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The Use of Cell Phone Support for Non-adherent HIV-Infected Youth and Young Adults: An Initial Randomized and Controlled Intervention Trial

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Abstract

This randomized behavioral trial examined whether youth living with HIV (YLH) receiving cell-phone support with study funded phone plans, demonstrated improved adherence and viral control during the 24 week intervention and 24 weeks post-intervention compared to controls. Monday through Friday phone calls confirmed medications were taken, provided problem-solving support, and referred to services to address adherence barriers. Of 37 participants (ages 15–24), 62 % were male and 70 % were African American. Self-reported adherence was significantly higher in the intervention group compared to the control at 24 and 48 weeks for the past month ($P = 0.007$) and log 10 HIV VL was significantly lower at both 24 weeks (2.82 versus 4.52 $P = 0.002$) and 48 weeks (3.23 versus 4.23 $P = 0.043$). Adherence and viral load showed medium to large effect sizes across the 48 week study. This is the first study to demonstrate sustained clinically significant reductions in HIV VL using youth friendly technology.

Keywords

Adherence; Adolescent; HIV; Cell phone; Support

Introduction

Adherence to antiretroviral treatment (ART) is critical not only to promote the health of the infected individual but also to prevent the spread of HIV, as transmission is less likely when HIV viral load (VL) is suppressed [1]. The high rates of non-adherence in adolescents and young adults with HIV [2] present a critical challenge to health care providers and to efforts highlighted in the National HIV/AIDS Strategy for the United States [3].

Most cross-sectional studies of ART adherence in youth have focused on social-cognitive predictors such as low self-efficacy for taking medications, depression, coping style, and social support [4–6]. Yet, when researchers ask youth why they miss medications, the three most common barriers endorsed by youth living with HIV (YLH) are forgetting, not having medication with them, or changes in their daily routine. A recent multi-site study reported that for 73 % of 498 non-adherent youth forgetting was the primary reason for non-adherence [7]. Thus, youth friendly interventions aimed at addressing these commonly cited barriers to adherence are needed.

There is limited literature on adherence interventions targeting HIV-infected youth and young adults and literature on adherence with other chronic health conditions indicates only minimal improvements with educational and behavioral interventions [2]. Gaur et al. (2010) conducted a pilot study of twenty youth non-adherent to ARVs who were provided a 12 week intervention of tapered directly observed therapy (DOT). While his study found reduced VL at the end of the intervention period, adherence waned 12 weeks post intervention. Greater baseline depressive symptoms, global beliefs about medicine, and viewing HIV as a potential threat predicted better DOT adherence [8, 9]. A randomized trial of four motivational interview sessions over 10 weeks for youth that included at least one of the following; non-adherence, substance abuse or unsafe sex, resulted in significantly lower VLs at 6 months but not at 9 months [10]. Furthermore, retention of youth in face-to-face multi-session interventions has been a barrier in several trials [10, 11].

Cell phones are a convenient and culturally relevant mechanism for intervention delivery, as younger adults and socioeconomically disadvantaged populations have been identified as having high rates of cell phone use [12]. Text message reminders (via mobile phones) and cell phone adherence interventions have shown some success in HIV-infected adults [13]. A pilot intervention using personalized, interactive, daily text messages in twenty-five 14-to-29 year olds with adherence under 90 % demonstrated significant improvements in self-reported adherence at the conclusion of their 24 week intervention but lacked the power to demonstrate improved VL [14]. A multi-site network trial for African adults found that weekly telephone support calls by trained nurses improved adherence; although adherence prior to the study was extremely high in both the control and adherence groups [15]. Two clinical trials conducted in Kenya with adults with HIV found that text messaging improved self-reported adherence [16, 17].

YLH are a highly stressed and marginalized population. One concern has been that consistent cell-phone support would be difficult in a population where cell phone access is variable (e.g., cell phone numbers are disconnected, prepaid phone cards expire). Another concern is that youth will not answer the phone for fear of disclosure or because they wish to avoid discussing HIV-related issues. In order to test feasibility, a small pilot study was

undertaken with eight youth non-adherent to ART medications who received a tapered schedule of daily cell phone reminder calls for 12 weeks. This study demonstrated intervention acceptance, and improved adherence during the 12 week intervention but waning adherence in the subsequent 12 weeks, suggesting reminders alone were inadequate [18]. Thus, while intervention delivery format was feasible, YLH may benefit from ongoing supportive communication with a provider [19, 20].

Studies have shown that social support is a strong predictor of good adherence to ARV medication [21–23] and retention to HIV care is predicted by clients' perceptions of providers as engaging, validating and partnering with clients in their treatment [24]. While the total construct of social support has predicted adherence in these studies, tangible or instrumental support (such as practical assistance) and informational support, along with problem focused coping were specifically found to be predictive of adherence in a study of adults with HIV [23]. Given the literature on reasons for non-adherence among HIV-infected adolescents, namely forgetting, not having medications with them and changes in daily routines we created an intervention delivered through brief cell phone calls to encourage consistent medication adherence. The content of calls (intervention content) validated the importance of daily adherence, prompted interactive problem-solving, and provided both informational support and instrumental support (in the form of relevant referrals) to any barriers to adherence as they emerged. In sum, this intervention used cell phones to provide instrumental and informational support and promote immediate problem focused coping in non-adherent adolescents with HIV to increase their consistent use of HIV medication.

This study was undertaken in order to determine if daily cell phone conversations with health care providers around self-care and taking HIV medications would lead to successful self-administration of ART in HIV infected adolescents with poor medication adherence. This longitudinal, experimental pilot study was designed to test a cell-phone adherence support intervention in a randomized trial at five sites within the National Institute of Health (NIH)-funded Adolescent Trials Network for HIV/AIDS Interventions (ATN). We hypothesized that YLH with a history of ART non-adherence randomly assigned to 24 weeks of cell phone support would show greater improvements in adherence and greater reductions in VL from baseline to 48 week follow-up than youth randomly assigned to standard care alone.

Methods

A cell-phone adherence support intervention guided by theories of social support was developed by coauthors. The nature of the cell phone interactions was designed to provide participating YLH with a consistent, accessible and supportive relationship in which problem solving solutions to adherence barriers along with tangible assistance and informational advice was offered. "Adherence facilitators" (AF) responsible for making daily cell phone contact with participants served as medication monitors reminding youth to take medications, but also allowed patients to (1) express their immediate needs and difficulties relevant to medication adherence; (2) engage in problem-solving with the facilitator; and (3) receive assistance in accessing clinic and community resources through timely referrals.

Study Participants

During 2010 a total of 37 evaluable participants were enrolled at baseline in this pilot study, with 19 YLH randomized to the intervention group and 18 to the control group. Inclusion criteria included documentation of HIV-positive status, aged between 15 and 24 years, and a history of non-adherence to one or more components of ART. A history of non-adherence

was defined by meeting one of the following criteria: (a) currently prescribed ART and reporting to care provider adherence <90 % and VL greater than 1,000 copies/ml (b) discontinued ART in the past while documented <90 % adherent to last regimen, or (c) agreed to start ART but never initiated. Subjects also had to understand and speak English and provide informed consent/assent. Exclusion criteria included evidence of cognitive impairment or other mental/substance abuse condition that limited ability to complete the intervention or assessments. Youth were not allowed to be participating in another behavioral intervention trial at the same time as the study.

Study Settings

YLH were recruited from five ATN sites located in Los Angeles, Washington DC, New Orleans, Ft. Lauderdale and San Francisco. All ATN sites were selected based on their programmatic access to comprehensive services including physicians, nurses, case manager/social workers, mental health providers and other staff experienced with YLH. YLH in the control arm received the individual sites usual care (which was not measured).

Procedures

The protocol was approved by each site's Institutional Review Board and a certificate of confidentiality was obtained from the NIH. On determination of eligibility, written informed consent was obtained from youth 18 and over while minors required parental permission with youth assent. Perinatally infected YLH were intentionally limited to half the recruits to ensure this research included adequate representation of youth behaviorally infected, the most prevalent population of YLH. Eligible participants were randomized within sites to either the intervention or control group in equal proportions using permuted block randomization.

Adherence Facilitator (AF) Selection, Training and Supervision—The five ATN sites were instructed to attempt to select AF familiar to subjects or provide an opportunity prior to intervention initiation to meet the participant in person in order to build rapport. AF were knowledgeable about HIV including treatment, skilled in interpersonal communication including the ability to maintain professional boundaries, and understood their local care systems in order to be able to refer to appropriate resources. Primary AF were expected to make the majority of calls and were not permitted to be licensed clinicians such as nurses, psychologists or master's level social workers. Two sites used research assistants, one site used a case manager and two sites initially used case managers that were replaced by research assistants. Because there is a considerable need for affordable adherence interventions that are easily replicable in community settings, the role of the AF was designed to be filled by less expensive staff such as case managers or non-licensed research staff. Sites were allowed one or two backup AFs that also had to be trained as above but could be nurses, master level social workers or licensed therapists.

All AF participated in a 2-h phone training covering the purpose of the intervention, conversational phone script, and procedures for maintaining contact and referral logs. To ensure consistency of the intervention, all calls were recorded and forwarded to a quality assurance manager (QAM). The QAM initially reviewed a randomly selected 20 % of calls from each site for two months and once sites demonstrated greater than 90 % adherence to protocol requirements, only 10 % of calls were reviewed for the remainder of the intervention. When the QAM determined that urgent feedback to AFs was required, she called and/or emailed the AF directly. The QAM also provided group feedback on monthly conference calls with the AFs and protocol team where ongoing concerns could be addressed by the protocol team.

Cell-Phone AF Intervention Description—Subjects randomized to the intervention met with the AF in person to establish rapport at the entry or baseline visit prior to the start of intervention phone calls. Together, they chose a start date and regular call times. Calls took place Monday through Friday (excluding holidays) for 24 weeks (approximately 120 days) either be once or twice a day corresponding to the daily frequency of the youth's ART regimen. AFs arranged calls to occur at a time after youth were scheduled to take their ART (as a check-in to see if medications had been taken correctly) but also at a time convenient for both the youth and the AF. Participants were allowed to change their call times during the study intervention period with AF agreement.

Phone Conversation Content—AF's followed a script outline that included medication review, problem solving support and scheduling relevant referrals. Medication review included the AF confirming that youth had taken medication or waiting for him/her to take medication if on hand. If medication was not taken or not on hand, the AF reviewed why the youth did not take their medication; discussed any new or ongoing problems; provided support around problem-solving to address these issues; and reinforced prioritizing medications. The final component of the phone conversation was scheduling relevant referrals (case managers, mental health providers, medical providers or substance abuse counselors); reminding participants about their scheduled appointments; and assessing the utilization of health services, including visits to the HIV clinic, other outpatient clinic visits, emergency room visits, inpatient stays and social services (e.g., housing, food banks, etc.) since the last call.

It was anticipated that the majority of calls would be less than 5 min and a sample script was provided to help organize the calls. Subjects were allowed to delay calls by contacting the AF via text or verbally prior to or at the time of the call. If the participant missed the call the AF would leave a message and call back in 30 min. If the follow-up call was not answered, the participant was deemed non-adherent to the intervention for that call.

Cell-Phone Plans, Usage and Participant Discontinuation Criteria—If participants chose to use their own cell phones and plans, \$45 was sent directly to their plan providers each month during the 6 month intervention. Subjects could also elect to have a phone and plan provided by the study site. Due to institutional requirements, each site had slight modifications for their cell phone plan. In general, youth had a minimum of 400 anytime minutes, free nights and weekends and unlimited texting. Most plans blocked outgoing calls once their minutes reached their cap. Most plans also prevented participants from making toll calls, downloading apps, calling information or any other procedures that would add additional cost and no sites reported problems with excessive costs. While internet provision was not the standard at the time of the study and was not included in the study provided plan, some current plans offer unlimited calls, texts and internet for the same cost (about \$45/month).

Youth non-adherent to more than 20 % of calls over one month were given a verbal warning and those who used their own cell phones and plans were required to switch to a study plan (to ensure that participants did not miss calls due to lack of phone access). Subjects were also notified that abuse of their study provided phone plans (e.g. repeated and excessive use of minutes, internet 411 calls, data usage or repeated lost or damaged phones) might result in intervention discontinuation.

Participants who missed more than 20 % of calls a month in two consecutive months, who went off medication for 14 or more consecutive days or who missed calls for 10 consecutive business days were discontinued from the study intervention. Cell phone plans were terminated but youth remained on study to complete all follow-up assessments. The 80 %

adherence requirement to phone calls was based on the protocol team perception that the provision of the cell phone services was a powerful incentive to maintaining regular contact and this contact would drive the benefits of the intervention.

Measures

Behavioral measures were collected via audio computer-assisted self-interview (ACASI) at baseline, 6, 12, 24, 36 and 48 weeks however the focus of this paper is on the adherence and viral load measures. HIV VL was abstracted from the medical record if less than 2 weeks prior to 6 and 12 week visits or within 4 weeks of subsequent visits or else collected at the time of the study visit. Self-reported adherence was measured in two ways: The Visual Analogue Scale (VAS) includes six items rated from 0 to 100 % in the last month and last 3 months. Prior reliability in an ATN protocol using Cronbach's alpha was 0.90, and validity was assessed by correlation with HIV VL ($r = -0.54$, $P < 0.01$). Additionally, continuous responses were categorized into a dichotomous variable based on clinical requirements for effective treatment defined as adherence <90 or 90 %.

Statistical Analysis

All statistical tests were performed using SASTM 9.2 software [SAS 9.2, 2009, SAS Institute, Cary, NC], and StatXACT v.10 by Cytel Software Corporation. Means and proportions were used to describe the study population. Chi square statistics or Fisher Exact test for categorical variables and ANOVA or Kruskal–Wallis test for continuous variables were used as needed to compare the youth in the intervention versus those in the control groups at week 24 (6 months) and week 48 (12 month) visits. Proportions, means and appropriate non-parametric statistics were used to explore differences in therapeutic success between intervention group participants who were prematurely discontinued versus those who completed the study. Differences between the intervention participants, after excluding those who were prematurely discontinued were also explored, as compared to the control group. Repeated measure analysis was used to examine the trends of preliminary therapeutic success over 6 and 12 months, as measured by lowered HIV VL, and self-reported adherence among intervention versus control group participants. Repeated measures analysis included Generalized Estimating Equation (GEE) models for dichotomous outcomes, and mixed models for continuous outcomes [25]. Effect sizes were also calculated using Cohen's d approach. All statistical tests were based on two-tailed alternatives, and $P < 0.05$ was considered significant [26].

Results

The mean age was 20.43 (STD = 2.57) years (range 15–24 years) (see Table 1). The majority of the subjects were male (62.16 %) and African-American (70.27 %). Fifty four percent acquired HIV sexually and 46 % perinatally.

Cell Phone Utilization

Fifty-eight percent of intervention subjects chose to use their own cell phone initially but by the end of the study only 27 % continued to use their own cell phone. Seven of the 19 youth assigned to the intervention were discontinued from receiving calls, five due to missing >20 % calls in consecutive months and 2 for missing calls for 10 consecutive days (one due to hospitalization and one incarceration). Figure 1 illustrates the timing for subjects coming off intervention or off study. Subjects who completed the intervention had a mean of 98.25 (SD = 9.42) first calls compared to 26.86 (SD = 17.08) first calls for those who were prematurely discontinued ($F = 140.17$, $P < 0.001$; using Mixed Models).

Self-Reported Adherence

Table 2 shows the effect of the intervention on adherence, with adherence defined as a dichotomous outcome; <90 versus ≥90 %. Higher proportions of youth in the intervention group reported being adherent versus the control group in all four time periods assessed; “Adherence-past 3-months” (OR = 2.85; 95 % CI 1.02–7.97), “Adherence-past 1-month” (OR = 3.09; 95 % CI 1.20–7.98), “Adherence-past 7-days” (OR = 3.76; 95 % CI 1.15–12.25) and “Adherence-last week-end” (OR = 3.62; 95 % CI 1.26–10.41).

We also looked at adherence as continuous variables (Table 3), and did not initially see significant differences between the mean percent adherence rates for intervention and control group participants, respectively at baseline for “Adherence-past 3-month” [35.74 % (SD = 38.50) and 35.59 % (SD = 42.08)], “Adherence-past 1-month” [31.26 % (SD = 38.17) and 33.75 % (SD = 42.52)], “Adherence-past 7-days” [48.50 % (SD = 41.96) and 46.64 % (SD = 41.51)] and “Adherence-last week-end” [41.23 % (SD = 43.87) and 43.83 % (SD = 43.53)].

Improvements in the mean percent adherence rates for the intervention versus the control group respectively, were then seen at week 24; for “Adherence-past 3-month” [77.20 % (SD = 37.93) and 47.69 % (SD = 42.77)], “Adherence-past 1-month” [77.67 % (SD = 37.52) and 40.67 % (SD = 42.67)], “Adherence-past 7-days” [65.71 % (SD = 41.40) and 35.12 % (SD = 35.56)] and “Adherence-last week-end” [57.78 % (SD = 46.23) and 21.41 % (SD = 36.88)].

Finally, the improvements in the mean percent adherence rates seen at week 24 were sustained throughout week 48 for all adherence measures, including “Adherence-past 3-month” [73.07 % (SD = 38.97) and 25.29 % (SD = 42.98)], “Adherence-past 1-month” [74.07 % (SD = 36.56) and 21.18 % (SD = 39.71)], “Adherence-past 7-days” [75.00 % (SD = 35.30) and 34.82 % (SD = 36.22)] and “Adherence-last week-end” [59.52 % (SD = 39.07) and 19.79 % (SD = 29.32)], respectively for intervention and control group participants.

Overall and taking into consideration all our 3 data points, improvements in percent adherence rates were significantly higher in the intervention versus the control group; and were seen as soon as week 24 and sustained throughout week 48; for “Adherence-past 3-month” (Mixed model estimate = 23.47 (SE = 9.67); $F = 5.89$, $P = 0.020$), “Adherence-past 1-month” (Mixed model estimate = 26.48 (SE = 9.21); $F = 8.26$, $P = 0.007$), “Adherence-past 7-days” (Mixed model estimate = 21.79 (SE = 9.97); $F = 4.78$, $P = 0.036$) and “Adherence-last week-end” (Mixed model estimate = 22.10 (SE = 10.08); $F = 4.81$, $P = 0.035$). (Table 3).

Viral Load

There were no significant differences in mean VL (Log₁₀ HIV VL) or history of non-adherence between the intervention and the control group at baseline. Mean VL was significantly lower in the intervention versus the control group at week 24 (2.82 versus 4.52, respectively), and week 48 (3.23 and 4.23, respectively), with a mixed model estimate of -0.79 (SE = 0.36) and a P value of 0.033 ($F = 4.90$) (Table 4). Participants receiving the intervention had greater changes in VL with a mean VL drop of 1.36 and 0.83 in the intervention group at week 24 and 48 versus 0.32 and 0.37 in the control group at week 24 and 48 (Mixed model estimate = 0.76 (SE = 0.35); $F = 4.73$, P value = 0.037). Using VL measure as a dichotomous variable (<400 versus ≥400 copies/ml), virological suppression below the level of detection (<400 copies per ml) was significantly higher in the intervention group than in the control group (OR = 4.18; 95 % CI 1.04–16.80) over the 48 week follow-up period (Table 4). For participants assigned to the intervention group and using Mixed models, we found that over the 48 weeks follow-up period subjects who completed the

intervention ($N = 12$) had significantly lower Log 10 VL measures ($F = 4.92$, $P = 0.040$) and greater Log 10 VL drop versus ($F = 4.93$, $P = 0.042$).

Effect Sizes

The between group effects sizes suggested improved adherence rates in the intervention versus the control group at weeks 24 and 48 visits. The effects sizes were medium to large for “Adherence-past 3-month” at week 24 (Cohen’s $d = 0.73$) and 48 (Cohen’s $d = 1.19$). Effects size were large for “Adherence-past 1-month” (Cohen’s $d = 0.92$ at week 24; and 1.39 at week 48), “Adherence-past 7-days” (Cohen’s $d = 0.79$ at week 24; and 1.12 at week 48) and “Adherence-last week-end” (Cohen’s $d = 0.87$ at week 24; and 1.15 at week 48) (Table 3). We found large effects size for “Log10 viral load” at both week 24 (Cohen’s $d = 1.28$) and week 48 (Cohen’s $d = 0.80$). Moderate to large effect sizes also suggested that the intervention group had a greater log 10 viral load drop than controls at week 24 (Cohen’s $d = 1.03$) and week 48 (Cohen’s $d = 0.38$) (Table 4).

Discussion

This small study of a cell-phone AF intervention for ART non-adherent YLH represents the first trial (either pilot or full scale) to demonstrate lasting (24 weeks post intervention) improvements in adherence and virologic control. The intervention had medium to large effect sizes across all time points. Previous adherence interventions for YLH include several pilot studies employing the use of cell phone reminders [17], DOT [8], and personalized text messaging [14]. None of these previous studies had a control group for comparison. The only other randomized intervention study examined the impact of four sessions of motivational interviewing and found a very small (0.41 log10) but significant reduction in HIV VL at 6 months, with waning improvement by 9 months [10].

Given the significant differences in the cost of these interventions there remain unanswered challenges. The first is whether reminders alone are as effective as reminders embedded in a supportive conversational interaction. Text messaging is less expensive, however a recent study boosting adherence to 90 % utilizing daily text messages with youth and young adults ages 14–29 (Dowshen, Kuhns, Johnson, Holoyda, Garofalo 2012) had much higher baseline adherence than the participants in our study (75 versus 36 %, respectively), as well as a lower baseline viral load (2,750 versus 265,000 copies/ml, respectively). These studies represent very different populations but the question of reminders versus support remains valid. Additionally, we hypothesized that the provision for the cost of the cell phone in return for a minimum of 80 % response to AF calls was a key to our intervention success. Because we did not have a comparison group that received the intervention via their own cell phone that they were paying for, this hypothesis could not be tested in the current study.

One final consideration is whether additional training for the AF, perhaps utilizing motivational interviewing or cognitive behavioral strategies might have improved the outcomes even further, both during and after the intervention. In future analyses of this data set, we will be able to look at our intervention’s impact on mediators based on the theoretical content of conversations including increases in self-efficacy, perceived social support, use problem-focused coping strategies, and decreases in perceived stress. Effects on additional outcomes including substance misuse, depression, and service utilization will be examined as well as characteristics of YLH who responded to our intervention. There are limitations to this study. The small number of participants precluded meaningful individual analyses for perinatally and behaviorally infected groups. However, it is noteworthy that self-reported adherence and VL improved in both subsets. Future research with a larger sample will enable us to determine the mediators responsible for the intervention effect on adherence. Another limitation is that we did not use an independent direct assessment of

adherence like pill counts or medication event monitoring devices to confirm self-reported adherence. Other limitations include lack of data on previous regimens, length of time in treatment and past viral resistance which could be addressed in a larger study. Lastly, it must be mentioned that cell phone technology and services included in plans are continuously changing. While our study attempted to control costs through limiting call minutes and excluding internet, these services are now almost universally included in plans at comparable cost to the study intervention plans. Future plans might easily include video chatting or other more youth friendly and technology savvy opportunities. That said, it is our belief that the provision of the cell-phone plan was a powerful incentive motivating sustained contact and that the nature of the personal contact was key in improving youth adherence.

Conclusions

This pilot study provides clear evidence that finding effective interventions for youth non-adherent to anti-retroviral HIV medication is achievable. Perhaps the most concerning data of this study demonstrated that adherence actually declined by 48 weeks in control participants and none had a VL less than 50 copies/ml (the true gold standard) despite receiving care at centers chosen based on their ability to provide comprehensive, interdisciplinary and youth specific care. This study and others point to the need for specific interventions that address the unique barriers to adherence of each struggling individual and that utilizing technology may be particularly attractive to youth. There is an unmistakable need for larger scale studies evaluating which patients might benefit sufficiently from reminders, versus those who would benefit from interpersonal contact and support. Studies should evaluate whether incorporating motivational interviewing or cognitive based counseling interventions improve adherence, whether incentives like free cell phone service are cost effective and lastly, which patients require an intervention lasting longer than 24 weeks. Based on the high cost of antiretroviral medications and the benefits to treatment as prevention [3], answers to these questions are imperative.

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Fig. 1.
Consort diagram

Table 1

Demographic and baseline characteristics by study group

	Overall (N = 37)	Intervention (N = 19)	Control (N = 18)	Statistic	P value
Age at baseline (years), mean (SD)	20.43 (2.57)	19.84 (2.52)	21.06 (2.53)	(2.22)	0.136
Gender, n (%)					
Male	23 (62.16)	11 (57.89)	12 (66.67)	(0.33)	0.737
Female	14 (37.84)	8 (42.11)	6 (33.33)		
Race/ethnicity, n (%)					
Non-Hispanic Black/African American	26 (70.27)	13 (68.42)	13 (72.22)	(1.11)	0.761
Hispanic	7 (18.92)	3 (15.79)	4 (22.22)		
Non-Hispanic white/other	4 (10.81)	3 (15.79)	1 (5.56)		
Most likely mode of transmission, n (%)					
Perinatal transmission	17 (45.95)	12 (63.16)	5 (27.78)	(5.03)	0.0932
Heterosexual contact	5 (13.51)	1 (5.26)	4 (22.22)		
Male-to-male sexual contact	15 (40.54)	6 (31.58)	9 (50.00)		
Log ₁₀ viral load, mean (SD)	4.54 (1.00)	4.39 (0.90)	4.71 (1.10)	(0.41)	0.523
<i>History of non-adherence</i>					
Currently prescribed HAART and reports to care provider less than 90 % adherence in previous month and has viral load greater than 1,000 copies/ml when last evaluated (within the last 4 weeks), n (%)					
Yes	14 (37.84)	9 (47.37)	5 (27.78)	(1.47)	0.313
No	23 (62.16)	10 (52.63)	13 (72.22)		
Discontinued HAART in the past while documented to be less than 90 % adherent during the most recent antiretroviral treatment, n (%)					
Yes	22 (95.65)	10 (100.0)	12 (92.31)	(0.75)	1.000
No	1 (4.35)	0 (0.00)	1 (7.69)		
Agreed to initiate antiretroviral treatment in the past, but never initiated, n (%)					
Yes	1 (100.0)	0 (0.00)	1 (100.0)	–	
No	0 (0.00)	0 (0.00)	0 (0.00)		

For continuous variables, the mean, standard deviation, median and range (min, max) are provided; P value is from non-parametric (Kruskal–Wallis) test

For categorical variables, the count and % are provided; P value is from Fisher's or Fisher–Freeman–Halton exact tests

Statistic statistical test value, SD standard deviation, N or n frequency

Table 2

Trends of preliminary therapeutic success at 6 and 12 months, measured by binary self-reported adherence between participants enrolled in intervention and control groups

Cutoff: 90 %	Baseline visit		Week 24 visit		Week 48 visit		Odds ratio (95 % CI)	(Statistic) <i>P</i> value ^a
	Intervention (N = 19)	Control (N = 18)	Intervention (N = 15)	Control (N = 16)	Intervention (N = 14)	Control (N = 17)		
Adherence-past 3-months								
Yes (90 %)	3 (15.79)	3 (17.65)	9 (60.00)	5 (31.25)	8 (57.14)	2 (11.76)	2.85 (1.02–7.97)	(1.99) 0.046 [*]
No (<90 %)	16 (84.21)	14 (82.35)	6 (40.00)	11 (68.75)	6 (42.86)	15 (88.24)		
(Statistic) <i>P</i> value ^b	(0.11)	1.000	(2.50)	0.157	(7.02)	0.018 [*]		
Adherence-past 1-month								
Yes (90 %)	3 (15.79)	3 (18.75)	9 (60.00)	4 (26.67)	8 (57.14)	2 (11.76)	3.09 (1.20–7.98)	(2.34) 0.019 [*]
No (<90 %)	16 (84.21)	13 (81.25)	6 (40.00)	11 (73.33)	6 (42.86)	15 (88.24)		
(Statistic) <i>P</i> value ^b	(0.14)	1.000	(3.28)	0.139	(7.02)	0.018 [*]		
Adherence-week (past 7-days)								
Yes (90 %)	4 (21.05)	3 (17.65)	7 (46.67)	2 (12.50)	6 (42.86)	1 (6.25)	3.76 (1.15–12.25)	(2.20) 0.028 [*]
No (<90 %)	15 (78.95)	14 (82.35)	8 (53.33)	14 (87.50)	8 (57.14)	15 (93.75)		
(Statistic) <i>P</i> value ^b	(0.13)	1.000	(4.22)	0.054	(5.37)	0.031 [*]		
Adherence-last week end								
Yes (90 %)	5 (26.32)	4 (22.22)	7 (46.67)	2 (12.50)	4 (28.57)	0 (0.00)	3.62 (1.26–10.41)	(2.39) 0.017 [*]
No (<90 %)	14 (73.68)	14 (77.78)	8 (53.33)	14 (87.50)	10 (71.43)	16 (100.0)		
(Statistic) <i>P</i> value ^b	(0.13)	1.000	(4.22)	0.054	(4.93)	0.036 [*]		

Statistic statistical test (Z) value, N or n frequency

^{*} P value < 0.05

^a P value is from Generalized Estimating Equations (GEE) models to test the trend of medication adherence over time between two study groups

^b P value is from Fisher's Exact Test to test the proportion of medication adherence between two study groups at a specific study visit

Table 3

Trends of preliminary therapeutic success at 6 and 12 months, measured by continuous self-reported adherence between participants enrolled in intervention and control groups

	Baseline visit		Week 24 visit		Week 48 visit		Estimate (SE)	(Statistic) <i>P</i> value ^a
	Intervention (N = 19)	Control (N = 18)	Intervention (N = 15)	Control (N = 16)	Intervention (N = 14)	Control (N = 17)		
Adherence-past 3-months								
N	19	17	15	16	14	17		
Mean	35.74	35.59	77.20	47.69	73.07	25.29	23.47 (9.67)	(5.89) 0.020*
SD	38.50	42.08	37.93	42.77	38.97	40.98		
(Statistic) <i>P</i> value ^b	(0.07)	0.843	(3.65)	0.056	(8.17)	0.004*		
Effect sizes (Cohen's d)				0.73		1.19		
Adherence-past 1-month								
N	19	16	15	15	14	17		
Mean	31.26	33.75	77.67	40.67	74.07	21.18	26.48 (9.21)	(8.26) 0.007*
SD	38.17	42.52	37.52	42.67	36.56	39.71		
(Statistic) <i>P</i> value ^b	(0.003)	0.958	(4.51)	0.034*	(8.73)	0.003*		
Effect Sizes (Cohen's d)				0.92		1.39		
Adherence-week (past 7-days)								
N	19	17	15	16	14	16		
Mean	48.50	46.64	65.71	35.12	75.00	34.82	21.79 (9.97)	(4.78) 0.036*
SD	41.96	41.51	41.40	35.56	35.30	36.22		
(Statistic) <i>P</i> value ^b	(0.01)	0.909	(5.55)	0.018*	(8.68)	0.003*		
Effect sizes (Cohen's d)				0.79		1.12		
Adherence-last week end								
N	19	18	15	16	14	16		
Mean	41.23	43.83	57.78	21.41	59.52	19.79	22.10 (10.08)	(4.81) 0.035*
SD	43.87	43.53	46.23	36.88	39.07	29.32		
(Statistic) <i>P</i> value ^b	(0.02)	0.884	(5.40)	0.020*	(7.47)	0.006*		
Effect sizes (Cohen's d)				0.87		1.15		

Statistic statistical test (F) value, SD standard deviation, N or n frequency, SE standard error

* P value < 0.05

^a P value is from the mixed effect models to test the trend of medication adherence over time between two study groups

^b P value is from non-parametric (Kruskal–Wallis) test to test the median differences of medication adherence between two study groups at a specific study visit

Table 4

Trends of preliminary therapeutic success at 6 and 12 months, measured by lowered HIV viral load (VL) between participants enrolled in intervention and control groups

	<u>Baseline visit</u>		<u>Week 24 visit</u>		<u>Week 48 visit</u>		Estimate (SE)/ odds ratio (95 % CI)	(Statistic) <i>P</i> value ^a
	Intervention (N = 19)	Control (N = 18)	Intervention (N = 15)	Control (N = 16)	Intervention (N = 14)	Control (N = 17)		
Log 10 HIV VL (copies/ml)								
N	19	18	15	15	14	17		
Mean	4.39	4.71	2.82	4.52	3.23	4.23	−0.79 (0.36)	(4.90) 0.033 [*]
SD	0.90	1.10	1.34	1.32	1.40	1.06		
Median	4.68	4.58	2.49	4.59	2.80	4.52		
(Statistic) <i>P</i> value ^b	(0.41)	0.523	(9.41)	0.002 [*]	(4.10)	0.043 [*]		
Effect sizes (Cohen's d)				1.28		0.80		
Log 10 HIV VL drop (copies/ml) ^c								
N	–	–	15	15	14	17		
Mean	–	–	1.36	0.32	0.83	0.37	0.76 (0.35)	(4.73) 0.037 [*]
SD	–	–	1.22	0.73	1.38	1.04		
Median	–	–	0.87	0.08	0.49	0.21		
(Statistic) <i>P</i> value ^b			(6.94)	0.008 [*]	(0.98)	0.321 [*]		
Effect sizes (Cohen's d)				1.03		0.38		
HIV VL (detectable versus undetectable)								
Detectable	19 (100.0)	18 (100.0)	8 (53.33)	15 (100.0)	12 (85.71)	17 (100.0)	–	
BLD (<50 copies per ml)	0 (0.00)	0 (0.00)	7 (46.67)	0 (0.00)	2 (14.29)	0 (0.00)		
(Statistic) <i>P</i> value ^d	–		(9.38)	0.006 [*]	(2.19)	0.196		
HIV VL (copies/ml)								
400	19 (100.0)	17 (94.44)	7 (46.67)	13 (86.67)	9 (64.29)	16 (94.12)	4.18 (1.04–16.80)	(2.02) 0.043 [*]
<400	0 (0.00)	1 (5.56)	8 (53.33)	2 (13.33)	5 (35.71)	1 (5.88)		
(Statistic) <i>P</i> value ^d	–		(5.24)	0.050	(4.13)	0.067		

Statistic statistical test (Z for GEE Models, and F for mixed models) values, SD standard deviation, N or n frequency, SE standard error

^{*} P value < 0.05

^a P value is from the mixed effect models to test the trend of viral load change over time between two study groups. Missing values were excluded in the P value calculations. Due to 0 cell frequencies in “below level of detection” group for binary viral load, the GEE estimation method from the generalized linear model (GENMOD) was not able to converge to a proper solution for VL detectable versus non-detectable, therefore, the P value was not provided

^b P value is from non-parametric (Kruskal–Wallis) test to test the median differences of viral loads between two study groups at a specific study visit. Missing values were excluded in the P value calculations

^c Log 10 viral load drop is the difference between baseline and week 24 (drop = baseline–week 24), baseline and week 48 (drop = baseline–week 48)

^d P value is from Fisher's exact test to test the proportion of viral load detection status between two study groups at a specific study visit. Missing values were excluded in the P value calculations