

Factors associated with discontinuation of combination antiretroviral therapy (ART) among HIV-positive adults receiving care at the Namacurra district capital health facility in Zambézia Province, Mozambique

Evaluation Final Report

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Executive summary

Background:

Human immunodeficiency virus (HIV) remains a major public health problem. While combination antiretroviral therapy (ART) has led to a significant reduction in HIV-associated morbidity and mortality, challenges of adherence and retention in care remain. Numerous studies have been published detailing the most common reasons for ART discontinuation among ART-treated adults residing in low- and middle-income countries (LMICs) globally, but few have been published about Mozambique, a country with the third highest HIV/AIDS burden globally. In addition, it is not known if the typical risk factors for ART discontinuation are the same in rural Mozambique, where people may face different challenges. As a result, we aimed to conduct an evaluation in rural Mozambique (the Namacurra district capital [“sede”] health facility in Zambézia Province) with the objective being to estimate the proportion of patients discontinuing ART (defined as failing to pick up ART for ≥ 60 days) and identifying the main factors associated with ART discontinuation in this setting.

Methods:

A cross-sectional study was performed utilizing data extracted from the electronic patient database (OpenMRS) from HIV-positive adults (age ≥ 15 years) enrolled in care between January 1, 2015 and December 31, 2016, with a follow-up period through May 8, 2018. Sample size was calculated using the formula for proportions (3% sample error, 50% discontinuation rate and 95% confidence level), with proportional sampling stratified by sex to avoid disproportionate inclusion of men and women. Associations with sociodemographic and clinical variables were assessed using chi-square and Fisher’s exact tests, and logistic regression modeling adjusted for significant variables. Analysis was supported by the statistical software package SPSS Version 25.

Results:

From the 2,641 adults in the cohort, 766 were included in the analysis (583 [76%] female and 183 [24%] male). Median age was 28 years (IQR: 22-35 years); 77% reported either no formal or primary-level education; and 90% reported being unemployed. The mean duration on ART was 19 months (standard deviation [SD] 12 months). The median for the most recent CD4 cell count was 394 cells/mm³ (IQR: 223–624 cells/mm³), and 73% had WHO clinical stage I or II disease. Overall, 50% of patients discontinued ART treatment in the evaluation period. Factors associated with ART discontinuation included being younger (< 35 years, $p=0.02$), unemployed ($p=0.02$), ART-experienced ($p=0.02$), without chronic diarrhea ($p=0.01$) or a prolonged cough ($p=0.04$), and having advanced immunosuppression (i.e., recent CD4 cell count of ≤ 200 copies/mm³ ($p<0.001$)). Adjusted analysis identified older age (≥ 35 years) as being protective (adjusted odds ratio [aOR]=0.97, 95%CI: 0.94-0.99; $p=0.01$), and having advanced immunosuppression (i.e., recent

CD4 cell count value of ≤ 200 copies/mm³) as risk factors (aOR=4.5, 95%CI: 2.084-9.837; p<0.001) for ART discontinuation.

Conclusions:

The rate of ART discontinuation is high in younger patients and those with advanced immunosuppression are at higher risk. Tailored strategies such as Young Adult Friendly Services and Community Adherence Support Groups with a specific focus on youth and young adults, combined with strengthened adherence counseling, should be explored.

Background

Globally, sub-Saharan Africa continues to have a disproportionate amount of people living with HIV/AIDS. Mozambique has the eighth highest prevalence worldwide, and Zambézia province, situated in the predominantly rural central region, has one of the highest HIV prevalence nationally.

According to national statistics from IMASIDA (2015), Mozambique's HIV prevalence was estimated at 13.2% among reproductive-aged (15-49 years of age) adults, with a higher rate among women (15.4%) compared to men (10.1%). For both sexes, prevalence is higher in urban (20.5% for women and 12.3% for men) compared to rural areas (12.6% for women and 8.6% for men). In Zambézia Province, HIV prevalence is estimated at 15.1%.

Evidence detailing the benefits of effective use of ART for increased survival and improved quality of life for HIV-positive patients is clear, and ART-treated individuals maintaining viral suppression (i.e., having consistent plasma viral load values below the lower limit of detection) will not transmit HIV to their HIV-negative partners; undetectable = untransmissible (U=U)[1].

However, the success of ART largely depends on the factors influencing individual patient adherence to ART including a variety of health-system (i.e., geographic distance, long wait times, poor quality of care, etc.) and individual-level factors (i.e., perceived stigma/discrimination, ARV medication-related side effects, etc.)[2-5].

Rates for retention to HIV services in Mozambique have been challengingly low, with a national retention rate of 69% at 12-months in 2018 (Ministry of Health [MoH] National Report).

Purpose and questions

The overall purpose of this evaluation was to quantify the rate of ART discontinuation and to identify the patient-related factors that contribute to it.

More specifically, this evaluation aimed to identify the sociodemographic and clinical factors that contribute to the discontinuation of ART among patients of the Namacurra district capital health facility in Zambézia Province, Mozambique.

Design/methods/limitations

Type

An observational, cross-sectional study was performed. For this outcome evaluation we conducted a secondary data analysis of individual- and health facility-level data routinely collected by district and provincial teams for programmatic monitoring and reporting purposes.

Stakeholder engagement

FGH technical teams have ongoing collaborations with key stakeholders working in the health facilities and communities in which we are supporting and engaging. This concept note and evaluation plan for secondary data analysis was developed in collaboration with the provincial district health authorities and approved by sponsoring institution CDC-Mozambique (CDC-MZ).

Sampling strategy

Sample size was calculated using a formula based on the proportion of previous ART discontinuation at this health facility site; sample size needed for this evaluation was then calculated for the current known population size. For a random sampling of eligible males and females proportional to the actual population seen at this health facility, sampling was stratified by sex (male and female). Considering that $Z_{\alpha/2} = 1.96$, given that the 95% confidence level (CI) is used, with a 3% margin of error (MOE = 0.03), we selected a sample size of 766 patients to be included in the evaluation. From this figure, the numbers corresponding to the identified proportions by sex were calculated: 24% of included patients were male (183 men) and 76% female (583 women).

Methods

Routinely collected patient-level data were obtained from a secondary data source, the OpenMRS, which is an electronic database where programmatic data are securely stored. These data are derived from patient medical records and their pharmacy-captured ART pick-up forms (FILA).

For data analysis, IBM Statistical Package for Social Science (SPSS) Version 25 and MS Excel 2016 were used.

To assess the association between categorical variables and ART discontinuation, chi-square test was performed; and if the conditions for this test were not met, Fisher's exact test was performed. For multivariate analysis, logistic regression was performed.

Ethical considerations

Prior to the execution of any of the procedures for this research, approval was sought by the Zambézia Bioethics Committee for Health. This secondary data analysis is covered under the VUMC/FGH's CDC-approved "blanket" protocol entitled, "*Quality Improvement for HIV Care and Treatment in Zambézia province of the Republic of Mozambique under the President's Emergency Plan for AIDS Relief (PEPFAR)*" (CGH HSR #: 2016-163a), also approved by Mozambique and VUMC IRB ethics committees.

Patient Confidentiality

All data included in this analysis were de-identified programmatic data.

Informed consent

For this research, the obtaining of informed consent was waived, since the source of data collection is secondary and there was no contact with the patients whose data were included in the analysis. Instead, a Data Use Agreement was made with the governing institution as a means of outlining and agreeing to the strictly limited access to de-identified individual-level data on data managers' computers or within databases located on FGH's secure servers.

Benefits

With the results of this research, it will be possible to design strategic approaches contextualized for the Namacurra District Health Center in order to mitigate ART discontinuation; thus, leading to lower morbidity and mortality rates among patients seen at that health facility or other patients with similar characteristics.

Risks

No risks are foreseen for the patients whose data was included in these analyses since there will be no interventions that can create physical, psychological and social damages, as only secondary data were collected and included.

Deviations from SOW/protocol

There was no deviation from any SOW or protocol.

Quality assurance

When the dataset was collected, the data were cleaned to ensure they are consistent with and appropriate for the evaluation's inclusion and exclusion criteria.

Data Analysis plan

An exploratory analysis was performed using descriptive statistics. For categorical variables, the proportions and their confidence intervals (CI) were calculated, the frequency tables constructed, and the results presented in appropriate tables and/or graphs. For numeric variables, the means or medians were calculated, and correspondingly the respective confidence intervals or interquartile ranges (IQR), the dispersion measures (variance, standard deviation, coefficient of variation) were calculated.

To assess the association between categorical variables and the variable of ART discontinuation, the chi-square test was performed, and when conditions for this test were not met, then Fisher's exact test was performed. Following the MoH's guidelines for ART care and treatment, discontinuation (i.e., abandonment) of ART was defined as not picking up one's ART within 59 days after the last scheduled pick-up date, or 90 days after the last ART medication pick-up.

For multivariate analysis, a logistic regression model was used in which ART discontinuation was the dependent variable, categorized as “1” if the patient had discontinued ART or “0” if not (i.e., patient was still active in care by the definition described above). Sociodemographic and clinical variables were included in the model as independent variables. The criterion for including the independent variables in the multivariate model was that the variables had a p-value less than or equal to 0.05 in the chi-square or Fisher's exact tests, thus these variables were included in the logistic regression model.

Limitations of design

The evaluation was conducted using data from patients at only one health facility in Zambézia Province, whereas inclusion of patients from additional health facilities in the region could presumably contribute to more generalizable results. In addition, it was not possible to explore the temporality component (as is done in prospective studies), thus the causality of the associated factors is not reported.

Findings and conclusions

Patient demographics

In the sample of 766 patients, 583 (76%) were female, the median age of the patients was 28 years (IQR of ± 13 years), 75% were under 35 years of age, 660 (90%) were unemployed (i.e., without a fixed income), 529 (77%) had either no education or only primary level education, 424 (73%) married or in common law relationships, 256 (77.8%) did not have a refrigerator in their home (Table 1). In the comparison of ages by sex, there is a difference between females and males. Females have a median age of 26 years (IQR ± 12 years) and males 34 years (IQR ± 15 years), with statistically significant differences identified by the Mann-Whitney test for independent samples (p-value < 0.001), i.e., 50% of ART-enrolled females are at least 26 years and males at least 34 years.

Patient clinical history

Regarding clinical history, 9 patients (5%) had a history of drug allergies, 9 (3%) were ART-experienced, 33 (6%) had a history of herpes zoster, 31 (6%) had a history of syphilis, 47 (9%) had a history of chronic diarrhea, 121 (23%) had a history of weight loss greater than 10% of their weight, 59 (11%) had a history of chronic cough, 533 (73%) had WHO clinical stage I or II disease, and 758 (99%) were on the ART regimen consisting of tenofovir (TDF), lamivudine (3TC), plus efavirenz (EFV). The mean duration on ART was 19 months (SD 12 months) and mean duration of being in HIV services clinical care was 30 months (range 0 to 135 months).

ART discontinuation

ART discontinuation among patients included in the analysis was found to be quite high at 50% (95% CI: 47%-57%). The median age of patients who dropped out of ART care was three years younger than that of individuals who continued treatment (i.e., remained active in care) and these

differences are statistically significant ($p < 0.001$), of which 26 years (IQR ± 12 years) for dropout patients and 29 years (IQR ± 15 years) for patients who continued treatment.

At a significance level of 5%, the variable for a patient's ART status (i.e., active on ART or discontinued ART) is associated with: age as 80% ($p=0.02$) of patients who discontinued ART were <35 years of age; occupation, where 93% ($p=0.02$) of those who discontinued ART reported being unemployed; being ART-naive, as 95% ($p=0.02$) of those who discontinued ART had no prior history of ART; cough symptom status ($p=0.04$), as 91% ($p=0.04$) of those who discontinued ART did not have a prolonged history of cough symptoms; latest CD4 cell count results, as 77% ($p < 0.001$) of those who discontinued ART had a most recent CD4 cell count >200 cells/mm³; and viral load, as 53% ($p=0.047$) of those who discontinued ART had a recent fully suppressed (i.e., <1000 copies/mL) at the time of their ART discontinuation.

Comparing proportions for the different categories between the patients active on ART treatment and those who discontinued, it was observed that among patients aged less than 35 years, 46% were active on treatment, whereas among patients aged 35 years or over 60% were active on treatment. Regarding patients' occupational status, among those who reported being unemployed, 48% were active on treatment and 52% had discontinued their prescribed ART, compared to those who reported being employed of whom 63% were active on ART with 37% discontinuing their prescribed ART. Among patients having a history of chronic diarrhea, 66% were active on treatment and 34% had discontinued, compared to those who had no prior history of diarrhea, of whom 46% were active on ART and 54% had discontinued their prescribed ART. Among patients with a history of prolonged cough, 61% were active on treatment and 39% had discontinued ART, compared to 46% and 54%, respectively, among those who did not have prolonged cough symptoms. With regards to the most recent CD4 cell count of patients having a value ≤ 200 cells/mm³, 31% were active on treatment and 69% had discontinued ART, compared to those having a most recent CD4 cell count value >200 cells/mm³ of whom 59% were active on ART and 41% had discontinued. Among patients having a fully suppressed (i.e., <1000 copies/mL) recent viral load, 85% were active on treatment and 15% had discontinued, compared with those with evidence of viremia (i.e., having a most recent viral load of $\geq 1,000$ copies/ml), of whom 75% were active on ART on 25% had discontinued their prescribed ART.

Table 1. **Bivariate analysis of factors affecting discontinuation**

	Active		Discontinued		Total		p-value
	n***	%	n***	%	n***	%	
Sex							0.27*
	Female	296	78%	287	74%	583	76%
	Male	84	22%	99	26%	183	24%
Age							0.02*
	<35 years	268	71%	310	80%	578	75%
	≥ 35 years	112	29%	76	20%	188	25%
Occupation							0.02*

Unemployed	318	87%	342	93%	660	90%	
Employed	46	13%	27	7%	73	10%	
Level of education							0.45*
None	106	31%	108	31%	214	31%	
Primary education	148	44%	167	48%	315	46%	
Secondary and/or technical education	85	25%	75	21%	160	23%	
Marital status							0.46**
Single	65	23%	67	22%	132	23%	
Separated/ divorced	0	0%	3	1%	3	1%	
Widowed	9	3%	12	4%	21	4%	
Married/ living together	208	74%	216	72%	424	73%	
Refrigerator at home							0.11*
No	137	82%	119	74%	256	78%	
Yes	31	18%	42	26%	73	22%	
Electricity at home							0.46*
No	133	76%	117	72%	250	74%	
Yes	43	24%	46	28%	89	26%	
Smoking							0.29*
No	299	97%	305	98%	604	98%	
Yes	9	3%	5	2%	14	2%	
Alcohol consumption							0.61*
No	217	92%	242	93%	459	92%	
Yes	20	8%	18	7%	38	8%	
Drug allergies							0.85**
No	82	94%	78	95%	160	95%	
Yes	5	6%	4	5%	9	5%	
History of prior ART							0.02**
No	159	99%	151	95%	310	97%	
Yes	1	1%	8	5%	9	3%	
Clinical history of Herpes Zoster							0.47*
No	235	93%	258	95%	493	94%	
Yes	18	7%	15	5%	33	6%	
History of oral candidiasis							0.28**
No	248	99%	263	98%	511	98%	
Yes	2	1%	6	2%	8	2%	
History of vaginal discharge							0.04*
No	217	85%	248	91%	465	88%	
Yes	37	15%	24	9%	61	12%	

Clinical history of syphilis								
	No	219	93%	242	95%	461	94%	0.46*
	Yes	17	7%	14	5%	31	6%	
Clinical history of chronic diarrhea								
	No	208	87%	244	94%	452	91%	0.013*
	Yes	31	13%	16	6%	47	9%	
Clinical history of weight loss >10%								
	No	182	73%	217	80%	399	77%	0.06*
	Yes	67	27%	54	20%	121	23%	
Clinical history of chronic cough								
	No	212	85%	245	91%	457	89%	0.04*
	Yes	36	15%	23	9%	59	11%	
WHO Clinical Staging								
	I and II	276	73%	257	74%	533	73%	0.73*
	III and IV	104	27%	91	26%	195	27%	
ART regimen								
	TDF+3TC+EFV	376	99%	382	99. %	758	99%	0.90**
	AZT+3TC+NVP	2	0.5%	3	0.8%	5	1%	
	d4T+3TC+NVP	1	0.3%	0	0.0%	1	0%	
	AZT+3TC+EFV	0	0.0%	1	0.3%	1	0%	
BMI								
	Low (≤ 18.5)	58	25%	47	20%	105	22%	0.30*
	Normal (18.6 -24.9)	151	64%	152	65%	303	64%	
	High ≥ 25	27	11%	36	15%	63	13%	
First CD4 cell count								
	≤ 200 cells/mm ³	67	18%	69	23%	136	20%	0.15*
	>200 cells/mm ³	302	82%	235	77%	537	80%	
Last CD4 cell count								
	≤ 200 cells/mm ³	32	9%	70	23%	102	15%	0.0*
	>200 cells/mm ³	336	91%	232	77%	568	85%	
First Viral load result								
	<1000 copies/ml	145	66%	27	55%	172	64%	0.19*
	≥ 1000 copies/ml	76	34%	22	45%	98	36%	
Last Viral load result								
	<1000 copies/ml	151	68%	26	53%	177	66%	0.05*
	≥ 1000 copies/ml	70	32%	23	47%	93	34%	

* chi-square test

** Fisher's exact test

Of the covariates in the logistic regression model, older age was found to be a significant covariate impacting ART discontinuation, namely, it is a protective factor whereby with every increase of one unit (i.e., one year) in age, the odds of ART discontinuation decreased by 3.5%, indicating that the older the patient is, the lower the probability of discontinuing ART (aOR=0.965; 95% CI: 0.94-0.99, p=0.01). Although only a small sample (9) of individuals were ART-experienced, analysis results indicated that ART-experienced individuals were 11% more likely to discontinue their prescribed ART (aOR = 0.11, 95% CI: 0.01-0.92, p=0.04) compared to ART-naïve individuals. Of note, individuals having a most recent CD4 cell count of ≤ 200 copies/mm³ had a nearly five-fold higher likelihood of discontinuing their prescribed ART.

Table 2. Regression analysis for patient-related factors impacting ART discontinuation

Variables	aOR (95% CI)	p-value
Age (years)		
<35	REF	0.01
≥ 35	0.965 (0.94-0.99)	
History of ART in past		
Yes	REF	0.04
No	0.11 (0.01-0.92)	
Last CD4 cell count		
>200 cells/mm ³	REF	<0.001
≤ 200 cells/mm ³	4.53 (2.08-9.84)	

Conclusions and Recommendations

In this evaluation, the rate of ART discontinuation was found to be quite high at 50%. Younger age, unemployment, advanced immunosuppression (i.e., having a recent CD4 cell count < 200 cells/mm³), and being viremic (i.e., having a most recent plasma viral load $> 1,000$ copies/mL) were identified as factors associated with ART discontinuation. In the multivariate analysis, age, prior ART experience, and advanced immunosuppression remained significantly associated. Tailored strategies such as Young Adult-Friendly Services or Community Adherence Support Groups (CASG) focused on youth, combined with strengthened adherence counseling, should be explored for reduction of treatment abandonment.

Dissemination plan

In an effort to share best practices and lessons learned from this evaluation, a CDC-Mozambique-approved abstract with these findings was presented in a poster format at the International Conference on AIDS and STIs in Africa (ICASA) in Kigali, Rwanda in December 2019. In addition, this report will be translated and shared with MoH and stakeholders at local level, where results will be discussed in order to improve strategies aimed at increasing retention.

Appendices

Approved protocol/ SOW

This evaluation is covered by and was approved by CDC-Mozambique Associate Director for Science (ADS) under the VUMC/FGH blanket protocol for secondary data analyses to evaluate and improve program outcomes using routinely collected HIV Care and Treatment data (CGH HSR #: 2016-163a).

Instruments

Not applicable

Informed consent

Informed consent was not required for use of data in this evaluation, as it was a secondary analysis of routinely collected, de-identified, programmatic data. A waiver of informed consent was approved, as the evaluation involved no more than minimal risk.

Bio-sketches

Not applicable.

Conflict of interest statement

The collaborators of this evaluation have no conflicts of interest to declare.

Evaluation costs

Not applicable.

Results or logical framework

Not applicable.

References

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