

**SCHOOL OF PUBLIC HEALTH
COLLEGE OF HEALTH SCIENCES
UNIVERSITY OF GHANA**

**ADHERENCE TO ANTIRETROVIRAL MEDICINES
AMONG ADULT HIV/AIDS PATIENTS AT THE KORLE
BU TEACHING HOSPITAL IN ACCRA, GHANA.**

**BY
DENNIS OCANSEY**

**THIS DESSERTATION IS SUBMITTED TO
THE UNIVERSITY OF GHANA, LEGON,
IN PARTIAL FULFILMENT OF THE REQUIREMENT
FOR THE AWARD OF MASTER OF
PUBLIC HEALTH DEGREE**

AUGUST 2009

DECLARATION

I declare that except for references to other people's investigations which have been duly acknowledged, this dissertation is the result of my own research and that this dissertation either in whole or in part has not been presented for another degree elsewhere.

AUTHOR

.....

DENNIS OCANSEY

(CANDIDATE)

.....

DR PHYLLIS ANTWI

PRIMARY SUPERVISOR

.....

DR. MARGARET LARTEY

SECONDARY SUPERVISOR

.....

DR. ADWOA AGYEI

FIELD SUPERVISOR

DEDICATION

I dedicate this dissertation to the King Eternal, Immortal, Invisible and only God.



ACKNOWLEDGEMENT

I am very grateful to my academic supervisors, Dr. Phyllis Antwi and Dr. Margaret Larney, as well as my field supervisor Dr. Adwoa Agyei, for their direction and inputs towards this dissertation to make it a master piece.

My thanks also go to my lovely wife, Mrs. Rosemond Naana Ocansey, and my two children, Akrofi Doe Ocansey and Nako Abena Ocansey for their immense support throughout the MPH programme.

I also express my profound gratitude to Ms Adelaide Amoako, a Public health Pharmacist for the invaluable guidance and contribution throughout the entire MPH course.

I sincerely appreciate staff of the ARV counselling section at the Pharmacy Department of the Korle Bu Teaching Hospital (KBTH) especially, Ms. Janet Antwi, Ms. Mary Dzifa Nordor, Ms. Vera Botchway and Ms Sabina Fremah Ansah for their assistance in collecting data throughout my research period at KBTH.

I also thank Mr. Jonathan Gordon and Mr. Samuel Addo jnr., who helped me in collecting data at the fevers unit of the Korle Bu Teaching Hospital

My appreciation also goes to Mrs. Grace Aboagye for her assistance in printing and compiling of my work.

I also express my gratitude to Mr. Daniel Ankrah, the head of manufacturing unit (KBTH) and Mr. David Mensah, a statistician at Noguchi memorial institute for their support and contribution to my work.

Table of Contents

DECLARATION	ii
DEDICATION	iii
ACKNOWLEDGEMENT	iv
ABSTRACT	ix
LIST OF TABLES	xi
Table 3-1: ARV Regimen at the Fevers unit	xi
Table 3-2: Independent variables affecting adherence.....	xi
Table 4-1: Demographic characteristics, socioeconomic status and education	xi
Table 4-2: Assessment of adherence to ART	xi
Table 4-3: Comparison of adherence using pill count and self report	xi
Table 4-4: Factors that contributed to optimal adherence	xi
LIST OF FIGURES.....	xii
LIST OF ABBREVIATIONS.....	xiii
CHAPTER ONE	1
1.0 INTRODUCTION	1
1.1 Background	1
1.2 Statement of the problem	3
1.3 Justifications for study	6
1.4 Study objectives	6
1.4.1 Specific objectives	6
CHAPTER TWO	7
2.0 LITERATURE REVIEW	7
2.1 Definition of adherence	7
Adherence is described as the engagement and accurate participation of an informed patient in a plan of care (Rabkin et al., 2003). The concept of ‘adherence’ has a broader meaning than compliance. It encompasses the extent to which a patient follows instructions and implies understanding, consent and partnership. It also includes entering into and continuing in a programme or care plan, as well as keeping appointments and tests as scheduled (Rabkin et al., 2003).	7
2.2 Measurement of adherence to antiretroviral medicines	7
2.2.1 Biological parameters	7
2.2.2 Therapeutic drug monitoring	8

2.2.3 Provider prediction of adherence	9
2.2.4 Review of pharmacy records.....	10
2.2.5 Patient self-report	10
2.2.6. Pill recognition.....	12
2.2.7 Pill counts	12
2.2.8 Electronic monitoring	13
2.3 Preferred adherence rate	14
2.4 Adherence rates in developing countries	14
2.5 Factors contributing to Adherence.....	17
2.5.1 Patient variables.....	17
Demographic and socioeconomic factors	18
Age	19
Level of education	19
Financial constraints.....	19
Social support	20
2.5.2 Treatment regimens	20
Simplifying treatment regimes to improve adherence (Pill burden)	21
Effects of ARV regimen on eating patterns	23
2.5.3 Patient - provider relationship	23
2.5.4 Clinic setting	23
Difficulties with re-supply of medicines	24
2.5.5 Disease characteristics.....	24
Depression and severe anxiety.....	25
Beliefs and knowledge	25
CHAPTER THREE.....	27
3.0 METHODS.....	27
3.1 Type of study.....	27
3.2 Study area	27
Successes of the unit.....	29
Challenges of the unit	29
3.3 Variables	30

3.4. Study population	30
3.5 Sampling	31
3.5.1 Sample size.....	31
3.5.2 Sampling method	31
3.6 Data collection technique/methods & tools.....	32
3.6.1 Quantitative data collection technique and tool	32
3.6.2 Qualitative data collection technique and tool	33
3.7. Quality control.....	33
3.8 Data processing and analysis	34
3.8.1 Quantitative data	34
Percentage adherence = $\frac{\text{Number of tablets taken}}{\text{Number of tablets should have been taken}} \times 100$	35
Number of tablets should have been taken.....	35
Pill count (three-month).....	35
Self-report (7-day recall)	36
Self-report (three-month recall).....	36
None	36
3.8.2. Qualitative data analysis.....	37
3.9 Ethical considerations/issues.....	37
3.10 Pretest.....	38
CHAPTER FOUR	39
4.0 RESULTS AND FINDINGS.....	39
4.1 Demographic Characteristics, Socioeconomic Status, and Education.....	40
4.2 Assessment of adherence to ARTs	40
Table 4-2 Assessment of adherence to ARTs.....	41
4.3. Comparison of adherence using pill count and self report.....	42
4.4 Factors that contribute to optimal adherence.....	43
4.5 Qualitative data.....	44
Background information	44
Experience with ART	44
Benefits of taking ART	46
Social support.	46
A desire to stay alive for others	47

Good quality adherence counseling programme.	48
Faith/ belief in God	48
CHAPTER FIVE	50
5.0 DISCUSSIONS	50
5.1 DEMOGRAPHIC CHARACTERISTICS OF THE PATIENTS	50
5.2 Assessment of adherence rates to ARTs.....	50
5.3 Comparison of adherence using pill count and self report.....	53
5.4 Factors that contribute to optimal adherence.....	55
5.5.1 Limitations of study	56
CHAPTER SIX	57
6.0 SUMMARY, CONCLUSIONS AND RECOMMENDATION	57
6.1 SUMMARY	57
6.2 CONCLUDING REMARKS.....	58
6.3 RECOMMENDATIONS	58
6.3.1 National AIDS Control Programme.....	58
6.3.2 Management of KBTH.....	59
6.3.3. Adult ARV users at KBTH (patients)	59
REFERENCES	59
APPENDICES.....	66
INFORMATION SHEET FOR PARTICIPANTS	66
ADHERENCE TO ANTIRETROVIRAL MEDICINES AMONG ADULT HIV/AIDS PATIENTS AT THE KORLE BU TEACHING HOSPITAL IN ACCRA.....	66
FOCUS GROUP DISCUSSION (FGD) GUIDE FOR PARTICIPANTS	73
Topics Discussed	74

ABSTRACT

It is very important to assess adherence to ARTs to understand why treatment fail. However, measurement of adherence especially in the clinic setting is very difficult as there is no single method that best measures it.

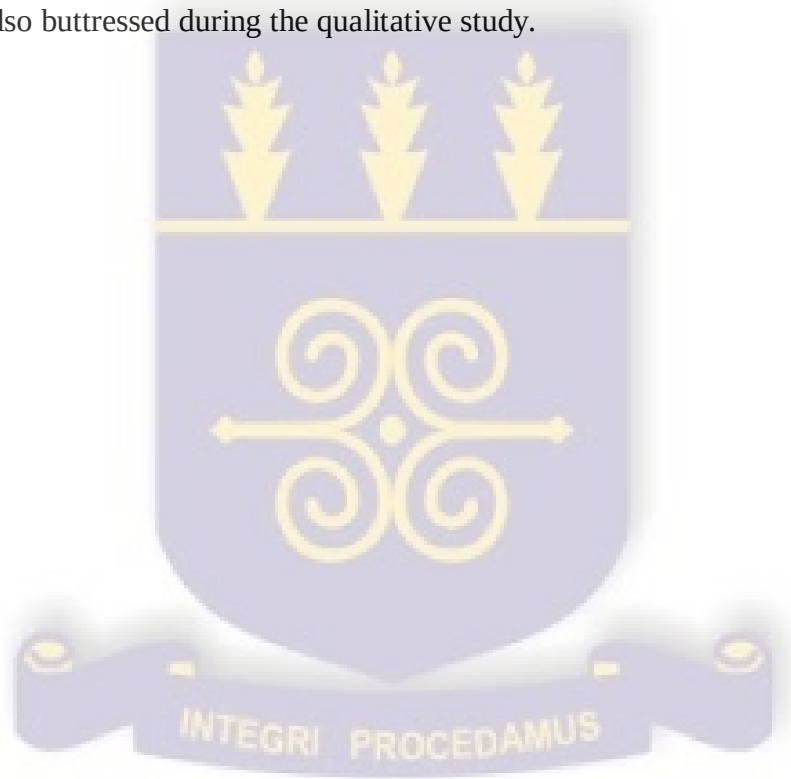
The main objective of this study was to measure adherence to ART among HIV patients (PLWHA) at the Korle Bu Teaching Hospital (KBTH) using, pill counts and Self-report and also to identify factors that contributes to optimal adherence.

The design was a cross sectional descriptive study which used systematic sampling to collect quantitative and qualitative data from adult ARV users who have been on ARTs for at least three months and attended clinic between May and July 2009. A t-test was performed to compare mean adherence and Multivariate logistic regression was used to determine factors that were associated with adherence. Analysis included 229 patients.

Of the three methods used, optimal adherence rate ($\geq 95\%$) was highest for 7- day recall (100%), followed by three-month pill count method (98%), and three-month visual line self report recorded the least adherence rate (77%). Overall rate of adherence was found to be 92%. This is higher than what some studies in developing countries have found. However, the overall adherence was below the minimum expected adherence of 95% which experts in ART management recommend.

Three month pill count recorded high optimal adherence compared to a visual line self report optimal adherence which was low but matched results from most African countries. Pill count method of measuring adherence should be used routinely to monitor patients on ARTs while self reported adherence should be used to identify patients who need extra support for adherence.

Quality of care was found to be a factor that contributes to optimal adherence, a finding that was also buttressed during the qualitative study.



LIST OF TABLES

Table 3-1: ARV Regimen at the Fevers unit

Table 3-2: Independent variables affecting adherence

Table 4-1: Demographic characteristics, socioeconomic status and education

Table 4-2: Assessment of adherence to ART

Table 4-3: Comparison of adherence using pill count and self report

Table 4-4: Factors that contributed to optimal adherence

LIST OF FIGURES

Figure 1-1: problem analysis diagram on factors affecting adherence

LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral therapy
DOT	Direct Observation Therapy
EDM	Electronic Drug Monitoring
GHS	Ghana Health Service
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
KBTH	Korle Bu Teaching Hospital
MEMS	Medication Events Monitoring System
MOH	Ministry of Health
NACP	National AIDS Control Programme
PLWHA	People Living with HIV/AIDS
PLWHIs	People living with HIV Infections

PMAQ	Patient Medication Adherence Questionnaire
UNAIDS	United Nations agency for AIDS
WHO	World Health Organization

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

The WHO/UNAIDS estimated that there were 33.2 million people living with HIV globally, of which 22.5 million people are in sub-Saharan Africa (WHO, 2007). There are currently about 300,000 AIDS infected persons in Ghana of which 15,000 are on anti-retroviral drugs (HIV Sentinel Survey Report, 2008).

Since the launch of the WHO ‘3 by 5’ initiative in 2003, many countries in sub-Saharan Africa have established national antiretroviral treatment (ART) programmes (WHO, 2005) including Ghana. One of the critical components of the care and support of PLWHAs is the administration of ARV therapy. Even as the issue of access to anti-retroviral drugs is being adequately addressed by the government of Ghana, another significant challenge that comes to the fore front as a result of access is adherence. Adherence to treatment is a critical factor in the success of ART. Patients must achieve at least 95% adherence in order to avoid treatment failure and the risk of developing drug resistant strains of the virus. (Paterson et al., 2000; Reiter et al., 2000; Chesney, 2000).

Measurement of adherence may be very important in detecting why patients fail anti-retroviral therapy. While adherence can be expressed quantitatively as a percentage of expected treatments actually taken; its accurate measurement is very difficult. There is no gold standard for adherence measurement. While adherence can be ensured by directly

observed treatment, this may not be practical for twice - daily therapy which has to be taken for life. As a result, levels of adherence can only be estimated by use of indirect measures. Many studies employ a number of methods, either alone or in combination to measure adherence. The most commonly used methods include pill counts, pharmacy refill records, various self - reporting tools such as questionnaires and visual analogue scales, measurement of blood levels, and electronic drug monitors, which monitor the number of times the cap of a pill container is removed.

According to Gill et al. (2005) the hierarchy of adherence measures ranks physician and self - assessment report the least accurate, pill count intermediate and electronic drug monitoring (EDM) the most accurate adherence marker. However, no single measure is appropriate for all settings or outcomes. It has been found that the use of more than one measure of adherence allows the strength of one method to compensate for the weakness of the other and to more accurately capture the information needed to determine adherence levels (Vitolins et al., 2000).

Studies in African settings have indicated optimal adherence rates (i.e., the proportion of patients who adhered to their ART schedule at least 95% of the time) ranging from 54% to 98% depending on the measure used (Weiser et al, 2003). African studies thus agree with international literature that more objective measures of adherence (e.g. unannounced pill counts and medication event monitoring systems) tend to be more sensitive to lapses in adherence (Liu .etal,2001). However, such measures are not feasible in resource-

limited settings with large-scale programs, and there is a need to determine the utility of simpler measures of adherence such as clinic-based pill-counts and self-report in predicting virological response in the African context.

As yet, there are limited studies on adherence rate at the Korle Bu Teaching Hospital (KBTH). This study sets out to measure pill count and self-report (seven-day recall and three-month visual analogue) adherence among adult HIV/AIDS patient at the KBTH.

1.2 Statement of the problem

There is growing concern about suboptimal adherence to ART as significant barriers to care in most resource poor countries especially in sub Saharan Africa. (Kityo et al, 2002). The issue now arises on how to measure adherence. Depending on which measures are used, a patient may have conflicting levels of adherence (Vincke et al, 2002). Direct Observation Therapy (DOT) may be considered the gold standard for measurement of adherence to HAART but is far from ideal since most regimens involve multiple daily doses which make DOT impractical. Self report is simple and inexpensive but patient may have difficulty to recall medicine intake over long period. Pill count is useful in clinical practice but is subject to manipulation by patient. Electronic device monitoring system is considered closest to a gold standard (Hardy, 2005) in measuring adherence, yet, it neither guarantees that patient swallowed medicine nor is it cheap especially in resource constraint country like Ghana. Currently, there is limited published study on

adherence measurement that employed more than one method to measure rate of adherence at the KBTH.

Furthermore, the Fevers unit of KBTH provides health care to about five thousand patients who are HIV positive. These are patients who have been on ART for different duration and are from diverse cultural, educational and socioeconomic backgrounds, factors that may impact significantly on adherence. The determination of levels of adherence and the factors affecting adherence in these patients will contribute greatly to the clinical approach and the development of programmes to improve adherence.

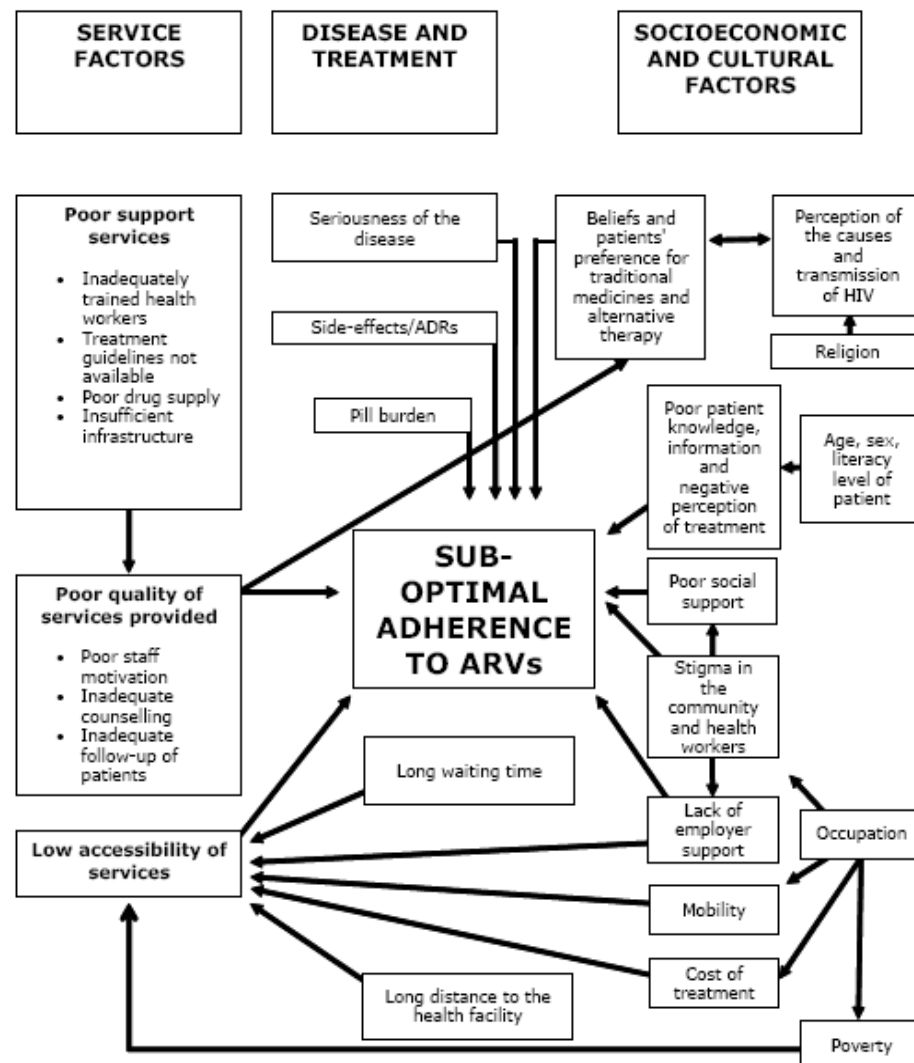


Figure 1-1: Problem Analysis Diagram on factors affecting ARV Adherence.

(Hardon et al, 2006)

1.3 Justifications for study

As more people gain access to ART, new initiatives are needed to help ensure that patients adhere to treatment. The maintenance of viral suppression requires maximum adherence to ART, at least 95%, which is difficult to achieve and maintain (Parades, 2000; Garcia et al., 2003). Insufficient adherence to ARVs may result in treatment failure and the emergence of drug resistant strains of HIV and require a change to second line treatment regimens, thereby greatly increasing treatment costs (Bangsberg, 2000). Increased treatment costs would either require more money or deny access to ARTs for more people. Such studies would help inform NACP/KBTH on the need to improving or sustaining adherence as access to ART is scaled up nationwide.

1.4 Study objectives

To assess adherence to ART among adult ARV users at the Korle Bu Teaching Hospital

1.4.1 Specific objectives

- To determine rates of adherence to ART among adult ARV users at KBTH.
- To compare rates of adherence to ART using pill count and self report.
- To identify factors that contribute to optimal adherence among adult ARV users at KBTH

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Definition of adherence

Adherence is described as the engagement and accurate participation of an informed patient in a plan of care (Rabkin et al., 2003). The concept of ‘adherence’ has a broader meaning than compliance. It encompasses the extent to which a patient follows instructions and implies understanding, consent and partnership. It also includes entering into and continuing in a programme or care plan, as well as keeping appointments and tests as scheduled (Rabkin et al., 2003).

2.2 Measurement of adherence to antiretroviral medicines

There are various methods of assessing adherence to antiretroviral medications. These include Electronic monitoring, Pill counts, Pill recognition, Review of pharmacy records, Patient self-report, Biological parameters, Provider prediction of adherence, and Therapeutic drug monitoring. None of these methods is considered the gold standard since each method has its strengths and weaknesses.(Paterson et al,2000)

2.2.1 Biological parameters

The mean corpuscular volume (MCV) has been used as a crude marker of adherence to zidovudine or stavudine. Among patients receiving these medications, a significant (and independent) association has been found between virologic response and the presence of macrocytosis (Duong et al, 2000), suggesting that an increase in MCV is correlated with adequate adherence to therapy. However, there are disease conditions that might also

cause an increase in MCV. These conditions include vitamin B12 deficiency, folic acid deficiency, alcoholism, and liver disease. Furthermore, use of the MCV in assessing adherence to ARTs is limited to zidovudine and stavudine.

Uric acid levels have been promoted as an indicator of adherence to didanosine use (Richardson et al, 1993). However, others have-not confirmed this association (Duong et al, 2000). It has been suggested that there may be a dose effect, with lower doses of didanosine (for example, 300 mg/day) not being associated with increased uric acid levels, while higher doses (for example, 500 mg/d or more) are associated with increased uric acid levels.

Lipid levels have been shown to have some correlation with adherence (Vergis et al, 2001). In particular, patients with an adherence rate of at least 80% to a protease inhibitor-containing regimen were significantly more likely to have elevated low-density lipoprotein levels compared with patients with an adherence rate of <80% (Vergis et al, 2001).

Hyperbilirubinemia is seen in some patients treated with indinavir. However, there is no significant association between hyperbilirubinemia and indinavir adherence (Duong et al, 2000). In one recent study, just 23% patients receiving indinavir had hyperbilirubinemia, and there was no correlation between hyperbilirubinemia and virologic outcome (Duong et al, 2000).

2.2.2 Therapeutic drug monitoring

Monitoring plasma concentrations of antiretroviral medications is pharmacologically possible for many drugs. More recently, studies have shown a link between low plasma

protease inhibitor levels and virologic failure (Duong et al, 2000). However, at the present time, procedures for sample collection, cross-validation of analytical procedures, and interpretation of assay results have yet not been standardized (Acosta, 2002).

It has also been noted that ‘white coat compliance’ or ‘the toothbrush effect’ (i.e., increased adherence immediately before clinic visits) is a well-known behavior that may limit the usefulness of therapeutic drug monitoring. Plasma drug levels can reflect only recent treatment adherence. Moreover, factors other than adherence (for example, drug interactions and diet) may be linked to low plasma concentrations of antiretroviral medications (Paterson et al, 2000).

2.2.3 Provider prediction of adherence

Physicians and other healthcare providers routinely make predictions of the adherence of their patients to antiretroviral therapy, especially prior to initiating therapy and when assessing reasons for poor virologic outcome. Nonetheless, a number of studies have shown that providers are poor estimators of adherence. (Paterson et al, 2000). In a study comparing physician prediction with adherence measured by electronic monitoring, 51% of patients in whom physicians predicted that adherence would be <80% actually had >80% adherence (Paterson et al, 2000).

This finding is alarming because physicians may potentially deny patients ARTs when they have cause to believe that patient is more likely to default leading to non-adherence. In spite of the lapses found in provider prediction of adherence, provider perception may improve with recognition that untreated mental illness (such as depression) and alcoholism may be important predictors of poor adherence (Paterson et al, 2000).

2.2.4 Review of pharmacy records

This can be a convenient measure of adherence assessment in situations in which a patient has a single source of antiretroviral medication e.g. as in the case of Ghana. Pharmacy refill records are used as an assessment of adherence for patients. However, even in this situation, a major problem may be one of drug hoarding, i.e., receipt of drugs from a pharmacy is not a guarantee that the drugs have actually been consumed (Paterson et al, 2000).

2.2.5 Patient self-report

Numerous methods have been applied to gain, from the patient, an assessment of antiretroviral drug adherence. Among the most common have been face-to-face inquiry or patient-completed questionnaires. It is known that how one asks about adherence may influence self report. (Paterson et al, 2000; Turner et al, 2001). There is a requirement that this inquiry be non-judgmental. This can be achieved with a preamble before the adherence questions to help patients understand that they are not being judged and that honest answers are being sought.

Some consider it ideal that the questioner not be a healthcare provider (Turner et al, 2001). In face-to-face interview, questioning about the number of doses missed during the past 7 days can be translated quantitatively into a percentage adherence. Shorter time periods are insufficient to determine whether adherence of <95% is likely. However, for some patients, recollection of pill taking for a 7-day period is not perfect. If shorter time periods are used, additional questions may be necessary to determine adherence over weekends compared with weekday because behaviors can differ in these two periods.

A structured questionnaire, the Patient Medication Adherence Questionnaire (PMAQ), has been devised. This is a self-administered questionnaire that contains 31 questions designed to evaluate drug adherence and to promote understanding of a patient's adherence behavior and its determinants (Duong et al, 2000). In one study, the adherence score from the PMAQ was significantly correlated with virologic response (Duong et al, 2000). A number of modifications to the PMAQ have been suggested to increase its usefulness (Duong et al, 2001).

Other alternative means of assessing self-reported adherence include computer-assisted self-interviewing (Bangsberg et al, 2002). This may encourage more honest answers than face-to-face interviewing. Finally, a patient diary of adherence represents another alternative mode of self report. This can be an inexpensive and accurate tool. Unfortunately, less compulsive persons may complete it retrospectively or not at all.

Since patient self-report is likely to be the simplest means of assessing adherence, it is important to determine its reliability in measuring adherence.

Liu et al. (Liu et al, 2001) found that adherence as measured by patient interview was considerably higher than adherence as measured by other means (electronic monitoring or pill count). A significant difference was observed between adherence (as measured by interview) in patients with detectable viral load and undetectable viral load at 24 weeks after initiation of adherence assessment. No such difference was observed at 8 weeks

after initiation of assessment. Although self-report is very simple and convenient, it overestimates adherence. Self-report is most useful for those patients who admit to poor adherence. Such patients truly are nonadherent (Murri et al, 2000).

2.2.6. Pill recognition

Parienti et al. (Parienti et al, 2001) developed a ‘pills identification test,’ in which HIV-infected patients were asked to identify the antiretroviral medications they had been prescribed from a board containing 23 antiretroviral pills and 2 similar appearing pills for each true antiretroviral pill. The authors compared the results from this test with a 4-item self-report measure. A significant correlation was found between the pill identification test and the 4-item adherence self-report. The ‘pills identification test’ seems to be a simple way to assess knowledge of an antiretroviral treatment regimen, but it has not yet been validated against a rigorous measure of adherence (Parienti et al, 2001) .

2.2.7 Pill counts

Pill counts are usually performed at the clinic, after patients have brought the pill bottle with them. A healthcare provider at the clinic counts the number of pills remaining in the bottle and computes the number of missed doses by comparing the difference between the actual and expected number of pills remaining in the bottle. Pill count however have some disadvantages which include the fact that patients dispose of pill (pill dumping) to make their adherence appear better than it may actually be.

To surmount this challenge, in research settings, the bottle may contain a random number of extra pills. Also, unannounced pill counts have also been used to guard against this occurrence (Bangsberg et al, 2001). Bangsberg et al (2001) successfully used this procedure in assessing adherence in HIV-infected homeless and marginally housed persons. Another disadvantage of unannounced pill counts is that some patients may regard them as an invasion of privacy.

2.2.8 Electronic monitoring

Electronic monitoring devices are the most sophisticated means of assessing adherence. The Medication Events Monitoring System (MEMS) cap is an example of electronic monitoring device. These devices are pill bottles with caps that contain an electronic chip that records each time the bottle is opened. The caps can be scanned, therefore, facilitating download of data. The data include time of opening of the pill bottle and can be readily analyzed to determine the level of adherence and also patterns of timing of pill consumption. Electronic monitoring has the advantage that it is extremely difficult to feign adherence as can be achieved with pill counts. Furthermore, the detail of analysis is considered the best. However, electronic monitoring may potentially underestimate adherence because patients may withdraw more than one tablet during each opening of the bottle (Parienti et al, 2001).

For example, a patient may withdraw two tablets each morning before going to work—one tablet for immediate consumption and the second for consumption at work. This will only be recorded by the device as one pill bottle opening in the morning—the lunchtime dose will be missed. This problem can be averted by informing patients at the outset that

during the monitoring period, tablets should not be removed from the pill bottle unless for immediate consumption.(Paterson et al,2000)

2.3 Preferred adherence rate

Recent evidence suggests that an 80% level with HAART adherence may be inadequate to prevent the development of antiretroviral drug resistance.(Holzemer et al.,1999; Paterson et al.,2002) This is significant in light of preliminary studies that suggest most individuals on HAART therapy are not 100% compliant.

The need for sustained viral suppression, increase in CD4 cell count and decreased morbidity from HIV/AIDs, makes adherence to ART an issue of paramount importance. Given the high rate of viral replication and the long-term survival of HIV reservoirs within treated patients, it has been estimated that at least 95% adherence with therapy is required to maintain HIV viral suppression and to prevent the emergence of drug resistance. (Paterson DL, et al., 2000; Reiter ,et al.,2000;Chesney ,2000; Orrell et al., 2003).Other data suggest that 100% adherence levels achieve even greater benefits (Fischl et al., 2000).

2.4 Adherence rates in developing countries

Studies in African settings have indicated optimal adherence rates (i.e., the proportion of patients who adhered to their ART schedule at least 95% of the time ranges from 54% to 98% depending on the measure used (Weiser et al., 2003).

A study conducted in La Côte d'Ivoire (Diabate' et al, 2007) reported that 74.3% of participants had adherence levels of 95% or greater using self report. Another study conducted in La Côte d'Ivoire showed the median self report adherence rate to be 78.0% using pill count (Eholie' et al, 2007). Another study conducted in Tanzania which used pill count, visual analogue and self report estimated a very low overall adherence (>95%) to be 21.0% (Irunde et al, 2005). However, Orrell (2003) reported a mean pill count adherence of 93.5% among HIV patients on ART in South Africa.

Furthermore, studies conducted by Byakika-Tusime (2003), reported good adherence of 67% using self report in Uganda. However, another study that was conducted in Uganda (Muganzi et al, 2004) using self report recorded high optimal adherence (>95%) of 98%. A randomized HIV/AIDS management trial in Uganda and Zimbabwe reported good adherence ($\geq 95\%$) which was found to have increased from 87% four weeks after initiation to 94% at forty-eight weeks using pill count and questionnaire (Muyingo et al, 2008).

Similar studies conducted in Blantyre, Malawi (Bell et al, 2007), discovered that the mean adherence using the medication event monitoring system MEMS cap (MC) was 88.1% whereas a significantly higher figure of 98.6% mean adherence was reported using the pill count method. Another study was conducted in Cameroon to compare adherence to antiretroviral therapy using drug level monitoring and self-report to explore the relation

between these 2 methods and viral load measurements. The study reported 88% optimal adherence using drug level monitoring compared to 97.5% optimal adherence using self report. (Kouanfack et al, 2008).

In looking at determinants of adherence to antiretroviral drugs among people living with HIV/AIDS in the Ife-Ijesa zone of Osun state of Nigeria, Muhammed et al.,(2009),found the overall adherence rate in the study population to be 44% using self report which is very low. Another study conducted in Nigeria (Erah PO and Arute JE,2008) measured adherence of HIV/AIDS patients to antiretroviral therapy in a tertiary health facility in Benin City using self-reporting and pill counting methods. Optimal adherence ($\geq 95\%$) between 58% to 60% was observed which was lower than those reported in many other sub-Saharan African countries. Furthermore, Daniel et al (2004) conducted similar study in Nigeria using interview administered questionnaire to collect data on 7 day recall of drug use. The study found an overall adherence ($\geq 95\%$) of 79.2% which is also quite low.

Hardon et al accessed adherence as well as factors that facilitate or constrain adherence to ART among adults at four public health facilities in Botswana using pill count, visual analog and self report. The study reported mean adherence rate of 95% using pill count, and 98.0% using two-day recall method whilst mean adherence rate for self report was 92.0%. The optimal adherence rate ($\geq 95\%$) for pill count, two-day recall and self report were 75.0%, 96.0% and 60.0% respectively (Hardon et al,2006).

These studies show that assessment of adherence using pill count is generally higher than self report adherence. Assessment of adherence using self report is also higher than electronic drug monitoring system.

2.5 Factors contributing to Adherence

Structural factors, disease or treatment factors, and socio-economic factors are the three broadly grouped factors that affect adherence (Weiser et al., 2003; Horne 1998; Eldred et al., 1998). These three broad groups are commonly divided into five intersecting categories (Reiter et al., 2003). These categories include patient variables, treatment regimens, disease characteristics, patient - provider relationship, and clinical setting.

2.5.1 Patient variables

Patient variables include socio demographic factors (age, gender, race, income, education, literacy, housing status, HIV risk factors) and psychosocial factors e.g. mental health, substance abuse, socio cultural issues and support, knowledge and attitude about HIV and its treatment (Carrieri, 2002; Nemes et al., 2003; Murphy et al., 2004; Machtinger and Bangsberg, 2005). Sociodemographic and psychological issues have great potential to impact on adherence. For instance, family support and religious beliefs about illness and medication may influence motivation and adherence (Haynes, et al., 1996).

The issue of disclosure has also been found to have serious implications for adherence (Ormazu, 2000; Klitzman et al., 2004). For example, the use of medication may inadvertently reveal a person's HIV status; poverty may prevent individuals from following treatment - related dietary advice; drug and alcohol abuse may impair judgment and the ability to adopt and maintain routine medication use; and family responsibilities may require adults to place the health care needs of others before their own. Furthermore, some studies have shown that patients who understand why they have to take their ARTs as recommended are more likely to adhere than those who do not have this knowledge. (Anderson, 1999; Horne, 2001).

Although side effects have been reported Although side - effects have been cited by some studies in developed countries as predictors of adherence, experience of symptoms and views about medications may be complex and may vary according to the type of regimen (Chesney, 2000; Carr and Cooper, 2000; Ammassari et al., 2001). Some studies attributed adherence to one's social groups but more recent studies have reported unpredictable adherence using certain social classes (Horne, 1998; Lerner, 1998; Carrieri, 2002).

Demographic and socioeconomic factors

Although the literature consistently demonstrates that demographic characteristics are not strong predictors of adherence, some correlates of adherence are described below together with socioeconomic factors.

Age

Age may influence adherence. Studies have found that, with the exception of the most elderly, adherence increases with age. Jones et al (1999) reported positive correlation between being younger and sub-optimal adherence to ARTs.

Level of education

A lower level of general education and poorer literacy may impact negatively on some patients' ability to adhere, while a higher level of education has a positive impact (Catz et al., 1999).

Financial constraints

Studies conducted in Africa reveal that the cost of medication is one of the most significant barriers to treatment adherence. In Botswana, Weiser et al. (2003) reported adherence difficulties related to the financial demands of therapy and an inability to afford medicines for varying periods. The study noted that 70% of patients claimed that the cost of ARVs posed a problem for them, and 44% of patients believed that the cost impeded their ability to adhere to treatment. Similarly, over one-half of health care providers (56%) believed that financial problems often or always impeded adherence to ART.

The extent to which financial difficulties played a key role in sub-optimal adherence is also reported in study findings in Uganda for patients receiving therapy that are not subsidized (Byakika-Tusiime et al., 2003). Medications and clinic visits cost money and may stretch an already meager budget. In resource-poor countries many people live below the poverty line and there is often no medical insurance or disability pension for people living with HIV (Katabira, 2002).

Social support

Living alone and a lack of support have been associated with an increase in suboptimal adherence (Williams and Friedland, 1997), and social isolation is predictive of sub-optimal adherence. Not living alone, having a partner, social or family support, peer interaction, and better physical interactions and relationships are characteristics of patients who achieve optimal adherence (Motashari et al., 1998).

2.5.2 Treatment regimens

These include the number of pills prescribed, the complexity of the regimen (dosing frequency and food instruction), the specific type of ARV and medication side - effects. The complexity of the regimen and side - effects caused by it are clearly associated with sub - optimal adherence (Chesney, 2000; Machtinger and Bangsberg, 2005).

Simplifying treatment regimes to improve adherence (Pill burden)

Simple regimens and regimens that fit into a patient's lifestyle enhance adherence.

Studies have shown that patients prefer regimen that are incorporated into their lives so that they can easily adapt to it (Erlon and Mellors, 1999). As a regimen increases in complexity, its inconvenience makes it difficult to incorporate into daily living. Much recent research is aimed at simplifying ART to twice daily or even once daily dosing (Grierson et al., 2000).

There are many kinds of ARVs, which attack the virus in different ways. For this reason, treatment today always involves a combination of ARVs. The most commonly used are from three classes: nucleoside reverse transcriptase inhibitors (NRTIs), non - nucleoside reverse transcriptase inhibitors (NNR - TIs) and protease inhibitors. A new class of drugs known as entry inhibitors prevents HIV from entering the T - cells, which are crucial in maintaining the individual's immune response. All ARVs have different side effects and these can have an impact both on how the medicines will be used and how patients take them. (Grierson et al., 2000)

For people on ART, a typical combination of medicines consists of three ARVs, plus other medication to prevent opportunistic infections. This can result in a high pill burden, taking medicine three times a day, dietary and dosing idiosyncrasies, large capsules or tablets, and specific storage instructions. The complexity of this regimen may have a significant impact on a patient's ability to adhere. Additional medications taken for

symptomatic relief (such as analgesics, and other common treatments) in patients with advanced disease further add to the pill burden and toxicity (Grierson et al., 2000).

A study in Senegal reveals that a high pill burden is associated with poor adherence among patients who have to take a large number of ARV pills (Dansburg et al., 2003). In Ghana, first-line treatment involves the use of the following combinations: lamivudine, zidovudine, and nevirapine (with stavudine as alternative to zidovudine, and efavirenz as alternative nevirapine). Second-line medicines used are didanosine, abacavir/ nelfinavir, with tenofovir serving as alternative to didanosine or lopinivir/ritonavir as alternative to nelfinavir (NACP annual report, 2007). Patients therefore take about four tablets a day for those on first line drugs while those on second line take more than that.

In some situations, several ARVs are combined in a single tablet, a fixed-dose combination (FDC), which ensures that patients always take multiple doses together. As a first - line treatment, antiretroviral therapy (ART) can be delivered relatively cheaply. However, if drug - resistance develops and these medicines are no longer effective, second - line ARVs may be required. These second - line ARVs are much more expensive than first - line medicines (WHO, 2003).

Effects of ARV regimen on eating patterns

Dietary restrictions add to the complexity of ART and often require adjustments in lifestyle. Patients can find their meal schedule compromised by ARVs that need to be taken on an empty stomach. This can be particularly difficult if workmates, family or friends are unaware of the patient's HIV status (Grierson et al., 2000). Complicated regimens with rigid dosing intervals may also interrupt sleep. The physical aspects of a particular medication (for example, taste, size or formulation) may also affect a patient's ability to adhere.

2.5.3 Patient - provider relationship

This includes the patient's overall satisfaction and trust in the provider and clinic staff; the patient's opinion of the provider's competency; the provider's willingness to include the patient in the decision - making process; the affective tone of the relationship (e.g. warmth, openness, cooperation); the compatibility of race/ethnicity between patient and provider; and the adequacy of referral. (Chesney,2000)

2.5.4 Clinic setting

This includes the availability of transport, general environment, flexibility of appointments, perceived confidentiality, and satisfaction with past experience with the health care system (Nemecheck &Tritle, 1998). Chesney (2000) found that dissatisfaction with the health services is a predictor of non - adherence.

Difficulties with re-supply of medicines

Obtaining a prescription during a clinic visit is reported as an obstacle to adherence. In some developing countries, just over 50% of ARV users are given a prescription which lasts for three months, 40% receive a prescription for one month and 12% for two months (Burgos et al., 1998). In addition, some dispensing pharmacies will only dispense one month's medication at a time (often on a single designated clinic day) and not all pharmacies are able to dispense ARVs. As a result of such difficulties in prescription procedures, some patients attend their local pharmacy for most prescription medicine and another separate pharmacy for their ARVs. This is a barrier to optimum adherence in that problems in obtaining or taking medicines have to wait until the designated clinic day, by which time patients may already be defaulting on their dose (Grierson et al., 2000).

2.5.5 Disease characteristics

This includes the stage and duration of HIV infection, associated opportunistic infections, and HIV - related symptoms. The severity of the illness could impact negatively or positively on adherence to ART (Chesney, 2000). Prior opportunistic infections, symptom severity and low CD4 counts are all predictors of adherence. Progression of disease creates a sense of urgency for treatment among patients. (Erlon and Mellors, 1999).

Seeing an improvement in the immunological and virological indices used to monitor ART (CD4 cell counts and HIV viral load) may be a powerful incentive to maintain adherence (Kaplin et al., 1999). However, caution should be exercised in emphasizing a patient's improved laboratory indices without assurance that adherence is almost

faultless. The value of these indices may improve in the short term, despite sporadic adherence and this may reinforce a patient's level of sub-optimal adherence. Lack of symptoms (despite laboratory evidence of the need for ART) may have an adverse effect on adherence (Jones, et al., 1999).

Depression and severe anxiety

Depression and severe anxiety are both predictors of sub-optimal adherence (Hirschorn et al., 1998). At some time in the course of their illness, most people with HIV, experience a psychiatric disorder (Buhrich and Judd, 1997). Depression and/or anxiety are reported in up to 70% of AIDS patients with symptomatic disease. Adherent patients demonstrate significantly less depression or other psychiatric disturbance (Catz et al., 1999). As the disease progresses, HIV may have an impact on the central nervous system and affect memory. AIDS-related dementia (AIDS Dementia Complex) is a common finding in patients with advanced disease and is characterized by abnormalities in cognitive and motor functions (Meisler et al., 1993). Even when cognition is unimpaired, it is difficult to remember when to take medications.

Beliefs and knowledge

Patient's beliefs about their illness and the effectiveness of medication are predictive of adherence. A good level of understanding about HIV by the patient, a belief that ART is effective and prolongs life, and recognition that poor adherence may result in viral

resistance and treatment failure (Wenger et al., 1999) all impact favorably upon a patient's ability to adhere. Conversely, a lack of interest in becoming knowledgeable about HIV and a belief that ART may in fact cause harm adversely affect adherence.

CHAPTER THREE

3.0 METHODS

3.1 Type of study

A cross-sectional descriptive study was used for the study. Quantitative and qualitative methods were used to assess adherence to ART among adult patients at KBTH.

3.2 Study area

The study was conducted at the Fevers unit of the Korle Bu Teaching Hospital which is a tertiary health institution in Ghana. The Fevers unit is one of the sub-units of the medical department of the Korle Bu Teaching Hospital. The unit sees mainly patients with rabies, tetanus and HIV/AIDS. However HIV patients form about 98% of the patients who are managed at the unit. Patients who visit the facility are first seen by counsellors and after registration, are enrolled into the treatment and care program. This is followed by consultation with a clinician who makes an assessment and documents the diagnosis and the WHO clinical staging. Laboratory /diagnostic tests are requested and co-trimoxazole prophylaxis is started if indicated as well as appropriate management of other opportunistic infection.

Patients are initially given a two week follow-up appointment for their second visit and during the second visit patients are enrolled into the comprehensive HIV/AIDS care and treatment programme. The patient's data is entered into the health information management system and an assessment for initiation of antiretroviral therapy according to national guidelines is conducted. Two sessions of adherence counselling are scheduled if the patient meets clinical criteria for initiating ART and subsequent administration of

ART is started after completion of the adherence counselling session (i.e. a third session of counselling is done at the pharmacy before ARVs are dispensed). Patients who have started ART are seen initially after two weeks, followed by once every month for the next three months and then bi-monthly, or every three months thereafter if there are no complications. Patients with complications are seen as and when the complications occur. Patients who do not qualify for ART are maintained on co-trimoxazole prophylaxis.

The fevers unit was one of the first facilities in a tertiary Hospital in Ghana which started ARTs in 2003. Currently the unit runs three clinics per week and manages about 350 patients a day. The facility has 5 medical doctors, 15 nurses, 2 data managers and 4 pharmacists who are directly involved in managing PLWHA at KBTH. There is an out-patient and in-patient section with a 30-bed capacity and 10,000 registered clients. There are about five thousand patients currently on ARTs

ART is subsidized by the government of Ghana and global AIDs fund and this includes laboratory monitoring. Patients however pay for viral load tests which are conducted outside the hospital as well as radiological investigations e.g. chest x-rays, ultrasound, and CT scans. Furthermore, Patients pay an amount of five Ghana cedis per month as service charge but those who cannot afford this amount are not precluded from treatment so that medication would not be a problem to adherence. Patients commute from both far and near e.g. other regions of the country and even outside the borders of Ghana.

Successes of the unit

Mortality among PLWHA being seen at the facility has generally reduced from 80% to 25%. Furthermore, there has been good treatment response by patients on ARTs at the facility. Also, the unit serves as training centre for other healthcare institution. In addition, a national guideline /policy have been developed.

Challenges of the unit

In spite of the successes, the unit has some challenges which include non-disclosure by patients and stigmatization. Also, drugs for managing opportunistic infections are sometimes not available and patients usually cannot afford. High patient load coupled with low staff strength lead to staff burn- out. Furthermore, there is poor motivation for staff at the unit. Again, there is inadequate bed and patients sometimes report too ill with some patients also being abandoned by family. Table 3-1 shows ARV regimen given at the Fevers unit of KBTH.

Table 3-1 ARV Regimen at the Fevers unit

1 st line drug	2 nd line drug
Zidovudine/Lamivudine/Nevirapine	Didanosine, Abacavir/Nelfinavir
Stavudine as alternative to Zidovudine	Tenofovir as alternative to Didanosine
Efavirenz as alternative to Nevirapine	Lopinivir/Ritonivir as alternative to Nelfinavir

3.3 Variables

The main dependent variable is the percentage of PLWHA who attained optimal adherence to ARTs. The independent variables that could affect optimal adherence are as in the table below (table 3-1)

Table3-2: INDEPENDENT VARIABLES AFFECTING OPTIMAL ADHERENCE

Service variable	Disease/treatment variable	Socioeconomic variables
• Limited accessibility of treatment • Lengthy waiting times • Attitudes and quality of care from health staff • Long distance to health facility.	• Seriousness of disease • Side effect • ADRs • Pill burden	• Illiteracy • Poverty • Stigma • Lack of social support • Poor knowledge and information

3.4. Study population

The study populations was PLWHA, 18 years and above, who have been initiated on ART for at least three months, mentally sound and had reported at the facility under study between May and July 2009.

3.5 Sampling

3.5.1 Sample size

The sample size was calculated based on the assumption that 74.3% of the patients achieve optimal adherence (Diabate' et al, 2007), a 6% margin of error, a study population of 5000, and at 95% confidence interval, a sample size of 203 was obtained using Epi Info 6 version 3.22 (July 2007). Making allowance for losses, it comes to approximately 230.

3.5.2 Sampling method

Based on the total number of patients on ART at the facility and the sample required, a sampling interval 'k' was calculated. Systematic sampling was used to select patients who have consented to be part of the study.

The first patient was randomly selected by balloting a set of balls numbered 1 to 21, and the number which was first picked then became the first patient. Beginning from the first patient picked as the starting point on the attendance register for that day, every 21st patient was selected. However, since some patients either declined, could not be easily located or did not have pills with them, every, 22nd, 23rd or 24th patient in the absence of the 21st patient, qualify to be selected. This continued until the total number of patients required for the sample was selected.

3.6 Data collection technique/methods & tools

The study involved the collection of quantitative data and qualitative data.

3.6.1 Quantitative data collection technique and tool

The technique used was an interview. Structured questionnaires were administered to selected respondents. The tool used was structured questionnaire. Some of the quantitative data were collected using the exit interview tool while part of the quantitative data were collected using an adherence tool (which was part of the questionnaire). The exit interviews which were conducted after patients had finished the consultation process, looked at demographic characteristics of patients, medical history of patients, patients' knowledge of ARTs, quality of healthcare as well as perceived problems and contributors of adherence. The remaining quantitative data were captured using the adherence tool to assess adherence prior to the patients collecting their medication at the pharmacy. One questionnaire was therefore administered to each patient. Patient records were also reviewed to confirm patient medical record i.e. date of HIV diagnosis, date of initiation of therapy and to ascertain record of previous pill count. This was subsequently confirmed by the primary investigator.

3.6.2 Qualitative data collection technique and tool

Four focus group discussions (FGD) were conducted, two each for both males and females using FGD guide. The selection of the patients was done through systematic sampling after determining the number of patients expected on that clinic day from the attendance register. Using the total number of patients required for the discussion and the number of patients expected on that clinic day, a sampling interval was obtained. The expected number of patients from the register was then divided by 16 to determine the 'kth' patient who would be picked and then every 'kth' patient was picked until the required number was obtained. If a patient was not willing to participate, the immediate next patient was selected.

Areas that the focused group discussion elicited information included patient background information, medical history of patient, knowledge/opinion of HIV/AIDs, perceived benefits of ART, disclosure, experience with ART, opinion of ARVs and herbal preparations, social support/networks, opinion of the quality of care in the facility, adherence problems and possible solutions.

3.7. Quality control

I) Quantitative data- To enhance quality, experienced field workers were used and all patients' record was critically examined at the end of each day. Field workers were also asked to cross-check the principal investigator's work. Almost all filled questionnaire were examined by the Principal Investigator and data collected was crossed checked with that in the patient's record for completeness and accuracy. At the end of each session the responses were examined critically to check that they were consistent and complete. At

the end of the data collection period there was double data entry using epiInfo version 3.4.1 and consistency was later checked for quality control purposes. SPSS version 11.5 was then used for the cleaning and analysis.

II) Qualitative data- all field workers were trained in qualitative data collection techniques. Transcription of focus group discussions were done two times by experienced research assistants. Small discussion groups of eight patients were used for each focus group discussion to facilitate easy running of the sessions. Good moderation of the discussion ensured that no single individual dominated the discussion and all notes well properly taken. All discussions were recorded and transcribed later.

3.8 Data processing and analysis

3.8.1 Quantitative data

Quantitative data collected with the help of structured questionnaire were entered twice in separate files and then validated using epiInfo version 3.4.1 database after creating a template. Data analysis was done using epiInfo and SPSS version 16. The optimal adherence for each measurement method and subsequently the overall adherence were estimated. A t-test was performed to compare adherence rate between pill count and self report .The hypothesis was that adherence measured by pill count and self report would be the same. The independent variables included age, sex, partner on medication, level of education, religion, , cure disease, get better, disclosure, social support, self motivation, side effect , cost and quality of care. Quality of care was measured as an aggregate of six factors. These factors included whether patient was listened to during consultation, whether patient was treated with respect, and also had opportunity to ask questions, and

whether patient had privacy during consultation as well as time spent during visit at the clinic. The presence of all these six factors during consultation and counselling was defined as quality of care.

The dependent variable (optimal self report adherence) was regressed on each of the independent variable for significance. After the univariate analysis, all the independent variables with a p-value of 0.05 or less were considered as significant. Quality of care ('Qcare'), ART cure disease ('curedx') and get better ('getbeta') had significant p-values of 0.002, 0.01 and 0.04 respectively. The three significant independent variables were regressed together to evaluate the group effect.

Adherence rates, measured as the percentage of pill intake over a specified time, was estimated using two methods: self report (i.e. 7-day recall and visual analogue) and a three-month pharmacy pill count. The overall adherence rate was estimated as a composite adherence rate which is calculated by finding the average of the pharmacy pill count adherence rate, visual analogue adherence rate and the 7-day recall adherence rate.

$$\text{Percentage adherence} = \frac{\text{Number of tablets taken}}{\text{Number of tablets should have been taken}} \times 100$$

Pill count (three-month)

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

determine the percentage adherence per participant. (Horizons/Population Council, 2004).

Self-report (7-day recall)

In the 7-day recall the patients were asked to recall the frequency and timing of medication over the previous seven days.

$$\% \text{ adherence over the last 7 days} = \frac{\text{No. of doses taken}}{\text{No. of doses should have been taken}} \times 100$$

From the formula, level of adherence by individual patients were classified into those with less than 95% adherence (sub-optimal adherence) and those with 95 % (or more) adherence i.e. optimal adherence.

Self-report (three-month recall)

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

None All

3.8.2. Qualitative data analysis

To process qualitative data, the recorded interviews were transcribed verbatim at the end of each interview with the help of field notes and translated into English and coded. Themes and sub themes were created from the transcripts; a matrix for each specific objective created and the relevant information were selected and added in discussion.

3.9 Ethical considerations/issues

Ethical clearance for the study was sought from the Ghana Health Service Ethical Committee. The permission to conduct the study was obtained from the Korle Bu Teaching Hospital Administration. The study was started after the ethical clearance had been provided and permission for the study granted. Participation of subjects conformed to the required ethical guidelines. Using a language well understood by the participants, all participants were well informed about the study, its objectives and method of data collection. Participants were also assured of strict confidentiality procedures and anonymity throughout the study. Furthermore, information received would be stored properly and used only with their consent. Participants were also informed that the outcome of study may be used to improve services received and that they were not going to be harmed in any way by participating in the study. Participants who agreed to be part of the study gave their consent by either a thumbprint or signature before being enrolled into the study and prior to data collection.

3.10 Pretest

Questionnaires were pre-tested at the Ridge Hospital and for a second time at the La General Hospital to address mistakes and omissions. Insight gained from focus group discussion was also taken into consideration in the questionnaire design. Certain sentences were rephrased and inclusions and subtractions made where necessary to properly address the issues under the study.

CHAPTER FOUR

4.0 RESULTS AND FINDINGS

Table 4-1 Demographic Characteristics, Socioeconomic Status, and Education

Characteristics of the Study Population (N=229)		
Characteristics	n (%)	
Sex		
Men	86 (37.6)	
women	143 (62.4)	
Age (y)		
<30	27 (11.8)	Mean = 40.5
30-39	86 (37.5)	S.D = 9.8
40-49	71 (31.0)	Min = 18
50-59	37 (16.2)	Max = 68
>59	8 (3.5)	
Marital status		
Married	91 (39.7)	
Unmarried	138 (60.3)	
Employment status		
Unemployed	30 (13.1)	
Artisan/trader	150 (65.5)	
Professional	44 (19.2)	
Unskilled	5 (2.2)	
Highest level of education completed		
None	39 (17.0)	
Primary/secondary	140 (61.1)	
Vocational	18 (7.9)	
Training college	23 (10.0)	
University	9 (3.9)	
Religion		
Christian	207 (90.4)	
Muslim	22 (9.6)	
Duration on ART (months)		
3-9	45 (19.7)	
10-15	50 (21.8)	
16-21	20 (8.7)	
22-24	35 (15.3)	
>24	79 (34.5)	

4.1 Demographic Characteristics, Socioeconomic Status, and Education

A total of two hundred and twenty-nine patients were interviewed between May and July 2009. The main characteristics are detailed in Table 4-1. The mean age was 40.5 years (S.D, 9.8). Majority of respondents were females (62.4%), unmarried (69%) artisan or traders (65.5%), had primary/secondary education (61.1%) and Christians (90.4). Thirty-five percent (35%) of respondents have been on ART for more than 24 months.

4.2 Assessment of adherence to ARTs

Assessment of adherence to ARTs is summarized in Table 4-2. The optimal adherence rates which indicates that a patient adhered to ARTs at least 95% of the time, using the pharmacy pill count, self report (visual line) and self report (7-day recall) were 98 %, 77% and 100% respectively.

Table 4-2 Assessment of adherence to ARTs

Finding		n=229 (%)
	Assessment of adherence visual line (three -months recall)	
	Optimal adherence ($\geq 95\%$)	176 (77.0%)
	Sub -optimal adherence ($< 95\%$)	53 (23.0%)
	Assessment of adherence (three-months pharmacy pill count method)	
	Optimal adherence ($\geq 95\%$)	225 (98.0%)
	Sub -optimal adherence ($< 95\%$)	4 (2.0%)
	Assessment of adherence(7 day recall)	
	Optimal adherence ($\geq 95\%$)	229 (100%)
	Sub -optimal adherence ($< 95\%$)	-
	Composite mean (average of 3 measures)	
	Mean Optimal adherence ($\geq 95\%$)	210 (91.7%)
	Mean Sub -optimal adherence ($< 95\%$)	19 (8.3%)

4.3. Comparison of adherence using pill count and self report

The mean pill count adherence rate to antiretroviral treatment was estimated at 97.0% (SD=2.5, median=90, IQR: 87.7-100) compared to the mean self –reported adherence rate of 92.0% (SD=9.5, median=90, IQR: 60-100). Two hundred and twenty-five (98.0%) compared to one hundred and seventy six (77.0%) of respondents had optimal adherence using three month pill count visual analogue self-report respectively. There was significant difference between self report and pill count adherence from the t-test performed as shown in table 4-3.

Table 4-3 Comparison of adherence using pill count and self report

	Paired differences					t	df	Sig. (2-tailed)
	Mean difference	Std. Deviation	Std. Error Mean	95% Confidence Interval of the mean Difference				
				Lower	Upper			
Pair 1 Average pill count-self report (%)	5.31004	9.8106	.64829	4.03263	6.5876	8.191	228	.000

4.4 Factors that contribute to optimal adherence

In a univariate analysis, only 3 variables of all the independent variables considered were associated with optimal adherence. These were Quality of care ($p < 0.05$), perception that ARTs cure disease ($p < 0.05$) and knowledge of getting better ($p < 0.05$). After these three significant variables were regressed together, quality of care was found to be significantly and independently associated with optimal adherence as shown in table 4-4.

Table 4-4 Factors that contributed to optimal adherence

Factor	Significance	95.0% Confidence Interval	
		Lower	Upper
Quality of care	0.014*	0.095	0.768
Thought that ARVs cure disease	0.055	0.029	1.036
Knowledge of getting better	0.20	0.343	1.274

4.5 Qualitative data

This section focuses on findings from the qualitative data on factors that contribute to optimal adherence among adult ARV users at the KBTH. The data are based on perspectives of respondents on ART. The views were grouped into themes/sub themes below.

Background information

Most of respondents interviewed said they have been on therapy between one and half years to five years. They said that usually after diagnosis, it took some time before they were initiated on HAART. One female ARV user said:

“After testing positive for the second time, my parents took me to a spiritualist for healing but my condition worsened and I became so ugly and horrible that my parents brought me back to see doctor. The doctor upon recognizing me was upset and was hesitant to treat me but after pleading with the doctor that I was taken to the spiritualist against my will, he changed his mind, treated me and today here I am”

Experience with ART

Some of the respondents said that they did not encounter any major problems with the ARVs contrary to what they were told by the health professionals whereas some of the respondents admitted that it was very difficult at the initial stages of taking ARVS but situations normalize after sometime. The main problems that were cited upon initiating ARV included rashes, drowsiness, dizziness, weakness, feeling terrible (‘maye basaa’), difficulty in sleeping and funny dreams.

“A male respondent explained, even though the counselors told me that I may encounter some problems with the pills, I didn’t know it would be like this. “The feeling was so bad

and the dream I had was terrifying such that I have to run from my room. It was my brother who came to hold me for sometime before I realized that I was dreaming.”

Most of the respondents explained after being on the therapy for a while, they do not experience any problem at all and that everything was normal. A female respondent explained,

“I know my condition is just like those with B.P or hypertension. They take their pills everyday without complaining and so why should I? The only reason why I will not take my medicine is if I forget/fell asleep or if I don’t have the pills with me when I have to take it or my pills are finished and I don’t have money to pay for the pills”.

Contributors of good adherence:

Acceptance of one’s status

Respondents explained that admitting that one actually has the disease was a difficult but very important step to good adherence. A number of the respondents identified acceptance of one status as the major step to good adherence.

“A female respondent said, in this world, nobody takes medicine for a sick person so until you admit that you have the disease as informed by the counselor, you would deceive yourself until you eventually visit your ancestors in the grave”.

Belief that one can take the medicine for good.

Most of the respondents said that the belief and conviction that they would be able to take the pills for the rest of their lives have made them adhere till date. They explained that once you make up your mind that you would take the medicines for the rest of your life, you definitely will do it.

“A male respondent explained, *“as a man you must be strong and take tough decisions-taking these medicines for the rest of your life is not easy but once I have made up my mind, whether rain or shine, I will take it.”*

Benefits of taking ART

Respondents explained that the immense benefit of ARTs is enough motivator to adhere.

They considered themselves fortunate enough to be on the therapy because ARVs have transformed their lives. It makes them stronger, healthier and live prolongs their lives. A respondent said,

“I was so thin like a broomstick that I was hiding from people and if today because of this pill, I can work, take care of my children and go anywhere I want ..., why should I stop?”

Social support.

Most of the respondents said that getting encouragement from close family members or friends contributed immensely to good adherence. Some admitted that they had support from their spouses whereas others identified their children as those who provided support. Respondents admitted that there were no recognized social networks but rather

make friends with fellow PLWH when they attend clinic and that is where they encourage each other and share ideas. Most of them admitted that they were supported when they disclosed to their confidants but because some of the people they confided have broadcasted what they told them, they are now very cautious.

A male respondent said,

“My wife has been there for me all these while, cooking, washing and taking care of me even when I’m coming to clinic even though she hasn’t got the disease. I couldn’t have made it without her especially when my own family has deserted me.”

One female respondent explained,

“My husband claim I brought the disease to him and so is very upset with me and has sacked me from the house. I am now staying with my in-laws who are treating me like an egg and that has brought me this far.”

Another said, *“They demanded that I bring someone before they would counsel me and give me medicine but the person I brought has broadcasted my status to everyone in the place I stay. Some people supported me when they got to know my status but others also shun my company”.*

A desire to stay alive for others

Most of the respondents identified the need to stay alive for others as one of the reasons why they took their medicines as recommended. Most of the male respondents said they have to bury their parents and not the reverse whereas most of the female respondents wondered what would happen to their children without them.

A female respondent said, *“it is only the mother of a child who knows what the child would eat, I’m happy that this pill has kept me strong and alive to take care of my children”*.

Another said, *“How can you possibly leave your parents to their fate especially in their old age? Why should they then bring you into this world in the first place? You are a disappointment then!”*

Good quality adherence counseling programme.

The respondents stated that they had received counseling at least three times before the initiation of HAART. According to the respondents, some of the issues covered included differences between HIV and AIDS, mode of transmission, prevention methods, how ARVs work, importance of adherence, side effects, interactions between ARVs and other medicines (including herbal medicine and alcohol), good nutrition, good hygienic practice. Respondents stated that they were very satisfied with the way the health professionals treated them.

A respondent said, *“Am very satisfied with everything but sometimes the time we spend here is too much and one more thing, to have the pharmacy close by at the other side.”*

Faith/ belief in God

Some of the respondents said they adhered because they had the belief that through the ARTs, God would miraculously heal/cure them of the disease while others admitted that they adhered because they believed that a medicine that cures the disease would soon be discovered. A respondent put it like this,

“As for me, I take my pills everyday because I know very well that God would cure me of this disease through these pills.”

CHAPTER FIVE

5.0 DISCUSSIONS

5.1 DEMOGRAPHIC CHARACTERISTICS OF THE PATIENTS

Though respondents were fairly sampled, there were more females (62.4%) than males (37.6%) consistent with current pattern of KBTH statistics on HIV enrolment. A significant number of the patients have also been on ART for more than two years (34.5%) and majority of respondents were not married (69.0%)

5.2 Assessment of adherence rates to ARTs

Adherence was defined in this study as the number of times that patients actually took their drugs during a given period as a proportion of the number of times they were recommended to do so.

Optimal adherence was defined as an adherent rate of 95% or higher since this level is strongly correlated with CD4 cell count increase, viral load suppression and a decrease in morbidity (Paterson et al, 2000). Levels below 95% were considered to be sub-optimal.

Three methods were used to measure adherence. These included pill count over three months, three months patients self report using a visual analogue and a seven-day recall. The optimal adherence ($\geq 95\%$) rates were 98% for the pill count, 77% for the three month visual analogue self report and 100% for the 7-day recall.

Measurement of optimal adherence using visual analogue self report recorded adherence levels that was lower (77%) than pill count adherence measurement (98%). This trend

was consistent with most results in developing countries that measured adherence using the pill count and visual analogue self report.

The various optimal adherence measures obtained were consistent with other findings from developing countries that recorded high optimal adherence. Orell reported mean pill count adherence of 94% in South Africa while Bell reported mean pill count adherence of 99% in Malawi. Muganzi found high optimal adherence of 98% in Uganda through self report. Other studies that found high optimal adherence with similar adherence measurement method included a study conducted in Uganda and Zimbabwe which recorded optimal adherence of 94% (Muyingo et al, 2008). Another study found high optimal adherence of 98% in Cameroun using self report (Kouanfack et al, 2008).

High optimal adherence was found in this study consistent with the above mentioned studies possibly due to so many factors. Some factors like the type of adherence measurement method and the threshold for defining optimal adherence could have accounted for high adherence. Other reason could also be due to the fact that the treatment centres in the above mentioned studies used similar combination therapy. The patients in the above mentioned studies could also possibly have similar socio-economic characteristics. It is also possible that some patients took in ARVs more than necessary.

However, optimal adherence of 98% for the pill count, 77% for the three month visual analogue self report and 100% for the 7-day recall showed that optimal adherence could be high in contrast to other studies that recorded low optimal adherence. Compared to

98% pill count optimal adherence in this study, Diabate' reported optimal adherence of 74%, while Eholie' reported adherence of 78% using pill count in La Co[^]te d'Ivoire.

Furthermore, compared to a self report adherence of 77%, a study conducted in Nigeria (Muhammed et al., 2009) reported low adherence rate of 44% using self report. Another study conducted in Nigeria (Erah and Arute, 2008) recorded an optimal adherence ($\geq 95\%$) using self report and pill count to be between 58% and 60%. Again, contrary to this study, Daniel et al (2004) reported an adherence ($\geq 95\%$) of 79.2% compared to 100% using seven- day recall of drugs.

This study measured adherence that was higher than that reported in some other countries, because although similar measurement methods were used, adherence could be defined differently. Another reason that could account for the different adherence rates could be the duration over which adherence was measured and also the type of combination therapy used by these treatment centres. Furthermore, the treatment centres in the above mentioned countries could have different socio-economic characteristics.

None of the three methods used to assess adherence can be referred to as the 'gold standard', because each has its advantages and disadvantages. The pill count to some extent is considered as quite objective, since it is used to determine the number of pills left over from the previous refill, thereby serving as a very good proxy indicator for actual pill intake. However, a patient who has not achieved optimal adherence, for fear of

hostile treatment from health professionals during dispensing may manipulate the number of pills remaining.

On the other hand, three-month visual analogue is simple and inexpensive but patients may have difficulty to recall medicine intake over such a relatively long period. The 7-day recall has the advantage of a relatively short time-span, which therefore implies that memory of medicine intake would possibly be good. However, the 7-day recall method could overestimate medicine intake (social desirability) because patients may feel guilty to admit to forgetting to take their ARTs just recently.

The study, in recognizing the limitations of each of these three methods measured composite adherence which was 92%. Although it is below the minimum expected adherence of 95%, the overall optimal adherence was considered to be high since it was found to be higher than the overall optimal adherence found in some other countries. A study conducted in Tanzania ((Irunde et al, 2005).) which used pill count, visual analogue and self report estimated a very low overall adherence (>95%) to be 21.0%. Another study that used similar measurement method reported overall adherence of 77% in Botswana (Hardon et al, 2006).

5.3 Comparison of adherence using pill count and self report

There was significant difference between pill count adherence and self report adherence even though the two methods measured adherence over the same period. The mean pill count adherence rate was 97% which was higher than mean self report adherence 92 %. The high pill count adherence over the self report is consistent with similar studies in south Africa, Malawi, Cameroun and Botswana (Orrell et al,2003 Bell,2007; Weiser et al,2003;Kouanfack et al,2008; Hardon et al,2006).

Pill counting is known to overestimate adherence and seems to be the case in this study as patients are able to manipulate pills remaining (Rudd et al.,1989). Patients who have missed doses may discard their excess tablets at the end of the period so as to seem more compliant. Pill counting alone would have suggested that adherence was high in the study. On the other hand, self report did not involve any health professional, and so patients were possibly less inclined to overestimate medicine intake. However, a degree of desirability bias is always possible, as is the inability to recall medicines intake over long period (Chesney et al, 2000).

Also, studies have shown that, patients who state that they are non adherent almost always are (Paterson, 2000). In one study, the adherence from self report was significantly correlated with virologic response (Duong et al, 2001). Self report adherence rate alone would have suggested that only 77% of patient achieved optimal adherence. In spite of these discrepancies, pill counting and self reporting serve a function in resource constraint setting by ensuring that, the issue of adherence is raised at each consultation or dispensing section.

5.4 Factors that contribute to optimal adherence

Knowledge that being on ARTs would make a person better, the thought that ARTs cure disease and Quality of care were found to independently affect optimal adherence at the univariate level. This finding is consistent with other studies conducted in resource constraint settings (Wenger et al.1999;Nemes et al,2003;Murphy et al,2004; Horne et al,2001).

However, of the three factors that were found to be associated with optimal adherence, only quality of care was found to affect optimal adherence in the multivariate analysis. From the study, quality of care affected optimal adherence. This finding is similar to other study findings (Chesney,2000;Nemecheck and Tittle,1998;Hardon et al,2006 ;Weiser et al,2003) in developing countries. The finding that quality of care contributed to optimal adherence was also buttressed by the qualitative study where a patient said, *“Am very satisfied with everything but sometimes the time we spend here is too much and one more thing, to have the pharmacy close by at the other side.”*

Considering that only quality of care impacted positively on optimal adherence, there could be other confounding factors that contributed to optimal adherence that the study could not identify. It could also be suggested that there are other factors that contribute to optimal adherence that have not been considered in this study.

5.5.1 Limitations of study

The level of adherence was not correlated to viral load or CD4 count to validate adherence measurement method used in the study.

Furthermore, this study used adherence measurement methods that relied on self report and was prone to response bias and pill manipulation.

Also, the study sampled respondents who are currently on ARTs which did not include individuals who had discontinued treatment for various reasons and were not attending clinic anymore. It is therefore possible that sampled patients did not include individuals who achieved sub-optimal adherence and did not attend clinic at the time of study.

Although most patients were on first- line medication that did not require food restrictions, measurement of adherence was not done in relation to the timing of drug and food intake for the few participants that were not on first-line drugs.

CHAPTER SIX

6.0 SUMMARY, CONCLUSIONS AND RECOMMENDATION

6.1 SUMMARY

There is an overall high adherence rate (92%) among adult ARV users at KBTH even though it is still below the minimum expected optimal adherence of 95%. The optimal adherence rates ($\geq 95\%$) for the three methods employed in measuring adherence were 98%, 77%, and 100% for the three-month pill count, three-month self report and 7-day recall respectively. Of the three methods used, optimal adherence rate was highest for 7-day recall (100%). Three month pill count method recorded a higher optimal adherence (98%) in comparison with visual line self report (77%).

There was significant difference between three month pill count adherence and self report adherence even though the two methods measured adherence over the same period. The mean pill count adherence rate was 97% which was higher than mean self report adherence 92 %. Self report adherence rate alone would have suggested that only 77% of patient achieved optimal adherence compared with 98% for pill count.

Quality of care was found to contribute positively on optimal adherence which was supported from findings from the focus group discussion.

6.2 CONCLUDING REMARKS

- The overall rate of adherence among adult ARV users at KBTH was very high (92%) in comparison to that of other developing countries.
- There was significant difference between mean pill count adherence rate (97%) and self report adherence rate (92 %).
- Quality of care impacted on optimal adherence.

6.3 RECOMMENDATIONS

6.3.1 National AIDS Control Programme

The group that was studied had been on ARTs for five years or less. Considering the fact that optimal adherence was high, and to get a better picture of what adherence to ART would be among patients who are on long term treatment, it would be useful to conduct similar study using bigger populations who have been receiving ART for more than five years.

A study using pill count as well as self report and validated by CD4 count and viral load measurement would be useful to confirm adherence

The study identified quality of care as a factor that contributes to optimal adherence. It is possible that there are other factors that contribute to optimal adherence that this study could not identify since adherence rate was very high and so require further study in this area.

Social support, disclosure, belief and benefits of ART were found to be themes that came out from the qualitative data. Further studies are needed to look at these variables in detail.

6.3.2 Management of KBTH

Pill counting is an important tool that is routinely used at KBTH to monitor and promote adherence among PLWH. However, there were some instances where pill counting were missed by some health professional and thereby making it difficult to measure adherence by pill count. Pill counting on clinic days needs to be strengthened.

6.3.3. Adult ARV users at KBTH (patients)

Some patients failed to bring their remaining pills for pill count with the excuse that, pill counting was sometimes not done even when they brought their pills. Patients must be educated on the importance of pill count and hence the need to bring along their pills on each clinic visit.

REFERENCES

Acosta EP, Gerber JG(2002). Position paper on therapeutic drug monitoring of antiretroviral agents. *AIDS Res Hum Retroviruses*; **18**:825–34.

- Ammassari A (2001). Self-reported symptoms and medication side-effects influence adherence to highly active antiretroviral therapy in persons with HIV infection. *Journal of Acquired Immune Deficiency Syndromes*, **28**(5):445-449.
- Anderson W, Weatherburn P. (1999). Taking HART? The impact of combination therapy on the lives of people with HIV (phase 2). London, Syria Research.
- Bangsberg DR (2000). Adherence to protease inhibitor, HIV-1 viral load and development of drug resistance in an indigenous population. *AIDS*; **14**:357-366.
- Beginnings of HIV and AIDS care and treatment in Ghana; the Korle Bu Teaching Hospital experience (January 2002-June 2005).
- Bell DJ, Kapita Y, Sikwese R, Oosterhout JV, Lalloo DG (2007). Adherence to Antiretroviral Therapy in Patients Receiving Free Treatment From a Government Hospital in Blantyre, Malawi ; *J Acquir Immune Defic Syndr* ; **45**:560–563
- Buhrich N, Judd FK (1997). HIV and psychiatric disorders. *Managing HIV*. Sydney, Australasian Medical Publishing Company.
- Burgos M (1998). Obstacles in treatment adherence: patient reasons. 12th World AIDS Conference, Geneva, Switzerland. Abstract no. 32400.
- Byakika-Tusiime J (2003). Ability to purchase and secure stable therapy are significant predictors of non-adherence to antiretroviral therapy in Kampala, Uganda. 10th Conference on Retroviruses and Opportunistic Infections. Boston, USA. Abstract no. 170.
- Carr A, Cooper DA (2000). Adverse effects of antiretroviral therapy. *Lancet*, 356:1423-30.
- Carrieri P, Caillefon V, Le moing V (2002). The dynamic of adherence to Highly Active Antiretroviral Therapy: Results from the French National APROCO cohort. *Journal of Acquired Immune Deficiency Syndromes*, **28**:232-9.
- Catz S, Heckman T, Kochman A (1999). Adherence to HAART therapy among older adults living with HIV disease. Fourth International Conference on the Biophysical Aspects of HIV Infection, Ottawa, Canada.
- Chesney MA (2000). Factors affecting adherence to antiretroviral therapy: *Clinical Infectious Diseases*, **30**:171-176
- Chesney MA, Ickovics JR, Chambers DB, Gifford AL, Neidig J, Zwickl B, Wu AW (2000). Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. Patient Care Committee & Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG). *AIDS Care*; **12**(3):255-66.
- Chesney MA, Ickovics JR, Hecht FM, Sikipa G, Rabkin J (1999). Adherence: a necessity for successful HIV combination therapy. *AIDS*; **13** Suppl A:S271-8. Review.

Cramer JA, Mattson RH, Prevey ML, Scheyer RD, Ouellette VL (1988). How often is medication taken as prescribed? A novel assessment technique. *JAMA*, **261**: 3273-3277.

Daniel OJ, Ogun SA, Odusoga OL, Falola RL, Ogundahunsi OA, Salako AA, Oladapo OT, Osho OB, Adenekan AA, Kolapo KO, Oluwole FA, Krain A, Boyle BA, Jacobs JL (2004). Adherence pattern to ARV drugs among AIDS patients on self-purchased drugs and those on free medications in Sagamu, Nigeria. XV International AIDS Conference. Bangkok, Thailand.

Dansburg D et al. (2003). Pill burden predicts adherence, regimen discontinuation or switch, viral load and CD4 cell response in nationwide US sample of HIV+ ARV naïve people on PI therapy. *Antiviral Therapy* **8**:395.

Diabate S, Alary M, Koffi CK (2007). Determinants of adherence to highly active antiretroviral therapy among HIV-1-infected patients in Côte d'Ivoire, *AIDS*, 21 1799-1803

Duong M, Piroth L, Peytavin G, Forte F, Kohli E, Grappin M (2001). Value of patient self-report and plasma human immunodeficiency virus protease inhibitor level as markers of adherence to antiretroviral therapy: *relationship to virologic response*. *CID* **33**:386-92

Eholie SP, Tanon A, Polneau S, Ouiminga M (2007). Field Adherence to Highly Active Antiretroviral Therapy in HIV-Infected Adults in Abidjan, Côte d'Ivoire. *J Acquir Immune Defic Syndr*; **45**:355–358

Eldred IJ, Wu AW, Chaisson RE (1998). Adherence to antiretroviral and pneumocystic prophylaxis in HIV disease. *Journal of Acquired Immune Deficiency Syndromes*, 18:117.

Erah PO and Arute JE(2008). Adherence of HIV/AIDS patients to antiretroviral therapy in a tertiary health facility in Benin City. *African Journal of Pharmacy and Pharmacology*, Vol. 2(7), pp. 145–152 .

Erlon JA, Mellors P (1999). Adherence to combination therapy in persons living with HIV:balancing the hardships and the blessings. *Journal of the Association of Nurses in AIDS Care*, 10(4):75–84.

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

Garcia R, Schooley R, Badaro R (2003). An adherence trilogy is essential for long term HAART success: *Brazilian Journal of Infectious Diseases*, 7(5):1-9.

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

Grierson J (2000). HIV futures II: The Health and Well Being of People With HIV/AIDS in Australia, Monograph Series No. 17.

Hardon A, Gerrits T, Hodgkin C(2006). From Access To Adherence: The Challenges Of Antiretroviral Treatment, studies from Botswana, Tanzania and Uganda.,World Health Organization, ISBN: 92-4-156328-1; 978-92-4-156328-4

Hardon A, Kgatlwane J, Ogenyi R, Ekezie C (2006) .Factors that facilitate or constrain adherence to antiretroviral therapy among adults at four public health facilities in Botswana: a pre-intervention study, World Health Organization, ISBN: 92-4-156328-1; 978-92-4-156328-4

Hardy H (2005). Adherence to antiretroviral therapy: The emerging role of HIV pharmacotherapy specialists. *J Pharm Prac*; **18**: 247–57.

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

HIV Sentinel Survey Report (2008); National AIDS/STI Control Programme, Ghana Health Service, Ministry of Health, Accra, Ghana

Hirschhorn L (1998). Highly active HAART therapy in the □ real world□ : experiences in an inner-city community health center. 12th World AIDS Conference, Geneva, Switzerland. Abstract 32334.

Holzemer WL, Corless IB, Nokes KM. et al (1999). Predictors of self-reported adherence in persons living with HIV Disease. *AIDS Patient Care and STDs*, **13**(3), 185-197.

Horizons/Population Council (2004) Adherence to Antiretroviral Therapy in Adults. A Guide for Trainers.1-130

Horne R, Buick D, Fischer M (2001). Perceptions of HIV and HAART as barriers to adherence. 5th AIDS Impact, Brighton, UK, 2001. Abstract no.105; 28:232-9.

[http://www.hivinsite.ucsf.edu\(17/03/09\)](http://www.hivinsite.ucsf.edu(17/03/09))

[http://www.mtctplus.org/intranet/pdf/ad treatment.pdf](http://www.mtctplus.org/intranet/pdf/ad_treatment.pdf) (04/05/09)

Irunde H, Temu F, Maridadi J,Nsimba S, Comoro C(2005). A study on antiretroviral adherence in Tanzania:a pre-intervention perspective,World Health Organization, ISBN: 92-4-156328-1; 978-92-4-156328-4

Jones JL, Nakashima AK, Kaplan JE (1999). Adherence to primary prophylaxis for pneumocystis carinii pneumonia: results from a multi-state interview project. 39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, USA.Abstract no. 586.

Kaplan A (1999). Adherence to protease inhibitor therapy and viral load. 6th Conference on Retroviruses and Opportunistic Infections, Chicago, USA. Abstract no. 96.

Kastrissios H, Blaschke TF (1977). Medication adherence as a feature in drug development. *Ann Rev Pharm Toxicol*, **37**: 451-474.

Katabira ET (2002). The promise and challenges of antiretroviral therapy in developing countries. Paper presented at the 9th Conference on Retroviruses and Opportunistic Infection. Symposium session 30.

Kityo C, Rabkin M, Atwine D, Mulindwa G, Kebba A, Kabuye G, Mugenyi P(2002). Adherence to antiretroviral therapy in Kampala ,International Conference on AIDS. ,Int Conf AIDS. 14: abstract no. WePeB5848.

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

Kouanfack C, Laurent C, Peytavin G, Laura L, Ngolle M (2008). Adherence to Antiretroviral Therapy Assessed by Drug Level Monitoring and Self-Report in Cameroon. *J Acquir Immune Defic Syndr*; **48**:216–219

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

Liu H, Golin C, Miller LG, Hays RD, Beck K, Sanandaji S, Christian J, Maldonado T, Duran D, Kaplan AH, Wenger NS (2001). A Comparison of Multiple Measures of Adherence to HIV Protease Inhibitors. *Annals of Internal Medicine*, **134**:968-977

Machtinger E, Bangsberg DR (2005). *Adherence to HIV antiretroviral therapy*. HIV Insite, University of California, San Francisco.

Meisler A (1993). Adherence to clinical trials among women, minorities and injecting drug users. Paper presented at the 9th International Conference on AIDS, Berlin, Germany.

Motashari F et al. (1998). Acceptance and adherence with HAART therapy among HIV infected women in a correctional facility. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, **18**:341-348.

Muganzi AM, Bondo MC, Draru J, Biryeri J (2004); Adherence to HAART in a rural resource limited country HIV/AIDS treatment program: The experience of Arua Anti-Retroviral (ARV) Treatment Program, Uganda. International Conference on AIDS , Int Conf AIDS. 2004 Jul 11-16; 15: abstract no. WePeB5760.

Muhammed O. Afolabi, Kayode T. Ijadunola, Adesegun O. Fatusi, Olayinka A. Olasode (2009) Determinants of adherence to antiretroviral drugs among people living with HIV/AIDS in the Ife-Ijesa zone of Osun state, Nigeria. *African Journal of Primary Health Care & Family Medicine*, Vol 1, No 1.

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

Muyingo SK, Walker SA, Reid A, Munderi P, Gibb DM, Ssali F, Levin J, Katabira E, Gilks C, Todd J, and the DART Trial Team (2008). Patterns of Individual and Population-

Level Adherence to Antiretroviral Therapy and Risk Factors for Poor Adherence in the First Year of the DART Trial in Uganda and Zimbabwe. *J Acquir Immune Defic Syndr*; **48**:468–475

Nemecheck P, Tritle D (1998). A survey evaluating pharmacy-related resources and their relation to drug adherence. 12th World AIDS Conference, Geneva, Switzerland. Abstract no. 98.

Nemes MB, Carvalho HB, Souza MFM (2004). Antiretroviral therapy adherence in Brazil. *AIDS* **18**(Suppl 3):15-20.

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

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

Parades R (2000). Predictors of virology success and ensuing failure in HIV positive patients starting HAART in Europe. *Archives of Internal Medicine*. **160**:1123-1132.

Parienti JJ, Verdon R, Bazin C (2001). The pills identification test: a tool to assess adherence to antiretroviral therapy. *JAMA*; **285**:412.

Paterson DL, Brian Potoski B, Blair Capitano B (2002). Measurement of Adherence to Antiretroviral Medications; *JAIDS Journal of Acquired Immune Deficiency Syndromes*, Vol. 31, Suppl. 3

Paterson DL, Swindells S, Mohr J, Brewster M, Vergis EN, Squier C, Wagener MN, Singh N. (2000). Adherence to Protease Inhibitor and Outcomes in Patients with HIV Infection. *Annals of Internal Medicine* **133**(1): 21-30.

Rabkin M, El- Sadr W, Abrahams E (2003). *MTCT-Plus clinical manual*. Mailman School of Public Health, Columbia University, USA.

Reiter GS, Stewart KE, Wojtusik L, Hewitt R, Segal-Maurer, Johnson M, Fisher A, Zackin R, Masters III H, Bangsberg D (2000). Elements of success in HIV clinical care: Multiple Interventions that promote adherence. *Topics in HIV Medicine*, **8**(5):21-30.

Richardson D, Liou SH, Kahn JO (1993). Uric acid and didanosine compliance in AIDS clinical trials: an analysis of AIDS Clinical Trials Group protocols 116A and 116B/117. *J Acquir Immune DeficSyndr*; **6**:1212–23.

Rudd P, Byyny RL, Zachary V, LoVerde ME; Titus C, Mitchell WD, Marshall G (1989). The natural history of medication adherence in a drug trial: limitations of pill counts. *Clinical Pharmacology and Therapeutics*, **46**(2):169-76.

Turner BJ (2002). Adherence to antiretroviral therapy by Human Immunodeficiency Virus-Infected Patients. *Journal of Infectious Diseases*, **185** (Suppl 2):143-151.

Vergis EN, Paterson DL, Wagener MM (2001). Dyslipidaemia in HIV-infected patients: association with adherence to potent antiretroviral therapy. *Int J STD AIDS*; **12**:463–8.

Vincke J, Bolton R (2002). Therapy adherence and highly active antiretroviral therapy: comparison of three sources of information. *AIDS Patient Care STDS*; **16**: 487–95.

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

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

Williams A, Friedland G (1997). Adherence, compliance, and HAART. *AIDS Clinical Care*, **9**(7):51-53.

Wenger N (1999). Patient characteristics and attitudes associated with HAART adherence. 6th Conference on Retroviruses and Opportunistic Infections, Chicago, USA. Abstract no. 981.

World Health Organization (WHO) Adherence to Long term therapies; Evidence for Action, Geneva: WHO 2003.

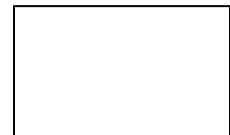
APPENDICES

INFORMATION SHEET FOR PARTICIPANTS

ADHERENCE TO ANTIRETROVIRAL MEDICINES AMONG ADULT HIV/AIDS PATIENTS AT THE KORLE BU TEACHING HOSPITAL IN ACCRA

I am a student of the school of Public Health of the University of Ghana, Legon. In doing my MPH dissertation, I am collecting information on how patients in Korle Bu Teaching Hospital are able to take their antiretroviral medicines regularly as they have been asked to do, and what enables them to take their pills. This information may be useful to the management of KBTH and national AIDS control program (NACP) in improving healthcare delivery in this facility. It will take between 10-15 minutes to complete. All information from this survey is confidential and using any records for this survey is voluntary. No names of patients will be collected. You can refuse to let me use any record. I am asking for your help to ensure that the information collected is accurate.

If you agree to take part in the study, please append your signature or thumbprint to indicate your consent. Thank you.



SIGNATURE or THUMB PRINT

.....

INTERVIEW DATE

.....

					Variable name
Respondent's Identification Number					idno
Interviewer code			Date:.....		idpat
Section 1: Demographic of Patients					Section1
1.	What is your age?				Q1age
2.	Sex?	Male Female	[1] [2]	☐	Q2sex
3.	What is your marital status?	Single Married Separated or Divorced Widowed Cohabiting	[1] [2] [3] [4] [5]	☐	Q3mar
4.	Is your partner HIV positive	Yes No I don't know	[1] [2] [3]	☐	Q4pathiv
5.	Is your partner on medication	Yes No I don't know N/A	[1] [2] [3] [4]	☐	Q5patmed
6.	What is your religious background?	Christian Muslim Traditional None	[1] [2] [3] [4]	☐	Q6religin
7.	What is your highest level of education?	None Primary/Secondary Vocational Training college University	[1] [2] [3] [4] [5]	☐	Q7educ

8.	Where do you live?	Town.....	Region.....	Q8reside	
9.	What work do you do?	Unemployed Artisan/trader professional Unskilled Other (specify).....	[1] [2] [3] [4]	☐	Q9employ
Section 2: Medical history of patient					Section 2
10.	How long ago were you diagnosed as HIV positive? Write date(month and years) mentioned by patient	...months years Don't know	[1] [2]	☐	Q10diag
11.	How long ago did you start taking the ARTs?	3- 9 months 10-15 month 16- 21 months 22-24 months 25+ Don't know	[1] [2] [3] [4] [5] [6]	☐	Q11stat
12.	Were you counseled about adherence before starting treatment?	Yes No Not sure	[1] [2] [3]	☐	Q12consl
13.	How many times were you counseled	Once Twice Three times	[1] [2] [3]	☐	Q13times
Section 3: Knowledge and Perception of Adherence to ARTs					
14.	What do you know about antiretroviral medicines? (Please tick all that apply)	Prolong life Improve quality of life Life-long treatment Have side effect Cure the disease	[1] [2] [3] [4] [5]	☐	Q14know

		don' know other (specify).....	[6] [7]		
15.	What do you think is the importance of taking your ARV medicines regularly as prescribed?	CD4 cells increase Patient gets better ARVs work better Viral load decreases	[1] [2] [3] [4]	☐	Q15tink
Section 4 :Quality of care					
16.	Do you feel listened to	Yes No Not sure	[1] [2] [3]	☐	Q16list
17.	Are you given the chance to state your problems and ask questions?	Yes No Not sure	[1] [2] [3]	☐	Q17free
18.	Are you treated with respect?	Yes No Not sure	[1] [2] [3]	☐	Q18Qresp
19.	Do you feel you can trust the health workers?	Yes No Not sure	[1] [2] [3]	☐	Q19trust
20.	Do you have privacy during consultation and counselling?	Yes No Not sure	[1] [2] [3]	☐	Q20priv
21.	How long did you spend altogether at the clinic when you last went for review?	Less than 3hrs 3-5hrs more than 5 hours	[1] [2] [3]	☐	Q21hlong
Section 5:Cost considerations					
22.	Do you lose any income as a result of your coming to the clinic	Yes No Not sure	[1] [2] [3]	☐	Q22incom

23.	Do you and your family have to give up anything in order to pay for your ARV treatment?	Yes No Not sure	[1] [2] [3]	☐	Q23family
24.	Has your being on ARVs resulted in changes in expenditure?	Yes No Not sure	[1] [2] [3]	☐	Q24expd
Section 6: Perceived problems and contributors of adherence					
25.	What is it that helps you to take your pills regularly and on time?	Cell phone /clock self discipline individual(monitor) Organizations None of the above	[1] [2] [3] [4] [5]	☐	Q25help
26.	Have you disclosed your status to anyone? (If no, move to question 28)	Yes No Not sure	[1] [2] [3]	☐	Q26discl
27.	If yes, do they help you take your pills regularly and on time?	Yes No N/A	[1] [2] [3]		Q27dhelp
28.	Apart from relatives or spouse, what else enables you to take your medicines regularly?	Self motivation Belief Workplace support Children	[1] [2] [3] [4]	☐	Q28delse
29.	Have you ever thought of stopping ARTs? If yes, move to question 31	Yes No Not sure	[1] [2] [3]	☐	Q29stop
30.	If no, why? (Please tick all that apply)	Want to live longer Want to be stronger Want to live for others N/A	[1] [2] [3] [4]	☐	Q30nowhy

31.	If yes, why?	Feel better Doubt if I have AIDs. Doubt if ARVs work tired of taking medicines	[1] [2] [3]	☐	Q31yswhy
32.	Over the last three months, did you perhaps miss any pill? (If no move to question 34)	Yes No Not sure	[1] [2] [3]	☐	Q32missp
33.	If yes, did any of the following made you miss a pill? (Please tick all that apply) ☐ A				
	☐ Side effect ☐ Pill burden ☐ Cost of ARVs ☐ Lack of food ☐ Simply forgot/fell asleep ☐ Felt better ☐ Clinic not accessible ☐ Lack of care/support ☐ Depressed ☐ Didn't have pills with you ☐ Shared pills ☐ Alcohol use ☐ Feeling that you had to hide your medication from those around you ☐ Religion (e.g. fasting) ☐ Hospitalized				
Section 7: Assessment of adherence					
34.	Now, try to remember the last 7days before this visit, Did you take all pills during that time?	All days (excellent) 5-6days/week (good) <5 days/week (poor)	[1] [2] [3]	☐	Q34adhe
35.	If you missed any, how many pills did you miss? (7-day Self report)	 N/A			Q35no

36.	Can we count your drugs (ARVs) to find out how many pills you have left please? Please indicate the following for each antiretroviral medicine: How many pills the patient should have taken since his/her last visit, and; How many pills he/she missed (i.e. how many pills were returned)																																																																	
<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 15%;">1ST LINE</td> <td style="width: 25%;">(3TC+AZT)= CBV</td> <td style="width: 15%;">EFV</td> <td style="width: 15%;">NVP</td> <td style="width: 15%;">D4T</td> <td style="width: 15%;">3TC</td> <td style="width: 15%;">AZT</td> </tr> <tr> <td>2ND LINE</td> <td>Kaletra</td> <td>ddl</td> <td>NFV</td> <td></td> <td>ABC</td> <td>TDF</td> </tr> </table>							1 ST LINE	(3TC+AZT)= CBV	EFV	NVP	D4T	3TC	AZT	2 ND LINE	Kaletra	ddl	NFV		ABC	TDF																																														
1 ST LINE	(3TC+AZT)= CBV	EFV	NVP	D4T	3TC	AZT																																																												
2 ND LINE	Kaletra	ddl	NFV		ABC	TDF																																																												
<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 35%;"></th> <th style="width: 15%;">Example</th> <th style="width: 15%;">Drug I</th> <th style="width: 15%;">Drug II</th> <th style="width: 15%;">Drug III</th> </tr> </thead> <tbody> <tr> <td>*Drug name</td> <td>Lamivudine</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Previous Date issued</td> <td>7 Mar</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Quantity taken home (total)</td> <td>60</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Quantity returned</td> <td>6</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Date returned</td> <td>4 Apr</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Days since last issue</td> <td>28</td> <td></td> <td></td> <td></td> </tr> <tr> <td>regimen</td> <td>1bid</td> <td></td> <td></td> <td></td> </tr> <tr> <td>*Total supposed to take</td> <td>56</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Should have returned</td> <td>60-56=4</td> <td></td> <td></td> <td></td> </tr> <tr> <td>*Pills missed</td> <td>6-4=2</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Percent adherence</td> <td>$((56-2)/56) * 100$</td> <td></td> <td></td> <td></td> </tr> </tbody> </table> *must fill row								Example	Drug I	Drug II	Drug III	*Drug name	Lamivudine				Previous Date issued	7 Mar				Quantity taken home (total)	60				Quantity returned	6				Date returned	4 Apr				Days since last issue	28				regimen	1bid				*Total supposed to take	56				Should have returned	60-56=4				*Pills missed	6-4=2				Percent adherence	$((56-2)/56) * 100$			
	Example	Drug I	Drug II	Drug III																																																														
*Drug name	Lamivudine																																																																	
Previous Date issued	7 Mar																																																																	
Quantity taken home (total)	60																																																																	
Quantity returned	6																																																																	
Date returned	4 Apr																																																																	
Days since last issue	28																																																																	
regimen	1bid																																																																	
*Total supposed to take	56																																																																	
Should have returned	60-56=4																																																																	
*Pills missed	6-4=2																																																																	
Percent adherence	$((56-2)/56) * 100$																																																																	
37.	Please make a mark on the line to show how many of your ARV pills you think you managed to take in the last three months: None All																																																																	

FOCUS GROUP DISCUSSION (FGD) GUIDE FOR PARTICIPANTS

- Participants per FGD (8)
- Adults on ART for at least 3 months (males and females conducted separately).
- 2 set of focus group for males and females
- A moderator, note –taker (2)
- Tape recorder, pen, and notebook
- Short introductory remarks
- Introduction of researcher and participants
- Thank patients for agreeing to participate in the discussion

Moderator explains purpose of study, purpose of the discussion, i.e. researcher is here to know the opinion of patients on ARTs, how ARVs work, share their experience i.e. importance of taking medicines as recommended, problems that affect adherence e.g. cost related issues, factors that contribute to adherence e.g. social support/networks, disclosure, good quality of care etc

- We are here to learn from participants.
- Reassurance on confidentiality and anonymity, discuss and reach consensus on ground rules.

Topics Discussed

- 1) What treatments do you know to be available for treating HIV? What is your opinion about these?(ARVs, Herbs, traditional medicine, spiritual healing, prayers and perceived benefits of treatment)
- 2) What is your experience of ART? (probe about adherence, side effects, pill burden, lack of food, lifestyle issues)
- 3) How do you think you are being treated by the health care providers? (Probe for privacy, confidentiality, respect, time spent with health provider, convenience i.e. integration with other services).What is the quality of care provided by the health care providers?
- 4) What do you think about the counseling that you receive? Are you counseled alone or in groups? (Probe especially on importance of adherence; effectiveness of counselling. What support are you given by the health care providers to help you adhere better to your medications? Have you disclosed?(at least to your partner)
- 5) What support is available for you in the community, in the family, in the workplace? (Probe about discrimination, stigma). Probe differences in perceived availability of social support verses social networks? Any negative social support?
- 6) What do you think are the key reasons for good adherence
- 7) What are the sources of motivation for adherence?
- 8) Duration of discussion (45mins); provide refreshments, Conclusion, thank participants.