The Effects of Teen Clubs on Adherence to Antiretroviral Therapy and Retention in HIV Care amongst Adolescents in Windhoek, Namibia

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Adherence
Viral Load Suppression
Teen Club
Lost to follow-up
Adolescent-friendly HIV services
Group interventions
ABSTRACT

Adolescents living with HIV (ALHIV) are notably underserved by national HIV programmes globally due to their unique needs. Of particular concern is limited access to and availability of adolescent-friendly ART services, which contributes to poor ART adherence and retention in care in many sub-Saharan African countries. Poor adherence in adolescents has been associated with medicine side effects, pill fatigue, non-disclosure of status to the child, inadequate information on HIV, caregiver-child communication, caregiver’s health beliefs and stigma, and lack of knowledge on the rationale of taking medicines. Several interventions have been developed to improve ART adherence and retention in care amongst ALHIV through peer groups and psychosocial support.

The Teen Club intervention was introduced in 2010 at Intermediate Hospital Katutura Paediatric ART clinic in Windhoek to improve ART adherence and retention in care amongst ALHIV by providing psychosocial support in a group environment. However, to date no formal evaluation of the effectiveness of the Teen Club intervention in Namibia has been conducted.

The aim of the study was to compare the effects of the Teen Club intervention against standard care on treatment outcomes for ART (i.e. adherence, retention in care and viral suppression) in adolescents at Intermediate Hospital Katutura Paediatric ART clinic in Namibia.

Methods: A retrospective cohort analysis of HIV positive adolescents aged 10-19 years, who were accessing ART between 1 July 2015 and 30 June 2017 was conducted. Patient data was extracted from the electronic Patient Monitoring System (ePMS), individual Patient Care Booklets and the teen club attendance register. Adherence to ART was measured through pill counts; and retention by kept clinic visits. Viral load results were assessed to measure levels of viral suppression. Adolescents with viral loads ≥ 1000 copies/ml were classified as not virally suppressed whilst those with viral loads <1000 are virally suppressed (with those <40 fully suppressed).

Results: The total sample was 385 participants; with 78 of them in the Teen Club (exposed) and 307 adolescents in standard care (unexposed).
The overall retention in care rates at 24 months among all adolescents was 90.1%, with no statistically significant difference between those in Teen Clubs (91%) and those in standard care (89%) (p = 0.956). Younger adolescents (10-14 years) had better retention rates than older adolescents (15-19 years) (94% vs. 86%; p=0.016). There were also statistically significant differences in retention rates between adolescents on first line ART regimen and those on second line (HR=0.333; p=0.028); between adolescents on ART ≥ 12 months and those on treatment < 12 months (HR=0.988; p=0.035); and between adolescents disclosed to and those not disclosed to (HR=0.131; p=0.016).

Viral load suppression at 24 months among participating adolescents was at 87% (68% fully suppressed, 19% suppressed). There was no statistically significant difference in viral load suppression between adolescents in Teen Club and those in standard care at 6 months (84% vs 89%; p=0.298), at 12 months (82% vs 86%; p=0.438) and at 18 months (80% vs 89%; p=0.113). Viral load suppression was higher in younger adolescents compared to the older adolescents at 6 months (93 % vs 83%, p= 0.015), at 12 months (90 % vs 80%, p= 0.021), and at 18 months (90 % vs 83%, p= 0.091). ART adherence as measured at clinical visits was rated as good (89%) over the 2 years of the study period. There was no statistically significant difference in ART adherence between adolescents in Teen Club and those in standard care (95% vs 90%; p=0.277).

**Conclusion:** This study found no significant differences in adherence to ART, viral load suppression and retention in care rates between adolescents that were in the Teen Club and those in standard care, although there were slightly higher adherence and retention rates among Teen Club members. Significant differences were found between younger and older adolescents on all three treatment outcomes. We concluded that in a specialized paediatric ART clinic, group-based interventions may not substantially improve treatment outcomes. Targeted, individual and age-specific interventions may provide additional benefits to the Teen Club intervention.
DECLARATION

I declare that *The Effects of Teen Clubs on Adherence to Antiretroviral Therapy and Retention in HIV Care amongst Adolescents in Windhoek, Namibia* is my work, has not been submitted for any degree or examination at any other university, and that all the sources I have used have been indicated in text and acknowledged in the references section.

Full Name: Farai Kevin Munyayi
Date: 23 February 2019

Signature: ___________________
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<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
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<td>ALHIV</td>
<td>Adolescents Living with HIV</td>
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<td>ART</td>
<td>Antiretroviral Treatment</td>
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<td>CD4</td>
<td>Cluster of Differentiation 4</td>
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<td>CI</td>
<td>Confidence Interval</td>
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<td>EDT</td>
<td>Electronic Dispensing Tool</td>
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<td>ePMS</td>
<td>electronic Patient Monitoring System</td>
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<td>HR</td>
<td>Hazard Ratio</td>
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<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>LTFU</td>
<td>Lost to Follow Up</td>
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<td>MoHSS</td>
<td>Ministry of Health and Social Services</td>
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<td>MSM</td>
<td>Men who have sex with men</td>
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<td>NAMPHIA</td>
<td>Namibia Population-based HIV Impact Assessment</td>
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<td>NNRTI</td>
<td>Non-Nucleoside Reverse Transcriptase Inhibitors</td>
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<td>OI</td>
<td>Opportunistic Infections</td>
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<td>PCB</td>
<td>Patient Care Booklet</td>
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<td>PI</td>
<td>Protease Inhibitors</td>
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<td>PLHIV</td>
<td>People Living with HIV</td>
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<td>RCT</td>
<td>Randomized Control Trial</td>
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<td>RCP</td>
<td>Red Carpet Program</td>
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<td>RNA</td>
<td>Ribonucleic Acid</td>
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<td>RR</td>
<td>Risk Ratio</td>
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<td>SRH</td>
<td>Sexual and Reproductive Health</td>
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<td>STYLE</td>
<td>Strength Through Youth Living Empowered</td>
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<td>TB</td>
<td>Tuberculosis</td>
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<td>UNAIDS</td>
<td>Joint United Nations Programme on HIV and AIDS</td>
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<td>WHO</td>
<td>World Health Organization</td>
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CHAPTER 1: INTRODUCTION

1.1 Background
Worldwide, an estimated 2.1 million adolescents between 10-19 years are living with the HIV; with sub-Saharan Africa home to an estimated 85% of them (Nabukeera-Barungi et al., 2015). The World Health Organization (WHO, 2013a) defines adolescents as children or young adults between 10-19 years of age. In many sub-Saharan Africa countries, HIV services are organized around adult or paediatric care, with the paediatric care facilities being responsible for treatment of younger adolescents (children) who are living with HIV. These facilities are often ill-equipped to give guidance on adolescent-specific issues for the older adolescents, such as information related to their needs to deal with sexual and reproductive health (SRH) concerns (Ssali et al., 2014). Adolescents living with HIV often fall and fail in the transition gap from paediatric to adult HIV programs; resulting in poor retention in care and adherence to antiretroviral therapy (ART) especially in the 15-19 years old age group (MacPherson et al., 2015). A study in Uganda reported that the risk of non-retention in HIV care was significantly greater in older adolescents (15–19 years) compared to younger adolescents (10–14 years) group (Ssali et al., 2014).

Adherence, characterised by “starting, managing and maintaining a given medication regimen at prescribed times, frequencies and conditions” (Mukumbang et al., 2016:2), is crucial in successful HIV care and treatment programs (Bygrave et al., 2012). Poor adherence is a major public health challenge and interventions to ensure consistent high levels of adherence to ART and persistent engagement in care are essential for sustaining substantial public health and individual benefits (Mukumbang et al., 2016). Health care providers are faced with challenges emanating from high rates of non-adherence to ART amongst adolescents. Some interventions used across the world to address adherence challenges include individual counselling, group counselling, mHealth platforms, community and home-based strategies, pharmacist counselling, task-shifting, patient fast-tracking, nutrition support and disability grants among others. However, common interventions among adolescents utilize group counselling interventions such as teen clubs (Ridgeway et al., 2018).
Kim, Gerver, Fidler and Ward (2014) described the 15-24-year age group (adolescents and young adults) as the fulcrum and centre of the epidemic with 42% of new infections occurring in this age group in 2010. They further argued that “poor ART adherence increases the risk of viral drug-resistance, limits treatment efficacy, leading to disease progression, and reduces future therapeutic options as well as increasing the risk of transmission due to unsuppressed viral replication” (p.1946). Nachega, Mills and Schechter (2010) concluded that although reported ART adherence is high globally (>95%), there is a concern about the waning adherence over time including loss of patients from HIV programmes when scaling up. The authors recommended monitoring of long-term adherence and retention in care, and the development of evidence-based interventions to address problems, especially amongst adolescents.

Namibia has adopted the Joint United Nations Programme on HIV and AIDS’ (UNAIDS) proposed fast track goals to achieve HIV epidemic control by 2030. The fast track goals are aimed at ensuring that 90% of PLHIV are identified; 90% of those identified are effectively linked and retained on ART; and 90% of these achieve viral suppression, i.e. the 90-90-90 targets (UNAIDS, 2014). Adolescents living with HIV have unique needs and are notably underserved globally and in national responses, which negatively affects their access to ART and results in poor retention in care and ART adherence and inferior treatment outcomes such as achieving and maintain viral load suppression (MacPherson et al., 2015). In Namibia, 15-19 year olds reportedly have only 62% viral suppression; which is below the national average suppression levels for adults (15-49 years) on ART at 87% (Mokenen, 2016). According to WHO, a maintained viral load of <1000 ribonucleic acid (RNA) copies per ml of plasma is considered evident of viral suppression (WHO, 2013b). In Namibia, in addition to the WHO viral suppression level of < 1000 copies/ml, a viral load of <40 copies/ml is classified as fully suppressed (Republic of Namibia Ministry of Health and Social Services, 2016).

Several factors including adolescents’ developmental stage, age, behaviour, psychosocial support, socioeconomic status and accessibility to adolescent-friendly health services have been attributed to the disparity in treatment outcomes between adolescents and
adults (MacPherson et al., 2015). Experimentation with sexual activities and drug and alcohol use increase the risk of contracting HIV during the adolescence phase (Lall, Lim, Khairuddin, & Kamarulzaman, 2015). Interventions targeting the youth should be a priority for national HIV programmes as they appear to be at most risk of not achieving and maintaining viral suppression (Mokenen, 2016). Poor ART adherence and retention in HIV care have been identified as some of the key factors negatively affecting the achievement of the last 90 of the HIV treatment cascade, particularly in adolescents. Several country HIV programmes have demonstrated the effectiveness of group-based interventions in improving retention in care and ART adherence. An evaluation study on the effect of a novel adolescent and youth Red Carpet Program (RCP) on linkage to care and outcomes conducted in healthcare facilities and schools in Homa Bay County, Kenya, showed that as compared to the pre-implementation cohort, retention on ART for the post implementation cohort increased from 66% to 90% at 3 months, and from 54.4 to 98.6% at 6 months (Ruria et al., 2017).

1.2 Problem Statement
A Teen Club intervention was established in 2010 at the Intermediate Hospital Katutura Paediatric ART clinic, in Windhoek, to address unique needs of adolescents on HIV treatment and care (Matjila, 2012). The Teen Club aims to improve ART adherence and retention in care through, amongst other activities, psychosocial support, adherence counselling and health education. To date, the effectiveness of the Teen Clubs on adolescents’ retention in HIV care and adherence to ART has not been formally evaluated in Namibia. Such an evaluation is necessary to assess the effectiveness of this intervention and inform decision makers on whether to scale-up the intervention to other facilities, or to modify implementation of the intervention.

1.3 Study Aim and Objectives
The aim of the current study was to compare the effects of the Teen Club intervention against standard care on treatment outcomes for ART (adherence, retention in care and viral load suppression) amongst adolescents at Intermediate Hospital Katutura Paediatric ART clinic in Windhoek, Namibia during the period 1 July 2015 to 30 June 2017.
The specific objectives of the study were:

- To describe the demographic and clinical characteristics of Teen Club members and adolescents in standard care;
- To compare adherence to clinic visits between Teen Club members and adolescents in standard care;
- To compare adherence levels, measured through pill counts and self-reporting between Teen Club members and adolescents in standard care;
- To compare viral load suppression between Teen Club members and adolescents in standard care; and
- To compare retention in care between Teen Club members and adolescents in standard care.

We hypothesise that if ALHIV who are on HIV treatment are enrolled in a Teen Club, then they will be retained better in HIV care, improve ART adherence and achieve higher viral load suppression levels.

1.4 Outline of thesis

This thesis is structured in six chapters beginning with an introduction to the study in chapter 1 above. Chapter 1 provides an overview of ART coverage and treatment outcomes worldwide, in the sub-Saharan region and in Namibia, and defines ART adherence, retention in care and viral load suppression. The introductory chapter narrows down to ART coverage and outcomes for adolescents, including challenges with adherence and retention in care among adolescents, and the aim and objectives of this study.

Chapter 2 looks at the literature, from both the global north and south, that has been published (some unpublished) on adolescent ART programmes focusing on adherence to ART, retention in care and viral load suppression levels, as well as intervention programs to improve treatment outcomes among adolescents.

Chapter 3 gives an outline of the study methodologies including the study design, study population and sampling, data collection processes, data management and data analysis, as well as the validity and reliability of the study observations. The chapter is concluded by the ethical considerations for the study.
The results of the study are outlined in chapter 4 with particular focus on a comparison of ART adherence levels, retention in care and viral load suppression between Teen Club members and adolescents in standard care. A discussion based on these results in chapter 5 is followed by conclusions and recommendations in chapter 6.
CHAPTER 2: LITERATURE REVIEW

2.1 Introduction
Adherence to ART is a key determinant of successful treatment outcomes for HIV and is crucial to mitigate against emergence of drug resistant viral strains (Thompson et al., 2012). The success of ART programmes has been limited by complexities of regimens patients on ART have to take and the long term nature of the treatment (Simoni, Amico, Pearson, & Malow, 2008). These complexities play themselves out differently in different age groups, and adolescents seem to have worse treatment outcomes due to their unique physical, social and mental changes and difficulties (Arrivé et al., 2012). Good adherence to ART is associated with suppression of HIV-1 RNA which is the aim of ART so as to achieve maximal clinical benefits for patients on treatment, and to reduce chances of HIV transmission (Mugavero, Amico, Horn & Thompson, 2013). Several interventions have been implemented to improve ART adherence and retention in care, and these can be either individual-based or group-based interventions. Bateganya et al. (2015) note that WHO proposes support groups as an intervention for improving ART adherence and retention in care for persons receiving ART. The authors argue that improved adherence and retention can be maximized if support groups are formed around homogenous population groups such as couples, men having sex with men or adolescents (Bateganya et al., 2015). Luque-Fernandez et al. (2013) provides further support for the positive effects of such interventions, noting that patient support groups are well recognised as measures to encourage retention in care and adherence to treatment.

2.2 Adherence to HIV treatment
Optimal adherence is essential for beneficial outcomes and preventing viral resistance, and adolescents may have worst adherence to ART due to their developmental stage and unique behavioural characteristics (Nachega et al., 2009). Adolescents are confronted with difficult choices regarding identity formation, sexual behaviour, romantic relations, alcohol and drug use, which become more complex for HIV-infected adolescents in addition to needing to stay in lifelong treatment and care (Reisner et al., 2009).
To start taking responsibility for their own health, HIV positive adolescents need to have an understanding of their sexuality and also come to terms with the identity of being HIV positive. Typical of any adolescent at this developmental stage, there is exploration of sexuality and forming of romantic relationships. In addition, HIV positive adolescents have concerns of transmission of the virus, re-infection, and future roles as an intimate partner, wife or husband, or being a parent (Meyersfeld & Vujovic, 2011). These concerns and their experiences are often clouded in fears of disclosing their HIV status and rejection by others, which further undermine their retention in care and adherence to ART. Adolescent experimentation with alcohol and other substance abuse impairs the individual ability to regularly and consistently take the medication at the right time and adherence to clinic appointments.

Treatment adherence levels below 90-95% (percentage of ARV doses patient took during the recall period) have been reported in adolescents; with some estimates between 50-75%, which is well below levels that are adequate for viral suppression (Davies et al., 2008). However, some studies have shown that viral suppression can be achieved at adherence levels as low as 54% with non-nucleoside reverse transcriptase inhibitors (NNRTI) (Nyogea et al., 2015). Müller et al. (2011) argue that some regimens containing Protease Inhibitors (PI) could show fully suppressed viral load results in situations where there is short-term poor adherence. This argument is based on the comparative efficacy of different types of antiretroviral medications, of which one type of antiretroviral drugs may have a longer acting effect than another.

Most of the available data on adolescents’ ART adherence and outcomes primarily comes from the global north, with limited information from sub-Saharan Africa (Nachega et al., 2009). Nyogea et al. (2015) also noted that less information is available on adolescents’ adherence to ART compared to adults, as most studies have focused on adults. A study conducted by Nachega et al. (2010) in South Africa showed that adolescents had significantly lower ART adherence and viral load suppression rates and immunologic recovery than adults.
However, studies at a Ugandan outpatients hospital-based clinic and a nationwide study on children and adolescents found excellent adherence at more than 95% (Nachega et al., 2010). A 2014 systematic review showed global adherence estimates ranging from 16% to 99% among adolescents whilst a meta-analysis of data for young adults and adolescents aged 12–24 years in 53 countries found an estimated pooled adherence at 84% in Asia and Africa. Rates of viral suppression (< 400 copies/mL) ranged from 52% to 87% in Asia, 27% to 89% in Africa, and from 37.5% to 49% in Central and South America (Ridgeway et al., 2018).

### 2.3 Factors associated with ART adherence in adolescents

Adherence barriers may be due to any combination of medication-related, disease-related, patient-related, structural, provider-related and psychological barriers (Agwu & Fairlie, 2013). Sociodemographic variables of interest in treatment outcomes amongst adolescents include the adolescents’ primary caregiver, level of education, employment status, day-to-day schedules, feeling healthy, disclosure and fear of stigma - which may lead to poor ART adherence and retention in care (Okoronkwo, Okeke, Chinweuba, & Iheanacho, 2013). A recent review of eleven studies done in sub-Saharan Africa identified a complex web of 44 barriers and 29 facilitators impacting ART adherence among adolescents, with stigma, lack of assistance, ART side-effects and forgetfulness as top barriers whilst top facilitators were caregiver support, knowledge of status and peer support groups (Ammon, Mason, & Corkery, 2018). Hudelson and Cluver (2015) highlighted potentially essential themes for ART adherence among adolescents from 15 studies conducted in low- and middle-income countries which included family structure, a burdensome ART regimen, attitudes about medication and the healthcare system factors.

#### 2.3.1 Mental health and adherence to ART

Several studies have provided evidence of a relationship between mental health and adherence to ART. Behavioral and emotional disorders have been reported in Africa throughout adolescence, with a study in Uganda reporting that 51% of adolescents living with HIV had psychological distress and 17% attempting suicide (Musisi & Kinyanda, 2009).
In Zambia, Menon, Glazebrook, Campain and Ngoma (2007) reported that 40% of HIV positive adolescents had mental health problems. Dow et al. (2016) argue that psychological and mental health difficulties have contributed to a 50% increase in AIDS related mortality amongst HIV positive adolescents. The authors conducted a study in Tanzania which administered a questionnaire to adolescents that included questions about school, home, ART adherence, stigma and mental health. The study concluded that mental health problems were prevalent amongst HIV positive adolescents and were associated with stigma and poor adherence, and addressing these “may improve ART adherence and virologic suppression, improving overall health of the individual and reducing the risk of HIV transmission to others” (Dow et al., 2016: 1).

2.3.2 ART adherence levels between younger and older adolescents
Several authors have described the developmental differences amongst different age groups of adolescents, and argue that these differences influence adolescent behavior and attitudes to treatment. Naswa and Marfatia (2010) divided adolescence into early (10-13 years), middle (14-16 years) and late adolescence (17-19 years) in terms of psychological, physiological and social development. These different adolescent age categories influence retention in care and adherence to ART. Slogrove, Mahy, Armstrong and Davies (2017) argued that different barriers and risks experienced during early adolescence (10–14 years) and later adolescence (15–19 years) may impact on HIV-related outcomes and on the risk for HIV acquisition. Whilst early adolescence is associated with increased physical changes and puberty, middle adolescence has greater peer influences and risk-taking behavior (Naswa & Marfatia, 2010). Alcohol and drug use increase during late adolescence and is associated with decreased ART uptake and adherence, retention in HIV care and viral suppression in this age group (Chander, Lau, & Moore, 2006). Younger adolescents are more likely to be living under more controlled environments with caregiver support where ART adherence and retention in care can be promoted at home and in school, and they are in early puberty and few have reached sexual debut, reducing HIV risk (Slogrove et al., 2017).
The older adolescents, who may naturally prefer some degree of independence, are increasingly faced with the sexual and reproductive health transitional challenges from childhood to adulthood, and identity and behavioral challenges that lead to poorer adherence and retention in care (Grey & Mwalabu, 2014).

### 2.3.3 Perinatally vs horizontally-infected adolescents

Perinatally HIV infected adolescents who were diagnosed late may present with unique challenges with growth stunting and pubertal delay a common feature. These adolescents often present with WHO clinical stage 3 or 4 characterized by presence of opportunistic infections, which subsequently leads to poor adherence to treatment due to altered pharmacokinetics, drug-drug interactions with other opportunistic infections treatment (e.g. TB), poor palatability of medications and gastrointestinal intolerance (Agwu & Fairlie, 2013). Treatment experienced adolescents who were initiated on treatment earlier commonly struggle with the disclosure process and the behavioral changes associated with the developmental, psychosocial and physiological evolution complexities.

### 2.4 Measures of Treatment Adherence

The methodology used to measure or assess adherence and the reported outcomes is crucial to validity of ART adherence studies. A number of variables are used by different researchers, and routinely, to assess adherence to ART. Chesney (2006) argues that there is no gold standard to assess ART adherence, as many seek for model interventions and optimal tools to assess and enhance ART adherence. The Medical Events Monitoring System arguably is the most accurate adherence measure if used correctly and has the closest correlation to viral load levels (Müller et al., 2011).
However, caregiver reports, pill counts, and pharmacy refill data are commonly used in Africa for monitoring adherence. Pill counts are conducted by healthcare workers during clinic visits by counting medication remaining in the pill bottles and comparing with expected quantity of pills at the time of the visit (Achieng et al., 2013). Self-reporting although inexpensive and readily available, is commonly used to assess adherence despite questions about its validity (Müller et al., 2011). Vreeman et al. (2014) suggests that caregivers may overestimate adherence of younger adolescents; hence there is need to validate adherence measures to strengthen reliability of information obtained.

Farley et al. (2003) outlined further options of measuring adherence and retention in care through use of physician/nurse assessments as well as appointment keeping by patients accessing ART. The finding that clinician assessments and appointment keeping behaviour correlated with virologic response was shown to be clinically useful (Farley et al., 2003). In support of Chesney’s (2006) argument, Berg and Arnsten (2006: 9) suggest that to improve assessing adherence, researchers and clinicians must develop “adherence improvement interventions with standardized and empirically tested adherence measures”. In Namibia, a combination of self-reporting, clinical assessments and pill counts by the health care worker are recommended for assessing ART adherence for all ages during each scheduled clinic visit (Ministry of Health and Social Services, 2016).

2.5 Retention in HIV care

Mugavero et al. (2013) outlined methods of measuring retention in care based on missed clinic visits (missed visits per measurement period) or based on kept clinic visits (proportion of kept visits/ scheduled visits). A cohort study utilizing another measure of retention defined as programme visits (any follow-up contact with an enrolled participant for the study sites and outreach services) every three months (Magnus et al., 2010). A novel retention in care programme named STYLE (Strength Through Youth Living Empowered) defined retention as attending at least one visit every four months in a 3 year period (Hightow-Weidman, Smith, Valera, Matthews, & Lyons, 2011). Retention variables of interest may include whether patient is alive and on continued ART, defaulted/lost, lost to follow-up (LTFU), transferred-out or died (Mutasa-Apollo et al., 2014).
Hoffman et al. (2017) argued that in addition to placing demands on healthcare systems, frequent dispensing of ART and clinic visits may lead to poor adherence, interruption of treatment or total disengagement from care. The authors suggested that 6-monthly visits, as compared to 3-monthly visits, may improve treatment outcomes including viral load suppression and retention in care due to reduced time and cost of frequent visits (Hoffman et al., 2017). A 2017 systematic review of 8 studies that reported on frequency of visits found that less frequent clinic visits almost doubled the odds of being retained in care (OR = 1.90; 95% CI; 1.21-2.99) (Mutasa-Apollo et al., 2017).

2.6 Viral suppression
Viral load is often used as a surrogate marker of good adherence (Müller et al., 2011). Other clinical variables of interest when evaluating ART programmes are treatment failure, which could be virologic failure (viral load >1000 copies/ml 6 months after ART initiation), clinical failure (HIV disease progression such as opportunistic infections) or immunological failure (assessed through CD4 counts) (MoHSS, 2016). Complexities and pill burden of different ART regimens, adverse side effects and duration of treatment are also important variables as they may lead to treatment fatigue, and subsequently virologic rebound characterized by unsuppressed viral loads (Claborn, Meier, Miller, & Leffingwell, 2015). Viral load monitoring is recommended at 6 months after initiating ART for all patients; thereafter every 6 months for children and adolescents aged 19 years and below, and every 12 months for adults. However shorter interval viral load measurements can be performed for unstable patients, who exhibit characteristics of treatment failure (Ministry of Health and Social Services, 2016).

2.7 Differentiated care models
Literature acknowledges the potential of differentiated care models in handling high volumes of patients on ART and the effectiveness of group-based models of ART service delivery to encourage retention in care and enhance ART adherence (Mukumbang, Van Belle, Marchal, & van Wyk, 2017a). Support groups have now evolved as possible mechanisms for additional service delivery such as symptom screening, dispensing of ART and decongesting health facilities (Luque-Fernandez et al., 2013).
Support groups can be facility-based or community-based interventions for treatment and support for individuals on ART. Although the role of support groups is strongly promoted, the “evidence of their impact on key health outcomes has not been fully assessed” (Bateganya et al., 2015: 2), and none of the literature seems to have examined the effects of group-based interventions specifically on promoting adolescent ART adherence.

Mukumbang, Van Belle, Marchal and van Wyk (2017b) objectively reviewed available literature on theories explicating why and how group-based ART interventions work, and the literature was predominantly reporting on stable adults receiving ART through differentiated care models. The four pillars of differentiated care models are based on 1) when (monthly, 2-, 3- or 6-monthly), 2) where (health facility, community, home), 3) who (clinician, pharmacist, community health worker, peer/family), and 4) what services will be in the package (ART initiation/refills, adherence support, clinical monitoring, laboratory tests, treatment of opportunistic infections, psychosocial support) (Grimsrud, Walker, Ameyan & Brusamento, 2018). Differentiated care models can be defined as streamlining ART services through adapting the HIV care components to the needs of differentiated groups of patients (Mukumbang et al., 2017a). Differentiated care models usually includes the core ART provision activities, as well as addressing common clinical care challenges such as long waiting times, poor access to medications and long distance to clinics, through quick ART refills, encouraging self-efficacy, adherence support and mutual support amongst similar groups of patients (Mukumbang et al., 2017a). Namibia has recognised the utility of the abovementioned models and incorporated differentiated care models in the 2016 National guidelines for ART (5th Edition), in addition to recommendations for developing facility-based Teen Clubs. Although the national guidelines recommend establishment of Teen Clubs at facilities taking care of adolescents, facilities are encouraged to work towards establishing community-based adherence groups in line with the four pillars for differentiated care models reviewed above.
2.8 Interventions to support adherence and retention among adolescents

Several innovative interventions to enhance ART adherence and encourage retention in care amongst adolescents have been developed and implemented from population level to individual level interventions (policy/health system level, provider/health facility level, community level and individual level) (MacPherson et al., 2015). MacPherson et al. (2015) reported that interventions at population level such as decentralization of pediatric/adolescent-friendly services (policy/health system level) or extended clinic opening hours and adolescent-friendly services provision (provider/health facility level) emphasize less on individual needs but have greater potential to reach a larger number of adolescents and uses fewer resources than individual-focused interventions. In contrast, individual-level interventions such as counselling and education, direct observed therapy, financial incentives and adherence support devices, and community-level interventions (family/peer support) are more intensive but more responsive to individual needs (MacPherson et al., 2015). Adherence reportedly improved through individual adolescents and caregivers counseling and education offered by nurses through home-based care, but more evidence is needed (Berrien, Salazar, Reynolds, Mckay, & HIV Medication Adherence Intervention Group, 2004).

In support of the individual-level interventions, Foster, McDonald, Frize, Ayers and Fidler (2014) reported improved immunological and virologic outcomes in adolescents offered financial incentives and motivational interviewing to improve adherence to their treatment. An evaluation assessing the effectiveness of a community-level intervention conducted in France reported that a peer support group intervention for perinatally infected HIV positive adolescents was associated with improved well-being and a positive influence on health outcomes such as perceived treatment inventory, self-esteem inventory and perceived illness experience scale (Funck-Brentano et al., 2005). At provider/health facility level, Davila et al. (2013) argued that if resources allow, expanding youth services and centralizing youth specific care within the health care system can improve retention in care and health outcomes amongst adolescents.
The authors examined differences in retention in care between HIV-infected youths enrolled in integrated services era, adolescent-specific services era, and a combination of adolescent-specific services and motivational interviewing (educational activities and support groups) era, and recommended advocating for the later intervention at policy/health systems level (Davila et al., 2013).

2.9 Summary
The available literature from studies conducted from the global north to the global south, including sub-Saharan Africa acknowledge that adolescents living with HIV present the remaining biggest gap towards achieving epidemic control by 2030. ALHIV face substantial difficulties accessing HIV services and have worse treatment outcomes than other age groups, with several studies reviewed showing suboptimal ART adherence levels and rates of retention in care. However, several studies have provided evidence that efforts to develop adolescent-specific interventions have not been in vain as these interventions, from population to individual level, have provided promising results on improving ART adherence, retention in HIV care, and viral load suppression among HIV-infected adolescents on treatment. The studies have recommended further research on group and individual-based interventions to improve treatment outcomes, particularly in low- and middle-income countries, including in Africa.
CHAPTER 3: METHODOLOGY

3.1 Study design
A retrospective cohort study was conducted using medical records of HIV positive adolescents between ages of 10-19 years receiving ART at a hospital-based paediatric clinic in Windhoek, Namibia. The study population was stratified into two groups of adolescents attending the Teen Club stratum and adolescents who were receiving standard care. Routine clinical records of the study population from 1 July 2015 to 30 June 2017 were reviewed. The design was appropriate for studying of adolescents, based on exposure, who are in the Teen Club and the influence of the intervention on ART adherence and retention in care, and compare with a similar group of adolescents who were not exposed to the intervention. The groups were assessed retrospectively to establish any temporal sequence of events (variables) that may be associated with the multiple (three) study outcomes in the exposed and unexposed groups.

3.2 Study population and sampling
All adolescents between the ages of 10 to 19 years attending the paediatric ART clinic between 1 July 2015 to 30 June 2017 as their initial enrolment site, were eligible for inclusion in the study. Adolescents transferred-in were excluded from the study. According to the 2014 Namibian National ART Guidelines, the child HIV disclosure process should be initiated as early as 6 years to 10 years of age (MoHSS, 2014). Once adolescents are aware that they are HIV infected, they become eligible to enrol in the Teen Club. The study sample was all inclusive of the study population. An estimated 720 children and adolescents are receiving ART at the clinic and around 480 of them are aged between 10-19 years; of which 85 are members of the Teen Club. The study sample was stratified into two strata consisting of adolescents in the Teen Club stratum and the other stratum with adolescents in standard care. Any adolescent who attended at least one Teen Club meeting was considered exposed to the intervention. The calculated minimum total sample size using Epi-Info was 272 participants; with 46 from the Teen club stratum (exposed) and 226 in the non-Teen Club stratum (unexposed). Parameters used to calculate sample size include: a power of 80%; an assumed 20% difference between the two groups; with a 95% Confidence interval; and an Unexposed/Exposed ratio of 5.
Electronic Patient Monitoring System (ePMS) with all clients on ART at Intermediate Hospital Katutura Paediatric ART clinic (N≈720)

Selected all adolescents (10-19 years) who were on ART at Intermediate Hospital Katutura Paediatric ART clinic between 1 July 2015 and 30 June 2017 (N=482)

Excluded adolescents who were transferred in from other facilities to Intermediate Hospital Katutura Paediatric ART clinic

Adolescents (10-19 years) who were initiated and on ART at Intermediate Hospital Katutura Paediatric ART clinic between 1 July 2015 and 30 June 2017 (N=385)

Selected adolescents (10-19 years) attending Teen Club at Intermediate Hospital Katutura Paediatric ART clinic between 1 July 2015 and 30 June 2017 (N=78)

Selected adolescents (10-19 years) in standard care at Intermediate Hospital Katutura Paediatric ART clinic between 1 July 2015 and 30 June 2017 (N=307)

Figure 3-1: Flow chart of sampling process for the study
3.3 Data collection and management

Patient demographics and visit details are completed routinely by healthcare workers into individual Patient Care Booklets (PCBs) during clinic and pharmacy visits. Patient information is then entered onto an electronic database, the electronic Patient Monitoring System (ePMS), by data clerks. Patient data was extracted from the electronic database into an excel spreadsheet. Teen Club members sign-in at every Teen Club meeting, and the Teen Club register was reviewed to match patient data from the electronic database and the teen club members using the unique ART numbers allocated as unique patient identifiers at the clinic. Patient Care Booklets for patients with incomplete records in the electronic database were retrieved, and the missing information was added to the excel spreadsheet. Extracted data was coded using R statistical package and transferred and saved onto a password protected excel file to ensure that the data could not be altered. Data cleaning and preparation (coding and creating new variables) was done on the excel file which was then exported into an SPSS file. Further coding and labelling of variable categories allowed conversion and compatibility with R. The dataset in both excel and SPSS format were subsequently exported to R for the data analysis.

The key outcome variable for the study is viral load suppression. Viral load suppression has been used in several ART adherence studies as the standard biomarker of adherence levels and evidence shows that it is a reliable predictor of good adherence (Duarte et al., 2015). Once viral load results are received from the laboratory, they are recorded in the PCBs and subsequently entered on the ePMS. Missing viral load results on the ePMS were extracted from the PCBs. Other adherence outcome variables examined include measured adherence by clinicians (self-reported and using pill counts) and adherence to pharmacy and clinic appointments (Sangeda et al., 2014). The most important exposure variable is the model of care, with Teen Club members in the exposed group and adolescents in standard care in the unexposed group. Other variables of interest that were collected are illustrated in the data extraction tool (see Appendix 2).
3.4 Data analysis
The data analysis included univariate analyses to describe demographic variables such as sex and age distribution including the range, average ages, median and mode; clinical variables such as model of care, disclosure status, period on ART and type of regimen; and treatment outcomes such as viral load suppression, adherence measured by clinicians, and retention as measured by attendance to clinic and pharmacy appointments at 24 months.

Bivariate analysis was performed using the Chi-square test to determine the significance of associations between viral load suppression, measured adherence by clinicians, retention in care and selected demographic and clinical variables. Cut-off for significance of associations was set at \( p<0.05 \). If the sample size was very small in any cell (<5), Fisher’s exact test was used as an alternative to the Chi-square test. Risk ratios were also calculated for comparison of viral load suppression, ART adherence and retention is care between Teen Club members and adolescents in standard care.

The Kaplan-Meier survival analysis with log-rank test was used to compare the survival curves in the Teen Club and adolescents in standard care groups, as well as younger and older adolescents’ groups. Multivariate analyses were performed using the Cox regression method (Cox Proportional Hazards model) to analyze differences in retention in care between Teen Club members and adolescents in standard care, and other variables of interest. Time-to-event was defined as time to defaulting/Lost, LTFU, transferred out or died.

3.5 Validity and reliability
Measures were put in place to ensure that the scientific observations actually measured what they were intended to measure and produce true conclusions. Selection bias was ruled out as all adolescents between 10-19 years who started ART at the clinic were included in the study. The facility (treatment environment), clinicians, and service practices were the same between the groups, except the participants’ exposure to the Teen Club intervention. A comparison group which was not exposed to the intervention reduced threats to validity from possible confounding or other unexpected factors.
Viral load measurements were reviewed to ensure that the same service provider (the Namibia Institute of Pathology), and methods and instruments were used to produce the results. Facility management was consulted to establish if there may be other interventions that may have influenced the variables under investigation during the study period.

Data quality assurance checks and validation were conducted to determine the reliability of the data from the routine clinical data sources. The same PCBs and ePMS database are used at all ART facilities in Namibia. Changes over time in recording, use of codes and reporting that could have resulted in unreliable or invalid data being collected were checked and resolved. The data sources which were used are routinely examined regularly by data clerks and M & E officers for reliability and validity. Quality checks include reviewing the database for missing and out of range values, checking for duplicate values, accuracy and consistency of data such as age, and completeness of data entry. Data for each participant was accurately matched between the three data sources using assigned codes for each participant. Validity and reliability of the overall project was enhanced through triangulation of the three data sources and assessment of different adherence and retention variables, including use of plasma viral load as a biomarker of adherence levels.

3.6 Ethics considerations
Health research that involves individuals becoming identifiable through the collection, preparation, or use of medical records requires strict compliance with ethical norms and conduct (Cash et al., 2009). This study was approved by the Namibian Biomedical Research Ethics Committee and Research Management Committee based at the MoHSS, and the University of the Western Cape Biomedical Research Ethics Committee and Senate Higher Degrees.

Permission was obtained from the MoHSS to access the Patient Care Booklets (PCB), electronic database and Teen Club register. To ensure confidentiality and respect for the privacy and dignity of the participants, no personal identifying information was extracted from the registers or during the review of individual PCBs.
As proposed by Polit and Hungler (1993), anonymized identification numbers were used instead of participants’ names and only aggregated data for the groups was reported to protect individual confidentiality.

All adolescents who originally enrolled at the clinic aged 10-19 years were included in the study. The study is justifiable (in including children in the sample) because of its social value and possible health benefits as it may lead to improvement of participants’ circumstances and service provision. Clients who were classified as lost (missed more than 30 days) and lost to follow-up (missed appointment for more than 90 days) were flagged and the list was forwarded to clinic staff for tracing and follow-up for returning into care. Routine data reviews identified gaps in service delivery processes and data capturing procedures that were addressed for improvements, thereby improving patient care at the facility. The study data was stored on a password protected personal computer and backed up on a personal external hard drive. Study results will be disseminated through presentations to the clinic staff and management, MoHSS Directorate of Special Programs and other partners. We will seek for approval to disseminate the results from the MoHSS, which may include publication of the results and presentations at local and international conferences.
CHAPTER 4: RESULTS

4.1 Introduction
This chapter will report on the results observed from this study and the analysis thereof. The results will include a description of the demographic and clinical characteristics of the study participants and comparing the distribution of these characteristics between the Teen Club and standard care groups. It will also include an analysis of retention in care differences between Teen Club members and adolescents in standard care and between younger and older adolescents, a description of viral load suppression levels among all adolescents, Teen Club members, adolescents in standard care, younger and older adolescents, and an analysis and comparison of ART adherence levels among Teen Club members and adolescents in standard care.

4.2 Realization of Sample
A total of 482 adolescents aged between 10-19 years attended the paediatric ART clinic during the 2-year study period. All records of the adolescents were extracted from the ePMS for the two-year period. Records of adolescents who were transferred in from other facilities, who had incorrectly entered demographic information, and those with missing files/PCBs were excluded from the final study sample. Of the total study population, 385 adolescents were eligible, with 78 of them being in the Teen Club.

4.3 Demographic and clinical characteristics of study participants
The average age amongst adolescents who were included in the study was 14 years and 51% of them were aged 10-14 years (younger adolescents) whilst 49% were aged 15-19 years (older adolescents). However, the proportion of older adolescents in the Teen Club was twice as much as that of the younger adolescents, with a statistically significant association for model of care and age at 5% level (p = 0.015). Older adolescents constituted 66.7% of the club members whilst 33.3% were younger adolescents. The majority of club members were female adolescents, at 59%, whilst 41% were males, and the correlation between model of care and sex was statistically significant at 1% level (p = 0.001).
Table 4-1: Demographic and clinical characteristics of adolescent participants on ART at Intermediate Hospital Katutura Paediatric ART Clinic (N = 385)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Standard care (%)</th>
<th>Teen Club members (%)</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>173 (56.4)</td>
<td>32 (41.0)</td>
<td>205</td>
<td>0.015*</td>
</tr>
<tr>
<td>Female</td>
<td>134 (43.6)</td>
<td>46 (59.0)</td>
<td>180</td>
<td></td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-14 years</td>
<td>171 (55.7)</td>
<td>26 (33.3)</td>
<td>197</td>
<td>0.001**</td>
</tr>
<tr>
<td>15-19 years</td>
<td>136 (44.3)</td>
<td>52 (66.7)</td>
<td>188</td>
<td></td>
</tr>
<tr>
<td><strong>Disclosure status (n=372)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disclosed</td>
<td>278 (94.2)</td>
<td>77 (100)</td>
<td>355</td>
<td>0.031*</td>
</tr>
<tr>
<td>Not disclosed</td>
<td>17 (5.8)</td>
<td>0 (0)</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td><strong>ART regimen</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line regimen</td>
<td>226 (73.6)</td>
<td>53 (67.9)</td>
<td>279</td>
<td>0.318</td>
</tr>
<tr>
<td>Second line regimen</td>
<td>81 (26.4)</td>
<td>25 (32.1)</td>
<td>106</td>
<td></td>
</tr>
<tr>
<td><strong>Duration on ART</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 12 months</td>
<td>3 (1.0)</td>
<td>0 (0)</td>
<td>3</td>
<td>0.382</td>
</tr>
<tr>
<td>≥ 12 months</td>
<td>304 (99.0)</td>
<td>78 (100)</td>
<td>382</td>
<td></td>
</tr>
<tr>
<td><strong>Retention in care @ 24 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In care</td>
<td>276 (89.9)</td>
<td>71 (91.0)</td>
<td>347</td>
<td>0.931</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>18 (5.9)</td>
<td>4 (5.1)</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Transfer Out</td>
<td>13 (4.2)</td>
<td>3 (3.9)</td>
<td>16</td>
<td></td>
</tr>
</tbody>
</table>

* Correlation is significant at 0.05 level (2-tailed)

** Correlation is significant at 0.01 level (2-tailed)

All (100%) the adolescents in the Teen Club had their HIV status disclosed to them, which is a minimum requirement for enrolment in the club, and of all the adolescents included in the study 95.4% had their HIV status disclosed to them. The association between model of care and disclosure status was also significant at 5% level (p = 0.031). As shown in Table 4-1, there was no statistically significant association between the model of care and duration on ART (p = 0.382), type of ART regimen (p=0.318) or retention in care at 24 months (p = 0.931). Only three adolescents had been on ART for less than 12 months at the beginning of the study and were in the standard care group. The median duration on ART among all adolescents was 10.3 years.
All the Teen Club members included in the study had been on ART for a minimum of 12 months whilst 99% of those in standard care were experienced patients. Most of the adolescents included in the study were on a first line ART regimen (72%). Approximately 68% of the adolescents in the Teen Club were on a first line ART regimen whilst the other 32% were on a second line regimen. The proportion of Teen Club members who were still in care at the end of the study period (24 months) was almost similar (91%) to that of adolescents in standard care (89%). Only 4.2% of the adolescents were transferred out to other facilities whilst 5.7% of the adolescents were lost to follow up during the 2-year study period. Overall, 20% of the adolescents included in the study were Teen Club members whilst 80% were receiving standard care.

4.4 Retention in care among Teen Club and standard care adolescents

Figure 4-1 shows that the probability of being retained in care in the first 500 days (16 months) among Teen Club members was higher as compared to adolescents in standard care. Beyond 500 days the probability of being retained in care was the same among the two groups. The likelihood of being retained in care among Teen Club members was almost 100% within the first 200 days (approximately 6-7 months) whereas loss of adolescents in standard care occurred much earlier, within the first 30 days (1 month). However, there was no statistically significant difference in retention in care between the Teen Club members and the adolescents who received standard care at 24 months (p = 0.9).
4.5 Retention in care by Sex, Disclosure, ART regimen and ART duration
There was no statistically significant differences in retention in care at 24 months between males and females (p = 0.343), between adolescents disclosed to and adolescents who did not have their HIV status disclosed to them (p = 0.343), between adolescents on a first line ART regimen and those on second line (p = 0.269), and between adolescents on treatment for less than 12 months and those who had been on treatment for 12 months and above (p = 0.847).

4.6 Association between retention in care and adolescents age group
Figure 4-2 shows that the probability of being retained in care is similar between the younger and older adolescents for approximately the first 500 days (16-17 months).
Thereafter, the likelihood of being retained in care was higher among the younger adolescents as compared to the older adolescents beyond 500 days during the study period. However, the log rank test showed that there was no statistically significant difference in the survival curves between the younger and older adolescents during the 2-year study period (p = 0.4).

However, there was sufficient evidence of a statistically significant difference at 5% significance level in retention in care at 24 months between younger and older adolescents (p = 0.016). The chance of being retained in care among older adolescents at 24 months was significantly less compared to younger adolescents (RR = 0.918; 95% CI = 0.858-0.982).
4.7 Loss to follow-up by Model of care

Table 4-2: Cox proportional hazards regression model

|              | coef  | exp(coef) | se(coef) | z     | Pr(>|z|) |
|--------------|------|-----------|----------|-------|----------|
| Care         | -0.498589 | 0.607387 | 0.669281 | -0.745 | 0.45629  |
| Age          | 0.266007  | 1.304744 | 0.100969 | 2.635 | 0.00843 ** |
| Sex          | -0.467084 | 0.626828 | 0.507478 | -0.920 | 0.35736  |
| Disclosure   | -2.031364 | 0.131157 | 0.844418 | -2.406 | 0.01614 * |
| Regimen      | -1.099095 | 0.333172 | 0.500542 | -2.196 | 0.02811 * |
| Duration     | -0.012241 | 0.987834 | 0.005798 | -2.111 | 0.03476 * |

Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
Concordance = 0.755 (se = 0.07)
Rsquare = 0.044 (max possible= 0.416)
Likelihood ratio test = 16.63 on 6 df, p=0.01
Wald test = 16.47 on 6 df, p=0.01
Score (log-rank) test = 17.99 on 6 df, p=0.006

The fitted Cox proportional hazards model was;

$$\log \left( \frac{h(t)}{h_0(t)} \right) = -0.499 X_1 + 0.266 X_2 - 0.467 X_3 - 2.031 X_4 - 1.099 X_5 - 0.012 X_6$$

Or equivalently,

$$\frac{h(t)}{h_0(t)} = \exp(-0.499 X_1 + 0.266 X_2 - 0.467 X_3 - 2.031 X_4 - 1.099 X_5 - 0.012 X_6)$$

$$= 0.607 X_1 + 1.305 X_2 + 0.627 X_3 + 0.131 X_4 + 0.333 X_5 + 0.988 X_6$$

where,

$h(t)$ = expected hazard of retention at time $t$
$h_0(t)$ = baseline hazard of retention at time $t$
$X_1$ = model of care
$X_2$ = age group
$X_3$ = sex
$X_4$ = disclosure
$X_5$ = regimen
$X_6$ = duration on ART

Table 4-2 shows that the hazard ratio for model of care was 0.607 meaning that the hazard rate for being lost from care among Teen Club members was approximately 40% less compared to adolescents in standard care.
Although the hazard ratio confirms that there was better retention in care among Teen Club members, there was no statistically significant difference in hazard rates on retention in care between those in Teen Club and the adolescents in standard care ($p = 0.456$). There was also no statistically significant difference in hazard rates of retention in care between males and female adolescents ($p = 0.357$).

### 4.8 Loss to follow-up by Age and ART regimen

The hazard ratio for age group was 1.305 meaning that the hazard rate for being lost from care among the older adolescents was approximately 30% more compared to the younger adolescents. The hazard ratio confirms that there was higher retention in care among younger adolescents. There was a statistically significant difference in hazard rates for retention in care between the younger and the older adolescents at 1% level ($p = 0.008$).

The hazard ratio for type of ART regimen was 0.333 meaning that the hazard rate for being lost from care among adolescents on a first line ART regimen was approximately 67% less compared to adolescents on a second line ART regimen. The hazard ratio confirms that there was higher retention in care among adolescents on a first line ART regimen. There was a statistically significant difference in hazard rates for retention in care between the first line and the second line ART regimen groups at 5% level ($p = 0.028$). The hazard rates for duration on ART (HR = 0.988; $p = 0.035$) and disclosure status (HR = 0.131; $p = 0.016$) were statistically significant at 5% level, showing that adolescents on ART for 12 months and more had less chance of being lost to follow up than those on ART for less than 12 months at the beginning of the study, and adolescents disclosed to had less chance of LTFU compared to those not disclosed. However, the numbers of adolescents on ART for less than 12 months and adolescents that were not disclosed to among the study participants were quite small.
4.9 Viral load suppression among Teen Club and standard care adolescents

Viral load suppression at amongst the adolescents who were included in the study at Intermediate Hospital Katutura Paediatric ART clinic was on average at 87% (68% fully suppressed, 19% suppressed) and 13% not suppressed for the 2-year study period. A similar trend was observed during the 2-year period, at 6 months, 12 months and 18 months visits.

Figure 4-3: Viral load status by model of care
Table 4-3: Demographic and clinical characteristics and viral load suppression

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>6 MONTHS</th>
<th></th>
<th></th>
<th>12 MONTHS</th>
<th></th>
<th></th>
<th>18 MONTHS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fully</td>
<td>Suppressed</td>
<td>Unsuppressed</td>
<td>p-value</td>
<td>Fully</td>
<td>Suppressed</td>
<td>Unsuppressed</td>
<td>p-value</td>
</tr>
<tr>
<td>Model of care</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teen Club</td>
<td>51 (69%)</td>
<td>11 (15%)</td>
<td>12 (16%)</td>
<td>0.298</td>
<td>50 (69%)</td>
<td>9 (12%)</td>
<td>13 (18%)</td>
<td>0.438</td>
</tr>
<tr>
<td>Standard care</td>
<td>195 (69%)</td>
<td>57 (20%)</td>
<td>30 (11%)</td>
<td></td>
<td>192 (68%)</td>
<td>50 (18%)</td>
<td>39 (14%)</td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-14 years</td>
<td>134 (72%)</td>
<td>38 (21%)</td>
<td>13 (7%)</td>
<td>0.015*</td>
<td>135 (73%)</td>
<td>31 (17%)</td>
<td>18 (10%)</td>
<td>0.021*</td>
</tr>
<tr>
<td>15-19 years</td>
<td>112 (65%)</td>
<td>30 (18%)</td>
<td>29 (17%)</td>
<td></td>
<td>107 (63%)</td>
<td>28 (17%)</td>
<td>34 (20%)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>126 (68%)</td>
<td>38 (20%)</td>
<td>22 (12%)</td>
<td>0.793</td>
<td>130 (69%)</td>
<td>35 (19%)</td>
<td>24 (13%)</td>
<td>0.38</td>
</tr>
<tr>
<td>Female</td>
<td>120 (71%)</td>
<td>30 (18%)</td>
<td>20 (12%)</td>
<td></td>
<td>112 (68%)</td>
<td>24 (15%)</td>
<td>28 (17%)</td>
<td></td>
</tr>
<tr>
<td>Disclosure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disclosed</td>
<td>233 (70%)</td>
<td>63 (19%)</td>
<td>39 (12%)</td>
<td>0.614</td>
<td>230 (69%)</td>
<td>57 (17%)</td>
<td>47 (14%)</td>
<td>0.122</td>
</tr>
<tr>
<td>Not disclosed</td>
<td>11 (69%)</td>
<td>2 (12%)</td>
<td>3 (19%)</td>
<td></td>
<td>10 (62%)</td>
<td>1 (6%)</td>
<td>5 (31%)</td>
<td></td>
</tr>
<tr>
<td>ART regimen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line</td>
<td>192 (74%)</td>
<td>43 (17%)</td>
<td>23 (9%)</td>
<td>0.012*</td>
<td>189 (74%)</td>
<td>36 (14%)</td>
<td>32 (12%)</td>
<td>0.004*</td>
</tr>
<tr>
<td>Second line</td>
<td>54 (55%)</td>
<td>25 (26%)</td>
<td>19 (19%)</td>
<td></td>
<td>53 (55%)</td>
<td>23 (24%)</td>
<td>20 (21%)</td>
<td></td>
</tr>
</tbody>
</table>

* indicates statistical significance at 5% level
Table 4-3 shows that there was no sufficient evidence of a statistically significant difference in viral load suppression levels at 6 months (p = 0.298), at 12 months (p = 0.438) and 18 months (p = 0.113) between Teen Club members and adolescents in standard care. No statistically significant differences were observed in viral load suppression levels between adolescents whose HIV status was disclosed to and those who were not disclosed to at 5% significance level. There was sufficient evidence of statistically significant differences in viral load suppression at 5% significance level between the younger (10-14 years) adolescents and older (15-19 years) adolescents at 6 months (p = 0.015) and at 12 months (p = 0.021), but there was no statistically significant difference at 18 months at 5% level (p = 0.091). There was also sufficient evidence of a statistically significant difference in viral load suppression between adolescents on a first line ART regimen and those on second line at 6 months (p = 0.012), at 12 months (p = 0.004), and at 18 months (p = 0.005). The adolescents on first line ART regimens were more likely to be suppressed than those on a second line regimen.

Table 4-4: Relative Risk for viral load suppression by Age, Sex and Model of care

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>6 Months RR (95% CI)</th>
<th>12 Months RR (95% CI)</th>
<th>18 Months RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model of care</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teen Club</td>
<td>0.94 (0.84 - 1.05)</td>
<td>0.95 (0.85 - 1.07)</td>
<td>0.90 (0.79 - 1.02)</td>
</tr>
<tr>
<td>Standard care</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-19 years</td>
<td>0.89 (0.83 - 0.97)</td>
<td>0.89 (0.81 - 0.97)</td>
<td>0.92 (0.85 - 1.00)</td>
</tr>
<tr>
<td>10-14 years</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.99 (0.93 - 1.08)</td>
<td>1.05 (0.96 - 1.15)</td>
<td>0.97 (0.89 - 1.05)</td>
</tr>
<tr>
<td>Female</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* indicates statistical significance
Table 4-4 shows that the chance of viral load suppression among Teen Club members at 6 months was about 6% less compared to viral load suppression among adolescents in standard care (RR = 0.938; 95% CI = 0.842-1.045), about 5% less at 12 months (RR = 0.952; 95% CI = 0.845-1.071), and about 10% less at 18 months (RR = 0.897; 95% CI = 0.792-1.016), such that adolescents in standard care had higher viral suppression levels than Teen Club members. However, the relative risk of viral load suppression between Teen Club members and adolescents in standard care was not statistically significant at all time points as the 95% confidence intervals include 1. There were also no statistically significant differences in viral load suppression levels between males and females at 6 months (88 % vs 89%, p= 0.793), 12 months (88 % vs 83%, p= 0.380), or 18 months (86 % vs 89%, p= 0.581).

The chance of viral load suppression among the older adolescents was about 10% less compared to viral load suppression among younger adolescents at 6 months (93 % vs 83%, p= 0.015), and 12 months (90 % vs 80%, p= 0.021), and about 8% less at 18 months (90 % vs 83%, p= 0.091).

4.10 Adherence levels among Teen Club and adolescents in standard care
The average measured ART adherence by the clinicians during clinical visits was 89% good, 6% fair and 5% poor amongst all the adolescents over the 2 years. Similar ART adherence levels were observed throughout each of the 3-monthly visits. Table 4-5 shows that there was no statistically significant difference in ART adherence between Teen Club members and adolescents in standard care (p = 0.277), between males and females (p = 0.980) and between adolescents on a first line and those on a second line ART regimen (p = 0.479) at the first 3 months clinic visit. There were statistically significant differences in measured ART adherence at 5% significance level between the younger and older adolescents (p = 0.033), between adolescents who were disclosed and those not disclosed (p = 0.035), and between adolescents who had been on ART for less than 12 months and those on ART for 12 months and above (p = 0.030).
Table 4-5: Demographic and clinical characteristics and ART adherence at 3 months

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model of care</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teen Club</td>
<td>74 (95%)</td>
<td>1 (1%)</td>
<td>3 (4%)</td>
<td>0.277</td>
</tr>
<tr>
<td>Standard care</td>
<td>276 (90%)</td>
<td>17 (6%)</td>
<td>12 (4%)</td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-14 years</td>
<td>179 (91%)</td>
<td>13 (7%)</td>
<td>4 (2%)</td>
<td>0.033*</td>
</tr>
<tr>
<td>15-19 years</td>
<td>171 (91%)</td>
<td>5 (3%)</td>
<td>11 (6%)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>186 (91%)</td>
<td>10 (5%)</td>
<td>8 (4%)</td>
<td>0.98</td>
</tr>
<tr>
<td>Female</td>
<td>164 (92%)</td>
<td>8 (4%)</td>
<td>7 (4%)</td>
<td></td>
</tr>
<tr>
<td>Disclosure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disclosed</td>
<td>327 (92%)</td>
<td>15 (4%)</td>
<td>13 (4%)</td>
<td>0.035*</td>
</tr>
<tr>
<td>Not disclosed</td>
<td>13 (76%)</td>
<td>3 (18%)</td>
<td>1 (6%)</td>
<td></td>
</tr>
<tr>
<td>ART regimen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line</td>
<td>255 (92%)</td>
<td>12 (4%)</td>
<td>10 (4%)</td>
<td>0.749</td>
</tr>
<tr>
<td>Second line</td>
<td>95 (90%)</td>
<td>6 (6%)</td>
<td>5 (5%)</td>
<td></td>
</tr>
<tr>
<td>Duration on ART</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 12 months</td>
<td>2 (67%)</td>
<td>0 (0%)</td>
<td>1 (33%)</td>
<td>0.030*</td>
</tr>
<tr>
<td>≥ 12 months</td>
<td>348 (92%)</td>
<td>18 (5%)</td>
<td>14 (4%)</td>
<td></td>
</tr>
</tbody>
</table>

* indicates statistical significance at 5% level

There was no consistent trend on the observed differences between ART adherence and age group, disclosure status or duration on ART over the 2-year study period. There was no observed difference in the chance for good ART adherence among Teen Club members as compared to adolescents in standard care at 3 months (RR = 1.001; 95% CI = 0.952-1.052). Generally, there were no statistically significant differences at 5% significance level in clinician-measured ART adherence between club members and adolescents in standard care.
Figure 4-4: Adherence levels by model of care

Figure 4-4 also shows that there was no statistically significant difference in ART adherence between Teen Club members and adolescents who were in standard care.

Sensitivity analysis

Compared to the primary findings, our study found no significant differences in the sensitivity analysis on viral load suppression rates between Teen Club members and adolescents in standard care by age groups at 6 months (p = 0.819) and 12 months (p = 0.427).
CHAPTER 5: DISCUSSION

5.1 Introduction
This study aimed to compare ART adherence, retention in HIV care, and viral load suppression between adolescents in a Teen Club and those who were receiving standard care at the Intermediate Hospital Katutura Paediatric ART clinic during the two-year period 1 July 2015 to 30 June 2017. Furthermore, the study also sought to describe the uptake of the Teen Club intervention among adolescents, as well as any observed association between the adolescents demographics (age, sex), other clinical variables (duration on ART, type of Regimen, HIV disclosure status), and the three outcome variables (ART adherence, retention in care and virologic suppression). Retention in care was determined by clinic attendance from the beginning of the study period up to 24 months whilst adherence to ART data was collected at 3-month intervals and viral load results collected at 6 months intervals. In the next section, the first topic of discussion is the data completeness.

5.2 Data completeness
The completeness of the data for all the variables ranged from 85% for the 18 months viral load results to 100% for age, sex and model of care variables among the eligible 385 adolescents. However, there was a substantial quantity of missing data on the ePMS and data had to be collected from the primary sources, the PCBs. Electronic data entry from the PCBs was incomplete and there is need to optimize the data entry processes. Some of the missing data on both the ePMS and in the PCBs can be attributed to adolescents who were lost to follow up or transferred out during the study period, although the percentage of adolescents lost to follow up and transferred out was only 9.9%. The lower level of data completeness on viral load results throughout the two-year study period may point to lower levels of viral load monitoring by the healthcare workers or suboptimal routine data collection. The considerably high level of data completeness on patient demographics may indicate emphasis and rigor in data collection completeness during the enrolment process, although there may be gaps in transferring that data from the patient
files to the electronic data base. As Makombe et al. (2008) argued, the level of data completeness may negatively impact site monitoring and national planning.

5.3 Retention in HIV care
This study found the overall retention in care rates to be approximately 90.1% at 24 months among all adolescents included in the study. Similar retention in care rates have been observed in other studies conducted in similar settings in Africa. A similar study conducted in South Africa reported retention in care rates of 89% which were also comparative to a report from a meta-analysis of six studies conducted in South Africa which reported 83% retention in care rates among adolescents at 24 months (Zanoni, Sibaya, Cairns, Lammert, & Haberer, 2017). The study conducted by Nabukeera-Barungi et al. (2015) in Uganda also reported that 90% of adolescents were retained in HIV care at 12 months after ART initiation whilst Ssali et al. (2014) reported rates of 96%, 90% and 83% at 6, 12 and 24 months respectively in another study in Uganda.

5.3.1 Retention among Teen Club members and adolescents in standard care
Although the study produced similar retention in care rates between adolescents in the club and those in standard care at 24 months, 91% and 89% respectively, there was better retention rates among Teen Club members. Comparable rates were reported by Zanoni et al. (2017) although the authors reported bigger differences of 95% retention among adolescents attending a dedicated adolescent clinic as compared to 85% (OR = 3.7; 95% CI 1.2, 11.1; p = 0.018) for adolescents in standard care, although the study defined retention as one clinic visit or pharmacy visit in the prior six months. A study in Kenya observed no differences in retention rates at 6 months and 12 months between adolescents accessing youth-friendly services and those who attended the selected facilities prior to implementation of the youth-friendly services (Teasdale et al., 2016). However, it was noted that the Kenya study may not have observed any differences because of the shorter follow-up time and temporal differences in the pre and post design. Decreasing rates of retention were also observed in our study in both the Teen Club group and the adolescents in standard care group. Decreases with time from high initial retention rates among adolescents have been previously documented in other studies in southern Africa (Zanoni et al., 2017).
5.3.2 Retention rates by adolescent age groups
Notably, there was a significant difference observed in this study in retention rates between the younger (10 – 14 years) and the older adolescents (15 – 19 years) at 24 months, with younger adolescents having better retention rates. This finding of comparatively poorer retention rates among older adolescents is supported by observations reported in other studies conducted in other low and middle income countries. Ssali et al. (2014) found the risk of non-retention among older adolescents to be 1.30 times higher than the risk in younger adolescents at 24 months (95% CI: 1.02 - 1.66). Evans et al. (2013) also reported lower hazard rates among younger adolescents on ART, arguing that the younger adolescents are less likely to be lost to follow up because the paediatric clinics are more designed to care for the younger adolescents than the older ones, and the younger adolescents are still under the care of a caregiver. The higher rate of attrition (loss to follow-up) among older adolescents may be due to challenges associated with the transition from paediatric to adult care, as the age group 15 – 19 years marks the transitional age range to adulthood. Reasons behind losses to follow up among older adolescents may also include changes in residence due to school/university and/or employment re-location. The fact that the Teen Club had twice as many older adolescents as the younger ones (with a statistically significant association between age group and model of care at 0.01 level) may have negatively influenced the comparative magnitude of the difference in the retention rates between the club members and adolescents in standard care, where the age distribution was more balanced.

5.3.3 Demographic and clinical factors associated with retention in care
This study did not find any evidence of differences in retention in care between female and male adolescents at 24 months. Other studies have reported differences in association between sex and rates of retention in care. Ssali et al. (2014) found that the risk of non-retention in care was significantly reduced in adolescent males compared to their female counterparts at 24 months. In contrast, a study involving adolescents conducted in America found better retention rates in males compared to female adolescents. However, the American study was done on a population that included men having sex with men (MSM), heterosexual men, heterosexual females, and females and males who use injectable drugs (Hall et al., 2012).
This arguably points to the importance of context in which studies are conducted, taking into consideration sexual and health behaviours in the population of interest and being aware of the local drivers of the epidemic.

The study also showed that adolescents who had been disclosed to were less likely to be lost to follow up. There was enough evidence in support of reduced hazard rates among adolescents who had their HIV status disclosed to them as compared to those who had not gone through the disclosure process. Disclosure of HIV status is an essential component of paediatric HIV care, long-term HIV management and an important step towards the transition from paediatric into adolescent and eventually adult care (Vreeman, Scanlon, et al., 2014). A study at County Referral Hospital in Kenya found a direct correlation between disclosure and retention in care, with overall retention at 64% for adolescents not disclosed to, 82% for partial disclosure, and 92% among adolescents who had full disclosure (Ouma, Tembula, McLigeyo, Njogu, & Kiare, 2016). Failure to disclose HIV status may result in poor understanding of why an adolescent need to stay in care, which may negatively influence retention rates among adolescents. The overall high rate of disclosure among all adolescents in the study may have contributed to the relatively high overall retention rate, and in particular better retention rates among adolescents in the Teen Club in which 100% of the adolescents were disclosed to. It is also valuable to note that there was a statistically significant association between disclosure status and the model of care (i.e. membership in Teen Club group or the adolescents who were in standard care), which may have contributed to better retention rates in the Teen Club group.

The observed reduced attrition among adolescents on a first line ART regimen as compared to adolescents on a second line ART regimen is likely due to the argument that adolescents on a second line regimen may have already been exhibiting poor outcomes on the first line regimen, which necessitated the switch to a second line regimen. In addition, there was no statistically significant association between model of care and the type of ART regimen.
Kyaw et al., (2017) reported that studies in Africa have shown rates of 13% to 40% poor treatment outcomes among patients on a second line ART regimen and described the different factors associated with second line treatment failure such as duration on first line ART, type of previous and current regimen, and late detection of first line ART failure.

5.4 Viral load suppression
In this study, the overall viral load suppression rates among the adolescents included in the study was at 87% - which almost reached WHO target of 90%. According to the 2017 Namibian National Guidelines for Antiretroviral Treatment, virologic status is classified in three categories namely, fully suppressed (< 40 copies/ml), suppressed (40-999 copies/ml) and unsuppressed (≥ 1000 copies/ml). The aim for this classification is for earlier identification of patients having suboptimal responses to therapy, whose immunologic and clinical responses may not have deteriorated at this stage, but persistently have viral loads of above 40 copies/ml. these patients undergo different clinical management, which includes intensive adherence counselling and support to achieve full suppression and avoid treatment failure that may necessitate switching to a second line ART regimen (Republic of Namibia Ministry of Health and Social Services, 2016). The results of this study showed that overall 68% of the adolescents included in the study were fully suppressed, 19% were suppressed, and 13% were not suppressed on average at the three 6-monthly visits during the 2-year study period. Viral load suppression levels were assessed at the 6 months, 12 months and 18 months visits. All children and adolescents aged 19 and below initiated on therapy are expected to routinely have viral load tests done every 6 months.

Similar viral load suppression levels among adolescents have been reported in other studies in Africa and in the sub-Saharan Africa region. The Zanoni et al. (2017) study in South Africa found viral load suppression rates among adolescents of 81% using a cut-off of < 400 copies/ml to define HIV-1 viral suppression. A literature review conducted by Ferrand et al. (2016) showed wider variations in studies that assessed viral load suppression rates among adolescents at 12 months after ART initiation, with viral load
suppression rates ranging from 27% to 89% in studies stratified by duration on ART and 28% to 87% in studies not stratified by duration on ART.

5.4.1 Viral suppression among Teen Clubs and adolescents in standard care
This study did not show any significant differences in viral load suppression rates between Teen Club members and adolescents who were receiving standard care. Overall, the viral load suppression rates were relatively high among all adolescents included in the study. The Intermediate Katutura Hospital Pediatric ART clinic is a specialized HIV clinic with dedicated staff for pediatric HIV management, which includes a physician, nurses, counsellors and other support staff. The quality of HIV care and treatment outcomes would generally be expected to be better than HIV care in an integrated primary healthcare (PHC) facility where you may not have dedicated specialized staff to manage pediatric HIV patients. The 2015 Namibia Preliminary Report for Adolescents Assessment reported viral load suppression rates of 74% and 70% among adolescent girls and boys respectively, and 73% and 63% among 10-14 years and 15-19-year olds respectively (Republic of Namibia Ministry of Health and Social Services, 2016). The study population consists mostly of adolescents who had been receiving specialized HIV care for more than 12 months, with a median period on ART of 10.3 years. This points to mostly treatment-experienced adolescents, and it is expected that generally viral load should reach undetectable levels by 6 months of therapy in fully adherent clients (Republic of Namibia Ministry of Health and Social Services, 2016). The meta-analysis done by Ferrand et al., (2016) reported on varied published viral load suppression results among adolescents, and emphasized the need to report suppression rates stratified by duration on ART and reporting of median duration on ART so as to contextualize treatment outcomes.

The Zanoni et al. (2017) study showed that there was better viral suppression levels in an adolescent-friendly HIV clinic (91%) compared to those in a standard pediatric clinic (80%). However, the adolescent-friendly clinic was based on a differentiated care model, providing HIV medication, psychosocial and peer support, education and sports, lunches and other entertainment activities through a Saturday clinic (Zanoni et al., 2017).
The model for the adolescent-friendly clinic reduced school absenteeism and stigma in addition to the services provided, resulting in better viral suppression levels and retention in care.

Our results suggest that the Teen Club intervention model implemented at the specialized paediatric HIV clinic may not offer adequate additional benefits to the club members on viral suppression, which may depend on other factors besides levels of adherence to treatment. Several reports have also showed reduced viral suppression levels amongst older adolescents and considering that 66.7% of the teen club members were older adolescents (p = 0.015), age could have influenced viral suppression levels among club members.

5.4.2 Viral load suppression levels among younger and older adolescents
The results showed that the Teen Club consists of twice as many older adolescents compared to younger adolescents. The association between age and the model of care was statistically significant at 5% level. There was also a statistically significant difference in viral load suppression levels between older and younger adolescents, with the older adolescents having about 10% less chance of viral load suppression compared to younger adolescents at 6 months and 12 months, and 8% less at 18 months. Similar results have been described in other studies in Africa, with Evans et al. (2013) reporting that older adolescents were more likely to be unsuppressed as compared to their younger counterparts at 6 months in a study conducted in adolescents and young adults in Mpumalanga (RR = 1.75; 95% CI = 1.25-2.47). The association between age and viral suppression was also described as a significant factor in other studies that compared viral suppression levels among young adults and adolescents, showing that younger adolescents had higher rates of viral load suppression (Nglazi et al., 2012; Nachega et al., 2009). As discussed earlier, the paediatric HIV clinics provide a more favourable environment for younger adolescents in general, and the younger adolescent is more likely to have better treatment outcomes due to closer caregiver support.
5.4.3 **Demographic and clinical factors associated with viral load suppression**

This study did not show any statistically significant association between sex and viral load suppression levels. Results from three sub-Saharan Africa countries showed differences in viral load suppression levels among males and females with surveys in Malawi and Zimbabwe showing better viral load suppression levels in women compared to men whilst in contrast, the Zambia survey showed better suppression levels in men compared to women (Avert, 2016). However, the Namibia Population-based HIV Impact Assessment (NAMPHIA) preliminary report of 2018 reported that among adults aged 15 – 64 years in Namibia, women had better viral load suppression levels than men (NAMPHIA, 2018).

Our study did not show any association between disclosure status and viral load suppression. Vreeman *et al.* (2014) argued that HIV disclosure is essential for HIV disease management although it is not well-characterised in resource-limited countries, and that more research is required to establish this association. In contrast, the type of ART regimen was consistently associated with viral load suppression at 6 months, 12 months and 18 months. The adolescents on a first line regimen were more likely to be suppressed than those on a second line ART regimen. As alluded to earlier, this may be due to the fact that the adolescents on second line would have been failing on the first line already and would be more likely to be unsuppressed than those on first line.

5.5 **Adherence to ART**

The results of this study showed that ART adherence among all adolescents included in the study was on average at 89% good, 6% fair and 5% poor as measured by clinicians during clinical visits. In Namibia adherence is classified as good at levels ≥ 95% adherence, fair at 85% - 94%, and poor below 85%. Similar ART adherence levels were observed throughout the 3-monthly visits during the 2-year study period. Taking at least 95% of all ART doses is widely regarded as a benchmark for good adherence (although some studies consider > 85% as good adherence) and a meta-analysis of studies conducted on adolescents in 53 countries in Africa and Asia found adherence levels of approximately 84% (Ridgeway *et al.*, 2018). A study of ART adherence in low-and middle-income countries estimated adherence levels between 49% and 100% (Vreeman,
Studies on ART adherence among adolescents have produced varied results and a systematic review and meta-analysis done in 2014 showed that overall, about 62% of adolescents and young adults were adherent to ART (as defined by > 85% to 100%) from studies globally (Kim et al., 2014).

The variability of the results is as much dependent on methodologies used for measuring adherence in the studies as it is differences in actual adherence levels among the adolescents. In Namibia, ART administration should be reviewed in detail and adherence levels determined during clinic visits. Adherence is assessed through pill counts by the clinicians, kept appointments, discussion about who administers the medicine routinely, and on holidays, when and where, self- or proxy-report of how many doses missed, as well as how medication times fit into the family schedule. However, patients’ or caregivers’ responses on ART adherence are subject to social desirability bias or recall bias. Some studies have utilized viral load suppression as a biomarker of ART adherence levels, but it should be noted that although viral load levels are a good indicator of ART adherence, an unsuppressed viral load is not necessarily always an indication of poor adherence (Wiener, Riekert, Ryder, & Wood, 2004). There are other causes of failure which need to be considered as well such as intercurrent Opportunistic Infections (e.g. TB), adverse drug-drug interactions, incorrect dosage of ARVs, poor absorption of medication and incorrect storage of medication (Republic of Namibia Ministry of Health and Social Services, 2016).

5.5.1 Adherence levels among Teen Club and adolescents in standard care
The results of this study did not show any statistically significant differences in ART adherence between Teen Club members and adolescents in standard care at any of the 3 monthly visits during the study period. This finding is in line with results showing no significant differences observed in retention in care rates and viral load suppression levels between the club members and adolescents in standard care, indicative of the strong association between the three outcomes. The relationship between adherence to ART and group-based interventions targeting adolescents on ART is not well described and studies have reported mixed results due to the complexities and substantially variable methods of measuring adherence.
Ridgeway et al. (2018) reported that among two studies that evaluated group counseling for ALHIV, one found statistically significant intervention effects and the other did not, whilst a pilot RCT in Thailand providing group counseling to adolescents aged 15–24 years found significant differences in the proportions of patients with ART adherence above 95% at 18 weeks (p<0.001). A second pilot RCT conducted in South Africa which evaluated a group counseling intervention delivered to young ALHIV aged 10–13 years and their family members did not find a significant treatment effect (p = 0.05). Ridgeway et al. (2018) argued that it was difficult to draw conclusions on mixed and limited data and although there were some significant findings on effects of some group interventions on adolescent ART adherence in some of the studies reviewed, further investigation of this relationship was warranted.

5.5.2 Demographic and clinical factors associated with ART adherence

The results of our study showed that there were statistically significant differences in ART adherence between younger and older adolescents at 3 months, with younger adolescents having better adherence levels. A similar trend was observed in viral load suppression levels and retention in care rates, pointing to the same factors, such as caregiver support, influencing better outcomes in the younger adolescents. Adolescents who had been on treatment for 12 months and more also showed significantly better adherence than those on treatment for less than 12 months. This finding supports the argument that treatment experienced adolescents may have better treatment outcomes as they would have most likely gone through the disclosure process, including disclosure to relations around them, making it much easier to take their medication at the right time with reduced fears of stigma. There was also a statistically significant difference in ART adherence between adolescents who were disclosed and those not disclosed. The relationship between ART adherence and disclosure of HIV status is not well described, and studies have reported mixed results. There are several reasons to suggest that HIV disclosure may lead to improved adherence, including better access to family and social support and increased personal responsibility for taking medication. On the other hand, there are also reasons why HIV disclosure might be associated with poor adherence.
The disclosure process may be a traumatic event for many children, and they may experience feelings of anger, rebellion, depression and hopelessness, which may result in temporary or longer-term problems with adherence to treatment. The negative effects of stigma, which may include efforts to keep their HIV status a secret by not taking or hiding medicines, may also negatively impact adherence for disclosed children more than those not disclosed to (Vreeman, Scanlon, et al., 2014).

5.6 Limitations of the study
The use of a retrospective cohort study design meant that we had to rely on the accuracy of the record keeping by the clinicians, counsellors and data clerks. The data collection process involved extraction of information entered on the electronic data base (ePMS), manually reviewing individual patient files (PCBs), and reviewing Teen Club attendance registers. Reliance on routinely collected data meant that we could not control the exposures and outcomes of interest in the study. The missing data affected the overall description of the study population characteristics and subsequent analysis of the data. There were also a number of missing files that could have been included in the study. The large amount of missing data could have potentially influenced the findings of the results. The inequivalence in sample sizes between the comparison groups (Teen club members vs adolescents in standard care) could also potentially result in a type II error.
CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions
Worldwide, adolescents who are on ART are reportedly at higher risk of non-retention in care, poor adherence to ART, and subsequently poor levels of viral load suppression compared to children and adults. Studies have shown that adolescent-friendly HIV services can lead to substantial improvements in treatment outcomes among adolescents on ART, which can be comparable to treatment outcomes among children and adults. Furthermore, retention in care and adherence support through peer support groups is reportedly an effective strategy to improve treatment outcomes for individuals on ART in general. The Intermediate Hospital Katutura Paediatric ART clinic provides specialized HIV services for children and adolescents, with dedicated staff, systems and a conducive environment to address children and adolescent-specific treatment issues. In addition, the clinic introduced the Teen Club as an intervention beyond standard care to further enhance adherence to ART and retention rates among adolescents through peer support, health education and psychosocial support. Thus, this study sought to compare the ART adherence levels, viral load suppression and retention in care rates between adolescents attending the Teen Club and those receiving standard care during the period 1 July 2015 to 30 June 2017.

Our study found no significant differences in adherence to ART, viral load suppression and retention in care rates between adolescents that were in the Teen Club and those in standard care, although there were slightly higher adherence and retention rates among Teen Club members. Overall, retention rates were at 90.1% at 24 months among all adolescents included in the study whilst adherence levels were on average 89% good (≥ 95%), 6% fair (85-94%) and 5% poor (< 85%) throughout the 2-year study period. Overall viral load suppression levels were at 87% (68% < 40 copies/ml and 19% 40-<1000 copies/ml) and 13% were unsuppressed. These relatively high retention rates, adherence levels and viral load suppression rates are comparable to rates reported in studies that assessed treatment outcomes in adolescents receiving treatment in adolescent-friendly HIV services.
Additionally, our study also sought to establish any associations between the treatment outcomes and other demographic and clinical characteristics of all the adolescents receiving treatment at the clinic. Of note, significant differences were found between younger and older adolescents on all three treatment outcomes (although there was no consistency in association with adherence), which is in line with what has been reported elsewhere globally. Viral load suppression rates were also found to be associated with the type of ART regimen the adolescents were taking during the study period, whilst there was no observed association with sex or disclosure status.

These results may only apply to this particular study population and setting. However, effects or effectiveness of the Teen Club intervention can reasonably be generalized to adolescents living with HIV who are between 10-19 years who are accessing ART at a specialized pediatric or adolescent-friendly ART clinic. We concluded that in a specialized paediatric ART clinic, group-based interventions may not substantially improve treatment outcomes among adolescents on ART. Targeted, individual and age-specific interventions may provide additional benefits to the Teen Club intervention. The results provide preliminary data that can be a vehicle for further research, modification of the intervention and development of future prospective studies.

6.2 Recommendations
The following recommendations are aimed at improving retention care, ART adherence and viral load suppression rates among adolescents on ART in general, in specialized pediatric ART clinics or adolescent-friendly settings, and within group-based interventions for adolescents such as Teen Clubs in particular. In addition to programmatic recommendations to optimize ART adherence and retention in care, we also include recommendations for a robust data collection and reporting system to optimize monitoring treatment outcomes among adolescents on ART.

6.2.1 Routine monitoring and data management
Generally, there is need to improve routine collection of patient monitoring data by healthcare workers during clinic visits. Although patient demographic data showed adequate completeness, there were gaps in clinical monitoring data collected in the PCBs
during subsequent visits. The data extracted from the ePMS showed further omissions, pointing to suboptimal entry of clinic visits data from the PCBs. Therefore, we recommend strengthening of training programs for data clerks, and supervisory and mentorship programs to routinely include regular data quality and completeness reviews, so as to improve the capacity of the programmes to monitor, analyse and evaluate adolescent outcomes with a higher degree of accuracy.

6.2.2 Optimizing viral load monitoring
Missing viral load results had the highest contribution to the overall missing data rate. There is need to ensure a robust viral load monitoring system, with prompt reminders for the healthcare workers to collect viral load when they are due to be collected, active following up of results, strengthening the results return systems, and documentation thereof when received, both in PCBs and the electronic database. It is also essential to empower the adolescents to remind the healthcare workers when their viral loads are due to be done.

6.2.3 Improving ART adherence, viral load suppression and retention in care
In specialized pediatric ART clinics where adolescent-friendly HIV services are provided, there is need to strengthen individual case management strategies for those adolescents with poor treatment outcomes. Although group-based interventions may improve overall adherence and retention in care rates among adolescents in general, special attention is needed for those failing treatment. Virologic failure may be due to a myriad of factors that could be patient-related such as active substance abuse (drugs or alcohol), depression, lack of disclosure or not feeling well among others. Factors negatively affecting viral suppression levels could also be healthcare system-related (dissatisfaction) or medication-related (type of ARVs, pill burden, side-effects), and these factors have to be explored on an individual basis to improve both adherence and viral load suppression. We recommend further research to explore factors contributing to poor treatment outcomes among these adolescents which may inform development of future interventions.

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The national programme should also consider scaling up differentiated care models, which may include weekend HIV services for adolescents, so as not to reduce chances of possible disruption of school attendance. Models tailored for the older adolescents may provide additional overall benefits for the Teen Club intervention, if some specific HIV services (such as medication dispensing, laboratory monitoring, SRH) could be included in the package during Teen Club meetings.

Although minimal additional benefits were realized in ART adherence and retention in care rates among adolescents in a Teen Club as compared to those in standard care in this particular study setting, there may be substantial benefits from the Teen Club intervention in facilities providing integrated PHC services. There is need for further research on the effectiveness of Teen Clubs in these integrated services facilities.

6.2.4 Age-specific interventions
The effect of age in the Teen Club cannot be underestimated. The club consisted of mostly older adolescents, an age group that evidently had poorer treatment outcomes compared to the younger adolescents. We recommend provision of age-specific interventions or activities within the Teen Club intervention. Instead of the Teen Club being all inclusive of all adolescents aged 10-19 years, there could be activities specifically targeting older adolescents that may include sessions on sexual and reproductive health (SRH), education and career concerns, and other issues on transition to adulthood among other concerns for older adolescents. We believe having two separate age-specific sessions may lead to improved treatment outcomes among the older adolescents in the Teen Club.

6.2.5 Teen Club programme implementation
Although overall differences in ART adherence, viral load suppression and retention in care rates between Teen Club members and adolescents in standard care were minimal, we found some significant differences especially in retention rates among club members earlier on during the study period. A sustained better retention rate for 16 months (6 months at 100%) among Teen Club members makes a case for further implementation and roll-out of Teen Clubs at other similar health facilities.
Overall, having a specialized pediatric HIV clinic demonstrated that improved treatment outcomes can be achieved among adolescents, which is imperative to close the gap towards achieving the 90-90-90 goals. National programmes have to consider decentralizing pediatric HIV services to more remote PHC facilities, with staff trained and equipped with the necessary knowledge and skills to provide adolescent-friendly HIV services.

Increased adolescent-friendly HIV services coverage, including implementation of settings specific group and individual-based interventions could substantially improve ART adherence, viral load suppression and retention in HIV care rates among adolescents, and close the gap between this underserved group, and children and adults.
REFERENCES


Duarte, H. A., Harris, D. R., Tassiopoulos, K., Leister, E., Negrini, S. F. B. de M.,


http://etd.uwc.ac.za/


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http://doi.org/10.7448/ias.18.2.19393


http://doi.org/10.1371/journal.pone.0056088


http://doi.org/10.1111/tmi.12517


http://doi.org/10.1097/QAI.0b013e3181b56404


Vreeman, R. C., Scanlon, M. L., Mwangi, A., Turissini, M., Ayaya, S. O., Tenge, C., &


APPENDICES

Appendix 1: Patient Care Booklet
<table>
<thead>
<tr>
<th>Unique Number:</th>
<th>Pharmacy Number / Code:</th>
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<tbody>
<tr>
<td>(Facility code)</td>
<td>(Facility code)</td>
</tr>
<tr>
<td>(Month)/Year)</td>
<td>(Sequential numbers)</td>
</tr>
<tr>
<td>(Sequential numbers)</td>
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</tbody>
</table>

**B SCREENING/CLINICAL FOLLOW-UP**

| Power (Y) or N | Pale exuus (Y) or N | Pneumonitis (Y) or N | Commonly on TB (Y) or N | Pregnant (Y) or N | CTX | ARV MEDICINE | ARV Side Effects | Child knows HIV status | Referral or emer-
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**PAEDIATRIC HIV CARE / ART CARD**
**Laboratory Results:**

- **Viral Load**: / / / / / / / / 
- **Hb**: / / / / / / / / 
- **ALT**: / / / / / / / / 
- **Creatinine / Cr CL**: / / / / / / / / 
- **CD4**: / / / / / / / / 
- **PAF smear Result**: / / / / / / / / 
- **HBsAg**: / / / / / / / / 
- **HBeAg**: / / / / / / / / 
- **RPR**: / / / / / / / / 
- **Others**: / / / / / / / / 

**TB TEST RESULTS**

- **Smear microscopy**: / / / / / / / / 
- **Xpert MTB/RIF**: / / / / / / / / 
- **TB Culture**: / / / / / / / / 
- **TST (in mm)**: / / / / / / / / 
- **Chest X-ray**: / / / / / / / / 
- **Other**: / / / / / / / / 

**TB Diagnosis, Treatment and Outcome**

- **TB Registration Number**: / / / / / / / / 
- **Site of disease (PTB or EPTB)**: / / / / / / / / 
- **Patient category (New or Previously Treated)**: / / / / / / / / 
- **Treatment Regimen**: / / / / / / / / 

**TB Preventive Therapy**

- **Date screened but NOT eligible for TB-IPT**: / / / / / / / / 
- **Reason**: / / / / / / / / 
- **Date screened and ELIGIBLE for TB-IPT**: / / / / / / / / 
- **TB-IPT Rejected; Reason**: / / / / / / / / 
- **Date (dd/mm/yy)**: / / / / / / / / 
- **Status (Codes for Stop)**: / / / / / / / / 
- **Adherence**: / / / / / / / / 
  - If "F" or "P", write code for why

**MUAC (cm) reference table**

Refer to National Guidelines for Antiretroviral Therapy pg.71

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Severe malnutrition</th>
<th>Moderate malnutrition</th>
<th>Normal nutritional status</th>
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<td>6-11 months</td>
<td>&lt;11.0</td>
<td>11.1-11.9</td>
<td>12.0-12.9</td>
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<td>12-23 months</td>
<td>15.6-17.5</td>
<td>17.6-19.5</td>
<td>19.6-21.5</td>
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**Codes for growth monitoring**

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<th>Growth chart</th>
<th>t-score (code)</th>
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<td>Height-for-age (HFA)</td>
<td>Infantile dwarfism (ID)</td>
</tr>
<tr>
<td>Weight-for-age (WFA)</td>
<td>Macrodactyly (MA)</td>
</tr>
<tr>
<td>Weight-for-length or BMI for age</td>
<td>Moderate malnutrition (MM)</td>
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</table>

**Codes for ART adherence**

<table>
<thead>
<tr>
<th>Adherence</th>
<th>%</th>
<th>Mixed BD doses per month</th>
<th>Mixed daily doses per month</th>
</tr>
</thead>
<tbody>
<tr>
<td>G (good)</td>
<td>&gt;99%</td>
<td>≤3 doses</td>
<td>&lt;2 doses</td>
</tr>
<tr>
<td>F (fair)</td>
<td>85-94%</td>
<td>4-5 doses</td>
<td>2-4 doses</td>
</tr>
<tr>
<td>P (poor)</td>
<td>&lt;85%</td>
<td>≥5 doses</td>
<td>≥5 doses</td>
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---

**PAEDIATRIC HIV CARE / ART CARD**

---

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### Appendix 2: Data Extraction Tool

<table>
<thead>
<tr>
<th>ART Nº (12-digit number)</th>
<th>Sex (M/F)</th>
<th>Age</th>
<th>Model of Care (TC/SC)</th>
<th>Disclosure status (D/ND)</th>
<th>ART start date</th>
<th>ART Regimen</th>
<th>Period on ART</th>
<th>VL1</th>
<th>VL2</th>
<th>VL3</th>
<th>Retention in care</th>
<th>Ad1 (G,F,P)</th>
<th>Ad2</th>
<th>Ad3</th>
<th>Ad4</th>
<th>Ad5</th>
<th>Ad6</th>
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**Notes:**

- **VL** - Viral Load result
- **Ad** - Adherence measured by healthcare worker during clinic visits.
- **D** - Disclosed
- **ND** - Not Disclosed
- **TC** - Teen Club
- **SC** - Standard care
- **G** - Good
- **F** - Fair
- **P** - Poor
- **LTFU** - Lost to Follow-Up
- **TO** - Transfer Out
Appendix 3: Ethics Approval

OFFICE OF THE DIRECTOR: RESEARCH
RESEARCH AND INNOVATION DIVISION

13 October 2017

Mr FK Muyayi
School of Public Health
Faculty of Community and Health Sciences

Ethics Reference Number: BM17/8/14

Project Title: The effects of teen clubs on adherence to antiretroviral therapy in retention in HIV Care amongst adolescents in Windhoek, Namibia.

Approval Period: 11 October 2017 – 11 October 2018

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project.

Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report in good time for annual renewal.

The permission from the health facility/provincial health department must be submitted for record-keeping

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms. Patricia Josius
Research Ethics Committee Officer
University of the Western Cape

PROVISIONAL REC NUMBER 130416-050
Appendix 4: Research Approval Letter from Ministry of Health and Social Services

OFFICE OF THE PERMANENT SECRETARY

Ref: 18/3/3 FM
Enquiries: Mr. L. Nghipangelwa

Date 12 January 2018

Mr. Farai Munyayi
University of the Western Cape
Cape Town
South Africa

Dear Mr. Munyayi

RE: The Effect of Teen Club on Adherence to Antiretroviral Therapy and Retention in HIV care among Adolescents in Windhoek, Namibia

1. Reference is made to your application to conduct the above-mentioned study.
2. The proposal has been evaluated and found to have merit.
3. Kindly be informed that permission to conduct the study has been granted under the following conditions:
   3.1 The data to be collected must only be used for academic purposes;
   3.2 No other data should be collected other than the data stated in the proposal;
   3.3 Stipulated ethical considerations in the protocol related to the protection of Human Subjects’ should be observed and adhered to, any violation thereof will lead to termination of the study at any stage;
   3.4 A quarterly report to be submitted to the Ministry’s Research Unit;
   3.5 Preliminary findings to be submitted upon completion of the study;
3.6 Final report to be submitted upon completion of the study;
3.7 Separate permission should be sought from the Ministry of Health and Social Services for the publication of the findings.

Yours sincerely,

Dr. D. Dhirab
Acting Permanent Secretary

[Signature]