Treatment failure to first line antiretroviral treatment among HIV-patients at Dodoma Regional Hospital, Tanzania

Degree Project in Medicine

Alisa Mundzic

THE SAHLGRENSKA ACADEMY

Treatment failure to first line antiretroviral treatment among HIV-patients at Dodoma Regional Hospital, Tanzania

Degree Project in Medicine

Alisa Mundzic

Programme in Medicine

Gothenburg, Sweden 2017

Supervisors: Prof. Rune Andersson, Professor in Global Health, MD, PhD Institute of Biomedicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Dr Boniface Nguhuni, MD, Medical Coordinator, Resource Centre for Infectious Diseases, Dodoma Regional Referral Hospital, Dodoma, Tanzania

Correspondence: alisa.mundzic@gmail.com

Table of Contents

Abstract

Introduction

HIV is not only a health problem but also as a socio-economic and development problem. Treatment failure contributes to development of drug resistance, the risk of transmission increase and inadequate treatment leads to death. Herbal medicines are sometimes used as a primary treatment for HIV/AIDS and HIV-related problems. It has been shown that herbal medications effect the serum levels of antiretroviral medications. Up to 80% use herbal medication in some parts of Africa. Stigma and the discrimination of people living with HIV are some of the biggest challenges when it comes to HIV prevention, treatment, care and support.

Aim

The aim of the study was to identify factors that are associated with therapy failure at Dodoma Regional Hospital, Tanzania.

Methods

Data was collected of 93 HIV-diagnosed men and women at Dodoma Regional Hospital, Tanzania. Treatment failure was determined following the WHO criteria for clinical and immunological treatment failure with some modification. SPSS were used to compare patients with successful treatment to patients failing treatment. In cases were a significant P-value was found the two groups were compared with odds ratios with 95 % confidence intervals for the underlying factors and outcome variables.

Results

Among the 93 patients, 77% were women and 23% were men and the mean age was 44 years. The prevalence of treatment failure among the patients monitored at the hospital was 15%. High transport costs (OR 5.74), long time traveling to the clinics (OR 11.26), and the advice from traditional healers to stop antiretroviral treatment (OR 40.8), were found to be significant predictors of treatment failure.

Conclusions

Long travels to the hospitals, high transport costs and advice from traditional healers to stop using antiretroviral treatment were factors associated with an increased risk of therapy failure.

Keywords

HIV, treatment failure, antiretroviral drugs, traditional healer.

Acknowledgements

I would like to thank Dr Rune Anderson for his guidance during this project, Dr Boniface Nguhuni who helped me with my work in Dodoma and Dr Siraji that supported me and translated the questionnaire. I also want to thank Dr Muzzna who helped me distributing the questionnaires to the patients, Halima that helped patients with difficulties reading and the rest of the staff at the Care and Treatment Clinic at Dodoma Regional Hospital.

1. Introduction

1.1 Background

1.1.1 Epidemiology

Approximately 36.6 million people around the world are estimated living with HIV. Around 2.1 million are annually getting infected by HIV and about 1.1 million people die from AIDS-related illnesses. Low - middle income areas have the highest prevalence of HIV.
Approximate 70 % of all people with HIV live in sub-Saharan regions where 65 % of new infections occur (1).

1.1.2 HIV

HIV (human immunodeficiency virus), is a retrovirus which has the ability to transform its RNA to DNA by using reverse transcriptase (RT).
HIV infects cells in the immune system by attaching to the CD4 receptor and co-receptors, found on the surface of T-helper cells, macrophages, langerhans cells and microglial cells. After the attachment, HIV can penetrate the cells, and the transcription of viral RNA begins. RT then transforms the RNA to DNA and another enzyme, integrase incorporate the DNA into the human genome.

New viruses can be produced in the infected cells by using the translation and transcription systems in the host cell. Proteases are important enzymes that cut the HIV-precursors to functional viral protein.

The presence of HIV strongly activates the immune system and a great loss of T-helper- and other immune cells are seen in HIV-positive patients due to apoptosis of the cells (2).

1.1.3 AIDS

The CD4 positive cells of the immune system plays an important role in fighting infections and some types of cancers. Therefore, a great loss of the CD4 cells results in immune deficiency. Untreated HIV gradually destroys the immune system and the HIV infection advances to AIDS (acquired immunodeficiency syndrome) which is the most advanced stage of HIV (3).

When diagnosed with AIDS the patient's immune system is badly damaged and opportunistic infections occurs. The diagnosis of AIDS is confirmed when a person with HIV infection gets one or more of the severe opportunistic infections or malignancies, for instance Kaposi sarcoma, cryptococcal meningitis, invasive cervical cancer, toxoplasmosis and CMV retinitis. This stage is equal with WHO stage 4 (4). AIDS leads to death if untreated (5).

1.1.4 Transmission of HIV

The most common cause of HIV transmission is sexual intercourse and HIV can be transmitted when practising anal, oral and vaginal sex without using condom, with a higher risk of getting an infection practicing anal sex. HIV can also be transmitted through blood and blood products, dirty needles and from mother to child transmission during pregnancy, childbirth and breast-feeding. Half of all new infections are transmitted from a newly infected person and the reason for this is a high viral load the first months after infection (2).

1.1.5 Antiretroviral treatment

HIV can't be cured. Antiretroviral treatment (ART) supress the viral replication so that people with HIV can live a long and healthy life and reduce the risk of transmission (1). Optimized treatment suppresses HIV-RNA load in plasma from 10^5-10^6 to <20 copies/ml Successful antiretroviral treatment results in lower viral loads allowing recovering of the immune system with an increase of the CD4 count. An important aspect of successful treatment of HIV is medication adherence. Medicament has to be taken at the right time every day to keep antiretroviral drug concentrations optimized and to prevent development of drug resistance. Patients with drug resistance have a higher risk of transmitting HIV due to higher viral load (2). All patients with confirmed HIV are recommended to initiate antiretroviral treatment, regardless of WHO clinical stage and at any CD4 cell count (6).

ART can be divided into 6 groups, NRTI (Nucleoside Reverse Transcriptase Inhibitor), NNRTI (Non-nucleoside reverse-transcriptase inhibitors), protease inhibitors (PI), integrase inhibitors, fusion inhibitors and CCR5 antagonists. HIV is most often treated with 3 different medications, usually from two different groups (2). Combining antiretroviral drugs supresses HIV-replication to lower levels and is less likely to develop drug resistance compared to monotherapy (7). In Tanzania 4 groups are available for use, (NRTIs), (NNRTIs), Nucleotide reverse transcriptase inhibitors (Nucleotide analogues) and protease inhibitors (Pl) (4). Since 2004, Tanzania offers free ART to HIV patients (8).

1.1.6 Impact of HIV and AIDS in sub-Saharan Africa

The HIV pandemic has had a big impact in the world, especially in the sub Saharan-Africa. The effect of the high prevalence of HIV in the area has resulted in restricted resources for other medical conditions. In Tanzania bed occupancy rate for HIV-positive patients in the bigger regional hospitals are estimated to 50-60%. Since some in the health care staff are HIV-positive as well there is lack of human resources at all health care facilities (4).

HIV is not only a health concern, but also as a socio-economic and development problem. HIV and AIDS has negatively affected economic growth (4).
Stigma and the discrimination of people with HIV are some of the biggest challenges when it comes to HIV prevention, treatment, care and support. Research shows that stigma is the reason why many patients don't seek treatment for HIV, disclose their HIV status to partners / family members and don't seek for information about HIV. Fear of violence and exclusion from the society are important reasons why HIV-patients keep a low profile when it comes to disclosing their HIV-status or getting their medications (9).

1.1.7 HIV in Tanzania

n 2015, approximate 1,400,000 people were living with HIV in Tanzania with an estimated prevalence rate of 4.7 % among adults aged 15-49 (10). The HIV prevalence varies regionally from 0.2 percent (Zanzibar) to 15.4 percent (Njombe) (11). Women accounted for 60% of the people living with HIV aged 15 or more (10). About 36,000 people die in AIDS related illnesses annually (11). Unprotected sex with infected partners account for more than 90% of HIV-infected in Sub-Saharan Africa including Tanzania (4).

1.1.8 Dodoma

The research was performed in Dodoma Regional Hospital situated in Dodoma.
Dodoma is the capital of Tanzania with a population of approximate 2.1 million people. The prevalence of HIV among adults aged 15-49 in the region was estimated to 2.9%, 2012 (12).

1.1.9 HIV monitoring, responses and therapy failure

There are 3 types of therapy failure defined by WHO (World Health Organization), viral-, immunological- and clinical failure (13). HIV can be monitored measuring viral loads, CD4 count and clinically. Measuring viral load is considered to be a more sensitive indicator of therapy failure compared to the immunological and clinical definitions. However, there is a limitation of accessibility of viral load testing in low income countries (14).

According to a review the current WHO criteria for immunological and clinical failure have low sensitivity and positive predictive value for identifying virological failure in individuals (13).

A study made in Tanzania included 2,403 patients and out of these 14.9 % had virological failure (15). Another study conducted in Tanzania included 243,844 patients from 348 clinics, 7% experienced immunological treatment failure (16).

1.1.10 HIV-testing and monitoring in Tanzania

Confirmation of HIV-diagnosis in adults and children > 18 years are usually done by detecting antibodies using two rapid tests or Enzyme Immunoassays (EIA) in whole blood, serum or plasma (4).

Because of limited ability to use viral load testing CD4 monitoring has frequently been used for monitoring the disease. Clinical and immunological monitoring are used to determine ART eligibility and treatment response. CD4 count is measured every 6 months. For adults the CD4 count has been reported in absolute number and for children CD4 has been reported in percentage (14).

1.1.11 Traditional healers and herbal medication use

According to WHO up to 80% of the population in Africa use traditional medicine, with variation from area to area (17). Herbal medicines are sometimes used as a primary treatment for HIV/AIDS and HIV-related problems (18). The use of traditional/alternative medicine is not only centred to Africa. In many high income countries many people have tried traditional medicine and the use is increasing rapidly in many parts of the world. (17). In France 75% had tried alternative medicine at least once. In Belgium and Canada 38% and 70% had used traditional medicine (17). The reason for a broad use of traditional medicine in low income countries is its accessibility and affordability (17). The reason for the wide spread of use of alternative medicine is that traditional healers are easy to access, many generations in Africa have been receiving advice from a traditional healer which give them credibility and acceptance among the population (19). The number of HIV-positive patients using herbal

medications as primary treatment is unknown (20). It has been shown that herbal medications effect the serum levels of antiretroviral medications through their effects on CYP3A4 and could contribute to therapy failure (21).

1.1.12 Factors associated with therapy failure

Adherence plays an important role of HIV viral suppression and is associated with therapy success with reduced rates of resistance, an increase in survival, improved quality of life and prevents the spread of HIV. Factors such as stigma, not having enough emotional support at home, little knowledge about ART, resistance developing, poor availability of monitoring clinics and lack of medication, effect the adherence negatively (4). Studies made in Tanzania have shown that drug resistance to first line ART due to poor medication adherence, increase the risk in developing drug resistance to second line ART (22).

1.2 Aim

The aim of the study was to determine the prevalence of antiretroviral treatment failure among patients over 18 years monitored at Dodoma Regional Hospital, Tanzania and to identify factors associated with therapy failure.

2. Material and Methods

2.1 Study design

The study was done as a cross sectional retrospective study of HIV-diagnosed men and women followed up clinically at Dodoma Regional Hospital, Tanzania during the period of 27th of February -15th of March 2017. A questionnaire consisting 39 questions were given to the patients. Included questions were age at diagnosis, treatment start, medication and dose, specific questions about adherence, difficulties with administration of medicaments, side effects, positive effects, presence of HIV-positive family members, socioeconomic status, demographic characteristics and distance to hospital, (see appendix). Parts of the questionnaire was borrowed from Emelie Thoren's master thesis, "High adherence to antiretroviral treatment despite frequent adverse effects among people living with HIV in Dodoma, Tanzania", and the other questions were new.

The questionnaire was written in English and translated into Swahili. Information about ART regime, ART-start date, CD4 counts and opportunistic infections were collected from the patient records that were written in English. Treatment failure was determined by using patients' medical records and following the WHO criteria for clinical and immunological treatment failure with some modification. Testing of HIV-viral load were not performed. Patients were selected following the inclusion criteria below when attending their scheduled appointment at the hospital. If the patient were suitable for the research, the doctor in charge of the patient informed about the study and handed over the questionnaire at the end of the consultation. An English and Swahili speaking nurse was available for answering any questions the patients had about the questionnaire. After completion of the questionnaire, they were put in the patient's medical record and labelled with a number. After labelling the

questionnaire data was extracted from the patient's medical record and afterwards the files were returned and questionnaires were saved for data input into an excel file. Patients that did not want to participate in the study or that did not fulfil the inclusion criteria were excluded. Few patients did not want to participate in the study.

2.2 Pre-testing

Both supervisors involved with the project checked the questionnaires and one of the doctors at the hospital translated the final English version into the final Swahili version. Thereafter the questionnaire was evaluated on 15 patients and the questions were modified during five test days to prevent any misinterpretations. Patients that participated in the test study were not included in this study.

s

Table 1. Therapy failure definitions used in the research, based on WHO's criteria for therapy failure

Failure definition		Comments
Clinical failure	**Adults and adolescents** New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition)[a] after 6 months of effective treatment	The condition must be differentiated from immune reconstitution inflammatory syndrome occurring after initiating ART
Immunological failure	**Adults and adolescents** CD4 count falls to the baseline (or below) or Persistent CD4 levels below 100 cells/mm^3 or *CD4 count falls with 50% from peak value after 6 months of effective treatment	Without concomitant or recent infection to cause a transient decline in the CD4 cell count
Virological failure	Plasma viral load above 1000 copies/ ml based on two consecutive viral load measurements after 6 months on ART, with adherence support	An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed

* Added criteria to WHO's definition of therapy failure.

Table 1 shows the criteria for clinical, immunological and virological failure defined by WHO, with some few modifications. To the immunological failure definition, a CD4 count fall with 50% from the peak value was added as an alternative way of defining failure. The definition of therapy failure in children has been removed since the study excluded children. Severe events of WHO clinical stage 3 were not included as therapy failure in this study.

2.3 Study population

The study population consisted of 93 HIV positive men and women, over 18 years with at least 6 months on first line antiretroviral treatment. Among the patients 77% were women and 23% men. Patients were selected by checking the medical records at their regular visit at the hospital. If they fulfilled the inclusion criteria the were included in the research and offered to participate, otherwise they were excluded together with patients that did not want to participate. Few patients did not want to participate, no data on the number of patients excluded were collected. Among the studied population 14% had a failing antiretroviral treatment.

2.4 Inclusion criteria

Inclusion criteria was HIV-positive patients (age ≥18 years), receiving first line ART for a minimum of 6 months.

2.5 Statistical methods

2.5.1 Population and data collection

Data collection included primary data from patient records on used drugs, CD4 cell counts, opportunistic infections together with a questionnaire. Data was registered into Excel using Google Forms and later transferred to SPSS version 24.

SPSS were used to compare patients with successful treatment by using the crosstabulation function. Depending on how many variables were analysed, significant differences were calculated by using likelihood Ratio or Fischer's exact test with a significant P-value of <0.05. In cases were a significant P-value was found, the two groups were compared with odds ratios with 95 % confidence intervals for the underlying factors and outcome variables. Patients that did not answer a question were excluded in the analysis.

3. Ethics

All participants received information about the study's purpose and use. Stressing that the participation was voluntary and did not affect the treatment if they did not want to participate. All personal information was strictly confidential and was only used for the study. No personal information was disclosed. Ethical approval was given by the medical coordinator at Dodoma Regional Hospital.

4. Results

The study population consisted of 93 patients aged 18-70 years and had a mean and median age of 44 and 45 years. Among these 23% were male and 77% were female.

4.1 Sociodemographic

Table 2 and 3 present the result of the general question section. There seems to be a tendency that a more in the of the group with failing treatment were farmers/peasants (P=0.124). No significant difference was found for the other factors regarding occupation, education levels, marital status, age and living conditions.

Table 2. Sociodemographic characteristics of the 93 participants in the study

	Study Population	%	Successful treatment	%	Failing treatment	%	Statistics	P=
Sex							Fisher's Exact Test	0.484
Male	21	23	17	22	4	31		
Female	71	77	62	78	9	69		
Total	92	100	79	100	13	100		
Percentage of the studied population		100		86		14		
Marital status							Likelihood Ratio	0.296
Married	23	25	20	25	3	23		
Single	20	22	15	19	5	39		
Divorced/Separated	14	15	13	16	1	8		
Widowed	23	25	20	25	3	23		
Cohabiting	3	3	2	3	1	8		
Boyfriend/Girlfriend	10	11	10	13	0	0		
Total	93	100	80	100	13	100		
Percentage of the studied population		100		86		14		
Occupation							Likelihood Ratio	0.124
Unemployed	8	9	7	9	1	8		
Employed	12	13	12	15	0	0		
Self-employed/ Business	29	32	27	35	2	15		
Student	2	2	1	1	1	8		
Peasant/Farmer	35	39	27	35	8	62		
Retired	5	6	4	5	1	6		
Total	91	100	78	100	13	100		
Percentage of the studied population		100		86		14		
Education							Likelihood Ratio	0.682
Never been to school	11	12	10	13	1	8		
Primary school	57	61	49	61	8	62		
Secondary school	20	22	16	20	4	31		
High school	1	1	1	1	0	0		
University/collage	4	4	4	5	0	0		
Total	93	100	80	100	13	100		
Percentage of the studied population		100		86		14		

Table 3. Age differences between patients with successful treatment and failing treatment.

	Mean age	Median age	Minimum age	Maximum age
Total study population	44.16	44.50	18	70
Failing treatment	41.85	47.00	19	60
Successful treatment	44.54	44.00	18	70

4.2 Treatment

The prevalence of therapy failure in the study population was 14%, out of these eight percent were diagnosed as clinical failure. The self-reported health status today compared to before initiating ART, 61% admitted they were feeling much better. In the group with failing treatment 73% had to take their medications two times per day compared to the group with successful treatment where 51% took their medication one time per day (n.s). No significant differences were found among the results of the treatment section in the questionnaire.

4.3 Economy and accessibility

Table 4. Amount of time patients spent traveling to the clinics

		Time to the clinic				
Therapy		Less than 30 min	30 min – 1 h	1 – 2 h	3 - 4 h	Total
Successful treatment	Count	27	33	16	3	79
	%	34%	42%	20%	4%	100.0%
Failing treatment	Count	2	5	2	4	13
	%	15%	38.5%	15%	31%	100.0%
Total	Count	29	38	18	7	92
	%	32%	41%	20%	8%	101.0%
Likelihood ratio: 0.034						

When comparing the time that was spent traveling to the clinics a significant difference was found between the groups (table 4). Patients failing ART had in 31% of the cases a travel time of 3-4 hours to the clinics, compared to the successful group where only four percent of the patients travelled for that long (P=0.034).

Patient with successful treatment had in 87% of the cases low to moderate costs for traveling and 13% had high costs. Among the failing group 46% reported high costs. Patients that have high traveling costs to the clinics have a 5.74 higher risk of therapy failure compared to

patients with low to moderate travel costs, see table 9.

In the study population 91% had never interrupted their medications due to economic reasons, there were no significant differences between the groups. Patients in the study population had multiple times got the information about the importance of HIV-medications, (81%).

4.4 Health

Smoking was not common in the study population, 95 % answered that they did not smoke. In the failing treatment group, none was smoking. No significant differences were found between the groups when comparing smoking and drinking habits.

4.5 Social network

In the study population 85% of the patients had at least one person to talk to about their HIV-diagnosis with no significant difference between the groups. Stigma was the most common reason why people did not want to talk to others about their HIV-diagnosis (25%). A fifth of the patients did not have a problem talking about their diagnosis and another 17% did not disclose their HIV-status because they did not want people to judge them and talk about them.

Table 5 Patients that received advice from a traditional healer about their HIV-treatment

		Received advice from a traditional healer		
Therapy		Yes	No	Total
Successful treatment	Count	2	74	76
	%	3%	97%	100%
Failing treatment	Count	2	10	12
	%	17%	83%	100%
Total	Count	4	84	88
	%	5%	96%	100%
Fisher's Exact Test P= 0.088				

Table 6 Patients that received the advice from a traditional healer to stop with their HIV-treatment

		Got the advice to stop their HIV-treatment		
Therapy		Yes	No	Total
Successful treatment	Count	0	77	77
	%	0.0%	100.0%	100.0%
Failing treatment	Count	2	9	11
	%	18%	82%	100.0%
Total	Count	2	86	88
	%	2%	98%	100.0%
Fischer's Exact Test P=0.014				

As illustrated in table 5, seventeen percent of the patients failing treatment had been in contact with a traditional healer and received advice regarding their HIV compared to three percent in the successful treatment group (P=0.088)

As many as 18% among the patients that were failing their treatment had gotten the advice to stop taking their HIV-medication from a traditional healer compared to none in the successful group (P=0.014).

Five percent of the study population admitted they had taken ART and herbal medications at the same time. In the failing treatment group eight percent we.re using both herbal medications and ART. The use in the successful group was four percent (n.s).

4.6 Contact with partners

In the group with failing patients 15% had a sexual relationship with more than one person and in the successful group five percent of patients had sex with more than one person.

Table 7. Number of patient that used a condom last time they had sex with a temporary partner

		Used a condom last time they had sex with temporary partner		
Therapy		Yes	No	Total
Successful treatment	Count	24	7	31
	%	77.%	23%	100%
Failing treatment	Count	2	4	6
	%	33%	67%	100%
Total	Count	26	11	37
	%	70.%	30%	100%
Fischer's Exact Test P=0.051				

A tendency towards a more frequent treatment failure was found among patients that did not use condom last time they had sex with a temporary partner (P=0.051), table 7.

4.7 CD4 cell counts

Table 8. CD4 cell counts of the patients

	Initial CD4	Last CD4
Study population		
Mean	173.11	460.96
Median	125	448.5
Failing treatment		
Mean	199.69	192.38
Median	160.00	146.00
Successful treatment		
Mean	168.79	505.15
Median	122.00	462.00

In total of 92 CD4 values used in the study for determining therapy failure, 75% were over one year old.

4.8 Risk of failing antiretroviral treatment

Table 9. Factors associated with therapy failure.

	OR (95% CI)	P-value
High transport costs	5.74 (1.60-20.6)	0.007
Long time to the clinic	11.26 (2.17-58.6)	0.0040
Advice from a traditional healer to stop *ART	40.8 (1.82-914)	0.019
Advice from a traditional healer	7.4 (0.94-58.5)	0.058

* ART (Antiretroviral treatment).

actors associated with therapy failure are listed in table 9. High transport costs gave a 5.74 times higher risk of therapy failure. Long transport time to the clinic gave a 11.26 times increased risk of therapy failure. Receiving advice from a traditional healer gave almost 41 times higher risk of therapy failure compared to a patient that did not receive any advice of stopping their treatment.

5. Discussion

The findings of this study show that factors such as long travels to the hospitals, high transport costs and advice from traditional healers could increase the risk of antiretroviral therapy failure.

5.1 Factors associated with therapy failure

It is not surprisingly that a traditional healer's advice to stop with the ART was the biggest risk factor for failing treatment. Many people in Africa and Tanzania seek for advice and care from traditional healers. A study of 442 HIV-infected patients, aged 18-64 years at Kilimanjaro Christian Medical Centre showed that as many as 56% of the patients had visited a local healer in the city of Loliondo. Five percent of the patients visiting the healer had gotten the device to stop ART. A significant but not a permanent decline in ART adherence was found among the patients that had been in contact with the healer (20). Another study that included 4489 patients from Tanzania, Uganda and Zambia showed that visiting a traditional healer, screening positive for alcohol abuse and greater levels of internalized stigma were actors significantly associated with incomplete adherence (23). It is well known that a decrease in adherence is associated with therapy failure (24). In our study two percent got the advice to stop with HIV-treatment due to a traditional healer's advice. A reason for traditional healers' big impact in Africa is the fact that spiritual beliefs have been influencing the culture for generations and herbal treatment is an accepted method for treatment. Some people choose to visit a traditional healer before going to a medical doctor. Traditional healers have a lot of support among the population and for some patients seeking them consider the traditional healers to be more reliable than medical doctors. For the doctors working in the hospitals the lack of trust can be an issue since the patients aren't always following the prescriptions or hiding the fact that they use herbal medications together with their ART. The

space between medical doctors and patients is something that could be improved by involving traditional healers in the HIV-care and providing them with education about HIV and when to encourage patients to seek a medical doctor.

Religion could also be a factor among patients falling treatment since religion is strongly influencing the society of Tanzania. In a study made in Arusha and Babati region 438 patients belonging to Catholic, Lutheran, and Pentecostal churches were given a questionnaire to examine the relation between religious beliefs and HIV-stigma, disclosure and attitude towards ART. The results showed that HIV-stigma was strongly associated with religious beliefs. HIV was considered as a punishment from God (P=0.01) (25). As high as 80.1% of the participants answered HIV could be cured by prayer. Unfortunate we did not look at religion and possible association with antiretroviral therapy failure in our study.

HIV-stigma is a big problem with HIV treatment and could explain why patients seek alternative medicine (26). Going to the clinics for doctor appointments or collecting HIV-medications could make people in the surroundings curious about their HIV-status. Many patients get their HIV-medication at the clinics and immediately after leaving the doctors room they go to the rest rooms to through away the packages so that nobody sees the HIV-medications. Some patients even take out the pills from the containers and put it in a small bag, bottle etc. Bathrooms at the clinic were full of containers and packages.
Another problem is the fact that some people fear medications and turn to traditional healers and herbal medications (17). Some patients on ART have problems with adverse effects a number of these patients stop taking their HIV-medications and turn to traditional healers and herbal medication believing that the herbal medications help them since they are not feeling the side effects form the ART. A research made in South Africa followed 222 patients that

reached out to a traditional healer that had been trained in HIV/STI, prevention and care. There were 18 HIV-positive patients (8.1%) and out of these 8 (44%) were using traditional medicine and ART at the same time (27). In this study, a total of five percent of the studied population admitted they were using herbal medication and ART at the same time. As mentioned in the background, it has been shown that herbal medications effect the serum levels of antiretroviral medications through their effects on CYP3A4 and could contribute to therapy failure (21). There are not so many studies made on herbal medications and the effects of the HIV-care and therapy failure (28). This could be interesting to continue investigating.

The study shows that high transport costs and a long time spent traveling to the hospitals increase the risk of therapy failure. Patients that have to travel for hours to the treatment clinics have to plan their trips in advance. Traveling 4h one way to the clinic the patients need a full day for the appointments. This might affect their work, economy and it could raise questions about the patient's absence in villages/cities. Some patients choose to get their HIV-care in other cities since they fear exclusion from the society if they receive care in their own city. There is a possibility that stigma is the reason why some patients decide to get their medications in other cities. A possible explanation why patients with high transport costs and long travel time are more often associated with therapy failure could be due to poor adherence. In case that medications are out of stock, or the patients miss their appointments it is likely that it is harder for patients living far away from the clinics to find time to get their medications and keep good adherence. Even though Tanzania have been fighting stigma and discrimination of people living with HIV there is still a lot to be done. In our study 25% of the population did not want to disclose their HIV-status because of stigma.

5.2 Contact with partners

On the question if the patients used a condom last time they had sex with a temporary partner, the results show that there is a tendency that patients that did not use condom had a higher risk of treatment failure. Among patients failing treatment 67% admitted they did not use a condom last time they had sex with a temporary partner, these patients risk transmitting HIV-infection. Only six out of thirteen patients failing treatment answered this question, the rest were excluded since they did not have a partner/ did not remember if they used protection. It would be interesting to know why patients with treatment failure prefer not to use a condom when having sex with a temporary partner.

5.3 Sociodemographic

In the city of Dodoma the population are estimated to consist of 51% men and 49 % women (29).

Our study had 23% male participants and 77% female, no significant difference was found between the failing and successful groups. An explanation to the fact that the majority of the patients were women could be that some male patients were ashamed of going to the appointments to get their medications. Instead they would send their wives / partners to get it for them and since the men did not show up they could not be included in the research. In a study of HIV-positive patients with immunological failure of first-line and switch to second-line antiretroviral therapy in Tanzania showed that being a male was a risk factor for therapy failure (16). We found no associations between sex therapy failure.

5.4 Methodological considerations

5.4.1 Strengths of the study

Using a questionnaire in this study made it possible to ask the patients private questions that could have been hard to ask when interviewing patients. The questions used in the research concerned many different areas and this resulted in a lot of valuable information. For patients that had difficulties reading or understanding the questions a secretary was available to assist. Translations were made by an English and Swahili speaking doctor and checked later checked in the testing phase. Determination of therapy failure was done by the same person to avoid bias.

5.4.2 Limitations of the study

The study was performed as an explorative retrospective study. The best way to look for potential factors associated with therapy failure would have been to do a case-control study as the original plan was. Due to logistic reasons a case-control study was not possible to do.

The HIV clinic had from time to time over 100 patients per day and sometimes patients were sitting close to each other or the treating doctor when filling in the questionnaires. This could have affected the answers given, since some patients tend to answer what they think is correct to answer. Since 100% privacy could not be guaranteed it is possible that some patients felt ashamed and wrote down another answer rather than the real answer.

We investigated many factors that could influence the therapy and there is a risk of getting false significance and therefore the results of the research should be used with this in concerned.

Another limitation is the fact that the studied population consisted of 93 patients which gives the study a lower power. To achieve greater statistical power, it would have been necessary to extend the study population and include more patients and if possible more hospitals in the city.

Furthermore, it is likely that the study population was not fully representing the HIV-population of Dodoma, since a small amount of men were included and patients that was very ill and potentially failing treatment were probably home or at the hospital getting treatment for severe infections.

To be able to determine a prevalence of therapy failure at Dodoma regional hospital the number of patients put on treatment, patients remaining on treatment, drop-out patients and the number of deaths in HIV/AIDS would have to be known and we did not have access to this information in this study.

The original plan was to use virological failure for determining therapy failure. Unfortunate this was not possible since the use of viral testing had not yet fully started. Instead we used WHO's criteria for immunological therapy failure and modified it a bit. A systematic review found that current WHO clinical and immunological failure had low sensitivity and positive predictive value for identifying patients with virological failure (13). Plan B was to use the updated CD4 values to determine whether patients were failing or not. Unfortunate 75% of the studied population had CD4-values that was more than one year old and this made it hard to determine whether the patients were failing their treatment at the time of the visit. Therefore, treatment failure was decided at the date last CD4 was measured.

Definition of clinical failure was only used once since the opportunistic infections and all data was collected from hand-written medical records of varied quality. In some cases, medical records were very old and information about the treatment was missing.

In the future, it would be of interest to further investigate the effects of alternative medicine on HIV- therapy in Dodoma. The Reliability of diagnosing treatment failure at the hospital using CD4 counts together with the clinical definition, could be compared to viral load testing in future studies.

6. Conclusions

High transport costs and long time spent traveling to get HIV-care increase the risk of therapy failure and could possibly be prevented by improved the accessibility.

A traditional healer's advice to stop ART was associated with a higher risk of therapy failure. Education and collaboration with traditional healers could be of interest to prevent that patients from stop using ART.

Some patients failing treatment admitted not using a condom when having sex with a temporary partner. It is important to educate patients but also the whole population with the risks of HIV-transmission and unprotected sex.

A majority of the patients at the treatment facilities are women. It is of importance to attract more men to the clinics to offer an equal HIV-care.

Stigma is still highly present I Tanzania. A more open community and acceptance for people living with HIV would be valuable for further progress of HIV-care. There is still more research to be done investigating the effects of herbal medications and antiretroviral treatment.

7. Populärvetenskaplig sammanfattning

Terapisvikt vid första linjens behandling med bromsmediciner, bland HIV-patienter vid det regionala sjukhuset i Dodoma, Tanzania.

Icke-fungerande HIV-behandling resulterar till ökade virusmängder, sämre immunförsvar, försämrad sjukdomsbild och ökad smittsamhet. Årligen dör 36 000 människor i AIDS-relaterade sjukdomar i Tanzania och behandling med bromsmediciner är livsnödvändig.

I en del afrikanska länder uppskattas det att ca 80% av invånarna har varit i kontakt med traditionella helare och alternativ medicin. Studier har visat att naturläkemedel ibland sänker den verksamma mängden HIV-läkemedel i blodet vilket kan försämra HIV-behandlingen så viruset får möjlighet att bli fler i antal.

HIV är inte bara ett hälsoproblem utan är också ett socioekonomiskt problem och påverkar den ekonomiska tillväxten negativt. Diskriminering av HIV-positiva patienter är en av de större utmaningarna i kampen mot HIV.

Vid användning av olika läkemedelskombinationer mot HIV är det viktigt att ha förståelse för olika faktorer som kan bidra till försämrad behandling. Vi ställde oss frågan: vilka faktorer bidrar till försämrad behandling på det regionala sjukhuset i Dodoma, Tanzania?

Studien var en retrospektiv tvärsnittsstudie av 93 HIV-positiva män och kvinnor som följdes upp på det regionala sjukhuset i Dodoma, Tanzania. Den studerade populationen delades in i två grupper, de med icke-fungerande behandling och de med fungerande behandling. Alla

HIV-positiva patienter över 18 år som hade använt första kombinationerna av antivirala läkemedel under minst 6 månader, inkluderades i studien. Icke fungerande behandling definierades enligt World Health Organization's, (WHO'S) kriterier för icke-fungerande behandling.

Andelen som hade icke-fungerande behandling bland de patienter som följdes på sjukhuset i Dodoma var 14%. Hela 67% av de som hade icke-fungerande behandling uppgav att de inte använde något skydd när de hade sex med en tillfällig partner.

Vår studie visade att höga resekostnader och lång transporttid till kliniken ökade risken för att drabbas av icke-fungerande behandling med ca 6 respektive 11 gånger. Ökad tillgänglighet av behandlande kliniker och bättre transportmöjligheter är ett sätt att bemöta höga resekostnader och längre transporttider.

Den allra största riskökningen såg vi hos patienter som hade fått rådet av en traditionell helare att sluta ta sina läkemedel, risken att drabbas av icke-fungerande behandling var hela 41 gånger förhöjd. Allmänna råd från en helare avseende patienternas HIV-behandling ökade risken att drabbas av icke-fungerande behandling med ca 7 gånger.

I Tanzania är förtroendet för traditionella helare stort, ibland större än för vanliga läkare. Helare har stort inflytande och bör i högsta grad involveras i kampen mot HIV/AIDS. Genom att utbilda helare om HIV och naturläkemedels negativa effekter på HIV-behandling skulle de kunna användas i kampen mot HIV. Helare skulle kunna samarbeta med läkare, sida vid sida.

References

1. UNAIDS. HIV/AIDS 2016 [Available from: http://www.who.int/mediacentre/factsheets/fs360/en/.
2. Iwarson PS. Infektionsmedicin epidemiologi, klinik, terapi. 6th ed. Sävedalen: Säve Förlag; 2014. 383 p.
3. Aaidsinfo.nih.gov. HIV Overview aidsinfo.nih.gov2016 [updated September 9, 2016. Available from: https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/19/45/hiv-aids--the-basics.
4. Welfare MoHaS. Tanzania national guideline for management hiv and aids Ministry of Health and Social Welfare National AIDS Control Programme; 2015. Available from: https://aidsfree.usaid.gov/sites/default/files/04_11_2016.tanzania_national_guideline_for_management_hiv_and_aids_may_2015._tagged.pdf.
5. Socialstyrelsen. Hiv/aids - B24 Socialstyrelsen.se [Available from: http://www.socialstyrelsen.se/riktlinjer/forsakringsmedicinsktbeslutsstod/hivaids-b24.
6. Organization WH. Consolidated Guidelines On The Use Of Antiretroviral Drugs For Treating And Preventing HIV Infection 2016 Recommendations For A Public Health Approach 2016. Available from: http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1.
7. Barnett T. Global HIV/AIDS Medicine 2008. Available from: https://books.google.se/books?id=fNU62HhYFT0C&pg=PA137&lpg=PA137&dq=combined+ARV+drug+resistance&source=bl&ots=r2AKtSLKJb&sig=4bkUk_zWQ3mdCnet034UOH-m17I&hl=sv&sa=X&ved=0ahUKEwiwq8WK4qnUAhWBESwKHZ4XBkg4ChDoAQhOMAY -v=onepage&q=combined%20ARV%20drug%20resistance&f=false.
8. (NACP) MoHaSWNACP. Implementation of HIV/AIDS Care and Treatment Services in Tanzania. Dar es Salaam - Tanzania2013. Available from: www.nacp.go.tz/site/download/bookreport3.pdf.
9. (UNAIDS). JUNPoHA. Reduction of HIV-related stigma and discrimination 2014 [Available from: http://www.unaids.org/en/resources/documents/2014/ReductionofHIV-relatedstigmaanddiscrimination.
10. UNAIDS. HIV and AIDS estimates 2015 [Available from: http://www.unaids.org/en/regionscountries/countries/unitedrepublicoftanzania.
11. USAID. HIV/AIDS Tanzania 2016 [Available from: https://www.usaid.gov/sites/default/files/documents/1860/Tanzania HIV-AIDS Fact Sheet 2016.pdf.
12. WELFARE TUROTMOHAS. HIV/AIDS/STI Surveillance Report Report Number 23 2013 [updated May 9, 2017. Available from: www.nacp.go.tz/site/download/report23.pdf.
13. UNAIDS. Table 7.15 WHO definitions of clinical, immunological and virological failure for the decision to switch ART regimens [Available from: http://www.who.int/hiv/pub/guidelines/arv2013/art/WHO_CG_table_7.15.pdf.
14. Programe URoTMoHaSWNAC. National HIV viral load testing guideline to support HIV and AIDS prevention, care and treatment. . Dar es Saalam: Ministry of Health and Social Welfare National AIDS Control Programme; 2015. Available from: https://aidsfree.usaid.gov/resources/tanzania-national-hiv-viral-load-testing-guideline-support-hiv-and-aids-prevention-care.
15. Hawkins C, Ulenga N, Liu E, Aboud S, Mugusi F, Chalamilla G, et al. HIV virological failure and drug resistance in a cohort of Tanzanian HIV-infected adults 2016

[updated JulPMC4896406]. 2016/04/15:[1966-74]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/?term=HIV+virological+failure+and+drug+resistance+in+a+cohort+of+Tanzanian+HIV-infected+adults.
16. Vanobberghen FM, Kilama B, Wringe A, Ramadhani A, Zaba B, Mmbando D, et al. Immunological failure of first-line and switch to second-line antiretroviral therapy among HIV-infected persons in Tanzania: analysis of routinely collected national data 2015 [updated JulPMC4672690]. 2015/03/18:[880-92]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4672690/.
17. Geneva WHO. WHO Traditional Medicine Strategy 2002–2005 2002 [Available from: http://www.wpro.who.int/health_technology/book_who_traditional_medicine_strategy_2002_2005.pdf.
18. Mills E, Singh S, Wilson K, Peters E, Onia R, Kanfer I. The challenges of involving traditional healers in HIV/AIDS care 2006 [updated Jun. 2006/06/01:[360-3]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16734953.
19. UNAIDS. Collaboration with traditional healers in HIV/AIDS prevention and care in sub-Saharan Africa.
20. Thielman NM, Ostermann J, Whetten K, Whetten R, Itemba D, Maro V, et al. Reduced adherence to antiretroviral therapy among HIV-infected Tanzanians seeking cure from the Loliondo healer 2014 [updated Mar 01PMC4006017]. 2014/02/15:[e104-9]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24525471.
21. Mills EF, Brian C; Heeswijk, Rolf vanc; Phillips, Elizabethd; Wilson, Kumanand; Leonard, Blaird; Kosuge, Kazuhirod; Kanfer, Isadore. Impact of African herbal medicines on antiretroviral metabolism [Januari 3, 2005:[95-7]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/15627040.
22. Ramadhani HO, Bartlett JA, Thielman NM, Pence BW, Kimani SM, Maro VP, et al. Association of first-line and second-line antiretroviral therapy adherence 2014 [updated SepPMC4281791]. 2015/03/04:[ofu079]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25734147.
23. Denison JA, Koole O, Tsui S, Menten J, Torpey K, van Praag E, et al. Incomplete adherence among treatment-experienced adults on antiretroviral therapy in Tanzania, Uganda and Zambia 2015 [updated Jan 28PMC4728173]. 2015/02/18:[361-71]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25686684.
24. (NACP) MoHaSWNACP. National guidelines for the management of HIV and AIDS Dares Salaam, Tanzania2012 [updated June 06, 2017. Fourth Edition:[Available from: https://aidsfree.usaid.gov/sites/default/files/hts_policy_tanzania.pdf.
25. James ZouEmail author YY, Muze John, Melissa Watt, Jan Ostermann and Nathan Thielman. Religion and HIV in Tanzania: influence of religious beliefs on HIV stigma, disclosure, and treatment attitudes [March 04, 2009:[Available from: https://bmcpublichealth.biomedcentral.com/articles/10.1186/1471-2458-9-75.
26. Katz IT, Ryu AE, Onuegbu AG, Psaros C, Weiser SD, Bangsberg DR, et al. Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis 2013 [updated Nov 13PMC3833107]. 2013/11/28:[18640]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/?term=Impact+of+HIV-related+stigma+on+treatment+adherence%3A+systematic+review+and+meta-synthesis.
27. Karl Peltzer NM. Patients Consulting Traditional Health Practioners in the Context of HIV/AIDS in Urban Areas in KwaZulu-Natal, South Africa [June 18, 2008:[Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2816585/ - R27.

28. Edward Mills VM, Dan Perri, Elizabeth Phillips, Gideon Koren. Natural health product–HIV drug interactions: a systematic review 2005 [March 01, 2005:[Available from: http://journals.sagepub.com.ezproxy.ub.gu.se/doi/abs/10.1258/0956462053420103.
29. Finance NBoSMo, Salaam De. 2012 Population And Housing Census [updated March, 2013. Available from: http://www.tzdpg.or.tz/fileadmin/documents/dpg_internal/dpg_working_groups_clusters/cluster_2/water/WSDP/Background_information/2012_Census_General_Report.pdf.

Appendices

Questionnaire

My name is Alisa and I am studying medicine in Sweden. This questionnaire is a part of my master thesis where I will examine how the HIV treatment is working here at the hospital in Dodoma. The questionnaire concerns different areas for example HIV treatment that you undergo, general questions and questions about your living conditions.

Participation in the study is voluntary and confidential. You can choose to leave the study without any specific reason. Care and treatment offered to you will be the same weather you choose to participate in the study or not. Participation in the study is valuable and helpful when it comes to understanding more about the factors that contribute to therapy failure.

I hope that you find this interesting and that you want to participate in the research.

Thank you!

Instructions:
Please tick the boxes for the appropriate answer. For some questions, more than one alternative can be chosen. Where a longer answer is required, please fill in your answers in the space provided.

A. General questions

1. Age: _____ years

2. Level of education:

- Never been to school
- Primary school
- Secondary school
- High school
- University/College

3. Occupation:

- Unemployed
- Employed
- Self-employed/business
- Student
- Peasant/ farmer
- Retired

4. Marital status:

- Married
- Single
- Divorced/Separated
- Widowed
- Cohabiting
- Boyfriend/girlfriend

5. Living conditions:

- Own house
- Rented house/apartment
- No stable place to live

B. Treatment

6. What is the main reason for taking your HIV drugs?

- To get cured from HIV
- To avoid getting symptoms of HIV
- The doctor tells me to take the medicine
- To live longer

7. Compared to before you started the treatment, how would you describe your health status now?

- Much worse
- Worse
- The same
- Better
- Much better

8. Have you experienced any of the following symptoms the last 6 months? (you may choose several options)

- Nausea
- Vomiting
- Diarrhea
- Abdominal pain
- Rashes/skin lesions
- Nightmares
- Problems to sleep
- Dizziness
- Reduced sensibility/numbness in arms or legs
- Fat loss in arms, legs or face
- Severe weight loss
- Muscle pain/joint pain
- Other_____
- No bad symptoms

9. How many times per day do you take your HIV drugs?

- 1 times a day
- 2 times a day

- 3 times a day

10. How many pills for HIV treatment do you take daily _____pills

11. Have you at any time not taken your medicine?

- Yes, many times
- Maybe some time
- No, never

12. In the past 4 weeks how many times did you not take your medication as prescribed?

- _____times

13. If you didn´t take your medication at any point, what was the reason? (You may choose several reasons)

- Simply forgot
- Side effects(please specify)_____
- Did not have enough pills at home
- Did not have time to get new pills
- Did not have enough money to get new pills
- Did not have access to a clinic where I could get the pills
- Other reason_____

14. Are you keeping your HIV-medications in the original package/tin?

- Yes I keep my HIV medication in the original container
- No I do not keep my HIV-medications in the original container(please specify how you keep your HIV-medication):

  _____

  _____

<u>C. Accessibility, availability, Economy</u>

15. How long time did you travel to get to the clinic?

- Less than 30 minutes
- 30 minutes – 1 hour
- 1 hour – 2 hours
- 3 hours - 4 hours
- More than 4 hours

16. How big are the economic costs of travel to the clinic for you?

- Not mentionable
- Low
- Moderate
- High
- Not bearable

17. Have you ever let down your medicine due to economic consequences? (For example costs to get to the clinic, costs to get the pills, have to stay home from work etc.)

- Yes, often
- A few times
- No never

18. How is the availability/access to the HIV-clinic?

- It is easy to contact the clinic and get a visit there when I need to
- It is hard to get a visit and to contact the clinic

19. A. Since the start of your HIV-treatment have you ever done any of the following? (You may choose several options)

- Stopped working
- Changed work
- Traveled to another city to get the HIV-medication
- Moved to another city
- Other_____
- No, I did not have to do any of the alternatives above.

<u>D. Knowledge of HIV and HIV drugs</u>

20. Are there any ways to cure HIV/AIDS?

- Yes
- No
- I don´t know

21. If you don´t take the HIV drugs continuously, may any of the following occur from this? (you may choose several options)

- The symptoms of HIV may return/increase
- The HIV drugs can stop working
- You can transmit HIV to others more easily
- Nothing will happen
- I will feel better
- Other

  _____
  _____

22. Have you got information about the importance of taking the HIV drugs regularly and why it is important?

- Yes, multiple times with detailed information
- Yes, a few times
- Yes, but only one time when I started treatment
- No, I never got the information
- I don´t know

E. Health

23. Have you had any of the following? (you may choose several options)

- Chest Pain
- Irregular heart beat
- Tuberculosis
- Kidney, bladder or urinary problems
- Liver disease – yellowness Jaundice
- Anemia

24. Do you smoke?

- Yes
- No
- No but I have been smoking in the past

25. Describe your smoking habits:

- Daily (please specify how many cigarettes per day)

  _____
- 4 or more times a week
- 2-3 times a week
- 2-4 times a month
- monthly or less
- I don't smoke.

26. How often do you have a drink containing alcohol?

- Daily (please specify how many alcoholic drinks per day)

  _____
- 4 or more times a week
- 1-3 times a week
- 2-4 times a month
- monthly or less
- I don't drink

F. Social network

27. Is there a person you can turn to if you need support or somebody to talk to?

- Yes I have many people I can talk to
- Yes I have a few people I can talk to
- Yes I have one person I can talk to

- o No I do not have anyone to talk to

28. Did you tell anyone about your HIV-diagnosis? (You may choose several options):

- o Yes, my partner
- o Yes, a family member
- o Yes, my mother
- o Yes, my father
- o Yes, my sister
- o Yes, my brother
- o Yes, my daughter
- o Yes, my son
- o Yes, several family members
- o Yes, a friend
- o Yes, a couple of friends
- o Nobody in my family knows about my HIV-diagnosis
- o My partner does not know about my HIV-diagnosis
- o None of my friends know about my HIV-diagnosis
- o Nobody but me and the health care workers know about my HIV-diagnosis

29. What is the reason for not telling people you know about your HIV-diagnosis?

- o I do not have a problem talking about my HIV-diagnosis
- o It is private
- o I do not want people to feel sorry for me
- o I do not want people to judge and talk about me
- o I think it could affect me Negatively (please specify in what way):

  _____

  _____
- o Stigma
- o Other(please describe):_____

30. Have you during your HIV-treatment received any HIV-treatment advice from a traditional healer?

- o Yes
- o No

31. Have you ever stopped using your HIV-medications/changed the way you use your HIV-treatment due to your traditional healer's advice?

- o Yes
- o No

32. Have you ever taken any herbal medication together with your HIV-medicine?

- o Yes
- o No

33. Are you currently using any herbal medications together with your HIV-medication?

- o Yes
- o No

G. Contact with partners

34. Do you know your partner's HIV status?

- o Yes, positive
- o Yes, negative
- o No, I don't know
- o I have no current sexual partner.

35. Do you have sexual relationships with more than one partner?

- Yes
- No

36. How many sexual partners do you have? (please specify with a number)

- No partner
- 1 partner
- 2 partners
- 3 partners
- 4 partners or more

37. Do you use condom during sex with your ordinary partner?

- Yes, always
- Most of the times
- Not very often
- No, never
- I have no partner

38. Do you use condom during sex with your temporary partner?

- Yes, always
- Most of the times
- Not very often
- No, never
- I have no partner

39. The last time you had sex with your temporary partner, did you use a condom?

- Yes
- No
- I do not remember
- I have no temporary partner
- I do not use condom at all

Medical records

AN: Sex
Male / Female

Date of birth (ddmmyy)_____

Date confirmed HIV (ddmmyy) _____

ART- start date (ddmmyy)_____

ART prescribed _____

ART Reason _____

Since treatment start how many times has the patient changed ART regime ____

Date (ddmmyy) first time ART was changed _____

Previous treatment _____

ART change reason _____

Date previous treatment (ddmmyy)_____

Nutritional status _____

Initial CD4_____

Date (ddmmyy) Initial CD_____

Last CD4_____

Date (ddmmyy) last CD4____

Lowest CD4 _____

Date lowest CD4 _____

Highest CD4 _____

Date (ddmmyy) Highest CD4____

Any opportunistic infections____

Number of opportunistic infections_____

Functional status (start) _____

OI treatment/prophylaxis and relevant CO-medications _____

Follow up status _____

BN: Therapy____
Successful / Failing

WHO clinical stage (1-4) (today) ____

Time from ART-start to first therapy change ____

Time from positive HIV result to ART-start _____

Years on treatment _____

Last CD4 taken within 1 year? ____

Transferred patient? ____