UNDERSTANDING PATIENTS' ADHERENCE TO ANTIRETROVIRAL THERAPY:

A MIXED-METHODS STUDY IN ARUSHA, TANZANIA

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ABSTRACT

Melissa H. Watt: Understanding Patients' Adherence to Antiretroviral Therapy:
A Mixed-Methods Study in Arusha, Tanzania

(Under the direction of Suzanne Maman, PhD)

Background: Over one million HIV-positive people in Africa are taking antiretroviral therapy (ART), and this number is increasing. Essential to the expansion of ART is ensuring patients' optimal adherence to therapy. This study combined qualitative and quantitative methods to understand ART adherence at one site in Tanzania where patients received free medication. The study measured ART adherence, identified factors associated with poor adherence, and explored how the social environment of patients' lives supported adherence. A theoretical framework using the Social Cognitive Theory (SCT) and social support guided the study.

Methods: Semi-structured interviews were conducted in Kiswahili with 36 adult ART patients and 6 health care providers. Patients described their experiences taking ART and managing adherence and providers described their experiences caring for patients. A structured survey was conducted with 340 patients. Adherence was measured by self report, and patients were identified as having poor adherence if they took less than 95% of their pills during either the previous four days or one month. The survey measured correlates of adherence informed by the SCT, along with demographic and treatment variables. Factors associated with adherence were considered in a logistic regression model.

Results: Only 5.9% (20/340) of patients reported poor adherence. Poor adherence was associated with: being young (19-30 years, vs. 31-40 years; OR=4.26, 95% CI 1.33-13.60);

being old (over 50 years, vs. 31-40 years; OR=7.59, 95% CI 2.10-27.43); having lower perceived quality of patient-provider interaction (for each one-point decrease, OR=3.18, 95%CI 1.29-7.83); and ever missing a clinic appointment (OR=3.75, 95% CI 1.29-10.89). Semi-structured interviews identified five factors to explain optimal adherence. First, respondents experienced improved health on ART, which motivated adherence. Second, they linked pill-taking with routine activities. Third, they were motivated to stay healthy to meet family responsibilities. Fourth, material and emotional support from others facilitated adherence. Finally, respondents trusted health care providers' instructions to adhere.

Conclusions: Adherence was high in this sample. Interventions to improve and sustain adherence should focus within the clinic to improve interactions between patients and providers and outside the clinic to bolster patients' social support. Different strategies may be necessary according to patients' ages.

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LIST OF ABBREVIATIONS

ART	Antiretroviral therapy
CTC	Care and Treatment Center (ART delivery site in Tanzania)
PEPFAR	United State's President's Emergency Plan for AIDS Relief
SCT	Social Cognitive Theory
STI	Sexually transmitted infection
USAID	United States Agency for International Development
VAC	Voluntary adherence counselor
WHO	World Health Organization

I. INTRODUCTION

Overview

Approximately 33 million people around the world are living with HIV/AIDS, and almost 70% of those infected live in Sub-Saharan Africa, where the epidemic has been driven by heterosexual transmission (UNAIDS, 2007). In 2007 alone, an estimated 1.6 million people died of AIDS-related illnesses in Africa, while a further 1.7 million people became infected with HIV, indicating that the epidemic in the region has not abated (UNAIDS, 2007). The impact of HIV/AIDS in Africa has been tremendous. Across the continent, life expectancy has fallen, in some cases as much as 20 years (World Health Organization, 2007). In addition to the social impact of losing loved ones in the prime of their lives, mortality among the most economically active members of society creates a spiral of poverty and a loss of human resources in sectors such as business, health and education.

Antiretroviral therapy (ART) offers an opportunity to extend the lives of people living with HIV and to rejuvenate societies and economies that have been affected by the epidemic. Funds have been mobilized to provide free ART to people in the most affected countries, most notably through the US President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund for HIV/AIDS, TB and Malaria. The East African country of Tanzania, which has an adult HIV prevalence of 6.5% (UNAIDS et al., 2006), is a priority country for these funding sources and its national government has made a commitment to providing ART across the health care delivery system (Government of Tanzania, 2003). As of December

2006, 54,000 people were receiving ART in Tanzania, out of a total 420,000 in need (UN Office for the Coordination of Humanitarian Affairs, 2007).

While access to ART is vital, it is equally important to ensure that people who are taking the medication achieve optimal adherence. Taking at least 95% of prescribed pills is a primary determinant of successful clinical outcomes for patients on ART (Paterson et al., 2000). Poor adherence can result in viral resistance, progression of disease and death (Bangsberg et al., 2000). Experience with other long-term therapies has provided lessons that adherence is difficult to achieve and is influenced by factors at the individual, inter-personal and institutional levels (World Health Organization, 2003). As ART services are expanded and sustained in Tanzania and throughout Africa, we must build a body of knowledge about patients' experiences adhering to the medication. This information will contribute to developing appropriate interventions and program models that can support adherence and therefore have the desired impact on improving patients' health.

Study aims

This study took place at a faith-based clinic in Arusha, Tanzania, where approximately 700 patients were receiving free ART. Based on a theoretical framework informed by the Social Cognitive Theory and the construct of social support, the study combined qualitative and quantitative methods to collect information about the factors that influenced patients' adherence to ART. The study was undertaken with four aims:

1. To assess the level of adherence in a sample receiving free ART in Tanzania;
2. To identify significant correlates of ART adherence;
3. To explore how the social environment of patients' lives supports ART adherence; and

4. To assess the role of mediating and moderating factors in the relationship between social support and adherence.

II. LITERATURE REVIEW

The Tanzanian context

Tanzania is an East African country about one and a half times the size of Texas and home to 36.3 million people (Figure 2.1). There are roughly 120 ethnic groups in Tanzania, none of which exceeds 10% of the country's total population. The country is united by the national language of Kiswahili, which is taught in schools and spoken by the vast majority of Tanzanians as a first or second language.

The city of Arusha is located in the north of the country and has a population of about 250,000 (2002 census). Situated at a high elevation on the slopes of Mount Meru, the area has a temperate climate that makes it well suited for both subsistence and commercial agriculture, in particular coffee and flowers. Being the gateway for visits to Tanzania's renowned national safari parks and Mount Kilimanjaro, the city is an epicenter of Tanzania's tourism industry. The area is traditionally inhabited by the Waarush, Wameru and Masaai ethnic groups, but the burgeoning economy of Arusha, combined with migration due to pressure on rural land in Northern Tanzania, makes Arusha an ethnic melting pot (Setel, 1999). The majority of Arusha residents are Christians and under a third are Muslims (Tanzanian National Bureau of Statistics et al., 2005).

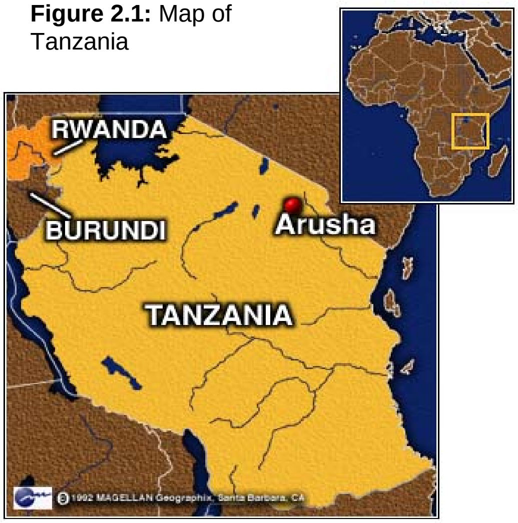


Figure 2.1: Map of Tanzania

Table 2.1: Development indicators for Tanzania, compared with the United States (United Nations Development Program, 2006)

	Tanzania	**US**
GDP per capital income	$674	$39,676
Per capita government expenditure on health	$29	$5,711
Adult literacy rate (% ages ≥ 15)	69.4%	>99%
Life expectancy at birth	45.9	77.5
Total fertility rate	5.0	2.0
Under 5 mortality rate (per 1000)	126	8

The World Health Organization (WHO) classifies Tanzania as a low income country, due to its low gross domestic product (GDP) per capita and poor health indicators (Table 2.1). Development indicators in Tanzania have declined in the last decade. The Human Development Index, which incorporates three dimensions (living a long and healthy life; being educated; and having a decent standard of living) has fallen steadily since 1990 (United Nations Development Program, 2006). The life expectancy of Tanzanians was lower in 2005 than in 1978 (World Health Organization, 2005b), due in part to the impact of HIV/AIDS on the country (Todd et al., 1997).

The history of Tanzania, and therefore the history of its healthcare delivery system, has been greatly impacted by colonialism and global political and economic forces. Prior to the late 19th century, Western medicine was unknown in the area, and people relied upon a diverse set of traditional healers, including both diviners and herbalists (Iliffe, 1998; Mandara, 1991). The colonial era introduced Western medicine to Tanzania and brought the first missionary hospitals, established both to control communicable diseases and to win converts to Christianity (Iliffe, 1998; Mandara, 1991; Nieuwkerk et al., 2001). Although basic social services were expanded during the period of British rule, these services were concentrated in areas where colonial administrators and missionaries were based and benefited relatively few Tanzanians.

When Tanzania gained independence in 1961, President Julius Nyerere vowed to forge a unique path of African socialism, which included nationalization of the country's economic resources and resettlement of people into collective *ujamaa* villages, where communities owned communal land and shared in both the burden and fruits of labor (Nyerere, 1968). It was in the context of this plan that Nyerere aimed to provide comprehensive preventive and curative health care to a largely rural population through village health posts. By 1971, 90% of the country's population was within walking distance of a rural health center (Barry et al., 1986). In the mid-1980s, however, the country's economic policies and the state of the global oil crisis sent Tanzania into a situation of economic disrepair. In 1985, Nyerere resigned and Tanzania's course was set for economic liberalization. Health care expenditure fell; structural adjustment programs imposed by the World Bank introduced user fees that kept health services out of reach of many Tanzanians; and international donors began to fund a significant proportion of the national health care budget (Shiner, 2003). Tanzania's healthcare system is now challenged by poverty, debt, poor water and sanitation systems, inadequate and insufficient financing systems, and lack of both technological and human resources (World Health Organization, 2002b). As an indication of the limited capacity of the health care system, by 2002 there was only one doctor to every 50,000 people in the country (World Health Organization, 2007).

Given the limitations of the government health infrastructure, church-based health facilities play a significant role in the provision of health care services in Tanzania. The

Lutheran church alone is responsible for 20 hospitals and 160 public health clinics, which they estimate to represent about 15% of all health services in the country (Evangelical Lutheran Church of Tanzania, 2007). There is some evidence that church-based health facilities provide better quality services than their government counterparts (Gilson et al., 1995) and that communities have a more favorable impression of church-based facilities (Gilson et al., 1994).

While formal health facilities may be the most recognizable health infrastructure to the outside eye, these facilities co-exist with a set of traditional health-seeking behaviors. Traditional healers (*waganga*) are a part of the healing system across tribal groups, offering treatment for a multitude of health ailments (Kayombo et al., 2007; Rekdal, 1999). People may seek treatment from traditional healers either serially or concurrently with biomedical care in health facilities. In an ethnographic study on the treatment of sexually transmitted infections (STIs) in a rural area of Western Tanzania, researchers found that health-seeking behavior was "pluralistic and opportunistic" (Plummer et al., 2006). People in this area often began treatment for suspected STIs with home remedies before seeking the services of a traditional healer. Only if those failed did they attend formal health facilities.

An important distinction that has often been made between traditional healing practice and Western biomedical care is that traditional practice engages the patient's larger social network, while Western care has taken a very individualistic approach (Turshen, 1984, p. 148). The focus of traditional healing practice on the patient's social network is consistent with what has been described as a "therapy management group," where a set of family members and friends mobilize around a patient with the purpose of "sifting information, lending moral support, making decisions and arranging details of the therapeutic process

(Janzen et al., 1978, p. 4)." This concept emphasizes the importance of formal health care facilities to make space for and engage the patient's social support system in the process of care.

The impact of HIV/AIDS in Tanzania

The first cases of AIDS in Tanzania were recorded in 1983, and since that time the impact of the virus has been felt increasingly around the country. In 2005 alone, approximately 140,000 people died of AIDS in Tanzania, and there are currently 1.3 million adults living with HIV in the country, of whom about 55% are women. In addition, approximately 110,000 children are living with HIV and over one million Tanzanian children have been orphaned by AIDS (UNAIDS et al., 2006).

At the end of 2006, UNAIDS estimated that approximately 6.5% of the adult population were infected with HIV (range: 5.8 – 7.2%) (UNAIDS et al., 2006). The UNAIDS estimate is derived from national-level data, which is based primarily on surveillance data of women attending antenatal clinic in sentinel sites. There is evidence that the HIV prevalence in Tanzania has steadied or declined over the last several years, although this appears to be more a factor of the rise in HIV-related deaths than a decline in new infections (Somi et al., 2006; Urassa et al., 2006).

The Tanzanian HIV/AIDS Indicator Survey is the first population-based survey of HIV/AIDS to cover all 21 regions in mainland Tanzania (Tanzanian Commission for AIDS et al., 2005). The representative probability sample included 6,900 households, including a total of 12,522 individual household members (55% female) ages 15-49. All adult household members completed separate questionnaires and provided blood samples for anonymous HIV testing, which were linked with their responses. The total HIV prevalence of the population was 7.0%, with variations by region, sex and age. The highest prevalence rates were found in Mbeya (13.5%) and Iringa (13.4%) regions, both located on the southern border of Tanzania, and in Dar es Salaam (10.9%), the capital city. Respondents in the Arusha region had an HIV prevalence of 5.3%. The HIV prevalence by age group and sex indicate that women become infected at younger ages than men (Figure 2.2). HIV prevalence was highest among women in the age group 30-34 and among men in the age group 40-44. This trend has been observed in other settings and is attributed to women's biological vulnerability to HIV at younger ages, as well as a tendency for women to be in relationships with older men (Glynn et al., 2001; Gregson et al., 2002; Pettifor et al., 2005).

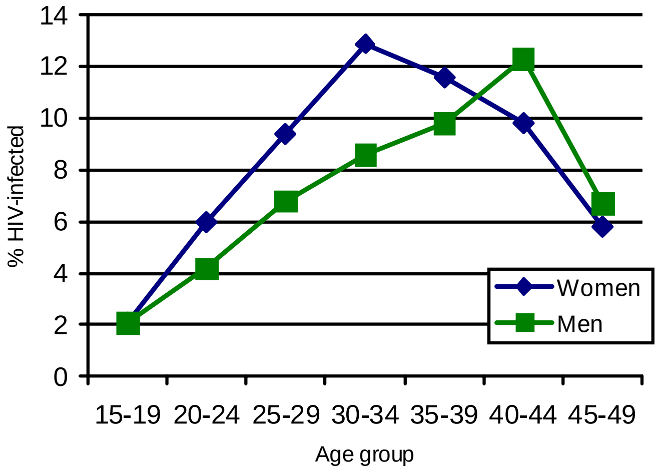


Figure 2.2: Percentage of Tanzania's population infected with HIV, by age group and sex (Tanzanian Commission for AIDS et al., 2005)

Little systematic research has been done on the social and economic impacts of the HIV epidemic in Tanzania. The Tanzanian government indicates that HIV/AIDS is draining the productive work force, with a negative macro and micro impact on the economy. They predict that Tanzania's GDP will be 15-20% lower in 2010 than it would have been without the AIDS pandemic. The provision of social services will be particularly impacted by increasing mortality. The Minister of Education has estimated that 114 teachers die of AIDS each month, presenting a gap in experienced personnel where there is often no replacement (Government of Tanzania, 2003). A similar impact is likely to be felt in the health sector, as nurses and doctors become infected with HIV.

There is evidence that HIV mortality is shifting the demographic distribution of the country. As early as 1992, a study in Mwanza Region of Tanzania found that with a relatively low prevalence of 4%, HIV had increased overall adult mortality in that region by more than 50% and more than doubled the number of deaths in the 20-29 year old age range (Todd et al., 1997). As a result of the long duration of illness and the plethora of AIDS-related infections, the epidemic is putting a great strain on already stretched hospital resources. In a large hospital in Moshi, in Northern Tanzania, a single-day, point-prevalence survey in 2001 found that 21% of all hospital inpatients were infected with HIV (Ole-Nguyaine et al., 2004). A methodologically similar study in urban Bukoba, in North-West Tanzania, found an HIV prevalence rate among admitted patients of 33%, with a prevalence of 53% among 25-34 year old patients (Kwesigabo et al., 1999). A study in rural North-West Tanzania found that in half of all HIV-related deaths, the person had never been admitted to the hospital, indicating a potentially large unmet need for HIV-related medical care (Ngalula et al., 2002).

The Tanzanian Government has acknowledged the broad-reaching impact of the HIV/AIDS epidemic and the need to provide a coordinated response. With technical assistance from the United States Agency for International Development (USAID) and the World Bank, the Tanzanian Commission for AIDS (TACAIDS) was launched in 2001 to coordinate the activities of all levels and sectors of government and to engage with multilateral donors in responding to the epidemic. The charge is guided by the National Multi-sectoral Strategic Framework on HIV/AIDS 2003-2007 and the National HIV/AIDS

Policy, both of which emphasize a multi-pronged approach of prevention, care and treatment involving multiple sectors of government and civil society.

Antiretroviral therapy as an opportunity to mitigate the impact of HIV

Antiretroviral therapy (ART) is one piece of a comprehensive response to mitigate the impact of the HIV/AIDS epidemic. ART, first introduced in the United States as combination therapy in 1996, has been an extraordinary life-prolonging tool for people living with HIV. ART regimens combine multiple drugs to reduce the amount of virus in the blood and increase the production of CD4+ T-cells, which allow the body to ward off infections. Just a few years after ART became widely available in the United States, studies reported 60% to 80% reductions in new AIDS-related illnesses, hospitalizations and deaths (Jensen-Fangel et al., 2004; Kaplan et al., 2000; Kleeberger et al., 2004; Paul et al., 1999). In Rio de Janeiro, Brazil, introduction of free ART reduced the number of AIDS deaths by 47.5% during the period 1995 to 2003 (Saraceni et al., 2005). Successful ART can change HIV from an illness that was almost always a death sentence into a chronic, manageable condition.

While ART was previously available only in resource-rich countries, generic production of ART has reduced the annual price of first-line regimens from approximately $10,000 in 2000 to $150 in June 2005, making the goal of universal access to ART more feasible (Medecins sans Frontieres, 2005). ART regimens have also become more simple to take and administer. Whereas initial formulations required patients to take several pills at multiple times of day, the newest regimens on the market require just one pill, once a day (Killingley et al., 2007). At the same time as there have been changes in the affordability and simplicity of ART, there has been a dedication of political will and resources to make ART available in developing countries, seen in large part because of the activism of HIV-positive individuals and organizations (Behrman, 2004). The call to expand ART services has increasingly been framed as an issue of human rights (Behforouz et al., 2004; Farmer, 2005; Galvao, 2005; Solomon, 2005). A rights-based approach is used to hold the international community accountable to responding to people living with HIV/AIDS, and to ensure access to affordable treatment for the world's poorest and most marginalized communities (Roseman et al., 2004).

In 2003, the World Health Organization (WHO) embarked upon an initiative to provide ART to 3 million people in developing countries by 2005. The strategy was underpinned by principles of urgency, equity and sustainability, and was embedded in a human rights framework. In launching what was called the '3 x 5' initiative, the WHO set the following goal:

> The goal of the Initiative is for WHO and its partners to make the greatest possible contribution to prolonging the survival and restoring the quality of life of individuals with HIV/AIDS, advancing toward the ultimate goal of universal access to antiretroviral therapy for those in need of care, as a human right and within the context of a comprehensive response to HIV/AIDS. By the end of 2005, 3 million eligible people in developing countries who need antiretroviral therapy will be receiving effective antiretroviral therapy. (WHOQOL Group, 1998)

It is now clear that the global community has made progress in the provision of ART but has missed the mark on meeting its ambitious target of three million on therapy. In June 2006, the WHO estimated that 1.6 million of the 6.5 million people who were in need of ART were receiving it (World Health Organization et al., 2006) (Table 2.2). The scale up of ART has been most dramatic in sub-Saharan Africa, increasing from 100,000 on ART at the end of 2003 to over one million on ART in mid-2006.

Table 2.2: ART coverage in low and middle income countries, June 2006 (World Health Organization et al., 2006)

Region	*Number receiving ART*	*Number needing ART*	*Coverage*
Sub-Saharan Africa	1,040,000	4,600,000	23%
Latin America & Caribbean	345,000	460,000	75%
East, South & S.E. Asia	235,000	1,440,000	16%
Europe & Central Asia	24,000	190,000	13%
N. Africa & Middle East	4,000	75,000	5%
TOTAL	1,650,000	6,800,000	24%

While these numbers present some progress on the scale-up of ART in developing countries, they fail to tell the full story. First, it is unclear how accurate the numbers are, given that they are based on generally weak routine health information systems. Further, the numbers beg additional questions, such as: How many people have survived once beginning ART? What has been the dropout rate of people starting ART? How many people have developed drug resistance and had to switch regimens?

In the next era of ART scale-up, an estimated US$27 billion is available or has been pledged from all sources to expand ART services in 2005-2007, but WHO estimates that an additional $18 billion is needed (World Health Organization, 2005a). Funds have been mobilized through the Global Fund to Fight AIDS, Tuberculosis and Malaria, PEPFAR, the World Bank, and other bi-lateral and multi-lateral initiatives. The challenge will be to ensure that the funds are used effectively to not only make drugs available, but also to build the physical and social infrastructure that will support patients to effectively take medications for the rest of their lives.

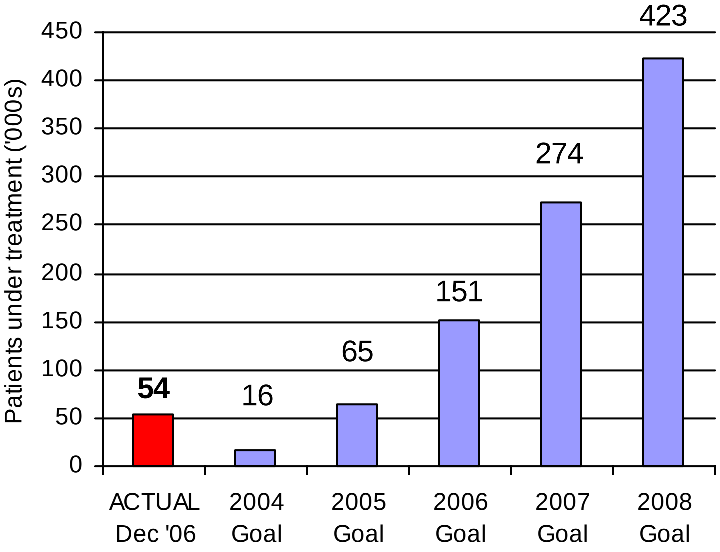
Antiretroviral therapy in Tanzania

Tanzania is committed to expanding ART access to all the people who are in need, and has received assistance from international donors to do so. The Tanzanian HIV/AIDS Care and Treatment Plan 2003-2008 guides the national scale-up of ART (Government of Tanzania, 2003). In this document, the Government set out four inter-related goals for treatment:

1. To provide quality, continuing care to as many HIV-positive people as possible
2. To strengthen the healthcare structure through expansion of healthcare personnel, facilities, and training in the care and treatment of HIV/AIDS
3. To foster communication efforts to increase public understanding of care and treatment alternatives and reduce HIV-related stigma
4. To strengthen social support for care and treatment of people living with HIV/AIDS, including home-based care, support groups and treatment partners

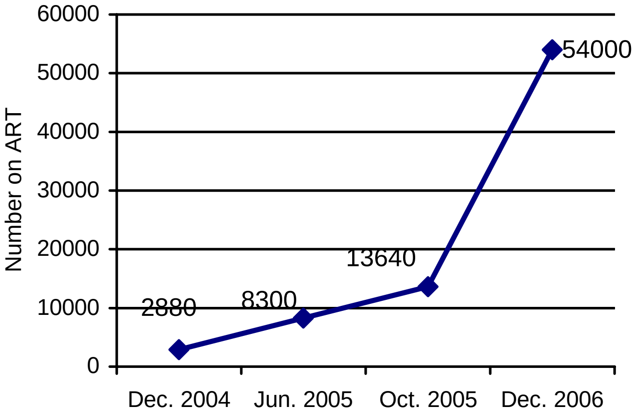
The national plan established specific target goals for the number of people on ART from 2004-2008 (Government of Tanzania, 2003). As of December 2006, 54,000 people were receiving ART across the country, out of 420,000 in need

Figure 2.3: Number receiving ART in Tanzania as of December 2006, compared with Government's goals (Government of Tanzania, 2003; UN Office for the Coordination of Humanitarian Affairs, 2007)



(UN Office for the Coordination of Humanitarian Affairs, 2007). This number falls far short of the government's goal of 151,000 on treatment by the end of 2006 (Figure 2.3). The reasons for this short-coming have not been identified, but potential challenges that were indicated in the national plan and that have been observed in other countries' experiences providing access to ART include: slow drug procurement, insufficient laboratory capacities, poor accessibility of voluntary counseling and testing services, lack of trained personnel, poor outreach to people in need of ART, and community-level stigma (Kober et al., 2004; McCoy et al., 2005). Even though the number of people on ART in Tanzania falls short of the government's stated targets, there has nevertheless been significant progress over the preceding two years (Figure 2.4).

Figure 2.4: Number receiving ART in Tanzania, as reported in 2004, 2005 and 2006 (UN Office for the Coordination of Humanitarian Affairs, 2007)



The national provision of ART is coordinated by the Tanzanian Department of Health. Sites that deliver ART are identified as care and treatment centers (CTC sites). As of December 2006, there were 200 CTC sites across the country, representing a mix of government, faith-based and charity-run health facilities (UN Office for the Coordination of Humanitarian Affairs, 2007). While provision of ART is disproportionately located in urban sites, there is increased commitment to making treatment available in rural areas.

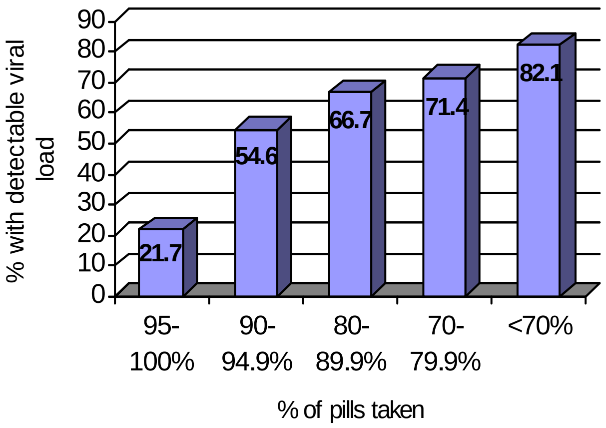
Financial resources are available to Tanzania to support its expansion of ART services. The Clinton Foundation, which provides technical and financial assistance for

HIV/AIDS treatment in Tanzania, estimates that Tanzania will spend $500 million in the next five years to provide ART to people living with HIV/AIDS (Clinton Foundation, 2006). This includes funds from the United States' PEPFAR program, which has committed $15 billion over five years to address HIV/AIDS in nine of the most affected countries including Tanzania, and the Global Fund to Fight AIDS, Tuberculosis and Malaria, which approved $216 million for Tanzania during the first four rounds of funding proposals (Global Fund to Fight AIDS TB and Malaria, 2005). However, even this fairly large infusion of funds may be insufficient to not only purchase the necessary medications, but also to build the supporting healthcare delivery system in a country where the per capita government expenditure on all health care costs is just $29 (United Nations Development Program, 2006).

Importance of adherence to antiretroviral therapy

One of the greatest challenges of rapid scale-up of ART services is to ensure patients' adherence to medications. Several studies have demonstrated that adherence to ART is the strongest predictor of progression to AIDS and death (Bangsberg et al., 2001; Garcia de Olalla et al., 2002; E. Wood et al., 2003b; E. Wood et al., 2002). The most commonly

Figure 2.5: Percentage of patients with virologic failure and adherence to ART (Paterson et al., 2000)



cited evidence of what constitutes ‘good’ adherence is a study by Paterson, Swindells et al (2000). Measuring both adherence and clinical outcomes in 99 ART patients in a U.S. hospital, the authors demonstrated that a threshold of 95% adherence was associated with less risk of virologic failure (defined as an HIV RNA level greater than 400 copies/ML) (Figure 2.5). In addition, at least 95% adherence was associated with an increases in CD4 lymphocyte count and lower hospitalization rates (Paterson et al., 2000). Using this study and subsequent evidence that greater than 95% adherence is associated with better clinical outcomes, 95% adherence is most often used as the threshold between poor and good adherence (Ammassari et al., 2001; Cederfjall et al., 2002).

While there appears to be a dose-response relationship between adherence and viral load, the relationship between adherence and the development of drug-resistant mutations of the virus has shown a different pattern. Several recent studies have demonstrated a skewed bell-shaped relationship between adherence and detection of drug-resistant mutations, in which high but imperfect adherence (80% - 90% adherence) was associated with the greatest risk of drug-resistant mutations (Bangsberg et al., 2004; Harrigan et al., 2005; M. S. King et al., 2005). These results do not negate previous data suggesting a dose-response relationship between adherence and disease progression and mortality (Bangsberg et al., 2001; Garcia de Olalla et al., 2002; E. Wood et al., 2003a; E. Wood et al., 2002), but they do suggest a renewed challenge to ensure that patients’ adherence is nearly perfect in order to guard against drug failure and poor health outcomes.

Suboptimal adherence to ART regimens has implications at both the individual and population levels. As noted above, at the individual level poor adherence is associated with progression to AIDS, increased risk of mortality and development of drug-resistant mutations of the virus. The drug-resistant mutations of the virus may render easier to administer first-line drugs ineffective for patients, requiring second-line drugs that are more complicated, more costly and carry greater side effects. This is particularly problematic in developing country settings, where second-line drugs are hard to come by and viral load testing is rarely available (Cohen, 2007). At the population level, drug-resistant viral strains can be transmitted through new infections, and implications for treatment may be similar to the spread of multi-drug resistant strains of tuberculosis (Alvarez et al., 2004). Small cohorts of patients in African populations have shown the emergence of drug-resistant strains of HIV in both treatment-naïve and ART-experienced patients (Laurent et al., 2005; Richard et al., 2004; Toni et al., 2003; Weidle et al., 2001; Weidle et al., 2002). Some suggest that unless the expansion of ART services is coupled with health and community systems that can support patients to adhere, it is possible that the rapid scale-up of ART services may do more harm than good (Gill et al., 2005; Harries et al., 2001).

Review of studies on ART adherence

Adherence is a challenge across chronic therapies. A review by the World Health Organization found that medication adherence across long-term therapies in developed countries is only in the range of 50% (World Health Organization, 2003). The authors of the report speculated that adherence may be even more problematic in developing countries, where there are additional challenges of access and supply. The findings of adherence to ART in Africa, however, have been fairly encouraging, holding at bay what some have termed as the potential of “antiretroviral anarchy” (Harries et al., 2001). A meta-analysis comparing ART adherence in North American settings and African settings found that patients in Africa had better adherence than their North American counterparts, with a pooled estimate of 77% of participants in African studies achieving adequate adherence, compared with just 55% in North American studies (Mills, Nachega, Buchan et al., 2006). In both settings, however, the measures of adherence were not consistent across the studies.

A review of studies in African settings that measured adherence and assessed factors associated with adherence identified seven studies (Table 2.3). Six of the seven studies measured adherence by patients' self-report, but these differed in the referent time interval (3 days, one week, one month, one year). One study measured adherence based on pharmacy pill count when patients returned for their monthly refill. All studies but one reported adherence as a dichotomous measure with patients compared to a standard of good adherence (most generally taking ≥95% of one's pills).

Table 2.3: Adherence measures and proportion of sample with poor adherence in studies in African countries

Reference	**Setting**	**Adherence measure**	**% of sample with poor adherence**
1. Byakika-Tusiime et al., 2005	Uganda	Self report: Proportion of doses taken in the past 3 days Adherence dichotomized at ± 95%	32%
2. Diabate et al., 2007	Ivory Coast	Self report: Proportion of doses taken in the past 3 days Adherence dichotomized at ± 95%	25.7%
3. Eholie et al., 2007	Ivory Coast	Self report: Proportion of doses taken in the past 7 days Adherence dichotomized at ± 95%	76%
4. Laniece et al., 2003	Senegal	Self report: Mean of pills taken over last 30 days Mean adherence: 91%	n/a
5. Nachega et al., 2004	South Africa	Self report: Proportion of doses taken in the past month Adherence dichotomized at ± 95%	12%

6. Orrell et al., 2003	South Africa	Monthly clinic pill-count: As a continuous measure, the median adherence for the cohort was 93.5% (mean, 87.2%). For analysis, adherence was dichotomized at ± 95%	54%
7. Weiser et al., 2003	Botswana	Self report: Proportion of doses taken in the past year Adherence dichotomized at ± 95%	46%

The measurement of adherence has been a consistent challenge. As Wu and colleagues state: “There is only vague consensus on what it is we are trying to measure, and there is a diversity of practice on when, how and what to measure” (Wu et al., 2002). Measures of adherence can be divided into two categories: subjective (patient self-report) and objective (pill count or technological devices) measures. Validation of adherence measures is generally done by looking at the correlation of the measures with patients’ HIV viral load (Montessori et al., 2004).

Self-reported measures of adherence are often chosen because they are easier, less costly and more feasible to administer than other more objective measures of adherence. Most self-report measures involve asking patients to recall the proportion of times that they correctly took their medications over the past 3-, 4-, 7-, or 28-day period (Reynolds, 2004). Self-reported measures have shown to consistently over-estimate adherence when compared with more objective measurements such as pill counts or electronic pill caps (Arnsten et al., 2001; M. A. Chesney, Ickovics et al., 2000; Liu et al., 2001; G. J. Wagner et al., 2000). For example, in a six month observational study, mean one-week estimates of adherence by self-report were 78%, but mean one-week estimates by electronic pill cap were 53% (Arnsten et al., 2001). Both of these measures were correlated with viral load, as has been seen in other studies (Arnsten et al., 2001; Duong et al., 2001; Fairley et al., 2005; Fletcher et al., 2005; Liu et al., 2001). Over-reporting adherence is often attributed to social desirability (Reynolds, 2004), but a small pilot study found that difficulties in recall played a more important role in accurate self-reporting than social desirability (G. Wagner et al., 2004). No social or cognitive variables have been identified to differentiate between those who accurately report adherence and those who do not accurately report adherence (Kimmerling et al., 2003). Despite the short-comings of self-reported measures of adherence, self report is nevertheless considered a robust and appropriate way to assess adherence (Simoni et al., 2006).

Multiple studies have considered the correlates of adherence in industrialized country settings, and several review articles have synthesized the findings (Ammassari, Trotta et al., 2002; M. Chesney, 2003; M. A. Chesney, 2000; Fogarty et al., 2002; Ickovics et al., 2002a, , 2002b; Mills, Nachega, Bangsberg et al., 2006; Reynolds, 2004; Tsasis, 2001). There is little consistency across studies of the predictor variables that are measured and hence those that are found to be associated with adherence. One review paper identified only a few factors have been consistently associated with poor adherence: side effects, psychological distress, lack of social or family support, complexity of the HAART regimen, low patient self-efficacy, and inconvenience of treatment (Ammassari, Trotta et al., 2002). In addition, supportive patient-provider relationships have been shown to be associated with better adherence (M. Chesney, 2003).

In order to synthesize findings on ART adherence in sub-Saharan countries, a systematic review of the literature in the Medline database was conducted using the key words: HIV, AIDS, adherence, compliance, ART, ARV, HAART. Studies were identified that met the following criteria: (1) considered adult adherence to ART as the dependent variable of interest; (2) used patient-level data to examine the correlates or predictors of adherence; and (3) were conducted in a sub-Saharan African country. Seven studies met these criteria, representing Uganda, the Ivory Coast, Senegal, South Africa and Botswana (Table 2.4). The sample sizes ranged from 66 to 591, with a mean sample size of 260. In six of the studies, at least some of the patients had to purchase ART. Four of the studies used a cross-sectional study design, while three used a prospective study design. All the studies involved face-to-face interviews, where the interviewer asked questions about adherence behaviors and the predictor variables.

Table 2.4: Characteristics of studies that looked at factors associated with adherence to ART in African countries

Reference	Setting	Sample	Study design
1. Byakika-Tusiime et al., 2005	Uganda 3 urban clinics	304 (all purchasing ART)	Cross-sectional structured interviews
2. Diabate et al., 2007	Ivory Coast 1 urban clinic	591 (unclear whether patients purchased ART)	Prospective: structured interviews
3. Eholie et al., 2007	Ivory Coast 3 urban clinics	308 (all purchasing ART)	Cross-sectional structured interviews
4. Laniece et al., 2003	Senegal 1 urban clinic	158 (1/2 purchasing ART; 1/2 receiving free ART)	Prospective: structured interviews
5. Nachega et al., 2004	South Africa 1 urban clinic	66 (1/3 purchasing ART; 2/3 receiving ART through clinical trials)	Cross-sectional structured interviews

6. Orrell et al., 2003	South Africa 1 urban clinic	289 (all receiving free ART through a clinical trial)	Prospective: structured interviews followed by monthly pill counts over 48 weeks
7. Weiser et al., 2003	Botswana 3 urban private clinics	109 (all purchasing ART)	Cross-sectional structured interviews

Similar to studies in industrialized country settings, there was little consistency across these studies of the factors that were measured as potential predictors and those that were found to be significantly associated with adherence. The factors that were studied fall into six broad categories. (A chart including the factors that were measured in each of the studies and their statistical significance in multivariate analysis is included as Appendix One).

- Demographic factors: All studies included measures of demographic variables. Age, gender, education and socio-economic status were measured in the majority of studies. Two studies found that younger age was associated with poor adherence in multivariate models (Nemes et al., 2004; Orrell et al., 2001). Gender was not associated with adherence in any of the studies. Two studies found that higher levels of education were associated with poor adherence (Eholie et al., 2007; Weiser et al., 2003). Only one study found an association between low socio-economic status (SES) and poor adherence, although SES was measured differently in each of the studies. Where SES was a significant predictor, it was measured as monthly income less than US$50 (Byakika-Tusiime et al., 2005). It is important that where SES was a predictor of adherence all patients were purchasing ART. One study found that poor adherence was associated with being single, which may be an indication of low social support (Byakika-Tusiime et al., 2005).

- Psychological factors: Four studies included measures of psychological variables. The only psychological variable that was significant in multivariate regression was

HIV optimism, measured by a single question of whether patients were less worried about their HIV infection now that treatment had improved (Diabate et al., 2007).

- <u>Social factors:</u> Four studies included measures of social influences. One study found that fear of stigmatization by a partner was significantly associated with worse adherence (Nachega et al., 2004), but this association was not explored in a multivariate model. Low social support was found to be a significant predictor of poor adherence in a study in Ivory Coast (Diabate et al., 2007), but was not significant in a study in Uganda (Byakika-Tusiime et al., 2005). Disclosure of HIV status was measured in a Botswana study and showed a trend of non-disclosure being associated with poorer adherence. In their study, 69% of patients did not disclose their HIV status to their families, and 94% did not disclose to people in their community. In an open-ended question of why patients missed ART doses, 15% reported missing doses due to stigma (Weiser et al., 2003).
- <u>Institutional factors</u>: Four studies included institutional variables in their measures, including access to the clinic, costs of medication and availability of counseling. Only cost of medication was a significant barrier to poor adherence. In a study in Botswana, patients who reported cost of ART as a problem were more likely to have poor adherence (Weiser et al., 2003), and in a study in Senegal, the reduction of the price of ART resulted in better adherence (Laniece et al., 2003).
- <u>Factors related to ART treatment:</u> All studies considered the relationship between adherence and treatment-related variables. An increasing number of pills and/or doses per day was significantly associated with poor adherence in two studies in multivariate analysis (Diabate et al., 2007; Orrell et al., 2003). In Senegal, patients taking regimens containing efavirenz had better adherence than patients taking regimens containing indinavir

(Laniece et al., 2003). The two studies that considered reported side effects did not find an association between side effects and adherence. There was also no association between time on ART and adherence in the four studies that measured this.

While the studies that have been conducted shed some insight on possible determinants of ART adherence in African settings, they also point to inconsistencies in both the predictor variables that were measured and those that were found to be significantly associated with adherence. The studies focused overwhelmingly on individual and clinical factors, with only scant attention to interpersonal or community dynamics that may influence adherence. None of the reviewed studies included a theoretical model, and none looked at mediated or moderated relationships of adherence, which would help to explain not only *what* factors are associated with adherence, but *how* those factors influence adherence. Further, most of the studies used a cross-sectional study design, which is limited in both its ability to show causation, as well as its ability to detect temporal differences in adherence rates (Spire et al., 2002). Very few studies on ART adherence in Africa have used qualitative methods, which would provide a more nuanced view of patients' experiences negotiating adherence (Crane et al., 2006; Hardon et al., 2007; Nachega et al., 2006).

III. THEORETICAL FRAMEWORK

Various theories have been used to explain variations in ART adherence and to inform adherence interventions. These include the trans-theoretical model (Rogers et al., 2001), the social cognitive theory (Fourney et al., 2003; Safren et al., 2001; Smith et al., 2003; Tuldra et al., 2000), the social action theory (Remien et al., 2003), the health belief model (Fourney et al., 2003; McPherson-Baker et al., 2000), the theory of group-mediated social control (Broadhead et al., 2002), the self-regulation theory (Reynolds, 2003), and the information, motivation and behavior skills model (Fisher et al., 2003; Harman et al., 2005). The use of theory in this field is young and disjointed. Amico and colleagues (2005) succinctly assess the limited use of theory in ART adherence research, and the importance of developing multivariate, theory-based models:

> Thus far, exploration of the determinants of ART adherence has been dominated by the 'single-variable,' predictive approach. While this work has provided valuable information regarding the associations between individual variables and adherence, it does not present a sufficiently complex view of the factors associated with ART adherence. Multivariate, theory-based models are only now emerging, and the evaluation of such models is critical in the development of effective interventions (Harman et al., 2005).

One of the problems with how theory has been applied in the field of ART adherence is that it has limited its lens to the individual level, failing to consider how the social context and interpersonal relationships influence patients' adherence. Studies of the correlates of adherence to ART have consistently found that adherence is influenced by variables at multiple levels of the social-ecological framework, including factors inherent to the individual, the individual's relationships, and characteristics of the physical and social environment (Ammassari, Antinori et al., 2002; M. Chesney, 2003; Fogarty et al., 2002; Ickovics et al., 2002b; Mills, Nachega, Bangsberg et al., 2006; Sankar et al., 2006; Vervoort et al., 2007).

This dissertation study integrated social support with constructs from social cognitive theory to explore the determinants of ART adherence. Social support is defined as assistance that is given through formal or informal relationships with the intention of being helpful for the beneficiary (Heaney et al., 2002), and has been categorized into four broad forms of supportive behaviors (emotional, instrumental, informational and appraisal) (Ferguson et al., 2002). Social cognitive theory is a behavioral theory that integrates intrapersonal and interpersonal levels of the social ecological framework and situates them together in a dynamic environment. The organizing concept of SCT is reciprocal determinism, which asserts continual interaction between the behavior, the person, and the physical and social environment (Baranowski et al., 2002). Albert Bandura, who has been refining the SCT since the 1970s, has identified five core constructs of SCT (Bandura, 1977):

1. Knowledge of health risks and benefits of a behavior
2. Self-efficacy to perform a behavior
3. Outcome expectations of a behavior
4. Goal setting and strategies to attain a goal of health behavior
5. Perceived facilitators and obstacles to performing a behavior

Drawing upon these theories, and considering empirical evidence of the determinants of ART adherence, I proposed a conceptual model to explain variations in patients' adherence to ART (Figure 3.6). This is a broad heuristic that asserts that adherence to ART is influenced by factors at multiple levels of the social-ecological framework. Below, I describe the ten predicted determinants, their theoretical underpinnings, and evidence of associations with ART adherence.

Individual level

Psychological and behavioral factors at the individual level are important for explaining ART adherence. All of the individual-level determinants are informed by the social cognitive theory.

1. *Perceived self-efficacy to adhere to ART*

Self-efficacy is defined as "the confidence a person feels about performing a particular activity, including confidence in overcoming the barriers to performing that behavior" (Baranowski et al., 2002). Bandura (2004) asserted that self-efficacy is perhaps the strongest determinant in influencing whether a person will undertake a particular behavior. For people who have never taken chronic medication before, the idea of taking pills every day, for the rest of one's life, can be daunting. This is particularly the case in the face of disrupting circumstances, such as experiencing side effects, traveling, or trying to hide one's HIV status. Adherence requires confidence that one can take the pills every day, even in the face of difficult circumstances. Self-efficacy has been associated with adherence in several studies (Catz et al., 2000; M. A. Chesney, Ickovics et al., 2000; Gifford et al., 2000; Godin et al., 2005; Wilson et al., 2004), including one study in a developing country setting (Pinheiro et al., 2002).

2. *Skills or strategies applied for taking ART*

The SCT identifies goal-setting and specific strategies to achieve goals as important for achieving behavior change (Bandura, 1977). Qualitative studies have identified the use of skills and strategies to ensure adherence including: pillboxes, alarm devices, carrying pills in a bag, and associating pill taking with other daily activities (Adam et al., 2003; C. Golin, Isasi et al., 2002; Kumarasamy et al., 2005; Ryan et al., 2003). In a study in Costa Rica, people who set out their pills on a daily basis had better adherence than people who did not use this strategy (Stout et al., 2004). In a prospective study in the United States, patients who used some adherence aids had significantly better adherence than patients who used no adherence aids (C. E. Golin, Liu et al., 2002b).

3. *Knowledge of ART*

The SCT views knowledge of the risks and benefits of a given health behavior as a precondition for embarking on changing behaviors (Bandura, 1977). For ART adherence, it is important that people have some basic comprehension of the mechanisms of ART, that they understand the long-term nature of ART, and that they grasp the potential negative impact of non-adherence. One study that specifically considered the association between knowledge of ART and adherence found that people with better ART knowledge were less likely to miss pills, compared with people with less ART knowledge (Weiss et al., 2003). In a longitudinal study in the United States, patients who had poor knowledge of their ART regimen at eight weeks after initiating treatment demonstrated poorer adherence (Miller et al., 2003).

4. *Outcome expectations of adherence*

Outcome expectations are what people expect will happen if they perform a given behavior. Outcome expectations may be either positive (expecting good things) or negative (expecting bad things). Positive outcome expectations increase the ‘pros’ of performing a behavior and therefore create incentives to perform a given behavior. These incentives may take the form of physical outcomes, social outcomes or self-sanctions (Fishbein, Triandis et al, 2001). Negative outcome expectations increase the 'cons' of performing a behavior and therefore present barriers to achieving a behavior. When people begin taking ART, they most likely have some positive expectations of taking the drugs. For example, they may expect that their health will improve, they will be able to return to work, or they will live longer. They may also have negative expectations, such as experiencing side effects, disrupting their normal routine, or having people find out that they are HIV-positive. The balance of positive to negative outcome expectations, which may change over time, may influence patients' motivation to adhere to ART. In a study in Brazil, low positive outcome expectations were associated with poor adherence (Pinheiro et al., 2002).

Interpersonal level

People live in a social environment where they are constantly being influenced by other people. It is critical to understand these interpersonal influences on ART adherence. Although all of the variables below are measured at an individual level, their influence, and therefore subsequent interventions, are at an interpersonal level.

5. *Patient-provider interaction*

A good relationship between patients and health care providers is recognized as vitally important for positive health outcomes (C. Golin et al., 2008; Lewis et al., 2002). When health care providers use communication tools that empower patients to be involved in their own care, health outcomes can be improved (Trummer et al., 2006). Positive interaction between patients and providers has been consistently associated with better adherence to ART in North American studies (Burke-Miller et al., 2006; Heckman et al., 2004; Wroth et al., 2006). Adherence is likely to be improved when patients feel they can ask questions and honestly share their experiences with health care providers, and when providers listen to their patients and impart relevant information and skills (Schneider et al., 2004).

6. Perceived levels of social support

Social support is positive assistance that is intentionally given from one person to another. As noted earlier, social support has been associated with adherence to medications in general (DiMatteo, 2004) and with adherence to ART in particular (Ammassari, Trotta et al., 2002). The mechanisms through which social support exerts an influence on adherence have not been studied as often. DiMatteo (2004) suggest that instrumental support may lead directly to adherence through the provision of practical support, while the relationship between emotional support and adherence may be mediated by a reduction in stress and depression, or an increase in self efficacy or self esteem.

7. HIV and ART disclosure experiences

Because of community-level stigma and fear of negative repercussions, many people do not disclose their HIV status to others (Blacker, 2004; Chandra et al., 2003; Petrak et al., 2001). Among women receiving HIV testing in a Dar es Salaam clinic, only 64% of those who tested positive disclosed their HIV status to their sexual partners (Maman et al., 2003). Among women who did not disclose, most reported that they were afraid of their partners' reactions. If the response is positive, disclosing one's HIV status to others – including family members, partners, friends and neighbors – may increase support for taking ART effectively. Hiding one's HIV status, or failing to disclose that one is taking ART, may make it difficult to take ART on a regular basis, both because of not wanting to take ART in front of others and lacking outside cues for assistance. A qualitative study among ART patients in the rural US found that many patients missed doses because of fear of being identified as HIV-positive

(C. Golin, Isasi et al., 2002). In Botswana, 69% of ART patients did not disclose their HIV status to their families and 94% did not disclose to people in their communities. Failure to disclose was moderately associated with poor adherence (p=.07) (Weiser et al., 2003).

Community level

While interpersonal influences deal with dyads, community influences deal with broader issues of group norms and cultural expectations. Again, while the variables below are measured at an individual level, their influence, and therefore subsequent interventions, occur at a community level.

8. Perceived stigma towards people living with HIV

Stigma is a prevailing societal judgment about a group of persons with a particular characteristic, which discredits these individuals and reduces them to lesser members of society (Goffman, 1963). Researchers distinguish between perceived or felt stigma and enacted stigma, which refers to identifiable forms of discrimination. In a mixed-methods study conducted on HIV stigma in Ethiopia, Tanzania and Zambia, people living with HIV/AIDS faced physical isolation from family, friends and community when their HIV status was known (Nyblade et al., 2003). Both perceived and enacted stigma led to isolation and a sense of hopelessness and resulted in the loss of access to physical and social resources. The study found that stigma resulted in people delaying HIV care until absolutely necessary and not getting the consistent care that was required. This impact of stigma could keep patients on ART from regularly attending clinic appointments and picking up their medications on time. In a South African study, ART patients who reported that they were afraid of being stigmatized by their sexual partners reported worse adherence than patients who did not express a fear of being stigmatized (Nachega et al., 2004).

9. Perceived normative beliefs of taking ART

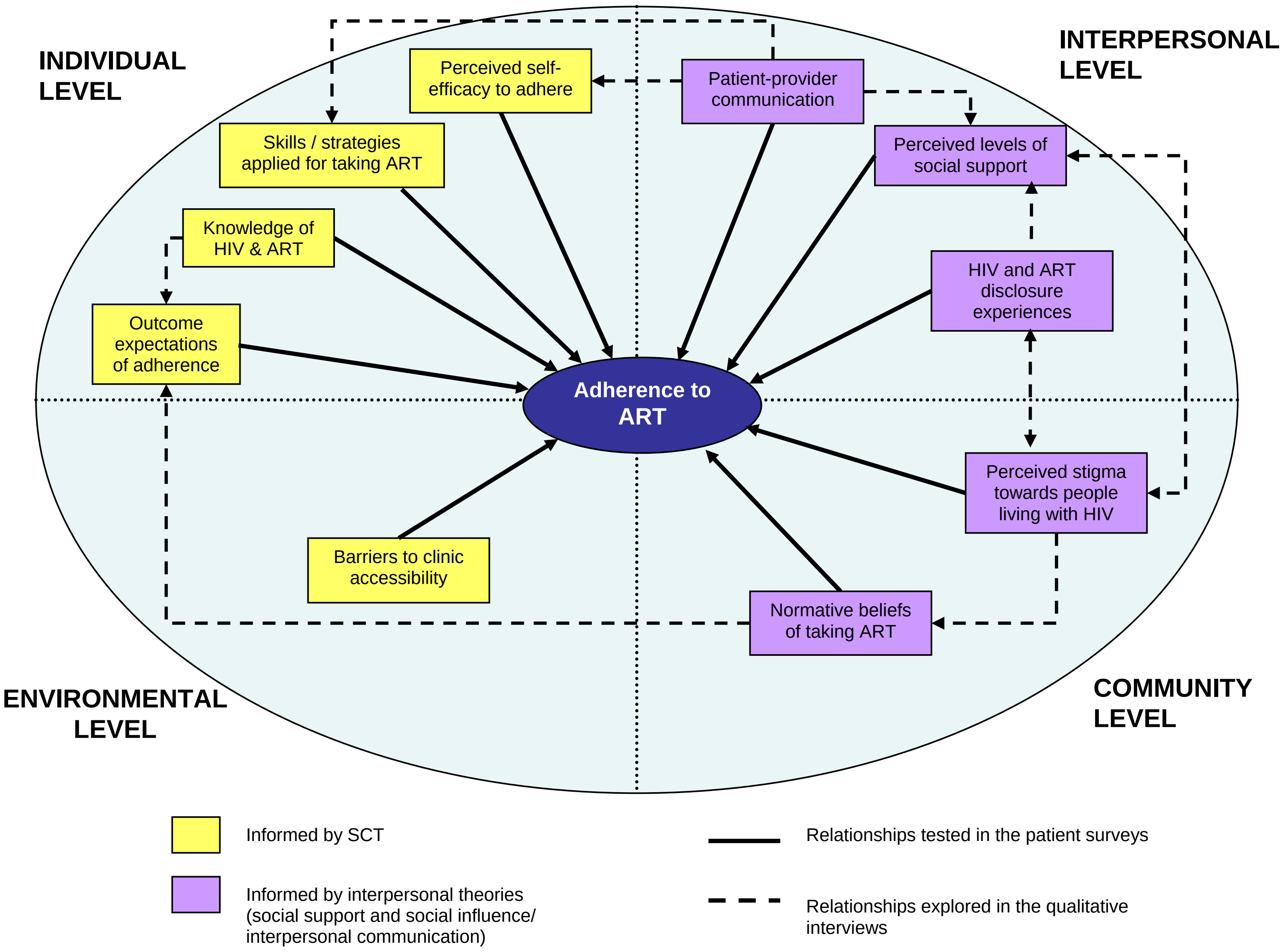
Normative beliefs refer to people's beliefs about whether individuals in their reference group would approve or disapprove of a given behavior. Normative beliefs make up a core construct of the theory of reasoned action (Montano et al., 2002), and are also inherent in the theoretical framework of social influence / interpersonal communication (Lewis et al., 2002). Normative beliefs of taking ART refer to whether people believe that others around them – family members, friends, religious leaders, physicians, etc. – approve or disapprove of their taking ART. Believing that most people in one's reference group think that taking ART is a good thing, and having strong motivation to comply with those people's beliefs, is likely to increase adherence to the medication. The impact of normative beliefs on ART adherence has not been previously documented in the literature.

Environmental level

10. Clinic accessibility

The SCT asserts that obstacles can make it nearly impossible to perform a health behavior, even if all other facilitators are in place. An obvious obstacle is physical accessibility to the clinic where one receives ART. Even with the strongest motivation, if people are not able to get to clinic appointments and pick up prescriptions on time, adherence can be impossible. Clinic accessibility can be a barrier if patients live far from the clinic, if they travel and can not return for clinic appointments and drug pick-ups, if they can not afford transportation to the clinic, or if the clinic has operating hours that are incompatible with patients' schedules. Difficulty finding or affording transportation to the clinic has been documented to negatively influence adherence (Hardon et al., 2007; Stout et al., 2004).

Figure 3.6: Conceptual model of the multiple factors influencing ART adherence



IV. STUDY OVERVIEW

Study site

The study took place at a health care facility in Arusha, Tanzania. The facility is under the direction the Evangelical Lutheran Church of Tanzania, one of the major health care providers in Tanzania (Flessa, 1998). The facility has been in operation since 1954 and includes a 120-bed hospital on the outskirts of the city and an outpatient clinic in the city center that houses the ART program. The facility is guided by a mission to respond to the physical, psychological and spiritual needs of the patients it serves.

Provision of ART at the study clinic began in October 2004, with funds from the United States' PEPFAR program. The clinic offers free clinical services to HIV positive patients, including laboratory exams, treatment of opportunistic infections and ART. Patients are eligible to start ART when their CD4 count drops below 200 or they present with opportunistic infections that represent a WHO clinical stage IV. At the time of the study, approximately 700 patients were receiving ART at the study clinic.

In addition to clinical services, patients at the study clinic meet with a counselor every month when they come to pick up their prescription for ART. At these brief meetings, the counselors discuss patients' progress and any concerns they might have regarding their physical or social condition. Patients are encouraged to bring a family member with them for their monthly appointments. Patients are also paired with voluntary adherence counselors (VACs), who are HIV positive people trained to provide follow-up and support for clinic patients. At the time of the study, 15 VACs were serving at the study clinic, and the clinic had plans to expand the program by training more VACs.

The United States Agency for International Development, which provides support to the study clinic through PEPFAR, has recognized the study clinic as one of the best models of care for providing ART services in Tanzania. In a reorganization of PEPFAR's support to ART sites in 2006, the study clinic was one of just two sites that graduated from having third-party supervision to being directly supported by USAID. This organizational change was due to USAID's perception that the study clinic had made significant progress in developing a comprehensive model of services for HIV positive individuals and that it had adequate organizational and human resource capacity to expand its provision of ART (Personal communication with USAID official, 2006).

Methods

Addressing the study aims required a combination of qualitative and quantitative methods. The use of mixed methods is valuable because it holds the potential to glean a fuller picture of the study topic and to transcend limitations in each of the methods (Borkan, 2004; Creswell et al., 2004; Steckler et al., 1992; Williamson et al., 2005). The study was conducted in three phases (Table 4.1).

Table 4.1: Overview of research methods

PHASE	Method	Sample size
1	Semi-structured interviews with patients on ART, treatment supporters, health care providers and voluntary adherence counselors	79 semi-structured interviews
2	Home visits to patients who participated in the qualitative interviews	42 home visits (2 visits each with 21 patients)
3	Structured face-to-face survey with patients on ART	340 face-to-face survey interviews

All interviews were conducted in Kiswahili by trained Tanzanian researchers. With the exception of the home visits, all interviews were conducted in the clinic. The UNC Institutional Review Board, the Tanzanian Commission for Science and Technology, and the Tanzanian National Institute for Medical Research all reviewed and approved the study protocol.

Introduction to the two manuscripts

The first manuscript, entitled "Factors associated with self-reported adherence to antiretroviral therapy in Tanzania," fulfills two functions. First, it presents the rate of adherence reported by the 340 patients who participated in the structured survey. Second, it uses logistic regression to explore the factors associated with adherence. Based on the high levels of optimal adherence reported in that sample, the second paper, entitled "*It's all the time in my mind*: A qualitative exploration of factors that facilitate adherence to antiretroviral therapy in Tanzania," uses the in-depth interviews with 36 patients and six health care providers to explore the factors that facilitated optimal ART adherence among patients in this clinic setting.

This dissertation study aims to inform the efforts to expand and sustain ART services in Tanzania and beyond. Survey data describes the population-based determinants of adherence, while qualitative information sheds light on the context of patients' experiences taking ART, including how adherence is influenced by patients' individual beliefs and motivations, social influences and routines of daily life. Together, this information can lead to the development of appropriate and effective interventions to support patients' adherence to ART.

V. MANUSCRIPT ONE:
Factors associated with self-reported adherence to antiretroviral therapy in a Tanzanian setting

Abstract

Background: Adherence to antiretroviral therapy (ART) is essential for clinical success among people living with HIV. The objective of this study was to determine the level of ART adherence and the factors associated with poor adherence among a convenience sample taken from a population of patients receiving free ART at one clinic in Tanzania.

Methods: Adult patients taking ART for at least one month were recruited into the cross-sectional study from a single clinic in Arusha, Tanzania. Self-reported adherence over four days and one month were assessed by structured patient interviews. Patients who reported less than 95% on either of the measures were considered to have poor adherence. In addition to demographic and treatment variables, the following potential correlates of ART adherence were measured: perceived quality of patient-provider interaction, social support, perceived HIV stigma, self-efficacy to adhere, depression, number of people to whom patients had disclosed their HIV status, personal beliefs about ART, normative beliefs about ART, and perceived side effects. Factors associated with adherence in unadjusted analyses ($\alpha=0.10$) were considered in a logistic regression model in forward stepwise fashion.

Results: A total of 340 patients participated in the study. Only 5.9% (20/340) of respondents reported less than 95% adherence in either the previous four days or one month. The final logistic regression model included the following factors significantly associated with poor adherence: being young (19-30 years old, vs. 31-40 years old; OR=4.26, 95% CI 1.33-13.60);

being old (over 50 years old, vs. 31-40 years old; OR=7.59, 95% CI 2.10-27.43); having lower perceived quality of patient-provider interaction (for each 1-point decrease in perceived quality of patient-provider interaction, OR=3.18, 95%CI 1.29-7.83); and reporting ever missing a clinic appointment (OR=3.75, 95% CI 1.29-10.89).

Conclusions: Adherence was very high in this sample. The factors associated with poor adherence highlight three specific needs: 1) to be sensitive to age-specific challenges of adherence and address these through appropriate counseling and support; 2) to be client-focused and address patients' perceived quality of patient-provider interaction; and 3) to emphasize and remind patients about clinic appointments.

Introduction

Antiretroviral therapy (ART) to manage HIV infection is increasingly available throughout Africa. Through an unprecedented international show of financial and political commitment to a health issue, ART coverage in Africa increased ten-fold in three years, from just 100,000 at the end of 2003 to over one million in mid-2006 (World Health Organization et al., 2006). In Tanzania, where 6.5% of the adult population is living with HIV, ART coverage has expanded from less than 3,000 people at the end of 2004 to 54,000 people at the end of 2006 (UN Office for the Coordination of Humanitarian Affairs, 2007). While access to medications is crucial, the success of the broad scale-up of treatment also depends on patients' abilities to adhere to the drugs. It is generally agreed that at least 95% adherence is needed to support clinical success to ART (Paterson et al., 2000). Poor adherence can lead to viral resistance, the failure of cheaper first-line treatment regimens, and the spread of multi-drug resistant forms of the virus (Bangsberg et al., 2000; Paterson et al., 2000; Stevens et al., 2004). Understanding the prevalence of poor adherence and the factors that are associated with poor adherence are important clinical and public health goals. This information is essential to inform ART programs and maximize patients' success on therapy.

A number of studies have been conducted in African settings to measure adherence to ART and explore the factors associated with adherence (Byakika-Tusiime et al., 2005; Diabate et al., 2007; Eholie et al., 2007; Laniece et al., 2003; Nachega et al., 2004; Orrell et al., 2003; Weiser et al., 2003). In these studies, between 12% and 76% of patients failed to achieve optimal adherence, most often measured at a cut-off of 95%. The variation in the adherence rates among these studies may in part be attributable to the variation in the conditions of the ART programs. In the Senegal study, for example, where 76% of patients failed to achieve adequate adherence, a quarter of patients who missed pills said the reason was that the pharmacy was out of stock (Eholie et al., 2007). In over half of the studies, patients were paying for pills out of pocket and their inability to consistently purchase pills was a substantial adherence barrier (Byakika-Tusiime et al., 2005; Eholie et al., 2007; Laniece et al., 2003; Weiser et al., 2003). Despite these structural barriers, a meta-analysis demonstrated that, overall, the adherence to ART of patients in African settings exceeded that observed in North American settings (a pooled estimate of 77% of participants in African studies achieving adherence vs. 55% of patients in North American studies) (Mills, Nachega, Buchan et al., 2006).

Most studies that have explored the factors associated with adherence to ART in African settings have been cross-sectional and measured adherence by self report. They have identified poor adherence as associated with: demographics (having low income, being single, being young, higher education, language spoken); psychological factors (low HIV optimism, lack of a lifetime commitment to ART); inter-personal factors (social support, fear of stigma); treatment-related factors (number of pills, number of doses, higher CD4 count at initiation of ART, ART regimen); and facility-related factors (cost of treatment). Studies in developed countries similarly have found that adherence is influenced by variables at multiple levels of the social-ecological framework (SEF), including factors inherent to the individual, the individual's relationships, and the clinic environment, as well as characteristics of the regimen itself (Ammassari, Trotta et al., 2002; M. Chesney, 2003; Fogarty et al., 2002; Ickovics et al., 2002a; Mills, Nachega, Bangsberg et al., 2006; Sankar et al., 2006; Vervoort et al., 2007). This evidence points to the need to understand and address potential barriers associated with adherence at multiple levels of influence.

This study is the first to assess the factors associated with adherence to ART in Tanzania. It is also the first study to look at these issues in an African setting where all patients are receiving free services and the large majority are taking single-pill, twice-a-day combinations of ART. The study addressed two research questions: (1) what proportion of patients achieved at least 95% adherence to ART; and (2) what factors are independently associated with having less than 95% adherence. The findings may be used to improve both existing and new ART programs in Tanzania and to inform further research.

Methods

Study site

The study took place at an urban, faith-based clinic in Northern Tanzania. With financial support from the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), the clinic provides free ART and related services (laboratory tests and treatment of opportunistic infections) to all HIV-positive patients with a CD4 measurement of less than 200 or a WHO clinical stage of IV. All patients at the study clinic are counseled about adherence before initiating ART and while taking therapy. In addition, patients are paired with HIV-positive peers who provide informational and emotional support. At the time of the study, approximately 700 adults were receiving ART from the clinic where this study was conducted.

Data collection

HIV-positive patients at the study clinic participated in a cross-sectional interviewer-administered face-to-face survey. Patients were eligible to participate in the study if they were 18 years or older, had been taking ART for at least one month, and had not participated in the qualitative phase of the study.

For a four week period, we consecutively approached all adult patients who came to the clinic to pick up their monthly supply of ART on designated HIV clinic days (Monday, Wednesday and Friday). The pharmacist screened all patients for eligibility and gave eligible patients a colored piece of paper, which indicated to a recruiter stationed next to the pharmacy that the patient was eligible to participate in the study. The recruiter told all eligible patients briefly about the study and, if they were interested in participating, referred them to an interviewer.

The Tanzanian interviewers, who had received standardized training, read an informed consent form to participants and administered the questionnaire orally in Kiswahili to those who provided written consent. To facilitate responses on scaled questions, interviewers used a visual aid that included circles of increasing sizes with the written response options underneath. Respondents could view the relative magnitude of the response choices and point to the appropriate circle to indicate their responses. Participants received

5,000 Tanzanian Shillings (approximately 4 US dollars) for participating in the one-hour survey.

The Institutional Review Boards of the University of North Carolina School of Public Health, the Tanzanian Commission for Science and Technology and the Tanzanian National Institute for Medical Research all reviewed and approved this study.

Table 5.1: Factors measured in the cross-sectional survey, with Chronbach's alpha reported for scale measures

Outcome variable
Self-reported adherence to ART
Correlates
Perceived quality of patient-provider interaction (α=.791)
Social support (α=.858)
Perceived HIV stigma (α=.899)
Self-efficacy to adhere (α=.720)
Depression (α=.846)
Extent of HIV disclosure
Personal beliefs about ART
Normative beliefs about ART
Skills used to adhere
Perceived side effects
Treatment-related variables
Time on ART
ART regimen
Demographics
Sex
Age
Religion
Education
Relationship status
Socio-economic status
Clinic accessibility

Measurements

The survey instrument was developed based on standard measurement scales and preliminary findings from the formative phase of the study (69 in-depth qualitative interviews about ART adherence conducted with patients, treatment supporters, health care providers and HIV-positive counselors). Table 5.1 lists the factors measured in the survey. All questionnaire items and response choices were translated into Kiswahili and back-translated into English. We conducted ten cognitive interviews with HIV positive patients to assess comprehension of individual questions. We pre-tested the questionnaire with 40 patients to assess the flow, timing and comprehension of the entire instrument.

Adherence

Development of adherence measure

The self-reported adherence measure was developed through multiple home visits to 21 ART patients who had participated in the qualitative phase of the research, using pill count as an objective criterion to validate the self-report measure. At the first home visit, the local interviewer observed where the participant kept his or her medication and recorded a pill count. At the second visit four days later, the interviewer administered three self-reported adherence measures: a four-day recall, a one-month linear visual analogue scale, and a one-month modified visual analogue scale using a jar of beads (method described below). Following each measure, the patient was asked to explain why they answered the way they did and whether they understood the question well. The interviewer then asked again to see the patient's medication and made a note of the number of pills left in the container. The results of the four-day pill count were compared with the results of the four-day self-report. In all but one case (95.2%) the four-day self report and pill count provided the same result. Patients reported confusion about the linear visual analogue scale, leading to the selection of the modified visual analogue scale using a jar of beads.

Description of adherence measure

Self-reported adherence to ART was measured with two sets of questions: a four-day recall and a modified one-month visual analogue scale (VAS). The four-day recall of adherence was adapted from the AACTG Adherence Instrument, developed for use in clinical trials conducted in the United States (M. A. Chesney, Ickovics et al., 2000) and adapted in multiple studies on the correlates of adherence in the U.S. and in Africa (Byakika-Tusiime et al., 2005; Nachega et al., 2004; Nemes et al., 2004; Weiss et al., 2003). The interviewer began by asking respondents to identify the regimen they were currently taking, using pill bottles to aid responses. The interviewer then confirmed with patients at what times of day they took their pills and the number of pills per dose. For each dosing period over the previous four days, the interviewer used memory recall prompts (e.g., asking respondents what time they woke up or what time they ate dinner that evening) and then asked whether they took morning and evening doses and, if so, at what time.

The one-month measure of adherence was based on the concept of a linear visual analogue scale (VAS), which asks respondents to indicate on a line on a piece of paper the proportion of prescribed ART pills they took in the previous month, from 0 to 100% (Walsh et al., 2002). We modified the VAS scale by using a visual tool of a jar of beads (Hardon et al., 2006). The interviewer explained that the jar contained the number of pills they *should* have taken in the previous month, and asked them to transfer to another jar the number of pills they actually *did* take in the previous month. The proportion of pills that respondents transferred from one bottle to another was an estimate of their adherence for the previous month.

The group of adherence questions was preceded by a statement acknowledging that people may miss taking pills for a variety of reasons and encouraging full disclosure of non-adherence. For any reported missed pills, the interviewer asked an open-ended question of why they had missed their pills.

Adherence was dichotomized to consider whether or not respondents had achieved optimal adherence. Optimal adherence was defined as reporting 95% adherence on both the

4-day and one-month recalls, while sub-optimal adherence was defined as failing to achieve 95% adherence on one or both measures.

Correlates

The potential correlate variables to study were chosen based on a theoretical framework drawing upon the Social Cognitive Theory (Baranowski et al., 2002) and the construct of social support (Heaney et al., 2002).

Perceived quality of patient-provider interaction was measured with a 9-item scale adapted from a study in Thailand (Panpanich et al., 2004). Items asked how much patients agreed with statements about their interactions with health care providers (staff give you enough time every time you come to the clinic; staff are willing to listen to your problems or your concerns; staff help you find solutions to health problems; staff explain things in a way you understand; you are able to contact staff when you need to; you are comfortable talking openly with staff; you get good care for your conditions from staff; staff provide advice for problems you have taking your medications; staff understand the difficulties you face taking your pills; and staff encourage you to take your pills) (α =.791). One additional question was dropped from the scale because it didn't load on the factor (staff advise you on how to reduce side effects to ARVs).

Social support was measured with a modified version of the Medical Outcomes Study (MOS) social support scale (Sherbourne et al., 1991). In addition to using the eight questions from the emotional/informational support sub-scale and the four questions from the tangible support sub-scale, we included five additional questions based on the types of support people mentioned during the qualitative interviews as important (how often do you feel you have: someone to remind you to take your pills; someone to give you courage in living with HIV;

someone to pick up your pills from the clinic if you're not able; someone to give you spiritual help; and someone to give you money if you don't have it). The questions about spiritual help and money were dropped on the final scale because they didn't load on the factor (α =.858).

Perceived HIV stigma was measured by adapting a 10-question scale on experienced stigma developed in a Tanzanian context (Nyblade et al., 2003). Items asked how worried respondents were about particular negative consequences if other people knew their HIV status (e.g., how worried are you that you would be excluded from a social gathering if people knew your HIV status) (α =.899).

Self-efficacy to adhere was measured with a 10-item scale adapted from studies in Thailand and Brazil (Panpanich et al., 2004; Pinheiro et al., 2002) and informed by the qualitative data. The scale included 9 items, each assessing respondents' confidence to take their HIV medication given a challenging situation (e.g., when you feel very healthy; when you are away from home) (α =.720).

Depression was measured using the 11 items that make up the psychological sub-scale of the Hopkins Symptoms Checklist that has been validated in the Tanzanian context (Kaaya et al., 2002). The items asked how often respondents had experienced depressive symptoms in the previous month (e.g., felt lonely, worried too much about things, cried easily) (α =.846).

The extent of disclosure of one's HIV status was measured with a single question: How many people have you talked with about your HIV status? HIV disclosure was analyzed both as a dichotomous measure of whether or not patients had disclosed to anyone and also as a categorical measure of how many people they had spoken with about their HIV status (no one, one person, two people, three or more people).

Personal beliefs about ART were measured with a set of eight questions, informed by the qualitative instrument, each assessing what patients know or believe about ART (e.g., whether ART can completely remove HIV from the body; whether ART are for life; and how ART impact CD4 and viral load). Beliefs about ART were measured as a continuous variable of the number of questions where patients expressed incorrect knowledge in their beliefs.

Normative beliefs about ART were measured with three questions: whether respondents had ever been told that taking ART would make them die sooner; whether they had been told that they should take traditional medicines instead of ART; and whether they had been told that they should pray instead of taking ART.

Skills used to adhere were measured with a set of six questions, informed by the qualitative interviews, about whether respondents had used different skills to remember to take their ART over the past month (e.g., listening to the radio, setting an alarm).

Perceived side effects were assessed with a single question of whether respondents had experienced any side effects related to their medication over the past month.

Treatment-related variables

Length of time on ART was measured with a single question asking when patients started taking ART. If respondents did not know the month and year, the interviewer checked their treatment card, which all patients must present at the pharmacy. *ART regimen* was measured with a single question. Interviewers presented respondents with pill bottles to assist in correct identification of the regimen.

Demographics

We measured *sex*, *age*, *religion*, *highest level of education* and *current relationship status*. *Socio-economic status* (SES) was calculated by a weighted sum of nine ownership items (radio, telephone, television, bicycle, car, refrigerator, cows, small animals, or a plot of land), electricity in the house, indoor plumbing, and a single question about food security in the previous month. Weights were assigned to individual SES items based on principal coordinate analysis (Bangdiwala et al., 2004). To assess *clinic accessibility*, we analyzed separately questions about how much time respondents spent traveling from their home to the clinic and how much it cost them to travel from their home to the clinic.

Data management and analysis

Data were double-entered in an Access database and compared for keystroke errors using Epi Compare. SPSS version 15.0 (SPSS Inc. Chicago, IL) was used for all analyses. Scaled measures were reviewed for internal consistency (reporting Chronbach's alpha) and item-by-item analysis was conducted to consider any items that should be dropped from the scales. Overall scaled scores were calculated by averaging the item responses and imputing missing responses. Scale items had, on average, fewer than two missing cases.

Logistic regression was used for analysis of unadjusted log odds of less than 95% adherence. Factors that were significantly associated with adherence at $\alpha = 0.10$ were considered in a multiple logistic regression model, as were potential control variables (sex, time on ART and SES) that affected the point estimate of predictor variables by +/-10%. The model was built with forward iterations, considering the limitation that five outcome events are required per predictor variable (Vittinghoff et al., 2007). Adjusted odds ratios and 95% confidence intervals are presented in the final model for the variables. Goodness of fit of the final model was assessed using the Hosmer and Lemeshow test. Non-significance of the chi square statistic from this test supported the model (Kinnear et al., 2006). Variables included in the final model were empirically investigated for multicollinearity.

Results

<u>Sample demographics</u>

A total of 340 patients participated in the cross-sectional survey. An additional 17 eligible patients (4.8%) were approached by the recruiter but declined to participate. The primary reason for declining was not having time available to complete the survey.

Table 5.2 describes the demographic characteristics of the study sample. The predominance of females in our sample was representative of patients receiving ART at the study clinic. The average age of participants was 39.5 years (range 19 to 77). Male respondents were on average older than female respondents (42.5 years vs. 38.4 years, p<.001).

Table 5.2: Demographic characteristics of respondents (n=340)

	n	**%**
Sex		
Male	88	25.9%
Female	252	74.1%
Age		
19-30	54	15.9%
31-40	160	47.1%
41-50	91	26.8%
51 and older	34	10.0%
Education		
Did not complete primary	69	20.3%
Completed primary only	207	60.9%
More than primary	64	18.8%
Religion		
Christian	74	78.0%
Muslim	263	22.0%
Electricity in house		
Yes	110	32.4%
No	230	67.6%
Indoor plumbing		
Yes	56	16.7%
No	283	83.3%
Problems getting food in past month		
Yes	242	71.4%
No	97	28.6%
Time to reach clinic		
< 1 hour	152	44.8%
> 1 hour	187	55.2%

Patients had been taking ART for an average of 13.9 months (range 1 to 62). The majority (311/340, 91.5%) were taking Triomune (manufactured by Cipla in Mumbai, India), a twice-a-day single combination ART pill containing Stavudine, Lamivudine and Nevirapine. An additional 27 respondents (7.9%) reported taking a two-pill combination of Combivir, containing Lamivudine and Zidovudine, and Efavirenz. This combination was usually prescribed to patients who were not tolerant of the Nevirapine contained in Triomune. The remaining two patients reported taking other ART combinations.

Adherence

Adherence in this setting was high, with 320 out of 340 respondents (94.1%) reporting at least 95% adherence on both the four-day and one-month self-report measures (Table 5.3). Of the 20 respondents who were classified as having poor adherence, 12 reported less than 95% adherence on the four-day measure, five reported less than 95% adherence on the one-month measure, and three reported less than 95% adherence on both measures. When asked why they had missed their pills, the most common response was that they simply forgot (45%), followed by being out of the house or traveling (20%), running out of pills because they had not come to the clinic on time for a refill (9%), intentionally not taking their pills due to illness or side effects (8%), or oversleeping (5%).

Table 5.3: Self-reported sub-optimal adherence by 4-day, one-month and cumulative measures (n=340)

	n	**%**
Respondents with <95% adherence		
4-day recall	15	4.4%
One-month estimate	8	2.4%
Cumulative	20	5.9%

Correlates of adherence

Results from bivariate associations of our correlate, demographic and treatment variables with our outcome variable included six significant factors at $\alpha=0.10$: age (being 19-30 years old or older than 51); having less than standard 7 education; having never been married; having lower self efficacy to adhere; reporting lower perceived quality of patient-provider interaction; and reporting having ever missed a clinic appointment (Table 5.4). The following correlate variables were not associated with adherence in our sample: social support, perceived stigma, depression, extent of HIV disclosure, normative beliefs about ART, personal beliefs about ART, skills used to adhere, and side effects.

The variables that were associated with adherence in the bivariate analysis at the 0.10 level or lower were considered in the multiple logistic regression model. The final model included three significant variables: age, missing a clinic appointment, and perceived quality of patient-provider interaction (Table 5.4). Marital status, education and self efficacy to adhere were not significant when controlling for the other variables, and were therefore not included in the final model. Missing a clinic appointment and perceived quality of patient-provider interaction were correlated, with patients who reported ever missing a clinic appointment having lower perceived quality of patient-provider interactions, compared with patients who reported never missing a clinic appointment ($F=21.07$, $p<.001$). When we included the interaction term of the two items in the model, it was not significant and was therefore not retained.

In the final model, age exhibited a U-shaped relationship with adherence. Respondents aged 19-30 years old were over four times more likely to report poor adherence, compared with respondents aged 31-40 (OR=4.26, 95%CI 1.33-13.60) and respondents over age 50 were over seven times more likely to report poor adherence, compared with respondents aged 31-40 (OR=7.59, 95% CI 2.10-27.43). Perceived quality of patient-provider interaction was also significantly associated with adherence. For each one-point decrease in the four-point scale, respondents were three times more likely to report poor adherence (OR=3.18, 95% CI 1.29-7.83). Finally, respondents who reported ever missing a clinic appointment were almost four times more likely to report poor adherence, compared with respondents who said they had never missed a clinic appointment (OR=3.75, 95% CI 1.29-10.89).

Discussion

Adherence was very high in this setting, with 94.1% of patients reporting that they took at least 95% of their prescribed pills during both the previous four days and previous one month. The rate of adherence in our sample was significantly higher than has been observed in other studies in African settings that also relied upon self report (Byakika-Tusiime et al., 2005; Diabate et al., 2007; Eholie et al., 2007; Laniece et al., 2003; Nachega et al., 2004; Weiser et al., 2003). The high adherence may be attributable to the nature of the study site. While most previous studies have been conducted in large government hospitals in capital cities, this study was conducted in a small faith-based clinic, which may have offered patients more personal attention. In addition, it is possible that the simple regimen (almost all patients were taking regimens that required just one pill twice a day) facilitated adherence. In previous studies in Africa, patients were taking regimens that included multiple pills at two or more dosing intervals. An increasing number of pills and doses has been associated with worse adherence (Ammassari, Trotta et al., 2002; M. Chesney, 2003; Diabate et al., 2007; Laniece et al., 2003; Orrell et al., 2003). Finally, while previous studies in Africa have often included patients who were paying out-of-pocket for ART drugs or related services, all HIV-related care at this site was offered free of charge to patients. Studies have consistently shown that ART adherence is higher when cost is not an obstacle (Byakika-Tusiime et al., 2005; Eholie et al., 2007; Weiser et al., 2003).

Several factors were associated with adherence in this sample. Both respondents who were younger (19 to 30 years old) and respondents who were older (50 years or more) were more likely to report poor adherence, compared with respondents ages 31 to 40. Younger age has been associated with poor adherence in other African studies (Diabate et al., 2007; Orrell et al., 2003), in Brazil (Nemes et al., 2004), and in India (Shah et al., 2007), as well as in North American settings (Barclay et al., 2007; Murphy et al., 2004; Schneider et al., 2004; Sullivan et al., 2007). The finding that young people were less likely to adhere was possibly related to younger people having less stable social and economic situations than their older counterparts and having less experience interacting with the health care system. The association between older age and poor adherence has not been documented elsewhere. A review of HIV infection among older people points out that scant attention has been given to the impact of the HIV epidemic on the older population (Knodel et al., 2003). The invisibility of older people in the epidemic is evident in the statistics published by UNAIDS, which reports HIV prevalence only among children (0-14 years) and “adults” (15-49 years), neglecting older people living with HIV (UNAIDS et al., 2006). More attention needs to be given to understanding the challenges faced by older individuals living with HIV and their experiences taking ART. Age- and sex-specific prevalence of HIV in Tanzania showed that women are infected at younger ages than men (Tanzanian Commission for AIDS et al., 2005), but there was no significant interaction between age and sex in the model.

Patients with less favorable assessments of their interactions with providers had worse adherence in this sample. Evidence from Africa confirms that patients value personal connections with providers, sometimes prioritizing the interpersonal domain over technical aspects of care (S. Haddad et al., 1995; S. Haddad et al., 1998; Unger et al., 2002). The association between adherence and patient-provider interaction has not been explored in other African studies, but has been identified in North American settings in both quantitative (Burke-Miller et al., 2006; Heckman et al., 2004; Schneider et al., 2004; Wroth et al., 2006) and qualitative studies (Abel et al., 2003; C. Golin, Isasi et al., 2002; Malcolm et al., 2003; Murphy et al., 2003; Murphy et al., 2000; Remien et al., 2003; Roberts, 2002; Sankar et al., 2002). Communication between patients and health care providers is recognized as vitally important for good health outcomes (C. Golin et al., 2008; Lewis et al., 2002). Adherence is likely to be improved when patients feel they can ask questions and honestly share their experiences with health care providers, when providers listen to their patients and impart relevant information and skills, and when providers exhibit warmth and empathy (Schneider et al., 2004; Squier, 1990). The successful use of motivational interviewing by health care providers in North American settings offers further support to the positive impact of patient-provider communication on adherence (Adamian et al., 2004; Cooperman et al., 2005). The quality of patient-provider interactions will be all the more important – and more challenging – as more patients enroll in ART programs, particularly given the shortage of health care workers throughout sub-Saharan Africa (Barnighausen et al., 2007; Kumar, 2007). Further research is needed to understand the aspects of patient-provider interactions most valued by patients in the Tanzanian setting, as well as the mechanisms through which patients' assessments of their interactions influence adherence outcomes.

Reporting ever missing a clinic appointment was associated with poor adherence. We do not have information about the reasons that patients missed appointments, but the fact that neither the amount of time nor the amount of money spent to reach the clinic were associated with adherence suggests that missing clinic appointments may be a function of personal motivation, rather than structural barriers of access, as have been identified in other studies (Hardon et al., 2007; Rosen, Ketlhapile et al., 2007). Missing a clinic appointment was associated with perceived quality of patient-provider interaction, with patients who missed appointments reporting lower perceived quality of interaction with their providers. The interaction between these two variables was not significant in the model of poor adherence, which may be attributable to the lack of power in the study due to the small number reporting poor adherence. More research is needed, ideally through a longitudinal study, to understand why patients miss clinic appointments and how or whether missed visits affect adherence or are just markers for other domains. Given the evidence of high loss to follow up in African ART programs, understanding and addressing missed appointments is of particular concern in and of itself (Rosen, Fox et al., 2007).

All other variables measured in the survey were not independently associated with adherence. However, this does not mean that these other psychosocial factors are not important to address in ART programs. Factors such as depression, stigma, disclosure and social support play important roles in the lives of people living with HIV, and successful ART programs should seek to positively influence these domains (Remien et al., 2007). Even though these factors did not distinguish good adherers from poor adherers in this setting, they likely have an impact on the quality of life of people living with HIV and may influence patients' retention in ART programs (Rosen, Fox et al., 2007). The scale measures adapted and developed for this study demonstrated strong internal reliability, suggesting that a lack of significance is not attributable to their measurement. The replication of these measures may be warranted in other studies with larger samples exploring these domains.

The findings highlight areas where interventions may be useful to improve adherence. First, counselors and health care providers should be aware that younger and older patients may have particular challenges adhering to their medications. They should seek to understand and respond to these challenges through directed counseling. Second, ART programs should make efforts to be client-focused and regularly assess and address the quality of interactions between providers and patients. This should be done at both the institutional level, for example in the time allotted for providers to spend with patients, as well as the interpersonal level of communication between providers and patients. Third, ART programs should emphasize to patients the importance of attending clinic appointment and look at innovative ways to remind patients about their appointments and assess and remove any barriers they face. Finally, the fact that the most common response to why patients had missed taking their pills was that they "just forgot" highlights the potential value of identifying appropriate reminder strategies, such as alarms, cell phone text messages, pill boxes, or engagement of household members to provide reminders (C. E. Golin, Liu et al., 2002a; Safren et al., 2003).

The results of this study must be interpreted in the context of its limitations. Although self-reported measures of adherence have been consistently correlated with viral load (Arnsten et al., 2001; Duong et al., 2001; Fairley et al., 2005; Fletcher et al., 2005; Liu et al., 2001) and have been deemed as robust and appropriate indicators of adherence (Simoni et al., 2006), they are nevertheless subject to social desirability and recall bias, and as such may under-estimate non-adherence compared with more objective measures such as pill counts and the use of electronic pill caps (Arnsten et al., 2001; M. A. Chesney, Ickovics et al., 2000; Liu et al., 2001; Reynolds, 2004; G. Wagner et al., 2004; G. J. Wagner et al., 2000). The fact that this study was cross-sectional means that it was impossible to establish temporal relationships. The study also failed to capture patients who had dropped out of the ART program altogether; by doing so, it may over-estimate adherence. Previous research in Africa has found that only 60% of patients who enter ART programs in Africa remained enrolled at two years, with loss to follow up accounting for over half of the attrition (Rosen, Fox et al., 2007).

The recruitment strategy employed in this study introduced the possibility of systematic bias and may have over-estimated adherence. The primary reason that patients declined to participate was being too busy, which may indicate that this group was different than patients who participated in the survey, with those who declined having less time available to attend clinic appointments and therefore having worse adherence. Additionally, we did not interview people who were picking up medication for someone other than themselves, which may mean that we missed patients who were too sick to attend their clinic appointments. Patients who missed their clinic appointments during the four-week recruitment period were also not included. Finally, we were not able to compare recruitment to the clinic roster and therefore lack information on which patients we missed approaching altogether.

Given the high adherence in the sample, there was limited power to detect differences between those who achieved adherence and those who failed to achieve adherence. The small number of poor adherers limited the number of predictors that could be considered in the final model and precluded the possibility of examining interaction terms. The allowance of five outcome events per predictor variable was acceptable (Vittinghoff et al., 2007), but not as conservative as other recommendations that ten outcome events are necessary per predictor variable (Peduzzi et al., 1996). Following the recommendation of five outcome events per predicator variable could have resulted in finding associations that did not exist (type I error).

Future studies of this type should include a larger sample size to provide more power to detect significant relationships. Longitudinal studies are needed in this setting to understand adherence over time and to explore the factors associated with discontinuation of therapy. It might also be beneficial to conduct qualitative and quantitative research to establish a 'best practice' for measuring adherence by self report in this setting.

This is the first study to look at correlates of ART adherence in Tanzania. It is also the first study of this type among a population receiving free ART and where almost all patients are taking a simple regimen of one combination ART pill twice per day. The results document encouraging high levels of adherence. The factors associated with adherence highlight the importance of understanding age-related factors that may influence adherence, of providing patient-centered quality services, and of ensuring adequate clinic access and follow-up to eliminate missed appointments.

Table 5.4: Factors associated with reporting <95% adherence. The adjusted model used forward stepwise regression to find the best four-factor model to predict <95% adherence.

	n	**% <95% adherence**	**Unadjusted OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**	**p-value**
Age						
19-30 years	54	11.1%	**3.80 (1.26 – 11.44)**	**.018**	**4.26 (1.33 – 13.60)**	**.015**
31-50 years	251	3.2%	REF		REF	
51 years and older	34	14.7%	**5.24 (1.61 – 17.08)**	**.006**	**7.59 (2.10 – 27.43)**	**.002**
Education						
Did not complete primary	69	10.1%	**2.24 (.86 – 5.85)**	**.083**		
Completed primary	271	4.8%	REF			
Marital status						
Married	128	5.5%	REF			
Single, never married	30	16.7%	**3.46 (1.011 – 11.78)**	**.047**		
Divorced or separated	83	3.6%	0.65 (.16 – 2.58)	.539		
Widowed	99	5.1%	0.92 (.28 – 2.99)	.889		
Missed clinic appointment						
Never missed appointment	280	3.9%	REF		REF	
Ever missed appointment	60	15.0%	**4.32 (1.70 – 10.94)**	**.002**	**3.75 (1.29 – 10.89)**	**.015**
Self efficacy to adhere						
For each 1-point decrease			**3.84 (1.42 – 10.36)**	**.008**		
Perceived quality of patient-provider interaction						
For each 1-point decrease			**3.48 (1.56 – 7.78)**	**.002**	**3.18 (1.29 – 7.83)**	**.012**

VI. MANUSCRIPT TWO:

"It's all the time in my mind": A qualitative exploration of factors that facilitate adherence to antiretroviral therapy in a Tanzanian setting

Abstract

Background: Studies show that HIV-positive patients' adherence to antiretroviral therapy (ART) is relatively high in African settings, but few have explored factors that facilitate adherence. Qualitative research that is informed by behavioral theory can help explain how and why patients adhere to ART. Understanding the dynamics of good adherence to ART may contribute to improving and sustaining high adherence.

Methods: The study was conducted at a faith-based clinic in Arusha, Tanzania, where participants were receiving free ART and HIV-related clinical services. Individual semi-structured interviews were conducted with 6 health care providers and 36 patients at the study site. All providers who spent the majority of time giving direct care to ART patients were eligible to participate. The patient sample was selected to include equal representation of men and women at various times on ART. Interviews were conducted in Swahili using interview guides informed by the Social Cognitive Theory. All interviews were audio-recorded, transcribed in Kiswahili, translated into English and coded for themes and patterns with Atlas t.i.

Results: Of the 36 patients (mean time on ART 9.8 months; range 1-23months), 32 reported perfect adherence in the previous month, three reported 98% adherence, and only one reported less than 95% adherence. Self-reported adherence was high despite potential barriers of economic hardship, depression, low rates of HIV disclosure and high perceived HIV-associated stigma. Five factors emerged to explain excellent adherence. First, all respondents experienced substantial improvements in their health after starting ART, which increased their confidence in the medication and motivated them to adhere. Second, respondents developed specific strategies to remember to take pills, particularly routinizing pill-taking by linking it with daily activities or events. Third, their perceived need to be able to meet their family responsibilities motivated respondents to stay healthy. Fourth, material and emotional support received from others facilitated adherence. Finally, respondents trusted the advice and instructions of their health care providers, who regularly emphasized adherence. Interviews with providers suggested that their interactions with patients reinforced patients' own motivations and mechanisms to adhere.

Conclusions: Almost all patients in this setting reported excellent ART adherence, despite the presence of potential barriers to adherence. The facilitating factors identified were consistent with the constructs of the Social Cognitive Theory to explain health behavior and highlight the importance of interventions that address multiple levels of influence on adherence.

Introduction

In 2007, 2.1 million people worldwide died from HIV and AIDS-related illnesses, with over 75% of those deaths occurring in Africa (UNAIDS, 2007). Antiretroviral therapy (ART) offers an unprecedented opportunity to avert deaths of people living with HIV/AIDS, and funds and political will have been mobilized to make ART available where it is most needed. In Tanzania, where approximately two million people (6.5% of the adult population) are living with HIV (UNAIDS et al., 2006), the government is committed to making free ART available to as many residents as possible (Government of Tanzania, 2003). Currently 54,000 people are receiving ART at 200 sites across the country (UN Office for the Coordination of Humanitarian Affairs, 2007).

The success of a national scale-up of ART depends on bolstering the capacity and reach of the health care system and shifting the system's orientation from an acute management model to a chronic care model (Swartz et al., 2002; World Health Organization, 2002a). At the same time, success on ART depends on patients' abilities to adhere to medications, which are influenced by factors extending beyond the clinic environment. Poor adherence can lead to the virologic failure of cheaper first-line treatment regimens and the spread of multi-drug resistant forms of the virus, resulting in a public health calamity (Paterson et al., 2000; Stevens et al., 2004). Poor adherence to all chronic therapies results in increased costs to health and society, in terms of direct financial costs of failed treatment and higher hospitalization rates, and indirect costs of lost productivity of patients and burden on family caregivers (Dunbar-Jacob et al., 2000; Sokol et al., 2005). The impact of sub-optimal adherence to ART is particularly concerning in countries that lack the capacity for regular viral load testing to detect drug resistance and where second-line regimens are prohibitively expensive or not available (Cohen, 2007).

Poor adherence to medication is a problem across chronic conditions. The World Health Organization, in a comprehensive report of adherence to long-term therapies, estimated that just 50% of patients in developed countries were adherent to chronic therapies. They speculated that adherence may be even lower in developing countries, where issues of unreliable supply and financial barriers to access present additional challenges (World Health Organization, 2003). Initial findings about patients' adherence to ART regimens in sub-Saharan Africa, however, show promising outcomes. A meta-analysis of studies on ART adherence found that a pooled estimate of 77% of patients in African settings achieved adequate adherence (most often measured as taking 95% of prescribed pills), compared with just 55% of patients in North American settings (Mills, Nachega, Buchan et al., 2006). A survey of 340 patients in the study site discussed in this article found that 94.1% of patients reported taking at least 95% of their pills over the previous four-day and one-month periods (Watt, unpublished).

At the same time as we are observing good adherence, there is evidence that retention in ART programs may be low. A meta-analysis of ART programs in Africa suggested that only 60% of patients remained enrolled in programs at the end of two years. The ambiguous category of "loss to follow up" accounted for 56% of attrition (Rosen, Fox et al., 2007). The potentially high levels of drop out from ART programs indicate that we require a better understanding of patients' experiences taking ART. Understanding how patients integrate ART in the context of their daily lives and what strategies and motivations they use to adhere may contribute to not only supporting and sustaining good adherence, but also to keeping patients in care over time.

While there is an emerging collection of quantitative studies looking at the factors that create challenges for adherence in Africa (Byakika-Tusiime et al., 2005; Diabate et al., 2007; Eholie et al., 2007; Hardon et al., 2007; Nachega et al., 2004; Orrell et al., 2003; Tadios et al., 2006; Weiser et al., 2003), few studies have explored the factors that facilitate adherence, and how the social and institutional context may contribute to optimal adherence. An exception to this gap in the literature is a study conducted in Kampala, Uganda, which considered factors that facilitated adherence through ten in-depth interviews with patients purchasing ART (Crane et al., 2006). The authors of that study found that near-perfect adherence was motivated by a belief that ART was responsible for keeping them healthy and by a desire to stay alive to look after the well-being of family members. The authors concluded that these motivators outweighed the challenges patients faced securing funds to purchase ART in Kampala.

Nearly all studies on factors that facilitate adherence, with the exception of the one in Kampala, have been conducted in North American settings, where there is a longer history of trying to understand and address adherence to ART. A published review of patient-reported barriers and facilitators to optimal ART adherence identified 23 qualitative studies conducted in North America (Mills, Nachega, Bangsberg et al., 2006). The facilitating factors that were reported consistently across the studies are detailed in Table 6.1. Similar to other chronic illnesses, including diabetes, hypertension and tuberculosis, the factors that influence adherence to ART span across individual, inter-personal and institutional levels (Costa, 1996; S. A. Munro, Lewin, Smith et al., 2007; World Health Organization, 2003).

Table 6.1: Patient-reported factors that facilitated adherence to ART, as identified in 23 qualitative studies in North America (Mills, Nachega, Bangsberg et al., 2006)

Individual level factors

- Having a sense of self-worth
- Having a routine for taking ART
- Belief in the efficacy of ART or expressing "faith" in treatment
- Understanding the need for adherence
- Accepting one's HIV positive status
- Using tools or strategies to remember to take pills
- Seeing positive results when adhering to the ART regimen

Inter-personal level factors

- Having a strong support network
- Being motivated to live for someone else, especially children

Institutional level factors

- Having a trusting relationship with health care providers

Conceptualizing adherence as a function of multiple levels of influence is particularly important in an African context, where health behavior has long been understood as more than an individual choice. In ethnographic research on health-seeking behavior in Central Africa, Janzen and Arkinstall described "therapy management groups", where sets of family members and friends mobilized around patients with the purpose of "sifting information, lending moral support, making decisions and arranging details of the therapeutic process" (Janzen et al., 1978, p. 4). A similar pattern of care has been documented in Tanzania (Juntunen et al., 2002). It is reasonable then to assume that one's kinship system and community, as well as the nature of their interaction with the health care system, play important roles in determining adherence to therapy in Tanzania.

Research on people's experiences taking long-term medication may benefit from the application of behavioral theory as an organizing framework (World Health Organization, 2001). The social cognitive theory (SCT) has been used as a theoretical lens for research and intervention on adherence to ART (Diiorio et al., 2007; S. Munro, Lewin, Swart et al., 2007). The organizing concept of the SCT is reciprocal determinism, which asserts that personal factors, social factors and behavioral factors all interact to determine behavior. According to the SCT, adherence is a function of one's self efficacy to adhere, which is influenced, among other things, by positive reinforcements received to adhere, observational experiences of adherence, skills used to regulate adherence, and expectations of adherence (Baranowski et al., 2002).

This article applied a theoretical framework of the SCT to explore how factors in the clinic setting, as well as in patients' lives outside the clinic, enhanced their motivation and capacity to adhere to ART. It is the first study to document the perspectives of both patients and their HIV care providers on what facilitates optimal adherence to ART in a Tanzanian setting. Understanding the motivations and mechanisms that patients are employing to adhere to their medications, and how these are reinforced in a health care setting, may provide important lessons for the expansion and sustainability of ART services in Tanzania and beyond.

Study setting

The study clinic was founded in 1954 by the Lutheran Church of Tanzania. It includes a 120-bed full-service hospital located on the outskirts of the Arusha metropolitan area and an outpatient clinic in the city center that houses the ART program. As a non-governmental health facility, the study clinic has been a mainstay of health services in Arusha, filling an important gap as government services have been affected by economic crises and structural adjustment measures for much of the last three decades (Lugalla, 2005). Its presence in Arusha is representative of the role that missionaries have played in providing social services in the area since the beginning of the colonial period (Turshen, 1984). The catchment area served by the study clinic includes over 500,000 people, representing the myriad of ethnic groups who either find their roots in or have migrated to urban Arusha. Residents of this area, like in the rest of Tanzania, utilize a combination of traditional healers and formal health facilities (Kayombo et al., 2007; Plummer et al., 2006).

The city of Arusha is home to people who work in manufacturing and in the area's tourism industry, as well as those who do petty business in Tanzania's burgeoning informal economy, including such activities as selling used clothing or hawking household wares on the street corners (Tripp, 1997). A significant portion also relies on farming or the keeping of livestock for their economic livelihood. Residents of this area are generally impoverished. According to the 2004 Demographic Health Survey, only 17% of households in the Arusha region had electricity and only 4% had flush toilets. The majority (67%) of housing had floors made of mud or sand (Tanzanian National Bureau of Statistics et al., 2005).

The first case of HIV in Tanzania was recorded in 1983, and since that time the disease has infiltrated the social landscape, taking on competing representations as a disease of migration, poverty, bad character, youth and modernity (Setel, 1999). The study clinic was among the first health care centers to respond to the epidemic in Arusha, with the establishment of its AIDS Control Program in 1986. First oriented to providing HIV education and prevention, as well as support to orphans and affected families, the clinic began providing ART on a cost basis in 2003. In 2004, with the support of the United States' President's Emergency Plan for AIDS Relief (PEPFAR), the study clinic began offering ART and related HIV services free to all eligible patients. At the time of data collection, approximately 700 adults were receiving ART at the study clinic.

Patients may begin ART at the study clinic after being assessed for clinical readiness and receiving counseling about the medications. Patients who have a positive HIV test result and a CD4 count of less than 200 or any symptoms representing a WHO clinical stage of IV qualify to start ART. Those who qualify are tested for TB and have appropriate blood tests done. The doctors discuss the results of these tests with patients and answer any questions they might have. In addition to clinical assessments, patients receive psychological support in individual meetings with trained counselors before initiating ART. The counselors reported that these pre-initiation sessions last an average of 20 minutes. The counselors provide information about the advantages of ART and what patients can expect, as well as potential side effects of the medication. They emphasize the life-long nature of ART and the importance of adherence, and they ask patients to make a commitment to using the medications as intended. Counselors encourage patients to bring a friend or family member to the clinic for the counseling sessions to ensure the patients have support for taking ART. It takes at least four visits (two weeks) from the time that patients first present to the clinic with an HIV positive test to the time that they are able to begin ART.

The study clinic offers a peer support program for all ART patients, which it launched in 2005. The program pairs voluntary adherence counselors (VACs) with ART initiates, matching them by their area of residence, whenever possible. VACs are HIV positive people who are trained to provide counseling to address problems patients might have taking their medications. The VACs are supposed to support and follow up with their assigned patients for an indefinite period of time. At the time of the study, 15 VACs were serving at the study clinic, and the clinic was making plans to expand the program by training more peer supporters. Patients meet with their VACs when they come for clinic appointments, and

VACs may also visit patients in their homes to understand their living situations, make necessary referrals, and provide supportive counseling to patients and their family members.

After initiating ART, patients must make monthly follow-up visits to the clinic. During these appointments, patients have their weight assessed by a nurse, discuss their progress with a clinic counselor, and meet with a pharmacist to pick up their monthly refill and discuss any problems with the medications. If patients have any clinical concerns, they may also meet with a physician. Patients have their CD4 count measured every six months, providing the only routine clinical marker of their progress on ART.

Methods

This study was part of a larger mixed-methods investigation of adherence to ART. The data presented in this paper include in-depth interviews with six health care providers from the clinic and 36 patients currently taking ART. Health care providers were eligible to participate in the study if the majority of their working time was spent providing direct care to patients who were preparing to take or were taking ART, as determined by the hospital director. Eligible providers included physicians, nurses, counselors and pharmacists. We introduced the study to health care providers at the clinic during a weekly meeting and then approached all eligible providers during working hours.

Patients were eligible to participate in the study if they had been taking ART for at least one month at the study clinic, were at least 18 years of age, and could give informed consent. We used maximum variation sampling with quotas (Patton et al., 2002) to ensure that we included both men and women who had been taking ART for various lengths of time (<6 months, 6-12 months, >12 months). We set a minimum of at least four respondents for each combination of sex and time on ART, and continued recruitment and interviews until we reached a saturation of themes. Participants were recruited by two clinic counselors who routinely met with all patients coming to the clinic to pick up their monthly supply of ART. A member of the study team informed the recruited patients about the study and, if they were interested in participating, read them the informed consent form.

Trained Tanzanian interviewers conducted the individual in-depth interviews with respondents in Kiswahili. Interviews took approximately 60 minutes and followed semi-structured interview guides informed by the Social Cognitive Theory. The interview guide for health care providers included questions and probes about the services they provided to patients and their impressions of patients' experiences taking ART. The interview guide for patients included questions and probes about how ART fit into their daily routines, strategies used to adhere, motivations to adhere, barriers faced in adhering, and self-reported adherence over the past month. All patients and providers who participated in the interviews received 5,000 Tanzanian Shillings (approximately four US dollars).

The research staff audio-recorded the interviews, transcribed them into Kiswahili and translated them into English. Transcription and translation occurred immediately after the interview. Interviews were reviewed in order to: 1) modify the interview guide to explore emerging themes; 2) give feedback to interviewers on their interviewing techniques; and 3) validate the quality and accuracy of translations.

Translated, transcribed interviews were coded using Atlas.ti (Atlas ti, 1997), a software program that facilitates the organization and analysis of qualitative data. In the first phase of coding, deductive codes were drawn from the interview guide and research questions. In the second phase, inductive codes were created and applied to identify additional themes, patterns and categories that emerged from the data (Patton et al., 2002).

The data were summarized through descriptive text-based summaries and data display matrices (Miles et al., 1994; Williamson et al., 2005). Representative, verbatim quotes were selected to illustrate key findings. In selecting the two case studies that illustrated common characteristics in the context of patients' lives, facts that were not relevant to the main theme were changed to protect respondents' confidentiality.

The study received ethical approval from the Institutional Review Board at the University of North Carolina's School of Public Health, The Tanzanian Commission for Science and Technology and the National Institute for Medical Research in Tanzania.

Results

The results are organized to first present the characteristics of the participants who took part in the study, followed by health care providers' perspectives on the clinical context. The social context of taking ART in this setting is then discussed, providing two case studies as illustrations. Finally, the five factors that emerged as facilitating ART adherence in this sample of patients are presented, supplemented by findings of how providers reinforced these facilitating factors with patients.

Characteristics of study participants

The health care providers interviewed represented all of the eligible clinic staff and included two physicians, two nurses, one professional counselor and one pharmacist. There were four male and two female providers, ranging in age from 35 to 49 (mean age 40).

The sample of patients included 19 females and 17 males. The demographic characteristics of the 36 ART patients who participated in in-depth interviews are presented in Table 6.2. The average age of patients was 41.6 years, with male patients being older than female patients (45.9 years vs. 37.7 years). Only 14% of patients had received education

beyond primary school and only 19% of patients had formal employment. Reporting no economic activity was more common for female patients than for male patients (57.9% of females had no economic activity vs. 11.8% of males).

All patients were taking Triomune (manufactured by Cipla in Mumbai, India), a single pill containing stavudine, lamivudine and nevirapine. The pill is intended to be taken twice per day at a 12 hour interval. Patients had been taking ART at the study clinic for an average of 9.8 months (range 1-23 months), although this is not necessarily representative of the study clinic, as our sample was selected for representation by time on ART.

Table 6.2: Demographic characteristics of 36 patients who participated in in-depth interviews

	N
Age	
20-29	5
30-39	13
40-49	11
50 or older	7
Education	
No education	2
Some primary	3
Completed primary	26
Post-primary	5
Religion	
Christian	28
Muslim	8
Marital status	
Never married	5
Currently married	14
Separated/divorced	6
Widowed	11
Main economic activity	
Petty trading	9
Farming/ livestock	7
Formal employment	7
No economic activity	13
Time from home to clinic	
< 1 hour	26
> 1 hour	10

Health care providers' perspectives on the clinical context

The comprehensive approach to services that the study clinic aimed to provide was reflected in the way that health care providers talked about their interactions with patients. Counseling was viewed as an integral part of on-going care and was considered the responsibility of all health care providers. As one provider explained,

> You need to understand a person. Therefore every person needs to be a counselor. Don't say a patient is for [one health care worker or another]. A

> patient is for everyone. Everyone who faces the person should give advice properly. That is how we were told.

Providers emphasized that the content of the counseling was not just about the clinical manifestations of the drugs, but also about the social context of patients' lives. Health care providers gave us the following examples of the types of questions they posed to patients during their meetings: "What are the things [you] encounter that make [you] despair, or things that encourage [you]? How do [you] face that?"; "How does the community see you now?"; "Do [you] get enough food? Does the food have all the nutrients the body needs?"; "How is home? Do people at home know that you are using medicine? Who usually helps you to use medicine?" Patients themselves confirmed having these types of conversations with providers.

All of the health care providers with whom we spoke talked about a personal motivation to serve patients, which was in part grounded in the faith-based orientation of the clinic. Although the clinic was not evangelical in its approach with patients, staff started each workday with a period of prayer and singing and closed all meetings with prayer. For at least two providers, their motivation to serve patients was related to the Christian ethic of the clinic, as one provider explained:

> We enjoy serving [patients] because this is a church center. Therefore when you serve the patient you see them like you are a part of their problem. So when you serve them you do it with all your heart.

Social Context

Patients described themselves as having some important characteristics that influenced their experiences living with HIV and taking ART. These characteristics, which were common across the majority of patients, shed some light on the life experiences of patients in this setting. First, almost all patients reported economic insecurity, exacerbated in many cases by long periods of HIV-related illnesses, losing a spouse, or both. Although no patients mentioned lack of food or money for transportation as a reason for non-adherence, both came up repeatedly as concerns for patients. When asked what additional support they would like from the clinic, the most common responses were food support and small loans to initiate business ventures. Second, many patients expressed feeling depressed or hopeless after being diagnosed with HIV, often related to a belief that HIV was a death sentence. For most patients, as their health improved with ART, so did their emotional state. Religion played an important role in regaining a sense of hope and purpose. Third, almost all patients disclosed their HIV status very selectively in their social networks. Patients decided whether to disclose based on the emotional closeness of a relationship, the perceived ability of a person to maintain their confidentiality, and how they thought a person would react to their HIV status. Patients reported that when they were around people to whom they hadn't disclosed their HIV status, they either hid their pills or told people the pills were for something other than HIV. Lastly, most patients expressed a fear that people would treat them differently if they knew they were HIV positive, although less than half reported directly experiencing any stigma themselves. As one man said, "I was hearing that if you tell people about this problem, they will stop coming to my house or they will discriminate against me."

To illustrate for readers the experiences of patients taking ART in this setting, two case studies are presented. Each case highlights some of the important characteristics consistent across the 36 patients who participated in this study.

Case study 1: Bahati (pseudonym)

Bahati is a 42 year old woman with a primary school education. She has never married but has had several long-term relationships, most recently with a married man. She lives with her three children in Arusha in a two-room mud house on a small plot of land next to her parents and brother. The house has electricity but no indoor toilet, and she must buy water from a public water pump 30 meters from the house. She keeps livestock as a means to support her children.

Bahati came to the clinic after suffering from recurring illnesses and weight loss. “I was fat before! All the clothes I used to wear didn’t fit me. I was losing weight with no reason.” At the clinic she was advised to test for HIV. When she was diagnosed in August 2006, she was very depressed. “The day I got my results was a difficult day. I didn’t sleep up to the next day. I mean, when I entered the room and my children called for me, I said they are calling me but I am going to die.” Soon after getting diagnosed Bahati became a “saved” Christian and found emotional support in religion that allowed her to accept her status and let go of her fear of death.

Bahati started ART two months after being diagnosed, and had been taking the pills for three months at the time of the interview. She has experienced significant improvements in her health since starting ART. “I am now energetic unlike before I started taking this treatment. For sure they have helped me, and I expect more good changes.” She understands the life-long nature of the pills and the importance of adherence. She takes her pills at 7am and 7pm and has arranged her schedule to make sure she is home during those times. She said she has not missed a single pill since starting ART, and she worries even if she’s a few minutes late in taking her pills.

Bahati has shared her status only with one female friend. She does not want to tell other friends or family because of a fear of abandonment. Her ability to conceal her HIV status is made easier by the fact that she has experienced clinical success on ART and appears healthier. Bahati says about her choice not to disclose: “You can tell someone and create another problem. But now I am living happily because no one knows, they are still cooperating with me very well. But what if they knew? They will isolate me.” She doesn’t see her non-disclosure as impeding her ability to take her pills, because she says people don’t know that the pills she is taking are for HIV.

When asked about taking ART for the rest of her life, Bahati responded that the medication has become part of her life. “I can’t stop because since I started to use the pills they help me. I can take care of my kids. I never asked for help; I do my work as usual; I’m strong; I have hope. So I do not worry and I must use my pills.”

Case study 2: Japhet (pseudonym)

Japhet, a 30 year old man, moved to Arusha from his village after completing primary school. He initially worked selling trinkets on the street and doing manual day labor (“pulling a wheelbarrow”) until he saved enough money to start a small shop selling basic food and household commodities. He married at the age of 19 and his wife gave birth to four children, one of whom died as an infant. At the time of the interview, his wife was pregnant with another child. He reported that he had several affairs with other women during times when he and his wife were not on good terms, and he believes that his infidelity was the source of his HIV infection.

Japhet suffered from recurring illnesses for an extended time before getting tested for HIV. He talked about seeking treatment without getting a clear diagnosis: “They told me at the hospital that it's malaria. After five months, I got malaria again, then typhoid. They gave me medicines but they were not telling me the problem." As his health deteriorated, he couldn't keep up his business and his capital dwindled. When his wife also began to get sick, he realized this may not be "normal illness" and decided to get an HIV test at a voluntary counseling and testing (VCT) center. After getting his result, Japhet was distressed. "I was disappointed and thinking a lot of things, like my children are still young and I'm going to die."

Japhet was referred to the study clinic from the VCT center, and started ART less than a month after his positive diagnosis. At the time of the interview, Japhet had been taking ART for five months. He had some nausea for the first few weeks, but then experienced great improvements in his health, which allowed him to go back to his normal activities: "Before I was getting up at 10am and felt tired by noon. But now I'm waking up at 6am without forcing myself." His daily routine is to wake up at 6am, open his shop, eat breakfast, brush his teeth and then take his pills. If he goes out of the house in the evening he takes his pills with him. During the first month he missed a day of taking his ART because he didn't return to the clinic in time for his refill. Now that he is familiar with the schedule of coming to the clinic for refills, he said he has not missed a single pill. However, Japhet expressed lack of knowledge about the life-long nature of ART ("I said to myself, 'Will I use these for the rest of my life?' I don't know.") and the importance of keeping to a regular timetable ("I usually take them at 7 in the morning and evening or 10 in the morning and evening. Tell me, is there any problem to do this?"). Despite his lack of understanding of the life-long nature of ART and the ideal 12-hour dosing schedule, Japhet continues to take his pills every morning and evening at the instructions of the doctor, and doesn't plan to stop until the doctor gives him permission.

Japhet's wife is also HIV positive but according to Japhet she has not started ART. She blames her husband for infecting her with HIV. She refuses to have sex with him, which has led him to sleep on the floor of his shop, while his wife and children stay in their rented room. Other than his wife, only his brother knows that he is HIV positive. Although this brother isn't able to support him financially, he goes to his brother when he has problems he needs to discuss. He hasn't told other relatives because he does not think they will be supportive. If people see him taking his pills at the shop he tells them "I have chest problems."

Although Japhet's health has improved considerably since starting ART, he still struggles with his economic situation and his relationship with his wife, as well as coming to terms with his HIV status: "Some of the time when I remember that I'm positive I get pain and think backwards [to the past]. But after a moment this disappears."

Self-reported adherence

The case studies above highlight some of the potential barriers to ART adherence in this sample, including economic insecurity, depression, limited HIV disclosure, and high perceived stigma. Despite these potential barriers, the majority of patients had perfect adherence as measured by a single question of how many pills they had missed over the past month. The question was preceded by normalizing language ("It is not unusual that patients miss taking a pill for various reasons"). In response to this question, 32 of 36 respondents said they had not missed any pills. Three patients said they had missed a single pill during the previous month (equivalent to 98% adherence), giving the following reasons:

- (Female, 30, 4 months on ART) Busy with an evening church event
- (Female, 35, 10 months on ART) Fell asleep early and missed an evening pill
- (Female, 53, 13 months on ART) Busy in the morning and forgot

One respondent had intentionally stopped taking her pills for ten days (Female, 31, 18 months on ART). The reason she gave for discontinuing therapy was that she had malaria and was vomiting. She said that when she explained this to the counselor at the next clinic appointment, she was advised to resume taking her pills and she did so.

Reasons for overall excellent adherence

Based on respondents' narratives of their experiences taking ART, we identified five primary factors that facilitated adherence (Table 6.3).

Table 6.3: Factors that facilitated ART adherence in the sample of 36 patients

1.) Patients experienced substantial improvements in their health by taking ART, increasing confidence in the medication and motivation to adhere.
2.) Patients were motivated to stay healthy and alive for the well-being of their family members, especially their children
3.) Patients made pill-taking part of their daily routine
4.) Patients received material and emotional support from others
5.) Patients trusted the advice to adhere given by service providers

1. Patients experienced substantial improvements in their health by taking ART, increasing confidence in the medications and motivation to adhere.

Most patients had suffered severe and sustained illness before being diagnosed with HIV. Twenty-five of the patients (71%) had a CD4 count of less than 200 at the time of diagnosis, requiring them to start ART immediately. As a result of having experienced long periods of illness, most patients had vivid illness narratives and an understanding of the devastating impact of HIV on their bodies. These periods of illness contrasted sharply with improved health after starting ART, which increased confidence in the medications.

> I was sick for a long time, since 2002 up to 2006, and my main food was soda and pain killers…. It's true that my life is good now. Since I started to take these drugs, I have no headache, no leg pains, and no body pains. (Male, 49, 6 months on ART)

Only about a third of respondents said they experienced side effects when starting ART (mostly abdominal symptoms), and all patients said that they had experienced improvements in their health on ART. Patients pointed to their increased weight, energy and the fact that they could return to work. The marked improvement in health and resumption of normal activities attributable to ART created a strong motivation to continue taking the drugs.

> I have no such idea of stopping to take them for sure, because I was too much tortured before. I was sick for a very long time, I was just sleeping in bed. But now I am not. Therefore it's not easy for me to stop them because they are the ones that made me better. (Female, 45, 17 months on ART)

The perceived benefits of adhering were closely linked in patients' minds to perceived negative consequences of not adhering. When asked about the impact of missing pills or stopping ART altogether, most patients mentioned a fear that they would return to their previous condition or die. The association between adherence and avoidance of severe illness or death was evident even among patients who had been on ART for over a year and whose health had plateaued at a healthy state.

> I will die if my previous situation comes again. I am worried about it. Therefore I carry pills anywhere; even now I have them in my bag, because I may go out and sometimes be late, so I must take them. (Male 55, 14 months on ART)

Health care providers said that they emphasized to patients the benefits of adhering to their ART for improving their health and prolonging their lives. A nurse said to a patient whom she suspected of poor adherence, “I told him that these medicines are for prolonging your life, and if you stop you will go back to the condition you had before.” Another provider said that he sometimes held up examples of other patients or the VACs to illustrate the positive benefits of ART. “Sometimes we give them live examples, comparing a patient when they first started to their present condition. That helps them not to lose hope, to show them the medicine helps them.”

2. Patients were motivated to stay healthy and alive for the well-being of their family members, particularly their children.

Patients’ desire to improve their health and prolong their lives was as much a social motivation as an individual one. HIV affects people at the height of their reproductive cycle, and as a result the majority of respondents (31 of 35) had children under the age of 18. Patients’ experiences of near-death illnesses and their diagnosis with HIV, which many initially assumed was fatal, was often accompanied by a fear of not being able to support their families financially or leaving their children as orphans. One man explained that his immediate reaction to his HIV diagnosis was asking, “Who will I leave my wife and kids with? I really wanted to see them start and finish their studies, the least I could do for them.” Taking ART offered patients an opportunity to return to work, support their families, and be around to take care of their children. Success on ART, achieved through adherence, allowed patients to resume or retain their roles in the lifecycles of their families.

The desire to be around for their family’s well-being was a motivator to become healthy and therefore to adhere. Children as a motivator was expressed by more men (7) than women (2). As one man said, “I could never give up because I have kids.” The following man had three children, ages 11 to 14. When we asked him how he felt about taking ART for the rest of his life, he replied:

> I use these drugs to prolong my life and to make sure my children go to school until they grow up. If you miss taking these drugs, you're going to die. And you will leave the children as orphans. (Male, 36, 10 months on ART)

Another man was married to two women, one of whom died of HIV and the other who left him after he told her about his HIV status. He felt responsible for his 16 children, and decided to start ART in order to act on that responsibility:

> I have a large family of 16 children, and my father is in [the village], and he is very old now. So I decided to use the drugs for me to be able to take care of my family. (Male, 49, 6 months on ART)

Two patients in our sample had only grown children. Those patients expressed shame about their HIV status and the burden they were placing on their children as a result of their illness. Although it was never explicitly mentioned, the desire to regain health in order to reduce the burden on adult children may also facilitate adherence. One man explained:

> It's hard to seek support, crying for support… I do not want to be a burden to them, because I am supposed to help my children, not my children helping me. (Male, 55, 14 months on ART)

Only one health care provider talked about drawing upon motivations for family obligations to support a patient's adherence. She was advising a female patient who struggled to take her ART by saying to her, "Your weapon is medicine because your children are still young. If it were not for the medicine you wouldn't be alive to support them."

3. Patients made pill-taking part of their daily routine.

The requirement that ART be taken at the same time every morning and evening meant that patients had to adapt their routines to incorporate taking their pills. Almost all patients explained that they had very consistent and predictable schedules, with little variation, which made it easier to incorporate pill-taking. The following woman explained how taking ART at 10AM and 10PM fit into her daily routine.

> I arranged to take them at 10AM. I can just wake up and do my work. I do the dishes, mop, take a shower, then at about 9:45 I take my tea. I look at my watch and at 10am I take my medicines. If I have somewhere to go, I go, and when I come back, I prepare food, prepare my children, they eat and take time watching sports. And my husband and I are just resting after we finish fetching water, because we normally fetch water at night. So after fetching water, the children have already eaten, and I sit down and eat. I just look at the time while eating. And when it reaches 10PM I stop eating and take my drugs. After that I take a short rest and I go to sleep. (Female, 30, 6 months on ART)

Patients talked about their efforts to keep regular schedules and prioritize the time to take their pills, as explained by the following woman.

> Using them becomes like a normal timetable, like that of a working schedule. For example if you have a cow, when you wake up you know at what time you're going to feed that animal, and this is the same with my drugs. I have the same timetable. I can't do my work without taking the drugs first, then after I take my drugs then I am free to work. (Female, 40, 4 months on ART)

When we asked patients how they remembered to take their pills on time, many simply said that it's "hard to forget" or "always on my mind." One patient said "I take it as food, which you have to eat every day." The dominance of ART in patients' daily thoughts and activities seemed to be related to a constant memory of their previous condition and the life-saving nature of their ART. One patient compared his consciousness about ART to a soldier who must always be aware of where his weapons are located.

> You know we are like soldiers who are taking care of the weapons and they're not supposed to leave it anywhere. So I always take my pills when I leave the house. (Male, 49, 4 months on ART)

The primary disruption in patients' schedules was traveling out of town for work or to visit family, or being busy and out of the house for long hours. When asked about this, respondents said that they prioritized pill taking and had strategies for carrying their pills, water and food. Patients who traveled out of town usually said that their pills were the first – and most important – thing they packed when getting ready for a trip.

> I can't forget - it's all the time in my mind. When I have a trip I'd better pack my pills and forget my clothes. And I go with enough water to last every day. (Male, 31, 13 months on ART)

Patients also talked about strategies they used to remember to take their pills. Four respondents said they set alarms on watches or cell phones (cell phones were common in this setting). More often, however, patients anchored the time of taking their pills with other regular activities, such as meal or tea times, brushing their teeth, prayer, or radio or television programs.

A doctor we spoke with told us how he advised patients about different strategies they might use to remember to take their ART.

> We normally advise them to use the alarm clock, so they set it in the morning at 7, or whatever time they decided to take the medication. So when the time comes the clock will ring. We also say that they should put the medication bottle close to where they put their toothbrush so when they go to brush their teeth they know that this is time for their medicine, so they take the medicine and they brush their teeth. So then they remember. Also when they go to sleep, if there is a place where they normally put something important they should put the medication at the same place; therefore when they go around they find their medicine right there.

4. Patients received material and emotional support from others to help them take their ART.

Social support facilitated adherence through direct reminders to take pills, material support of food and money, and emotional encouragement. As mentioned earlier, most patients disclosed their HIV status selectively within their social networks. Twenty-nine told a select group of people they were HIV positive, six told everyone in their social network, including family, friends and neighbors (although one man in this group said he did not want his elderly mother to know and one woman was withholding the information from her landlord), and only one person told no one. Respondents made decisions about whether or not to disclose to people in their lives based on perceptions of support they would receive from each person. As this woman shared: “Some people when you tell them they will feel you are dying now. It seems as you shock them. They are not happy and you are not happy either. Therefore it is not in all situations that you are open.” Disclosure was often seen as a strategy to garner support for living with HIV and taking ART.

The most direct way that patients received support to adhere was through explicit reminders to take their pills. Fourteen respondents said they had someone who provided these reminders. When the patient’s spouse or partner was also taking ART (five respondents), they usually reminded each other. As one man said of his wife, “She is the one who reminds me about the pills and gives me food. We help each other a lot.” Ten respondents said that their children reminded them of the time to take their pills, even if they hadn’t directly disclosed their HIV status to their children. One woman, whose own child was only three, had engaged other children in the neighborhood to remind her: “At the place I am living there are children. So I told those children to remind me when it reaches 8:00. I told them to come to tell me wherever I am.” Other respondents had family members call them or visit them to remind them to take their pills.

Most respondents (24 of 36) received material support, primarily from family members, in the form of food and money. Respondents gave the impression that the supporters gave material support because of the general hardships the respondents were facing in their lives, not explicitly because of their HIV status or to help with taking their ART. Nevertheless, respondents spoke about the importance of this type of support for taking ART, as this respondent related: “If you want to enjoy taking these pills and have them help you, you must have some food. If you have some food, then there is no other problem."

Although our questions about support first elicited responses about reminders and material support, probing by interviewers also revealed that patients received important emotional support that made it easier for them to take their pills. Almost all respondents (29 of 36) talked about receiving some emotional support, often related to general encouragement or to 'normalizing' HIV and giving examples of other people with HIV who were living productive lives. One female patient who was taken in by her brother and his family after she became ill said that her brother and sister-in-law not only reminded her to take her pills, but also encouraged her to live positively with HIV, which seemed to increase her motivation to take her ART properly.

> They really help me, give me advice. Even encourage me, because sometimes I feel heartbroken. To some extent they help to give me courage, so that I can see it as a normal thing. (Female, 30, 4 months on ART)

While the vast majority of patients said it was family members who provided the most important support to them, two patients pointed to friends in this role. One woman explained how her in-laws took all her property after her husband died of HIV and insisted that she come live with them in the village. When she decided to stay in town, she was given support by a close friend of her deceased husband. The friend rented her a room and put her in touch with a church that could provide her with food support. He bought her a mobile phone so that she could set an alarm to remind her of the time to take her pills and so that he could call her to check that she had taken them.

The voluntary adherence counselors (VACs) at the clinic also played an important role in providing support to patients. Almost all respondents (33 of 36) said they had a VAC assigned to them. Of those, 26 said that their VACs gave them important information relevant to adherence, and 14 said that their VACs gave them some form of emotional support. The fact that the VACs were also HIV positive made the information and emotional connection even more salient. As one woman said, “When you talk with a person with the same problem as you it’s easy to understand each other well.” The importance of emotional support provided by the lived experiences of their HIV positive peers was expressed by the following respondent.

> She told me that she was so sick (before), only sleeping at home…. She told me she was suffering, until people were afraid. But today they forgot that she was like that. She gave me hope because of how she changed and improved. She gave me hope so that I’m serious about using ART. (Female, 40, 4 months on ART)

Health care workers spoke about their efforts to engage family members or friends in patients’ care. They did this by encouraging patients to bring their supporters to clinic appointments, counseling the supporters when they attended, and having VACs follow up with family members in the home. This doctor talked about the benefits of engaging the patient’s support system.

> It is a benefit, especially for adherence to the medication. It is believed that if they involve a second person, it reduces stigma first and then it improves adherence to the medication. And these people can also assist them to take medication, like telling them that they forgot this medication today. Or sometimes the patient asks the relative to come and collect the medication, in case they can’t come themselves.

5. Patients trusted the advice of service providers

Lastly, patients expressed an absolute trust in the advice of service providers at the study clinic, which motivated them to adhere. Patients consistently said that counselors, doctors and VACs all emphasized the importance of adherence in their interactions. Patients accepted this advice without reservation, in no case questioning the expertise or advice of these providers. Having trust in the advice of service providers allowed patients to overcome any lack of knowledge about the impact or long-term nature of ART. When we asked the following patient if he believed that the ART might cure him completely of HIV, he said he wasn't sure. When we followed up to ask if he would ever stop taking his ART, he told us that he would not stop until instructed to do so by the doctor.

> I will not stop, even if there are side effects, because I was told to use it. If I stop for some reason, it will be bad. If the doctor who gave me the pills tells me that I'm supposed to stop, I will stop, but apart from that I will use it, even if there are side effects. (Male, 49, 4 months on ART)

Overall, patients felt very positively about the services they received at the study clinic, particularly comparing the study clinic to other clinical settings they had experienced. The things they appreciated about the clinic were the information they received on taking ART and the openness of staff to addressing their problems. One patient told us:

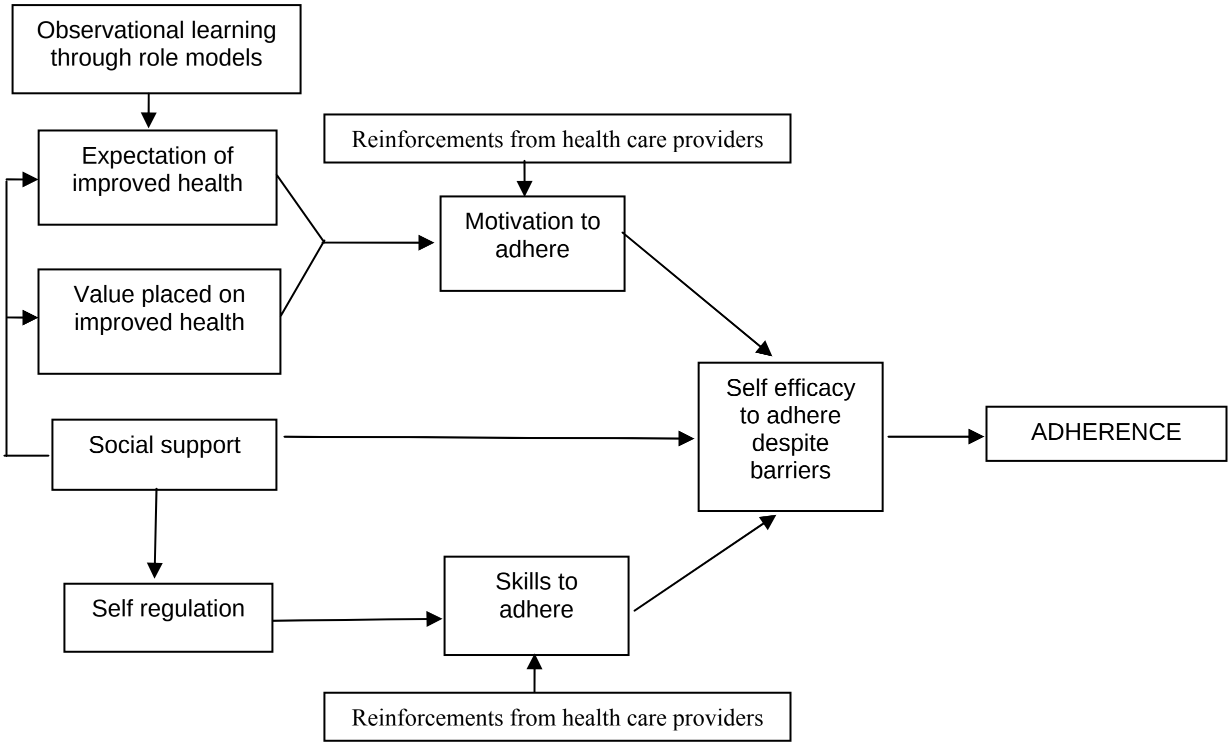
> There are good services here compared to other clinics, where they don't want to listen to patients. There, when you talk to a doctor they already call in the next person. So these services here are good. Let them keep it up. (Male, 49 years old, 3 months on ART)

Trusting health care providers may in part have to do with the relationships that providers tried to build with patients. One provider explained how he related to patients: "I make jokes sometimes to make patients feel comfortable, so you can explore their insights and they can tell you how they feel…. You feel free to chat with patients and they feel free to chat with you." Another provider recognized the importance of building such relationships when she said, "It is important that they trust you a lot. So we are trying to build good relationships between the patients and the staff."

Synthesis of facilitating factors

The factors that emerged as facilitating adherence to ART in this setting resonated with the constructs of the Social Cognitive Theory (Baranowski et al., 2002). Factors at the individual, inter-personal and institutional levels interacted to positively influence adherence. Patients drew upon their own personal experiences (being ill and recovering with ART) as well as role models of the VACs to develop expectations of positive adherence outcomes that motivated their behavior. The desire to support their families placed added value on the outcomes of renewed health and sustained life. Emotional support in the form of "normalizing" HIV increased motivation to adhere. Patients exhibited self regulation in developing strategies to integrate adherence in their daily routines, which was supported by reminders from friends and family. Health care provider reinforced patients' inherent motivations and skills. Together, these factors appeared to positively influence patients' self efficacy to adhere to ART, despite the presence of potential barriers (Figure 6.1).

Figure 6.1: Explanatory model of factors that facilitated ART adherence in this sample



Limitations of the study

The results of this study must be interpreted in light of the study's limitations. First, the high adherence we found in this setting must be interpreted cautiously because of the possibility of self-reporting bias (Bell et al., 2007). Self-reported measurements of adherence likely over-estimate adherence due to recall bias and social desirability (Arnsten et al., 2001; M. A. Chesney, Morin et al., 2000; Liu et al., 2001), but self-reported adherence measurements have nevertheless shown to be associated with other, more 'objective' measurements of adherence (Arnsten et al., 2001; Oyugi et al., 2004) and to be associated with viral load (Arnsten et al., 2001; Duong et al., 2001; Fairley et al., 2005; Fletcher et al., 2005; Liu et al., 2001). Second, the themes reported in this paper are limited to the issues that individual respondents chose to discuss during the interviews. While the interview guide included broad questions and probes for follow-up, the depth of discussion on the topics was not standard across the interviews. The proportion of patients reporting various factors must be interpreted as descriptive only, bearing in mind that not all patients were asked the same questions in the exact same way. Additionally, no observations were conducted of patient-provider interactions, requiring us to rely solely on self report, which is subject to social desirability bias. Finally, as applies to any qualitative study, the results are not meant to be statistically generalizable to a larger population, but to illuminate aspects of experience and context that may be shared by others.

Discussion

This qualitative inquiry suggests that the contexts of patients' lives present potential barriers to ART adherence that have been observed in other studies. These include poverty, emotional distress, low rates of HIV disclosure, and high levels of perceived HIV-associated stigma (Fogarty et al., 2002; Hardon et al., 2007; Mills, Nachega, Bangsberg et al., 2006; Sankar et al., 2006; Vervoort et al., 2007). Despite the potential barriers, self-reported adherence was excellent for this sample, with 32 of 36 patients reporting perfect adherence over the past month and only one patient reporting less than 95% adherence.

Similar to other studies (Abel et al., 2003; Adam et al., 2003; C. Golin, Isasi et al., 2002; Misener et al., 1998; Murphy et al., 2000; Remien et al., 2003), a primary factor that facilitated adherence in our sample was a belief in the efficacy of the medications to improve health and prolong life. This belief came from patients' subjective experiences transitioning from debilitating illnesses before starting ART to improved health after initiating therapy. Recalling their previous illness served as a strong motivator to adhere to their medication. The clinic environment, including having the VACs as role models and the counseling provided by health care providers, likely reinforced the benefits of ART for patients and enhanced their motivation to adhere.

A desire to be alive to support their families also motivated patients to adhere, as has been documented in other studies (C. Golin, Isasi et al., 2002; Murphy et al., 2003; Remien et al., 2003; Richter et al., 2002; Sankar et al., 2002; Stone et al., 1998; S. A. Wood et al., 2004). However, while most of these other studies have documented patients' desire to be around to "see their children grow up," respondents in this study spoke more about their responsibility for the economic well-being of their children, particularly to ensure that their children get an education. In addition, while most North American studies have documented family as a facilitating factor of adherence primarily among women (Misener et al., 1998; Remien et al., 2003; Richter et al., 2002; S. A. Wood et al., 2004), in this study it was a more salient theme among male patients. This must be understood within the context of the patrilineal system of Northern Tanzania, where men are often the key decision makers in areas of child rearing and care that require significant outlays of funds, including post-primary education, vocational training, or semi-formal apprenticeships that children might receive to establish their own economic independence. Men feel an obligation to meet these costs and see their children 'established' in this way (Personal communication with Philip Setel, 2007).

Patients reported consistent and predictable daily routines, which made it easier for them to integrate pill-taking into their daily lives. North American studies have documented unstable lives, shifting routines, and the fact that "every day is different" as one of the primary challenges to taking ART on schedule (Adam et al., 2003; C. Golin, Isasi et al., 2002; Murphy et al., 2000; Ryan et al., 2003). Because patients in this sample had consistent routines, they could anchor their pill-taking to daily events like morning tea, brushing their teeth, or bedtime. Having a simple medication regimen (one pill twice a day) may also have contributed to more ease in integrating pill-taking into their daily routines. Regimens that have fewer pills and doses have been associated with better adherence to ART and other chronic therapies (Bangalore et al., 2007; Diabate et al., 2007; Mills, Nachega, Bangsberg et al., 2006; Orrell et al., 2003). The greatest disruption to daily routines in this sample was travel, but patients who traveled talked about strategies for carrying their pills with them and taking their pills while out of the house. The self-reported consistency of patients' routines would benefit from validation by ethnographic observations, which might reveal changes over time and across seasons that were not reported in the interviews.

The positive influence of social support on adherence has been documented in both qualitative (Adam et al., 2003; Campero et al., 2007; Klitzman et al., 2004; Malcolm et al., 2003; Remien et al., 2003; Sankar et al., 2002; Weiss et al., 2006) and quantitative studies (Diabate et al., 2007; Gonzalez et al., 2004; Gordillo et al., 1999; Murphy et al., 2004; Vyavaharkar et al., 2007). Social support arose as an important facilitating factor among this sample, taking the form of direct reminders, financial help and emotional support. While reminders and emotional support have been documented as facilitating adherence in the qualitative studies cited above, the expressed importance of financial help was unique to this setting. This is likely related to the poverty in our sample, the lack of public assistance, and the potential barriers to adherence of hunger and transportation costs, which have been documented in other African settings (Hardon et al., 2007).

The support that people received to cope with their HIV infection appeared to be more on the basis of individual, one-on-one support, rather than a group of people mobilizing to support the patient, as has been found in response to acute illnesses (Janzen et al., 1978). This may be due in part to the nature of disclosure (and non-disclosure) of HIV, as well as the fact that respondents were discussing the sustained, rather than illness-focused, support that they received. Health care providers in the study clinic recognized the influence of patients' support networks on adherence and encouraged patients to involve their supporters in routine care. The VACs at the clinic also provided information and emotional support that particularly resonated because of the VACs' personal experience living with HIV.

Finally, patients' trust in the advice of health care providers and VACs facilitated adherence in this sample. Patients perceived these providers as referent authorities whose advice they should follow without question, and the advice they were being provided was to adhere to their medication. The influence of patient-provider relationships is consistent with findings from other qualitative studies (Abel et al., 2003; C. Golin, Isasi et al., 2002;

Malcolm et al., 2003; Murphy et al., 2003; Murphy et al., 2000; Remien et al., 2003; Roberts, 2002; Sankar et al., 2002). Providers in the study clinic recognized the importance of building trusting relationships with patients, and did so by having thoughtful conversations with patients and attempting to reduce the gap between provider and patient.

The clinical environment itself likely had a positive influence on adherence in this setting. The health care providers we spoke with all expressed a personal motivation to do their work, grounded in an ethic of service that seemed in part influenced by the faith-based orientation of the clinic. The fact that the study clinic aimed to provide a continuum of care to patients by offering a range of services for people living with and affected by HIV/AIDS reflected a broader commitment to seeing patients as whole people with needs and influences outside of the clinic setting. Strong patient-provider relationships are essential components of a chronic care model that can support and sustain adherence over time (Swartz et al., 2002; World Health Organization, 2002a). Although this study was not a formal evaluation of the VAC program, the findings do suggest there was a positive influence of this peer support program for people taking ART. The HIV positive peer supporters provided role models for how HIV positive individuals may return to good health by making a commitment to taking ART. Counseling that these peers provided to patients based on their own personal experience was particularly salient. In addition, home visits by these peers have the potential to further engage the patients' natural support systems. A future direction of research is to examine the VACs program for its impact on patients' adherence.

The findings presented in this paper highlight the importance of, first, understanding the motivators and strategies that patients are employing to adhere and, second, integrating that understanding into the health care system so that providers can recognize and reinforce patients' inherent motivators and strategies. The implication for practice is that ART programs and their targeted interventions must address not only each of the levels of influence, but also find ways to ensure connections and reinforcements among these levels. Comprehensive ART programs that make these connections and are grounded in the unique social context of their settings have shown success in promoting and sustaining adherence (Koenig et al., 2004; Mukherjee et al., 2006; Weidle et al., 2006).

Future research on this topic may benefit from different methodological approaches using qualitative methods. Observations of patient-provider interactions would provide more information about the nature of communication and would validate self-reported findings from providers. To understand how patients' support systems influence adherence, studies should seek the perspectives not only of patients, but also of other actors in patients' lives essential to sustaining adherence. Finally, because adherence is a dynamic process that may change over time, multiple contacts with respondents may be more useful than single interviews (Conrad, 1990).

Despite the limitations faced in the study, this is the first qualitative study on the factors that facilitate patients' adherence to ART in Tanzania, and it therefore increases our understanding of why adherence might be high in a low-resource setting, despite the presence of potential barriers.

VII. CONCLUSIONS

Summary of findings

Guided by a theory-informed conceptual framework, this study set out to understand the factors that influenced patients' adherence to antiretroviral therapy in a single clinic in Tanzania. The study was undertaken with four aims: to assess the level of adherence in a sample receiving free ART in Tanzania; to identify significant correlates of ART adherence; to explore how the social environment of patients' lives supports ART adherence; and to assess the role of mediating and moderating factors in the relationship between social support and adherence. The qualitative and quantitative methods used to address these aims complemented each other and produced a richer understanding of adherence in this setting.

<u>*Aim one*: Assess the level of adherence in a sample receiving free ART in Tanzania</u>

The study identified high levels of adherence in this sample. As reported in the first manuscript, over 94% of patients in the survey interviews reported optimal adherence in both the previous four days and previous month. The finding of high adherence is encouraging, as it represents better adherence than has been measured by self report in other African settings (Byakika-Tusiime et al., 2005; Diabate et al., 2007; Eholie et al., 2007; Nachega et al., 2004; Weiser et al., 2003). The high adherence may in part be explained by characteristics of the clinical services. All patients in the study were receiving ART and related laboratory and treatment services at no cost, removing a financial barrier that has been observed as an adherence barrier in other settings (Byakika-Tusiime et al., 2005; Eholie et al., 2007; Weiser et al., 2003). Additionally, almost all patients in the study were taking very simple ART regimens that involved one pill twice a day, which has not been the case for previous studies on adherence in Africa. An increasing number of doses and pills have consistently been associated with poorer adherence (Ammassari, Trotta et al., 2002; M. Chesney, 2003; Diabate et al., 2007; Laniece et al., 2003; Orrell et al., 2003).

Aim two: Identify significant correlates of ART adherence

While adherence was high in this setting, not all patients managed to adhere to their medication. Three factors emerged that differentiated those who achieved adequate adherence from those who did not achieve adequate adherence. Both patients who were younger (19-30 years) and older (over 50 years) were at greater risk for poor adherence, compared with patients ages 31-49. Patients who had ever missed a clinic appointment were more likely to report poor adherence. In addition, patients who had a lower assessment of the quality of their interaction with providers reported poorer adherence.

Aim three: Explore how the social environment of patients' lives supports ART adherence

The in-depth interviews, presented in the second manuscript, helped to explain the factors that facilitated adherence in this setting. The facilitating factors represented influences at the individual, inter-personal and institutional levels. The most important facilitator appeared to be patients' belief in the efficacy of the medication based on their personal experience. All patients were able to contrast their poor health prior to starting ART with their improved health after starting the medication, which increased their motivation to adhere. Patients believed that if they did not take their drugs properly, they would likely face illness or death, and they wanted to avoid this in order to be around to support their families. Their families in turn provided them with reminders, material assistance and emotional support that helped their adherence. Patients had very predictable and consistent routines that allowed them to easily integrate a schedule of taking their medication regularly and on time, and they developed skills and strategies to remember to take their pills properly. Finally, patients trusted the advice of their providers, and providers worked to build strong and trusting relationships with patients.

As this was not a comparative study, it is impossible to definitively attribute the high adherence in this setting with the characteristics unique to the study clinic. However, the interviews with patients and providers give reason to believe that the nature of the setting had some positive influence on adherence. The mission of the clinic to "serve, treat and minister to the whole person, in body, mind and spirit" appeared to contribute to clinic staff respecting and responding to the patients' social context. Counseling was a central component of the ART services and providers encouraged patients to bring their family members with them to appointments. Clinic staff expressed a motivation to serve patients, grounded in the faith-based orientation of the institution, which might have resulted in better quality of care compared with their counterparts at large government-run hospitals.

The data from the second manuscript underscored the contribution of the social cognitive theory and the construct of social support for understanding adherence in this setting. The in-depth interviews highlighted how patients' expectations of adherence outcomes, the values placed on those expectations, observational learning from role models, social support and behavioral capability influenced patients' motivations and skills to adhere to their ART. Theses motivations and skills, reinforced by health care providers, increased patients' self efficacy to adhere and allowed them to overcome potential barriers to take their medication as instructed.

Aim 4: To assess the role of mediating and moderating factors in the relationship between social support and adherence

Social support was not a significant predictor of adherence in the survey, making it impossible to address this aim statistically. The lack of association may be due to inadequate power in our sample, or it may be an appropriate reflection that those who achieved adherence in this setting did not necessarily have higher levels of perceived social support from those who did not achieve adherence.

The qualitative data, on the other hand, points to the importance of social support in facilitating good adherence. Patients talked about three forms of support they received from family members: reminders to make medication, emotional support that helped to 'normalize' HIV, and material support in the form of food and money. Reminders that patients got from others contributed to their adherence skill set and directly helped them remember to take their medication on time. Emotional support increased patients' motivation to adhere by providing an expectation that they could achieve good health and by placing greater value on good health. Material support assisted patients to overcome direct barriers of lack of food and transportation fees, which may have otherwise hindered adherence. In this way, the qualitative data suggests that social support influences adherence by increasing patients' skills and motivations to adhere and also by directly impacting their self efficacy to adhere, despite potential barriers.

Study limitations

The study was limited by several factors. In the survey, adherence may have been over-estimated due to social desirability bias in patients' self report. Additionally, the recruitment strategy missed individuals who have dropped out of the ART program or who did not come to clinic during the recruitment period, which may have introduced an over-estimation of adherence. The small number of cases who reported poor adherence limited the number of predictor variables that could be included in the final model and precluded the investigation of interactions among the predictor variables.

The in-depth interviews were similarly subject to social desirability bias. Single contacts with respondents meant that the interviewers had limited time to build rapport and probe for inconsistencies in self reports. No observations were conducted of patient-provider interactions to confirm what patients and providers reported. The semi-structured nature of the interview guide meant that the depth of discussion on topics was not consistent across respondents, making the presentation of proportions of respondents reporting various factors descriptive only.

In both the survey and in-depth interviews, social desirability bias was minimized to the extent possible by using normalizing language (e.g., "It is normal for patients to not take their pills as they are supposed to") and by training interviews on strategies to gain respondents' trust and elicit honest responses. Limitations that were specific to the methods – such as inadequate power to detect differences in the survey and lack of consistency in the qualitative interviews – were reduced by the use of complementary methods. The in-depth interviews provided a more detailed and nuanced exploration of the factors that influenced adherence than was possible in the survey interviews, while the survey data allowed us to make more generalizable conclusions about the data than was possible from the in-depth interviews.

Implications for research and practice

The findings reported here have implications for research and practice. First, the findings highlighted several characteristics of the clinic setting that may have attributed to the excellent adherence in this sample. Studies are needed that compare multiple sites and ART program models, in order to identify the characteristics that best support patients' adherence. This may include comparisons of different size clinics and faith-based versus government facilities. The VACs program may have also contributed to the high adherence in this sample, and deserves evaluation as an intervention model.

The influence of patient-provider interactions on adherence emphasizes the importance of training health care providers to ensure a patient-centered approach. As ART programs expand to include more patients, it will be important to ensure that providers have enough time with patients to develop and sustain trusting relationships. Peer educators may help to fill the gap where medical professionals are overstretched or unavailable. Additional research is needed to determine what aspects of interactions with providers patients most value and have the strongest influence on adherence.

The association between age and adherence deserves further attention. Both younger and older patients may need additional support when starting ART. Further research on the challenges that both of these groups face may help develop tailored counseling messages and support mechanisms. The experience of older people living with HIV is particularly neglected and deserves further attention.

Although adherence was high in this setting, there is nevertheless need to develop interventions to sustain and support adherence, particularly as access to ART expands. Models for adherence interventions in developing countries often rely on intensive individual counseling, telephone follow up, or mechanisms such as pagers or financial incentives (Cote et al., 2005; M. Haddad et al., 2000; Simoni et al., 2003). In developing country settings, where limited financial and human resources do not permit such interventions, a community-based approach that mobilizes social support is often used to promote patients' adherence (Behforouz et al., 2004; Coetzee et al., 2004; Koenig et al., 2004; MSF, 2004). The findings of this dissertation study suggest that an approach that mobilizes social support would be valuable in this setting. At the same time, our findings indicate that health care providers need to be trained and mobilized to support patients' adherence. Providers' willingness and ability to appropriately communicate with patients and to identify and support their motivations and skills in taking ART are essential for supporting and sustaining patients' adherence over time.

Pilot intervention

The findings from this research have already been leveraged into a small study to develop and pilot test an intervention for ART initiates and their treatment supporters at the study clinic. A group intervention was chosen as the delivery mode because we found that social support helped patients to live positively with HIV and adhere to their medication, but at the same time patients feared disclosing in their social networks due to perceived stigma. Informal conversations with the research team and clinic staff suggested that a group seminar for patients and their supporters may not only deliver important information, but it may also help to normalize HIV, leading to increased disclosure and support. During the home visits, patients were asked about their interest and willingness to participate in a seminar with a treatment supporter. All patients responded that they would come and felt they would benefit from such a seminar.

The content of the half-day seminar was informed by the findings of the dissertation, a review of other adherence interventions, and ten focus group discussions that we conducted with patients, their treatment supporters and health care providers. Because the dissertation work pointed to the saliency of the Social Cognitive Theory, we used constructs from the SCT to inform the intervention. The application of these constructs included: introducing role models by having HIV positive facilitators lead the seminar; practicing emotional coping, behavioral capability and self control through appropriate role plays; increasing self efficacy by anticipating barriers to adherence and brainstorming challenges to overcome those barriers; and making patients' social environments more conducive to taking ART by equipping patients' self-identified supporters with knowledge and skill to provide appropriate support.

We recruited 38 patients to participate in the pilot testing of the seminar, and 29 (76%) attended. Of those, 12 (41%) brought treatment supporters, including seven relatives and five friends. Feedback on the seminar was positive. When asked to rate the helpfulness of the seminar on a scale of one to five, 24 patients (83%) and eight supporters (67%) gave the seminar a five as "very helpful". Focus group discussions with patients and supporters in the week following the seminar elicited feedback on ways to improve the intervention. While the results of the pilot are still being analyzed, the preliminary findings demonstrate that most patients were willing and able to attend the seminar and almost half brought treatment supporters. In the evaluation of the pilot, participants rated the sessions favorably, providing evidence that this may be a useful model for improving quality of life and supporting adherence to ART at this site.

Future topics for data analysis

This dissertation study has only begun to touch on the many available research topics in the data collected. Below are several additional research areas outside of the issue of adherence that can be undertaken with the data at hand.

1. *Social support from perspectives of ART patients and their supporters*: Social support emerged as an important facilitator of adherence in the in-depth interviews. A qualitative analysis of the patient interviews, paired with their supporters, will provide a better understanding of the nature of social support in this sample and how ART programs and interventions may maximize social support.
2. *Role of religion*: Religion emerged as prominent in the in-depth interviews with patients. Patients talked about finding support and hope in their faith, but said they rarely heard messages about living with HIV from their mosques and congregations and were reluctant to disclose in their religious communities for fear of stigma. These findings may identify missed opportunities for religious organizations to support people living with HIV.
3. *Patterns of HIV disclosure*: It is important to understand HIV disclosure in order to inform HIV prevention efforts and to ensure that HIV positive people access and are retained in care (R. King et al., 2007). Data from the survey and in-depth interviews with patients can be combined to shed light on the groups of people to whom people are disclosing (e.g., brothers, sisters, neighbors, church leaders), the order in which they disclosed, reasons for disclosing and not disclosing, and experiences of 'indirect disclosure'.

4. *Measurement of perceived stigma*: The stigma scale that was developed for the survey was adapted from measurement work done by the International Center for Research on Women (Nyblade et al., 2003). The adapted scale measured perceived stigma, instead of experienced stigma as was the case for the original scale, because this seemed to be the most important influence from the qualitative findings. Understanding the scale properties may improve and standardize measurement of perceived stigma in other settings.
5. *Predictors of depression*: Depression has been well documented for people living with HIV in North America (Berg et al., 2007; Ciesla et al., 2001; Valente, 2003), and emerged as prevalent in this study. The survey data can be used to identify the types of depressive symptoms people reported and factors associated with reporting high depression.
6. *Perspectives of HIV positive lay health advisors:* The interviews with VACs revealed that they not only perceived their contributions for improving the adherence and quality of life of the clinic patients, but that they also perceived benefits of the program for their own well-being. The impact of lay health advisor programs on the lay health advisors themselves has been studied in the United States (Marino et al., 2007), but has not been explored in Africa, where such intervention models are increasingly being used.

APPENDIX ONE

Factors considered as determinants of poor adherence to ART in eight African studies

The table below provides the factors considered as determinants of non-adherence to ART in eight studies (study numbers correspond to list below). Odds ratios and 95% confidence intervals are included for factors that were significantly associated with poor adherence at alpha=.05. Blank cells mean that the factor was not measured in the study and 'n/s' means that the factor was studied but found not significant.

	1	**2**	**3**	**4**	**5**	**6**	**7**
Demographic variables							
Age (younger)	n/s	**1.45 (1.17-1.78)**	n/s			**1.03 (1.01-1.06)**	n/s
Gender	n/s		n/s		n/s	n/s	n/s
Marital status (being single)	**2.77** **(1.64-4.67)**						n/s
Education (higher levels)	n/s		**3.08 (1.25-7.60)**		n/s		**3.87 (1.21-12.40)**
Religion	n/s						
Employment					n/s		n/s
Income / socio-economic status (low SES)	**2.93 (1.32-6.50)**	n/s	n/s		n/s	n/s	
Psychological variables							
HIV optimism		**1.26 (1.01-1.58)**					
Outcome expectations / confidence in ART	n/s						
Knowledge / beliefs about ART	n/s				n/s		
Knowledge / beliefs about HIV					n/s		
Depression / negative affect	n/s						
Worries about side effects					n/s		
Impact of illness on work and relationships							n/s
Attitude toward western medicine							n/s
Use of alcohol and drugs	n/s						
Social variables							
Social support	n/s	**1.66 (1.24-2.24)**					
Fear of stigmatization by a partner					**8.0** **(1.4 – 50)**		
Disclosure of HIV status							n/s

Health facility and provider variables							
Vicinity of residence to the clinic	n/s						
Costs of medication or reporting cost as a barrier	n/s			**Sig**			**9.09 (3.33 – 25.0)**
Ever received counseling			n/s				
Treatment-related variables							
Regimen	n/s		n/s	**Sig**	n/s		n/s
Time on ART	n/s		n/s	n/s			n/s
Side effects of medication	n/s						n/s
Number of pills / doses per day (more)		**1.47 (1.14-1.91)**	n/s			**3.07 (1.40 – 6.74)**	n/s
Requirement to take pills on an empty stomach						n/s	
Use of traditional medicines							n/s
CD4 count at initiation		**1.43 (1.10-1.88)**					

Studies reviewed:

1. Byakika-Tusiime, J., J. H. Oyugi, et al. (2005). "Adherence to HIV antiretroviral therapy in HIV plus Ugandan patients purchasing therapy." International Journal Of Std & Aids 16(1): 38-41.

2. Diabate, S., Alary, M., & Koffi, C. K. (2007). Determinants of adherence to highly active antiretroviral therapy among HIV-1-infected patients in Cote d'Ivoire. *Aids, 21*(13), 1799-1803.

3. Eholie, S. P., Tanon, A., Polneau, S., Ouiminga, M., Djadji, A., Kangah-Koffi, C., et al. (2007). Field adherence to highly active antiretroviral therapy in HIV-infected adults in Abidjan, Cote d'Ivoire. *J Acquir Immune Defic Syndr, 45*(3), 355-358.

4. Laniece, I., Ciss, M., Desclaux, A., Diop, K., Mbodj, F., Ndiaye, B., et al. (2003). Adherence to HAART and its principal determinants in a cohort of Senegalese adults. *Aids, 17 Suppl 3*, S103-108.

5. Nachega, J. B., D. M. Stein, et al. (2004). "Adherence to antiretroviral therapy in HIV-infected adults in Soweto, South Africa." AIDS Res Hum Retroviruses 20(10): 1053-6.

6. Orrell, C., D. R. Bangsberg, et al. (2003). "Adherence is not a barrier to successful antiretroviral therapy in South Africa." Aids 17(9): 1369-1375.

7. Weiser, S., W. Wolfe, et al. (2003). "Barriers to antiretroviral adherence for patients living with HIV infection and AIDS in Botswana." J Acquir Immune Defic Syndr 34(3): 281-8.

APPENDIX TWO:
Survey questionnaire

Study ID: ____ ____ ____	**Date:** ____ / ____ / _2007_ **mm dd YYYY**
Clinic ID: ____ - ____ - ____	**Interviewer:** ________________________

I. DEMOGRAPHICS

1. [Mark this – do not ask] What is the patient's gender	1. Male 2. Female
2. What is your birth date?	___ / ___ / ________ mm dd YYYY
If birthdate is unknown 3. How old are you?	1. I am _____________________ years old
4. How many years of school have you completed?	1. No education 2. Less than Standard 7 3. Completed Standard 7 only 4. Some secondary school 5. Completed secondary school 6. Some post-secondary education
5. What language do you speak most often in the home?	1. Kiswahili 2. Masaai 3. English 4.Other, specify:______________________________

6. What is your religion?	1. Muslim 2. Christian, specify: ______________________________ 3. Other, specify: ________________________________ 4. I have no religion
7. How often do you go to church or mosque?	1. Every day 2. More than once a week 3. Once a week 4. In a month I go ____ times 5. Less than once a month 6. Never
8. Are you currently married?	1. Yes 2. No
9. *If yes:* In the past month, have you lived together with your spouse?	1. Yes, we live together all the time 2. Yes, but my spouse also lives somewhere else. Reason: ________________________________ 3. No, my spouse lives somewhere else Reason: ________________________________
10. Is your spouse HIV positive?	1. Yes 2. No 3. Never tested
11. *If yes:* Is your spouse taking ARVs?	1. Yes 2. No
12. *If no:* What is your relationship status?	1. Widowed 2. Divorced 3. In a relationship, living with partner 4. In a relationship, not living with partner

	5. Single, never married, no current partner
13. *If widowed:* Did your spouse die of HIV?	1. Yes 2. No 3. S/he never tested
14. *If divorced or separated:* Was the divorce/separation due to HIV?	1. Yes 2. No 3. Don't know
15. How many children do you currently have?	__________ children [If 0, go to 18]
16. How many of these children have their primary residence in your home?	__________ children
17. How many of these children are HIV positive?	__________ children 88. Don't know
18. Have you had any children who have died?	__________ children [If 0, go to 20]
19. How many of those children who do you think died of HIV?	__________ children 88. Don't know

Does your household own:		
	Yes	**No**
20. Radio or music system?	1	2
21. Television?	1	2
22. Bicycle?	1	2
23. Car?	1	2
24. Telephone?	1	2
25. Refrigerator?	1	2

26. Cows?	1	2
27. Small animals, like goats and chickens?	1	2
28. A farm or a plat of land?	1	2
Does the house where you live have:		
29. Electricity?	1	2
30. Piped water inside the house?	1	2

31. What kind of toilet does your household use?	1. Drop toilet 2. Flush toilet 3. No toilet facility
32. Do you share the toilet with any other households?	1. Yes 2. No
33. What is your house made of?	1. Block 2.Mud house with iron roof 3.Mud house with grass roof 4.Other: ______________________________
34. Do you own or rent your house?	1. Own 2. Rent
35. How many rooms does your house have?	__________ rooms
36. Including you, how many people 18 years and older live in your house?	__________ adults
37. How many people under 18 years live in your house?	__________ children
38. How many meals do you usually have per day?	__________ meals

39. How often in the last month did you have problems in satisfying the food needs of the household?	1. All the time 2. Some times 3. A few times 4. No times at all
40. Have you ever received food support from this clinic?	1. Yes. Number of times: __________ 2. No
41. In the past year, have you ever received food support from any other organization?	1. Yes 2. No
42. What type of economic activities do you do?	1. Not working 2. Farming 3. Petty trading 4. Employed with a salary 5. Other: ________________________
43. Does your work require you to travel outside of Arusha?	1. Yes 2. No
44. In the past month, how much did you earn from your economic activities?	Tsh ______________________________

II. TREATMENT AND HIV-RELATED VARIABLES

1. When did you first learn your HIV status?	___ / ___ / ________ mm dd YYYY
2. When did you start taking ART? [If they don't know, check their patient card]	___ / ___ / ________ mm dd YYYY

III. SOCIAL SUPPORT

People sometimes look to others for companionship, assistance, or other types of support. I'm now going to ask you about how often different types of support are available to you if you need it. For each type of support that I mention, please tell me how often you feel that support is available to you. You can answer: none of the time, a little of the time, some of the time, most of the time or all of the time.

	None of the time	**A little of the time**	**Some of the time**	**Most of the time**	**All of the time**
1. Someone you can count on to listen to you when you need to talk	1	2	3	4	5
2. Someone to give you information to help you understand a situation	1	2	3	4	5
3. Someone to give you good advice about a crisis	1	2	3	4	5
4. Someone to confide in or talk to about yourself or your problems	1	2	3	4	5
5. Someone whose advice you really want	1	2	3	4	5
6. Someone to share your most private worries and fears with	1	2	3	4	5

	None of the time	**A little of the time**	**Some of the time**	**Most of the time**	**All of the time**
7. Someone to turn to for suggestions about how to deal with a personal problem	1	2	3	4	5
8. Someone who understands your problems	1	2	3	4	5
9. Someone to help you if you were confined to bed	1	2	3	4	5
10. Someone to take you to the doctor if you needed it	1	2	3	4	5
11. Someone to prepare your meals if you were unable to do it yourself	1	2	3	4	5
12. Someone to help with daily chores if you were sick	1	2	3	4	5
13. Someone to remind you to take your pills	1	2	3	4	5
14. Someone to give you spiritual help	1	2	3	4	5
15. Someone to give you courage in living with HIV	1	2	3	4	5
16. Someone who can pick up your pills at the clinic if you're not able	1	2	3	4	5
17. Someone to give you money if you don't have it	1	2	3	4	5

IV. ADHERENCE TO ART

1. Which pills do you take for your HIV?	1. Triomune 30 2. Triomune 40 3. Combivir / EFV 4. Other: ___________________
2. What time do you generally take your morning dose?	Time: _________________
3. What time do you generally take your evening dose?	Time: _________________

We understand that it is common that people forget to take their pills or have reasons for deciding not to take their pills. That's normal. I'm going to ask you some questions about YOUR experiences taking ARVs. `Remember what you say to me will not be shared with anyone and I personally don't care what your answer is.`

For each day, first ask a question to get them thinking about the day (What did you do yesterday?). Then ask about whether they took a pill in the morning and in the evening and at what time. Record the time taken in the box below. If the patient reports *not* *taking a dose, put an X in the cell.*

4. Please circle: What day of the week is TODAY?

1)Monday 2)Tuesday 3)Wednesday 4)Thursday 5)Friday 6)Saturday 7)Sunday

	Previous four days **[Write the appropriate days of the week on the lines below]**				
	5. _____ **Today**	6. ______ **Yesterday**	7. ______ **2 days ago**	8. ______ **3 days ago**	9. ______ **4 days ago**
a. **Morning dose**					▨
b. **Evening dose**	▨				

FOR CODER: 1)Took dose on time, 2)Took dose 1 hr. or more earlier than usual, 3)Took dose 1 hr. or more later than usual, 4) Took dose but not sure of time, 5) Not sure if s/he took dose, 6)Didn't take dose, 7) Time for dose has not arrived

For each missed dose or dose taken at least one hour later than the time they say they normally take their pills, ask the question:

10. MISSED DOSE 1: What was your reason for not taking that dose / taking it late?	
11. MISSED DOSE 2: What was your reason for not taking that dose / taking it late?	
12. MISSED DOSE 3: What was your reason for not taking that dose / taking it late?	
13. MISSED DOSE 4: What was your reason for not taking that dose / taking it late?	

Take out the container of beads.

Now I want you to think about the past *month* and how many of your prescribed ARV pills you have taken. In this jar is 60 beads. This represents all the pills you should have taken in the past month. We know that not all patients take all their pills for different reasons. I want you to show me how many of these pills you took by putting into this other container the number of these pills you think you actually took in the past month.

14. *Record the number of beads in the original jar.*	Number of beads: ______________
15. *If there are any beads in the original jar:* What were your reasons for not taking these pills?	

V. BELIEFS ABOUT ARVs

Now I'm going to read you some things people believe about HIV and ARVs. Please tell me how you feel about each one.

1. Do you think antiretrovirals can: totally remove HIV from your body, improve your health but not remove HIV from your body, or do they not help much at all?	1. Totally remove HIV from your body 2. Improve your health but not remove HIV from your body 3. They do not help much at all
2. Once people start feeling better, should they: stop taking antiretrovirals immediately, keep taking them for a while longer and then stop, or keep taking them for the rest of their lives?	1. Stop taking ARVs immediately 2. Keep taking them for a while longer to make sure the symptoms have really stopped, and then stop taking them 3. Keep taking them for the rest of their lives
3. When should you take your ARVs: only when you're feeling sick, only when you're feeling healthy, or all the time, no matter if you feel sick or healthy?	1. Only when you're feeling sick 2. Only when you're feeling healthy 3. All the time, no matter if you feel sick or healthy
4. Do people who are on antiretrovirals need to use condoms when they have sex or are those people no longer able to spread HIV so they don't need condoms?	1. Need to use condoms 2. Those people are no longer able to spread HIV so don't need to use condoms
5. If a man and a woman are both HIV positive and taking ARVs, should they: stop having sex altogether; reduce the frequency of having sex; or continue having sex as often as before?	1. Stop having sex altogether 2. Reduce the frequency of having sex 3. Continue having sex as before
6. When should people take their ARVs: at the same time every morning and evening; anytime, as long they take it in the morning and evening; or it doesn't matter as long as they take two pills per day?	1. At the same time every morning and evening 2. Anytime, as long as they take it in the morning and evening 3. It doesn't matter when as long as they take two pills per day

7. If someone in your family is sick with HIV, is it okay to share you antiretrovirals with that person or should you make sure you never give your ARVs to someone else to take?	1. It's okay to share your ARVs 2. You should never give your ARVs to anyone else
8. When you take antiretrovirals, does the amount of body immunity / CD4 increase, decrease or stay the same?	1. Increase 2. Decrease 3. Stay the same
9. When you take antiretrovirals, does the amount of virus in your body increase, decrease or stay the same?	1. Increase 2. Decrease 3. Stay the same

VI. HIV DISCLOSURE EXPERIENCES

Now I want to talk to you about whether or not you have ever talked to different people about your HIV status and about the fact that you are taking medication for HIV. Different people do different things when they learn they are HIV-positive. Some people tell their friends, families and sexual partners, others don't tell anyone. Please remember that I will not tell anyone what you tell me in this interview.

	a. Have you talked to this person about the fact that you're HIV-positive?			b. After you told this person you were HIV+, would you say that their response was positive, negative or neutral?			c. *If haven't disclosed directly:* Do you think this person knows that you're HIV positive, even if you didn't tell them directly?		d. Does the person know that you are taking ARVs?		e. Does this person give you any help in remembering to take your ARVs?		f. *If yes:* Would you say he/she gives you: a little support or a lot of support to help you remember to take your ARVs?	
	Yes	**No**	**N/A**	**Pos**	**Neg**	**Neut.**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**A little**	**A lot**
1. Spouse or partner	1	2	3	1	2	3	1	2	1	2	1	2	1	2
2. Mother	1	2	3	1	2	3	1	2	1	2	1	2	1	2
3. Father	1	2	3	1	2	3	1	2	1	2	1	2	1	2
4. Any blood brothers	1	2	3	1	2	3	1	2	1	2	1	2	1	2
5. Any other brothers	1	2	3	1	2	3	1	2	1	2	1	2	1	2
6. Any blood sisters	1	2	3	1	2	3	1	2	1	2	1	2	1	2
7. Any other sisters	1	2	3	1	2	3	1	2	1	2	1	2	1	2
8. Any brothers- or sisters-in-law	1	2	3	1	2	3	1	2	1	2	1	2	1	2

9. Any uncles	1	2	3	1	2	3	1	2	1	2	1	2	1	2
10. Any aunts	1	2	3	1	2	3	1	2	1	2	1	2	1	2
11. Any children over age 15	1	2	3	1	2	3	1	2	1	2	1	2	1	2
12. Any friends	1	2	3	1	2	3	1	2	1	2	1	2	1	2
13. Any neighbors	1	2	3	1	2	3	1	2	1	2	1	2	1	2
14. A pastor or other religious leader	1	2	3	1	2	3	1	2	1	2	1	2	1	2
15. Any workmates	1	2	3	1	2	3	1	2	1	2	1	2	1	2
16. The person who owns your house	1	2	3	1	2	3	1	2	1	2	1	2	1	2
17. Your house boy/girl	1	2	3	1	2	3	1	2	1	2	1	2	1	2

18. Who did you tell about your status first, second and third?	1. ________________________________ 2. ________________________________ 3. ________________________________
19. How many people outside this clinic have you told about your status?	_____________ people [If respondent says they've disclosed to 'all or 'many', confirm that it is more than 5 and write '>5' on line above]

VII. PERCEIVED STIGMA

There are a lot of social and emotional aspects of having HIV. Some people have bad experiences because of having HIV, or are afraid that people will react badly because they have HIV. I'm going to ask you how afraid you are of certain things happening if people knew your HIV status. I want you to respond by telling me whether you are: not afraid at all, just a little afraid, somewhat afraid, or very afraid.

	Not worried at all	**Just a little worried**	**Some-what worried**	**Very worried**
1. How worried or not worried are you that you would be treated differently / shunned at a social gathering if people knew your HIV status? Are you:	1	2	3	4
2. How worried or not worried are you that you would be abandoned by your family / sent away to the village if people knew your HIV status? Are you:	1	2	3	4
3. How worried or not worried are you that you would be isolated in your household (made to eat along / made to use separate eating utensils / made to sleep alone in your room) if people knew your HIV status? Are you:	1	2	3	4
4. How worried or not worried are you that you would no longer be visited or would be visited less by family and friends if people knew your HIV status? Are you:	1	2	3	4
5. How worried or not worried are you that you would be teased, insulted or sworn at if people knew your HIV status? Are you:	1	2	3	4
6. How worried or not worried are you that you would lose customers to buy your produce / goods or lose a job if people knew your HIV status? Are you:	1	2	3	4
7. How worried or not worried are you that you would lose housing or not be able to rent housing if people knew your HIV status? Are you:	1	2	3	4
8. How worried or not worried are you that you would be denied religious rites/services (marriage, communion, burial, singing in the choir, prayer) or not be allowed to go to church or mosque if people knew your HIV status? Are you:	1	2	3	4

9. How worried or not worried are you that you would lose respect / standing within the family or community if people knew your HIV status? Are you:	1	2	3	4
10. How worried or not worried are you that you would be gossiped about if people knew your HIV status? Are you:	1	2	3	4

VIII. DEPRESSION

Sometimes people lose hope or courage when they have different problems in day-to-day life. I'm going to ask you how often you felt different ways in the past month.

	Never	**Seldom**	**Some of the time**	**Very often**
1. Felt hopeless about the future	1	2	3	4
2. Felt worthless	1	2	3	4
3. Felt blue	1	2	3	4
4. Thought of ending your life	1	2	3	4
5. Felt trapped or caught	1	2	3	4
6. Blamed yourself for things	1	2	3	4
7. Felt lonely	1	2	3	4
8. Worried too much about things	1	2	3	4
9. Cried easily	1	2	3	4
10. Felt everything is your fault	1	2	3	4
11. Not felt interested in things	1	2	3	4

IX. PERCEIVED SELF-EFFICACY TO ADHERE

There are a lot of situations that people talk about that make it difficult for people who are HIV positive to take their pills every day and on time. Now I want to ask you about some of those situations. I'd like you to tell me how confident or not confident you are that you can take your pills correctly if you were in these different situations.

	Amount of confidence			
	Almost no confidence	**A little confidence**	**Some confidence**	**A lot of confidence**
1. If you have side effects from taking ARV, how much confidence do you have that you will be able to take your ARV medications? Do you have:	1	2	3	4
2. If you travel away from home, how much confidence do you have that you will be able to take your ARV medications? Do you have:	1	2	3	4
3. If you are very busy with work, how much confidence do you have that you will be able to take your ARV medications? Do you have:	1	2	3	4
4. If you are busy participating in community events, such as funerals, weddings, how much confidence do you have that you will be able to take your ARV medications? Do you have:	1	2	3	4
5. If you are busy with activities in the church or mosque, how much confidence do you have that you will be able to take your ARV medications? Do you have:	1	2	3	4
6. If you become sick, how much confidence do you have that you will be able to take your ARV medications? Do you have:	1	2	3	4
7. If you are feeling very tired, how much confidence do you have that you will be able to take your ARV medications? Do you have:	1	2	3	4

	Amount of confidence			
	Almost no confidence	**A little confidence**	**Some confidence**	**A lot of confidence**
8. If you are with someone when you have to take your medications who doesn't know that you HIV+, how much confidence do you have that you will be able to take your ARV medications? Do you have:	1	2	3	4
9. In the situation when you don't have food, how much confidence do you have that you will be able to take your ARV medications? Do you have:	1	2	3	4
10. In the situation where you health has improved greatly, how much confidence do you have that you will be able to take your ARV medications? Do you have:	1	2	3	4

X. NORMATIVE BELIEFS

1. Has anyone ever told you that taking ARVs makes you die sooner?	1. Yes, Who: _________________ 2. No [Go to 3]
2. Do you value the opinion of the person who told you that: a lot, a little, or not much at all?	1. A lot 2. A little 3. Not much at all
3. Has anyone ever said to you that you should take traditional medicines <u>instead of</u> taking ARVs?	1. Yes, Who: __________________ 2. No [Go to 5]
4. Do you value the opinion of the person who told you that: a lot, a little, or not much at all?	1. A lot 2. A little 3. Not much at all

5. Has anyone ever told you that you should pray <u>instead of</u> taking ARVs?	1. Yes, Who: __________________ 2. No [Go to next section]
6. Do you value the opinion of the person who told you that: a lot, a little, or not much at all?	1. A lot 2. A little 3. Not much at all

XI. SKILLS AND STRATEGIES APPLIED FOR TAKING MEDICATION

Some people do things so that they are better able to remember to take their ARV medications every day, on time. I'm going to tell you about some different strategies people have used to remember to take their pills, and I want you to tell me whether you have ever done this in the past month.

In the last month …

	Yes	**No**
1. …have you carried your pills in your pocket or handbag if you leave home?	1	2
2. ...have you timed taking your pills so that it corresponds to another event, like having a bath, brushing your teeth, or saying your prayers?	1	2
3. …have you placed your pills in an open space so that you remember to take them?	1	2
4. …have you set an alarm to remember to take your pills?	1	2
5. …have you used a radio or TV program to remind you that it's time to take your pill?	1	2
6. …have you had someone remind you to take your pills?	1	2

XII. PERCEIVED SIDE EFFECTS

1. In the last month, have you experienced any side effects related to the ARVs?	1. Yes 2. No
2. *If yes:* Please describe those side effects.	

XIII. PATIENT-PROVIDER COMMUNICATION

I am going to ask you some questions about is your relationship with the hospital staff, namely with the doctors, nurses, counselors and pharmacists. Remember, your answers are confidential and we will not share what you say with the clinic staff.

When you come into the clinic to receive care, how often do you feel that…

	Never	**Sometimes**	**Usually**	**Always**
1. …the hospital staff give you enough time every time you come to the clinic? Do you feel that way:	1	2	3	4
2. …the hospital staff are willing to listen to you problems or to your concerns? Do you feel that way:	1	2	3	4
3. ..the hospital staff help you to find solutions to problems related to your health?	1	2	3	4
4. …the hospital staff are able to explain things to you in a way that you can understand? Do you feel that way:	1	2	3	4
5. … you are able to contact or meet the hospital staff whenever you need to? Do you feel that way:	1	2	3	4

	Never	**Sometimes**	**Usually**	**Always**
6. …you are comfortable talking openly with the care providers at the hospital? Do you feel that way:	1	2	3	4
7. …you get good care for your conditions from the hospital staff? Do you feel that way:	1	2	3	4
8. …the hospital staff help-provide advice to you for any problems you have in taking your medications? Do you feel that way:	1	2	3	4
9. …the hospital staff understand the difficulties that you face taking your ARV medications? Do you feel that way:	1	2	3	4
10. …the hospital staff advise you how to reduce side affects from your ARV medications? Do you feel that way:	1	2	3	4
11. …the hospital staff encourage you to take your ARV medications? Do you feel that way:	1	2	3	4

XIV. VOLUNTARY ADHERENCE COUNSELORS

1. The VACs are the people who come on clinic days and are supposed to help patients take their pills. Do you have a VAC?	1. Yes 2. No 3. Don’t know
2. *If yes:* Who is your VAC?	Name: ___________________________

3. When you come to the clinic, how often do you talk to your VAC?	1. Never 2. Sometimes 3. Usually 4. Always
4. Has this person ever visited you at home?	1. Yes 2. No
5. Do you belong to any organizations for people living with HIV?	1. Yes 2. No

XV. ACCESSIBILITY TO THE CLINIC

1. How many minutes does it usually take you to get from your house to this clinic?	1. ________ minutes
2. What form of transportation do you <u>usually</u> use to get from your house to the clinic?	1. Walk 2. Personal car 3. Car of relative or friend, Cost each way: ________ 3. Hired taxi, Cost each way: ________ 4. Daladala, Cost each way: __________ 5. Bicycle
3. Since you started taking ARVs, how often have you missed an appointment at the clinic for the time to pick up your ARVs?	1. Never 2. Once 3. 2-3 times 4. More than 3 times

4. What were your reasons for missing the appointments? (Circle all that apply)	1. Travelling outside of Arusha 2. No transportation fare 3. Unable to come due to weather 4. Forgot 5. Sick 6. Other reasons:__________________

These are all the questions I have for you. Is there anything you would like to add about your experiences living HIV or taking antiretroviral medications?

Do you have any questions for me?

THANK YOU for taking the time to be part of this study. The information you provided will help to improve services for people living with HIV.

APPENDIX THREE:
In-depth interview guide for ART patients

I. INTRODUCTION/PERSONAL INFORMATION

To begin, I want to know a little about yourself.

1) Where were you born? In what year? [If they don't know the year, how old are you?]

2) How much school did you complete?

3) Your religion? How is your involvement in this religion? (frequency, etc)

4) What types of economic activities are you involved in? Has it changed since being HIV positive? Do you get enough money to support yourself?

5) Where do you live now?

6) How much time does it usually take you to get from where you live to the clinic? How do you usually travel here? Do you ever find problems in coming to the coming?

7) Who do you live with at your home?

8) Are you currently married? [Probe: relationship status]

9) Do you have children? How many? Ages?

HIV in the family

Now I would like to talk with you about HIV/AIDS in your life and your family.

1) Is anyone else in your family HIV-positive? [probe for spouse]

2) Has anyone in your family died of AIDS?

II. EXPERIENCE BEING DIAGNOSED WITH HIV

I would like to know how you found out you were HIV positive, and what you have done since then.

1) Please tell me about the events that led you to get tested for HIV [Probe: Motivation for being tested, illness, where tested, who went with them to get a test]

2) When did you learn that you were HIV- positive? [Probe: Month and year]

3) How was it for you after you learned your HIV status? [Probe: First month, feelings, reactions, intentions and decisions]

4) When you went for the HIV test, did you know about these drugs (ARVs)? What did you know about them?

5) How do you think you became infected?

6) Apart from going to the clinic, many people try to find other ways to get relief from HIV. For example they go to traditional healers and herbalists. How about you?

III. EXPERIENCE TAKING ARVS

I am interested in learning about your experiences taking medication for your HIV.

1) [Show him/her antiretroviral medications] Which of these medicines do you take?

2) When did you start taking ARVs?[Probe: Month and year]

3) Please tell me the events that led you to start taking these drugs. [Probe how did you find out about them, what did you know about them, who or what persuaded you to look for medication]

4) How has taking ARVs changed your life? [Probe for both positive and negative changes]

5) How do you think these drugs work in your body?
    - Do they cure you? Why not?
    - What will happen if you stop taking them?
    - What will happen if you don’t take them every day?

6) You know, when you come to the clinic, they often mesaure your CD4. Do you know what this CD4 indicates?

IV. ADHERENCE

I would like to understand how taking ARVs fits into your daily life

1) Tell me about your normal timetable, from the time you get up in the morning to the time you go to sleep at night, and taking ARVs fits into this? [Probe: time when they eat and when they take ARVs]
    - How many meals do you get per day?
    - Are there other days that have different time schedules? [Probe: how this affects taking ARVs]

2) What things do you do so that you are able to take your antiretrovirals on time? [Probe for strategies to help them remember their pills]

3) Some people have times when it is <u>hard</u> for them to take their ARVs when they are supposed to. In what circumstances do you find it hard to take your pills? [Probe: Side effects, remembering, traveling, hiding the drugs, running out of pills, not having food]

4) Do you travel? Is it hard to take your ARVs when you travel or just the same when you are at home? *Then:* Tell me your experiences taking ARVs when you are traveling.

5) Please think about the last time you missed taking your ARVs. Tell me about that time.

6) In the last month about how often do you think you missed taking your antiretroviral medications. [Probe for reasons]

V. RELIGION

I would like to understand the role of religion in your life and how it helps you in using ARVs.

1) Since you learned that you were infected, how was your involvement (in religion) changed?

2) What kind of support do you get from the church / mosque?

3) Do people at your church / mosque know that you're HIV positive? (probe: pastor, imam)

4) What do you hear them say about AIDS? ARVs?

5) Have you heard of anyone being cured of HIV because of prayer?

VI. DISCLOSURE, SOCIAL SUPPORT AND STIGMA

Now I would like to know a little about who in your life knows that you are HIV-positive, other than people at this clinic.

1) Who is the first person you told about your HIV status? When? Why? What was the reaction?

2) Who is the second person you told about your HIV status? When? Why? What was the reaction?

3) Who is the third person you told about your HIV status? When? Why? What was the reaction?

4) Who else knows apart from these three?

5) [If more than 3 mentioned] Of these people, which three are most important to you?

For each person mentioned [up to three]:

1) How has your relationship with this person changed since telling them about your HIV status?

2) Has this person given you help in dealing with your HIV status? If yes, Tell me how this person has helped you deal with your HIV status. [Probe for examples]

3) Does this person know you are taking ARVs? [If no, probe for reasons]

4) Has this person given you help in taking ARVs? If yes: Please tell me how this person has helped take ARVs [Probe for examples]

Social support

1) Which of these people you have told me about has provided the most help to you since you have started taking ARVs? Why do you say this?

Disclosure

1) Is there any one who does not know that you are HIV positive? **(**Probe: Family, friends, neighbors, workplace)

If someone in the household does not know they are HIV-positive:

- What made you decide not to tell this person your HIV status?
- What do you think would happen if this person knew?

Stigma

There are things we've heard from the radio that some people are discrimated against because they are HIV positive.

1) Have you ever heard anyone else being treated differently because they are HIV positive? Tell me about that.

2) Has any one ever treated you differently because you are HIV positive? Tell me about that.

VII. RELATIONSHIP WITH SERVICE PROVIDERS

Support from VACs

Now I would like to know about your relationship with VACs who work at this clinic.

1) Do you know who these VACs are?

2) Do you have a VAC? Who?

3) Where do you meet? Clinic? Home? When? How often?

4) What kind of things do you talk about with [VAC]?

5) What kind of help do you get from your VAC?

6) What other things would you like your VAC to help you with?

Support from the clinic

1) Is there anything else that this clinic can do to better support you, and other people like you, in taking ARVs?

VIII. CONCLUSION

Now I have asked you all my questions.

1) Do you have anything else you would like to tell me about your experiences as a person living with HIV or your experiences taking ARVs?

APPENDIX FOUR:
In-depth interview guide for health care providers`

1. INTRODUCTION / PERSONAL INFORMATION / HISOTRY

Can you please tell me a little about yourself.

- Where are you from?
- How old are you?
- What is your level of education?
- Who do you live with at your home?

[Verify position /work in the clinic]

Can you explain to me how you became a nurse/doctor/councellor/ pharmasist, and how come you are a worker in this clinic?

- What motivated /attracted you to become a health worker?

2. RELATIONSHIP WITH ART PATIENTS AND THE SYSTEM OF ASSISTING THEM

I would like to know what type of work you do in this clinic. Could you please explain your daily activities. What do you normaly do from morning to evening until when you finsh /complete your work.

- What type of service did you offer?
- How many patients did you attend?
- How long did you take to attend each patient?
- Generally what part of your work do you enjoy most.
- What challenges do you face in your work?
- How do other working days differ from this particular day?

Explain to me your experience of caring for patients who use ARVs.

- What kind of service and assistance do you give to patients who use ARVs?
- What type of conversation do you have with patients who use ARVs. Give examples
- Do patients who use ARVs tell you what kind of problems they have? Give examples. How do you assist them(Give examples)

What are your experiences working with friends, partner or family members who come to the clinic with ART patients?

- Who do patients bring with them to the clinic? (Differentiate by patients' gender and age)
- How often do you meet with them?
- What kind of conversation do you normally have with them? Tell me about the problems they talk to you about and solutions you offer them. (Give examples)
- What are the benefits of patients coming to the clinic with their helpers/assistants? (Differentiate by gender/age)
- How do patients who come to the clinic with helpers differ from those who come without helpers?
- Beside family members/relatives who else usually assist the patients who use ARVs?

Please tell me the changes you have noticed from people since they started using ARVs.

- What are the positive or negative changes?
- Do these changes differ for women and men?
- What are the differences between young and old people?

3. PERSPECTIVE OF THE WAYS PEOPLE MANAGE ADHERENCE

Tell me the challenges/problems which patients can face by using medicine daily and in the period they are supposed to use them.

For each problem/challenge mentioned, enquire for more examples about the type of advice they gave.

- In what environment/situation is it difficult for patients to follow their medicine regulations? Examples.
- In these situations, what type of advice do you give them? Examples.
- What types of patients get more problems using ARVs?
- How do family members/relatives help patients to use of medicine? Example.
- Are there patients who do not have help from family or friends? What do they do? Examples.
- What things do people do to remeber to take their medications as they are supposed to? Examples.
- When do the patients get more problems using the medicine? When they just start, or after they have used for a long time? Why do you think so?
- Do you know patients who reject using their medications? (Example, reasons)
- Are there patients who have stopped using the drugs completely? (Example, reasons)
- Patients of which gender have the most problems taking ARVs, males or females? What about old and young peopel? Why do you think so? Examples.

Think about a patient you take care of who has a lot of problems taking their medications every day as they should. Tell me about this person.

What about a person who you take care of who is good in taking medications every day as they should. How is that person?

- Is it a man or a woman?
- How old is the patient?
- What is the person's living situation? Married? Children?
- Who knows that the person is living with HIV and is taking medication?
- What kinds of help does the person get from others? From which people does the person get help?
- In which situations does the person get difficulties adhering to the medications?
- What strategies does the person use to take the medications?
- How has the person's adherence changed over different time periods?
- How is the person's state of mind / mental health?
- How do you support the person to take his/her medicines?

Are there other things we have not yet talked about which can help me to understand how you help patients to take their drugs every day and on time?

4. CONCLUSION / THEIR EXPECTATIONS FOR PROGRESS AT WORK

Finally, think about your work as a doctor/ nurse / counselor / pharmacist. What types of changes do you see in your work five years from now? Whether or not you remain working in this clinic.

- What kinds of training will help you to give care in this position?
- What types of career aspiritations do you have?

What what about this clinic? What types of changes do you see in five years from now?

- Which other types of care will be importatnt to provide to patients in this clinic?
- What types of extra training will people in this clinic need?
- Are there any challenges you see facing this clinic?

Do you have any questions?

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