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Individualized Texting for Adherence Building (iTAB) for Methamphetamine Users Living with HIV: A Pilot Randomized Clinical Trial

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ABSTRACT

Background: Methamphetamine (METH) use poses a barrier to antiretroviral therapy (ART) adherence. We evaluated the efficacy of the individualized texting for adherence building (iTAB) intervention among persons living with HIV (PLWH) who meet criteria for METH use disorder. We examined daily associations between ART adherence and text-reported METH use and depressed mood.

Methods: We conducted a single site, 2-arm, 6-week, pilot randomized clinical trial comparing a personalized, bidirectional, text messaging system (iTAB; n=50) to an active control condition (n=25). All participants received adherence psychoeducation and daily texts assessing METH use and depressed mood. The iTAB group received personalized daily ART reminder texts. ART adherence was monitored using Medication Event Monitoring System (MEMS) caps.

Results: Response rates to daily ART reminder texts were high (79%), with good concordance between MEMS-derived and text-reported ART adherence ($p<.001$). Intervention groups did not differ in MEMS-derived ART adherence (68% iTAB, 70% active control; $p=.68$); however, participants in the iTAB group had fewer METH use days (median 14.4 iTAB, 22.0 active control; $p=.05$). Text-reported METH use, but not depressed mood, was associated with poorer MEMS-derived ART adherence.

Conclusions: High text response rates and good concordance between MEMS-derived and text-reported adherence suggests text messaging is a feasible intervention delivery approach that provides a valid indication of ART adherence. Reductions in METH use among iTAB participants suggest daily health reminders may help attenuate substance use. Further research is needed to substantiate daily text messaging as a harm reduction approach.

This trial is registered with the ClinicalTrials.gov # NCT01317277.

Keywords: Medication Adherence; HIV/AIDS; Methamphetamine; Stimulant; mHealth; Behavior Modification

1. Introduction

Antiretroviral therapy (ART) is the standard of care for persons living with HIV infection (PLWH). Suboptimal ART adherence can lead to disease progression and development of drug-resistant strains of HIV (Flandre et al., 2002; Nachega et al., 2011). Persons with substance use disorders demonstrate poorer adherence to ART compared to those without substance use disorders (Hinkin et al., 2004; Meade et al., 2011; Westergaard et al., 2012). Methamphetamine (METH) use is particularly concerning in the context of HIV care, given its high prevalence among PLWH, particularly in San Diego (Wagner, 2014), and its association with poor ART adherence (Hinkin et al., 2007; Marquez et al., 2009; Moore et al., 2012).

Text messaging is a potentially effective and low-cost means of both assessing medication adherence using ecological momentary assessment (EMA) and delivering medication adherence interventions (Horvath et al., 2012). High rates of concordance have been observed in self-reported ART adherence obtained via two-way text messaging and ART adherence assessed by electronic pill bottle caps (Harris et al., 2010). Thus, we developed the Individualized Texting for Adherence Building (iTAB) intervention, an automated, personalized, bidirectional, text messaging system that draws on aspects of the Health Belief Model (HBM), Theory of Planned Behavior (TPB), and Social Cognitive Theory (SCT) (Bandura, 2001; Becker, 1974; Godin & Kok, 1996). In particular, the iTAB message content was structured to fall into domains (e.g., social support, self-esteem) addressing individual and interpersonal factors that may influence ART adherence. Message content was designed to promote self-efficacy and reciprocal determinism (SCT), support adherence behavioral intentions (TPB), and promote the perception of benefits derived from engaging in the target health behavior (HBM). The iTAB intervention demonstrated efficacy for improving ART adherence with respect to dose timing in a study

involving PLWH with bipolar disorder (Moore et al., 2015). Other studies have used text messaging to deliver intervention content to support health behaviors among PLWH with comorbid substance use disorders (Glasner-Edwards et al., 2016; Ingersoll et al., 2015).

Based on growing evidence indicating the efficacy of text message interventions to support ART adherence (Pellowski & Kalichman, 2012) and need to better understand daily factors of nonadherence among substance users, the goal of the present study was to evaluate the iTAB intervention among PLWH who use METH. We hypothesized that participants assigned to iTAB (i.e., standard-of-care adherence psychoeducation, daily ART reminder texts, and daily texts assessing METH use and presence of depressed mood) would show better ART adherence rates as compared to participants in the active control condition (i.e., same components as iTAB except the daily ART reminder texts). We also examined whether METH use and depressed mood were related to ART adherence, and we hypothesized that a higher frequency of METH use and presence of depressed mood would correlate with poorer ART adherence among participants in both the active control and iTAB conditions. Secondary analyses examined the frequency of METH use between study arms.

2. Methods

2.1. Trial design

The study was a two-armed, parallel-design pilot randomized clinical trial (RCT). Target enrollment was 75 participants. With a randomization strategy of 2:1 to the iTAB intervention (n = 50) and active control arm (n = 25), we had 80% power to detect an effect size d of .71 for the difference in adherence rates between the two intervention arms (Wilcoxon-Mann-Whitney critical t = 1.99, df = 69.6). The unbalanced design was selected to maximize ability to investigate data within the iTAB condition. The intervention period was six weeks with in-

person assessments occurring at pre- and post-intervention. This study length was chosen as an adequate amount of time to assess changes in viral load, based on a published recommendation for measurement of plasma viral load following initiation or modification of ART regimen (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2011). The local Human Research Protection Program approved the current study.

2.2. Participants

Participants were recruited from ongoing studies of HIV infection and substance use conducted at the University of California, San Diego – HIV Neurobehavioral Research Program from November 2011 to May 2014. Inclusion criteria were the capacity to provide informed consent, age 18 years or older at enrollment, documented HIV infection, DSM-IV-TR diagnosis of METH abuse or dependence via the Composite International Diagnostic Interview (World Health Organization, 1997), self-reported METH use within 45 days of baseline, and an active prescription for ART to treat HIV. Plasma HIV viral load detectability was not an inclusionary criterion. Participants with other comorbid substance use conditions were deemed eligible if they met recruitment criteria. Participants had to be willing to respond to text messages and utilize electronic medication tracking devices (i.e., Medication Event System Monitoring TrackCaps, MEMS, AARDEX, Sion, Switzerland). Exclusion criteria were minimal (i.e., unable to show capability of responding to texts at baseline by direction observation) to enhance generalizability.

After meeting study inclusion requirements, interested participants provided written informed consent. Participants were informed that some participants would be randomly selected to receive daily ART reminder texts. Participants received monetary compensation for the initial ($50) and follow-up ($35) assessments and for returning the MEMS device ($25). Participants were reimbursed for additional costs incurred by participating in the study over their regular cell

phone use. A mobile phone with a texting plan was loaned to participants who did not own a cell phone or were unable to receive texts on their current phone (n=17 iTAB and n=11 in active control arm received a loaned phone).

2.3. Intervention (iTAB)

The iTAB intervention has been described previously in detail (Moore et al., 2013; Moore et al., 2015); therefore, the following sections briefly describe the components of the RCT.

2.3.1. Personalized ART Reminder and Reinforcement Text Messages. For this pilot RCT, iTAB was refined through focus groups to derive patient-centered intervention content for use among PLWH who use METH (Montoya et al., 2014). As a result of the focus groups, 40 ART reminder text messages that fall into eight thematic reminder stems (i.e., social support/responsibility to others, self-esteem, dangers of non-adherence, harm reduction, direct reminder, spirituality, celebration of health, and disease control) were developed.

During the first study visit, all participants selected, modified, and/or created ten personalized ART reminder text messages from the list of 40 predetermined ART reminder text messages. For participants in the active control group, these messages were printed out for participants to take with them and use as desired. The active control group did not receive daily ART reminder texts during the intervention. iTAB participants provided their preferred name and a description of their tracked ART medication to be used in the text messages. The ART reminder text was sent during the iTAB participants' specified dosing time. An example ART reminder text might read, "John, you can have fun and take ur meds. Time 4 ur big blue pill now. Pls reply A) took D) didn't G) snooze."

The iTAB system had automated features designed to optimize adherence, including a "snooze" option for the ART reminder text (i.e., the reminder was re-sent one hour later). If iTAB participants indicated they did not take his or her ART, they were sent an additional text to identify the reason for the missed dose. After three consecutive days of non-responses to the ART reminder texts, the automated system sent an "adherence alert" message to the participant and study coordinator. The study coordinator called the participant after five days of failure to respond to the ART reminder texts and each subsequent five days until the participant began responding to the system or the study period closed.

iTAB participants also selected, modified, and/or created ten reinforcement text messages from a list of 20 predetermined messages (e.g., "Great job, every dose helps" and "Keep up the good work."). The reinforcement texts were sent to reinforce events where the participant reported taking his or her ART medication. A reinforcement text might read, "Great job! Ur current adherence: 75%. Adhr when u take ur next dose: 80% (4/5 doses)."

2.3.2. Text Messages to Assess METH Use. Both groups received a daily text asking, "Have you done anything in the past 24 hours? Y) yes N) no" to assess for METH use. To protect participants from potential legal or personal ramifications associated with disclosure of METH use, the word "methamphetamine," or variants thereof, were not included in the texts. At the first study visit, participants were informed this daily text was in reference to METH use. It was emphasized that the response to this inquiry would not impact individuals' participation in the study. For each participant, we calculated the responsiveness to texts assessing METH use (# of texts responded to / # of texts received) and the proportion of days a participant endorsed METH use (# of days endorsing METH use / # of texts responded to).

2.3.3. Text Messages to Assess Depressed Mood. Both groups received a daily text assessing depressed mood and had the following response options: 0 – not at all depressed, 1 – a little depressed, 2 – moderately depressed, 3 – very depressed, and 4 – extremely depressed. For each participant, we calculated the responsiveness to texts assessing depressed mood (# of texts responded to / # of texts received) and the average severity of depressed mood endorsed during the study period (range of 0 to 4).

2.3.4. ART Adherence Psychoeducation. All participants received up to 30-minutes of ART adherence psychoeducation individually delivered by research staff via PowerPoint at the first study visit. The ART adherence psychoeducation component presented the health benefits of adherence, potential adverse ART and METH use effects, potential adherence difficulties, and practical adherence strategies. Participants had an opportunity to ask questions and speak about their own experiences adhering to medications.

2.4. Pre-Intervention Assessments

Substance use and mood disorder diagnoses were determined using the lay-administered Composite International Diagnostic Interview (World Health Organization, 1997). Severity of current depressive symptomatology was assessed via the Beck Depression Inventory-II (Beck et al., 1996), and severity of current anxiety-related symptoms was assessed via the Beck Anxiety Inventory (Beck & Steer, 1993). Participants were administered a detailed substance use interview, recording both frequency and quantity of METH use. Each participant completed a standardized medical history interview, structured neurological and medical examination, and collection of blood and urine samples consistent with previous studies at the HNRP (Heaton et al., 2011). Trained research staff conducted all medical history interviews, and a clinician (i.e., RN, NP or MD) performed the neuromedical examination

2.5. Primary Outcome: ART Adherence

2.5.1. Objective Medication Adherence. MEMS TrackCaps, which provide an electronic record of the date and time the cap is removed, were used to track ART adherence during the study period. Two primary outcome variables were derived from the MEMS data:

2.5.2. Overall MEMS Adherence. One of the primary outcome variables for analysis was overall MEMS adherence over the study period. In analyses assessing between-group differences (iTAB vs. active control), overall MEMS Adherence was defined as the percentage of taken doses (i.e., ([# of bottle openings)/ (# of prescribed doses)] *100%). In multilevel models examining daily adherence, overall MEMS adherence was a binary variable that denoted the occurrence (or non-occurrence) of MEMS Trackcap openings.

2.5.3. MEMS Adherence Based on Dose Timing. The second primary outcome variable for examining between-group differences was MEMS adherence based on dose timing (i.e., [(# of bottle openings within a ± two-hour time window of the intended dosing time)/ (# of prescribed doses)] *100%). In multilevel models examining daily adherence, MEMS adherence based on dose timing was a binary variable that indicated whether or not MEMS Trackcap openings occurred within two hours of intended dosing times.

2.6. Randomization

Prior to study enrollment, a series of participant ID's were randomly assigned to the iTAB or active control condition by a statistician. Research associates providing the psychoeducational component of the study were blinded to these assignments. A separate research staff member kept the randomization code and informed the participant of their assignment after provision of the adherence psychoeducation (but ahead of the set-up of daily text messages).

2.7. Data Analytic Strategy

Group differences between iTAB and active control participants on MEMS adherence and responsiveness to texts were examined using non-parametric methods (Wilcoxon Rank-Sum test). Two iTAB participants had brief periods when they were unable to respond to texts (e.g., incarceration), and data from these days were treated as missing rather than as non-adherent.

To account for within-subject correlations that are inherent to repeated measurements and to examine daily relationships between text responses and adherence outcomes, multilevel models were used (Bolger & Laurenceau, 2013). These analyses were carried out in Mplus v7.4 (Muthén & Muthén, 1998-2012) using robust maximum likelihood estimation, which provides standard errors for parameters that are robust to non-normality and missing data; non-response to text messages was considered as missing and modeled under standard missing data assumptions (Yuan & Bentler, 2000).

3. Results

Figure 1 provides a study CONSORT diagram detailing study enrollment and retention (Schulz et al., 2010). The demographic and clinical characteristics of the 66 study participants who completed follow-up and had analyzable MEMS adherence data are provided in Table 1.

3.1. MEMS Adherence by Intervention Arm

We examined MEMS-derived ART adherence by intervention arm and found the iTAB and active control groups did not significantly differ on the MEMS adherence outcome variables (Table 2). Given the intervention arms differed on race/ethnicity, employment status, and proportion meeting criteria for current major depressive disorder (*p's* < 0.05), we explored the relationship between these covariates and overall MEMS adherence within the whole sample. Of the three covariates, only employment status was associated with overall MEMS adherence, such

that those with employment achieved higher adherence rates (Median: 84.0% [72.6%, 90.5%]) compared to unemployed participants (Median: 69.0% [34.5%, 90.1%]; $Z = 2.59$, $p = 0.01$). The interaction of intervention group and employment status was not significantly associated with overall MEMS adherence ($p > 0.05$).

We examined the association of HIV disease indicators and MEMS-derived ART adherence outcomes. Neither estimated duration of HIV nor current CD4 count were significantly associated with overall MEMS adherence or MEMS adherence based on dose timing (p's > 0.05). AIDS status was significantly associated with overall MEMS adherence (t (62) = 2.4, $p = 0.02$, g = -0.61) but not with MEMS adherence based on dose timing ($p > 0.05$). Having an undetectable plasma viral load was significantly positively associated with overall MEMS adherence (t (63) = 3.3, $p = 0.002$, g = -0.89) and MEMS adherence based on dose timing [Welch's t (45.4) = 3.9, $p < 0.01$, g = -0.94].

3.2. Responsiveness to Text Messages by Intervention Arm

iTAB group participants were sent a median of 42 ART reminder texts. Both iTAB and active control groups received a median of 42 texts assessing METH use and depressed mood across the 42-day study period. iTAB participants responded to a median of 78.6% [64.3%, 90.5%] ART reminder texts. There were no significant differences in the responsiveness rates to METH (iTAB: Median = 79.8% [69.05%, 91.6%] vs. active control: Median = 83.3% [70.0%, 92.7%]; Z = 0.56, $p = 0.57$) or mood (iTAB: Median = 83.3% [71.4%, 92.9%] vs. active control: Median = 88.1% [69.1%, 90.5%]; Z = 0.10, $p = 0.92$) texts. Regarding text-reported METH use, participants in the iTAB group reported fewer days of METH use than participants in the active control group (iTAB: Median = 14.4 [0, 33.6] vs. active control: Median: 22.0 [7.3, 65.6]; Z = -

1.97, $p = 0.05$). Severity of depressed mood responses did not differ by intervention arm (iTAB: Median = 0.33 [0.07, 0.93] vs. active control: Median: 0.48 [0.04, 0.86]; $Z = -0.09$, $p = 0.92$).

3.3. Daily MEMS adherence and daily ART text responses

Within the iTAB group, the most common response to ART reminder text was 'Took', at 68.4%, followed by a non-response at 23.9%, 'Snooze' at 5.4%, and 'Didn't Take' at 2.3%. The relationship between MEMS adherence and text-reported ART adherence was examined in correlations and in multilevel regression models that took into account the effect of progression of time in the study. The correlation between overall MEMS adherence and text-reported ART adherence was significant at the within-person ($r = 0.19$, $p < .001$) and between-person levels ($r = 0.44$, $p < .001$). Similarly, the correlation between MEMS adherence based on dose timing and text-reported ART adherence was significant at the within-person ($r = 0.13$, $p < .001$) and between-person levels ($r = 0.46$, $p < .001$). When these relationships were examined in multilevel models accounting for time (Table 3), text-reported ART adherence was significantly associated with overall MEMS adherence ($B = 2.12$, $OR = 8.31$, $p < .001$) and MEMS adherence based on dose timing ($B = 2.86$, $OR = 17.48$, $p = .001$). This was such that, on a day on which a participant text-reported ART adherence, he/she had greater odds of a MEMS cap opening and greater odds of the cap opening occurring within 2 hours of his/her dosing time. Associations between MEMS outcomes and text-reported ART adherence were similar at the between-person level such that individuals with a higher rates of text-reported ART adherence had significantly greater overall MEMS adherence ($B = 6.27$, $p = .023$) and significantly greater MEMS adherence based on dose timing ($B = 8.50$, $p = .001$).

3.4. Daily MEMS adherence and daily reports of METH use and depressed mood

We examined associations between MEMS adherence outcomes and text-reported METH use and depressed mood during the study period. Among iTAB participants, text-reported METH use was significantly correlated with lower overall MEMS adherence (r= -0.07, p = 0.03) and lower MEMS adherence based on dose timing (r = -0.05, p = 0.04) at the within-person level, indicating that when individuals reported METH use via text, they were generally non-adherent. At the between-person level, text-reported METH use was marginally associated with MEMS adherence based on dose timing (r = -0.30, p = 0.08), indicating that participants who report METH use also report poorer adherence. Among active control participants, text-reported METH use was significantly correlated with overall MEMS adherence and MEMS adherence based on dose timing at the between-person level only (r = -0.46, p = 0.01 and r = -0.52, p < 0.001). No significant correlations were observed between MEMS adherence outcomes and text-reported severity of depressed mood among either iTAB or active control participants.

When examined in multilevel regression models (Table 4), at the within-person level, text-reported METH use was marginally associated with a decreased same day probability of MEMS adherence based on dose timing (B = -0.26, OR = 0.77, p = .08), above and beyond concurrent depressed mood severity. No significant daily associations were found between text-reported METH use and overall MEMS adherence, controlling for text-reported depressed mood. At the between-person level, individuals with greater reports of METH use tended to have poorer overall MEMS adherence (B = -2.08, p = .01) and poorer MEMS adherence based on dose timing (B = -2.57, p = .002). No significant between-person associations were found for text-reported depressed mood, above the effect of METH use, group assignment, and time.

4. Discussion

The present study examined the efficacy of an automated, personalized, bidirectional, text messaging system to support ART adherence among PLWH with recent and ongoing METH use. The iTAB group did not significantly differ from the active control group in overall rates of ART adherence based on monitored pill cap openings; however, participants in the iTAB group reported using METH on fewer days during the intervention period. For the iTAB group, we observed a daily association between text-reported ART adherence and MEMS adherence. Although previous studies have found good concordance between self-reports of adherence and MEMS adherence, these studies have used global retrospective recalls of adherence or daily average text-reported adherence, rather than daily correlations between the two (e.g., Harris et al., 2010; Walsh et al., 2002). Thus, this study is the first to report significant day-day within-person associations between text-reported adherence and MEMS adherence. Last, for the combined pool of iTAB and active control participants, we observed a daily association between text-reported METH use and poorer ART adherence. Overall, this study supports the feasibility of using text messaging to explore the contemporaneous relationship between METH use and ART adherence.

Contrary to the primary hypothesis, the iTAB and active control groups did not significantly differ in their levels of MEMS-derived ART adherence during the study period. Furthermore, intervention arms did not differ in post-study HIV disease characteristics related to ART adherence (i.e., CD4 count and viral load). This lack of a significant effect of daily ART reminder texts and related outcomes in the iTAB group may be the result of our active control condition, which involved psychoeducation and receipt of daily texts assessing METH use and depressed mood. Many of the bidirectional-texting studies for ART adherence that have shown significant effects had passive control conditions without daily texts (e.g., Ingersoll et al., 2015;

Finitsis et al., 2014). Results from a recent meta-analysis suggest mobile health interventions with active control conditions generally yield smaller effect sizes than interventions without active control conditions (Firth et al., 2017). Indeed, during debriefing, some participants in the active control arm reported the daily METH use and depressed mood prompts served as daily reminders for ART adherence, which is consistent with participant feedback from a previous study indicating EMA prompts increase self-awareness of behaviors (Freedman et al., 2006).

We hypothesized that METH use and depressed mood would negatively impact ART adherence. We found that METH use was associated with a decrease in probability of on-time ART adherence on the same day, above and beyond depressed mood. Individuals with greater METH use across the study period tended to be those with poorer adherence. These results, showing daily and adverse effects of METH use on adherence, confirm prior research that has shown day specific effects of METH use on ART adherence (Parsons et al., 2013). Interestingly, we observed that participants in the iTAB arm reported fewer days of METH use during the intervention period than those in the active control arm. A possible reason underlying the lower rates of METH use among iTAB participants may be that the daily texts, generally rooted in models of health behavior change, may have promoted greater self-efficacy and awareness of substance use. Thus, although this study did not directly aim to intervene on METH use, these results suggest the possibility that daily reminders to attend to one's health (e.g., adhering to a medication regimen) may moderate substance use. Additional intervention studies utilizing a harm reduction approach are needed to substantiate this possibility.

Some limitations of this study should be noted. Although MEMS caps are considered to be a gold standard method of assessing medication adherence, their use has some drawbacks. MEMS caps may be potentially inaccurate when individuals use other methods of medication

storage (e.g., pillboxes), and use of MEMS caps as a monitoring tool may alter participants' adherence behaviors. Given the high correlation between text-reported ART adherence and MEMS data among iTAB participants, utilization of the MEMS cap likely approximated actual medication-taking behavior. Although text message content variability and personalization were provided to participants, we hypothesize that greater variability in message content may enhance novelty. Future studies may want to consider greater content variability and text-message systems capable of adaptively responding to the nuances of participant responses. Despite these limitations, results suggest the possibility of modest to good engagement in text messaging interventions among individuals with active substance use.

In summary, this study sought to examine the effect of a bidirectional text messaging system on ART adherence among PLWH with comorbid METH use. Although no between-group differences were found between the intervention and active control group, we found the intervention to be feasible and to have good participant response rates. Additionally, participants in the iTAB group had fewer reported days of METH use than those in the active control group. Furthermore, METH use was observed to have deleterious daily and cumulative effects of on ART adherence, underscoring the necessity of harm reduction as a concomitant goal in interventions to improve medication adherence among those with active substance use.

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Figure 1. CONSORT 2010 Flow Diagram

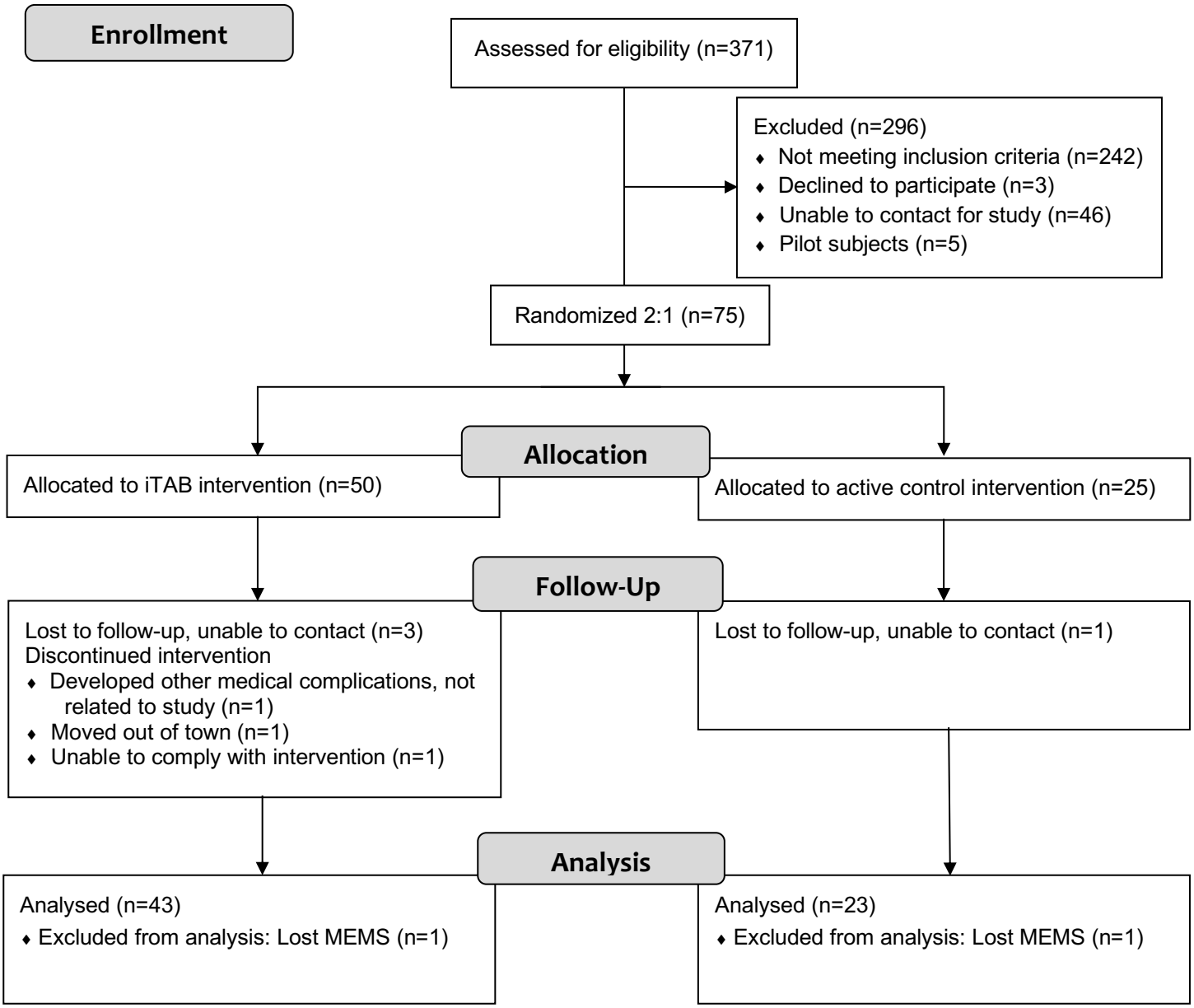

Table 1. Baseline participant characteristics by intervention arm (N = 66)

	iTAB (n = 43)	**Active Control** (n = 23)	***p*-value**	**Effect size**
Descriptive				
Age; mean (SD)	45.4 (7.7)	46.0 (8.9)	.78	g = -0.07
Years of education; mean (SD)	13.1 (2.8)	13.7 (2.5)	.45	g = -0.20
Male; n (%)	40 (93.0%)	23 (100%)	.55	-
Sexual orientation			.32	
Gay/bisexual; n (%)	37 (86.0%)	17 (73.9%)		OR = 2.18
Heterosexual; n (%)	6 (14.0%)	6 (26.1%)		OR = 0.46
Race/Ethnicity			.04	
Non-Hispanic white; n (%)	23 (53.5%)	7 (30.4%)		OR = 2.63
Black; n (%)	15 (34.9%)	7 (30.4%)		OR = 1.22
Hispanic; n (%)	5 (11.6%)	8 (34.8%)		OR = 0.25
Pacific Islander; n (%)	0 (0.0%)	1 (4.3%)		-
Employed; n (%)	15 (34.9%)	2 (8.7%)	.04	OR = 5.63
HCV infected; n (%)	10 (23.3%)	4 (17.4%)	.75	OR = 1.44
HIV Disease Characteristics				
Estimated duration of HIV (years); median [IQR] [a]	10.6 [4.4, 19.6]	13.5 [4.7, 19.7]	.64	g = -0.10
AIDS; n (%) [b]	25 (62.5%)	13 (56.5%)	.64	OR = 1.28
CD4 Count; median [IQR] [a]	595 [375, 775]	479 [178, 605]	.07	g = 0.49
Nadir CD4 Count; median [IQR] [c]	167 [42, 360]	196 [12, 280]	.48	g = 0.22
Undetectable plasma viral load (<50 cp/ml); n (%) [c]	31 (73.8%)	14 (63.6%)	.40	OR = 1.61
Antiretroviral therapy (ART)				
Prescribed once daily regimen; n (%)	41 (95.4%)	21 (91.3%)	.61	OR = 1.95
Months on current regimen; median [IQR] [d]	25.5 [11.9, 50.3]	17.9 [5.0, 44.5]	.19	g = 0.36
Months on any ART regimen; median [IQR] [b]	75.9 [33.8, 134.1]	93.6 [49.7, 177.0]	.31	g = -0.27
Methamphetamine (METH) Use Characteristics				
Age of first use; median [IQR] [e]	23.0 [15.8, 27.8]	16.5 [9.5, 23.5]	.09	g = 0.34
Days since last use; median [IQR] [f]	4.5 [2.0, 20.8]	4.0 [1.5, 14.0]	.75	g = 0.10
Quantity (grams) consumed in past year; median [IQR] [d]	8.4 [2.6, 39.3]	9.8 [1.5, 41.5]	.90	g = 0.13
Days of use in past year; median [IQR] [d]	24.0 [11.0, 52.6]	19.9 [4.3, 104.2]	.63	g = 0.34
History of treatment for METH use; # (%)	33 (76.7%)	17 (73.9%)	1.00	OR = 1.16

Psychiatric				
BAI Total; median [IQR]	26 [23, 38]	27 [22, 32]	.48	g = 0.32
BDI-II Total; median [IQR]	13 [3, 19]	14 [1, 21]	.61	g = 0.15
Lifetime MDD; # (%)	29 (67.4%)	14 (60.9%)	.60	OR = 1.33
Current MDD; # (%)	9 (20.9%)	0 (0%)	.02	-
ADHD; # (%) [c]	7 (16.7%)	0 (0%)	.09	-
ASPD; # (%) [c]	14 (33.3%)	5 (22.7%)	.57	OR = 1.70

Note: Nadir CD4 count is calculated as the lowest of self-reported or laboratory generated value. Effect size compared iTAB to active control. BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory-II; HCV = Hepatitis C Virus; g = hedge's g, which is based on standardized mean difference; IQR = interquartile range; MDD = Major Depressive Disorder; OR = odds ratio.
[a] n=50, [b] n=63, [c] n=64, [d] n=65, [e] n=58, [f] n=61,

Table 2: Between-group differences in MEMS adherence (N = 66)

	iTAB	**Active Control**	**Difference Test**	**Effect Size**
	Mean (SD)	Mean (SD)	Wilcoxon-Rank Statistic	
Overall MEMS Adherence (%)	68.0 (0.3)	70.4 (0.3)	$Z = 0.42$, $p = 0.68$	$r = 0.05$
MEMS dose timing (mins)	181.0 (133.1)	195.2 (129.9)	$Z = 0.51$, $p = 0.61$	$r = 0.06$
MEMS adherence based on dose timing (%)	43.9 (32.2)	45.5 (30.5)	$Z = 0.06$, $p = 0.95$	$r = 0.01$

Note. The effect size, *r*, was calculated as *Z*/sqrt(n) (Rosenthal, 1991).

Table 3. Multilevel Models of Daily ART Text Responses Predicting Daily MEMS Adherence among Participants in the iTAB Arm (n = 43)

Effect	Odds Ratio	Estimate	Standard Error	95% Confidence Interval	
				Lower	Upper
Outcome: MEMS overall adherence					
Within-person level					
Text Response	8.306	2.117***	0.501	1.135	3.099
Study day	0.960	-0.041***	0.009	-0.059	-0.024
Between-person level					
Text Response	-	6.269*	2.753	0.874	11.665
Outcome: MEMS adherence based on dose timing					
Within-person level					
Text Response	17.479	2.861**	0.827	1.240	4.482
Study day	0.966	-0.035***	0.007	-0.049	-0.021
Between-person level					
Text Response	-	8.501**	2.480	3.639	13.362

Note.
† p <.10. * p < .05. ** p < .01., *** p < .001.

Table 4. Multilevel Models of Daily Meth and Depressed Mood Text Responses Predicting Daily MEMS Adherence (N = 66)

Effect	Odds Ratio	Estimate	Standard Error	95% Confidence Interval	
				Lower	Upper
Outcome: MEMS overall adherence					
Within-person level					
METH	0.809	-0.212	0.207	-0.617	0.193
Mood	0.964	-0.037	0.102	-0.236	0.163
Study day	0.969	-0.032***	0.008	-0.047	-0.016
Between-person level					
METH	-	-2.081**	0.791	-3.631	-0.532
Mood	-	0.182	0.262	-0.332	0.696
Group	-	-0.606	0.470	-1.527	0.315
Outcome: MEMS adherence based on dose timing					
Within-person level					
METH	0.775	-0.255†	0.145	-0.540	0.030
Mood	0.879	-0.129	0.089	-0.303	0.046
Study day	0.975	-0.025***	0.006	-0.037	-0.012
Between-person level					
METH	-	-2.566**	0.826	-4.185	-0.947
Mood	-	0.409	0.261	-0.102	0.919
Group	-	0.572	0.505	-1.562	0.419

Note. $N = 66$ individuals (23 active control and 43 intervention).
† $p < .10$. * $p < .05$. ** $p < .01$., *** $p < .001$.