



Paediatric ART Adherence in South Africa: A Comprehensive Analysis

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Abstract

Adherence to antiretroviral therapy (ART) remains a challenge for HIV-infected children. In this cross-sectional study, we used structured interview-administered questionnaires and medical records to measure adherence levels and factors associated with adherence and viral suppression. We included 195 South African children aged 2.1–12.9 on ART. Adherence levels ranged between 20.5% (pill count) and 89.1% (self-report). Boys were less adherent according to self-report, girls were less adherent according to pill count. Caregivers ensured medication was taken when the condition directly affected daily life. Well-functioning families and families with high SES provide a context supportive of adherence. Non-disclosure and difficulties administering medication negatively affected adherence and viral suppression. This study shows challenging levels of adherence impacting directly on viral suppression in a South African paediatric HIV program. Gender roles, non-disclosure and difficulty administering medication may undermine adherence and should be taken into account for clinical guidelines, policy design and inform strategies.

Keywords Adherence · Child · Paediatric · HIV · South Africa

Introduction

In 2016, South Africa was home to 0.9% of the world's children (age 0–14 years) [1] and 15.2% of the global human immunodeficiency virus (HIV) infected children [2, 3]. South Africa has more people on anti-retroviral treatment (ART) than any other country in the world [4]. Paediatric ART coverage is 55% [3]. Since 2010, paediatric ART

service delivery has been decentralized to the primary healthcare level [5], which is based on nurse-driven service through clinics [6]. The country has developed national consolidated guidelines for the management of HIV in children, adolescents and adults [7].

Despite these efforts, non-adherence is common and adherence levels in young South Africans range between 36 and 58%. Between 67 and 78% of children on ART are virally suppressed [8, 9]. HIV-related deaths in South African youth (10–19) increased by 77.1% between 2006 and 2016 [10] and non-adherence was an important contributing factor [11]. Paediatric ART failure is an under-recognized issue that receives inadequate attention in the field of paediatrics and within HIV treatment programmes. Clinicians are often uncertain how to assess adherence of HIV-infected children and their caregivers, as well as how to provide structured adherence support at the time of treatment failure. Too often, proper basic adherence counselling is only provided once the child has begun failing treatment [12].

To address non-adherence, it is important to understand paediatric adherence and factors impacting adherence and retention in care [11]. Although South Africa has accepted strategic plans to address HIV, there is inadequate capacity to deliver critical health-care interventions [13]. National

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guidelines address adherence [7], however, this information is not specifically tailored to children. Paediatric adherence is a dynamic process [14] which is not only affected by health system challenges [15], but also clinical, child, caregiver and socio-economic characteristics [16]. Often it is simple adherence support strategies that healthcare providers can use in busy clinics that greatly improve the quality of patient support that children and their caregivers receive before the child reaches a high viral load [12].

In order to inform strategies to support paediatric adherence, we aimed to assess adherence with multiple measures in a paediatric population. In addition, we aimed to provide a comprehensive understanding of paediatric adherence, the context in which adherence behaviour is stimulated and factors that hinder paediatric adherence.

Methods

For this cross-sectional study, children aged 2–14 years who were on treatment at TC Newman clinic—a semi-urban ART clinic in the Western Cape, South Africa—and their caregivers were considered for participation between September 2012 and September 2013. We assessed level of adherence and explored all associations between selected potential predictors of adherence and treatment efficacy. Structured questionnaires were administered by trained research staff in the caregiver's primary language (English, Xhosa or Afrikaans) during interviews while patients were waiting to see the doctor and was supplemented with medical record data.

Ethical Considerations

Stellenbosch University's human research ethics committee approved this study. All caregivers provided written informed consent for their and their child's participation. In addition, all children (≥ 7 years) provided written informed assent for their participation.

Adherence Measures

To assess adherence, a combination of adherence monitoring measures and definitions were included. Pill count was calculated using the number of pills taken or volume for liquid formulations (dispensed minus returned) as a percentage of medication prescribed. Self-reported measures of adherence for the last three and 30 days were recorded during caregiver interviews using the validated Paediatric AIDS clinical trials group (PACTG) adherence modules [17, 18]. Adherence was defined as pill count of 95% and more, 95–105 and 95–100%, or no self-reported missed dosages within the indicated time period. Although health outcome (viral suppression and immune response) is not synonymous

for adherence behaviour [19], these measures were included as indicators of treatment efficacy. Viral suppression was defined by non-detectable viral load (< 50 copies/ml) and immune response was defined by CD4 count (> 500 cells/mm³) which was assessed as part of general clinical practice and included retrospectively when available from medical records between 6 months before up to 3 months after inclusion.

Potential Prediction Measures

General demographic and clinical data from medical records were supplemented with caregiver interviews using validated questionnaires to provide a comprehensive analyses of adherence predictors. Health-related quality of life (HRQoL) and the impact of paediatric chronic health conditions on family and caregivers (family impact) were measured using PedsQL questionnaires [20–22]. The HRQoL scale (measuring physical-, emotional- social- and school-functioning) combined a caregiver proxy-report and a child self-report (all children ≥ 5 years). Family impact consisted of scores for caregiver functioning (physical, emotional, social cognitive, communication and worry) and family functioning (daily activities and family relationships). The worry component of caregiver functioning considers concern about the child's treatment, side effects, others reactions, the child's condition, effects of illness on family and future. The daily activity component of family functioning considers time, effort and energy to finish household tasks. Socio-Economic Status (SES) was calculated using 21 questions from the Census 2011 [23]. A higher score (%) indicated better HRQoL, family functioning and SES. Based on caregiver interview, health care provider report and medical files, we categorised disclosure status as non-disclosure (the child is unaware of their condition and its effect on the body), partial disclosure (the child is aware of their condition without actually naming HIV) and full disclosure (the child is made aware of their condition which is named as HIV) [24].

Statistical Analyses

Analyses were done with IBM statistics version 24. Univariate logistic regression for associations between potential predictors and adherence (self-report, pill count) or treatment outcome (viral load) are presented in tables with odds ratio (OR) and 95% confidence interval (CI) unless otherwise specified. Fisher's exact *p* value was presented for cell size less than five. Confounding and effect modification for the child's sex and age was investigated using multivariate analyses for all associations studied. The associations not affected or which remained after correction are highlighted in the result section. Significance was measured at $p=0.05$. Forward selection procedure was used to construct

prediction models. This method considered all predictors of adherence (self-report, pill count) or treatment outcome (viral load) by adding the predictor with the lowest p-value under 0.05 to the crude model, which was repeated until no additional predictor had a p-value < 0.05. The percentage correct classified cases and Hosmer and Lemeshow Chi square test with p-value for goodness of fit are presented for each model (good fit is indicated by p-value > 0.05).

Results

At the start of the study, 238 active patients on ART aged 2–14 attended the clinic. One caregiver declined participation because the child (13 years) was not disclosed to and 42 patients were missed because caregivers did not visit on the appointment date (relocated to another province or did not attend the clinic on an allocated paediatric days when research staff was present). One hundred and ninety-five children were included. For five households with two children in the study, only the child enrolled first was considered for SES analyses (n = 190).

Adherence and Health Outcome

Adherence varied depending on the measure and definition used. Pill counts were available for 195 children (100%), two children (1%) had pill counts for two of three medicines, one child (0.5%) had pill counts for one of three medicines in their regimen. Adherence measured by pill count was 20.3% when defined as 95–100% (35.9% defined as 95–105%, and 54.7% when defined $\geq 95\%$). Although mean adherence was 94.5%, this includes pill counts up to 192%. Self-reported adherence was 79.6% in the previous 30 days and 89.1% for three-day recall (n = 195, 100%). In addition, 66.7% of the children were virally suppressed (n = 129, 66.2%) and 92.6% had a CD4 count > 500 cells/mm³ (n = 121, 62.1%). Figure 1 provides an overview stratified by sex. The majority of caregivers indicated sole responsibility for medication adherence (77.1%), the child solely (6.8%) or joint between them (3.1%).

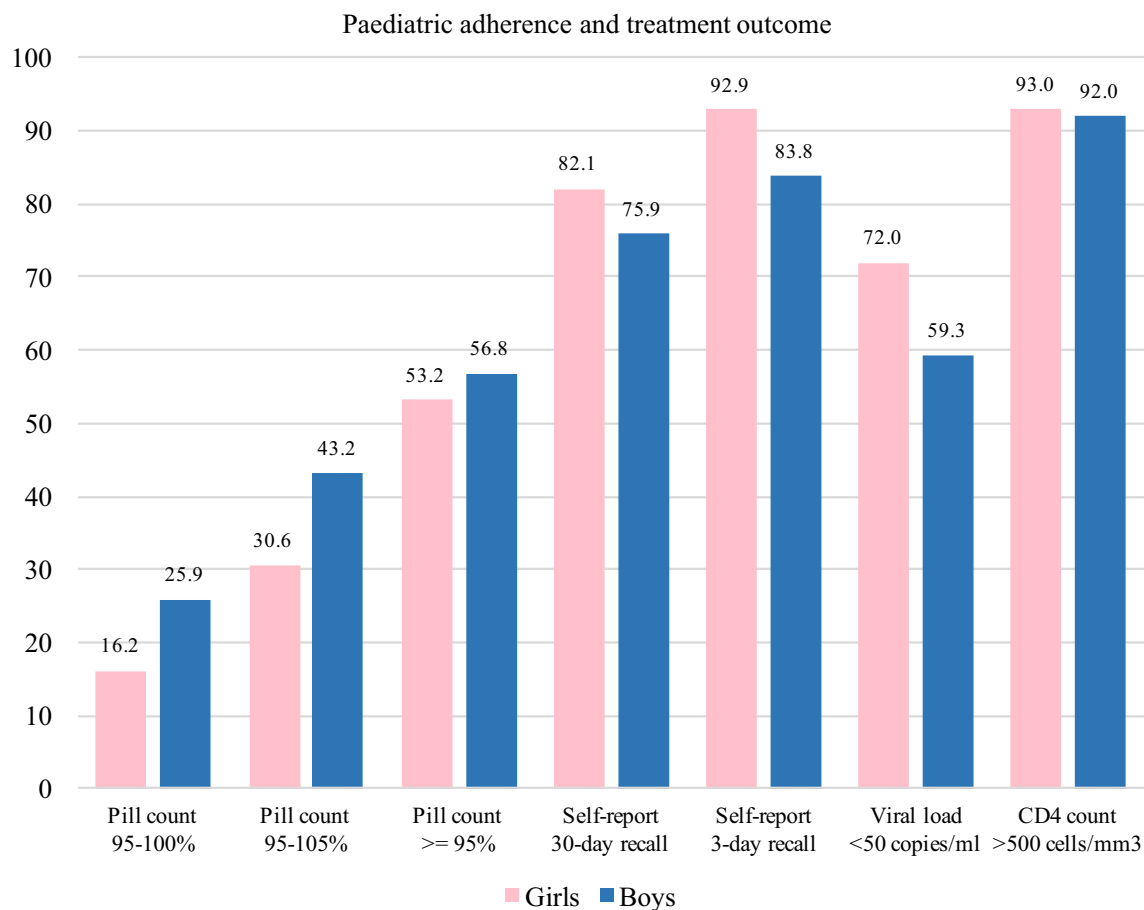


Fig. 1 Paediatric adherence and treatment outcomes (%)

Child Characteristics

Table 1 provides an overview of all child characteristics and their potential univariate association with adherence (self-report and pill count) and viral load. Controlling for confounding and effect modification, we found older children (self-report OR 14.70, 1.77–121.99, $p=0.013$; pill count OR 5.70, 2.05–15.88, $p=0.001$), children of school going age (≥ 6 years) (self-report OR 3.74, 1.45–9.65, $p=0.006$; pill count OR 3.16, 1.46–6.84, $p=0.003$), girls (self-report OR 2.93, 1.11–7.74, $p=0.030$), children who's school functioning was not affected by their condition (pill count for both caretaker proxy-report OR 2.79, 1.02–7.63, $p=0.046$; and child self-report OR 3.00, 1.07–8.43, $p=0.037$) were more adherent. Children with good health-related quality of life scores more likely had a non-detectable viral load (OR 3.31, 1.05–10.51, $p=0.042$).

Caregiver Characteristics

Table 2 provides an overview of all caregiver characteristics and their potential univariate association with adherence (self-report and pill count) and viral load. Controlling for potential confounding and effect modification, we found older caregivers (self-report OR 12.5, 1.37–106.34, $p=0.025$), foster parents/family members (self-report OR 10.18, 1.33–77.72, $p=0.025$; pill count OR 10.80, 1.84–63.32, $p=0.008$ for children < 6 years), children who received disclosure (self-report Fisher's Exact for partial/full $p=0.005$; partial $p=0.028$) and caregivers who worried more (pill count OR 3.88, 1.69–8.91, $p=0.001$) were more adherent. Children who received disclosure more likely had a non-detectable viral load (partial/full; OR 4.42, 1.22–16.00, $p=0.024$; partial OR 6.76, 1.41–32.32, $p=0.017$).

Clinical Characteristics

Reported complications were fever, oral ulcers, thrush, other infections and tuberculosis (one child, 0.5%). Caregivers identified difficulties to adhere to treatment as running out of medication, flavour, forgetting, side effects, multiple caregivers, illness, depression and being away from home. Side effects reported were fever, rash, sleep disturbance and pain. A life-event (e.g. passing of caregiver or discontinuation of care due to travel to Eastern Cape Province) or non-adherence (e.g., caregiver inability to cope with regimen or inability to visit clinic), contributed to children defaulting, all of whom subsequently re-started treatment. Most regimens included three medicines (86.7%) from a variation of 11 medicines (fixed drug combinations were used). Table 3 provides an overview of adherence and viral suppression per medicine. Table 4 provides an overview of all clinical characteristics and their potential univariate association with

adherence (self-report and pill count) and viral load. Controlling for potential confounding and effect modification, we found boys with clinical stage three (pill count OR 14.45, 1.51–138.16, $p=0.020$) or stage four (pill count OR 12.72, 1.08–149.65, $p=0.043$), children who experience complications in the last 30 days (adjusted pill count 95–100% OR 2.75, 1.13–6.70, $p=0.026$), caregivers who did not experience difficulties administering medication (self-report OR 31.11, 6.95–139.36, $p<0.001$; pill count OR 12.51, 4.28–36.53, $p<0.001$), girls who started treatment after the first year of life (pill count OR 5.05, 1.46–17.43, $p=0.010$) and children on tablet formulations only (pill count Fisher's Exact $p=0.001$) were more adherent. Caregivers of children (< 6 years) who did not report any problems administering medication (OR 28.75, 3.16–261.41, $p=0.003$), regimens without didanosine (OR 3.70, 1.13–12.12, $p=0.030$) or including lamivudine (OR 4.04, 1.36–12.02, $p=0.012$) more likely had a non-detectable viral load.

Socio-economic Characteristics

Table 5 provides an overview of all socio-economic characteristics and their potential univariate association with adherence (self-report and pill count) and viral load. Controlling for potential confounding and effect modification, we found families who own a TV (self-report OR 4.02; 1.22–13.24 $p=0.022$), fridge (self-report OR 2.91, 1.11–7.65, $p=0.031$) or bicycle (self-report Fisher's Exact $p=0.028$; pill count OR 2.56, 1.14–5.72, $p=0.022$), boys with high family functioning scores (pill count OR 5.66, 1.12–28.61, $p=0.036$) and caregivers who reported problems with daily activities (pill count OR 3.37, 1.18–9.63, $p=0.023$) were more adherent.

Prediction Models

The prediction model for adherence included three variables: problems reported (self-report OR 33.44, 7.15–156.36, $p<0.001$; pill count OR 13.87, 4.62–41.59, $p<0.001$), school going age (self-report OR 0.26, 0.08–0.79, $p=0.018$; pill count OR 0.33, 0.15–0.76, $p=0.009$) and sex of the child (self-report OR 3.42, 1.11–10.50, $p=0.032$; pill count OR 0.47, 0.23–0.93, $p=0.030$). The prediction model for viral load included six variables: problems reported (OR 7.10, 2.23–22.65, $p=0.001$), HRQoL (OR 0.07, 0.01–0.33, $p=0.001$), disclosure (OR 0.09, 0.02–0.37, $p=0.001$), adherence (pill count 95–105% OR 0.25, 0.08–0.80, $p=0.019$), family impact score (OR 3.32, 1.12–9.83, $p=0.031$) and age of patient (OR 3.03, 1.04–8.85, $p=0.043$). The percentage correctly classified cases was 90.1% (self-report), 72.5% (pill count) and 78.4% (viral load). The Hosmer and Lemeshow Chi square test for goodness of fit was 9.9 with $p=0.196$ (self-report), 4.3 with

Table 1 Child characteristics of adherence and treatment efficacy

Child characteristics—univariate		3 Day recall self-report (N = 195)				Pill count 95-105% (N = 195)				Viral load (N = 129)			
		n (%)	Mean (sd)	Non-Adherent	Adherent	OR (95% CI)	Non-Adherent	Adherent	OR (95% CI)	Detectable	LDL	OR (95% CI)	
Age (N = 195)													
Mean	8.0 (2.7)	6.2 (2.6)	8.2 (2.7)	–	–	7.5 (2.8)	8.8 (2.3)	–	7.8 (2.9)	7.8 (3.0)	–	–	
2.1–5.7	49 (25.1)	10 (47.6)	38 (22.1)	1 (ref)	–	42 (34.1)	6 (8.7)	1 (ref)	11 (25.6)	28 (32.6)	1 (ref)	–	
5.8–8.2	49 (25.1)	5 (23.8)	43 (25.0)	2.26 (0.71–7.21)	–	28 (22.8)	20 (29.0)	5.00 (1.79–14.01)*	12 (27.9)	17 (19.8)	0.56 (0.20–1.54)	–	
8.3–10.1	47 (24.1)	5 (23.8)	42 (24.2)	2.21 (0.6907.05)	–	26 (21.1)	21 (30.4)	5.65 (2.02–15.85)*	11 (25.6)	16 (18.6)	0.57 (0.20–1.61)	–	
10.2–12.9	50 (25.6)	1 (4.8)	49 (28.5)	12.90 (1.58–105.18)*	–	27 (22.0)	22 (31.9)	5.70 (2.05–15.88)*	9 (20.9)	25 (29.1)	1.09 (0.39–3.07)	–	
Age (N = 195)													
Preschool age	54 (27.7)	11 (52.4)	42 (24.4)	1 (ref)	–	43 (35.0)	10 (14.5)	1 (ref)	12 (27.9)	31 (36.0)	1 (ref)	–	
School age	141 (72.3)	10 (47.6)	130 (75.6)	3.41 (1.35–8.58)*	–	80 (65.0)	59 (85.5)	3.17 (1.47–6.82)*	31 (72.1)	55 (64.0)	0.69 (0.31–1.53)	–	
Sex (N = 195)													
Female	113 (57.9)	8 (38.1)	105 (61.0)	1 (ref)	–	77 (62.6)	34 (49.3)	1 (ref)	21 (48.8)	54 (62.8)	1 (ref)	–	
Male	82 (42.1)	13 (61.9)	67 (39.0)	0.39 (0.16–0.99)*	–	46 (37.4)	35 (50.7)	1.72 (0.95–3.13)	22 (51.2)	32 (37.2)	0.57 (0.27–1.19)	–	
HRQoL (N = 192)													
Mean	90.4 (10.5)	87.6 (13.8)	90.6 (10.1)	–	–	90.7 (11.0)	91.0 (5.5)	–	89.4 (9.7)	91.0 (10.6)	–	–	
23.8–87.5	47 (24.5)	5 (25.0)	42 (24.7)	1 (ref)	–	30 (25.0)	16 (23.2)	1 (ref)	14 (32.6)	19 (22.6)	1 (ref)	–	
87.6–92.9	49 (25.5)	7 (35.0)	42 (24.7)	0.71 (0.21–2.43)	–	34 (28.3)	14 (20.3)	0.77 (0.32–1.84)	10 (23.3)	24 (28.6)	1.77 (0.64–4.86)	–	
93.0–96.6	47 (24.5)	4 (20.0)	43 (25.3)	1.28 (0.32–5.10)	–	29 (24.2)	18 (26.1)	1.16 (0.50–2.71)	13 (30.2)	15 (17.9)	0.85 (0.31–2.34)	–	
96.7–100	49 (25.5)	4 (20.0)	43 (25.3)	1.28 (0.32–5.10)	–	27 (22.5)	21 (30.4)	1.46 (0.63–3.35)	6 (14.0)	26 (31.0)	3.19 (1.04–9.83)*	–	
HRQoL (N = 158)													
Self-report mean	91.5 (11.3)	90.7 (22.4)	91.7 (9.3)	–	–	91.8 (13.0)	91.0 (8.3)	–	91.5 (12.0)	90.6 (9.2)	–	–	
6.5–88.0	37 (23.4)	4 (23.5)	32 (22.9)	1 (ref)	–	20 (21.1)	17 (28.3)	1 (ref)	9 (26.5)	19 (27.9)	1 (ref)	–	
88.1–93.5	42 (26.6)	1 (5.9)	41 (29.3)	5.13 (0.55–48.12)	–	23 (24.2)	18 (30.0)	0.92 (0.38–2.25)	6 (17.6)	20 (29.4)	1.58 (0.47–5.29)	–	
93.6–98.9	41 (25.9)	4 (23.5)	37 (26.4)	1.16 (0.27–5.00)	–	23 (24.2)	16 (26.7)	0.82 (0.33–2.03)	9 (26.5)	17 (25.0)	0.90 (0.29–2.78)	–	
99.0–100	38 (24.1)	8 (47.1)	30 (21.4)	0.47 (0.13–1.72)	–	29 (30.5)	16 (15.0)	0.37 (0.14–0.98)*	10 (29.4)	12 (17.6)	0.57 (0.18–1.80)	–	
HRQoL school (N = 176)													
Proxy mean	81.4 (19.2)	85.0 (14.6)	81.3 (19.3)	–	–	84.2 (15.8)	76.4 (23.8)	–	79.5 (20.3)	80.3 (19.7)	–	–	
5.0–70.0	38 (21.6)	4 (21.1)	33 (21.2)	1 (ref)	–	18 (16.2)	19 (30.6)	1 (ref)	10 (26.3)	17 (22.4)	1 (ref)	–	
70.1–85.0	58 (33.0)	4 (21.1)	54 (34.6)	1.64 (0.38–6.99)	–	36 (32.4)	21 (33.9)	0.55 (0.24–1.28)	13 (34.2)	28 (36.8)	1.27 (0.46–3.52)	–	
85.1–95.0	40 (22.7)	6 (31.6)	34 (21.8)	0.69 (0.18–2.66)	–	28 (25.2)	11 (17.7)	0.37 (0.14–0.96)*	7 (18.4)	15 (19.7)	1.26 (0.38–4.14)	–	
95.1–100	40 (22.7)	5 (26.3)	35 (22.4)	0.85 (0.21–3.43)	–	29 (26.1)	11 (17.7)	0.36 (0.14–0.93)*	8 (21.1)	16 (21.1)	1.18 (0.37–3.73)	–	
HRQoL school (N = 150)													
Self-report mean	83.1 (18.1)	86.7 (24.7)	82.7 (17.4)	–	–	85.9 (16.9)	78.2 (19.5)	–	79.1 (22.9)	82.6 (16.2)	–	–	
5.0–70.0	34 (22.7)	3 (20.0)	31 (23.1)	1 (ref)	–	16 (17.6)	18 (32.1)	1 (ref)	9 (28.1)	13 (19.7)	1 (ref)	–	

Table 1 (continued)

Child characteristics—univariate		3 Day recall self-report (N = 195)				Pill count 95–105% (N = 195)				Viral load (N = 129)			
		n (%)	Mean (sd)	Non-Adherent	Adherent	OR (95% CI)	Non-Adherent	Adherent	OR (95% CI)	LDL	LDL	LDL	LDL
70.1–85.0	41 (27.3)	1 (6.7)	39 (29.1)	3.77 (0.37–38.09)	24 (26.4)	16 (28.6)	0.59 (0.24–1.49)	9 (28.1)	24 (36.4)	1.85 (0.59–5.80)			
85.1–95.0	32 (21.3)	2 (13.3)	30 (22.4)	1.45 (0.23–9.31)	19 (20.9)	12 (21.4)	0.56 (0.29–1.51)	4 (12.5)	15 (22.7)	2.60 (0.65–10.45)			
95.1–100	43 (28.7)	9 (60.0)	34 (25.4)	0.37 (0.09–1.47)	32 (35.2)	10 (17.9)	0.28 (0.10–0.74)*	10 (31.3)	14 (21.2)	0.97 (0.30–3.14)			

OR odds ratio, CI confidence interval, *sd* standard deviation, *HRQoL* health related quality of life, *LDL* undetectable viral load

*p-value < 0.05

$p = 0.509$ (pill count), and 7.6 with $p = 0.373$ (viral load). Of note is that caregivers report girls are more adherent (three-day recall self-report) where defining adherence by pill count (95–105%) we find the opposite where boys are more adherent.

Discussion

Adherence in this South African paediatric cohort was 20.3–54.7% for pill count, 79.6–89.1% for self-report and 66.7% viral suppression. When the condition had a prominent effect on daily life (health-related quality of life, school functioning, WHO staging, complications, worry, daily activities), caregivers ensured medication was taken resulting in higher levels of paediatric adherence and viral suppression. Well-functioning households and households with high SES provide a context supportive of treatment adherence and viral suppression. Non-disclosure and difficulties administering medication negatively affected adherence and viral suppression.

Self-reports are influenced by social desirability and tend to overestimate adherence. Pill counts are more accurate and reliable [19]. The variation between adherence measures could be explained by the measuring periods (3-day self-report or pill count over a month period) and different definitions used (a more strict definition will find less children adherent). Pill counts up to 192% could be due to vomiting and re-administering the dose, too many pills taken, or disposing of pills. This informed the recommendation to include upper levels when defining adherence. Monthly visits represent a convenient and appropriate time to address difficulties administering medication rather than non-adherence (self-report), providing a good estimate of adherence and an opportunity to resolve problems while reducing social desirable answers and stigmatisation before the child starts failing treatment.

Child characteristics affecting adherence and treatment efficacy were age, sex, school functioning and health-related quality of life. A child's age and sex are important factors associated with adherence in the South African context [25–27], although not all studies confirm this association [8, 25]. Self-reports identified girls more adherent, pill counts indicated boys as more adherent. Girls progress to disease more slowly compared to boys [28], possibly explaining lower pill counts for girls (less impact of condition on daily life). The social construct of gender roles could explain this difference. A study in a similar setting identified the pervasiveness of traditional gender roles [29]. Translating these roles to children and their medication taking behavior, daughters are expected to be at home, assume a caring role and responsibility for their treatment (high caregiver-reported adherence). Sons spent more time outside and are

Table 2 Caregiver characteristics of adherence and treatment efficacy

		3 Day recall self-report (N = 195)				Pill count 95-105% (N = 195)				Viral Load (N = 129)				
		% Mean (sd)		OR (95% CI)		Non-adherent		Adherent		Detectable		LDL		OR (95% CI)
Age (N = 195)														
Mean	39.1 (11.2)	32.3 (3.8)	40.0 (11.5)	-	38.2 (10.8)	41.0 (11.9)	-	37.6 (10.2)	39.7 (12.0)	-				
16.0-31.2	48 (24.6)	11 (52.4)	37 (21.5)	1 (ref)	35 (28.5)	12 (17.4)	1 (ref)	12 (27.9)	23 (26.7)	1 (ref)				
31.3-37.2	49 (25.1)	6 (28.6)	43 (25.0)	2.13 (0.72-6.32)	30 (24.4)	18 (26.1)	1.75 (0.73-4.21)	13 (30.2)	18 (20.9)	0.72 (0.27-1.96)				
37.3-44.1	49 (25.1)	3 (14.3)	44 (25.6)	4.36 (1.13-16.81)*	32 (26.0)	16 (23.2)	1.46 (0.60-3.55)	7 (16.3)	23 (26.7)	1.71 (0.57-5.13)				
44.2-74.4	49 (25.1)	1 (4.8)	48 (27.9)	14.27 (1.76-115.55)*	26 (21.1)	23 (33.3)	2.58 (1.09-6.12)*	11 (25.6)	22 (25.6)	1.04 (0.38-2.85)				
Sex (N = 195)														
Female	180 (92.3)	21 (100.0)	157 (91.3)	1 (ref)	114 (92.7)	63 (91.3)	1 (ref)	39 (90.7)	77 (89.5)	1 (ref)				
Male	15 (7.7)	0 (0.0)	15 (8.7)	0.379†	9 (7.3)	6 (8.7)	1.21 (0.41-3.55)	4 (9.3)	9 (10.5)	1.14 (0.33-3.94)				
Relation (N = 195)														
Parent	136 (69.7)	20 (95.2)	114 (66.3)	1 (ref)	35 (81.4)‡	4 (40.0)‡	1 (ref)	29 (67.4)	59 (68.6)	1 (ref)				
Other	59 (30.3)	1 (4.8)	58 (33.7)	10.18 (1.33-77.72)*	8 (18.6)‡	6 (60.0)‡	6.56 (1.49-28.83)**	14 (32.6)	27 (31.4)	0.95 (0.43-2.08)				
Language (N = 195)														
Afrikaans	58 (29.7)	7 (33.3)	50 (29.1)	1 (ref)	35 (28.5)	22 (31.9)	1 (ref)	12 (27.9)	18 (20.9)	1 (ref)				
Xhosa	130 (66.7)	13 (61.9)	116 (67.4)	1.25 (0.47-3.32)	84 (68.3)	44 (63.8)	0.83 (0.44-1.59)	31 (72.1)	62 (72.1)	1.33 (0.57-3.11)				
Other	7 (3.6)	1 (4.8)	6 (3.5)	0.84 (0.09-8.05)	4 (3.3)	3 (4.3)	1.19 (0.24-5.85)	0 (0.0)	6 (7.0)	0.079†				
Marital status (N = 195)														
Not married	140 (71.8)	19 (90.5)	119 (69.2)	1 (ref)	92 (74.8)	47 (68.1)	1 (ref)	30 (69.8)	62 (72.1)	1 (ref)				
Married	55 (28.2)	2 (9.5)	53 (30.8)	4.23 (0.95-18.82)	31 (25.2)	22 (31.9)	1.39 (0.73-2.66)	13 (30.2)	24 (27.9)	0.89 (0.40-2.00)				
Education (N = 194)														
PS incomplete	29 (14.9)	2 (9.5)	27 (15.8)	1 (ref)	16 (13.1)	13 (18.8)	1 (ref)	7 (16.7)	13 (15.1)	1 (ref)				
Primary school	140 (72.2)	17 (81.0)	121 (70.8)	0.53 (0.12-2.42)	90 (73.8)	47 (68.1)	0.64 (0.29-1.45)	29 (69.0)	62 (72.1)	1.15 (0.42-3.19)				
High school	25 (12.9)	2 (9.5)	23 (13.5)	0.85 (0.11-6.53)	16 (13.1)	9 (13.0)	0.69 (0.23-2.07)	6 (14.3)	11 (12.8)	0.99 (0.26-3.82)				
Disclosure (N = 195)														
Not disclosed	150 (76.9)	21 (100.0)	127 (73.8)	1 (ref)	100 (81.3)	48 (69.6)	1 (ref)	38 (88.4)	61 (70.9)	1 (ref)				
Partial/full	45 (23.1)	0 (0.0)	45 (26.2)	0.005**†	23 (18.7)	21 (30.4)	1.90 (0.96-3.77)	5 (11.6)	25 (29.1)	3.12 (1.10-8.83)*				
Disclosure (N = 195)														
Not disclosed	150 (76.9)	21 (100.0)	127 (73.8)	1 (ref)	100 (81.3)	48 (69.6)	1 (ref)	38 (88.4)	61 (70.9)	1 (ref)				
Partial	28 (14.4)	0 (0.0)	28 (16.3)	0.028*†	17 (13.8)	10 (14.5)	1.23 (0.52-2.88)	2 (4.7)	16 (18.6)	4.98 (1.09-22.90)*				
Full	17 (8.7)	0 (0.0)	17 (9.9)	0.132†	6 (4.9)	11 (15.9)	3.82 (1.33-10.94)*	3 (7.0)	9 (10.5)	1.87 (0.48-7.34)				
FI worry (N = 193)														
Mean	89.2 (11.3)	88.4 (12.0)	89.3 (11.3)	-	91.6 (10.2)	85.7 (11.8)	-	90.1 (8.8)	89.7 (11.7)	-				
50.0-80.0	47 (24.4)	5 (23.8)	42 (24.7)	1 (ref)	19 (15.4)	25 (37.3)	1 (ref)	8 (19.5)	18 (20.9)	1 (ref)				

Table 2 (continued)

Caregiver characteristics—univariate										
Total	3 Day recall self-report (N = 195)			Pill count 95–105% (N = 195)			Viral Load (N = 129)			
	% Mean (sd)	Non-adherent	Adherent	OR (95% CI)	Non-adherent	Adherent	OR (95% CI)	Detectable	LDL	OR (95% CI)
80.1–90.0	59 (30.6)	8 (38.1)	49 (28.8)	0.73 (0.22–2.40)	39 (31.7)	20 (29.9)	0.39 (0.17–0.87)*	14 (34.1)	26 (30.2)	0.83 (0.29–2.37)
90.1–95.0	24 (12.4)	21 (14.3)	21 (12.4)	0.83 (0.18–3.83)	18 (14.6)	6 (9.0)	0.25 (0.08–0.76)*	9 (22.0)	9 (10.5)	0.44 (0.13–1.54)
95.1–100	63 (32.6)	5 (23.8)	58 (34.1)	1.38 (0.38–5.08)	47 (38.2)	16 (23.9)	0.56 (0.11–0.59)*	10 (24.4)	33 (38.4)	1.47 (0.49–4.37)

OR odds ratio, CI confidence interval, *sd* standard deviation, *PS* primary school, *FI* family impact, *LDL* undetectable viral load

**p*-value < 0.05

†*p*-Value Fisher's exact test (cell size less than 5)

‡Presented for children < 6 years

assumed to require more involved caregiver guidance regarding their treatment (high pill counts). Gender roles should be taken into account when interpreting adherence measures in clinical practice, the development of interventions and future research. Quality of life of the child is confirmed by multiple studies as an important factor in paediatric adherence [26, 27, 30]. We find children with high health-related quality of life scores were less adherent to their treatment but more likely had a non-detectable viral load. When the condition has a prominent effect on daily functioning (detectable viral load, low health-related quality of life and school functioning scores), adherence to the regimen seems more urgent. When the child is well (non-detectable viral load, high health-related quality of life and school functioning scores) this urgency is not as prominent.

Caregiver characteristics associated with paediatric adherence and treatment efficacy were age, relationship, disclosure and worries. Our study is unique in confirming an association between adherence and age of caregiver and child-caregiver relationship [8, 9, 16]. Disclosure of HIV status to the child was associated with better adherence as reported by others [16, 26, 27] although not all research confirms the association [8]. A child's understanding of a condition and active knowledge on how to manage it are important for adherence [19]. Disclosure is encouraged, however, we emphasize the process can only be successful when a supportive social context is present [31]. Similar to the condition affecting the child's daily life, caregivers who worry and who's daily activities are affected by the chronic condition, are more likely adherent. Literature supports caregiver anxiety and depression are associated with adherence [27].

Clinical characteristics associated with paediatric adherence were WHO clinical staging, complications, difficulties administering medication, commenced within first year of life, formulation and regimen. Clinical characteristics [9] and clinical staging are important in paediatric adherence [30]. We cannot confirm treatment fatigue [16], rather we found a more adherent population at older age and longer on treatment. This could be explained by young non-adherent children who not yet defaulted, where children who were non-adherent and on treatment for a longer period would likely default and excluded from our study. Liquid formulation palatability could contribute to non-adherence in young children [16], we find children on tablets only more adherent. Reported difficulties experienced with administering medication was not before associated with paediatric adherence [9]. Regimens with didanosine were associated with non-adherence and literature confirms low adherence for didanosine [32]. Current paediatric guidelines recommend to replace didanosine regardless of viral load [7]. Regimens including lamivudine were associated with good adherence as does a study

Table 3 Clinical characteristics of adherence and treatment efficacy

Clinical characteristics—univariate		3 Day recall self-report (N = 195)		Pill count 95-105% (N = 195)		Viral Load (N = 129)					
		Non-adherent	Adherent	OR (95% CI)	Non-adherent	Adherent	OR (95% CI)	Detectable	LDL	OR (95% CI)	
WHO clinical (N = 189)											
Stage 1	19 (10.1)	4 (19.0)	15 (9.0)	1 (ref)	9 (19.6) [§]	1 (3.0) [§]	1 (ref)	2 (4.9)	10 (11.9)	1 (ref)	
Stage 2	49 (25.9)	4 (19.0)	44 (26.5)	2.93 (0.65–13.21)	11 (23.9) [§]	7 (21.2) [§]	5.73 (0.59–55.60) [§]	9 (22.0)	24 (28.6)	0.53 (0.10–2.92)	
Stage 3	87 (46.0)	10 (47.6)	77 (46.4)	2.05 (0.57–7.42)	19 (41.3) [§]	19 (57.6) [§]	9.00 (1.04–78.17) [§]	20 (48.8)	36 (42.9)	0.36 (0.07–1.81)	
Stage 4	34 (18.0)	3 (14.3)	30 (18.1)	2.67 (0.53–13.48)	7 (15.2) [§]	6 (18.2) [§]	7.71 (0.75–79.77) [§]	10 (24.4)	14 (16.7)	0.28 (0.05–1.57)	
Complications (N = 187)											
No	156 (83.4)	15 (75.0)	139 (84.2)	1 (ref)	128 (86.5) [¶]	26 (72.2) [¶]	1 (ref)	37 (88.1)	66 (81.5)	1 (ref)	
Yes	31 (16.6)	5 (25.0)	26 (15.8)	0.56 (0.19–1.68)	20 (13.5%) [¶]	10 (27.8) [¶]	2.46 (1.03–5.87) [¶]	5 (11.9)	15 (18.5)	1.68 (0.57–5.00)	
Difficulties (N = 192)											
No	133 (69.3)	2 (9.5)	131 (76.6)	1 (ref)	68 (55.7)	63 (94.0)	1 (ref)	1 (9.9) [‡]	23 (74.2) [‡]	1 (ref)	
Yes	59 (30.7)	19 (90.5)	40 (23.4)	0.03 (0.01–0.14) [*]	54 (44.3)	4 (6.0)	0.08 (0.03–0.23) [*]	10 (90.1) [‡]	8 (25.8) [‡]	0.04 (0.00–0.32) ^{**}	
Side effects (N = 186)											
No	165 (88.7)	19 (95.0)	144 (87.8)	1 (ref)	103 (88.0)	59 (89.4)	1 (ref)	35 (83.3)	70 (87.5)	1 (ref)	
Yes	21 (11.3)	1 (5.0)	20 (12.2)	2.64 (0.34–20.80)	14 (12.0)	7 (10.6)	0.87 (0.33–2.28)	7 (16.7)	10 (12.5)	0.71 (0.25–2.04)	
Tx duration (N = 195)											
Mean	5.1 (2.4)	4.1 (2.5)	5.3 (2.3)	–	4.8 (2.4)	5.6 (2.2)	–	4.8 (2.3)	4.9 (2.5)	–	
0.1–3.3	48 (24.6)	7 (33.3)	39 (22.7)	1 (ref)	37 (30.1)	11 (15.9)	1 (ref)	12 (27.9)	26 (30.2)	1 (ref)	
3.4–5.3	50 (25.6)	8 (38.1)	42 (24.4)	0.94 (0.31–2.84)	33 (26.8)	16 (23.2)	1.63 (0.66–4.01)	13 (30.2)	20 (23.3)	0.71 (0.27–1.89)	
5.4–7.0	50 (25.6)	3 (14.3)	47 (27.3)	2.81 (0.68–11.61)	27 (22.0)	22 (31.9)	2.74 (1.14–6.59) [*]	8 (18.6)	21 (24.4)	1.21 (0.42–3.51)	
7.1–9.8	47 (24.1)	3 (14.3)	44 (25.6)	2.63 (0.64–10.89)	26 (21.1)	20 (29.0)	2.59 (1.06–6.30) [*]	10 (23.3)	19 (22.1)	0.88 (0.31–2.45)	
Tx 1st life year (N = 195)											
No	133 (68.2)	10 (47.6)	121 (70.3)	1 (ref)	27 (58.7) [§]	29 (82.9) [§]	1 (ref)	31 (72.1)	58 (67.4)	1 (ref)	
Yes	62 (31.8)	11 (52.4)	51 (29.7)	0.38 (0.15–0.96) [*]	19 (41.3) [§]	6 (17.1) [§]	0.29 (0.10–0.85) ^{**}	12 (27.9)	28 (32.6)	1.25 (0.56–2.79)	
Tx interrupted											
No	178 (92.2)	20 (95.2)	156 (91.8)	1 (ref)	109 (90.1)	66 (95.0)	1 (ref)	36 (83.7)	79 (94.0)	1 (ref)	
Yes	15 (7.8)	1 (4.8)	14 (8.2)	1.80 (0.22–14.39)	12 (9.9)	3 (4.3)	0.41 (0.11–1.52)	7 (16.3)	5 (6.0)	0.33 (0.10–1.10)	
Regimen (N = 195)											
Standard 3 meds	169 (86.7)	19 (90.5)	149 (86.6)	1 (ref)	110 (89.4)	57 (82.6)	1 (ref)	40 (93.0)	77 (89.5)	1 (ref)	
Less (1 or 2)	24 (12.3)	2 (9.5)	22 (12.8)	1.40 (0.31–6.44)	13 (10.6)	10 (14.5)	1.48 (0.61–3.59)	3 (7.0)	8 (9.3)	1.39 (0.35–5.51)	
More (4 meds)	2 (1.0)	0 (0.0)	1 (0.6)	1.000 [†]	0 (0.0)	2.9 (2.9)	0.121 [†]	0 (0.0)	1 (1.2)	1.000 [†]	
Regimen (N = 195)											
Tablets	117 (60.6)	8 (38.1)	109 (63.4)	1 (ref)	64 (52.5)	51 (75.0)	1 (ref)	25 (59.5)	50 (58.1)	1 (ref)	
Syrups	14 (7.3)	7 (33.3)	7 (4.1)	0.07 (0.02–0.26) [*]	14 (11.5)	0 (0.0)	0.001 [†]	5 (11.9)	6 (7.0)	0.60 (0.17–2.16)	

Table 3 (continued)

Clinical characteristics—univariate										
Total	3 Day recall self-report (N = 195)			Pill count 95-105% (N = 195)			Viral Load (N = 129)			
	% Mean (sd)	Non-adherent	Adherent	OR (95% CI)	Non-adherent	Adherent	OR (95% CI)	Detectable	LDL	OR (95% CI)
Tablets + syrups	62 (32.1)	6 (28.6)	56 (32.6)	0.69 (0.23–2.07)	44 (36.1)	17 (25.0)	0.49 (0.25–0.95)*	12 (28.6)	30 (34.9)	1.25 (0.55–2.85)
Regimen (N = 195)										
No lamivudine	25 (12.8)	3 (14.3)	22 (12.8)	1 (ref)	13 (10.6)	9 (13.0)	1 (ref)	10 (23.3)	6 (7.0)	1 (ref)
Lamivudine	170 (87.2)	18 (85.7)	150 (87.2)	1.14 (0.31–4.18)	110 (89.4)	60 (87.0)	0.79 (0.32–1.95)	33 (76.7)	80 (93.0)	4.04 (1.36–12.02)*
Regimen (N = 195)										
No didanosine	176 (90.3)	20 (95.2)	154 (89.5)	1 (ref)	112 (91.1)	61 (88.4)	1 (ref)	35 (81.4)	81 (94.2)	1 (ref)
Didanosine	25 (9.7)	1 (4.8)	18 (10.5)	2.34 (0.30–18.47)	11 (8.9)	8 (11.6)	1.34 (0.51–3.50)	8 (18.1)	5 (5.8)	0.27 (0.08–0.88)*
Regimen (N = 195)										
No lop/rif syrup	151 (77.4)	14 (66.7)	135 (78.5)	1 (ref)	85 (68.1)	63 (91.3)	1 (ref)	34 (79.1)	64 (74.4)	1 (ref)
Lop/rif syrup	44 (22.6)	7 (33.3)	37 (21.5)	0.55 (0.21–1.46)	38 (30.9)	6 (8.7)	0.21 (0.09–0.54)*	9 (20.9)	22 (25.6)	0.56 (0.54–3.13)
Regimen (N = 180)										
No PI base	80 (41.0)	78 (38.1)	70 (40.7)	1 (ref)	43 (35.0)	34 (49.3)	1 (ref)	18 (41.9)	30 (34.9)	1 (ref)
PI + D4T/DDI	33 (16.9)	3 (14.3)	30 (17.4)	1.14 (0.28–4.61)	23 (18.7)	10 (14.5)	0.55 (0.23–1.31)	6 (14.0)	16 (18.6)	1.60 (0.53–4.83)
PI + ABC/AZT	67 (34.4)	9 (42.9)	58 (33.7)	0.74 (0.27–2.03)	49 (39.8)	18 (26.1)	0.47 (0.23–0.94)*	14 (32.6)	33 (38.4)	1.41 (0.60–3.33)
PI + other	15 (7.7)	1 (4.8)	14 (8.1)	1.60 (0.19–13.83)	8 (6.5)	7 (10.1)	1.11 (0.37–3.36)	5 (11.6)	7 (8.1)	0.84 (0.23–3.05)

OR odds ratio, CI confidence interval, *sd* standard deviation, *Tx* treatment, *Lop/rif* lopinavir/ritonavir, *PI* protease inhibitor, *D4T* stavudine, *DDI* didanosine, *ABC* abacavir, *AZT* zidovudine, *LDL* undetectable

**p*-value < 0.05

[†]*p*-Value Fisher's Exact test (cell size less than 5)

[‡]Presented for children < 6 years

[§]Presented for boys

[¶]Presented for PC 95–100%

Table 4 Adherence and treatment efficacy by medication

Medication (N = 192)	In regimen n (%)	Mean PC % (sd)	Min–max PC %	Adherent SR n (%)	Adherent PC n (%)	LDL VL n (%)
NRTIs	192 (98.5)	–	–	170 (89.5)	69 (35.9)	86 (67.2)
Didanosine	19 (9.9)	91.7 (17.2)	38–107	18 (94.7)	8 (42.1)	5 (38.5)
Stavudine	56 (29.2)	93.5 (17.7)	35–148	49 (89.1)	21 (37.5)	26 (66.7)
Zidovudine	66 (33.8)	92.2 (19.2)	38–144	60 (90.9)	20 (30.3)	28 (62.2)
Abacavir	66 (34.4)	95.8 (18.4)	21–153	55 (85.9)	23 (34.8)	31 (70.5)
Lamivudine	170 (87.2)	96.0 (22.3)	21–192	150 (89.3)	60 (35.3)	80 (70.8)
Tenovovir	1 (0.5)	84.0 (–)	84–84	1 (100.0)	0 (0.0)	1 (100.0)
NNRTIs	67 (34.4)	–	–	61 (93.8)	28 (41.8)	30 (63.8)
Efavirenz	65 (33.9)	96.5 (11.3)	46–118	59 (93.7)	27 (41.5)	29 (64.4)
Nevirapine	2 (1.0)	93.0 (9.9)	86–100	2 (100.0)	1 (50.0)	1 (50.0)
PI	115 (59.0)	–	–	102 (88.7)	35 (30.4)	56 (69.1)
Lopinavir/ritonavir	115 (59.0)	92.3 (20.0)	32–131	102 (88.7)	35 (30.4)	56 (69.1)
Tablets	71 (37.0)	91.9 (19.1)	32–117	65 (91.5)	29 (40.8)	34 (68.0)
Syrups	44 (22.9)	93.0 (21.7)	34–131	37 (84.1)	6 (13.6)	22 (71.0)
Ritonavir	1 (0.5)	118.0 (–)	118–118	0 (0.0)	0 (0.0)	0 (0.0)

NRTI nucleoside reverse transcriptase inhibitors, *NNRTI* non-nucleoside reverse transcriptase inhibitors, *PI* protease inhibitor, *PC* pill count, *SR* self-report, *LDL* undetectable, *VL* viral load

in children [17]. The presence of side effects (didanosine) or lack thereof (lamivudine) could explain our findings.

Socio-economic characteristics associated with paediatric adherence and treatment efficacy were specific assets, family functioning and activities. Although socio-economic status is often poorly addressed [8], literature reports an association between better socio-economic status and good paediatric adherence [8, 9, 30], including specific household assets like a fridge [9]. Similar to the child and caregiver's life being affected by the child's condition, we find an association between the impact of a chronic health condition on family life and paediatric adherence. This provides unique insight in the social impact of the dynamic adherence process.

Relying on medical records for available viral load and CD4 count limited available data and having both the caregiver and child present during their respective interviews was a potential limitation to our study. The children not included in the study potentially defaulted on treatment which could have introduced bias and an overestimation of adherence. We suggest doing similar research in other settings to ensure generalizability of data. Strengths of our

study include reasonable sample size and inclusion of all children aged 5 years and older for health-related quality of life. We used multiple measures for paediatric adherence and provide a comprehensive analysis of a wide range of potential predictors including child, caregiver, clinical and socio-economic characteristics.

Conclusion

This study shows challenging levels of adherence impacting directly on viral suppression in a South African paediatric HIV program and provides a unique comprehensive analysis of potential predictors with multiple measures and definitions. Adherence is a dynamic, multifactorial process including child, caregiver, clinical and socio-economic characteristics. Measuring adherence is important. Definitions for pill counts should include both lower and upper limits. Monthly clinic visits represent a convenient and appropriate time to address difficulties administering medication and an opportunity to resolve problems while reducing social desirable answers and stigmatisation. Gender roles, non-disclosure and difficulty administering medication may undermine adherence and should be taken into account for clinical guidelines, policy design and when informing strategies.

Table 5 Socio-economic characteristics of adherence and treatment efficacy

		3 Day recall self-report (N = 195)				Pill count 95-105% (N = 195)				Viral load (N = 129)									
		% Mean (sd)		OR (95% CI)		Adherent		Non-adherent		Adherent		OR (95% CI)		Detectable		LDL		OR (95% CI)	
Socio-economic characteristics—univariate																			
Family impact (N = 194)																			
Mean	90.4 (11.3)	87.1 (14.6)	91.0 (10.5)	–	–	92.1 (9.8)	–	–	–	88.7 (13.2)	90.4 (10.7)	–	–	–	–	–	–	–	–
41.9–87.1	47 (24.2)	8 (38.1)	38 (22.2)	1 (ref)	17 (37.8) [§]	3 (8.6) [§]	1 (ref)	1 (ref)	1 (ref)	13 (30.2)	22 (25.9)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
87.2–93.8	50 (25.8)	5 (23.8)	45 (26.3)	0.53 (0.16–1.75)	10 (22.2) [§]	9 (25.7) [§]	0.20 (0.04–0.90) ^{§§}	0.20 (0.04–0.90) ^{§§}	0.20 (0.04–0.90) ^{§§}	10 (23.3)	22 (25.9)	0.77 (0.28–2.12)	0.77 (0.28–2.12)	0.77 (0.28–2.12)	0.77 (0.28–2.12)	0.77 (0.28–2.12)	0.77 (0.28–2.12)	0.77 (0.28–2.12)	0.77 (0.28–2.12)
93.9–98.4	52 (26.8)	7 (33.3)	44 (25.7)	0.76 (0.25–2.28)	10 (22.2) [§]	12 (34.3) [§]	0.15 (0.03–0.65) ^{§§}	0.15 (0.03–0.65) ^{§§}	0.15 (0.03–0.65) ^{§§}	14 (32.6)	20 (23.5)	1.19 (0.45–3.12)	1.19 (0.45–3.12)	1.19 (0.45–3.12)	1.19 (0.45–3.12)	1.19 (0.45–3.12)	1.19 (0.45–3.12)	1.19 (0.45–3.12)	1.19 (0.45–3.12)
98.5–100	45 (23.2)	1 (4.8)	44 (25.7)	0.11 (0.01–0.90) [*]	8 (17.8) [§]	11 (31.4) [§]	0.13 (0.03–0.59) ^{§§}	0.13 (0.03–0.59) ^{§§}	0.13 (0.03–0.59) ^{§§}	6 (14.0)	21 (24.7)	0.48 (0.16–1.51)	0.48 (0.16–1.51)	0.48 (0.16–1.51)	0.48 (0.16–1.51)	0.48 (0.16–1.51)	0.48 (0.16–1.51)	0.48 (0.16–1.51)	0.48 (0.16–1.51)
FI activities (N = 194)																			
Mean	91.5 (15.1)	88.9 (18.1)	91.8 (14.8)	–	–	89.8 (15.5)	–	–	–	91.1 (19.4)	92.2 (13.8)	–	–	–	–	–	–	–	–
25.0–83.3	44 (22.7)	6 (28.6)	37 (21.6)	1 (ref)	22 (17.9)	21 (30.9)	1 (ref)	1 (ref)	1 (ref)	6 (14.3)	18 (20.9)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
83.4–91.7	30 (15.5)	5 (23.8)	25 (14.6)	1.23 (0.34–4.48)	23 (18.7)	7 (10.3)	3.14 (1.11–8.84) [*]	3.14 (1.11–8.84) [*]	3.14 (1.11–8.84) [*]	8 (19.0)	15 (17.4)	1.60 (0.45–5.65)	1.60 (0.45–5.65)	1.60 (0.45–5.65)	1.60 (0.45–5.65)	1.60 (0.45–5.65)	1.60 (0.45–5.65)	1.60 (0.45–5.65)	1.60 (0.45–5.65)
91.8–100	120 (61.9)	10 (47.6)	109 (63.7)	0.57 (0.19–1.66)	78 (63.4)	40 (58.8)	1.86 (0.92–3.78)	1.86 (0.92–3.78)	1.86 (0.92–3.78)	28 (66.7)	53 (61.6)	1.59 (0.57–4.45)	1.59 (0.57–4.45)	1.59 (0.57–4.45)	1.59 (0.57–4.45)	1.59 (0.57–4.45)	1.59 (0.57–4.45)	1.59 (0.57–4.45)	1.59 (0.57–4.45)
SES index (N = 188)																			
Mean	52.2 (16.8)	45.4 (18.0)	53.2 (16.5)	–	–	54.9 (17.5)	–	–	–	50.1 (17.7)	52.7 (16.4)	–	–	–	–	–	–	–	–
9.5–42.9	40 (21.3)	6 (28.6)	33 (20.0)	1 (ref)	26 (22.0)	14 (20.9)	1 (ref)	1 (ref)	1 (ref)	10 (25.0)	20 (23.5)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
43.0–55.0	49 (26.1)	6 (28.6)	42 (25.9)	0.79 (0.23–2.66)	34 (28.8)	15 (22.4)	1.22 (0.50–2.97)	1.22 (0.50–2.97)	1.22 (0.50–2.97)	10 (25.0)	19 (22.4)	1.05 (0.36–3.09)	1.05 (0.36–3.09)	1.05 (0.36–3.09)	1.05 (0.36–3.09)	1.05 (0.36–3.09)	1.05 (0.36–3.09)	1.05 (0.36–3.09)	1.05 (0.36–3.09)
55.1–61.9	46 (24.5)	8 (38.1)	38 (22.9)	1.16 (0.36–3.68)	32 (27.1)	13 (19.4)	1.33 (0.53–3.31)	1.33 (0.53–3.31)	1.33 (0.53–3.31)	10 (25.0)	25 (29.4)	0.80 (0.28–2.30)	0.80 (0.28–2.30)	0.80 (0.28–2.30)	0.80 (0.28–2.30)	0.80 (0.28–2.30)	0.80 (0.28–2.30)	0.80 (0.28–2.30)	0.80 (0.28–2.30)
62.0–100	53 (28.2)	1 (4.8)	52 (31.2)	0.11 (0.01–0.92) [*]	26 (22.0)	25 (37.3)	0.56 (0.24–1.31)	0.56 (0.24–1.31)	0.56 (0.24–1.31)	10 (25.0)	21 (24.7)	0.95 (0.33–2.77)	0.95 (0.33–2.77)	0.95 (0.33–2.77)	0.95 (0.33–2.77)	0.95 (0.33–2.77)	0.95 (0.33–2.77)	0.95 (0.33–2.77)	0.95 (0.33–2.77)
SES asset (N = 189)																			
No TV	20 (10.6)	5 (23.8)	14 (8.4)	1 (ref)	14 (11.8)	6 (9.0)	1 (ref)	1 (ref)	1 (ref)	4 (10.0)	9 (10.6)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
TV	169 (89.4)	16 (76.2)	152 (91.6)	0.30 (0.09–0.93) [*]	105 (88.2)	61 (91.0)	0.74 (0.27–2.02)	0.74 (0.27–2.02)	0.74 (0.27–2.02)	36 (90.0)	76 (89.4)	1.07 (0.31–3.69)	1.07 (0.31–3.69)	1.07 (0.31–3.69)	1.07 (0.31–3.69)	1.07 (0.31–3.69)	1.07 (0.31–3.69)	1.07 (0.31–3.69)	1.07 (0.31–3.69)
SES asset (N = 189)																			
No fridge	38 (20.1)	8 (38.1)	29 (17.5)	1 (ref)	29 (24.4)	9 (13.4)	1 (ref)	1 (ref)	1 (ref)	8 (20.0)	19 (22.4)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Fridge	151 (79.9)	13 (61.9)	137 (82.5)	0.34 (0.13–0.91) [*]	90 (75.6)	58 (86.6)	0.48 (0.21–1.09)	0.48 (0.21–1.09)	0.48 (0.21–1.09)	32 (80.0)	66 (77.6)	1.15 (0.46–2.91)	1.15 (0.46–2.91)	1.15 (0.46–2.91)	1.15 (0.46–2.91)	1.15 (0.46–2.91)	1.15 (0.46–2.91)	1.15 (0.46–2.91)	1.15 (0.46–2.91)
SES asset (N = 189)																			
No bicycle	159 (84.1)	21 (100)	136 (81.9)	1 (ref)	106 (89.1)	51 (76.1)	1 (ref)	1 (ref)	1 (ref)	36 (90.0)	73 (85.9)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Bicycle	30 (15.9)	0 (0.0)	30 (18.1)	0.028 [†]	13 (10.9)	16 (23.9)	0.39 (0.18–0.87) [*]	0.39 (0.18–0.87) [*]	0.39 (0.18–0.87) [*]	4 (10.0)	12 (14.1)	0.68 (0.20–2.24)	0.68 (0.20–2.24)	0.68 (0.20–2.24)	0.68 (0.20–2.24)	0.68 (0.20–2.24)	0.68 (0.20–2.24)	0.68 (0.20–2.24)	0.68 (0.20–2.24)

OR odds ratio, CI confidence interval, *sd* standard deviation, FI family impact, SES socio-economic status, LDL undetectable viral load

^{*}p-value < 0.05

[†]p-Value Fisher's exact test (cell size less than 5)

[§]Presented for boys

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Compliance with Ethical Standards

Conflict of interest The authors have no conflict of interest to declare.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Stellenbosch University's human research ethics committee approved this study (reference number N11/11/329).

Informed Consent All caregivers provided written informed consent for their and their child's participation. In addition, all children (≥ 7 years) provided written informed assent for their participation.

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