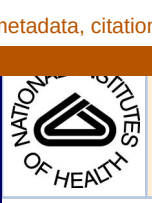

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Effect of Directly Observed Antiretroviral Therapy Compared to Self-Administered Antiretroviral Therapy on Adherence and Virological Outcomes among HIV-Infected Prisoners: A Randomized Controlled Pilot Study

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Abstract

The effect of directly observed therapy (DOT) versus self-administered therapy (SAT) on antiretroviral (ART) adherence and virological outcomes in prison has never been assessed in a randomized, controlled trial. Prisoners were randomized to receive ART by DOT or SAT. The primary outcome was medication adherence [percent of ART doses measured by the medication event monitoring system (MEMS) and pill counts] at the end of 24 weeks. The changes in the plasma viral loads from baseline and proportion of participants virological suppressed (<400 copies/mL) at the end of 24 weeks were assessed. Sixty-six percent (90/136) of eligible prisoners declined participation. Participants in the DOT arm (n = 20) had higher viral loads than participants in the SAT (n = 23) arm (p = 0.23). Participants, with complete data at 24 weeks, were analyzed as randomized. There were no significant differences in median ART adherence between the DOT (n = 16, 99% MEMS [IQR 93.9, 100], 97.1 % pill count [IQR 95.1, 99.3]) and SAT (n = 21, 98.3 % MEMS [IQR 96.0, 100], 98.5 % pill count [95.8, 100]) arms (p = 0.82 MEMS, p = 0.40 Pill Count) at 24 weeks. Participants in the DOT arm had a greater reduction in viral load of approximately −1 log 10 copies/mL [IQR −1.75, −0.05] compared to −0.05 [IQR −0.45, 0.51] in the SAT arm (p value = 0.02) at 24 weeks. The proportion of participants achieving virological suppression in the DOT vs SAT arms was not statistically different at 24 weeks (53 % vs 32 %, p = 0.21). These findings suggest that DOT ART programs in prison settings may not offer any additional benefit on adherence than SAT programs.

Keywords

Directly observed therapy; Antiretroviral therapy; Adherence; Prisoners; HIV/AIDS; Protease inhibitors; Clinical trial

Introduction

Suboptimal adherence to antiretroviral therapy (ART) can lead to continued viral replication, viral drug resistance, disease progression, and increased infectiousness [1–5]. However, achieving levels of adherence sufficient to maintain viral suppression is challenging for many patients. Directly observed therapy (DOT) has been proposed as an intervention to ensure “near perfect” adherence to ART [5, 6]. It has been widely adopted in prisons and other supervised settings where it is used for both HIV and non-HIV-related medications.

Despite the widespread use of DOT in prison, there are several factors that make DOT ART in prison challenging. First, prisoners often have to wait in long lines to receive their medications [7]. Second, the medications may be given at inconvenient times. Further, prisoners waiting in the DOT line may experience lack of confidentiality and feel stigmatized [8–10]. Finally, prisoners often do not trust the correctional officers and nurses staffing the DOT line to administer the correct antiretroviral medications [11].

Despite these factors, several studies of HIV infected prisoners have reported high levels of adherence or virological suppression with ART delivered by DOT but have had major methodological limitations [12, 13]. One study found greater viral suppression among

prisoners in Florida receiving ART via DOT compared to non-incarcerated HIV clinical trial participants who self-administered ART (SAT) [14]. The non-randomized design of the Florida study precluded the ability to distinguish the effects of the use of DOT from other confounding factors [14]. A trial involving four state prison systems, found that prisoners who received ART by DOT reported 94 % adherence with 85 % achieving virologic suppression [15]. However, this trial lacked an SAT comparison group. In contrast, in two observational studies, there were no differences in ART adherence between prisoners who received ART either by DOT or SAT [12, 16].

Because DOT is a common, expensive, labor-intensive policy adopted for ART administration among many prison systems, studies with more rigorous designs are warranted to determine the efficacy of DOT in enhancing ART adherence and virological outcomes in prisons [17, 18].

To compare the effect of DOT versus SAT on medication adherence in a correctional setting, we conducted a pilot of a randomized controlled trial of DOT versus SAT delivery of ART in a state prison system. Our primary objective was to determine the efficacy of DOT versus SAT in enhancing adherence to ART at 24 weeks. Our secondary objectives were to compare the adherence of both arms at 48 weeks, and to compare the changes in plasma HIV RNA levels and $CD4^+$ lymphocyte cell counts between both arms at 24 and 48 weeks. Because our non-randomized pilot research had not demonstrated the superiority of DOT over SAT on ART adherence [12], we hypothesized that there would be no difference in adherence between prisoners receiving ART by DOT or self-administration.

Methods

Study site and Participants

The study was conducted in the North Carolina State prison system from 8/5/2003–2/16/2005. At the time of the study, 640 HIV-infected men and women were incarcerated at 74 correctional facilities across the state [19, 20]. Sixty percent of the total HIV-infected prison population were housed in 11 of the largest 74 facilities [19]. We limited our study to these 11 facilities because of their capacity to directly observe antiretrovirals every day of the week.

Men and women prisoners were consecutively recruited from three prison-based HIV clinics where approximately 85 % of the total HIV-infected population received outpatient HIV care. Prisoners were eligible for the study if they were: documented to have HIV infection; currently receiving or initiating ART; housed at one of the 11 participating facilities with no planned inter-prison transfers; had a Karnofsky score ≥70, indicating capability for self-care; were at least 18 years of age; expected to be incarcerated ≥6 months; and had a $CD4^+$ T-lymphocyte count and a plasma HIV RNA level within 60 days of study entry. Potential participants were excluded if they had active mental illnesses or conditions that would preclude informed consent or completion of study requirements.

All participants provided informed consent before enrollment. Consent was obtained in a private room by research personnel. Participants were informed that joining the study would

not affect their health care, terms of confinement, or release from prison. The study was approved by the University of North Carolina Biomedical Institutional Review Board, North Carolina Department of Public Safety's (NCDPS) Human Subjects Review Committee, and the US Department of Health and Human Services Office of Human Research Programs (OHRP). Participants received no incentives, financial or otherwise (per NCDPS Human Subjects Review policy), for study participation.

Standard of Care and Intervention Design

Standard of Care—At the time of the trial, it was standard of care per prison policy for prison staff (nurses, nursing assistants or correctional officers) to administer all doses of protease inhibitors by DOT to enhance adherence and reduce downstream costs due to non-adherence [12, 21]. Non-nucleoside and nucleoside reverse-transcriptase inhibitors could either be directly observed or self-administered. After each DOT event, prison staff would record whether or not the inmate took the ART. Per North Carolina prisons' protocol, if prisoners missed more than 3 days of directly observed antiretrovirals, the prison staff were to notify the prison physicians, nurses or HIV clinicians. Prisoners participating in the self-administered medication program were directed to turn in any remaining medications at each monthly refill.

Intervention Design and Randomization—Participants were randomly assigned in a 1:1 ratio to DOT or SAT using permuted block randomization. The randomization schedule was maintained by personnel at a central study site away from study personnel.

DOT Arm—In the DOT arm, prison staff observed each inmate ingest all of their antiretroviral medications per prison DOT protocol.

SAT Arm—In the SAT arm, participants received monthly allotments of all of their antiretroviral medications, including their protease inhibitors, from prison staff and were required to sign for each antiretroviral medication bottle.

Optional Adherence Counseling—After week 24, all participants had the option of receiving two standardized Motivational Interviewing sessions by trained health educators focused on helping them identify strategies to address adherence to ART.

Study Outcomes

Primary Outcome

The primary outcome was ART Adherence at 24 weeks. This was determined by the percent of prescribed ART doses taken during 20–24 weeks as measured by Medication Event Monitoring System pill caps (MEMS; Aardex, Switzerland) and Pill Count in both arms.

Secondary Outcomes

We assessed the percent of prescribed ART doses taken at 48 weeks (44–48 week period) as well as the odds (DOT vs. SAT) of achieving greater than or equal to 95 % adherence over the entire 24 and 48 week time period. We assessed for the change in plasma HIV-1 RNA

levels (log_{10} copies/mL) and $CD4^+$ T-lymphocyte counts from baseline values to 24 weeks and baseline values to 48 weeks. We also determined the plasma HIV-1 RNA levels (log_{10} copies/mL) and proportion of participants virologically suppressed (plasma HIV RNA level ≤400 copies/mL) at the end of weeks 24 and 48.

Data Collection

Participants' demographic, clinical, and laboratory data were abstracted from prison administrative and medical records using standardized chart abstraction forms. Participants received laboratory assessments (plasma HIV RNA levels, $CD4^+$ T-lymphocyte counts) at approximately 0, 12, 24, 36, and 48 weeks. Participants' MEMS caps and pill bottles were collected at the end of each 4-week period. The MEMS caps were sent to UNC CH and downloaded to a designated research computer. The pill bottles were sent to the main prison pharmacy to determine the remaining pills in each bottle using an automatic pill counter.

Measurement of Adherence

We assessed antiretroviral adherence using MEMS (Aardex, Switzerland) and Pill Count. Adherence was measured as the number of MEMS events (pill bottle openings) in one4 week time period divided by the number of prescribed doses, multiplied by 100 [22]. Prison pharmacy staff placed a MEMS device on one pill bottle from each participant's antiretroviral regimen at monthly refills. The MEMS device was placed on the bottle of the antiretroviral medication with the most complexity. We used the following to rank the complexity of each antiretroviral medication: Rank = daily pill frequency + (total number of pills taken daily/2) [5, 23–26]. We used the same complex antiretroviral per regimen (as above) to determine the Pill count. The Pill count was determined as the (number of pills dispensed-number of pills left)/number of pills dispensed) multiplied by 100. See the Appendix—Supplementary materials for examples.

Statistical Analyses

All statistical analyses were conducted using SAS version 9.3 and R version 2.15. Descriptive statistics were used to summarize baseline demographical and clinical characteristics. We compared the adherence, immunological and virological outcomes between the two study arms. All participants with complete data were included in the 24 and 48 week analyses, respectively. All participants were analyzed as randomized.

Wilcoxon rank sum tests were used to compare adherence levels between the DOT and the SAT arms during both the 20–24 and the 44–48 week time periods. Logistic mixed models were employed to estimate the odds ratios (OR) for achieving greater than 95 % adherence between the two arms. These models included time since randomization as a linear continuous covariate and an interaction term between time and study arm. Random effects included participant specific time slopes and intercepts. Because of the attrition of participants at 24 and 48 weeks, we conducted a sensitivity analysis to determine the extent that loss of these participants may have affected the tests to determine differences in adherence between the two arms (see Appendix—Supplementary materials).

To compare the $CD4^+$ T lymphocyte counts and HIV RNA levels (log_{10} copies/mL) between the DOT and SAT arms at the end of weeks 24 and 48, respectively, we used the Wilcoxon rank sum tests. To compare HIV RNA levels at the end of 24 and 48 weeks between the two arms (adjusting for baseline log_{10} viral loads), we used the *t* test. To compare the proportion of participants virally suppressed at ≤400 copies/mL between the two arms at the end of weeks 24 and 48, we used the Fisher's exact test.

Linear mixed models were fit to assess the effect of study arm on the changes in $CD4^+$ T lymphocyte counts and HIV RNA levels (log_{10} viral load) from baseline to weeks 24 and 48. Logistic mixed effects models were used to assess the effect of study arm on the binary outcome of interest (virological suppression defined as <400 copies/mL). The models included as fixed effects time since randomization, study arm, and interaction between time and study arm. Random effects included participant specific time slopes and intercepts.

Results

Participation and Sample Baseline Characteristics (Table 1)

Eleven of the 20 participants (55 %) in the DOT arm and 8 of the 23 (35 %) participants in the SAT arm were ART na(x000EF)ve prior to randomization ($p = 0.23$). Participants in the DOT arm had significantly higher HIV-1 RNA levels (log_{10} copies/mL) at baseline study entry compared to their SAT counterparts ($p < 0.05$). A higher proportion of participants randomized to the SAT arm were virologically suppressed as compared to the DOT arm ($p < 0.05$).

The disposition of patients screened and enrolled is shown in Fig. 1. During the initial phase of recruitment (8/05/03–11/26/03), 36 % (13/36) of eligible prisoners refused. The most commonly reported reason was unwillingness to change their mode of antiretroviral administration. Thus, eligible prisoners (both those who, at the time of study recruitment, were taking their ART medication as DOT and those who were taking it as SAT) preferred to keep their current mode of antiretroviral administration. Because of our experiences of eligible prisoners declining participation in the RCT due to ART mode preference, we offered prisoners an additional study option during the second phase of study recruitment (12/05/03–9/03/04). Prisoners were offered the option to participate in a parallel observational cohort study of ART adherence. In this observational study, participants were allowed to continue their current mode of ART. Findings from the observational cohort study are described elsewhere (unpublished data). During this second phase of recruitment, 83 % (83/100) of participants agreed to participate in either study. Twenty elected to participate in the RCT and 60 elected to participate in the observational cohort study. Thus, the RCT refusal rate during the second phase was 77 % of eligible (77/100) prisoners with 77 % of those refusing the RCT (60/77) electing to participate in the observational cohort study. Overall, 66 % (90/136) of eligible participants, declined participation in the RCT. Approximately half ($n = 22$) of the original participants remained in the trial at week 48. This was largely due to the slow pace of recruitment leaving insufficient time for those recruited later in the study to reach 48 weeks. Nine of the DOT participants and 14 of the SAT participants opted to receive adherence counseling approximately 25 and 26 weeks after randomization. There were no deaths in either arm during the 48 week study period.

Adherence Outcomes

There were no clinically or statistically significant differences in MEMS or Pill Count adherence between the DOT and SAT arms at 24 or 48 weeks (Table 2). At 24 weeks, the median MEMS adherence was 99.0 % [IQR 93.9, 100] in the DOT arm and 98.3 % [IQR 96.0, 100] in the SAT arm ($p = 0.82$). The median pill count adherence at 24 weeks was 97.1 % [IQR 95.1, 99.3] in the DOT arm and 98.5 % [IQR 95.8–100] in the SAT arm ($p = 0.40$). Similarly, there were no difference between study arms in MEMS or pill count adherence at 48 weeks ($p = 0.79$ and $p = 0.84$ respectively). There was no statistically significant difference in the odds of achieving greater than 95 % adherence in the DOT versus SAT arm respectively as measured by MEMS or pill count (OR_{mems} 0.77, $p = 0.77$; $OR_{pill\ count}$ 1.28, $p = 0.75$).

We conducted a sensitivity analysis for the MEMS and Pill count adherence outcomes to determine if the loss of trial participants resulted in a statistically significant difference in adherence between the DOT and SAT arms. We found no statistically significant differences in adherence between the two arms at 24 or 48 weeks (see Appendix—Supplementary materials).

Virological and Immunological Outcomes

There was a significantly greater decrease in HIV-1 RNA levels (log_{10} copies/mL) from baseline in the DOT arm as compared to the SAT arm at both 24 ($p = 0.02$) and 48 weeks ($p = 0.01$). Because the baseline viral load was higher in the DOT arm, we adjusted for baseline differences between the two arms. In the adjusted analysis, there was no difference in the final HIV-1 RNA levels (log_{10} copies/mL) at the end of 24 or 48 weeks (p 0.27 vs. p 0.16).

Similarly, the proportion of participants achieving viral suppression did not differ significantly between the two study arms at week 24 or 48 (p 0.21 vs. 0.48, see Table 3). In the adjusted analysis (for baseline viral load), there remained no differences in the proportion of participants achieving viral suppression at week 24 or 48 (data not shown). Further, using a linear mixed model (adjusting for baseline viral load) we found no differences in plasma HIV RNA levels (log_{10} copies/mL) between the two arms ($p = 0.93$). Using a logistic mixed effects model, we again found no significant differences between the two arms in achieving viral suppression ($p = 0.47$).

There was also no significant increase or decrease in $CD4^+$ T lymphocyte counts (from baseline) between the two arms at the end of weeks 24 ($p = 0.69$) or 48 ($p = 0.98$). In multivariate analysis (linear mixed effect model) adjusting for baseline viral load, we again found no significant differences between the two arms with respect to change in $CD4^+$ T lymphocyte from baseline to week 48 ($p = 0.21$).

Discussion

In this randomized controlled trial in a prison of DOT versus SAT, we found no difference in antiretroviral adherence or $CD4^+$ T-lymphocyte counts between prisoners receiving DOT versus SAT. Median antiretroviral adherence in both arms was high at greater than 95 % throughout the study. At the end of 24 weeks, DOT participants had a significantly greater

viral load reduction of −1 $\log_{10}$ copies/mL from baseline compared to a 0 reduction in the SAT participants. However, there were no differences between the two arms in HIV RNA levels or proportion virologically suppressed at the end of 24 or 48 weeks.

Several possibilities may explain the greater virological reduction without differences in adherence in the DOT arm compared to the SAT arm. First, the differences in the decrease in viral load from baseline between the two arms could have been attributable to baseline differences and not to randomization. Alternatively, DOT could be superior to SAT in achieving virological benefits without improving adherence, as seen by Altice et al. [27]. For example, participants receiving DOT may receive closer monitoring by clinicians resulting in modifications to regimens as needed to improve their efficacy [27]. Further, our major adherence outcomes measured adherence at the end of weeks 24 and 48. However, differences in the earlier weeks of adherence could have affected viral load. Further, we did not compare the patterns of adherence which may have differed between the two arms and have been shown to affect virological outcomes [28].

We were not able to demonstrate any overall advantage of DOT in terms of adherence, immunological outcomes, or achievement of virological suppression. Our results were consistent with findings from recent systematic reviews and meta-analyses of DOT versus SAT ART when restricted to randomized controlled trials [29]. However, our results do not definitively demonstrate that DOT has no role in supporting ART adherence in prisons. DOT interventions may be particularly effective in prisoners and non-prisoners with poor adherence [27, 29, 30].

Our results contrast with findings of non-randomized prison trials of DOT ART, which show that DOT produces greater virological suppression than SAT [13, 14]. While DOT may not be superior to SAT, previous prison studies of DOT were nonrandomized and their positive results may be due to confounding. Also, the components of the DOT intervention in our study may be substantially different than the DOT components in other prison studies. Third, even if the intended DOT intervention components were similar, the non-randomized studies may not have been designed to maintain the same degree of fidelity to the DOT protocol [29].

This study has several limitations. First, due to its small sample size, it lacked power to detect small differences in adherence and to detect differences in later secondary outcomes at 48-week follow-up. Given the high levels of adherence in both arms, it is doubtful that an increase in sample size would have yielded clinically significant differences of 10 % adherence [31, 32]. Refusals during participant recruitment may have introduced selection bias. However, it is reassuring that prisoners felt comfortable refusing study participation given the ethical imperative to avoid coercive prison research participation [33, 34]. Finally, DOT and SAT may differ in their effects on other important health outcomes, like prisoner satisfaction, quality of life, hospitalizations or costs, which was beyond the scope of this pilot trial.

We were surprised by the high refusal rate in this study given our previous research showing a general dislike of DOT. We believed that prisoners on DOT ART would agree to

participate in a study where they had a chance to change their mode of ART administration. However at the time of the study, prisoners were increasingly being prescribed non-nucleoside reverse transcriptase inhibitors (NNRTI). These medications do not require direct observation per prison policy. Therefore, we had fewer eligible participants on DOT than expected, and who were willing to risk an ART administration change. In addition, some prisoners on DOT ART preferred to have their antiretrovirals directly observed by prison staff.

Despite these limitations, our study does not support DOT as more efficacious at enhancing adherence to complex ART medications or at achieving virological suppression than SAT among HIV infected prisoners. HIV-infected prisoners achieved near-perfect adherence under both sets of conditions, suggesting widespread use of DOT ART among incarcerated populations should be questioned [35]. These findings add to a much needed evidence-base for ART adherence interventions for HIV-infected inmates. The greater challenge is to determine the best strategies to help HIV-infected prisoners maintain their high levels of adherence and virological suppression after release into their communities [36, 37].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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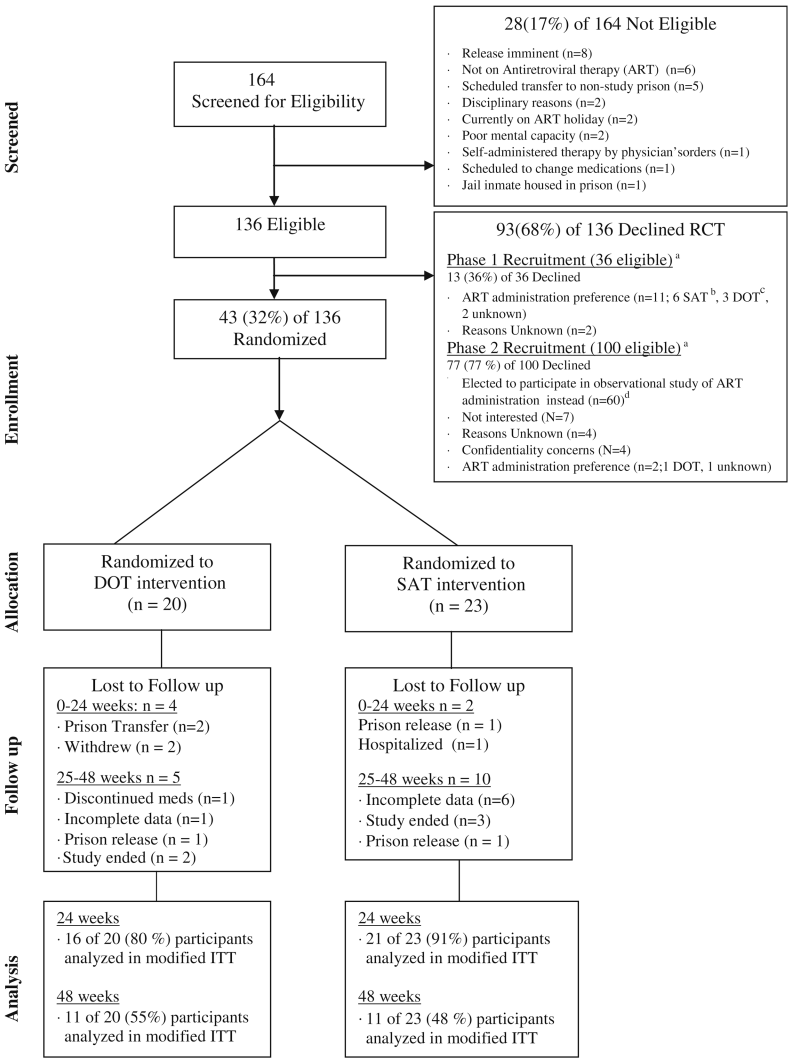

[a] After the first 4 months of recruitment (phase1), participants who met eligibility criteria for the RCT studywere also given the option of participating in a parallel observational study of ART administration during the remaining 11 months of recruitment (phase 2).
[b] SAT: Self-Administered Therapy vs [c] DOT : Directly observed Therapy). [d] Participants in the observational study were allowed to continue their current ART mode (DOT or SAT) of administration.

Fig. 1. The disposition of study participants

Table 1

Baseline characteristics of the 43 randomized controlled trial prison participants administered antiretrovirals by direct observation (DOT) versus self-administration (SAT)

Characteristic	DOT *N* = 20 (%)	SAT *N* = 23 (%)	*p*
Age, median years [IQR]	38 [34, 38]	39 [36, 39]	0.39
Male sex	17 (85 %)	20 (87 %)	1.00
Race/Ethnicity			0.26
African-American	13 (65 %)	18 (78 %)	
White	2 (10 %)	1 (4 %)	
Native American	3 (15 %)	0 (0 %)	
Hispanic/latino	0 (0 %)	1 (4 %)	
Multiracial or other	2 (10 %)	3 (13 %)	
Highest educational level[a]			0.18
8th grade or less	1 (5 %)	0 (0 %)	
Some High School	6 (30 %)	12 (52 %)	
High School Graduate/GED	4 (20 %)	5 (22 %)	
Some College	2 (10 %)	5 (22 %)	
College Graduate	5 (25 %)	1 (4 %)	
More than 4 year College Degree	1 (5 %)	0 (0 %)	
Baseline laboratory values			
Plasma HIV RNA level <400 copies/mL	2 (10 %)	12 (55 %)	0.004
HIV-1 RNA level, median $\log_{10}$ copies/mL [IQR]	3.35 [2.94, 4.47]	2.60 [2.09, 3.20]	0.01
$CD4^+$ T Lymphocyte count, median cells/μL [IQR]	461 [249, 911]	465 [312, 655]	0.96
Antiretroviral naive before study entry	11 (55 %)	8 (35 %)	0.23
Antiretroviral regimens received at study entry			0.47
PI + NRTIs	5 (25 %)	7 (30 %)	
Ritonavir-boosted PI + NRTIs	6 (30 %)	4 (17 %)	
NNRTI + NRTIs	7 (35 %)	9 (39 %)	
NRTIs only	1 (5 %)	1 (4 %)	
PI + NNRTI + NRTIs	1 (5 %)	0 (0 %)	
Ritonavir-boosted PI + PI + NRTIs	0 (0 %)	2 (9 %)	
HIV risk factor or mode of transmission[b]			0.82
Homosexual contact (MSM)	1 (5 %)	2 (9 %)	
Heterosexual contact	13 (65 %)	16 (70 %)	
Injection drug use	7 (35 %)	8 (35 %)	
Other	0 (0 %)	0 (0 %)	
Illegal substance abuse history[a,c]	16 (80 %)	20 (87 %)	0.69
Depression[d]	4 (20 %)	8 (35 %)	0.32

[a] Missing data for education level (*n* = 1, DOT arm) and substance abuse history (*n* = 1 DOT, arm, *n* = 2, SAT arm)

[b] Participants could be in more than one category if they listed multiple risk factors

[c] Participants were classified as having an illegal substance abuse history if they had ever used amphetamines, crack/cocaine, ecstasy, heroin or marijuana

[d] At study entry, participants were asked two emotional well-being items from the short-form health survey (SF-36). The questions were how much of the time during the past 4 weeks have you felt 1) “down in the dumps that nothing could cheer you up” or 2) “downhearted and depressed?” Participants were classified as depressed if they answered “all” or “most of the time” to either of the two items

Table 2

Median (%) adherence to ART regimens administered by direct observed therapy (DOT) versus self-administered therapy (SAT) among HIV-infected prisoners

At 24 weeks			*p*	At 48 weeks		*p*
Measurement Method	**DOT (*N* = 16)**	**SAT (*N* = 21)**		**DOT (*N* = 11)**	**SAT (*N* = 11)**	
MEMS						
Median % [IQR]	99.0 [93.9, 100]	98.3 [96.0, 100]	0.82	99.8 [96.3, 100]	99.9 [85.2, 100]	0.79
Pill count						
Median % [IQR]	97.1 [95.1, 99.3]	98.5 [95.8, 100]	0.40	100 [94.8, 100]	99.5 [97.0, 100]	0.84

Table 3

Virological and immunological outcomes among HIV-infected prisoners administered antiretroviral regimens by directly observed therapy (DOT) or by self-administered therapy (SAT)

At 24 weeks				At 48 weeks		
Measure	**DOT (*N* = 14)**	**SAT (*N* = 18)**	***p***	**DOT (*N* = 16)**	**SAT (*N* = 17)**	***p***
Change in $CD4^+$ T lymphocyte counts (median [IQR]) from baseline	−29.5 [−70, 147] (*N* = 17)	−2.5 [−82, 105] (*N* = 22)	0.69	9.0 [−108.0, 142.5] (*N* = 15)	31.0 [−43.0, 105.0] (*N* = 17)	0.98
Change in HIV-1 RNA levels (median $\log_{10}$ plasma viral load [IQR]) from baseline	−1.15 [−1.75, −0.05]	0.05 [−0.45, 0.51]	0.02	−0.69 [−2.64, −0.34]	0.10 [−0.18, 0.80]	0.01
Adjusted HIV-1 RNA levels (median $\log_{10}$ plasma HIV-1 viral load [IQR])[a]	2.60 [1.98, 3.08]	2.76 [2.50, 3.24]	0.27	2.44 [1.83, 2.88]	2.69 [2.24, 3.29]	0.16
Proportion of participants virological suppressed (plasma HIV-1 RNA <400 copies/mL^3)	53	32	0.21	56	44	0.48

[a] *p* values were adjusted for baseline HIV-1 RNA level