

Adherence to highly active antiretroviral therapy among HIV-infected children in Kano, Nigeria

Abstract

Background: HIV has emerged as one of the leading causes of childhood mortality and morbidity in sub-Saharan Africa. Antiretroviral therapy (ART) in children in Africa has resulted in dramatically improved survival. However, excellent adherence is one of the most important factors in determining treatment success and preventing viral resistance. While studies of African adults showed that good adherence to ART is possible despite poor social circumstances, there are limited data on ART adherence among African children, and hence the need for the current study. This study determined factors associated with adherence to highly active antiretroviral therapy (HAART) among HIV-infected children in Kano, Nigeria.

Method: A cross-sectional study was conducted at the Special Treatment Clinic (STC) of Aminu Kano Teaching Hospital, Kano, Nigeria. The study population comprised HIV-infected children taking ARV medications, which accessed care at the Clinic between June and August 2010, and met the eligibility criteria. A list of all children who were on HAART and had a clinic appointment within the study period was generated. From this list, participants were randomly selected using a computer-based random number generator. Caregivers were interviewed at the clinic using a structured questionnaire

Results: A total of 122 children [64% males] out of 130 contacted, whose caregivers provided consent, were recruited into the study. The median age of the study children was 5.5 years (IQR: 1.3 to 14 years). A total of 80 children (65.6%) were adherent to the prescribed antiretroviral drugs for the 7 days preceding the interview. Non-adherence was found to be significantly associated with caregiver's report of missing at least one clinic appointment in the last six months (p -value 0.000) and children on second line HAART regimen (p -value 0.01). However, children whose caregivers were older than 25 years (p -value 0.012) were more likely to be adherent than their respective counterparts.

Conclusion: Adherence to HAART in children in Kano, Nigeria was similar to reported adherence levels from other sub-Saharan African countries. Keeping clinic appointments was strong predictor of good adherence to HAART.

Keywords: Adherence, HAART, Children

Volume 2 Issue 2 - 2015

Bashir Zubayr,¹ Muatassim Ibrahim,² Jibreel Jumare,¹ Fatima Hassan Hanga,³ Mahmoud J Gambo,³ Patrick S Dakum,¹ Kareem Airede,⁴ Nicaise Ndambi¹

¹Institute of Human Virology, Nigeria

²Umar Musa Yar Adua University Katsina, Nigeria

³Aminu Kano Teaching Hospital/ Bayero University Kano, Nigeria

⁴University of Abuja, Nigeria

Correspondence: Bashir Zubayr, Institute of Human Virology, Nigeria, Email bashonipe@yahoo.com

Received: December 15, 2014 | **Published:** January 28, 2015

Introduction

In 2013, an estimated 35.2 million people were living with HIV worldwide and 3.5 million of these were children under 15 years of age.¹ Furthermore, in 2012, 260,000 children less than 15 years were newly infected with HIV and 210,000 died from AIDS-related causes. In the last decade, HIV has emerged as one of the leading causes of childhood mortality and morbidity in sub-Saharan Africa.¹

Antiretroviral therapy (ART) in children in Africa has resulted in improved survival, due to improvement in clinical, immunological, and virological status.^{2,3} Excellent adherence remains one of the most important factors that determine a successful treatment outcome, mainly by preventing viral drug resistance.^{2,4} However, the need for near-perfect adherence to lifelong therapy from an early age has been identified as a major challenge in the administration of ART to HIV-infected children.^{2,6} Using unannounced pill counts, one study reported good adherence levels among Ugandan children.⁷ Poor adherence was found to be more common in situations where a child's HIV status was only known to the primary caregiver.⁷ The findings of this study, however, were questioned because children on syrups and suspensions were excluded.

Another study found similar levels of self-reported adherence in children receiving ART in Kampala, Uganda, which were comparable to the reported levels in resource-rich settings.⁸ In addition, the study found that financial constraints in purchasing ARV medications were

a major barrier to adherence. An earlier report also found financial constraints to be the most common reason for non-adherence among children on ART in Nigeria.⁹ However, this study had a sample size of 40 children and it would be difficult to draw comparative conclusions given the small sample size. While studies of African adults showed that good adherence to ART is possible despite poor social circumstances,¹⁰⁻¹² there are limited data on ART adherence among African children, and hence the need for the current study. To address this, our study determined the rates and factors associated with adherence to highly active antiretroviral therapy (HAART) among HIV-infected children in Kano, Nigeria.

Methods

Study design and area

The was cross-sectional study conducted at Aminu Kano Teaching Hospital, a 400-bed tertiary health facility located in Kano metropolis, Northwestern Nigeria. It is the largest referral center in the region. The hospital offers free HIV/AIDS services through the President's Emergency Plan for AIDS Relief (PEPFAR), courtesy of the United States of America (USA).

Study population

The study population comprised HIV-infected children aged 6 months to 15 years, taking ARV medications for at least 6 months, who

accessed care at the HIV Clinic of Aminu Kano Teaching Hospital (AKTH) between June and August 2010, and whose caregivers provided consent. A list of all children who were on HAART and had a clinic appointment within the study period was generated. From this list, participants were randomly selected using a computer-based random number generator. One hundred and thirty children/caregiver pairs who were eligible were enrolled into the study.

Ethical clearance

Approval for the study was obtained from the Medical Ethics Committee of Aminu Kano Teaching Hospital, Kano, Nigeria, before the commencement of the study.

Data extraction

Personal information was obtained from parents or caregivers at study enrollment. The information obtained included age, gender, duration of treatment and patient's abode. Other information obtained included socio-demographic characteristics of the child and caregiver, such as educational status, occupation, religion, and belief in the effectiveness of ARV drugs.

Caregiver-reported or self-reported adherence was then assessed by an interviewer-administered questionnaire for the week preceding each visit. Structured questions were asked about the drug regimen the child was on, including dosing schedule; number of pills or amount of syrup taken each day; relationship of drug administration and meals; number of doses missed the 7 days prior to the visit; and the reasons for missing doses.

The number of clinic appointments missed during the previous six months was sought and recorded for each patient, along with the method of drug storage. Other information obtained included the relationship of the caregiver to the child; the HIV status of the

caregiver, whether the caregiver was also receiving ARV drugs (if HIV positive); and whether the child was aware of his or her HIV status. Medical case notes were reviewed to collect anthropometric data and WHO clinical stage of HIV disease prior to the initiation of HAART. Clinical, laboratory, and anthropometric parameters were also documented at enrolment. In this study a child was said to be adherent if their caregiver reported that he/she took $\geq 95\%$ of the prescribed doses for one week prior to the interview

Data analysis

Data were analyzed using SPSS version 18 statistical packages. Descriptive statistics were used to summarize the socio-demographic and clinical characteristics as well as adherence rate of the participants. Pearson χ^2 test was used for bivariate analysis. Variables associated with ARV non-adherence in the bivariate analyses were included by a stepwise selection procedure in a multivariable logistic regression model with adherence level as the dependent variable. In the bivariate analysis, only variables that showed significant association with a p-value of <0.05 were included in the final model.

Results

Socio-demographic and economic characteristics of children and their caregivers

A total of 130 children respondents were contacted and 122 caregivers consented to participate, giving a response rate of 94%. The median age of the study children was 5.5 years (IQR: 1.3 to 14 years), 78 (64%) of whom were male. Ninety three (76.2%) of the study subjects were on HAART for a duration of 12 months or more and 29 (23.8%) were on HAART for a duration of six to 11 months. The median age of the caregivers was 35.2 years (range: 20 to 55 years). One-hundred-and-eleven (91%) were female (Table 1).

Table 1 Caregiver-related Factors Affecting HAART Adherence

Variable	Response	Adherent (N=80)	Non-adherent (N=42)	Odds ratio (CI)	p-value
Age of caregiver	>25 years	44	11	3.44 (1.52 -7.79)	0.003*
	≤ 25 years	36	31		
Gender of caregiver	Female	70	41	0.17 (0.02-1.38)	0.06
	Male	10	1		
Marital status	Married	43	8	0.20 (0.08 - 0.49)	0.000*
	Not married	37	34		
Socio-economic class	Classes II and III	3	2	0.78 (0.10-7.0)	0.78
	Classes IV and V	77	40		
Administration of medications	Mother	64	28	2.0 (0.86 – 4.64)	0.91
	Other Caregiver	16	14		
Religion	Muslim	64	31	0.72(0.27-1.83)	0.43
	Christian	16	11		
HIV status	Positive	68	30	0.44(0.17- 1.09)	0.07
	Negative or unknown	12	12		
Disclose to child	Yes	10	7	1.43(0.42-1.45)	0.54
	No	70	35		
Identify medications	Yes	66	30	0.53(0.20-1.40)	0.15
	No	14	12		
Believes ART effective	Yes	78	32	0.08(0.02 - 0.39)	0.002*
	No	2	10		
Drugs related to mealtimes	Yes	63	21	0.26(0.12 -0.61)	0.001*
	No	17	21		
Missed appointment	Yes	10	31	19.72(7.53-68.3)	0.000*
	No	70	11		
Number of pills/syrup	Two tablets	55	27	0.81(0.37- 1.80)	0.61
	>Two tablets	25	15		
Child has side effects	Yes	17	12	1.48(0.58-3.79)	0.37
	No	63	30		

*=Significance =p <0.05; CI = confidence interval

Relationship of caregivers to study subjects

Eighty-five (85/122) of the caregivers were biological mothers of the children and all (9%) male caregivers were biological fathers. The 26 (21.3%) non-biological parents or guardians comprised 23 maternal aunts and three grandmothers.

HIV status of caregivers and belief in efficacy of ART

Ninety five (77.9%) care-givers were HIV infected, out of which 81 (85.2%) were on HAART. One hundred and five (86.1%) caregivers reported that their children were unaware of their HIV status, while the efficacy of HAART was endorsed by 110 (90.2%) caregivers.

Socio-economic status of caregivers study subjects

Majority (76.2%) of the caregivers had no formal education, whereas 23.8% had at least a primary school education. A total of 88 (72.1%) caregivers were unemployed, 18 (14.8%) were junior public servants, 11 (9%) were laborers, three (2.6%) were artisans, and two (1.5%) were medium-grade public servants. Fifty-one (41.8%) caregivers were married, 48 (39.3%) were widowed, 17 (13.9%) were divorced, and six (5.0%) were single parents.

Clinical characteristics of children on HAART

Ninety-eight of the children (80.3%) had World Health Organization (WHO) clinical stage I disease at enrollment into the study, 10 (8.2%) children were in WHO clinical stage II, and the remaining 14 (11.5%) children had WHO clinical stage IV disease.

Caregivers' reports of adherence

All 122 caregivers were responsible for administering medications to their children or wards. Forty-two (34.4%) caregivers reported that they missed giving more than one dose of medication to their child or ward in the week preceding the study (indicating <95% of medication consumed by each child or ward during that week) while 80 (65.6%) were adherent administering medications.

Caregiver reasons for missing medications

Among caregivers who missed giving medications to their child or ward in the previous week, the most common reasons for missing medications were forgetfulness (59.5%), travel out of town (21.4%), and inter current illness (14.3%)(Figure 1).

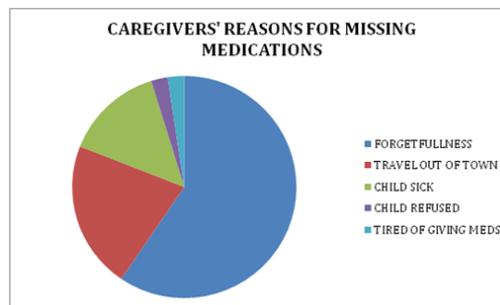


Figure 1 Reasons for Missing Medications by Caregivers.

Child-related factors associated with pediatric adherence to Antiretroviral Therapy

For children aged less than 5 years, 35.6% of their caregivers were non-adherent, while 33.3% of caregivers of children more than 5 years were non-adherent in administering medications. Of the 103 children living with their biological parents, 34% were non-adherent to HAART compared to 37% of children not living with their biological parents ($p=0.89$; $OR=0.88$; $CI: 0.31-2.44$).

Furthermore, 30% of children who were on a first-line HAART regimen were non-adherent to HAART, in contrast to 55% of children who were on a second-line HAART regimen ($p=0.03$, $OR=2.79$, $CI: 1.05-7.43$). The relationship between treatment duration and adherence to HAART was also explored. Seventeen (55%) children whose duration of treatment was less than 12 months at the time of the study were non-adherent to HAART, while 25 (28%) of their peers who had been on HAART for more than 12 months recorded non-adherence ($p=0.006$; $OR=3.21$; $CI: 1.37-7.45$). In addition, 87/122 (71.3%) children had complete virological suppression, that is, undetectable viral load in the serum, while thirty-five (28.7%) had viral load of 400 copies or more /ml, that is, they did not achieved virological suppression despite HAART. Furthermore, 53 (64.6%) of the children attending school were adherent to medication, while 27 (67.5%) of the children not attending school were adherent to their medication ($p=0.75$; $OR=0.87$; $CI: 0.39-1.96$). In addition, 69 (65.7%) children who had WHO clinical stages I and II disease at enrolment in the study were adherent to HAART compared to 11 (64.7%) children having WHO clinical stages III and IV disease ($p=0.93$, $OR=0.95$, $CI: 0.32-2.79$) (Table 2).

Table 2 Child-related Factors Affecting HAART Adherence

Variable	Response	Adherent (N=80)	Non-adherent (N=42)	Odds ratio (CI)	p-value
Age group	<5 yrs	38	21	1.1 (0.52 - 2.33)	0.79
	>5 yrs	42	21		
Gender of child	Female	30	14	1.20 (0.54 - 2.63)	0.64
	Male	50	28		
Duration of treatment	<12 months	14	17	3.21 (1.37 - 7.45)	0.006*
	>12 months	66	25		
Attending school	Yes	53	21	0.87 (0.39 - 1.96)	0.75
	No	27	13		
Resident with parents	Yes	68	35	0.88 (0.31 - 2.44)	0.89
	No	12	7		
WHO clinical stage	I - II	69	36	0.96 (0.32 - 2.79)	0.98
	III - IV	11	6		
HAART regimen	First line	71	31	2.79 (1.05 - 7.43)	0.03*
	Second line	9	11		

*=Significance = p-value <0.05; CI = confidence interval

Caregiver-related factors associated with pediatric adherence to Antiretroviral Therapy (Table 1)

Using care-giver reported adherence, 40.3% of children whose care-givers were less than 25 years of age were non-adherent to HAART compared to 20% of children whose care-givers were older than 25 years of age. This difference in proportion was statistically significant. ($p=0.003$, OR = 3.44, CI: 1.52 – 7.79).

Similarly, 15.6% of children whose care-givers were married were non-adherent to HAART; in contrast to a corresponding 47.2% of children whose care-givers were single parents. This difference was statistically significant (p -value=0.001, OR=0.20, CI: 0.08 – 0.49). 30.1% of Children whose care-givers were HIV infected were non-adherent to HAART in contrast to 50% of children whose care-givers' HIV status were either unknown or negative and this was not statistically significant (p -value=0.07, OR= 0.44, CI: 0.17 – 1.09). However, belief in the efficacy of ART was associated with high adherence (p -value=0.02, OR= 0.08, CI: 0.02 – 0.39).

Table 3 Independent Factors Affecting HAART Adherence *= Significant ; P< 0.05 ; CI = Confidence Interval

Variables	P-value	Non-Adherent	N = 42	Adherent	N = 80	Crude OR (CI)	P-value	Adjusted OR	P-value
Duration of treatment	<12 months	17		14		3.20(1.37-7.45)	0.006	3.25 (0.81 - 13.10)	0.09
	>12 months	25		66					
HAART Regimen	First line	31		71		2.79(1.05-7.43)	0.03	8.61(1.70-44.10)	0.01*
	Second line	11		9					
Age of care giver	≤12 months	31		36		3.44(1.52-7.79)	0.003	4.81(1.37-16.82)	0.012*
	<12 months	11		44					
Married	Yes	8		43		0.20(0.08-0.49)	0.000	0.38(0.10-1.37)	0.04
	No	34		37					
Belief in ART Effective	Yes	32		78		0.08(0.02-0.39)	0.001	0.38(0.38-3.51)	0.08
	No	10		2					
Drugs related to meals time	Yes	21		63		0.26(0.12-0.61)	0.001	0.29(0.08-1.18)	0.08
	No	21		17					
Missed Appointments	Yes	31		10		19.72(7.59-51.26)	0.000	31.18(7.53-24.6)	0.00*
	No	11		70					

*= Significant ; P< 0.05 ; CI = Confidence Interval.

Discussion

Our findings suggest that approximately one-third (34.4%) of children were reported to have missed one or more doses during the previous week. This level of non-adherence is relatively low compared to findings in some studies in children.^{5,12} One study reported 42% non-adherence based on a retrospective review of pharmacy records during the first 180 days of HAART.⁵ Similarly, another study reported that 43% of caregivers had missed one or more doses in the week preceding the interview-based study.¹²

Possible explanations for the greater adherence in the present study may be ascribed to the higher use of the more patient-friendly, twice-daily dosing schedule (e.g. Zidovudine/Lamivudine/Nevirapine combinations). It may also be partly attributed to the hospital's policy of giving comprehensive pre-treatment adherence counselling sessions in which the need for strict adherence to ART instructions are emphasised. The majority of caregivers (90.2%) in the present study believed in the efficacy of HAART. This is likely to lead to a favourable attitude toward administration of ARV to their children and wards. In the present study, reasons for non-adherence among those who had missed at least one dose of their medications included forgetfulness (59.5%), travelling away from home (21.4%), and presence of other disease conditions (14.3%). These findings are similar to other studies from Malawi,¹³ but differ remarkably from the observations in an earlier study from our study site (AKTH). In this

Only 25% of Children whose care-givers timed their administration of medication to meal times were non-adherent to HAART. When this was compared with the 55.3% of children whose caregivers' administration of medications was not related to mealtimes, the difference was statistically significant ($p=0.001$, OR= 0.26, CI: 0.12 – 0.61). Similarly, 75.6% of children whose care-giver reported missing at least one clinic appointment in the preceding 6 months were non-adherent to HAART compared with 13.6% of those who did not miss clinic appointments. This difference was again statistically significant (p -value=0.0001, OR=19.72, CI: 7.53 – 68.30).

Independent factors affecting adherence to HAART:

After controlling for the confounding effects of other variables, three variables were found to be independently associated with adherence to HAART in children. They include regimen type, age of care-giver and missing clinic appointments (Table3).

earlier report,⁸ the most common reasons for non-adherence were cost of transportation and cost of medications. At the time of that earlier report, HIV care was not entirely free, and patients had to bear some costs of laboratory tests and medications for opportunistic infections. With funding from the PEPFAR program, comprehensive HIV care is now being provided for free, meaning that patients no longer face the key adherence barrier of medication costs. This is a positive step that has the potential of enhancing access to HAART for poor adults and children living with HIV. Free treatment services may also partly explain why the socio-economic classification does not appear to predict adherence because all patients, irrespective of their socio-economic group, enjoyed the same service at the PEPFAR-supported HIV clinic.

This was similar to the findings of a study on adherence among Ugandan children.⁷ In the current study, multivariate analysis indicated that three variables were independently predictive of adherence to HAART, including the type of regimen (either a first-line or second-line regimen). The complexity of the therapeutic regimen, as well as multiple medications and frequent dosing, adversely affect adherence.¹⁴ Similarly, data from a large cohort of HIV-infected patients (1322 persons living with HIV/AIDS) who were receiving antiretroviral combination therapies demonstrated that reducing dosing frequency or pill burden significantly increased adherence.¹⁵ It was therefore not surprising that the present study demonstrated poor adherence among patients on a second-line regimen, which

is a more complex regimen with multiple medications having an unpalatable taste. Keeping clinic appointments was found to be a strong independent predictor of adherence. Caregivers who missed clinic appointments may not have medications at home to give their children or wards while others may have traveled. It is important for care providers to not just ask questions about medication adherence but to also inquire about keeping clinic appointments.

This may help identify caregivers that may have potential adherence issues before virologic failure sets in. In addition, this study found that older caregivers were more likely to be adherent than their peers who were younger. This finding is similar to another report where adherence was found to increase with age, except in the most elderly.¹⁶ It is conceivable that older caregivers may have more understanding of the dynamics of disease and health. However, several reports did not find any association between age and adherence.¹⁷ This study also found that a child's age does not have a significant association with adherence level. This is not surprising as all the caregivers in this study were responsible for administering medications to their children despite the low number of adolescents in the cohort.

It is worth noting that marital status of caregivers, belief in ART efficacy and timing of medications were all predictors of adherence in the bivariate analysis but not in the multivariate analysis. Furthermore, religion, disclosure of HIV status to the child, dosing interval and school attendance did not appear to predict adherence in the present study. In addition, the caregiver's relationship to the child or ward did not appear to predict adherence. This may be due to the high percentage of biological caregivers in the present study. This finding is similar to those in earlier reports from South Africa.¹⁸

Limitations

There were a number of methodological limitations in this study. There is no gold standard assessment of adherence. In this study, adherence was measured using self-reports from caregivers, and self-reports tend to overestimate the prevalence of adherence. Another limitation is that adherence classification cut off points may not be perfect in different settings to compare and contrast the findings.

Conclusions and recommendation

Adherence level among HIV-infected children in Kano, Nigeria, was similar to several reports from other parts of Africa. The main reasons for non-adherence among children in this study include caregiver forgetfulness, travelling away from home, and children inter current illness. Keeping clinic appointments was found to be strong predictors of adherence. Therefore, care providers should emphasise keeping clinic appointments by caregivers, and target those who miss clinic appointments for intensive adherence counselling to avert treatment failure.

Acknowledgements

Our sincere gratitude to staff and patients of the Special treatment clinic, Aminu Kano Teaching Hospital for their cooperation during the study.

Conflicts of interest

None.

References

- UNAIDS 2013 Report on the global HIV/AIDS epidemic, Geneva, Switzerland.
- Eley B, Nuttall J, Davies MA, et al. Initial experience of a public sector antiretroviral treatment programme for HIV-infected children and their infected parents. *S Afr Med J*. 2004;94(8):643–646.
- UNICEF: A call to action: Children the missing faces of AIDS. UNAIDS; 2005.
- Paterson DL, et al. Adherence with protease inhibitor therapy for human immunodeficiency virus infection [abstract I-172]. In: Program and abstracts of the 38th Inter-science Conference on Antimicrobial Agents and Chemotherapy (San Diego). Washington, DC: American Society for Microbiology 419. 1998.
- Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353(9):487–497.
- Watson DC, Farley JJ. Efficacy of and adherence to highly active antiretroviral therapy in children infected with human immunodeficiency virus type 1. *Pediatr Infect Dis J*. 1999;18(8):682–689.
- Nabukeera-Barungi N, Kalyesubula I, Kekitiinwa A, et al. Adherence to antiretroviral therapy in children attending Mulago Hospital, Kampala. *Ann Trop Paediatr*. 2007;27(2):123–131.
- Byakika-Tusiime J, Oyugi JH, Tumwikirize WA, et al. Adherence to HIV antiretroviral therapy in HIV+ Ugandan patients purchasing therapy. *Int J STD AIDS*. 2005;16(1):38–41.
- Mukhtar-Yola M, Adeleke SI, Gwarzo D, et al. Preliminary investigation of adherence to antiretroviral therapy among children in Aminu Kano Teaching Hospital, Nigeria. *African Journal of AIDS Research*. 2006;5(2):141–144.
- Orrell C. Antiretroviral adherence in a resource-poor setting Current HIV/AIDS Reports. 2005;2(4):171–176.
- Sethi AK, Celentano DD, Gange SJ, et al. Association between adherence to antiretroviral therapy and human immunodeficiency virus drug resistance. *Clin Infect Dis*. 2003;37(8):1112–1118.
- Nachege JB, Hislop M, Dowdy DW, et al. Adherence to highly active antiretroviral therapy assessed by pharmacy claims predicts survival in HIV-infected South African adults. *J Acquir Immune Defic Syndr*. 2006;43(1):78–84.
- Reddington C, Cohen J, Baldillo A, et al. Adherence to medication regimens among children with human immunodeficiency virus infection. *Pediatr Infect Dis J*. 2000;19(12):1148–1153.
- Weigel R, Makwiza I, Nyirenda J, et al. Supporting children to adhere to anti-retroviral therapy in urban Malawi: multi method insights. *BMC Pediatr*. 2009;9:45.
- Davies MA, Boule A, Fakir T, et al. Adherence to antiretroviral therapy in young children in Cape Town, South Africa, measured by medication return and caregiver self-report: a prospective cohort study. *BMC Pediatr*. 2008;8:34.
- Klosinski LE, Brooks RN. Predictors of non-adherence to HIV combination therapies [abstract 32375]. In: Program and abstracts of the 12th World AIDS Conference. Geneva: Marathon Multimedia. 1998.
- Mehta S, Moore RD, Graham NM. Potential factors affecting adherence with HIV therapy. *AIDS*. 1997;11(14):1665–1670.
- Singh N, Squier C, Sivek C, et al. Determinants of compliance with antiretroviral therapy in patients with human immunodeficiency virus: prospective assessment with implications for enhancing compliance. *AIDS Care*. 1996;8(3):261–269.