of HIV patients enrolled on ART programmes also found that fear of disclosure was the most consistently cited barrier to treatment.52 As well as discussing structural and socio-cultural issues, some research has concentrated on identifying which patient groups are most likely to become LTFU. Younger age at treatment initiation53, lower CD4 count at presentation,54 type of ART regimen55 and the occurrence of side effects56 have all been found to be associated with LTFU in the early stages of treatment. Later on, a risk of LTFU arises from patients experiencing an improvement in health and subsequently assuming that treatment is no longer necessary; 28.3% of patients LTFU in rural Malawi cited improved health as their primary reason for leaving the programme.56

HIV and ART in Malawi

Malawi’s HIV prevalence is one of the highest in the world; with the most recent Malawi Population-Based HIV Impact Assessment report estimating that 10.6% of the population (over 1 million people) are living with HIV.57 The epidemic has affected all sectors of society, disproportionately targeting the youngest and most productive age groups, and has played a significant role in the country’s life expectancy of only 54.8 years.58 This burden is compounded by a shortage of health workers; the ratio of 1 physician per 50,000 people in Malawi is well below the WHO threshold of 1 per 1000. Furthermore, substances used to reduce the burden of HIV in Malawi have been made over the last decade, bringing about significant reductions in morbidity, mortality and transmission. New infections have declined from 98,000 in 2005 to 34,000 in 2013, gaining 1.4 million life-years as well as a 67% reduction in mother-to-child transmission over the same period.59 This has largely been attributed to remarkable increases in ART coverage across the country, with over 300,000 individuals initiated on ART since the introduction of free universal provision in 2004.60

Prior to this, ART was only available at a cost of US$25 for a month’s supply. However, ART adherence is variable. In 2012, only 79% of adults and children were on ART in Malawi were taking them 12 months later, suggesting a significant proportion of patients LTFU. National Reports 2009, 2010 and 2012 have shown rates of LTFU of 12%, 15% and 21% respectively, the problem is increasing61 and with it, the impact on individuals. Patients missing visits in the first year of treatment have a two-fold increase in long-term mortality.62 There is also a health risk to the general public posed by the likely increase in drug resistance.63 In response to this, in 2014, Malawi launched the 2015-2020 National HIV/AIDS Strategic Plan. A key objective involves “maintaining high levels of adherence and retention in ART programs”64. This study is a contribution to this objective; as the number and demographics of patients LTFU from ART at Malawi was not known, it provides this missing information and gives insight into the frequency and reasons patients may be LTFU locally.

Methods

Study design

This was a retrospective notes-based review.

Setting

MMH is a mission hospital located in southern Malawi, close to the border with Mozambique. The hospital serves a catchment of 650,000 people who mainly live in rural villages and are reliant on farming for subsistence. The largest part of the hospital’s workload is in the assessment and treatment of HIV/AIDS, with 10,714 HIV tests done and 74,136 ART clinic attendances during 2015 alone. The most recent prevalence study in the area found that 18% of the population was living with HIV, significantly more than the national prevalence of 10.3%.65

Data collection

Using an existing clinical dataset, all patients on adult antiretroviral formulations at MMH, who were classified as ‘defaulters’ (the previous 12 months (2nd quarter 2015 – end of 1st quarter 2016), were included in the study. According to the local 2014 Malawian ART guidelines, defaulting was defined as “patients missing a scheduled follow-up visit by more than two months”66; a time frame that has recently been shown by Rachlis et al to represent the period (>9 weeks) after which returning to clinic reduces substantially.67

Data was collected from the patient cards stored in the outpatient ART clinic. The following variables were included in the analysis: gender, age, months on ART, time of year LTFU, WHO clinical stage, ART regimen, reported side effects, number of doses missed in the previous 12 months, whether the patient has been followed up in the community and if so, the length of time elapsed before follow up. To highlight comparisons amongst the studied population (the LTFU group), a control group was identified and their data analysed. The control group was selected by using all of the patients who attended the ART clinic between 18th and 22nd July 2016, and who had never defaulted.

Statistical analysis

Comparison data for LTFU and controls were analysed using the chi squared (χ²) test, with alpha levels set at 0.05.

Ethical considerations

Ethical approval was sought and approved by the MMH medical director and hospital board. Confidentiality was maintained by coding the patient ART cards anonymously so that data was inputted and analysed separately from any patient identifiable information.

Results

In all, 136 patients had been LTFU over the previous 12 months at MMH. Of these, 43 patients had been missing ART cards, so the records of 93 patients LTFU were analysed. In the control group, 93 datasets were also analysed.

Table 1: Comparison data for LTFU and comparison groups

| Gender | Male | Female | Controls (n=93) |
|--------|------|--------|----------------|
|        | 42 (55%) | 28 (30%) |                |
|        | 51 (45%) | 65 (70%) |                |
| Age (years) |        |        |                |
| ≤20 | 3 (3.2%) | 5 (5.4%) |                |
| 21-30 | 22 (23.7%) | 13 (14.0%) |                |
| 31-40 | 36 (38.7%) | 36 (38.7%) |                |
| 41-50 | 22 (23.7%) | 23 (24.7%) |                |
| >50 | 2 (2.2%) | 7 (7.5%) |                |
| WHO Clinical Stage at Initiation of ART |        |        |                |
| 2 | 18 (19.4%) | 15 (16.1%) |                |
| 3 | 30 (32.3%) | 26 (28.0%) |                |
| 4 | 6 (6.5%) | 5 (5.3%) |                |
| Duration of treatment on ART (months) |        |        |                |
| 0-12 | 18 (19.4%) | 10 (10.8%) |                |
| 13-24 | 20 (21.5%) | 17 (18.3%) |                |
| 25-36 | 9 (9.7%) | 11 (11.8%) |                |
| 37-48 | 18 (19.4%) | 14 (15.1%) |                |
| >49 | 28 (30.1%) | 41 (44.1%) |                |
| Number of Doses of ART missed in last 12 months |        |        |                |
| 0-3 | 48 (52%) | 61 (66%) |                |
| ≥4 | 45 (48%) | 32 (34%) |                |
had documented side effects in the previous 12 months (1 peripheral neuropathy and 1 hepatitis). The mean length of time on ART was 39.3 months for the LTFU group and 47.3 months in the control group, with a mean difference of 8.3 months less in the LTFU group (p=0.06). The mean number of doses of ART missed in the previous 12 months was 13.15 in the LTFU group and 4.74 among the controls, giving a mean difference of 8.41. When comparing time on ART and the likelihood of being LTFU, this finding was further evidenced by a recent retrospective cohort study in Neno District which found that ART decentralisation halved the distribution of ART during the rainy season. This has been further evidenced by a recent retrospective cohort study in Neno District which found that ART decentralisation halved the average distance to health centres and was associated with a 70% increase in retention in care.

ART regimen and length since initiation of ART

Two of the most instructive findings from the study came from an examination of the relationship between the length of time on ART and the likelihood of LTFU. The mean length of time on medication was 8.3 months less in the LTFU group, with a p-value of 0.05, emphasizing the need for more intensive follow-up in the early stages of treatment, when patients are at the highest risk of LTFU. Patients were also more likely to get LTFU if they had missed 4 or more doses in the previous 12 months (p-value=0.05); however, this relationship could be used as an early indicator for what might be needed to improve adherence rates and gaps and contained inconsistencies. The 43 initial missing records represent a potential selection bias if there are systematic differences between these patients and those analysed. Even when patient ART cards were available, some of the data was not entered: 8 ages were not recorded and for many patients, only their year of birth (not date) was documented. Absence of accurate data could have been a source of measurement error.

Furthermore, there was no follow-up of two thirds of the LTFU patients; so their outcomes represented an unknown fraction of the data was susceptible to significant selection bias.

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