Factors Associated with Untimely Antiretroviral Drug Pick-up by Patients in Bindura District.

Masters in Public Health (Health Promotion)
Faculty of Medicine
College of Health Sciences
University of Zimbabwe

By
Isaac Taramusi

Dissertation submitted in partial fulfilment of Masters in Public Health [Health Promotion] Degree University of Zimbabwe
Declaration

This dissertation is the original work of Isaac Taramusi. It has been prepared in accordance with the guidelines for MPH [Health Promotion] dissertations in the University of Zimbabwe. It has not been submitted elsewhere for another degree or any other university.

1. Name of student: Isaac Taramusi

   Signature: ___________________ Date: ______________

2. Name of Supervisor 1: Professor S Rusakaniko

   Signature____________________ Date: ______________

3. Name of Supervisor 2: Dr J Maradzika

   Signature____________________ Date: ______________

4. Chairman, Community Medicine, University of Zimbabwe Medical School.

   Signature____________________ Date: ______________
Abstract

Introduction
Timely antiretroviral drug pick up is one of the early warning indicators for monitoring HIV drug resistance. Timely antiretroviral drug pick up is essential in the prevention of emergence of HIV drug resistance. The scale up of ART programme is not directly proportional to clients picking their drugs on time. This study sought to establish ART drug pick up patterns of ART clients, prevalence of untimely drug pick up and the associated factors.

Methods: The study was an analytic cross-sectional study. Two hundred and seventy-seven (277) respondents were randomly selected from attendees of ART clinics at ART sites. Interviewer-administered pretested questionnaires were used to collect data. Epi info version 3.5.1 was used to create frequencies and proportions were calculated as well as Odds ratios to determine associations. Logistic regression analysis was done to identify independent risk factors and to control for confounding variables.

Results: Two hundred and seventy-seven (277) ART clients were included in the study. The prevalence of untimely drug pick up was 40.4%. The median number of times participants missed drug pick on time in the past 12 months was 1 (Q1=1; Q3=2) and the main reason for not picking up drugs on time was social problems like attending funerals and not having bus fares. Those who had short time (0-6 months) on treatment [POR = 0.45 (95% CI: 0.27 - 0.77)] and having one month or less supply [POR = 0.50 (95% CI: 0.30 - 0.81)] were significantly associated with a lower likeliness of missing drug pick up time. Barriers such as adverse effects [AOR = 1.84 (95% CI: 1.13 - 3.01)], user fees [AOR = 1.96 (95% CI: 1.06 - 3.60)], and long distances to ART sites [AOR 1.96 (95% CI: 1.11 – 3.47)] were significantly associated with high likeliness of missing drug pick up time. These factors remained statistically significant on logistic regression analysis and stratified analysis showed that age was modifying the relationship between distance and drug pick up time.

Conclusion and Recommendations
ART clients were mainly missing drug pick up time due to long distance to ART sites, user fees and adverse effects to drugs. The District Health Executive need to scale up ART outreach in order to provide services for those who stay far away from ART sites.

Key Words
Antiretroviral, Untimely drug pick, Bindura
**Acknowledgement**

I would like to express my sincere gratitude to the Provincial Medical Director of Mashonaland Central province Dr C Tshuma and his staff for all the support rendered in this project. I would also want to express my gratitude to my field supervisor Dr T Magure for the guidance and support throughout this project. I also want to acknowledge the Department of community medicine for all the support rendered to me. My sincere gratitude also go to the Bindura District Health Executive team and all sister in charge for ART sites for their unwavering support. Many thanks also to all the clinic nurses for assisting me during the study and guidance in their areas of jurisdiction. I would also want to thank all the study participants for taking their time and agreeing to take part in this study. My uttermost gratitude goes to Professor S Rusakaniko and Dr J Maradzika for the guidance throughout the whole process of preparing this project.

I would also like to finally thank the National AIDS Council for taking part in the funding of the project.

Isaac Taramusi

University of Zimbabwe, August 2013
Table of Contents

Declaration........................................................................................................................................... ii

Abstract.................................................................................................................................................. iii

Acknowledgement ................................................................................................................................. iv

Table of Contents .................................................................................................................................... v

List of Figures .......................................................................................................................................... vii

List of Tables .......................................................................................................................................... vii

CHAPTER 1: BACKGROUND .................................................................................................................. 1

1.0 Background information ................................................................................................................... 1

1.1.1 HIV and AIDS Situation .......................................................................................................... 1

1.1.2 Treatment of HIV ..................................................................................................................... 2

1.1.3 Early Warning Indicators (EWIs) for HIV treatment................................................................. 4

1.1.4 Drug pickup .................................................................................................................................. 5

1.2 Problem statement ............................................................................................................................ 6

CHAPTER 2: LITERATURE REVIEW ..................................................................................................... 8

2.1 Untimely drug pick up ..................................................................................................................... 8

2.2 Factors Known to Hinder Timely Drug pick-up ........................................................................... 9

2.2.1 Demographic or patient related factors ................................................................................... 9

2.2.2 Health service related factors ................................................................................................ 9

2.2.3 Treatment related factors ....................................................................................................... 10

2.3 Justifications .................................................................................................................................... 11

2.4 Research question .......................................................................................................................... 11

2.5 Objectives ....................................................................................................................................... 11

2.5.1 General objective: .................................................................................................................. 11

2.5.2 Specific objectives .................................................................................................................. 12

2.6 Conceptual Framework .................................................................................................................. 12

CHAPTER 3: STUDY METHODS .......................................................................................................... 14
3.1 Study design.......................................................................................................................... 14
3.2 Study setting............................................................................................................................ 14
3.3 Study population ................................................................................................................... 14
3.4 Study Unit................................................................................................................................ 14
3.5 Inclusion criteria ..................................................................................................................... 15
3.6 Exclusion criteria .................................................................................................................... 15
3.7 Sampling .................................................................................................................................. 15
3.7.1 Sampling frame.................................................................................................................... 15
3.7.2 Sample size ......................................................................................................................... 15
3.7.3 Sampling methods .............................................................................................................. 16
3.8 Study variables....................................................................................................................... 16
3.9 Data collection process .......................................................................................................... 17
3.9.1 Data Collection Tools ........................................................................................................ 17
3.10 Data management.................................................................................................................. 18
3.10.1 Quality control .................................................................................................................. 18
3.10.2 Entry process ..................................................................................................................... 18
3.10.3 Data cleaning ..................................................................................................................... 18
3.10.4 Data Analysis ..................................................................................................................... 18
3.10.5 Data Storage ...................................................................................................................... 19
3.11 Permission to proceed.......................................................................................................... 19
3.12 Ethical issues......................................................................................................................... 19

CHAPTER 4: RESULTS .................................................................................................................. 20
4.1 Demographic characteristics of respondents........................................................................ 20
4.4 Multivariate analysis ............................................................................................................. 27

CHAPTER 5: DISCUSSIONS ......................................................................................................... 29
Conclusions................................................................................................................................... 33
Recommendations......................................................................................................................... 34
List of Figures

Figure 1: Trends in Adult (15+) HIV Prevalence, Zimbabwe 1970-2015 .............................................. 1
Figure 2: ART coverage and gap in Zimbabwe ......................................................................................... 2
Figure 3: Number of people on ART by year in Zimbabwe ..................................................................... 3
Figure 4: ART coverage versus drug pick up in Zimbabwe ....................................................................... 7
Figure 5: Reasons of not picking up drugs on time .................................................................................... 22
Figure 6: Proportion Underlying Conditions ............................................................................................... 24
Figure 7: Challenges in picking up drugs .................................................................................................... 27

List of Tables

Table 1: EWI survey results ......................................................................................................................... 4
Table 2: Study variables .............................................................................................................................. 16
Table 3: Demographic characteristics respondents .................................................................................. 20
Table 4: Demographic factors associated with untimely drug pick up ................................................. 23
Table 5: Treatment related factors associated with untimely drug pick up ........................................... 25
Table 6: Health service related factors associated with untimely drug pick up ....................................... 26
Table 7: Logistic regression analysis .......................................................................................................... 28
### Acronyms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3TC</td>
<td>Lamivudine</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired Immuno-Deficiency Syndrome</td>
</tr>
<tr>
<td>AOR</td>
<td>Adjusted Odds Ratio</td>
</tr>
<tr>
<td>ART</td>
<td>Anti-Retroviral Therapy</td>
</tr>
<tr>
<td>ARV</td>
<td>Anti-Retroviral</td>
</tr>
<tr>
<td>AZT</td>
<td>Zidovudine</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>CROI</td>
<td>Conference on Retroviruses and Opportunistic Infections</td>
</tr>
<tr>
<td>CSO</td>
<td>Central Statistics Office</td>
</tr>
<tr>
<td>d4T</td>
<td>Stavudine</td>
</tr>
<tr>
<td>DMO</td>
<td>District Medical Officer</td>
</tr>
<tr>
<td>EWIs</td>
<td>Early Warning Indicators</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>HIVDR</td>
<td>Human Immunodeficiency Virus Drug Resistance</td>
</tr>
<tr>
<td>JREC</td>
<td>Joint Research Ethics Committee</td>
</tr>
<tr>
<td>LTFU</td>
<td>Lost to Follow up</td>
</tr>
<tr>
<td>MoHCW</td>
<td>Ministry of Health &amp; Child Welfare</td>
</tr>
<tr>
<td>MRCZ</td>
<td>Medical Research Council of Zimbabwe</td>
</tr>
<tr>
<td>NAC</td>
<td>National AIDS Council</td>
</tr>
<tr>
<td>NVP</td>
<td>Nevirapine</td>
</tr>
<tr>
<td>OI</td>
<td>Opportunistic Infections</td>
</tr>
<tr>
<td>PMD</td>
<td>Provincial Medical Director</td>
</tr>
<tr>
<td>POR</td>
<td>Prevalence Odds Ratio</td>
</tr>
<tr>
<td>StatCalc</td>
<td>Statistical Calculator</td>
</tr>
<tr>
<td>UNAIDS</td>
<td>United Nations Joint Program on HIV and AIDS</td>
</tr>
<tr>
<td>USD</td>
<td>United States Dollar</td>
</tr>
<tr>
<td>UZ</td>
<td>University of Zimbabwe</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>ZDHS</td>
<td>Zimbabwe Demographic Health Survey</td>
</tr>
</tbody>
</table>
CHAPTER 1: BACKGROUND

1.0 Background information

1.1.1 HIV and AIDS Situation
Zimbabwe has a generalized HIV epidemic with adult prevalence of 15%\(^1\) and an incidence of 1.07%\(^2\). The prevalence peaked in 1997 at 26.48% (24.96 – 27.77%) and started declining thereafter as shown by figure 1 bellow.

Figure 1: Trends in Adult (15+) HIV Prevalence, Zimbabwe 1970-2015

![Trends in Adult (15+) HIV Prevalence, Zimbabwe 1970-2015](image)


The increased burden of HIV and AIDS increased AIDS related deaths to 114,440 in 2005, reduced productivity and increased morbidity due to HIV and AIDS. In response the government of Zimbabwe embarked on a number of strategies to prevent transmission of new infection and in 2004 introduced the Ante-retroviral (ARV) Treatment in order to reduce morbidity and mortality due to HIV and AIDS. There is an estimate of 1,384,254 living with
HIV (1,208,617 are adults aged 15-49, and 175,637 children younger than 15 years)\(^2\). A total of 836,384 were in need of ART by December 2012\(^2\). There were 899,300 estimated AIDS orphans, and 46,653 estimated annual AIDS deaths by December 2012\(^2\).

1.1.2 Treatment of HIV
Since the advent of HIV, people sought treatment from traditional healers that is traditional medicine\(^3\) up until the government of Zimbabwe introduced antiretroviral treatment programme in April 2004 and ‘Plan for the Nationwide Provision of ART that was finalized in December 2004 covering the period (2004-2007). There are 128 ART initiation facilities and 382 follow up sites in Zimbabwe. The ART coverage increased from 29% in 2007 to 40% for children and 56% for adults in 2010. The following figures show ART coverage and gap since 2004.

Figure 2: ART coverage and gap in Zimbabwe

Source: MOHCW presentation by Dr. T Mutasa-Apollo (National ART Programme Manager)
The increase in ART coverage over the past years is a makeable achievement for ART programme in Zimbabwe as shown by figure 2 above, but on the other hand only 5% of the sites offering ART services had their patients picking up drugs on time. This has a negative impact on the programme through development of HIV drug resistance (HIVDR).

There were 565, 675 (518,801 adults and 40,605 children) on ART in Zimbabwe by December 2012\(^4\), Mashonaland central had 41,798 adults and 3500 children, and Bindura had 10,370 adults and 594 children on ART\(^5\). Bindura Provincial Hospital serves 26% of the patients on ART in Mashonaland Central province and there is a challenge of drug pickup.

The following figure shows yearly ART progress in Zimbabwe. Figure 3 bellow shows that there was a rapid increase in number of people on ART from 2004 to 2010.

**Figure 3: Number of people on ART by year in Zimbabwe**

![Graph showing yearly ART progress in Zimbabwe](image-url)
1.1.3 Early Warning Indicators (EWIs) for HIV treatment

HIV drug resistance monitoring is routinely carried out by conducting Early Warning Indicator (EWI) Survey. The HIV DR Early Warning Indicators are ART site-based indicators associated with HIV DR prevention. Based on routinely collected data in the existing medical and pharmacy records, Zimbabwe is monitoring the following WHO suggested HIVDR EWIs: ART prescribing practices: proportion of patients lost to follow up (LTFU) 12 months after ART initiation; proportion of patients still on appropriate first line ART 12 months after initiation; on time antiretroviral (ARV) drug pick-up; on time clinic appointment keeping; and ARV drug supply. The following table shows the results of the EWI survey from 2008 to 2011 for Zimbabwe.

<table>
<thead>
<tr>
<th>Early Warning Indicator (EWI)</th>
<th>EWI Target for all clinics</th>
<th>Percentage of ART clinics that met the EWI target</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2008 n=40</td>
</tr>
<tr>
<td>Percentage of site with 100% appropriate initial ART regimen prescribed</td>
<td>100%</td>
<td>92.5</td>
</tr>
<tr>
<td>Percentage of sites with ≤ 20% patients starting first-line ART, lost to follow-up at 12 months after initiation</td>
<td>≤ 20%</td>
<td>52.5</td>
</tr>
<tr>
<td>Percentage of sites with patient retention on first line 12 months after ART initiation ≥ 70%</td>
<td>≥ 70%</td>
<td>35</td>
</tr>
<tr>
<td>Percentage of sites with ≥ 90% patients picking up all prescribed drugs on time</td>
<td>≥ 90%</td>
<td>NC</td>
</tr>
<tr>
<td>Percentage of sites with ≥ 80% patients who attended all clinical consultations on time</td>
<td>NC</td>
<td>60 (n=10)</td>
</tr>
<tr>
<td>Percentage of sites with no ARV drug stock-outs</td>
<td>≥ 100%</td>
<td>57</td>
</tr>
</tbody>
</table>

Only 3.7% of ART sites met the target for timely drug pick up in 2011 as shown by table 1 above. There is still a challenge of on time drug pick up which need to be researched on.
1.1.4 Drug pickup

According to MOHCW HIV DR strategy, drug pick-up is the collection of all ARV drugs by patient as per the prescription from ART sites. In Zimbabwe the EWI monitoring survey started to collect information on drug pick-up in 2009. In 2009 no site managed to meet the EWI target out of the 21 sites studied. In 2010 only 4.7% of the 43 studied sites met the EWI target. According to WHO, all ART sites are supposed to meet the target of $\geq 90\%$ of all patients on ART picking up their drugs on time. Bindura provincial hospital had only 18% for 2009 and 21% for 2010 and 2011, ART patients picking up their drugs on time$^6$.

If ART drugs are not picked on time and taken as per the prescription, there will be high risk of HIV drug resistance. In order to prevent HIV drug resistance ART drugs are supposed to be taken as per prescription. According to 2011 EWI report, most patients were not picking up their drugs as per schedule. Untimely drug pick up was not quantified and factors associated to drug pick up were not assessed.

Operational definition

According to WHO Early Warning Indicators Survey guidelines 2009, untimely drug pick-up is defined as: “Drug pick-ups that occurred after the previous ARVs would have run out if taken as prescribed considering the one week buffer”. A person is considered to have missed drug pick up if she/he runs out of the previous ARVs prescription including the buffer. The standard drug pick-up schedule for first line ART is as follows:

First line: Tenofovir (TDF) /Stavudine (d4T), Lamivudine (3TC) and Nevirapine (NVP)

Alternative first line: Zidovudine (AZT), Lamivudine (3TC) and Nevirapine (NVP)

Let $T$ be the appointed time of drug pick up.
$T_0$ – Time of initiation on ART (Starter pack)

$T_{1/2}$ – Time for step up of NVP after finishing Starter pack.

$T_1$ – Time for re-supply for a month, doctor’s review and monitoring of IRS and adverse effects

$T_2$ - Time for re-supply for a month, doctor’s review and monitoring for delayed adverse effects

$T_3$ – Time for re-supply for 3 months, doctor’s review and monitoring for delayed adverse effects

$T_n$ - Time for subsequent re-supply for 2 or 3 months depending with the logistic supply system, drug stock, condition of the patient, distance from the ART site and other factors.

The patient then picks the drugs from the pharmacy according to the schedule. Every supply was having a week buffer.

**Timely drug pick up** = $T_0 + T_{1/2} + T_1 + T_2 + T_3 + … + T_n$; where $T$ is the appointed time for drug pickup. (Collection of drugs that was done by the patient before running out of the previous ARVs prescription)

According to Ministry of Health and Child Welfare HIV Drug Resistance Prevention Strategy, missing any of the $T_1$ to $T_n$ is classified as untimely drug pick up or missed drug pickup.

**1.2 Problem statement**

Anecdotal evidence has shown that, ART coverage has improved, whilst the proportion of patients picking up drugs on time still remained very low below 35% and the gap between
recommended ART pick up and actual drug pick up was widening since 2006 as illustrated by figure 4 below;

**Figure 4: ART coverage versus drug pick up in Zimbabwe**

A study on EWIs for HIV treatment (2011) has shown that only 21% (44/212) of the patients on ART at Bindura provincial hospital were picking up drugs on time\(^4\). WHO recommend that all sites providing ART should have more than 90% of the patients picking up drugs on time. The proportion of drug pick up in Bindura district and the factors associated with drug pick up were not known, while on average, 115 people are initiated on ART on a monthly basis in Bindura district. Late drug pick up increases the chances of HIV drug resistance which have negative implication to ART programme. Drugs are supplied by Logistic Support Unit using the push delivery system, where supply depends on ordering system.
CHAPTER 2: LITERATURE REVIEW

In 2011, UNAIDS estimated that 34.0 million [31.4 million–35.9 million] people were living with HIV globally. Of this population, 23.5 million [22.1 million -24.8 million] reside- in Sub-Saharan Africa, representing 67% of the global HIV burden. Zimbabwe has total population of 12,973,808 (Male - 6,234,931 and Females - 6,738,877)\(^7\). The country has a generalized HIV epidemic with a prevalence of 15%\(^1\) and an incidence of 1.07%\(^2\).

2.1 Untimely drug pick up

On-time drug pick-up is one of the early warning indicators monitored for HIV drug resistance. The indicator code is EWI 4a and the WHO benchmark is ≥90% of the ART patients picking up all their drugs on time.

Population-based Monitoring of HIV Drug Resistance in Namibia with Early Warning Indicators was done by Steven Y. Hong et al in 2010. The findings from this study indicated that, data for On-time ARV drug pick-up was unavailable except at one site where the proportion of patients picking up pills on time was 72%, which fell significantly short of the suggested WHO target of ≥90%. The study recommended monitoring of EWI in order to optimize the quality of care. Little has been done in monitoring the EWI on time drug pick-up. Zimbabwe started abstracting data on this indicator in 2009.
2.2 Factors Known to Hinder Timely Drug pick-up

2.2.1 Demographic or patient related factors

Zulu carried out a cross-sectional survey and an observational qualitative study and study indicates that that death of a relative, travel and migration, religious beliefs about illness, work schedule and commitments were the main causes for not attending scheduled drug pick-ups and clinic visits. Skhosana et al (2006) and Deribe et al (2008) reported that social demographic issues have great impact on patients continuing with treatment. For instance family and community support and religious beliefs about illness and medication influence patients to discontinue ART.

Excessive consumption of alcohol and hard drugs like cocaine and cannabis has also been associated with defaulting among patients on ART. Some defaulting patterns of patients on ART were as a result of patients visiting traditional healers or using traditional medicine. Wanjohi (2009) in Kenya carried out a study on factors influencing non-adherence to ART and he found out that age, level of education, occupation, transport cost and user fee for other medical services influenced non-adherence to ART.

2.2.2 Health service related factors

An operational study done by Sethi in 2011 in Uganda pointed that in rural areas, patients in rural areas tend to live far from the clinic and distance is a barrier to picking up HIV medication refills on time. A qualitative study done in Nepal by Wasti et al (2013) pointed out that cost (travel, registration and diagnostic), distance to health service, short period prescription, limited counselling services, transport problems, limited family support and adverse side-effects were the major barriers to ART drug pickup. A study done Maskew et al
(2007) in Ethiopia found out that poverty and lack of money for transport were the major causes of default to ART.

Hordon et al (2006) found out that attitude and quality of care provided by health care staff, lack of appropriate counselling, long waiting hours, seriousness of disease, adverse drug reaction and side effects, poor patient knowledge and information on HIV and illiteracy had negative influence on patients continuing with treatment in Tanzania.

### 2.2.3 Treatment related factors

In a study done by Adegoke in Abuja, results showed that; those that had any refill from the fourth refill onwards scheduled for less than 30 days were 4.1 times more likely to miss their appointment OR=4.1 95% CI:1.9-8.8. Results of the study showed that frequency of drug refill is a major predictor of treatment adherence. Similarly a study done by El-Khatib et al (2009) pointed out that a cumulative adherence of <95% to drug-refill visits was significantly associated with both virologic and immunologic failure (p<0.01). Skhosana and Hordon et al (2006) suggested that provision of several months’ supply of medicines per visit would help to reduce cost and minimize patient expenditure and defaulting incidence. Another study by Weiser et al (2003) pointed that side effects constrained patients on ART from sticking to agreed treatment plans in Botswana.
2.3 Justifications

Surveillance data for MoHCW (2011) revealed that only 21% were picking up drugs on time at Bindura provincial hospital but, the magnitude of untimely drug pick up and factors associated with drug pick up in Bindura district were not assessed. No studies were done in Bindura district to quantify the magnitude of late drug pick up and assess factors associated with drug pick up. Late drug pick up leads to the emergence of HIV drug resistance. It was therefore crucial to determine the prevalence of on time drug pick up and assess factors associated with drug pick-up in order to prevent the emergence HIV drug resistance. The results of this study provides evidence on drug pick-up and informs program managers on how best to improve drug pick up by patients on ART, quality of care for ART patients, reduce cost of putting people on second line and reduce morbidity and mortality of people on ART. The results also initiate further studies.

2.4 Research question

1. What is the magnitude of untimely drug pick-up and associated factors in Bindura District?

2.5 Objectives

2.5.1 General objective:

➢ To determine factors associated with untimely drug pick-up by ART patients in Bindura district by December 2012.
2.5.2 Specific objectives

- To determine prevalence of untimely drug pick up by ART patients in Bindura district.
- To assess demographic factors that influence untimely drug pick up by patients on ART in Bindura district.
- To assess health service related factors that influence untimely drug pick up by patients on ART in Bindura district.
- To assess treatment related factors that influence untimely drug pick up by patients on ART in Bindura district.

2.6 Conceptual Framework

The study used the Health Belief Model and borrowed constructs from PRECEDE-PROCEED Model to determine factors associated with drug pick up in Bindura district. The Model suggests that behaviour is a product of Modifying, Enabling and Reinforcing factors, Perceived susceptibility, Perceived barriers and Cues to action. Drug pick up was modelled to be a product of these factors.
**Perceived Susceptibility:**
HIV drug resistance

**Modifying Factors:**
Age, sex, marital status, occupation, co-morbidity, alcohol use, level of education, place of residence

**Perceived Barriers:**
User fees, Distance to ART site, Frequency of drug refill, Side effects, Availability of traditional medicine

**Enabling Factors:**
- Health Service Related factors: Drug stocks, Mode of transport to health facility, user fees
- Treatment related factors: line treatment, Frequency of drug refill, time on ART

**Reinforcing Factors:**
Religion, Time on ART, magnitude of supply, Adherence Counselling, attitude of health workers

**Cues to Action:**
support from family and colleagues, Reminders - dates

*Modified from; The Health Belief Model by Rosenstock*
CHAPTER 3: STUDY METHODS

3.1 Study design
An analytical cross sectional study was carried out where ART clients were drawn in the study and their drug pick up pattern was ascertained at the same time with measurement of the determinants variables. This was the most appropriate design since the proportion of drug pick up and factors associated are not known. This study design enabled the researcher to establish the proportion of ART clients who are not picking their drugs on time and explain factors associated drug pick up in Bindura district. Patients were assessed for drug pick up pattern and were classified into timely and untimely pick-ups for bi-variate analysis. The two groups were compared to determine factors associated to untimely drug pick up.

3.2 Study setting
The study was carried out in Bindura district. Bindura district is one of the 8 districts in Mashonaland Central province. The district has 24 health facilities and 16 of them offer ART services. Patients were interviewed from all the 16 ART sites in Bindura district.

3.3 Study population
The study population were all ART clients residing in Bindura district during the period of the study. The district ART registers has a total of 10,370 clients expected to pick up their drugs on time.

3.4 Study Unit
An ART client from the ART registers of Bindura district
3.5 Inclusion criteria

ART clients who are registered in Bindura district who;

- Are 16 years and above
- On ART for at least a month
- Consented
- Permanently resides in Bindura district

3.6 Exclusion criteria

The study excluded ART clients who;

- are paediatrics
- Visited Bindura district.

3.7 Sampling

3.7.1 Sampling frame: ART registers of ART initiating and follow up sites in Bindura district and participants were drawn from these registers.

3.7.2 Sample size

Epi-Info version 3.5.1 StatCalc function was used to calculate the sample size. According to NAC 2012 ART report, the number of people on ART in Bindura district was 10,370. The proportion of patients picking-up their drugs on time for Bindura provincial hospital was 21% (MOHCW EWI Report 2011). The sample size calculated at 95% significance level and worst acceptable results of 16% was 249. Assuming 90% response rate, however 28 participants were included to cater for non-responses, participants interviewed were 277.
3.7.3 Sampling methods

Participants were selected from all 16 sites proportional to size. Ratio of patients by sites was calculated and more clients were selected from high volume sites, few clients were selected from low volume sites. Study participants were randomly selected from each site using Microsoft Excel Random function [=RANDBETWEEN(1, n)]

3.8 Study variables

Table 2: Study variables

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Study Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untimely drug pick-up</td>
<td><strong>Patient related factors</strong></td>
</tr>
<tr>
<td></td>
<td>Age</td>
</tr>
<tr>
<td></td>
<td>Sex</td>
</tr>
<tr>
<td></td>
<td>Marital Status</td>
</tr>
<tr>
<td></td>
<td>Level of Education</td>
</tr>
<tr>
<td></td>
<td>Religion</td>
</tr>
<tr>
<td></td>
<td>Employment status</td>
</tr>
<tr>
<td></td>
<td>Place of residence</td>
</tr>
<tr>
<td></td>
<td>Support from colleagues</td>
</tr>
<tr>
<td></td>
<td>Co-morbidity ie Psychological disorders</td>
</tr>
<tr>
<td></td>
<td><strong>Treatment related factors</strong></td>
</tr>
<tr>
<td></td>
<td>Time on ART</td>
</tr>
<tr>
<td></td>
<td>Line of regimen</td>
</tr>
<tr>
<td></td>
<td>Side effects</td>
</tr>
<tr>
<td></td>
<td>Frequency of drug refill/ Magnitude of supply</td>
</tr>
<tr>
<td></td>
<td>Treatment Adherence Counselling</td>
</tr>
<tr>
<td></td>
<td><strong>Health service related factors</strong></td>
</tr>
<tr>
<td></td>
<td>ART Drug stock outs</td>
</tr>
<tr>
<td></td>
<td>User fees</td>
</tr>
<tr>
<td></td>
<td>Distance from ART site</td>
</tr>
<tr>
<td></td>
<td>Attitude of health workers</td>
</tr>
</tbody>
</table>
3.9 Data collection process
An interviewer-administered questionnaire was used to collect data from the participants (See Annex 3). The questionnaire was created based on the constructs of the conceptual framework. Questionnaire administration was done in Shona. Timely drug pick up was measured from ART patient facility held cards and patients cards and verified by checking pharmacy registers. Each site had ART registers, pharmacy registers and patient cards. ART clients who had came for ART services at all 16 sites in Bindura district were randomly selected and interviewed using a questionnaire. A data extraction form (See Annex 4) was used to verify client’s information with pharmacy registers; facility held cards, patient notes and facility stock cards. The data collection exercise was done in a period of one month from 24 June to 19 July 2013.

3.9.1 Data Collection Tools
A questionnaire was developed and was used to collect data from participants. The questionnaire was translated to the appropriate vernacular language (Shona) by an independent person and another person retranslated it to English to check for consistency in the meaning of the questions after translation. The questionnaire was pre-tested for validity in Bindura district and where necessary adjustments were made. A data extraction form was developed and was used to extract data from patient records and registers, and the information was bi-angulated with the one provided by the client.
3.10 Data management

3.10.1 Quality control
In order to ensure quality control at data collection, questionnaires and data extraction forms were piloted and the questionnaires were translated in vernacular. Independent back translation was done to check and maintain meaning of the questions. Completed questionnaires were checked for completeness and consistence in responses and all responses were coded. A list of codes was kept for data analysis and interpretation.

3.10.2 Entry process
Data was entered into the Epi Info package version 3.5.1. Errors were checked as the data was entered whether the correct variable codes were correctly assigned by cross checking with the variable list. Double entry was done to correct errors where possible.

3.10.3 Data cleaning
In the field questionnaires were checked for completeness and consistency in the responses. During data entry, the researcher ensured that correct variables codes were entered without modifications. Entered data were checked for outliers, duplicates and inconsistencies.

3.10.4 Data Analysis
Epi Info version 3.5.1 was used to analyse data. Frequencies and proportions were generated. Prevalence odds ratios (POR) were used to determine strengths of associations between the independent variables and the outcome of interest (timely drug pick up). The outcome of interest was whether one was picking drugs on time or not. 95% confidence intervals for
PORs were used to determine the significance of associations between independent variables and the outcome of interest. Logistic regression analysis was performed to identify independent risk factors for factors associated with un-timely drug pick up among ART clients and to control for confounding variables. The logistic regression model included all variables with a p-value of 0.25 or less.

3.10.5 Data Storage

Data was stored on computer Epi Info database with backup files on memory stick. Hard copies of the completed questionnaires were kept in office under lock.

3.11 Permission to proceed

Written permission was sought from the Health and Child Welfare Provincial Medical Director of Mashonaland Central province and the letter was copied to District Medical Officer Bindura district (See Annex 5). This was done two weeks prior to data collection.

3.12 Ethical issues

Ethical approval for the protocol was sought from the Joint Research Ethics Committee and the Medical Research Council of Zimbabwe and was granted (See Annex 6 and 7). The study protocol was explained in full to all study participants in Shona (their local language). Written informed consent was obtained from all study participants using a consent form (See Annex 1 and 2). No force, coercion or persuasion by any means was used to recruit study participants. Study participants were allowed to terminate their participation at any time they felt like doing so. Confidentiality was assured and maintained throughout the study.
CHAPTER 4: RESULTS

A total of 277 ART clients who were on treatment for at least a month were interviewed in Bindura district. Most (65.7%) participants had been on ART for more than 6 months. Treatment was first sought from a health facility by 260 (93.9%) of the participants while the remaining 15 (5.4%) first sought treatment from faith healers, 2 (0.7%) and traditional healers. Median age of respondents was 35 years (Q1 = 30 years; Q3 = 42 years) and 174 (62.8%) were from urban, 56 (20.2%) were from rural and 47 (17.0%) were from farms. Females constituted 70.4% of the participants and males 29.6%.

4.1 Demographic characteristics of respondents

Table below 3 shows the socio demographic characteristics of the respondents

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (N=277)</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>82</td>
<td>29.6</td>
</tr>
<tr>
<td>Females</td>
<td>195</td>
<td>70.4</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>150</td>
<td>34.5</td>
</tr>
<tr>
<td>Widowed</td>
<td>58</td>
<td>20.9</td>
</tr>
<tr>
<td>Divorced</td>
<td>39</td>
<td>14.1</td>
</tr>
<tr>
<td>Single</td>
<td>30</td>
<td>10.8</td>
</tr>
<tr>
<td>Variable</td>
<td>Frequency (N=277)</td>
<td>Proportion (%)</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Religion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apostolic</td>
<td>106</td>
<td>38.3</td>
</tr>
<tr>
<td>Pentecostal</td>
<td>61</td>
<td>22.0</td>
</tr>
<tr>
<td>Catholic</td>
<td>19</td>
<td>6.9</td>
</tr>
<tr>
<td>Traditional African</td>
<td>44</td>
<td>15.9</td>
</tr>
<tr>
<td>Orthodox</td>
<td>6</td>
<td>2.2</td>
</tr>
<tr>
<td>Protestant</td>
<td>41</td>
<td>14.8</td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No formal education</td>
<td>31</td>
<td>11.2</td>
</tr>
<tr>
<td>Primary</td>
<td>96</td>
<td>34.7</td>
</tr>
<tr>
<td>Secondary</td>
<td>147</td>
<td>53.1</td>
</tr>
<tr>
<td>Tertiary</td>
<td>3</td>
<td>1.1</td>
</tr>
<tr>
<td>Employment Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formally employed</td>
<td>31</td>
<td>11.2</td>
</tr>
<tr>
<td>Informally employed</td>
<td>61</td>
<td>22.0</td>
</tr>
<tr>
<td>Not employed</td>
<td>180</td>
<td>65.0</td>
</tr>
<tr>
<td>Student</td>
<td>5</td>
<td>1.8</td>
</tr>
</tbody>
</table>

### 4.2 Prevalence of untimely drug pick up

The prevalence of untimely drug pick up for 16 ART sites in Bindura district was 40.4% (n=277). Stratified by gender the proportion of females who missed drug pick up time were 42.6% as compared to 35.4% of males. The median number of times participants missed drug
pick on time in the past 12 months was 1 (Q1=1; Q3=2) and the reasons of not picking up drugs on time are presented in the figure 5 below.

**Figure 5: Reasons of not picking up drugs on time (n=112)**

![Figure 5: Reasons of not picking up drugs on time (n=112)]

Figure 5 above provides a distribution of responses for not picking up drugs on time. The greatest proportion (24%) of ART clients who missed drug pick up time mentioned social problems like death of friends and relatives, and other social commitments as the main reason for not picking up drugs on time. A marked proportion (17%) mentioned travelling as a reason for not picking up drugs on time. Only 1% mentioned most frequent drug refill as a reason for not picking up drugs on time.

### 4.3 Factors associated to untimely drug pick up.

#### 4.3.1 Demographic factors associated with untimely drug pick up

Table 4 shows demographic factors that are associated to untimely drug pick up.
Table 4: Demographic factors associated with untimely drug pick up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Untimely drug pick up</th>
<th>Timely drug pick up</th>
<th>POR (95% CI)</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (n=277)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>83(42.6%)</td>
<td>112(57.4%)</td>
<td>1.35 (0.79 - 2.31)</td>
<td>0.327</td>
</tr>
<tr>
<td>Male</td>
<td>29(35.4%)</td>
<td>53(64.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low level of education (n=277)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (Primary and below)</td>
<td>53(41.7%)</td>
<td>74(58.3%)</td>
<td>1.10 (0.68 - 1.79)</td>
<td>0.778</td>
</tr>
<tr>
<td>No (Secondary and above)</td>
<td>59(39.3%)</td>
<td>91(60.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural resident (n=277)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (Rural and Farms)</td>
<td>44(42.7%)</td>
<td>59(57.3%)</td>
<td>1.62 (0.71 - 1.91)</td>
<td>0.639</td>
</tr>
<tr>
<td>No (Urban)</td>
<td>68(39.1%)</td>
<td>106(60.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital Status (n=277)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>54(36.0%)</td>
<td>96(64.0%)</td>
<td>0.67 (0.41 - 1.08)</td>
<td>0.131</td>
</tr>
<tr>
<td>Single (Never married, Divorced and Widowed)</td>
<td>58(45.7%)</td>
<td>69(54.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employment status (n=216)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed (Formally and informally employed)</td>
<td>11(35.5%)</td>
<td>20(64.5%)</td>
<td>0.77 (0.35 - 1.70)</td>
<td>0.655</td>
</tr>
<tr>
<td>Unemployed (Not employed and Student)</td>
<td>77(41.6%)</td>
<td>108(58.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underlying Conditions (n=234)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>19(51.4%)</td>
<td>18(48.6%)</td>
<td>1.96 (0.96 - 3.98)</td>
<td>0.09</td>
</tr>
<tr>
<td>No</td>
<td>69(35.0%)</td>
<td>128(65.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (n=277)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-35 years</td>
<td>66(46.2%)</td>
<td>77(53.8%)</td>
<td>1.64 (1.01 - 2.66)</td>
<td>0.04*</td>
</tr>
<tr>
<td>36-68 years</td>
<td>46(34.3%)</td>
<td>88(65.7%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Statistically significant

Females were more likely to untimely pick up drugs/miss drug pick up time than males, however the relationship is not statistically significant with POR = 1.35 (95% CI: 0.79 - 2.31). Those with low level of education, primary and below are more likely to miss their drug pick up than those with high level education (secondary and above) but the relationship is not statistically significant with POR = 1.10 (95% CI: 0.68 - 1.79). Those who stay in rural and farms were more likely to miss drug pick up time than those staying in urban areas but the association is not statistically significant with POR = 1.62 (95% CI: 0.71 - 1.91). Being
married is protective to untimely drug pick up, however the relationship is not significant with POR = 0.67 (95% CI: 0.41 - 1.08). Those who are aged 16 – 35 years are more likely to miss drug pick up time than those who are 36 – 68 years and the relationship is statistically significant with POR = 1.64 (95% CI: 1.01 - 2.66). Those who have underlying conditions were more likely to miss drug pick up time than those without underlying conditions but the relationship is not statistically significant with POR = 1.96 (95% CI: 0.96 -3.98). The following figure shows the proportion of the underlying conditions.

**Figure 6: Proportion Underlying Conditions (n=37)**

![Figure 6: Proportion Underlying Conditions (n=37)](image)

Tuberculosis was reported to be the most prevalent (43%) underlying condition and cancers and diabetes mellitus were the least.

**4.3.2 Treatment related factors associated with untimely drug pick up.**

The following table shows treatment related factors that are related to untimely drug pick up.
Table 5: Treatment related factors associated with untimely drug pick up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Untimely drug pick up</th>
<th>Timely drug pick up</th>
<th>POR (95% CI)</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Support from household/colleagues (n=277)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>64</td>
<td>108</td>
<td>0.70 (0.43 - 1.15)</td>
<td>0.203</td>
</tr>
<tr>
<td>No</td>
<td>48</td>
<td>57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Belonging to a support group (n=116)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>18</td>
<td>39</td>
<td>0.67 (0.31 - 1.44)</td>
<td>0.409</td>
</tr>
<tr>
<td>No</td>
<td>24</td>
<td>35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adherence counselling (n=277)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>97</td>
<td>153</td>
<td>0.51 (0.21 - 1.13)</td>
<td>0.139</td>
</tr>
<tr>
<td>No</td>
<td>15</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse effects to ART (n=277)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>56</td>
<td>58</td>
<td>1.84 (1.13 - 3.01)</td>
<td>0.019*</td>
</tr>
<tr>
<td>No</td>
<td>56</td>
<td>107</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration on treatment (n=277)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 - 6 months</td>
<td>27</td>
<td>68</td>
<td>0.45 (0.27 - 0.77)</td>
<td>0.005*</td>
</tr>
<tr>
<td>More than 6 months</td>
<td>85</td>
<td>97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency of drug supply (n=277)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One month or less supply</td>
<td>55</td>
<td>109</td>
<td>0.50 (0.30 - 0.81)</td>
<td>0.007*</td>
</tr>
<tr>
<td>Two months or more supply</td>
<td>57</td>
<td>56</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Statistically significant

Support from colleagues or household member was protective to untimely drug pick up, however the relationship was not statistically significant with POR = 0.70 (95% CI; 0.43 - 1.15). Adherence counselling is protective to untimely drug pick up although the relationship is not statistically significant (POR = 0.51; 95% CI: 0.21 - 1.13). Those who had adverse effects to treatment were more likely to miss their drug pick up time than those who did not have, and the relationship is statistically significant with POR = 1.84 (95% CI; 1.13 - 3.01). Those who had short time (0-6 months) on treatment were less likely to miss their drug pick up time than those with more than 6 months on treatment and the relationship is statistically significant with a POR = 0.45 (95% CI; 0.27 - 0.77). Having one month or less supply was
protective to untimely drug pick up, and the relationship is statistically significant (POR = 0.50; 95% CI: 0.30 - 0.81).

4.3.3 Health service related factors associated with untimely drug pick up.

The following table shows health service related factors that are related to untimely drug pick up.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Untimely drug pick up</th>
<th>Timely drug pick up</th>
<th>POR (95% CI)</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance from ART site</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤10 km radius</td>
<td>79</td>
<td>136</td>
<td>0.51 (0.29 - 0.90)</td>
<td>0.029*</td>
</tr>
<tr>
<td>≥10 km radius</td>
<td>33</td>
<td>29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pay consultation fees/User fees</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>94</td>
<td>120</td>
<td>1.96 (1.06 - 3.60)</td>
<td>0.041*</td>
</tr>
<tr>
<td>No</td>
<td>18</td>
<td>45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mode of transport</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foot and bicycle</td>
<td>83</td>
<td>127</td>
<td>0.85 (0.49 - 1.49)</td>
<td>0.687</td>
</tr>
<tr>
<td>Motor Vehicle</td>
<td>29</td>
<td>38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stock outs of medicines</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>23</td>
<td>22</td>
<td>1.68 (0.88 - 3.19)</td>
<td>0.153</td>
</tr>
<tr>
<td>No</td>
<td>89</td>
<td>143</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Statistically significant

Residing within 10km radius to ART was protective and the association is statistically significant (POR = 0.51; 95% CI: 0.29 - 0.90). Those who pay consultation fees or user fees were more likely to miss drug pick up time than those who don’t pay and the relationship is statistically significant with POR = 1.96 (95% CI; 1.06 - 3.60). On average (n=44) clients were paying a consultation fee of $1-00 (min=1; max=5). Those who reported that they had been referred to other sites because of stock out of ART medicines were more likely to miss their drug pick up time, however the relationship was not statistically significant (POR = 1.68; 95% CI: 0.88 - 3.19).

The following figure 7 shows the challenges faced by ART clients in picking up drugs.
Figure 7: Challenges in picking up drugs (n=176)

The most frequent challenge was user fees (48%) followed by long distance from ART site (26%). Only 2% of participants mentioned that they were facing challenges of stock outs.

4.4 Multivariate analysis

Multivariate analysis was done in order to estimate the measures of association while at the same time controlling for confounding variables. All variables that were significant at 0.25 level (P-value < 0.25 in the bi-variate analysis) were included in the multivariate logistic regression model.

Step wise regression model was used, where the - model was started off with one variable. Other variables were added one by one into the model. Variables that were not significant were eliminated from the model until left with significant variables at 0.05 level. Goodness of fitness test (GoF) was done to test adequacy of the model using likelihood ratio test and it was found to be significant (p = 0.0000). The following table shows variables which were
found to be significant after forward elimination process. The adjusted odds ratios (AOR) and 95% confidence intervals (95% CI) from the final model are presented below.

**Table 7: Logistic regression analysis**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted OR (95% CI)</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance from ART site (≥10Km radius)</td>
<td>1.96 (1.11 - 3.47)</td>
<td>0.021</td>
</tr>
<tr>
<td>Pay consultation fees/User fees (Yes/No)</td>
<td>1.96 (1.06 - 3.60)</td>
<td>0.031</td>
</tr>
<tr>
<td>Adverse effects to ART (Yes/No)</td>
<td>1.84 (1.13 - 3.01)</td>
<td>0.014</td>
</tr>
<tr>
<td>Duration on treatment (&gt; 6 months)</td>
<td>2.21 (1.30 - 3.76)</td>
<td>0.003</td>
</tr>
<tr>
<td>Frequency of drug supply (&gt; 2 months)</td>
<td>2.02 (1.23 - 3.30)</td>
<td>0.005</td>
</tr>
<tr>
<td>Constant</td>
<td>*</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Long distance (≥10km) from ART site [AOR 1.96 (95% CI: 1.11 – 3.47) p = 0.021], user fees [AOR 1.96 (95% CI: 1.06 - 3.60) p = 0.031], adverse effects to ART [AOR 1.84 (95% CI: 1.13 - 3.01) p = 0.014], long duration on treatment [AOR 2.21(95% CI: 1.30 – 3.76) p = 0.003] and frequency of drug supply [AOR 2.02 (95% CI: 1.23 – 3.30) p = 0.005] were independent factors associated with the likelihood of untimely drug pick up in Bindura district.
CHAPTER 5: DISCUSSIONS

The study sought to establish the prevalence of untimely ART drug pick up and factors associated with drug pick up in the district. Forty percent (40%) of ART clients in Bindura district missed to pick up drugs at least once in the past 12 months period (June 2012 to June 2013). Furthermore 32.1% of the study participants missed more than one supply. The prevalence is high compared to WHO recommended standard of ≤10%. This confirms that there is a problem of untimely ART drug pick up in Bindura District. Missing ART drug pick up time will lead to HIV drug resistance and this will worsen treatment outcomes. The main reasons for not picking up drugs on time were social problems (i.e. death of friends and relatives, lack of money for transport) and travel, were the same as the main reasons for non-attendance to scheduled drug pick-ups identified by Zulu (2009).

Age was the only demographic factor which was found to be significantly associated with timely drug pick up. Those who were 16 – 35 years were more likely to miss drug pick up time than those 36 – 68 years. This is in line with the findings of Wanjohi (2011) who stated that those of younger age group were less likely to adhere to ART in Kenya, and the reasons being that they were committed to work and school. These reasons apply in Zimbabwe situations where 8% and 3% mentioned work and school commitments as reasons of not picking up drugs on time respectively. After logistic regression and stratified analysis; age
modified the relationship between distance from ART site and duration on treatment, and ART drug pick up time.

Level of education was not significantly associated with drug pick up time. This is contrary to the findings of Wanjohi (2011) who stated that level of education was a significant factor in determining drug pick up time in Kenya\textsuperscript{10}. In the Zimbabwean situation, there might be more important factors such as availability and overall accessibility of ART services that could rule out the significance protective effect of level of education. Those who are highly educated are expected to be aware of the effects of not picking drugs on time and are expected to be picking drugs on time, however there is no statistically significant association between level of education and drug pick up time.

Having underlying conditions like psychotic disorders was not statistically significant and this contrary to the findings of Hardon et al (2006) who found out that; underlying conditions has a negative influence for patients to continuing on ART in Tanzania\textsuperscript{11}. However the underlying conditions are of clinical importance to management and treatment of ART clients. Treatment regiment and frequency of supply may depend on the underlying condition. The most reported condition was tuberculosis and some TB treatment drugs interact with some ARVs.

Treatment related factors which were found to be statistically significant were adverse effects to drugs, duration on treatment and magnitude/frequency of drug supply. Side/adverse effects of ART may be mild or severe and they de-motivate patients from taking drugs on time because the patient might be sick or might be afraid of recurrence of adverse effects. This is concurring with the study done by Weiser et al, who pointed that side effects constrained
patients on ART from sticking to agreed treatments plans in Botswana\textsuperscript{12}. Those who are on treatment for less than six months were protected from missing drug pick up time because they will be new to the system and will adhere to treatment with motivation to getting well. Clients given one month supply or less were protected from missing drug pick up time. In Zimbabwe situation, clients who are given one month or less supply are the ones who will be starting ART and most of these patients will be not feeling well since the bulk of patients are initiated based on WHO clinical staging criteria. These clients will pick up drugs on time with motivation to recover. These results are contrary to results of Hardon et al (2006) who suggested that provision of several months’ supply of medicines per visit would help to reduce cost and minimize patient expenditure and defaulting incidence\textsuperscript{11}.

Support from family members/colleagues is very important in reminding one of the times for drug pick up and providing support when one is ill. Adherence counselling is of clinical importance in order to motivate clients to pick their drugs on time. It imparts knowledge on the cons of non-adherence and explores ways to reduce defaulting. However support from family members/colleagues and adherence counselling was not statistically significant. This is in tandem with results of a study by Wasti et al (2011) which pointed out that limited counselling services and limited family support were major barriers to ART drug pick up\textsuperscript{13}. Adherence counselling play a major role since this includes a one-to-one interaction between the health care provider and the client where issues about treatment are also clarified. Adherence counselling however remains an important factor to ART drug pick-ups as shown in this study that adherence counselling is protective to untimely drug pick up.

\textsuperscript{11}
Line of treatment was not compared because there were few people on second line and all of them had missed drug pick up time. This means untimely drug pick up was prevalent in all ART second line clients.

Health service related factors which were significantly associated with drug pick up were; distance from ART sites, user fees and challenges in ART drug pick up. Staying within a 10km radius to health facility was protective and this confirm findings from a study done by Ajay Sethi in Uganda (2011) that pointed suggested that in rural areas, patients tend to live far from the clinic and distance is a barrier to picking up HIV medication refills on time. In Bindura district most clients will not be working and will not have bus fare for subsequent drug refill. Hence it’s a major obstacle that was highlighted by clients. Living long distances from the health facility lowers accessibility of health services even in situations where services are readily available. Those who paid user fees were more likely to miss drug pick up time, since some will not have the money by the time they are suppose to go for drug refill and most (66.8%) these clients are not working. This concurs with a study done by Wasti et al (2011) which pointed out that cost for travel, registration/consultation and diagnosis were major barriers to ART drug pick up. Those who mentioned that they had challenges like distance, health worker attitude and long waiting time ware more likely to miss drug pick up time because challenges will hinder clients from picking up their drugs. This concurs with results from a study done by Hardon et al (2006) that mentioned that; attitude and quality of care provided by health care staff, long waiting hours, had negative influence on patients continuing with treatment in Tanzania. Most health facilities in Zimbabwe are short staffed hence there will be long waiting hours for a service to be delivered. Furthermore due to lack of incentives, the attitude and quality of services provided will be compromised.
Stock outs of ARV drugs are of public health importance and the study has shows that those who experienced stock outs were more likely to miss drug pick up time. However the association was not statistically significant and conflicts with the results of the study done by Maskew et al (2007), which mentioned that stock outs of ARV drugs was one of the main causes of non-adherence to ART\textsuperscript{14}. ART facilities in Zimbabwe normally will rather give a supply of less than a month than to turn away patients because of stock outs. Stock outs are mainly due to logistic challenges in ordering of drug and also delivery system which is a push system.

**Conclusions**

Timely drug pick is enabled by magnitude of supply and the behaviour to pick up drugs on time is reinforced by attitude of health workers. This study has shown that distance from ART sites, side effects and user fees are barriers to ART drug pick up. Age is a modifying factor to ART drug pick up. The major independent factors associated to ART drug pick up are; distance from ART site, user fees, side effects of ARVs, time on treatment and frequency of drug supply.
Recommendations

- The District Health Executive through the pharmacy department must ensure uninterrupted supply of ART drugs at all ART sites.

- The Ministry of Health and Child Welfare should put a policy to exempt ART clients from payment of user fees.

- The District Health Executive should intensify ART outreach activity in order to provide services to those who stay far away from ART sites.

- District Health Executive through the pharmacy department must speed up transitioning from Stavudine based regimen to Tenofovir based regimen so as to reduce side effects of ART drugs.

- The health promotion officer must sensitize health workers on Patient/Clients charter.

- The health promotion officer must develop IEC materials to empower communities with information on effects of untimely drug pick up.

- There is need for further research on the effects of underlying conditions and adherence counselling on ART drug pick-up time.
References

1. ZIMSTAT: Zimbabwe Demographic Health Survey 2010-2011, Harare (2011)
9. Zulu : Factors associated with default of scheduled drug pick-up and clinic visits by patients on ART, South Africa (2009), Stellenbosch University


17. Deribe et al: Disclosure experience and associated factors among HIV positive men and women clinical service users in South West Ethiopia. BMC, Public Health Volume 8; Pages 1-34


Factors Associated with Timely Antiretroviral Drug Pick-up by Patients in Bindura District.

Mashonaland Central Province Zimbabwe:

2013

Principal Investigator: Isaac Taramusi

Phone number: 0773924183
Introduction

My name is Isaac Taramusi. I am a Public Health student with the University of Zimbabwe attached to National AIDS Council. I am conducting a study on the factors associated with Antiretroviral Drug pick-up by patients in Bindura District. Before you decide to volunteer for this study, you must understand its purpose, how it may help you, the risks to you and what is expected of you.

Purpose of the study

You are being asked to participate in a research study of factors associated with drug pick up by patients in Bindura district. The purpose of the study is to establish the factors which may be causing ART patients to miss their drug pick up time. Timely drug pick-up has been shown in other studies to reduce treatment failure or drug resistance among ART patients. You were selected as a participant in this study because you are one of those who have been on ARV treatment in the district. The results of this study could potentially benefit ART patients in the district as the recommendations could be used to improve ARV treatment services in Bindura district. This study will have a total 277 participants in Bindura district. The information obtained will be used on designing interventions on how to improve ART services, improve ART review visits among ART patients so as to improve treatment outcomes.

Procedures and Duration

If you decide to participate in this study, you will undergo an interview which may take 15 - 20 minutes to complete. You will be asked questions about yourself and your pattern of drug pick up. I will also require with your permission, to check your treatment card to verify drug pick up, and scheduled dates as well as the regimen you are on. You are free to ask for
clarification on any questions that you do not understand at any point during the interview. If you have questions about the study, you may ask at any time.

**Risks and Discomforts**

Some of the questions that you will be asked are of a personal nature so you may feel embarrassed to respond to them. If you feel very uncomfortable, you are free to decline answering any question that you do not want to answer. The answers you provide will be kept private and confidential.

**Benefits and or Compensation**

There are no direct benefits/compensation that will come from participating in this study. You will get an opportunity to learn more about the importance of timely drug pick-up in reducing treatment failure and drug resistance.

**Alternative Procedure or Treatments**: there are no interventions or treatments that will be done in this study.

**Confidentiality**

If you indicate your willingness to participate in this study, your participation will be on a voluntary basis. You are free to withdraw from the study at any point. Information collected about you and your responses will be treated with confidentiality. The questionnaire to be used during the interview will be identified by a coded number instead of your name. This consent form will be separated from the coded questionnaires and stored in a secure place.

**Additional Costs**: You will not incur any expenses from participating in this study.
Offer to Answer Questions

If you have any questions on any aspects that are not clear to you about this study, please feel free to ask me before you sign this form. You are free to take as much time as you can to think about it.

Authorization

By signing this form, it means that you have read and understood the information provided above, had all your questions answered, and decided to participate voluntarily without being coerced and can choose to stop your participation at any time without loss of any benefits entitled to you. You authorize myself, field and academic supervisors to access the information that you will have provided. The information you provide will only be used for the purpose of this study.

Client Name…………………… Signature of Client.................. Date...........................
Name of Researcher………………Signature of Researcher……………….. Date..................
Name of Witness…………………..Witness Signature ……………….. Date.................. 
For any further information pertaining to this study, Joint Research Ethics Committee at:

University of Zimbabwe,

College of Health Sciences

Department of community medicine

PO Box A178, Avondale,

Harare

Zimbabwe
YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP

If you have any questions concerning this study or consent form beyond those answered by the investigator, including questions about the research, your rights as a research subject or research-related injuries: or if you feel that you have been treated unfairly and would like to talk to someone other than a member of the research team, please feel free to contact the The Joint Research Ethics Committee on Telephone 04-708140
ANNEX 2: GWARO RECHITENDERANO

Nhanganyaya


Chinangwa cheongororo

Murikukumbirwa kuti muve nhengo yeongororo yekutsvaka zvikonzero zvinoita kuti varwere veHIV ne AIDS vari pamishonga yema ARVs vasaenda kukiriniki kana kuchipatara kunotora mapiriti avo pamazuva avo akatarwa muno mudunhu reBindura. Nekudaro, chinangwa chikuru cheongororo iyi ndichekuwana zvikonzero zvinotadzisa varwere kutora mishonga yavo pamazuva avakatarirwa. Zvakawonekwa mune dzimwe tsvakurudzo zhinji kuti kutorwa kwemishonga panguva dzakatarwa kunoderedza dambudziko rekupanduka nekusadavira mishonga kwe chirwere ichi muvanhu vanorwara nacho. Ongororo iyi ichaitwa muvanhu vana mazana maviri ane makumi manomwe nenomwe (277) vanorwara nechirwere ichi muno mudunhu reBindura.

Zvichaitwa muongororo: Kana makasununguka kuva muongororo ino, ndichakubvunzai mibvunzo inogona kutora nguva iripakati pemaminitsi gumi nemashanu kusvika makumi

**Njodzi dzamungasangana nadzo**

Hapana njodzi yamungasangana nayo kuburikidza nekuva muongororo ino. Kana musina kusununguka kupindura mimwe mibvunzo, makasununguka kurega kuipindura. Mhinduro dzichange dzakavanzika, hakuna vamwe vanhu vanotenderwa kuziva zvamunenge mapindura.

**Zvakanakira kuva muongororo ino**

Hapana muhoro wamuchawana kuburikidza nekuva muongororo ino asi kuti muchawana mukana wokudzidza zvakawanda maererano nezvakanakira kutora mishonga yenyu pamazuva akatarwa.

**Kurapwa:** Hakuna Kurapwa kuchaitwa muongororo ino

**Kuvimbika kwetsvakurudzo**

**Dzimwe mari dzingangodikanwa:** Hapana mari inodikanwa kubva kwamuri kuti muve mutsvakiridzo ino.

**Kupindurwa kwemibvunzo**

Kana paine mibvunzo yamuchaona isina kujeka makasununguka kundibvunza ikozvino, chero pane imwe nguva. Makasununguka kutora nguva yekuti mumbofunga.

**Mvumo**

Kusayina kwamuchaita panzvimbo inoteversa zvinoratidza kuvuma kuni maverenga mukanzwisisa uye maziviswa maerano neongororo iyi, hamuna kumanikidzwa kuva nechokuita nayo, uyezve kuti zvamauzwa kana kuverenga mugwaro rechitenderano iyi zvaita kuti mugone kunyatonzwisisa njodzi uye zvingakubatsirai zvamungawana mutsvakurudzo iyi zvekare kuti munokwanisa kusarudza kuti hamuchada kuenderera mberi nekupindura mibvunzo pasina zvamungarasikirwa nazvo. Zvamunenge mazivisa
patsvakiridzo ino zvichabvumidza ini pamwe nevarairidzi vangu kuti tizvishandise muongororo ino bedzi.

Zita reMupinduri................................ Dharangidzo................................ Zuva..............................
Zita reMuongorori................................ Dharangidzo................................ Zuva..............................
Zita reChapupu.................................. Dharangidzo................................ Zuva..............................

Kana paine zvamunoda kunzwisisa, ivai makasununguka kunyorera pa kero inoti:

Joint Research Ethics Committee
University of Zimbabwe
College of Health Sciences
Department of community medicine
PO Box A178, Avondale
Harare
Zimbabwe

**MUCHAPIHWA RIMWE GWARO RECHITENDERANO KUTI MUGARE NARO**

Kana muine imwe mibvunzo isina kupindurwa nemuongorori, kana mibvunzo yakanangana nekubatwa kwamaitwa mutsvakurudzo iyi, kana kodzero dzenyu, kana kusabatwa zvakanaka kwamunenge maitwa makasununguka Kutura neveJoint Research Ethics Committee panhamba dzerunhare dzinoti: 04-708140
ANNEX 3: QUESTIONNARE

UNIVERSITY OF ZIMBABWE

Factors Associated with untimely Antiretroviral Drug Pick-up by Patients in Bindura District.
Mashonaland Central Province Zimbabwe:

2013

Principal Investigator: Isaac Taramusi (MPH trainee)
Phone number: 0773924183
Questionnaire

Introduction
My name is Isaac Taramusi. I am a Public Health student with the University of Zimbabwe attached to National AIDS Council. I am conducting a study to understand why ART patients are not picking up drugs on time. This study will help in solving the problem of un-timely drug pick up. You have been chosen to be one of the respondents of this study. You are free to decline participation in this study or to ask any question concerning this study at anytime. The information that you are going to provide will be kept confidential. If you are willing to participate in this study, please endorse below:

Patient OI/ART No…………………… Signature of Client.........................
Date............................

Section A: Demographic characteristics
I am now going to ask you questions about yourself. Feel free to answer and clarify questions you don’t understand/ Ikozvino ndichakubvunzai mibvinzo maererano nemi, sunungukai kuipundura uye kuti munyatsojekeserwa panenge pasina kujeka.

1. Sex M [ ] F [ ]
2. What is your age at last birth day/Mune makore mangani ................. Years
3. What is your marital status/ Makaroorwa/ra here?
   □ Single
   □ Married
   □ Divorced
   □ Widower/d
   □ Co-habiting
4. What is your level of education/Makafunda kusvika danho ripi?
   - No formal education
   - Primary
   - Secondary
   - Tertiary

5. What is your employment status/Munosevenza basa rei?
   - Student
   - Not employed
   - Informal employment
   - Formally employed

6. What is your religion/Munotevedzera chitendero chipi?
   - Apostolic
   - Pentecostal
   - Catholic
   - Orthodox
   - Traditional African Religion
   - Other (Specify) .................................................................

7. What is your place of residence/Munogara kupi?
   - Rural
   - Urban
   - Farm

Section B: Treatment related questions/ Mibunzo yakakanangana nekurapwa kwenyu

I am now going to ask you questions about the treatment you are getting. Feel free to answer. / Ikozvino ndichakubvunzai mibvinzo maererano nekurapwa kwenyu, sunungukai kuipundura.
8. Where did you first seek treatment for HIV and AIDS/Makatanga kunorapwa kuna ani?
   - Traditional healer
   - Faith healer
   - Health Facility

9. Are there any HIV and AIDS support groups/networks in your area? Munharaunda menyu mune mapoka evanorwara ne HIV ne AIDS here?
   - Yes
   - No
   a. If Yes; Do you belong to any of the groups/Kana ariko; Ko imi muri umwe wemapoka aya here?
      - Yes
      - No

10. Do you receive support from household members or colleagues on your treatment/Munowanawo hererutsigiro kubva kuhama kana shamwari pakurapwa kwenyu?
    - Yes
    - No

11. What ART drugs are you taking/Mari kutora mishonga ipi?
    - First line (Stalanev, Zidovudine+Lamivudine+Nevirapine/Efavirenz,
      Tenofovir+Lamivudine+Nevirapine/Efavirenz)
    - Second line (Zidovudine+Lamivudine+Lopinavir/Ritonavir,
      Tenofovir+Lamivudine+Lopinavir/Ritonavir, Abicavir+Didanosine+Lopinavir/Ritonavir)

12. How long have you been on ART/Mavaneguva yakadii muchitora mishonga yenyu?
    - < 3 months
    - 3 – 6 months
    - > 6 months

13. Did you suffer any adverse effects of ART drugs/Makamborwara here nemhaka yekusapindirana nemishonga?
14. How often do you collect your drugs/Munotora mishonga yenyu panhambo dzakadii?
- Yes
- No
- Twice per month
- Once per month
- Once in ≥ 2 months

15. Do you receive adherence counselling/Munombopangawo here mazano maererano nekutora mishonga?
- Yes
- No

a) If Yes; How often/Kana mati hongu, nenhambo dzipi? ..............................................

16. Have you ever missed picking up your drugs on time/Makambodarika here nguva dzamakapiwa dzekunotora mishonga?
- Yes
- No

a) If Yes; How many times in the last 12 months/Kana mati hongu; kangani pamwedzi gumi nembiri yapfuura? .................................................................

b) If No; what makes you pick up all drugs on time/Kana mati kwete; chii chinoita kuti mutore mishonga yenyu nenguva iyo makatarirwa?
Section C: Health Service related questions/Mibvunzo yakanangana nekuwana rubatsiro

I am now going to ask you questions about the health services you are getting. Feel free to answer. / Ikozvino ndichakubvunzai mibvinzo maererano nekuwana kwenyu rebatsiro kuchipatara kana kiriniki, sunungukai kuipundura.

17. What is the distance from the nearest ART site/Kure nemusha wenyu zvakadini kusvika ku Kiriniki kana Chipatara chamunotorera mishonga?
   - [ ] ≤ 10km radius
   - [ ] ≥ 10km radius

18. What mode of transport do you use to go to your nearest ART site/Munoshandisa zvífambiso rudzii kuenda kuchipata kana kiriniki iri pedyo nemi yamunotorera mishonga yenyu?
   - [ ] On foot
   - [ ] Scotch-cart
   - [ ] Bicycle
   - [ ] Motor vehicle
   - [ ] Others (Specify)..............................................................................................

19. Do you pay for ART services/Munobhadhara here pamunoenda kunotora mishonga yenyu?
   - [ ] Yes
   - [ ] No
   a) If Yes; How much do you pay/Kana muchibhadhara; munobhadhara marii?
      ............................................................................................................................

20. Did you ever fail to have your refill because of stock outs in the past 12 months/mumwedzi gumi nemiviri yaphuura (12 months) makamboenda here kuchipatara/kiriniki pamazuva enyu akatarwa mukawana kusina ARVs?
   - [ ] Yes
   - [ ] No
   a) If Yes; How many times/Kana mati hongu; kangani kamakashaiwa mishonga?..............................................................
21. Are you facing any problem in picking up your drugs/ *Munedambudziko here nekukutora mishonga yenyu neguva dzakatarwa*?

☐ Yes
☐ No

a) If Yes; What are the problems/ *Kana mati hongu; ndeapi matambudziko acho*?

..................................................................................................................................................................
..................................................................................................................................................................
..................................................................................................................................................................
..................................................................................................................................................................
..................................................................................................................................................................
..................................................................................................................................................................

Thank you/ *Tatenda*
ANNEX 4: DATA EXTRACTION FORM
(For Data Bi-angulation)

UNIVERSITY OF ZIMBABWE

Factors Associated with Untimely Antiretroviral Drug Pick-up by Patients in Bindura District.
Mashonaland Central Province Zimbabwe:

2012

Principal Investigator: Isaac Taramusi (MPH trainee)
Phone number: 0773924183
Section A: Demographic characteristics

22. Sex  M [  ]            F [  ]

23. Age at last birth day……………… years

24. Marital status
   □ Single
   □ Married
   □ Divorced
   □ Widowed
   □ Co-habiting

25. Employment status
   □ Student
   □ Not employed
   □ Informal employment
   □ Formally employed

26. Religion
   □ Apostolic
   □ Pentecostal
   □ Catholic
   □ Orthodox
   □ Traditional African Religion

Other (Specify) ..............................................................................................................

27. Place of residence
   □ Rural
   □ Urban
   □ Farm
28. Is the person suffering from any other conditions?
   ☐ Yes
   ☐ No
   a) If Yes; What is the condition ..............................................................

Section B: Treatment related factors

29. Line of treatment
   ☐ First line (Stalanev, Zidovudine+Lamivudine+Nevirapine/Efavirenz,
                            Tenofovir+Lamivudine+Nevirapine/Efavirenz)
   ☐ Second line (Zidovudine+Lamivudine+Lopinavir/Ritonavir,
                            Tenofovir+Lamivudine+Lopinavir/Ritonavir, Abicavir+Didanosine+Lopinavir/Ritonavir)

30. Time on ART
   ☐ < 3 months
   ☐ 3 – 6 months
   ☐ > 6 months

31. Frequency of refill
   ☐ Twice per month
   ☐ Once per month
   ☐ Once in ≥ 2 months

32. Adherence counselling
   ☐ Yes
   ☐ No
   a) If Yes; check how often.........................................................

33. Missed picking up drugs on time
   ☐ Yes
   ☐ No
c) If Yes; check how many times in the last 12 months ..........................

Section C: Health Service related factors

34. Payment for ART services
   □ Yes
   □ No
   b) If Yes; Check how much  ......................................................................

35. Experienced stock outs in the past 12 months
   □ Yes
   □ No
   b) If Yes; check how many times .................................................................
ANNEX 5: PERMISSION TO PROCEED FROM PMD
ANNEX 6: APPROVAL LETTER FROM JOINT RESEARCH ETHICS COMMITTEE
ANNEX 7: APPROVAL LETTER FROM MEDICAL RESEARCH COUNCIL OF ZIMBABWE