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Impact of Multi-Month Dispensation of Antiretroviral Therapy on Retention among People Living with HIV in Zambia

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Abstract

HIV/AIDS continues to be a global public health concern. At the end of 2019, an estimated 38 million people were living with HIV globally of which 87% knew their HIV status, 67% were on antiretroviral therapy and 59% had achieved HIV viral load suppression with no risk of infecting others. WHO recommends multi-month dispensing of ART for up to 6 months in patients who are clinically stable due to the positive effects of reducing the burden on health systems, and saving time and opportunity costs for patients. The study was a retrospective cohort study based on secondary data collected routinely from health facilities with a sampling frame covering the entire country extracted from SmartCare. Both adults and children who had received ART between 1st January 2015 and 30th June 2020 were included in the study and were tracked through to 30th June 2021. This study revealed that HIV-positive patients on ART and receiving multi-month dispensation are more likely to be retained in HIV care and treatment compared to those on the standard of care dispensation. In conclusion, this study has revealed that a multi-month dispensation of ART is an effective intervention to improve retention among people living with HIV. Therefore, there is a need to continue scaling up multi-month dispensation for all stable patients on ART in Zambia.

Keywords: *ART, HIV, MMD, Multi-Month Dispensation, People Living with HIV.*

Introduction

HIV has been one of the world's biggest health and development challenges since the first cases were reported in 1981. An estimated 76 million people have been infected with HIV since it was first discovered. Currently, approximately 38 million people are living with HIV with over 10 million people dying of AIDS-related causes since the beginning of the epidemic [16]. Despite the availability of antiretroviral therapy that can control HIV and reduce viral transmission, HIV is still a leading cause of death. In 2019, approximately 690,000 people died of AIDS-related causes and 1.7 million people were newly infected with HIV [2]. In 2013, UNAIDS announced the 90-90-90 fast-track targets to help end the AIDS epidemic: By 2020, 90% of all people living with HIV will know their HIV status. By 2020, 90% of all people diagnosed with HIV infection will receive sustained antiretroviral therapy. By 2020, 90% of all people receiving antiretroviral therapy will have viral suppression [15]. According to the UNAIDS report, in 2019, 81% of people living with HIV knew their HIV status. Among people who knew their status, 82% were accessing treatment. And among people accessing treatment, 88% were virally suppressed. Of all people living with HIV, 81% knew their status, 67% were accessing treatment and 59% were virally suppressed in 2019 [16].

In 2020, UNAIDS reported that 1,500,000 adults and children were estimated to be living with HIV representing 8.4% of the total

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population. A total of 1,200,000 people were estimated to be living with HIV at the end of 2019 of which 1,100,000 (90%) knew their HIV status, 1,084,942 (86%) were on antiretroviral therapy and 960,000 (77%) have achieved viral load suppression. In addition, approximately 17,000 people died of AIDS-related causes and 15,000 people were newly infected with HIV (UNAIDS, 2020). However, in 2020, approximately 17,000 people died of AIDS-related causes with 15,000 people being newly infected with HIV [16].

Adherence to ART among PLHIV has the potential to result in a near-to-normal life expectancy for individuals who remain on treatment and achieve viral load suppression. Several barriers to achieving ART retention and viral load suppression both at patient and health system levels have been identified in settings with high prevalence like the southern African region and include the need for frequent clinic visits for clinical evaluations and medication refills, long waiting time in ART clinics, long distances to and from ART clinics, high costs for travel to clinics, and missed wages as a result of time away from work. For patients who are considered clinically stable, frequent clinical visits might not be necessary as this may result in an avoidable burden on the health system especially on health care providers. Multi-month dispensing of ART is one strategy to reduce the frequency of medication refill visits, which can reduce barriers to care at both the patient level and the health-system level. There is now an increasing need to extend dispensing intervals up to six months, driven by the PEPFAR to have fully implemented six-monthly ART dispensing by the end of the fiscal year 2021 in all supported countries [12].

The observational studies conducted so far have suggested that clinical outcomes of patients on multi-month dispensation of ART in sub-Saharan Africa are favourable. However, the magnitude of evidence from studies of this intervention is rated as very low to low due to selection bias [9]. In the era of treat all antiretroviral treatment eligibility, differentiated service delivery models are now critical for improved services to meet the needs of people living with HIV and reduce burdens on the health care system, particularly in sub-Saharan Africa, the region has almost 70% of the people living with HIV globally [3]. However, there are several factors negatively associated with adherence to ART among people living with HIV which include improved health status, stigma, running out of medication and lack of systems to facilitate reminders to HIV patients on ART [7].

A study conducted in Malawi to determine the outcome using differentiated models of care to achieve national HIV treatment goals showed that multi-month dispensing was being implemented nationally and had already generated cost savings and efficiencies in the country for patients and the health system. However, they observed that only 72.9% of the eligible patients and 42.3% of ineligible patients received multi-month dispensation of ARVs. This inconsistency in the recruitment criteria may result in negative outcomes for patients [11].

A study conducted in six countries (i.e. Botswana, Lesotho, Swaziland, Malawi, Uganda and Tanzania) showed that transitioning children and adolescents to the multi-month dispensation of ARVs was feasible and there was evidence of favourable health outcomes in terms of immunologic status, ART adherence, viral suppression, retention, and mortality [6]. Another cohort-based study conducted in Zambia showed that six-month clinic return intervals were associated with fewer missed visits, gaps in medication and LFTU. However, the study recommended the need to assess viral load suppression among patients on extended

clinical follow-up and pharmacy refills for up to six months [8]. Furthermore, Failure to adhere to antiretroviral therapy (ART) continues to be the leading cause of treatment failure among PLHIV and new infections [5].

The objective of this study was to estimate retention among people living with HIV on antiretroviral therapy and determine the impact of multi-month dispensation of ART on retention.

Methods

This study was a retrospective cohort study based on secondary data collected routinely from health facilities with a sampling frame covering the entire country. Both adults and children who had received ART between 1st January 2015 and 30th June 2020 were included in the study and were tracked through to 30th June 2021. This provided an ideal window to review their health outcome (viral load suppression) and retention for those started on multi-month dispensation of ART. The starting point of 2015 for the study was selected because WHO recommended VL testing as the preferred monitoring approach to diagnose and confirm treatment failure in 2013 and this took time to be fully operational across resource-limited countries, especially in the southern Africa region [18]. All patients with an HIV-positive status but not started on ART on or before 30th June 2020 were excluded from the study, including those who started on ART after 30th June 2020.

Data for this study was extracted from Smart Care, which is the national medical records system used for routine HIV care and treatment in Zambia. SmartCare is an electronic medical records system that stores patient information for easy retrieval at facility, district, provincial and national levels. The system captures patient-level identification data and health-related information, which includes HIV/AIDS, PMTCT, TB, and other services that are later transferred into the Health Management Information System (HMIS).

The dataset extracted from SmartCare contained patients' demographic characteristics when they tested HIV positive when they were started on ART and the regimen type they are taking. The dataset went through a thorough process of data cleaning where it was reviewed for correctness, consistency and completeness. The cleaned dataset was then analysed using R studio software.

This research used quantitative data; therefore, a descriptive analysis was conducted to describe the population under study by age, sex, length of treatment, regimen type, viral load testing, MMD of ART and region. In addition, a descriptive analysis was conducted to estimate eligible people living with HIV on multi-month dispensation of antiretroviral therapy by age, sex and province. A bivariate logistic regression analysis was conducted at a 95% confidence interval (95% CI) to determine the association between MMD and viral load suppression and retention. Finally, a multivariable logistic regression model was used to determine the probability of achieving retention for HIV patients receiving MMD of ART.

Results

The study covered a total of 1,305,275 PLHIV on ART and registered in SmartCare. The mean age of respondents was 41 years, with the majority of the patients being in the age group 40-44 years, representing 17% of the total patients on ART, followed by 35-39. Females were the majority of the patients on ART, representing 63%, while males represented 37%. Lusaka Province has the majority of the PLHIV on ART in Zambia at 30% followed by Copperbelt Province with 19% while North Western and Muchinga Provinces have the least representing 3% and 2% respectively. A total of 589,340 (45%)

received ART drugs for less than 3 months, 546,632 (42%) received 3-5 months of ART drugs and 160,048 (12%) received for more than 6 months. (Table 1)

Table 1. Characteristics of the Population

		Frequency	**Percentage**
Age	0-4	2,975	0%
	5-9	16,955	1%
	10-14	22,050	2%
	15-19	25,825	2%
	20-24	48,361	4%
	25-29	117,475	9%
	30-34	166,113	13%
	35-39	211,521	16%
	40-44	216,235	17%
	45-49	185,695	14%
	50-54	129,798	10%
	55-59	74,878	6%
	60-64	44,703	3%
	65+	42,691	3%
Sex	Male	489,421	37%
	Female	815,854	63%
Province	Central	165,106	13%
	Copperbelt	254,446	19%
	Eastern	128,135	10%
	Luapula	60,383	5%
	Lusaka	386,802	30%
	Muchinga	31,787	2%
	Northwestern	44,944	3%
	Northern	45,060	3%
	Southern	99,102	8%
	Western	89,510	7%
Viral Load Testing	Valid Viral Load Result	745,939	57%
	Invalid Viral Load Result	559,336	43%
MMD	Less than 3 months	589,340	45%
	3-5 months	546,632	42%
	6 months and above	160,048	12%
	Missing Data	9,255	1%
Total		**1,305,275**	**100%**

The data shows that the majority of those below the age of 15 received ART drugs for less than 3 months: 0-4 years (78%), 5-9 years (72%) and 10-14 years (55%). Only 18% and 4% of those aged 0-4 years received 3-5 months and more than 6 months of ART drugs, respectively. In addition, the data shows that MMD coverage was higher among those

aged 35 years and above. Overall, 46% of the patients received less than 3 months of ART drugs, 42% received 3 to 5 months and only 12% received ART drugs for 6 months and above. (Table 2).

Table 2. Multi-Month Dispensation

		Multi-Month Dispensation		
		Less than 3 months	**3-5 months**	**6 months and above**
Age	0-4	2,315 (78%)	542 (18%)	107 (4%)
	5-9	12,224 (72%)	3,680 (22%)	960 (6%)
	10-14	12,168 (55%)	7,615 (35%)	2,160 (10%)
	15-19	12,267 (48%)	10,376 (40%)	3,014 (12%)
	20-24	25,225 (53%)	17,671 (37%)	5,047 (11%)
	25-29	61,543 (53%)	42,789 (37%)	12,226 (10%)
	30-34	82,637 (50%)	63,469 (39%)	18,676 (11%)
	35-39	99,078 (47%)	85,701 (41%)	25,093 (12%)
	40-44	94,095 (44%)	93,062 (43%)	27,574 (13%)
	45-49	75,090 (41%)	84,445 (46%)	24,865 (13%)
	50-54	50,226 (39%)	60,710 (47%)	18,084 (14%)
	55-59	28,126 (38%)	35,789 (48%)	10,527 (14%)
	60-64	16,726 (38%)	21,448 (48%)	6,243 (14%)
	65+	17,620 (42%)	19,335 (46%)	5,472 (13%)
Sex	Male	365,637 (45%)	342,248 (42%)	101,783 (13%)
	Female	223,703 (46%)	204,384 (42%)	58,265 (12%)
Province	Central	73,126 (44%)	76,584 (46%)	15,203 (9%)
	Copperbelt	115,252 (45%)	105,059 (41%)	33,960 (13%)
	Eastern	57,129 (45%)	51,956 (41%)	18,413 (14%)
	Luapula	31,261 (52%)	21,802 (36%)	6,960 (12%)
	Lusaka	188,224 (49%)	151,007 (40%)	42,505 (11%)
	Muchinga	12,981 (41%)	15,848 (50%)	2,849 (9%)
	Northwestern	18,891 (42%)	19,806 (44%)	5,905 (13%)
	Northern	21,455 (48%)	15,976 (36%)	7,364 (16%)
	Southern	34,064 (35%)	49,394 (51%)	14,060 (14%)
	Western	36,957 (42%)	39,200 (44%)	12,829 (14%)
Total		**589,340 (46%)**	**546,632 (42%)**	**160,048 (12%)**

Retention in HIV care and treatment was higher among patients who received 6 months and above MMD of ART, with 83% of the patients retaining, followed by those that received 3-5 months with 67%, while those that received less than 3 months recorded the lowest retention of 14%. In addition, the data shows that retention was higher in the older population than in the younger population. Furthermore, retention was higher among males at 46%, while among females, it was at 43%. Finally, retention was higher in the Southern province at 58%, while the Eastern province had the lowest retention at 29%. (Table 3**).**

Table 3. Retention

		Retention on ART	
		Retained	**Not retained**
MMD	Less than 3 months	80,743 (14%)	508,597 (86%)
	3-5 months	365,587 (67%)	181,045 (33%)
	6months and above	132,606 (83%)	27,442 (17%)
Age	0-4	1,039 (35%)	1,925 (65%)
	5-9	6,435 (38%)	10,429 (62%)
	10-14	10,166 (46%)	11,777 (54%)
	15-19	12,385 (48%)	13,272 (52%)
	20-24	18,326 (38%)	29,617 (62%)
	25-29	43,678 (37%)	72,880 (63%)
	30-34	66,368 (40%)	98,414 (60%)
	35-39	90,365 (43%)	119,507 (57%)
	40-44	98,026 (46%)	116,705 (54%)
	45-49	89,142 (48%)	95,258 (52%)
	50-54	64,491 (50%)	64,529 (50%)
	55-59	37,763 (51%)	36,679 (49%)
	60-64	22,158 (50%)	22,259 (50%)
	65+	18,594 (44%)	23,833 (56%)
Sex	Male	368,647 (46%)	441,021 (54%)
	Female	210,289 (43%)	276,063 (57%)
Province	Central	78,596 (48%)	86,317 (52%)
	Copperbelt	122,906 (48%)	131,365 (52%)
	Eastern	37,308 (29%)	90,190 (71%)
	Luapula	24,684 (41%)	35,339 (59%)
	Lusaka	165,164 (43%)	216,572 (57%)
	Muchinga	15,758 (50%)	15,920 (50%)
	Northwestern	20,986 (47%)	23,616 (53%)
	Northern	18,157 (41%)	26,638 (59%)
	Southern	56,407 (58%)	41,111 (42%)
	Western	38,970 (44%)	50,016 (56%)
Total		**578,936 (45%)**	**717,084 (55%)**

The PLHIV on 3-5 months multi-month dispensation of ART was 93% (AOR=0.075; p-value < 0.001; and 95% CI=0.074 – 0.076) less likely not to be retained on ART than those on less than 3 months multi-month dispensation. Similarly, those that were on 6 months and above multi-month dispensation of ART were 97% (AOR=0.029; p-value<0.001; and 95% CI=0.029 – 0.030) less likely not to be retained on ART than those on less than 3 months multi-month dispensation. (Table 4).

There was sufficient evidence that if a patient on ART is in a different age group besides 0-4 years, the odds that they achieve viral load suppression varied across Provinces. If a patient was in the age group 25-29 years, they are 2.1 (AOR=2.123; p-value <0.001; and 95% CI=1.940– 2.321) more likely to be retained on ART than those in the age group 0-4. In addition, if a patient is in the age group

5-9 years, they are 14% (AOR=0.171; p-value <0.001; and 95% CI=0.148 – 0.198) less likely not to be retained on ART than those in the age group 0-4 years. Males are 20% (AOR=1.195; p-value <0.001; and 95% CI=1.184 – 1.206) more likely to be retained on ART compared to females. (Table 4).

There was sufficient evidence that if a patient on ART is in a different province besides Central province, the odds that they will be retained on ART varied across Provinces. If a client was in Eastern Province, they are 3.3 (AOR=3.319; p-value <0.001; and 95% CI=3.258 – 3.382) times more likely to be retained on ART than in Central Province. In addition, if a patient is in the Southern province, they are 24% (AOR=0.776; p-value <0.001; and 95% CI=0.761 – 0.792) less likely not to be retained on ART than in the Central Province. (Table 4).

The PLHIV that have been on ART between 3-5 years is 37% (AOR=1.366; p-value <0.001; and 95% CI=1.345 – 1.388) more likely to achieve viral load suppression compared to those that have been on ART for less 3 years. Similarly, those who have been on ART for 5 years and above are 58% (AOR=1.583; p-value <0.001; and 95% CI=1.559 – 1.608) more likely to be retained on ART compared to those who have been on ART for less than 3 years. (Table 4).

Table 4. Multivariable Logistic Regression Outputs for Retention

Variable		**Coefficients**	**Std. Error**	**Z value**	**Pr (>|z|)**	**AOR**	**C.I.**	
MMD	Intercept	0.803333	0.045681	17.586	<2e-16***	2.233	2.043	2.443
	3-5 months	-2.590662	0.004906	-528.064	<2e-16***	0.075	0.074	0.076
	6months and above	-3.532894	0.007898	-447.336	<2e-16***	0.029	0.029	0.030
Age	5-9	-0.148841	0.048921	-3.042	*0.00235***	0.862	0.783	0.948
	10-14	-0.049435	0.048235	-1.025	*0.30542*	0.952	0.866	1.046
	15-19	0.130146	0.047817	2.722	*0.00649***	1.139	1.037	1.250
	20-24	0.705612	0.046597	15.143	<2e-16***	2.025	1.848	2.218
	25-29	0.752719	0.045742	16.456	<2e-16***	2.123	1.940	2.321
	30-34	0.638221	0.045566	14.006	<2e-16***	1.893	1.731	2.069
	35-39	0.524776	0.045493	11.535	<2e-16***	1.690	1.545	1.847
	40-44	0.452497	0.045508	9.943	<2.3e-16***	1.572	1.438	1.718
	45-49	0.361176	0.04558	7.924	*<2e-15****	1.435	1.312	1.569
	50-54	0.300481	0.04575	6.568	*<5.103e-11****	1.351	1.234	1.477
	55-59	0.283719	0.046136	6.15	*<7.77e-10****	1.328	1.213	1.453
	60-64	0.334314	0.046735	7.153	*<8.46e-13****	1.397	1.274	1.530
	65+	0.550893	0.04682	11.766	*<2e-16****	1.735	1.582	1.901
Sex	Male	0.178212	0.004645	38.365	<2e-16***	1.195	1.184	1.206
Province	Copperbelt	-0.040738	0.007866	-5.179	<2.23e-07***	0.960	0.945	0.975
	Eastern	1.199785	0.009493	126.383	*<2e-16****	3.319	3.258	3.382
	Luapula	0.189445	0.012044	15.73	*<2e-16****	1.209	1.180	1.237
	Lusaka	0.122968	0.007336	16.763	*<2e-16****	1.131	1.115	1.147
	Muchinga	-0.00544	0.015062	-0.361	*0.71798*	0.995	0.966	1.024
	Northwestern	0.143297	0.013215	10.843	*<2e-16****	1.154	1.125	1.184
	Northern	0.406232	0.013466	30.167	*<2e-16****	1.501	1.462	1.541
	Southern	-0.253414	0.010058	-25.196	*<2e-16****	0.776	0.761	0.792

	Western	0.393612	0.01027	38.327	*<2e-16****	1.482	1.453	1.512
Length on treatment	3-5 years	0.312137	0.008149	38.301	*<2e-16****	1.366	1.345	1.388
	5 years and above	0.459456	0.00781	58.831	*<2e-16****	1.583	1.559	1.608

Discussion

This study has estimated retention to be at 45% among patients who had a pharmacy interaction between 1 January 2015 and 30 June 2020. The number of people living with HIV estimated to be on ART between January 2015 and June 2020 was 1.3 million, which is slightly higher than the 1.2 million estimated by UNAIDS in 2020. One factor that can contribute to this is the duplication factor of PLHIV who may start ART at one health facility and decide to start at another health facility without disclosing their known HIV-positive status at the new health facility. This leads to a patient having two unique identifiers in the electronic medical record. In addition, during the period under review, patients who were transferring from one facility to another were still counted as active in the initial sites until they were late for more than 28 days from the last expected visit date. Out of the 1,305,275 PLHIV estimated to be on ART, 589,340 (45%) patients received less than 3 months of ART drugs, 546,632 (42%) received 3-5 months and only 160,048 (12%) received 6 months and above of ART drugs. Furthermore, 63% of the patients on ART are females, while 37% are males and this aligns with the 2018 ZDHS, which shows that prevalence is higher among females (14.2%) compared to males (7.5%) [20].

The study went further to review the impact of multi-month dispensation on retention among patients receiving ART. The results showed that patients who received longer multi-month dispensations had less likelihood of not retaining HIV care and treatment. For example, the study showed that patients who received 6 months or more of ART drugs were 97% less likely not to retain ART. This aligns with the study conducted in six countries (i.e. Botswana, Lesotho, Swaziland, Malawi, Uganda and Tanzania) which showed that transitioning children and adolescents to the multi-month dispensation of ARVs was feasible and there was evidence of favourable health outcomes in terms of immunologic status, ART adherence, viral suppression, retention, and mortality [6]. A study conducted in Uganda suggested that transportation costs can compromise both ARV adherence and access to care for PLHIV [14], and in another systematic review study, it was found that reduced frequency of clinic visits and drug refills may lead to improvements in program retention and patient outcomes among PLHIV [1, 9]. This aligns with the findings of this study, as multi-month dispensation reduces health facility visit frequency.

The World Health Organization (WHO) 2016 ART guidelines recommend multi-month ART refills for clinically stable patients (WHO, 2016). This is also supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) COP 2020 guidance, where it was stated that providing 6-month multi-month dispensation of antiretroviral drugs to all eligible clients would improve retention. Through improved adherence and retention, PEPFAR Zambia will aim to achieve 95% viral load (VL) suppression [10]. Aligning this study to the predicted positive health outcomes stated by PEPFAR, the study confirms that multi-month dispensation does lead to improved retention, which ultimately leads to improved viral load suppression. In addition to improving health outcomes for PLHIV on ART, multi-month dispensation in the era of treatment all of antiretroviral treatment eligibility, differentiated service delivery models are now critical for improved services to meet the needs of people living with HIV and reduce burdens on the health care system,

particularly in sub-Saharan Africa, the region has almost 70% of the people living with HIV globally [3].

Conclusion

In conclusion, this study has reviewed that multi-month dispensation of antiretroviral therapy is an effective intervention to improve retention among people living with HIV. Multi-month dispensation offers a variety of advantages not only to the patient but to health facility staff, too, because they are not overwhelmed with monthly visits by clinically stable patients. Therefore, there is a need to continue scaling up multi-month dispensation for all stable patients on ART in Zambia for positive health outcomes among PLHIV on ART and to reduce the burden on the already overwhelmed health system arising from frequent visits by patients. Finally, there is a need to consider comparing the differentiated services available as recommended by the World Health Organization and determine which other model provides the highest impact on retention in addition to multi-month dispensation.

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