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Treatment outcomes among HIV-positive adolescents initiated on antiretroviral therapy in Sedibeng district, Gauteng

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TREATMENT OUTCOMES AMONG HIV-POSITIVE ADOLESCENTS INITIATED ON ANTIRETROVIRAL THERAPY IN SEDIBENG DISTRICT, GAUTENG

Submitted in partial fulfilment of the requirements for the degree of

Master of Public Health in Maternal and Child Health,

School of Public Health,

Faculty of Health Sciences,

University of the Witwatersrand,

Johannesburg, South Africa,

by

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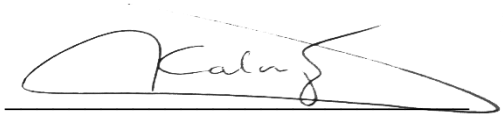
FEBRUARY 2022

Declaration

I, Njiba Kalonji-Makaloni, hereby, declare that the work contained in this research report is my original work unless otherwise acknowledged. No part of this report has been submitted in the past or is being submitted for a degree or examination at any other university or institution of higher education. I designed the study, analysed the data, and wrote the current report. I recognize the help I have received from my supervisors Prof Olufemi Babatunde Omole and Prof Lee Fairlie further declare collaboration with other scientists during this project. Parts of this work has been selected and/ or for publication with peer-reviewed journals.



Njiba KALONJI-MAKALONI

Date; 28/02/2022

Acknowledgements

It was told to us at the beginning of the journey some years back that many people attempt the journey to a master's degree but not all of them make it to the finish line. For me, it is a great personal honour that I could make it to the end.

I am, nonetheless, indebted to many with whom I have interacted and worked throughout this journey. I am grateful to God Almighty for the gift of life, the strength to carry this work to its end.

I thank my supervisors, Prof Lee Fairlie and Prof Olufemi Babatunde Omole for how they empowered me to do and complete my research. I am grateful to both of you for providing the necessary guidance.

Thank you to the staff and colleagues from the University of the Witwatersrand, my friends and my family who were supportive at different levels.

I also wish to thank the staff from the Sedibeng District Health Information Service for facilitating access to the database.

Dedication

I would like to dedicate this master's dissertation to my husband Kalam Makaloni, my best friend for the last 27 years…

To him and my three children Dorty Ange Sanduk Makaloni, Chloé Anzor Makaloni, Kevin Kalonji Makaloni, I will forever be indebted to them for their unyielding support throughout my master's journey. Thank you for always believing in me.

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CHAPTER 1
Introduction and overview

1. Introduction

1.1. Background

Adolescence is a transition period in age between 10 and 19 years (1). In 2019 there were 1.2 billion adolescents, globally, with the majority living in under-developed countries. These adolescents, especially young women, continue to be affected disproportionately by the human immunodeficiency virus (HIV). In 2019, about 170 000 new HIV infections were registered in this population group worldwide (2). In Sub-Saharan African, the world region disproportionally impacted by HIV epidemics, five in six new infections among adolescents between 15–19 years are among girls (3).

In 2018, South Africa had the highest HIV burden worldwide with an estimated 7.5 million people HIV infected and 200 000 new infections recorded. Alongside women of reproductive age, adolescents generally compose an important epidemiological group in terms of morbidity and mortality around the world, owing in part to increased risk of disengagement with care during the transition from paediatric to adolescent HIV programmes (4,5). In 2018, about 720000 adolescents were living with HIV in South Africa; among these, there were 37200 new infections (6).

In order to work towards the eradication of HIV, the 90–90–90 targets in the HIV programme were set by the United Nations General Assembly. This entailed that by 2020, 90% of people living with HIV should know their HIV status, 90% of those diagnosed HIV positive should be initiated on antiretroviral therapy (ART), and 90% of those receiving ART should be virally suppressed (7).

In light of the targets of the 90-90-90 strategy, recent data showed that only 47% of HIV-positive youths had access to ART in 2018 (6). Data from a national survey conducted in 2017 showed that among people 15 years and above who were HIV-positive, 84.8% knew their HIV-positive status, among them 70.7% were on ART, and 87.4% of these had their viral load suppressed (8). Increasing access to ART among adolescents is key to controlling the spread of infections to their sexual partners and improving and prolonging the health of adolescents living with HIV (6,9,10). Despite these known benefits, life-long ART has created several other challenges such as difficulty with retaining adolescents on ART (11).

Retention on ART has been noted as a global challenge particularly for adolescents (5,12). Treatment adherence and retention into care constitute the main challenges facing ART programmes in Southern Africa (13–16). At a global scale, 74% of adolescents who tested HIV-positive are retained into care at 24 months and 60% at 60 months (17). Data published in a 2015 metanalysis review of six studies conducted in South Africa reported a rate of retention into care of 83% at twenty-four months on ART (18), highlighting that other factors such as psychosocial and environmental conditions affect long-term success of HIV care.

Another South African study showed that only 84% of adolescents on ART achieve a suppression of their viral load (<400 copies/mL) during the first twelve months from ART initiation, declining with time to 77.4% and 68.8% at 12 and 24 months respectively. This trend has been closely observed in several other cohorts in South Africa and elsewhere (11,13,19–21). Given the wide differentiation between geographical areas and communities (resourced vs non-resourced, urban vs rural etc.), it is difficult to capture the success of ART in a few cohorts (22–25). There is a need for studies in different contexts and areas, especially where HIV treatment outcome measures have not been explored in detail. These data are important for tracking the success of treatment interventions such as the 90-90-90 strategy (8,26).

1.2. Statement of the problem

The rapid expansion of the ART programme globally and in South Africa has also seen a considerable increase in the number of studies analysing the success of the treatment (13,19,27,28). However, in view of the large exposure scenarios and wide socio-economic differences, treatment outcomes are projected to vary across different settings (5,12,24). Information is lacking on retention in care and LFTU (define acronyms the first time) for HIV-positive adolescents attending HIV care in the Sedibeng Health District. Moreover, adolescence is also a period with high-risk for disengagement from care, resulting in poor treatment outcomes with low viral load suppression rate (12,22,23). Whether this is true for the Sedibeng district is not known. Such area-specific information is needed, both to guide the implementation of targeted national interventions and bridge research gaps regarding treatment outcomes among HIV-positive adolescents.

1.3. Rationale and motivation for the study

Several studies have attempted to explore outcomes of ART or retention in care among adolescents in South Africa (11,13,16,27–29) but none have included the Sedibeng district. In

addition, variations in treatment contexts and psychosocial environments may make generalization of their findings to our study setting problematic. Therefore, it is important to explore treatment outcomes trends more broadly in South Africa to inform policies and interventions.

1.4. Purpose of the study

The purpose of this study is to provide local evidence regarding HIV treatment outcomes among adolescents and build and advance the understanding of existing knowledge on ART. It is envisaged that the results will benefit the HIV program in Sedibeng Health District by identifying factors affecting HIV care and treatment success in this context.

1.5. Aim and objectives

1.5.1. Aim

To assess ART treatment outcomes among adolescents aged 10-19 years in the Sedibeng District from 2010 to 2015.

1.5.2. Objectives

a) To obtain and describe baseline (Time of ART initiation) demographic information including age and sex, pregnancy status (if female), type of facility where ART was initiated, ART regimen, and immunologic characteristics.
b) To determine the immunologic (CD4+ T-Cells counts) and virologic outcomes (viral loads) at 6, 12, 24, 36, 48 and 60 months after ART initiation.
c) To determine the time to viral load suppression.
d) To explore the associations between those remaining in care, LTFU, transfer out, death, viral loads, and demographic variables (age, sex, ART regimen and type of facility).

2. Methods

2.1. Study design

This was a cross sectional study using retrospective review of routinely collected data of ART naïve patients from the time of initiation of treatment in 2010 and followed up to 60 months post initiation (See Figure 2.1).

2.2. Study Setting

The study was conducted in the Sedibeng District, Gauteng Province, Republic of South Africa. Sedibeng District is situated in the Southern part of Gauteng Province and comprises three sub-districts namely, Emfuleni, Midvaal and Lesedi.

According to the District Health Information System (DHIS), in 2010, Sedibeng's general population was estimated at 867 625, of which 152,089 were adolescents aged 10-19 years old (30). The same reports showed that the proportion of males and females were equal in the adolescent population as well as in the total population. Sedibeng DHIS data is collected from one regional hospital, two district hospitals and 39 primary health care clinics (31).

2.3. Study population and sampling

The study population consisted of adolescents aged between 10 and 19, HIV-positive, treatment naïve, initiated on ART at healthcare facilities registered in the Sedibeng DHS. In the present study, the adolescent population was categorized into young (10-14years) and older adolescents (15-19 years), respectively, in line with categories used in most literature (27,28).

All patients who were initiated on ART from 1st January 2010 until December 31st of the same year were identified on the Tier.Net and their data extracted for the study.

Inclusion criteria for the study were:

- Being registered on Tier.Net (a government online registry Software for routinely collected data for HIV since 2018 that includes tuberculosis (TB) patients)(32).
- HIV-positive adolescents 10-15 years with CD4 count $\leq$ 350 cells mm^{-3} or those meeting the WHO clinical staging 4 or were co-infected with TB.

- HIV-positive adolescents 16-19 years with a CD4 count ≤ 200 cells mm^{-3} or those meeting the WHO clinical staging 4 or were co-infected with TB, and
- HIV-positive pregnant adolescents with CD4 count ≤ 350 cells mm^{-3} or corresponded to stage 3 or 4 or individuals co-infected with TB (33).

Patients were excluded from the final sample population if their folders could not be found in the facilities or if at least 30% of their information could not be retrieved either on Tier.Net registry or hardcopy files or they were not ARV naive. Essentially, if the absence of vital information regarding the sex, age, regimen type, 3 viral load data monitored successively or at different points during the sixty months were missing, the patient was dropped from the final list of participants.

A total 259 files were retrieved, of which 254 were included in the final analysis.

2.4. Measurement tool and data collection

ART clinical and treatment data are routinely recorded at the PHC clinics, first on a hardcopy, and then entered in the TIER.Net software.

TIER.Net is a three-tiered Software used in government healthcare facilities to capture information of all HIV positive patients initiated on ART at a point in time. TIER.Net evolved since its introduction in 2010 to include in addition to the HIV module, another module focusing on TB treatment.

Regarding recruitment, the investigators requested and received permission to access and review participants' medical health records from the Sedibeng DHS management. The investigators first reviewed the data from the Tier.Net Software and obtained hardcopy files of patients whose information were incomplete on the software, if needed to bridge any information gap. The main input data from the HIV modules included patients' demographic information, i.e.: age, sex, and contact details, treatment data, i.e. regimen type, treatment outcomes including death, LTFU, transfer out and remaining into care (34).

The participants' HIV treatment records were also extracted from the Tier.Net software and recorded primarily on a standard Excel datasheet which was designed by the researchers, then tested and pre-tested for ease of recording and fitness for data analysis. The data was reviewed and edited manually by the principal investigator. Data gathering and recording started from

the date each participant was initiated on ART in January 2010 till the end of the study at 60 months or when the patient died if, sooner. Unpublished TIER.Net HIV treatment covering a period of five years, from January 1st, 2010, to December 31st, 2015, were extracted for analyses in this report. Extracted data included specific patient regimen code, and demographic information (healthcare centre for ART initiation, age at the start of ART, sex, and for female, pregnancy status) specific for each patient. Treatment outcome data were also recorded and included patient's immunologic (CD4 count) and virologic (viral load) progression indicators at baseline (CD4 count only) and at 6, 12, 24-, 36-, 48- and 60-months' intervals and whether a participant died, was LTFU, remained in care or was transferred out.

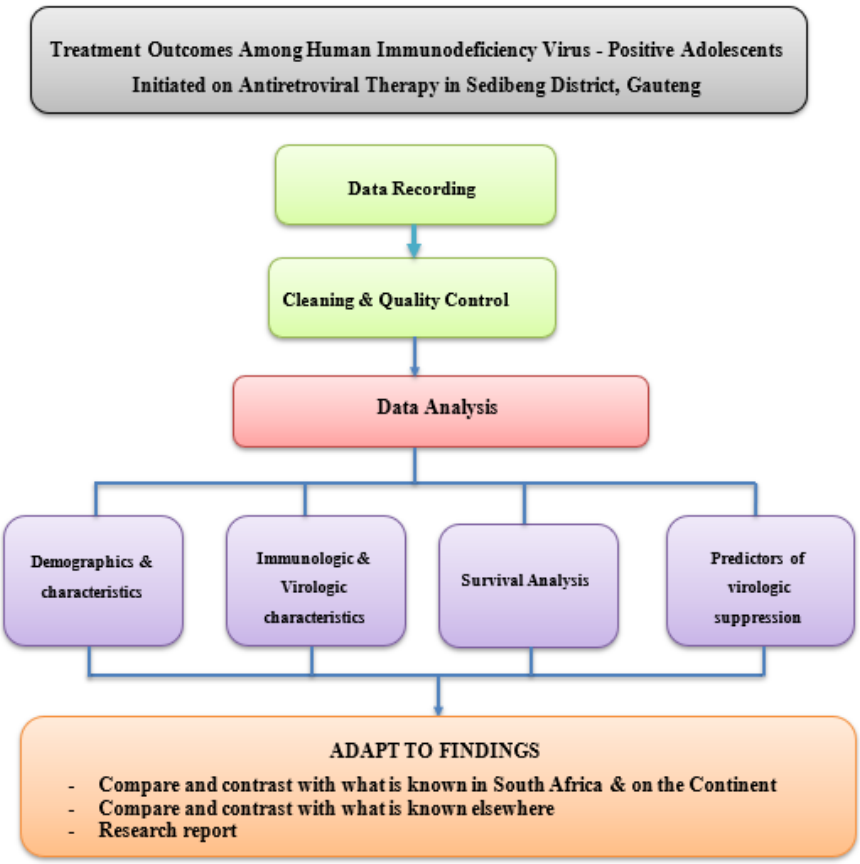


Figure1: Schematic diagram of the overall study design.

2.5. Data management & quality control

To ensure the reliability of data, two independent data collectors (clinic data clerks) extracted and recorded data, while the other investigators checked the recorded data for coherence, consistency, and corrected errors if any. Where participants' data were not fully complete on Tier.Net, the researcher followed up with the clinics and reviewed the hard copy of the

participant's medical files, recorded the missing information on Tier.Net and then transferred the information into Excel. A total of 259 files were retrieved of which 254 were included in the analysis. The remaining five had substantial incomplete information (>30%).

In order to protect the patient's confidentiality and the medical records' integrity as per the clinical research code, a participant identification number (PIN) was assigned to each patient by the principal investigator. The PIN was linked to the medical record of each patient, and the data was kept in a password-controlled database on a password-controlled laptop and only the principal investigator had access to the final data.

2.6. Data analysis

STATA (Stata Corp, Texas, USA) version 15 was used to analyse data. The student defined the analytical framework, computed, cleaned, and analysed the dataset along with statisticians from the University of Witwatersrand and a private biostatistician.

Participants were stratified into two age groups: 10-14 years and 15-19 years. The demographic and treatment information were described by age group using proportions for categorical variables and median and interquartile range (IQR) for continuous variables. Survival probabilities from ART initiation for the sixty months of follow-up were calculated using the Life table and Kaplan-Meier methods. The survival time was computed in months with the time interval between the date of ART initiation and events experienced by the participants. The log-rank test was used to test whether observed differences in survival experiences were statistically significant. All variables with a p-value ≤ 0.05 were considered statistically significant. Finally, the Cox proportional hazard regression model was fitted to identify predictors of virologic failure among participants. The results are reported as tables and figures.

2.7. Ethical clearance and approval

Ethical clearance and approval were obtained from the Wits Human Research Ethics Committee (HREC), Faculty of Health Sciences with reference no M160845 (Annexure A). Permission to use the data was obtained from the Sedibeng District Management for access to Tier.Net (Annexure B).

Table 2.1: Data variables of participants extracted from the Tier.Net.

Measures	
Demographic information	
Sex	Male or Female
Age	Defined from 10 to 19, then divided into two groups 10 to 14 and 15 to 19
Pregnancy status	a female patient will be defined as pregnant or not pregnant when starting ART
Facility type	Hospitals and clinics
Treatment Outcomes	
Remain in care	a patient who was still on ART in Sedibeng at the end of the study period (60 months).
Died	a patient-reported dead while on treatment.
Transferred out	a patient, who for any reason, was transferred to a different district health service then Sedibeng.
LTFU	a patient who has failed to attend the clinic for ≥12 weeks but was not reported dead or transferred out.
ART start/ initiation date	The date when a patient started ART.
ART initiation guidelines at time of study	• HIV-positive adolescents 10-15 years with CD4 count ≤ 350 cells mm^{-3} or those meeting the WHO clinical staging 4 or were co-infected with TB. • HIV-positive adolescents 16-19 years with a CD4 count ≤ 200 cells mm^{-3} or those meeting the WHO clinical staging 4 or were co-infected with TB, and • HIV-positive pregnant adolescents with CD4 count ≤ 350 cells mm^{-3} or corresponded to stage 3 or 4 or individuals co-infected with TB
Date of outcome	The date one of the outcomes is confirmed.
CD4 count Baseline	The CD4 Cell count of the patient when they initiate treatment, reported in cells per mL.
Viral load	Viral load measured at different points in time, i.e.: six months, twelve months, etc. This was reported as copies per mL. In the context of this study, viral load suppression data are described (1) <50 copies/mL and (2) <1000 copies/mL. When copies of HIV cannot be detected by standard viral load tests, they are expressed as viral load <50 copies/mL, or undetectable viral load (35).

Results

A total of 259 participants' records were retrieved from Tier.Net software from 1st January 2010 to 31st December 2010. After data cleaning and editing, 5 patient files were removed from the final analysis because of substantial incompleteness (≥30%).

2.8. Socio-demographic characteristics of participants

Most participants were aged 15-19 years (η = 132; 52%) - Figure 3.1. The median age of the participants was 15 years (IQR: 12-18).

In terms of sex, 173 (68.1%) were females (Table 3.1). Most participants attended their ART visits in PHC clinics (η = 170, 70.9 %), with only 74 (29.1%) initiated in hospitals (Table 3.1).

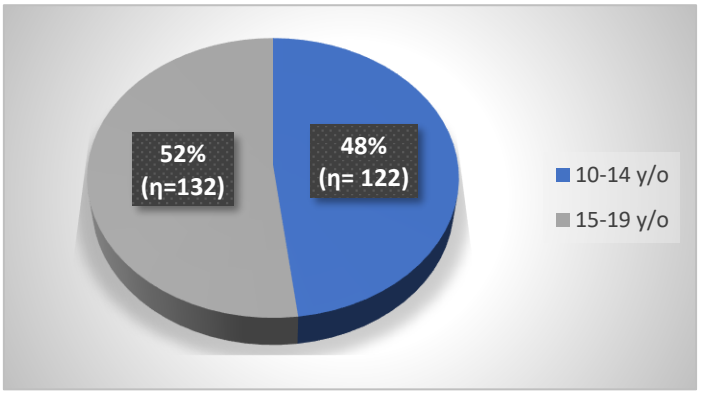


Figure 3.1: Age groups distribution (η= 254).

Table 3.1: Participants distribution by sex, type of facility (η = 254).

Characteristics		age (years)						
		10-14 N=122		15-19 N=132		Total N=254		*p* value
		n	Col %	n	Col %	n	Col %	
Sex	**Female**	61	50	112	84.8	173	68.1	**<0.001**
	Male	61	50	20	15.2	81	31.9	
Type of facility	**Clinic**	86	70.5	94	71.2	180	70.9	
	Hospital	36	29.5	38	28.8	74	29.1	

2.9. Pregnancy status of female participants

As shown in Figure 3.2, there was no pregnancy reported for the participants in the younger age group, but in the older group, 20.5 % (η =23) were pregnant at initiation of ART.

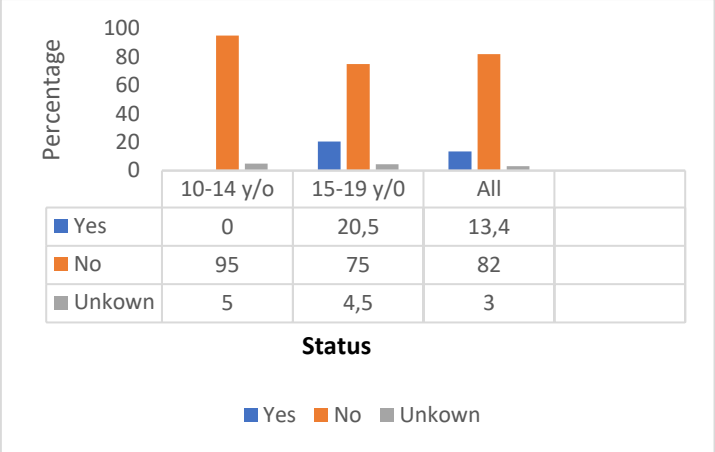


Figure 2.2: Proportion of female participants who were pregnant at the initiation of ART (η= 173**).**

2.10. Treatment regimen characteristics of participants

Table 3.2 and 3.3 present the findings of the participants' regimen at the beginning and the end of the study stratified by sex. The regimens were grouped into three categories: Efavirenz, Nevirapine and Lopinavir/ritonavir-based regimens. Most participants 232 (91.3 %) were likely to be initiated on an efavirenz-based regimen (Table 3.2). The remaining 8.7% participants included 7.5% (η =19) initiated on Nevirapine-based regimen and 1.2% (η =3) on Lopinavir/ritonavir-based regimen. Most participants remained on Efavirenz-based regimen (n=247; 97.8%) at the point of exit in the study (Table 3.3).

Female adolescents were mostly initiated on an Efavirenz -based regimen (*p* 0.017). There was, however, no statistical difference (***p*** 0.249) between male and female adolescents taking either regimen at the time the participants exited the study. For the 132 participants remaining in care, 110 (83.3%) were taking efavirenz-based regimens and 19 (14.4%) and 3 (2.28%) were on Nevirapine and lopinavir/r-based regimens, respectively.

Table 3.2: Type of participant regimen at baseline and when they exited the study (η = 254).

Characteristics		Sex						
		Female		Male		Total		*p*-value
		n	%	n	%	n	%	
Regimen at Baseline (Categories)	Efavirenz	154	89	78	96.3	232	91.3	**0.017**
	Nevirapine	18	10.4	1	1.2	19	7.5	
	Lop/r	1	0.6	2	2.5	3	1.2	
Last ART Prescription Code (Categories)	Efavirenz	168	97.1	79	97.5	247	97.2	0.249
	Nevirapine	5	2.9	1	1.2	6	2.4	
	Lop/r	0	0	1	1.2	1	0.4	

Table 3.3: Last regimen prescription for participants remaining in care (η = 132).

Variables	N	Percent.
Efavirenz -based regimen	110	83.33
Nevirapine -based regimen	19	14.4
Lop/r -based regimen)	3	2.28
Total	132	100

2.11. Treatment outcomes

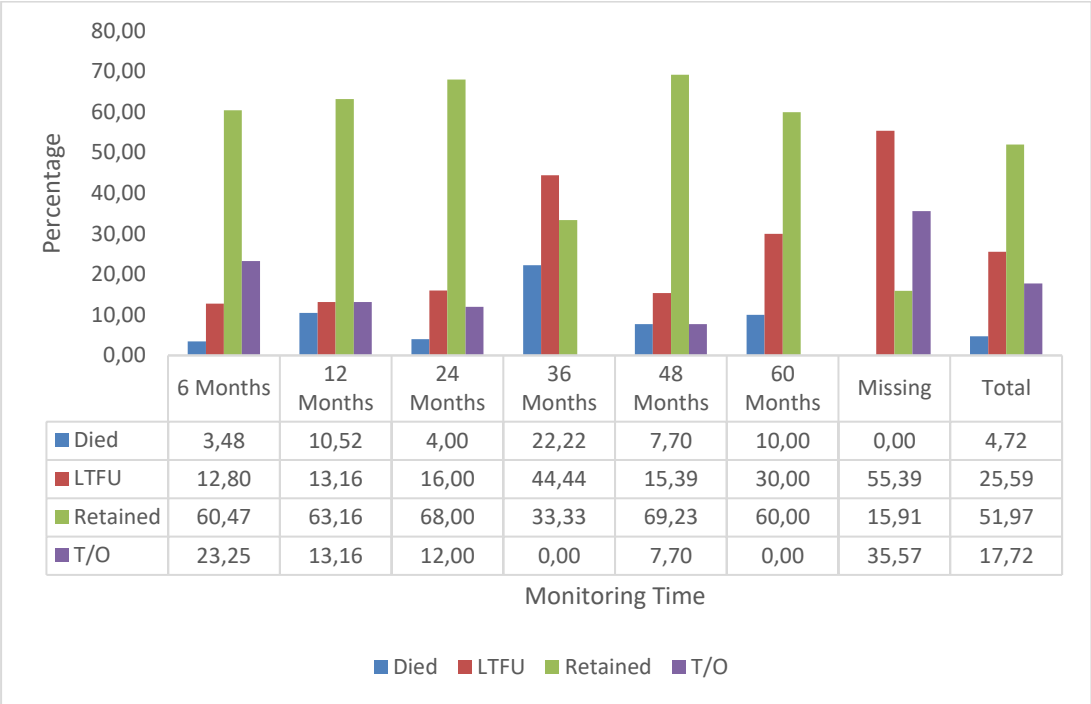
A total of 132 (52%) participants remained into care at the end of the study period (Table 3.4). Of this number, 97 (73.5%) were initiated in PHC clinics.

As shown in Table 3.4 and Figure 3.3, the proportion of those who died during the study was 4.7% (η =12), while most deaths occurred around 36 months, with a higher proportion (η =8) amongst the older adolescents. A total of 65 (25.6%) were LTFU, and 45 (17.8%) were transferred out.

There was no statistical difference in terms of treatment outcomes between those who were initiated on ART at hospitals and those initiated in PHC clinics (p <0.181).

Table 3.4: Outcome by facility type (η = 254).

Outcome	Clinic		Hospital		Total	
	n	%	n	%	n	%
Died	4	1. 57	8	3.14	12	4.7
Lost to follow up	16	21.6	49	27.2	65	25.6
Remain in care	35	47.3	97	53.9	132	52
Transferred/Moved out	19	25.7	26	14.4	45	17.7
Total	74	100	180	100	254	100
***p*-value: <0.181 (Fisher's exact test)**						



	6 Months	12 Months	24 Months	36 Months	48 Months	60 Months	Missing	Total
Died	3,48	10,52	4,00	22,22	7,70	10,00	0,00	4,72
LTFU	12,80	13,16	16,00	44,44	15,39	30,00	55,39	25,59
Retained	60,47	63,16	68,00	33,33	69,23	60,00	15,91	51,97
T/O	23,25	13,16	12,00	0,00	7,70	0,00	35,57	17,72

Figure 3.3: Outcome's trend over time (η =254).

Legend: Figure 3.3 shows that the highest percentage of LFTU and death occurred around 36 months post ART initiation.

2.12. Immunologic outcomes

Table 3.5 presents the immunologic outcomes over time by age groups. Participants were monitored at 6, 12, 24, 36, 48- and 60-months intervals. Overall, the median CD4 count increased significantly (p <0.001) with time spent on ART across the two age groups. The median baseline CD4 count for younger adolescents was 135 cells mm^{-3} (IQR: 32-232) and 172 cells mm^{-3} (IQR: 62-252) for older adolescents. Older adolescents had a higher median CD4 count throughout the study period; however, the difference was not statistically significant (all p's > 0.05) at each point in time.

Table 2.5: Immunological outcome of participants (η = 254).

Immunologic characteristics	10-14 years old			15-19 years old			All			
	n	median	IQR	N	median	IQR	n	median	IQR	*p* value
Baseline CD4	113	135	32-232	130	172	62-252	243	161	40-245	0.371
CD4 at 6 months	64	295	173.5-547.5	60	398.5	263.5-549	124	371	204-549	0.212
CD4 at 12months	62	440	226-653	61	376	291-569	123	413	245-592	0.578
CD4 at 24months	65	463	321-712	54	438	252-627	119	462	268-676	0.242
CD4 at 36months	70	522.5	280-708	50	527	323-720	120	525	319-711.5	0.719
CD4 at 48months	66	508.5	236-661	48	581	352.5-770	114	550.5	297-729	0.091
CD4 at 60months	58	493.5	272-680	35	560	367-715	93	514	297-695	0.141
***p*-value <0.001**										

Figure 3.4 gives the combined CD4 count progression considering sex and age characteristics. The median CD4 count for older males was lower compared to that of the same age group in females (***p* 0.007**). Females appeared to have a significantly progressive CD4 count increase compared to males **(*p* 0.007)**.

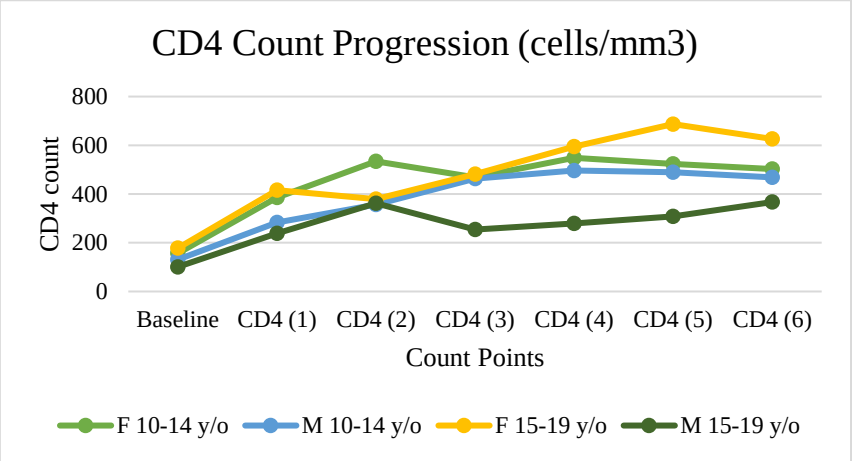


Figure 3.4: Comparison of CD4 count progression (cells/mm3) according to sex and age groups (η =254**) (*p* 0.007).**

2.13. Virologic outcomes

Table 3.6 presents the findings of the virological outcome by age group. Out of the 123 viral loads done at 6 months, 54 were below 200 copies/mL. Younger adolescents had a statistically significant higher (*p* 0.023) median viral load, 541 copies/mL at six months compared to older ones whose median viral load was 124 copies/mL at the same time period. However, the overall increase or decrease in viral load was not statistically significant for both younger (*p* 0.711)

and older (*p* 0.078) adolescents and both groups combined (*p* 0.222). It was also noted that viral load increased in both age groups by 36 months post ART initiation, though, the differences were not statistically significant (*p* 0.934).

Table 3.6: Virologic outcome by age groups (η = 254).

Virological characteristics	10-14 years old			15-19 years old			All			
	n	median	IQR	n	median	IQR	n	Median	IQR	p-value
VL at 6months	69	541	124-2602	54	124	40-1169	123	323	101-1889	**0.023**
VL at 12months	65	237	110-775	51	161	124-1795	116	198.5	124-1304	0.849
VL at 24months	76	171	72-3171.5	56	124	124-1499	132	137.5	116-2696.5	0.945
VL at 36months	78	354.5	53-18961	55	188	124-1739	133	233	99-3437	0.934
VL at 48months	71	147	61-11550	50	124	41-419	121	124	59-2322	0.111
VL at 60months	84	124	101-2480	48	124	40-452	132	124	66.5-1940	0.100
***p*-value**		0.711				0.078			0.222	

Table 3.7 and Figure 3.5 showed that there was a significant **(*p* 0.002)** variation in viral load for older males compared to the younger males and the females. The study found that older females were more likely to experience viral loads below 1000 copies/mL than their male counterpart at 24 (***p* 0.031**) and 60 (*p* **0.047**) months.

Table 3.7: Virologic outcome by Sex and age combined (η = 254).

Virologic characteristics	10-14 years old					15-19 years old				
	Female		Male			Female		Male		
	N	Median (IQR)	N	Median (IQR)	p-val	N	Median (IQR)	N	Median (IQR)	p-val
VL at 6months	**35**	810(124-3869)	**34**	361(124-1579)	0.325	**48**	148.5(40-1183.5)	**6**	124(101-621)	0.978
VL at 12months	**34**	176(60-2712)	**31**	244(124-775)	0.541	**43**	141(124-1045)	**8**	689.5(124-13244)	0.333
VL at 24months	**38**	270(82-17316)	**38**	154.5(62-1145)	0.588	**49**	124(124-1004)	**7**	3285(124-189162)	**0.031**
VL at 36months	**40**	491.5(107.5-16188)	**38**	152.5(40-22157)	0.462	**47**	168(124-1246)	**8**	1013.5(178.5-12084)	0.330
VL at 48months	**36**	167(111.5-4686)	**35**	124(50-39506)	0.564	**41**	124(49-343)	**9**	299(40-10273)	0.178
VL at 60months	**39**	124(103-3600)	**45**	124(99-1090)	0.536	**40**	124(40-242.5)	**8**	2106(124-10145.5)	**0.047**
***p*-value: 0.002**										

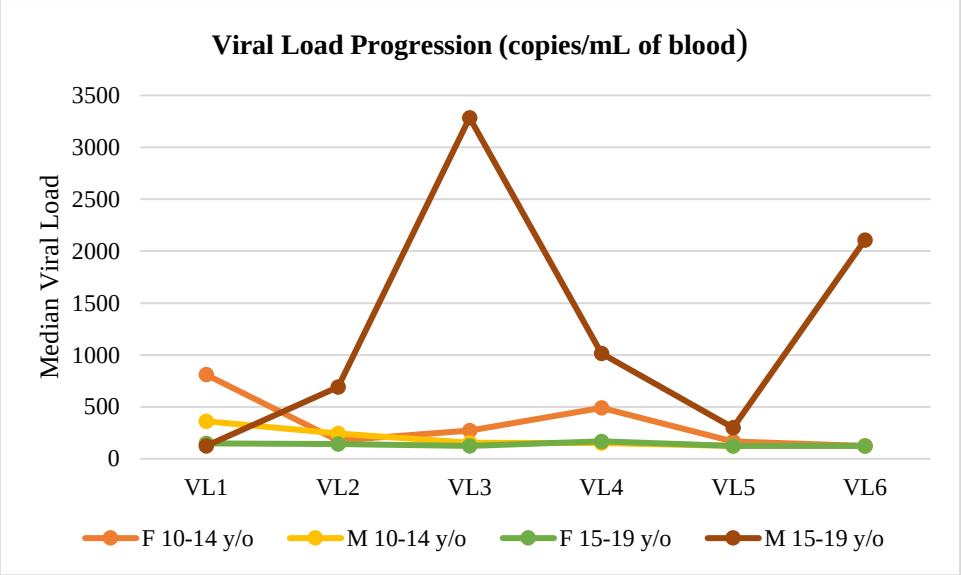


Figure 3.5: Viral Load Progression (copies/mL) combining age groups and sex (η = 254) (*p* 0.002).

Table 3.8 presents the variation in viral load below 1000 copies/mL grouped by age, sex, and facility type.

Of the 116 viral loads done at 12 months, 85 (73,3%) had a viral load below 1000 at 12 months. At the end of the study period (60 months), of the 132 viral loads done, 94 (71%) were below 1000 copies/mL.

Table 3.8: Comparison between virally suppressed and unsuppressed adolescents (<1000 copies/mL).

Time scale	Viral Load: Suppressed (<1000 copies/mL) by Sex						
	Male		Female		Total		
	η	%	n	%	H	%	*p*-value
Suppressed 6m	29	72.5	54	65.1	83	67.5	0.409
Unsuppressed 6m	11	27.5	29	34.9	40	32.5	
Suppressed 12m	28	71.8	57	74	85	73.3	0.798
Unsuppressed 12m	11	28.2	20	26	31	26.7	
	Viral Load: Suppressed (<1000 copies/mL) by Age						
Time Scale	**10-14 y/o**		**15-19 y/o**		**Total**		
	η	%	n	%	η	%	*p*-value
Suppressed 6m	43	62.3	40	74.1	83	67.5	0.167
Unsuppressed 6m	26	37.7	14	25.9	40	32.5	
Suppressed 12m	49	75.4	36	70.6	85	73.3	0.562
Unsuppressed 12m	16	24.6	15	29.4	31	26.7	
	Viral Load: Suppressed (<1000 copies/mL) by Type of facility						
Time Scale	**Hospital**		**Clinic**		**Total**		
	η	%	η	%	η	%	*p*-value
Suppressed 6m	34	60.7	49	73.1	83	67.5	0.143
Unsuppressed 6m	22	39.3	18	26.9	40	32.5	
Suppressed 12m	40	67.8	45	78.9	85	73.3	0.175
Unsuppressed 12m	19	32.2	12	21.1	31	26.7	

On association testing, the proportion of males (72.5%, η = 29) with suppressed levels at six months were higher than those of females (65.1%, η = 54), but the difference was not statistically significant (all *p values* >0.05).

In terms of age, about 75.4% (η = 49) of younger adolescents had a viral load below 1000 copies/mL at twelve months. This number included only patients who had their viral loads assessed or reported at such a time. The proportion of older adolescents who had a viral load below 1000 copies/mL at six months dropped from 74.1% (η = 40) to 70.6% (η = 36) at twelve months. Nonetheless, there was no statistical difference (all *p's* >0.05) between those with viral load below 1000 copies/mL and those who had higher viral loads.

In terms of facility types, 49 (73.1%) and 45 (78.9%) participants whose treatment was initiated at PHC clinics were virally suppressed at six and twelve months, respectively, compared to less than 70% of those initiated in hospitals. However, there were no statistically significant differences (all *p*'s >0.05) between those with viral loads below 1000 copies/mL and those with higher viral loads.

On association testing (< 50 copies/mL), younger adolescents were significantly (*p* 0.041) more likely to have higher viral loads than older adolescents at six months (Table 3.9). However, no statistical difference (*p* 0.375) was detected at 12 months. No statistical differences (*p* >0.05) were also found between those who were virally suppressed and those who were not in terms of sex and facility type.

Table 3.9: Comparison between virally suppressed and unsuppressed adolescents (<50 copies/mL).

Time scale	Viral Load: Suppressed (<50 copies/mL) by Sex						
	Male		Female		Total		
	η	%	η	%	η	%	*p*-value
Suppressed 6m	7	17.5	19	22.9	26	21.1	0.37
Unsuppressed 6m	33	82.5	64	77.1	97	78.9	
Suppressed 12m	5	12.8	15	19.5	20	17.2	0.37
Unsuppressed 12m	34	87.2	62	80.5	96	82.8	
	Viral Load: Suppressed (<50 copies/mL) by Age						
Time Scale	**10-14 y/o**		**15-19 y/o**		**Total**		
	η	%	η	%	η	%	*p*-value
Suppressed 6months	10	14.5	16	29.6	26	21.1	**0.041**
Unsuppressed 6months	59	85.5	38	70.4	97	78.9	
Suppressed 12months	13	20	7	13.7	20	17.2	0.375
Unsuppressed 12months	52	80	44	86.3	96	82.8	
	Viral Load: Suppressed (<50 copies/mL) by Type of facility						
Time Scale	**Hospital**		**Clinic**		**Total**		
	η	%	η	%	η	%	*p*-value
Suppressed 6m	11	19.6	15	22.4	26	21.1	0.71
Unsuppressed 6m	45	80.4	52	77.6	97	78.9	
Suppressed 12m	13	22	7	12.3	20	17.2	0.164
Unsuppressed 12m	46	78	50	87.7	96	82.8	

2.14. Kaplan Meir Estimate of Time to viral load ≤ 1000 copies/mL of participants at Sedibeng Health District

The Kaplan Meir failure estimates are shown in Figure 3.6. Participants were stratified by sex, age, facility type, and type of regimen. The probability of viral load suppression increased quickly in the 1st year of ART treatment. In terms of facility type, the probability of viral load suppression is almost constant after twelve months of treatment. Participants in PHC facilities

had a slower progression compared to those initiated in hospitals, but the difference was not statistically significant (*p* 0.3265, Log-rank test).

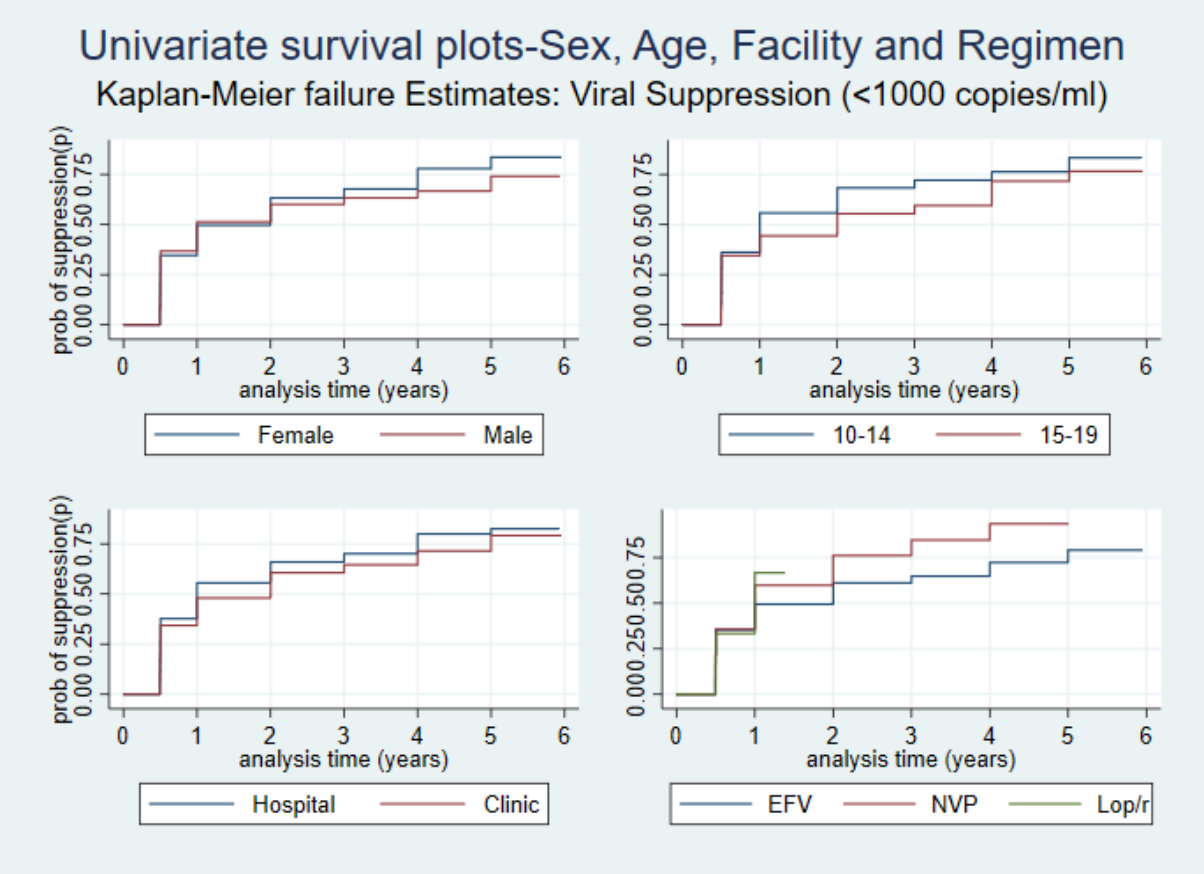


Figure 3.6: Kaplan Meir Survival estimates of participants presented by sex, age at the start of ART, facility type, and baseline regimens (2010/01/01 to 2015/10/01).

At the end of the study, younger adolescents showed a higher probability of viral load suppression than older adolescents, but there was no statistically significant difference between groups (*p* 0.2539). Participants initiated on the Nevirapine-based regimen also showed a higher probability of viral load suppression compared to those initiated on other regimens. However, the differences were not statistically significant (*p* 0.3076).

Generally, the average incidence of virologic failure was estimated at 2.59 per 1000 person-months (95% CI: 2.05, 3.32). The younger adolescents had a higher incidence rate (IR) of virologic failure, 2.78 (95% CI: 2.06, 3.85), compared to older adolescents who had an IR of 2.36 (95% CI 1.64, 3.53) per 1000 person-months. Females experienced a virologic failure rate of 2.4 (95% CI: 1.78, 3.32) per 1000 person-months, which was lower than the 2.95 (95% CI: 2.05, 4.41) found in male participants. The incidence rate of virologic failure was 2.04 (1.50,

2.86) for participants who were initiated on ART at PHC facilities and twice as high, 4.03 (95% CI: 2.85, 5.89) for those who were seen in hospitals. The incidence of virologic failure was 2.67 (95% CI: 2.10, 3.44) per 1000 person-months for participants on Efavirenz-based regimen and 1.89 (95% CI: 0.61, 8.54) per 1000 person-months for participants on Nevirapine-based regimens.

The Cox regression model (Table 3.10) showed that the probability of experiencing virologic failure was not significantly different in males and females (*p* 0.87). Younger adolescents had a 6.11 increased risk of experiencing virologic failure compared to older adolescents. Participants with an initial low CD4 count had a 3.19 Hazard Ratio (HR) of virologic failure compared to those who were put on treatment with a high CD4 count. Those who were initiated at hospitals had virologic HR = 2.01 compared to those who attended ART in PHC clinics.

Table 3.10: The Cox regression multivariate analysis, the hazard ratio of suppression of ART participants at Sedibeng Health District, 2010-2016.

Variables		Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	*p*-value
Sex	*Male*	Ref		Ref	
	Female	0.95 (0.55,1.66)	0.87	1.62 (0.83,3.14)	0.156
Age	*15-19*	Ref		Ref	
	10-14	1.34 (0.76,2.35)	0.295	6.11 (1.15,32.32)	**0.033**
Facility	*Clinic*	Ref		Ref	
	Hospital	2.49 (1.45,4.27)	**0.001**	2.01 (1.12,3.61)	**0.019**
Regimen*	*EFV*	Ref		-	-
	NVP	0.487 (0.118,2)	0.275	-	-
BaselineCD4	-	0.998 (0.996,1.00)	**0.035**	0.998 (0.996,1.000)	0.113
Age*Sex	-	-	-	3.19 (1.01,10.09)	**0.048**

2.15. Association between remaining in care and age, sex, baseline regimen, baseline CD4 count as well as the type of facility (2010 to 2015)

In Table 3.11, female participants were more likely to be LTFU, transferred out or remain in care compared to male participants. The odds of death were equal for both sex (*p* 0.019).

In terms of age groups, older adolescents had a higher risk of death, and presented with increased risk of being transferred out or LTFU in comparison to young adolescents who mostly likely remained in care (*p* 0.001).

Furthermore, there is a significant difference in outcomes depending on the baseline CD4 count (*p* 0.049) with patients with the lowest median CD4 count at ART initiation having significantly (*p* 0.049) higher risk of death compared to those with higher baseline CD4 count. There was no statistical difference (*p* 0.468) observed between being LTFU, dying, transferred out during the study or, remaining into care and the type of regimen given to participants at the beginning of the study.

Table 3.11: Association between sex, age, baseline regimen, baseline CD4 count, facility type and clinical outcomes (2010-2015).

		Died		LTFU		Remain into Care		Transferred Out		Total		
Variables		**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	***p*-value**
Sex	Female	6	50	52	80	81	61	34	76	173	68	**0.019**
	Male	6	50	13	20	51	39	11	24	81	32	
Age	14-10 years old	5	42	22	34	80	61	15	33	122	48	**0.001**
	15-19 years	7	58	43	66	52	39	30	67	132	52	
Baseline Reg	Efavirenz-based regimen	11	92	59	91	122	93	40	93	232	92	0.468
	Nevirapine based-regimen	1	8	6	9	9	7	3	7	19	8	
	Lop/r based-regimen	0	0	0	0	1	1	2	5	3	1	
Facility Type	Hospital	5	42	19	29	40	30	30	67	94	37	**<0.001**
	Clinic	7	58	46	71	92	70	15	33	160	63	
		n	**Median (IQR)**	**n**	**Median (IQR)**	**n**	**Median (IQR)**	**n**	**Median (IQR)**	**n**	**Median (IQR)**	***p*-value**
Baseline CD4*[1] [N, Median (IQR)]	-	11	29 (10-135)	64	160.5 (58-281.5)	124	124 (39.5-225.5)	44	178 (117.5-261)	243	161 (40-245)	**0.049**

3.9 Results of multivariate logistic regression

As shown in Table 3.12, after adjusting for sex and facility type, those in the age group of 10 to 14 years had significantly (*p* 0.007) reduced the risk of being LTFU by 60% than the older

*[1] Because baseline CD4 count is a continuous variable, Kruskal-Wallis statistical test was used, and the values presented are rather median and IQR.

adolescents and of transfer out by 70% (*p* 0.003). Being initiated in hospital significantly (*p* <0.001) increased the risk of being transferred out compared to those initiated at the clinics.

Table 3.12: Multivariate analysis of participants on ART in Sedibeng District, Gauteng Province, South Africa, 2010 - 2015.

N=243	Died RRR (95% CI)	p-value	LTFU RRR (95% CI)	p-value	Transferred or Moved out	*p*-value
Sex						
Male	1.0		1.0		1.0	
Female	0.39 (0.11-1.43)	0.155	1.75 (0.82-3.73)	0.149	1.15 (0.49-2.7)	0.751
Age						
15-19	1.0		1.0		1.0	
10-14	0.31 (0.08-1.17)	0.084	0.4 (0.2-0.78)	**0.007**	0.3 (0.14-0.66)	**0.003**
Facility Type						
Clinic	1.0		1.0		1.0	
Hospital	1.85 (0.54-6.27)	0.325	1 (0.51-1.97)	0.995	5.03 (2.38-10.64)	**<0.001**

3. Discussion

This study investigated HIV treatment outcomes among adolescents in the Sedibeng District Health Services over a 5-year period. The main finding of the study is that there was an improvement in patients' CD4 count, however, overall, the treatment outcomes including viral suppression and patient retention in care were poor. This study supports the results of other national cohorts (27,29), and suggests that adolescents are a key population group for interventions aimed at improving retention in care, achieving suppression of viral load, and ultimately reducing the HIV transmission in South Africa.

As per the ART guideline in 2010, at the beginning of the study, younger adolescents qualified for initiation on ART with a higher CD4 count (≤350 cells mm-3) than older adolescents (≤200 cells mm-3). But the present study found that the median CD4 count at ART initiation was similarly low for young adolescents 135 cells/mm3 [IQR: 32-232] and older adolescents CD4 count of 172 cells/mm3 [IQR 62-252], p= 0.371.

The low CD4 count at initiation reflects the fact that HIV treatment was initiated late, at an advanced stage among adolescents (36). Some adolescents were infected vertically when, in the country, prevention of mother to child transmission guideline was not well established nor well implemented as it is currently. This undoubtedly played a role in late treatment initiation (37) characterised by HIV progression and low baseline CD4 count.

The initiation of ART yielded a significant increase in the CD4 count levels for patients in both age groups. These findings corroborate with other studies (11,29) and justify the need for sustained implementation of the universal testing and treating policy. Other recommendations regarding early diagnosis of HIV and immediate initiation of ART include community outreach campaigns through which community members are educated on the benefits of regular HIV testing and treatment (38). With the development of social media platforms, future campaigns could target the dissemination of treatment support messages through platforms such as Facebook, Instagram, and Twitter, including television. Mobile short messages service (SMS) reminders can be used at the community level and television messages in waiting areas of community healthcare facilities (38,39).

The low numbers of adolescents having VL testing done (48.4%) and the fluctuation of viral load during follow-ups is a cause for concern. The latter is usually related to suboptimal

adherence to treatment but may also indicate intercurrent opportunistic infections, incorrect ART dosage, drug-to-drug interaction (i.e.: with anti-TB treatment) and the development of resistance to antiretroviral drugs (40).

When the definition of viral load suppression was made more stringent (< 50 copies/mL), the proportion of those achieving viral suppression fell dramatically to 21.1% (n= 26) and 17.2% (η = 20) by six and twelve months, respectively. This indicate a poor ART programme performance most likely due to suboptimal treatment adherence by patients(41,42). Efavirenz and lamivudine have a low genetic barrier to resistance and therefore it is likely that many of these patients had developed resistance to their ART regimen. Very few adolescents were switched to Lopinavir/ritonavir-based treatment as per the guideline, again indicating programmatic failure. This finding results in diminished chances of achieving 90-90-90 strategic targets (8) and raise a need for measures to address adherence issues. Multidisciplinary approach involving dieticians, social workers, and the creation of adolescent support group with peer educators may assist in this regard. These factors can be embedded in a youth-friendly service that has been fully implemented in some areas in South Africa (23,43).

Recent data showed that 92% of HIV-positive people in South Africa are aware of their HIV status. However, only 75% of these are on treatment, and a total 64% are virally suppressed (44). While the present findings marginally exceed the suppression figure, it is important to note that they represent suppression after 6 months (below 1000 copies/mL). Viral load remained high for most participants throughout the remainder of the follow-up period. This indicates that even though viral suppression is reached, HIV-positive patients still experience some viral rebound as reported by Omole and Semenya (29). Thus, the present results emphasize the need for investments into intensive pre-ART and ongoing adherence counselling to HIV-positive adolescents. This strategy could be extended to include home-based HIV counselling and support (45) as well as afternoon and weekend HIV services for school-going adolescents (46).

Omole and Semenya (29) also pointed to the importance of ongoing adherence support by the healthcare provider; the need to fully involve adolescent patients in the management of their condition and improve their understanding of the disease as well as the advantage of the treatment plan (29). It was further argued that healthcare providers play a role in the monitoring of laboratory and clinical parameters to assess the need for adjustment or change of the

treatment (29). Such factors could also be deployed to address the challenges relating to suboptimal viral load or low-level viremia in patients on ART.

The absence of any statistically significant difference in virologic suppression between the groups in the present study is similar to reports from in other African settings (53, 54). In contrast to the current study and those from Ethiopia and Uganda, reports from developed countries have demonstrated the significance of factors such as HIV treatment regimen, age, sex and types of healthcare facility on viral suppression (49,50).

The observation that virologic failure (Figure 3.6) was highest amongst hospital participants in the 10-14 age group is consistent with other studies (51). It was expected that young adolescents were at less risk of virologic failure compared to the 15-19-year-old because they are under parental or guardian's care and control. The results of this study contradict this proposition and may indicate poor treatment supervision/oversight by parents/guardians. It may also highlight the need to intensify treatment support, reduce stigma by promoting transparency and disclosure, and reduce the burden of treatment by simplifying drug regimens using fixed drug combinations and simplified dosages.

The proportion 52% (η =132) of adolescents retained in care is concerning considering the long-term ART needs for this population. The present findings are similar to several other national and international cohorts (27,29,52,53), but better than recent findings by van Wyk et al. (16), who found less than 50% of retention after a three year follow-up. Retention in care, especially for adolescents requires and effective ART programme. Adolescents undergo a range of psychosocial and physiological development which have been identified as barriers to treatment success (54). Consequently, adolescent-tailored treatment programmes are needed to achieve better treatment outcomes. An evaluation by Mackenzie et al. (55) in Malawi revealed greater retention in care among adolescents on antiretroviral treatment using the adolescent treatment adapted approach. This finding has also been supported by empirical and review studies (24,46,56) thus highlighting the need for investments on adolescents adapted adherence support and service delivery models.

A study incorporating HIV patients of all ages in the Tshwane District found a retention rate of 40.9% for similar follow-up times as the current study (11). Likewise, an investigation in KwaZulu-Natal, South Africa showed decreasing retention rates for adults after two years of follow-up (57). It was further stated that psychosocial factors including depression is one of

the factors influencing non-retention in care even in adults (57). Therefore, the present findings justify the need for approaches to address other common challenges to retain HIV patients in treatment programmes. Adolescence remains a period with high risk for disengagement from care. Several common challenges such as stigma, mental health issues and lack of social support at home and school impede successful treatment adherence and the consequent need to remain in the ART programme (23,24,58,59). Addressing such challenges requires good family support, skilled adolescent treatment teams (youth-friendly services), and the provision of facilitated care. These may assist in restoring any disrupted adolescent-clinician relationship (60). Another intervention is the use of ward-based outreach team (WBOT) to reach out/ trace adolescents in the community.

Female participants were more likely to be LTFU, transferred out or remain in care compared to male participants. The present findings were particularly predictable as females composed over 68% (n= 173) of participants in this cohort. Nevertheless, the findings were not statistically significant. Meyer et al. (61) findings showed that females were likely to experience optimal HIV-treatment outcomes including remaining in care (50%). However, the present findings is supported by continued reports regarding the disproportionate distribution of HIV infections by sex in the sub-Saharan African where most females have been found to be at risk of worse treatment outcomes (3).

Both males and females had significantly (p 0.019) equal chances of dying during the study period. In terms of age groups, older adolescents had a higher risk (*p* 0.001) of death and presented an increased risk of being transferred out or LTFU in comparison to younger adolescents. Indeed incidences of mortality have been previously reported in studies investigating treatment outcomes of HIV-positive population (62). Although it is difficult to investigate the specific reasons for mortality, the incidence of mortality in this study is similar to those reported in a study in Zimbabwe (62). Possible causes for mortality could be other comorbidities or advanced HIV (21,63). As the aims of antiretroviral therapy include among others prolonging patient life, there is a need to work on achieving this especially for young HIV population such as adolescents.

The low retention in care could also have been impacted by unreported deaths (64). Similarly, patient-level factors mentioned previously together with other factors such as ART toxicity and false beliefs that the patients are cured have previously been reported to contribute to a low rate

of retention in care (43). Despite the fact that such factors were not investigated in this research, they have been documented previously in South Africa and elsewhere (24,43,60) and warrant further investigation to determine to what extent they apply in this research setting.

It was not possible to determine whether pregnancies were planned but the finding that 20.2% of females (η = 35) were reported pregnant in this study are similar to a previous report in South Africa (65) that reported a 19.2% adolescent pregnancy rate. Of note in this study is that all pregnancies were reported among older adolescents confirming a previous report that most 10-14 year old adolescents may not be engaging in active sexual activities (66). This provides a window of opportunity to offer early sexual health education integrated within the HIV-treatment programmes, particularly because unplanned pregnancies have been associated with poor clinical and treatment outcomes (29,67).

Studies have demonstrated that adolescent pregnancy results from risky sexual behaviours and is mainly associated with an increase in the incidence of sexually transmitted infections, including HIV (22,23). Teenage pregnancy is also a major contributor to other comorbidities that have been reported to affect optimal treatment outcomes including violence and mental health disorders (23). Although these behaviours were not investigated in this study, it is possible that if present, they may have also contributed to poor treatment outcomes amongst the study subjects. A priority task in the healthcare provider-patient relationship is to promote and sustain sexual health service and improve health counselling regarding safe sex-practice and family planning as an integral part of HIV care for female adolescents (29).

Adolescent females constituted the majority of participants in this cohort, confirming previous reports that females are disproportionately affected by HIV in South Africa (3,27). This highlights the need for interventions such as increased testing (including self-testing) in order to initiate early treatment, safe-sex practice such as using condoms during sexual intercourse and limiting the number of sexual partners. The need for increased testing capacity is also key to ensuring a high uptake of adolescents in ART programmes and meeting the currently unachieved objectives of the 90-90-90, which includes in addition to testing, the treatment uptake and viral suppression. However, such interventions should also be extended to their male counterpart as they also showed low CD4 count at ART initiation. Regardless of these clinical issues, social interventions that promote autonomy of sexual choices need to be promoted among adolescents.

In this study, explorative objectives included several associations encompassing time, demographics, biologic, and clinical parameters (Table 3.11). For example, a patients' time on ART was associated with an increase in CD4 count level. Such a finding is a positive and similar to results of another study conducted in different states in the United States of America (68), and adds to the arguments that ART initiation and uptake by patients is essential for immune reconstruction.

Moreover, being young and having low baseline CD4 count levels were significantly associated with an increased risk of virologic failure. This finding is similar to reports elsewhere (69). It should be noted that low CD4 cell count is an important risk factor for immune disruption and can lead to opportunistic infections such as TB (70). Studies conducted in South Africa (70), and Uganda (71) have shown low CD4 levels as well as higher viral load in HIV patients co-infected with TB. These results justify the need for early testing and initiation on ART as alluded to earlier.

Apart from age (adjusted HR), facility type and baseline CD4 count, none of the remaining factors examined predicted the risk of virologic failure in the Cox regression model (Table 3.10). The few recent studies investigating virologic failure during HIV treatment have shown variable results in some areas but certainly demonstrated that low baseline CD4 cell counts or decreasing CD4 cell levels increases the risk of virologic failure (72,73). This confirms the need for increased testing capacity, including extending self-testing capacity to help individuals know their status during early stage of the disease and initiate treatment.

In the multivariate logistic model (Table 3.12), after adjusting for sex and facility type, the findings that younger adolescents had a low risk of loss to follow up and more prone to remaining in care is significantly consistent with many previous studies (47,73). These results highlight the principle that ART is not solely the responsibility of the patient. Parental supervision could also yield desirable treatment outcomes; hence the need to involve parents at all levels of adolescent HIV care including counselling (23).

In conclusion, in this cross-sectional study of adolescents in Sedibeng, ART initiation was accompanied by significant immune reconstitution and viral load suppression within 12 months. However, the observed high viral loads at initiation and resurgence at 36 months, and low CD4 count levels at initiation of ART, calls for increased early testing and uptake of adolescents into ART programmes at the early stages of the disease.

Adolescents have poor rates of retention in care and the high number of patients that LTFU during chronic treatment such as ART. These two challenges are a barrier to reaching several national targets including 90-90-90 strategies, and ultimately make it difficult to eradicate the HIV epidemic in the country. The present study calls for actions in adolescent-adapted treatment programmes in order to boost good treatment outcomes.

4. Study limitations

Notwithstanding the findings of this research, some limitations should be acknowledged. The accuracy and completeness of routinely collected national data cannot be ascertained. This study entirely relied on a single research site and a small sample size, thus limiting the generalizability of the findings. The research protocol for this study was completed and approved in 2017. Changes in treatment guidelines over time in South Africa have also prompted changes in indicators of treatment success and these could have influenced the CD4 and viral load interpretation and therefore action taken. However, all current analyses were carried out considering earlier treatment guidelines. Information regarding the cause of death of HIV patients was not available in the Tier.Net database and therefore the mortality outcome of those LTFU was unknown in this study. This might have led to misclassification of some of dead patients as being lost to follow up.

Missing data lead to bias and may impact the accuracy and reliability of research findings (74) and could have occurred due to human error from the service personnel (data clerk) or omission by the clinician to draw blood when the patient is due for blood test monitoring. However, only five of the 259 medical files reviewed had significant information deficit (74).

5. Conclusions

In conclusion, there was a sizeable number of HIV-positive adolescents in Sedibeng who were all initiated on ART treatment in 2010 and followed for five years. The findings from this study may be important for the planning and implementation of HIV services corresponding to the needs of adolescent population in Sedibeng. Adolescents attending ART in this area experience high rates of LTFU, low retention in care and poor viral load suppression. As the country works on eradicating HIV epidemics, the results of the present study emphasize the need to target adolescents for present and future interventions aimed at improving clinical outcomes and retention in care. The observed poor treatment outcomes call for programmes tailored at responding to adolescent specific needs in the healthcare system. With the current universal

testing and treatment programme in the country, health care system needs to prepare for the increase of HIV-positive adolescents that should be closely monitored. The perceptions held by health care providers in SA public healthcare services that it is a taboo or inappropriate behaviour for adolescents to engage in sex could stigmatize them and negatively affect the care received. This could in turn affect adolescents' health seeking behaviours and result in poor treatment adherence and LTFU. Hence, healthcare professionals should also be trained to be aware of their own prejudices and on non-judgemental approach to clinical care to limit stigma and its negative effects on care.

6. Recommendations

- Emphasis should be placed on routine HIV testing including self-testing (where people can test at their convenient time), community mass testing and testing mobilisation through schools. Such practices are vital for the early detection of HIV, which in turn can lead to early initiation of treatment, a key factor in ensuring viral suppression, increase in CD4 count, hence better outcomes.
- Future interventions aiming to better treatment outcomes should invest in counselling of both patients and their parents/guardians. Such counselling should be focused on dealing with stigma, mental health issues, false beliefs and other negative psychosocial issues. Counselling will also improve the knowledge of the benefits of adherence to treatment and collaboration with healthcare providers.
- Weekend and afternoon HIV care may be implemented to accommodate adolescent attending school and therefore increase the number of adolescents returning for follow-up.
- Patient tracking can be strengthened through Ward-Based Outreach Team who can liaise with a community member to reach the patient after working hours. Such programmes can help curb the gap in patients LTFU.
- Youth friendly services need to be implemented fully in all health facilities to achieve sustained viral suppression and retain adolescents in care. Topics such as physiological start to sexuality in adolescence, stigma or maltreatment in clinic, modes of transmission, reflecting on one's own sexuality when they were younger … need to be addressed.

- The 3rd year or month 36 of ART need to be considered as a critical milestone in adolescent HIV management since an increased in viral load, LTFU and death were reported at this time. Attention need to be given to treatment adherence counselling in adolescence on HIV treatment and intensified from 24 months onwards to stem the surge in viral loads at 36 months of treatment
- Further qualitative research is required to understand the challenges affecting good HIV treatment outcomes within and beyond the study setting. It could also explore the perceptions of patients, healthcare practitioners and public health managers on the best way to address these challenges and achieve the intended health outcomes.

- To minimise missing data, a checklist can be inserted in all patients' files where the clinician can tick all actions taken at each visit and cross where not appropriate. In addition, the patients need to be educated about the importance of blood monitoring and informed about their next due date. One other possible solution is to institute teams of data recording, verification, and follow-up in all facilities to ensure that all treatment information is properly recorded.

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8. Appendices

Appendix A: Plagiarism declaration

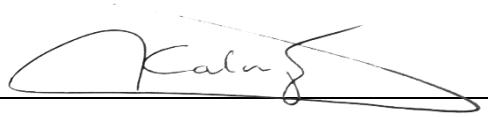
PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I, NJIBA KALONJI-MAKALONI (Student number: 501764) am a student registered for the degree of MASTERS OF PUBLIC HEALTH in the academic year 2021.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature:  Date: 28/02/2022

Appendix B: Ethics clearance certificate

R14/49 Dr Njiba Kalonji-Makaloni

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160845

NAME: (Principal Investigator)	Dr Njiba Kalonji-Makaloni
DEPARTMENT:	School of Public Health Maternal and Child Health Sedibeng District Health Services
PROJECT TITLE:	Treatment Outcomes amomg Human Immunodeficiency Virus - Positive Adolescents Initiated on Antiretroviral Therapy in Sedibeng District, Gauteng
DATE CONSIDERED:	26/08/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Lee Fairlie and Olufemi Babatunde Omole
APPROVED BY:	Professor P Cleaton-Jones,Chairperson, HREC (Medical)
DATE OF APPROVAL:	16/09/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004, 10th floor, Senate House/3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in August and will therefore be due in the month of August each year.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix C: Research authorisation letter

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

Enquiries: Dr. Victor Figueroa
Directorate: Family Medicine
Tel: 016 9506116
Fax: 016 950 6034
Cell: 082 3716077
1/6/2

TO	:	Sedibeng District Management
FROM	:	Dr. Victor Figueroa – Research Coordinator (Sedibeng DHS)
DATE	:	07 June 2016
SUBJECT	:	CONSENT FOR CONDUCTING RESEARCH TO DR. N KALONJI ON TREATMENT OUTCOMES AMONG HIV+ ADOLESCENTS INITIATED ON ANTIRETROVIRAL THERAPY

This is to certify that Dr. N. Kalonji – Makaloni, currently a Medical Officer in HAST services and will be conducting a research as part of the requirement of the Faculty in pursuing her Master Degree in Public Health.

The title of the study is: Treatment outcomes among HIV+ adolescents initiated on antiretroviral therapy in Sedibeng District.

I, Dr. Victor Figueroa in my capacity as Sedibeng District Research Co-ordinator recommend and support for permission to be granted to the above researcher.

Regards,

DR. VICTOR FIGUEROA
RESEARCH CO-ORDINATOR
SEDIBENG DISTRICT HEALTH SERVICES

DATE: 2016/06/07

MRS. S. HLAHANE
DIRECTOR – SEDIBENG DHS

DATE: 15/06/2016

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