DOI: 10.21522/TIJPH.2013.11.03.Art021

Assessing the Impact of Universal Test and Treat Implementation Strategy on Retention to Antiretroviral Therapy in HIV Care: A Retrospective Cohort Review

Caeser Magumba^{1*}, Peace Mary Mbulangina², Emma Shiikwa³
¹School of Public Health, Texila American University, Guyana
²Outapi ART Clinic, Ministry of Health, Namibia
³Okahao ART Clinic, Ministry of Health, Namibia

Abstract

Namibia has an adult HIV prevalence of 12.6% according to the Namibia population-based HIV impact assessment survey of 2017 making it one of the highest in the world. Early initiation of antiretroviral therapy (ART) has excellent outcomes for both morbidity and mortality. The National Strategic Framework for HIV and the Namibia Ministry of Health and Social Services (MoHSS) rolled out the WHO 2015 UTTS guidelines making Namibia one of the first African countries to implement UTTS. With UTTS guidelines, rolled out in October 2016, clients who test HIV positive are initiated on ART immediately preferably the same day or within seven days regardless of their HIV clinical stage or CD4 count. Retention in care is required for optimal clinical outcomes in patients with HIV infection. However, after two years of adopting the strategy, it is not well understood whether UTTS affects the retention to care. We therefore sought to establish any emerging differences in retention of ART care after the implementation of UTTS. We used a retrospective cohort review study design that employed both quantitative and qualitative methods. 879 client records were reviewed, 678 clients were initiated on treatment two years prior to the UTTS and 201 were initiated after January 2017 when the UTTS was fully rolled out and had been on treatment for at least 12 months. Data analysis was done using Excel and Statistical Package for Social Sciences (SPSS) version 23.0 software. The overall retention after 12 months of follow-up was (822/879) 93.5% (95% CI: 91.3% to 95.7%). The retention rate at 12 months among clients in the UTTS cohort was 95.5% (95% CI: 93.5% to 97.5%) and somewhat higher than that in the pre-UTTS cohort 92.9% (95% CI: 90.6% to 95.2%). At the end of the review period, attrition was higher in the pre-UTTS cohort 251/678 (37.0%; 95% CI 34.8 to 39.2) versus 42/201 (21.0%; 95% CI 19.0 to 23) during UTTS. Retention on ART was nearly 5% higher after UTTS implementation but young adults and men between 31 and 40 years of age had higher chances of attrition at the time of ART initiation. We recommend that all facilities in Namibia and other parts of sub-Saharan Africa should embrace the UTTS strategy to benefit their clients.

Keywords: Antiretroviral therapy, Retention, Retrospective cohort review, Universal test & treat.

Introduction

Namibia has an adult HIV prevalence of 12.6% according to the 2017 Namibia Population HIV Impact Assessment (NAMPHIA) results and this makes it one of the highest in the world [1]. Among adults aged 15-

64 years, the prevalence of HIV varies geographically across Namibia, ranging from 7.6% in Kunene to 17.9% and 22.3% in Ohangwena and Zambezi, respectively. Regions with higher prevalence tended to have it higher among females than males [1].

There are extensive efforts that have

 contributed to the containment of the HIV epidemic, however, some challenges to meeting the 95-95-95 UNAIDS targets still exist [1]. The National Strategic Framework for HIV and the Namibia Ministry of Health and Social Services (MoHSS) rolled out the 2015 World Health Organization (WHO) guidelines for Universal Test and treatment (UTTS), making Namibia one of the first African countries to implement UTTS on a national programme level [2, 3].

With the new UTTS guidelines, rolled out in October 2016, clients who test HIV positive should be initiated on ART immediately preferably the same day or within seven days regardless of their HIV clinical stage or CD4 count [2].

There is enough evidence to support the benefits for early ART initiation and these may include decreased HIV morbidity and mortality, improved uptake and linkage to care, slower disease progression and decreased HIV transmission [4, 5, 6 and 10]. However, these benefits cannot be obtained unless optimal retention and ART adherence are maintained.

To achieve robust clinical outcomes for patients with HIV infection, retention of care is very crucial. As ART naïve patients waited to initiate antiretroviral therapy (ART) in the pre-UTTS era, retention in care allowed the provision of prophylactic medications for opportunistic infections, ongoing staging, prevention of mother-to-child transmission (pMTCT), and prompt initiation of ART once indications arose [3, 4]. During this era of UTTS, retention in care is of paramount importance since it allows for ongoing refills of ART, assessing for possible drug reactions, and recognizing treatment failure early enough such that appropriate regimen switches can be done. Since HIV is a lifelong and yet complicated disease, retention is needed such these patients can benefit from the much-needed social support and education messages targeting secondary prevention [3, 4, 7].

Retention on ART can be defined as once a client is enrolled on ART, they should be able to

attend an HIV clinic as scheduled for proper follow-up and management [3 &10]. Both retention to care and adherence are critical factors in achieving virological suppression, which forms the basis for individual ART benefits and on a public health aspect, the two have the potential to prevent or stop HIV transmission since the population viral load will be very low [8, 9, 10].

Almost two years into the strategy of UTTS, it is not known whether UTTS impacts the retention of clients into care since most of them are initiated on ART when they seemingly look healthy and with higher CD4s which can explain their easy loss to follow up [6]. There are also some concerns that clients are not prepared well in terms of counseling before being initiated on ART and this is thought to affect retention to care [10, 11].

We therefore designed this retrospective cohort review to establish any emerging differences in retention of ART care after the implementation of the universal test and treat strategy in Namibia.

The primary project objective was to establish any emerging differences in the retention of ART care after the implementation of the universal test and treatment strategy in Namibia. The Specific objectives were.

- 1. To examine which other factors influence retention at ART Care.
- 2. To examine adherence in patients initiating ART with higher CD4s and without any underlying illness.
- 3. To compare ART adherence levels in clients starting before and after the test and treatment implementation.

Methodology

Overview

The protocol was developed with guidance from experienced health professionals in the Ministry of Health including senior HIV clinical mentors, quality improvement coaches and advisors. This was operational research using both qualitative and quantitative methods. Data

collection instruments were developed with technical input by data personnel and a statistician. The investigator was assisted by research assistants who were already employed as nurses and data clerks.

The study reviewed 879 client records who were active on ART. 678 clients were those initiated on treatment two years prior to the UTTS and 201 were initiated after January 2017 when the UTTS was fully rolled out and had been on treatment for at least 12 months.

The sample size of 879 client records was thought sufficient to give at least 80% power to detect if there was any difference in terms of retention to care between the UTTS group and the pre-UTTS group. Assessing retention to care in those two groups was critical because it impacts HIV virological suppression.

Study Settings

The study was conducted at the community level in Okahao district, Namibia and seven (7) health facilities that provided ART services were involved. Okahao district is one of the four districts in Omusati region of Namibia, with a total population of 43,645 and HIV prevalence of 16.9% among adults [1]. The district has seven health facilities. Four of the facilities were using the electronic patient medical record system (ePMS) for client registration and data collection, and the Electronic Data Tool (EDT) for pharmacy dispensing. The other three use the paper-based systems. All HIV clinics in these health facilities were managed by the MOHSS or by the Catholic Health Services and supported by the Center for Infectious Disease Control and under the President Prevention (CDC), Emergency Plan for AIDS Relief (PEPFAR) a United States-based entity during the time of the study.

Study Design

The study was a retrospective cohort review that involved both quantitative and qualitative methods. The quantitative methods involved a review of client records of attendance at the ART clinics and pharmacy at the seven (7) health facilities. The qualitative methods consisted of factors related to ART adherence.

We created two cohort categories with equal follow-up duration, one pre-UTTS and the other UTTS. In the pre-UTTS cohort, records for clients who started ART between October 2014 and June 2015 and had been on ART for at least 12 months were recruited. The UTTS cohort included clients who started ART after October 2016 under UTTS guidelines and were on ART for at least 12 months.

Data Collection

We recruited 70 client records files daily for a period of ten days. The proportion of records from each facility was determined by the number of active clients in a particular facility.

All data was extracted from routinely collected MOHSS client monitoring and evaluation records showing at least 12 12-month period of follow-up. All the information collected from the patients' files was captured into a created digital database. We used standardized MOHSS ART definitions [3], as follows: "Lost to follow-up" (LTFU), not returned to the clinic three months beyond the given review date "Stop ART," the patient is alive, but they stopped their treatment for whatever reason; "Dead," having died from any cause after initiating ART. Transfer out" Clients who transferred to care at another ART facility.

The primary study outcome was retention to care where a live patient has maintained their treatment for at least 12 months of regular clinic visits. Retention to care is a universal outcome for all ART programs where the patient is alive and taking their treatment which excludes those patients visiting the clinic but not taking their medicines. Attrition is interpreted as the total number of patients who have either died, lost to follow up or have stopped their ART.

Patients who were "Transferred out" were excluded because their outcomes could not be established correctly after their transfer out.

The following information was collected:

- 1. Number of active clients registered in the clinic before and after the UTTS.
- The number of clients known to be lost to follow up before and after the UTTS (3) Age (4) Gender (5) TB status at initiation of ART (6) WHO stage at ART initiation and the ongoing treatment stage (7) Standardized ART outcomes like Stop ART, Dead, Alive on ART or Transfer out.

Inclusion Criteria

We included clients who were registered with the health facility and presumed to have been on treatment for a period of at least twelve months and had no known history of treatment interruptions.

Sample Size

We used a convenient sampling process for getting the client record files from the electronic database (ePMS).

The latest version of Stata was used to determine the sample size for the primary objective.

Data Analysis

The quantitative data was analyzed using SPSS on computers with assistance from the statistician and some quantitative study outcomes were measured as percentages (%). Any detectable associations were assessed for their significance using the 95% confidence interval.

We further adjusted for any confounders that were detected during the process and a

sensitivity analysis was conducted to limit any observations brought about by certain factors, for example, those in less severe stages and advanced stages of disease. We did a multivariable Cox regression analysis for other factors thought to be independently associated with attrition to care.

Ethical Consideration

The study was implemented following the routine way in which the facility clients were being followed up. However, the project protocol was submitted to the institutional review board at the Ministry of Health for their notification. Unique identifiers were used, and a few selected study members handled the clients' records.

Study Duration

The project was for eight months from April 2019 to December 2019

Results

Characteristics of the Cohorts and Treatment Outcomes

We recruited 879 client record files, of whom 678 started ART between October 2014 and June 2015 (pre-UTTS cohort) and 201 clients started ART after October 2016 (UTTS Cohort). Most clients were between 20 and 40 years old at the time of ART initiation (68.3%) in both cohorts. It was noted in both cohorts that more females initiated ART (70.5% for females compared to 29.5% for males) as seen in Table 1.

Table 1	Raceline	Characteristics and Outcomes
Table 1.	Daseillie	Characteristics and Outcomes

Variable	Total n (%)	Pre-UTTS n (%)	UTTS n (%)
Patients enrolled	879	678	201
Age Categories			
1-10	30	23	7
11-20	49	35	14
21-30	262	183	79
31-40	277	225	52
41-50	165	132	33
>50	96	80	16

Gender Category(n=879)				
Female	620(70.5)	483	137	
Male	259(29.5)	195	64	
TB status at ART initiation				
Yes	46	36	10	
No	772	602	170	
Missing	61	40	21	
WHO clinical stage at initiation	475	344	131	
Ι	38	28	10	
II	18	13	5	
III	41	40(5.9)	1(0.5)	
IV	307	253(37.3)	54	
Standardized ART outcomes (%)				
Stop ART	0	0	0	
Dead	29	23(3.4)	6(2.9)	
LTUF	28	25(3.8)	3(1.5)	
Alive on ART	586	427(62.9)	159(79.1)	
Transfer out	236	203(29.9)	33(16.5)	

As seen in Table 1, we never found any important differences between the two cohorts in age and sex but there was a higher degree of missing WHO clinical stage at initiation data in the pre-UTT cohort. There were 36 clients with Tuberculosis at ART initiation in the pre-UTTS cohort compared to only 10 in the UTTS cohort. There were also more clients with WHO clinical stage IV at initiation in the pre-UTTS (40) cohort than in the UTTS cohort (1).

Of 879 clients we reviewed 586(66.7%; 95% CI 64.7 to 68.9) were retained alive and 241 (27.4%; 95% CI 26.0 to 28.8) were recorded as Transfer-out. 30 (3.4%; 95% CI 2.5 to 4.3) clients were recorded as dead during the review period with a higher proportion in the pre-UTTS cohort: 23(3.4%) in comparison to the UTTS cohort 6(2.9%) from Table 1.

Attrition was higher in the pre-UTTS cohort 251/678 (37.0%; 95% CI 34.8 to 39.2) versus 42/201 (21.0%; 95% CI 19.0 to 23) during UTTS as reflected in Table 1.

Retention on ART and Predictors of Attrition

The overall retention after 12 months of follow-up was (822/879) 93.5% (95% CI: 91.3% to 95.7%). The retention among clients in the UTTS cohort was 95.5% (95% CI: 93.5% to 97.5%) and somewhat higher than that in the pre-UTTS cohort 92.9% (95% CI: 90.6% to 95.2%). The least observed retention was among adults aged 31 to 40 (63.2%; 95% CI: 60.8% to 65.6%) as seen in Table 2.

Table 2. Overall Retention in Care After 12 Months of Follow-Up

Variable	Retention Outcome		
	Not Retained n (%)	Retained n (%)	
Pre-UTTS	251(37.0)	427(63.0)	
UTTS	42(20.9)	159(79.1)	
Age			
1-10	10(33.3)	20(66.7)	

11-20	16(34.8)	33(65.2)	
21-30	76(29)	186(71)	
31-40	102(36.8)	175(63.2)	
41-50	53(32.1)	112(67.9)	
>50	36(33.7)	60(66.3)	
Gender			
Female	207(33.4)	413(66.6)	
Male	86(33.2)	173(66.8)	
TB status at ART initiation			
No	259	513	
Yes	13	33	
Missing	21	40	
WHO clinical staging			
I	174	301	
II	21	17	
III	10	8	
IV	25	16	
Missing	63	244	

We performed a multivariable regression analysis and found an independent association between ART initiation in the pre-UTTS cohort (hazard ratio (HR) 1.44; 95 % (CI: 1.13-1.75)

and a p-value of 0.006. Age category 31 to 40 years (HR 1.75; 95% CI: 1.28 to 2.22 p-value 0.004) was associated with high rates of attrition as seen in Table 3.

Table 3. Cox Regression Analysis of Predictors of Attrition to Care

Variables	n (%)	HR (95%)	P-value
Cohort (n=879)			
Pre-UTTS	251(37.0)	1.44(1.13-1.75)	0.006
UTTS	42(20.9)	Ref=1	
Age(n=879)			
1-10	10(33.3)	0.94(0.69-1.43)	0.779
11-20	16(34.8)	Ref=1	0.144
21-30	76(29.0)	0.9(0.57-1.23)	0.004
31-40	102(36.8)	1.75(1.28-2.22)	-
41-50	53(32.1)	Ref=1	-
>50	36(33.7)	0.76(0.50-1.18)	-
Gender			
Female	207(33.4)	Ref=1	0.435
Male	86(33.2)	1.16(0.89-1.43)	

Discussion

Retention was higher among clients who started ART under UTTS guidelines than those who started pre-UTTS (95.5 vs. 92.9%). High

attrition rates were seen among adults aged 31 to 40 years.

In clinical trials conducted in Kenya and Uganda, it was observed that 95.5% retention can be achieved within one year of ART

initiation while being young and having a low baseline CD4 count was linked to attrition [12, 16]. Retention to care is needed for the success of ART programs and it plays a big role in achieving mainly the last component the 95-95-95 UNAIDS global targets. However, there are great concerns about whether it is possible to achieve optimum adherence and retention of ART under UTTS at a national level, especially in the subpopulation of asymptomatic patients with high CD4 counts [3, 13-15].

After the 12 months of follow-up with the implementation of UTTS in Namibia, program data shows that retention is at 77% among adults with HIV infection [2]. Much as there were great concerns regarding retention, especially those with high CD4s and in clinical stage one, our study provides reassuring results.

The implementation of UTTS mildly increased retention on ART in general, however certain patient groups still have higher chances of defaulting treatment under UTTS.

Children, adolescents, and young adults always face challenges to remain in HIV care, as their transition to adult life presents with physiological and psychological demands, plus the need to assume responsibility for one's own treatment and HIV-associated stigma and discrimination [17]. Findings from this study are in line with studies from Malawi and Kenya [10,16,], where retention of ART in 15- to 24-year-olds was much lower compared to older persons (81% vs. 90% to 94%). Having a family member living with HIV staying with an infected youth improves retention [16]. Adolescents belonging to peer support groups show improved retention of care [18].

Other factors like travelling distances to hospitals, high transport fairs, medicine side effects, severe illness, and non-comprehension of ART education [19], ART initiation on the day of HIV testing [20], models of HIV care at the health facility [21] and non-disclosure of HIV status between spouses [22] were identified by various studies as barriers for pregnant and breastfeeding women.

Our study has various strengths. The programme analysis gave us an opportunity to highlight different outcomes that are witnessed in daily HIV care, adding a deep understanding of UTTS implementation to knowledge from clinical trials. ART outcomes from our study results were somewhat like recent national reports from the MOHSS, which use facility-level data.

Our study had some limitations that call for interpretation of results with that in mind. First, the differences observed between the pre-UTTS and UTTS cohorts could be due to some undetected changes that have occurred over time due to our before/after kind of design.

We excluded clients who were transferred to other health facilities from the analysis because their outcome status could not be clearly established. This exclusion could not allow us to observe these clients since they were no longer visiting these same facilities where ART was initiated. This could have led to an underestimation of retention, but it is less likely to have varied by cohort.

We relied on routine HIV data collection, and this resulted in incomplete information on WHO clinical stage, and TB status at initiation. Due to the missing information about pill counts done routinely, this data was not part of the analysis done. With these highlighted limitations of our study, there is a need for other cohorts to be studied with a long duration of follow-up whilst paying extreme attention to data collection methods.

Conclusion

In our retrospective cohort design project, we analyzed ART outcomes two years after the adoption of UTTS guidelines in Namibia. Retention on ART was nearly 5% higher after UTTS introduction but young adults and men between 31 and 40 years of age at the time of ART initiation had higher rates of attrition. This therefore calls for individualized care for these subgroups to achieve the 95-95-95 UNAIDS targets in the UTTS timing. Our results indicate

that UTTS improves retention to care as opposed to earlier fears that it would negatively affect it.

All facilities in Namibia and other parts of sub-Saharan Africa should embrace the UTTS strategy to benefit their clients because we have established that the retention rates are better when ART is initiated as soon as a client is confirmed HIV positive.

References

- [1] Namibia Population-Based HIV Impact Assessment, 2016-2017 https://phia.icap.columbia.edu/wp/content/uploads/2 018/10/NAMPHIA-pdf.
- [2] Namibia National Guideline for Antiretroviral Therapy 2016: https://aidsfree.usaid.gov/sites/default/files/na_natio nal guidelines art.Pdf.
- [3] World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. 2018: http://apps.who.int/iris/bitstream/10665/208825/1/.
- [4] Temprano ANRS 12136 Study Group. A trial of early antiretrovirals and isoniazid preventive therapy in Africa. N England J Med. 2015.
- [5] Antiretroviral Therapy Cohort Collaboration. Causes of death in HIV-1 –infected patients treated with antiretroviral therapy, 1996–2006: collaborative analysis of 13 HIV cohort studies. Clin Infect Dis. 2010; 50(10):1387–96.
- [6] Insight Start Study Group. Initiation of antiretroviral therapy in early asymptomatic HIV infection. N Engl J Med. 2015; 373(9):795–807.
- [7] Messeri PA, Abramson DM, Aidala AA, et al. The impact of ancillary HIV services on engagement in medical care in New York City. AIDS Care. 2002; 14(Suppl 1): S15–S29.
- [8] Ulett KB, Willig JH, Lin HY, Routman JS, Abroms S, Allison J, et al. The therapeutic implications of timely linkage and early retention in HIV care. AIDS Patient Care STDS. 2009; 23(1):41–9.
- [9] Mugavero MJ, Lin HY, Willig JH, Westfall AO, Ulett KB, Routman JS, et al. Missed visits and mortality among patients establishing initial

Conflict of Interest

No conflict of interest to declare.

Acknowledgement

We would like to appreciate the support from the nurses and data clerks who helped with this project. Special thanks to all sites that were part of this project.

outpatient HIV treatment. Clin Infect Dis. 2009; 48(2):248–56.

- [10] Alhaj Mohammad, Amberbir Alemayehu, Singogo Emmanuel Banda Victor, Lettow Monique, Matengeni, Alfred (2019) et al. Retention on antiretroviral therapy during Universal Test and Treat implementation in Zomba district, Malawi: a study. retrospective cohort Journal of the International **AIDS** Society. 22. e25239. 10.1002/jia2.25239.
- [11]McCreesh N, Andrianakis I, Nsubuga RN, Strong M, Vernon I, McKinley TJ, et al. Universal test, treat, and keep improving ART retention is key in cost effective HIV control in Uganda. BMC Infect Dis. 2017; 17(1):322.
- [12] Brown LB, Havlir DV, Ayieko J, Mwangwa F, Owaraganise A, Kwarisiima D, High levels of retention in care with streamlined care and Universal Test and Treat in East Africa. AIDS. 2016; 30(18):2855–64.
- [13] Dodd PJ, Garnett GP, Hallett TB. Examining the promise of HIV elimination by 'test and treat' in hyper-endemic settings. AIDS. 2010;24(5):729.
- [14] Bigna JJ, Plottel CS, Koulla-Shiro S. Challenges in initiating antiretroviral therapy for all HIV-infected people regardless of CD4 cell count. Infect Dis Poverty. 2016;5(1):85.
- [15] Hayes R, Sabapathy K, Fidler S. Universal testing, and treatment as an HIV prevention strategy: research questions and methods. Curr HIV Res. 2011;9 (6):429–45.
- [16] Brown LB, Ayieko J, Mwangwa F, Owaraganise A, Kwarisiima D, Jain V, et al. Predictors of retention in HIV care among youth (15–24) in a Universal Testand-Treat setting in Rural Kenya. J Acquir Immune Defic Syndr. 2017;76 (1): e15–8.

[17] Wolf HT, Halpern-Felsher BL, Bukusi EA, Agot KE, Cohen CR, Auerswald CL. "It is all about the fear of being discriminated [against]. . . the person suffering from HIV will not be accepted": a qualitative study exploring the reasons for loss to follow-up among HIV-positive youth in Kisumu, Kenya. BMC Public Health. 2014; 14:1154.

[18] MacKenzie RK, Lettow M, Gondwe C, Nyirongo J, Singano V, Banda V, et al. Greater retention in care among adolescents on antiretroviral treatment accessing "Teen Club" an adolescent-centred differentiated care model compared with standard of care: a nested case—control study at a tertiary referral hospital in Malawi. J Int AIDS Soc. 2017;20(3): e25028.

[19] Tweya H, Gugsa S, Hosseinipour M, Speight C, Ng'ambi W, Bokosi M, et al. Understanding factors, outcomes, and reasons for loss to follow-up among women in Option B+ PMTCT programme in Lilongwe, Malawi. Trop Med Int Health. 2014;19(11):1360–6.

[20] Chan AK, Kanike E, Bedell R, Mayuni I, Manyera R, Mlotha W, et al. Same day HIV diagnosis and antiretroviral therapy initiation affects retention Option B+ prevention of mother-to-child transmission services at antenatal care in Zomba District, Malawi. J Int AIDS Soc. 2016;19(1):20672. [21] Lettow M, Bedell R, Mayuni I, Mateyu G, Landes M, Chan AK, et al. Towards elimination of mother-to-child transmission of HIV: performance of different models of care for initiating lifelong antiretroviral therapy for pregnant women in Malawi (Option B+). J Int AIDS Soc. 2014;17(1):18994. [22] Jasseron C, Mandelbrot L, Dollfus C, Trocm e N, Tubiana R, Teglas JP, et al. non-disclosure of a pregnant woman's HIV status to her partner is associated with non-optimal prevention of mother-tochild transmission. AIDS Behav. 2013; 17(2):488-97.