

# Predictors of First Line Antiretroviral Therapy (ART) Failure among ART Patients in Gutu District, Masvingo Province, Zimbabwe, 2016

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## ABSTRACT

**Background:** First Line ART Failure is one of the challenging programmatic public health problems in HIV response. Surveillance of ART in Gutu district indicated that an increasing number of patients were moving to second line therapy. The aim of this study was to identify predictors of first line ART failure

**Methods:** A 1:1 case-control study was conducted where 300 ART patients were enrolled into the study who had been on ART for at least 6 months, failed first line ART and had been switched to second line ART. Controls were patients who have been on ART for at least 6 months, failed first line ART and were still on first line interviewer administered questionnaire was used to interview patients on ART at selected health facilities. Bivariate and multivariate analyses were used to establish the predictors for first line ART failure among ART patients.

**Findings:** A total 150 cases, 150 controls were recruited; females were majority with 58% and 53% in both arms. Multivariate analysis generated 3 risk factors-poor adherence(AOR=3.17,95%CI:1.42-7.09),baseline WHO stage 3 or 4(AOR=1.85,95%CI:1.03-3.30) and TB infection while on ART (AOR=2.68, 95%CI:1.51-4.76) , 2 protective factors-being a member of an HIV/AIDS support group(AOR=0.27,95%CI:0.15-0.48) and condom use(AOR=0.41,95%CI:0.23-0.71).

**Conclusions:** The findings of this study confirm that First line ART failure was related to poor adherence to ART, TB infection while on ART, baseline WHO stage 3 or 4 which were key factors for first ART failure in Gutu district.HIV response interventions should focus on adherence counseling and institute education and awareness programmes for early treatment seeking behavior.

**Key Words:** First line ART failure, risk factors, protective factors, independent factors

## INTRODUCTION

### Epidemiology of HIV at global level

The human immunodeficiency virus (HIV) pandemic is most severe in Sub-Saharan Africa where over 60% of all people living with HIV reside. Globally, 15% of women living with HIV are aged 15-24 years, of whom 80% live in Sub-

Saharan Africa and over 70% of all new HIV infections occur here. <sup>[1]</sup>

Therefore there is need to focus on high transmission areas and key populations, together with the implementation of evidence-based combination prevention strategies that have the ability to substantially reduce HIV transmissions and achieve epidemic control,

potentially transforming the pandemic to lower level endemic epidemics. [2] Effective ART first introduced in 1996, led to dramatic reduction in morbidity and mortality. [3]

In 2013, an estimation of about 35.0 million people was living with HIV worldwide. Countries mostly affected in southern Africa included South Africa (25%), Nigeria (13%), Zimbabwe (6%), Tanzania (6%) and six more all accounting for about 8 in every 10 of all people living with HIV. [4]

### Epidemiology of HIV nationally (in Zimbabwe)

According to the Zimbabwe Demographic and Health Survey (ZDHS) (2012) national estimates of HIV prevalence rates stood at 15%, estimating 12% infection rate for men and 18% for women respectively [5] A study by Sharma M (2015) found that expanding home and mobile testing and outreach to key populations with facilitated linkage can decrease the HIV burden and increase the proportion of men, young adults, and high-risk individuals who are linked to HIV prevention and treatment. [6]

### Antiretroviral Therapy (ART) Failure

ART failure according to WHO guidelines 2010, treatment failure has 3 definitions as follows:

**Virological failure**-it occurs when the viral load is persistently above 1000copies/ml<sup>3</sup> within at least 2 consecutive results spaced by three months.

**Immunological failure**-occurs when the CD4 count goes down to below baseline CD4 or when there is 50% drop from a given threshold (if it is known) when on

treatment or when CD4 count levels are persistently below 100cells/mm<sup>3</sup>.

**Clinical failure**- occurs when there is a new WHO stage 4 or reoccurring WHO stage 4 in an ART patient who has been on ART for at least 6 months.

### Problem Statement

Gutu District has been experiencing continuous rise in the number of patients being switched to a second line from first line ART regimen. The rise was almost exponential and still the number was increasing at the time of the study.

Gutu catered for 10 865 and 352(3.26%) of these patients were on second line ART. These 352 accumulated over the past 5 years. On average, 71 patients were switched to second line ART each year or 1 to 2 patients per every week.

Figure1 below shows an upward trend, almost exponential cumulatively over the past 5 years. The aim of the study was to identify predictors of first line ART failure leading to switching of first line ART patients to second line therapy.

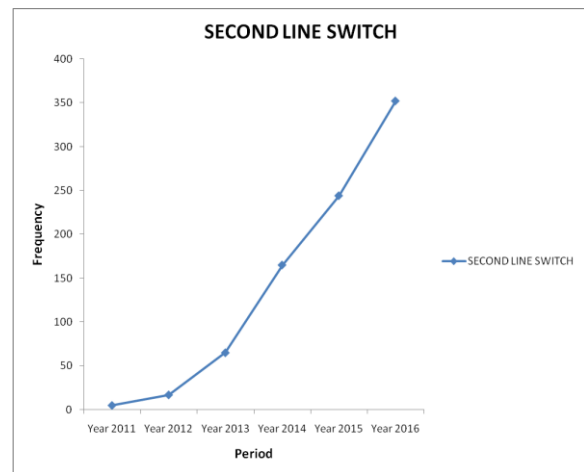


Figure 1: Second Line increment over the years 2011-2016

Table 1: Districts ART coverage in Masvingo province

District	1 <sup>st</sup> line ART patients	2 <sup>nd</sup> line patients	Proportions	Proportions of 2 <sup>nd</sup> line in %	Ranking of Proportions
Bikita	9152	60	60/9212=0.007	0.7%	7 <sup>th</sup>
Chiredzi	17765	361	361/18126=0.020	2.0%	2 <sup>nd</sup>
Chivi	10699	52	52/10751=0.005	0.5%	6 <sup>th</sup>
<b>Gutu</b>	<b>10 513</b>	<b>352</b>	<b>352/10865=0.032</b>	<b>3.2%</b>	<b>1<sup>st</sup> (double the provincial)</b>
Masvingo	20455	355	355/20810=0.017	1.7%	3 <sup>rd</sup>
Mwenezi	9449	48	48/9497=0.005	0.5%	5 <sup>th</sup>
Zaka	10772	144	144/10916=0.013	1.3%	4 <sup>th</sup>
<b>TOTAL</b>	<b>88830</b>	<b>1347</b>	<b>1347/90177=0.015</b>	<b>1.5%</b>	(Provincial totals)

Source: Provincial Health Information Office and Gutu District Health Executive (DHE).

## **Literature Review**

Studies reviewed provided an insight into the predictors of first line ART failure which included demographic factors, socio-economic factors, behavioural factors, clinical factors, healthcare provider factors and social factors. In this study the socio-ecological model was used. A study by Baral et al (2013) using the social ecological model in the context of HIV found that the model is useful in interpreting the complicated associations among social, structural, individual behaviours and practices, the physical surroundings (environment) and health. [7]

### **Demographic factors of ART failure**

Studies conducted in Zimbabwe according Matare et al (2015) in Zvishavane and Chimbetete et al (2014) at Newlands clinic all concurred that age was demographic risk factor of first line ART failure, those less than 18 years old were 1.7 times more likely to fail 1st line than those above 18 years. [8,9]

### **Behavioural Factors**

Non-adherence has been found to be a risk factor in a study by Getnet et al (2014) in public hospitals in Addis Ababa, Ethiopia; those who had poor adherence had a higher risk of 2.73 of failing ART than those with good adherence. [10]

Alcohol intake was found to be a risk factor for ART failure as evidenced by findings from Braithwaite et al (2010). [11] Unprotected sexual activities were found by Pingen et al (2012) to be a risk factor since it leads to re-infections and in some cases super-infections. [12]

Therefore correct and consistent condom use is critical according to Shewamene et al (2015) as a key effective preventive measure against HIV transmission among ART patients; this is an important concept that impedes HIV transmission and therefore improves the health of the patient. [13]

### **Clinical Factors**

A study by Getnet et al (2014) found that those in WHO stage 4 had the highest risk of ART failure than those in WHO

stages 2 and 3 with risks of 1.2 and 1.18 except for stage 1 which showed no association. [10]

### **Healthcare Provider factors**

Having incurred challenges in ART accessibility was found to be a risk factor for first line ART failure among ART patients. [14] According to Eholie et al (2012) accessibility challenges were found to be a risk of ART failure affecting ART including transport to health facility. [15]

One study by Grace et al (2010) documented that care provided in village clinics was less likely to achieve virological suppression compared to care provided at country level hospital. There are few studies examining these other factors and data are scanty to make a strong conclusion (gaps for further research). [16]

According to Gupta et al (2013) TB at baseline and incident TB during ART were strongly associated with even increased risk of mortality apart from ART failure. [17]

### **Justification**

Gutu district had the highest proportion of second line ART patients among all the seven districts in Masvingo Province. The trend for the increase in numbers over the years was almost exponential. It was actually above the provincial magnitude of second line ART patients. The provincial second line patients stood at 1.5% and Gutu was more than double the provincial at 3.20%. It was important to conduct this study. Comprehensive analysis of the factors associated with first line ART failure so as to unearth the specific factors that influence ART failure in Gutu district. Useful and helpful information and conclusions to practicing managers, planners, policy makers and other agencies concerned were drawn from the study. Continual failure leads to development of resistant strains that are more difficult to treat therefore a need to remain on first line for a patient to be safe. Moreover second line has more pill burden.

Quite a number of studies focused much on patient-inclined factors and not

giving the same attention to other factors that may have a bearing on ART failure. ART failure could be as a result of a wide combination of factors since patients exist in an ecosystem with healthcare system, family setup and community fabric some which may stigmatize HIV positive status. In addition to focus on patient related factors this study also focused on the

holistic environment of the patient for example social support, healthcare service as viewed by patients, cultural factors and socio-economic factors contribution to first line ART failure. A study by Kumar et al (2009) identified ecological factors as determinants of the uptake of HINI influenza vaccine in the USA. [18]

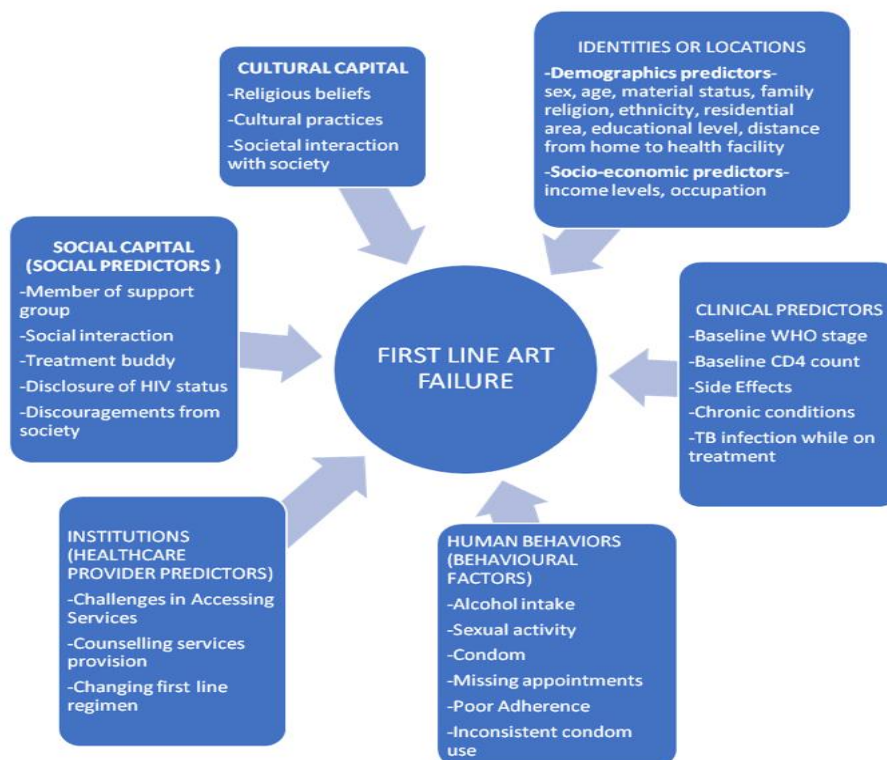


Figure 2: Theoretical framework -Modified Social Ecological Model

## OBJECTIVES

### Research question

- What are the predictors of first line ART failure among ART patients in Gutu district, Masvingo province, Zimbabwe, 2016? (with reference to the social ecological model constructs)

### Broad objective

- To assess the predictors of first line ART failure among ART patients in Gutu district, Masvingo province, Zimbabwe, 2016.

### Specific objectives

Objectives were based on the theoretical framework -Social capital, cultural capital, clinical predictors, human behaviours), Institutions (healthcare provider factors).

- To determine the demographic characteristics of the study participants in Gutu District, 2016.
- To determine the socio-economic factors that are associated with first line ART failure among ART patients in Gutu, 2016.
- To determine the behavioural factors that are associated first line ART failure in Gutu, 2016.
- To determine the clinical predictors that are associated with first line ART failure in Gutu, 2016.
- To determine healthcare provider factors that are associated with first line ART failure in Gutu, 2016.

- To determine the socio-cultural factors that are associated with first line ART failure among ART patients in Gutu District, 2016.

## **MATERIALS AND METHODS**

### **Study design**

A1: 1Unmatched Case-control study design was used in which the study population constituted patients receiving ART in Gutu district who were on Antiretroviral Therapy (ART) for at least 6 months during the study period.

A Case was defined as patient who has failed 1st line ART after taking the regimen for at least 6 months and had been switched to second line regimen because of ART failure.

A Control was defined as a patient who has been on first line ART for at least 6 months and has NOT failed 1st line treatment and the patient is still receiving 1st line ART during the study period.

### **Study Setting**

This study was conducted in Gutu District in Masvingo Province, Zimbabwe.

### **Data collection techniques**

A review of patients' files and interviewing of patients on first line ART (controls) and second line ART patients (cases) was done. Moreover an interviewer-guided questionnaire and a checklist were used to ensure all areas on the questionnaire were covered

### **Study population**

The study population were all the ART patients whether on first line ART or second line ART in Gutu District, Masvingo Province and this study population were selected from a sample frame of ART registers which capture and record all the ART patients in the district. ART failures occurred among the ART patients and therefore the study population appropriate for the study with an outcome of interest.

### **Study units**

These were individual cases and controls on antiretroviral therapy in Gutu district.

### **Sample size determination**

According to C. Chimbetete et al in 2014 on Factors associated with first line ART failure among patients at Newlands Clinic, Harare, Zimbabwe, they found out significantly that one of the predictors of First Line ART failure was marital status, participants who were married to those who were not (i.e. single, divorced or widowed), those NOT married were 2.04; (OR: 2.04; 95%CI: 1.38-3.04) times more likely to fail treatment than those married.

Using the StatCalc function of Epi info, exposure being defined as marital status and the outcome defined as treatment failure. Exposure in the control group was 40.5%. Using an odds ratio of 2.04, 95% confidence interval and 80% power, factoring in attrition of 10% for refusal rate the minimum required sample size was calculated to be 150 cases and 150 controls.

### **Sampling procedures**

Purposive sampling was conducted on selection of health facilities on the basis of high volume sites of first line and second line ART patients. Then proportion sampling was conducted to determine the number of participants to be taken per each health facility selected. Simple random sampling using the lottery method was conducted to select individuals who were eligible for inclusion into the study.

Simple random sampling was used for participants on first and second line ART participants where they were selected basing on proportions of the ART patients at each health facility that were in the study. High volume sites health facilities were eligible for the study and the proportion of ART patients to determine the study participants were selected from that particular health facility.

### **Inclusion and Exclusion criteria**

Exclusion procedures that were applied in the study were that any ART patient who had been on ART for less than 6 months was NOT eligible and was NOT included in the study.

## Selection and recruitment procedures

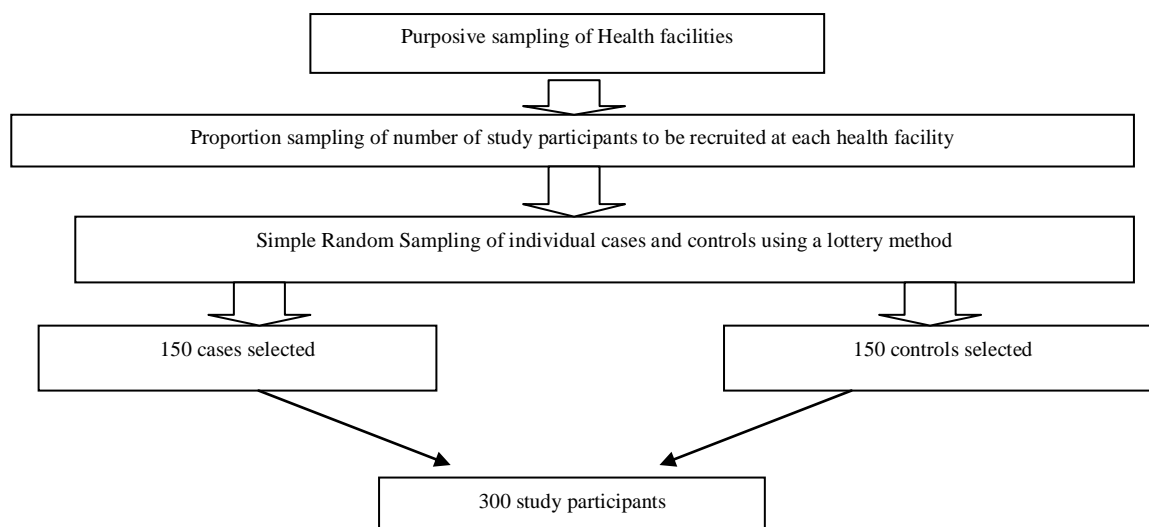


Figure 3: Illustrated Sampling Procedures that were conducted

### Study variables / Social ecological framework

#### Dependant variable

In this study the dependent variable was First Line ART Failure.

#### Independent variables

The study variables were those highlighted in the Socio-ecological model constructs.

#### Developing data collection tools

An interviewer administered questionnaire was developed based on the objectives of the study and the variables defined in the social ecological model.

#### Measures to control bias

As a measure to control bias purposive sampling of health facilities and proportion sampling random sampling was used to avoid selection bias.

#### Ethical Considerations

Ethical approval to conduct the study was obtained from Joint Research Ethics Committee for University of Zimbabwe, College of Health Sciences and the Parirenyatwa group of Hospitals (JREC Ref:173/16). A clearance to conduct the study was also obtained from Medical Research Council of Zimbabwe (MRCZ/B/1114). In the study setting permission was sought from the Provincial Medical Director and Gutu District Health Executive.

### Ethical issues in data collection

Written informed consent to participate and confidentiality, voluntarism, with the option of withdrawal from participation at anytime was assured.

## RESULTS

### 1. DESCRIPTIVE EPIDEMIOLOGY

#### *Demographic characteristics of the research participants*

Table 2 below shows demographics for a total of 300 participants comprising 150 cases and 150 controls with median ages of 40 years ( $Q_1=32$ :  $Q_3=47$ ) among the cases and 40 years ( $Q_1=32$ :  $Q_3=46$ ) and median family size was 4 for both cases ( $Q_1=3$ :  $Q_3=4$ ) and controls ( $Q_1=4$ :  $Q_3=6$ ). Other demographics included were marital status and educational level.

### 2. ANALYTIC EPIDEMIOLOGY

#### *(2A) Bivariate Analysis*

#### **Risk and Protective factors for First Line ART failure among the participants**

A bivariate analysis for various variables under each category was done so as to identify predictors of First Line ART failure among ART patients.

#### **Socio-economic and demographic predictors of First Line ART failure among the participants**

In this study marital status was found to be a protective factor of first line ART failure among ART patients, those married were 20% less likely to develop ART failure than the unmarried [OR=0.80 (95% CI : 0.47-1.37)].

Unemployment was a predictor of ART failure, those who were unemployed were 1.95 times more likely to fail ART as compared to those who were employed (95% CI: 1.22-3.12).

Gender was found to be a risk factor, females were 1.21 times more likely to fail ART as compared to males (95% CI: 0.77-1.91). Age was also found in this study to be a risk factor, those aged below 18 years were 2.30 times more likely to fail first line ART as compared to participants above 18 years, the result was not significant (95% CI: 0.78-6.78).

**Table 2: Socio-economic and demographic predictors**

Variable		Cases n=150(%)	Controls n=150(%)	(OR)	(CI)	P-value
Marital Status	Married	111(74)	117(78)	0.80	0.47-1.37	0.211
	Unmarried	39(26)	33(22)			
Occupation (Unemployment)	Yes	101(67)	77(51)	1.95	(1.22-3.12)	0.002
	No	49(33)	73(49)			
Sex	Female	87(58)	80(53)	1.21	0.77-1.91	0.210
	Male	67(42)	70(47)			
Age	<18years >18years	11(7)	5(3)	2.30	0.78-6.77	0.067
		139(93)	145(97)			

### Behavioural predictors of First Line ART failure among the study participants

Quite a number of behavioural factors were found to be significant risk factors in this study, condom use was found to be a protective factor, those who used condoms during sexual intercourse were 45% less likely to fail ART as compared to those who did not use condom as a measure of safety during sexual intercourse [OR=0.55, (95% CI: 0.33-0.92)].

However on the other hand inconsistent condom use was found to be a significant risk factor since those who were inconsistently using the condom were 3.11 times more likely to fail first line ART

as compared to those who consistently used a condom as a safety measure (95% CI: 1.55-6.24).

Poor adherence was found to be a significant risk of first line ART with a magnitude of 4.71 more likeliness to fail ART among those with poor adherence as compared to those who had good adherence ART (95% CI: 2.66-8.34).

Alcohol intake as a lifestyle behaviour was found to be one of the significant predictors of ART failure, alcohol consumers were 1.91 times more likely to fail ART than non-alcohol consumers (95% CI: 1.06-3.59).

**Table 3: Behavioural predictors of First Line ART failure among the study participants.**

Variable		Cases n=150(%)	Controls n=150(%)	OR	C.I	P-value
Alcohol intake	Yes	31(21)	18(12)	1.91	(1.06-3.59)	0.022
	No	119(79)	132(88)			
Inconsistent condom use	Yes	104(78)	66(55)	2.88	(1.55-6.24)	0.001
	No	30(22)	55(45)			
Poor adherence	Yes	63(42)	20(13)	4.71	(2.66-8.34)	0.000
	No	87(58)	130(87)			
Condom use	Yes	76(51)	85(57)	0.55	(0.33-0.92)	0.011
	No	58(49)	36(43)			

### Clinical predictors of First Line ART failure among the study participants.

The study found that those who developed side effects of ART were 2.32

times more likely to fail ART as compared to those who did not (95% CI: 1.46-3.68).

Baseline WHO staging was also found in this study to be a significant risk factor of ART failure, those who had

baseline WHO stage of 3 or 4 were 3.62 times more likely to fail ART than those in stage 1 or 2 (95% CI: 2.23-5.89).

TB infection history while on ART was found to be a significant risk factor for first line ART failure, those who had TB

while on therapy were 2.0 times more likely to fail ART as compared to those with no history of TB co-infection (95% CI: 1.24-3.22).

**Table 4: Clinical predictors of First Line ART failure among the study participants**

Variable		Cases n=150(%)	Controls n=150(%)	OR	C.I	P-value
Developed side effects of art medicines	Yes	94(63)	63(42)	2.32	(1.46-3.68)	0.000
	No	56(37)	87(58)			
Baseline WHO stage 3 or 4	Yes	111(74)	84(56)	3.6224	(2.23-5.89)	0.000
	No	39(26)	66(44)			
TB infection history while on ART	Yes	68(45)	44(29)	2.00	(1.24-3.22)	0.002
	No	82(55)	106(71)			

### Healthcare provider related predictors of ART failure among study participants

On healthcare provider inclined factors in this study those who had some challenges in the past of accessing ART

were 5 times more likely to fail ART as compared to those who had not experienced challenges in accessing ART medicines (95% CI: 2.01-12.62).

**Table 5: Healthcare provider related predictors of ART failure among study participants**

Variable		Cases n=150(%)	Controls n=150(%)	OR	C.I	P-value
Ever incurred challenges in accessing ART	Yes	26(17)	6(4)	5.03	(2.01-12.62)	0.000
	No	124(83)	144(96)			

### Social-cultural predictors of First Line ART failure among study participants

On the social factors those who had religious beliefs that discourage ART uptake in their society were 1.62 times more likely to fail ART as compared to those in a society without such dynamics (95% CI:

0.61-4.29). Those who were members of a health support group were 65% less likely to fail first line ART as compared to those who were not in any health support group [OR=0.35(95% CI: 0.20-0.62)].

**Table 6: Social predictors of First Line ART failure among study participants**

Variable		Cases	Controls	OR	C.I	P-value
Social and religious beliefs that discourage ART uptake	Yes	11(7)	7(5)	1.62	(0.61-4.29)	0.173
	No	139(93)	143(95)			
Being a member of a support group	Yes	101(67)	128(85)	0.35	(0.20-0.62)	0.000
	No	49(33)	22(15)			

### (2B) MULTIVARIATE ANALYSIS (LOGISTIC REGRESSION ANALYSIS)

After the bivariate analysis of risk factors for first line ART failure then regression analysis to identify and estimation of association measures for independent risk factors for first line ART failure among the ART patients in Gutu District. This was done to control for confounding variables so that those that are statistically clear independent risk factors remain. This was accomplished through a forward step wise logistic regression

analysis. Initially those variables identified in the bivariate analysis with p-values less than 0.25 (p<0.25) were identified and selected for use in the model. All the variables in each category from socio-economic and demographic factors, behavioural factors, clinical factors, healthcare provider inclined factors and social factors were included in the logistic regression model.

Variables were entered into the model adding one by one while dropping or removing all those that had p-values of



greater than 0.05( $p > 0.05$ ), the model would indicate those that were supposed to be dropped out and finally all the variables were entered and those that were significant independent predictors of first line ART failure were identified.

The sequence of logistic regression was pyramidal in manner where in bivariate analysis there was a wide spectrum of statistically significant variable and as the variables were entered into the model and

some dropped the number of variable become lesser and lesser until a few were left which were independent risk factors of first line ART failure among ART patients in Gutu District.

In logistic regression adjusted odds ratios, confidence intervals and p-values were generated and the table below shows the selected independent risk factors of first line ART failure.

**Table 7: Predictors/Independent Factors associated with First Line ART failure among ART patients in Gutu District**

Independent Risk Factors	Crude OR	Adjusted Odds Ratio(AOR)	Confidence Interval(CI)	P-value
Poor Adherence	4.71	3.17	1.42-7.09	0.005
Baseline WHO stage 3 or 4	3.62	1.85	1.03-3.30	0.004
TB infection history whilst on ART	2.00	2.68	1.51-4.76	0.001
Being a Member of an HIV/AIDS support group	0.35	0.27	0.15-0.48	0.000
Condom Use	0.55	0.41	0.23-0.71	0.002

As shown on the table 7 above, there were 3 independent risk factors that were associated with first line ART failure in Gutu District and 2 protective factors, poor adherence to antiretroviral therapy, baseline WHO stage 3 or 4 and TB infection history while on ART.

The 2 Significant protective factors identified were being a member of an HIV/AIDS support group and condom use.

## DISCUSSION

### Risk factors and Protective Factors for First Line ART failure

In this study, predictors of first line antiretroviral therapy failure were identified and were categorized according to the research objectives.

Poor adherence was found to be a significant risk factor, poor adherence is consistent with findings from Matare et al (2015), they found that those who has poor adherence were 5.14 times more likely to fail ART as compared to those who adhered after adjusting for possible confounders. [8]

Another study by Chesney et al (2000) found that electronic monitoring systems such as Medication Event Monitoring Systems (MEMS) are crucial where they are inserted into a medication bottle containing a computerized chip which

records the date and time of opening and closing of the bottle. [19]

Gender was found to be a risk factor; females were found to be at a higher risk of failing first line ART of 1.21 as compared to men. This is contrary to what Matare et al (2015) and Chimbetete et al (2014) have found where males had a higher risk of failing first line ART than females because of poor health seeking behavior of males. [8,9]

However to support the findings of this study some studies have cited that females have less tolerance to ART and its side-effects than males and are therefore more likely to fail ART than males. A study by Otofokun et al (2003) found that sex differences occur in several aspects of Human Immunodeficiency Virus infection and its management, including differences in the tolerability of some antiretroviral medicines. [20]

Another study by Squires et al (2011) found that incidence of adverse events as a risk factor to ART failure is greater among females as compared to male. [21]

Marital status in this study was found to be a protective factor. This was consistent with Getnet et al (2014) who found similar results. [10] Married people have reinforced social and moral support

structure from partners that improves uptake of ART.

Unemployment as one of the socio-economic factor was found to be a risk factor for first line ART failure in Gutu district. Unemployment can affect the finances needed to travel to health facilities for ART services, finance to purchase basic needs all which are compromised when there is limited income to cater for them. This finding was consistent with findings from Matare et al (2015). [8]

Alcohol consumption was found to be a risk factor; alcohol consumers had a greater risk of ART failure than non-consumers. Alcohol consumption according to Braithwaite et al (2010) reduce adherence to antiretroviral therapy and thereby compromising the effectiveness of ART in the body of the patient. [11]

On sexuality, sexual activity if unprotected through example condom use exposes both partners to super-infection or re-infections which poses another risk of acquiring new strains of viruses that may be resistant to the initial strains on which the patient was being treated for and may result in rapid disease progression. [12]

In this study 64% (68/104) of inconsistent condom users were females and 36% (39/107) were males. Females have lesser negotiating skills for condom use and therefore are not well empowered to advocate for condom use.

Missing clinical appointments was found to be a risk factor for first line ART failure in Gutu district. Some studies have explained missing appointments as an issue of concern. According Yalew et al (2012) a study conducted in Ethiopia proved that a good perception of good communication (patient-physician) by a patient is associated with low likelihood of patients missing clinical appointments whereas in another study done in China assessing missed visits to health facilities, it was found that women who were not accompanied to a health facility were more likely to miss medical appointments. It was also found in several studies that unaccompanied adult males

were more likely to not attend medical appointments in resource-limited settings. [22]

WHO stage 3 or 4 in this study was also found to be a significant risk factor, the finding was consistent with findings from Kwobah et al in Kenya (2012). [14] This shows delay by majority of patients to commencement on ART it is therefore important for health workers to emphasize early HIV testing and early initiation in ART for positive clients.

Challenges in accessing ART were found to be a significant risk factor in this study. Chimbete et al (2014) found similar findings. [9] Challenges in the study setting included accessibility of services in the past when ART services were centralized, ART patients had to travel long distances to acquire ART medicines in the district at a centralized institution.

Having TB infection while on ART was found to be a significant risk factor associated with first line ART failure in study. According to Lawn et al, 2013, it was found that TB is one of the causes of death among ART patients in sub-Saharan Africa. [23]

All people who test HIV positive should all be screened for TB infection and vice-versa to reduce effect of co-morbidity leading to first line ART failure.

In this study being a member of a support group was found to be an independent significant protective factor for first line ART failure among ART patients in Gutu district. Support groups in studies conducted in Mozambique it was found that the rolling out of health clubs (known as adherence clubs) further caters for impediments to ART access and increases adherence through allowing easier and faster accessibility to treatment. [24]

Beliefs that discourage ART uptake were found to be a risk factor although statistically not significant in this study, a study by Zou et al (2009) in Tanzania have found that although religious beliefs were associated (significantly) with shame-related HIV stigma, the impact of them on people's

willingness to get medical treatment for HIV was minimal. [25]

## CONCLUSION

In this study in Gutu District after adjusting for confounding and effect modification the 3 independent risk factors generated and significantly associated with ART failure in Gutu district should be addressed. These need to be taken into cognizance in public health programming in order to alleviate first line ART failure in Gutu district. Good adherence to prevent TB infection while on ART, HIV testing services and early ART initiation to be intensified.

Protective factors generated are also vital in promoting positive outcomes of antiretroviral therapy, condom promotion and joining support groups to be encouraged among ART patients.

First line ART failure is a problem of public health concern because second line ART is more expensive and even more expensive for third line ART. Failure of ART may lead to development of resistant strains in the long run.

## RECOMMENDATIONS

1. Healthcare providers (clinicians and counselors) to ensure that adherence counseling is provided universally to all ART patients irrespective of adherence status. District Health Executive (DHE) to ensure all health works comply and that this is documented as evidence of work done to reach ART clients.
2. Health workers to ensure that all HIV positive clients are tested for potential TB infection and vice versa so as to commence care early for TB-HIV co-infection.
3. Healthcare providers to embark on counseling for alcohol use and any other drug abuse among ART patients so as to prevent treatment failure since alcohol compromises the effectiveness of ART.
4. Health care providers to offer a comprehensive package of ongoing health education concerning condom use and its consistent use among ART patients so as to prevent re-infections and potential super-infections. Village health workers to be also

engaged in this important role to create demand.

5. HIV Testing Services(HTS) to be intensified to the communities in Gutu so that people get to know their status early and then get initiated on ART if tested positive for HIV infection while their baseline CD4 count and baseline WHO stages are still at safe levels(Healthcare providers to attend).
6. Healthcare providers to initiate and roll out support groups formation in the district to all willing ART patients since they help in strengthening the important community social support systems especially for ART patients which is protective in ART failure in the district.

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