

Adherence to Highly Active Antiretroviral Therapy and Associated Factors among HIV Positive Adolescents in Kenya

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ABSTRACT

Background: Optimal adherence to antiretroviral therapy (ART) is a serious challenge for adolescents living with HIV. The poor adherence is associated with poor treatment outcome. Currently, adolescence is the only age group where HIV related mortality is not declining. This study aimed at determining the proportion of adolescents adhering to antiretroviral therapy (ART) and the correlates of non-adherence to ART.

Method: A total of 85 adolescents were enrolled consecutively as they sought services at the Comprehensive Care Centre (CCC) of Murang'a County Hospital. Interviews were conducted using an interviewer-administered semi-structured questionnaire. Chi square test was used to assess the associations between the dependent and independent variables.

Results: The study found that 75.3% of the subjects adhered to ART (95% confidence interval (CI) 16.8% to 34.8%). Most frequently reported reason for non-adherence was forgetting (62%) followed by travelling (14%). Younger adolescents (< 18 years) had higher odds of being non-adherent to ART (adjusted odds ratio (aOR) 97.40 (95% CI 2.22 - 4282.91) for those aged 10 to 13 years and aOR 522.46 (95% CI 4.87 - 56101.59) for those aged 14 to 17 years). A student enrolled in a day school had 90% lower likelihood of being non-adherent to ART when compared to his counterparts in boarding schools (aOR 0.10 (95% CI 0.02 - 0.58)). Experiencing adverse effects on taking ARVs was associated with increased odds of poor ART adherence (aOR 16.17 (95% CI 1.76 - 148.28)) while finding the hours of CCC's operation being convenient lowered the odds of being non-adherent to ART by 98% (aOR 0.02 (95% CI 0.00 - 0.65)).

Conclusion: Our study showed a substantial proportion of self-reported suboptimal ART adherence among adolescents living with HIV. This is likely to place this cohort at an increased risk of ART failure and the attendant risk of disease progression. The findings suggest that interventions designed specifically for the adolescent population are further needed.

Key words: HIV/AIDS; Antiretroviral Therapy; Adherence; Adolescents

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I. INTRODUCTION

Antiretroviral therapy (ART) is effective at improving quality of life, progression to AIDS and death (Palella et al 1998; Vittinghoff et al 1999). Recently, ART has been proven to prevent HIV transmission (Cohen et al 2011). However, studies have shown that, over time, deaths associated with HIV/AIDS have not decreased in the adolescent population. Between 2004 and 2011, AIDS-related deaths increased by 50% in this population (Kasedde et al 2013; Ammon et al 2018). It is estimated that, globally, 1.8 million adolescents are living with HIV/AIDS with the majority (85%) living in Sub Saharan Africa (UNAIDS 2018).

Once ART is initiated, adherence should be strictly maintained to suppress viral load and prevent drug resistance (Matson et al 2018). 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 (Vittinghoff et al 1999; Cohen et al 2011).

Adolescence is a period of enormous developmental, social, and biological transition. This multifaceted transition creates a combination of risk factors for several health outcomes. Sexual debut during this period brings with it a risk of pregnancy, as well as sexually transmitted infections, and the psychological, socio-economical, and legal circumstances of adolescents render this group especially vulnerable to the consequences of these events (Matson et al 2018). Optimal adherence to ART is a key challenge for adolescents living with

HIV (ALWH). It is estimated that, worldwide, 40% of ALWH are non-adherent to ART (Kim et al 2014). Additionally, adolescents show low rates of HIV testing, poor linkage to care, and high loss to follow-up from ART programs (Idele et al 2014; Ronen et al 2017; UNICEF 2018).

There is a shortage of published literature focusing on ART adherence among adolescents living in a resource-limited settings of SSA countries such as Kenya. Moreover, the few studies on ART adherence were not conducted in the current era of simple, once-daily ART. To fill the aforementioned gaps, at least in part, the current study aimed at describing the adherence to ART among ALWH and also the correlates of sub-optimal ART adherence in this population.

II. METHODS

Study population

The study population comprised of all HIV positive adolescents (10 to 19 years) seeking services at the CCC of Murang'a County Hospital and had been on ART for at least six months. The inclusion criteria were as follows: being HIV positive adolescent, being enrolled for care and treatment at the CCC, being on ART for at least six months, having assented/consented to participate in the study and consent being given by the caregiver for adolescents aged below 15 years. The exclusion criteria included being under influence of drugs, being mentally challenged and/or being very sick.

Data collection procedure

Study participants were recruited consecutively as they sought services at the CCC. Primary data was collected using semi-structured interviewer-administered questionnaire. Secondary data was abstracted from the hospital's database.

Statistical analysis

Data were analyzed using IBM SPSS 22.0. Categorical data were described using frequencies and proportions while continuous data was presented using mean \pm standard deviation (sd) or median (interquartile range (IQR) where appropriate. Chi square (χ^2) test was used to evaluate the association between the independent variables and the dependent variable. Variables that were found to be associated with adherence to ART by bivariate analysis were subjected to binary logistic regression. The threshold for statistical significance was set at $p < 0.05$.

Ethical Statement

The study was approved by Kenyatta National Hospital/University of Nairobi Ethical Review Committee. Permission to conduct the study was also obtained from the Ministry of Health, Murang'a County, and the hospital's management. Assented to participate in the study was sought from adolescents aged below 15 years as well as consent from their caregiver. In addition, informed written consent was sought from adolescents aged 15 years and above.

III. RESULTS

Characteristics of the study participants

Sociodemographic characteristics of the study participants

Their age of the study participants ranged from 10 to 19 years with a mean \pm sd age of 16 ± 2.3 years. Respondents who were aged 18 years and above comprised 37% of the study sample. Majority of the study participants were Christians (95%) and were pursuing secondary school education (60%). Additionally, most of the participants were enrolled in day schools (61%) and were still dependent on their parents (77%). None of the study participants was married. Most of the adolescents enrolled in the study reported that their main caregivers were the biological parents (mother and/or father). Furthermore, minority mentioned that their caregivers were not related to them biologically (7%). A vast majority of the adolescents were aware of their HIV status (97%). Inquiries into the disclosure status among those who knew of their HIV status revealed that of the 76% had disclosed their HIV status. The proportion of respondents who responded on the affirmative on being asked if they had ever been 'treated differently' because of the medications they were taking was 11%. Of the 36 adolescents who said that they took alcohol or abused other substances (42%), 21 (58%) reported that they had ever missed taking the medicines because of taking alcohol or abusing other substances (Table 1).

Table 1 - Sociodemographic characteristics of the study participants

Characteristics	Frequency (n=85)	%
Gender		
Female	41	48.2
Male	44	51.8
Age (years)		
10 to 13	18	21.2
14 to 17	36	42.4
18 to 19	31	36.5
Religion		
Christian	81	95.3
Muslim	4	4.7
Education		
Tertiary	9	10.6
Secondary	51	60.0
Primary	25	29.4
Type of school		
Day	49	61.3
Boarding	31	38.8
Source of your livelihood		
Depends on parents	65	76.5
Depends on Relatives	17	20.0
Depends on well wishers	1	1.2
Employed	2	2.4
Rating of the support provide caregiver		
Good	78	91.8
Fair	6	7.1
Poor	1	1.2
Caregiver's support affects how I take medicines		
No	35	41.2
Yes	50	58.8
Knows his/her HIV status		
Yes	82	96.5%
No	3	3.5%
Ever been treated differently because of the medications		
Yes	9	10.6
No	76	89.4
Drinks alcohol or abuses other substances		
Yes	36	42.4
No	49	57.6

Clinical/drug-related attributes of the study participants

Those who were on the first line and second line of ART at the time the study was undertaken constituted 66% and 15% of the respondents. Minority of the study respondent's had ever experienced adverse effects from ART (14%)(Table 2).

Table 2– Clinical/Drug-related attributes of the study participants

Attribute	Number (n=85)	%
Therapy		
First line	56	65.9
Second line	13	15.3
Not sure	16	18.8
Daily frequency of drugs		
Once	8	9.4
Twice	77	90.6
Ever experienced a bad side effect due to the medicines		
Yes	12	14.1
No	73	85.9

Analysis of the daily pill burden is displayed in Figure 1. Six percent of the participants took ARV once daily while the frequency of taking ARV was twice and thrice daily for 31% and 47% of the participants respectively.

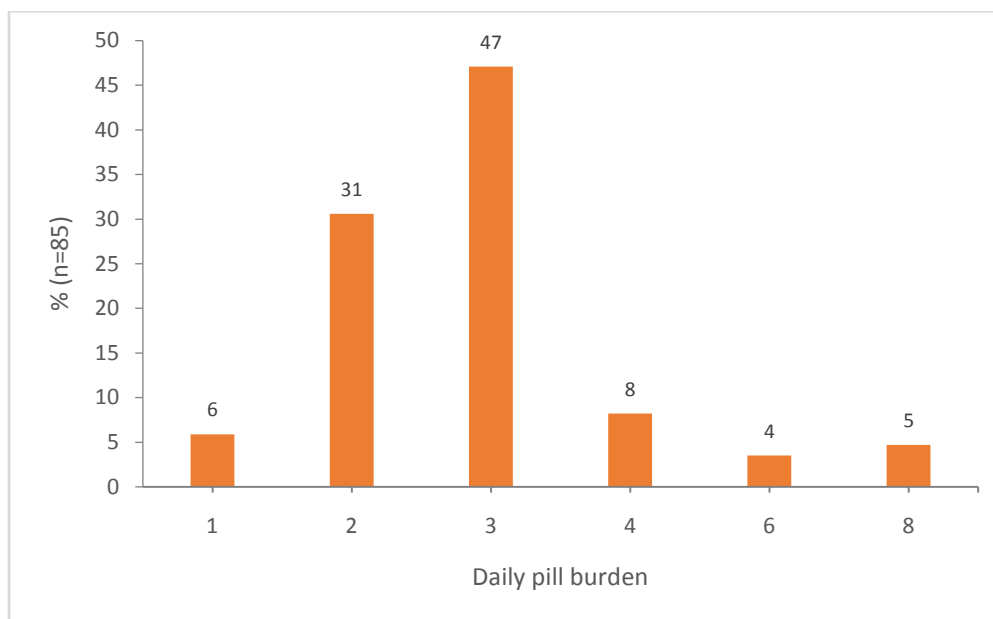


Figure 1 - Pills taken on a daily basis (24hrs)

Health-system related attributes

Asked to rate the distance from home to the hospital, 45% and 44% said it was far and near respectively. Those who rated the healthcare workers as ‘good’ in terms of being caring, friendly and listening were 87% while 86% opined that the CCC working hours were convenient. Waiting time during your clinic appointments was rated as appropriate by 69% of the adolescents who were recruited in the study. Majority of the respondents found the psychosocial support groups very helpful (94%) (Table3).

Table 3- Health-system related attributes

Attributes	Frequency (n=85)	%
Distance from home to the hospital		
Very far	10	11.8
Far	38	44.7
Near	37	43.5
Rating healthcare workers (caring, friendly and listening)		
Good	74	87.1
Average	9	10.6
Poor	2	2.4
CCC working hours convenient		
Yes	73	85.9
No	12	14.1
Waiting time during your clinic appointment		
Appropriate	58	69.0
Long	26	31.0
Psychosocial support groups are:		
Very helpful	80	94.1
Not sure	5	5.9

Adherence to ARV

Twenty one of the 85 adolescents who took part in the current study reported that they had missed taking the ARVs thus a non-adherence level of 24.7% (95% confidence interval (CI) 16.8% to 34.8%).

Factors associated with adherence to ART

Demographic factors and adherence to ART

The age of the respondents who had ever missed any of your prescribed medications was not significantly different from that of their counterparts who had never missed the medications (mean ± standard error 15.1±0.46

years and 16.2±0.29 years, respectively, p=0.048). Adolescents aged between 10 and 13 years were about seven times more likely to be non-adherent to ART when compared with their older colleagues of 18 to 19 years (odds ratio (OR) 7.250 (95% CI 1.278-41.139), p=0.039). Similarly, those who were aged between 14 and 17 years had approximately 8 times higher odds of being non-adherent compared to those who were at least 18 years old (OR 8.196 (95% CI 1.678 - 40.033), p=0.007). None of the adolescents in the aged between 10 and 12 years reported ever missing medications. Analysis of adherence by sex showed that a higher proportion of boys reported that they had ever missed taking the ARVs (37% for boys and 14% for girls, OR 3.654 (95% CI 1.253 - 10.654), p=0.014). A significantly higher proportion of the respondents who were in boarding school reported ever missing their medications compared to those who were in enrolled in day schools (45% versus 14% respectively, OR 0.202 (95% CI 0.070 - 0.589), p=0.002). Other demographic factors including education, source of livelihood and religion failed to show any significant relationship with adherence to ART (Table 4).

Association between drug-related factors and adherence to ART

The daily pill burden was a significant factor associated with adherence to ART. Lower pill burden (1 or 2 pills daily) was associated with 87% lower odds of being non-adherent to ART (OR 0.127 (95% CI 0.027-0.591), p = 0.003). The line of the ARVs prescribed to the adolescent, daily frequency of drugs and timing of taking the drugs were not significant factors for adherence to ART among the adolescents (Table 5).

Table 5 – Association between drug-related factors and adherence to ART

Characteristic	Ever missed		OR* (95% CI [§])	P-value
	Yes(n=21)	No(n=44)		
Therapy				
Second line	4(30.8)	9(69.2)	1.22(0.33-4.54)	0.772
Not sure	2(12.5)	14(87.5)	0.39(0.08-1.93)	0.235
First line	15(26.8)	41(73.2)	Ref	
Daily frequency of drugs				
Once	2(25.0)	6(75.0)	1.03(0.19-5.47)	0.984
Twice	19(24.7)	58(75.3)	Ref	
Pills taken daily (24hrs)				
1 or 2	2(6.5)	29(93.5)	0.13(0.03-0.60)	0.003
3 +	19(35.2)	35(64.8)	Ref	
Ever experienced bad side effects				
Yes	6(50.0)	6(50.0)	3.87(1.09-13.71)	0.028
No	15(20.5)	58(79.5)	Ref	

*Odds ratio §Confidence interval

Association between health system factors and adherence to ART

Those who reported that the healthcare workers in the CCC were good in terms of being caring, friendly and listening were found to have about 80% lower odds of having ever missed their medications (odds ratio (OR) 0.212 (95% CI 0.057-0.789), p=0.023). Respondents who said that the psychosocial support groups were very helpful had significantly lower odds of being non-adherent to ART compared to those who had a different opinion about the helpfulness of the groups (OR 0.067 (95% CI 0.007-0.644), p = 0.012). Study participants who responded on the affirmative on being asked if they found the CCC working hours' convenient were significantly less likely to be non-adherent (OR 0.169 (95% CI 0.047 - 0.614), p = 0.008). Other health system attributes assessed in the survey were not significantly related to the adherence to ART in adolescents (Table 6).

Table 6 – Association between health system factors and adherence to ART

Factor	Ever missed		OR* (95% CI [§])	P-value
	Yes(n=21)	No(n=44)		
Distance from hospital				
Very far Far	15(31.3)	33(68.8)	2.35 (0.81-6.82)	0.111
Near	6(16.2)	31(83.8)	Ref	
Rate: healthcare workers are caring, friendly and listening				
Good	15(20.3)	59(79.7)	0.21(0.06-0.79)	0.023
Average/Poor	8(61.5)	5(38.5)	Ref	
CCC working hours convenient				
Yes	14(19.2)	59(80.8)	0.17(0.05-0.61)	0.008
No	7(58.3)	5(41.7)	Ref	
Rate: waiting time on appointment				

Appropriate	10(17.2)	48(82.8)	0.284(0.10-0.80)	0.016
Long	11(42.3)	15(57.7)	Ref	
Psychosocial support groups				
Very helpful	17(21.3)	63(78.8)	0.067(0.01-0.64)	0.012
Not helpful/Not sure	4(80.0)	1(20.0)	Ref	

* Odds ratio §Confidence interval

Multivariate analysis

Compared to those aged 18 years and above, the younger adolescents had higher odds of being non-adherent to ART (p=0.031). Additionally, being a student in a day school was associated with a 90% decrement in odds of being non-adherent to ART when evaluated against those enrolled in boarding school (adjusted odds ratio (aOR) 0.10 (95% CI 0.02 - 0.58), p=0.010). Those who reported ever experiencing adverse effects on taking ARVs were more likely to non-adherence to ART (aOR 16.17 (95% CI 1.76 - 148.28), p=0.014). Adolescents who found the CCC working hours being convenient were had a 98% lower likelihood of being non-adherent to ART (aOR 0.02 (95% CI 0.00 - 0.65), p=0.029) (Table 7).

Table 7 – Outputs from binary logistic regression

Variables	aOR*	95% CI§		P-value
		Lower	Upper	
Age(years)				0.031
(10 – 13 vs. 18+) years	97.40	2.22	4282.91	0.018
(14 – 17 vs. 18+) years	522.4		56101.5	
	6	4.87	9	0.009
Sex (Male vs. Female)	2.96	0.57	15.43	0.197
Type of school (Day vs. Boarding)	0.10	0.02	0.58	0.010
Pills taken daily (1 or 2 vs. 3 +)	0.45	0.06	3.32	0.436
Ever experienced bad side effects (Yes vs. No)	16.17	1.76	148.28	0.014
Rate: healthcare workers are caring, friendly and listening (Good vs. Average/Poor)	1.11	0.10	12.37	0.936
CCC working hours convenient (Yes vs. No)	0.02	0.00	0.65	0.029
Waiting time on appointment (Appropriate vs. Long)	0.88	0.14	5.53	0.889
Psychosocial support groups (Very helpful vs. Not helpful/Not sure)	0.06	0.00	1.08	0.057

*Adjusted odds ratio §Confidence interval

IV. DISCUSSION

The findings in this study demonstrated high self-reported non-adherence to antiretroviral therapy amongst ALWH. About one in four adolescents who took part in the study were found to be non-adherent to ART. The poor adherence among adolescents documented in this study is a significant concern, given the limited ART options available and the substantial risk of development of drug resistance associated with non-adherence to ART. A study done in Malawi reported much higher levels of self-reported non-adherence with nearly half (45%) of all ALWH in this setting reporting missing ART in the month (Kim et al 2017). A recent study done in Zambia showed that 28.3% were non-adherent to ART (Okawa et al 2018). A survey in Southwest Ethiopia and reported that 36% of the study participants had poor adherence to ART (Abera et al 2015). Non-adherence rates in Uganda were 18% while a survey done in Rwanda reported a non-adherence rate of 37% (Okawa et al 2018; Abera et al 2015). The observed variations in statistics on non-adherence could be attributed to differences in demographic characteristics, socio-economic and cultural contexts under which the studies were conducted. For instance, the research in Zambia focused on adherence to ART among late adolescents (15 to 19 years) (Okawa et al 2018). The current study focused on both early and late adolescents (10 to 19 years). Further, the Ethiopian study was done at the ART Clinic of Jimma University Teaching Hospital and recruited People Living with HIV/AIDS rather than adolescents alone (Abera et al 2015).

Being in a day school was associated with lower odds of being non-adherent compared to boarding school. The most likely explanation to this finding is that adolescents who are in day school have more access to psychosocial support and also have some support from caregivers and family members (Mutumba et al 2016; Fawzi et al 2016). The finding perhaps is a pointer to the fact that the caregiver's and/or parents' presence is vital for adolescents' well-being, particularly in terms of economic and emotional stability in their daily life (Kikuchi et al 2014). Indeed a study conducted in Uganda noted that adolescents reported stigma and discrimination at school by teachers and fellow students (Mutumba et al 2016). Those in boarding schools lacked privacy to take their medication, which lead to missing doses. Additionally, those who did not disclose

their HIV status to the school authorities found it very difficult to get permission to leave school to keep a clinic appointment (Nabukeera-Barungi et al 2007).

The present study showed no significant association between religion and adherence to ART. Similarly, a study done in Nigeria no association between the two variables (Ashraf et al 2017). Previous studies have also reported an association between religion and adherence. Research done in Zambia showed that spiritual beliefs and religious healing played a role in incomplete adherence to ART among ALWH (Denison et al 2015).

Bivariate analysis showed that disclosure of HIV status was associated with decreased risk of non-adherence to ART among the study participants. This is not surprising as one can speculate that when a patient does not understand the reasons for taking a prescribed medication, the cooperation needed could be compromised. In line with this, disclosure might help the patient/client understand why he or she is taking daily medications and the benefits thereof (Nichols et al 2017). Based on such evidence, the American Academy of Pediatrics (1999) has recommended age-appropriate disclosure of HIV status to children, with full disclosure occurring by adolescence in order to achieve better disease outcomes and assist with the child's psychological adjustment to knowing his or her status. The WHO published a similar set of guidelines in 2011 which recommended beginning the disclosure process at 6 years old, with full disclosure being accomplished by the age of 12 (WHO 2011). Research undertaken, with patients aged 10 to 19 years, in Eastern Cape, South Africa, showed a significant association between disclosure of HIV status and adherence (OR 2.65, 95 % CI [1.34–5.22]) (Cluver et al 2015). A recent study done in Tanzania associated HIV status disclosure with an eight-fold increment in the odds of being adherent to treatment (aOR 8.173, $p < 0.05$) among children aged 6 to 17 years (Bulali et al 2018).

Contrary to what is reported in our survey, a study done in Zambia implicated not knowing one's HIV status on incomplete adherence ((Denison et al 2015). In a study done in South Africa, it was noted that early and full disclosure was strongly associated with improved adherence amongst ART-initiated adolescents (Cluver et al 2015). A study of children (339 out of 792 were aged over 10 years) in four 'Academic Model Providing Access to Healthcare' (AMPATH) clinics in Kenya found that disclosure was associated with non-adherence based on the child's report (Vreeman et al 2014). A hospital-based study conducted in Thailand, 260 children and adolescents aged 6 to 19 years, of which 228 were over 10 years old, indicated no significant association between HIV disclosure and ART adherence, using measures of pill count, CD4 cell count or viral load (Sirikum et al 2014). In Nigeria, a study of 213 children (45 were over 10 years old) used caregiver or child report and found improved adherence wherein HIV status was disclosed (Ugwu & Eneh 2014). The differences in findings could be explained by the differences in demographic characteristics of the study participants, specifically age, as well as the variations in the study settings. Besides, the mixed results observed in these studies could be due to the fact that disclosure is increasingly being understood not as a single event, but as a complex dynamic process and can include disclosure of parental HIV-status (Dima et al 2014; Qiao et al 2013). This can include 'partial disclosure' wherein a child may know that they have an illness, but not that it is HIV/AIDS. Full disclosure is often described as naming HIV, but research indicates that HIV-positive children or adolescents may not fully understand the meaning of positive serostatus (Sirikum et al 2014). Caregiver's support was associated positively with adherence to therapy in the current study. Previous studies have shown similar findings. For example, a Zambian study documented that the families of ALWH supported them in uptake of therapy. This support ranged from occasional reminders to direct observation of swallowing the pills (Denison et al 2015).

Our survey showed that experiencing adverse events while being on ART as a significant barrier to ART adherence. This is in agreement with research carried out in Zambia which reported side effects among the reasons for incomplete adherence to ART among ALWH (Denison et al 2015).

Working hours of CCC being convenient was associated with higher odds of adherence to ART. This is in concordance with the findings of a survey done in central Uganda which indicated that adolescents are attracted to adolescent friendly services (Atuyambe et al 2009). Other health system's facilitators of adherence noted in the Ugandan study included scheduling clinic visits during school holidays, providing food support, transport to clinics, short waiting time, telephone calls from the facilities and text messages (Nabukeera-Barungi et al 2007). Overall, the findings on health system factors emphasize the need to create and sustain an adolescent-friendly treatment spaces (both physical and social environments) in order to increase self-efficacy for medical care engagement (Mellins et al 2011). Primary care providers working with ALWH also need to be trained on the cultural and developmental needs of this group.

The present study is not without limitations. The study utilized a cross-sectional study design. Stronger and definitive conclusions on the associations between various factors and adherence to ART would be possible with a longitudinal cohort study. Additionally, the study population was majorly drawn from a rural area. Observations may be different in an urban set-up. Another potential limitation is that adherence was assessed only through adolescent self-report. Incorporating the viral load data was very helpful in providing insights on

the clinical relevance of self-reported adherence. A major challenge with self-report is potential overestimation of adherence due to social desirability bias. Nevertheless, in this study, self-reporting of ART adherence was done anonymously thus potentially reducing the attendant bias. Moreover, self-reporting of medication adherence by adolescents has been found to be relatively accurate and rates of non-adherence reported in studies using laboratory assays are consistent with rates reported in studies using self-report (Mellins et al 2011; Buchanan et al 2012).

V. CONCLUSIONS AND RECOMMENDATIONS

Our study found that a notable proportion of self-reported suboptimal ART adherence among ALWH. This is likely to place this cohort at an increased risk of ART failure, disease progression as well as increased risk of HIV transmission and increased mortality. The study also identified a set of modifiable risk factors to suboptimal ART adherence including being in early adolescence (<18 years), being a student in a boarding school, experiencing bad side effects and inconvenient CCC operational hours. The findings highlight the pressing need for better interventions targeting ALWH to facilitate optimal adherence to ART, retention in care and improved treatment outcomes.

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