From access to adherence:

the challenges of

antiretroviral treatment

University of Amsterdam

World Health Organization

Royal Tropical Institute

From access to adherence: the challenges of antiretroviral treatment

Studies from Botswana, Tanzania and Uganda
2006

Anita Hardon
University of Amsterdam

Sheila Davey
Writer/Editor

Trudie Gerrits
University of Amsterdam

Catherine Hodgkin
Royal Tropical Institute, Amsterdam

Henry Irunde
Principal Investigator, Tanzania

Joyce Kgatlwane
Principal Investigator, Botswana

John Kinsman
University of Amsterdam

Alice Nakiyemba
Principal Investigator, Uganda

Richard Laing
World Health Organization

European Community

This document has been produced with the financial assistance of the European Community. The views expressed herein are those of the authors and can therefore in no way be taken to reflect the official opinion of the European Community.

Contents

Acknowledgments

Acronyms and abbreviations

ACHAP	African Comprehensive AIDS Partnership (Botswana)
ACP	AIDS Control Programme (Uganda)
ADR	Adverse drug reaction
AIDS	Acquired Immune Deficiency Syndrome
AMREF	African Medical and Research Foundation
ART	Antiretroviral therapy
ARVs	Antiretroviral medicines
BHP	Botswana Harvard Partnership
BOTUSA	Botswana-USA project
CSO	Central Statistical Office (Botswana)
CTC	Care and Treatment Clinics (ART clinics)
EDM	Electronic drug monitoring
FGD	Focus Group Discussion
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
GoT	Government of Tanzania
HIV	Human Immunodeficiency Virus
IDCC	Infectious Disease Control Centre
IEC	Information, education and communication
INRUD	International Network for Rational Use of Drugs
JCRC	Joint Clinical Research Centre (Uganda)
JRRH	Jinja Regional Referral Hospital (Uganda)
KIT	Royal Tropical Institute (Amsterdam, the Netherlands)
KITSO	Knowledge, information and technology shall overcome (HIV and AIDS)
MDH	Muhimbili University College of Health Sciences (MUCHS), Dar es Salaam City Council and Harvard School of Public Health
MEDUNSA	Medical University of South Africa
MNH	Muhimbili National Hospital, Dar es Salaam, Tanzania
MoH	Ministry of Health

MSD	Medical Stores Department
MSF	Médecins Sans Frontières
MUCHS	Muhimbili University College of Health Sciences, Dar es Salaam, Tanzania
NACA	National AIDS Coordinating Agency (Botswana)
NACP	National AIDS Coordinating Programme (Tanzania)
NGO	Nongovernmental organization
NIMR	National Institute of Medical Research (Tanzania)
NTC	Nile Treatment Centre (Uganda)
PASADA	Pastoral Activities and Services for AIDS in Dar es Salaam Archdiocese, Tanzania
PEPFAR	(United States) President's Emergency Plan for AIDS Relief
PLWHIV	People living with HIV
pMTCT	Prevention of Mother-to-Child Transmission
Portakabin	Prefabricated building used in treatment centres
PRDUC	Promoting Rational Drug Use in the Community
SIDA	Swedish International Development Agency
SOP	Standard Operating Procedures
SSI	Semi-structured Interview
STG	Standard Treatment Guidelines
TASO	The AIDS Support Organisation (Uganda)
TFDA	Tanzania Food and Drugs Authority
UAC	Uganda AIDS Commission
UDSM	University of Dar es Salaam
UDVL	Undetectable viral load
UNAIDS	United Nations Joint Programme on AIDS
VCT	Voluntary counselling and testing for HIV
WHO	World Health Organization

Foreword

The devastating impact of AIDS in the world – especially in sub-Saharan Africa - has led to an unprecedented global effort to ensure access to antiretroviral (ARV) medicines to treat the disease in every country where HIV is a threat. While the World Health Organization (WHO) goal of ensuring access to antiretroviral treatment (ART) for 3 million people by end-2005 was not achieved, an estimated 1.3 million people who would not otherwise have been treated now have access to ART. This book is a testament to the early treatment successes and the hidden challenges of antiretroviral therapy (ART) in resource-poor settings. It is also a wake-up call to the risk of treatment failure and the development of widespread ARV resistance unless all patients are given the continuing support they need to achieve full adherence to ARVs. AIDS is particularly challenging because of the need to achieve very high (at least 95%) levels of adherence to prevent treatment failure and the generation of ARV-resistant virus.

This book has arisen from the fieldwork undertaken by participants attending the Promoting Rational Drug Use in the Community (PRDUC) course in Pretoria, South Africa, in September 2004. Since it was first offered in Bangkok, Thailand, in 1999, this course – jointly organized by the University of Amsterdam, the Netherlands, the Royal Tropical Institute (KIT), Amsterdam, and WHO – has focused on community aspects of medicine use. The participants at the Pretoria course identified adherence to ARVs to be the major problem in medicine use being faced today in many of their countries. To enable the participants to undertake pre-intervention studies on this, three groups were selected through a competitive process to receive financial and technical support. An initial planning workshop was held in Bagamoyo, the United Republic of Tanzania, in February 2005, followed by on-site assistance in data analysis from PhD students from the University of Amsterdam in July and August, leading to a report writing workshop in Jinja, Uganda, in November 2005. The country teams included pharmacists, doctors, social scientists and ministry of health staff. The different country and support groups assisted each other in undertaking these studies in the short time available.

The authors report on the experiences from successful treatment programmes in three countries in sub-Saharan Africa at the forefront of the roll-out of ARVs. The voices of the patients, their families, community members and the health workers who care for them have been reported faithfully by the country study authors. Their real life experience is valid and needs to be considered by health programme managers who are planning the expansion of ART programmes.

In all three countries, people living with AIDS speak of the impact of ART on their daily lives and of the key challenges involved in sustaining the necessary high level of adherence to treatment. These include treatment-related hunger, the burden of out-of-pocket expenses (including the cost of transport to often distant treatment centres, lost wages, registration fees and monthly user fees), side-effects, long waiting times at the treatment centres, and fear of stigma and discrimination – in the workplace, the community, and even within their own families.

Elsewhere, health care staff highlight the pressure of work at some treatment centres and the lack of adequate resources, especially the shortage of adherence counsellors. Some health workers complain of a heavy workload due to staff shortages, of poor facilities (especially a lack of laboratory facilities) and occasional stock-outs of ARVs.

Although regular counselling is a key requirement for successful ARV adherence, the frequency and quality of counselling varied greatly among and within the three countries involved. Meanwhile, stigma and discrimination were said to be a continuing problem in all three countries and a major constraint to adherence for people who were unable to disclose their HIV status. Without disclosure, people rarely had access to an adequate social support network – identified as a key factor for successful adherence.

The three studies have each generated a number of practical recommendations such as establishing an appointments system to help reduce long waiting times at the public sector facilities; providing vouchers to cover transport costs; providing "food baskets" during the first six months of therapy; offering more frequent and longer opening times at the facilities; and ensuring that adherence counsellors are available to do pill counts and provide adherence support. However, as yet none of these recommendations or the many others made have been subject to intervention testing and evaluation. The country studies were pre-interventional and now need to be followed up by careful evaluation of the measures suggested. As the world invests billions of dollars in ensuring access to ARVs, there needs to be simultaneous investment in testing approaches to ensuring long-term optimal adherence in varied settings.

The roll-out of ARVs in many resource-poor countries has been a remarkable expression of international solidarity. However, starting patients on ARVs without ensuring full adherence through an adequate support system is likely to lead to treatment failure and the emergence of drug-resistant virus which can be transmitted to others. Drug-resistance is a potentially major threat to achieving universal access as it could mean that more and more people have to switch to second-line ARVs, which are more expensive and more difficult to use. The major increase in programme costs that this would entail would limit the total number of people with access to treatment.

To ensure that AIDS can continue to be treated, it is essential that effective adherence support should be an integral part of any treatment programme. As treatment roll-out is increased to meet the global target of achieving universal access to ART by 2010 for all who need it, the need for effective adherence support mechanisms will intensify. Failure to tackle this will jeopardize the future of treatment programmes, and may result in the failure of the immense global and national efforts to provide hope to people living with HIV through the provision of treatment to those most in need.

Efforts to increase access to ARVs should go hand-in-hand with the efforts needed to ensure that every ART patient receives adequate adherence support. This book illustrates some of the key challenges in achieving and maintaining optimal adherence and points to possible solutions. We hope that the evidence presented, the personal experiences related and, in some cases, the unanswered questions identified will encourage policy-makers, planners, funding organizations, AIDS doctors and patients to work together towards sustainable ART: access and optimal adherence.

Anita Hardon
University of Amsterdam

Catherine Hodgkin
Royal Tropical Institute (KIT), Amsterdam

Richard Laing
World Health Organization

Geneva
July 2006

1. On hunger, transport costs and waiting time: a synthesis of challenges to ARV adherence in three African countries

Anita Petra Hardon, Dorothy Akurut Aurugai, Christopher Comoro, Cosmas Ekezie, Henry Irunde, Trudie Gerrits, Catherine Hodgkin, Joyce Kglatwane, John Kinsman, Richard Kwasa, Janneth Maridadi, Alice Nakiyemba, Stephen E.D. Nsimba, Robert Ogenyi, Thomas Oyabba, Florence Temu, Richard Laing.

Introduction

Since the launch of WHO's '3 by 5' initiative in 2003, many countries in sub-Saharan Africa have established national antiretroviral treatment (ART) programmes. Although the WHO target of providing access to ART for 3 million people by 2005 was not achieved, by end-2005 an estimated 1.3 million people in low- and middle-income countries had access to treatment (about 20% of those estimated to be in need) (WHO and UNAIDS, 2006). By mid-2005, the WHO target had already been overtaken by an even more ambitious aim. In July 2005, the G8 group of industrialized countries committed to the goal of achieving 'as close as possible to universal access to treatment for all those who need it by 2010.' (UNAIDS, 2006, G8 Gleneagles Summit, 2005). Nonetheless, the challenges in the region remain great. Health systems are weak, and the target orientation of ART programmes risks an emphasis on initiating people on ART at the expense of ensuring effective use of medicines. As discussed in Chapter 2, extremely high levels of adherence (at least 95%) are needed to ensure positive treatment outcomes and prevent the development of drug-resistance (Paterson et al., 2000).

Up till now, only limited operational research has been carried out to identify adherence problems in resource-poor settings and to strengthen adherence support (Jaffar et al., 2005; Bennet, Boerma and Brugha, 2006; Kent et al., 2003; Akileswaran et al., 2005; Farmer et al., 2001). Previous studies on adherence to ART in Africa have provided quantitative estimates of adherence and data on clinical outcomes, mainly from experimental settings (Ivers, Kendrick and Doucette, 2005; Coetzee et al., 2004; Orrell et al., 2003; Koenig, Léandre and Farmer, 2004; Gill et al., 2005). A recent review of six of these studies reported that 68%-99% of patients took at least 95% of their medicines. The authors, Ivers et al., conclude that adherence levels in Africa are high, i.e. comparable to those in industrialized settings. However, Gill and colleagues (2005) and Laurent et al., 2002) stress that there is no room for complacency, noting that adherence rates tend to deteriorate over time.

There is little evidence as to *why* some ARV users do not achieve optimal adherence rates or about how to improve adherence support in resource-poor settings (Koenig, Léandre and Farmer, 2004; Gill et al., 2005). Reports on sub-optimal adherence to ART in developed countries indicate that the key factors are patient- and treatment-related, including substance and alcohol abuse, complexity of dosing regimen and 'pill burden', dietary restrictions and side-effects (DiMatteo, 2004; Chesney, 2000; American Public Health Association, 2004; WHO, 2004). The few studies conducted in Africa suggest that in resource-poor settings other factors may predominate (Hardon, Hodgkin and Fresle 2004). Weiser et al., in a study in Botswana in 2003, identified financial constraints as the major obstacle to adherence. Ivers and colleagues (2005) found in their meta-analysis of 10 studies conducted in resource-poor settings that providing

medication free of charge to patients was associated with a 30% higher probability of having an undetectable viral load at months 6 and 12. In resource-poor settings, cost appears to be an important determinant of adherence.

Methods

Our pre-intervention country studies were designed to estimate adherence levels in ART programmes in resource-poor settings under routine health care conditions, to identify reasons for sub-optimal adherence from the perspective of both ARV users and front-line health workers, and to recommend context-specific ways of improving adherence support. In this chapter we present an overview of the results of these three-country studies of adherence to ART conducted in Botswana, Tanzania and Uganda, and propose recommendations for action. The countries differ in HIV prevalence, density of ART sites, and in their level of ART coverage by December 2005 (see Table 1).

Table 1: Overview of ART in Botswana, Tanzania and Uganda, 2005

Country	Population size	Estimated percentage adult HIV prevalence	Number of treatment sites	Number of people in need of treatment	Estimated percentage treated as of December 2005*
Botswana	1.8 million	24%	32	84 000	85%
Tanzania	37 million	6.5%	44	315 000	7%
Uganda	25 million	6.7%	175	148 000	51%

*   For this table we refer to the WHO/UNAIDS '3 by 5' Report of 2006 and the UNAIDS 2006 Report on the Global AIDS Epidemic (see references), which have some discrepancies with the data for 2005 reported in the country studies.

Our study used rapid appraisal techniques (Vitolins et al., 2000) for collecting both quantitative estimates of adherence levels and qualitative data as to why sub-optimal adherence occurs. The methods used to collect data were: (i) semi-structured interviews (SSIs) with ARV users, health workers and key informants; (ii) focus group discussions (FGDs) with ARV users and key informants; (iii) adherence interviews with ARV users; and (iv) exit interviews and observations. Rapid appraisals tend to use a mix of methods to increase the validity of results. In this way, the evidence collected with different instruments can be compared and used to validate findings. The strongest evidence is that which emerges from different 'angles', i.e. through 'triangulation'. The qualitative methods (SSIs and FGDs) were mainly used to find out *why* people do not adhere. The quantitative adherence interviews were used to find out *how often* they do not adhere. The exit interviews allowed us to interview users about the information flows between health workers and users, as well as the quality of care

provided. The observations were used to check on the availability of medicines and laboratory facilities, and to observe interactions between health workers and patients and the quality of care.

Ethical approval for the national studies was provided by national authorities in each of the three countries. Sample sizes are shown in Table 2.

Table 2. Number of respondents by data collection instrument

	Number of facilities	SSIs with health staff	SSIs in community	No. of adherence interviews with ARV users	No. of focus group discussions	No. of exit interviews
Botswana (four regions)	4 public	16	23	514	16	163
Tanzania (Arusha and Dar es Salaam)	3 public 4 private	28	30	107	8	70
Uganda (Jinja only)	1 public 1 private	10	20	71	10	20

SSI: semi-structured interview

The adherence measurement tools

Given the lack of a gold standard for measuring adherence (Kent et al., 2003; Vitolins et al., 2000), and the pros and cons of different kinds of adherence measures, the Tanzania and Botswana teams selected three measurement tools for this study: (i) two-day self-report recall (ii) one-month visual analogue and (iii) pharmacy pill counts. The two-day self-report and one-month visual analogue recall methods have been found by Oyugi and colleagues (2004) to be valid instruments for estimating adherence in a recent study in Uganda.

The visual analogue method used in Botswana and Tanzania differed. In Botswana, ARV users were asked to indicate their adherence rate over the past month using a 10-centimetre long 'visual analogue' line. The beginning of the line indicated not taking the medications at all in the past month, while the end meant taking all of them as prescribed. The patient's mark was then measured using a 10 cm ruler and translated into percentages. The Tanzanian team used a glass-full of beads representing the total number of pills that the patient should have taken over the previous month. The researcher then asked ARV clients to pour the beads from one glass into another in order to estimate the number and percentage of pills they had not taken over the past month. The researchers used a centimetre measure to calculate the proportion of beads not 'consumed'. To calculate this, they divided the height of the remaining beads in the glass by the original height of the beads (representing the total number of pills to be taken over one month).

Each of these three measures has strengths and limitations. In order to reduce desirability bias, the trained researchers who conducted the two-day recalls and the one-month visual analogue methods were encouraged to be sympathetic to the problems experienced by respondents. The two-day recall has the advantage of a short time-span, which means that memory of medicine intake is likely to be good. However patients may feel ashamed to report specific instances of non-adherence that occurred in the 48 hours prior to visiting the health facility, especially if they have to specify on the chart exactly when they failed to take a pill and then to explain why. In terms of desirability bias, the one-month visual analogue methods are likely to be better. By estimating the number of pills missed over a one-month period, patients are confronted less with each specific non-adherent event. The pill-counts can be defined as the most 'objective' of the three approaches, measuring the actual number of pills left over since the previous refill. However, patients who fear the possible repercussions of revealing to the dispensing pharmacist that they have not achieved optimal adherence, may present fewer pills to the pharmacist than were actually left over. All three methods are likely to overestimate adherence.

The key to measuring adherence accurately is to ensure that respondents do not feel threatened when reporting in one way or another a non-adherent event. Rather than measuring exact levels of adherence, these measures should be seen as producing 'good enough' estimates of adherence. Given that the optimum level of adherence is at least 95%, the aim of adherence measures should be to determine to what extent such near-complete adherence is actually being achieved. Since lapses in adherence can lead to treatment failure and the emergence of drug-resistant HIV, poor adherence is not only a problem to users but to public health in general. For individual patients, the adherence tools can perhaps best be used as points of reference in counselling sessions on adherence, in order to discuss the reasons for sub-optimal adherence and ways to overcome these constraining factors.

Sampling frame

Since the low budget for these studies did not allow for a representative sample of the countries' ART sites, the sampling frame used was multi-staged. Health facilities were selected purposively, with the aim of including a diversity of facilities as well as limiting travel costs and time. In Tanzania, seven health care facilities were chosen in two cities (Dar es Salaam and Arusha). They included both public facilities and private/faith-based facilities which had been providing ARVs for at least three months. In Uganda, two study sites were selected in Busoga region, a sub-region of eastern Uganda which has both a public health facility and a private facility providing ART, each site relatively research-naïve. In Botswana, the study sites were located in three of the country's nine districts: North West (Maun), Central (Serowe and Mahalapye) and Kweneng (Molepolole). Serowe and Maun were among the pilot sites, while Mahalapye and Molepolole were second-generation facilities.

In Tanzania and Botswana, sample-size calculations were conducted to determine the number of users to be interviewed for the purpose of estimating adherence levels at the facilities. In Tanzania, sample size calculation for ARV users using the adherence tool was based on the results of the pilot study (mean overall adherence rate=98% at 95% confidence intervals) which gave 24 per each health facility (estimated total of 168 ARV users for seven facilities). ARV users were randomly chosen using the outpatient attendance register. Inclusion criteria were: adult, aged 18 years or over; willing to participate in the study; and on ART for at least three months. Only 107 ARV users met the inclusion criteria in Tanzania during the days of data collection.

In Botswana, the sample size for the quantitative data required to obtain estimated proportions with 95% probability level was estimated using the CSURVEY design in Epi Info 6, version 3.22 (Centers for Disease Control and Prevention, 2004), based on the assumption that 85% of the patients achieve optimal adherence (i.e. at least 95%). The sample size required was 93, 96, 95 and 93 (total 377) for the four selected facilities (Mahalapye, Serowe, Maun and Molepolole respectively). However, a total of 514 users were interviewed at the four sites. From the determined sample size, the number of patients to be interviewed each day over the five-day period was determined. The number of patients expected on a given day was determined from the consultation appointments at the data clerks' office and from the dispensary appointments. This number was then divided by the number of patients to be interviewed, to determine the Xth patient who was to be picked for the interview. From then on, every Xth patient was picked until the required numbers of patients were interviewed per day. If the patient declined, the immediate next patient was selected.

In Uganda, the study population consisted of patients aged 18 years or over who were receiving treatment at the two study sites. All patients visiting the sites during the study period who were in this age range, on ART, and willing to participate in the study were included. Systematic sampling was used to select the final sample, comprising every third patient visiting the clinic on the day of the fieldwork. Wherever a patient was not interested in being included in the study, the next patient was considered. A registry file from each facility's reception was used as a sampling frame from which ARV users were selected for the study using systematic sampling. In Uganda, a total of 71 ARV users were interviewed for the adherence estimates.

Study period

Data collection took place between May and September 2005. Quantitative analysis involved a standard Access data entry and analysis programme. Qualitative data were analysed thematically, either manually or with NUDIST software. The research and training activities undertaken prior to the study and after data collection was completed are given in Chapter 3.

Quantitative results: adherence estimates

Tables 3 and 4 present the adherence estimates by adherence measurement tool.

Table 3. Average percentage of doses taken at the right time in the study population, by adherence measurement instrument

	Two-day recall	One-month visual analogue	One-month pill count
Botswana	98% (n=508)	92% (n=496)	93%(n=443)
Tanzania	100% (n=107)	83% (n=107)	98% (n=107)

The levels of adherence appear high, based on the average percentage of drugs taken at the right time. The estimates are highest for the two-day recall method, suggesting a relatively high desirability bias. For Botswana, the visual analogue and pill count methods produced a remarkably similar average level of adherence. For Tanzania, adherence levels measured by visual analogue method show lower levels of adherence than by pill-counts. In Uganda, a two-day recall was used. No sub-optimally adherent events were reported, suggesting either optimal adherence or a high level of desirability bias. Because only one measure for assessing adherence was used and we doubt the validity of the results, we do not present the Ugandan quantitative data.

Table 4. Percentage of respondents with optimal ARV adherence rates (at least 95%), by adherence measurement instrument

	Two-day recall	One-month visual analogue	One-month pill count
Botswana	96% (n=508)	60% (n=496)	75% (n=443)

Table 4 shows the percentage of patients who achieved the optimal level of at least 95% adherence, as calculated in the Botswana study. The estimates based on both the visual analogue recall method and pill counts are low. On the basis of pill counts, an estimated one in four patients in Botswana failed to achieve this level. When measured by visual analogue, the proportion of users who failed to achieve optimal adherence is even higher, 40% in Botswana. The Botswana study also quantified the reasons reported by ARV users for missing a dose of ARVs, see Table 5.

**Table 5. Reasons reported for missing medications in Botswana
(N = 514 ARV users)**

Reason	No. of ARV users reporting this reason	% of ARV users reporting the reason
Simply forgot	90	17.5
Logistics and transport costs	67	13
Work or home duties	61	11.8
Stigma	36	7
Lack of care/support	18	3.5
Misunderstood instructions	16	3.1
Lack of food	11	2.1
Distance to the health facility	10	1.9
Being in hospital	9	1.7
Alcohol abuse	9	1.7
Depressed	6	1.2
Feeling better	3	0.6
Pill burden	3	0.6

Qualitative results: what are the constraints to optimal adherence?

The qualitative findings from these three country studies suggest that although patients are highly motivated to take ARVs as prescribed, constraints such as transport costs, user fees, long waiting times, hunger, stigma, side-effects and lack of appropriate counselling undermine their intentions to do so. Meanwhile, front-line health workers have to contend with heavy workloads, a lack of laboratory facilities and occasional stock-outs of ARVs. However, despite these health system constraints, the perceived quality of care among users is relatively good. In the section below we discuss the most commonly reported challenges to ARV adherence.

Transport costs and user fees

Although participants in all three studies received medicines free of charge, transport costs are an important reason why ARV users fail to visit the health facility for follow-up and refill. These accounts from semi-structured interviews illustrate the problems:

"I came from very far, over 50 kilometres from here. Before I come to the hospital I have to plan the money for a journey fare to the clinic. In fact my extra drugs got finished yesterday." (Male ARV user, Uganda)

A minibus delivers researchers for fieldwork in South Africa, but for many ARV users the cost of transport to health facilities and the general lack of transport in rural areas are serious problems.

For others, the lack of a means of transport - especially from remote areas - can be an additional challenge:

> *"I once missed my appointment for refill because there were no vehicles coming here. I was in the stop from early morning and by noon I went back home. Fortunately I still had some medications."* (Male ARV user, Botswana)

An ARV user in Uganda suggested opening more treatment centres that were closer to home:

> *"I have very many people in the village, they are dying because they don't have money to transport themselves to the hospital. You need to have this money monthly. Like me, from the village where I come from, getting up to this place costs 15 000 Shillings (US$ 8.50). To and fro is 30 000 Shillings (US$ 17.00), which is a lot of money. And getting that money is a problem. So maybe, like people in Kyoga, if they can send that drug up to Kyoga, I think that could be good. Right now only Lira Referral Hospital gives ARVs, and that is 130 kilometres from our place (Kyoga). Very far!"*

However, problems can persist even when treatment centres are more locally available, as explained by a respondent in Tanzania, who complained that he was denied access to a centre that had opened close to his village:

> *"I was registered to start ART in Kilimanjaro Christian Medical Centre (KCMC) in Moshi a year ago. At that time there was no ART clinic near my village. Now there is a clinic near my home but I am denied transfer from KCMC to my home clinic. KCMC is very far from here, about 170 km away. Some times I do not have the fare to travel to KCMC, hence I miss my doses."* (Male ARV user, Tanzania)

Health workers in all three countries were well aware that transport costs impede adherence. As one health worker in Uganda reported:

> *"Some people have failed to report to the clinic on time because they failed to get transport to reach the clinic. Some people come from the islands, and they will tell you that they did not get money to cross the waters and that is why they did not come on time. And when you are told that, you cannot do much but to hope that when the next visit comes, he can afford to come on time."*

In addition to recurrent transport costs, patients have to pay registration and user fees in private facilities in Uganda and Tanzania. In Uganda, a fee of US$ 3.00 was charged in the private facility at each visit. In Tanzania, the private facilities charge user fees with a range of US$ 1.50 to US$ 3.00 per visit, and an additional US$ 15.00 for laboratory investigations.

Waiting times

In all three studies, the problem of long waiting times was cited as a major challenge to adherence. In Tanzania, the mean time spent at the clinic was six hours. About half (12/28) of the health workers interviewed in Tanzania identified long waiting times as a problem. In Botswana, most respondents reported that they spent around four hours at the clinic. Nearly half of the respondents spent even more than that, with the longest wait being 12 hours, as shown in Figure 1.

Figure 1. Distribution of the time spent by Botswana participants at the clinic (N=128 exit interviews with ARV users)
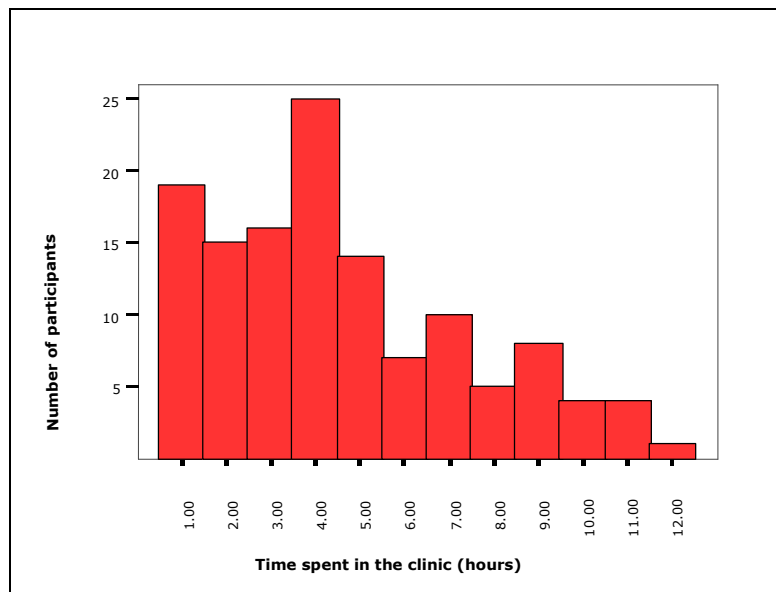
In Uganda, the average waiting time for ARV users was five hours in the public facility and one hour in the private facility. The findings suggest that ARV users may miss one working day per month in order to get ARV refills. This can be a problem for some ARV users whose employers do not know that they are HIV-positive or do not support their need for care. One ARV user in Botswana said:

> *"I resorted to asking my relative to pick up my medications, because my employer refuses to release me to go and pick up my medications."*

Hunger

ARV users in all three countries complained about hunger during the initial stages of treatment, when the body needs extra nutrition as it regains strength and weight. They said they could not afford the amount of food needed to satisfy their increased appetites. The following quotes illustrate this.

"The problem I have with ARVs is related to food. I have no money and ARVs increase appetite. I am not capable of buying food.
(Male ARV user, Tanzania)

"I want to eat all the time and fear the hunger will eat into my stomach, since I have ulcers already. Sometimes I wake up in the night to eat food. This is a difficult situation for me."
*(*Male ARV user, Uganda)

"Majority of people say the ARV treatment makes them to eat a lot. They go to an extent of begging for old age pension from their grandparents. Others quit the treatment because they complain about the lack of food." (FGD participant, Botswana)

Carrying home food parcels from a health care facility in South Africa - but not everyone is so fortunate. Some participants in the studies reported that hunger had an adverse effect on adherence, particularly in the initial stages of ART.

"Some patients have expressed lack of food as a reason for not wanting to swallow the life-saving drugs. In fact we have one woman who has declined her life-saving drugs because she does not have enough food to feed herself." (Doctor, Uganda)

In Tanzania, a female participant of a FGD reported that, because some ARVs have to be taken with food, some patients take their medicines only once a day in the evening (instead of twice daily), because that is the only time they have food.

In Uganda, some patients receive food support (soya flour, cooking oil, rice, sugar and maize flour) from TASO, the nongovernmental AIDS Support Organisation. In Botswana, the Government provides a food basket for ARV users who have been assessed by social workers and found to meet certain criteria.

Stigma

All three country studies reported on ARV users' experiences of stigmatization and discrimination and lack of social support. Some ARV users reported that after disclosing their HIV-positive status they had lost their job (Tanzania); were abandoned or badly treated by their partners (Botswana); or were isolated by community members (Uganda). Fearing such stigmatization, ARV users often decide to hide their HIV status, from colleagues, friends and others.

If ARV users do not disclose their HIV-positive status it may affect adherence in different ways. Firstly, non-disclosure may lead to patients taking their ARV medicines secretly and irregularly, as illustrated by quotes from ARV users in Uganda and Botswana:

"I cannot take my drugs when people are seeing. I always go and hide when I take them. Otherwise, people start whispering about you all the time." (ARV user, female FGD, Uganda)

"I usually miss my medications when I visit friends because I have not told them about my HIV and so I do not want them to see my medications." (Male ARV user, Botswana)

Moreover, when ARV users do not disclose their HIV-positive status to others they will not receive adequate social support and encouragement to take their drugs regularly and on time. The Tanzania study found that of 30 ARV users interviewed, 94% had disclosed their HIV-positive status and 83% received various forms of help from family and friends on the use of drugs (e.g. transport support, food, reminding them to take drugs).

In all three countries, children were found to be important sources of support for ARV users, as illustrated here:

"My children after seeing the state I was in and after getting ARVs, I called them and told them about my state. They got encouraged and as a result they buy me passion fruits and sugar because they know the drugs I am taking are so strong. I even wrote my file number in TASO on the wall and told them that just in case I am badly off they can go to TASO and get me help. My children know very well that because of my drugs I have to drink enough and to eat on time. One thing that motivated me to tell them is because I thought I could be so weak to collect my refill of the drugs (ARVs). They even know the name of my counsellor." (ARV user, mother of five, Uganda)

Side-effects

The side-effects most frequently mentioned by ARV users were: body rash, swollen legs, nausea, headache, increased heart rate, diarrhoea and vomiting. In Tanzania and Uganda, the occurrence of side-effects was mentioned as an important reason for skipping doses.

"I had side-effects and decided to take medication only once per day." (Male FGD, Tanzania)

"Feeling a lot of heat in the body, especially after taking the drug and excess sweating makes one embarrassed in public. So, you feel like postponing the drug to a later time when you are not relating with people." (Male ARV user, Uganda)

In most cases, side-effects disappear over time. However, ARV users in Tanzania and Uganda have not always been given this important information. By contrast, in

Botswana, where side-effects are discussed extensively in pre-treatment counselling, of the 58% of ARV users (n=514) who reported that they had experienced side-effects, only 8% cited them as one of the reasons for missing their medication, suggesting that effective counselling increases tolerance.

Lack of counselling

Counselling is a key requirement for successful ARV adherence. However, the frequency and quality of counselling was found to differ greatly both between the different countries and among the different facilities within each country. In Botswana, well-trained counsellors (nurses, social workers and lay counsellors) are available in all health facilities providing ARVs. In the public facility in Uganda, the counselling was done by nurses, who were not well trained because the public health facility could not afford to pay for good quality training courses for counsellors. ARV users in Uganda valued support from the community-based volunteers of TASO, many of whom are HIV-positive themselves. In Tanzania, the quality of counselling was found to be different in Dar es Salaam and Arusha. While patients in Dar es Salaam appreciated the quality of the counselling received, several ARV users in Arusha complained about the quality of their counselling due to the lack of trained counsellors. The exit interviews confirm that only a small proportion of ARV users see a counsellor (21%), while, in contrast, almost all (97%) see a doctor.

Table 6: Categories of health staff seen by patients in Tanzania
(N=70 exit interviews with ARV users)

Cadre of staff	No. of patients who consulted with this category of health worker	Percentage
Counsellor	15	21%
General nurse	20	29%
Pharmacist	54	77%
Doctor	68	97%

As one FGD participant commented:

> *"You find 25 patients and only one person attending all these patients and he just tells you to go and collect your medication."* (Male FGD participant, Tanzania)

Heavy workloads

At the public facilities in both Uganda and Tanzania, the scaling up of ART had occurred without any increase in personnel to cater for the increasing numbers. As a result, health workers were visibly overworked as they struggled to cope with the large number of patients on clinic days. One health worker in Uganda said:

> *"You overwork like this without even a break because there are too many people all coming one day and yet you are very few."* (Health care worker FGD, Uganda)

Table 7 shows the main challenges reported by 28 health workers in Tanzania.

Table 7: Challenges most frequently mentioned by health workers in Tanzania (N=28)

Challenges	Number of respondents	Percentage
Low motivation	26	92.9
Heavy workload	23	82.1
Inadequate training	20	71.0
Long waiting hours for patients	12	42.9
Too few staff	11	39.3
Work fatigue	5	17.9
Being faced with difficult or non-compliant ARV users	3	10.7

Commenting on the large number of clients attending ART clinics, a female participant of a FGD in Tanzania said:

> *"If the situation remains like this, doctors will be tired and the last patient will not be attended (to) properly."*

It is remarkable that, despite these heavy workloads, patients in all three countries expressed satisfaction with the quality of care at the facilities. In Botswana, 99% of ARV users interviewed in exit interviews at the facilities said that they felt listened to. In Tanzania, 80% of the ARV users at the facilities reported that they had been asked about their experiences in taking ARVs. In Uganda, out of 26 users in the public facility, 16 said the services offered were good, 8 rated them as fair and only two said they were poor. In contrast, all 20 participants interviewed at the private facility said the services were very good. With the exception of two users at the public facility, participants at both the public and private facility felt that the service providers listened to them. They trusted the health workers.

Lack of space for confidential consultations

The findings suggest that space for consultations is generally adequate in private facilities, but can be lacking in the public sector. In Uganda, the public facility lacked enough room to accommodate patients for counselling and to discuss personal issues. As a result, the nurses took them to any free space available, thereby compromising confidentiality. In contrast, the private facility in Uganda was very well organized, with comfortable seating, less waiting time and everybody was attended to. In Tanzania, space for the ART clinics was generally adequate in both Dar es Salaam and at the faith-based organizations in Arusha. However, at one public hospital in Arusha there was no separate room for consultation and thus no confidentiality. At the time of the study, three doctors at this facility were sharing a single room and consulting with three different ARV users at the same time. In Botswana, the space for consultation was found to be inadequate in two of the four public health facilities.

Lack of CD4 machines and ARV stock-outs

In Botswana and Tanzania, health facilities were found to lack laboratory facilities to conduct CD4 counts, which are needed to monitor the efficacy of the treatment and also to decide when to initiate treatment. In Uganda, the private facility conducted all recommended tests for HIV management within the centre while the public facility had to send out some of their samples for CD4 and viral load testing. This implied that people who were very sick had to wait at least two weeks before they could be put on therapy.

In Tanzania, four of the seven facilities studied lacked a CD4 machine. In Botswana and Uganda, both ARV users and health workers complained about inoperative testing facilities. Even where CD4 machines were available, reagents were sometimes out of stock. Moreover, two of the seven facilities also reported stock-outs of ARVs, which is a major challenge to adherence. Although the supply of ARVs was reliable in most of the facilities at the time of the study, some patients expressed concern about possible future stock-outs, as one respondent from Uganda explained:

> *"We are grateful for the government for bringing medicine to the people, but we hear it is only for five years. Whenever I take these drugs, I am wondering whether in the next five years I will still have them free. Actually I get disturbed by that."* (Male ARV user, FGD, Uganda)

Discussion

Our study involved a rapid appraisal of adherence problems confronting ARV users and front-line health workers in resource-poor health facilities in three sub-Saharan countries. The findings suggest that patients are experiencing problems in their efforts to attain optimal adherence rates. Although the adherence rates seem high when measured as an average percentage of doses taken at the correct time, the Botswana study suggests that around one out of three users do not achieve the optimal adherence rate of at least 95% needed to minimize the risk of treatment failure and the development of drug-resistance. While adherence support and ART provision is well-established in Botswana – one of the first countries in sub-Saharan Africa to scale-up access to ART - levels of optimal adherence are likely to be lower elsewhere.

All the facilities studied in Botswana, Tanzania and Uganda provide ARVs free of charge, but other related costs (e.g. transport expenditures, registration and user fees at the private health facilities, and lost wages due to frequent clinic visits and long waiting times) are obstacles to optimal adherence. It is significant that these same financial concerns were expressed in all three country studies and at all the sites involved. Hunger in the initial treatment phase (when the patient is recovering) is an added concern for poor patients not covered by food support in the three countries. ARV treatment programmes need to find ways to confront these constraints. Clearly it is not enough to provide treatment free of charge.

Treatment programmes also urgently need to find ways to reduce waiting times for ARV patients coming for refills and take into consideration the work schedules of ARV users. Evening and early morning clinics may be a good option, though these would be an additional burden for health workers. Patients could also be given appointments to reduce waiting times. In addition, workplace policies should include provisions for patients to take time off work to attend to their treatment needs.

The studies showed that health workers have heavy workloads and are working in health facilities with sub-optimal health infrastructures. While the Botswana programme seems to have overcome some of these infrastructure problems, in Uganda and Tanzania the lack of CD4 machines to monitor treatment outcomes on-site and the reported stock-outs of ARVs in Tanzania are major challenges to the ART programmes. A regular and reliable supply of the needed drugs is a pre-requisite for optimal adherence.

A dynamic approach to adherence support is needed (Spire et al., 2002). As reported by Carrieri et al. in 2003, optimal adherence appears to be most critically important in the initial treatment phase, in terms of achieving undetectable viral loads. In the initiation stage, many patients also suffer side-effects, some of which disappear over time. Treatment programmes need to emphasize adherence support in this stage. Health care workers should properly inform patients about the adverse effects they can expect, and how to confront these. The treatment programmes should consider providing or subsidizing both transport and food support to patients who are too poor to pay.

Once the health status of ARV users has improved, and optimal adherence levels are being achieved, these must be maintained. To this end, recurrent costs for ARV users can be reduced by providing patients with three-month refills, rather than the one-month refills that are current practice in the facilities studied. It is ironic that the system of one-monthly refills, intended to help monitor adherence, in practice creates a constraint to adherence because of the transport costs incurred. Transport costs can also be reduced by setting up a more extensive network of facilities where ARV users can go for refills, adherence monitoring and counselling. In addition, treatment programmes need to set up transfer mechanisms for ARV users to allow them to attend newly established facilities closer to home.

Pharmacists and nurses can play an important role in this follow-up care. Their involvement can also reduce the workload of doctors. To provide good quality care, all auxiliary health workers should be trained to recognize clinical signs of treatment failure, such as emergent opportunistic infections, and to provide adequate adherence support. When treatment failure occurs, intensified adherence monitoring by means of electronic monitoring devices or self-report could be used more systematically to investigate whether sub-optimal adherence is causing the treatment failure. This would help prevent unnecessary recourse to second-line ARVs.

Adequate counselling services are needed at health facilities or in communities in both the initiation and continuation phases of ART to help patients cope with the side-effects of ART, identify and confront the social constraints to adherence, and address the financial problems that ARV users face. The country reports highlighted the lack of designated rooms for counselling in some facilities and, in one glaring example, a room being used by three counsellors and ARV users at the same time. These kind of conditions are likely to inhibit patients from discussing personal issues. Adequate space and privacy is needed to ensure the confidentiality and trust needed for effective adherence counselling.

In Botswana, all the facilities appraised had well-trained counsellors. The Tanzanian and Ugandan teams found that the quality of the counselling varied greatly. In the public facility studied in Uganda, nurses were given the task without adequate training. Yet training programmes for ARV counselling exist in sub-Saharan Africa and could be used more fully. Ministries of health and the agencies funding and providing technical support for ART programmes need to acknowledge that the provision of ARVs will not lead to positive treatment outcomes unless accompanied by the necessary adherence support in all health facilities. The Ugandan ARV users were very positive about the treatment support provided by TASO's community-based volunteers, many of whom are HIV-positive and can therefore better relate to the problems of people living with HIV (PLWHIV). Health facilities need to strengthen their ties with PLWHIV groups and other community organizations in order to strengthen community support mechanisms for ARV users.

More specifically, adherence support programmes need to find ways to help ARV users remember to take their pills on time, for example through alarms on mobile phones, or through using popular radio programmes as a prompt. Our studies suggest that, in all three countries, children play a role in reminding their parents to take their pills. Adherence support could recognize the potential role of children in adherence support, and provide them with adequate information on ART, for example through school education programmes, to empower them in their role as treatment supporters.

Stigma was found to be a key constraining factor in all three countries. Most treatment programmes try to reduce stigma by encouraging disclosure to at least one person, who then becomes a treatment supporter. Our findings show that ARV users value such treatment support, but still find it hard to take their drugs when they are among people to whom they have *not* disclosed their HIV status, such as co-workers, or friends. ARV users are likely to have to take their medicines in social contexts where they have not disclosed their HIV status, especially if their work shifts vary or if they lead irregular social lives. Public and workplace education on ART is needed in high prevalence areas to help reduce the stigma attached to AIDS.

The researchers involved in our studies are now working with staff from the health facilities to help improve adherence support mechanisms along the lines of these recommendations. However, many of our recommendations cannot be implemented without external support (for transport, food and better counselling and monitoring facilities).

Conclusion

With some adjustments, the self-report methods used in this study were endorsed and recommended by the Adherence Working Group at a WHO meeting on the development of generic tools to facilitate operational research on HIV treatment and prevention in resource-limited settings (16-18 January 2006, Geneva). The Working Group agreed that self-report methods can be used to monitor the effectiveness of adherence support mechanisms, and recommended that both average adherence levels and the percentage of patients achieving at least 95% adherence should be used as outcome measures. The latter is the preferred public health measure. Average adherence levels can appear high, but if only a fraction of users are achieving optimal adherence then adherence support programmes clearly have a long way to go. The Working Group also recognized that there is a need to validate self-report methods in resource-poor settings. Viral loads can be used for this purpose, as well as electronic monitoring devices.

We have shown that small-scale studies using a combination of qualitative and quantitative rapid assessment tools, conducted by local researchers in collaboration with front-line health workers, can be used to estimate adherence levels, identify factors that facilitate or constrain adherence and indicate possible solutions. ART planners locally and globally need to encourage such studies and acknowledge their findings in order to improve the effectiveness of ART programmes. Such operational research will help to ensure that initiatives towards universal access to ART achieve positive health outcomes. In the absence of adequate guidelines on adherence monitoring and support, health facilities throughout Africa are developing their own methods for this. There is an urgent need to develop the evidence about which of the likely interventions proposed in the recommendations are most effective in supporting adherence. Those found to be effective should be scaled up.

Without adequate adherence support, ART programmes will be confronted with a high proportion of treatment failure and the development of drug-resistance, together with a related increased demand for second-line treatments - currently 10 times more expensive than first-line treatments. Global donors and national programmes need to emphasize the importance of treatment effectiveness and adherence in order to ensure the sustainability of current efforts to scale up access to ART. This should include providing resources for routine use of simple measures to monitor adherence and to evaluate innovative adherence support measures, as well as scaling up adherence support measures of proven effectiveness. The percentage of ARV users *continuing* treatment after one year and the percentage of users achieving optimal adherence should be key indicators used by donors to assess national programme efforts. At present, the main achievement indicator is the number of people *initiated* on ART – an inadequate measure of programme performance, as it defines performance in terms of access rather then the adherence that is necessary for sustained health benefits and to safeguard public health.

References

1. Akileswaran C et al. (2005). Lessons learned from use of highly active antiretroviral therapy in Africa. *Clinical Infectious Diseases*; 41:376-385.

2. American Public Health Association (June 2004). *Adherence to HIV treatment regimens*: recommendations for best practices. Available at: www.apha.org/ppp/hiv.

3. Bennet S, Boerma JT, Brugha R (2006). Scaling up of HIV/AIDS evaluation. *Lancet*, 367:79-82.

4. Carrieri MP et al. (2003). Impact of early versus late adherence to highly active antiretroviral therapy on immuno-virological response: a 3-year follow-up study. *Antiviral Therapy*, 8(6):585-94.

5. Chesney MA (2000). Factors affecting adherence to antiretroviral therapy. *Clinical Infectious Diseases*, 30 (Suppl 2):S171-176.

6. Coetzee D et al. (2004). Promoting adherence to antiretroviral therapy: the experience from a primary care setting in Khayelitsha, South Africa. *AIDS*, 18(Suppl 3):S27-31.

7. DiMatteo MR (2004). Variations in patients' adherence to medical recommendations. A quantitative review of 50 years of research. *Medical Care*, 42:200-209.

8. Farmer F et al. (2001). Community-based approaches to HIV treatment in resource-poor settings. *Lancet*, 358:404-409.

9. G8 Gleneagles Summit. Chair´s summary, 8ʰ July 2005. Available at: http://www.g8.gov.uk/

10. Gill CJ et al. (2005). No room for complacency about adherence to antiretroviral therapy in sub-Saharan Africa. *AIDS*, 19:1243-1249.

11. Hardon A, Hodgkin C, Fresle D. *How to investigate the use of medicines by consumers*. Geneva, World Health Organization, 2004.

12. Ivers LC, Kendrick D, Doucette K (2005). Efficacy of antiretroviral therapy programmes in resource-poor settings: a meta-analysis of the published literature. *Clinical Infectious Diseases*, 41:217-224.

13. Jaffar S et al. (2005). Antiretroviral treatment in resource-poor settings: public health research priorities. *Tropical Medicine and International Health*, 2005; 10:295-299.

14. Kent DM et al. (2003). Suitable monitoring approaches to antiretroviral therapy in resource-poor settings: setting the research agenda. *Clinical Infectious Diseases*, 37 (Suppl 1):S13-24.

15. Koenig SP, Léandre F, Farmer PE (2004). Scaling-up HIV treatment programmes in resource-limited settings: the rural Haiti experience. *AIDS*, 18 (Suppl 3):S21-25.

16. Laurent C et al. (2002). The Senegalese Government's highly active antiretroviral therapy initiative: an 18-month follow-up study. *AIDS*, 16:1363-1370.

17. Orrell C et al. (2003). Adherence is not a barrier to successful antiretroviral therapy in South Africa. *AIDS*, 17:1369-1375.

18. Oyugi JH et al. (2004). Multiple validated measures of adherence indicate high levels of adherence to generic HIV antiretroviral therapy in resource-limited setting. *Journal of Acquired Immune Deficiency Syndrome*, 36:1100-1102.

19. Paterson DL et al. (2000). Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine*, 2000;122:21-30.

20. Spire B et al. (2002). Adherence to highly active antiretroviral therapy (HAART) in HIV-infected patients: from a predictive to a dynamic approach. *Social Science and Medicine,* 54(10):1481-96.

21. UNAIDS. *2006 Report on the global AIDS epidemic.* Geneva, United Nations Joint Programme on AIDS, 2006.

22. Vitolins MZ et al. (2000). Measuring adherence to behavioral and medical interventions. *Controlled Clinical Trials* 2000; 21:188S-194S.

23. Weiser S et al. (2003). Barriers to antiretroviral adherence for patients living with HIV infection and AIDS in Botswana. *Journal of Acquired Immune Deficiency Syndromes*, 34:281-288.

24. WHO. *Adherence to HIV treatment.* Geneva, World Health Organization, 2004.

25. WHO/UNAIDS. *Progress on global access to HIV antiretroviral therapy: a report on "3 by 5" and beyond*. Geneva, World Health Organization/United Nations Joint Programme on AIDS, 2006.

2. Overview of antiretroviral therapy, adherence and drug-resistance

Richard Laing
Catherine Hodgkin

Background

This overview is intended to provide the context and scientific background to a number of key issues relating to the AIDS pandemic and in particular to the issue of treatment adherence. There are many important aspects of the pandemic which are not discussed in this overview – for example, the importance of prevention, strategies for harm reduction and the need to tackle stigma and address the needs of vulnerable populations. The UNAIDS *2006 Report on the global AIDS epidemic* provides detailed information on these and other aspects of the epidemic.

Since it was first recognized in 1981, Acquired Immune Deficiency Syndrome (AIDS) has killed more than 25 million people worldwide, making it one of the most destructive pandemics in recorded history. In 2005 alone, AIDS claimed an estimated 2.8 million lives and an estimated 4.1 million people were newly infected with the virus. In 2005, an estimated 38.6 million people worldwide were living with the human immune deficiency virus (HIV), of whom 24.5 million live in sub-Saharan Africa (UNAIDS, 2006).

AIDS is caused by HIV, which can be spread through sperm, blood, breast milk and vaginal secretions. The most common route of transmission is unprotected sex. However, among particular risk groups, other methods of transmission may be dominant. For instance, among intravenous drug users the use of contaminated needles is a major cause of transmission. HIV spreads rapidly in situations where conflict, disasters, or socioeconomic pressures contribute to the displacement of people and disruption of family life. In these situations, women and children are especially vulnerable.

When a person is initially infected by HIV, they may experience a mild flu-like illness and then become asymptomatic, remaining well for an average of about eight years. However, throughout that period, they are able to infect other people. Once the infection progresses, the immune status of the individual becomes depressed and they become vulnerable to a range of different illnesses (opportunistic infections). The first of these is often tuberculosis, but many other conditions can emerge, including pneumonia, some cancers, meningitis and fungal infections. AIDS kills because the individual's immune system is not able to fight infections.

It is possible to measure the effect that HIV has on an individual by measuring the number of CD4 cells (key components of the immune system) in the blood stream and, where the required equipment is available, the actual viral load. The normal count is about 1000. Once the CD4 count falls, the individual is likely to suffer from various different infections unless they are treated with antiretroviral medicines (ARVs). When the CD4 count falls below 200, treatment with ARVs is usually started. However, if

there are AIDS-defining conditions and a CD4 count below 350, treatment may also be started. People in these two categories are referred to as "people in need of treatment." Of particular concern in Africa is the impact of AIDS on the nutritional status of the individual. Wasting and weight loss are very common in AIDS patients. The causes of wasting are complex and due to a wide range of factors. As reported by Strawford and Hellerstein (1998), they include a reduction in appetite and calorific intake as well as more complex physical alterations caused by illness and stress. The three country studies which follow suggest that treatment causes an unusually large increase in appetite – especially during the first six months – which in these settings often cannot be met. The need to ensure nutritional support for AIDS patients was recognized by UN Member States in the Political Declaration issued at the UN General Assembly Special Session (UNGASS, 2006) on HIV/AIDS in New York from 31 May-2 June 2006).

Antiretroviral therapy (ART)

The introduction of ARVs in the 1990s brought new hope to people living with HIV. More recently, the increased availability of treatment has dramatically improved survival rates and lowered the incidence of opportunistic infections in people with AIDS (UNAIDS, 2005). Those who have access to ARVs and the care needed to maintain therapy can live for many years with what is now considered to be a complicated but manageable chronic disease. Although ARVs are not a cure for HIV, they are very effective in controlling the virus, and can even reduce the level of the virus to a point where it is no longer possible to detect any HIV in the blood. These medicines prevent HIV from multiplying rapidly and, at the same time, boost the body's immune system. In this way, they can increase the length and quality of life and enable people to lead full and productive lives. There are many kinds of ARVs, which attack the virus in different ways. For this reason, treatment today always involves a combination of ARVs. The most commonly used are from three classes: nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNR-TIs) and protease inhibitors. A new class of drugs – entry inhibitors – prevent HIV from entering the T-cells, which are crucial in maintaining the individual's immune response. All ARVs have different side-effects and these can have an impact both on how the medicines will be used and how patients take them.

In some situations, several ARVs are combined in a single tablet, a fixed-dose combination (FDC), which ensures that patients always take multiple doses together. As a first-line treatment, antiretroviral therapy (ART) can be delivered relatively cheaply. However, if drug-resistance develops and these medicines are no longer effective, second-line ARVs may be required. These second-line ARVs are much more expensive than first-line medicines (see Figure 1).

Figure 1: Current prices (US$) of first- and second-line ARVs in Africa

Price of ARVs in Africa 2005

Dollars per year

$1 500

$1 000

$500

$0

$136

$1 400

First-line   Second-line
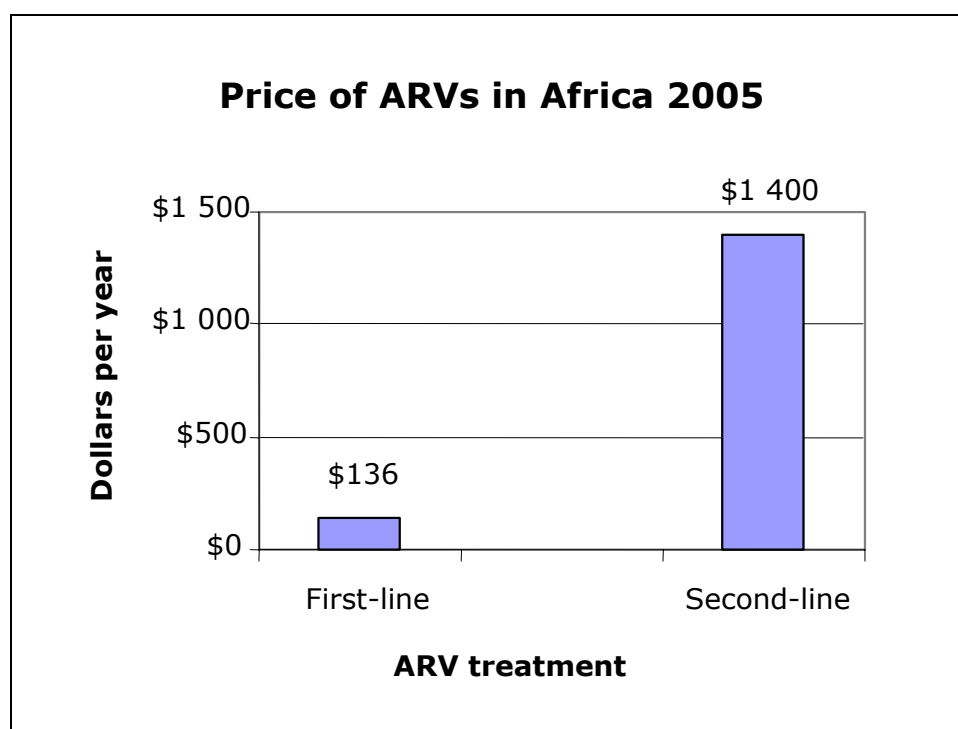
ARV treatment

Source: Médecins Sans Frontières (MSF) with data from Clinton Foundation HIV/AIDS
Initiative and WHO Global Price Reporting Mechanism

Epidemic in sub-Saharan Africa: new initiatives and treatment roll-out

Sub-Saharan Africa is the global epicentre of the AIDS pandemic and remains the region worst affected. Although it has little over 10% of the world's population, the region is home to more than 60% (24.5 million) of the people living with HIV. In 2005, an estimated 2 million people died of AIDS-related illnesses in this region, while a further 2.7 million people became newly infected with HIV (UNAIDS, 2006). The catastrophic impact of HIV in sub-Saharan Africa is threatening development in all sectors of society. While people of all ages are affected by HIV, most of those infected are in the 25-45 age group. This group is particularly important not only in terms of economic productivity but also as carers, parents and providers. The loss of productive workers and increases in spending on health care and social services require difficult decisions about resource allocations across all government sectors (UNAIDS, 2005).

In response to the epidemic and the need to ensure the availability of ARVs in resource-poor settings – a major focus of global advocacy efforts – a number of strategic partnerships and new organizations have been established and new initiatives launched. Meanwhile, the price of most first-line ARVs has fallen substantially due to the involvement of Indian generic pharmaceutical companies which have produced ARV formulations at prices that allow patients to be treated for less than US$ 1.00 per day. The first of these initiatives to improve ART availability was the Accelerating Access Initiative, a partnership established in 2000, involving UN organizations and a

number of pharmaceutical companies which offered to make their products available at reduced prices. In 2001, the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) was established. Although essentially a financing organization, the Global Fund has assisted many countries in their efforts to obtain ARVs. The Global Fund aims to provide ART to 1.8 million people over five years and to support many more people with voluntary counselling and testing for HIV, medical services and community care. In 2003, WHO launched the "3 by 5" initiative, which aimed to ensure that 3 million patients were on ART by the end of 2005. Although this milestone was not reached, many hundreds of thousands of patients who would not otherwise have been treated were initiated on therapy, particularly in sub-Saharan Africa. Also in 2003, the United States Government established the President's Emergency Plan for AIDS Relief (PEPFAR). This initiative focuses on 15 high-burden countries and provides substantial resources, not only for ARVs, but also for systems support. The target of PEPFAR is to treat 2 million patients within 5 years.

This book focuses on the early treatment experiences of three countries in sub-Saharan Africa: Botswana, the United Republic of Tanzania and Uganda. Botswana received early support from both the Gates Foundation and Merck (the Merck Company Foundation/Merck & Co., Inc.). Tanzania has received support from both the Global Fund and PEPFAR. Uganda was very active during the Accelerating Access Initiative and in the "3 by 5" activities, and also benefits from PEPFAR funding. Thus, in all three countries, multiple organizations have been providing support. Access to ARVs has improved dramatically, and many patients have been started on treatment. However, taking ARVs twice a day is a challenging task for people who may be ill and who may also face obstacles to regular adherence.

Drug-resistance

Drug-resistance is a well-recognized biological phenomenon occurring with infectious organisms including bacteria, viruses and parasites such as malaria. When an infectious organism is exposed to an antibiotic, an antiviral agent or an antiparasitic agent such as chloroquine, some of the organisms will be very sensitive to the agent while others will be partially resistant, due to genetic variation. If the course of therapy is interrupted, those organisms that were sensitive will have been killed, while the more resistant organisms will have survived and can replicate. If there are repeated interruptions in treatment, only drug-resistant organisms will survive. In the case of HIV, the problem is complicated by the very rapid replication of the virus and the fact that it can go into a non-active state where it is not affected by ARVs. When the viral load is very high, as it is at the beginning of therapy, high adherence to ARVs is required (Carrieri et al., 2003). If an individual misses a few doses at this stage, the danger of the development of drug-resistant organisms is far higher than it would be after six months of regular treatment, by which time the person is likely to have a low viral load. To prevent the development of drug-resistance, an adherence level of at least 95% is required for the duration of therapy and especially in the first six months (Paterson et al., 2000). This is very difficult to achieve.

If an individual develops resistance to ARVs, two problems occur. Firstly, the first-line ARVs will no longer work and the individual will start to suffer from multiple opportunistic infections. Secondly, the individual may transmit the drug-resistant virus to their contacts and when those individuals go for treatment they will discover that their virus does not respond to the first-line therapy. Once a person develops resistance to first-line medicines they will need to be changed to second-line ARVs. However, at present these products are substantially more expensive than the first-line ARVs and have a different range of side-effects. Moreover, the decision to change a person from first-line to second-line therapy is a difficult one to make, especially if CD4 and viral load testing equipment is not available. At present, the cost of second-line therapy is about 10 times more than first-line therapy. The danger is that if too many patients progress to second-line therapy, the increased costs involved will limit access to treatment for many people who would benefit from first-line therapy. Therefore, every effort should be made to ensure a high level of adherence (at least 95%) to the first-line ARVs in order to delay the emergence of drug-resistance and enable individuals to be treated for many years with first-line ARVs.

Adherence

Drug-resistance is not the only cause of treatment failure. The natural history of HIV infection is very unpredictable and people respond to treatment regimes in different ways, as reported by O'Brien et al. (2000). Sub-optimal adherence itself is an important cause of failure. If people are sharing ARVs or interrupting their daily dosage regimes they simply do not get enough of the medicines for effective treatment and they will generate drug-resistance. Inappropriate use of ARVs is a multifaceted problem increasing the likelihood of drug-resistance and contributing to direct treatment failure. Policies and programmes that aim to provide increased or universal access to treatment face a key challenge: in order to succeed, these programmes need to achieve an exceptionally high level of adherence for an indefinite period of time. An extensive review of interventions for improving adherence was undertaken by Haynes et al. in 2005. The authors define adherence as the extent to which patients follow the instructions they are given for prescribed treatments. In this review, the term compliance, which is less commonly used today, is considered to be, in terms of measurement, the same as adherence. The term adherence is intended to be non-judgmental, a statement of fact rather than of blame of the patient, prescriber or treatment.

Measurement of adherence: particular requirements for ARVs

While adherence can be expressed quantitatively as a percentage of expected treatments actually taken, its accurate measurement is very difficult. There is no gold standard for adherence measurement. While adherence can be ensured by directly observed treatment, this may not be practical for twice-daily therapy which has to be taken for life. As a result, levels of adherence can only be estimated by use of indirect measures. The most commonly used methods include pill counts, pharmacy refill records, various self-reporting tools such as questionnaires and visual analogue scales,

measurement of blood levels, and electronic drug monitors, which monitor the number of times the cap of a pill container is removed. A recent report from Malawi has compared three of these methods of measuring adherence. The authors compared four-day recall, visual analogue scale (using visual measurement tools to capture self-reports) and self-administered questionnaires, and found that self-reporting on the basis of four-day recall was the best predictor of viral load (Ferradini et al., 2006).

When reporting adherence to ART, two measures are frequently used. The first is the overall adherence recorded as the number of tablets taken correctly as a proportion of those which were prescribed. This measure is an important marker for the clinical evaluation of individual patients, as well as for counselling purposes. The second measure, which is more sensitive to the particular requirements of ART, reports the percentage of patients taking at least 95% of their tablets correctly, and is essential for programmatic or public health evaluation.

When reporting population adherence rates, it is critically important to include the percentage of patients who achieve the optimal adherence rate of at least 95%. Thus the average (mean) overall population adherence rate may be 85% (i.e. 85% of all pills that should have been taken were taken) but only 60% of this same population may have achieved the optimal adherence rate of at least 95%. The first measure of overall adherence is important for individual counselling, while the second, which is a population measure of adherence, is useful for evaluation and planning. Although having both measures in any study complicates analysis, both are needed, in particular the second measure. Both measures can be collected in the same way with pill counts, patient recall, visual analogue scales or electronic monitoring.

Adherence to treatment for chronic diseases

Considerable experience exists in dealing with the challenges of long-term adherence to medication for chronic diseases other than AIDS. In 2004, DiMatteo reported on 50 years' research on adherence to medical recommendations. Within the more than 500 studies, adherence ranged from as low as 4.6% to 100% with an average of about 75% adherence for the different conditions. Only eight studies of the treatment of AIDS were included and the mean adherence in these studies was 88%. Vermeire et al., (2001) reviewed patients' adherence to treatment over the past 30 years. In addition to identifying the difficulties in measurement, they discuss the causes of poor adherence, pointing out that these are not well understood. They discuss aspects such as features of the disease, the referral process, the clinical setting and the therapeutic regimen, noting that these do not appear to affect adherence. Demographic variables are also poor indicators of adherence. Factors related to poor adherence include psychiatric disorders, treatment factors such as the duration of treatment, the number of medicines prescribed, the cost, and the frequency of dosages. Factors which can increase adherence include increased supervision, and parenteral administration. Surprisingly, side-effects are rarely seen as a reason for sub-optimal adherence. The patient's own beliefs and lifestyle are found to be important in affecting adherence. Social factors such as having positive attitudes in the community are also seen to improve adherence. The quality of the doctor-patient relationship is regarded as a very important factor.

However, the amount of research which has measured this is limited. The Uganda country report in the present publication provides an extensive review of the existing literature.

Many reasons exist for non-adherence to medical regimens, including problems with the regimen such as: adverse effects, poor instructions, poor provider-patient relationship, poor memory, patients' disagreement with the need for treatment, problems in accessing the facilities providing treatment or inability to pay for it (Haynes et al., 2005).

ARVs: a special case

While experience of adherence to treatment for chronic diseases has great relevance, ART is exceptional in requiring adherence rates of at least 95% to prevent treatment failure or drug-resistance. In 2000, Chesney reviewed the factors affecting adherence to ART, based on the US experience. She reported a strong correlation between the level of medication adherence and the percentage of patients without detectable level of the virus. When patients achieved less than 80% adherence, 87% of them had detectable virus. When adherence was between 80% and 90%, treatment failure occurred in 47% of the patients; and when adherence was more than 95%, detectable virus occurred in only 10% of patients. Although this occurred in a small number of patients, it does underline the importance of high levels of adherence. There were many factors which were reported to negatively affect adherence. These were grouped under patient factors, medication factors and the system of care factors. The reasons for sub-optimal adherence included the patients forgetting or being too busy, being away from home, a change in daily routine, side-effects, depression or illness and a lack of interest or desire to take a "drug holiday". A number of strategies were suggested to help improve adherence. These included directly observed treatment, providing clear instructions, using personal treatment plans, tailoring the drug regimen to suit the patient's lifestyle, showing patients how to keep a diary, and making the clinic appointments both convenient and pleasant. The evidence as to which intervention was most effective was not presented.

In an opinion piece published in 2005, Gill et al. suggested that there was no room for complacency about adherence to ARVs in sub-Saharan Africa. They pointed out that after initial optimism about adherence in Africa, recent reports reflected medium-to-poor adherence in the few studies that reported longitudinal data. In particular, they quoted the experience from Senegal, where 95% of patients had adherence levels exceeding 80% after one month of therapy, but after 18 months only 80% remained above that level. The 80% level of adherence would not be high enough to prevent treatment failure or the development of drug-resistance. Meanwhile, the percentage of patients with undetectable viral loads fell from 80% to 59% over time. In Cameroon, Akam was quoted as reporting that mean self-report adherence was initially under

68% and declined further over time. One of the key conclusions of the Gill et al. paper was that external multinational funds should be allocated to supporting and studying adherence. The authors also suggested that qualitative research into the behavioural reasons for patient non-adherence is urgently needed. The studies presented in this publication are intended to help fill that gap.

References

1. Carrieri MP et al. (2003). Impact of early versus late adherence to highly active antiretroviral therapy on immuno-virological response: a 3-year follow-up study. *Antiviral Therapy* 8:1-198.

2. Chesney MA (2000). Factors affecting adherence to antiretroviral therapy *Clinical Infectious Diseases*, 30(Suppl 2):S171-6 2000.

3. DiMatteo MR (2004). Variations in patients' adherence to medical recommendations. A quantitative review of 50 years of research *Med Care*, 42:200-209.

4. Ferradini L et al. (2006). Scaling up of highly active antiretroviral therapy in a rural district of Malawi: an effectiveness assessment. *Lancet*, 367:1335–42.

5. Gill CJ et al. (2005). No room for complacency about adherence to antiretroviral therapy in sub-Saharan Africa. *AIDS*, 19:1243-1249.

6. Haynes RB et al. Interventions for enhancing medication adherence. *The Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD000011. DOI: 10.1002/ 14651858. CD000011. pub2.

7. O'Brien SJ et al. (2000). Polygenic and multifactorial disease gene association in man: lessons from AIDS. *Annuf Genetics,* 34: 563-91.

8. Paterson DL et al. (2000). Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine*, 133:21–30.

9. Strawford A, Hellerstein M (1998). The etiology of wasting in the human immunodeficiency virus and acquired immunodeficiency syndrome. *Seminars in Oncology*, 25 April, (Suppl 6):76-81.

10. UN General Assembly Special Session (UNGASS) on HIV/AIDS, 2006. Final Draft Political Declaration. 2 June 2006. Para 28. Available at: http://www.ungasshiv.org

11. UNAIDS. P*rogress made in the implementation of the Declaration of Commitment on HIV/AIDS*. Report of the Secretary General. New York, United Nations, 2005.

12. UNAIDS. *2006 Report on the gobal AIDS epidemic*. Geneva, United Nations Joint Programme on HIV/AIDS, 2006. http://www.unaids.org/en/HIV_data/2006GlobalReport/default.asp

13. Vermeire E et al. (2001). Patient adherence to treatment: three decades of research. A comprehensive review. *Journal of Clinical Pharmacy and Therapeutics,* 26: 331-342.

3. From training to action:
the process of engaging health professionals in operational research on adherence to antiretroviral therapy

Trudie Gerrits
John Kinsman

Introduction

Health care workers tend to assume that patients follow the instructions and advice they are given about medicine use. The studies presented in this book are based on the view that consumers – especially those with chronic conditions – are the key decision-makers in medicine use. Various factors – at individual, household, community, health service institution, national and international levels – influence medicine use by consumers. Consumers may have very rational reasons to use medicines 'irrationally'. Interventions to improve rational medicine use should be based on a thorough analysis and understanding of these reasons.

Over recent years, a shared view on how to study the multi-level influences which shape individual medicine use behaviour has evolved between WHO, the Medical Anthropology Unit of the University of Amsterdam and KIT. The expertise of all three institutions together provide a unique multidisciplinary approach, by including public health, anthropological and health systems perspectives.

This chapter describes the development of the Promoting Rational Drug Use in the Community (PRDUC) course – designed by the three institutions and conducted in collaboration with partner institutes in Africa and Asia. The chapter focuses in particular on the course conducted in 2004, which concentrated on issues surrounding ARV adherence. In line with the previous courses, it included the combination of public health, anthropological and health systems perspectives that characterizes the PRDUC course. The chapter also describes how the subsequent operational ART adherence studies – the results of which are presented and discussed in this publication – evolved, from proposal design through to the reporting of findings.

Through this process, we demonstrate that the combination of (i) a synthesis of perspectives; (ii) ongoing training and support; and (iii) strong commitment from both country-based researchers and international technical advisers, can produce comprehensive results that are fully 'owned' by the participating countries. This in turn means that study recommendations are more likely to be incorporated into national policies and guidelines, and subsequently implemented.

Promoting the rational use of drugs

Since the beginning of the 1980s the essential drugs concept has become one of the cornerstones of international and national health policy. The selection and rational use of medicines are accepted as key principles of health service quality and management (Hardon, Hodgkin and Fresle, 2004). WHO has defined rational use of drugs as the situation in which *'Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community'* (WHO, 1985). Common patterns of inappropriate medicine use include, for example, using too many medicines per patient, inappropriate use of antimicrobials, over-use of injections, failure to prescribe according to clinical guidelines, and inappropriate self-medication (WHO, 2002; Hardon, Hodgkin and Fresle, 2004). Improper prescription, inappropriate use, and lack of access to medicines are all part of the problem of irrational drug use. Over the past two to three decades, many efforts have been made to improve the use of medicines, such as the development of national medicines policies, the strengthening of drug regulation, ensuring access to essential medicines, and efforts to improve the rational use of medicines by providers and consumers. Hardon and colleagues in 2004 reported that despite substantial progress in this area, health policy-makers have tended to focus more on the provision and regulation of medicines, and on efforts to improve health workers' prescribing habits, rather than on efforts to ensure rational use of medicines by consumers.

A 1997 global survey of consumer-oriented interventions aimed at improving the rational use of medicines, carried out in collaboration with Health Action International, revealed that few of these interventions had been designed appropriately, most were found to be non-sustainable, and there had been very little monitoring and evaluation of interventions (WHO, 1997). These survey findings prompted the then-Essential Drugs and Medicines Policy Department of WHO, together with the Medical Anthropology Unit of the University of Amsterdam and KIT to design the PRDUC course. The aim of the PRDUC course is to develop a better understanding of medicine use in the community, and to design, implement and evaluate effective interventions to improve medicine use in the community.

The contents and approach of this course were not completely new. They built on long-term collaboration and a shared vision among staff members of the participating institutions. In particular, the research component of the course built on two publications: *How to investigate drug use in communities* (WHO, 1992); and *How to investigate drug use in health facilities* (WHO, 1993). Both of these publications, which give detailed guidance on how to conduct operational research in the area of medicine use, have been a source of inspiration for several studies in this field (e.g. Rasmussen et al., 1996; Adome et al., 1996; Birungi, 1996; van Staa and Hardon, 1996; Senah, 1997, Sringernyuang, 2000; Hogerzeil et al., 1993).

Promoting Rational Drug Use in the Community course

Approach and contents

The PRDUC course starts from the principle that it is important not only to know the type and extent of irrational medicine use in a certain community, but also to understand *why* medicines are used irrationally. Only by understanding *why* people do what they do, can appropriate, efficient and feasible strategies to change medicine use practices be identified and developed (Hardon et al., 2004). A multi-level perspective is therefore adopted, which includes analysis of factors at the individual, household, community, health service institution, national and international levels.

Studies on the use of medicines should be an integral part of the process by which interventions are developed to help ensure more appropriate medicine use by consumers at community level. The PRDUC training model proposes an intervention cycle, which entails research activities in almost all its steps (see Table 1).

The first week of the two-week PRDUC course focuses on investigating and prioritizing medicine use problems; the second week is devoted to developing effective strategies and interventions for change. See Table 1 for an overview of course modules in both weeks.

Table 1: Overview of PRDUC course modules per week

Course modules week 1: Research	Course modules week 2: Intervention
Setting the scene What influences drug use in the community Investigating drug use patterns Prioritizing drug use problems Conducting a rapid assessment Sampling Fieldwork Data analysis Monitoring and evaluation Linking research with interventions	Face-to-face education Designing printed material Pre-testing Mass media Working with journalists Advocacy and networking Managerial and regulatory strategies 'Country' proposals

The studies presented in this publication are 'Step 3' (see Figure 1) or pre-intervention studies, which involve analysing problems and identifying solutions.

Figure 1: Steps in developing an effective intervention aimed at enhancing rational drug use by consumers
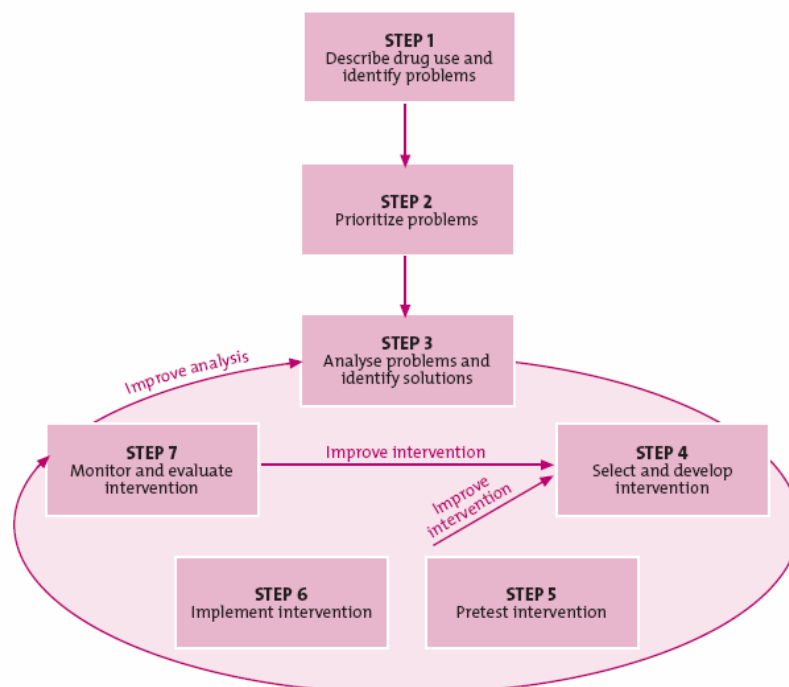
As Figure 1 suggests, research can play a role in the different steps of intervention development. The various course sessions address each of these different steps.

The PRDUC *research* training modules are based on the WHO publications mentioned above (WHO, 1992 and 1993) and on chapters of the *Manual for applied health research* (Hardon et al., 2001). Having successfully used these research training modules in the first three PRDUC courses, they have now been transformed into the manual, *How to investigate the use of medicine by consumers* (Hardon et al., 2004). The *intervention* training modules have been developed in close collaboration with communication specialists and journalists with long experience in the field of international health, in particular of medicine use and communication in health (http://www.healthcomms.org/; Haaland et al., 2005). The course material used in the intervention modules is currently being developed into a second manual. All course materials, including exercises and additional reading and audiovisual materials are available at the PRDUC website (http://mednet3.who.int/PRDUC).

The PRDUC course is participatory in nature, and builds on the knowledge, skills and experiences of participants. Interactive teaching methods, including role-play, discussions, and various group exercises are applied throughout the course. In the first week, a fieldwork activity is held during which data collection techniques that have been taught during the course – such as focus group discussion, semi-structured interviews, structured observations and simulated client visits – are put into practice. Topics of fieldwork activities are defined in close collaboration with the local organizing institution, and to date have included community medicine use for malaria, coughs and colds, diarrhoea, sexually transmitted infections (STIs) and HIV. National

organizing institutes (see below) are responsible for writing background papers on these issues in their countries, which participants use to prepare the fieldwork activities.

At the end of the second week, course participants develop and present 'country' proposals, in which they elaborate all the steps of the intervention cycle with regard to a topic that they have prioritized in their own country or region. Generally participants from one country or geographical region work together in this exercise. In the past, course participants have always been encouraged to further develop these proposals and to submit them for funding to relevant agencies. However, in the 2004 course, for the first time, limited funds were available to support a number of participants' project proposals. This funding led to the studies presented in this publication.

PRDUC courses in practice: national organizing institutes, faculty members and participants

The PRDUC courses are coordinated by the Medical Anthropology Unit of the University of Amsterdam, in close collaboration with KIT and WHO's Department of Medicines Policy and Standards (PSM) and the national organizing institute. The course has a core faculty of teachers who have been involved in the development of the course, and other expertise is brought in as needed.

Each PRDUC course is organized in close collaboration with national organizing institutes in developing countries. Four international PRDUC courses have been held to date, in Thailand (2000, 2002), Uganda (2001) and South Africa (2004). The national organizing institutes – including the Centre for Health Policy Studies, Mahidol, Thailand; the Child Health and Development Centre at Makerere University, Kampala, Uganda; and the School of Pharmacy of the Medical University of South Africa (MEDUNSA) in Pretoria – had all previously carried out (community) medicine use studies. Faculty members of the host organizations prepared and organized fieldwork in advance of the course, and were also involved in some of the training modules.

Between 25 and 33 people have participated in each course to date, mainly originating from Asian and African countries, though occasionally participants have come from Europe, the Middle East and South America (see Annex 1). Pharmacists have been the most represented profession, with medical doctors, health educators, community workers and social scientists also taking part. Participants tend to come from ministries of health, universities, NGOs, district level government and hospitals. Despite efforts by the course organizers to attract more NGO workers and others working at community level, both groups are under-represented in the PRDUC course. The number of women and men participating has been more or less equal in each course.

Raising funds to cover the cost of participation at the PRDUC courses is a major challenge for both applicants and the course coordinators. The course fee (including accommodation but excluding travel costs) is US$ 2 950 per participant. Annex 1 shows the high dependence on WHO funds, either from headquarters or regional and country offices. In every course a substantial number of potentially strong applicants have not

been able to participate because of lack of funding. In the 2002 course, for example, 35 such people – from universities (21), ministries (9) and NGOs (5) – had to be turned away. Difficulty in raising funds is an indicator of the low priority given by national and international funding organizations to efforts to reach out to consumers as a means of improving the rational use of medicines.

From the outset, the PRDUC course organizers have encouraged others to use and adapt the course materials as much as possible. All the course materials have been translated into Spanish, with funding from WHO, and the course has subsequently been conducted in Latin America. It has also been held in India.

Major changes in the 2004 PRDUC course

In 2004, the fourth PRDUC course took place in Pretoria, South Africa, in the context of major changes - both in the world of medicines and in the availability of resources to support local operational research on the rational use of medicines. These changes were instrumental in the realization of the ARV adherence studies presented in this publication.

A changing context: the focus on AIDS medicines

Since the first PRDUC course was held in 2000, there has been a dramatic shift in the availability of ARVs. Although AIDS was a major problem in many developing countries at that time, ART was too expensive for most people and treatment was limited to managing opportunistic infections. Since then, the substantial reduction in prices of ART and the establishment of large donor organizations, such as the Global Fund and PEPFAR, have led to the scaling up of ART in many low- and middle-income countries.

However, the increasing availability of ARVs has prompted concerns about their proper use (Richard et al., 2004). High levels of adherence (at least 95%) are needed to ensure positive treatment outcome (Paterson, 2000). This changing situation, which touches on the core of the PRDUC course – i.e. emphasizing the importance of appropriate medicine use at community level – provided the course faculty members with new challenges. In response, it was decided to focus the 2004 PRDUC course on *"medicine use to alleviate the AIDS pandemic"*. Accordingly, the course objectives were expanded to include a focus on studying how AIDS patients were using AIDS medicines, what prevented them from using ARVs appropriately, and what could be done to improve their use.

At the time of the course, the extent and quality of operational research to identify problems with ARV adherence in resource-poor conditions and to strengthen adherence support mechanisms was very limited, and remains so today. Faculty members were therefore challenged to adapt existing course modules, to identify lessons that could be used from other chronic disease treatment programmes, and to explore new strategies for promoting ARV adherence. Reading materials covering ARV adherence issues were added and discussed in a number of PRDUC modules. In

addition, a completely new module was developed to cover regulatory and managerial interventions. New issues in the course included, for example, the selection of patients to enrol for treatment, human resource needs, the types of peer support that ARV users may need, issues of price control and drug registration. Among other tools used was a case study of the Médecins Sans Frontières (MSF) pilot ART roll-out programme in Khayelitsha, South Africa, which was intensively discussed to sensitize participants to the new challenges faced in ART programmes, and to encourage them to think about ways of addressing these (Kasper et al., 2003). It was recognized that communication strategies alone would not be enough to change people's medicine-use behaviour, and that other interventions are needed to create an enabling environment for optimal adherence to ART. This applies not only to ART but to other medicines as well.

In accordance with the course focus on AIDS medicines, all fieldwork activities in the 2004 PRDUC course were dedicated to ARV adherence issues. Six health facilities in the Pretoria area involved in ART roll-out were visited by groups of course participants, and data were collected using different data collection techniques. Subsequently, participants analysed the data and presented their initial findings and conclusions. The data collected during the field visits yielded a broadly positive picture of the situation in the Pretoria area, and raised the hope among course participants and faculty members that effective ARV treatment in resource-poor settings was indeed possible. As research findings in this field were (and remain) limited, course faculty members and participants decided to write up fieldwork findings, which resulted in an article in the WHO *Essential Drugs Monitor* (Abah et al., 2005), which is included here as Chapter 4.

A participant in the 2004 PRDUC course arrives at the fieldwork site near Pretoria to begin collecting data on ARV adherence.

Using new media: CD-ROM and websites

Another innovation in the fourth course was the intensive use of new electronic media. A CD-ROM, containing all training materials and related documents, was produced and distributed to course participants before they left the course. In addition, two PRDUC course websites were set up, one public site and one site with access restricted to course participants and faculty members. All materials included in the CD-ROM were made available on the PRDUC websites as well. The CD-ROM enables course participants to use course materials when not having access to a properly functioning Internet connection.

The two websites serve different purposes. The public site includes all course materials and related documents, and is accessible for anyone working on the Internet (http://mednet3.who.int/prduc). The second website, which is restricted to course participants and faculty members, allows for the distribution and sharing of work-in-progress – i.e. work not yet ready to be disseminated widely but which might be a source of inspiration for others currently working on the same topic. During the course, for example, the fieldwork instruments were posted on this site. At a later stage, the restricted website contained different versions of participants' research proposals and faculty members' comments on these proposals (see below). The restricted website was also used to circulate the research tools developed for the ARV adherence studies, the interim reports, and draft versions of the final reports. In this way the website enabled participants to continue learning from each other's work.

Both the CD-ROM and websites came into being through cooperation between the WHO staff member involved and a MEDUNSA data manager, who also became the webmaster of both sites.

Availability of financial resources: developing operational research proposals

Another major difference compared to the three previous PRDUC courses was the availability of additional financial resources, provided by the European Union (EU) as part of their support to WHO, in order to develop and pursue the 'country' plans as developed during the course. Participants were informed that three proposals would be funded and receive technical assistance. A Call for Applications for Promoting Rational Drug Use was announced to the 2004 PRDUC course participants (see Annex 3). Participants were encouraged to generate operational research proposals with a maximum budget of US$ 12 500. In addition, technical assistance would be provided by medical anthropologists from the University of Amsterdam. The proposals would be reviewed by a selection committee on the basis of their scientific merit, their relevance to improving medicine use in the community, and the potential for strengthening operational research capacities. In addition, participants were strongly encouraged to ensure effective collaboration with community partners and stakeholders in all phases of the project development. The selection committee consisted of PRDUC course faculty members. Draft proposals were submitted and core faculty members reviewed them extensively. Proposals and comments were placed on the restricted PRDUC website, and applicants were recommended to read and learn from each other's proposals and the comments, as part of 'continuing learning' after the PRDUC course. In this way, while developing their own proposals they were also providing input for each other's work.

In the first round, eight draft proposals were submitted, with five in the second round. In each round, two people commented on each proposal. After three cycles of production, review and re-submission, four viable proposals were generated, of which there were funds for only three. They included three proposals on ARV adherence (from Botswana, Uganda and Tanzania) and one on HIV-TB co-infection (from Kenya) (see URLs for each proposal in Annex 2). All four proposals were of good quality,

fulfilling the criteria as indicated in the Call for Proposals. After intensive deliberations it was decided to fund the three study proposals that focused on community aspects of adherence to ARVs. This decision had less to do with the quality of the otherwise strong Kenyan proposal, than with the fact that three proposals dealing with ARV adherence together would enable the development of a joint comparative, multi-country study. Synthesizing results from such a comparative study, it was thought, would lead to synergy among the three study teams and to added value in terms of study findings. In addition, assisting three teams in a similar study is more time-efficient than giving support to teams with different study objectives and approaches. This publication shows that both assumptions have proved to be valid. While efforts have been made to raise funds for the Kenyan proposal, unfortunately these have not been successful to date.

Three ARV adherence studies: the process

Study design and planning

With the proposals for the three ARV studies approved, a series of workshops was planned to run throughout 2005, in order to provide training and support to the country teams who would conduct the research. Regular e-mail contact was also maintained between country teams and facilitators in order to ensure a free sharing of ideas and information. The first of these workshops took place over five days in Bagamoyo, Tanzania, in February 2005. Ten participants attended from four countries – Tanzania, Uganda, Botswana and South Africa – including pharmacists, medical doctors and social scientists. Three staff members from the University of Amsterdam acted as facilitators.

The primary objectives of the Bagamoyo workshop were (i) to review each of the country proposals and to define common ground for a comparative study; (ii) to develop common and/or country-specific research objectives and methodologies; and (iii) to work out detailed country plans (including the selection and training of fieldworkers and pre-testing research instruments) and budgets. The workshop was designed to be fully participatory, and it opened with participants presenting peer reviews of each other's proposals. Based on the discussions arising from these critiques, a shared research objective was formulated: *To identify factors that facilitate or constrain adherence to ART among adults through a pre-intervention study.* The objective was to work towards the design and subsequent implementation of interventions that would promote optimal adherence to ART. On this basis, the participants expressed their willingness to make the country studies as comparative as possible, while still keeping country-specific issues in mind.

Two further guiding principles for the studies were also agreed upon: (i) teams would use a mix of quantitative and qualitative research methods; and (ii) they would adopt a multi-level perspective, meaning that they would investigate issues of ARV adherence from several different points of view: individual ARV users; the community; health facilities (including all cadres of staff); and policy-makers and other national level actors.

From this starting point, the remainder of the workshop involved formulating more detailed research questions, identifying relevant variables (for the quantitative tools) and themes (for the qualitative tools), and then designing appropriate research instruments. Research tools used in the 2004 course, questionnaires from a *Horizons* ARV adherence survey conducted in Mombasa, Kenya, as well as other literature (*Horizons*, 2005; Farmer, 1999; Vitolins et al., 2000; Sankar et al., 2002) were handed out to provide additional input. Eleven draft research instruments were produced by the end of the workshop, from which individual countries could select and adapt as necessary (http://mednet3.who.int/prduc/Bagamoyo/Bagamoyo.htm).

Initial planning of fieldwork was also undertaken, for example in relation to sampling frames. This included deciding upon the categories of health facility to be investigated – e.g. NGO, private-for-profit, government – and in which areas of the country they would be. This was not always a straightforward process: some areas of at least one of the participating countries were 'over-researched', and it was hard for this team to find a facility that had not been previously subjected to (usually clinical or epidemiological) investigation.

With respect to ARV users, the number of respondents was considered, as well as the importance of systematic selection criteria in order to reduce bias to a minimum. It was also stressed that selection should be conducted in such a way as to ensure that people would not be stigmatized as a result of their participation in the studies. Finally, there was discussion about data management as an ongoing process throughout the fieldwork period.

During the evaluation of the Bagamoyo workshop, the participants conceded that it was only at this stage that they could fully appreciate the extent of the work that lay ahead, and – in relation to this – how small their budgets were. However, by the end of the workshop a shared research objective had been defined; high quality research instruments had been produced; and the revised country plans and budgets were well on their way to being finalized.

Fieldwork

Fieldwork took place in Uganda, Tanzania and Botswana between April and July 2005. Between the Bagamoyo workshop and the start of fieldwork, each country selected the research instruments they wanted to use from the 11 draft versions that had been produced, and then adapted these to local conditions. This adaptation included translation to the vernacular, pilot testing, and subsequent fine-tuning.

Each of the country teams was composed of people from very different backgrounds, including pharmacists, doctors, social scientists and administrators. This combination of backgrounds, levels and disciplines produced a dynamic synergy of complementary skills. In addition, data collection personnel were hired and trained in each of the three countries. These were either social science graduates or social workers based at the various health facilities. The general feeling from each of the three country teams was that health workers, community members and ARV users were highly cooperative and willing to participate, but it was not always so easy to access those working at the national level.

Data collectors receiving training in Tanzania.

The main constraints faced by the teams were financial and logistical. The budget was extremely tight for all of them, and since a number of people were involved in the various studies, the researchers sometimes had to use their own personal funds for accommodation, meals and transport. While undoubtedly causing some hardship, this is nonetheless an indication of the high level of motivation and commitment by members of the three teams. In addition, it was a major challenge for people who already had full-time jobs to meet – in some cases, hundreds of kilometres from where they lived – in order to organize and conduct the work.

Contact between the teams was maintained on their own initiative, with regular e-mail exchanges, text messages, and occasional phone calls. These discussions concerned both data collection and initial analysis. In addition, the team members from the University of Amsterdam and WHO also kept in touch with the teams via e-mail throughout the fieldwork.

Analysis and writing up

Analysis workshops were held in each of the three countries in July 2005, attended by the principal investigators from each country (all of whom had attended the Bagamoyo workshop) and their national research colleagues. Direct assistance was provided by two medical anthropology Ph.D. candidates from the University of Amsterdam, one visiting Botswana, the other visiting Uganda and Tanzania. This was a key moment for each of the three country studies, since these visits prompted the national participants to come together to consider what they had found during their fieldwork. In view of their work commitments, it was not always easy for the team members to coordinate meetings for analysis and writing. Furthermore, few of them had any training in either quantitative or qualitative data analysis, so this was an occasion for hands-on 'learning by doing' in the company of a colleague who had well-developed analytical skills.

These analysis workshops followed the principles of technical assistance that have been developed over the last decade by the University of Amsterdam during collaborative studies on a number of health topics, including immunization, medicine use, malnutrition and reproductive health.

Given that most of the researchers did not come from a research background, it was important to provide guidance in analysis technique. A number of issues were therefore stressed throughout the three analysis workshops. With the multi-level perspective adopted in each of the three studies, for example, it was important to try to understand respondents' 'emic' perspectives. This assumes that 'there is no one correct view', which is a helpful premise when considering the thoughts and opinions of ARV users, providers and the community as a whole, since it permits a nuanced interpretation of what has been reported by a wide variety of respondents.

The research teams were also advised (i) to think critically about data validity, and to look out for reporting bias; (ii) to think of how the quantitative and qualitative data could best be triangulated and used together; and (iii) always to bear in mind the ultimate objective: *designing workable intervention/s to improve ARV adherence*.

The analysis approach taken with the qualitative data is given in Table 2. Quantitative data analysis was facilitated by a system devised by the South African team who had attended the Bagamoyo workshop, and assistance was received from them over the phone during the course of the analysis workshops.

Table 2: Steps taken in qualitative analysis

1. Organize and order the 'raw data'
2. Code interviews and fieldwork notes
3. List and sort data
4. Categorize, summarize and display the data
5. Interpret the data
6. Triangulate and validate
7. Draw conclusions and seek to verify

The workshops ended with the production of suggested report outlines to be worked on in the run-up to the final writing workshop in Jinja, Uganda, in November 2005. Individual team members were given specific tasks and deadlines, and as the country teams developed their reports, they distributed them via the Internet and received technical and editorial input from each other as well as from the team members at the University of Amsterdam and WHO. Thus each country report went through several reviews and revisions before a final report writing workshop.

Report writing workshop

The objectives of this five-day workshop, held in Jinja, Uganda, in November 2005, were (i) to discuss and work towards finalizing the draft country reports; (ii) to write a short 500-word policy brief for each country; and (iii) to start work on a synthesis article for publication. The workshop was attended by eight full-time participants from the three countries, and was facilitated by five technical advisers (three from the University of Amsterdam and two from WHO).

The workshop started with a series of peer review sessions, during which members from two of the participating country teams would review the draft report of the other country team, with additional input from the course advisers. This peer review process focused on the following: (i) adequacy and clarity of the presentation of data; (ii) appropriateness of analysis and conclusions (iii) reflection on differences and similarities in findings between the three countries; and (iv) formulating recommendations for improvements.

A WHO editor – one of the two WHO advisers – provided additional advice on presentation and style. Some of the 'key tips' provided are given in Table 3 below. The importance of the reports having a clear 'red thread' was also stressed, linking the data with the interpretation of findings, and subsequently with the recommendations for future interventions and/or policy changes.

Table 3: Key tips for report writing

- Consider your audience. Policy-makers are often not technically minded, so keep it simple.
- Avoid being long-winded: very long, turgid sentences don't work well.
- Avoid unnecessary jargon.
- Keep acronyms and abbreviations to a minimum.
- Adopt the four Cs: always be Clear, Concise, Complete, Correct.

A second important activity at the workshop was the initial drafting of a 500-word policy brief, based on the essential 'take home' message that the country teams wanted to stress. A role play exercise, entitled 'Four floors with the minister', was conducted to encourage the teams to distil their message. The idea was that they were in a lift with the Minister of Health, and would be travelling up four floors together: what was the message they wanted to put across in that short time?

The hands-on work then began on the reports, with team members from each country sitting together alongside one of the course advisers. Each of the teams restructured parts of their report according to the suggested outline provided by the WHO editor. As soon as a chapter or section was completed, the editor was then able to start work. This work continued throughout the final three days of the workshop. The initial draft

of a synthesis paper outlining the main collective findings of the reports was also produced. The workshop concluded with the production of a time-line for the finalization of reports.

Intervention development

Since this was a 'pre-intervention' study aimed at designing interventions to promote ARV adherence, a session was held during the Jinja workshop to define three possible intervention approaches for each of the country teams. It was recognized that a mix of interventions may work synergistically, ensuring that the whole is greater than the sum of the parts. A ranking exercise, which had already been introduced to the participants during the PRDUC course, was suggested for prioritizing the various suggested interventions. Six additional criteria were defined that could assist in the prioritization of interventions, including: (i) anticipated cost; (ii) likely impact; (iii) feasibility; (iv) sustainability; (v) acceptability at various levels; and (vi) likelihood of harm and/or unintended consequences. See Table 4 for a list of the suggested interventions.

Table 4: Interventions suggested during the Jinja report writing workshop

- Address HIV-related male gender issues
- Facilitate social support and reminders
- Train health staff in adherence counselling
- Raise awareness of potential side-effects during initial 6-month treatment stage
- Institute pill counting at treatment centres
- Increase distribution points for ART (initiation at hospitals, with subsequent transfer to a more local setting)
- Promote community sensitization on ARV use
- Provide transport subsidies where needed to cover the cost of transport to treatment centres
- Strengthen home-based care
- Provide food support during the initial stage of treatment
- Ensure availability of adherence counsellors at each facility
- Institute a follow-up system for treatment defaulters
- Provide family-based voluntary counselling and testing, as an entry point for ART
- Provide feedback to the community on the study, as an entry point for future interventions

It was also agreed that country teams would report back to the various stakeholders who had participated in the research, and present their proposals for future interventions. Limited funds were made available from HealthLink to facilitate this activity. While the initial recommendations for future interventions were derived from the data collected during the studies, it was recognized that additional and potentially important issues regarding the interventions would emerge during such consultations.

Funding for these interventions and their evaluations has not yet been obtained, and country teams were encouraged to seek funds from Embassies, PEPFAR, the Centers for Disease Control and Prevention, USA, and other funding organizations.

Publications

Output from the ARV studies included the following:

- Individual study reports, for in-country distribution to stakeholders at local and national levels.
- A synthesis article, based on the findings from all three countries.
- The current publication.
- Conference papers, including abstracts from each of the three countries, submitted to the 2006 International AIDS Conference in Toronto.

How the process was funded

The cost of the process is an important benchmark, both in terms of value for money of the study itself, and also as a guide for researchers who may wish to follow certain aspects of the study in future. The costings presented here are therefore divided into two sections: (i) the 2004 PRDUC course, which laid the groundwork for the study; and (ii) the study itself.

The 2004 PRDUC course held in Pretoria was attended by 34 participants, each of whom paid (through their respective funders) US$ 2950. This did not include travel costs. Part of these course fees and additional costs were covered by the WHO and Merck & Co., Inc., who contributed US$ 37 500 and US$ 10 000 respectively to the course. The proposal review (after the course) was done by PRDUC faculty members and a MEDUNSA staff member on a voluntary basis. The Dutch Ministry of Foreign Affairs (DGIS) financially supported the technical assistance provided by KIT throughout the process (development of PRDUC course material, lecturing at the PRDUC course, proposal review and editing of the current publication).

US$ 25 000 was made available by WHO, with funds provided by the EU for WHO support, for each of the three country studies, making a total expenditure of US$ 75 000. Each country's US$ 25 000 was divided equally between the country research teams and the University of Amsterdam, which provided the necessary administrative and technical support, as explained below.

From the US$ 12 500 received by each country team, they had to cover all the study expenses, including fieldwork preparations, the actual fieldwork, analysis of data, writing up and correcting/editing the reports. According to the budget, approximately one third of the project money was allocated to pay research staff. Given the amount of time that country team members have invested in the studies, it is clear that a great deal of volunteer work has been carried out during each phase of the study.

The US$ 37 500 (three times US$ 12 500) received by the University of Amsterdam was used (i) for the overall coordination of the three studies; (ii) to finance the two workshops in Bagamoyo and Jinja; and (iii) for the technical assistance and advice provided throughout the project. Technical assistance took place during the workshops; through numerous e-mail contacts; and through the two medical anthropology PhD candidates who visited each country team once during the analysis phase. The majority of the funding was spent covering travel and accommodation expenses for country team participants and technical advisers. In addition, the University has invested approximately 100 person/days in this project to cover the major part of the technical assistance provided.

In addition to the personnel input from country teams and the University, other people and institutions have also provided technical assistance, advice and input. These include: (i) a WHO staff member, who has played a role as adviser and facilitator in the process; (ii) a WHO editor, who facilitated during the writing workshop; (iii) a MEDUNSA data analyst, who provided – on a voluntary basis - assistance in the development of the quantitative research tools; and (iv) a consultant editor, who edited this entire publication, and who was financed by additional funds provided by WHO.

Discussion and conclusion

The process of conducting this three-country study on ARV adherence has highlighted a number of issues that warrant consideration by anyone planning a similar study. There were four key strengths of the study, and it would be useful for any similar future study to seek to emulate these points.

Firstly, we conducted basic training, followed by intensive, ongoing technical support, both face-to-face during country visits and over the Internet. This provided both sustained motivation and support to the sometimes over-stretched research teams, without which it is possible that none of the studies would have been completed.

Secondly, each of the studies involved a collaboration of expertise at different levels, including local, national and international actors. This ensured that no one perspective dominated, an essential component of any study attempting to unravel the complexities of such a multi-faceted phenomenon as medicine use. It was also clear that the inclusion of national level actors as respondents, and especially those with connections to key policy-makers, ensured that there was significant interest in the results of the study from within the respective country's ministry of health. In addition, all researchers involved were very committed to bring the study to a successful conclusion, and invested a great deal of time and energy into the entire process, from developing the proposal to writing up the results.

Thirdly, the studies sought to combine the primarily medical, public health perspective of WHO with the medical anthropological approach of the University of Amsterdam and the health systems perspective of KIT. Again, this permitted the complexities of what was being observed to be analysed from equally important, complementary perspectives.

Fourthly, a key principle underlying the whole process was one of continuous learning, made possible by a strong support and coordination component, run primarily from the University of Amsterdam. People were kept in touch with each other, and, whenever technical, financial or other problems arose, promptly directed to somebody who might be able to assist. Internet accessibility was critical in this, since it instantaneously linked up Geneva and Amsterdam with the respective national partners as well as district hospital personnel. Such a study would therefore have been impossible before the Internet, and would not be possible today in any context where the Internet is not well established. This consistent and positive contact between participants facilitated a general sense of goodwill within and between facilitators and country teams, which meant that people were committed to completing work within the agreed time-frame.

Despite these key strengths, a number of challenges had to be faced during the course of the studies, which would need to be taken into account in any similar study in the future. Firstly, there was only limited money available for each country team, which meant that difficult decisions had to be made about the limits of what could be done during the research itself, as well as during the analysis and writing process. There is, however, a positive aspect to this problem, in that priority setting became crucial to the success of the exercise and only those who were highly motivated stayed involved.

Secondly, the logistics for the country teams were complicated, with long distances to travel for discussion, analysis and writing meetings. Although e-mail contact between team members helped considerably, in large countries the problem of distance is more or less unavoidable.

Thirdly, few of the participants had either a scientific background or significant research experience, which meant that this study had higher support demands than most 'conventional' research. However, if such support can be provided, this should not be seen as a serious limitation either, not least because engagement in the whole process from conceptualization through to study design, fieldwork, analysis and writing up, constitutes an enormous capacity-building exercise.

Finally, a balance had to be struck by the facilitators between ensuring national ownership of the respective country studies and attempting to develop comparability between country studies. This project was not set up as a multi-country study in the sense that a single protocol was to be followed in each country. However, the similarity of the country study topics and approach – in the initial study proposals - made it tempting to make them more comparable and to design communal data collection instruments. In the event, it was left to the country teams to decide on the actual use of these research instruments in their respective countries. This led to variation in the kind of data collected per country and, in particular, to a significant variation in the amount of quantitative data collected.

We can conclude that this approach to researching the use of ARVs in Africa contains principles that could be usefully applied to any of the other medicine use issues that have previously been addressed by the PRDUC courses – such as acute respiratory infections or diarrhoea. Low-budget research that is conducted with strong technical support can produce findings at least as valuable as more heavily funded studies.

References

1. Abah SJ et al. (2005). There's hope – early observations of ARV treatment roll out in South Africa. *Essential Drugs Monitor* No.34:16-17.

2. Adome RO, Reynolds-Whyte S, Hardon A (1996). *Popular pills. Community drug use in Uganda*. *Community Drug Use Studies*. Amsterdam, Het Spinhuis, 1996.

3. Birungi, H. *Injection use and practices in Uganda*. Geneva, World Health Organization, 1995.

4. Farmer KC (1999). Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clinical Therapeutics,* 21(6):1074-1090.

5. Haaland A, Molyneux C. C*oll*ecting *quality information: training manual on practical communication skills for researchers and project personnel*. Geneva, World Health Organization, 2005.

6. Hardon A. *Confronting ill health: medicines, self-care and the poor in Manila*. Quezon City, Health Action Information Network, 1990.

7. Hardon AP, Hodgkin C, Fresle D (2004). *How to investigate the use of medicines by consumers*. Geneva, World Health Organization, 2004.

8. Hardon A et al. *Manual for applied health research. Anthropology of health and health care*. Amsterdam, Het Spinhuis, 2001.

9. Hogerzeil HV et al.(1993). Field tests for rational drug use in twelve developing countries. *Lancet*, 4 December:1408-1410.

10. Kasper T et al. (2003). Demystifying antiretroviral therapy in resource-poor settings. World Health Organization *Essential Drugs Monitor* No.32:20-21.

11. Paterson DL et al. (2000). Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine,* 133:21-30.

12. Population Council Horizons (2005). T*esting different approaches to promoting adherence to HAART in Mombasa, Kenya.* Available at: http://www.popcouncil.org/horizons/AIDSquest/summaries/ssmombasaARVs.html,

13. Rasmussen ZA et al. *Enhancing appropriate medicine use in the Karakoram mountains. Community Drug Use Studies*. Amsterdam, Het Spinhuis, 1996.

14. Richard N et al. (2004). High prevalence of antiretroviral resistance in treated Ugandans infected with Non-subtype B Human Immunodeficiency Virus Type 1. *AIDS Research and Human Retroviruses*, 20(4):355–364.

15. Sankar A et al. (2002). Adherence discourse among African-American women taking HAART. *AIDS Care*, 14(2):203–218.

16. Senah KA. T*he popularity of medicines in a rural Ghanaian community. Community drug use studies.* Amsterdam, Het Spinhuis, 1997.

17. Sringernyuang L. *Availability and use of medicines in rural Thailand*. University of Amsterdam, 2000 [Dissertation].

18. van Staa A, Hardon A. *Injection practices in the developing world: a comparative review of field studies in Uganda and Indonesia*. Geneva, World Health Organization, 1996.

19. Vitolins MZ et al. (2000). Measuring adherence to behavioral and medical interventions. *Controlled Clinical Trials*, 21:188S–194S.

20. WHO (1985). *Rational use of drugs*. Report of the Conference of Experts, Nairobi, Kenya, 25-29 November. Geneva, World Health Organization.

21. WHO (1992). H*ow to investigate drug use in communities*. Geneva, World Health Organization.

22. WHO (1993). *How to investigate drug use in health facilities*. Geneva, World Health Organization.

23. WHO (1997). *Public education in rational drug use*. Geneva, World Health Organization.

24. WHO (2002). *Promoting rational use of medicines: core components*. WHO Policy Perspectives on Medicines, No.5. Geneva, World Health Organization.

Annex 1: PRDUC course participants by region, type of institution, sex and source of funding

	2000 Thailand	2001 Uganda	2002 Thailand	2004 South Africa	TOTAL
Total number of participants	**23**	**29**	**29**	**33**	**114**
Sex					
Men	9	13	14	18	54
Women	14	16	15	15	60
Region					
Africa	11	20	3	25	59
Asia	10	6	19	5	40
Others	2	3	7	3	15
Institution					
MoH	7	4	18	10	39
University	6	9	5	3	23
Hospital	2	1	2	7	12
District level	3	1	-	-	4
NGOs	1	3	4	7	15
Others	4	11	-	6	21
Source of funding					
WHO-HQ	2	17	3	13	35
WHO-regional	-	-	16	2	18
WHO-country	7	2	4	4	17
Gvt.	5	2	1	4	12
NGO	-	2	-	2	4
UN organizations	3	-	2	-	5
Bilateral donor	1	1	-	1	3
Pharm. ind.	-	-	-	3	3
Other	5	5	3	4	17

Annex 2: URLs for country proposals

http://mednet3.who.int/PRDUC/ FinalProposalARVAdherenceStudyBotswana.pdf
http://mednet3.who.int/PRDUC/ FinalProposalARVandTBStudyKenya.pdf
http://mednet3.who.int/PRDUC/ FinalProposalARVAdherenceStudyTanzania.pdf
http://mednet3.who.int/PRDUC/ FinalProposalARVAdherenceStudyUganda.pdf

Annex 3: Call for proposals

World Health Organization, University of Amsterdam, Royal Tropical Institute

Call For Applications for Promoting Rational Drug Use in the Community

The Essential Drugs and Medicines Programme within the World Health Organization (WHO) in collaboration with the University of Amsterdam and the Royal Tropical Institute (KIT) is pleased to announce the CALL FOR APPLICATIONS for the PRDUC operational research project from ACP participants attending the PRDUC Pretoria course. Please note that the deadline for application is 15th December 2004.

Objectives

The PRDUC operational research programme (PRDUC-OR) aims to facilitate and strengthen community drug use operational research in ACP countries of participants attending the Pretoria PRDUC course. The PRDUC-OR supports research projects by funding, on a competitive basis, research that contributes to the promotion of the rational use of drugs in the community. Priority will be given to projects integrating operational research activities that either provides information as to the underlying reasons for particular problem behaviours or evaluates an intervention that addresses a community drug use problem.

Applications for 2005

The Programme will support research activities that meet the above-mentioned objectives. Duration for support is 12 months with maximum financial support of US$ 12 500. Three proposals will be supported financially and with technical assistance. Applications are invited from participants who attended the Pretoria PRDUC course.

How to apply

The principal investigator should submit electronically the completed proposal to Trudie Gerrits at the University of Amsterdam by December 15th 2004. Prior to submission of the completed proposal, applicants are strongly encouraged to submit drafts according to the following schedule. They will receive prompt comments on these drafts.

First Draft submitted by 15th October 2004 Comments returned by October 30th.
Second Draft submitted by 15th Nov 2004 Comments returned by Nov 30th.
Final Draft submitted by 15th Dec 2004.

Proposal

The final proposal should contain the following information:

- Project Summary (1 page).
- Full names, addresses and others for principal investigator and other personnel.
- Name of the project.
- Justification of the study (2-3 pages).
- Objectives (1 page) Detailed description of the study design and methodology. (5-8 pages) If an intervention is undertaken, details of how the intervention will be developed, pretested, monitored and evaluated should be provided (5-8 pages).
- Mechanisms to ensure effective collaboration between the investigators and community partners and stakeholders at all levels of project development (1 page).
- Details of requested technical assistance (1 page).
- Expected results and potential contribution of the project (1 page).
- Ethical permissions (1 page).
- Activity timeline.
- An outline budget for the proposed work. Please be prepared to submit details if requested. Budgets in excess of U$12 500 may be submitted if details as to where the additional funding will be provided from are submitted. Such details should include a commitment letter.
- Brief curriculum vitae of key participants in the proposal. Letters of commitment should be submitted.
- Bank Details

The proposal should be submitted electronically. **Any applications that are submitted after December 15th 2004 will not be considered for funding.** Curriculum vitae of one page: this should clearly indicate the investigator's name, affiliation and complete address (including telephone number, e-mail address, fax number), sex, date of birth, nationality; qualifications and the nature of the applicants current and previous posts.

Bank details (Account number, clearing code, and bank address) should also be provided.

Selection process

The submitted proposals will be reviewed by the selection committee according to their scientific merit, relevance to improving drug use in communities and the potential for strengthening operational research capacities. The principal investigators of proposals that meet the above criteria and selected for funding will be informed by 31 December 2004. The support group will assist the principal investigators in finalizing their proposals through reviewing drafts of the proposal.

Draft and Final Proposals should e-mailed to: Trudie Gerrits (g.j.e.gerrits@uva.nl).
Deadline for receipt of applications is 15th December 2004.

4. There's hope - early observations of ARV treatment roll-out in South Africa

S.J. Abah, E. Addo, P.C. Adjei, P. Arhin, A.A.S. Barami, M.A. Byarugaba, C.S. Chibuta, A.K. Chowdhury, L. Dlamini, C.C. Ekezie, J. Essobe, T. Gerrits, L.N. Gitau, J.E.P. Hadiyono, H. Irunde, B. Kafoa, L. Kekana,   J. Kgatlwane, G. Kibria, R. Kwasa, R. Laing, A. Lupupa, M.J.P. Machai, H.N. Madaki, U. Mehta, S. Murithi, M.A. Naarendorp, V. Nawadra-Taylor, E. Ngemera Mwemezi, J.K.N. Nyoagbe, R. Ogenyi, E. Osafo, S. Suryawati, H. Zeeman.

In this chapter, we present data from an exploratory study on adherence to ARVs undertaken as a field exercise for the Promoting Rational Drug Use in the Community (PRDUC) course (see Chapter 3) held in Pretoria, South Africa, in September 2004. The course was organized by WHO, the University of Amsterdam, the Royal Tropical Institute (KIT) Amsterdam, and the Medical University of South Africa, (MEDUNSA), Pretoria. A major activity of the course was field visits to ARV treatment sites. The report of these visits is included below. A full course report is available at: http://mednet3.who.int/prduc/coursereport/PRDUC_Report.pdf

In South Africa in 2002, HIV prevalence in the 15-49 age group was estimated to be almost 30% (National Household HIV Prevalence and Risk Survey of South African Children). The public sector roll-out programme for the prevention of mother-to-child transmission with nevirapine started at 18 pilot sites in 2002. An ARV treatment plan was published in 2003 and roll-out of treatment started at 32 accredited sites in April 2004, aiming to treat all South Africans needing therapy (1.4 million by 2009). Although stigma, discrimination and cultural beliefs still affect voluntary testing and recognition of HIV and AIDS, in 2004 many more patients were initiated on ARV therapy.

A group photograph at the 2004 Promoting Rational Drug Use in the Community course.

Twenty ARV products are currently available in South Africa. Current first-line treatment is a twice-daily triple ARV regimen including two nucleoside reverse transcriptase inhibitors and either nevirapine or efavirenz. At least 95% adherence is required for this regimen to be fully effective and prevent the development of drug-resistance. Achieving this high level of adherence remains a concern. At all the treatment sites, patients are assessed by a multidisciplinary team. Patients are enrolled in the ART programme when they have a CD4 count below 200 and/or WHO stage III or IV AIDS-defining illness, and are committed to following the regimen strictly.

Methodology

Six health facilities which provide ART were included in the qualitative study undertaken over a single day in Gauteng and North-West Provinces. These units consisted of three public clinics - one primary, one secondary and one tertiary - two NGO-based primary clinics, and a private-for-profit primary clinic.

Different qualitative methods were used to study factors influencing sub-optimal or non-adherence to ARV treatment. Thirty-eight ARV users, 22 women and 16 men, were interviewed using exit questionnaires (17 people) and semi-structured interviews (21). These interviews aimed to study: patients' history of ARV treatment; experience in taking medicines; cost of treatment; perception of the quality of care given at the clinics; and availability of social support. In-depth interviews were also conducted with 24 health workers, including five doctors, 11 counsellors, five nurses and three pharmacists. The purpose of the interviews was to study the functioning of the ARV programme, information provided to ARV users, availability of ARVs and other resources, perceived job satisfaction, problems (and possible solutions), and other

> One female responded to the question of how she felt she was being treated by health staff, with the following: *"Nice! Even the doctors, they are nice to you".*

relevant information. In addition, two focus group discussions were conducted, one with patients and one with health care workers. There were structured observations of 13 consultations to study the interaction between the providers and ARV users. The availability of supplies of ARVs in the six clinics was also assessed. Information was collected on data collection forms and tabulated into a matrix using word processing software. These matrices were then synthesized across facilities to produce summary result tables. The heads of individual facilities, health workers and the patients gave their permission prior to the study.

Patients in the study were between 20 and 60 years old, and their educational backgrounds ranged from those who had reached Grade 3, up to diploma and degree holders. Most lived in areas surrounding the facilities, and the reasons for their visits ranged from initiation of treatment to follow-up and other illness. Among the 21 ARV users interviewed using a semi-structured format, 16 had started therapy in 2004, while five had started more than one year previously. The length of treatment as recorded at the time of the survey ranged from three months to four years. One female patient had not started treatment, despite a diagnosis of AIDS nine months previously, due to a fear of being on ARVs for life. Nineteen of the patients interviewed had never used ARVs and 10 people in the study had been diagnosed in the previous year.

Results

Facility profiles

All six facilities have treatment guidelines, although their sources varied (e.g. WHO, Catholic Society). Three had diagnostic facilities in their hospital while another three send their specimens elsewhere for analysis. The criteria for all sites for starting ARV treatment are HIV-positive status, a CD4 count of less than 200, and WHO stage III or IV of AIDS. All the clinics have a "preparedness for ARV treatment" programme, which varies in intensity and duration. Some of these programmes work with AIDS patients on an individual basis, while others prepare them in groups. Some clinics require proof of adherence to prophylaxis against opportunistic infections, usually cotrimoxazole and in some cases isoniazid. All the clinics carry out pre-training for new ARV users, which includes history-taking, adherence courses of varying lengths and some form of contract agreement.

Only two clinics have a pharmacist on the staff. Elsewhere, in one clinic the prescription is filled in another facility and a nurse then dispenses the ARVs, while in another clinic a pharmacist comes to dispense ARVs on fixed clinic days. In clinics where a pharmacist is available, the pharmacist counsels the patient and issues leaflets on drug schedules and, in some cases, a leaflet on side-effects and a pill intake card. Counselling was conducted at all clinics, either by medical doctors (in two clinics) or by trained HIV counsellors (in four clinics). Where a nutritionist is available, patients are counselled on dietary needs.

Although ARVs are issued free of charge in all the public clinics visited, ARV users pay a registration fee which ranges from 17-30 Rand per visit. The cost in the private clinic ranges from 800-2000 Rand per visit, most of which was said to be covered by insurance. (Exchange rate at time of interview: US$ 1.00 = R 6.35).

At the time of the survey, all the drugs needed for ART were available and there were no stock-outs reported over the previous two months. With regard to support to health workers, de-briefing sessions are carried out in four clinics, three have in-service training for staff, and one clinic provided no support services.

Quality of care

Perceived quality of care may be a crucial issue affecting adherence to ARV treatment in the long term. Data on this were collected from in-depth and exit interviews with ARV users, and observations on interactions between health workers and patients.

Privacy. In all six clinics visited, patients' right to privacy was respected and they were attended to by health workers in a private setting. In one clinic, privacy was seen as a major issue, even during the study interviews, which were carefully planned so that the patients would not meet each other. The-doctor-in-charge stressed the importance of privacy by giving an example of one person who lived around the corner from the clinic, and had started ARV treatment there, but then decided to continue the treatment elsewhere for fear of meeting someone who knew him. In another clinic ARV users

could meet, have tea, and support each other on a daily basis. They felt knowing, supporting and sharing experiences with each other made it easier to follow the treatment. Clearly, the importance of privacy depends on the overall set up of the ARV treatment centres.

Respectful treatment. Almost all ARV users interviewed expressed their satisfaction about the way they are treated by the health workers. Most are greeted cordially and feel that they can express their concerns and ask questions. For example, one woman was pregnant and she asked about the implications of her pregnancy for her treatment, and the risk of transmitting her illness to the baby.

Information given to ARV users. This is reportedly a major influence on increased adherence. In this study the information given to patients on their initial visit was observed, and questions were also asked in the exit interviews. In particular, patients were asked: whether health workers provide information about how the medicines work; how to administer the medicines; why continuous treatment is needed; what possible interactions can occur; what to do when they forget to take medicines; what possible side-effects may occur; and where to get ARV re-supply.

All ARV users interviewed said that they get a substantial amount of information, and this was supported by the findings from observations (Table 1). One patient reported having only received information about the possible interaction of ARVs with alcohol. This person showed low self-esteem and exhibited defensive behaviour.

Table 1.
Components of information received by patients initiating ARV treatment
at two different facilities

	Component of information	**From exit interviews (n=4 females)**	**From observations (n=3 males)**
1.	How ARVs work	4	2
2.	How to use them	4	2
3.	Why continuous treatment is needed	4	2
4.	What possible interaction may occur with other treatment	4	3
5.	What to do when they forgot taking medicines	4	2
6.	Which side-effects may occur and what to do if they occur	4	2
7.	What requirements for (breast)feeding	4	N/A
8.	When and where to get ARV re-supply	4	2

Commenting on the beneficial effects of treatment: *"I have power, I have energy, can even sweep…"*, *"I could not walk last week, today I can walk."*

<u>Waiting time</u>. Avoiding long waiting times is crucial in maintaining high adherence levels over a long period. Waiting times ranged from 30 to 90 minutes, and some ARV users reported that the time they had to spend waiting for treatment was a problem for them.

Waiting times and food were issues raised by some participants in all of the studies carried out. Additional spending on snacks and meals due to long waiting times at treatment centres was one concern. Here a stall outside the hospital in Molepolole, Botswana, sells food items.

Factors influencing adherence

Almost all ARV users reported feeling better. Only one person said that the treatment made him more sick, and another was unsure due to the limited period of treatment. Fifteen out of the 21 patients on ARV treatment reported no missed doses, while six reported missing at least one dose since their last visit.

Both health workers and ARV users mentioned several factors that complicate adherence to treatment, sometimes leading to non-adherence for a period, but often just making adherence more difficult.

<u>Costs</u>. Both ARV users and health workers said that the cost of ARV treatment and blood tests, especially in the private facilities, was a major constraint to adherence. Even the ARV users who are covered by Medical Aid complained of costly treatment since the insurance does not cover all expenses. Cost was found to be a major factor that affects adherence. One man said: *"... It can take three months for me before I come back when I don't have money..."*

<u>Food</u>. Both the health workers and ARV users reported that food complicates adherence and can also be a cause of non-adherence. In a number of cases treatment with ARVs made people hungrier, but they could not afford the cost of additional food. Some centres recommend and/or provide nutritional food, such as fortified high protein supplements.

Food
As one woman said with a sigh: *"... if we have no money to buy food, then this medicine is a problem..."*

<u>Family support</u>. This is an important factor in supporting adherence, and was mentioned by most of the health workers interviewed. However, ARV users are usually shocked when they first realize they have contracted HIV, and often find it difficult to disclose to family members, and so do not receive support.

Family support
A 47-year old man who had been on ARVs for four years whispered in pain: "*... I have to keep this in to me... I do not tell anybody..*". In contrast, a teenaged ARV user was very optimistic: "*... I told my mother, I told my brother, they all support me ...*".

<u>Side-effects</u>. Health workers at two centres mentioned side-effects as a serious problem. Some ARV users reported that they had experienced side-effects initially but that these passed with time. Of the 21 people interviewed, 11 reported not experiencing any adverse reactions or side-effects. Others complained about various problems, such as rash, nausea and pain in the feet.

<u>ARV users' knowledge about ART</u>. Some health workers reported limited information about ART, especially the importance of treatment adherence. While this factor, in itself, may lead to failures in adherence, it may be even more problematic in those cases where ARV users have received conflicting information from different sources.

In addition to the factors described above, various health workers from two centres mentioned "depression due to HIV status" as a factor complicating adherence to ARV treatment. Health workers also highlighted the concomitant use of traditional medicines as a factor influencing treatment. In terms of adherence to ART, most health workers observed that females appeared to achieve higher levels of adherence than males, and that people aged over 30 years appeared to achieve better levels of adherence to treatment than those in younger age groups. In addition, the level of education appears to have an impact on adherence. ARV users also admitted that they sometimes simply forgot to take the medicines, especially when beginning the treatment.

Efforts to improve services

All clinics have taken several measures to help improve adherence to ARV treatment. Written information in the form of leaflets is available in all clinics. Follow-up programmes vary in intensity from a daily direct observation of treatment, to weekly and to monthly clinical reviews. Some clinics keep a diary of appointments, while others use phone calls and short messaging services. In one clinic, the pharmacist provides patients with leaflets on the treatment schedule, and in some cases provides a diary card, or an alarm clock.

PRDUC course participants were impressed by the high quality of counselling provided by health workers at all clinics. From the observations of 13 counselling episodes, it was reported that most patients were greeted in a friendly way and were listened to carefully. Results from the exit interviews with 17 ARV users also supported

this finding. Most of them were satisfied with the services, and said that they respected and trusted the health workers. In the private clinic, participants admired the efforts to ensure privacy by establishing procedures which minimized the chance of patients meeting each other during the visit.

To support the health workers, most clinics have conducted a pre-service training programme, a Care-for-Carer training programme, or debriefing sessions, which varied in intensity, frequency and length. Interviews with health workers indicated that most of them were extremely enthusiastic and committed, although some health workers complained about the heavy workload and tiring counselling process, low remuneration, or the inadequate recognition by the Government of certain aspects of the work. Some health workers expressed their hope that the Government would help create a more enabling environment for ARV treatment by providing a community-focused sensitization programme, to positively influence the support system needed by people on ART.

Discussion

Although this was a small study, the use of in-depth interviews and observation provided comprehensive information about behaviour and practices. Many of the observations and comments were consistent across the range of different facilities.

Most of the sites visited had been operating an ARV roll-out programme for less than six months and the availability of ARVs did not appear to be a problem. However, factors including sex, age and level of education were observed to influence adherence. The national ARV programme uses a multidisciplinary approach in which different health workers in the team and other patients and support groups care for patients. Written information and materials to reinforce adherence are available.

> *Counselling*
> A teenaged ARV user who was interviewed expressed her feelings about the counselling she received: " *.. they are very, very, very supportive...*"

Although the patients interviewed were generally happy with the outcomes of therapy, in some facilities patients complained about side-effects and the demanding nature of ARV regimens. Patients said they trusted the health care workers and felt that they were listened to, respected and given a chance to ask questions. Health workers were enthusiastic and seemed to enjoy their work.

Transport costs were said to be a burden for some patients and a treatment-related increase in appetite posed an additional challenge, especially for those who were poor. However, the Government provides some nutritional support if needed. At most of the facilities, health workers expressed concern about the expected increase in the number of patients to be treated, which could result in overloading existing facilities and human resources. There was also concern at the lack of Care for Carer programmes to support health care staff at the health facilities.

Other problems highlighted included the shortage of social workers and counsellors in the facilities, the need to expand the range of ARVs to include paediatric formulations, and the need for capacity building to improve service delivery. There was widespread concern about the limited numbers of staff available and their capacity to cope with the anticipated increase in patient load.

Conclusion

This study was undertaken over a single day in a small number of health facilities by participants attending a training course. The facilities visited were among the first to provide ARVs to the general population. The staff were enthusiastic and committed to their patients. The patients appreciated the care they were receiving and generally felt better on therapy. Health workers expressed concern about both the present and anticipated future workload. Patients were concerned about treatment-related hunger and the need to take ARVs regularly and for life.

These are early days for the roll-out of ARV therapy in South Africa but there appears to be hope that many more patients could be treated. Many problems persist, including heavy workloads for health care staff, the need to promote adherence, and treatment-related hunger, especially among ART patients who are poor. However, there is also a feeling of enthusiasm among staff and hope among patients - suggesting that the roll-out of ARVs has begun successfully in the health facilities studied.

Factors that facilitate or constrain adherence to antiretroviral therapy among adults at four public health facilities in Botswana:
a pre-intervention study

Joyce Kgatlwane
Botswana Essential Drugs Action
Programme
PO Box 639, Gaborone, Botswana
Tel. +267 3632070 cell: +267 72565815
E-mail: jkgatlwane@gov.bw
jkgatlwane@yahoo.com

Robert Ogenyi
Mahalapye District Hospital
PO Box 49, Mahalapye, Botswana
Tel. +267 4710333 cell: +267 71427344
E-mail: robagumu@yahoo.com

Cosmas Ekezie
Sekgoma Memorial Hospital
PO Box 120, Serowe, Botswana
Tel. +267 4630333 Cell +267 71446186
E-mail: costee_akataka@yahoo.com

Haruna Ngbo Madaki
Scottish Livingstone Hospital
Private Bag 001, Molepolole, Botswana
Tel: +267 592 0333.
Cell: 267 71461135 Fax 5920335.
E-mail: harmadaki2@yahoo.com

Sikhulile Moyo
Botswana-Harvard School of Public
Health
AIDS Initiative Partnership
Private Bag BO 320, Gaborone
Botswana
Tel: +267 3902671 cell: +267 71400471
E-mail: smoyo@bhp.org.bw

Tirelo Modie Moroka
University of Botswana
Social Work Department
Private Bag 0022 Gaborone, Botswana
Tel: +267 3550000
E-mail: modiet@mopipi.ub.bw

Contents

Acknowledgements

Acronyms and abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ACHAP	African Comprehensive AIDS Partnership
ART	Antiretroviral Therapy
ARVs	Antiretrovirals
BHP	Botswana Harvard Partnership
BOTUSA	Botswana-USA project
CSO	Central Statistical Office
EDM	Electronic drug monitoring
FGD	Focus Group Discussion
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
HIV	Human Immune Deficiency Virus
IDCC	Infectious Disease Control Centre
KITSO	Knowledge, information and technology shall overcome (HIV and AIDS)
MoH	Ministry of Health
NACA	National AIDS Coordinating Agency
PLWHIV	People Living with HIV
pMTCT	Prevention of Mother-to-Child Transmission
Portakabin	Prefabricated building used in treatment centres
SOP	Standard Operating Procedures
STG	Standard Treatment Guidelines
UNAIDS	United Nations Joint Programme on AIDS
VCT	Voluntary Counselling and Testing

Executive summary

Introduction

Botswana is one of the countries hardest hit by the HIV epidemic, with a prevalence of 37.4% among pregnant women attending Government antenatal clinics (National AIDS Coordinating Authority (NACA), 2003). In 2002, Botswana became the first country in sub-Saharan Africa to launch a free national antiretroviral therapy (ART) programme in the public health sector.

While ART has improved the lives of many worldwide, lack of adherence to ART is still a major challenge to AIDS care and has serious public health consequences. Lack of adherence to ART often leads to treatment failure and is likely to accelerate the emergence of drug-resistant strains of HIV. As Botswana scales up access to ART in all health facilities, there is a critical need to estimate and monitor the rates of adherence. It is also important to understand factors that influence adherence in order to design appropriate interventions. This study was part of a three-country study on adherence to ART carried out in Botswana, Tanzania and Uganda.

Study objective

To determine adherence levels and identify factors which facilitate or constrain adherence to ART among adults in Botswana, and to identify and recommend possible interventions to improve adherence.

Methods

The study used a cross-sectional survey method, with both quantitative and qualitative research methods of enquiry. Adherence rates were measured using patient self-report methods (two-day recall, one-month visual analogue) and one-month pharmacy pill count. Information on how certain factors influenced adherence was collected using in-depth interviews, semi-structured interviews and focus group discussion (FGD) with ARV users, policy-makers, health care providers and the community.

Results

A total of 514 patients were interviewed, using a structured questionnaire. The mean adherence measures were: two-day recall 98% (N=508), one-month self-recall (visual analogue) 92% (N=496); and one-month pharmacy pill count 93% (N=443). The optimal adherence rates (defined as the proportion of those who take their medication at least 95% of the time) were 75% using the pharmacy pill count, 60% using the self-report (visual line), and 96% using the self-report (two-day recall method). The composite optimal adherence rate (average of the optimal adherence rates using the three

methods) was estimated to be 77%. The quantitative data revealed that the most common reasons cited for missing medication were: forgetfulness (18%), logistics and costs (13%), work and home duties (12%), stigma (7%), lack of care/support (4%), misunderstood instructions (3%), lack of food (2%) and alcohol abuse (2%). There was no association observed between gender and adherence. A higher proportion of those who were employed (65%) achieved optimal adherence rates than those who were unemployed (55%).

The qualitative data suggested that some of the facilitators of adherence were: acceptance of HIV status and disclosure; self-motivation to adhere to medication (self-efficacy and the ability to take and adhere to ART); belief in the efficacy of treatment (ARVs); pre-treatment health state; the need to care for others (especially children and the elderly); perceived availability of social support; and an effective adherence counselling programme. Factors that constrain adherence were identified by interviewees as: non-acceptance of HIV status; non-disclosure of HIV status and of being on ART; perceived lack of social support; stigma; logistics; treatment-related costs; and alcohol abuse. While concerns about long waiting times at the health facilities and lack of food were brought up during the interviews and discussions, these were viewed as inconveniences and not necessarily linked to sub-optimal adherence. In addition, information from policy-makers suggests that the unreliable availability of ARVs at Central Medical Stores and some health facilities could have an impact on patients' ability to adhere to ART.

Conclusions and recommendations

The adherence rates found in this study are comparable to other studies in developing countries. Adherence is a complex issue and multi-dimensional approaches are required to both address the constraints and strengthen the key facilitators of adherence. Efforts to determine the level of adherence among patients on ART is complicated by the general methodological difficulties of adherence assessment. There is no gold standard of adherence assessment. While the two-day recall measure may be useful for on-the-spot individual patient adherence counselling, we recommend using the visual analogue scale and the pill counts for routine adherence monitoring.

In this study the critical barriers to adherence identified were: forgetfulness, lack of transport fare to the health facility, non-acceptance of HIV status, fear of discrimination and stigma, alcohol abuse, and non-supportive home and work environments. Although side-effects occur in a significant proportion of users, this was not perceived as a barrier to adherence.

Facilitators of adherence were found to include self-efficacy, social support, an effective adherence counselling programme, perceived benefits of the medication, and a desire to stay alive for the sake of others.

Efforts to improve the level of adherence require a collaborative approach involving the patient, the community, health workers and policy-makers, and a focus on ways of addressing environmental and structural constraints.

Some of the recommendations identified include the development of practical guidelines for implementing adherence management strategies. These should include guidelines for: continuous adherence counselling; bringing treatment closer to home; adoption of a family care model approach to ART; use of practical reminders; adherence case management; and the use of medication organizers (pill boxes partitioned to display the daily or weekly sequence of pills to be taken). In addition, the establishment of a transport voucher scheme should be considered for people who genuinely cannot afford the cost of transport to collect their medication. Such interventions should be evaluated to assess their effects on adherence.

Furthermore, since acceptance of HIV status, disclosure and gender were found to be the main emerging themes in the qualitative data, further studies are needed to explore these variables in greater depth. Programmes targeting men to inform them about HIV-related issues should also be developed. This would help increase the enrolment of men in ART programmes, help them to better understand the gender issues around HIV, and mobilize them to be protectors and supporters of women in the fight against HIV.

Chapter 1: Introduction

In 2005, Botswana had a population of almost 1.8 million people, of whom an estimated 350 000 people were living with HIV (UNAIDS/WHO, 2005). In 2002, Botswana became the first country in sub-Saharan Africa to launch a national antiretroviral therapy (ART) programme in the public health sector. The ART is provided free to all citizens who are eligible for treatment.

While ART has improved the lives of many worldwide, lack of adherence to ART is still a major challenge to AIDS care. Failure to achieve optimal adherence to ART may lead to an increase in the replication of HIV and the development of viral mutations. This can result in treatment failure and accelerate the emergence of drug-resistant strains of HIV, with severe consequences for public health (Bangsberg et al., 2000; Turner, 2002).

As Botswana scales up access to ART in all its health facilities, there is a critical need not only to estimate the rates of adherence but also to understand the key factors (motivators and barriers) that influence adherence, and to apply the lessons learnt in order to improve both existing and future ART programmes. In order to do this, this study targeted antiretroviral (ARV) users, health workers, policy-makers, community members and other stakeholders in an effort to identify key factors which influence adherence. It was designed to facilitate the development with other stakeholders of specific interventions to improve adherence.

1.1 Research problem

Antiretroviral therapy has been available through the public sector in Botswana since 2002. But there is continuing concern at the level of adherence. Studies conducted in Botswana have reported adherence levels of 83% (Nwokike, 2004) in the public sector and 54% (Weiser et al., 2003) in the private sector – rates below the minimum level of 95% required for treatment success and to help delay the emergence of drug-resistant strains of HIV.

To date, studies in Africa have mainly reported on adherence rates (Gill et al., 2005). However, qualitative studies are also needed in order to identify barriers and facilitators to adherence. Kumarasamy et al., (2005) identified the main barriers as treatment-related costs, privacy, and stigma, while the facilitators were the perceived benefits of ART, awareness of the consequences of sub-optimal adherence, and social support mechanisms.

1.2　Research questions

♦　What is the rate of adherence to ART?

♦　What constitute barriers to adherence in patients on ART?

♦　What are the facilitators of adherence to ARVs among patients on ART?

♦　What factors at the community, facility and national level influence adherence to ART?

1.3　Study objectives

To identify factors which facilitate or constrain adherence to ART among adult ARV users in Botswana.

1.3.1 Specific objectives

♦　To quantify rates of adherence to ART.

♦　To determine what motivates and sustains good adherence.

♦　To determine barriers to good adherence.

♦　To determine factors at the community, health institution and national levels that influence adherence.

♦　To determine the relationship between the factors identified and adherence.

♦　From the lessons learnt, to identify and recommend possible interventions to improve adherence.

Chapter 2: Background

2.1   History of HIV and AIDS in Botswana

Botswana's first AIDS case was reported in 1985 and since then HIV prevalence has continued to rise dramatically. Today, HIV prevalence in Botswana is among the highest in the world. In 2003, Botswana's second generation surveillance system (National AIDS Coordinating Agency (NACA)) Technical Report, November 2003: Botswana 2003 Second Generation HIV/AIDS) estimated HIV prevalence to be 37% among pregnant women aged 15-49 attending Government antenatal clinics. This level appears to be stabilizing at around 30%-40%. In 2004, a first population-based survey estimated that 17% of the population aged 1.5-89 years were living with HIV.

Botswana mounted a strategic response to the HIV epidemic in three phases. The first phase (1987-89) focused mainly on the screening of blood to eliminate the risk of HIV transmission through blood transfusion. The second phase (1989-97) saw the introduction of an information, education and communication (IEC) programme. The third phase (1997-2002), was multi-pronged, with a focus on areas including education, prevention, comprehensive care and the provision of ART. The NACA, which was established in 2000, was given responsibility for mobilizing and coordinating a multi-sectoral national response to HIV (NACA, 2003).

2.2   Botswana's ART programme

In March 2001, the President of Botswana, Festus Mogae, announced that the Botswana Government would provide ARVs free of charge to all citizens of Botswana who qualify for treatment. The programme became known as '*Mas*' (the Setswana word for 'dawn'). An assessment of the Botswana health care system and infrastructure was carried out in May 2001, led by NACA, the Ministry of Health (MoH), African Comprehensive HIV/AIDS Partnership (ACHAP), and consultants from McKinsey & Company. The consultants concluded that a national AIDS treatment programme could be realistically and practically implemented using a phased roll-out approach to reach a total of 110 000 people in need of treatment over the next 6-8 years. The strategic recommendations to implement the programme concerned the wide-scale recruitment of skilled human resources, strengthening capacity for HIV diagnosis and testing, the implementation of counselling, education and support services and development of an information technology (IT) infrastructure.

The UNAIDS-brokered Accelerating Access Initiative was established at the international level in May 2000 to help increase access to AIDS care and treatment in developing countries, including high-burden middle-income nations. It is now a partnership of the UN with seven pharmaceutical companies (Abbott Laboratories, Boehringer Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline, F. Hoffmann La-Roche,

Gilead Sciences and Merck & Co., Inc.). The initiative provides a framework for bilateral company-government negotiations, and does not necessarily involve UNAIDS or other UN organizations. The MoH and the supplying companies in Botswana have individual agreements with the companies participating in the Accelerating Access Initiative (except for Merck, which is handled via ACHAP). In 2001, the Government of Botswana set up a cross-Government Task Force for ARV Drugs Price Negotiations to prepare for the launch of an ART programme in 2001–2002. The Task Force met with individual company representatives to agree on initial supply arrangements and prices, according to the framework of the Accelerating Access Initiative. Since then, companies have continued to offer price reductions to Botswana, in line with overall company discount strategies. The government-negotiated prices are for distribution in public sector or Government-supported health facilities. Significant (but lower) discounts are also negotiated by wholesalers serving the private market, particularly for use by the insured sector.

In 2002, Botswana officially launched an ART programme on a national scale. The national ARV roll-out in Botswana also involved a public-private partnership arrangement. The major partnership involved the Government, the Bill and Melinda Gates Foundation, the Merck Company Foundation/Merck & Co., Inc. and ACHAP. Other key partnerships include the Botswana Harvard Partnership (BHP) and the Botswana-USA (BOTUSA) project. Established in July 2000, ACHAP supports the goals of the Government to reduce the incidence of HIV and significantly increase the rate of diagnosis and treatment of the disease, by rapidly advancing prevention programmes, access to AIDS treatment and care, and patient management. The Bill and Melinda Gates Foundation and the Merck Company Foundation have each dedicated US$ 50 million over five years towards the project. Merck & Co., Inc. is donating two ARVs for appropriate treatment programmes developed by the Government for the duration of the initiative. The BHP provides training and technical support for health care workers involved in the programme, and directs operational research for programme improvement.

The ART programme was launched initially in four sites in Botswana, two referral hospitals and two district hospitals. The programme expanded to such an extent that by end-2004, all 32 district and primary hospitals throughout the country were providing ART. By end-2005, an estimated 85% of those in need of treatment were reported to be on ART (WHO, 2006). Overall, approximately 63% of the ART patients are female and most are aged 30-40 years. The next phase involves plans to roll out ART to clinics that serve as satellite clinics and also to strategically target areas from which the current sites are inaccessible.

2.3 Literature review

A dramatic reduction in HIV-related morbidity and mortality has been recognized in countries where ART has been made widely available (Anna et al., 2002). However it is also recognized that extremely high levels of adherence to ART (at least 95%) are needed to ensure optimal benefits, and that this may often be complex in terms of the pill burden, dietary restrictions and dosing frequency. Where adherence is sub-optimal,

HIV rapidly selects for resistance (Papella et al., 1998), in part due to rapid and error-prone replication (Perelson et al., 1996) but also often aided by the low genetic barrier of several ARVs to resistance (Kuritzes et al., 1996). Though effective adherence levels have not been fully defined for ART, levels of adherence below 95% have been associated with poor virological and immunological responses (Paterson et al., 2000; Orrell et al., 2003). Other data suggest that 100% adherence levels achieve even greater benefits (Fischl et al., 2000). Estimates of average rates of adherence to ART range from 50% to 70% in many different social and cultural settings, and the risks associated with sub-optimal adherence are extensive at both individual and societal levels (Chesney et al., 2000; Bangsberg et al., 2000; Liu et al., 2001; Nemes et al., 2004; Saferen et al., 2005).

Concerns about low adherence have been cited by those who question the feasibility of rapid scaling up of ART programmes in resource-poor settings (Stevens et al., 2004; Gill et al., 2005). Harries et al. (2001) argued that adherence problems would constitute a perceived significant barrier to the delivery of ART in sub-Saharan Africa. They warned that unregulated access to ARVs in sub-Saharan Africa could lead to the rapid emergence of drug-resistant viral strains and individual treatment failure, curtailing future treatment options and leading to the transmission of drug-resistant strains of HIV. The authors also maintained that, at present: there are few health care providers skilled in the provision of ART and in the management of patients who are on treatment; the existing health infrastructure is incapable of monitoring viral load, immune status, or the side-effects of ARVs; medicine procurement and distribution systems are weak; and interruptions in the medicine supply chain are likely. In addition, they highlighted current concern about the theft of medicines from health institutions for sale in the market, shops and private clinics, and across national borders.

2.3.1 Measurement of adherence

There is no gold standard by which to measure adherence to medication. Many studies employ a number of methods, either alone or in combination to measure adherence. The most common include: electronic drug monitoring (EDM) devices, pill counts, biochemical markers, pharmacy refill records and various self-reporting tools such as questionnaires and visual analogue. According to Gill et al. (2005) the hierarchy of adherence measures ranks physician and self-assessment report the least accurate, pill count intermediate and EDM the most accurate adherence marker. However, no single measure is appropriate for all settings or outcomes. It has been found that the use of more than one measure of adherence allows the strength of one method to compensate for the weakness of the other and to more accurately capture the information needed to determine adherence levels (Vitolins et al., 2000).

Studies in African settings have indicated optimal adherence rates (i.e., the proportion of patients who adhered to their ART schedule at least 95% of the time) ranging from 54% to 98% depending on the measure used: Botswana (Weiser et al., 2003: 54%); Nigeria (Daniels, 2004: 79%); South Africa (Ferris et al., 2004: 77%; Darder et al., 2004: 80%); Uganda (Byakika-Tusime, 2003: 67%; Munganzi, 2004: 98%); and Rwanda (Omes, 2004: 87%).

2.3.2 Factors affecting adherence

A number of factors have been associated with adherence to ART and are commonly divided into five intersecting categories (Reiter et al., 2003). These categories are: patient variables, treatment regimens, disease characteristics, patient-provider relationship, and clinical setting.

Patient variables

Patient variables include sociodemographic factors (age, gender, race, income, education, literacy, housing status, HIV risk factors) and psychosocial factors (mental health, substance abuse, sociocultural issues and support, knowledge and attitude about HIV and its treatment) (Carrieri et al., 2002; Nemes et al., 2003; Murphy et al., 2004; Machtinger and Bangsberg, 2005).

Sociodemographic and psychological issues have great potential to impact on adherence. For instance, family support and religious beliefs about illness and medication may influence motivation and adherence (Becker, 1990; Haynes, et al., 1996; Chesney, 1997). The issue of disclosure has also been found to have serious implications for adherence (Ormazu, 2000; Klitzman et al., 2004; Zea et al., 2005). For example, the use of medication may inadvertently reveal a person's HIV status; poverty may prevent individuals from following treatment-related dietary advice; drug and alcohol abuse may impair judgment and the ability to adopt and maintain routine medication use; and family responsibilities may require adults to place the health care needs of others before their own. Mental health problems such as depression have been associated with low adherence in HIV-positive adults and adolescents as have other psychological variables such as perception of one's ability to follow a medication regimen, or self-efficacy (Singh, 1996; Eldred, 1998; Murphy, 2001; Tuldra, 2002). Beliefs about health and illness, in particular about the necessity of medication to ward off illness and concerns about potential medicine-related adverse events have been found influential in both HIV and other disease areas (Horne, 2001).

Although side-effects have been cited by some studies in developed countries as predictors of adherence, experience of symptoms and views about medications may be complex and may vary according to the type of regimen (Chesney, 2000; Carr and Cooper, 2000; Ammassari et al., 2001; Carr, 2002; Murphy et al., 2004). Symptoms may stimulate the use of medications by acting as a reminder or reinforcing beliefs about the necessity for treatment. However, patients' expectations of symptom relief are also likely to have an important effect. This could be problematic if expectations are unrealistic, or where treatment is given for asymptomatic disease, as occurs with HIV infection (Horne, 2001). In addition, patients' concerns about the potential harm of ART may be entirely rational. Horne and colleagues have proposed that for some individuals missed doses may be a logical attempt to moderate this risk by taking fewer medications (Horne, 2001). Patients who understand the rationale for ART and treatment failure report higher adherence levels than those without this information (Anderson, 1999; Horne, 2001). Efforts both to reinforce information provided verbally with written information to take home and to check that information has been correctly understood are likely to be beneficial, as patients commonly misunderstand their

health care provider's instructions. One study found that 13% of patients prescribed ART were not taking their medication correctly, despite believing that they were (Bangsberg, 2001).

However, studies investigating the role patient variables play as predictors of adherence have produced largely inconsistent results. The tendency to ascribe low adherence to (often deprived) social groups is a well-established trend in the general literature (Horne, 1998). However, as later experience with antibiotics would demonstrate, low adherence is not restricted to certain social classes but is widespread and unpredictable (Lerner, 1998). Moreover, adherence rates vary not just between individuals but within the same individual over time (Carrieri, 2002). Adherence is therefore best thought of as a variable behaviour rather than as a stable characteristic of an individual. Most people will exhibit low adherence some of the time (Horne, 1998).

Treatment regimens

These include the number of pills prescribed, the complexity of the regimen (dosing frequency and food instruction), the specific type of ARV and medication side-effects. The complexity of the regimen and side-effects caused by it are clearly associated with sub-optimal adherence (Machtinger and Bangsberg, 2005).

Patient-provider relationship

This includes the patient's overall satisfaction and trust in the provider and clinic staff; the patient's opinion of the provider's competency; the provider's willingness to include the patient in the decision-making process; the affective tone of the relationship (e.g. warmth, openness, cooperation); the compatibility of race/ethnicity between patient and provider; and the adequacy of referral.

Clinic setting

This includes the availability of transport, general environment, flexibility of appointments, perceived confidentiality, and satisfaction with past experience with the health care system. Chesney (2003) found that dissatisfaction with the health services is a predictor of non-adherence.

Disease characteristics

This includes: the stage and duration of HIV infection, associated opportunistic infections, and HIV-related symptoms. The severity of the illness could impact negatively or positively on adherence to ART.

2.4 Definition of concepts

Adherence to ART

Adherence is defined as the "extent to which a client's behaviour coincides with the prescribed health care regimen as agreed through a shared decision-making process between the client and the health care provider" (KITSO Manual, 2004; Carter, 2004). For the purpose of this study, adherence has been defined as the use of ARVs at the right frequency of dosing. We also checked the number of pills (correct dose) and the time patients were taking them, using a 'sun and moon chart'. Ability to keep to this

pattern of utilization is defined as 100% adherence, while adherence of ≥95% is accepted as optimal adherence. Levels of adherence below 95% are considered to be sub-optimal. A composite adherence measure was computed as the means of the optimal adherence rates of the three measures used.

Knowledge about HIV and ART

The Oxford Dictionary defines *knowledge* as the information, understanding and skills that is gained through education or experience. For the purpose of this study, knowledge shall be assessed in terms of: what HIV is and how it can be transmitted; how ARVs work and how they should be used; whether the ARV users know that ARVs are not a cure and that they have to be taken for life. The level of knowledge was graded on a scale of 0 – 8, with a score of 75% and above depicting good knowledge.

Side-effects

For the purposes of this study, medicine-related side-effects have been categorized according to patient/ARV user and biomedical perspectives. Where pills were missed because a patient assumed that they might be responsible for certain symptoms that are not measurable, this has been classified as a patient/ARV user perspective, while those instances where side-effects can be recorded and assessed in observable terms were regarded as a biomedical perspective.

Disclosure

For the purposes of this research, disclosure was deemed to have taken place if a patient on ART had shared his or her status and the fact of being on treatment with at least one friend and/or any other person (including family members) for the purpose of deriving support if needed.

Treatment costs

Botswana offers ARVs free of charge to any citizen who is eligible for treatment. Weiser et al. (2003) found the cost of ARVs to be a major predictor of low adherence in their cohort. However, since this study is conducted in the public health sector, where there is no longer a charge for ARVs, this study will focus on other treatment-related costs such as transport fares, foregone wages, expenditure on snacks and meals while waiting to be seen at the clinic, and increased spending on food as a result of being on ART.

Chapter 3: Methodology

3.1 Introduction

This study was part of a three-country study on adherence to ART, which included Botswana, Tanzania and Uganda. The study proposals were submitted by participants of a WHO-run workshop on Promoting Rational Drug Use in the Community, conducted in Pretoria, South Africa, in September 2004. The proposals were appraised using a collaborative peer review process, following which research tools were designed at a workshop involving all three countries in Bagamoyo, Tanzania, in February 2005. Fieldwork took place in May and June 2005, and an analysis workshop for the Botswana team was held in Gaborone in July. The report was then prepared and finalized following a third workshop in Jinja, Uganda, attended by all three country teams. Technical advice was provided throughout by the Medical Anthropology Unit, University of Amsterdam, and by WHO.

3.2 Study design

This is a cross-sectional study which used both quantitative and qualitative methods to investigate the facilitators of and constraints to adherence to ART among adult patients in four public health facilities in Botswana. The research questions necessitated the triangulation of methods and this procedure was adopted in the study.

3.3 Study population

The study was conducted in four district hospitals across Botswana which were providing ART. The study population consisted of policy-makers, patients on ART (18 years and above) at the study sites, health workers and members of the local community.

3.4 Description of study sites

Botswana is a landlocked country in southern Africa, to the north of South Africa. Its population is mainly concentrated in the eastern part of the country and it has borders with Namibia, South Africa and Zimbabwe. The country is divided into nine districts and five town councils*: Central, Francistown*, Gaborone*, Ghanzi, Jwaneng*, Kgalagadi, Kgatleng, Kweneng, Lobatse*, North West, North East, Selebi-Pikwe*, South East and Southern. The study sites were located in North West (Maun), Central (Serowe and Mahalapye) and Kweneng (Molepolole) districts. Serowe and Maun were among the pilot sites and Mahalapye and Molepolole were the second generation facilities (Figure 3.1).

Figure 3.1: Map of Botswana showing the study sites

3.4.1 Maun

Maun is located in the north of Botswana and is a peri-urban tourist village with a population of over 124 000 (Ngami and Okavango) (Central Statistics Office (CSO), 2001). The village is home to a wide range of people of different backgrounds and a number of tourist companies are based there. It is the capital village of the North West district and most of the major council offices are located there. The Government hospital is situated in the central part of the village. At the time of the report, the hospital had 2690 registered patients, of whom most (2492) were on ART. There are three primary hospitals within 300 kilometres which also offer ARVs (Ghanzi to the south-west, Gumare to the north and Gweta to the south-east of Maun).

The ART patients are seen at the Infectious Disease Control Centre (IDCC) clinic which is located in a Portakabin close to the hospital entrance gate. The clinic is open Monday to Friday from 0730 hours. All the different units required to serve the patients are enclosed to form a quadrangle. The building is spacious and clean and has a waiting area that is large enough to accommodate patients. The entrance opens onto the reception area, where patients are registered for the day and given appointment numbers, and patient files are prepared and taken to the relevant officer. The clinic starts with a morning prayer and health talk organized by the staff for all patients in the clinic. The patients then disperse, moving on to the appropriate unit for their appointments.

3.4.2 Serowe

Serowe is a peri-urban village situated in the central part of the country. It is the capital of the Central District Council and many Government offices and other departments are located there. It is home to the Bangwato tribe. There are two tertiary institutions: Serowe College of Education and the Institute of Health Sciences. The Botswana Defence Force training camp is located about 40 kilometres from the hospital.

Sekgoma Memorial Hospital, a district hospital, was built over 75 years ago. However, regular maintenance has ensured that the buildings and surroundings are clean. The hospital serves the over 42 000 residents of Serowe (CSO, 2001), as well as patients from its catchment area which has a population of over 153 000. At the time of the study, the hospital had 3403 patients – all of them on ART. The ART programme was started in the hospital in May 2002. At that time, the treatment centre consisted of a resource centre and a prefabricated unit with a conference room and two consulting rooms with a very small reception area. This unit and what would later be the definitive IDCC building were built through funding from ACHAP. The IDCC is now a very large pre-fabricated structure located by the hospital entrance gate. It has two major entrances, one leading to the reception for consultations and counselling and another leading to the ARV dispensary. The unit provides adequate space for patients and health care workers. The clinic is open Monday to Friday from 0730 hours. It also opens occasionally on public holidays to cater for patients who may have run out of pills. Patients are received within the reception area and issued with numbers on a first-come-first-served basis, although priority is given to very sick patients and emergencies. A member of the health team, invited priests and others lead the patients in morning prayers and devotion. This is followed by a health talk about HIV, AIDS and ARVs which is given by a nurse or lay counsellor (usually a person living with HIV (PLWHIV)). This talk includes the use of audiovisual aids and covers HIV infection, prevention, disease progression, treatment with ARVs and monitoring, side-effects, nutrition and adherence issues. Patients are registered by data clerks, and nurses check their vital signs before directing them to the appropriate room for consultation or counselling. The hospital now has capacity for CD4 testing, but this was not available at the time of the study.

3.4.3 Mahalapye

Mahalapye is a peri-urban village located in the central part of the country. It is the capital of the Mahalapye central sub-district and most of the council's major offices are located here. Mahalapye Government Hospital is in the central part of the village. It is a 95-bed hospital which offers outpatient services, maternity services and general inpatient care. It serves as a referral facility for 44 health facilities in the sub-district, comprising one primary hospital, 15 clinics, 28 health posts and mobile clinics. Mahalapye sub-district has a total population of almost 110 000 people (Mahalapye District Health Team, 2005). It has four satellite clinics which refer patients to the IDCC when treatment is initiated. The hospital is located 200 kilometres to the north of Gaborone, along the main trunk road that runs across the country from the south to the

north. There is one primary hospital within 100 kilometres of this village which also provides ART.

At the time of the report, the hospital had 1960 registered patients of whom 1836 were on ART. Patients are seen at the IDCC clinic which is in a separate block of buildings located behind the main hospital. It is open on weekdays, with the exception of public holidays. All the different units required to serve the patients are grouped together, with the exception of the laboratory which is in the main hospital complex. The clinic is spacious and clean, but has only a small waiting area for patients. Patients meet the nurse on duty and their files are processed from the booking register, according to the order in which they arrived. They then queue to see the medical officer before going to the pharmacy to collect their medications.

3.4.4 Molepolole

Molepolole is a peri-urban village 50 kilometres to the west of Gaborone. It is the capital village for Kweneng district, which has a population of over 230 000 (CSO, 2001). The Scottish Livingstone Hospital is one of the second generation hospitals to offer ART. At the time of this report, the hospital had 2284 patients enrolled, of whom 1879 were on treatment. Although there is a primary hospital 40 kilometres south of Molepolole which also offers ART, there are no hospitals to the north and west which provide treatment services. As a result, some patients travel up to 200 km to access treatment at the Scottish Livingstone Hospital. The hospital consists of old buildings but a new ultra-modern hospital is currently under construction on an adjacent site. The existing hospital does not have a separate building for ART patients. All outpatients are attended to in the hospital outpatients unit, which has two separate consulting rooms for patients who come for AIDS management.

The ARV clinic operates four days a week from Monday to Thursday. All outpatients have their vital signs checked at the same reception area. Then patients who have come for AIDS management are given a number in a patient card - which is a different colour from the cards given to other outpatients - and join the queue for one of the two consulting rooms reserved for them. After the consultation, the ART patients go to collect their medication from the pharmacy which is housed within the outpatients department, while the other patients go to a different building to collect their medications. Adherence counselling and HIV-related specimen collection are provided at the resource centre, a Portakabin situated very close to the outpatients department. There is a television in the reception area/waiting room, and a conference room where patient education and counselling is done. Some reference books and videos are also available for patients' use. The Portakabin is often packed to capacity and some patients wait outside on the stone-paved area. Ambulances from different health posts and clinics are parked within the hospital. Ambulance transport is provided free of charge for ART patients who are very sick. Other ART patients can sometimes avail themselves of this transport if there is available space or if there is no public transport available to take them to the treatment centre.

3.5 Inclusion and exclusion criteria

All adult patients (aged 18 years or above) on ART at the four participating facilities who were willing to take part in the study were eligible for inclusion. Those who had just been referred or transferred from another site to the study site were excluded.

3.6 Selection and training of data collectors

The data collectors comprised research associates and social workers. An effort was made to ensure appropriate gender balance, so that any concerns about gender-sensitive issues could be addressed. Prior to data collection, a four-day training workshop was organized for the data collectors, which included the following: an overview of how the study came about; a presentation of the study proposal with a special emphasis on the objectives, methodology and data analysis; and a detailed collective review of the research tools. This involved detailed presentation and discussion in English, followed by discussion of the translated (Setswana) version of the research questions (since the data collectors would be interviewing respondents in Setswana). This training was followed by pre-testing of the tools at Palapye primary hospital, which was not involved in the study. Lessons learnt were discussed by both the data collectors and the researchers to help further modify the tools and clarify some of the issues. The following week, the tools were finalized, centrally coded and sent to the different study sites ready for data collection.

3.7 Qualitative data collection

Qualitative data were obtained using observations, semi-structured interviews, exit interviews and FGDs. The selection criteria are discussed under each tool below.

3.8 Observations

Health facilities

These were observed with a focus on issues such as structural outlay, privacy, conducive environment (structure, cleanliness, and workers' attitudes, availability of Standard Treatment Guidelines (STG) and Standard Operating Procedures (SOP); availability of medicines, adherence reminders, and availability of adherence support strategies.

Health workers

Four client visits (for ART users) per facility were observed during consultation. The type of health workers observed varied from site to site and included: receptionist/data clerks; nurses; doctors; social worker/lay adherence counsellors; and pharmacy personnel. The laboratory personnel were not observed because blood tests relating to AIDS treatment management were done by the IDCC nurses. The duty roster for each cadre was used to randomly select the staff members to be interviewed during the day of the visit. The clients observed were randomly selected from the register or as they waited for their consultation. Patients were observed over two days with two observations per day at different times of the day.

The focus was on the following: attitude; greetings; whether the patient was invited to ask questions and listened to; whether the health worker examined the patient when necessary; whether the patient was allowed to talk about any symptoms they were experiencing; whether patients were told what to do, where to go and when to come for medicine refill and review, and asked about possible side-effects; how well patients understood the instructions given and what kind of questions patients asked.

3.9 Semi-structured interviews

Health workers

At each study site, four health care workers involved in ART patient care were interviewed. This included the nurse, doctor, social worker/counsellor and pharmacy personnel. The health workers were randomly selected from the duty roster of the day from among health workers who had been involved in the management of AIDS patients for a minimum of three months.

Health workers at Maun Clinic, Botswana, take time from their busy schedules to entertain a young visitor.

The questions focused on the following: level of formal and non-formal training; use of SOP/STG; perception of the job; information and communication; availability of medicines; facilities and technical skills; perceived job satisfaction; problems and possible solutions. The interview also solicited demographic, socioeconomic and cultural information, general assessment of adherence, report of adherence in the previous three months, reasons for low adherence, reasons for high adherence, opinions on the quality of health care provided and on ways of improving adherence. It also assessed the counselling support available for health care workers caring for AIDS patients (care of carers).

ART patients

Five semi-structured interviews were conducted at each site. The patients were randomly selected from the register after determining the number of patients expected on the day of the site visit. Since the proportion of female patients among ART patients is higher than that of males, a gender mix of three females and two males was established. These interviews focused on the following: background information on the informant; perceived benefits of ART; adherence problems and possible solutions; social network and support; perception of quality of care in current treatment centre; cost considerations; views and experiences of ART; brief history of diagnosis and treatment.

Policy-makers

The interviews with policy-makers proved to be difficult because none of those selected for interview could be contacted. As a result, information was obtained from the Programme Manager of the National ARV Programme (MASA), the Chief Pharmacist at the MoH and the Principal Pharmacist at Central Medical Stores. The questions focused on the following: national roll-out plan; procurement of medicines; availability and sustainability of medicine supply and budgeting; adherence support and maintenance strategies; and national monitoring and evaluation system.

Key informants

The teams had planned to interview two to five key informants selected among the community members involved in HIV-related issues, using semi-structured interviews. However, most of the sites did not manage to do so. Only one site managed to interview the health workers who had accompanied patients from the referring facilities and one officer from one of the orphanages which also hosts a PLWHIV support group. The interviews were supposed to be held with community members such as: a church leader, home-based care volunteer, councillor, AIDS support group leader and a traditional healer. The aim was to focus on the following: support for ART patients to help them adhere to treatment; strategies in place to help them adhere; and some of the factors that may lead to sub-optimal adherence. Although these different leaders were not interviewed due to limited time for the data collection, all of the above-mentioned community members were represented in the FGDs.

3.10 Exit interviews

A total of 163 exit interviews were conducted with adult ART patients at the four sites. The selection of patients was done systematically and the interviews were spread out over several days, with five patients interviewed per day. From the determined sample size, the number of patients to be interviewed each day over the five-day period was determined. The number of patients expected in a given day was obtained from the data clerk's registry for those coming for doctors' review and laboratory tests, and from the dispensary for those coming for medicine refill but also for verification of the doctors' appointments. The expected number of patients was then divided by five to determine the Xth patient who would be picked and then every X^{th} patient was picked until five patients had been interviewed per day. If the patient declined, the immediate next patient was selected.

3.11   Focus group discussions

The FGDs were conducted with ART patients and with representatives of the local communities at the different sites.

ART patients

Administrative records, which include the pharmacy refill register, medical consultation appointment visit, and information from lay counsellors at the health facilities, were used to recruit the participants for the FGDs with ARV users. Efforts were made to include some of the patients who had been identified as having adherence problems. A total of eight FGDs were conducted, two per site, consisting of 8-10 persons per group. At each site, there was one FGD with female ART patients and another with the male patients.

The FGD was designed to provide insight into: patients' knowledge and perceptions of their illness and response to it; knowledge, perceptual understanding and expectations of treatment and social support. The FGDs also explored whether adherence was a problem among ARV users; and if so, what were the causes of sub-optimal adherence and the reasons for failure to adhere; and how some patients managed to maintain high levels of adherence.

Community members

The participants for community FGDs were selected with the assistance of the district HIV coordinators and leaders of PLWHIV support groups. Most FGDs included representatives from the PLWHIV support groups, traditional healers, members of faith-based organizations and home-based care volunteers. There were two FGDs per site for the community members, one for males and another for females.

The aim of the community level FGDs was to investigate community perceptions and beliefs about HIV, AIDS and ARVs as well as their perception of factors affecting adherence to ARVs. The FGDs also sought to elicit views on possible solutions and interventions that might improve adherence.

At the end of each FGD (for patients and the community), there was a debriefing session to give a general overview of what had been discussed, the problems identified and the possible solutions offered. Plans were made to refer patients, where necessary, for social, clinical or emotional support, but none of the participants needed referral. The focus group meetings were not audio-taped, and the importance of confidentiality was reinforced. The groups were facilitated by one member of the research team, with another member taking detailed notes and recording specific quotations when possible. At times there was more than one note-taker, which enabled the notes to be more detailed. The note-taker and the facilitator debriefed each other after each focus group, and the notes from the group discussion were then typed up.

3.12 Quantitative data

3.12.1 Sample size calculations

The sample size for the quantitative data required to obtain estimated proportions with 95% probability level was estimated using the CSURVEY design in Epi Info 6 version 3.22 (Centers for Disease Control and Prevention (CDC), 2004). The estimated total numbers of adults on ART in the study sites at the time of the study were 1425, 2400, 2055 and 1308 for Mahalapye, Serowe, Maun and Molepolole respectively. This was based on the assumption that 85% of the patients achieve optimal adherence (i.e. have adherence rates of ≥ 95%). These estimates were arrived at using the reports from the health care providers and predicted rates for Botswana (Weiser et al., 2003). Using the CSURVEY design in Epi Info 6, version 3.22 (CDC, 2004) (with expected rates 85% and worst acceptable estimate 78%) the sample size was estimated to be 93, 96, 95 and 93 for Mahalapye, Serowe, Maun and Molepolole respectively.

3.12.2 Sampling and data collection

Some of the quantitative data were collected using the exit interview tool, while the bulk of these data were collected using an adherence tool. The exit interview was carried out at the end of the patient's visit after collecting the medication, while the adherence tool was administered at any point during the consultation process but before collecting the medication.

Research associates conducted interviews for health workers, national level policy-makers and carried out the observations of health facilities. The research associates and the social workers conducted the 23 semi-structured interviews, 163 exit interviews and 514 adherence questionnaires with ARV users, while a research associate moderated 16 FGDs for community members and ARV users. Research associates collected the data and supervised the data collectors in a site where they are not resident. This was meant to increase the objectivity of the data collected and to address the issue of bias that might arise if research associates collected data in the facilities where they were employed.

3.13 Data analysis

Quantitative data

Quantitative data were initially stored in an Access database (Microsoft Access, 2003). Statistics were generated using Epi Info and SPSS version 13.0. The crude prevalence of adherence was estimated and its 95% confidence interval calculated. The Chi-square test was used to compare adherence rates among two or more categories. Logistic regression models were used to determine predictors of adherence and to estimate the independent and multiple effects of selected factors on adherence. All hypotheses were tested using $\alpha = 0.05$ level of significance.

Adherence rates, measured as the percentage of pill intake over a specified time, were estimated using three methods: two-day recall using a 'sun and moon chart', which depicted the sun at different times of the day and the moon at night; visual analogue (a one-month recall using an uncalibrated 10 cm line); and a one-month pharmacy pill count. In the visual analogue, respondents were requested to indicate, by marking on the line, how they perceived their adherence over the past month. The overall adherence rate was estimated as a composite measure (i.e. the average of the one-month visual analogue, pharmacy pill count (one-month) and the two-day recall.

Pill count (one-month)

Pill counts were calculated by subtracting the number of pills returned from the number of pills issued. This provided the amount of medication used by the patient during this period. The amount used is then divided by the expected amount and multiplied by 100 to determine the percentage adherence per participant.

Self-report (two-day recall)

In the two-day recall the patients were asked to recall the frequency and timing of medication as well as their food intake over the previous two days. The data were captured in the sun and moon chart.

Self-report (one-month recall)

Participants were asked to indicate their adherence rate using a visual analogue line measuring 10 cm. The distance from zero to the tick on the line multiplied by 10 was considered to be the estimated percentage adherence rate.

Most of the patients interviewed were on first-line regimens, which include: efavirenz, lamivudine and zidovudine. These do not have any food requirements. However, some patients may choose to take them after meals to reduce nausea. Therefore since most of the ARV combinations used for first-line regimen in Botswana do not necessarily require that they be taken with food, the variable timing of taking medication and whether the drugs were taken with food or not were dropped in the analysis.

Qualitative data

The qualitative data collected were analysed with a view to gaining understanding of the factors that influenced adherence to ART. The data analysis process included a four-day workshop, with technical assistance provided by the University of Amsterdam. The work involved reading through the data from the qualitative research tools – which included the semi-structured interviews with health workers and ARV users, and the FGDs with ARV users and the community – in order to identify key themes. Initially, 28 themes were identified. The quotes were then manually pasted onto theme cards for easy perusal. A general thematic analysis was then conducted, focusing on similarities and differences of perspective between different groups of respondents. Further analysis revealed that the themes appeared to be linked, and these were then analysed together. Information was analysed to capture the different perspectives of the different actors: ARV users, health workers and community members. Where there were agreements or conflicting views, these were shown.

3.14   Emic perspective

As a research team, we agreed to take into account the emic perspective which assumes that 'there is no one correct view'. This is a helpful premise when considering the thoughts and opinions of ARV users, health care workers and the community, first differently and then collectively. This approach permits a nuanced interpretation of what has been reported by a wide variety of respondents.

Emic perspective is described as the "insider's" or "native's" interpretation of or "reasons" for their customs or beliefs. It describes what things mean to the members of a society. Emic measures focus on local and idiosyncratic content. In this context, the emic assessments provided a qualitative description of the idiosyncratic meaning ascribed to adherence. To understand the cultural context of health problems as it relates to adherence to ART in Botswana, it is essential to work with this key concept. The emic perspectives are useful for examining when we are seeing things from our own point of view and when we are trying to understand someone else's view of things. The emic perspective shows the meaning that people attach to things from their own cultural perspective. For example, some cultures view worms (Ascaris) in children as normal and believe they are caused by eating sweets.

Experience shows that health programmes that fail to recognize and work with indigenous beliefs and practices fail to reach their goals. Similarly, research to plan and evaluate a health programme must take cultural beliefs and behaviours into account in order to understand why programmes are not working and what to do about it.

Health and illness are defined, labelled, evaluated and acted upon in the context of culture. If you wish to help a community improve its health you must learn to think like the people of the community. Before asking a group of people to assume new health habits, it is wise to ascertain the existing habits, how these habits are linked to one another, what functions they perform, and what they mean to those who practise them. This approach is relevant to our research since it is based on an intervention outcome.

3.15   Ethical considerations

Health research unit approval

Approval was obtained from the Botswana MoH, through the National Health Research Committee and the managements of the four study sites.

Informed consent

The informed consent process involved the data collector giving a verbal explanation to each potential participant on the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits involved, and any discomfort it might entail. Each potential participant was also informed that participation in the study was completely voluntary and that they could withdraw at any time, and that withdrawal of consent would not affect their subsequent treatment or relationship with the facility staff or any other person.

The participants were also assured that all information gathered would be treated as confidential and would be accessible only to the researchers, who would be responsible for its safekeeping. There would be anonymity in the reported findings.

3.16   Feedback

Feedback was given to the health workers in a group discussion in order to share the preliminary results but also to clarify some of the issues where necessary. Study participants, institutions' managements, as well as various stakeholders will be given the study report when it is available. Providing feedback will hopefully be an opportunity for interaction with stakeholders in generating ideas about the possible interventions that may increase adherence. This is also important for ensuring ownership of any intervention strategies that may be developed.

Chapter 4: Quantitative results

This chapter details the quantitative findings from the adherence measurement tool and the exit interviews from the cross-sectional study of ARV adherence in Botswana.

4.1 Adherence measurement tool results

4.1.2 Demographic data and patient characteristics

Demographic data and patient characteristics are summarized in Table 4.1. A total of 514 participants from four study sites participated in this study. Of these, 122 (24.7%) were from Maun, 128 (24.9%) from Mahalapye, 115 (22.4%) from Molepolole and 149 (29%) from Serowe. The mean age was 38.3 years (95% confidence interval 37.4 – 39.2). Most of the patients are in the age range 20-40 (60.2%) and 15% were aged over 50 years. The sample included more women (67.6%) than men (32.4%) consistent with the current pattern of the Botswana statistics on ARV enrolment. Almost 35% had secondary school education level and 42% reported not being in any form of employment.

Table 4.1 Demographic data

Finding		No. (%)
Age (years) (n=507)	<30 30-39 40-49 >50	95 (18.7) 211 (41.6 127 (25.0) 74 (14.7)
Sex (n=510)	Male Female	165 (32.4) 345 (67.6)
Level of education (n=505)	None or incomplete primary Primary Secondary Tertiary or Vocational	152 (30.1) 153 (30.3) 178 (35.2) 22 (4.4)
Employment status (n=511)	Employed Unemployed	298 (58.3) 213 (41.7)

4.1.2 Distance to health facility

About 25% of the participants travelled more than 50 km to the health facility and the maximum distance travelled was 200 km.

4.1.3 Time on treatment

Most of the participants (90%) had been on treatment for less than 24 months, with an average and median of 11 and 9 months respectively (Figure 4.1). This reflects the nature of the expansion of the programme.

Figure 4.1: Distribution of the months on treatment (N=505)
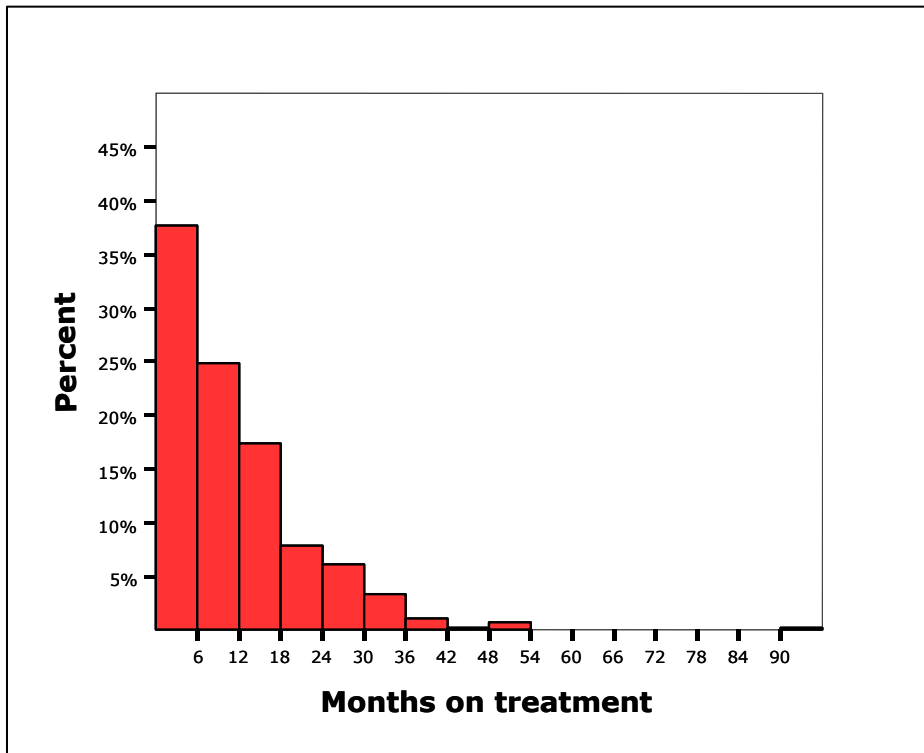
4.2   Rates of adherence to ARVs

Assessments of adherence to ART are summarized in Table 4.2. The optimal adherence rates (indicative of being adherent at least 95% of the time) using the pharmacy pill count, self-report (visual line) and self-report (two-day recall method) were 75%, 60%, and 96% respectively. The composite mean adherence was estimated at 77%. The raw means of all measures (uncategorized) are summarized in Annex I.

Table 4.2: Adherence rates

Finding	Facility/No. (%)					95% confid-ence inter-val
	Maun	Mahalapye	Molepolole	Serowe	Total (%)	
Self-assessment of adherence (visual line one-month recall)	(n=112)	(n=124)	(n=114)	(n=146)	(n=496)	
Optimal adherence (at least 95%)	57 (51)	91 (73)	67 (59)	80 (55)	295 (60)	55.7 – 64.3
Sub-optimal adherence (<95%)	55 (49)	33 (27)	47 (44)	66 (45)	201 (40)	35.7 – 44.3
Assessment of adherence (pharmacy pill count method)	(n=106)	(n=107)	(n=109)		(n=322)	
Optimal adherence (at least 95%)	97 (92)	63 (59)	82 (75)	*	242(75)	70.3 – 79.7
Sub-optimal adherence (<95%)	9 (8)	44 (41)	27 (25)	*	80 (25)	20.3 – 29.7
Assessment of adherence (Two -day recall)	(n=121)	(n=125)	(n=115)	(n=147)	(n=508)	
Optimal adherence (at least 95%)	109 (90)	122 (98)	111 (97)	144 (98)	486 (96)	74.3 – 97.7
Sub-optimal adherence (<95%)	12 (10)	3 (2)	4 (3)	3 (2)	22 (4)	2.3 – 5.7
Composite mean (average of 3 measures)						
*Mean optimal adherence (at least 95%)	77.3	76.7	77.0	*75.5	77	73.1 – 80.9
Sub-optimal adherence (<95%)	22.7	23.3	23	24.5	23	19.1 – 26.9

* Serowe composite mean optimal adherence rate calculated without pill count data because of data quality problems (pill count records) found at the site during data collection.

4.3 Reasons for skipping medication

The most common reasons cited for missing medication were: forgetfulness (18%), costs and logistics (13%), work and home duties (12%), stigma (7%), lack of support (4%), lack of food (2%) and alcohol abuse (2%). See Table 4.3 below.

Table 4.3: Reasons for missed medication

Reason	No. cited as reason	% reported
Simply forgot	90	17.5
Logistics and costs	67	13
Work or home duties	61	11.8
Stigma	36	7
Lack of care/support	18	3.5
Misunderstood instructions	16	3.1
Lack of food	11	2.1
Distance	10	1.9
Hospitalized	9	1.7
Alcohol abuse	9	1.7
Depressed	6	1.2
Feeling better	3	0.6
Pill burden	3	0.6
Shared pills	2	0.2

4.4 Factors affecting adherence to ART

4.4.1 Costs

Consistent with the current policy on registration costs, most participants either reported paying 2 pula/P2 (about 40 US cents) or did not pay anything. The P2 charge is the normal administrative fee payable by anyone who visits a health facility. Twenty-nine per cent of the participants indicated that they had experienced a loss of income as a result of coming to the clinic and 57% indicated changes in general expenditures. However, there was no significant association between employment status and reported loss of income (χ^2=1.526; p=0.217). The median cost of travelling to the facility was P10 (approx US$ 2.00) and 80% of the participants reported spending less than P15 (approx US$ 2.50) for transport. The mean cost of transport was not significantly different between the optimally adherent and sub-optimally adherent (t=0.0208; P=0.978).

4.4.2 Gender and employment

Using the visual analogue method, no association was observed between gender and adherence (χ^2=0.743; P=0.389). However, there is a significant association between employment status and adherence (χ^2=5.116; P=0.024), suggesting that people who are employed are more likely to adhere to treatment. A higher proportion of the employed (65%) had optimal levels of adherence compared to 55% among the unemployed.

Figure 4.2: Adherence rates (measured by visual analogue) by sex and occupation
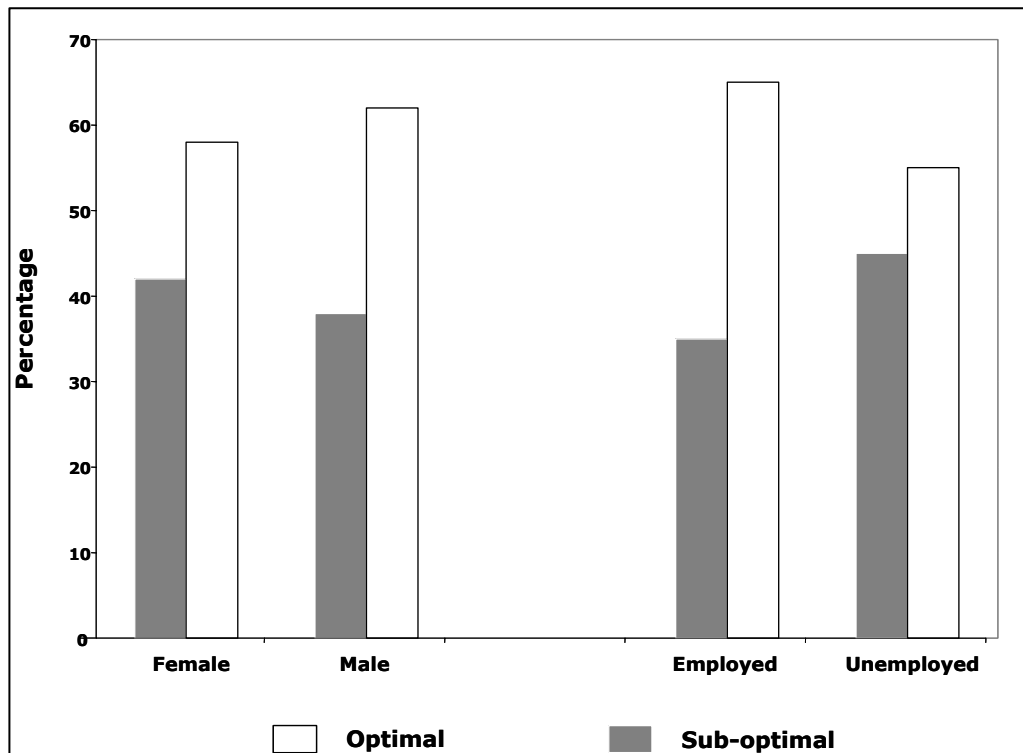
4.4.3 Knowledge of HIV and ARVs

The knowledge about HIV and ARVs was rated using eight questions worth one point each. Fifty-eight per cent of the participants got a score of at least 75%. For the purpose of evaluating the impact of knowledge on adherence, a cut-off of 75% was used (>75% good knowledge). A significant correlation was observed between knowledge of HIV and ARVs and adherence level (optimal and sub-optimal) for pill count (χ^2=13.558; P<0.0001) and visual analogue (χ^2=3.890; 0.049). However, there was no correlation between knowledge of HIV and ARVs and adherence levels in the two-day recall measure (χ^2=1.127; P=0.288).

Table 4.4: Association between knowledge of HIV and ARVs with level of adherence and measures used

Measure	Level of Adherence	Good	Poor	χ^2 value	P-value
Pill count* (N=322)	Sub-optimal	69	11	13.558	<0.0001
	Optimal	156	86		
Two-day recall (N=496)	Sub-optimal	9	13	1.127	0.288
	Optimal	255	231		
Visual analogue (N=508)	Sub-optimal	95	106	3.890	0.049
	Optimal	166	129		

* Serowe data excluded from the analysis.

4.4.4 Education

There was no association between educational levels and adherence rates ($\chi 2$ =3.44; p=0.751).

4.4.5 Quality of health care services

The majority of the participants (92%) were satisfied with the quality of health care services.

4.4.6 Side-effects

Of the 58% of participants who reported having experienced side-effects, 8% reported having skipped their medication as a result.

4.4.7 Treatment supporters/reminders and appointments

Most of the participants (74%) said they had someone to remind them to take their medication. Twenty per cent reported having missed some appointments.

4.5 Predictors of adherence to ART

Multivariate logistic regression analysis was performed on the measures of adherence using selected explanatory variables including age, gender, occurrence of side-effects, education, occupation, cost of transport, other treatment-related costs, loss of income, months on treatment, missed appointments, and knowledge of HIV and ART (Annex 2). The variable of missed appointments was a significant predictor of adherence (Wald statistic χ^2=4.851; p=0.028) and was associated with levels of adherence to ARV treatment (χ^2=5.86;P=0.016). This finding was also reported by Nemes et al. (2004).

Independent t-tests between the sub-optimal and optimal groups for age, distance to facility, cost of transport and months on treatment indicated no significant differences (P>0.05) in both one-month recall methods (Table 4.5).

Table 4.5: Independent t-tests for comparisons between optimal and sub-optimal adherence groups

Variable	Visual line one-month recall		One-month pharmacy pill count	
	t-test	P-value	t-test	P-value
Age (n=442)	0.031	P=0.975	-0.781	0.435
Distance to facility (n=492)	-0.047	P=0.749	-1.746	0.082
Cost of transport (n=479)	0.028	P=0.978	-1.502	0.134
Months on treatment (n=489)	1.182	P=0.238	0.233	0.816

4.6   Quantitative results of exit interviews

Exit interviews were carried out with 133 (63%) participants, mostly females. This gender imbalance may reflect the fact that more females than males are infected with HIV in Botswana and/or the better health-seeking behaviour of females. Most of the participants were in the 30-44 age groups (Figure 4.3), 58% were not employed and over 80% had been on treatment for less than 24 months.

Figure 4.3: **Age distribution of participants (N=128)**
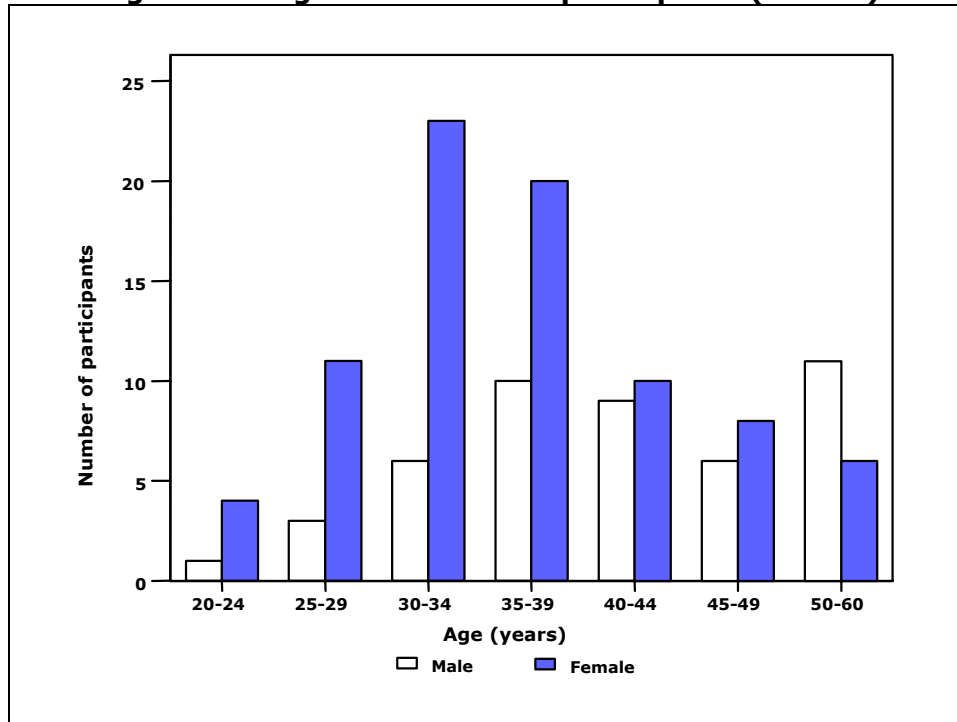
The respondents were asked what issues were covered in their discussion with the health worker during consultation. They reported that the issues discussed with the health workers were counting of pills (97%), side-effects (32%), refill and check-up dates (19%), medication schedule and referral for counselling for any missed doses (32%), and effects of missing doses and other medications taken (18%). Seventy-seven per cent of the participants admitted to have missed some doses since they started treatment. In order to remind themselves to take their medication the participants mentioned the use of mechanical devices (80%) (i.e. radios, cell phones, watches), a partner or family member (11%) and self-discipline (9%).

In terms of costs, 44% reported an increase in expenditure and 37% reported loss of income due to clinic visits. Respondents were largely satisfied with the quality of care they received. Generally the participants felt they: were listened to (99%); were given a chance to state their problems and ask questions (99%); were treated with respect (98%); trusted the health workers (94%); and were allowed privacy during consultations (89%). The major issue that was raised by the participants was the length of time they

had to spend waiting to be attended to at the health facility (Figure 4.4). Over half (53%) of the respondents reported spending at least four hours at the clinic. In some cases, participants spent the whole day there after arriving two hours ahead of opening time (Figure 4.5)

Figure 4.4: Satisfaction with the amount of time spent at the clinic (N=133)
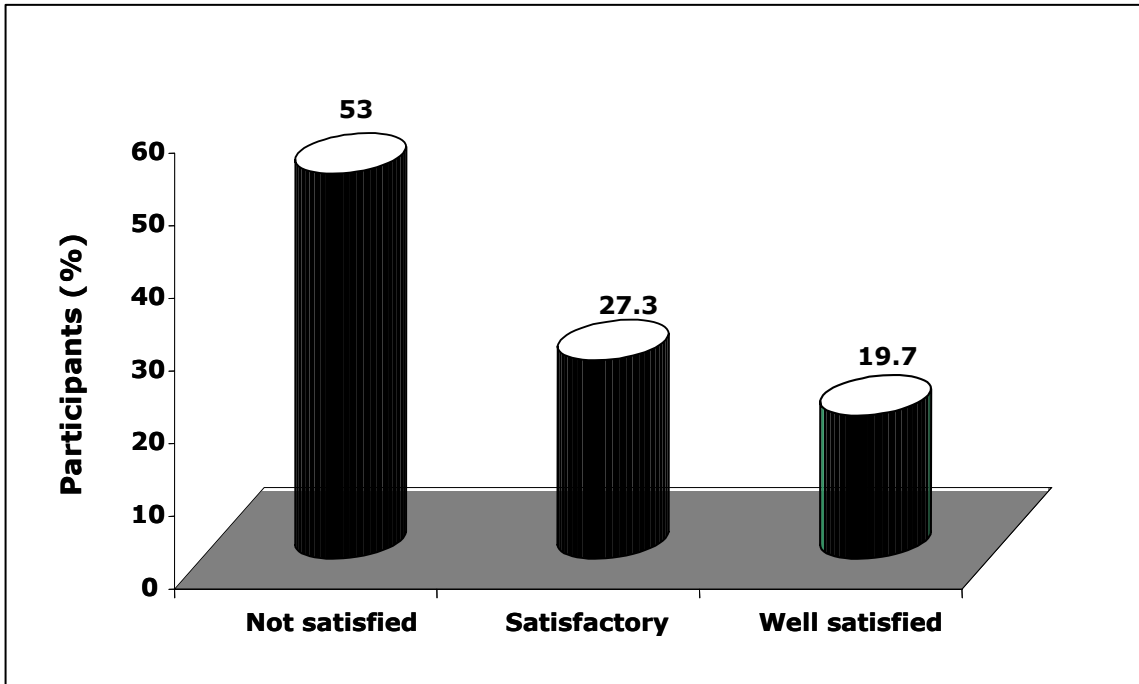
Figure 4.5: Distribution of the time spent by participants at the clinic (N=128)
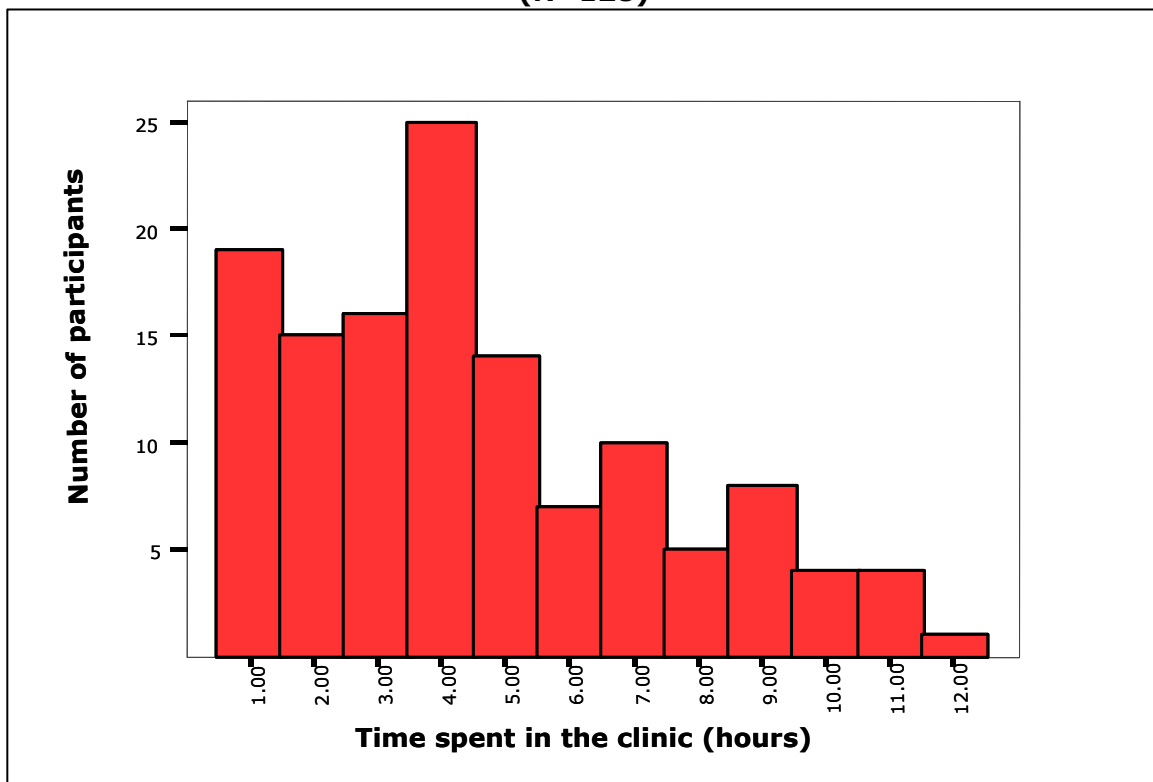
Chapter 5: Qualitative results

This chapter focuses on the findings from the qualitative data on the constraints and motivators of adherence to ART among adult patients at the four public health facilities in Botswana (Table 5.1). These data are based on the perspectives of patients on ART, the community and health care workers.

5.1 Constraints to adherence to ART

In the discussions on constraints to adherence, the study identified six interrelated themes. These are presented below, without any order of priority.

5.1.1 Gender and non-acceptance of HIV status

Gender was identified as being strongly associated with acceptance of HIV status. Respondents stated that women talk about HIV and test early, and so are more likely to accept their status than men. Men were said to avoid testing for HIV. But when their partners test first, they often blame them for bringing the virus. As a result, men can become angry and violent and tell the partner not to bring the medication into the ('his') home. In Maun, there were stories of women who were hiding their ARVs in a neighbour's house for fear that their husband would discover that they were still taking the pills. This interfered with adherence in that most of the time these women would be dependent on their neighbour's schedule for access to their medication. Women were also reported to avoid telling their partners about their HIV-positive status in order to protect the relationship. This results in re-infection and in the hiding of medication.

Most respondents agreed that individual acceptance of positive HIV status is key to the behavioural changes that are required for a good health outcome. Non-acceptance of positive HIV status and of life-long dependency on ART for survival were perceived by many respondents as a major barrier to adherence. A female ARV user put it succinctly:

> *"In life people feel shy to tell other people about their status and that they are on ARVs. People do not advise them because they do not know they are on treatment. When one has a visitor, he/she will start skipping treatment. They end up dying because they fail to take the treatment."*

When an ARV user is in a state of denial, it is difficult to disclose to others, medicines are hidden from friends and relatives, and when necessary they skip medication to ensure that friends and family do not discover that they are HIV-positive. A male ARV user explained:

"I usually miss my medications when I visit friends because I have not told them about my HIV and so I do not want them to see my medications."

Meanwhile, a female ARV user said:

"My boyfriend did not tell me his status and was against me going to test for HIV because I was pregnant. As a result he hid his ARVs from me. He kept all the other medications on the dressing table but one time when I was cleaning, I saw some bottles of medications hidden away. I wrote the names on the paper and went and asked the nurse about them. She told me they were ARVS. I went back and asked him why he did not tell me. I think he wanted me and the baby to die because he did not want us to get help by testing."

Many respondents thought that women were more likely to accept their HIV status than men and that women generally have better health-seeking behaviour than men. Some women consider the better health-seeking behaviour of women to be due to their desire to stay alive in order to care for their children and other loved ones, despite being blamed by men for the disease. Health care workers attributed the greater acceptance of positive HIV status by women and their better health-seeking behaviour to the fact that women have always been very close to the health care system through the maternal and child clinics.

One ARV user in a female FGD explained:

"Women accept their status easily; we chat and get encouragements from other people. We like to know our HIV status even while still young without having children; we would like to know so that we may help significant others."

Another female ARV user said:

"Men are stubborn. I had a partner and we had a child who later passed away. I tested and my husband accepted me but he refused to test himself. I wonder why he refused."

One of the men said:

"Men are brave, strong. We believe in our tradition/culture. It is not easy for us to go and consult the doctor. Men believe in herbs but the disease doesn't tolerate that."

Respondents generally agreed that acceptance of status could result in increased disclosure and possibly in improved adherence.

5.1.2 Non-disclosure

Non-disclosure was one of the themes that emerged as a barrier to adherence. Respondents stated that failure to tell someone (e.g. a friend or family member) could be due to reasons such as: fear of being discriminated against, stigma, job loss or abandonment. It was not uncommon to hear of people who were rejected by their

partners because they had revealed their HIV status. This problem is highlighted by the following quotes from a FGD involving female ARV users:

"Those on treatment at times do not tell their partners."

"Some women hide their status fearing to be dumped by their partners after disclosing their HIV status."

"A man will leave you if you tell him."

Men, on the other hand, complained that women do not disclose their status in order to keep them in the relationship. One of them said:

"Those who get pregnant while on treatment might not have told their partner."

The male respondents also maintained that no man would refuse to use a condom if they knew that the woman was HIV-positive. Meanwhile, young adults who were in relationships also found it difficult to disclose their status, because they are tested independently and do not necessarily know the status of their partner. One ARV user explained:

"For us the unmarried youth, you will find that even when you know your status, it is not easy to disclose because you do not know your partner's status. You end up hiding medications because when you tell them, they disappear after a short period. We usually weigh the situation because we would not want our names to be defiled."

If one partner is on ART, they may resort to pill hiding, occasional skipping of medications and failing to keep clinic appointments for refills or review, so their partner does not find out that they are on ART.

5.1.3 Perceived lack of social support, fears about stigma and privacy concerns

Many participants discussed issues relating to lack of social support, fears about stigma and privacy concerns that acted as constraints to adherence. These issues are presented under the following three levels: individual, family/friends, and workplace.

Individual level

Some respondents identified the personality traits of the individual as being important in determining how they perceive stigma, privacy issues, and the availability of social support. Lack of self-motivation was said to result in low adherence. People who lack self-motivation are less likely to disclose their status and therefore less likely to attract social support. And even where social support is available, there may be a tendency not to use it. This was supported by a female respondent who said:

"My younger brother who was on treatment refused to take his ARVs, and even to talk to the social workers visiting at home. He never did well and ultimately died."

Some respondents perceived the partial integration of ART with other health services as exposing them to the likelihood of being stigmatized, as one ARV user at a semi-integrated health care facility explained:

> *"We will like to have our own clinic instead of being mixed with these other people. They are always staring at us, especially when we come to this door (labelled "ARV Dispensary"). I like it at Princess Marina Hospital* (in Gaborone) *where ARV users are isolated from the rest of the people. Some people fail to come and refill here because they are shy to be seen by their friends."*

Family/friends

Family social support and acceptance of a relative or friend living with HIV/AIDS, was found to depend on the nature of the existing bonds before the illness and how the individual has contributed to the relationship. A male ARV user said:

> *"If you don't have a partner you are in trouble. The partner can take care of you when you are sick. The parents may say you only know them when you are sick, you used to go around with other ladies when you were fit. They deny you and offer you negative support."*

A female home-based care volunteer observed that:
> *"Some of the patients are suffering. There is one man who is suffering because his wife does not want to care for him. She does not cook for him and does not give him his medicines. We sometimes try to bring him food but when she sees us, she chases us away. The man is so thin."*

Within the same family, some members may be more supportive than others, as a female ARV user explained:

> *"I get support from my sister and my children. My nieces, they are always laughing at me and telling people that I have the virus. They would not even give me my medications when I am too sick."*

Most ARV users said they would not disclose their HIV status and the fact that they are on treatment to anyone if they believed it would result in stigmatization and a lack of support. Unresolved family conflicts may also result in lack of support. This was captured in the story of an ARV user, who said:

> *"My discrimination did not start with my HIV status but emanated from family conflict. I ended up moving out of the family home with my children. I continued to meet obligation to the family but when I got ill and was hospitalized, they never visited me. Currently my parents have passed away. However, if there is illness or death of one of our relatives I do assist."*

Workplace

The reaction of employers and employees towards HIV/AIDS in the work environment is a reflection of the attitude of the community and its culture. A supportive work environment creates a conducive atmosphere in which PLWHIV do not have to fear about stigma and discrimination.

Many of the respondents interviewed, especially those who worked as shop assistants, farm workers and for safari companies, cited non-release by employers as a barrier to adherence to treatment. Many of these workers said they could not even freely discuss the issue of their HIV status and treatment at work, for fear of being victimized by their employers. One ARV user said:

> *"I was once ill-treated in my workplace and forced to transfer to a place about 400 kilometres away but I am supposed to see the doctor. I resigned from the work because I preferred to stay close to my treatment site."*

A female ARV user, who works as a shop assistant said:

> *"I resorted to asking my relatives to pick up my medications because my employer refuses to release me to go and pick up my medications."*

In northern Botswana, freehold farms and safari companies are the major employers of unskilled labour. These work settings are sometimes located in difficult terrains, a long distance from the ART clinics. For some safari company employees, access to a treatment centre may be by air. In some of these settings, employees work for periods of three to four months before being entitled to a free flight back to the mainland. For these people, difficulties with transportation to attend clinics for treatment monitoring and medicine refills were major issues of concern.

One of the health workers explained:

> *"For the employees in the ranches and cattle posts, transport to health facilities poses a problem. Some employers do not release their workers."*

There were reports of cases where individuals who worked on ranches and for construction companies were forced to take pay cuts for attending clinics. These attitudes by employers were said to constitute a barrier to adherence as people remained at work instead of attending the clinic. Most of the ARV users interviewed believed that more should be done by the Government to protect PLWHIV in the workplace, as this would help improve adherence.

5.1.4 Logistics and costs

In Botswana, patients do not pay for ARVs offered within the public sector. Logistics and costs were therefore viewed in terms of the availability of transport, transport-related costs, lost wages, money spent on snacks and food while attending appointments, and other treatment-related costs, as perceived by the ARV users.

In the qualitative survey, the health workers reported lack of transport – either no means of transport or no money to pay the fare - as the reason most frequently cited by patients for failing to attend the clinic for treatment review or medicine refill. Many ARV users, especially those who were not employed, said that lack of money to pay for transport was a problem. Some ARV users complained that the treatment centre was too far away and not always easy to access. An ARV user who had to travel from an outlying cattle post to the village to get a medicine refill said:

> *"I once missed my appointment for refill because there were no vehicles coming here. I was in the stop from early morning and by noon I went back home. Fortunately I still had some medications."*

Another ARV user from one of the remote villages said:

> *"The clinic vehicle used to transport us. Now they say we are better so we should transport ourselves. I usually get 'piece jobs' and use the money to come and pick up my medicines."*

5.1.5 Misconceptions

There were some concerns among ARV users about the language used to communicate the results of laboratory tests to patients. As one ARV user said:

> *"One of the patients stopped the medicines because he was told that his viral load was undetectable, so he stopped taking his pills because he thought he was cured."*

5.1.6 Alcohol and substance abuse

Alcohol abuse was cited as one of the reasons why some patients are not adhering to medication. It was reported that even the local newspapers had on several occasions cited alcohol abuse as one of the reasons for non-adherence. One of the respondents said:

> *"Some of the patients who take alcohol end up forgetting to take their tablets or omitting treatment."*

Another respondent said:

> *"Those who take alcohol sometimes lose their drugs in the bars when they are drunk."*

5.2 Facilitators of adherence to ART

In our efforts to identify facilitators to adherence six main themes emerged. These are presented below, not in order of priority.

5.2.1 Acceptance of HIV status and disclosure

Most respondents (ARV users, community and health care workers) agreed that individual acceptance of HIV status was key to the necessary behavioural change that is required for good health outcomes.

One of the ARV users said:

> *"Since the beginning, I told myself that this disease is just a disease like any other disease. You should accept yourself."*

Similarly, another ARV user said:

> *"As long as one has accepted his/her situation and is committed to treatment, there will be no problems."*

5.2.2 Self-efficacy and the ability to take and adhere to ART

Self-efficacy refers to patients' beliefs about their capabilities and their ability to exercise personal control. Perceived self-efficacy was stated as one of the key variables that was critical to adherence. Some respondents stated that it was important to be convinced that it was possible to take the medication correctly.

One ARV user explained:

> *"Taking these medicines is a personal decision. When the time to take them comes, I take them regardless of whether I am hungry or not."*

One of the strategies suggested by respondents was abandoning a previous lifestyle (e.g. alcohol abuse, womanizing) in order to focus on treatment. Some participants maintained that people who are highly motivated are more likely to be adherent to treatment.

One ARV user described the treatment as one that requires commitment and control:

> *"This treatment controls one's movement. When you go out, you got to return and take them."*

Another ARV user said:

> *"Problem why patients fail to take treatment is because they lack self-discipline."*

5.2.3 Belief in the efficacy of ARVs in treatment/pre-treatment health state

The fear of relapse or perceived vulnerability to negative outcomes from sub-optimal adherence was considered to be a major motivator of adherence. Most of the respondents stated that, despite being often preoccupied with their own health concerns and fears, the availability of ARVs had given them a "new lease of life." Some of the respondents stated that individuals were motivated to begin treatment if they experienced a decline in their health status, believed that therapy would prolong life, and believed that they could cope with the treatment regimen and its potential side-effects. One of the respondents, who had recovered as a result of taking the ARVs stated:

"If you had seen me a few months ago I could hardly get out of bed. I was like this (showing the smallest finger). Now here I am. You cannot even believe it. If you have been there, you will take them (ARVs)."

Another male ARV user also stated in Setswana that *"rona re ka bo re seyo,"* which means: *"Some of us would not be here if it were not for the ARVs."*

5.2.4 The need to care for others

The desire to stay alive can be greatly reinforced by the recognition that your loved ones might not cope in your absence. Women were found to be always concerned about their children and aged parents. The desire to continue to be around for them for their sake was found to be a critical motivator for most women. These sentiments were shared by other female respondents:

"We give birth to children, and we don't want to orphan our children… I don't want my children to be raised by a step-mother. Fathers are not good at raising children."

"As women, we feel pity for our aging parents, especially if the other children are irresponsible. You wonder who is going to take care of the parents if you were to die first."

"I feel I'm the best thing for my children. I'm afraid of dying and my baby has to suffer without me. My children are the best things that ever happened in my life. And I'm wondering how they would feel if they had to lose me."

5.2.5 Social support

Social support is based on the kind of relationships and interactions that provide individuals with assistance or feelings of attachment. Generally, most respondents agreed that the availability of social support was critical for good adherence to ART.

Children were reported to be among the main providers of social support, with older (primary or secondary school age) children taking a leading role in reminding the parent (often their mother) of pill times. For those in stable relationships, the availability of social support from the partner was determined by whether that partner had tested and, if so, whether they had accepted their status.

One of the respondents said:

> *"I once went to my mother and told her that I am taking life-long treatment and she accepted me. My husband also accepted me. He is the one who wakes me up to come for treatment."*

Another said:

> *"My husband is HIV-negative but he always reminds me to take my ARVs. My children also remind me."*

5.2.6 Effective adherence counselling

Adherence counselling is aimed at promoting adherence to ARVs and preventing further transmission of HIV. The respondents stated that they had received counselling before the initiation of therapy. The issues covered included: HIV and AIDS; mode of transmission; prevention methods; how ARVs work; the importance of adherence; side-effects and how to minimize them; interactions between ARVs and other medicines (including traditional medicines) and alcohol. The effectiveness of the counselling process was highlighted by some respondents who stated that, even though they do experience side-effects, they continue to take the medicines because they were warned about possible side-effects and informed that they would go away. Some also said they were given written information about this to take home.

One of the female ARV users said:

> *"I learnt that I should not skip the medicines and I should adhere to the stipulated time. At one stage I skipped them and took them after the stipulated time. I told my nurse and I was assisted."*

Some of the participants pointed out that there was also a need for continued counselling. One female ARV user said:

> *"Even though initially we are given a lot of information, counselling is not adequate because it is only done once. Follow-up at home should be done to find out if one is really taking the medicines."*

Similarly, a health care provider pointed out that:

> *"Patients are given information during the initiation of treatment but it is necessary to continue reminding them."*

5.3 Observation of health facilities

5.3.1 Structural issues

At the Maun, Serowe and Mahalapye study sites, patients gather at the IDCC clinics for their ARV consultations, adherence counselling, laboratory schedules and collection of their medications. These clinics are largely separate from the rest of the units within the hospital. In contrast, at the Molepolole study site, all outpatients were received at the hospital outpatients unit, which had two consulting rooms for people on ART. Two of the health facilities (Serowe and Maun), which happened to be first generation sites, had adequate space. The structures provided for adequate confidentiality, good counselling, laboratory services with adequate shade, and seats provided for the patients in the waiting area. However, in Mahalapye and Molepolole there was a lack of space, seats and shade in the waiting areas, and patients resorted to sitting in makeshift waiting areas. The little cover and shade that is available is inadequate to shelter patients if the weather is bad. In all four facilities the environment was found to be clean. At each of the facilities posters were strategically placed within the IDCC clinics, mainly explaining the importance of adherence to ARVs and the fact that these medicines suppress the virus but are not a cure for the disease. Some of the posters were in English and others in Setswana.

The service and staffing details are outlined in Tables 5.1 and 5.2.

Table 5.1: Service details of each participating facility, as of May/June 2005

Sites	Date started ART	Total no. on treatment at facility by July 2005	Average no. of patients consulted per day	Average no. of patients for ARV medication refilling per day
Maun	July 2002	2492	40	100
Serowe	May 2002	3403	60	150
Mahalapye	Oct 2003	1836	40	90
Molepolole	Oct 2003	1879	50	100

Table 5.2: Summary of staffing for the IDCC at the time of data collection

Sites/ numbers	Medical officers	Nurses	Social workers	Pharmacy personnel	Laboratory personnel	Data entry clerks	Auxiliary staff
Maun	4	6	3	4	6	4	3
Serowe	2	8	3	3	6	3	2
Mahalapye	1	6	3	2	6	2	1
Molepolole	1	4	4	3	6	1	3

5.3.2 Service provision

All facilities operated Monday to Friday, with the exception of Molepolole which opened only four days per week. The eligibility criteria were the same in all the facilities since they followed the national guidelines for commencement of therapy. The patients were encouraged to come with adherence support partners but the lack of a partner did not disqualify anyone from being put on ART.

At the Maun, Molepolole and Mahalapye sites, pre-treatment adherence counselling was done in a group session, whereas in Serowe this was done on a one-to-one basis. At Mahalapye, adherence counselling was done by a team of health workers consisting of a nurse, pharmacy staff, social worker, and dietician, while at the other sites it was done by one health worker at a time with a group of patients.

Seeking shade from the sun in Molepolole: patients wait for their appointments in the hospital grounds, outside the hospital chapel.

The adherence support mechanisms varied between the sites, in both the method of counselling used and in the follow-up of patients who were not achieving optimal adherence or who had stopped taking the ARVs. The similarities included the use of pill counts (with the exception of Serowe), encouraging patients to bring an "adherence buddy" at the start of therapy, and the use of cell phone alarm settings to remind them to take their medicines. A basket of food rations was also available for patients who were unemployed or no longer working because of illness and who did not have any other source of income. This was determined on the basis of an assessment by social workers, which included home visits.

At the time of the study, equipment for measuring CD4 counts and viral load was not available at any of the facilities. Maun, for instance, sends its viral load and CD4 samples to reference facilities by air courier and the other sites transport their samples by road to their tertiary referral hospitals. Other laboratory investigations, such as haematology, cultures and urine analysis were done on site. Since the completion of the study, Serowe has acquired the capacity for CD4 testing.

Language barriers were observed to be a problem during interactions between some expatriate health workers and patients.

5.4 National level policy issues

The interviews with policy-makers proved to be difficult because the respondents originally targeted could not be reached. The few interviews conducted revealed that the programme roll-out in Botswana has been proceeding according to plan. However, concerns about the availability, affordability and sustainability of ARVs, as well as the shortage of human resources were raised by the respondents and considered to be major challenges for the future.

Chapter 6: Discussion, conclusion and recommendations

6.1 Discussion

This report describes the findings of a study that explored factors affecting adherence to ART in four public facilities in Botswana. The study used both quantitative and qualitative methods. The strength of this mixed-method approach is its usefulness in addressing the complexity associated with issues relating to adherence. The aim of the study was to help design interventions that can assist in maintaining high rates of adherence, a critical need if the danger of widespread resistance to treatment is to be avoided (Paterson et al., 2000; Orrell et al., 2003, Stevens et al., 2005). Paterson reported that ARV patients who achieved less than 80% adherence have a virological failure rate of 87%. As Botswana scales up access to ART, it is important to maintain high levels of adherence.

This section will first present the discussion on the quantitative results and then explore the integration of the quantitative and qualitative results. The quantitative data were collected using an adherence survey tool and exit questionnaires. The qualitative data were collected using exit interviews, semi-structured interviews, FGDs and observations. The respondents included ARV users, health workers, members of the local community and policy-makers.

A total of 514 respondents participated in the quantitative part of the study. Adherence in this study was defined as the number of times that patients actually take their drugs during a given period as a proportion of the number of times that they are recommended to do so. Optimal adherence was defined as an adherence rate of 95% or higher, since this is the level generally deemed necessary for treatment success and to avoid the development of resistance to treatment (Paterson et al., 2000). Levels of adherence below 95% were considered to be sub-optimal.

Three tools were used to measure adherence: pill counts over one month; one-month patient self-report with a visual analogue; and two-day recall using a 24-hour 'sun and moon chart'. The mean adherence rates were 95% for the pill count, 92% for the one-month self-report and 98% for the two-day recall. Using the pill count method it was found that 75% of the ART users achieved the optimal adherence levels of over 95%. Sixty per cent of participants reported optimal adherence using the visual line one-month recall and 96% reported optimal adherence using the two-day recall.

All three of these measures have both strengths and weaknesses. The pill count is in some ways the most 'objective', since it measures the number of pills left over from the previous refill, and can act as a very good proxy indicator for actual pill intake. It is, however, subject to manipulation by patients who may fear a bad response from health workers during dispensing if they have not achieved optimal adherence. In contrast, the one-month self-recall did not involve any health workers in this study. It was administered by researchers who were trained to act empathetically to the potential problems faced by respondents. As a result, ARV users might have been less inclined to overestimate medicine intake. However, a degree of desirability bias is always possible; as is the inability to recall medicine intake over such a relatively long period. The two-day recall has the advantage of a short time-span, which means that memory of medicine intake is likely to be good. However, it can overestimate medicine intake because patients may feel ashamed to admit to forgetting to take their medications so recently. While the two-day recall measure may be useful for on-the-spot individual patient adherence counselling, it may not be useful for long-term adherence monitoring. We recommend that both one-month recall (using visual analogue scale) and the pill counts be undertaken for routine adherence monitoring.

Recognition of the limitations of each of these three individual measures resulted in our calculating a composite adherence rate in the expectation that this would allow the strengths of one method to compensate for the limitations of the others. This composite adherence rate was calculated by taking the mean of the three measures and was found to be 77%. This is comparable to the adherence rates found in other countries (Bangsberg et al., 2000; Chesney, 2000; Liu et al., 2001; Nemes et al., 2004; Safren et al., 2005). Weiser et al. (2003) predicted that if treatment costs were removed as a barrier, adherence rates in Botswana would rise from 54% to 74%. We found that waiting times, costs and logistics are challenges to adherence.

The finding that 23% of patients had sub-optimal adherence rates is still unacceptably high. In view of the serious implications of non-adherence for public health, there is a critical need for targeted intervention strategies to increase the level of adherence. Monitoring and evaluation of the adherence strategies are an important component of any ART programme and can be useful in determining rates and identifying the factors that influence adherence. There is also a need for studies to investigate changes in patient adherence over time. As Horne (1998) argued, adherence should not be considered as a *stable* characteristic of any group of individuals but rather as a *variable* behaviour of an individual that can change over time.

The analysis of qualitative data was by thematic approach and 28 themes were initially identified. Further analysis identified the following key factors as facilitators or constraints of adherence (not in order of importance): the inter-related issues of disclosure: social support; acceptance of HIV status; treatment adherence partner; gender; remembering or forgetting to take the medicines; alcohol/substance abuse; transport costs and distance to health facility; side-effects; food; education; perceived effectiveness of treatment; self-efficacy; counselling; implementation of national guidelines; and a management system for addressing adherence and quality of care.

The study collected data at individual/household, community, health system and national levels. The following key issues relating to adherence operate primarily at the individual and household level, but they also incorporate aspects from the community and health facility.

The interrelated issues of disclosure, social support, acceptance of HIV status, treatment support partner and gender

The qualitative data showed that acceptance of one's HIV status and belief in the efficacy of treatment were important facilitators of adherence to treatment, while non-acceptance of HIV status was reported to be a major constraint. Respondents agreed that individual acceptance of HIV status translated into the kind of behavioural changes that are required for a good treatment outcome. For example, when ARV users are in a state of denial about their HIV status, ARVs are often hidden from friends and relatives and medication may be skipped to avoid discovery when other people are around.

The data also suggested that those who had accepted their HIV status were more likely to disclose to other people. Since acceptance is closely related to disclosure, most ARV users felt that non-disclosure of HIV status or of being on ART was a likely predictor of sub-optimal adherence to ART. Without disclosure it becomes difficult to use medication in the presence of other people. In view of the complexity of the medication schedule (in terms of time and consistency), it is difficult to have the privacy that would keep people from noticing regular medicine use. However, even though a significant number of respondents believed that disclosing to relatives and friends had the potential to improve adherence, some of them also perceived that disclosure carried a number of risks such as: emotional injury, loss of intimate relationships and job loss. Other studies have also found that disclosure is a complex process with varying consequences, such as greater intimacy or rejection, feeling of relief or remorse and enhanced status or 'spoiled image' (Ormazu, 2000; Klitzman et al., 2004; Zea et al., 2005). It was generally believed that without disclosure, the level of social support would not be adequate.

Adherence to the treatment regimen was also related to the availability of information material as well as emotional support from family members. The positive role of children in reminding parents when it was time to take their pills was found to be a common facilitating and supportive factor. In addition, the level of family social welfare (income status, collective efficacy, successful resolution of previous conflict, trust) was found to determine the kind of social support an ARV user receives. Men complained that where people had not invested in family social welfare, there was more negative energy/emotion in the family characterized by neglect, sarcasm, negative affective states and constant reminders of the recipient's dependency. Where a husband had previously deserted the family home and where lack of forgiveness prevailed, social support was often lacking. Investment in family social welfare was found to be essential for future social support.

Gender was perceived to have an influence on acceptance of status. Many respondents agreed that women were more likely to accept their status and to seek health care. The desire for women to stay alive in order to care for their children and other loved ones, despite being blamed by men for bringing the disease, was said to be a major facilitator of adherence. The better health-seeking behaviour of women was attributed to the fact that women have always been close to the health care system through the maternal and child health clinics, a system which pre-dates the HIV era. Prior involvement in prevention of mother-to-child transmission (pMTCT) programmes before starting on ART also meant that women were better sensitized and specifically targeted with HIV interventions. While women were thought to accept their HIV status more readily than men and were therefore more likely to seek help from the treatment centres, men were perceived to be difficult, refusing to accept their status or to disclose. This may partly explain why more women than men are on treatment. Since acceptance of HIV status, disclosure and gender were found to be the main emerging themes in the qualitative data, further studies are needed to explore these variables in greater depth.

Positive attitude and belief in the efficacy of ART

The FGDs revealed that, despite being often preoccupied with their own health concerns and fears, a majority of participants reported that the availability of ARVs had given them a "new lease of life." ARV users tended to have adequate information about the natural progression of HIV. The study also found that one of the strongest qualitative predictors of medication adherence was a personal belief in the efficacy of ART. This belief was also buttressed by the fact that ARVs are potent and as such, better than traditional herbs. There was an overriding belief among ARV users that traditional herbs do not increase CD4 count in the body or decrease the viral load, while ARVs do. This is a critical finding, in a country where patients tend to use both traditional and modern medicine. Those who held this belief also said that HIV was increasingly a manageable disease. In deciding whether or not to start taking ARVs and to continue taking the medication, a patient has to weigh up the costs and benefits of treatment.

Other studies have confirmed an association between adherence and a belief in the efficacy of the pills used in treatment (Eldred, 1997; Ferris, 1996; Smith, 1997). Several studies have shown that patients with a higher level of knowledge about the effectiveness of ART and belief that poor adherence could promote viral resistance and treatment failure have a greater ability to adhere to their medication.

Remembering/forgetting, alcohol and substance abuse

Forgetfulness was the most common reason cited by those who had problems with adhering to their medication, a finding that is consistent with other studies (Brigido et al., 1998; Chesney et al., 2000; Golin et al., 2002; Turner, 2002). However, the specific reasons for forgetfulness could not be quantified. Respondents cited work and home duties, travelling for work (e.g. cattle posts) or social events (e.g. funerals and weddings) as factors that led to forgetfulness. The qualitative data highlighted alcohol abuse as a major barrier to adherence to ART. ARV users, health workers and members of the community all identified a direct link between alcohol abuse and sub-optimal or non-adherence. The participants acknowledged the use of mechanical devices (radios,

cell phones, and watches), children, parents and partners as helpful ways of being reminded to take their medicines.

Distance to health facility, employment status and costs

The Government of Botswana is responsible for the overall management of the national ART programme and for making treatment available free of charge. However, the study data suggest that patients are burdened by the cost of transportation to and from facilities and by the cost of food while waiting to be attended to. Forty-four per cent of the patients in our quantitative survey reported an increase in expenditures as a result of being on ART, 37% reported a loss of income, and of those who had missed an appointment, 12% said it was for lack of funds to pay for transport to reach the health facility. One in four ARV users interviewed said they had to travel at least 50 km to visit the treatment centre and the maximum distance travelled was 200 km. These findings suggest that many patients have significant treatment-related financial problems, even though the Government is providing ARVs free of charge.

Quantitative data suggested that there was an association between employment and optimal adherence in that respondents who were employed were more likely to adhere than those who were unemployed. It makes conceptual sense that treatment-related costs (e.g. transport) could be a reason why the unemployed failed to achieve optimal adherence. However, the cost of transport can also be a serious problem for workers on a daily rate, the self-employed and casual workers, who not only have to pay for their trip to and from the clinic, but who are also likely to have to forego their daily wage in order to keep appointments at the health facility. Based on this finding, the provision of travel vouchers or reimbursement of travel expenses would be potent facilitators of adherence.

Side-effects

Quantitative data revealed that of the 58% of ARV users who reported having experienced side-effects, only 8% cited side-effects as a reason for failure to achieve optimal adherence. This is contrary to other studies carried out in developed countries where the most frequently cited reason for stopping medication was side-effects. (Chesney et al., 2000; Ammassari et al., 2001). There are several possible reasons for these differences in results. First, in the case of Botswana, the entry level for ART is CD4 count ≤ 200. At this level, patients may be so sick that the side-effects experienced could be perceived as a symptom of the disease itself. Second, a sociocultural belief exists among Batswana that it is easy and painless for a disease to get inside the body, but difficult and painful for the disease to get out. According to this belief, the experience of side-effects may be interpreted as the disease exiting from the body and therefore may be tolerated. Third, pre-treatment counselling, where patients are educated about the ARV treatment plan, including possible side-effects, may result in the perception of side-effects as a reasonable risk to be tolerated in view of the magnitude of benefits expected and the alternatives available. These reasons could explain the under-reporting of side-effects/adverse events as stated by one of the health workers in the qualitative interview. This could also suggest that, despite lack of continuity in counselling, this service seems to have an impact on adherence.

The treatment-related increase in food demand did not appear to have a significant impact on adherence. Although 2% of respondents in the quantitative study cited lack of food as a reason for sub-optimal adherence to ART, subsequent interviews revealed that, while lack of food was an inconvenience, it did not stop them taking their ARVs. Education level is usually used as a measure of socioeconomic status but most studies so far did not find education as a predictor of adherence when controlled for other socioeconomic factors (Carrieri et al., 2002; Nemes et al., 2003; Murphy et al., 2004). Our study also confirms this finding and may also be an indicator that information, education and communication is working well.

Health facility level

Health care workers performed different activities such as: pre-treatment counselling; ongoing counselling; referral to social workers of patients with adherence problems; pill counts; and collation of adherence data and submission of monthly statistics to the national programme. The health workers all maintained that there is no strategic management system for addressing ART adherence problems.

All four of the facilities surveyed use the *Botswana Guidelines on Antiretroviral Treatment*. The current version (2005) recognizes sub-optimal adherence as a common reason for treatment failure and the most important cause of the emergence of drug-resistant strains of HIV. The guidelines recommend seven strategies to improve adherence, including: establish trust with the patient and family; serve as an educator and source of information; provide ongoing support and monitoring; intensify management in periods of low adherence by more frequent visits, recruitment of friends and family and deployment of other team members; utilize a health team approach; provide training to support the ART staff; use the family care model approach and provide care to the family as a unit.

While these recommendations are excellent, there is no clarity as to how the health care worker should achieve the objectives. The guidelines acknowledge the need to involve family and friends in coping with the demands of adherence, but fail to address the ethical issues involved in areas such as privacy, autonomy and confidentiality, which are genuine concerns for patients and health workers.

Study limitations

It would have been interesting to examine the adherence rates in relation to the timing of drug and food intake. However, due to the fact that most of our study participants were on first-line medication that did not require food restrictions and the fact that a previous question included the times medication were taken, these measures could not be used. This study had several limitations. For example, some of the data collection methods used in this study relied on self-reports of adherence behaviour, which is prone to response biases. In addition, the study used a client sample that was currently on ART and did not include individuals who had discontinued treatment. It is also possible that people who achieved sub-optimal adherence may no longer be visiting the treatment facilities.

6.2 Conclusions

Although the adherence rates found in this study are comparable to those of other studies in developing countries, these rates are still low for good clinical outcomes. Adherence is a complex issue and multi-dimensional approaches are required to both address the constraints and strengthen the key facilitators of adherence. Efforts to determine the level of adherence among patients on ART is complicated by the general methodological difficulties of adherence assessment. There is no gold standard of adherence assessment. While the two-day recall measure may be useful for on-the-spot individual patient adherence counselling, we recommend the use of the visual analogue scale and the pill counts for routine adherence monitoring.

In this study the critical barriers to adherence identified were: forgetfulness, lack of transport fare to the health facility, non-acceptance of HIV status, fear of discrimination and stigma, alcohol abuse, and non-supportive home and work environments. Although side-effects occur in a significant proportion of users, this was not perceived as a significant barrier to adherence.

Facilitators of adherence were found to include self-efficacy, social support, an effective adherence counselling programme, perceived benefits of the medication, and a desire to stay alive for the sake of others.

Efforts to improve the level of adherence require a collaborative approach involving the patient, the community, health workers and policy-makers, and a focus on ways of addressing environmental and structural constraints.

Some of the recommendations identified include the development of practical guidelines for implementing adherence management strategies. These should include guidelines for: continuous adherence counselling; bringing treatment closer to home; adoption of a family care model approach to ART; use of practical reminders; adherence case management; and the use of medication organizers (pill boxes partitioned to display the daily or weekly sequence of pills to be taken). In addition, the establishment of a transport voucher scheme should be considered for people who genuinely cannot afford the cost of transport to collect their medication. Such interventions should be evaluated to assess their effects on adherence.

Acceptance of HIV status, disclosure and gender were found to be the main emerging themes in the qualitative data. Further studies are needed to explore these variables in greater depth. Programmes targeting men to inform them about HIV-related issues should also be developed. This would help increase the enrolment of men in ART programmes, help them to better understand the gender issues around HIV, and mobilize them to be protectors and supporters of women in the fight against HIV.

6.3 Recommendations

♦ Development of practical guidelines for implementing adherence management strategies. These should include guidelines for: continuous adherence counselling; bringing treatment closer to home; adoption of a family care model approach to ART; use of practical reminders; adherence case management; and the use of medication organizers.

♦ Consideration of the establishment of a transport voucher scheme for people who genuinely cannot afford the cost of transport to collect their medication.

♦ Adoption of a uniform adherence monitoring system at all facilities in Botswana, with simple and practical tools such as pill count register and the visual line one-month recall. These measures need to be validated and standardized. Data generated should be reviewed periodically in order to monitor the rate and trend of adherence to ART.

♦ Sustained community mobilization aimed at mitigating stigma and discrimination in an effort to create an environment in which people can disclose and take their ARVs without fear of discovery.

♦ Enforcement of appropriate legislation to protect the rights of people in employment to access to treatment without fear of discrimination. Efforts are also needed to sensitize people to their HIV-related rights in the workplace, including the establishment of toll-free lines to enable people to complain if their rights are violated.

♦ Development of programmes targeting men to inform them about HIV-related issues. This would help increase the enrolment of men in ART programmes, help them to better understand the HIV-related gender issues, and mobilize them to be protectors and supporters of women in the fight against HIV.

♦ Development of new tools to sustain and improve adherence rates and influence behavioural change. This includes using radio stations, TV stations and mobile phone operators to send periodic signals with jingles reminding people to take their medication.

♦ Continuous operational research on adherence.

♦ Development of interventions targeting men to help reduce the HIV-related consequences of alcohol abuse.

♦ Behavioural change interventions designed to modify the work and home-related barriers to adherence should be developed and evaluated. For example, patients could be given small medicine envelopes (commonly known as 'seed bags') to carry some of their medicines when they go to places where they do not want to be seen taking medicines from original containers (e.g. when visiting friends, going to funerals or to work).

♦ Acceptance of HIV status, disclosure and gender were found to be the main emerging themes in the qualitative data. Further studies are needed to explore these variables in greater depth.

References

1. Ammassari A et al. (2001). Self-reported symptoms and medication side-effects influence adherence to highly active antiretroviral therapy in persons with HIV infection. *Journal of Acquired Immune Deficiency Syndromes*, 28(5):445-449.

2. Anderson W, Weatherburn P. *Taking heart? The impact of combination therapy on the lives of people with HIV (phase 2)*. London, Syria Research, 1999.

3. Bangsberg DR et al. (2000) Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. *AIDS*, 14:357–366.

4. Brigido LFM et al. (1998). *Low adherence in antiretroviral users at Sao Paulo, Brazil*. 12th World AIDS Conference, Geneva, 28 June-3 July 1998. Abstract no. 32370.

5. Byakika-Tusiime J et al. (2003). *Ability to purchase and secure stable therapy are significant predictors of non-adherence to antiretroviral therapy in Kampala, Uganda.* 10th Conference on Retroviruses and Opportunistic Infections. Boston, USA. 10-14 February 2003. Abstract no. 170.

6. Carr A (2002). Improvement of the study, analysis and reporting of adverse events associated with antiretroviral therapy. *Lancet*, 360:81-85

7. Carr A, Cooper DA (2000). Adverse effects of antiretroviral therapy. *Lancet*, 356: 1423-30.

8. Carter M. Adherence – information series for HIV-positive people. 2nd ed. London, NAM, 2004.

9. Carrieri P, Caillefon V, Le moing V (2002). The dynamic of adherence to Highly Active Antiretroviral Therapy: Results from the French National APROCO cohort. *Journal of Acquired Immune Deficiency Syndromes*, 28:232-9.

10. Chesney MA (2000). Factors affecting adherence to antiretroviral therapy. *Clinical Infectious Diseases*, 30(Suppl 2):S171-6.

11. Chesney MA, Morin M, Sherr L (2000). Adherence to HIV combination therapy. *Social Science & Medicine*, 50:1599-1605.

12. Chesney MA et al. (1999). Adherence: a necessity for successful HIV combination therapy. *AIDS*, 13(Suppl A):5271-5278.

13. Daniel OJ et al. (2004). *Adherence pattern to ARV drugs among AIDS patients on self-purchased drugs and those on free medications in Sagamu, Nigeria*. XV International AIDS Conference. Bangkok, Thailand. 30 March - 2 April 2004.

14. Darder M et al. (2004). *Determinants of short and long-term adherence to antiretroviral treatment in resource-poor settings*. XV International AIDS Conference. Bangkok, Thailand. 30 March - 2 April 2004. Abstract no. B11852.

15. Eldred I J, Wu Aw, Chaisson RE (1998). Adherence to antiretroviral and pneumocystic prophylaxis in HIV disease. *Journal Acquired Immune Deficiency Syndromes*, 18:117.

16. Ferris DC et al. (2004). S*elf-reported adherence to antiretroviral therapy and virologic outcomes in HIV-infected persons in Durban, KwaZulu Natal, South Africa*. XV International AIDS Conference. Bangkok, Thailand. 30 March - 2 April 2004. Abstract no. WePeB5829.

17. Fischl M, Rodriguez A, Scerpella E. (2000). *Impact of directly observed therapy on outcomes in HIV clinical trials*. 7th Conference on Retroviruses and Opportunistic Infections, San Francisco, USA. 30 January - 2 February 2000. Abstract no. 71.

18. Gill CJ et al (2005). *No complacency about adherence to antiretroviral therapy in sub-Saharan Africa*. *AIDS*, 19:1243-1249.

19. Gillford AL et al. (2000). Predictors of self-reported adherence and plasma HIV concentrations in patients on multidrug antiretroviral regimens. *Journal Acquired Immune Deficiency Syndrome*, 23(5):386-95.

20. Golin CE et al. (2002). A prospective study of predictors of adherence to combination antiretroviral medication. *Journal of General Internal Medicine*, 17:756-765.

21. Government through Presidential Directive CAB: 35/93, 17th November 1993. Gaborone. (UNDP, 2001) Botswana human development report, 2000, p.41-42.

22. Harries AD, et al. (2001). Preventing antiretroviral anarchy in sub-Saharan Africa. *Lancet*, 358:410–414.

23. Horne R. Adherence to medication, a review of existing research. In: Myers L, Midence K (eds.). *Adherence to treatment in medical conditions* (pp.285-310). London, Harwood Academic, 1998.

24. Horne R. Compliance, adherence and concordance. In: Taylor K and Harding G (eds.), *Pharmacy practice* (pp.165-184). London, Taylor & Francis, 2001.

25. KITSO. Harvard Institute HIV/AIDS. *KITSO training manual for health workers in Botswana*, 2004

26. Klitzman RL et al. (2004). Intricacies and inter-relationships between disclosure and HAART: a qualitative study. *AIDS Care*, 16(5):628-640.

27. Kumarasamy N et al.(2005). Barriers and facilitators to antiretroviral medication adherence among patients with HIV in Chennai, India: A qualitative study. *AIDS Patient Care and STDs*, 19(8):526-537.

28. Lerner BH, Gulick R M, Dubler NN. Rethinking non-adherence: historical perspectives on triple-drug therapy for HIV disease. *Annals of Internal Medicine*, 1998, 129(7):573-578.

29. Liu H, et al. (2001). A comparison of multiple measures of adherence to HIV protease inhibitors. *Annals of Internal Medicine,* 134:968-997.

30. Machtinger E, Bangsberg DR (2005). *Adherence to HIV antiretroviral therapy*. Available at: http://hivinsite.ucsf.edu/InSite?page=kb-03-02-09

31. Muganzi AM et al. *(*2004). *Adherence to HAART in a rural resource limited country HIV/AIDS treatment programme: the experience of Arua Anti-Retroviral (ARV) Treatment Programme-Uganda*. XV International AIDS Conference. Bangkok, Thailand. 30 March - 2 April 2004. Abstract no.: WePeB5760.

32. Murphy DA et al. (2004). Predictors of antiretroviral adherence. *AIDS Care*, 16(4): 471-484.

33. National AIDS Coordinating Agency (NACA). B*otswana sentinel year book 2003*. Available at: http://www.naca.gov.bw/about.htm.

34. National AIDS Coordinating Agency (NACA) website: http://www.naca.gov.bw

35. Nemes MIB, Carvalho HB, Souza MFM (2004). Antiretroviral therapy adherence in Brazil. *AIDS* 18(Suppl 3):S15-S20.

36. Nwokike J (2004). *Baseline data and predictors of adherence in patients on antiretroviral therapy in Maun General Hospital, Botswana*. International Conference on Improving Use of Medicines (ICIUM). Bangkok, Thailand. Abstract no. HI012, 2004.

37. Ormazu JA (2000). Disclosure decision model: determining how and when individuals will self-disclose. *Personality and Social Psychology Review*, 4:174-185.

38. Omes C et al. (2004). *Adherence to antiretroviral (ARV) therapy among advanced-stage, indigent patients in the funded ESTHER programme in Kigali, Rwanda*. XV International AIDS Conference. Bangkok, Thailand. 30 March - 2 April 2004. Abstract no. B12315.

39. Orrell C, Bangberg DR, Badri M, Wood R (2003). Adherence is not a barrier to successful antiretroviral therapy in South Africa. *AIDS*, 17:1369-1375.

40. Palella FJ Jr et al. (1998). Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *New England Journal of Medicine*, 338:853–860.

41. Paterson DL et al. (2000). Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine*, 133(1):21–30.

42. Perelson AS, Neumann AU, Markowitz M (1996). HIV-1 Dynamics in viro; viron clearance rate, infected cell life span, and viral generation time. *Science*, 271(5255): 1582-6.

43. Poppa A et al. *Guidelines on provision of adherence support to individuals receiving antiretroviral therapy.* London, British HIV Association/British Association for Sexual Health and HIV, 1993.

44. Ramotlhwa (2005). ARV statistics. (Personal communication).

45. Reiter GS et al. (2000). Elements of success in HIV clinical care. *Topics in HIV Medicine* 8:67.

46. Safren SA et al. (2005). ART adherence, demographic variables and CD4 outcome among HIV-positive patients on antiretroviral therapy in Chennai, India. *AIDS Care*, 17(7):853-862.

47. Singh N et al. (1996). Determinants of compliance with antiretroviral therapy in patients with human immunodeficiency virus: prospective assessment with implications for enhancing compliance. *AIDS Care*, 8:261-269.

48. Stevens W, Kaye S, Corrah T (2004). Education and debate: antiretroviral therapy in Africa. *British Medical Journal*, 328:280-2.

49. Tuldra A, Fumaz C R, Ferrer MJ (2000). Prospective randomized two arm controlled study to determine the efficacy of a specific intervention to improve long term adherence to highly active antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndromes*, 25:221-8.

50. Turner BJ (2002). Adherence to antiretroviral therapy by Human Immunodeficiency Virus-Infected Patients. *Journal of Infectious Diseases*, 185(Suppl 2):S143-51.

51. UNAIDS/WHO (2005). *The AIDS epidemic update - Special report on HIV prevention.* Available at: http://www.who.int/hiv/epiupdate2005/en/.

52. Vitolins MZ et al. (2000). Measuring adherence to behavioral and medical interventions. *Controlled Clinical Trials*; 21:188S-194S.

53. Weiser S et al. (2003). Barriers to antiretroviral adherence for patients living with HIV infection and AIDS in Botswana. *Journal Acquired Immune Deficiency Syndrome,* 34:281–288.

54. WHO. *Progress on global access to HIV antiretroviral therapy. A report on "3 by 5" and beyond*. Geneva, World Health Organization, 2006.

55. Zea et al. (2005). Disclosure of HIV status and psychological well-being Among Latino gay and bisexual men. *AIDS and Behavior*, 9(1):15-26.

Annex 1:
Mean of rates adherence

Raw averages of the different measures

a) Self assessment of adherence using the visual analogue method

	Mean	**Median**	**Mode**	**Minimum**	**Maximum**
Maun	.91	.95	1.00	.50	1.00
Mahalapye	.95	.99	.99	.56	1.00
Molepolole	.91	.98	1.00	.30	1.00
Serowe	.89	.96	1.00	.44	1.00
All	**.92**	**.97**	**1.00**	**.30**	**1.00**

(There were problems noted on-site with the Serowe pill count recording).

Self assessment of adherence using patient self-report method (two-day recall)

Facilities	**Mean**	**N**	**Std. Error of Mean**
Maun	.94387	121	.018158
Mahalapye	.99267	125	.004639
Molepolole	.98333	115	.009775
Serowe	.99206	147	.004644
Total	.97876	508	.005227

Pill counts (including Serowe data)

	Mean	**Median**	**Mode**	**Minimum**	**Maximum**	**Count**
Maun	.972	1.000	1.000	.000	1.000	122
Mahalapye	.930	.963	1.000	.567	1.000	128
Molepolole	.954	.982	1.000	.667	1.000	115
Serowe	.855	.879	1.000	.321	1.000	149
Total	**.925**	**.967**	**1.000**	**.000**	**1.000**	**514**

Annex 2: Multivariate logistic regression analyses on the predictor variables

Multivariate logistic regression analyses on the predictor variables

Variables	Parameter estimate	Wald χ^2	O.R.	O.R. (95% C.I.)	p-value
Side-effects	-0.0674	0.105			0.746
Distance	0.000589	0.0430			0.836
Sex	-0.185	0.598			0.439
Age	0.0107	0.885			0.347
Education	-0.00298	0.000512			0.982
Occupation	0.370	2.681			0.102
Cost of transport	-0.00711	0.169			0.681
Loss of income	-0.285	1.207			0.272
Other costs	-0.334	2.267			0.132
Months on treatment	-0.0129	1.477			0.224
Counselling	-16.024	0.0000249			0.996
Partner reminder	-0.283	1.298			0.255
Missing appointment	-0.575	4.851	0.572	(0.363; 0.902)	0.028
Implications of missed dose	0.443	1.116			0.291
Knowledge about HIV and ARVs	0.323	2.063			0.151

Annex 3: Questionnaires

1.   Focus group discussion (FGD) for antiretroviral users: Questionnaire

- Participants per FGD (6-8)

- Adults (= or >18 years, men and women separately – may want also to split into high- and low-adherers, if easily identifiable, depending on what country teams want to do)

- One moderator, one note-taker (*and* use of tape recorder)

- Neutral venue outside the facility

- Two FGD per facility (one with men and one with women)

Short introductory remarks

- Introduction of researchers and participants

- Thank participants for agreeing to participate, all share a common feature – they are on ARV treatment, are here to share their thoughts about ARVs and difficulties in taking ARVs: we want to learn from participants

- Explain purpose of study, purpose of this discussion, reassurance about confidentiality, agree on rules.

Topics for discussion

1. What treatments do you know to be available for treating HIV? What is your opinion about these? (e.g. ARVs; herbs; traditional medicines; spiritual healing; prayers; and perceived benefit (s) of treatment).

2. What is your experience of ART? (probe about adherence, adverse effects, pill burden, lack of food, lifestyle issues).

3. How do you think you are being treated (handled) by the health care workers (probe: privacy, confidentiality, respect, being listened to, time spent with patient, waiting time, integration with other services). What is the quality of care provided by health care workers?

4. What do you think about the counselling that you receive? (probe especially on importance of adherence effectiveness of counselling). What support are you given by the health workers to help you adhere better to your medications? Have you disclosed?

5. What support is available for you in the community, in the family, in the workplace? (probe about discrimination, stigma). Probe differences in perceived availability of social support versus social networks? Any negative social support? Any stress exacerbation?

6. What do you think could be done to help people adhere more easily to their treatment?

7. What do you think are the key reasons for non-adherence and good adherence? What are the sources of motivation for adherence?

8. Duration of discussion (1½ hours); provide refreshments

9. Conclusion, thank participants

2. Focus group discussion for community members: Questionnaire

1. Explore the role of participants in HIV/AIDS. Explore whether the members know about ARVs; what it is and the current practice of service delivery in ARV use. Explore where people obtain medicines for HIV/AIDS (ARVs) in the area. Assess accessibility to information on ARV.

2. What are the perceptions/beliefs/attitudes of the community on HIV/AIDS, treatment modalities? What are the perceptions of the community on current criteria for inclusion in ARV treatment? Probe for reasons for perceptions. What criteria should be used for starting antiretroviral therapy?

3. How easy/accessible is it for people in your community for people who are taking ARVs? (Probe on stigma, discrimination, logistical issues for reaching the clinic etc.)

4. Can existing infrastructure be modified and strengthened to adapt to antiretroviral provision? What resources are needed to make antiretroviral widely available in your area?

5. In your view, what are the current barriers to adherence for the individuals living with HIV in your community?
   a) Demography (age, sex, ethnicity/language, socioeconomic status)
   b) Information (knowledge, self efficacy, coping, etc)
   c) Motivation (beliefs, depression, drug use)
   d) Behaviour skills (pill taking, scheduling)
   e) Provider – expertise, trust
   f) Regimen – simplicity, toxicity, disruption of daily activities
   g) Disease stage
   h) Clinical setting

Probe on how cultural, psychological behavioural and contextual circumstances influence adherence?

6. Solutions: In your view, how can adherence be enhanced in your community? What activities take place at the moment in your community to help people adhere to their medication? (Probe on support, HBC, individual coping capacity. Probe on existing strategies to improve adherence.). How can therapeutic effectiveness, adverse side-effects, and the emergence of drug resistance be monitored?

What should be done to assist people on ARVs to take their medications as instructed?

7. Are there barriers/obstacles different in different health care systems for primary care centres as in private practice? How can the situation be improved?

3. Semi-structured interview with health care workers

Guidelines for semi-structured interviews with health workers
(to be adapted for use with different type of health workers – medical doctors,
nurses, counsellors, pharmacists, social workers)

Name of facility:
Name interviewer:
Interview number:
Date:

(Introduction of the interviewer (s), introduction of the study)

Background information on informant (health worker)

a) Sex	M / F
b) Age	years
c) Profession	
e) Role in ARV programme	
f) Involved in programme since ….	

Tasks and training

a) What specific training have you received for this job in relation to ARV programme? Tell me about the training (Details)

b) Do you think this training has been sufficient? (Details)

Drugs, treatment and procedures

a) Which treatment guidelines for HIV/AIDS management do you use at this facility? (Give details if necessary, e.g. national guidelines etc)

b) Are the drugs you prescribe always available? (If not, give details – how often, reason, what do you do about it)

c) Are the drugs in the guidelines you use to dispense always available? (Give details – how often, reason, what do you do about it)

d) Have you had periods where your patients have not been able to get their medications because they were not available in stock?

e) How reliable are your lab and diagnostic support services? Do results come in on time? Details.

f) What is your procedure when a patient is put on ARV drugs for the first time?

g) What is your procedure when a patient switches regimens?

h) In what ways are ARV-users informed about and prepared for ARV treatment?

i) What kind of information do they receive? Please describe it to us:

- The disease process (i.e. HIV and AIDS)   ☐
- How the disease affects the body   ☐
- How ARVs work   ☐
- How to use them   ☐
- The need to continue treatment   ☐
- What to do if a pill is forgotten   ☐
- Possible interactions with other drugs
  (including traditional medicines)   ☐
- Which side effects can occur & what to do if they occur   ☐
- (Breast) feeding requirements   ☐
- When and where to get re-supply   ☐

Who is giving this information?

Adherence issues

a) Generally speaking, do your patients keep their appointments?

b) How do you think your patients do, generally speaking, in terms of adherence to ART?

c) Could you estimate the percentage of your patients who you think are "sufficiently adherent" to ART? (Respondent gives their definition of 'sufficiently adherent' what level is that?) **

d) What do you use to determine adherence (probe: appointments, refills?)

e) We would like to get your views on the following (probe): From your experience

- How would you compare adherence between women and men?
- How would you compare adherence between older patients and younger patients?
- How does a patient's educational level affect adherence?
- How do you think that cost to patients influences adherence?

f) How do you think the distance to the health facility affects adherence?

g) From your experience how do you think the following affect adherence?

- Having or not having a treatment-support partner?
- Duration of treatment?
- Side effects?
- Lack of food?
- Knowledge about ART?

h) What strategies are in place to monitor adherence?

i) What strategies are in place to support adherence? (probe: family/community involvement).

j) What are the main challenges you face in supporting your patients to adhere to ARV drugs (especially for longer term users)?

Challenges and staff support

a) What are the main challenges you and your colleagues face more generally in your work? (if necessary, prompt re workload, stress, burnout)

b) Have you ever been afraid of being infected with HIV through your work? What were you specifically afraid about? How do you feel now about the HIV-infection risks? Do you take any extra precautions when working with them?

c) Have these challenges changed in any way since you started working at the ARV clinic?

d) Is any special support made available for staff engaged in management of HIV/AIDS at this facility? If no, do you think there is a need to have such support?

e) Is there anything you would like to see done differently in this facility? If yes, what?

Is there anything else you would like to tell us or ask us?

Thank you very much for your participation in this interview.

4.   Semi-structured interview with ARV users

Name of the interviewer:

Interview number:

Name of health facility where patient contacted:

Date:

NB:
- Informed consent
- ARV-user will be contacted initially at the health facility, but the interview will be conducted at another time and place.

Introduction of the interview, introduction of the study, consent requested with option not to participate. Statement of confidentiality.

Sociodemographic information on informants

a) Sex	M / F
b) Age	Years
c) Educational level	
d) Who do you live with? (spouse, children, mother etc.)	
e) What do you do for a living	
f) Distance from facility (in time or distance)	

Medical history of patient

a) When were you first diagnosed with HIV?

b) What made you decide to go for testing?

c) When did you start treatment for HIV (ARVs)?

d) How do you feel about your health since you started treatment?

e) How would you describe your health since you started treatment?
- Better
- Same
- Worse

Patient knowledge about HIV/AIDS

We would like to understand what people actually know about the illness that they have. Can you tell me what you know about HIV/AIDS? (Allow patient to say what they want, then probe on the following: cause of HIV infection, cause of AIDS, prevention, life-long infection).

Apart from this, is there anything else you may have heard from your community that explains AIDS in a different way?

Patient knowledge about ARVs

We would like to understand what people know about HIV/AIDS medicines. Could you help us with this by telling me what you know about ARVs? (Allow patient to say what they want, then probe on the following: prolongs life, improves quality of life, life long treatment, knowledge about side effects).

Assessment of adherence and non-adherence

We are trying to find out how patients manage to take their medicines – for some people it's not a problem, but we also know that others don't always find it easy. Please feel free to be open about the problems you face with this. Everything you say here will remain confidential, and will not be shared with anyone at the clinic.

a) Do you have your medicines with you? May I see them? Please can you tell me when you take each of the medicines?

b) Are there any other medications you are taking (e.g. traditional medicines, herbs, medicines from other hospitals, clinics, shops/chemist, etc.)

c) Over the last two days, when did you take your pills? (Not including today – starting from last night and back.) (Complete 'sun-and-moon chart', or other checklist)

d) Did you perhaps miss any? (Confirming (c), sympathetic manner. Details if yes.)

e) This is a very important question. We appreciate how difficult it can be to take pills on a daily basis. If you sometimes miss a dose, please can you tell me what causes this to happen? Can you give an example or two? (Include even if 'simply forgot').

f) On the other hand, what is it that *helps* you to take your pills regularly and on time? (e.g. buddy, relatives, individuals, cell-phone, clock etc.)

g) Have you disclosed your status to any one? If so, who? Do they help you to take your pills? [If not covered in (f)]

h) Have you had your treatment changed at any moment since you were started on ARVs? If yes, why? (e.g. treatment failure, side-effects, drug not available).

i) Have you ever missed an appointment at your IDCC? (Reasons, and details on type of consultation: review/refill, counselling etc.)

j) What do you think happens in your body if you skip your ARV medicines?

k) Have you ever thought about stopping HIV/AIDS medicines (ARVs)? If yes, details.

Perception about HIV/AIDS, ARVs and stigma

Have you ever had any experience of being treated differently because of your HIV status? (in your family, at work, at the church etc)

Cost considerations

a) How much do you have to pay to cover your travel expenses when you visit the clinic?

b) What is the cost of registering at the clinic (if any)?

c) What is the cost of the ARV medicines that you take (if any)?

d) Do you lose any income as a result of your coming to the clinic?

e) Do you incur any other costs as a result of your taking ARVs?

f) What have you and/or your family had to give up in order to be able to take your medicines regularly?

Quality of care

(a) What do you think of the service you receive at this clinic? (General, open-ended, and then prompt, as below: ask for details as necessary)

- Do you feel listened to? Yes ☐ No ☐

- Are you given the chance to state your problems and ask questions?
  Yes ☐ No ☐

- Are you treated with respect? Yes ☐ No ☐

- Do you feel you can trust the health workers? Yes ☐ No ☐

- Do you have privacy during consultation and counselling?
  Yes ☐ No ☐

- How do you find the environment of the clinic?

(b) How long did you spend altogether at the clinic when you last went for review?

(c) How long did you have to wait before being attended to?

Perceived problems and possible solutions

a) What do you perceive as the biggest problem regarding taking ARV treatment?
b) What do you think could be done to improve this?

Do you have any questions for me?

Thank you for your time and co-operation!

5. Adherence measurement tool for antiretroviral users: Questionnaire

ARV adherence questionnaire

Page 1 of 4

Date [   ] Interviewer: [   ] Facility: [   ] Study No: [   ]

(Introduce yourself)

(Explain purpose of interview:) You have come here to get your ARV medication. We know that it can be very difficult to take this medication every day, and we are doing some research to find out whether patients manage to take their medicines correctly. Would you have a few minutes to answer some questions? We will not record your name, and this information will not go to anyone here at the clinic.

1. Sex: [   ] 2. Age: [   ]

3. Level of Education (tick:)
None, or Primary not completed
Primary completed
Secondary
Tertiary or vocational

4. Occupation:

4a: Employment category:
[   ]

5. How far did you have to travel today to come to the clinic (km) [   ]

(If distance not known, record here where patient lives):

6. How much to you pay for travel when you visit the clinic? (state amount) [   ]

7. What did you have to pay to register at this clinic? (state amount) [   ]

8. What do you pay for a month's supply of your ARV medicines? (amount) [   ]

9. Do you lose any income as a result of your coming to the clinic? (Y/N) [   ]

10. Do you or your family have to give anything up in order to be able to pay for your ARV treatment? (Y/N) [   ]

11. Has your being on ARVs resulted in any changes in expenditure? [   ]
(1=same; 2=more; 3=less)

12. When did you start treatment? (approximate date, e.g. mid-May 04) [   ]

13. Were you counselled about adherence before starting treatment? (Y/N) [   ]

14. Have you experienced any side effects with your ARV medication? (Y/N) [   ] *If yes:.............* 15. Has this been a reason for you to skip your medication at any time?

16. What do you think would happen in your body if you skipped your ARV medication?

DO NOT prompt the patient. Record "Yes" if patient mentions one or more of the following: viral load increases, patient's health gets worse, virus becomes resistant (Y/N) [   ]

17. Do you have anyone to remind you to take your ARV medication? (Y/N) [   ]

18. Do you use a medication diary or calendar? [   ]

19. Have you ever missed an appointment at this clinic? (Y/N) [   ]

20. What do you know about HIV infection?
(Give 1 point each if patient knows about: cause of HIV, cause of AIDS, prevention, that infection is life-long)

21. What do you know about antiretroviral medicines?
(Give 1 point each if patient knows: Prolong life, improve quality of life, life-long treatment, knowledge about side-effects

22. Quality of life (feeling respected, listened to, privacy, given chance to ask questions)

3=very good, 2=good, 1 = poor

+Have any of the following ever made you skip your medication +:

Ask for each box 23-38, mark with "+" if yes

(15. Side effects/adverse effects) [   ]

23. Felt better: [   ] 24. Clinic not accessible [   ] 25. Cost of ARVs: [   ] 26. Lack of food: [   ]

27. Pill burden: [   ] 28. Lack of care/support [   ] 29. Hospitalized: [   ] 30. Depressed: [   ]

31. Did not understand instructions: [   ] 32. Shared pills: [   ] 33. Distance: [   ]

34. Alcohol use: [   ] 35. Didn't have pills with you: [   ] 36. Simply forgot: [   ]

37. Feeling that you had to hide your medication from those around you: [   ] 38. Other (describe): [   ]

We would like to get your best guess about how much of your ARV medication you have managed to take recently. We would be surprised if this was 100% for most people. We will try several ways to estimate this.

39. Please make a mark on the line to show how many of your ARV pills you think you managed to take in the last month:

None ————————————————————— **All**   cm: [   ]

Can I see your medicine, please? (Complete names and number of pills/day for each medicine)

Drug A: _____ Pills per day: _____
Drug B _____ Pills per day: _____
Drug C _____ Pills per day: _____
Drug D _____ Pills per day: _____

40. Now remember the last seven days. Did you miss any pills in that time? If yes, how many pills?

(If any, ask:) "Can you remember why?" Let patient state reasons, tick boxes 15 and 23-38 on page 1 (again) with "x" if mentioned

41. Now, try to remember the last two days. When did you take each medicine, and when did you have meals?

On the slip below, fill in patient's medicines (as on page 2) and study number (as on page 1).

Please take this slip to the pharmacy to complete. We will collect it from there.
THANK YOU VERY MUCH FOR SHARING YOUR EXPERIENCE WITH US.

To the pharmacist:
Please indicate for each antiretroviral medicine:
1. How many pills the patient **should have taken** since his last visit, and
2. How many s/he missed (how many **extra pills were returned**).

You can follow the example given if it helps, but only the two bold, shaded lines need to be completed.

	Example	Drug A	Drug B	Drug C	Drug D	Study number
Drug name (as on page 2)						
Previous Date issued	6 Jan					(as on page 1)
Qty taken home (total)	67					
Qty returned	15					
Date returned	3 Feb					
Days since last issue	28					
Regimen	2 bid					
1. Total supposed to take	56	[ ]	[ ]	[ ]	[ ]	
Should have returned	67-56=11					
2. Pills missed	15-11=4	[ ]	[ ]	[ ]	[ ]	
Percent adherence	(56-4)/56 * 100					

6.   Exit interviews with ARV users

Guideline for exit interviews with PLWHIV using ARVs
(To be conducted after pharmacy visit, i.e. when all their business at the health facility is completed).

Name of facility

Name of interviewer

Interview number

Date

(Introduction of the interviewer (s), introduction of the study, consent requested with option not to participate, assurance of confidentiality)

Background information on informant

a) Sex	M/F
b) Age	Years
c) Educational level	
d) What do you do for a living	
e) Distance from facility (in time or distance) (NB village or ward)	

Whom did you visit today? (Can include more than one)

- Counsellor
- Nurse
- Medical doctor
- Pharmacist
- Other

What was the reason for your visit today?

- Counselling
- To start using ARV/AIDS medicines
- Routine follow-up, if yes: when did you start using the AIDS medicines?
- Other reason:

What was the result of the visit?

- I got ARV medicines for the first time
- They gave me a refill of my ARV medicines
- They gave me a different kind of ARV medicines
  If yes, why did the doctor prescribe different medicines?

- Other

If you were given AIDS medicines for the first time *today*, or were given a new kind of AIDS medicine *today*, what did the health worker tell you? (Open ended, then probe on following topics)

What HIV/AIDS is?   By whom?

How ARVs work?   By whom?

How to use them?   By whom?

The need to continue treatment   By whom?

What to do if a pill is forgotten   By whom?

Possible interactions with other drugs   By whom?
(including traditional medicine)

Which side effects can occur with (state the   By whom?
drugs the patient is taking) & what to do if
they occur

(Breast) feeding requirements   By whom?

When and where to get re-supply   By whom?

What is required when you come for re-   By whom?
supply (bring unused medicines?)

(If client was given a repeat prescription, ask him/her the following; if new patient, proceed to 8)

What did you discuss with the health worker?

_____

Probe for:
a) Did you talk with the health worker about your experience of using your medicines? (Side effects, perceived effects)

- Did the health worker ask you if you have missed a dose?

Yes ☐   No ☐

b) If yes, did the health worker explain what the effects are of missing a dose?

Yes ☐   No ☐

c) Did your health worker count your pills before giving you a new supply?

Yes ☐   No ☐

d) Did the health worker ask you if you were taking any other medicines?

Yes ☐   No ☐

Assessment of adherence and non-adherence

a) Do you have your medicines with you?

Yes ☐   No ☐

b) May I see them? Please can you tell me when you take each of the medicines?
    (Refer to table with sun and moon, or other checklist)

c) Are there any other medications you are taking
    (e.g. cotrimoxazole, traditional medicines, herbs etc)

Yes ☐   No ☐

d) Over the last two days, when did you take your pills? (Not including today -
    from yesterday evening and back.)

e) Did you perhaps miss any?
    (Confirming (c), sympathetic manner. Details if yes.)

___

f) What do you do to remind yourself to take your pills?

___

Cost consideration

a) How much do you have to pay to cover your travel expenses when you visit
    the clinic?

b) Do you lose any income as a result of your coming to the clinic?

Yes ☐   No ☐

c)   (Do you incur any other costs as a result of your taking ART?

Yes ☐   No ☐

d) Do you and your family have to give anything up in order to be able to pay for
    your ART?   Yes ☐   No ☐

Quality of care in the ARV Clinic
I would like to ask you some more questions about the way you
were treated in the clinic today.

a) What do you think of the service you receive at this clinic? (General, open-
    ended, and then prompt, as below: ask for details as necessary)
    Do you feel listened to?   Yes ☐   No ☐

    Are you given the chance to state your problems and ask questions?

Yes ☐   No ☐

    Are you treated with respect?   Yes ☐   No ☐

    Do you feel you can trust the health workers?   Yes ☐   No ☐

    Do you have privacy during consultation and counselling?

Yes ☐   No ☐

    How do you find the environment of the clinic?   Yes ☐   No ☐

b) How long have you spent altogether at the clinic today?

_____

c) How long did you have to wait before being attended to?

(For consultation   … … min/hours   For dispensing   …….min/hrs

d) Did you receive any written information?   Yes ☐   No ☐

Perceived problems and possible solutions

a) What do you perceive as most problematic regarding taking the ARV treatment?

b) What do you think could be done to improve this?

Anything else to say or ask?

Is there anything else you would like to tell us or ask us?

Thank you very much for your participation in this interview.

7.   Guide for observation of health facility

Name of observer
Name of health facility
Date/time observation took place

This observation shall be conducted by the researchers.
The purpose is to give a descriptive of the setting under which care takes place.

1.   Describe hospital setting in general.

2.   Describe the location and setting of the ARV clinic and support services (pharmacy, laboratory, social welfare/counselling).

3.   Describe the sanitary condition of the environment, how clean or dirty is it, check out the toilets. Describe

4.   Where are patients received? Is there privacy? Describe what you see

5.   What is the general attitude of health workers, are they receptive and willing to assist clients or are they impatient? Describe what you see what notices or information are displayed for clients to read, describe

6.   Specifically look through where patients get ARVs to see if there is any piece of information emphasizing the need for good adherence or telling people how to improve adherence.

8.   Observation of consultation with health workers

Study no ☐

(Medical doctor, Nurse, Pharmacist, Social worker/Counsellor, Receptionist, laboratory personnel).

<u>Guide has to be adapted, taking into account the type of consultation to be observed</u>

(*Don't forget informal, unstructured observations!!!*)

Name of facility   _____
Date   _____
Interviewer   _____

Consultation: Start time: ------   End time: --------

Observation of consultation with: ....
- ❑   Medical doctor
- ❑   Nurse
- ❑   Social worker/counsellor
- ❑   Pharmaceutical staff
- ❑   Receptionist
- ❑   Laboratory personnel
- ❑   Other: ………………………..

1.   Background information on informant

a) Sex	M/F
b) Age	…….. Years (ask or estimate)

2.   Reason / Aim of the consultation:
- Counselling
- Initiation of active ARV treatment
- Routine follow-up
- Other reason: ………………………….

3.   Is patient well received?   Yes ☐   No ☐

      (If not, describe)

      _____

4.   Was the client greeted in a friendly manner?   Yes ☐   No ☐

5.   Does the consultation take place in privacy?   Yes ☐   No ☐

6. Does the health worker ask about any symptoms?   Yes ☐   No ☐

7. Is the patient invited to ask questions?   Yes ☐   No ☐
    (If yes, what do they ask? Was the question addressed?)
    Details:

8. Is the patient told what to do next
    (within the health facility)?   Yes ☐   No ☐

    Is the patient told where to go for that?   Yes ☐   No ☐

9. Is the sequence of events in relation to treatment protocols explained
    to *new* patients? (Requires training for observer)   Yes ☐   No ☐

10a. **If *new* patients, d**o they receive comprehensive general information about
      ARVs? *(Tick if covered, X if not covered):*

- How ARVs work ☐
- How to use them ☐
- The need to continue treatment ☐
- What to do if a pill is forgotten/missed ☐
- Possible interactions with other drugs, including traditional

  medicines ☐
- Which side-effects (for the different drugs) may occur ☐
- What to do if they occur ☐
- (Breast) feeding requirements ☐
- When and where to get re-supply ☐
- Requirement to bring unused medicines ☐

10b. Are patients (especially new and those switching regimens) given the following
      information about ARVs: *(Tick if covered, X if not covered):*

- Dosage (number of tablets to take and how often) ☐
- Times of when to take the medicines ☐
- How to take them in relation to meals (where necessary) ☐
- What to do if vomit the pill ☐
- What to do if forgets to take medicine on time ☐
- What to do if dose is missed ☐
- What to do if travelling? ☐

10c. **For *follow-up* users only:**
Does the health worker ask if the patient missed a dose?

Yes ☐   No ☐

If yes, does the health worker explain the effects of missing dose?

Yes ☐   No ☐

Does the health worker offer support to not miss the doses?

Yes ☐   No ☐

If yes, describe

---

11.   Did the provider listen carefully to the client?   Yes ☐   No ☐

12.   Was any written information given? **(new patients)**   Yes ☐   No ☐
If yes, bring a copy of it if possible.

13.   For follow up patients only:
Does the health worker count the patient's pills before giving
him/her a new supply?   Yes ☐   No ☐

14.   Does the health worker ask the patient if they are taking
any other medicines   Yes ☐   No ☐

15.   Does the patient receive specific tools to remind them
to take their medicines?   Yes ☐   No ☐

9. Semi-structured interview with site manager

Name of interviewer
Place of interview
Date of interview
Officer interviewed

Interviewer appropriately greets person to be interviewed, explains purpose of the interview.

The main purpose of these interviews shall be to ascertain to what extent adherence to medication was considered important prior to programme commencement.

- What strategies were put in place to encourage good adherence.
- What strategies were put in place to monitor adherence.
- What strategies are being put in place to improve adherence.

The interviewer shall probe where relevant - the questions below are merely a guide.

But we shall start with these questions.

1.   When did the facility start providing ART?

2.   Number of workers & type of staff involved in ART?

3.   Number of staff trained & type of training?

4.   Total number of patients on treatment at the facility?

5.   Total number of patients seen per day?

6.   Availability of reference materials, formularies etc.?

7.   Criteria for eligibility to ART (documentary/verbal)?

8.   We would like to know about the national roll out of ARVs, when and how did it all happen?

9.   How was your office involved in it?

10.   What in your opinion do you reckon to have been the greatest challenge you faced with the rollout?

11.   How did you overcome the challenge?

12.   What number of patients would you be looking at in the next one year by your projections?

13. Do you always receive your order as at and when due?

14. There had been times in the past when your patients had their ARV supply rationed because of inadequate stock, what do you know about this?

15. What mechanisms do you have to ensure availability and sustenance of ARV supply?

16. What do think the adherence levels of your patients' in terms of taking ARVs is?

17. What strategies have you in place to ensure patients receiving ARVs adhere well enough to their treatment?

18. Do you have any reporting and monitoring system for this?

19. Given your experience with your ARV programme is there any thing you would like to see done differently?

20. Do you think there are opportunities for improvement in your programme, if yes probe?

21. The Botswana rollout programme has drawn attention from all over the world, what do you think other countries contemplating national rollout for ARVs can learn from you?

Thank you very much for your time.

10. Questionnaire guideline for key informant interview

List of possible key informants and topics

This is a guide to help researchers remember different issues that may be discussed with key informants of different types. They include general topics, which could be discussed with all these people; and additional topics as under each category. The list could be added to as new issues arise.

General topics

Handling of misconceptions about ARVs
Beliefs about illness (HIV)
Beliefs about ARVs/alternative ways of treatment
Community participation (pre-intervention sensitisation, communication channels, community response to sensitisation)
Community support system; Support systems for people living with HIV/AIDS: home-based care, compassionate visits (by whom, for what purposes)
Stigma/discrimination
Disclosure
Workplace
Employer support

Key informant categories

Member of council/Local Authority
Support systems for people on ARV treatment (transport, food baskets etc.)

Chief
Cultural support/discrimination

Religious leader
Spiritual support, prayers

Home-based care volunteers
Collecting medication
Administering medication
Pill counts at home

'Family Welfare Educators'
Education packages available
Follow up of non-adherent patients

Traditional healers
Handling of patients being treated with ARVs
"Referral" of patients

PLWHIV Association
Support systems
Stigma
Issues faced my members in relation to adherence, accessing drugs etc.

11. Semi-structured interview with national level policy makers

Name of interviewer
Place of interview
Date of interview
Officer interviewed

- Interviewer appropriately greets person to be interviewed, explains purpose of the interview.

- The main purpose of these interviews shall be to ascertain to what extent adherence to medication was considered important prior to programme commencement.

- What strategies were put in place to encourage good adherence.

- What strategies were put in place to monitor adherence.

- What strategies are being put in place to improve adherence.

The interviewer shall probe where relevant. The questions below are for guidance only.

We would like to know about the national roll-out of ARVs, when and how did it all happen?

a) How was your office involved in it?

b) What in your opinion do you reckon to have been the greatest challenge you faced with the rollout?

c) How did you overcome the challenge?

How many patients nationwide are on ARVs presently?

a) What number of patients would you be looking at in the next one year by your projections?

b) Where do you source your ARVs from?

c) Who does the procurement?

d) Do you always receive your order as at and when due?

e) There had been times in the past when your patients had their ARV supply rationed because of inadequate stock, what do you know about this?

f) What mechanisms do you have to ensure availability and sustainability of ARV supply?

What do think the adherence levels of your patients' in terms of taking ARVs is?

a) What strategies have you in place to ensure patients receiving ARVs adhere well enough to their treatment?

b) Do you have any reporting and monitoring system for this?

Given your experience with your ARV programme is there any thing you would like to see done differently?

a) Do you think there are opportunities for improvement in your programme, if yes probe?

The Botswana rollout programme has drawn attention from all over the world, what do you think other countries contemplating national rollout for ARVs can learn from you?

A study on antiretroviral adherence in Tanzania: a pre-intervention perspective, 2005

Henry Irunde, Florence Temu, Janneth Maridadi, Stephen Nsimba, Christopher Comoro.

Research team

Principal investigator:
Henry F.H. Irunde
Ministry of Health
Tanzania Food and Drugs Authority
PO BOX 77150, Dar es Salaam
Tanzania
E-mail: irunde@yahoo.com

Co-researchers:
Florence Temu
AMREF - Tanzania Country Office
PO BOX 65000, Dar es Salaam
Tanzania
E-mail: fsipora@yahoo.com

Janneth Maridadi
National Institute of Medical Research
PO BOX 9653, Dar es Salaam
Tanzania
E-mail: mashaka_2000@yahoo.com

Stephen E.D. Nsimba
Muhimbili University College of Health Sciences
PO .BOX 65010, Dar es Salaam
Tanzania
E-mail: snsimba@muchs.ac.tz
Or: nsimbastephen@yahoo.co.uk

Christopher Comoro
University of Dar es Salaam
PO BOX 35043, Dar es Salaam
Tanzania
E-mail: topher06@uccmail.co.tz

Contents

Acknowledgements

Acronyms and abbreviations

ADR	Adverse drug reaction
AIDS	Acquired Immune Deficiency Syndrome
AMREF	African Medical and Research Foundation
ART	Antiretroviral therapy
ARVs	Antiretroviral medicines
CTC	Care and Treatment Clinics (also known as ART clinics)
FGD	Focus group discussion
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
GoT	Government of Tanzania
HIV	Human immunodeficiency virus
IEC	Information, education and communication
INRUD	International Network for Rational Use of Drugs
MDH	Muhimbili University College of Health Sciences (MUCHS), Dar es Salaam City Council and Harvard School of Public Health
MNH	Muhimbili National Hospital
MoH	Ministry of Health
MSD	Medical Stores Department
NACP	National AIDS Coordinating Programme
NGO	Nongovernmental organization
NIMR	National Institute of Medical Research
PASADA	Pastoral Activities and Services for AIDS in Dar es Salaam Archdiocese
PEPFAR	President's Emergency Plan for AIDS Relief (USA)
PLWHIV	People living with HIV
SIDA	Swedish International Development Agency
SSI	Semi-structured interview
TFDA	Tanzania Food and Drugs Authority
UDSM	University of Dar es Salaam
WHO	World Health Organization

Executive summary

In Tanzania, the burden of HIV is second only to malaria, with an estimated prevalence of 7% among adults (Tanzania Commission for AIDS, 2005). Today, the HIV epidemic is recognized not only as a major public health problem but also as a socioeconomic and developmental crisis that affects all sectors. The Tanzanian Government has recently initiated the roll-out of free antiretroviral therapy (ART). Although antiretroviral medicines (ARVs) can be effective in controlling the disease, they do not provide a cure and pose new challenges due to potential side-effects and the emergence of drug-resistant strains of HIV. However, the introduction of ARVs has dramatically reduced rates of mortality and morbidity, improved the quality of life for people living with HIV (PLWHIV), revitalized communities and transformed the perception of AIDS from that of a plague to a manageable, chronic illness.

Adherence to treatment is a critical factor in the success of ART. Patients must achieve at least 95% adherence in order to avoid treatment failure and the risk of developing drug-resistant strains of the virus. In Tanzania, up till now there has been no attempt to document the level of adherence to ARV treatment or to identify possible factors contributing to sub-optimal adherence. The present study was designed to help fill that gap. The aim has been to measure adherence and to identify possible factors and operational barriers facilitating or constraining adherence to ART among AIDS patients and to suggest possible ways of improving adherence.

A cross-sectional study on ARV adherence was conducted in Arusha and Dar es Salaam in June and July 2005, involving a total of seven health care facilities in the two regions. A multi-disciplinary team of researchers collected the data from ARV users through exit interviews, semi-structured interviews, adherence measurement, focus group discussion (FGD) and key informant interviews. In seeking information from health care staff, the tools used were semi-structured interviews, observation of staff while conducting consultations, and pharmacy stock controls.

A total of 207 ARV users were involved in the study, 26 observations were made, 28 staff were interviewed, 8 FGDs and 10 key informant interviews were conducted, and 6 pharmacy stock checks were carried out in health care facilities.

The mean age of ARV users studied was 43 for males and 37 for females and most of the ARV users studied were females (64%). Most male ARV users were either employed in the private sector or self-employed in a small-scale business, while female ARV users were either not employed or involved in minor trade. Of the staff interviewed, most were nurses.

In this study, adherence is considered from the perspective of both the ARV user and the health worker. From the ARV users' perspective (based on two-day recall, visual analogue and the pill count method) the mean level of adherence was 95%, while from the health workers' perspective it was found to be 88% (range 60%-100%). The composite measure of adherence using 28-day visual analogue and pill count method was 90%. However, only 21% of ARV users interviewed reported achieving the optimal level of adherence (over 95%) as measured by the composite adherence rate. The remaining 79% self-reported to achieve only moderate adherence (85%-95% adherence rate) and are therefore at risk of treatment failure and the development of drug-resistant forms of the virus.

While most patients seemed to be knowledgeable about ART, a few patients were not well-informed about treatment and the consequences of sub-optimal adherence to ARVs. The main ways of providing this information at the health facilities involved in the study included leaflets, seminars, adherence counselling, verbal counselling, television and video.

The standard of counselling was considered to be good in Dar es Salaam but there was less satisfaction with the counselling services provided in Arusha. Despite widespread information about HIV and AIDS, the idea of bewitchment as the source of HIV was still reflected in the perception of some patients. And although most of the 30 ARV users interviewed during semi-structured interviews (93.5%) had disclosed their HIV status, social stigma was said to be widespread. Respondents said that PLWHIV are often stigmatized both at home and in the workplace (especially in the private sector).

The cost of once-monthly travel to the clinic for ARV users was significant, ranging from Tshs 200-30 000 (approximately 20 US cents to US$ 30.00), while the distance patients had to travel ranged from 1 km to 246 km.

Both ARV users and key informants said that lack of food was a problem for most ARV users. This was exacerbated by a treatment-related increase in appetite and by the additional demands of needing to take some medicines together with food. However, this did not appear to affect treatment adherence among the ARV users involved in the study. Of the ARV users who cited lack of food as a problem, all maintained that they had persisted in taking their ARVs. Other interviewees remained concerned at the potential impact of hunger on adherence to ART. For example, it was reported that some patients take their medication only once a day, in the evening, because that is the time when they have food, and that some patients were selling ARVs in order to buy food. This implies that food scarcity can be a drawback to adherence.

The study identified a number of structural problems in the health facilities involved. For example, it was found that consultations carried out in some of the public facilities in Arusha were not as conducive to confidentiality as consultations in the public facilities in Dar es Salaam. Elsewhere, at the private facilities in both Dar es Salaam and Arusha, confidentiality was said to be satisfactory. In addition, ARV users reported that they could spend up to 10 hours in the health care facility waiting to be attended to during their monthly visits.

According to both ARV users and staff, laboratory services were inadequate in some of the public facilities surveyed. Problems cited included the unavailability of CD4 reagents and machines, thus delaying the required tests. The private facilities were better equipped than the public facilities.

The prescribed ARV medicines were generally available in the health care facilities involved. Only five of the staff interviewed (including four from Government facilities) reported occasional shortages of prescribed medicines. Although medicines for opportunistic infections were reported to be available in most of the facilities, these were not always dispensed free of charge.

The staff involved complained of low motivation, inadequate training, and of being overloaded with work. Other complaints included long waiting times for patients due to the limited number of staff.

Suggestions for ways of improving the ARV programme included: providing food and financial loans to ARV users; adequate counselling; using education and information to help reduce stigma; efforts to reduce waiting times; an increase in the number of ART clinics and in staffing levels; ensuring a reliable medicine supply chain; improvements in staff motivation and training; providing transport for staff involved in home-based care (i.e., treatment monitoring and adherence counselling); and an increase in laboratory services.

While the relatively high rate of adherence reported in this study is encouraging, more efforts are needed to ensure optimal adherence among the large group (79%) of ARV users who are currently taking less than the critical 95% of their dosage. There is much that could be done to sustain and improve the current adherence rate. Many potential activities or interventions could be implemented and evaluated to determine which are most effective. As ARVs are rolled out to meet the challenging targets set by the Government, it is critically important to determine how to ensure optimal adherence for good clinical outcomes and to prevent the emergence of drug-resistance.

Chapter 1: Introduction

1.1   Background

The United Republic of Tanzania is one of the world's poorest countries. It has a gross domestic product of US$ 600 per capita, and life expectancy at birth is 44 years (CIA World Factbook, 2003). HIV is a serious public health problem in Tanzania, second only to malaria, with an estimated prevalence of 7% among adults (Tanzania Commission for AIDS, 2005). HIV is a major development crisis that affects all sectors. It has had a major impact on health, economic and social progress – reducing life expectancy, deepening poverty, and contributing to and exacerbating food shortages (National AIDS Coordinating Programme (NACP), 2003).

The advent of ART in 1996 changed the way people in the world's richest countries view HIV (UNAIDS, 2004). Although ARVs do not provide a cure and pose additional challenges due to potential side-effects and the emergence of drug-resistant strains of HIV, they have dramatically improved rates of mortality and morbidity, improved quality of life, revitalized communities and transformed the perception of AIDS from that of a plague to a manageable, chronic illness (UNAIDS, 2004).

Tanzania receives various sources of funding for HIV from organizations such as the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), the US President's Emergency Plan for AIDS Relief (PEPFAR), the Clinton Foundation, the Swedish International Development Agency (SIDA) and the Tanzania Multi-country HIV/AIDS Programme. The Government of Tanzania (GoT) has been vigorously engaged in efforts to combat HIV and has launched initiatives to increase the availability of ARVs as well as other medicines for the management of HIV-related opportunistic infections. The Tanzania Food and Drugs Authority (TFDA) has registered more than 50 ARV formulations, enabling private pharmaceutical companies and hospitals to stock and sell ARVs (TFDA, 2004). Government efforts are also supported by an increasing number of nongovernmental organizations (NGOs) and private companies which are promoting and establishing HIV policies and treatment programmes for their employees (e.g. the African Medical and Research Foundation (AMREF) and the Tanzania Cigarette Company).

Over the past few years, the price of ARVs has fallen dramatically. In 2000, the price of a first-line WHO-recommended ARV regimen to treat one patient for one year was between US$ 10 000 and US$ 12 000 on world markets. By 2004, the price for some generic combinations was approximately US$ 300 per person per year (UNAIDS, 2004). The decrease in prices is attributed to increased funding from the Global Fund and PEPFAR and competition from generic manufacturers.

The GoT has ambitious plans to put more than 400 000 people on ARVs within a five-year period (October 2004-September 2009). The Government's interim goal of putting 44 000 people on ART by end-2005 was not met. The National AIDS Control Programme reported that, as of January 2006, an estimated 25 300 people were on treatment. As ART is scaled up in Tanzania, there is a need for community mobilization and empowerment in order to address social factors that constrain adherence to ART. An understanding of these factors is crucial in order to plan for the scaling up of access to ART.

1.2   Rationale

As more people gain access to ART, new initiatives are needed to help ensure that patients adhere to treatment. The maintenance of viral suppression requires maximum adherence (at least 95%) to ART (Parades, 2000; Garcia et al., 2003). Insufficient adherence to ARVs may result in treatment failure and the emergence of drug-resistant strains of HIV and require a change to second-line treatment regimens, thereby greatly increasing treatment costs (Bangsberg et al., 2000).

The availability of ARVs in Tanzania is relatively recent. Therefore this study was designed to investigate key factors associated with adherence and non-adherence to ARV medication, with a view to suggesting possible intervention measures to sustain or improve adherence. The study focused on health facilities where ARVs had been provided for at least three months. It is part of a multi-country study also carried out in Botswana and Uganda.

1.3   Literature review

Adherence is described as the engagement and accurate participation of an informed patient in a plan of care (Rabkin et al., 2003). The concept of 'adherence' has a broader meaning than compliance. It encompasses the extent to which a patient follows instructions and implies understanding, consent and partnership. It also includes entering into and continuing in a programme or care plan, as well as keeping appointments and tests as scheduled (Rabkin et al., 2003). In low-income countries, adherence can be a problem for a number of reasons. Yet studies have shown no significant difference in adherence between resource-limited and resource-rich countries, which suggests that patients in all environments have trouble adhering to medicines 100% of the time. It is therefore recommended that all ARV programmes worldwide should have a concurrent plan for adherence assessment and support (Rabkin et al., 2003; Weiser et al., 2003).

For the purposes of this study, '*Near perfect adherence*' has been defined as 95% and above adherence. The ability to consistently take the medicines at exactly or approximately the same times each day depends on the individual's frame of mind as well as the support of family members, the people around them, and the community at large. Administration of ARVs imposes constraints on the daily schedule and lifestyle and it can be difficult for individuals to adapt to these demands, especially on a long-term basis.

Previous studies in Tanzania on other diseases have indicated that patients often do not have enough knowledge and/or do not remember how to use various prescribed medicines, contributing to their irrational use (Mnyika et al., 1995; Massele et al., 1993; MoH, 2002). This has also been observed in settings where ARVs are used. For example, in a previous study in Botswana, 54% of patients reported optimal adherence (defined as completing greater than or equal to 95% of prescribed doses) and 56% were seen as achieving optimal adherence on the basis of provider assessment (Weiser et al., 2003). The main factors affecting ARV use in Botswana were structural, disease-related and treatment-related factors, and socioeconomic and cultural factors. For instance, patients lacked funds and had to travel long distances to the clinics providing ARVs. If cost was eliminated as a barrier, then the adherence rate was predicted to increase to 74% (Weiser et al., 2003). The Botswana Government has taken several initiatives to improve adherence, including increasing access to ARVs in the public sector, improving the distribution of ARVs, increasing the availability of clinical and laboratory monitoring, and strengthening health infrastructures for delivering care.

The role of sociodemographic characteristics, such as gender, race, age, exposure category and educational level as predictors of adherence has produced largely inconsistent results (Horne et al., 1998). The tendency to ascribe low adherence to (often deprived) social groups is a well established trend in the general literature, dating back to 1990 when tuberculosis control occupied public health officials (Lerner et al., 1998). However, as later experience with antibiotics demonstrated, low adherence is not restricted to certain social classes but is widespread and unpredictable. Research in the HIV field supports this perspective. Moreover adherence rates vary not just between individuals but also for the same individual over time (Carrieri et al., 2001). Adherence is therefore best thought of as a variable behaviour rather than as a constant characteristic of an individual. Most people will exhibit low adherence some of the time (Horne et al., 1998).

Psychological factors, including mental health problems such as depression, have been associated with low adherence in HIV-infected adults and adolescents, as have other psychological variables such as perception of one's ability to follow a medication regimen, or self-efficacy (Singh et al., 1996; Murphy et al., 2001; Eldred et al., 1998; Tuldra et al., 2000). Beliefs about health and illness, in particular about the necessity of medication to ward off illness and concerns about potential adverse events, have been found to be influential in both HIV and other disease areas (Horne et al., 2001 and 2002).

1.4 Problem statement

A comprehensive study of ARV adherence and possible factors facilitating or constraining adherence to ART in Tanzania has not yet been attempted. Elsewhere, studies in other countries have described a range of factors affecting ARV treatment adherence at various levels, including individual, community and health facility levels (Weiser at al., 2003; Horne 1998; Eldred et al., 1998). These factors can be broadly grouped into three categories: structural factors, disease and treatment factors, and social and economic factors. The structural factors include inadequate support services,

limited accessibility of treatment, long distances to the health facility, lengthy waiting times, and the attitudes and quality of care of the health care staff. The disease and treatment factors include the seriousness of the disease, adverse drug reactions, and side-effects. The socioeconomic factors include poor patient knowledge and information, illiteracy, lack of social support, poverty, stigma, misconceptions about HIV and AIDS, and communication barriers between patients and doctors/care-givers (see Figure 1 below).

1.5 Objectives

1.5.1 Broad objective

The purpose of this study was to identify possible factors which constrain or facilitate adherence to ART among AIDS patients and suggest possible ways to improve adherence.

1.5.2 Specific objectives

The study aimed to:

♦ determine the proportion of patients who achieve/do not achieve optimal adherence to ART in selected health facilities in Tanzania

♦ identify factors (structural, socioeconomic, cultural and disease-related) contributing to sub-optimal adherence

♦ assess the quality of the operating structures for the provision of ARVs in the selected health facilities

♦ assess the quality of the processes involved in providing ART services for patients attending the selected sites

♦ document suggestions and proposals for improving ART adherence from ARV users, health care providers and key informants.

1.6 Output

The study addressed:

♦ The degree of ART adherence and sub-optimal adherence in two regions of Tanzania

♦ Possible factors (structural, socioeconomic, disease-related) contributing to sub-optimal adherence to ART

♦ Possible operational barriers to ART adherence

♦ Possible interventions to be undertaken to improve ART adherence.

Figure 1: Problem analysis diagram on factors affecting ARV adherence
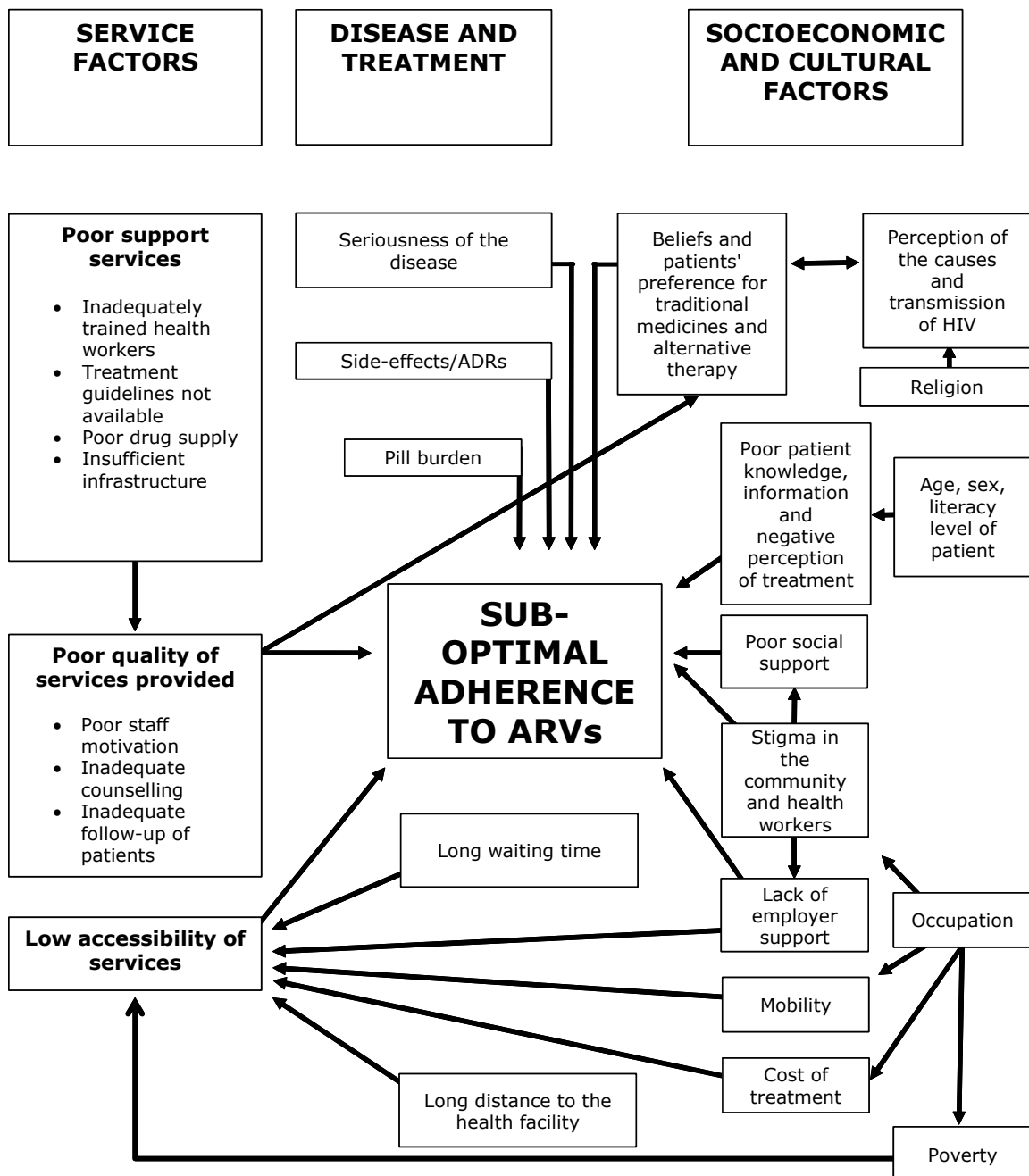
Chapter 2: Methodology

2.1 Study design

The study was based on a cross-sectional study design using rapid appraisal techniques for collecting both qualitative and quantitative data.

2.2 Study population

The study population included:

♦ ARV users from seven health care facilities who met the criterion of being on ART for at least three months

♦ staff at the seven health care facilities who were involved in counselling and providing ARV medicines (e.g., nurses, doctors) and the pharmacists who were dispensing and stocking drugs

♦ key informants who were identified from among the communities to which the ARV users belonged (e.g., AIDS activists from NGOs, coordinators of HIV programmes and representatives of local government).

2.3 Inclusion and exclusion criteria for interviewees

Inclusion criteria:
   Patients
   - Adult, 18 years or over and willing to participate in the study
   - On ART for at least three months
   Health care workers
   - Staff working at the ART clinic and willing to participate in the study
   - Well-informed about ARV users

Exclusion criteria
   Patients
   - Not willing to be interviewed
   - Below age 18
   - Not on ARV treatment
   Health care workers
   - Not willing to be interviewed
   - Working at the ART clinic for less than one month
   - Not directly interacting with ARV patients.

2.4   Quantitative data

Most of the quantitative data were collected using an adherence tool and some were collected using exit interviews, semi-structured interviews and a checklist for pharmacy stock. The adherence tool was administered before the patients collected medication from the pharmacy. The exit interview was conducted after the patient had been attended to.

2.5   Qualitative data

Qualitative data were obtained using an observation checklist, semi-structured interviews, exit interviews, focus group discussions (FGDs) and interviews with key informants.

2.6   Data collection tools

A combination of data collection tools were used to gather the information in this study. Tools used for data collection from ARV users were exit interviews, semi-structured questionnaires, adherence tool and FGDs. These tools were originally developed at a multi-country workshop held in Bagamoyo in February 2005, and were then adapted after pilot testing. They are included in this report as Annexes. The following tools were used with other population groups: semi-structured interviews with staff, observation, pharmacy stock controls and key informant interviews with identified community members.

Instruments used to measure adherence were:

♦   Two-day recall, involving the use of 'sun and moon' charts to measure the consistency of the times respondents took their medicine over the previous two days (Annex 4).

♦   Visual analogue, in which ARV users were asked to pour beads from one glass into another to indicate the number of pills they would have taken over a one-month period. The remaining beads in the first glass were deemed to be the pills which the ARV user had forgotten to take during the course of the month. Adherence was recorded on the basis of the line marked from 0-10 on the first glass (Annex 4).

♦   Pill count method undertaken by the dispensing pharmacist, in which the numerator was the number of pills supposed to have been taken over a given period minus the number of pills missed and the denominator was the total number of pills supposed to have been taken (Annex 4).

♦   Health workers' assessment, comprising the estimate of the level of adherence to treatment by ART clients over a period of not less than three months (Annex 6).

2.7   Pilot study

Following the multi-country workshop to develop instruments in early 2005, a planning meeting of Tanzanian medical and social scientists was held at the FDA at Mabibo in Dar es Salaam. The purpose of this meeting was to review research tools, to train the research assistants and conduct a pre-test of the tools in a selected health facility in Dar es Salaam. Amana Hospital in Ilala municipality was used as the pilot site. The pilot study was done two weeks prior to the main study, to determine the suitability of data collection instruments, sampling frame and techniques, and estimates of mean adherence, so as to calculate the sample size required for the adherence tools. The research tools were modified and finalized for the Arusha and Dar es Salaam data collection.

Following the pilot study results, the tools were refined into a good Kiswahili translation to make them clearer for the study population. The visual analogue method for estimating adherence level was modified from weekly to monthly recalls. In addition, a new category denoting the occupation of the respondent was added to the ARV user tools, as this was found to be important.

2.8   Sample size and sampling strategy

The sample size calculation for ARV users using the adherence tool was based on the results of the pilot study (mean overall adherence rate = 98%, $p*(1-p) = 0.015605$, and α at 95% confidence interval) which gave 24 per each health facility (estimated total of 168 ARV users for seven facilities). The adherence tool was used for 107 ARV users, while 100 ARV users were studied through exit interviews and semi-structured interviews (see Table 1). In some health facilities, the sample size was smaller than planned for the adherence tool because some identified users did not meet the criteria of being on treatment for at least three months. ARV users were randomly chosen using the outpatient attendance register. Each ARV user chosen was administered a single tool.

Twenty-six observations were made to see how the patient was received and dealt with in the ARV clinics and 28 health workers were also interviewed. The health workers interviewed were those who were working in the ART clinics. However, the number of staff varied between the different health facilities and therefore the expected sample size was not consistent in all facilities.

Eight FGDs were conducted with ARV users and 10 key informant interviews were carried out. In six of the health care facilities, stocks of ARV medicines were checked to assess availability.

Table 1 shows the total study population in the seven health facilities in both Arusha and Dar es Salaam according to data collection tools.

Table 1:
Study population of selected health facilities in Arusha and Dar es Salaam

	Facilities	Adherence tool	Exit interview	SSI client	SSI staff	FGD	Key informant	Observation consultation	Stock check
ARUSHA	Selian	15	17	3	4	1	2	5	1
	St Elizabeth	10	5	5	2	1	1	-	-
	Arumeru	5	5	5	5	1	1	4	1
	Mt. Meru	19	9	1	2	1	1	2	1
DAR ES SALAAM	M/nyamala	23	15	5	5	2	2	5	1
	PASADA	22	14	5	5	2	2	5	1
	Hindu Mandal	13	5	6	5	-	1	5	1
	Total	**107**	**70**	**30**	**28**	**8**	**10**	**26**	**6**

SSI: Semi-structured interview. FGD: Focus group discussion

2.9   Data collection

Data were collected by the research team and research assistants. Research assistants dealt with the adherence measurement tools and exit interviews under the supervision of the research team. Research team members conducted semi-structured interviews, FGDs, key informant interviews, observation of consultation and pharmacy stock checking. Review meetings were conducted each evening in order to share the daily experiences. In addition, the principal investigator checked the completeness of the collected data on a daily basis. In order to maintain consistency, the same team collected data in both Arusha and Dar es Salaam.

2.9.1   Data entry and analysis

Data for the adherence tool were entered into the prepared MS Access database while the remaining data were entered into Epi Info 2000. Data entry was checked by the principal investigator. Analysis was undertaken using both MS Access and Epi Info 2000. Descriptive analysis was done for the basic demographic characteristics. Means and standard deviation were calculated for quantitative data. For qualitative data, coding was done and data were summarized using themes. Methods used for estimating adherence included both ARV users` self-assessment, health workers` perception, pill count and visual analogue.

2.10   Ethics

The National Institute for Medical Research Committee issued ethical clearance for this study. Permission was also obtained from the respective regional health authorities and from the facilities involved. Consent was obtained from all the clients interviewed and from staff and key informants.

Chapter 3: Study areas

The study was conducted in Arusha and Dar es Salaam. Arusha is situated in a highland area in the north of Tanzania and has a population of almost 1.3 million, while Dar es Salaam lies in the coastal region and has a population of almost 2.5 million (National Bureau of Statistics, United Republic of Tanzania, 2003). These two cities were chosen because they had already been providing ARVs for at least three months at the time of the study. Arusha is a major tourist city which is known as the "Geneva of Africa" because it hosts many national and international conferences and meetings. Dar es Salaam is the major commercial city in Tanzania, which attracts many people both from other parts of the country and from abroad.

**Figure 2: Map of Tanzania showing the study areas of Arusha
and Dar es Salaam**

ARV adherence study sites shown by arrows.

3.1   Health care facilities

Seven health care facilities were selected, including both public facilities and private/faith-based facilities. In Arusha, four health care facilities were involved in the study: Selian and St Elizabeth Hospitals (both faith-based facilities) and Mount Meru and Arumeru Hospitals (both public facilities). Selian is operated by the Lutheran Church, while St Elizabeth is run by the Roman Catholic Church. Both hospitals are located within Arusha City and are beneficiaries of PEPFAR funding. The Selian Hospital launched its ART programme in 2003, while the St Elizabeth programme started in early 2005. At the time of the study, Selian had a total of 535 registered ARV users, of whom 353 were females and 182 males. At St Elizabeth Hospital there were 299 (215 female and 84 male) ARV users. Community counsellors were helping ARV users in Selian and St Elizabeth Hospitals.

Of the public health facilities, Mt. Meru is a regional hospital located in the centre of Arusha City. At the time of the study, it had 344 (212 female and 132 male) registered ARV users. Arumeru, a Government district hospital, is located 15 km outside the city and had only registered 87 ARV users (42 females and 45 males). Both hospitals started an ART programme in late-2004 and are funded by the Government and the Global Fund. Some of the facilities in Arusha did not operate on a daily basis, leading to time constraints for the research team as well as for ARV users.

In Dar es Salaam, three health care facilities were studied: Mwananyamala Hospital, Hindu Mandal Hospital, and PASADA (Pastoral Activities and Services for AIDS in Dar es Salaam Archdiocese) Hospital. Mwananyamala is a public district hospital, located in Kinondoni municipality; Hindu Mandal is a private hospital in Ilala municipality, which is owned and run by Tanzanians of Indian origin; and PASADA is a faith-based hospital run by the Roman Catholic Church in Temeke municipality. PASADA and Mwananyamala started their ART programmes in 2003 and 2004 respectively, while Hindu Mandal Hospital started in 2002. The Mwananyamala programme receives support from both the Government and the Global Fund, and is also a beneficiary of a HIV project run jointly by three institutions: Muhimbili University College of Health Sciences (MUCHS), Dar es Salaam City Council and Harvard School of Public Health (known as the MDH project). Funding of study facilities is shown in Table 2 below. At the time of the study, Mwananyamala Hospital had 1791 registered ARV users (907 females and 884 males); PASADA had 508 registered ARV users (364 females and 144 males); and Hindu Mandal had 178 ARV users (102 females and 76 males).

Table: 2 Summary of characteristics of the surveyed health care facilities

	Facilities	Public/ Private	Initiation of ART	ARV funding sources	ARV users	No. of clinics per week
ARUSHA	Selian	Private/ Lutheran	2003	PEPFAR Global Fund GoT	535	3
	St. Elizabeth	Private/ RC	2005	PEPFAR Global Fund GoT	299	3
	Arumeru	Public	2004	Global Fund GoT	87	5
	Mt. Meru	Public	2004	Global Fund GoT	344	1
DAR ES SALAAM	M/nyamala	Public	2004	Global Fund GoT MDH	1791	5
	PASADA	Private/ RC	2003	PEPFAR Global Fund GoT	508	5 clinics organized on the basis of age
	Hindu Mandal	Private	2002	Global Fund GoT	178	6

GoT: Government of Tanzania

Patients waiting for services at Mwananyamala Hospital, Dar es Salaam, one of the public health care facilities in the study.

Chapter 4: Quantitative results

Quantitative data were collected from exit interviews, semi-structured interviews and adherence tools.

4.1   Demographic characteristics of ARV users

Age and sex distribution

See Table 3 for the average ages of patients by sex and type of instrument used for data collection.

Table 3: Age and sex distribution of ARV users (N =207)

Sex	Age	Tool			Total/Mean
		SSI	Exit interview	Adherence tool	
		N=30	N=70	N=107	207
Male N=68	Mean age	45.4	43.5	39.6	42.8
	Range	24-57	18-60	27-51	18-60
Female N=139	Mean age	36.4	35.2	38.3	36.6
	Range	18-50	18-56	18-64	18-64

Combining all the three tools for ARV users, the mean age of male ARV users surveyed was 43 years and for females it was 37. Three interview tools were used but each ARV user was subjected to only one of these. Females featured most in all types of tools of data collection (67%).

Levels of education

Most of the ARV users participating in this study (almost 60%) had completed primary education and just over 30% had completed secondary education (see Figure 3 below).

Figure 3: Sex distribution of the ARV users by level of education
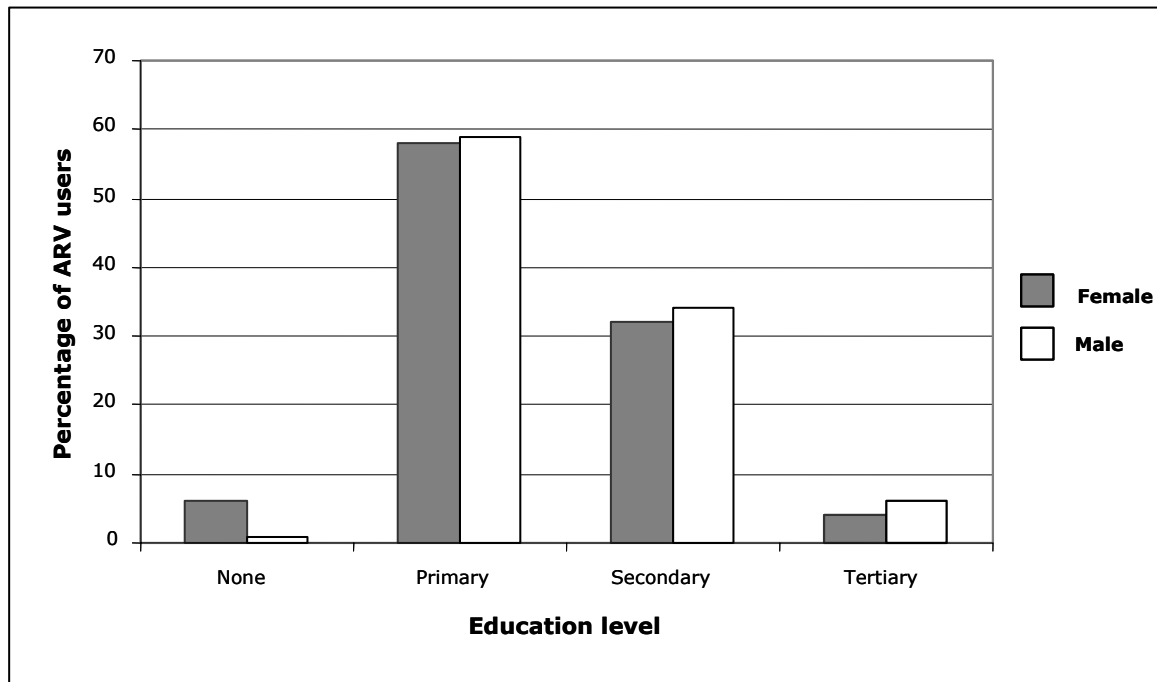
Occupation

ARV users: out of 65 females interviewed (exit interview or semi-structured interview), the largest group (37%) were not employed, followed by 35% who were working in a business. Among the 35 males interviewed, the most prominent occupations were private employee and business owner (each accounting for 29%).

Health care staff: a total of 29 staff were interviewed, including:

♦   5 medical doctors, 3 of them managers

♦   9 nurses

♦   5 counsellors, one of whom was also a social worker

♦   6 pharmacists

♦   1 dietician

♦   1 laboratory technician

♦   1 receptionist.

4.2   Adherence rates

The following is a summary table showing the level of adherence of ARV users by facility.

Table 4: Adherence of ARV users by facility (N=107)

Hospital		Two-day recall (sun and moon chart)	Visual analogue (glass of beads)	Pill count (pharmacy slips)	Composite adherence (one-month visual analogue and pill count)
ARUSHA	Arumeru (Government) **N=4**	100%	83%	100%	91%
	Mt. Meru (Government) **N=23**	100%	83%	97%	90%
	St Elizabeth (Private) **N=8**	100%	82%	98%	90%
	Selian (Private) **N=16**	100%	79%	100%	89%
	Weighted means*	100%	82%	98%	90%
DAR ES SALAAM	Mwananyamala (Government) **N=19**	100%	83%	98%	90%
	PASADA (Private) **N=24**	100%	83%	97%	90%
	Hindu Mandal (Private) **N=13**	100%	82%	99%	91%
	Weighted means *	100%	83%	98%	90%

* Weighted by number of patients at each facility.

The composite adherence for one month (for the seven health facilities involved) was 90%. In the public health facilities, the mean composite level of adherence for one month was 90.1%, while in the private facilities it was 89.9%. The weighted mean adherence rates for the ARVs users in Arusha and Dar es Salaam were similar (90%). The majority of clients seemed to be observant of their routine daily schedule for taking ARVs and used watches, radios and alarm clocks to remind themselves of medication times. However, a few people did not take their medication at the correct times. FGD participants observed that it was difficult to adhere to the exact schedule for taking ARVs.

> "*There is problem of adhering strictly to time and if you forget it is a problem.*"
> (Female FGD, Selian Hospital, Arusha)

From the health workers' perspective (using the semi-structured questionnaire), the mean percentage of adherence was estimated to be 87.8% (range 60%-100%). According to health staff, adherence was interpreted to mean using medicines as prescribed, at the right time and at the correct dosage, and attending the facilities as scheduled for follow-up checks.

Table 5: Number and percentage of ARV users according to adherence rate in the health facilities studied (N=107)

28 day mean composite adherence rate	Arusha		Dar es Salaam		Total
	Private No. (%)	Government No. (%)	Private No. (%)	Government No. (%)	
Moderate adherence (85%-95%)	19 (79)	18(67)	29 (78)	19 (100)	85 (79)
High adherence (>95%)	5 (21)	9 (33)	8 (22)	0(0)	22 (21)
Total	**24 (100)**	**27 (100)**	**37 (100)**	**19 (0)**	**107 (100)**

Table 5 shows that only 21% of ARV users achieved optimal adherence (as measured by a combination of monthly visual analogue and pill count) while 79% achieved only moderate adhererence.

Table 6: Number and percentage of ARV users according to adherence rate and sex in health facilities studied (N=107)

28 day mean composite adherence rate	Male	Female	Total
	No. (%)	No. (%)	No. (%)
Moderate adherence (85%-95%)	28 (85)	57 (77)	85 (79)
High adherence (>95%)	5 (15)	17 (23)	22 (21)
Total	**33 (100)**	**74 (100)**	**107 (100)**

Table 6 above shows that a slightly higher proportion of females achieved optimal adherence (23%) compared to males (15%) among the ARV users studied. However, overall there was no significant difference between males and females in adherence ($X2 = 0.4$, $p=0.51$).

Table 7 below shows the comparison of the adherence rates according to the education level of ARV users. There appears to be no association between education and adherence rates.

Table 7: Comparison of composite adherence rates among ARV users according to education level (N=107)

Level of education	Adherence rates		Odds ratio (95% confidence interval)
	Moderate adherence (85%-95%)	High adherence (>95%)	
No education/primary not completed	5	2	1
Primary completed	53	10	2.12 (0.24-15.46)
Secondary	27	8	1.35 (0.15-10.67)
Tertiary	0	2	0.0 (0.0-3.59)

Chapter 5: Qualitative results

The qualitative information reported below was collected from FGDs, key informant interviews and from semi-structured interviews with ARV users.

5.1 Factors that influence adherence to ARVs from the users' perspective

Information about HIV, AIDS and ART

While the majority of patients seemed to be knowledgeable about ART, a few patients were not well-informed about how ARVs work and were not aware of the consequences of sub-optimal adherence to ARVs. Perceptions about ARVs were not uniform among the users. Some described ARVs as having significant side-effects, while others perceived ARVs to be very helpful medicines which were decreasing the "fierceness" of the disease in the body. Several men said that if they stopped taking the ARVs the virus would increase and body resistance would decline, while most of the women indicated that taking ARVs makes the virus "sleep" and lengthens the patient's life. In FGDs, some of the participants observed that it was difficult to keep taking the medicines at the correct time.

Both male and female ARV users who had learned about the use of ARVs had positive opinions. One female client from Arumeru indicated that:

> *"ARVs have improved my quality of life. If I stop using them I will die."*

Similarly, a male client from the same area noted that:

> *"ARVs have helped to increase my body immunity, my health is improving. If I stop using ARVs, the disease will come back."*

A female ARV user attending an FGD in Dar es Salaam said:

> *"Drugs bring our energy back and we are getting hope of living."*

A male participant in an FGD in Dar es Salaam was also positive about the impact of ARVs:

> *"My CD4 cell counts were down but after using ARVs now they have gone up. I'm not getting opportunistic infections."*

Despite widespread information about the AIDS pandemic, the idea of bewitchment as a source of HIV was still reflected in the perception of some patients. A few of them thought that AIDS was therefore inevitable and that everyone was at risk of infection. From their perspective, someone with AIDS was presumed to be already a dead person. Three options for AIDS treatment were advanced: traditional healers, faith healing and the use of ARVs.

Although there was a difference between the study settings, in general there was no difference in perceptions about HIV and AIDS between the different groups of informants. Most key informants interviewed who worked in HIV-related fields commented that at the community level there was a lack of knowledge about ARVs and this was a threat to treatment adherence. Key informants stressed the importance of adherence counselling to ensure that patients do not drop out. They said that although medication was considered to be very effective, good counselling could help motivate patients to be more adherent. Although some key informants noted that belief in links between witchcraft and HIV infection still prevails in some population groups and reliance on traditional healing persists, many people increasingly put their trust in ARV medicines. Many more patients are now attending HIV treatment clinics and, as a result, these are becoming more congested.

Counselling in ARV administration is now increasingly included in information sessions for patients on ART. One male patient from Mt. Meru hospital who had received some counselling said he remembered to take his medication *"due to fearsome instructions from doctors."* However, a female patient from a faith-based facility in Arusha reported that she was not told what would happen if she stopped taking the medication. In Arusha, FGD participants expressed similar concerns about the quality of counselling. Participants at one male FGD reported that:

> *"You find 25 patients and only one person attending all these patients and he just tells you to go and collect your medication."* (Male FGD participant, Selian, Arusha)

Similarly, a participant in a female FGD said:

> *"I did my HIV test (in AMREF Dareda) and was told that I am infected, (but) without proper preparation,"* meaning that she was not adequately counselled. (Female FGD, Selian, Arusha)

In contrast, patients in Dar es Salaam, commented on their appreciation of the quality of the counselling they received. According to male participants in different FGDs, the majority believed that counsellors were providing a good service, including providing information on nutrition. A participant in a female FGD in Dar es Salaam reported that:

> *"We are advised to bring our husbands here so that we are both counselled on how to live in harmony. Voluntary counselling and testing staff are very helpful to direct people where to go for ARVs."*

According to interviewees, the main modes of channelling health-based information in the surveyed health facilities included leaflets, seminars, adherence counselling, television and video. Meanwhile, conversation between patients provided an additional source of information.

Disclosure and social support system

Out of 100 ARV users interviewed (70 exit interviews and 30 semi-structured interviews), only eight were living alone in a household. It was found that 93.5% of the 30 semi-structured interviewees who were on ARVs had disclosed their HIV status, with 82.7% of them receiving some form of treatment support, such as transport support, food assistance and reminders to take medicines.

However, interviews with key informants and FGD participants revealed that stigma is still prevalent in society. PLWHIV were said to be affected by stigma both at home and in the workplace. This could affect both disclosure and adherence. According to a participant in a female FGD (Selian, Arusha):

> *"My utensils were put separate, including my spoon. All your belongings are not touched and you feel bad."*

The situation was worst for those employed in the private sector:

> *"I was a driver. I lost my job when my relative went to tell my boss that I was HIV-positive."* (Male FGD, Mwananyamala, Dar es Salaam)

> *"I lost my job after my boss noticed that I was HIV-positive."* (Female FGD, Selian, Arusha)

> *"I work in a drug store. I am told not to touch medicine because my hands have black spots and have been told that if customers notice, they will stop buying medicine from our store."* (Female FGD, Mwanayamala, Dar es Salaam)

> *"If I disclose I will be stigmatized. They look at us as if we are prostitutes. We are treated like leprosy patients."* (Male FGD, Mwananyamala, Dar es Salaam)

> *"Disclosure brings problems. You can lose business. Sometimes I am not invited to attend ceremonies because I have disclosed."* (Female FGD, Sinza, Dar es Salaam).

On the other hand, some respondents indicated that they had received some support as a result of disclosing their HIV status:

> *"I have told my family and if the time of taking medication comes they remind me."* (Male FGD, Selian, Arusha)

> *"My husband knows my status and we are helping each other. We cannot disclose in a workplace."* (Female FGD, Mwananyamala, Dar es Salaam)

Reminders to take medicines

A substantial percentage (44%) of respondents (42 out of 95) who were on ARVs reported that without any help they were able to remember the routine schedule for taking their medicines. Some of them commented that, as a result of strong counselling they had received they did not miss taking the ARVs. Meanwhile, 33 respondents (34%) reported having family carers, including a spouse and children, who used to remind them to take their medicines and 19 others (20%) said they used reminders such as clock alarms and calls to prayer at the mosque (*adhana)*. Twenty respondents (21%) reported having forgotten to take their ARVs at some time since they started treatment.

Adherence to ARVs was also affected by other circumstances, such as forgetting to take medicines when travelling or very busy. One female FGD participant observed that failure to disclose and the need to ensure confidentiality can also inhibit people from taking medicine.

Food

Lack of food was cited as a problem for most ARV users. According to FGD participants, lack of food disrupted the daily schedule for taking medicines and affected adherence. Both male and female ARV users complained that the medicines were increasing their appetite and that they did not have enough food. A male ARV user at St Elizabeth Hospital explained:

> *"The problem I have with ARVs is related to food. I have no money and ARVs increases appetite. I am not capable of buying food."*

However, none of the ARV users interviewed for the study said they had stopped taking ARVs despite a lack of food. The persistence of ARV users in continuing treatment even when they went hungry was also corroborated by staff interviewed in the health facilities. A male doctor in Arumeru hospital observed that:

> *"Food is a big problem, patients are getting appetite when they use drugs, but have not stopped using medication."*

Other interviewees remained concerned at the potential impact of hunger on adherence to ART. For example, a female FGD participant observed that some patients take their medication only once a day, in the evening, because that is the time when they have food, and a key informant in Sinza, Dar es Salaam, noted that some patients were selling ARVs in order to buy food. This implies that food scarcity can be a drawback to adherence.

Complexity of treatment regimen

It was also observed that the complexity of the treatment regimens is a problem for some ARV users. Patients on ART are required to take their prescribed medicines at the same times of day on a regular basis. However, ARV users had different perceptions of

the treatment regimen and the correct time for taking the medicines. A female client from Arumeru commented that:

"It is a problem to take the medicines at the right time every day."

This particular client indicated that she was taking her first dose of the day at 0700 hours and the second one at 2100 hours, thereby exceeding the recommended time of 12 hours between doses. Another popular misconception was revealed by a male FGD participant in Dar es Salaam:

"It is true you can forget taking drugs according to schedule but it is not good to exceed the recommended time interval by more than five hours."

Most ARV users interviewed in Dar es Salaam indicated that they were taking their ARVs according to the required schedule, compared with a smaller proportion of those in Arusha.

According to the health staff interviewed in both Dar es Salaam and Arusha, most ARV users were following the required treatment schedule. A female nurse from Arumeru in Arusha said:

"Most patients follow the instructions given them on proper use of ARVs."

Similarly, a nurse from a facility in Dar es Salaam stated that:

"A few patients do not follow their appointments but the majority are using ARVs properly."

Meanwhile, a pharmacist in Dar es Salaam noted that:

"A few patients have difficulties in following the correct drug regimen."

Side-effects

Although ARVs are known to cause some side-effects in the initial stages of treatment, these usually subside over time. However, this important information is not common knowledge among patients on ARVs. For example, patients in Arusha said:

"I was not informed of side-effects and what will happen to me if I stop taking medication." (Male ARV user, Arumeru)

"I don't know, I have not been told of impending side-effects." (Female ARV user, Selian)

In one of the male FGDs, side-effects were cited as one of the reasons for missing a dose of ARVs. One male FGD participant from Dar es Salaam offered the following information on side-effects:

"When I started using medication I was feeling very cold. I went to ask at the hospital and they asked me, "Do you want to stop medication? Did we not tell you that the medicine had some side-effects?" Three days later I was fine." (Male FGD, Sinza)

However, in Arusha, a male FGD member reported that side-effects had affected his treatment schedule:

"I had side-effects and decided to take medication only once per day." (Male FGD, Arumeru)

Most ARV users reported experiencing some side-effects in the initial stages of treatment but these had largely subsided over time. However, in some cases, the treatment regimen had to be changed. Some of the common side-effects mentioned were body rash, swollen legs, nausea, headache, increased heart rate, diarrhoea and vomiting.

It was suggested by one respondent that adequate counselling and education about the appearance and disappearance (over time) of side-effects would help to better prepare ARV users for possible side-effects and make them more bearable.

"If side-effects are very severe patients may stop medication, but due to continuous counselling and education we give them we advise to continue and most follow." *(*Female receptionist, Selian Hospital, Arusha)

5.2   Quality of operating structures

The information below was derived mainly from structured observations and from notes taken by researchers who visited the facilities.

Structural issues

Both health care providers and ARV users highlighted a number of structural problems in the health facilities which had a potential impact on adherence to ART. At Mount Meru in Arusha, for example, there was no separate room for consultation and thus no possibility of confidentiality for patients. At the time of this survey, three doctors were sharing a single room and consulting with three different ARV users at the same time. However, ARV users frequently mentioned that they were accorded respect. Elsewhere, at St Elizabeth, the waiting area was limited. In Arusha, the faith-based facilities generally had better operating structures than those in the public sector, where confidentiality was compromised by lack of space and the number of consultation rooms that were shared.

In contrast, consultations in Dar es Salaam took place in more appropriate consultation rooms. Although the quality of the infrastructure varied between the different facilities, it provided for adequate confidentiality, good counselling and adequate laboratory services.

The public health facilities in Dar es Salaam are well-endowed due to their involvement in the MDH project and operate on a daily basis unlike most of the facilities in the Arusha region. For instance, of the two public sector hospitals studied in Arusha, Mt. Meru had only one ART clinic per week, while Arumeru was running ART clinics daily (Monday to Friday), and the faith-based facilities were operating ART clinics three days per week.

Other structural problems highlighted included: the lack of prescribing capacity at Arumeru Hospital, where ARV users went home without medication on days when the hospital's only prescriber was not on duty; limited waiting space at the Hindu Mandal private facility in Dar es Salaam, which was difficult for both ARV users and care providers; lack of transport for the staff involved in home-based care services; and lack of medicines at ART clinics for the treatment of HIV-related opportunistic infections.

In addition, a female FGD participant in Arusha complained about the rigid bureaucratic procedures involved in transferring to another ART clinic closer to home:

> *"I was registered to start ART clinic in Kilimanjaro Christian Medical Centre (KCMC) in Moshi a year ago. At that time there was no ART clinic near my village. Now there is a clinic near my home but I am denied transfer from KCMC to my home clinic. KCMC is very far from here, about 170 km away. Sometimes I do not have the fare to travel to KCMC, hence missing my doses."*

Key informants also maintained that there were not enough health care facilities providing ART. Meanwhile, ARV users complained that services in the few existing facilities were deteriorating due to the increasing number of patients. One key informant from Kinondoni, Dar es Salaam, suggested that:

> *"ART clinics should be increased and more private hospitals should also be included in the programme."*

There were reports of wide variations in the length of time ARV users had to wait at the clinics. According to ARV users, waiting times varied from less than one hour to 10 hours (see Table 8 below).

Table 8: Average time spent by ARV users in health facilities studied

Number of ARV users interviewed		Hours spent before being attended to	Hours spent while being attended to at the clinic
Exit interview (N=70)	Mean time spent	2.5	4.8
	Range	1-8	1-10
	Waiting time most frequently experienced (mode)	1 (48.6%)	6 (21.4%)
SSI patients (N=30)	Mean time spent	3.8	5.1
	Range	1-8	1-9
	Waiting time most frequently experienced (mode)	1 (25.8%)	6 (22.6%)

SSI: Semi-structured interview

Staff qualifications and working conditions

A total of 28 staff were interviewed (including 16 from the four nongovernmental facilities). They included a dietician, laboratory technicians, counsellors, medical doctors, pharmacists and social workers. Only one of them had primary school education only and five had studied up to secondary education level only. The remaining 22 (78%) had undergone various tertiary education, including college education.

On the day of the exit interview, 97% of all patients saw the doctor and 77% saw a pharmacist while only 21% saw a counsellor, as presented in Table 9.

Table 9: Categories of health staff seen by patients on day

of exit interview (N=70)

Cadre of staff	No. of patients who consulted with this category of health worker	Percentage
Counsellor	15	21%
General nurse	20	29%
Pharmacist	54	77%
Doctor	68	97%

The staff interviewed had worked in ART clinics for a period ranging from 3 to 36 months, with an average of approximately 15 months. Some staff (21.4%) had 12 months' experience of working in ART clinics. However, only three (10.7%) of the respondents reported that the training they had received for ARV management was adequate. Twenty respondents (70.7%) said that the training they received was too short and that they needed additional training.

A major complaint was the pressure of work. A nurse in one facility in Dar es Salaam said:

> *"There is a lot of work in this ART clinic and we are overworked."*

As a result, many of the ART staff had multi-functional roles. For instance, one counsellor was responsible for routine nursing duties as well as administrative and supervisory duties. Out of 28 respondents, 11 (39.3%) were involved in adherence counselling in addition to other routine duties. In addition, nine nurse-counsellors were also dispensing drugs.

All the health facilities surveyed indicated that they were receiving an increasing number of ARV users, thereby adding to their workload. A female participant of an FGD in Mwananyamala said:

> "*If the situation remains like this, doctors will be tired and the last patient will not be attended properly.*"

Meanwhile, a staff member from a hospital in Arusha suggested that doctors should start the clinic earlier.

In Dar es Salaam (but not in Arusha), the staff in public facilities are provided with some topping-up allowances. However, the majority of health care workers (93%) expressed low motivation. Other challenges are shown in Table 10 below.

Table 10: Challenges most frequently mentioned by health staff (N= 28)

Challenges	Number of respondents	Percentage
Low motivation	26	92.9
Heavy workload	23	82.1
Inadequate training	20	71.0
Long waiting hours for patients	12	42.9
Too few staff	11	39.3
Work fatigue	5	17.9
Being faced with difficult or non-compliant ARV users	3	10.7

In summary, staff complained of the increased workload involved in treating ARV patients, for which they were not adequately trained. In contrast, patients largely expressed appreciation for the quality of care provided, despite complaints about long waiting times.

Availability of guidelines and diagnostic equipment
A number of facilities lacked the necessary laboratory and diagnostic equipment. This led to delays for patients as they had to return again in order to get the results of tests (see Table 11).

Table 11: Status of diagnostic facilities in health facilities studied

Type of facility (N=7)	ELISA machine for HIV testing	CD4 machine	Biochemistry tests	Adequate laboratory space
Government (N=3)	1	1	1	2
Non-Government (N= 4)	4	2	2	4
TOTAL	5	3	3	6

The table shows that of the seven health facilities, only three had both CD4 and biochemical testing machines. According to both ARV users and staff, the services of the laboratory and testing were inadequate in some of the surveyed facilities. Problems cited included the unavailability of CD4 reagents and of CD4 cell count machines. As a result, test results were delayed because they had to be carried out in other facilities elsewhere.

All the facilities had NACP guidelines for ART. In addition, one nongovernmental facility in Dar es Salaam had WHO guidelines as well. The MDH project had also provided guidelines to its sites in Dar es Salaam. However, none of the facilities visited had their own policy guidelines.

Staff from all seven facilities reported that they had adequate HIV testing facilities and reagents and had no problem with processing results. However, two facilities in Dar es Salaam were concerned about delays in obtaining results.

Availability of medicines

The prescribed ARV drugs were usually available in all seven facilities. Of the interviewed staff, only five (including four from government facilities) reported periodic shortages of prescribed medicines, requiring them to borrow medicines from nearby facilities. However, it was learned retrospectively during the course of this study that ARV drugs were out of stock for a whole month in Arumeru Hospital, causing an interruption in treatment for ARV users. The unavailability of ARVs was linked to a delay in supplies from the Medical Stores Department. However, this situation has now been rectified. About 36 patients were on ARVs at that time and were asked to get their supply from the nearby Mt. Meru Regional Hospital.

During the survey period, there was also a shortage of supplies of Triomune 40 at the Mt. Meru Hospital. When needed for dispensing during the clinic day, the hospital had to borrow supplies from Arumeru Hospital.

Although medicines for opportunistic infections were reported to be available in some of the facilities, these were not provided free of charge in faith-based and private facilities with the exception of anti-tuberculosis medicines. In Arumeru Hospital in Arusha, medicines such as fluconazole and other antifungal medicines were not available, and there was no substitute drug for clients who had experienced an adverse drug reaction after using cotrimoxazole.

Since all facilities providing ART were getting medicine supplies from the Medical Stores Department, there were no significant variations in the available stock of ARVs. However, Hindu Mandal and Selian, both faith-based facilities, showed some slight variations in stocked medicines. For example, Hindu Mandal stocked indinavir and didanosine and Selian stocked abacavir and didanosine, medicines that were not available in other surveyed facilities. In addition, there were no fixed-dose combinations for syrup preparations, which poses a problem for paediatric treatment. In some of the facilities surveyed, there was inadequate space for drug storage and for counselling during the dispensing of ARVs.

Provider-patient interaction regarding use of ARVs

In all the ART facilities studied (both public and private) respondents stated that providers showed respect for ARV users. This may be the result of initial training, which was conducted by NACP under the MoH. One male FGD participant said:

> *"Providers show a warm relationship to clients and provide good services."* (Male FGD, Mwananyamala, Dar es Salaam)

However, hospital support staff who had not received any training on how to deal with AIDS patients were reported to be stigmatizing ARV users and behaving in an unethical manner towards them. For example, it was reported that a hospital cleaner in one of the public facilities in Dar es Salaam had shouted loudly to indicate the place where ARV users were seated, waiting to be attended to. This had been a major source of embarrassment for all involved.

As part of the follow-up on treatment adherence, health staff were expected to ask specific questions on the use of ARVs. Figure 4 below summarizes the questions most frequently put to ARV users. These data were obtained during the observation of consultation phase of the study.

Figure 4: Questions most frequently asked by health workers during follow-up in ART clinics (N=64)
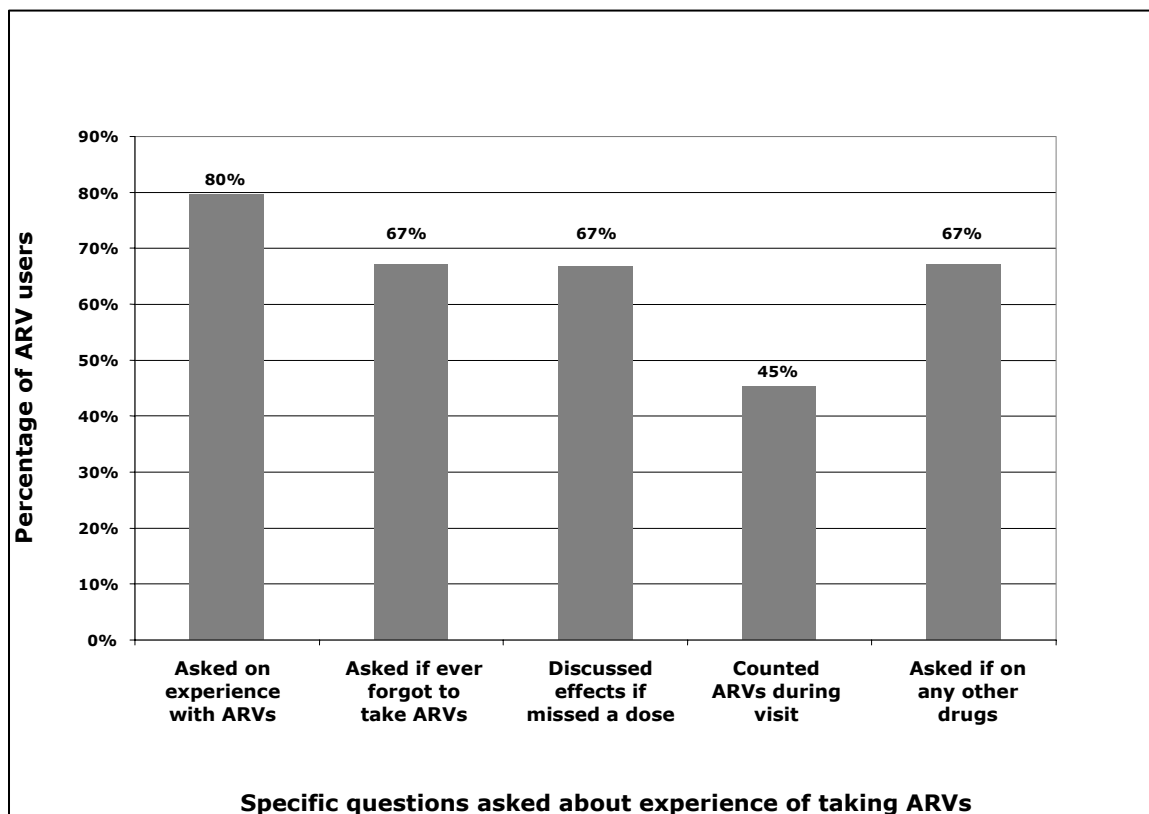
During observation of consultations, seven new ARV users who came to start treatment were told about the possible side-effects, six were told about the importance of continuing with treatment, five discussed how to use ARVs, and four were informed about what to do if they forgot to take a dose. However, there was no discussion about other reproductive health needs, such as contraception and safer sex, in any of the observed consultations.

Costs

The cost of travel to the health facility for ARV users ranged between Tshs 200 to Tshs 30 000 (approximately 20 US cents to US$30.00), while the distance travelled ranged from 1 km to 246 km. Most patients had started ART less than one year ago (mean 8.7 months, range 3-36 months). Costs were described as a constraint to adherence. Some ARV users said they were unable to keep their appointments because they could not afford the cost of travel. Patients also cited other costs, including registration and consultation fees. A registration fee of Tshs 1500 (US$ 1.50) was levied at all facilities in Arusha except Mount Meru, where the registration fee was Tshs 3000 (US$ 3.00). Elsewhere at Selian Hospital in Arusha, in addition to the registration fee, patients were also charged a consultation fee of Tshs 3000 (US$ 3.00) per visit and Tshs 15 000 (US$ 15.00) for each laboratory investigation to monitor the CD4 cell count. With the exception of the private Hindu Mandal Hospital, which charged a monthly consultation fee of Tshs 1000 (US$ 1.00), the facilities surveyed in Dar es Salaam were not charging any fees.

5.3 Opinions and suggestions given by respondents to improve provision of ARVs

Most of the clients interviewed were very thankful that they were on ART and commended the Government's efforts to roll out the ARV programme. They described the ART programme as a "life-saving" one which had given them new hope:

"Drugs bring our energy back and we are getting hope of living."

Both ARV users and staff in the facilities involved offered a number of suggestions on ways of improving the provision of ARV services. Some of the ARV users suggested that separate rooms for consultation should be made available in the facilities and that ARV medicines should be dispensed in consultation rooms to enhance client confidentiality. There were frequent requests from patients for an increase in the number of staff in order to help reduce waiting times. It was also suggested that frequent seminars should be held to remind ARV users of the importance of the appropriate use of ARVs. Other suggestions included ensuring the availability of laboratory services (including reagents) at health facilities and ensuring that medications to treat opportunistic infections were provided free of charge. In addition, some staff at Arumeru Hospital suggested that the working environment at that hospital should be improved, particularly the waiting rooms and consultation rooms.

There was a request that the Government should provide financial support to facilitate sustainable income-generating projects and food assistance for ARV users who are poor. Meanwhile, the local government was encouraged to raise awareness of HIV-related issues at community level in order to help reduce stigma. Some patients also proposed that researchers should visit them once a year to ask about the kind of problems they are facing.

Staff in the various facilities had a range of different opinions on employment-related issues, such as staffing and conditions of service, education and training, and working conditions. The most common request was that more staff should be employed in order to cope with the increasing number of ARV users. Staff working with ARV users also called for the payment of a topping-up allowance. Even those currently receiving some allowances indicated dissatisfaction at the meagre amount they receive and argued that they should be paid adequate salaries. Staff also suggested that transport should be made available for staff who provide home-based care for ARV users (monitoring treatment progress and counselling both ARV users and family members on treatment adherence). Another suggestion was that nurses on ARV programmes should be exempted from routine ward work. Meanwhile, a pharmacist working in a private health care facility in Dar es Salaam recommended that at each treatment facility a pharmacist should be responsible for dispensing ARVs.

On the issue of education and training needs, the staff recommended that community-based education and training should be made available for both ARV users and carers to help ensure that patients follow prescription instructions properly. In addition, the staff said there was a need to train staff members in HIV-related health issues, such as minimizing the risk of tuberculosis infection when caring for patients who are co-infected with tuberculosis and HIV.

Chapter 6: Discussion, conclusion and recommendations

6.1   Discussion

A comprehensive study of ARV adherence in Tanzania has not yet been attempted. This study has been conducted in order to identify factors which constrain or facilitate adherence to ART and to suggest possible ways to improve adherence. Reports from other countries have emphasized that sub-optimal adherence is the main cause for the failure of ARV therapy. The unforgiving nature of HIV requires that levels of adherence be higher (>95%) and more sustained than in most other areas of medicine (Garcia et al., 2003; (Paterson, 2000).

The present study examined a range of factors that can have a negative impact on adherence, including: stigma, poor social support, mistaken beliefs, lack of food, side-effects, inadequate counselling, long waiting times at treatment facilities, transport-related and other costs, and long distances to the health facility. Factors which can help facilitate adherence which were investigated included: adherence counselling, disclosure of HIV status to family members, social support, a reliable medicine supply chain, information and education.

Adherence measurement

Three different adherence measurements were used in this study. Two-day recall was found not to be discriminatory. Use of tablet counts and 28-day recall using a visual device (beads) were combined to produce a composite adherence measure. However, there were substantial differences between the results of these two measures. As there is no gold standard for adherence measures, further studies are needed to validate these different measures by comparing the different results with viral load counts, as has recently been undertaken by Carrieri et al. in Malawi.

The results of this survey indicate a composite one-month average adherence rate of 90% for ARV users at the seven facilities involved. This meant that 90% of all the pills that should have been taken over the previous month by those interviewed were taken. However, only 21% of ARV users interviewed reported achieving the optimal level of adherence (over 95%) as measured by the composite adherence rate. The remaining 79% self-reported to achieve only moderate adherence (85%-95% adherence rate) and are therefore at risk of treatment failure and the development of drug-resistant forms of the virus.

There was little difference in the composite adherence rate among ARV users interviewed in Arusha and Dar es Salaam, and there was no difference in adherence rates between males and females. In addition, there was no significant difference in

adherence rates among ARV users with different levels of education. These findings were similar to the observation by DiMatteo in 2004 that adherence was generally unrelated to variables such as gender, education or socioeconomic status.

In a study conducted in Cameroon, Akam et al. (2004) found an overall adherence rate of 68%. In that study, the constraining factors were found to be the cost of medication and some side-effects. Elsewhere, a study conducted in Botswana by Weiser et al. (2003), reported that between 54% and 56% of patients were achieving the optimal adherence rate of at least 95%. In the Weiser study, financial constraints were identified as one of the principal barriers to adherence. However, it was estimated that if cost was eliminated as a barrier, then the adherence rate would increase to 74%.

Our study would appear to confirm Weiser's findings, which suggest that at population level there are many patients who do not achieve optimal (95%) adherence and who are therefore at risk of treatment failure and the development of drug-resistant virus. We remain interested in investigating further the differences in our various measurements of adherence – ideally comparing these with viral loads, as was recently undertaken in Malawi (Carrieri et al., 2001).

Structural issues

Administering an effective ARV programme is a daunting task. In the present study, there was no uniformity among the treatment facilities in terms of follow-up monitoring and checking of drugs. Some facilities, especially the private ones, did not have procedures for asking patients to come with their medicines for pill count monitoring and to check on patients' adherence to medication. Some health care facilities did not have proper medicine storage facilities, which may compromise the quality of the medicines.

Some of the health care facilities studied did not ensure adequate confidentiality for patients. The worst example of this was a situation in which three doctors were sharing one consultation room and consulting with three different patients at the same time. This can inhibit some patients from attending consultations or from communicating openly, and so impair adherence.

In this study, a major issue for patients was the lengthy waiting times. ARV users spent an average of five hours waiting and being attended to at a facility. Lengthy waiting times could have a negative impact on both attendance at clinics and adherence. Patients complained that staff working at ART clinics were overworked, and in some health care facilities they started the clinic late. Some patients had to travel long distances, and then had to wait for a long time at the facility, sometimes for 10 hours. In addition to the impact of this on adherence, the long waiting times were said to strain the relationship between staff and patients. Food was also a related issue since patients had to buy food while waiting for treatment, thereby incurring additional costs.

In administering ARVs, efforts should be made to minimize waiting times. In many settings it may be possible to provide patients with appointment times, so they do not

have to wait all day. Another improvement that could be considered is an increase in the provision of laboratory services at the treatment facilities. At present, many ARV users continue taking medicines without regular checks to monitor their CD4 counts and liver and kidney function. The availability of laboratory services could also help motivate adherence since patients would know through the laboratory results that they were improving. This is an area that needs to be strengthened.

Counselling

Although counselling is a key requirement for successful adherence to ART, the importance of the need for regular ongoing counselling is not always recognized. This was confirmed in our study by the fact that only 21% of patients saw a counsellor on the day of their exit interview. Patients are counselled intensively prior to treatment and at the time they start treatment. However, once on treatment there is very little counselling unless they have a particular problem. Yet it is well recognized by Horne and others that adherence rates decline over time (Horne et al., 2001). Patients need to be counselled whenever they come for refills and if they are achieving at least 95% adherence, they should be congratulated and encouraged. If they are not, the counsellor should be able to spend time with patients and suggest adherence strategies. If a patient forgets, possible solutions are the use of alarm clocks or reminders from a treatment "buddy." ARV users also mentioned using calls to prayer at the mosque as well as reminders from family members. If the patient has not disclosed that they are on treatment, the counsellor could suggest approaches to disclosing or finding a treatment supporter.

Costs

Poverty is a serious problem in Tanzania, which can have a negative impact on adherence. Both key informants and ARV users said that many patients complained that these medicines increase the appetite and cause hunger. Since lack of food has been described as a problem for most people on ARVs, food shortages among the general population in Tanzania are a serious concern. It was reported that some patients were taking their ARVs only once a day, in the evening, because that was the time when they had food, and that some patients were selling their ARVs in order to buy food. This implies that food scarcity can be a drawback to adherence.

Although ARV users received medicines free of charge, the additional costs incurred were cited as an important reason for not visiting the health facility for follow-up and medicine refill. These costs included travel costs, registration or consultation fees at health facilities, and money spent on food while attending the treatment facilities. In addition, some patients had to travel long distances to the facilities and, in some cases, had to stay overnight near the clinic, thereby incurring additional accommodation expenses. Costs were seen as a constraint to adherence. Some ARV users suggested that they should be given loans to run small-scale businesses to help them cope with the additional costs incurred through being on ART.

Knowledge and beliefs

To be successful, an ART programme depends on a certain level of knowledge and awareness among ARV users. However, this study found wide variation in the level of

knowledge among ARV users about HIV, AIDS and ART. While knowledge about HIV and AIDS is generally good, beliefs that people have been bewitched, had a spell cast on them or been afflicted by an AIDS devil/spirit (a *'jini'*) are commonplace and inhibit adherence to ART. Greater efforts are needed to educate both the community and ARV users about HIV in an effort to dispel beliefs about witchcraft.

Stigma

According to the testimonies of some ARV users, stigma remains a major problem. Moreover, disclosure and stigma seem to be different sides of the same coin. On the one hand, disclosure may cost the individual their job, social support and their family. On the other hand, a substantial number of ARV users who had disclosed were receiving support from family members. This support included financial assistance for travel costs and food, as well as reminders to ensure that they take their medicines on time. Although disclosure can have both negative and positive effects on adherence, it was more generally linked to better adherence, since 82% of those who had disclosed received various forms of help on the use of medicines. Efforts to ensure that the community is better educated about HIV and treatment would go a long way towards reducing stigma and encouraging disclosure.

Side-effects

A study conducted by Weiser et al. (2003) in Botswana indicated that side-effects did not pose a major barrier to adherence. The study found that while 51% of respondents experienced some side-effects, less than 10% of them reported side-effects as a significant barrier to treatment adherence. This was also noted by Akam et al. (2003) who found that very few side-affects were noted or cited as a cause of poor adherence (5%). In the present study, very few ARV users cited side-effects as a constraint to adherence. While some ARV users who participated in FGDs mentioned side-effects as a cause for skipping doses or taking medication only once per day, in most cases the side-effects were reported to disappear over time. However, this important information was not always communicated to ARV users in advance. In order to promote adherence, ARV users should have access to adequate education about potential side-effects and their likely duration.

Study limitations

There were some limitations to this study. First, the very few clients who refused to be interviewed or to turn up for FGDs may have significant information which has not been captured by this study. Second, the budget and time for this study were limited. Third, the method of determining adherence rates included self-assessment by ARV users and the literature suggests that patients tend to overestimate adherence (Chesney, 2000). Fourth, we were unable to relate the obtained adherence rate to viral loads and CD4 cell responses since this was not in our original plan, due to financial and logistical barriers to frequent laboratory monitoring in this setting. However, the combination of different approaches and respondents permitted extensive triangulation and gave us a comprehensive set of results in spite of the various problems faced.

6.2 Conclusion

Despite obstacles to ARV adherence, the overall mean composite adherence rate of 90% in the two areas surveyed is encouraging. However, more efforts are needed to ensure optimal adherence among the large group (79%) of ARV users who are currently taking less than the critical 95% of their dosage. The large variation in the results between pill counts and visual analogue demands an explanation. Therefore the two measures need to be validated against viral load, as was done by Carrieri et al. in Malawi.

Key challenges to optimal ARV adherence identified in this study include: the inadequate number of ART clinics; lengthy waiting times; travel costs and other treatment-related costs; an unreliable supply of ARVs in some facilities; stigma; lack of confidentiality; staff shortages; and a lack of incentives for staff. Such problems need to be tackled in order to ensure the smooth running of the ART programme and sustain optimal levels of adherence. Consideration should be given to providing support to ARV users to help alleviate poverty (including food support and loans to help people run their own business) and community education to help reduce stigma. In addition, more training is needed for staff in ART clinics to enable them to update their knowledge more frequently.

The GoT has established ambitious targets for ART and made a good start in rolling out ARVs. Many patients now have access to treatment and there is widespread appreciation of the Government and of the health workers involved in the programme. However, unless due attention is paid to the critical issue of adherence, the emergence of drug-resistance will be accelerated and the early treatment achievements could be reversed.

6.3 Recommendations

The following are presented as suggestions for interventions that we believe may promote ARV adherence rates among patients in Tanzania. They have not yet been evaluated and we would welcome the opportunity to undertake such intervention studies.

♦ **Institute pill counting**. Pill counting is an important monitoring and adherence promotion tool for both providers and users. However, in many facilities this system is not used. Although public facilities in Dar es Salaam have started pill counting, the system is weak and many patients do not bring their drugs for counting on clinic days. Pill counting will also help clear up suspicions that some patients are selling their ARVs.

♦ **Employ adequate numbers of well-trained staff.** More trained staff are needed to cope with increasing workloads in ART clinics. This will also help clients by reducing waiting times.

♦ **Increase access to ART clinics, as well as improving facility infrastructures and laboratory services.** This can be done both by increasing the opening hours of existing clinics and by opening new clinics closer to where people live. Such clinics might be used to review patients who have initiated treatment at a larger hospital facility.

♦ **Establish reliable drug supply**. There was some concern that the medicine supply chain is not yet reliable. A reliable supply of medicines needs to be instituted and efforts made to assure clients and providers that the supply chain is reliable.

♦ **Create proper referral networks of ARV users between facilities.** Such a referral and transfer network should allow patients to be treated as close to their homes as possible with minimum waiting times and travel costs.

♦ **Train staff in adherence counselling and continuously update their knowledge about HIV and AIDS.** This implies that not only pharmacists and dispensers have a responsibility for adherence counselling. Everyone from clerk to nurse to doctor to counsellor has a responsibility to encourage full adherence, recognizing how difficult it is for patients to maintain full adherence.

♦ **Train and support community counsellors who operate from their home (as seen in Arusha).** The use of community counsellors has been shown to be effective in other countries as well as in Tanzania. Creating training opportunities for such counsellors and involving them in follow-up and support of ARV patients should occur at every ART facility.

♦ **Prepare IEC material focusing on adherence to ARVs, stigma and disclosure.** These materials should emphasize that patients on ARVs need support to achieve optimal adherence and that patients on treatment can be healthy and fully able to work.

♦ **Waive registration and consultation fees.** Registration and consultation fees should be waived for AIDS patients.

♦ **Conduct intervention studies.** Intervention studies are recommended in order to sustain and promote adherence to ARVs. It is the wish of this research group to continue with intervention studies if funds are made available.

♦ **Loans and food support.** Due to the prevailing poverty in the country, loans and food support to ARV users should be considered by the Government and NGOs.

6.4   Proposed interventions

The following are the proposed interventions from this study.

INTERVENTION	SPECIFIC TARGET	METHOD OF EVALUATION	EXPECTED IMPACT
Managerial	Institute pill counting.	No. of clients bringing pills for counting.	Improve adherence rate.
	Employ adequate numbers of staff.	No. of new staff employed.	Reduce waiting time and improve counselling.
	Ensure reliable supply of medicines.	Availability of reliable medicine supply chain.	Improve adherence rate.
	Increase the no. of ART clinics.	No. of new ART clinics.	Reduce workload in ART clinics.
	Facilitate the transfer of ARV users to ART clinics closer to home.	No. of users transferred to ART clinics closer to home.	Improve adherence rate.
	Open clinics early and minimize waiting time.	No. of clinics open on time.	Reduce waiting times.
	Provide rooms for consultation that offer greater patient confidentiality.	No. of clinics with consultation rooms that offer patient confidentiality.	Improve attendance and adherence rate.
Educational: Training of provider	Update knowledge of staff.	System to update staff knowledge in place.	Improve adherence rate.
	Train staff in adherence counselling (emphasize initial side-effects).	No. of staff trained in adherence counselling.	Improve adherence rate.
	Train staff to be supportive, in an effort to minimize stigma.	No. of supportive staff trained.	Reduce stigma.
Educational: Training of the public	Train community counsellors who operate from home (as seen in Arusha).	No. of community counsellors trained.	Improve adherence rate.
	Prepare IEC materials focusing on promoting disclosure and reducing stigma.	No. and types of IEC materials prepared.	Increase disclosure rate and reduce stigma.
	HIV-related education for the public through radio, TV and newspapers.	No. of programmes produced.	Increase disclosure rate and reduce stigma.

References

1. Akam AW et al. (2004). *Anti-retroviral adherence in a resource poor setting*. International Conference on AIDS, 11-16 July 2004. 15. Abstract no. B12311.

2. Bangsberg DR et al. (2000). Adherence to protease inhibitor, HIV-1 viral load and development of drug resistance in an indigenous population. *AIDS*;14:357-366.

3. Carrieri P, Caillefon V, Le moing V. (2001). The dyanamic of adherence to Highly Active Antiretroviral Therapy: Results from the French National APROCO cohort. *Journal of Acquired Immune Deficiency Syndromes*, 28:232-239.

4. Chesney MA (2000). Factors affecting adherence to antiretroviral therapy. *Clinical Infectious Diseases*, 30(Suppl 2):S171-S176.

5. CIA. *The world factbook 2003, (Tanzania).* Available at: http:/www.cia.gov/cia/publications/factbook/geos/tz.html.

6. DiMatteo MR (2004). Variations in patients' adherence to medical recommendations. A quantitative review of 50 years of research. *Medical Care*, 42:200-209.

7. Eldred I J, Wu Aw, Chaisson RE (1998). Adherence to antiretroviral and pneoumcystic prophylaxis in HIV disease. *Journal of Acquired Immune Deficiency Syndromes*, 18:117.

8. Garcia R, Schooley, R, Badaro R (2003). An adherence triology is essential for long term HAART success. *Brazilian Journal of Infectious Diseases*, 7(5):1-9.

9. Horne R, Buick D, Fischer M (2001). *Perceptions of HIV and HAART as barriers to adherence*. 5th AIDS Impact, Brighton, UK, 2001. Abstract no.105. 2002; 28:232-9.

10. Horne R. Compliance, adherence and concordance. In: Taylor K, Harding G, eds. *Pharmacy practice.* London, Taylor & Frances, 2001:165-184.

11. Horne R. Adherence to medication, a review of existing research. In: Myers L, Midence K, eds. *Adherence to treatment in medical conditions.* London, Harwood Academic, 1998:285-310.

12. Lerner BH, Gulick RM, Dubler NN. Rethinking non-adherence:historical perspectives on triple-drug therapy for HIV disease. *Annals of Internal Medicine*, 1998, 129(7):573-578.

13. Ison CA, Dillon JA, Tapsall JW. The epidemiology of global antibiotic resistance among *Neisseria Gonorrhoeae* and *Haemophilus ducreyi*. *Lance*, 1998:351(Suppl 3):8-11.

14. Massele AY et al. (1993). Knowledge and management of malaria in Dar es Salaam, Tanzania. *East African Medical Journal*, 70(10):639-42.

15. Massele AY, Ofori-Adjei D, Laing RO. (1993). A study of prescribing patterns with special reference to drug use indicators in Dar es Salaam Region, Tanzania. *Tropical Doctor*, 23(3):104-7.

16. Mhalu F. *The impact of globalization on spread of emerging and re-merging diseases.* Keynote address to NIMR's 19th Annual Joint Scientific Conference AICC, 15-17 March 2004.

17. Ministry of Health. *National guidelines for malaria diagnosis and treatment.* (2000). Malaria Control Series 1. Dar es Salaam, Ministry of Health of the United Republic of Tanzania, 2000.

18. Ministry of Health. *Report of the baseline survey of the pharmaceutical sector in Tanzania*. Dar es Salaam, Ministry of Health of the United Republic of Tanzania and World Health Organization, 2002:22-23.

19. Mnyika KS, Killewo JZ, Kabalimu TK. Self-medication with antimalarial drugs in Dar es Salaam, Tanzania. *Trop Geogr.Med*. 1995;47(1):32-4.

20. Murphy DA, Wilson CM, Durako SJ (2001). Antiretroviral medication adherence among the REACH HIV-infected adolescent cohort in the USA. *AIDS Care*,13,(1) 27-40.20.

21. NACP(2003). *HIV/AIDS/STI Surveillance Report,* No.17.

22. National Bureau of Statistics-United Republic of Tanzania (2003). *National population and housing census general report 2002*. Dar es Salaam, Central Census Office, National Bureau of Statistics, President's Office Planning and Privatisation, Tanzania.

23. Parades R (2000). Predictors of virology success and ensuing failure in HIV positive patients starting HAART in Europe. *Archives of Internal Medicine*. 160:1123-1132.

24. Rabkin M, El- Sadr W, Abrahams E (2003). *MTCT-Plus clinical manual*. Mailman School of Public Health, Columbia University, USA. Available at: http://www.mtctplus.org/intranet/pdf/ad treatment.pdf

25. Simonen M (2003). *Population and Development Perspective,* No. 9.

26. Singh N, Squier C, Sirek C (1996). Determinants of compliance with antiretroviral therapy in patients with HIV: prospective assessment with implications for enhancing compliance. *AIDS Care*, 8:281.

27. Tanzania Food and Drugs Authority. List of registered drugs, 2004. Available at: http://www.tfda.or.tz.

28. Tuldra A, Fumaz C R, Ferrer M J (2000). Prospective randomized two arm controlled study to determine the efficacy of a specific intervention to improve long term adherence to highly active antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndromes*, 25; 221-8.

29. UNAIDS 2004. *Report on the global AIDS epidemic*. Available at: http:/www.unadis.org/bangkok2004/GAR2004 html.

30. UNAIDS 2004. *Report on the global AIDS epidemic.* Executive summary. Available at: http://www.Unaids.org/bangkok2004/ GAR2004 html/ ExecSummary en/ExecSumm en 04.htm#P225 26561 accessed on 11/8/2004.

31. United Republic of Tanzania. *HIV/AIDS care and treatment plan 2003-2008*. (Draft document).

32. Weiser S et al. (2003). Barriers to antiretroviral adherence for patients living with HIV infection and AIDS in Botswana. *Journal of Acquired Immune Defiiency Syndromes*, 34:281-288.

ANNEX 1: Exit interview with ARV users

Name of the interviewer:

Interview number:

Name of health facility:

Date:

- Greeting
- Assurance of confidentiality

1.   Sociodemographic information on informant

a) Sex

b) Age

c) Educational level (no education, primary, secondary, tertiary)

d) Who do you live with (spouse, children, house girl etc)?

e) Employment status (unemployed, self, government, NGO)

f) Distance from facility (in time or distance)

2.   Whom did you consult/visit today? (can include more than one)

- Counsellor
- Nurse
- Medical doctor
- Pharmacist
- Other

3.   What was the reason for your visit today?

- To start using AIDS medicines
- Routine follow-up, if yes: when did you start using the AIDS medicines?
- Other reason

4.   What was the result of the visit?

- I got AIDS medicines for the first time
- They gave me a refill of my medicines
- They gave me a different kind of medicine. If yes, why did the doctor prescribe different medicines?
- Other (describe)

5.   If you were given AIDS medicines for the first time *today*, or were given a new kind of AIDS medicine *today*, what did the health worker tell you? (Open-ended, then probe on following topics)

- How ARVs work
- How to use them
- The need to continue treatment
- What to do if a pill is forgotten
- Possible interactions with other drugs
- Which side-effects can occur and what to do if they occur
- (Breast) feeding requirements
- When and where to get re-supply

6.   (If client was given a repeat prescription, ask him/her the following; if not applicable, proceed to 8)

a) Did you talk with the health worker about your experience of using your medicines?
b) Did the health worker ask you if you have missed a dose? If yes, did the health worker explain what the effects are of missing a dose?
c) Did your health worker count your pills before giving you a new supply?
d) Did the health worker ask you if you were taking any other medicines?

7.   Assessment of adherence and non-adherence

a) Do you have your medicines with you? May I see them? Please can you tell me when you take each of the medicines? (Refer to table with sun and moon, or other checklist)
b) Are there any other medications you are taking (e.g. septrin, herbs etc)
c) Over the last two days, when did you take your pills? (Not including today - from yesterday evening and back.)
d) Did you perhaps miss any? (Confirming (c), sympathetic manner. Details if yes.)
e) What do you use to remind yourself to take your pills?

8.   Cost consideration

a) How much do you have to pay to cover your travel expenses when you visit the clinic?
b) What is the cost of registering at the clinic (if any)?
c) What is the cost of the ARV medicines that you take (if any)?
d) Do you lose any income as a result of your coming to the clinic?
e) Do you incur any other costs as a result of your taking ART?
f) Do you and your family have to give anything up in order to be able to pay for your ART?

9. Quality of care in the centre

I would like to ask you some more questions about the way you were treated in the centre today.

(a) What do you think of the service you receive at this clinic? (General, open-ended, and then prompt, as below: ask for details as necessary)
- Do you feel listened to?
- Are you given the chance to state your problems and ask questions?
- Are you treated with respect?
- Do you feel you can trust the health workers?
- Do you have privacy during consultation and counselling?
- How do you find the environment of the clinic?

(b) How long did you spend altogether at the clinic when you last came for review?

(c) How long did you have to wait before being attended to?

(d) Did you receive any written information?

10. Perceived problems and possible solutions

a) What do you perceive as most problematic regarding taking the ARV treatment?

b) What do you think could be done to improve this?

Have you any questions for me?

Thank you for your time and cooperation!

ANNEX: 2: Semi-structured interview with ARV users

Name of the interviewer:

Interview number:

Name of health facility:

Date:

- Greeting (to create rapport with ARV user)
- Statement of confidentiality.

1. Sociodemographic information on informants

a) Sex

b) Age

c) Educational level (no education, primary, secondary, tertiary)

d) Who do you live with (spouse, children, house girl etc)?

e) Employment status (unemployed, self, government, NGO)

f) Distance from facility (in time or distance)

We would like to understand a bit about how it is for people taking ARVs. Could you tell me how you spend a normal day? How do you spend your spare time? What do you do to relax?

2. Medical history of patient

a) When where you first diagnosed?

b) What made you decide to go for testing?

c) When did you start treatment for HIV (HAART)?

d) How do you feel about your health since you started treatment?How would you describe your health since you started treatment?

- Better
- The same
- Worse

3. Patient knowledge about HIV/AIDS

We would like to understand what people actually know about the illness that they have. Can you tell me what you know about HIV/AIDS? (Allow patient to say what they want, then probe on the following: cause of HIV infection, cause of AIDS, prevention, life-long infection). Apart from this, is there anything else you may have heard from your community that explains AIDS in a different way?

4. Patient knowledge about ARVs

We would like to understand what people know about their treatment. Could you help us with this by telling me what you know about ARVs? (Allow patient to say what they want, then probe on the following: Prolongs life, Improves quality of life, Life long treatment, Knowledge about side effects.)

5. Assessment of adherence and non-adherence

We are trying to find out how patients manage to take their medicines – for some people it's not a problem, but we also know that others don't always find it easy. Please feel free to be open about the problems you face with this. Everything you say here will remain confidential, and will not be shared with anyone at the clinic.

a) Do you have your medicines with you? May I see them? Please can you tell me when you take each of the medicines? (Refer to table with sun and moon, or other checklist)

b) Are there any other medications you are taking (e.g. cotrimoxazole, herbs etc)

c) Over the last two days, when did you take your pills? (Not including today - from yesterday evening and back.)

d) Did you perhaps miss any? (Confirming (c), sympathetic manner. Details if yes.)

e) This is a very important question. We appreciate how difficult it can be to take pills on a daily basis. If you sometimes miss a dose, please can you tell me what causes this to happen? Can you give an example or two?

f) On the other hand, what is it that helps you to take your pills regularly and on time? (e.g. organizations, individuals, clock etc)

g) Have you disclosed your status to any one? If so, who? Do they help you to take your pills? [If not covered in (f)]

h) Have you had your treatment changed at any moment since you started on ART. If yes, why? (e.g Treatment failure, Side effects)

i) Have you ever missed an appointment at your ART clinic? (Reasons, and details on type of consultation: review/refill etc.)

j) What do you think happens in your body if you skip your ARV medication?

k) Have you ever thought about stopping ART? If yes, details.

6. Perception about HIV/AIDS, ARVs and stigma

Have you had any experience of being treated differently because of your HIV status?

7. Cost considerations

a) How much do you have to pay to cover your travel expenses when you visit the clinic?
b) What is the cost of registering at the clinic (if any)?
c) What is the cost of the ARV medicines that you take (if any)?
d) Do you lose any income as a result of your coming to the clinic?
e) Do you incur any other costs as a result of your taking ART?
f) Do you and your family have to give anything up in order to be able to pay for your ART?

8. Quality of care

a) What do you think of the service you receive at this clinic? (General, open-ended, and then prompt, as below: ask for details as necessary)
   - Do you feel listened to?
   - Are you given the chance to state your problems and ask questions?
   - Are you treated with respect?
   - Do you feel you can trust the health workers?
   - Do you have privacy during consultation and counselling?
   - How do you find the environment of the clinic?
b) How long did you spend altogether at the clinic when you last came for review?
c) How long did you have to wait before being attended to?

9. Perceived problems and possible solutions

a) What do you perceive as the biggest problem regarding taking ARV treatment?
b) What do you think could be done to improve this?

Have you any questions for me?

Thank you for your time and cooperation!

ANNEX 3: ARV users, FGDs

- Name of ARV-providing health facility
- Participants per FGD (6-8)
- Adults (= or >18 years, men and women separately)
- One moderator, one note-taker (*and* use of tape recorder)
- Neutral venue outside the facility
- One FGD with men, and one with women per facility

Short introductory remarks

- Introduction of researchers and participants
- Thank participants for agreeing to participate, all share a common feature – they are on ARV treatment, are here to share thinking about ARVs and difficulties to take ARVs, want to learn from participants
- Explain purpose of study, purpose of this discussion, reassurance about confidentiality, agree on rules

Guide for discussion

1. What treatments do you know to be available for treating HIV? What is your opinion about these? (e.g. alternative treatments; traditional remedies; healing; spiritual; prayers; perceived benefit of treatment).
2. What is your experience of ART? (probe about adverse effects, pill burden, lack of food, lifestyle issues, adherence).
3. How do you think you are being treated (handled) by the health care workers (probe, *in relation to adherence*: privacy, confidentiality, respect, being listened to, time spent with patient, waiting time, integration with other services, under-the-counter payments)
4. What do you think about the counselling that you receive? (probe especially on importance of adherence)
5. What support is available for you in the community, in the family, in the workplace? (probe about discrimination, stigma)
6. What do you think could be done to help people to adhere more easily to their treatment?

Duration of discussion (1½ hours); provide refreshments
Conclusion, thank participant

ANNEX 4:
Adherence measurement tools

Date: _____

Name of the interviewer: _____

Name of health facility
providing ARV: _____

a) Interviewer introduces him/herself
b) Explain purpose of exercise: "You have come here to get your ARV medication. We know that it is very difficult to take this medication, and we are doing some research to find out whether patients manage to take their medicines correctly – would you have a few minutes to answer some questions?"

1.   Sociodemographic issues

a) Sex
b) Age
c) Level of education completed
d) How far did you have to travel today?

2.   Cost considerations

a) How much do you have to pay to cover your travel expenses when you visit the clinic?
b) What is the cost of registering at the clinic (if any)?
c) What is the cost of the ARV medicines that you take (if any)?
d) Do you lose any income as a result of your coming to the clinic?
e) Do you incur any other costs as a result of your taking ART?
f) Do you and your family have to give anything up in order to be able to pay for your ART?

3.   Treatment and adherence issues

a) How long have you been on ART?
b) Have you experienced any side-effects with your ARV medication? (If yes, has this been a reason for you to skip your medication at any time?)
c) Has distance to the clinic ever been a reason for you to skip your medication at any time?

d) Has cost ever been a reason for you to skip your medication at any time?
e) What do you think happens in your body if you skip your ARV medication?
f) Does a lack of food ever make you skip your medication?
g) Do you have anyone to remind you to take your medication?
h) Have you ever missed an appointment at your ART clinic?
i) Have you ever had to skip a dose because you felt you had to hide your medication from others around you?

4. Adherence counts

"We would like you to get your best guess about how much of your ARV medication you have managed to take in the last month. We would be surprised if it is 100% for most people."

We will take several approaches to measuring adherence:

I. Two-day recall diary

Three elements within this, as in sun and moon chart

Over the last two days, when did you take your pills? (Not including today - from yesterday evening and back.) Please mark with a cross when you took pills on the form below.

	When did you take your medicine yesterday?																		
	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	Morning						Midday						Evening					Night	
Name of medicine																			

	When did you eat yesterday?																		
	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	Morning						Midday						Evening					Night	

II.   *Visual analogue approach*

(a) Ask patient to pour one lot of beads (representing <u>all</u> the pills they would take in any given month, <u>note</u> separately for each medicine), A glass full of beads is marked with 0-10 cm line, after pouring beads to an empty glass, estimate pills not taken by looking at the mark of beads remaining in the first glass.

III.   *Pill count*

Train the pharmacist to do pill count and fill the slip shown below.
Ask the client to take the slip to the pharmacy to be completed. Collect the slip from the pharmacy.

ANNEX 5: Key informant interview

- Participants are community leaders, coordinators of ART, or people who have had some direct experience with ART;
- Adults (= or >18 years)
- One moderator, one note-taker (*and* use of tape recorder)
- Neutral venue in the community

Short introductory remarks, explain purpose of study, define what we mean by 'adherence', purpose of this discussion, reassurance about confidentiality

Introduction of researchers and participant.

1. Do you know where people can obtain ARVs in this area? (Probe also perceptions on ART, availability of traditional healers in that area etc.)
2. How does your community view for people who are taking ART? (Probe on stigma, discrimination, logistical issues for reaching clinic etc.)
3. Do they face any problems with adherence to their medication? (Probe on poverty, hunger, access to ART etc.)
4. What activities take place at the moment in your community to help people adhere to their medication? (Probe on support, home based care, individual.)
5. What *should* be done to ensure that people on ARVs take their medications as instructed?

Duration of discussion (1 ½ hours)
Conclusion, thank participants

ANNEX 6: Semi-structured interviews (with staff)

Name of facility:

Date:

Interviewer:

- Questions 1,2,3,4,17,18,19,20 should be answered by all categories of persons

- Questions 10 should be answered by Doctors and Pharmacists only.

- Questions 7 should be answered by a Pharmacist only

- The rest of questions see asterisk guidance [*]

Number	Question	M	Dr	N	P	So/Co	Di	R
Tasks and training								
1	What is your job in this clinic?	*	*	*	*	*	*	*
2	How long have you been doing this job?	*	*	*	*	*	*	*
3	What specific training have you received for this job in relation to ART? Tell me about the training (Details)	*	*	*	*	*	*	*
4	Do you think this training has been sufficient? (Details)	*	*	*	*	*	*	*
Drugs, treatment and procedures								
5	Which treatment guidelines for ART do you use in this facility? (Give details if necessary, e.g. national guidelines etc.)	*	*	*	*	*	*	
6	Are the drugs you prescribe always available? (If not, give details – how often, reason, what do you do about it)	*	*	*	*	*	*	
7	Are the drugs in the guidelines you use to dispense always available? (Give details – how often, reason, what do you do about it?)				*			
8	How reliable are your lab and diagnostic support services? Do results come in on time? Details.	*	*	*	*	*	*	
9	What is your procedure when a patient is put on ART for the first time?	*	*	*	*	*	*	
10	What is your procedure when a patient switches regimens?		*		*			

Number	Question	M	Dr	N	P	So/Co	Di	R
Adherence issues								
11	How do you think your patients do, generally speaking, in terms of adherence to ART?	*	*	*	*	*	*	
12	Generally speaking, do your patients keep their appointments?	*	*	*	*	*	*	
13	Could you estimate the percentage of your patients who you think are sufficiently adherent to ART? (Respondent gives their definition of 'sufficiently adherent'.) **	*	*	*	*	*	*	
14	We would like to get your views on the following (probe): a) How would you compare adherence between women and men? b) How would you compare adherence between older patients and younger patients? c) How does a patient's educational level affect adherence? d) How do you think that cost to patients influences adherence? e) How do you think the distance to the health facility affects adherence? f) In what way does having or not having a treatment-support partner affect adherence? g) Duration of treatment? h) Side effects? i) Lack of food? j) Knowledge about ART?		*	*	*	*		
15	Do you have a standard practice at this facility to support your patients to adhere to their treatment? If yes, is it documented? Can we see it? In what way is it used?	*	*	*	*	*	*	
16	What are the main challenges you face in supporting your patients to adhere to ART (especially for longer term users)?	*	*	*	*	*	*	
Challenges and staff support								
17	What are the main challenges you and your colleagues face more generally in your work? (if necessary, prompt re workload, stress, burnout)	*	*	*	*	*	*	*
18	Have these challenges changed in any way since you started here?	*	*	*	*	*	*	*
19	Is any special support made available to staff engaged in ART at this facility?	*	*	*	*	*	*	*
20	Is there anything you would like to see done differently in this facility? If yes, what?	*	*	*	*	*	*	*

Key

Managers – M	Counsellor – Co
Doctor – Dr	Social workers – So
Nurse – N	Receptionist – R
Pharmacist – P	Dieticians – Di

ANNEX 7: Observation (consultations)

Don't forget informal, unstructured observations!!!

Name of facility:
Date:
Observer:
Time observation started:
Time observation ended:

Person observed
  2. Doctor – Dr
  3. Dieticians – Di
  4. Nurse – N
  5. Pharmacist – P
  6. Receptionist – R
  7. Counsellor – Co
  8. Social workers – So

Things to note for observation
- Questions 2,6,7,8,19,20,21 should be answered by all categories of persons
- Questions 1,3,4,5,9,10,11,12,13,15,16,18 should be answered by Doctors, Nurses, Pharmacists and Social workers
- Questions 14 and 17 should be answered by a Pharmacist only
- Suggest a 'one-in, one-out' approach for conducting observations – follow one patient in for observation; take time to write up notes while the next one goes in; then follow the next patient in.
- Response forms should include 'yes/no' boxes to be ticked where relevant, with space for writing down other details.

Number	Topics for checklist	Yes	No	Not applicable	Details
1	What is the reason for the visit?				
2	Is patient well received? (If not, describe.)				
3	Does the consultation take place in privacy? (describe consultation room and environment)				
4	Does the health worker ask about any symptoms?				
5	Is the patient invited to ask questions? (If yes, what do they ask? If yes, was the question addressed? Details.)				
6	Is the patient told what to do next (within the health facility)?				
7	Is the patient told where to go for that?				
8	Is the patient told when to come back for refill and review?				
9	Is the sequence of events in relation to treatment protocols explained to *new* patients? (Requires training for observer)				
10	Do *new* patients receive comprehensive general information about ART? (How ARVs work, How to use them, The need to continue treatment, What to do if a pill is forgotten, Possible interactions with other drugs, Which side effects can occur & what to do if they occur, (Breast) feeding requirements, When and where to get re-supply) Are new patients asked if they were previously exposed ARVs through PMTCT, Or buying themselves from medical stores?				
11	Are *new* patients and those switching regimens given information about importance of adherence to ART: (i) dose, (ii) timing, (iii) what will happen if vomit up the pill, (iv) forgets timing, (v) misses dose, (vi) travelling?				
12	For follow-up users only: is there any discussion about the patient's experience of using their medicines? (specifically side effects)				
13	For follow-up users only: Does the health worker ask if the patient missed a dose? If yes, does the health worker explain what the effects are of missing a dose?				
14	For follow-up users only: Does the health worker count the patient's pills before giving him/her a new supply?				
15	Does the health worker ask the patient if they are taking any other medicines?				
16	Is the importance of adherence to ART reinforced?				

Number	Topics for checklist	Yes	No	Not applicable	Details
17	Does the patient receive specific tools to remind them to take their drugs? (eg pill calendar)				
18	Is the patient asked anything about their adherence strategies (include categories for adherence support partner/s, clock, mobile phone, other)?				
19	Is there any effort made to confirm whether or not the patient understands the information and instructions given?				
20	Does the clinician/nurse/counsellor *listen*? (details?)				
21	Do the health workers ever act or speak in any negative way (impatient, judgemental etc) towards patients? (If yes, describe)				

ANNEX 8: Observation of antiretroviral (ARV) stock

Clinic:…………… Name of interviewer:... Date:…./…../ 2005

1. ....Availability of drugs in stock:

Active ingredient(s)	Brand name	Dosage form	Strength(s)	In stock? (Y/N)	Out of stock in the past days?
-d4T/3TC/NVP	Triomune 30	Tab	D4T30mg/3TC150mg / NVP 200mg		
"	Triomune 40	Tab	D4T40mg/3TC150mg / NVP 200mg		
Efavirenz	Stocrin®, Sustiva®	Tab	50, 200, 600mg		
"	"	Oral sol.	150mg/5ml		
Lamivudine	3TC®	Tab	150mg		
"	"	Oral sol.	50mg/5ml		
Lopinavir+ ritonavir	Kaletra®	Tab	133,3mg+33.3mg		
Nevirapine	Viramune®	Tab	200mg		
"	"	Oral susp.	50mg/ 5ml		
"	"	Oral sol.	400mg/5ml		
Stavudine	D4T, Zerit®	Tab	30, 40mg		
"	"	Oral sol.	5mg/5ml		
Zidovudine	Retrovir®	Tab	100, 250mg		
"	"	Syrup	50mg/ml		
"	"	Infusion	10mg/ml		
Zidov+ Lamiv.	Combivir®	Tab	300mg+150mg		

2. Are buffer stocks written in the stock record card?   Yes ☐   No ☐

3. Is there a written policy for emergency procurement of ARV?

    Yes ☐   No ☐

4. Is the storage condition satisfactory?   Yes ☐   No ☐

5. Is storage room / space / size satisfactory?   Yes ☐   No ☐

6. Are stock register/records with respect to prescription maintained?   Yes ☐   No ☐

Factors that facilitate or constrain adherence to antiretroviral therapy among adults in Uganda: a pre-intervention study

Alice Nakiyemba, Dorothy A. Aurugai, Richard Kwasa, Thomas Oyabba.

Alice Nakiyemba
Busoga University
P.O. Box 154
Iganga, Uganda (Office)
P.O.Box 5028
Jinja-Uganda (Home)
Tel: +256-772-450371
Fax: +256-43-122103
E-mail: nakiyembaa@yahoo.com

Richard Kwasa
Pharmacy Department
Jinja Regional Referral Hospital
P.O.Box 43
Jinja, Uganda
Tel: +256-772-408948
Fax: +256-43-120007
E-mail: kwasarichard@yahoo.com

Dorothy A. Aurugai
P.O. Box 29396
Kampala, Uganda
E-mail: dakurut@yahoo.com
Tel: +256-752-653554

Thomas Oyabba
Busoga University
Department of Humanities
P.O. Box 154
Iganga, Uganda
Tel: +256-712-629471
E-mail: oyaxtoma@yahoo.com

Contents

Acknowledgements

Acronyms and abbreviations

ACP	AIDS Control Programme
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral therapy
ARVs	Antiretrovirals
EDM	Electronic drug monitoring
FGD	Focus group discussion
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
HIV	Human Immune Deficiency Virus
JCRC	Joint Clinical Research Centre
JRRH	Jinja Regional Referral Hospital
MoH	Ministry of Health
NTC	Nile Treatment Centre
PLWHIV	People living with HIV
pMTCT	Prevention of Mother-to-Child Transmission
SSI	Semi-structured interview
TASO	The AIDS Support Organisation
UAC	Uganda AIDS Commission
UNAIDS	United Nations Joint Programme on AIDS
UDVL	Undetectable viral load
VCT	Voluntary counselling and testing for HIV

Glossary

ADHERENCE	Adherence to antiretroviral treatment means taking the medicines in the right quantities, at the right time and taking all the medicines as prescribed. Poor adherence rates (less than 95% adherence) can lead to treatment failure and to the emergence of drug-resistant strains of HIV.
ANTIRETROVIRALS (ARVs)	Medicines designed to suppress the replication of HIV and prevent the progression of AIDS.
ANTIRETROVIRAL THERAPY	HIV treatment involving the use of a triple combination of ARVs.
CD4 T-CELL	A type of immune system cell that is depleted during the progression of HIV infection. A blood test involving a CD4 cell count can be used to determine the stage of the disease and is one of the criteria that can be used for deciding when to start ART and to monitor response to therapy.
CLIENTS	People who use the AIDS treatment services available at the health facilities.
UNDETECTABLE VIRAL LOAD	When the virus is not detected in the blood after a laboratory test.
VIRAL LOAD	Levels of virus found in the blood per 10 millilitres (mls).

Executive summary

AIDS is a serious public health problem in Uganda, together with malaria and tuberculosis. In the early 1990s, Uganda had the highest prevalence rate of HIV in the world. In response, the Government implemented strong preventive measures through a policy of openness, public information, communication and education, and national and international collaboration through a partnership involving both the private and public sectors. This approach succeeded in lowering the prevalence of HIV from over 30% in some sentinel sites to the current level of 7% (Ministry of Health, 2005). While these rates remain unacceptably high, Uganda offers one of the most hopeful scenarios in Africa.

Although antiretroviral (ARV) medicines do not provide a cure and are associated with other problems such as side-effects and drug resistance, they can increase the length and quality of life as well as the productivity of patients on antiretroviral therapy (ART). Antiretroviral regimens have improved survival rates and lowered the incidence of opportunistic infections in people with AIDS. Strict adherence to ART is crucial in order to maintain a low viral load and prevent the development of drug-resistant strains of the virus. However, some clients do not return for follow-up on schedule and the likely outcome for such patients is sub-optimal adherence to prescribed ARV regimens and possible treatment failure.

In Uganda, by October 2005, over 65 000 people had access to ART through accredited treatment centres (both public and private treatment centres). This exceeded the country's target of 60 000 that was set for end-2005 (i.e. the WHO "3 by 5" target for Uganda which was designed to reach 50% of people estimated to be in need of treatment).

It is estimated that in Uganda each year about 50 000 additional AIDS patients require ART (UN Integrated Regional Information Networks, 2005). As the number of people able to benefit from ART increases, the problems associated with sub-optimal adherence to ARVs are also likely to increase.

The purpose of this study was to identify factors that facilitate or constrain adherence to ART among adults in Uganda and to suggest possible interventions at one public health facility and one private facility. It is hoped that these suggestions will also have relevance for other public and private facilities in Uganda. This pre-intervention study used a variety of methods, both quantitative and qualitative, and involved the use of focus group discussions (FGDs), ethnographic observation, key informant interviews, semi-structured interviews (SSIs), exit interviews and the use of pharmacy records. The total sample survey included 200 participants from the two study sites. The study, part of a multi-country study also carried out in Botswana and Tanzania, was conducted in

Busoga region at Jinja Regional Referral Hospital (a public facility) and at Nile Treatment Centre (a private facility) during May and June 2005. Ethical issues were considered throughout the study; approval and permission were sought from the research unit of the Ministry of Health of Uganda. All those who participated in the study did so voluntarily and gave their informed consent, and the confidentiality of the participants was assured.

The study found that some people reported problems with adherence while others had not experienced any. A number of key issues were identified. Costs, including user fees, transport and other overhead costs, had a very large impact on adherence, even for those who tried their best to be adherent. In addition, hunger was identified as a threat to the future success of ART in Uganda. The study found that many patients on ART cannot afford to feed themselves as their body metabolism improves and their appetite increases. Although stigma and discrimination are not a major problem overall in Uganda, they still exist at local levels and sometimes pose a problem for people living with HIV (PLWHIV). While social support was identified as a good motivator which can boost adherence, inadequate social support can have a negative impact on adherence.

Participants in the study were worried about dependency on medicines which they would have to take for life. Some participants also worried about treatment fatigue, including some who were found to be giving themselves 'drug holidays' when they felt like doing so. These kinds of lapses in adherence will affect viral suppression and lead to the emergence of drug-resistant strains of the virus. Meanwhile, as more patients become resistant to first-line drugs, necessitating a switch to second-line regimens, it will become impossible to scale up ART in Uganda if more expensive second-line regimens are needed for all. Another finding was that ARV users often doubted whether they were receiving the best treatment currently available, leading to inconsistent adherence to ART.

The report makes a number of recommendations on possible ways to improve adherence to ART in Uganda, including: instituting pill counting in all facilities providing ART; training more adherence counsellors to support ARV users; informing communities about the availability of ART and of the critical importance of adherence; the launch or scaling up of home-based care programmes; providing a 'food basket' during the initial six months on ART, when the increase in appetite is greatest; and encouraging spot checks for adherence.

The implementation of the recommendations of this study would focus mainly on instituting pill counting throughout the country through training health workers and ARV users about the importance of pill counting in promoting adherence. The impact of this intervention would be evaluated on the basis of how many users are able to count their pills, the keenness of health workers on the method, and efforts by health workers to keep records of pill counts.

An additional key intervention strategy emerging from this study would be educational interventions for health workers, ARV users and community members. This would include training in adherence counselling and educating ARV users and community members about the availability of ARVs and the importance of adherence. The methods used would include the use of participatory training in communities through outreach activities and the use of posters, leaflets and local FM radio programmes using mainly local languages. In each case, the approach would need to be tailored to the educational levels of the communities involved. The impact of these would be evaluated on the basis of how many people are reached, whether there is an impact on their knowledge, and whether the knowledge gained would be sustainable in the long term and lead to increased levels of adherence and general improvements in health.

The interventions suggested above have been selected because they are expected to be appropriate for the target group, are likely to have an impact on both the primary and secondary targets, are sustainable, and are likely to require resources for only a limited period of time. For example, it is easy to get access to the local media and this can be used to achieve the communication objectives in both the short and long term.

The study concludes that although Uganda has made a good start in scaling up ART, which is widely appreciated, it appears to be moving very quickly to scale up access to ARVs without addressing some of the critical issues relating to adherence. These include the need to address factors which have a negative impact on adherence such as hunger, the burden of transport and other overhead costs, and long waiting times at the facilities. Meanwhile efforts to promote adherence should include a focus on the importance of pill counting, efforts to sensitize the community to both the availability of ART and the importance of adherence, as well as the need to train adherence counsellors and have them available in all facilities.

Chapter 1: Introduction

1.1 Background

AIDS is a serious public health problem in Uganda, together with malaria and tuberculosis. Although measures by the Government and nongovernmental organizations to prevent HIV have helped lower the estimated prevalence from over 30% in the early 1990s to an estimated 7% in 2005, the current prevalence is still unacceptably high (Ministry of Health (MoH), 2005).

Emerging data suggest that among segments of Ugandan society there have been important behavioural changes. People report that they have reduced the number of sexual contacts, based on Government advice that people love carefully, love faithfully or stick to one sexual partner. However, this does not mean that Ugandans are no longer vulnerable to HIV infection.

By October 2005, over 65 000 people with AIDS in Uganda had access to ART – more than half of the people estimated to be in need of treatment. However, it is estimated that each year an additional 50 000 people will require access to ART (UN Integrated Regional Information Networks, 2005).

1.2 Research problem

In Uganda, there is growing concern about loss to follow-up and sub-optimal adherence to ART as significant barriers to care (Kityo et al., 2002). Although Uganda is described in most literature as a success story to emulate in sub-Saharan Africa (Green, 2003), there was a need to assess the quality of care and adherence among people receiving these life-extending medicines. Since the service was newly introduced, it was vital that studies be conducted to evaluate and assess levels of adherence among people on ART and factors affecting adherence in both private and public facilities. Such studies would help inform the MoH and other policy-makers in Uganda on ways of improving or maintaining adherence to ART as access to ARV medicines is scaled up nationwide.

1.3 Research objective

The main objective of the study was to identify factors that facilitate or constrain adherence to ART among adults in Uganda.

1.3.1 Specific objectives

(a)   Determine patients' knowledge, attitudes and perceptions on the use of ARVs.

(b)   Establish patients' information sources and the communication channels most acceptable to them.

(c)   Determine beliefs and practices that affect adherence to ARVs.

(d)   Establish the type of services delivered to patients receiving ARVs in selected sites in Uganda.

(e)   Establish the kinds of social support given to patients taking ARVs.

(f)   Gather information from ARV users, support groups and health workers on improving ARV adherence, which can be useful for planning an intervention.

Chapter 2: Background to the study

2.1 History of AIDS in Uganda

In the early 1990s, Uganda had the highest prevalence of HIV in the world. In response, the Government implemented strong preventive measures through a policy of openness, public information, communication and education, and national and international collaboration through a partnership involving the private and public sectors (Uganda AIDS Commission (UAC), 2001). This approach succeeded in reducing HIV prevalence from over 30% in some sentinel[1] sites to the current level of 7% (MoH, 2005). Although HIV prevalence remains unacceptably high, Uganda offers one of the most hopeful scenarios in Africa and is seen as a model to emulate (Green, 2003).

In 1986, Uganda established the AIDS Control Programme (ACP) in the MoH. The UAC was established in 1992 to coordinate multisectoral approaches to HIV, of which one of the major initiatives was the introduction of interventions for the prevention of mother-to-child transmission (pMTCT) of HIV through the UNAIDS-brokered Accelerating Access Initiative. This initiative is a partnership involving UN agencies and a number of pharmaceutical manufacturers who have offered to supply products at reduced prices in resource-poor countries. Other Government strategies for prevention include an emphasis on the "ABC" strategy (Abstinence, Be faithful, Condom use) (UAC, 2001).

2.2 History of ARVs in Uganda

Since 1996 Uganda has pioneered the use of ART in sub-Saharan Africa. The ARVs were initially imported and distributed to those patients who could afford to buy them. Joint initiatives between international organizations such as UNAIDS and private organizations such as the Joint Clinical Research Centre (JCRC) helped to reduce the cost of ARVs, making them accessible to many more people. The importation of cheaper generic drugs into the country by private institutions such as JCRC has caused pharmaceutical companies to significantly reduce the price of some patented ARVs (Mugyenyi, 2001).

As AIDS became the second highest cause of death in Uganda after malaria, the JCRC was established in 1991, with support from the Government, as the country's first AIDS treatment research centre. However, since ART was very expensive only a few government officials and other high-income people could access the medicines. Even

---

[1] HIV sentinel sites are those where blood samples from clients of antenatal and sexually transmitted infection (STI) clinics are collected, using unlinked anonymous methods. The blood samples are collected on a quarterly basis for testing at the Uganda Virus Institute. Results from these sites are generalized to establish HIV prevalence in Uganda.

after securing permission to import generic ARVs, prices were still prohibitively high for the general population.

ARV medications became more widely available in Uganda in 2004 when the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) and the US President's Emergency Plan for AIDS Relief (PEPFAR) came in to support the provision of ART for people with AIDS. These two agencies provided unprecedented multilateral support and enabled the scaling up of access to ART (Gill et al., 2005).

In June 2004, the Government of Uganda implemented an ARV programme in one national referral hospital (Mulago), in all 11 regional referral hospitals and 11 district hospitals, providing ARVs to 2700 patients. At the time of this study, the Uganda Government, under the National Strategic Framework for Expansion of HIV/AIDS Care and Support – 2001/2-2006/7, was providing ARVs through 140 accredited sites. Most of these are district hospitals and health centre IVs (rural health units offering primary health care, usually staffed by one doctor, one clinical officer, three nurses and three midwives). By September 2005, 14 300 patients were accessing ARVs through these Government facilities (National Strategic Framework for Expansion of HIV/AIDS Care and Support – 2001/2-2006/7).

In addition to the Government facilities, some nongovernmental (private not-for-profit) organizations also provide ART. The foremost of these are: The AIDS Support Organisation (TASO) with 6600 patients; JCRC which provides ARVs to 18 000 people through its various sites across the country; and Mildmay International Centre with 2500 clients on ART. Others include Uganda Cares, Medical Access and the Uganda Business Coalition for HIV/AIDS.

Chapter 3: Literature review

The literature on ART reviewed in this chapter relates mainly to non-African countries, where most studies have been conducted so far. There is a great need for African studies of experience with ART in order to help fill this gap. However, where evidence is available from some sub-Saharan African countries, this is also included.

3.1   Importance of adherence to ART

Since 1996, an overwhelming amount of evidence from clinical trials has been published validating the use of ART for the treatment of AIDS. The biological and clinical goals of treatment have been defined as the suppression of viral replication, restoration of the immune response, a halt in the progression of disease, increased survival rates, reduced morbidity and a better quality of life. In countries where access to this level of care is available, AIDS-related mortality and morbidity have significantly declined (Pallela et al., 1998).

Maximum and sustainable suppression of HIV viral replication to below the level of detection is necessary to achieve these biological and clinical goals. To achieve success requires near-perfect adherence to combination ARV regimens. Adherence to an ARV treatment regimen involves taking all pills in the correctly prescribed doses, at the right time, and in the right way (Carter, 2005). It involves the following elements:

♦ Taking all the medicines which make up the ARV combination in the correct quantities.

♦ Taking the pills at the right times. Taking the medication at the wrong time can cause a rise in viral load and this may lead to the development of drug resistance.

♦ Ensuring that the medication is taken with or without food, according to the instructions. Some medicines need to be taken with food to ensure that the body absorbs them properly while others need to be taken on an empty stomach, a certain amount of time before or after eating. It can also be important that the patient eats the right kind of food; for example, the amount of fat eaten can make a difference to how well some drugs are absorbed.

♦ Checking for interactions with any other medication or drugs. This includes medicines that have been prescribed for the patient, or bought at a pharmacy, supermarket or health store, including complementary or alternative therapies. Some recreational and illegal drugs can have potentially dangerous interactions with ARVs.

The best response to ART is seen when adherence is 100%. Levels of adherence below 95% have been associated with poor suppression of HIV viral load and a lower increase in CD4 count (Carter, 2005).

♦ If a patient is taking once-daily treatment, 95% adherence means missing no more than one dose a month.

♦ If a patient is taking treatment twice a day, 95% adherence means missing no more than three doses a month.

♦ If a patient is taking treatment three times a day, 95% adherence means missing no more than four doses a month.

However, many people with AIDS do not manage to achieve such high levels of adherence. Failure to suppress viral replication completely inevitably leads to the selection of drug-resistant strains, limiting the effectiveness of therapy. Sub-optimal adherence to ART is the strongest predictor of failure to achieve viral suppression below the level of detection and most often underlies treatment failure. Evidence suggests that greater than 95% adherence may be necessary to adequately suppress viral replication, produce a durable response and halt disease progression (Paterson et al., 1999). This means that missing more than one dose of a regimen per week may be enough to cause treatment failure. In addition to leading to disease progression this may result in the development and transmission of drug-resistant viruses which cannot be treated with first-line (lower cost) medicines. This will require treatment with second- and/or third-line medicines, which are more expensive, associated with many side-effects and are complex to manage.

The challenge of adherence in the face of potential viral resistance, treatment failure, disease progression and the spread of drug-resistant virus to sexual partners is of great concern. Patients on long-term ART with undetectable levels of HIV still harbour replication-competent virus (Furtado et al., 1999). For this reason, with current medications, ART is a life-long process. While conscientious treatment adherence is difficult under any circumstances, the unforgiving nature of HIV replication, the complexity of the ART regimens, and the associated short- and long-term toxicity of the medicines all pose particularly difficult challenges for patients.

It should be recognized that adherence to ART is a critical issue, and it is clear from the literature that the factors that influence a patient's ability to adhere are multiple and complex. A multitude of variables such as income, education and marital status have all been shown to affect adherence to ART, to differing degrees. In addition, some studies of ART in developing countries show that resistance is already circulating among patients starting their first "official" course of therapy (i.e. when somebody has acknowledged their HIV status, is willing to speak about it freely, and is seeking treatment from an accredited site for proper monitoring and follow-up) (Mugyenyi, 2002). Before ART was scaled up, fear of stigma led many people to seek ARVs clandestinely on the black market. As a result, people sometimes took medicines on the

basis of instructions from the person selling them on the black market and the use of ART was poorly monitored.

3.2   Measurement of adherence

Researchers who have tried to measure adherence have realized that there is no gold standard by which it can be quantified (Farmer, 1999). The many methods employed by the different studies include: pill counting, electronic drug monitoring (EDM), pharmacy refill records, biochemical markers and other self-reporting techniques such as visual analogue and recall methods. The relative accuracy of adherence measures ranks from physician assessment and self-assessment being the least accurate, to pill counting being intermediate, and EDM being the most accurate (Gill et al., 2005).

Electronic drug monitoring more accurately predicts undetectable viral load (UDVL) than self-report or pill count. Its main advantages are that it provides data on the timing of doses taken and permits monitoring over long periods. Since adherence can be known precisely, the link between adherence levels and UDVL can be established with a high degree of confidence. Arnsten et al (2001) noted that patients whose EDM data indicated high adherence (above 90%) were far more likely to achieve UDVL than patients self-reporting the same level of adherence. Other studies have reported similar results on the relationship between UDVL and EDM-rated adherence: Paterson et al (2000) observed UDVL in 80% of those with above 95% adherence, while in a trial conducted by Kirkland et al (2002) mean adherence was 94% with 85% of the patients achieving UDVL. However, no single measure is appropriate for all settings or outcomes. It has been found that the use of more than one measure of adherence allows the strengths of one method to compensate for the weakness of the other and to more accurately capture the information needed to determine adherence levels (Vitolins et al., 2000).

3.3   Factors affecting adherence to ART

3.3.1 Demographic and socioeconomic factors

Although the literature consistently demonstrates that demographic characteristics are not strong predictors of adherence, some correlates of adherence are described below together with socioeconomic factors.

3.3.2 Age

Age may influence adherence. Studies have found that, with the exception of the most elderly, adherence increases with age. In two studies associated with ART adherence, sub-optimal adherence showed a positive correlation with being younger (Jones et al., 1999).

3.3.3 Level of education

A lower level of general education and poorer literacy may impact negatively on some patients' ability to adhere, while a higher level of education has a positive impact (Catz et al., 1999).

3.3.4 Financial constraints

Studies conducted in Africa reveal that the cost of medication is one of the most significant barriers to treatment adherence. In Botswana, Weiser et al. (2003) report adherence difficulties related to the financial demands of therapy and an inability to afford medicines for varying periods. They note that 70% of patients claimed that the cost of ARVs posed a problem for them, and 44% of patients believed that the cost impeded their ability to adhere to treatment. Similarly, over one-half of health care providers (56%) believed that financial problems often or always impeded adherence to ART. The extent to which financial difficulties played a key role in sub-optimal adherence is also reported in study findings in Uganda for patients receiving non-subsidized therapy (Byakika-Tusiime et al., 2003). Medications and clinic visits cost money and may stretch an already meagre budget. In resource-poor countries many people live below the poverty line and there is often no medical insurance or disability pension for people living with HIV (PLWHIV) (Katabira, 2002).

3.3.5 Social support

Living alone and a lack of support have been associated with an increase in sub-optimal adherence (Williams and Friedland, 1997), and social isolation is predictive of sub-optimal adherence. Not living alone, having a partner, social or family support, peer interaction, and better physical interactions and relationships are characteristics of patients who achieve optimal adherence (Motashari et al., 1998).

3.4   Impact of the drug regimen on adherence

Almost all of those who are currently on ART are on a regimen of three or more ARVs (Grierson et al., 2000). The likelihood of a patient's adherence to a given regimen declines with polypharmacy, the frequency of dosing, the frequency and severity of side-effects, and the complexity of the regimen (Williams and Friedland, 1997). Drug hypersensitivity is common in patients with HIV and regimen-associated toxicity is a common predictor of, and reason for sub-optimal adherence, which has been identified across many studies. Side-effects associated with each individual ARV medicine have been well documented and, while not universal for every patient, can be predicted. Although these side-effects usually subside after the first few weeks of therapy, for some people they persist. The anticipation and fear of side-effects also have an impact on adherence. Poor adherence has also been associated with patients' desire to avoid embarrassing side-effects (like sweating) in certain situations such as on a date or at a job interview (Burgos et al., 1998).

For people on ART, a typical combination of medicines consists of three ARVs, plus other medication to prevent opportunistic infections. This can result in a high pill burden, taking medicine three times a day, dietary and dosing idiosyncrasies, large capsules or tablets, and specific storage instructions. The complexity of this regimen may have a significant impact on a patient's ability to adhere. Additional medications taken for symptomatic relief (such as analgesics, cough remedies and other common treatments) in patients with advanced disease further add to the pill burden and toxicity. In Uganda, first-line treatment involves the use of the following combinations: lamivudine, stavudine, and nevirapine or efavirenz; and zidovudine, lamivudine, and nevirapine or efavirenz. Second-line medicines used are didanosine; lopinivir or ritonivir; and stavudine or zidovudine.

The generic fixed-dose combination Triomune, which is provided by the Global Fund/MoH consists of three ARVs (lamivudine, stavudine and nevirapine) in a single pill. However, PEPFAR provides these same ARVs as three separate pills. As a result, patients taking the separate pills have to take three times as many pills as those on Triomune, with significant implications for adherence. A study in Senegal reveals that a high pill burden is associated with poor adherence among patients who have to take a large number of ARV pills (Dansburg et al., 2003).

3.4.1 Effects of ARV regimen on eating patterns

Dietary restrictions add to the complexity of ART and often require adjustments in lifestyle. Patients can find their meal schedule compromised by ARVs that need to be taken on an empty stomach. This can be particularly difficult if workmates, family or friends are unaware of the patient's HIV status (Grierson et al., 2000). Complicated regimens with rigid dosing intervals may also interrupt sleep. The physical aspects of a particular medication (for example, taste, size or formulation) may also affect a patient's ability to adhere.

3.5   Treatment characteristics affecting adherence

3.5.1 Physical state and disease stage

Prior opportunistic infections, symptom severity and low CD4 counts are all predictors of adherence. One patient described the progression of disease as "*creating a sense of urgency for treatment.*" Another said: "*As I first entered the study, I had a T-cell count below 10. I was at the hospital 20 some times...... The grim reaper was standing above me.*" (Erlon and Mellors, 1999).

Seeing an improvement in the immunological and virological indices used to monitor ART (CD4 cell counts and HIV viral load) may be a powerful incentive to maintain adherence (Kaplin et al., 1999). However, caution should be exercised in emphasizing a patient's improved laboratory indices without assurance that adherence is almost faultless. The value of these indices may improve in the short term, despite sporadic adherence and this may reinforce a patient's level of sub-optimal adherence.

Lack of symptoms (despite laboratory evidence of the need for ART) may have an adverse effect on adherence (Jones, et al., 1999). Most patients with untreated HIV infection have a median AIDS-free time of 11 years, and ART is often begun when patients have laboratory evidence of disease progression but are essentially asymptomatic and feeling well. In Uganda, the policy is to initiate treatment in patients with documented HIV infection and:

♦ WHO Stage IV disease, irrespective of CD4 cell count; or

♦ Advanced WHO Stage III disease, including persistent or recurrent oral thrush and invasive bacterial infections, irrespective of CD4 cell count or total lymphocyte count: or

♦ With a CD4 cell count of 200/mm^3 or less for patients in WHO Stage I, II or III; or

♦ Tuberculosis with a CD4 cell count of 200-350/mm^3.

3.5.2 Depression and severe anxiety

Depression and severe anxiety are both predictors of sub-optimal adherence (Hirschorn L et al., 1998). At some time in the course of their illness, most people with HIV, experience a psychiatric disorder (Buhrich and Judd, 1997). Depression and/or anxiety are reported in up to 70% of AIDS patients with symptomatic disease. Adherent patients demonstrate significantly less depression or other psychiatric disturbance (Catz et al., 1999).

As the disease progresses, HIV may have an impact on the central nervous system and affect memory. AIDS-related dementia (AIDS Dementia Complex) is a common finding in patients with advanced disease and is characterized by abnormalities in cognitive and motor functions. Although studies describing adherence and AIDS Dementia Complex were not found, cognitive deficits have a negative impact on adherence to ART (Meisler et al., 1993). Even when cognition is unimpaired, it is difficult to remember when to take medications.

3.5.3 Beliefs and knowledge

A patient's beliefs about their illness and the effectiveness of medication are predictive of adherence. A good level of understanding about HIV by the patient, a belief that ART is effective and prolongs life, and recognition that poor adherence may result in viral resistance and treatment failure (Wenger et al., 1999) all impact favourably upon a patient's ability to adhere. Conversely, a lack of interest in becoming knowledgeable about HIV and a belief that ART may in fact cause harm adversely affect adherence.

3.6 The clinic setting and service provision

The effect that the clinic setting has on adherence should not be underestimated. Clinic characteristics that impact on adherence include: proximity to the patient's home or place of work, the expense of getting there, lengthy delays between appointments, clinic opening and closing times, long waiting times, lack of services such as child care, privacy, confidentiality, and unsympathetic or inconsiderate staff (Nemecheck and Tritle, 1998).

3.6.1 Difficulties with re-supply of medicines

Obtaining a prescription during a clinic visit is reported as an obstacle to adherence. In some developing countries, just over 50% of ARV users are given a prescription which lasts for three months, 40% receive a prescription for one month and 12% for two months (Burgos et al., 1998). In addition, some dispensing pharmacies will only dispense one month's medication at a time (often on a single designated clinic day) and not all pharmacies are able to dispense ARVs. As a result of such difficulties in prescription procedures, some patients attend their local pharmacy for most prescription medicine and another separate pharmacy for their ARVs. This is a barrier to optimum adherence in that problems in obtaining or taking medicines have to wait until the designated clinic day, by which time patients may already be defaulting on their dose (Grierson et al., 2000).

3.7 Simplifying treatment regimes to improve adherence

Simple regimens and regimens that 'fit into' a patient's lifestyle enhance adherence. Patients talk of *"incorporating the regimen into their lives and of it becoming a way of life"* (Erlon and Mellors, 1999). As a regimen increases in complexity, its inconvenience makes it difficult to incorporate into daily living. Much recent research is aimed at simplifying ART to twice daily or even once daily dosing (Grierson et al., 2000).

3.8 Conceptual framework

The conceptual framework (Figure 1) was developed during the proposal development process. It identifies service factors, patient factors and socioeconomic and cultural factors leading directly and indirectly to sub-optimal adherence to ARVs. This study aimed to investigate all of the identified factors to assess which were the most important in the Ugandan context and which were amenable to intervention.

Figure 1: Factors leading to sub-optimal adherence to ARVs
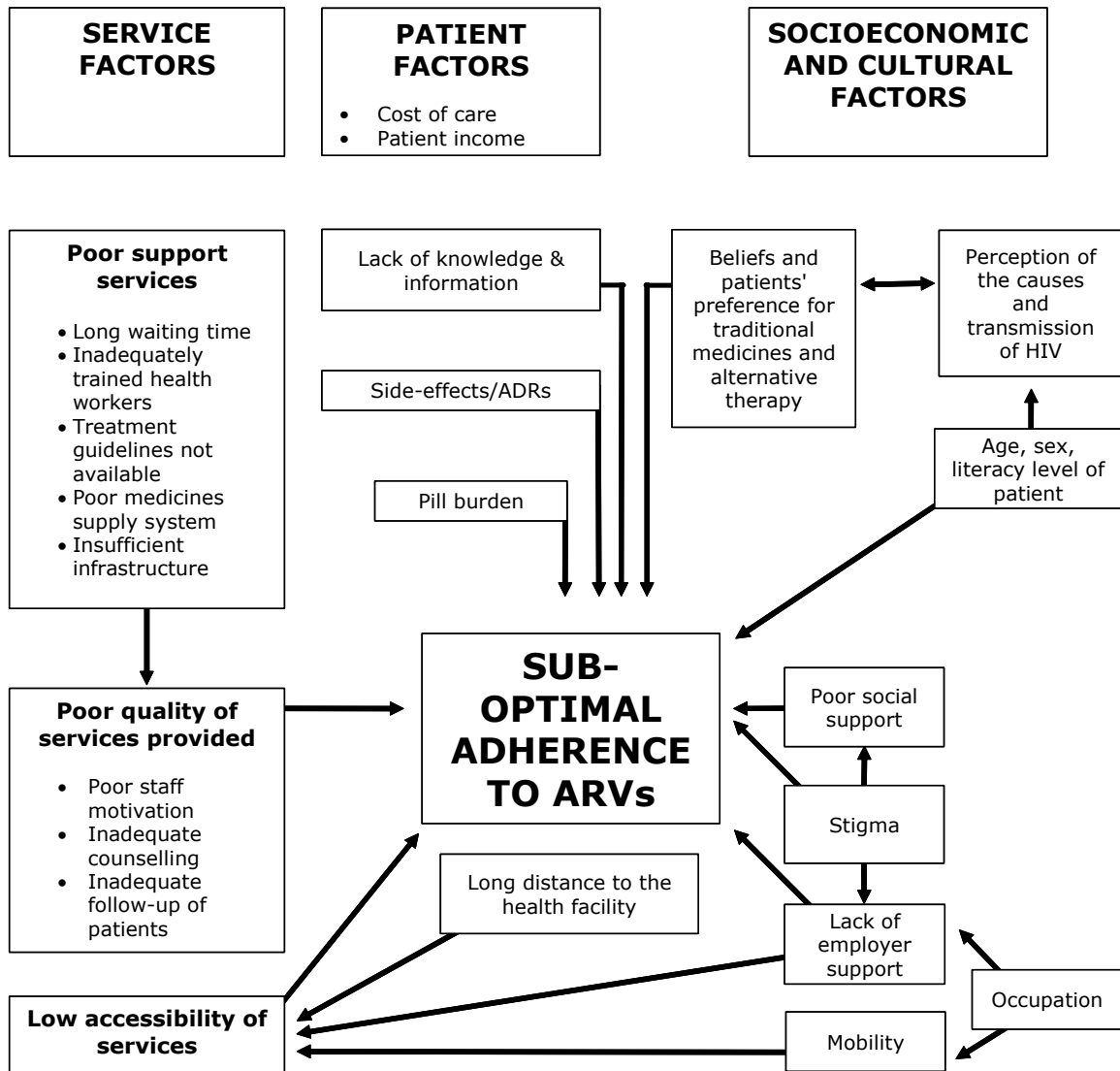
Chapter 4: Methodology

4.1 Study design

The study investigated factors that facilitate or constrain adherence to ART for people on treatment at one public facility and one private facility in Uganda. The study used both quantitative and qualitative methods. These two approaches complemented each other. This research is part of a multi-country study carried out in Uganda, Tanzania and Botswana.

Data were collected at three different levels: individual, community and facility levels. The research team, comprising the principal investigator, three research associates and one data collector, collected data through interviews and observations, with the use of tape recorders. Data were collected during May and June 2005.

4.2 Study population

The study was conducted at two facilities providing ART in the Busoga region of Uganda. The study population consisted of patients aged 18 years or above who were receiving treatment at the study sites, and health workers and community members at the selected sites.

4.3 Inclusion and exclusion criteria

The study sites in Busoga region, a sub-region of Eastern Uganda were selected according to the following criteria:

1.   The area has both a public and private facility supplying ARVS.
2.   The sites were relatively research naïve.

Two facilities were chosen for the purpose of this research. One of these, the Jinja Regional Referral Hospital (JRRH), is accredited to offer ART through the Global Fund. At the time of this study, the services available at this facility included ART, voluntary counselling and testing (VCT) for HIV and treatment for opportunistic infections. The hospital collaborates with TASO, to which they refer their patients for continuing support.

The other facility, the Nile Treatment Centre (NTC), is a nongovernmental agency in Jinja. Since January 2004, NTC has been providing AIDS care and treatment for opportunistic infections for about 600 inpatients. In addition, NTC has outpatient facilities for AIDS treatment and VCT. However, it has no support programme for PLWHIV.

All patients attending the two facilities who were at least 18 years of age, on ART, and willing to participate in the study were included. Systematic sampling was used to select the final sample, based on the selection of every third patient visiting the clinic on the day of the fieldwork. Where a patient was not interested in being included in the study, the next patient was considered instead (except when selecting participants for the focus group discussions (FGDs) according to sex, when the next female or male patient was chosen, as appropriate).

4.4 Sample size and selection

A registry file from each facility's reception was used as a sampling frame from which ARV users were selected for the study, using systematic sampling. This was done to avoid bias in the sample. A total of 200 people participated in the study. Of these, 130 were ARV users interviewed through the use of one of the following tools: FGD guide, adherence tool, semi-structured interview (SSI) guide, exit interview guide, key informant interview guide and observation guide. Fifty of the study participants were community members interviewed using the FGD guide and key informant interview guide. The remaining 20 participants were staff members interviewed using the FGD guide, SSIs and the pharmacy records tool.

The study included 10 FGDs, (five with ARV users, four with community groups who were categorized by sex, and one with health workers) which helped clarify issues raised by participants. Twenty exit interviews were undertaken with ARV users to establish the quality of care, procedures and conduct while at the facility. Another 20 ART users completed adherence measurement interviews to assess levels of adherence. Two pharmacy stock records were completed.

Table 1: Summary of study participants

Tool	Public Facility Jinja Regional Referral Hospital	NGO Facility Nile Treatment Centre	Total
FGD* – staff	1x8	-	8
FGD - ARV users	3x10	2x10	50
FGD - community	2x10	2x10	40
SSI** - staff	5	5	10
SSI - ARV users	10	10	20
Key informants	10	10	20
Exit interviews	10	10	20
Adherence tool	10	10	20
Pharmacy records	1	1	2
Observations	5	5	10
Total	109	91	200

   * Focus group discussion, ** Semi-structured interview

4.5 Data collector selection and training

After completing the study materials and having obtained permission from the MoH research unit and both of the facilities involved, the research team selected and trained data collectors. The selection criteria for data collectors involved having a multi-disciplinary team including one social scientist and one health worker with adequate experience in conducting health-related research. The research team was gender balanced, comprising two female and two male members. The data collectors were trained in the various methodologies of data collection and also on critical ethical issues. As part of the training, the data collectors participated in pre-testing the instruments with the guidance of the principal investigator.

4.6 Pilot testing

The research team conducted a pre-test of the instruments with two FGDs (one per facility) involving four AIDS patients (two per facility) and two service providers (one from each facility). The pre-test served to rectify and revise instruments as well as the research procedures in general. Changes made included omitting the pill count method since it is not used at the facilities.

4.7 Data collection

While many of the planned data collection methods were used, some modifications had to be made in response to a broadening focus and the need to adapt to the local culture. However, the main emphasis remained on using a mix of qualitative and quantitative methodologies to collect the information. This strategy was chosen because triangulation of methods would yield different types of information, and such a mixture would not only enable a cross-validation of data, but also minimize bias. Some tools provided both quantitative and qualitative data.

4.7.1 Quantitative data

Quantitative data were collected using a coding manual which had been developed earlier and answers were recorded using the manual. Information on demographics, timing of drug administration, and some default interruptions leading to non-adherence were entered in the manual. Additional quantitative data were collected using SSIs, observation (consultations), exit interviews, and pharmacy records. Information collected on demographics included age, religious background, educational level, knowledge, attitude, perception and experience in the use of ARVs.

4.7.2 Qualitative data

The bulk of the data for the study were based on qualitative methodologies because the key problem studied, sub-optimal adherence to ART, could best be captured in this way. The following qualitative methods were used: FGDs, observations, in-depth interviews, SSIs and exit interviews. FGDs were administered to the following study populations: four groups in the community categorized by sex, five groups of ARV users, and three groups of health workers who were not categorized according to type

since it was assumed that all health workers face similar challenges as they interact with PLWHIV and those on ART. Key informant interviews were conducted with local council and opinion leaders, cultural leaders, religious leaders, traditional healers and PLWHIV support groups. Semi-structured interviews were conducted with ARV users, service providers from both facilities, and ethnographic observations were conducted in both facilities with notes compiled on themes related to adherence. Other techniques used included: exit interviews with ARV users, checking pharmacy records with staff, and the use of the adherence tool with ARV users.

Focus group discussions

Focus group discussions, organized by age and sex, were conducted both with community members and with people on ART and enrolled at the selected sites. The aim was to identify difficulties that were being encountered by people on ART. The moderator had an FGD guide, used to keep the research focused on the main themes of the study. Ten FGDs were conducted (four with the community, five with ARV users and one with health workers). The location was considered when selecting participants for the FGDs (i.e. urban, peri-urban and rural setting). The FGDs were used to: determine community knowledge, beliefs, attitudes and behaviour in relation to the use of ARVs; investigate social support given to PLWHIV; and to get suggestions on ways of improving adherence to ARVs. Four of the 10 FGDs focused on getting the views of community leaders and other opinion leaders on the use of ARVs as well as the community's perception of and solutions to the problem. At each facility the counsellor helped select participants for the discussion.

In-depth interviews

These involved the use of semi-structured, open-ended interview guides with flexible probing, ideal for investigating personal experiences of ART from the subjective perspective of each respondent. The exit interviews were helpful in assessing the quality of care. They served as a back-up to the FGD findings. Twenty key informant interviews were conducted, 10 at each facility. The aim was to establish: beliefs about HIV and ARVs; community participation in HIV-related activities; support systems in place for people on ARVs; and the problem of sub-optimal adherence.

Observation (consultation)

Ten observations, five at each facility, were conducted with a doctor, pharmacist, nurse, counsellor/social worker and receptionist. The aim was to explore aspects such as interactions between clients and service providers in health facilities, the availability of ARV stocks, stigma, and the length of time spent at the facility, privacy, and organizational procedures. Observational notes were taken and later used in data analysis. The notes were used to help fill in any gaps in the data obtained during FGDs or in-depth interviews, and to triangulate data.

4.8 Data analysis

Data checking and cleaning were done by the entire research team under the direction of the principal investigator. At the end of every field day, data were checked for completeness and consistency, and FGDs were transcribed. All relevant sources of data were considered to allow for triangulation. After transcribing and cleaning, data were converted to rich text format and entered into Nudist Nvivo, a package used for analysis of textual data. A code book was developed which was used for coding the text, after which searches related to adherence were run. Quantitative data were entered using the MS Access 2000 database, and descriptive and bivariate analyses were completed using SPSS version 11.01.

4.9 Evaluation of methods

The mix of methodologies was very useful in both urban and rural settings, and in the public and private facilities. It allowed for both flexibility and cross-validation of data. The FGDs were particularly informative. The study yielded a large amount of additional qualitative data. Wherever possible, this information has been used. The in-depth interviews, which were carried out in both rural and urban settings, yielded not only information on factors facilitating or constraining adherence but also more general information on trends in the use of ARVs in Uganda. Although originally the research team believed that, for ethical reasons, treatment observations may not be possible, the researchers were allowed by staff and patients to observe while consultations were going on.

4.10 Ethical considerations

Approval and permission for the study were requested from the MoH health research unit. Due care was taken to ensure that all those who agreed to participate in the study did so voluntarily, and gave their written informed consent. To this end, the researchers explained the aims and objectives of the study to all those involved and they were given an opportunity to ask for any clarification. Participants were informed that any information collected was to be kept confidential and that no names would appear on research documents, only identity (ID) numbers.

Chapter 5: Description of the study sites

5.1 Jinja Regional Referral Hospital

Jinja Regional Referral Hospital (JRRH) is located in the industrial town of Jinja, 80 km east of the capital city, Kampala, in the eastern region of Uganda. Established in the 1920s, it now serves as both a primary contact hospital and as a regional referral hospital for seven districts (Bugiri, Iganga, Jinja, Kaliro, Kamuli, Kayunga and Mayuge) with an overall population of 3.5 million people. The hospital has 500 beds and a staff of 360 instead of the 480 approved by the MoH.

In addition to the usual medical care programmes, the hospital is involved in regional training programmes for the Integrated Management of Childhood Illnesses (IMCI), pMTCT, VCT, and ART.

The hospital's HIV clinic runs all HIV-related programmes including ART. The hospital has three programmes for ART access:

- Free MoH programme
- Free Treat Orphans programme (JCRC-coordinated)
- Cash and Carry programme for paying patients (JCRC-coordinated).

All participants in the study at this facility were chosen from the free MoH programme. This was because the other free programme, the Treat Orphans programme, caters only for children. The patients on the free programmes collect their refills on the weekly clinic day, while the patients in the Cash and Carry programme can come on any working day to collect their refills. The Cash and Carry programme is available for anyone who does not want the inconvenience of queuing for treatment and is able to pay for the medicines.

A total of 300 patients are currently enrolled on ART through these programmes (230 on the free MoH programme, 65 on the free Treat Orphans programme and five on the Cash and Carry programme). The hospital uses the MoH treatment policy and criteria and thus offers the recommended treatment regimens for ART.

The clinic attends to all HIV-related cases one day a week. During other days of the week, patients with HIV-related problems are identified and advised to attend the weekly HIV clinic.

On a typical weekly HIV clinic day, two rooms are converted to one reception and one consultation room (on other days the same rooms are used for other routine hospital activities). Two doctors and seven nurses are assigned to attend to the HIV patients,

including those on ART. Some of the nurses act as both receptionists and counsellors. About 80 patients attend the weekly clinic, of whom about 50 are already on ART. The clinic opens at 0830 hours and patients start arriving as early as 0700 hours. The patients report to reception, where their names and numbers are taken and their file retrieved from the filing cabinet. The patient's file is taken to the counsellor, who calls in the patient from the shady waiting area. After the counselling session, the patient has to queue again if they need to see the doctor. Otherwise the counsellor/nurse writes a refill prescription for the patient, who then takes the prescription to the pharmacy and sits outside waiting to be called in.

5.2 Nile Treatment Centre

The Nile Treatment Centre (NTC) which opened in January 2004 is a nongovernmental agency located on the Jinja to Kampala highway, 5 kilometres from Jinja. The location makes it less accessible than the public facility and allows for greater privacy. NTC is funded by PEPFAR and is under the aegis of the Uganda Business Coalition against HIV/AIDS, which has two other centres in Kampala.

NTC has 12 staff members: three doctors, two counsellors, two phlebotomists, one dispenser, one pharmacist, two nurses, and one medical assistant who offer services to PLWHIV. It is open five days a week and the staff work a half-day on Saturdays. The Centre receives 30 patients a day on average and the doctor patient ratio is 1:15, with two doctors on duty at any one time. Like JRRH, NTC follows the National Antiretroviral Treatment and Care Guidelines and offers similar regimens.

NTC opens at 0830 hours. On arrival patients are welcomed into comfortable seats and welcomed by a receptionist who then asks for the patient's confidential number. The receptionist keys this number into the computer and checks whether the patient has come for their appointment on the correct day. She then refers the patient to the health workers they are scheduled to meet that day.

For all new patients, the importance of near-perfect adherence is emphasized by the adherence counsellor on the first visit. This counselling is carried out in groups or individually on request. Patients are then sent to the doctor, who assesses the patient's condition and requests blood or other tests, including a repeat HIV test. Prior to testing, the phlebotomist checks that the client is aware of the critical importance of adherence. A similar check is carried out by the pharmacist before releasing medicines to any patient.

5.3 Study limitations

The study focused on patients who are accessing ART through only two facilities, one private and the other public. Furthermore, the quantitative data on adherence were limited and have not been presented in this report.

Patients' waiting area at Jinja Hospital.

The pharmacy window and waiting area,
Nile Treatment Centre.

One of the three consulting rooms for doctors at
the Nile Treatment Centre.

Chapter 6: Results

6.1 Demographic characteristics of ARV users

The study was conducted at Jinja Regional Referral Hospital (JRRH) and Nile Treatment Centre (NTC) both in Busoga region. A total of 200 respondents (109 from JRRH and 91 from NTC) participated in the study. Demographics were calculated for all the ARV users who participated in the study from adherence, exit and semi-structured interviews. Twenty six (37%) of the ARV users were male and 44 (63%) were female. Fifty-six per cent of the participants had been on ART for two years or less and the rest (44%) had been on ARVs for more than two years (Table 2).

Table 2: Length of time participants have been taking ARVs, by site

Duration taking ARVs (months)	JRRH		NTC		Total	
	Number	Percent	Number	Percent	Number	Percent
< 3 months		0	4	11	4	6
3 - 6	4	11	14	39	18	25
7 - 12	13	37	5	14	18	25
13 - 18	3	9	3	8	6	8
19 - 24	3	9	0	0	3	4
25 - 30	2	6	2	6	4	6
31 - 36	2	6	2	6	4	6
37 - 42	0	0	2	6	2	3
43+	8	23	4	11	12	17
Total	35	100	36	100	71	100

Of the 71 respondents interviewed, 40 (56%) had finished secondary education, 17 (24%) had completed primary education and 14 (20%) had completed tertiary education. The lowest educational level was seven years' schooling (Table 3).

Table 3: Educational status of study participants

Education Level	Number who completed	Percentage (%)
Primary	17	24
Secondary	40	56
Tertiary	14	20
Total	**71**	**100**

While ARVs were provided free of charge at the public facility (JRRH), most patients (97%) at the private facility (NTC) reported a monthly expenditure of Ushs 5000 (US$ 3.00) in the form of user fees. Overall, 82% (58) of the patients at the two facilities incurred additional costs associated with obtaining or taking ARVs. Only 18 % (13) did not incur such additional costs (Table 4). There were no significant differences in the additional costs between the two facilities.

Table 4: Costs incurred by ARV users per month

ARV costs in Uganda shillings*	JRRH N=35	NTC N=36	Total N=71
	Percent	Percent	Percent
<5000	97	0	48
>5000 <10000	3	97	51
10000+	0	3	1
Total	**100**	**100**	**100**
Other Costs			
No	17	19	18
yes	83	81	82
Total	**100**	**100**	**100**

* US$ 1.00 = approx. 1700 Uganda shillings (Ushs)

The average distance travelled to the health facility was 20 km, with the minimum distance being 1 km and the maximum distance travelled 184 km. Distances were considered because they had implications for costs, which in the long run may affect adherence (Table 5).

Table 5: Distance travelled to the health facility by ARV users on each visit

Distance (km)	JRRH		NTC		Total	
	Number	Percent	Number	Percent	Number	Percent
1 - 10	24	69	18	50	42	59
11 - 20	3	9	3	8	6	8
21 - 30	2	6	4	11	6	8
31 - 40	4	11	2	6	6	8
41 - 50	1	3	3	8	4	6
51+	1	3	6	17	7	10
Total	**35**	**100**	**36**	**100**	**71**	**100**

A considerable number of patients on treatment had to travel at least 10 km to the clinic which may also be a significant factor in relation to adherence. This implies that some of them had to travel by taxi or hire a bicycle, entailing extra cost for the client, while those who came from far away had no alternative but to shoulder the additional transport costs.

6.2   Factors influencing adherence to ART

6.2.1 Costs

Although all the respondents were receiving medicines free of charge, additional costs incurred through travel to the facilities and user charges at the private facility have implications for adherence, as indicated in the following quotes:

> *"Sir, I came from very far. Over fifty kilometres from here. Before I come to the hospital I have to plan the money for journey fare to the clinic. In fact my extra drugs got finished yesterday."* (Male ARV user, JRRH)

"I have many people in the village. They are dying because they don't have money to transport themselves to the hospital. You need to have this money monthly. Like me, from the village where I come from, getting up to this place costs Ushs 15 000 (US$8.50). To and fro is Ushs 30 000 (US$17), which is a lot of money…Right now only Lira Referral Hospital gives ARVs, and that is 130 km from our place (Kyoga). Very far!" (ART user)

"Some people have failed to report to the clinic on time because they failed to get transport to reach the clinic. Some people come from the islands, and they will tell you that they did not get money to cross the waters and they will tell you that is why they did not come on time. And when you are told that, you cannot do much but to hope that when the next visit comes, he can afford to come on time." (Health worker)

The issue of cost was even worse at the private facility, where there is a user fee of Ushs 5000 (US$ 3.00) payable at each monthly visit in addition to transport costs. It is possible that these costs could contribute to sub-optimal adherence in the near future.

Another respondent receiving treatment at NTC complained about the user fee charged at the private facility, explaining how it had affected his budget. When asked whether he and his family had to give up anything to be able to pay for ART, he said:

"Yes it is a sacrifice. I am considering going to a government hospital which is completely free." (Male, semi-structured interview, NTC)

Group discussions with men on ART also highlighted some cost-related factors that have made taking ARVs difficult and may in the long run affect adherence.

"I can no longer pay school fees for my children because I am burdened by extra costs of maintaining my health." (Male ARV user, FGD)

Another man said:

"The compromising nature of the treatment is very difficult to adhere to. You have to sacrifice others for the sake of yourself." (Male ARV user, FGD)

Travel costs were also identified by health workers as one reason why they could not follow up on some of their patients who failed to turn up to refill their drugs on time. The health workers were worried that travel costs for patients would affect adherence in the near future. One said:

"People coming from very far will always have an extra cost especially where barriers are included. For instance, some patients have to cross waters to come to the centre. You cannot keep blaming them for defaulting. It is really hard." (Doctor, NTC)

Lack of money for travel seemed even worse for patients at the public facility which provides services for ARV users who are very poor. Some of the patients had already

started missing follow-up, mainly due to lack of transport to come to the centre. One health worker stated:

> *"It is really good the Government brought this medicine but many people who attend this clinic are poor. Sometimes they fail to come back to refill the drugs because they failed to raise just 1000 shillings* (about 60 US cents) *so they lose follow-up like that and eventually die."* (Nurse, JRRH)

6.2.2 Hunger

ARV medicines tend to increase the user's appetite. Patients who were interviewed at both facilities reported having an insufficient supply of food to match their rising appetite as they began to feel better. Lack of food was seen to frustrate patients' determination to take and adhere to ART since they had nothing to eat as their appetite improved. A doctor at the private facility told a story of one patient who declined ARVs, saying:

> *"Some patients have expressed lack of food as a reason for not wanting to swallow the life-saving drugs. In fact we have one woman who has declined her life-saving drugs because she does not have enough food to feed herself."* (Doctor, NTC)

Another said:

> *"I missed on Sunday because I could not find what to eat and yet I had to eat first before taking the tablets."* (Female ARV user, SSI)

This finding is echoed by a report in Uganda's Daily Monitor newspaper (see below) about patients on ART at another organization, Uganda Cares, who were threatening to stop ART because they lacked food.

Daily Monitor

October 19, 2005

100 hungry people stop ARV Treatment

This drug enhances one's appetite and many AIDS patients on ARVs don't have the capacity to get enough food to match their appetite. They have therefore decided to do away with the drugs. Unless the Government and the World Food Programme come in and help, a number of patients on ARV treatment in the district will soon die. (LC5 Chairman Rakai District, Mr Vincent Semakula)

Another ARV user said:

> *"I want to eat all the time and fear the hunger will eat into my stomach since I have ulcers already. Sometimes I have to wake up in the night to eat food. This is a difficult situation for me."* (Male ARV user, JRRH)

These findings apply to a majority of the clients in the study facilities, most of whom either do not have a regular income or whose income is low. This is one of the key factors that should be taken into account when designing future interventions.

Some patients at the public health facility are currently getting food support (soya flour, cooking oil, rice, sugar, maize flour) as a food basket provided by TASO-Jinja for registered members. This has acted as a motivator for those reluctant to join.

> *"When people hear our testimony and they see the way we look like they may get encouraged to join. They even start asking about how you improved."* (Male, community FGD)

6.2.3 Stigma and disclosure

In Uganda, HIV-related stigma and discrimination have been reduced through the Government's committed efforts to demystify HIV and AIDS and through strong political support from the President. While this approach has been successful in reducing the level of stigma and discrimination at the national level, these problems persist at the local level (i.e. between individuals, in families and in communities). PLWHIV said that while it is not easy to disclose their status to community members they do not know well, it is very easy to do so among other PLWHIV. Focus group discussions with PLWHIV generated many comments about stigma, discrimination and disclosure:

> *"Disclosing status is not easy, especially to those who don't know you. They talk about you in small groups and when you join them they pretend they don't mind. Yet they have been discussing you. We are OK disclosing to fellow PLWHIV, who understand our problem."* (PLWHIV, female FGD)

People with AIDS may receive negative reactions from their community once they are known as ARV users. They feel they are being looked upon as useless. Though this definitely hurts them, it does not always affect their behaviour, as is clearly expressed by a female ARV user:

> *"It is my husband who died first. So, I also thought I was next. But when I started ARVs I got better and better. But some time in between I lost two of my relatives. When I lost my two brothers in between, what, however, weakened me was that when people heard the bad news they came out thinking it was me. Actually, on the day of the burial of my relatives, people kept pointing fingers at me wishing that I should have died instead of my relatives. People were saying I was of no use any more, while people who were of use are being buried. I felt so bad. I could not sleep that night but I could not stop taking my drugs. These did not or do not affect me to tell them the truth about my status and ART."* (Female, FGD)

Another ARV user reported having received similar negative comments from community members. Sometimes community members do not seem to understand why AIDS patients need to be treated instead of letting them die:

"People wonder why they bring me drugs instead of leaving me to die. So, as a result, people in my village look at me as nothing and I also do not value them." (Female, ARV user)

As people with AIDS do not feel accepted and understood by community members, this may lead to them taking their ARVs secretly:

"I cannot take my drugs when people are seeing. I always go and hide and take them. Otherwise, people start whispering about you all the time." (ARV user, female FGD)

For other ARV users, negative reactions from community members make them withdraw entirely from any contact with the community, and rely entirely on the support of family members, as one ARV user confided to us:

"At first I got so scared to tell people because of the stigma but ever since I started on ARVs they have began to wonder what has happened. In fact I hear some say why they don't inject her and put her to rest otherwise she is going to finish everybody. Because of these I remained alone. So I remained with only a few of my family members who I cooperate with. The counsellor advised us to tell our family members about it. In fact these helped me so much when I told them I became free about my status and up to now I have a lot of courage and strength with the ARVs." (ARV user, SSI)

While several ARV users complained about being stigmatized by community members, others experienced similar reactions from their own spouses. A number of ARV users reported that they were abandoned by their spouses because of their HIV status:

"My wife abandoned me the moment I disclosed my status to her. She left me with the children. And to make it worse, my own family said I deserved harsh treatment because I infected my wife with the deadly virus." (Male, semi-structured interview)

The above reactions to people with AIDS are both discriminative and stigmatizing, both of which can lead to non-disclosure, and hence to non-adherence.

6.2.4 Social support

Participants in the FGDs stressed the importance of their children in providing treatment support:

"My children after seeing the state I was in and after getting ARVs, I called them and told them about my state. They got encouraged and as a result they buy me passion fruits and sugar because they know the drugs I am taking are so strong. I even wrote my file number in TASO on the wall and told them that just in case I am badly off they can go to TASO and get me help. My children know very well that my drug needs to drink enough and to eat on time. One thing that motivated me to tell them is because I

thought I could be so weak to collect my refill of the drugs (ARVs). They even know the name of my counsellor." (ARV user, mother of five).

ARV users report that their children support them in different ways. As illustrated in the example above, children may help them to have food and meals at regular times. In addition, the children know where to go and whom to contact in case their mother feels too ill to collect her refill herself. Another participant said that he was so pleased he had told his children he is an ARV user, as his children remind him to take his drugs on time.

"I would fall sick so often. So my children kept asking me what I was suffering from. They kept advising me to go and find out and promised me all the help whatever the illness could be. So when I went there I was put on ARVs and told them immediately when I went back home. They have been very supportive in my adherence ever since. Because I told my children that I take the drug on time they endeavour to rush to any one who has a watch or radio and ask the time for me to take my drug. Telling them has helped me so much because of the comfortable relationship that exists between me and my children and neighbours." (ARV user, FGD)

However, not all children are equally supportive, as shown in the following complaint:

"It is only my young children who give help. They cook for me and bring me whatever I send them. But my elder children abandoned me yet I told them about my status." (Female ARV user, SSI)

Children are not the only source of support. ARV users also feel greatly supported by people from the TASO clinic. Meeting other ARV users who are equally or even worse affected than they are encouraged them to start and continue ART.

"One thing that strengthened me was the people I met at the TASO clinic. There were people who were so badly off. So I asked myself: if such people still have the hope of getting better then what about me. I saw those with bad rashes, others almost losing their eyes." (Male, group discussion)

ARV users are very much aware of the important role they can play as role models in encouraging people to open up, disclose their HIV status and seek treatment.

"We - the people living with HIV - we get back and tell them about the medicine. And when people look at some of us and see how we were and how we look now, they get the guts and come to ask us what has helped to make us look better. They pretend to have a patient and ask us to help their patients as well." (Female, FGD)

TASO committees, which visit communities to help sensitize people to the availability of ART, are considered to play a very important role in the education of the public.

"When my husband died, he had not been tested. However, when we shifted to this place most people who saw him knew what the cause was. My neighbours – after the

death of my husband - came out and encouraged and advised me to go and test early. So, when the different [TASO] people came to me, some were HIV-positive themselves, they told me about ART treatment in Jinja. They have continued to support me throughout. These TASO committees who come visiting homes have helped to teach and sensitize people about ART." (Female, semi-structured interview)

Other people learn to overcome stigmatization and are encouraged to start using ARVs through hearing the testimonies of people who are already on ART:

"Drama groups like ours called 'White' helps people to come out from stigma."

and

"(We have) our own networks like the Jinja Net for People Living with AIDS. Whenever we gather people are forced to ask why (we attend) the meeting and as a result we tell them about the medicine." (Female ARV user)

Some clients also acknowledged support from relatives and friends, while emphasizing that most of the support would normally come from the immediate family.

"Yes, friends and extended family members may help but you are better off when your immediate family gets involved in your sickness. For me my brother brought me here and he has supported me throughout." (Male ARV user)

6.2.5 Drug regimen

ARV users take at least a three-drug combination and they have to take these ARVs at different times, sometimes alongside other medicines for the treatment of opportunistic infections. Some participants complained about the demanding drug regimens and about the size of the individual pills they had to take (especially those on efavirenz). This often becomes a problem over time, especially when too many different medicines have to be taken at once. A 50-year-old male graduate underlined how the size and number of medicines can frustrate adherence even when people know that the treatment is essential to save their life:

"Strocrin (efavirenz) tablets are strenuous when you take them. It is as if they have stuck to the throat; they are big and sometimes this causes people to postpone or dodge taking it intentionally." (Male ARV user)

Because health workers are aware of the potential side-effects of ARVs and understand that adherence is not always easy, they persist in emphasizing the importance of adherence:

"Sincerely, adherence is not a joke. Sometimes when people fail we feel it. But you have to keep pumping them about the importance of adherence. It can be worse when you have to combine ART with treatment for opportunistic infections." (Doctor, NTC)

The number of medicines to be taken was felt to be even more problematic when these had to be combined with prophylaxis for opportunistic infections, such as tuberculosis, cryptococcal meningitis or malaria.

6.2.6 Side-effects

Some respondents experienced adverse effects that discouraged them from taking the medicines. In particular, people complained about nausea, skin rash and dizziness. Participants also reported having "weird" dreams that made them frightened to take the medicines.

> *"You fear to take the drug because of the weird dreams. You can see dead bodies and you are walking with them. You are in races struggling and many other struggles. It frustrates and soon you get fed up."* (ARV user, female FGD)

The physical and social impact of side-effects is also a concern for ARV users and can have an adverse effect on adherence. As one man said:

> *"Feeling a lot of heat in the body, especially after taking the drug, and excess sweating makes one embarrassed in public. So, you feel like postponing the drug to a later time when you are not relating with people."* (Male ARV user, JRRH)

Side-effects often appear with the initiation of ART but disappear over time. Those who were being treated at the private facility were better informed about side-effects as a result of ongoing adherence counselling. When asked whether they inform their clients about side-effects one health worker said:

> *"We tell them about the side-effects so that they know what is bound to happen but it so happens that women get more worried when you tell them about side-effects especially rash. The men don't express fear but I think they also worry."* (Adherence counsellor, NTC)

ARV users expressed mixed feelings about the drugs: while people appreciated the fact that the medicines are effective, at the same time they feared the medicines. When asked whether they were happy about ART, one participant said:

> *"I only fear the side-effects of the life-saving drug. I fear it will kill us instead of the HIV."* (Female ARV user, FGD)

During FGDs some women expressed similar beliefs about ARVs. It was assumed that ART was designed to kill people, because most of people who had taken them had died, as shown by the quotes below:

> *"By the time I began the drug I heard of it killing people. So, when I began I knew I was taking this drug and it was going to kill me. And sincerely the time I began I collapsed three times. I could take the drug but without faith. I knew I was taking this drug and it was going to kill me so it was after some time that I got used. The third time I really*

died because I collapsed at 1600 hours and came back on earth at 0100 hours. It took me
time to believe that the drug could heal." (Female, FGD)

As a result of these fears, some people reported delaying taking their medications, even when they had the opportunity to do so:

"I also want to add that I only just joined TASO this year [2005] because I was always
hearing that their main objective was, to finish these people [PLWHIV] off because they
are getting sick and they are not getting better. So I never wanted to go to TASO. At
first they were saying, why don't you go to TASO? I said no way. I had that belief
until 2005 and yet I had heard something about ARVs in 1994."(Female, FGD)

6.2.7 Dependency and treatment fatigue

Participants knew that they would have to remain on ARVs for life. Some feared that the time would come when they would get tired of taking the medicines and would fail to achieve optimal adherence:

"I don't think it is realistic to take drugs or treat a disease until you die. Treatment
should be for a limited time and the disease is treated and you don't have it any more.
So, now we have nothing to do. It is like a failure." (ARV user, female FGD)

Although most of the respondents had been on ARVs for less than two years, they had already started to complain about treatment fatigue. A female ARV user, a graduate in her late thirties, felt it was not worth living with AIDS when the medicine to cure her illness has still not been found. She felt it was a failure and useless to take the ARVs unless they could cure her. Therefore, on several occasions she decided to take a "drug holiday", without consulting her doctor. This kind of personal decision without a physician's expert advice has serious implications for adherence, and should be addressed when designing interventions or providing adherence counselling.

ARV users also questioned whether they were actually receiving the best treatment currently available:

"We hear rumours that there are some drugs which came out and cure. But they are
still in America. So I just request the Government if it can at least bring those drugs so
that we are helped and get cured." (ARV user, female FGD)

6.2.8 Patients' information sources and communication channels

TASO was the first AIDS support organization to be established in Uganda and it is not surprising to hear participants say that TASO was the first to offer ART. In fact, TASO initially provided support for PLWHIV through offering VCT and providing a fortnightly food basket to boost their nutritional needs. TASO was also the major source of information on HIV and AIDS in Uganda.

> *"The food support we get from TASO motivates people to ask how we come to get it and as a result we tell them about the medicine. We get soya, cooking oil, etc."* (Female ARV user, FGD)

In collaboration with JRRH, TASO set up a research programme on HIV and AIDS. Subsequently, information was decentralized to TASO centres throughout the country and the emphasis was placed on VCT, and on the prevention and treatment of opportunistic infections. Community seminars were held to inform people that ART was available and was going to be provided free of charge in Uganda.

As discussed in 6.2.4 above, people also learn about ART through testimony from people who are already on ART:

> *"We the people living with AIDS, we get back and tell them about the medicine."* (Male ARV user, FGD)

In Uganda the main source of information for the general public is the radio. Radio stations, especially local FM stations, broadcast programmes about HIV and AIDS.

6.2.9 Sustainability

In view of the fact that medicines have to be taken for life, participants were anxious to know what would happen if the free medicines were phased out. They wondered whether the Government would take on the responsibility for providing the drugs. This anxiety about the continuing availability of medicines could have an adverse affect on their future adherence.

> *"We are grateful to the Government for bringing medicine to the people, but we hear it is only for five years. Whenever I take these drugs, I am wondering whether in the next five years I will still have them free. Actually, I get disturbed by that."* (ARV user, male FGD)

6.2.10 Structural/health facility issues

Throughout the study, structural issues relating to access and service provision were observed. Both ARV users and health workers commented on the level of infrastructure established for service provision, especially at the public facility. The public facility was facing difficulties in that the scaling up of ART had occurred without any increase in personnel to cater for the increasing number of patients. For example, while the doctor-patient ratio was 1:15 a day at the private facility it was only 1:25 a day at the public facility. Health workers were visibly overworked and they struggled to attend to the large number of patients on a clinic day. As one health worker explained:

> *"You overwork like this without even a break because there are too many people all coming one day and yet you are very few."* (Health worker FGD, JRRH)

The public facility had no adherence counsellors and did not have adequate designated rooms/offices for counselling or for patients to discuss personal issues with the health workers. At times, the health workers have to try and locate a suitable room before they can start a counselling session or private discussion with a patient. In contrast, the private facility was very well organized, with comfortable seating, shorter waiting times than at the public facility, and everybody was attended to. There were two adherence counsellors, all patients were required to have adherence counselling, and spot checks on adherence were also carried out at various sections of the facility.

At the private facility, all recommended tests for AIDS management were done within the centre. In contrast, the public facility had to send out some of their samples for CD4 and viral load testing. This implied that people who were very sick had to wait at least two weeks before they could be put on therapy. This lack of up-to-date equipment was another limiting factor at the public facility.

6.2.11 Quality of care issues

Forty-eight ARV users seen during exit and semi-structured interviews were asked to comment on the quality of the services provided in the clinic in terms of: trusting the health workers; privacy during counselling; respect from the health workers; whether the health workers listened to the ARV users; and the general environment.

Out of 26 users in the public facility, 16 said the services offered were "good", eight rated them as "fair", and two felt they were "poor". In contrast, all 20 participants interviewed at the private facility said the services provided were "very good". With the exception of two users at the public facility, patients at both facilities felt the service providers listened to them. They said they trusted the health workers, and that they were allowed privacy in both facilities.

On the issue of waiting times, patients at the public facility waited five hours on average compared to only one hour at the private facility. Long waiting periods were acknowledged to be a demotivating factor for already sick patients, some of them very weak.

It was also observed that services at the private facility were quite fast and each patient had adequate time to discuss issues with the health care providers. However, patients at the public facility had to queue for a long time at the once-weekly HIV clinic and the time spent with the health worker was very limited. This may be the reason why some of the study participants reported inadequate counselling at the public facility. There were no long waits at the private facility, which had a very welcoming atmosphere and was open six days a week.

Chapter 7: Discussion, conclusions and recommendations

7.1   Discussion

Two hundred participants including key informants (such as religious leaders and traditional herbalists), health workers and ARV users were enrolled in this study and interviewed using one of the instruments designed to collect data. This research lays the groundwork for future quantitative studies as well as informing future interventions aimed at improving adherence.

This study was largely qualitative rather than quantitative. By directly quoting statements from the study participants, we present qualitative information that would otherwise be missed by the quantitative data. The qualitative data provide in-depth insight into people's experiences with ARVs.

It is important to note that 56% of the ARV users who took part in the study had only been on ART for a year or less (Table 2). As a result, the issues which patients currently face in these settings may not be the same as those faced by people who have been on therapy for a longer time. It is likely that the results of follow-up studies would deviate from the current findings as people face treatment fatigue.

Both facilities involved in the study had first-line ART according to the Uganda national guidelines. Medicines to prevent opportunistic infections were available in the public facility but not at the private facility. The public facility used generic medicines while the private facility used patented medicines.

Scaling up ART in developing countries is not an easy task since there is a lack of uniformity in the way different organizations carry out this function. While many studies have indicated that Uganda's overall achievement in its approach to HIV is a success story which could be emulated, there are many aspects of adherence which need further investigation. Although the Uganda National Treatment Guidelines (November 2003) are comprehensive, the issue of adherence is addressed on only one page. Uganda has increased access to free ART, especially in the MoH centres. However, some institutions, particularly the private facilities, still charge a user fee, while other larger institutions such as JCRC, which have championed the use of ART in the country, have paying patients as well as patients who are treated free of charge. Both Government and private ART facilities in Uganda lack organized procedures for carrying out pill counts. Meanwhile, many health workers argue that carrying out pill counts is an additional burden on their already heavy workload.

Costs

Costs such as user fees, transport and other overhead costs were reported to be a concern that may influence adherence. ARV clients frequently complained about the cost of transport and other treatment-related costs incurred as a result of being on ARVs. Some patients failed to report on time to get their refills because they were still trying to get together the money needed to pay for transport to the clinic. This is a serious problem that is likely to affect adherence, even for those who try to be adherent. It is also not cost-effective if people fail to achieve optimal adherence and rapidly develop resistance to the first-line drugs.

Hunger

Some nongovernmental organizations such as TASO provide food support (soya flour, cooking oil, rice, sugar, maize flour) to their ARV clients to help them meet the increased demand for food as their body metabolism improves. However, such food support schemes are not available in any of the private health facilities providing ART, and are rarely available at the public sector treatment centres. As a result, many ARV clients in need of food support are not receiving it. This threatens the future success of ART in Uganda. Hungry people are inclined to stop taking ARVs because they cannot afford to feed themselves as their body metabolism improves and the demand for food increases. ART programmes will continue to face serious challenges unless the Government addresses the problem of low-income subsistence farmers who do not have a reliable and regular supply of food. Food supplementation for low-income patients, as occurs in Botswana, should be considered in Uganda.

Stigma and discrimination

Patients who are stigmatized may avoid taking their medicines in the presence of other people. If this situation continues (for example, when patients have to attend large traditional funerals which usually last for several days), it is likely to have an impact on adherence. Although HIV-related discrimination and stigma have been (and are still) vigorously addressed in Uganda, many of the ARV clients interviewed at both facilities said stigma and discrimination were still a problem, especially at the micro-level. Some had experienced stigma even within their immediate families. At least two clients (a man and a woman) described being abandoned or divorced by their spouse because of their HIV status. In their accounts of receiving negative criticism and discrimination within their own communities, some patients reported taking their doses in private for fear that they would be discriminated against. However, ARV users felt they were free to disclose their status to fellow ARV users without any fear.

Social support and children

While social support was seen as motivating adherence, lack of such support can have a negative impact. Some ARV users acknowledged the support they received from their immediate families. In particular, some stressed the importance of support from their children to ensure they took their medicines at the right time. However, not all children are equally supportive. Some were reported to have abandoned their parents without any support. Many ARV users felt extremely well supported by TASO and

suggested that people who were afraid to take ARVs should be encouraged by hearing testimonies from other people who were on treatment.

Drug regimen and side-effects

For ART to achieve viral suppression, combined treatment with at least three ARVs is needed. Some patients experienced side-effects; others none at all. For those experiencing side-effects, the impact seemed so pronounced that they said it might affect their ability to adhere to the medicines, which have to be taken for life. Some participants said that the side-effects (e.g. dizziness or scratching due to a rash) were sometimes a nuisance when they were in public, especially when in an office. The study also revealed that some side-effects were feared due to the belief that ART was designed to kill people. As a result, some people were afraid to take the ARVs in case they died and others delayed starting ART even when they had the opportunity.

Dependency and treatment fatigue

From the literature it is clear that sub-optimal adherence is a widespread problem. Internationally, estimated rates of sub-optimal adherence to ART range from 10%-92% with an average of 50%, while reports of optimal adherence (usually defined as taking 80% or more of the prescribed regimen) range from 25%-85% (Bachiller, Arrando, Liceago, Iribarren and Olloquiegui, 1998). However, in patients on ART, 80%-90% adherence has been associated with failure to achieve complete viral suppression in 50% of patients (Paterson et al., 1999).

It was therefore not surprising to find participants who were worried about the long-term consequences of depending on medicines for the rest of their lives (treatment fatigue), and some who were found to be giving themselves a "drug holiday". However, it will be impossible to scale up access to ART in Uganda if many patients become resistant to first-line ARVs and more expensive second-line medicines are needed instead. Another finding was that ARV users often doubted both whether they were receiving the best treatment currently available and whether the free treatment would remain available over time.

Quality of care

Despite the fact that this study was carried out at two facilities in the same region, there were remarkable differences between the two facilities in terms of organization, doctor-patient ratios, length of waiting times, and the kind of services that were available. The private facility was well organized and had strict treatment protocols. For instance, patients were given spot checks on adherence when they returned for follow-up. Patients were asked to say something they remembered about adherence issues and if a patient declined to participate the medicines would be withheld. The doctor-patient ratio of 1:15 a day at the private facility was much better than at the public facility, where it was 1:25 a day.

The public facility was usually crowded and slow in its procedures. Large numbers of people had to be attended to within the space of a few hours in the morning because the clinic closed at 1300 hours. The limited opening hours were a problem since many people travelled long distances to the clinic but might end up missing their

appointment, either because they arrived late after the clinic had closed or because not all the patients could be seen on one day. In the group discussions, some patients said they thought that the quality of counselling at the public facility was not as good as that provided by TASO. This is an important observation since counselling is an integral part of AIDS management. The nurses at the public facility had a dual role as counsellors and nurses. This double burden on the nurses, who are usually overworked and so cannot give quality counselling to their patients, could be the reason why some of the patients reported them as being rude.

The once-weekly clinic day is a limiting factor in offering quality care to ARV users. It is also possible that some people had to spend the night in nearby towns in order to arrive at the clinic early, thereby incurring additional costs.

7.2   Conclusions

The strength of this study lies in the qualitative data, in which we present views about adherence by reporting statements from the study participants themselves. This qualitative data supports the quantitative findings reported in other studies, such as the Tanzania and Botswana studies.

We anticipate that as ART is rolled out in Uganda, optimal adherence will be difficult to achieve. The costs involved in terms of transport, waiting times and other overhead costs are already impeding adherence and some patients are dropping out of treatment as a result.

Hunger is usually a major concern among those who have just started therapy. One organization reported that 100 patients were threatening to stop taking their ARVs because of increased food needs which they could not meet. This is a serious threat to adherence. Unless programmes are designed to provide food assistance in the first months of ART, optimal adherence is going to be difficult to achieve.

In this study, it was reported that the level of infrastructure for service provision and the quality of care provided were better at the private ART-providing facility than at the public facility. Structural problems at the public facility included overcrowding at the ART clinic, lack of training for health workers and the inability of the few that are trained to cope with the growing number of people on ART. Unless these kind of structural issues are addressed by the Government as ART is rolled out in Uganda, it will be difficult to ensure adherence. Other challenges that will also have to be addressed include the lack of social support, stigma and discrimination, and treatment fatigue.

Uganda has made a good start in scaling up ART and this is widely appreciated. However, Uganda appears to be moving very quickly to scale up access to ARVs without addressing critical issues such as the problem of additional costs, hunger and excessive time spent at the facilities, as well as the need for pill counting, training of adherence counsellors, community sensitization and home-based care services.

Efforts to minimize constraints and improve adherence levels will require the efforts of the community, health workers and patients as well as Government commitment to resolve key structural problems.

7.3   Recommendations

The following recommendations are made on the basis of the pre-intervention study. However, we recognize that these have not been subject to intervention testing or evaluation. We therefore propose that such studies should be undertaken as a matter of urgency.

♦ **Institute pill counting across the country:** Only a very small number of ART facilities in Uganda have adopted the use of pill counting, which is a major shortcoming. Pill counting will help track the use of ARVs as well as help in calculating adherence rates throughout the country. However, this will require an increase in financial and human resources for both Government and private facilities providing ARVs, in order to institute and operate a pill counting system.

♦ **Train more adherence counsellors:** In order to support ARV users, more staff should be trained specifically in counselling. This would help ensure that nurses do not have to double up as counsellors and enable adherence counselling to be scaled up countrywide. This would help in delivering quality adherence counselling and may also contribute to efforts to reduce the long waiting times.

♦ **Sensitize the community** on the availability of treatment and the importance of adherence. This would help to educate and inform caregivers who work as treatment buddies. Community sensitization could also help in reducing discrimination, thereby encouraging more people to disclose their HIV status as stigma is reduced.

♦ **Increase provision of home-based care:** As the disease progresses, some people may not be able to go to the clinic to get a medicines refill. Such people should be attended to in the home for both refills and counselling services, which the entire family can benefit from. Therefore, facilities providing ART should initiate or scale up (as appropriate)   home-based care programmes.

♦ **Provide food baskets:** Food baskets should be provided at the start of ART to counter the excessive hunger experienced by ARV users.

While we have not yet developed intervention studies to evaluate these recommendations, we would welcome the opportunity to do so. We set out below some thoughts on possible intervention and evaluation studies.

The implementation of these recommendations would mainly focus on instituting pill counting through training health workers and ARV users about the importance of pill counting in relation to adherence. This would be done by counting the number of dosage units that the patient has not taken by the scheduled appointment or clinic visit.

The impact of this intervention would be evaluated on the basis of how accurately pill counts are undertaken, the use of pill count data to guide adherence counselling and the keenness of health workers to use the method.

Health workers in all facilities that provide ART would be trained in adherence counselling through formal training seminars. In addition to evaluating changes in the level of knowledge of health workers, adherence measurements through pill counts would be used to assess the impact of this training.

Meanwhile, ARV users and other community members would be sensitized about the availability of ARVs and the importance of adherence. The methods involved would include the use of participatory training in communities through outreach programmes and local FM radio programmes using mainly local languages, posters and leaflets tailored to the educational levels of the communities involved. Accessibility to the local media is easy and could achieve communication objectives in both the short and long term. The impact of these approaches would be evaluated on the basis of how many people are reached, and if there is an impact on the level of their knowledge. It would also be evaluated in the long term on the basis of whether the knowledge gained was sustainable and led to increased levels of adherence.

References

1. Arnsten JH et al. (2001). Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: comparison of self-report and electronic monitoring. Clinical Infectious Diseases, Oct 15;33(8):1417-23.

2. Bachiller P et al. (1998**).** Drug compliance in patients starting saquinavir. 12th World AIDS Conference, Geneva, Switzerland. Abstract no. 32392.

3. Buhrich N, Judd FK. HIV and psychiatric disorders. In: G. Stewart ed. *Managing HIV*. Sydney: Australasian Medical Publishing Company, 1997.

4. Burgos M et al. (1998). Obstacles in treatment adherence: patient reasons. 12th World AIDS Conference, Geneva, Switzerland. Abstract no. 32400.

5. Byakika-Tusiime J et al. (2003). Ability to purchase and secure stable therapy are significant predictors of non-adherence to antiretroviral therapy in Kampala Uganda [abstract]. Tenth Conference on Retroviruses and Opportunistic Infections, Boston, USA, February 2003.

6. Carter M (2005). Adherence. Information series for HIV-positive people. NAM. Available at: http://www.aidmap.com

7. Catz S, Heckman T, Kochman A (1999). Adherence to HAART therapy among older adults living with HIV disease. Fourth International Conference on the Biophysical Aspects of HIV Infection, Ottowa, Canada.Poster 18.

8. Dansburg D et al. (2003). Pill burden predicts adherence, regimen discontinuation or switch, viral load and CD4 cell response in nationwide US sample of HIV+ ARV naïve people on PI therapy. *Antiviral Therapy* 8:395.

9. Erlon JA, Mellors P (1999). Adherence to combination therapy in persons living with HIV: balancing the hardships and the blessings. *Journal of the Association of Nurses in AIDS Care*, 10(4):75–84.

10. Farmer KC (1999). Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clinical Therapeutics,* 21(6):1999.

11. Furtado MR et al. (1999). Persistence of HIV-1 transcription in peripheral blood mononuclear cells in patients receiving potent HAART therapy. *New England Journal of Medicine*, 340(21): 1614–1622.

12. Gill CJ et al. (2005). No room for complacency about adherence to antiretroviral therapy in sub-Saharan Africa. *AIDS*, 19(12):1243-1249.

13. Green EC. *Rethinking AIDS prevention. Learning from success in developing countries.* Westport, USA, Praeger, 2003.

14. Grierson J et al. *HIV futures II: the health and well being of people with HIV/AIDS in Australia.* Monograph Series No. 17, Melbourne, La Trobe University, 2000.

15. Hirschhorn L et al. (1998). Highly active HAART therapy in the "real world": experiences in an inner-city community health center. 12th World AIDS Conference, Geneva, Switzerland. Abstract 32334.

16. Jones JL, Nakashima AK, Kaplan JE (1999). Adherence to primary prophylaxis for pneumocystis carinii pneumonia: results from a multi-state interview project. 39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, USA. Abstract no. 586.

17. Kaplin A et al. (1999). Adherence to protease inhibitor therapy and viral load. *6*th Conference on Retroviruses and Opportunistic Infections, Chicago, USA. Abstract no. 96.

18. Katabira ET (2002). The promise and challenges of antiretroviral therapy in developing countries. Paper presented at the 9th Conference on Retroviruses and Opportunistic Infection. Symposium session 30.

19. Kirkland LR et al. (2002). Response to lamivudine-zidovudine plus abacavir twice daily in antiretroviral-naïve, incarcerated patients with HIV infection taking directly observed treatment. *Clinical Infectious Diseases*, 34: 511-8.

20. Kityo et al. (2002). A trial of regimens to suppress HIV/AIDS in Ugandan adults. Paper presented at the 13th International Conference on HIV/AIDS, Barcelona, Spain, July 2002.

21. Meisler A et al. (1993). Adherence to clinical trials among women, minorities and injecting drug users. Paper presented at the 9th International Conference on AIDS, Berlin, Germany.

22. Ministry of Health. National strategic framework for expansion of HIV/AIDS care and support 2001/2-2006/7. Kampala, Ministry of Health of Uganda, 2001.

23. Ministry of Health. *National HIV/AIDS Sero-Survey 2005*. Kampala, Ministry of Health of Uganda, 2005.

24. Motashari F et al. (1998). Acceptance and adherence with HAART therapy among HIV-infected women in a correctional facility. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, 18:341-348.

25. Mugyenyi P. No second best in AIDS care. In: A*merican Foundation for AIDS Research HIV/AIDS treatment directory.* American Foundation for AIDS Research, New Yor*k*, 2001.

26. Mugyenyi P (2002). HIV/AIDS situation in Africa. Statement by P. Mugyenyi, Director, Joint Clinical Research Centre, Kampala, Uganda.

27. Nemecheck P, Tritle D (1998). A survey evaluating pharmacy-related resources and their relation to drug adherence. 12th World AIDS Conference, Geneva, Switzerland. Abstract no. 98.

28. Pallela FJ et al. (1998). Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *New England Journal of Medicine*, 338 (13):853-860.

29. Paterson DL, Swindells S, Mohr J (1999). How much adherence is enough? A prospective study of adherence to protease inhibitor therapy using MEMSCaps. 6th Conference on Retroviruses and Opportunistic Infections, Chicago, USA. Abstract no. 92.

30. Paterson DL et al. (2000). Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine*,133(1):21-30.

31. Uganda AIDS Commission. Twenty years of HIV/AIDS in the world: evolution of the epidemic and response in Uganda. Kampala, Uganda AIDS Commission, 2001. Available at: http://www.aidsuganda.org/pdf/20_yrs_of_hiv.pdf

32. UN Integrated Regional Information Networks. Uganda: AIDS treatment capacity overwhelmed, says NGO Official. October 17, 2005.

33. UNAIDS/WHO. *AIDS epidemic update*: Geneva, Joint United Nations Programme on AIDS and World Health Organization, 2005.

34. UNAIDS (2005). *Progress made in the implementation of the Declaration of Commitment on HIV/AIDS*. Report of the Secretary-General. New York, United Nations, 2 June 2005.

35. Vitolins MZ et al. (2000). Measuring adherence to behavioral and medical interventions. *Controlled Clinical Trials* 21:188S-194S.

36. Weiser S et al. (2003). Barriers to antiretroviral adherence for patients living with HIV infection and AIDS in Botswana. *Journal of Acquired Immune Deficiency Syndromes*, 34(1): 281–288.

37. Wenger N et al. (1999). Patient characteristics and attitudes associated with HAART adherence. 6th Conference on Retroviruses and Opportunistic Infections, Chicago, USA. Abstract no. 981.

38. Williams A, Friedland G (1997). Adherence, compliance, and HAART. *AIDS Clinical Care*, 9(7):51-53.

"A timely, evidence-based, first-hand, real-time, untold story of ART beyond access and the numbers. The lessons as told by the people inside the unfolding, complex ART world. An excellent and invaluable handbook on ARV adherence for ART policy-makers, programme managers, funding organizations, treatment and care providers, and patients on ART." *Kizito Lubano (Technical Adviser, PMTCT Section, Global AIDS Programme, CDC, Kenya)*

"Essential reading for those interested in understanding why patients in Africa do - or do not - take their antiretroviral medications. Of particular value is the authors' decision to rely heavily on qualitative methods to probe into the pressing question of adherence." *Christopher J. Gill (Assistant Professor, Center for International Health, Boston University School of Public Health, USA)*

"This book is a poignant and persuasive witness of a new ART era. It documents the second great challenge after scaling up ART: how to promote adherence to life-long treatment in resource-poor settings. By innovatively merging quantitative and qualitative research, it gives us new insights into the additional barriers to adherence that patients, providers and carers have to face in developing countries, and also suggests the possible solutions." *Patrizia Carrieri (Epidemiologist, INSERM, France)*

"Does successful roll-out of ARVs mean that we are winning the battle against AIDS? This book will make you realize that we are only beginning to confront the crisis. It challenges everyone to consider the many barriers to optimal patient use of ARVs." *Michael Montagne (Professor of Social Pharmacy, Associate Dean of Graduate Studies, Massachusetts College of Pharmacy, Adjunct Professor of International Health, Boston University School of Public Health, USA)*

"Patients with AIDS need to take almost all their antiretroviral medicine to avoid treatment failure and the development of drug resistance. Yet, with the international focus on access to medicine, there has been no standardization in measuring either patient or facility adherence levels, and very little understanding of what interventions in what facilities may be effective in improving them.

The authors and investigators of this fascinating volume are to be praised for highlighting such a vital area of work by reporting initial studies in Botswana, Tanzania and Uganda showing the difficulties individual patients face taking all of their medicine. It is no surprise that simply forgetting may be the commonest reason, but the cost of time and transport to get to the clinic, the need for food with medicine, and the fear of the stigma still attached to sufferers of the disease are among the many important factors involved. To find out which affordable interventions will have maximal effect, and where they should be targeted are the next pressing challenges." *John Chalker (Management Sciences for Health; Coordinator of the International Network for the Rational Use of Drugs Initiative on Adherence Measurement)*