

# Antiretroviral Therapy Discontinuation among Adults Receiving HIV Care in Kadoma City in 2015-2019

Godwell Nhidza<sup>1</sup>, Daniel Chirundu<sup>2</sup>, Tsitsi Patience Juru<sup>1</sup>, Emmanuel Govha<sup>1</sup>, Notion Gombe<sup>1,3</sup>, Addmore Chadambuka<sup>1</sup>, Mufuta Tshimanga<sup>1</sup>

<sup>1</sup>Department of Primary Health Care Sciences, Family Medicine/Global and Public Health Unit, University of Zimbabwe, Harare, Zimbabwe

<sup>2</sup>Kadoma City Health Department, Kadoma, Zimbabwe

<sup>3</sup>African Field Epidemiology Network, Harare, Zimbabwe

Email: achadambuka1@yahoo.co.uk

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## Abstract

**Background:** Discontinuation remains a legitimate threat to the long-term success of antiretroviral therapy (ART) scale-up in Zimbabwe. Furthermore, the characteristics associated with ART discontinuation and trends are poorly understood in developing countries like Zimbabwe. We analysed the HIV/AIDS data to describe the characteristics associated with ART discontinuation and the trends from 2015 to 2019. **Methods:** We conducted an analytical cross-sectional study using secondary data from Electronic Patient Management System (ePMS) in Kadoma City. We interviewed eighteen health care workers to find the reasons for ART discontinuation. Data were analysed using Microsoft Office Excel 2016 and Epi info 7 version 7.2.2.6. Microsoft office excel was used to generate linear graphs to demonstrate the trends in ART discontinuation in Kadoma City in 2015-2019. Epi info 7 was used to generate frequencies, means, prevalence odds ratios p-values, and 95% confidence intervals (CI) and significance testing. Backward stepwise logistic regression analysis was done to determine the independent factors associated with discontinuation. **Results:** A total number of 2833 patients were enrolled on ART from 2015 to 2019. One hundred and seventy-three 173/2833 (6.1%) discontinued ART, 415/2833 (14.7%) transferred out, 69/2833 (2.4%) died and 2176/2833 (76.8%) were retained on ART. Out of those who discontinued ART, sixty-five percent (112/173) were females. Approximately two-thirds had immunological failure 110/173 (64%). The trend in ART discontinuation decreased over the years but was not statistically significant ( $R^2 = 0.57$ ,  $p > 0.05$ ). ART discontinuation was independently associated with being  $<40$  years of age (adjusted pOR = 2.3, [95% CI: 1.6 - 3.2],  $p = 0.001$ ), having never

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attended school (adjusted pOR = 3.9, [95% CI: 2.5 - 6.0],  $p = 0.003$ ) and having immunological failure (adjusted pOR = 6.2, [95% CI: 4.5 - 8.6],  $p = 0.0001$ ). The reasons mentioned by the health care workers which cause people living with HIV (PLHIV) to discontinue ART were health state not improving 13/18 (72.2%), participating in artisanal mining activities 11/18 (61.1%), change in marital status 9/18 (50.0%), medical side effects of ART 8/18 (44.4%), living far from health facilities 5/18 (27.8%) and relocating to neighbouring countries 3/18 (16.7%). **Conclusion:** We concluded that the characteristics associated with ART discontinuation were having never attended school, being less than forty years of age and having immunological failure. The reasons why patients discontinue ART were health state not improving, participating in artisanal mining activities, change in marital status, medical side effects of ART, living far from health facilities, and relocating to neighbouring countries. We recommended continuous provision of health education, enhanced adherence counselling sessions to those with unsuppressed viral loads and investigating the cause of virologic failure.

## Keywords

ART Discontinuation, Secondary Data Analysis, HIV, Zimbabwe

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## 1. Introduction

Globally, 38 million people were living with human immunodeficiency virus (HIV), 1.7 million new HIV infections, and 690,000 HIV/AIDS-related deaths in 2019 [1]. Among these, 61% were residing in Eastern and Southern Africa [2]. Zimbabwe is a low-income country in Southern Africa with a population of approximately 13 million people as of 2012 and is one of the worst affected by the HIV epidemic [3]. By the end of 2019, Zimbabwe had 1.3 million people living with HIV. Eighty-six percent of them knew their status while 97% of those who knew their status were on antiretroviral therapy (ART) [4].

If the quality of life and survival of people living with HIV (PLHIV) are to be improved, further efforts need to be made to ensure ART retention and its positive outcomes [5]. ART discontinuation is a loss to follow-up, defaulting, and/or stopping medication while remaining in HIV care [6]. Discontinuation from ART (hereon referred to as discontinuation) is a major contributor to attrition, and further to poor quality of life and death [7].

PLHIV on ART who are not retained in care are at increased risk of developing HIV drug resistance [8]. HIV drug resistance (HIVDR) is the ability of HIV to mutate and reproduce in the presence of antiretroviral (ARV) drugs [9]. The consequences of drug resistance include treatment failure, the transmission of drug-resistant HIV, as well as increased direct and indirect costs, for patients and health systems, due to more expensive, complex, and toxic second- and third-line ARV regimens [9].

The prevalence of ART discontinuation in 2009 and 2012 was between 9% - 34% in Asia [10] and between 13.7% - 57.4% in Africa [2]. Several studies done in low resource settings have revealed demographics characteristics, clinical characteristics and institutional characteristics as factors associated with ART discontinuation. A retrospective cohort study that was done to analyse the data from 2012-2015 in Zimbabwe in 2020 on retention and factors associated with attrition, did not assess important clinical characteristics which are viral load suppression, immunological failure and TB/HIV co-infection [11].

In Zimbabwe, since the inception of HIV prevention programs in the late 1990s, all patient-related data were collected using manual, paper-based systems. By 2008 the system in Zimbabwe was not functioning properly due to the increase in the volume of patients requiring treatment, which by 2014 had increased to over 740,000 [12]. This increase affected the accurate monitoring and reporting of patients accessing HIV services, as the paper-based patient information systems could not cope, and also translated into a huge workload, straining the already over-burdened health worker [13].

To address this gap, the Ministry of Health and Child Care (MoHCC), in consultation with its partners, resolved to establish an electronic system to collect and manage HIV and TB data at the patient level, with the ultimate aim of phasing out paper registers throughout the Country [12] [13]. This led to the decision to develop an Electronic Patient Management System (ePMS). This system captures common patient registrations, demographic details, past medical history, patient follow-up visits, laboratory investigations, and prescription and dispensing of the drug [14]. The ePMS was first piloted in 2012 and by 2014 about 246 health facilities were using it in Zimbabwe [12]. In Kadoma City, the ePMS was started in March 2015.

According to the ePMS data of Kadoma City, 417 clients were initiated on ART in 2018. Out of the 417, 46 (11%) were lost to follow-up (LTFU) and 71 (17.1%) defaulted at 12 months. The retention for Kadoma city in 2019 was 71.9%. This was low according to the WHO HIV drug resistance (HIVDR) early warning indicators of 2016, which states that at least 85% should be retained in care 12 months after antiretroviral therapy initiation. The characteristics associated with ART discontinuation and the trends are poorly understood in developing countries, particularly in Zimbabwe. We analysed the HIV/AIDS data to describe the characteristics associated with ART discontinuation and its trends from 2015 to 2019.

## 2. Methods

### 2.1. Study Design

We conducted an analytical cross-sectional study using a secondary data set.

### 2.2. Data Source

Data were obtained from ePMS in Kadoma City and interviews with health care

workers in the health facilities. Data from health care workers were collected using an interview guide.

### **2.3. Study Sites**

The study sites were five Kadoma city health facilities including Rimuka maternity clinic and Rimuka Integrated HIV and TB Care clinic located in Rimuka high-density suburb, Waverly clinic located in Waverly high-density suburb, Ingezi clinic located in Ingezi high-density suburb and Chemukute clinic located six kilometres from the Kadoma central business district in the mining location of Rio-Tinto. All the health facilities had a total catchment population of 93,716.

### **2.4. Study Population and Sampling**

The study populations were records/entries of HIV patients enrolled on ART entered in the ePMS in all the Kadoma City Health facilities for the period March 2015 to December 2019. We conveniently recruited the eighteen health care workers as key informants.

### **2.5. Study Variables and Treatment Outcome**

The data were extracted from ePMS. The data extracted included demographics (age, sex, marital status) and clinical variables (viral load at 6 months, baseline CD4 counts, HIV/Tb co-infection). Programmatic data collected included facility of care, date of HIV testing, date of enrolment, and date of ART initiation. Date of last clinic visit, date of next scheduled clinic visits, and date of transfer-out/death/stopping ART was collected and used to determine the patient status (*i.e.*, active on treatment, LTFU, dead, transferred out, or stopped ART). The patient status was determined on the date of data abstraction, regardless of previous treatment interruptions.

### **2.6. Study Variables and Measurements**

The dependent variable was discontinuation and was dichotomized as 1) alive and on ART (No), and 2) discontinued (Yes). Discontinuation referred to LTFU, defaulting and/or stopping medication while remaining in care. LTFU refers to patients who had been on ART treatment and had missed at least three clinical appointments but had not yet been classified as “dead” or “transferred out” (transferred). Stopping medication referred to patients who had stopped treatment due to any reason while they have remained in care. Transferred is an official transferring of a patient to another ART clinic within or outside a catchment area.

### **2.7. Permission**

Permission to carry out the study was sought and obtained from the Director of Health and Environmental Services (DHES) of the Kadoma City Council and Health Studies Office (HSO).

## 2.8. Ethical Considerations

Ethical principles in research privacy and confidentiality were applied. Benefits for Kadoma City health facilities were maximized by continuously giving feedback to the health facilities during and after the study.

## 2.9. Data Analysis

Data were analysed using Microsoft Office Excel 2016 and Epi info 7 version 7.2.2.6. Microsoft office excel was used to generate linear graphs to demonstrate the trends in ART discontinuation in Kadoma City in 2015-2019. Epi info 7 was used to generate frequencies, means, prevalence odds ratios, p-values, and 95% confidence intervals (CI) and significance testing. Backward stepwise logistic regression analysis was done to determine the independent factors associated with discontinuation. All variables that were associated with ART discontinuation with a p-value  $\leq 0.25$  were included in the logistic regression model. Variables were introduced, and then eliminated one by one starting with the one with the highest p-value until significant factors were obtained. The variables with a p-value less than 0.05 were considered significant.

## 3. Results

### 3.1. Data Analysis

We analysed data from 2833 records from ePMS from the health facilities in Kadoma City. The reviewed records had most variables filled in 2748/2833 (97%) and the remaining records had missing viral load results.

The total number of patients who were initiated on ART in 2015 to 2019, whose records were extracted from ePMS were 2833. The number of patients who were transferred to other health facilities was 415/2833 (14.6%), those who died 69/2833 (2.4%), and those who discontinued ART 173/2833 (6.1%).

### 3.2. Demographic and Clinical Characteristics of Patients Who Discontinued ART

Focusing on the patients who discontinued the majority were females 112/173 (65%). Those who were separated constituted the most at 75/173 (43%). Approximately two-thirds had immunological failure 110/173 (64%). Patients who were co-infected with Tb/HIV were 98 (57%). Three quarters attained primary level 129/173 (75%) (**Table 1**).

### 3.3. Trends in ART Discontinuation and Death in Kadoma City 2015-2019

The trend in percentages of people on ART dying decreased significantly between 2015 and 2019 from 5.2% to 0.8% ( $R^2 = 0.90$ ,  $p < 0.05$ ). For every increase in one year, the proportion of patients on ART who died decreased statistically by 1.11%. ART discontinuation showed a downward trend but the decrease was not statistically significant ( $R^2 = 0.57$ ,  $p > 0.05$ ). For every increase in one year

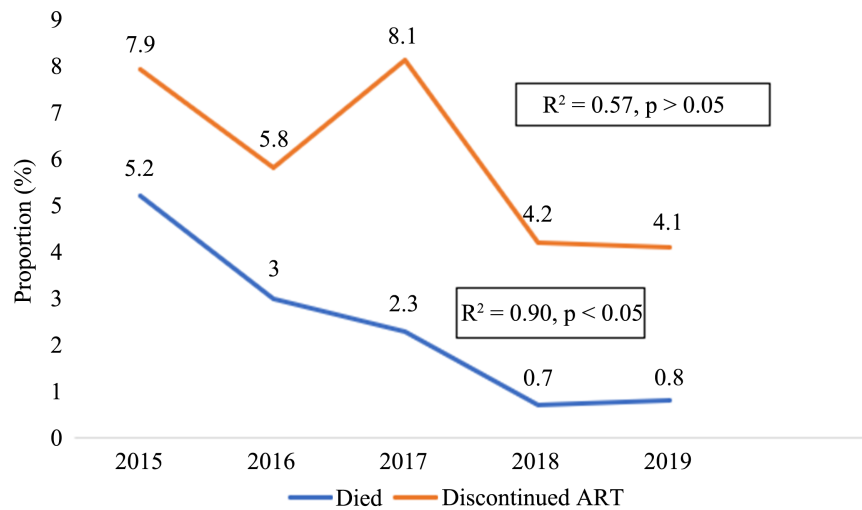
**Table 1.** Demographic and clinical characteristics who discontinued ART in Kadoma City from 2015-2019.

Variable	n (%), n = 173	
Age	15 - 25	51 (30)
	25 - 50	77 (45)
	>50	25 (15)
	Median (range)	36 (Q1 = 14; Q2 = 49)
Sex	Male	61 (35)
	Female	112 (65)
Marital status	Single	15 (8)
	Widowed	30 (17)
	Married	53 (31)
	Separated	75 (43)
Education level	No education	30 (17)
	Primary	129 (75)
	Secondary and above	14 (8)
Employment status	Formally employed	20 (12)
	Not employed	62 (38)
	Self-employed	14 (5)
+Baseline CD4 counts (cells/mm <sup>3</sup> )	<200	110 (64)
	>200	63 (36)
History of TB/HIV co-infection	Yes	98 (57)
	No	75 (43)
HIV viral load at 6 months	<1000	63 (36)
	>1000	110 (64)

the proportion of patients on ART who discontinued decreased by 0.92% (Figure 1).

### 3.4. Characteristics Associated with ART Discontinuation in Kadoma City 2015-2019

On multivariate analysis, discontinuation was independently associated with being <40 years of age (adjusted pOR = 2.4, [95% CI: 1.6 - 3.2], p = 0.001), having never attended school (adjusted pOR = 4.0, [95% CI: 2.5 - 6.0], p = 0.003) and immunological failure (adjusted pOR = 6.2, [95% CI: 4.2 - 8.6], p = 0.0001). (Table 2).



**Figure 1.** Trends in the proportions of death and ART discontinuation in HIV-infected people enrolled on ART care in Kadoma City, Zimbabwe, 2015-2019.

**Table 2.** Characteristics associated with ART discontinuation in HIV-infected people enrolled on ART care in Kadoma city from 2015 to 2019.

Variable	ART Discontinuation		Crude prevalence Odds Ratio	Adjusted prevalence Odds Ratio	p-value
	Yes n = 173	No n = 2176			
Age ≤ 40	Yes	118	2.3 (1.6 - 3.2)	2.4 (1.6 - 3.2)	<0.05
	No	55			
Being female	Yes	61	1.0 (0.7 - 1.4)	1.1 (0.9 - 1.5)	>0.05
	No	112			
Being married	Yes	53	0.5 (0.4 - 0.7)	0.6 (0.3 - 0.7)	>0.05
	No	120			
Never went to school	Yes	30	3.9 (2.5 - 6.0)	4.0 (2.5 - 6.0)	<0.05
	No	143			
CD4 < 200	Yes	110	5.9 (4.5 - 7.5)	6.2 (4.2 - 8.6)	<0.05
	No	63			
Virally suppressed (<1000)	Yes	63	0.1 (0.1 - 0.2)	0.2 (0.1 - 0.3)	>0.05
	No	110			
TB HIV coinfection	Yes	98	5.2 (3.9 - 7.2)	4.9 (3.2 - 7.8)	>0.05
	No	75			

### 3.5. Reasons for ART Discontinuation from Health Care Workers

We summarised the reasons mentioned by health care workers as to why PLHIV discontinued ART. The sister in charge at one of the health facilities said, “*You hear a patient when he/she comes to collect medicines saying I think these drugs*

*are not compatible with me, if I don't see any changes this time I will stop taking them*".

One of the nurses also said "*Some PLHIV especially young men say we go to mine gold very far away from home and sometimes we don't get time to come for ART refill, so we end up stopping taking the medicines*".

The reasons cited by the health care workers interviewed at the health facility on why patients discontinue ART were health state not improving 13/18 (72.2%), participating in artisanal mining activities 11/18 (61.1%), change in marital status 9/18 (50.0%), medical side effects of ART and toxicity 8/18 (44.4%), living far from health facilities 5/18 (27.6%) and relocating to neighbouring countries 3/18 (16.7%).

#### 4. Discussion

We conducted an analytical cross-sectional study on a secondary data set analysis on ART discontinuation in Kadoma, one of the cities in Mashonaland West in Zimbabwe. This study sought to determine the characteristics associated with ART discontinuation and the trends. In this study, we found that the characteristics which were independently associated with ART discontinuation were being less than forty years, having never attended school and immunological failure. The trend of proportions of PLHIV on ART dying decreased significantly between 2015 and 2019. The reasons cited by the health care workers interviewed at health facilities on why PLHIV discontinued ART were health state not improving, participating in artisanal mining activities, change in marital status, medical side effects of ART, living far from health facilities, and relocating to neighboring countries.

In the study, we found that the odds of discontinuing ART were more among females than among men although the association was not statistically significant in this study. This finding can be explained by the fact that most females have lower literacy status than males, which is a challenge that prevents them from optimizing the benefit of HIV care. People who have lower literacy do not fully comprehend the benefits of taking ART for lifetime. Having most women discontinuing ART has a negative implication on attaining the targets of eliminating mother-to-child transmission of HIV. A study from Ethiopia by Nash *et al.* (2015) reported that one of the reasons why females discontinue ART is that females consult traditional healers more than men, who tell them to stop taking medicines to rely on herbs [15].

Those who were younger than forty were two times more likely to discontinue ART than those more than forty years, these findings were similar to those by Makurumidze *et al.* (2015) which was done in Zimbabwe [11]. Kadoma is characterized by artisanal mining activities, and about seventy-five percent of those who participate in these activities are young people below the age of 40. We speculate that since they are highly nomadic discontinuing ART is possible. This finding can also be explained by rigid scheduling not taking into account



school-going age group at the local health facilities and unavailability of peer caregivers.

We also found that those who had never attended school were four times more likely to discontinue ART. The causal relationship is not clear, but it is expected that educated people have a better understanding of the disease process which could affect their attitude against ART discontinuation [16]. More so, educated people are more likely to adhere to their medication because they understand the benefits of taking their medication consistently.

Having immunological failure was six times more likely to be associated with discontinuing ART. Patients with immunological failure were prone to discontinuation because of morbidity. This is biologically plausible because once the CD4 counts are below 200 copies/mL, the body becomes prone to various opportunistic infections. These findings were similar to those by Duncan *et al.* (2017) from Tanzania who reported that HIV-infected patients with immunological failure were susceptible to multiple opportunistic infections and progress to the advanced stage of HIV/AIDS rapidly leading to quick deterioration of their health status thereby discontinuing ART [17].

The trend in the proportions of PLHIV on ART who were dying, significantly decreased between 2015 and 2019. This may be attributed to the “treat all” strategy which was introduced by the WHO and adopted by Zimbabwe in 2017, where all patients who tested positive on HIV were initiated on ART despite the CD4 count. This significantly decreased the number of patients who progressed to full-blown HIV/AIDS and has increased the life expectancy of people living with HIV. This also meant that patients were now being initiated on ART with higher CD4 counts this helped to maintain the immune competence. In addition to the treat all strategy, the period between 2015 and 2018 was characterized by decentralization of HIV care services, hence PLHIV were now receiving medicines at local clinics, so this improved accessibility and finally adherence.

Most of the health workers who were interviewed as key informants, reported that when PLHIV who were taking medicines realized that their health state is not improving discontinued ART. Considering the pill burden and the side effects of the medicines some patients may fail to realize the reason why they should continue taking the medicines if their health state is not improving. This finding was similar to that from Tanzania, which reported that health status not improving can also be among significant factors associated with stopping medicines [17]. Another reason cited was change in marital status, so usually, when some PLHIV on ART who were single get married they do not disclose their HIV status to their new partners hence discontinue ART to pretend as if they were not taking ART.

Some discontinued ART because they live far from health facilities, so sometimes they do not have money for bus fare to come to collect their medicines. We speculate that decentralization of HIV care services helped in the reduction of ART discontinuation during the period under study. This finding is consistent with that by Balogun *et al.* (2019) from Nigeria who reported that staying

far from health facilities and having no money for transport was associated with ART discontinuation [18]. Another reason cited was relocation to neighbouring countries, due to economic hardship in our country some PLHIV migrated to neighbouring countries like South Africa, Botswana and Namibia in search of “greener pastures”. So they finally discontinue ART because they do not come home as usual for ART refill. Others discontinued ART because they failed to tolerate the medical side effects of ART medicines. This calls for counselling and provision of the health education on ART. A study from Nigeria reported similar finding, where the risk of discontinuation of treatment was higher in patients-initiated on treatment regimen with Tenofovir disoproxil fumarate (TDF) containing regimen compared to Zidovudine (AZT) [19].

## 5. Limitation

The major limitation was the inability to get the patient’s perspectives on the reasons for ART discontinuation since it was secondary data analysis.

## 6. Conclusions and Recommendations

We, therefore, concluded that the characteristics that were associated with ART discontinuation were having never attended schools, being less than forty years and having immunological failure. We further conclude that reasons why patients discontinue ART were health state not improving, participating in artisanal mining activities, change in marital status, medical side effects of ART and toxicity, living far from health facilities, and relocating to neighboring countries.

Based on our findings we recommended the continuous provision of health education to patients on the importance and benefits of taking ART consistently and properly transferring from one facility to another. We also recommended continuously enhanced adherence counselling sessions for those with unsuppressed viral loads.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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## Abbreviations

ePMS: Electronic Patient Management System

HIV: Human Immunodeficiency Virus:

MOHCC: Ministry of Health and Child Care;

UNAIDS: The Joint United Nations Programme;

WHO: World Health Organisation

ART: Antiretroviral Treatment

AIDS: Acquired Immunodeficiency Syndrome

PLHIV: People Living with HIV

Adjusted pOR: Adjusted prevalence Odds Ratio