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# **Low retention in care among HIV positive patients receiving antiretroviral treatment in Dodoma, Tanzania**

Degree Project in Medicine

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# Abstract

## **Introduction**

There have been great scale-ups of antiretroviral therapy (ART) in sub-Saharan Africa recent years. ART is very efficient in treating HIV, but it needs to be taken with strict adherence and life-long. Thus, the current challenge is to keep patients in the treatment programmes.

## **Aims**

The aim of this study was to find the proportion of patients starting ART 2012-2015 that remain in treatment the following four years at Dodoma Regional Referral Hospital. Furthermore, to find out whether patients lost to follow-up differed from patients remaining in care. Finally, to find out about patients' experiences of being treated with ART.

## **Methods**

Data was gathered from Dodoma Regional Referral Hospital's local database concerning 2333 patients, from 200 patient files and from 100 answered questionnaires. SPSS was used for analysing data.

## **Results**

Retention in treatment was 60% one year after treatment start, with further decrease to 47% after four years. Patients starting ART 2012 were more likely to remain in care than patients starting later. Having advanced HIV classified as WHO clinical stage 3 at treatment start was found to be a factor that increased the risk of being lost to follow-up (OR 3.19, 95% CI 1.81-8.59).

Incomplete adherence was shown in 22% of patients, where patients had missed to take at least one dose of ART the last four weeks before time of investigation. Side effects increased the risk for poor adherence. Stigma was seen; 22% of patients chose not to tell others about being HIV positive because of fear of being discriminated and 10% because of fear of being excluded from their families.

### **Conclusions and implications**

Retention in treatment was low and needs to be increased. By inquiring for factors associated with being lost to follow-up patients in need of extra resources to remain in treatment could be identified.

### **Keywords**

Antiretroviral therapy, retention, adherence, Tanzania.

# Introduction

## History and epidemiology

The first cases of AIDS (acquired immunodeficiency syndrome) were described in 1981 and the virus HIV (human immunodeficiency virus) causing the disease was discovered in 1983. By then, the disease was thought to be a threat to only special risk groups (1). Since then humanity has learned the hard way that AIDS in fact was a disease that could affect anyone and plenty of people have been affected by the epidemic. Since 1981 more than 70 million people have been infected by HIV and more than 35 million people have died because of HIV/AIDS. The current number of HIV positive people globally is estimated to 37 million, which corresponds to about 0.8% of the world's adults aged 15-49 years (2). The burden of disease varies between countries and continents, the epidemic has been most severe in low-income countries, especially in sub-Saharan Africa (SSA) where about two thirds of the HIV positive people can be found (3).

One of these Sub-Saharan African countries where the epidemic has been devastating is Tanzania. Statistics from year 2015 show that 1.4 million people were living with HIV by that time in Tanzania, corresponding to an estimate of 4.7% of adults aged 15-49 years. The same year 36,000 people died from AIDS in Tanzania. In only Tanzania there were by 2015, 790,000 orphans aged 0-17 years due to HIV/AIDS (4). The suffering has been tremendous and so has also the impact on economy and social welfare been (3).

## Transmission and risk groups

The main route of HIV transmission in Tanzania is heterosexual intercourse, which is estimated to account for 80% of the HIV cases (5). Historically, mother to child transmission

has been high, but is declining and by 2016 the coverage of ART was 86% for pregnant women living with HIV. However, there were still 10,000 new HIV infections in children by 2016.

The Joint United Nations Programme on HIV/AIDS (UNAIDS) has identified five key populations where more active measures need to be taken against HIV. These populations are sex workers, people who inject drugs, gay men and other men who have sex with men, transgender people and prisoners. By the year of 2016 28% of sex workers in Tanzania were estimated to be HIV infected and the corresponding number in men who have sex with men was 18%. The remaining three key populations have no corresponding numbers registered (6).

### 90-90-90

UNAIDS has decided on a treatment target to succeed with ending the AIDS epidemic. It is called 90-90-90 and this goal shall be met at year 2020 which is part of the final goal to end AIDS by 2030. The goal with 90-90-90 is that by 2020:

- 90% of all HIV positive people are to know their HIV status.
- 90% of all people with diagnosed HIV will receive antiretroviral therapy (ART).
- 90% of all people receiving ART will have viral suppression.

This will sum up in that at least 73% of all people living with HIV should be virally suppressed (7).

UNAIDS has presented data reflecting the situation in Tanzania by 2016, showing that Tanzania is currently at 70% knowing about their HIV status, 62% are on treatment and the number of virally suppressed is unknown (6). These statistics show us that Tanzania has a long way to go and the probability that the 90-90-90 goal will be met seems to be low.

However, there is definitely hope; new infections are declining and people dying of AIDS are significantly fewer every year (5). The factor behind these progresses and the reason that UNAIDS has set this ambitious goal is that there is treatment available that has been very successful and that treatment is antiretroviral therapy (ART) (6).

## Antiretroviral therapy

### *Pathophysiology*

HIV is a retrovirus that exists in two subtypes; type 1 and type 2. HIV-1 is more contagious than HIV-2 and it is HIV-1 that is responsible for all the cases of HIV infections in Tanzania, therefore HIV-1 will from now on be called HIV in this report (1, 3). HIV binds to the cellular receptor CD4 which is found mainly on helper T-lymphocytes, commonly called CD4-cells. The infected CD4-cells eventually die and that makes measuring CD4 count one way to monitor virus activity. Being a retrovirus, HIV is able to turn its RNA into DNA through the enzyme reverse transcriptase. In this process there are a number of different steps that are targets for ART (1).

### *Antiretroviral drugs*

There are currently six different categories of ART:

- Nucleoside reverse transcriptase inhibitors (NRTIs)
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- Integrase inhibitors (II)
- Protease inhibitors (PI)
- Entry inhibitors (EI) (subgroups: Fusion inhibitors and Chemokine receptor antagonist)

These drugs are taken in different combinations, commonly three different drugs from two different groups (8). The first line treatment in Tanzania is tenofovir (NRTI) + lamivudine (NRTI) + efavirenz (NNRTI). Depending on side-effects and other impacting factors the treatment can be modified, the Tanzanian guidelines for treatment include multiple different treatment regimens, including second line treatment. In Tanzania there are ten different ART pharmaceuticals; six NRTIs, two NNRTIs and two PIs which are used in different combinations (3). This is in comparison with almost 30 different ART drugs in Sweden (9).

### ***Indication***

The indication for treatment has been changed from different levels of CD4+ cells and clinical stage of disease to the present regimen which is simply to treat all, regardless of CD4 count.

After a positive HIV test the patient's eligibility for ART will be assessed (lab tests, psychological factors and so on) and when everything is in order treatment will start (6). This *treat all* regimen is according to WHO's guide lines from 2015 as part of the struggle to achieve the 90-90-90 goal (10). However, parts of this study will be investigating patients starting treatment in year 2012-2015 and by that time other guidelines were used. By then the indications for treatment of confirmed HIV positive adults were as follows (3):

- CD4 count 350 cells/ $\mu$ L or less.
- WHO clinical stage 3 or 4.
- Pregnant women.
- Breastfeeding women.
- TB co-infected.



### *Effects of ART and resistance*

ART has been a success story. It reduces the risk of developing AIDS, prolongs life and decrease mother to child transmission. If the therapy is successful the viral load can be decreased from  $10^5 - 10^6$  copies/ml to less than 20 copies/ml. When virus levels decrease the immune system recovers and the amount of CD4+ cells increase. ART has its effect through stopping replication of HIV which means that the virus is unable to infect new cells. There are, however, cells that keeps on living infected but in a latent phase, not replicating. These latent cells make it impossible to completely eradicate HIV from an infected person, since ART can only stop new cells from being infected and not treat the already infected ones (1).

The treatment sets high demands on the patient; it has to be taken exactly according to the prescription, which is daily (one, two or three times) and lifelong. Just a few missed doses and the virus could start replicating again, it has been shown that if less than 95% of doses are taken replication can occur. If replication occurs in presence of medicines resistance against these medicines could easily be developed. There are documented cases of resistance for all antiretroviral drug classes, either through therapy failure or through therapy-naïve patients that has been infected with drug-resistant viruses (1, 8). Given these factors it is of great importance that retention to treatment and adherence is absolute.

Several studies from sub-Saharan Africa have showed the connections between adherence, virological suppression/failure and drug resistance. In a review article that includes studies from 18 sub-Saharan African countries where the definition of virological failure was  $>1000$  copies/mL, virological failure occurred in 22% of patients after six months of ART, in 24% after twelve months and in 33% after 24 months of ART (11). There is currently no HIV drug

resistance surveillance system in Tanzania. However, roughly 71-90% of patients with virological failure have been showed to have evidence of resistance (12).

### *Side effects*

Despite the many advantages with ART there are some disadvantages too; it can cause several different side effects and it is common. Among the most commonly reported are for instance diarrhoea, peripheral neuropathy, lipodystrophy, fatigue, headache and rash (13). Typically, the older drugs are the ones causing the most side effects and it is also the older drugs that have been the most common in low-income countries due to lower price. This has, however, changed during the last decade since prices on more ARTs has decreased and the possibility of changing drugs if side effects occur has increased (14).

### Factors associated with adherence

Retention to treatment programmes is a determinant of adherence, since patients must attend an ART care programme to monitor their HIV clinical indicators and to receive their prescriptions. The coverage of ART for HIV positive people has increased a lot, the challenge remaining is, however, not to be underestimated and that is to have a total adherence and retention (15).

A study from Moshi, Tanzania showed that few patients were aware of which drugs of treatment they have and the limited future treatment options available. Results from that study suggested that the patients possessing that knowledge were more likely to be adherent in their treatment. In conclusion, it is of importance that health care personnel educate patients in these aspects (16).

Risk factors for non-adherence to treatment in SSA have been shown to be among others (15, 17):

- Patients of young age (<30 years).
- Patients with baseline WHO clinical stage 3 or 4.
- Ambulatory and bedridden patients at baseline (compared to working or active patients).
- Loss of body weight by more than 10% at baseline.
- Low baseline CD4 count (<50 cells/ $\mu$ L).
- Accessing care from higher level healthcare facilities.

Moreover, social and behavioural factors have been showed to be of importance. A large study performed in SSA found the following independent factors that were associated with incomplete adherence: high internalized stigma, positive screen for alcohol abuse and consulting traditional healers due to HIV (18). Stigma associated with HIV in Tanzania is one of the country's main challenges concerning HIV. Stigma is a common factor for poor adherence and non-retention to care (19).

In addition to medical adherence, retention in care is of importance for monitoring patients and for ensuring on-time medical refill. Several barriers to retention have been identified. A study performed in eastern Africa, including Tanzania, categorizes barriers to retention in structural (external environment), clinic based (healthcare environment) and psychosocial (patient-based). This study suggest that structural barriers contribute the most to patient transferring without announcing it ("silent transfer"), while psychosocial barriers such as social and psychological ones tend to result in long-term care discontinuation (20).

## Aim

To my knowledge there are no reports focusing on retention, investigating predictors for poor adherence and ways to improve adherence done at Dodoma Regional Referral Hospital, which is where this report aims to fill in the blanks.

The purpose of this study was to follow up how many of the patients that for the first time received ART in January 2012 to December 2015 at Dodoma Regional Referral Hospital that still remained on treatment after 1, 2, 3 and 4 years after starting treatment. Furthermore, the study focused on factors leading to low adherence and to leaving care and treatment.

### *Specific Objectives*

- How many of patients starting treatment in January 2012 to December 2015 remained in the treatment program after 1, 2, 3 and 4 years?
- To compare sociodemographic baseline data and medical factors between patients leaving the treatment program and patients remaining in care.
- To investigate patients' experiences of antiretroviral treatment and factors that might influence adherence to the treatment.

# Material and methods

## Study setting

This study was performed at Dodoma Regional Referral Hospital, which is a governmental hospital. Dodoma is the capital of Tanzania and has a population of roughly 400,000.

Dodoma region, however, has a population of just over 2 million people. The total HIV prevalence in the region was estimated to 2.9% in 2012 (21). The hospital is one of the bigger among plenty of hospitals in Dodoma. The care and treatment clinic (CTC), where data was collected currently, has a cumulative number of around 9200 HIV positive patients in all ages that have ever been enrolled in care at the clinic. However, the number of patients that attended the CTC during the third quarter of 2017 was 2959 of which 69% were women and 31% were men. Since 2004 all appointments at CTCs are free of charge and so are also all antiretroviral drugs, this is the case in the entire country.

Patients enrolled in care at the CTC at Dodoma Regional Referral Hospital are to attend the clinic every other month.

## Study design

There are three parts of this study, part A, B and C:

- A retrospective cohort study (part A) with numbers of how many of the patients that started treatment from January 2012 to December 2015 that still remained in care after 1, 2, 3 and 4 years.
- A case control study (part B) where randomly sampled groups of 100 patients that remain in care and 100 patients that were lost to follow-up will be compared in sociodemographic and medical factors.

- A general observation study (part C) of patients attending the clinic through a questionnaire, which aimed to assess adherence and factors associated with it.

The period of January 2012 to December 2015 was chosen due to the fact that the same national guidelines on HIV were applied throughout that time (which are the 2012 National Guidelines for the Management of HIV and AIDS). Since then the guidelines have been changed.

Patients were supposed to come to the CTC in every two months. In case a patient did not present itself to the clinic within three days of the booked appointment staff from the clinic tried to reach that patient through telephone and if that was not successful community health care workers tried to get in contact with the patient physically for getting the patient back in care. If none of these two methods were successful and the patient did not show up at the clinic in three months after the missed appointment the patient was labelled “lost to follow-up” (LTFU).

Some data about patients were registered in Dodoma Regional Referral Hospital’s local database. From that database, the quantitative data being used for part A; assessing retention to treatment was retrieved. All the data needed for assessing retention was present in the database. However, data for part B; the comparison between the patients remaining in care and the ones lost to follow-up was retrieved from the patients’ medical files that were physical paper files.

Files for patients still in care and for patients that has been lost to follow-up were kept in different rooms at DRRH. One hundred files for patients in care and 100 files for patients lost

to follow-up were randomly chosen through convenient sampling. (Not all files were kept and that was the reason for the convenient sampling. Random generator could not be used in a doable way since not all the files were kept and there was no register over the files. The ones that were present were the ones we had to use and, therefore, it was decided that convenient sampling should be used). When a file had been used or just controlled for inclusion criteria it was put back at a special place to avoid getting data from those files twice.

Inclusion criteria for the database collection (part A) were all patients at the clinic who were HIV positive and started ART between January 2012 and December 2015. The same applied for part B (the comparison of the medical files) but in addition for part B inclusion criteria were also that patients had to be of age 18 years or older. The data used for part A included all patients in all ages and it was impossible to sort out only patients 18 years and older, therefore all ages were included in part A. The definition of lost to follow-up or dropping out of the program was, as mentioned above, for a patient not to show up at the CTC for three consecutive months after a missed appointment.

Among the files for the retained patients, files were found that indicated that the patients had been lost to follow-up but were now back in care, these files were excluded.

The hospital does not automatically get information about when a patient belonging to the hospital dies. If a patient dies in care, that patient's file is taken away from the other ones. However, if a patient dies out of care and no relative informs the hospital about it and community health care workers do not get the information that patient would be lost to follow-up. The same applies for patients transferring. If it is an official transfer the hospital will send the file to the new hospital, but if it is a "silent transfer" (where the patient change

hospitals without announcing it to the old one) and the hospital fail to reach the patient this would also be a case of false labelling of lost to follow-up.

A general observation of the people presenting to the clinic was made through a questionnaire (part C), which aimed to assess the patients' experience of the treatment, adherence and factors associated with adherence. The questionnaires were handed out to patients that presented to the clinic during seven days in October 2017. The goal was to get 100 answered questionnaires, which was met during this period of time.

The questionnaire was created by using some questions from a present questionnaire (from a previous degree project made by Ebba Niméus and Emma Bokström, named "Reasons behind interrupted antiretroviral treatment in rural Tanzania") and by creating some new questions. The questionnaire was then translated into Swahili by a medical doctor. Along with the questionnaire the patients got written information about the study and that answering was voluntary and anonymous.

A pilot was made where ten questionnaires were handed out to patients. After the pilot one question was changed to make it more understandable. The results from the pilot questionnaires were not included in the results of this study.

Inclusion criteria in part C were all patients presenting to the clinic with the age 18 years and above during seven days in October 2017 that had been treated with ART for at least six months. When patients arrived at the clinic their medical files were controlled for if they had been on ART for six months or more, if they had they were asked if they could fill in the form. A total of four patients were not willing to participate, giving lack of time as reason.



The literate patients answered the questionnaires by themselves but were informed of whom to ask for clarifications if necessary. The not literate patients got help from CTC personnel with reading the questions.

All in all, 103 questionnaires were distributed and 100 answered questionnaires were collected. The remaining three disappeared after being distributed, which was thought to be because of lack of time before the doctor's appointment.

## Statistical methods

All collected data was registered in Excel files. These files were later on imported to the statistics programme SPSS Statistics version 25. Calculations and graphs were then made through using SPSS Statistics. Statistical calculations used were multivariate logistic regression, Fisher's exact test, z-test and Mann-Whitney U test. The multivariate regression analysis was performed on baseline variables that had a p-value of 0.1 or less and was calculated with 95% confidence intervals. Missing values were always excluded from statistical calculations.

## Ethics

All patients participating in the questionnaire received written information about the study stressing that participation was voluntary and anonymous. There was no way of identifying patients' identity through the questionnaires. The data retrieved in the file study was confidential with no collection of personal information and the integrity of the patients was respected. Ethical approval for this study was given by the Head of Dodoma Regional Referral Hospital.

The study could be interpreted as a part of quality assurance work, where the data being used is already available. That kind of work would in many countries (including Sweden) not require ethical approval, on the contrary it is something the hospital is required to do. This would not be considered research and would, according to Tanzanian law, not require Research Clearance or Research Permit (22). Some could however argue that the questionnaire handed out is beyond this quality assurance work. However, the questionnaire aimed to find out the patients' experiences of their care and treatment. Patients filled in questionnaires while waiting for their doctors' appointments, they were not asked to come earlier to the clinic or to stay after their appointments. This means that the study did not claim any additional time from the patients.

The Tanzanian supervisors for the project were in charge over getting the ethical approvals demanded by Tanzanian law for conducting the study. Their assessment was that this study was not research, therefore, it did not require any extra approvals than from the Head of the hospital.

# Results

## Part A - Total retention in care

The study population in this part consisted of 2333 patients who started antiretroviral treatment (ART) between January 2012 and December 2015 at Dodoma Regional Referral Hospital (DRRH) or another hospital but later transferred to DRRH. All patients, in all ages, were included. Table 1 shows yearly retention rates in care of all these patients.

Table 1. Total retention of patients after 1, 2, 3 and 4 years for all patients starting antiretroviral therapy (ART) during the years 2012-2015.

<i>Time after ART start (years)</i>	<i>N patients starting ART during cohort years adjusted for transfers</i>	<i>N patients still in care</i>	<i>Percentage</i>	<i>CI (95%)</i>
1	2333	1402	60.1	58.1-62.1
2	2209	1146	52.9	50.8-55.0
3	1591	766	48.1	45.7-50.6
4	1030	489	47.5	44.4-50.5

The proportion of patients remaining in care was 60% after one year with further decrease the following years, see table 1. In addition to that, there was a tendency for the retention proportion to fall for every passing year of ART start which is demonstrated by figure 1.

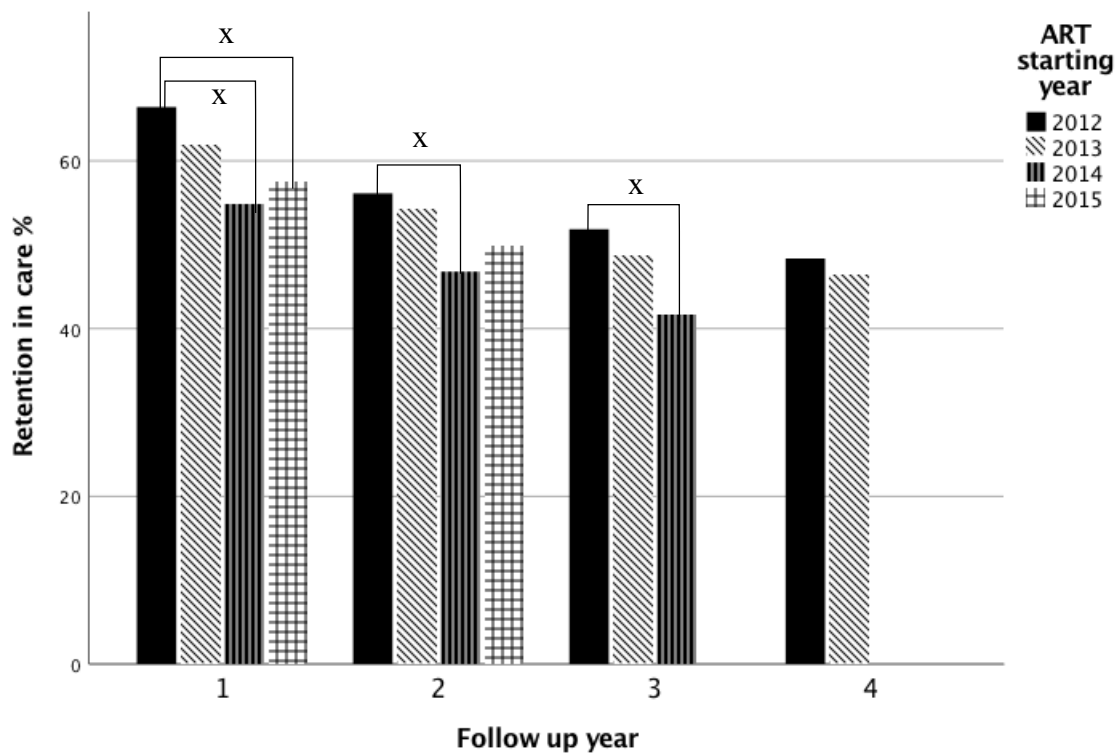


Figure 1. Retention in care by follow-up year and by year of starting antiretroviral therapy (ART). The data in Dodoma Regional Referral Hospital's database covered statistics until August 2017. Chart is calculated based on all 2333 patients. X= p<0.05.

The proportion of patients remaining in care after one year was significantly higher for patients starting treatment in 2012 with 66.4% (95% CI 62.3-70.5) compared with 54.9% (95% CI 50.8-58.9) in 2014 and 57.6% (95% CI 53.7-61.5) in 2015. At two years follow-up, there was a significantly higher proportion of patients remaining that started treatment in 2012 with 56.1% (95% CI 52.0-60.2) compared with 46.8 (95% CI 42.8-50.8) with starting in 2014. The same applied for follow-up year three with 51.9% remaining (95% CI 47.7-56.0) of patients starting ART in 2012 and 41.7% (95% CI 36.9-46.6) of patients starting in 2014.

## Part B - File study

### *Demographics*

Through file studies 200 patients were included in this part of the study, 100 that were already labelled lost to follow-up and 100 that remained in care. Table 3 present the characteristics of the participants. Table 3 shows that married patients had a greater probability to remain in care than patients with another civic status ( $p=0.019$ ).

Table 2. Demographic characteristics of the 200 participants in the file study. P-values calculated with Fisher's exact test.

<b>Demographics</b>		<b>Lost to follow-up n (n=100)</b>	<b>In care n (n=100)</b>	<b>Total n</b>	<b>P-value</b>
<b>Sex</b>	Women	65	71	136	0.45
	Men	35	29	64	
<b>Age (years)</b>	18-25	9	3	12	0.053
	26-30	16	18	34	
	31-35	24	14	38	
	36-40	21	15	36	
	41-45	6	12	18	
	46-50	11	13	24	
	51-60	9	21	30	
	61-70	3	4	7	
	>70	1	0	1	
<b>Marital status</b>	Married	38	56	94	0.019
	Cohabiting	2	0	2	
	Single	25	11	36	
	Divorced/ separated	21	17	38	
	Widower	11	11	22	
	Missing value	3	5	8	
<b>Total number of patients</b>		100	100	200	

As seen in table 3, patients working at baseline were more likely to remain in care than patients that were either bedridden or ambulatory ( $p=0.010$ ). There was a tendency for

remaining patients to have lower WHO clinical stage at baseline than patients lost to follow-up (p=0.059).

Table 3. Medical status of the participants at baseline and at one year follow-up. P-values calculated with Fisher's exact test except for value marked with \* where p-value is calculated with Mann-Whitney U test.

		Baseline			1 year follow-up		
		Lost to follow-up n (n=100)	In care n (n=100)	P-value	Lost to follow-up n (%) (n=48)	In care n (%) (n=100)	P-value
<b>Functional status</b>	Working	74	90	0.010	47 (98)	100 (100)	0.324
	Bedridden	4	1		0	0	
	Ambulatory	22	9		1 (2)	0	
<b>WHO clinical stage</b>	1	8	8	0.059	5 (10)	8 (8)	0.44
	2	24	40		9 (19)	34 (34)	
	3	51	34		29 (60)	38 (38)	
	4	17	18		5 (10)	20 (20)	
<b>CD4 count (cells/<math>\mu</math>L)</b>	0-50	12	17	0.52	2 (4)	1 (1)	0.674
	51-100	17	14		1 (2)	3 (3)	
	101-150	9	10		2 (4)	5 (5)	
	151-200	8	18		1 (2)	4 (4)	
	201-250	11	11		3 (6)	5 (5)	
	251-300	12	11		2 (4)	7 (7)	
	301-350	8	4		2 (4)	5 (5)	
	>350	12	11		3 (6)	17 (17)	
Missing value	11	4	32 (67)	53 (53)			
<b>Median CD4 count (cells/<math>\mu</math>L)</b>		195	171	0.327*	254	295	0.361*
<b>Signs/Symptoms</b>	Experiencing symptoms				15 (31)	24 (24)	0.426
	No symptoms				33 (69)	76 (76)	
<b>TB positive/negative</b>	Negative				45 (94)	78 (78)	0.019
	Positive				3 (6)	22 (22)	

TB=tuberculosis. WHO clinical stage 1=Asymptomatic HIV infection or consistent generalized lymphadenopathy. WHO clinical stage 2=HIV infection causing light weight loss (<10%) or milder opportunistic infections e.g. seborrheic dermatitis or herpes zoster. WHO clinical stage 3=HIV infection causing severe weight loss (>10%) or more advanced opportunistic infections e.g. pulmonary TB and oral candidiasis. WHO clinical stage 4= HIV infection causing wasting syndrome or advanced opportunistic infections such as pneumocystis pneumonia or Kaposi's sarcoma.

Table 4. Antiretroviral therapy (ART) of the patients at baseline and one year follow-up. P-values calculated with Fisher's exact test.

	Baseline			1 year follow-up			
		Lost to follow-up n (n=100)	In care n (n=100)	P-value	Lost to follow-up n (%) (n=48)	In care n (%) (n=100)	P-value
<b>ART start year</b>	2012	28	14	0.068	12 (25)	14 (14)	0.406
	2013	32	31		13 (27)	31 (31)	
	2014	22	32		15 (31)	32 (32)	
	2015	18	23		8 (17)	23 (23)	
<b>ART combination regimen</b>	No ART	0	0	0.11	2 (4)	0	0.075
	1g	36	53		17 (35)	52 (52)	
	1e	24	16		11 (23)	27 (27)	
	1f	2	1		2 (4)	1 (1)	
	1b	10	12		4 (8)	12 (12)	
	1h	1	0		1 (2)	0	
	1c	27	18		10 (21)	16 (16)	
	2 <sup>nd</sup> line	0	0		1 (2)	2 (2)	
<b>Treatment supporter</b>	Yes	93	95	0.77	44 (92)	95 (95)	0.472
	No	7	5		4 (8)	5 (5)	
<b>ART status</b>	Continue				39 (81)	96 (96)	0.006
	Change				7 (15)	4 (4)	
	Stop				2 (4)	.	
<b>Reasons for changed ART</b>	Out of stock				1 (2)	.	1.000
	Poor adherence				1 (2)	.	
	Side effects				1 (2)	.	
	Treatment failure, immunological				2 (4)	3 (3)	
	Not specified				1 (2)	.	
	Anemia				1 (2)	.	
	Rash				1 (2)	.	
	Other reason				1 (2)	1 (1)	
	Missing value (=no changes)				39 (81)	96 (96)	
<b>Assessed ART adherence status*</b>	Good				35 (73)	93 (93)	0.002
	Poor				13 (27)	7 (7)	

\*) Assessed ART adherence status is assessed during the patient's clinic appointment by a medical doctor. No forms are used, it is the doctor's personal assessment based on conversation with patients. ART=Antiretroviral Therapy. 1g) tenofovir+lamivudine+efavirenz, 1e) tenofovir+emtricitabine+efavirenz, 1f) tenofovir+emtricitabine+nevirapine, 1b) zidovudine+lamivudine+nevirapine, 1h) tenofovir+lamivudine+nevirapine, 1c) zidovudine+lamivudine+efavirenz.

At one year follow-up, as seen in table 3, a bigger proportion of patients remaining in care was positive for tuberculosis than patients lost to follow-up (p=0.019). After one year of treatment 15% of the patients lost to follow-up had changes in their ART compared to 4% of

the patients remaining in care ( $p=0.006$ ). Table 4 shows that 27% of patients lost to follow-up were assessed to have poor treatment adherence whereas the corresponding percentage was 7% for patients remaining in care ( $p=0.002$ ).

At two years follow-up 70% of “lost to follow-up patients” had their disease classified as WHO clinical stage 3 which was significantly higher than the patients remaining in care where the corresponding number was 39% ( $p=0.028$ ). In addition, at three years follow-up 29% of the patients lost to follow-up experienced symptoms compared to 8% of the remaining patients ( $p=0.030$ ).

At two years follow-up 52% of patients remaining in care were treated with tenofovir + lamuvidine + efavirenz (TDF+3TC+EFV) which was significantly higher than the corresponding 23% of the lost to follow-up patients ( $p=0.002$ ). This also applied for follow-up year three, where 31% of patients remaining in care and none of the lost to follow-up patients were treated with TDF+3TC+EFV ( $p=0.007$ ). At two years follow-up 13% of lost to follow-up patients got their ART changed which was a significantly higher proportion compared to 1% of remaining patients that to a greater extent continued with the same treatment ( $p=0.011$ ). This also applied for follow-up year three, where 36% of lost to follow-up patients stopped their treatment (mainly motivated by poor adherence) compared to none of the remaining patients ( $p<0.001$ ). Finally, at three years follow-up the proportion of patients with assessed poor adherence status were 24% in the lost to follow-up group but none in the group with patients remaining in care ( $p=0.001$ ).



## Regression analysis

Table 5 demonstrates that being working at start of ART was linked to lower risk of being lost to follow-up (OR 0.332). Also, advanced HIV with WHO clinical stage 3 increased the risk of being lost to follow-up.

Table 5. Multivariate logistic regression analysis of baseline patient factors. Analysis performed for all baseline patient factors with  $p < 0.1$ . Values are predicted for getting lost to follow-up. Last value in all categories was used as reference.

		OR	95% CI	P-value
Age (years)		0.971	0.941-1.003	0.073
Marital status	Married	0.516	0.180-1.480	0.219
	Cohabiting	NA	NA	NA
	Single	1.914	0.530-6.908	0.322
	Divorced/ separated	0.680	0.199-2.325	0.538
	Widower			0.092
Functional status	Working	0.332	0.124-0.887	0.028
	Bedridden	5.211	0.401-67.719	0.207
	Ambulatory			0.018
WHO clinical stage	1	2.160	0.520-8.973	0.289
	2	1.040	0.364-2.977	0.941
	3	3.185	1.181-8.589	0.022
	4			0.017
ART start year	2012	1.799	0.616-5.255	0.283
	2013	1.130	0.435-2.939	0.801
	2014	0.618	0.238-1.600	0.321
	2015			0.182

ART=Antiretroviral Therapy. NA=Not Applicable. For explanation of WHO clinical stages see text under table 3.

## Part C - General observation through questionnaire

This part of the study is a general observation of 100 patients presenting to the Care and Treatment Clinic that filled in a questionnaire. All patients that were willing to participate, aged 18 years or more and that had been on ART for at least six months were included.

## Demographics

The study population in the questionnaire part of the study consisted of 100 patients, who all filled in the questionnaire. Of these 63% were women and 37% were men. Mean and median age in study population was 44 and 42 years.

Table 6. Demographic characteristics of the 100 patients answering the questionnaire.

		n (n=100)
Sex	Women	63
	Men	37
Age (years)	18-25	4
	26-30	6
	31-35	9
	36-40	18
	41-45	24
	46-50	7
	51-60	18
	61-70	10
	>70	1
	Missing value	3
Marital status	Married	28
	Long term relationship	6
	Single	23
	Divorced	18
	Widower	25
Level of education	Never been to school	10
	Primary school not finished	2
	Primary school	65
	Secondary school	17
	University/College	5
	Missing value	1
Current social situation	Employed	13
	Self-employed	51
	Not employed	25
	Student	3
	Other grant	4
	Missing value	4
Religious affiliation	Christian	76
	Muslim	22
	Missing value	2

The earliest year of HIV diagnose in the study population was 1995 and the latest 2016. Mean year of diagnose was 2010 and median 2011. The earliest start of treatment was 1996 and latest 2017, with a mean year of 2011 and median 2012.

Table 7. Medical factors of the 100 participants in the questionnaire study.

		n (n=100)
Experienced health status before treatment start	1 (Very poor)	40
	2	20
	3	13
	4	15
	5 (Excellent)	12
Experienced health status currently	1 (Very poor)	3
	2	0
	3	7
	4	26
	5 (Excellent)	63
	Missing value	1
Prescribed doses/day	One	56
	Two	44
Missed medicine doses last 28 days	0	74
	1-2	14
	3-4	4
	5-6	0
	7-10	1
	More than 10	2
	Missing value	5
Ever interrupted/stopped treatment	Yes	7
	No	90
	Missing value	3

Patients were asked to fill in their self-experienced health status before treatment start and currently (which corresponds to after at least six months of treatment). This was made through marking a number on a scale from one to five, where one represented very poor and five represented excellent, the results are shown in table 7. Health status before start of ART was filled in by all patients and resulted in a mean value of 2.39 and median value of 2. Health at time of investigation was filled in by 99 (99%) of patients and issued in a mean and median value of 4.47 and 5. Women had a significantly higher median value of 2 before treatment start than men with a value of 1 ( $p=0.042$ , calculated with Mann-Whitney U test).

There was however no significant difference in current health status between women and men.

*Adherence in treatment*

Patients were questioned about whether they had missed to take any doses of ART in the last four weeks or not, 95 patients out of 100 answered the question, 22% stated that they had missed to take at least one dose. No significant difference was found between men and women in number of missed ART doses the last 28 days.

Patients were asked what the reason was if they ever missed to take their medicine, 46 patients did not fill in any of the reasons and 56 patients filled in one or more alternative. The distribution of the answers of those 56 patients is shown in figure 2.

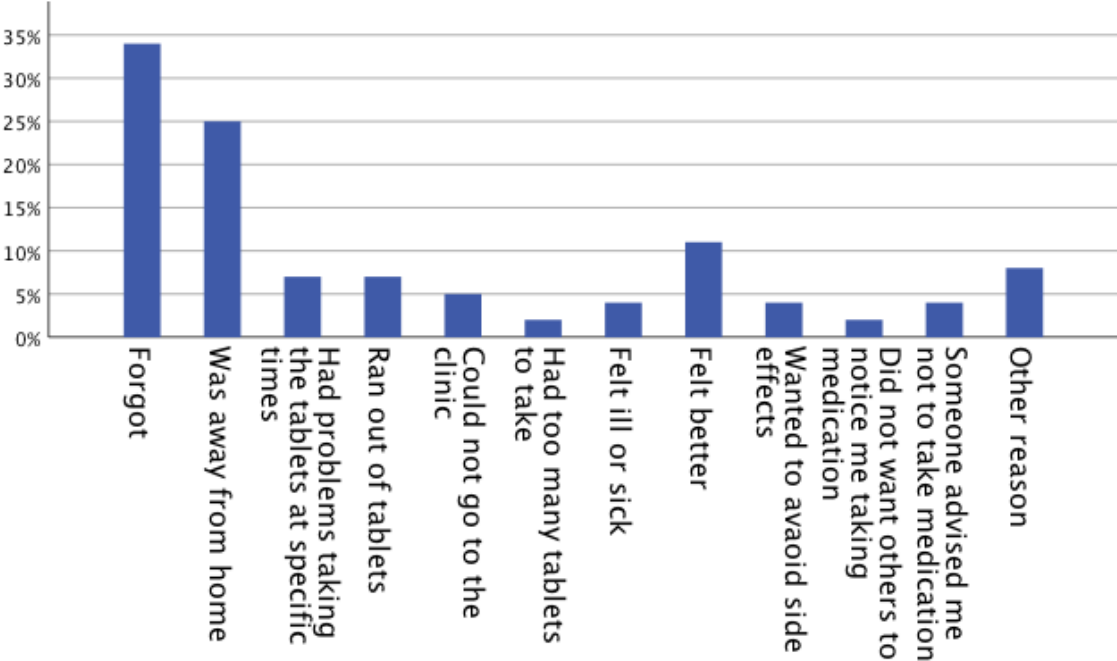


Figure 2. Reasons given by patients for ever forgetting to take medicine. Chart is based on 63 answers given by 56 patients.

Answers from men and women did not differ significantly. However, patients that had missed any doses the last four weeks did to a significantly higher proportion (10%) answer that they wanted to avoid side effects than patients that had not missed any doses (0%) (p=0.047).

Patients were also asked what they thought could be done to prevent them from missing to take medicine or to not interrupt the treatment. The answers were not significantly different between men and women nor between patients with or without missed doses the last four weeks. There were 47 patients stating that they agreed with one or more of the alternatives and 53 patients did not tick any of the alternatives. These answers are showed in figure 3.

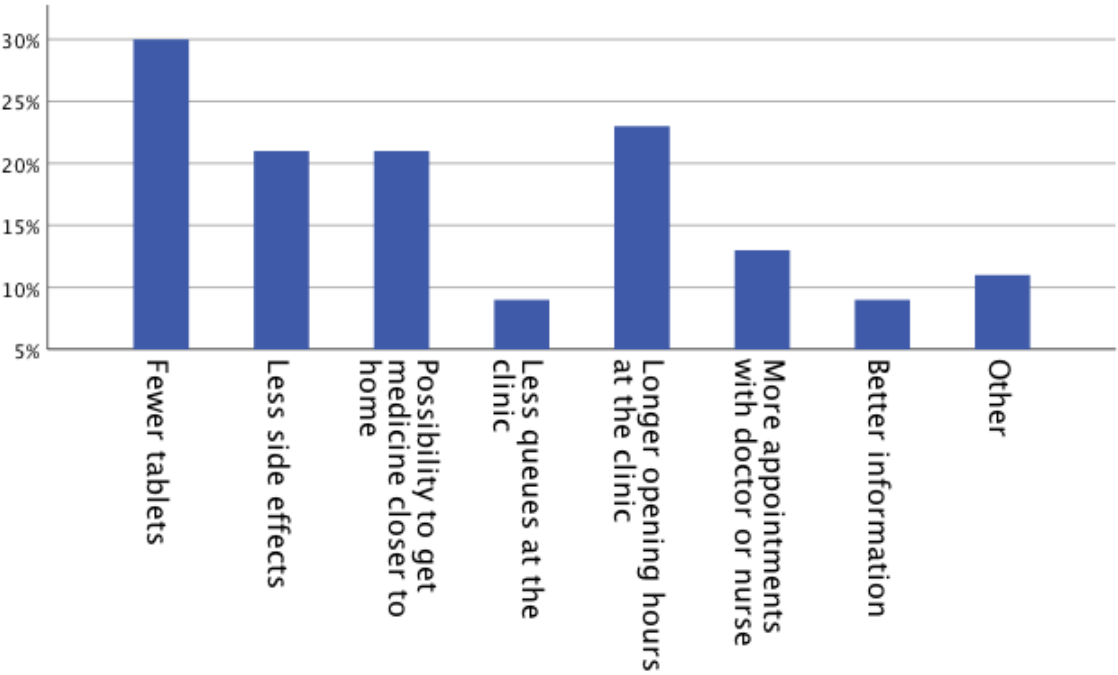


Figure 3. Factors that patients think could help preventing missing to take medicine or interrupting the treatment. Chart is based on 64 answers given by 47 patients.

Patients were also asked what they believed was going to happen if they do not take their HIV medicine regularly, 93 answers were registered and 7 were missing. There were three alternatives given and the percentages of answers given were distributed as follows: 8% “nothing will happen”, 45% “I will feel worse” and 47% “after some time the medicine will no longer have any effect”.

### *Experience of antiretroviral treatment*

Furthermore, patients were questioned about if they have experienced any positive effects since they started ART. There were five alternatives and 96 out of 100 patients gave one or more answers to the question. Answers were distributed as seen in figure 5. No significant differences between men and women or between patients with or without missed doses the last four weeks were found.

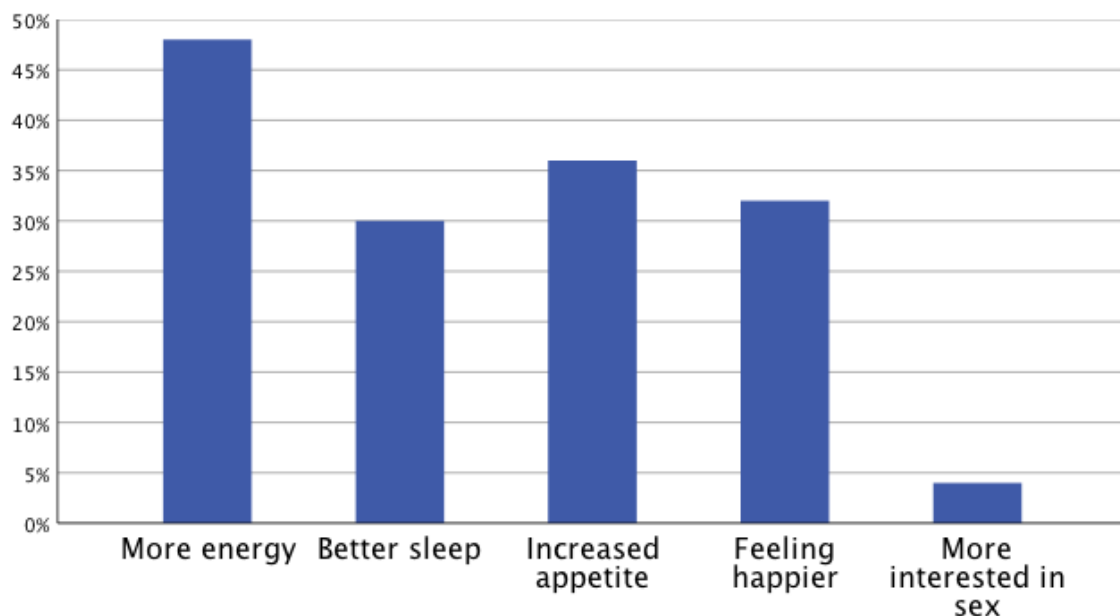


Figure 5. Patient-experienced positive effects since start of ART. Chart based on 144 answers given by 96 patients.

Patients were also asked for experienced negative effects since they started ART. There were 61 patients stating that they had experienced at least one of the alternatives and 39 patients stating that they had none of the listed negative effects. A significantly higher proportion of the women (24%) had experienced weight loss than the men (5%) ( $p=0.025$ ). Also, regarding patients that had missed at least one dose the last four weeks they were to a significantly higher proportion experiencing loss of appetite and headache than patients that had taken all doses ( $p=0.012$  respectively  $p=0.013$ ) which is showed in table 8.

Table 8. Patient-experienced negative effects since start of antiretroviral treatment (ART), answers categorized after if patient had missed to take any doses of ART the last four weeks or not. Table based on answers of 95 patients. Multiple answers were allowed. P-values calculated with Fisher's exact test.

	<i>Patients with no missed doses n (%) (n=74)</i>	<i>Patients with missed doses n (%) (n=21)</i>	<i>P-value</i>
<i>Less energy</i>	4 (5)	4 (19)	0.069
<i>Sleeping disturbances</i>	9 (12)	1 (5)	0.450
<i>Loss of appetite</i>	7 (9)	7 (33)	0.012
<i>Feeling depressed</i>	7 (9)	3 (14)	0.687
<i>Less interest in sex</i>	12 (16)	1 (5)	0.285
<i>Diarrhoea</i>	2 (3)	1 (5)	0.532
<i>Headache</i>	5 (7)	6 (29)	0.013
<i>Skin rashes</i>	8 (11)	3 (14)	0.703
<i>Losing weight</i>	10 (14)	4 (19)	0.503
<i>Thinner face</i>	1 (1)	1 (5)	0.395
<i>Slim legs</i>	3 (4)	1 (5)	1.000
<i>More abdominal fat</i>	6 (8)	1 (5)	1.000
<i>Absent or abnormal sensation in feet</i>	5 (7)	2 (10)	0.648
<i>None</i>	32 (43)	5 (24)	0.132

Furthermore, patients were asked what gives them motivation to take their medicines. Table 9 shows the result. There was no significant difference between answers from women and men.

Table 9. Patients' given motivations for continuing to take their ART. Patients were asked to answer in their own words, the answers were then divided in to the categories beneath. There were 12 missing answers and 88 patients that answered the question.

	<i>n (%)</i>
<i>To have a good health</i>	34 (39)
<i>To live a good life</i>	28 (32)
<i>To live a long life</i>	16 (18)
<i>To have strength for work</i>	11 (13)
<i>My disease makes it necessary to take the medicine</i>	8 (9)
<i>It is good for me</i>	10 (11)
<i>To be able to fulfil my dreams</i>	3 (3)
<i>To stay happy</i>	3 (3)
<i>Other reason</i>	14 (16)

### *Social support*

Patients were questioned about who they had told about their HIV status, answers are presented in table 10. The proportion of men that informed their fathers about their HIV status was 61% which was significantly higher than the 39% of the women (P=0.030). A trend of more men (41%) than women (25%) informing their partners was seen (p=0.124). The most

common person to inform was sister or brother. It is however not entirely sure to be the case; in Swahili, the words for sister and brother could also describe a woman or man in general (often that you are related to or close with).

Table 10. Information given by patients about who they have informed about their HIV status, answers shown divided by sex. Table based on 187 answers given by all 100 patients, multiple answers were allowed. P-values calculated with Fisher's exact test.

	Women n (%) (n=63)	Men n (%) (n=37)	P-value
Partner	16 (25)	15 (41)	0.124
Mother	24 (38)	13 (35)	0.832
Father	7 (11)	11 (30)	0.030
Sister or brother	30 (48)	17 (46)	1.000
Children	23 (37)	15 (41)	0.831
Friends	6 (10)	6 (16)	0.352
None	2 (3)	2 (5)	0.625

Moreover, patients were questioned about reasons for not informing people about being HIV positive. Answer frequency of the alternatives were distributed in accordance to table 11.

There were no significant differences in the answers seen to sex nor if patients had missed to take medicine the last four weeks or not.

Table 11. Reasons for patients not to inform people about being HIV positive. There were 98 answers given by 82 patients, multiple answers were allowed. 18 patients did not fill in any alternative.

	n (%)
<i>I am afraid my partner would leave me</i>	4 (5)
<i>I am afraid my partner would not be intimate with me</i>	4 (5)
<i>I am afraid my family would exclude me</i>	10 (12)
<i>I am afraid my friends would exclude me</i>	5 (6)
<i>I am afraid I would lose my job</i>	1 (1)
<i>I am afraid I would be discriminated</i>	22 (27)
<i>I feel ashamed that I have HIV</i>	6 (7)
<i>Nobody else needs to know</i>	36 (44)
<i>Other reason</i>	10 (12)

Finally, patients were asked if the people they had informed about being HIV positive gave them support. Answer frequency was 100%, 76% of patients stated that they got support and 16% that they did not. Moreover, 2% stated that the people they informed gave them more



problems than support. In addition, 4% answered that they had not informed anybody about their HIV status. Finally, 2% filled in that they had no answer.

## Discussion

We found that only 60% of patients starting antiretroviral therapy (ART) at Dodoma Regional Referral Hospital (DRRH) January 2012 to December 2015 remain in care one year after their treatment start. Having advanced HIV classified as WHO clinical stage 3 at start of treatment increased the risk of leaving care and treatment.

## Demographics

The file study (part B) included 200 patients of which 68% were women and 32% were men and the study population of 100 patients filling out the questionnaire (in part C) consisted of 63% women and 37% men. This corresponds well to the proportions at the Care and Treatment Clinic (CTC) at DRRH, where there were 69% women and 31% men visiting the last three months. In Tanzania in general 57.7% of the HIV positive adults are estimated to be women and 42.3% men (4), that does not however mean that the percentage of people in care are the same. A study performed in, among other east African cities, Morogoro in Tanzania had a percentage of 69.1% women and 30.9% men when including all patients at that hospital (20). In conclusion, fewer men than expected (when looking at numbers of HIV positive men) attended clinics. One factor behind this could be that men, due to stigma, send their wives or female partners to receive medicine for them. In addition, male sex has been shown to be a risk factor for leaving treatment programmes in several studies performed in east Africa (15).

## Retention in care

This study found a surprisingly low proportion of patients remaining in treatment after one year, with only 60.1% remaining after one year with further decrease to 47.5% after four years. A study, performed in Tanzania and other east African countries, with more than 18,000 patients enrolled showed a retention of 67% after two years of treatment but only 26% were actually lost to follow-up, others had transferred or died. Adjusted for transfers and death in that study results in 74% of patients remaining in care after two years of treatment, which corresponds to 52.9% in our study (20). Another study performed on data from 101 Tanzanian clinics showed that 18% of patients were lost to follow-up after one year of treatment and 36% after three years of treatment (23).

This study showed that the proportion of patients remaining in care was significantly higher for patients starting ART in 2012 compared to 2014. In addition, there was a tendency for retention proportions to be lower for every passing year of ART start from 2012 to 2015. This is in contrast to other studies that have shown improvement in retention over time (24, 25).

One of the underlying reasons for the decrease could be that the years before 2012 the CTC at DRRH received economical donations and health care workers from Italy as a part of a project to improve their healthcare for HIV positive patients. This project was ended in 2012 and the CTC does not receive Italian contributions anymore. Lack of resources could, of course, make it difficult to keep the same standard as before and might be what happened in this case.

## Factors linked with being lost to follow-up

The patients lost to follow-up were on median 36 years old compared to 42 years for patients remaining in care ( $p=0.009$ ). This suggests that a lower age increases the risk of being lost to

follow-up. The result is in line with other studies from Tanzania and other countries, where low age has been identified as one of the main risk factors for becoming lost to follow-up (15, 26).

Furthermore, having advanced HIV with the disease classified as WHO clinical stage 3 increased the risk of being lost to follow-up (OR 3.19, 95% CI 1.18-8.59). Having a higher WHO stage equals a poorer health status and has been shown to increase the risk of leaving treatment in previous studies (15, 17). Patients with a more advanced HIV are obviously more likely to die than patients with a less severe HIV and this could be one explanation behind the result. The results emphasize the importance of early detection and treatment of HIV.

After one year of treatment fewer patients lost to follow-up (LTFU) had tuberculosis (TB) than remaining patients. This could be connected to the fact that TB positive patients might have had additional visits at the clinic and staff might have stressed the importance of treating both diseases with good adherence. In Tanzania, the aim is to manage coinfections of HIV and TB integrated, which repeatedly has been shown to be effective in previous studies, this could also be a factor behind the result (3, 27).

Moreover, patients labelled LTFU were more likely to have their treatment adherence assessed as poor than patients remaining in care. This appears to be a reasonable result. The question is however why not more of the LTFU patients than 27% after one year of treatment and 24% after three years were assessed to have bad adherence? Maybe it reflects the actual situation, but it would seem natural that many patients might, as a pre-stage, have a poor adherence before leaving treatment. Patients that were identified to have poor adherence status need extra support to make sure they improve their adherence.

Further findings suggest that patients experiencing symptoms during the following years after treatment start are more likely to be LTFU. (Symptoms included both adverse reactions and HIV related symptoms. Among the most common were cough, rash, headache, abdominal pain and skeletal pain). This reasonable result confirms what previous studies have shown; that a patient experiencing symptoms (both side effects and HIV related symptoms) after starting treatment is less likely to have a complete adherence and to remain on treatment (13, 28). A study from, among other countries Tanzania, shows that side effects are common factors for incomplete adherence and in the study every additional symptom increased the odds of incomplete adherence by 12% (13). Sometimes side effects of ART can be more disabling for patients than the disease appeared to be, this makes it difficult for patients to put out with side effects and keep a good adherence in treatment. This also comes hand in hand with the results in this study showing that LTFU patients also were more likely to have had changes done in their ART. Some of them due to stock out, some because of immunological treatment failure, side effects or poor adherence. This appears to be a reasonable result; poor adherence and bad retention is coupled. Also, statistics tend to show that the longer patients stay on ART, the fewer side effects, thus the side effects tail away. This is likely to be false, since patients experiencing side effects are prone to quit therapy. Being one of the main factors behind poor adherence side effects are to be taken seriously and should be requested at patient's appointments. Furthermore, treatment with tenofovir + lamuvidine + efavirenz (TDF+3TC+EFV) was the best (of the combinations they had access to in Tanzania in 2012-2015) for keeping patients in care and treatment. This combination is known to have fewer side effects than many other combinations and is therefore linked to better adherence and retention.

## General observation among patients on treatment through questionnaire

Patients' self-experienced health status on a scale of one to five was increased from a mean of 2.39 before ART start to 4.47 at the point of investigation. Since ART has been successful in decreasing the burden of disease, this result was not unexpected but yet satisfactory. Women declared a higher health status before treatment than men, but after at least six months of treatment the difference had evened out. It has been showed before that men enter health care with a more advanced disease than women (29). This could be due to different explanations; men are, unlike women, not screened because of pregnancy and they do not partner test to the same extent as women (30). The study population in this part of the study was quite homogenous, where all patients were attending the clinic and had a rather high adherence to treatment, which goes hand in hand with the good results of ART seen in rise of self-experienced health status.

### *Adherence to treatment*

We found that 22% of the patients reported missing at least one dose of ART the last four weeks. This was lower than findings in a study performed in Tanzania, Uganda and Zambia, where 58% of patients reported taking less than 100% of their ART doses the last 30 days (18). If the results from this study do not entirely reflect the truth, this difference could be due to the fact that patients were anxious to fill in the right answer because they were afraid their treating doctor would find out and disapprove. However, the result could also be correct. In that case, one reason for a higher adherence than the other study could be that the study population, as written before, was a group of patients that actually had a good retention.

When patients were asked about what could prevent them from missing doses, the most common answers were: fewer tablets, longer opening hours at the clinic, less side effects and

possibility to get medicine closer to home. Fifty-six percent of the patients have a single dose per day regimen and the rest had two doses per day. There is currently no ART regimen with less than one dose per day. Longer opening hours at the clinic could be considered a reasonable improvement. Patients had to leave their daily occupation to come to the CTC in the middle of the day, which was more or less complicated for all patients due to travel distance, occupation and so on. Side effects could to some extent also be considered avoidable, not entirely but by giving low-income countries access to the same types of new ART drugs as high-income countries have, since most new drugs have less side effects than older drugs. It is an economical question. Something that could be done is to make sure that patients experiencing side effects get to try another treatment regimens, since Tanzania have different first line and second line treatment combinations to try (although not nearly as many as high-income countries). The suggestion to get medicine closer to home will actually be fulfilled in year 2018 when ART patients in Tanzania will be offered to get medicine delivered to their homes. This has been proven to be a successful intervention for increasing retention before (15).

### ***Experience of antiretroviral treatment***

There were 97 patients out of 100 filling in at least one experienced positive effect since start of ART, which is a pleasing result. In addition to positive effects, 61/100 patients filled in one or more negative effects since ART start. Women experienced weight loss to a higher extent than men. One explanation for the greater weight loss in women could be that the drugs are prescribed in fixed doses with the same dose for all adults. Women often have lower body weight than men and the doses can sometimes be too high for them and result in more adverse effects. Adjusting doses after body weight could be successful in lowering side-effects.

Moreover, patients that stated that they had missed to take medicine at least one time the last

four weeks were more likely to experience loss of appetite and headache than patients with no missed doses. These patients (that had missed to take doses) also answered that the reason for not taking all doses wanted to avoid side effects to a higher extent than patients that had taken all doses. As stated before: side effects could be reason enough for nonadherence.

### *Social support*

When patients were asked about reasons for not informing others about their HIV status a high level of stigma remaining in the Tanzanian society could be seen. There were 22/100 patients stating that they were afraid to be discriminated if their HIV status was revealed, also 10/100 patients were afraid their families would exclude them. Several previous studies have shown that stigma increases the risk of poor adherence to antiretroviral treatment (19, 31, 32). Interventions for lowering stigma are necessary, both within the group of HIV positive patients and in the rest of society. As long as HIV-related stigma continue to be high it will be difficult to reach the 90-90-90 goal; not enough people will be tested neither will adherence to treatment be high enough.

### Strengths and Weaknesses

A strength of this study is that it is one of few studies that look into how many HIV patients that actually remain in care and treatment and that does not just focus on the patients that are still in treatment. Another strength was that there was enough data gathered to actually get significant results. There were also three different parts of the study that enlightened different aspects.

A great limitation to this study is that it was not certain that the patients that had been labelled lost to follow-up were in fact lost to follow-up, they could be dead or transferred. This makes it impossible to say that the risk factors for becoming lost to follow-up identified in this study are risk factors for just leaving care. They are, however, risk factors for becoming lost to follow-up where the term included patients that had left care, transferred to another clinic or died. This especially applied for the file study (part B), considering part A data was supposed to have been adjusted for deaths and transfers.

Another weakness is the design of the questionnaire. There were several questions that lacked the alternative “no answer” or that none of the other alternatives applied. This resulted in that some questions had low answering frequency, which can be assumed to mean that patients thought that none of the alternatives applied, but we cannot know whether it actually was that way or just that patients did not answer that question for some other reason.

In addition, another weakness concerning the questionnaire is the question of how many medicine doses patients had forgotten to take the last four weeks. The alternatives there were none, 1-2, 3-4 etcetera. This makes it impossible to know exactly how many doses patients missed and, therefore, we cannot say whether patients had a complete or non-complete adherence (incomplete adherence is usually described by more than 5% missed doses). The limit would be at more than one for patients taking one dose per day and for patients taking two doses per day the limit would be more than two missed doses. Because of this, analyses were done with patients divided into groups based on if they had any missed doses or not.

Patients that were not literate were helped with filling in the questionnaire by a nurse. It is likely that this lack of privacy and decreased anonymity would affect how patients answer.



Also, patients were often sitting close to each other in the waiting room while answering the questionnaire which also affected the privacy.

Since parts of this study were retrospective review of patients' files, it was not possible to assess other structural and socioeconomical important predictors for retention, such as transports to clinic, income and level of education. There were also missing data in the files, for instance CD4 count after one year was only measured in 43% of patients.

Finally, it would have been good to have bigger study populations to increase the power of the study.

### **Further studies**

It would have been interesting to search for patients that have actually left care and treatment and ask them about why they left. This is, however, a study that demands more time than this study was given.

Also, it would be interesting to see what the results would be like if patients had been divided into different outcome categories, such as: retained at original clinic, known transfers, silent transfers, deaths in and deaths out of care.

## Conclusions

Main conclusions:

- Retention to care and treatment at Dodoma Regional Referral Hospital was low and was decreasing during the years 2012-2015. Efforts need to be made to increase the retention.
- One factor that was linked to non-retention was amongst others having HIV classified as WHO clinical stage 3 at treatment start.
- There were fewer men attending the clinic and men sought help at a later stage. This needs to be improved and campaigns need to target men specifically.
- HIV-related stigma was still high in Tanzania and further actions need to be taken to diminish it. As long as there is a high level of stigma HIV will never be sufficiently reduced.
- Side effects can be a sole reason for leaving treatment. There is need to pay thorough attention to side effects and to trying to bring them down.
- By enquiring for factors which has been linked with getting lost to follow-up patients with increased risk can be identified and given extra attention.

## Future perspectives

Currently the patients meet a doctor during all their appointments at the Care and Treatment Clinic (CTC) at Dodoma Regional Referral Hospital. This results in very short and rapid appointments where patients have to be really on toe if they want to ask something or have any complaints. It might be better to sparse out these appointments and make them fewer but longer. Instead patients could have regular meetings with nurses or other staff at the CTC as long as everything is going well and just meet doctors when something concerning the

treatment is not going well. Since doctors are the most expensive and limited resource at the CTC this could be a way to use the doctors' time in a meaningful way.

Another suggestion that goes hand in hand with the previous one is to use volunteers that are HIV positive themselves. These volunteers could get some education and then work with educating new HIV patients or even with having the appointments (between doctors' appointments) at the CTC. This could be a way to gain patients' trust; knowing that the person you talk to actually share your experiences can make it easier to get an honest and open conversation.

All in all, these suggestions could lead to more thorough appointments, more efficiency both economically and time-wise and finally they could lead to improved adherence and retention in treatment.

## Acknowledgements

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# Populärvetenskaplig sammanfattning

## **Låg andel HIV-positiva patienter kvar i vård vid uppföljning på Dodomas regionsjukhus, Tanzania**

Det finns bra behandling för HIV-sjuka människor som kallas antiretroviral terapi. För att hjälpa måste dock denna behandling tas med stor noggrannhet och det är nödvändigt att ta medicin dagligen livet ut. Gör man det beräknas man leva lika länge som en icke HIV-positiv person.

Tanzania är ett land som drabbats hårt av HIV, men som på senare år kraftigt har ökat antalet patienter som behandlas. Nu är utmaningen att dessa patienter ska fortsätta att komma på mottagningsbesök och ta sin behandling och dessutom göra det med den noggrannhet som krävs.

Denna studie är utförd i Tanzania och målet med studien var att undersöka hur stor andel av de patienter som började med HIV-behandling på Dodomas regionsjukhus från år 2012 till 2015 som fortfarande går kvar på sjukhuset och tar sina mediciner. Ett annat mål var att undersöka om patienter som slutar med behandling på något sätt skiljer sig från de som fortsätter. Till slut gjordes även en enkätundersökning där syftet var att ta reda på patienters upplevelse av HIV-behandling och vad som kan göras bättre.

Det visade sig att endast 60% av de som började med behandling under 2012–2015 var kvar på behandling efter ett år, andelen fortsatte sedan att sjunka och fyra år efter behandlingsstart var det bara 47%. Detta är en oväntat låg andel och man måste med största allvar jobba för att förbättra detta.

Studien visade att de som vid behandlingsstart hade HIV i ett allvarligt stadium (som kallas WHO stadium 3) hade ökad risk att lämna behandlingen. Det var också fler av de som slutade med behandling som hade upplevt biverkningar av läkemedlen.

Enkät svar visade att 22% av de svarande patienterna inte talar om för andra att de är HIV-positiva på grund av att de är rädda för att bli diskriminerade. Vidare angav 10% att de var rädda för att bli uteslutna ur sina familjer om deras HIV-status avslöjades. Dessa resultat visar på att stigmatisering kopplat till HIV fortfarande är utbrett i Tanzania. Detta är också något som behöver jobbas med, både på patientnivå och sett till samhället i stort. Så länge stigmatisering är vanligt förekommande kommer det inte att gå att stoppa spridningen av HIV.

Genom att efterfråga faktorer som är kopplade till att ha en hög risk för att sluta med behandling kan man identifiera vilka patienter som på olika sätt behöver extra insatser och på så sätt kan förhoppningsvis avhopp förebyggas. Det är i detta arbete resultaten från denna studie kan användas.

## Abbreviations

AIDS – Acquired Immuno Deficiency Syndrome

ART – Antiretroviral Treatment

CTC – Care and Treatment Clinic

DRRH – Dodoma Regional Referral Hospital

EI – Entry Inhibitors

HIV – Human Immunodeficiency Virus

II – Integrase Inhibitors

LTFU – Lost to Follow-up

NNRTI – Non-Nucleoside Reverse Transcriptase Inhibitors

NRTI – Nucleoside Reverse Transcriptase Inhibitors

PI – Protease Inhibitors

PLHIV – People living with HIV

SSA – Sub-Saharan Africa

TB – Tuberculosis

UNAIDS – The Joint United Nations Programme on HIV/AIDS

WHO – World Health Organization

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# Appendix

## Patient questionnaire

This is a questionnaire about HIV treatment which is part of a study about what makes patients stay on antiretroviral treatment. The questionnaire is anonymous and participation is voluntary.

We are grateful for your participation. If you have any questions regarding the survey, please contact:

Dodoma Regional Referral Hospital  
Jenny Bodell, medical student  
Supervisors: Dr Boniface Nguhuni and Dr Siraji Shaban, Dodoma Regional Referral Hospital, Prof Rune Andersson, Gothenburg University, Sweden.

### 1. Gender:

- Female
- Male

2. Age (years): \_\_\_\_\_

### 3. Marital status

- Married
- Long term relationship
- Single
- Divorced
- Widower

### 4. Level of education

- Never been to school
- Primary school not finished
- Primary school
- Secondary school
- High school
- University/College

### 5. Actual social situation

- Employed
- Self-employed
- Not employed
- Student
- Disability pension
- Other grant: \_\_\_\_\_

### 6. Religious affiliation

- Christian
- Muslim
- Indigenous religion
- No religion

### 7. When were you diagnosed HIV positive?

Year: \_\_\_\_\_  
Month: \_\_\_\_\_

### 8. When did you start your HIV treatment at this clinic?

Year: \_\_\_\_\_  
Month: \_\_\_\_\_

### 9. How many times per day do you take your medicine?

- One time
- Two times
- Three times
- Others: \_\_\_\_\_

### 10. How would you describe your general health status?

Very poor 1 2 3 4 5 Excellent

### 11. How would you describe your general health status before starting HIV treatment?

Very poor 1 2 3 4 5 Excellent

**12. How many times did you miss to take your medication against HIV the last four weeks?**

- 0
- 1-2
- 3-4
- 5-6
- 7-10
- More than 10

**13. Have you ever interrupted or stopped the HIV treatment?**

- Yes
- No

**14. If you ever missed taking your medication, what was the reason?** (You can tick several boxes)

- Forgot
- Was away from home
- Had problems taking the tablets at specific times
- Ran out of tablets
- Could not go to the clinic
- Had too many tablets to take/
- Felt ill or sick
- Felt better
- Wanted to avoid side effects
- Did not want others to notice me taking medication
- Someone advised me not to take my medication
- Other reason:  
\_\_\_\_\_

**15. What do you think could be done to prevent you from missing to take tablets or interrupt the HIV treatment?** (You can tick several boxes)

- Fewer tablets
- Less side effects
- Possibility to get medicine closer to home
- Less queues at the clinic
- Longer opening hours at the clinic
- More appointments with a doctor or

nurse

- Better information
- Other: \_\_\_\_\_

**16. What will happen if you do not take your HIV medicine regularly?**

- Nothing will happen
- I will feel worse
- After some time the medicine will no longer have any effect

**17. Have you experienced any of the following positive effects since you started HIV treatment?** (You can tick several boxes)

- More energy
- Better sleep
- Increased appetite
- Feeling happier
- More interested in sex

**18. Have you experienced any of the following negative effects since you started HIV treatment?** (You can tick several boxes)

- Less energy
- Sleeping disturbances
- Loss of appetite
- Feeling depressed
- Less interest in sex
- Diarrhoea
- Headache
- Skin rashes
- Losing weight
- Thinner face
- Slim legs
- More abdominal fat
- Absent or abnormal sensation in feet
- None

**19. What motivates you to keep taking your HIV medication?**

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Thank you very much for your participation. By filling out this questionnaire you help us to improve the future care of you and other HIV positive people.

**20. Who have you told that you are HIV positive? (You can tick several boxes)**

- Partner
- Mother
- Father
- Sister or brother
- Children
- Friends
- None

**21. If you choose to not tell other people that you are HIV positive, what are your reasons? (You can tick several boxes)**

- I am afraid my partner would leave me
- I am afraid my partner would not be intimate with me
- I am afraid my family would exclude me
- I am afraid my friends would exclude me
- I am afraid I would lose my job
- I am afraid I would be discriminated
- I feel ashamed that I have HIV
- Nobody else needs to know
- Other reason:

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**22. Do the people that you informed about being HIV positive give you support?**

- Yes
- No
- More problems than support
- I have not informed anybody about my HIV status
- No answer