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Correlation between Use of Antiretroviral Adherence Devices by HIV-infected Youth and Plasma HIV RNA and Self-reported Adherence

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Abstract

Our objective was to investigate antiretroviral adherence device use by HIV-infected youth and assess associations of device use with viral suppression and self-reported adherence. This cross-sectional, multisite, clinic-based study included data from 1,317 HIV-infected individuals 12-24 years of age that were prescribed antiretroviral therapy. Mean adherence in the past seven days was 86.1% and 50.5% had an undetectable HIV RNA. Pillbox was the most commonly endorsed device. No specific device was independently associated with higher odds of 100% adherence. Paradoxically, having an undetectable HIV RNA was inversely associated with use of adherence devices (OR=0.80; p=0.04); however, among those with <100% adherence, higher adherence was associated with use of one or more adherence devices (coefficient=7.32; p=0.003). Our data suggest that adolescents who experienced virologic failure often used adherence devices which may not have been sufficiently effective in optimizing adherence. Therefore, other tailored adherence-enhancing methods need to be considered to maximize virologic suppression and decrease drug resistance and HIV transmission.

Keywords

antiretroviral medication adherence; adherence devices; youth; adolescent; HIV

Introduction

Adherence to antiretroviral (ARV) therapy is strongly correlated with an increase in survival and improvement in quality of life[1,2] and modest reductions in adherence have been

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associated with loss of virologic control and treatment failure[3-5]. Despite the necessity to maintain high levels of adherence, research has shown a consistent association between younger age and lower ARV adherence and higher risk of virologic failure[6-10]. ARV adherence in HIV-positive adolescents and young adults (i.e., youth) in the past month has been estimated to be as low as 28.3% in one study[11] and 41% in another[12]. In addition to having similar adherence barriers as HIV-positive adults, including stigma, substance use, concerns with regimen complexity, depression, and intolerance of adverse effects, youths' ARV adherence may be further challenged by other major factors, such as having less autonomy, privacy, peer support, and mobility compared to adults[13].

In 2009, youth aged 13-24 years accounted for 8,294 new HIV infections in the United States among 40 states with HIV reporting, representing approximately 20% of all new diagnoses that year[14]. More than half of this population remained unaware of their HIV status [15], leading to increased likelihood of late diagnosis and worse clinical outcomes. Taken together, young individuals have a disproportionately high rate of HIV infection and late diagnosis, an increased risk of ARV non-adherence, and therefore, an elevated chance of disease progression and transmission.

Few studies have examined barriers to ARV adherence in HIV-positive youth[11,16,17]. These barriers have included: forgetting to take ARVs, a change in daily routine, not having medications, pharmacy-related issues, not feeling like taking medications, life-style barriers (e.g., alcohol or substance use and homelessness), and medication adverse effects. Even fewer studies have examined the use of ARV adherence devices and facilitators in general[18-20]. In a qualitative interview study of HIV-infected individuals in four U.S. cities, belief and trust in ARVs and health care providers and the belief that the treatment is beneficial to health and survival were among the strongest facilitators of adherence[18]. In another qualitative study among HIV-infected pediatric patients in Ethiopia, caregivers identified the presence of mobile/wall alarms, follow-up counseling, improved health of the child, ARV clinic setups, and disclosure of HIV serostatus as adherence facilitating factors[19]. Lastly, in a systematic review, important self-reported adherence facilitators in developed countries included having a sense of self-worth, seeing positive effects of ARVs, acceptance of positive serostatus, understanding the need for strict adherence, using reminder tools, and having a simple ARV regimen[20].

Given sparse data on adherence device use in youth and a greater focus on barriers to ARV adherence, we investigated the use of ARV adherence devices (e.g., pillboxes, beepers, timers, etc.) among HIV-infected youth and the correlation of the use of these devices with plasma HIV RNA and self-reported ARV adherence. We hypothesized that with use of more adherence devices there is a higher likelihood of virologic suppression and having higher ARV adherence. As a secondary objective, we compared the association between ARV adherence and plasma HIV RNA and adherence device use among three sub-groups: 1- perinatally versus behaviorally HIV-infected youth, 2- those reporting versus not reporting forgetfulness to take ARVs as an adherence barrier, and 3- those reporting versus not reporting problematic substance use. We investigated the first sub-group because perinatally HIV-infected youth are more likely to have lengthy ARV treatment histories, more drug resistance, complicated ARV regimens, and advanced stages of HIV disease than

behaviorally HIV-infected youth[21,22]. Therefore, these HIV risk groups are likely to have unique treatment needs and may be distinct in adherence device use. Additionally, we examined differences in device use among those reporting versus not reporting forgetfulness to take ARVs because forgetting to take ARVs is the most commonly stated reason for non-adherence[20] and therefore, several studies[23-25] have examined the impact of the use of pagers, timers, and reminder devices on ARV adherence. Lastly, substance use is highly prevalent among HIV-positive youth[26] and has been associated with poor ARV adherence[12]; therefore, we wanted to examine the influence of problematic substance use on the association between ARV adherence and plasma HIV RNA and adherence device use.

Methods

Study design

We conducted a secondary data analysis of cross-sectional data collected as part of Adolescent Trials Network (ATN) 086 and ATN 106 to examine the correlation of ARV adherence devices with participants' plasma HIV RNA and self-reported ARV adherence.

Setting

ATN 086 and ATN 106 were cross-sectional, multi-site studies conducted in 15 and 5 Adolescent Medicine Trials Units (AMTUs), respectively, in the U.S. and collected information on ARV adherence, sexual risk behavior, substance use, and mental health concerns. ATN 086 initiated in October 2009 and concluded in March 2011 and the study duration for ATN 106 was from February 2011 through August 2012.

Subjects and recruitment

Participants were behaviorally or perinatally HIV-infected youth (12-24 years of age) who were aware of their HIV-positive serostatus, were in care at the AMTU (at least one clinic visit during the one year study enrollment period), and understood written and/or spoken English (ATN 086 and 106) or Spanish (ATN 106 only). Those with serious psychiatric symptoms, appearing visibly distraught, intoxicated, under the influence of alcohol or other substances at the time of consent or data collection were excluded. Participants were approached and recruited during regularly scheduled clinic visits or during supportive activities and HIV infection was confirmed through documented test results from earlier HIV screening. Unique participant identifiers were generated and used to avoid participant duplication between ATN 086 and 106.

ATN 086 included 1,704 HIV-infected youth aged 12-24 years, 58.4% of whom were on ARVs at the time of the study. Among this sample, 25.7% were perinatally HIV-infected, 65.1% were HIV-infected through a behavioral route, and 9.2% did not know the route or reporting being HIV-infected by other routes (e.g., blood products). ATN 106 included 509 HIV-infected youth, 63.5% of which were on ARVs. Primary routes of HIV infection in this sample were 34.2% perinatal, 59.9% behavioral, and 5.9% other or unknown route.

Measurement and data collection

Data were collected through biomedical chart extraction and/or laboratory testing and by Audio Computer Assisted Self Interview (ACASI). Participants received compensation for their time and transportation in an amount determined by their local Institutional Review Board (IRB).

ARV Adherence Devices—In ACASI, participants were asked to select the devices that they used to help them remember to take their ARV medicines in the past seven days from an eight-item checklist. These adherence devices included use of labels, calendars, pillboxes, beepers, timers, medication event monitoring caps (MEMS), programmable wrist watches, and diaries. The adherence device variables were operationalized in two ways: 1) dichotomized (yes/no) for use of a specific adherence device from the eight-item checklist; and 2) categorized as use of 0, 1, 2, or ≥3 adherence devices.

ARV Adherence—Participants were asked to state the total number of ARV doses they were prescribed to take per day and to estimate how many times they had missed taking a dose in the past seven days. “Dose” was defined as “quantity of pills or medicines prescribed to be taken at one particular time (for example, 3 pills before bedtime)”. ARV adherence or percentage of doses taken in the past seven days was calculated as the number of doses taken divided by total number prescribed doses per week. Adherence was operationalized as a continuous variable and by dichotomizing at 100%. Despite the fact that 100% adherence is no longer necessary to achieve an undetectable plasma HIV RNA, we used this cut-off given the median adherence of our sample and the overestimation of self-reported ARV adherence[27].

Biomedical Information—Plasma HIV RNA and CD4+ cell count were obtained from medical chart review and abstraction. Participants who did not have plasma HIV RNA and CD4+ cell count evaluations within six months of the study had blood collected for these measurements. Because the study took place in clinical sites across the United States, various viral assays were used, including Bayer/Siemens Versant HIV-1 RNA 3.0 (bDNA) (lower limit of detection [LLD] = 75 copies/mL), Roche Amplicor® HIV-1 Monitor - Standard (LLD = 400 copies/mL) or Ultrasensitive (LLD = 50 copies/mL), Roche COBAS AmpliPrep/COBAS® Taqman® HIV-1 Test, v1.0 (LLD = 48 copies/mL) and v2.0 (LLD = 20 copies/mL), Chiron Quantiplex HIV-1 RNA 3.0 (bDNA) (LLD = 50 copies/mL), Organon-Teknika/bioMerieux NucliSENS® EasyQ HIV-1 Assay (LLD = 10 copies/mL), and Abbott RealTime HIV-1 Assay (LLD = 40 copies/mL). Therefore, we used the corresponding study site's plasma HIV RNA assay cut-off for the lower limit of detection (LLD) of HIV RNA to designate viral suppression. Plasma HIV RNA was examined as a dichotomous (undetectable versus detectable) and a continuous ($\log_{10}$ transformed) variable.

Psychological Symptoms—Psychological symptoms were assessed by the Brief Symptom Inventory (BSI)[28]. The BSI generates nine primary symptom scales (e.g., anxiety dimension, obsessive-compulsive dimension, depression dimension, etc.) and global indices and has established norms for adolescents and adults. We used the global severity Index (GSI) T-score as a continuous variable and a dichotomous variable with a score of ≥63

and/or the presence of any two BSI dimensions as the clinical cutoff for psychological distress[28].

Route of Infection—Participants were asked how they thought they were HIV infected. Multiple choice responses were coded as perinatal route and behavioral route (sex and injection drug use). Those who did not know their route of HIV infection or reported being infected through other routes were placed in the 'other' category.

Substance Use—Lifetime use or no use of alcohol, marijuana, stimulants (crack, cocaine, amphetamines) and other substances (inhalants, sedatives, hallucinogens, and opioids) was assessed. CRAFFT (Car, Relax, Alone, Forget, Friends, and Trouble), a six-item behavioral health screening tool designed for youth, was used to assess the consequences of alcohol, drugs, and/or marijuana use[29]. A score of two or greater is highly suggestive that the individual has a high risk of alcohol or drug-related disorder. In our study, CRAFFT was used as a continuous variable and dichotomized with a score of two or more as suggestive of problematic substance use, abuse, or dependence.

Analysis

We used descriptive statistics to characterize the sample overall and used two-sided *t*-, chi-square, and Wilcoxon rank sum test as appropriate.

Self-reported use of adherence devices constituted our focal predictor variables (categorized as 0, 1, 2, ≥3 devices). Our non-focal variables (i.e., potential confounders) included age; sex at birth; race/ethnicity; sexual orientation; education; employment; income; ever being incarcerated; route of HIV infection; use of alcohol, marijuana, stimulants, or other drugs; CRAFFT and BSI GSI scores; and prescribed dosing frequency of ARV regimen per day (i.e., once-daily versus twice-daily or more).

Our outcome measures consisted of self-reported ARV adherence and plasma HIV RNA. Because both outcomes are highly skewed (at 100% adherence or undetectable plasma HIV RNA), we used a two-component method for our analysis[30]. The benefit of a two-component model is that it maximizes power, minimizes loss of valuable data, and presents a fuller picture of the variability in the data. Specifically, we used logistic regression models to assess the association between device use and adherence (100% versus <100%) and plasma HIV RNA (undetectable versus detectable). Next, we used linear regression models to examine the correlation between device use and continuous adherence and $\log_{10}$ transformed plasma HIV RNA for those with <100% adherence and detectable plasma HIV RNA, respectively.

In our two parallel analyses, we initially examined associations in unadjusted models. We then assessed multivariate regression models to examine the association between the outcomes and our focal predictor variable while controlling for all non-focal variables with a p-value <0.25 in unadjusted analyses[31]. Using backward elimination, non-focal variables were removed until all remaining variables had a p-value <0.05.

For our secondary objective, using logistic regression, we compared the association between our outcome variables and adherence device use among three sub-groups: 1- perinatally versus behaviorally HIV-infected youth; 2- those who reported versus did not report "forgot" to take ARVs in the past seven days as an adherence barrier; and 3- those with versus without problematic substance use, operationalized as a CRAFFT score of two or more versus less than two. A two-sided p-value<0.05 was considered statistically significant. All analyses were conducted using Stata, version 13 (StataCorp, College Station, TX).

Due to the variety in plasma HIV RNA assays used in various study sites, we conducted sensitivity analyses on three subsets of data: 1) six cases for which the assay's LLD was <400 copies/mL; 2) nine cases where the assays were unknown; and 3) 30 cases in which the symbol qualifier (i.e., <, >, or =) and reported plasma HIV RNA did not correspond with the LLD of the reported assay. These sensitivity analyses did not result in any significant changes in results, and thus the authors included these data.

Ethical considerations

ATN 086 and 106 protocols and informed consent documents were reviewed and approved by each study site's IRB with a waiver of parental/legal guardian permission for youth <18 years of age. A certificate of confidentiality was obtained from the National Institutes of Health. Informed consent was obtained from all participants.

Results

We examined data from 1,317 HIV-infected individuals who were 12-24 years old (mean age =20.0 years), were on ARVs, and were behaviorally (52.7%) and perinatally (39.1%) HIV infected (Table 1). Mean self-reported ARV adherence over the past 7 days was 86.1% (median =100%), 50.5% of the sample had an undetectable plasma HIV RNA, and mean CD4+ cell count was 526 cells/mm^3. Among 735 youth who reported 100% adherence, 311 (42.3%) had a detectable plasma HIV RNA. Plasma HIV RNA and ARV adherence were highly correlated (coefficient = -0.01; 95% confidence interval [CI] = -0.013, -0.008; p<0.0001). The mean lag time between plasma HIV RNA assessment and the ACASI data collection was 48 days (standard deviation [SD] = 44). The majority (63.5%) of participants did not use adherence devices and among those who reported device use, the most commonly endorsed device was a pillbox (24.6%). Beepers, programmable wrist watches, diaries, and MEMS were the least used adherence devices (Table 1).

ARV Adherence

In unadjusted analysis, there was no statistically significant association between reporting 100% adherence and use of one or more adherence devices (odds ratio [OR] =0.84; 95% CI =0.68, 1.05; p=0.13; results not shown) or the number of devices used (overall p-value =0.76; Table 2). Additionally, no specific adherence device was independently associated with higher odds of reporting 100% adherence (all p-values >0.16). Other covariates associated with higher odds of reporting 100% adherence included: male sex at birth; behavioral route of HIV infection; non-heterosexual orientation; never having gone to jail;

lower mean CRAFFT score; never using alcohol, marijuana, cocaine, or amphetamines; lower mean BSI GSI score; and once-daily dosing frequency of ARV medications. Among those reporting<100% adherence (N =566), higher ARV adherence was associated with the use of one or more adherence devices (coefficient=7.32; 95% CI =2.43, 12.21; p=0.003; results not shown) and with the use of more devices (overall p-value =0.0001; Table 2).

In the final adjusted model, there was no significant association between the odds of reporting 100% adherence and the number of devices used (overall p-value=0.97) when controlling for other variables (i.e., sex at birth, CRAFFT score, ARV dosing frequency, and route of HIV transmission). However, among those with <100% adherence, higher reported adherence was associated with number of adherence devices used (coefficient for 1 device =8.90 [95% CI =1.78, 16.02; p =0.01], 2 devices =9.23 [95% CI =1.92, 16.53; p =0.01], ≥3 devices =6.04 [95% CI =-0.32, 12.39; p =0.06]compared to use of no devices; overall p-value =0.02) when controlling for sex at birth, race, psychological distress, CRAFFT score, ARV dosing frequency, and use of other substances.

Plasma HIV RNA

In unadjusted analysis, having an undetectable plasma HIV RNA was inversely associated with the use of one or more adherence devices (OR =0.80; 95% CI =0.64, 0.99; p =0.04;results not shown) and the number of adherence devices (overall p-value = 0.009; Table 2). Other covariates associated with higher odds of having an undetectable plasma HIV RNA included male sex at birth, behavioral route of HIV infection, more than high school education, being employed, lower mean CRAFFT score, and once-daily dosing frequency of ARV medications. Among those with a detectable plasma HIV RNA (N =650), there was no association between plasma HIV RNA and use of one or more adherence devices (coefficient =-0.03; 95% CI=-0.22, 0.16; p=0.74; results not shown) or the number of devices used (overall p-value = 0.23; Table 2). Among specific adherence devices, use of calendar, timer, and diary had inverse associations with undetectable plasma HIV RNA (calendar: OR =0.74;95% CI = 0.55, 1.00; p =0.05 / timer: OR =0.73; 95% CI= 0.54, 1.00; p =0.05 / diary: OR =0.58; 95% CI = 0.33, 1.02; p =0.06).

In the adjusted model, there was a statistically significant inverse association between having an undetectable plasma HIV RNA and number of adherence devices (OR for 1, 2, or ≥3 devices, in comparison to no reported use of adherence devices, was 0.64 [95% CI=0.45, 0.91; p=0.01], 1.14 [95% CI=0.80, 1.64; p =0.46], and 0.62 [95% CI=0.43, 0.89; p=0.009], respectively [overall p-value = 0.004]) when controlling for sex at birth, education, mean CRAFFT score, and ARV dosing frequency. In adjusted models among those with a detectable plasma HIV RNA, number of adherence devices was not associated with mean $\log_{10}$ plasma HIV RNA (overall p-value =0.10) even after controlling for sex at birth, alcohol, and marijuana use.

Secondary analyses

Table 3 summarizes the comparison between perinatally and behaviorally HIV-infected youth. Perinatally HIV-infected youth were significantly more likely to endorse the use of pillboxes and behaviorally HIV-infected youth were more likely to report the use of beepers.

Irrespective of the route of HIV infection, participants were similar with regard to the number of adherence devices used. Additionally, the route of HIV infection did not modify the association between having an undetectable plasma HIV RNA or reporting 100% adherence and specific adherence devices, with the exception of the use of timers, for which there was a lower odds of undetectable plasma HIV RNA in perinatally HIV-infected youth (OR =0.50; 95% CI = 0.29, 0.87; p =0.01).

Four-hundred-seventy-one (35.8%) youth reported forgetfulness as a barrier to ARV adherence. There was no statistically significant difference with the use of any specific adherence device (all p-values>0.10) or more adherence devices used between those who reported and did not report forgetfulness as a barrier to adherence (p-value=0.50). Among those reporting forgetfulness, the use of labels, calendars, and pillboxes was significantly associated with higher odds of reporting 100% adherence; however, none of these or other specific devices were associated with higher odds of undetectable plasma HIV RNA in this population.

Lastly, among those who did not have problematic substance use, there was lower odds of having an undetectable plasma HIV RNA with the use of calendars (OR =0.59; 95% CI = 0.38, 0.92; p =0.02), beepers (OR =0.52; 95% CI = 0.27, 0.98; p =0.04), and timers (OR =0.59; 95% CI = 0.38, 0.92; p =0.02). Having problematic substance use did not modify the association between having undetectable plasma HIV RNA or reporting 100% adherence and adherence device use.

Discussion

In this study, we analyzed the use of ARV adherence devices among HIV-infected youth. Among the list of devices, using a pillbox was the most commonly endorsed adherence device and beepers, programmable wrist watches, diaries, and MEMS were the least reported devices. Most participants did not report use of any adherence devices and, interestingly, those who did not report using adherence devices had a higher odds of having an undetectable plasma HIV RNA despite not reporting 100% adherence. Additionally, the use of any adherence device was not associated with higher odds of reporting 100% adherence; however, among those who reported any level of non-adherence, the use of adherence devices was associated with higher mean ARV adherence. These seeming paradoxes may be due to an effect-cause rationale, whereby those exhibiting virologic failure and/or ARV non-adherence were more likely to have been offered adherence devices by their providers. Given the cross-sectional nature of this study and the lag time between ACASI data collection and plasma HIV RNA evaluation, it is unknown if non-adherent participants who reported higher adherence with use of devices actually had improved adherence, which was not yet reflected in their plasma HIV RNA due to a delay in HIV RNA improvements or if they overestimated their adherence due to social desirability bias. It is likely that individuals with an undetectable plasma HIV RNA may have successfully developed other non-device-based adherence-facilitating methods, such as associating medication-taking with activities of daily living (i.e., routinizing medication-taking behavior[32]) and did not require the use of other methods. Therefore, longitudinal studies of

HIV-infected youth are needed to disentangle the temporal sequence of adherence patterns and clinician recommendations regarding the use of devices to promote adherence.

Perinatally and behaviorally HIV-infected sub-groups did not differ in terms of the number or specific adherence devices used, with the exception of pillboxes and beepers. The higher use of pillboxes in perinatally HIV-infected youth may have been related to the potentially higher parental or guardian assistance and support. It is also possible that perinatally HIV-infected youth had more complex ARV regimens, because they were less likely to have once-daily regimens and were more likely to be taking protease inhibitors or other ARVs generally prescribed for treatment-experienced patients (such as CCR5 inhibitors, integrase inhibitors, and fusion inhibitors).

Finally, we examined the difference in the use of adherence devices among those who reported and did not report forgetfulness as a barrier to ARV adherence. In our study, there was no association between citing forgetfulness as an adherence barrier and any specific adherence device or the number of devices used. Therefore, despite the fact that perinatally HIV-infected youth have unique treatment needs compared to behaviorally HIV-infected youth[21,22], that forgetting to take ARVs is the most commonly stated reason for non-adherence[20], and that substance use has been associated with poor ARV adherence[12], the route of HIV infection, forgetting to take ARVs, and problematic substance use did not modify the association between undetectable plasma HIV RNA and use of specific adherence devices. Future research should examine other underlying reasons behind self-reported adherence barriers (e.g., forgetfulness) and the individual-specific factors that are important in tailoring facilitators of adherence.

The results of the current study are valuable because they demonstrate that the use of devices alone or cumulatively may not be enough to minimize non-adherence and virologic failure and that evidence-based tailored approaches are needed to improve outcomes. However, it is important to note that our results are based on secondary data analysis of data collected for other purposes; therefore, we believe our findings are preliminary and exploratory and should be further assessed in future research. Nevertheless, given the lack of data on the use of adherence devices, especially among HIV-infected youth, we believe our study is a logical step forward to inform future trials. Other limitations include the cross-sectional nature of our study, the use of measures assessing key variables over different timeframes, and the use of a clinic-based convenience sample which may not be generalizable to all HIV-infected youth. Additionally, we relied on self-reported measures for variables such as ARV adherence, psychological well-being, and substance use. It is important to note that a disadvantage with the use of self-reported medication adherence data is that respondents tend to overestimate adherence due to social desirability bias and/or self-denial.

Future research on HIV-infected youth should focus on capitalizing and improving devices that are more commonly used and should minimize more obsolete devices (e.g., label, beeper, programmable wrist watch, and diary). Additionally, future research should examine more ubiquitous devices that were not as widely used by youth when ATN 086 and 106 were conducted, such as mobile telephones (especially smartphones), but also concentrate

on methods of improving adherence that are above and beyond adherence devices alone. Given the high number of youth with detectable plasma HIV RNA, we believe more research is needed to examine youth-friendly and tailored methods to improve adherence and engagement in HIV care. Several research projects are currently examining these methods[33-35]. It is imperative for youth experiencing virologic failure to be re-engaged in their care by receiving a thorough evaluation and counseling to assess adherence barriers and having discussions about what adherence-facilitating methods can be used and tailored to enhance medication-taking.

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Table 1
Characteristics of all participants on antiretroviral therapy

Characteristic		Total (N= 1,317)
Mean age, years (SD)		20.0 (3.0)[a]
Male at birth (%)		860 (65.3)
Race/Ethnicity (%)		
	Black	831 (63.3)
	White	114 (8.7)
	Latino	273 (20.8)
	Other	94 (7.2)
Route of HIV infection (%)		
	Perinatal	514 (39.1)
	Behavioral	693 (52.7)
	Other	109 (8.3)
In school (%)		758 (57.8)
Education (%)		
	Less than high school	446 (34.3)
	High school or equivalent	431 (33.1)
	More than high school	425 (32.6)
Employed (%)		434 (33.1)
Sexual orientation (%)		
	Heterosexual	684 (52.1)
	LGBQQ & other	630 (48.0)
Ever jail (%)		352 (26.8)
Mean CRAFFT score (SD)		2.1 (1.9)[b]
Problem-level substance use (CRAFFT score ≥2) (%)		660 (51.8)
Ever… (%)		
	drink alcohol	1,008 (76.5)
	use marijuana	751 (57.0)
	use cocaine or amphetamines	302 (23.0)
	use inhalants, sedatives, hallucinogens, or opioids	293 (22.3)
Psychological distress (GSI ≥63 and/or any 2 dimensions) (%)		157 (12.6)
Mean BSI GSI (SD)		49.2 (6.2)[c]
ARV dosing frequency (%)		

Characteristic		Total (N= 1,317)
	Once-daily	918 (70.0)
	≥Twice-daily	393 (30.0)
Use pill box (%)[d]		324 (24.6)
Use calendar (%)		197 (15.0)
Use timer (%)		189 (14.4)
Use label (%)		162 (12.3)
Use beeper (%)		90 (6.8)
Use programmable wrist watch (%)		63 (4.8)
Use diary (%)		53 (4.0)
Use MEMS (%)		33 (2.5)
Number of adherence devices		
	0	836 (63.5)
	1	165 (12.5)
	2	156 (11.9)
	≥3	160 (12.2)
Mean adherence, % (SD)		86.1 (23.9) [e]
Undetectable HIV RNA (%)		664 (50.5)
Mean log10 HIV RNA, copies/mL (SD)		2.51 (1.18) [f]
Mean CD4+ cell count, cell/mm^3 (SD)		526 (292) [f]
ARV regimen		
	PI-based	760 (57.7)
	NNRTI-based	498 (37.8)
	Other (RAL, MVC, ENF)	120 (9.1)

ARV: antiretroviral; BSI: Brief Symptom Inventory; CRAFFT: Care, Relax, Alone, Forget, Friends, and Trouble; ENF: enfuvirtide; GSI: Global Severity Index; LGBQQ: lesbian, gay, bisexual, queer, questioning; MVC: maraviroc; MEMS: medication event monitoring system; NNRTI: non-nucleoside reverse transcriptase inhibitor; PI: protease inhibitor; RAL: raltegravir; SD: standard deviation

[a] N= 1313

[b] N= 1275

[c] N= 1242

[d] Among N= 1,317

[e] N= 1302

[f] N= 1314

Table 2

Unadjusted associations of selected covariates with ARV adherence and plasma HIV RNA

		100% Adherence		Adherence Level (if <100% adherent)		Undetectable HIV RNA		Log10 HIV RNA (if detectable)	
		OR (95% CI)	p-value	Coefficient (95% CI)	p-value	OR (95% CI)	p-value	Coefficient (95% CI)	p-value
Mean age		1.01 (0.97, 1.05)	0.64	-0.47 (-1.15, 0.22)	0.18	1.01 (0.97, 1.04)	0.77	-0.01 (-0.04, 0.23)	0.64
Female at birth		0.68 (0.54, 0.86)	0.001	-3.47 (-8.81, 1.57)	0.18	0.74 (0.59, 0.94)	0.01	0.26 (0.12, 0.40)	<0.001
Race/Ethnicity [b]		-	0.27 [a]	-	0.004 [a]	-	0.18 [a]	-	0.74[a]
	Black	0.78 (0.52, 1.16)	0.22	-10.73 (-18.81, -2.66)	0.009	0.74 (0.50, 1.09)	0.13	0.10 (-0.24, 0.45)	0.56
	Latino	0.83 (0.53, 1.30)	0.42	-3.87 (-11.88, 4.14)	0.34	0.91 (0.59, 1.42)	0.68	0.04 (-0.35, 0.44)	0.83
	Other	0.58 (0.33, 1.01)	0.06	-6.03 (-11.88, 4.14)	0.20	0.98 (0.57, 1.70)	0.95	0.23 (-0.26, 0.72)	0.36
Route of HIV infection[c]		-	0.0005 [a]	-	0.97 [a]	-	0.02 [a]	-	0.60[a]
	Behavioral	1.51 (1.20, 1.91)	<0.001	-0.14 (-4.98, 4.71)	0.96	1.35 (1.07, 1.70)	0.01	-0.10 (-0.30, 0.10)	0.31
	Other	1.79 (1.16, 2.76)	0.009	-1.18 (-12.08, 9.72)	0.83	0.97 (0.64, 1.46)	0.88	-0.08 (-0.40, 0.23)	0.61
In school		0.99 (0.79, 1.24)	0.93	5.37 (0.18, 10.56)	0.04	0.94 (0.76, 1.17)	0.59	-0.02 (-0.19, 0.15)	0.80
Education [d]		-	0.24 [a]	-	0.37 [a]	-	<0.001	-	0.09[a]
	High school or equivalent	0.95 (0.73, 1.25)	0.73	3.80 (-1.79, 9.39)	0.18	1.07 (0.82, 1.39)	0.64	-0.25 (-0.48, -0.01)	0.04
	More than high school	1.19 (0.91, 1.56)	0.20	0.39 (-5.72, 6.49)	0.90	1.63 (1.24, 2.13)	<0.001	-0.22 (-0.46, 0.02)	0.07
Employed		1.18 (0.93, 1.49)	0.17	2.18 (-3.35, 7.71)	0.44	1.32 (1.05, 1.67)	0.02	-0.24 (-0.46, -0.02)	0.03
Sexual orientation [e]	LGBQQ & other	1.42 (1.14, 1.77)	0.002	1.37 (-3.13, 5.86)	0.55	1.19 (0.96, 1.48)	0.11	-0.05 (-0.21, 0.12)	0.59
Ever jail		0.78 (0.61, 1.00)	0.05	-5.77 (-9.76, -1.78)	0.005	0.80 (0.63, 1.02)	0.08	0.01 (-0.19, 0.22)	0.89
Mean CRAFFT score		0.82 (0.78, 0.88)	<0.001	-1.61 (-3.00, -0.21)	0.02	0.94 (0.89, 1.00)	0.05	-0.02 (-0.06, 0.03)	0.51
Ever…	drink alcohol	0.75 (0.58, 0.98)	0.04	-4.28 (-8.58, 0.03)	0.05	0.97 (0.75, 1.25)	0.81	-0.12 (-0.29, 0.05)	0.18
	use marijuana	0.65 (0.52, 0.81)	<0.001	-3.70 (-8.69, 1.30)	0.15	0.83 (0.67, 1.03)	0.10	0.11 (-0.05, 0.28)	0.19
	use cocaine or amphetamines	0.72 (0.55, 0.93)	0.01	1.55 (-2.78, 5.87)	0.48	0.94 (0.73, 1.22)	0.64	-0.22 (-0.41, -0.03)	0.02

		100% Adherence		Adherence Level (if <100% adherent)		Undetectable HIV RNA		Log10 HIV RNA (if detectable)	
		OR (95% CI)	p-value	Coefficient (95% CI)	p-value	OR (95% CI)	p-value	Coefficient (95% CI)	p-value
	use inhalants, sedatives, hallucinogens, or opioids	0.96 (0.74, 1.25)	0.79	4.75 (0.05, 9.46)	0.05	1.14 (0.88, 1.47)	0.34	-0.16 (-0.37, 0.05)	0.14
Mean BSI GSI		0.97 (0.95, 0.99)	0.001	-0.55 (-0.84, -0.22)	0.001	0.98 (0.97, 1.00)	0.06	-0.003 (-0.02, 0.01)	0.67
ARV dosing frequency [f]	≥ Twice-daily	0.61 (0.48, 0.78)	<0.001	12.16 (8.06, 16.26)	<0.001	0.67 (0.53, 0.85)	0.001	0.09 (-0.08, 0.26)	0.29
Number of adherence devices [g]		-	0.76[a]	-	0.0001 [a]	-	0.009[a]	-	0.23[a]
	1	0.96 (0.68, 1.34)	0.79	11.08 (5.48, 16.68)	<0.001	0.66 (0.47, 0.92)	0.02	-0.16 (-0.43, 0.10)	0.23
	2	1.19 (0.84, 1.69)	0.33	8.66 (3.66, 13.65)	0.001	1.17 (0.83, 1.65)	0.37	0.16 (-0.12, 0.43)	0.26
	≥ 3	1.05 (0.75, 1.48)	0.78	4.04 (-1.45, 9.53)	0.15	0.69 (0.49, 0.96)	0.03	0.09 (-0.22, 0.40)	0.56

ARV: antiretroviral; BSI: Brief Symptom Inventory; CI: confidence interval; CRAFFT: Care, Relax, Alone, Forget, Friends, and Trouble; GSI: Global Severity Index; LGBQQ: lesbian, gay, bisexual, queer, questioning; OR: odds ratio

[a] p-value for the omnibus Wald test

[b] "White" as reference category

[c] "Perinatal" as reference category

[d] "Less than high school" as reference category

[e] "Heterosexual" as reference category

[f] "Once-daily" as reference category

[g] "0" adherence devices as reference category

Table 3
Comparison between behaviorally and perinatally HIV-infected participants

Characteristic		Behaviorally HIV-infected (N= 693)	Perinatally HIV-infected (N= 514)	p-value
Mean age, years (SD)		21.6 (1.9)[a]	17.9 (3.0)[b]	<0.001
Male at birth (%)		561 (81.0)	233 (45.3)	<0.001
Race/Ethnicity (%)				0.33[c]
	Black	449 (64.8)	321 (63.1)	
	White	60 (8.7)	45 (8.8)	
	Latino	143 (20.6)	99 (19.5)	
	Other	41 (5.9)	44 (8.6)	
Sexual orientation (%)				<0.001[c]
	Heterosexual	169 (24.4)	458 (89.3)	
	LGBQQ & other	524 (75.6)	55 (10.7)	
Mean CRAFFT score (SD)		2.5 (1.8)[d]	1.49 (1.7)[e]	<0.001
Mean BSI GSI (SD)		50.2 (6.8)[f]	48.1 (5.2)[g]	<0.001
ARV frequency (%)				<0.001 [c]
	Once-daily	600 (86.6)	237 (46.6)	
	≥Twice-daily	93 (13.4)	272 (53.4)	
Adherence facilitators (%)				
	Pill box	162 (23.4)	147 (28.6)	0.003
	Calendar	108 (15.6)	78 (15.2)	0.85
	Timer	114 (16.5)	65 (12.7)	0.07
	Label	82 (11.8)	69 (13.4)	0.41
	Beeper	61 (8.8)	25 (4.9)	0.009
	Programmable wrist watch	34 (4.9)	28 (5.5)	0.67
	Diary	33 (4.8)	19 (3.7)	0.37
	MEMS	15 (2.2)	18 (3.5)	0.16
Number of adherence facilitators (%)				0.48 [c]
	0	435 (62.8)	319 (62.1)	
	1	80 (11.5)	74 (14.4)	
	2	86 (12.4)	59 (11.5)	
	≥3	92 (13.3)	62 (12.1)	
Mean adherence (SD)		87.3 (22.9)[h]	84.0 (24.9)[i]	0.02
Mean log10 HIV RNA, copies/mL		2.43 (1.18)[a]	2.61 (1.17)	0.007

Characteristic		Behaviorally HIV-infected (N= 693)	Perinatally HIV-infected (N= 514)	p-value
Mean CD4+ (SD)		491 (238) [j]	570 (345) [k]	<0.001
ARV regimen (%)				
	PI	327 (47.2)	363 (70.6)	<0.001
	NNRTI	294 (42.4)	168 (32.7)	0.001
	Other (RAL, MVC, ENF)	29 (4.2)	89 (17.3)	<0.001

ARV: antiretroviral; BSI: Brief Symptom Inventory; CRAFFT: Care, Relax, Alone, Forget, Friends, and Trouble; ENF: enfuvirtide; GSI: global severity Index; LGBQQ: lesbian, gay, bisexual, queer, questioning; MVC: maraviroc; MEMS: medication event monitoring system; NNRTI: non-nucleoside reverse transcriptase inhibitor; PI: protease inhibitor; RAL: raltegravir; SD: standard deviation

[a] N= 690

[b] N= 513

[c] p-value for the omnibus Wald test

[d] N= 686

[e] N= 481

[f] N= 666

[g] N= 474

[h] N= 689

[i] N= 506

[j] N= 691

[k] N= 513