

Contents lists available at ScienceDirect

Preventive Medicine Reports



journal homepage: www.elsevier.com/locate/pmedr

Smartphone-based incentives for promoting adherence to antiretroviral therapy: A randomized controlled trial

Anthony DeFulio^{a,*}, Amanda Devoto^a, Haily Traxler^a, David Cosottile^a, Michael Fingerhood^b, Paul Nuzzo^c, Jesse Dallery^d

^a Western Michigan University, United States

^b Johns Hopkins University School of Medicine, United States

 $\stackrel{\rm c}{}$ University of Kentucky, United States

^d University of Florida, United States

ARTICLE INFO

Keywords: Antiretroviral therapy HIV Adherence Incentives Contingency management Smartphone mHealth remote intervention

ABSTRACT

Antiretroviral therapy can improve the lives of people living with HIV and reduce the rate of transmission. However, high levels of adherence are required. Some people living with HIV, including people who use drugs, are at elevated risk for non-adherence. Contingency management is a promising intervention for promoting adherence to antiretroviral therapy. Barriers to adoption of contingency management include lack of provider expertise and implementation effort. To address these barriers, a smartphone-based adherence intervention was developed. HIV + people with a substance use disorder were required to submit video selfies of medication consumption that met validity criteria. Monetary incentives were delivered to participants via reloadable debit cards, contingent upon a valid video. The intervention was evaluated in a small (n = 50) randomized controlled trial. Intervention participants submitted 75% of possible videos, and 81% of videos met validity criteria, indicating a high level of usability. Participants also rated the intervention as highly acceptable. Adherence was measured as the percent of participants who achieved a 95% adherence threshold, and also as the overall percent of days in which participants were adherent to their antiretroviral therapy. The former showed a significant effect for group, (p = .034) but this was not maintained when adjusting for stratification variables as covariates (p = .094). The latter measure showed a significant group \times time interaction. Smartphone-based contingency management is a promising method for promoting adherence to antiretroviral therapy. Assessing the cost-benefit of the intervention and development of strategies for long-term adherence are priorities for future research.

1. Introduction

Injection drug use and crack cocaine use are major factors that underlie the transmission of HIV (HIV/AIDS and Drug Abuse: Intertwined Epidemics, 2012). An analysis of communities with high rates of poverty and HIV found that heterosexual injection drug users and non-injecting crack cocaine users have substantially higher rates of HIV seroprevalence (9.5% and 11.1%, respectively) when compared to individuals reporting no drug use (3.2%) (Kuo et al., 2011). In addition to being major risk factors for HIV transmission, injection drug use and cocaine use are complicating factors in the treatment of HIV and are associated with reduced ART adherence (Rosen et al., 2013).

Antiretroviral therapy (ART) increases life expectancy and quality of

life for individuals infected with HIV, and can reduce the chance of HIV transmission (Cohen et al., 2011; Hull and Montaner, 2011). These personal and public health benefits require a high level of medication adherence (King et al., 2005; Pham, 2009) High rates of virologic suppression can be achieved with an adherence rate of 90% (Bangsberg, 2006), but adherence of 95% or more produces the best combination of a higher probability of virologic suppression and a lower probability of the development of resistance to the medications (Lucas, 2005; Raffa et al., 2008). For these reasons, behavioral interventions designed to promote ART adherence in low-income people who have opioid or cocaine use disorders may be helpful for the people receiving the intervention and beneficial for their communities.

Several types of interventions have been effective in promoting

https://doi.org/10.1016/j.pmedr.2021.101318

Received 22 August 2020; Received in revised form 23 November 2020; Accepted 21 December 2020 Available online 7 January 2021 2211-3355/© 2021 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0y).

^{*} Corresponding author at: Department of Psychology, Western Michigan University, 1903 Western Michigan Ave., Mail Stop 5439, Kalamazoo MI 49009, United States.

E-mail address: anthony.defulio@wmich.edu (A. DeFulio).

short-term ART adherence in individuals who use drugs. Reminders and counseling strategies each have modest beneficial effects (Altice et al., 2010). Other approaches have been even more successful. This includes directly administered ART (DAART; akin to the more generic Directly Observed Therapy; DOT), medication-assisted therapy (e.g., methadone), contingency management (i.e., provision of incentives contingent upon adherence), and multi-component nurse delivered interventions (Binford et al., 2012). However, a core problem with all ART adherence interventions is that their effects do not appear to last after the interventions are discontinued (Simoni et al., 2010). Commenting on this in their systematic review of ART adherence interventions for drug users, Binford et al. (p. 287) Binford et al. (2012) expressed concern over the "virtual lack of interventions with sustained post-intervention adherence and virologic benefits." The common finding of postintervention dissipation of effects suggests that ART adherence interventions may need to be implemented as long-term or permanent adjuncts to ART for drug users.

A fundamental question for any intervention designed for long-term implementation is whether that intervention's effects are actually sustained when the intervention is maintained over the long-term. Contingency management interventions have a well-established history of long-term efficacy. When targeting drug abstinence, the effects of contingency management are durable over one to three years (Silverman et al., 2004, 2002, 2012; DeFulio et al., 2009). Contingency management has also been a broadly effective approach in promoting adherence to a variety of medications, including antiretrovirals (see DeFulio and Silverman, 2012 for a review) (DeFulio and Silverman, 2012). Thus, contingency management adjunct to ART because it has proven efficacy in improving short-term ART adherence and in improving long-term drug abstinence.

Implementation of long-term behavioral intervention can be burdensome to care providers and patients. Computer and mobile technologies can greatly reduce these burdens by automating functions that previously required ongoing human attention and reducing the effort associated with participation. Smartphones are especially promising as delivery devices for behavioral interventions because they contain all the necessary functionality and because they have been adopted by people of all income levels. A systematic review of SMS interventions reveals only "limited evidence on the effectiveness of mobile phone messaging for HIV care," (Van Velthoven et al., 2013) but smartphones are capable of delivering a more intensive intervention because they are not limited to SMS technology. The long-term durable nature of incentive interventions in particular recommends their inclusion in smartphone-based intervention, which may otherwise have limited effects in the long-term care of high-risk populations (De Jongh et al., 2012).

The purpose of the present study was to conduct a preliminary evaluation of the usability, acceptability, and efficacy of a smartphonebased incentive intervention designed to promote adherence to ART in low-income drug users. The intervention included provision of monetary incentives contingent upon ART adherence as demonstrated by usersubmitted selfie videos, as well as medication reminders and easy access to adherence-related information.

2. Method

2.1. Participants

Fifty individuals living with HIV participated in this study. Participants were recruited from the Baltimore area through flyers, in-person contact during medical appointments, and phone recruitment based on IRB-approved lists collected as part of other HIV studies. Participants were recruited between May 2016 and October 2017, and data collection was completed in March 2018. Participants were included in the study if they were 18–100 years old, HIV-positive, received HIV related

care including Antiretroviral Therapy (ART) from a HIV care provider, met DSM-5 criteria for a substance use disorder spoke fluent English, and could operate a smartphone. Participants were excluded if they reported suicidal or homicidal ideation, active hallucinations, or were enrolled in another HIV or medication adherence related study.

3. Materials

All participants received a Medication Event Monitoring System (MEMS)® cap which was affixed to their primary HIV medication bottle in place of the standard cap. The MEMS® cap recorded each time a participant opened their medication bottle. These data were used as a measure of adherence for all participants. All participants received a reloadable debit card. The debit card functioned as a credit card in that it could be used to purchase items but not to make cash withdrawals. The card did not work at liquor stores or bars. Researchers loaded money onto the gift cards using CTPayer®, a HIPAA-compliant financial service used for making anonymous payments in the context of clinical trials.

In addition to the materials described above, participants in the intervention condition (described below) also received a Samsung Galaxy PrevailTM smartphone for six months. The phone and phone service were provided to the participants at no cost throughout the study period. At the end of the study, participants could choose between receiving \$100 in exchange for the phone or keeping the phone. Each smartphone was pre-loaded with the intervention app.

4. Procedures

Design. This randomized controlled pilot study featured a two-group parallel design. Participants were assigned to receive the smartphone-based intervention as well as usual care (intervention group) or usual care only (control group). Study participation lasted for 6-months.

Study enrollment. Participants who met initial inclusion criteria based on a brief screen were asked to provide informed consent prior to completing an intake assessment to fully determine eligibility. An outreach coordinator met with participants to obtain informed consent and determine eligibility based on inclusion/exclusion criteria and ability to use a smartphone. If a participant met inclusion criteria, the complete intake assessment interview was conducted immediately.

Surveys. During all intake and monthly assessments, participants completed surveys. Surveys were conducted using Qualtrics® survey software. The intake assessment surveys were completed independently with remote supervision and minimal guidance from a research staff member who had access to their computer screen using TeamViewer© software and audio contact with the participant via a headset. All monthly assessments were administered over the phone. Table 1 displays each survey used in the study and the time of administration. Surveys included the Smartphone Assessment Protocol, Test of Functional Health Literacy in Adults (TOFHLA) (Parker et al., 1995; Kerr et al., 2012), Visual Analog Scale for self-reporting ART adherence (VAS) (Buscher et al., 2011), Medical Outcomes Study HIV Health Survey (MOS-HIV) (Wu et al., 1997), Addiction Severity Index-Lite (ASI-Lite) (McLellan et al., 1985), Patient Reactions Assessment (PRA) (Galassi et al., 1992), SteadyRx Satisfaction Questionnaire, and Software Usability Measurement Inventory (SUMI) (Kirakowski and Corbett, 1993).

Randomization and initial training. Urn randomization was used to determine group assignment with a 1:1 allocation ratio for groups. Three dichotomous stratification variables were used. These included current depression, self-reported drug use within the last 30-days, and whether their score on the TOFHLA was higher than the rolling median. These variables were selected because they have been shown to correlate with low levels of ART adherence (Rosen et al., 2013; Springer et al., 2012; Kalichman et al., 2008). The stratification routine was carried out by a study team member who had no direct contact with study participants.

Once the group assignment had been determined, the outreach

Table 1

List of survey assessments and timepoints of survey delivery.

Survey	Description	Intake	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
Smartphone Assessment Protocol	Assesses participants' ability to use a smartphone.	Х						
TOFHLA	Standard measure of health literacy used to predict ART adherence*	Х						
VAS	Provides highest quality self-reports of ART adherence in recent studies $$	Х	Х	Х	Х	Х	Х	Х
MOS-HIV	Assessment of quality of life for patients with HIV. Assesses perceived physical/mental health	Х	Х	Х	Х	Х	Х	Х
ASI-Lite	Assesses drug use and related problem severity	Х	Х	х	х	х	х	Х
PRA	Assesses patients' perceived ability to initiate communication about illness. Used to determine effect of consult element of SteadyRx	Х	Х	Х	Х	Х	Х	х
SteadyRx Satisfaction Questionnaire	Assesses satisfaction of services provided by SteadyRx application		Х	Х	Х	Х	Х	х

* see Kalichman et al. (2008).

** see Buscher et al. (2011).

coordinator was informed and provided all relevant materials to the participant. Participants assigned to the intervention condition then received training specific to the use of the app. After intake, all participants were paid \$50 via the reloadable debit card.

Intervention smartphone app. The intervention smartphone app was called "SteadyRx." Each participant in the intervention condition received a unique username and password, which were required to access the app. Successful entry of username and password opened a menu screen with three options displayed as buttons. From this screen the user could navigate to any of the three parts of the app.

The "PillWatch," part of the app was for recording and submitting selfie videos demonstrating ART adherence. Videos were time stamped and could only be recorded during a 6-hour dosing window that was consistent with the participants' prescription. The videos were checked daily by two researchers. In order to qualify for the incentive the participant was required to (1) show the pill bottle to verify it was the proper medication, (2) remove the cap, (3) remove a pill, (4) place the pill in their mouth, (5) swallow, and (6) perform a mouth check after swallowing. Participants had to follow all steps on camera for acceptance. For the first seven video submissions participants completed in the study, all attempts to submit a video were accepted independent of whether they met the criteria, and detailed feedback was provided. After the training period, participants received specific feedback on all submitted videos, but submissions that did not meet one or more criteria were not approved. To further facilitate successful submission of timely videos, the app sent daily SMS notifications to the participant's smartphone 30 min prior to the start of the dosing window.

The "MyRewards" part of the app allowed participants to monitor their monetary incentive earnings. Participants could see the number of consecutive days of medication adherence, days left until a bonus was earned, total earnings, and the current balance of incentives that had been earned but were pending disbursement to their cards. Earnings were disbursed within 24 h anytime that the pending amount exceeded \$10. Finally, "InTouch" part of the app provided listings and contact information for a variety of community resources, pdf files that explained the benefits of ART adherence, and instructional materials related to the use of the app.

Adherence incentives. Intervention participants received \$2 for each video that met the criteria described above. When a participant submitted three videos that met criteria on three successive days, that participant received a \$6 bonus. Participants who submitted correct videos on 29 out of every 30 days also received a \$20 bonus. Thus, 30 days of perfect adherence yielded payments totaling \$140.

Monthly assessments. All participants were scheduled for six 30-day assessments. Participants brought their medication bottle with the MEMS® cap to the outreach coordinator, who placed the cap on an automatic reader to upload the complete record of pill bottle openings. Participants were paid \$20 for bringing their MEMS® cap to the

outreach coordinator. All participants could also provide CD4/RNA lab work and were paid up to \$100 twice throughout the study for undetectable RNA levels (i.e., <20 copies/ml) on tests conducted after study enrollment. After the outreach coordinator completed the MEMS® cap reading and obtained lab work, the surveys scheduled for that assessment were administered over the phone. Participants were paid \$30 for completing surveys.

4.1. Data analysis

Groups were compared on intake variables using Fisher's exact tests for dichotomous variables, chi-square tests for categorical variables with more than two categories, and t-tests for continuous variables. The primary outcome measure was a dichotomous (Y/N) measure of whether a participant achieved 95% adherence in each study month, as measured by MEMS. This measure was analyzed with generalized estimating equations (GEE) (Zeger et al., 1988), including and excluding the stratification variables as covariates. GEE results presented use the covariate model unless otherwise specified. Planned comparison t-tests were used to compare between and within groups on outcome measures at time points 1 and 6. The secondary outcome measure for adherence was the percentage of adherence achieved by each participant in each month as measured by MEMS. Exploratory analyses were also conducted on mental and physical well-being scales of the MOS-HIV survey, selfreported drug use on the ASI-Lite, and the relationship with care providers as assessed by the PRA. All secondary and exploratory analyses were conducted using mixed models with group and time as factors. Analyses were intent-to-treat and conducted using SAS version 9.3. Missing data were treated as missing-missing. Analyses were two-tailed with statistical significance set at alpha of 0.05. Because participants only submitted biometric data when it showed undetectable viral load, analyses for these variables were not conducted. Note that because this study was a pilot clinical trial that was designed principally to show feasibility and acceptability of the intervention, no power analysis was conducted. Instead, the data collected in this study were intended to be the basis of a power analysis for a fully powered future study. However, in order to understand the magnitude of effects that could be detected in the present study, effect sizes were calculated for the primary and secondary measures.

5. Results

Participant flow and demographics. Sixty-three people were invited to complete the intake interview (see Fig. 1). Twelve people were excluded because they did not meet all of the inclusion/exclusion criteria. Fifty-one people were randomized, but one person deleted the app off of the phone before the intervention started the next day and was lost to the study. The remaining 50 people were included in the analysis.

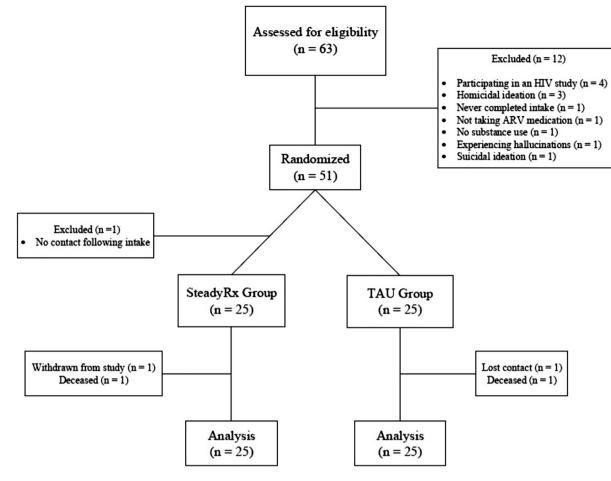


Fig. 1. Participant flow throughout study.

Participant demographics are represented in Table 2. The participants were largely middle aged, Black, unemployed, and low-income. Over 90% of both groups had an undetectable viral load at intake. Gender was the only demographic characteristic that was significantly different between groups, with more female participants in the intervention group (p = 0.047).

Medication adherence. Fig. 2 shows the percent of participants in each group that were adherent to ART on at least 95% of days in each study month as measured by MEMS. The difference between the groups

Table 2

Participant demographics with means and standard deviations. These measures were collected during the intake assessment.

Variable	Steady Rx (N $=$ 25)	TAU (N = 25)
% Female	68	36
Age (years)	52.36 ± 10.69	54 ± 7.81
Race % (B/W/O)	92/4/4	84/12/4
Education (years)	11.96 ± 1.24	11.88 ± 2.13
% Employed	20	24
TOFHLA score*	85.16 ± 12.36	80.28 \pm
		15.27
% Clinically depressed*	36	44
% Self-reported use of opiates or cocaine, last 30 days*	36	24
% Self-reported use of opiates or cocaine, lifetime	96	92
Annual income, USD	8.9 K (4.4)	9.9 K (6.1)
% Undetectable Viral Load, intake	91.3	96

Note. * indicates a stratification variable. Bolded variables indicate a statistical difference at the 0.05 level.

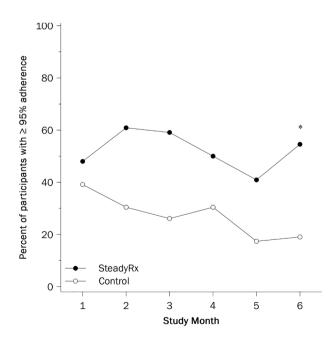


Fig. 2. Percent of groups that were 95% adherent or greater across study months as measured with MEMS. Significant differences between groups is represented with *.

that were 95% adherent increased over the study months. At the end of month one the groups were somewhat similar, at 39% and 48% for the control and intervention groups, respectively, p = .717. The groups separated across time, with percent of adherent participants decreasing in the control group, resulting in a significant difference between groups at study month 6, p = .037. GEE analysis showed a significant effect for group, $\chi^2(1, N = 50) = 4.48$, p = .034. This effect was small ($\phi = 0.143$). When adjusting for the stratification variables as covariates, the group difference was not significant, $\chi^2(1, N = 50) = 2.8$, p = .094.

Fig. 3 shows group means for percent adherence across study months as measured by MEMS. The intervention group increased from 81.7% to 89.9% from month 1 to month 2 and remained relatively stable across the remaining months. The control group was 80.4% adherent in study month 1, then decreased across study months. At the end of month 6, the difference between groups was approximately 16 percentage points. The covariate excluded and covariate included models both showed a significant group × time interaction, F(5, 214) = 3.3, p = .007 and F(5,214) = 3.35, p = .006, respectively. The model with no covariates had a significant difference between the groups at month six, p = .036, but the covariate model did not. As with the primary dependent measure, this effect was small ($\eta 2 = 0.027$). The TOFHLA and depression variables were significant covariates in this model, p = .009 and p = .041, respectively.

On average, the control group self-reported 91.10% (*SEM* = 1.42%) adherence and the intervention group reported 94.34% (*SEM* = 0.94%). There were no significant differences between groups, F(1, 45) = 0.66, p = .42, and no group × time interactions, F(6, 258) = 1.3, p = .257.

Smartphone application usability and acceptability. Fig. 4 shows the percent of possible selfie videos that were submitted, and of those that were submitted, the percentage that were accepted. These data include only intervention participants, as control group participants did not have the opportunity to submit videos. Intervention participants submitted between 3% and 100% of possible videos, with a mean of 75%. The percent of submitted videos that were accepted ranged from 25% to 100% across participants, with a mean of 81%.

Fig. 5 shows acceptability of the intervention from the intervention participants. The top left panel shows a composite acceptability score made up of the mean of the participants' responses to the questions. Overall, the intervention had high acceptability that was maintained

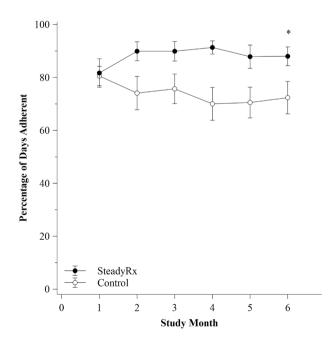


Fig. 3. Medication adherence of groups across study months as measured with MEMS. Error bars represent SEM. Significant differences between groups is represented with *.

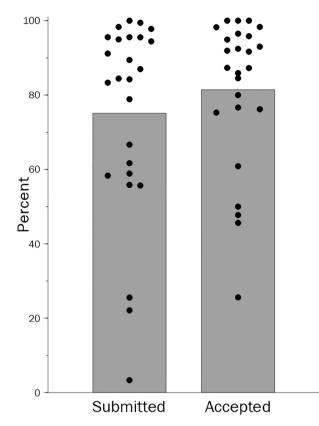


Fig. 4. Percentage of videos that were submitted and percentage of videos that were accepted across all study time points. Dots represent individual participants, and the bar represents the mean.

over time.

Overall well-being. The control group had a mean Mental Health score on the MOS-HIV questionnaire of 51.37 (*SEM* = 0.97) and the SteadyRx group had a mean score of 54.61 (*SEM* = 0.66), indicating slightly higher scores than the normal population. This difference was not statistically significant, F(1, 45) = 2.52, p = .119. At month 6, there was no significant difference between the control group (M = 51.12, *SEM* = 2.66) and the SteadyRx group (M = 56.03, *SEM* = 1.74), p = .073.

For Physical Health scores on the MOS-HIV questionnaire, the control group had an overall mean of 42.75 (SEM = 1.02) and the SteadyRx group had an overall mean of 45.63 (SEM = 0.91), indicating slightly lower scores than the normal population. This difference was not significant, F(1, 45) = 1.11, p = .296. At month 6, there was no significant difference between the control group (M = 40.67, SEM = 2.93) and the SteadyRx group (M = 46.88, SEM = 2.80), p = .068.

Depression was a significant covariate for both Mental Health scores (p = .014) and Physical Health scores (p = .007). Recent drug use at intake was a significant covariate for Physical Health scores (p = .020) but was not significant for Mental Health scores (p = .057).

Drug use. The proportion of recent opiate or cocaine use ranged from 0.17 to 0.30 for the control group and 0.10 to 0.28 for the SteadyRx group across study months. No significant differences were found between groups or across time (p > .05). Those in the control group reported significantly less problems with alcohol use from intake to month 6 (p = .045). Group level differences were not found for self-reported drug or alcohol use (as measured by ASI composite scores) (p > .05). Drug use at intake was a significant covariate for alcohol use (p = .014), but not drug use (p = .076).

Relationship with care providers. Participants in the control group scored, on average, 81.80 (SEM = 81.79) on the PRA. SteadyRx group participants scored 86.84 (SEM = 0.83) on average, but this difference was not significant, F(1, 45) = 3.36, p = .073. There were significant

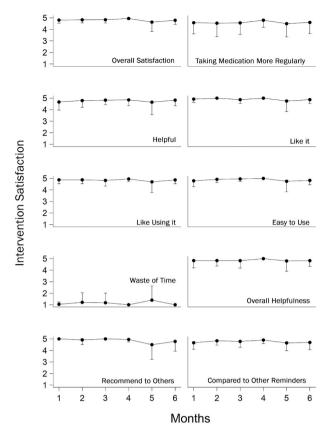


Fig. 5. Intervention satisfaction data as a function of study month. Higher scores represent higher agreement. Error bars represent standard deviation.

group differences for some individual questions of the PRA, shown in Table 3. Overall, SteadyRx group participants better understood their medical plan and what changes to expect during treatment, felt that any procedures were well described, and found it easier to ask questions of their healthcare provider than control participants.

6. Discussion

The results of the present study are consistent with prior studies that support preliminary efficacy of contingency management as a method of supporting antiretroviral adherence in people with a history of drug use (DeFulio and Silverman, 2012). In fact, despite being substantially underpowered, the study showed a significant difference on the primary outcome measure of proportion of participants achieving 95% adherence at the final study time point. This study extends prior findings by showing that delivering such an intervention via a smartphone application is feasible. This smartphone-based contingency management intervention was convenient to implement and easy to use for the overwhelming majority of participants. Participants found the intervention useful and highly acceptable overall. Further, there were some improvements participants understanding their own care, and feeling empowered to ask their providers questions about their care.

The present study is also consistent with a larger trend of using mobile devices to implement contingency management procedures (DeFulio et al., 2021; Kurti et al., 2016; Moore et al., 2015). This approach to implementation offers several advantages that should greatly facilitate adoption of contingency management interventions for health behaviors. First, these interventions have nationwide reach, because the technologies involved (i.e., smartphones and smart debit cards) work everywhere in the United States. Second, this approach eliminates provider burden and lack of expertise, two of the most critical barriers to dissemination (Kirby et al., 2006). Table 3

PRA Individual Q	Questions	based on	pooled	data fro	om monthl	y assessments.

Question	Control Group Mean (SEM)	SteadyRx Group Mean (SEM)	р
I understand the possible side effects of the treatment	5.68 (0.09)	5.70 (0.09)	0.734
If this person tells me something that is different from what I was told before, it is difficult for me to ask about it in order to get it straightened out	5.12 (0.13)	5.48 (0.11)	0.367
He (she) is warm and caring toward me	5.73 (0.07)	5.91 (0.06)	0.111
If I don't understand something the person says, I have difficulty asking for more information**	5.20 (0.13)	5.65 (0.10)	0.238
The person told me what he (she) hopes the treatment will do for me	5.48 (0.90)	5.72 (0.09)	0.398
This person makes me feel comfortable about discussing personal or sensitive issues	5.58 (0.10)	5.84 (0.09)	0.139
It is hard for me to tell the person about new symptoms**	5.39 (0.11)	5.71 (0.09)	0.495
It is hard for me to ask how my treatment is going**	5.35 (0.11)	5.85 (0.09)	0.085
This person really respects me	5.53 (0.09)	5.75 (0.08)	0.120
I understand pretty well the medical plan for helping me	5.67 (0.07)	5.96 (0.07)	0.042*
After talking to this person, I have a good idea of what changes to expect over the next weeks and months	5.51 (0.08)	5.89 (0.07)	0.018*
When I talk to this person, I sometimes end up feeling insulted**	5.42 (0.11)	5.83 (0.08)	0.067
I have difficulty asking this person questions**	5.30 (0.11)	5.85 (0.08)	0.025*
The treatment procedure was clearly explained to me	5.53 (0.09)	5.95 (0.06)	0.009*
This individual doesn't seem interested in me as a person**	5.31 (0.11)	5.75 (0.09)	0.029*

Note. * indicates a significant difference at the 0.05 level. ** indicates that the scores for the question were reverse coded.

Cost remains as a barrier to adoption that is not overcome by mobile implementation of contingency management intervention. This raises the priority of cost-benefit studies and underscores the need for commercialization of contingency management services in a manner that is consistent with the literature on effective contingency management intervention design. Mobile contingency management interventions for drug and alcohol use, smoking, diabetes care, and medication non-adherence are effective (Dallery et al., 2007; Raiff and Dallery, 2010; Raiff et al., 2016; Koffarnus et al., 2018; DeFulio et al., 2021). Given the high cost associated with care for these health problems, it seems reasonable that mobile contingency management interventions designed to address these problems may be cost-effective as well and thereby attractive to health care payers. However, more data is needed to understand the most cost-effective approaches to incentivizing medication adherence. For example, it may be possible that intermittently providing incentives based on biomarkers of ART adherence is equally effective but less costly than the approach used in the present study. Whether applying incentives to the everyday processes required to produce an outcome versus to the outcome itself has been a matter of ethical debate as well (Schmidt et al., 2012).

The other critical issue for the use of contingency management as an ART adherence intervention is how best to use its efficacy in the longterm care of people living with HIV. Over the six-month course of the intervention, adherence was well maintained in the intervention group, but adherence deteriorated in the control group. The reasons for the deterioration observed in the control group are not clear, and other studies have shown that there is substantial variation within and a cross studies in terms of the deterioration of ART adherence over time (Wilson et al., 2013). In all likelihood, this is because the causes of nonadherence are many and varied, and include occasional intentional non-adherence in some patients (Kardas et al., 2013; Lehane and McCarthy, 2007). Whatever the cause of this deterioration, successful long-term implementation of contingency management as a drug abuse intervention (Silverman et al., 2012) suggests that the effects of contingency management interventions to support ART medication adherence have the potential to be durable for as long as the intervention is maintained. Thus, implementing contingency management as a lifelong adjunct to care for individuals with HIV is likely to be effective for many people. Whether this is practical depends fundamentally on the costbenefit of the intervention. The other option is to develop interventions that use the potency of contingency management as part of a larger effort to produce life-long behavior change. This may involve the development of patterns of behavior in which medication consumption becomes ingrained in the everyday lives of the patients, ongoing support from no-cost interventions such as medication reminders, lower levels of incentives for key behaviors such as prescription refills, or strategies tailored to individual patients to address their specific barriers to longterm adherence. Whether these strategies are more cost-effective than contingency management as a lifelong adjunct to care is ultimately an empirical question, but the development of a broad array of strategies for promoting health behaviors over the long term is a critical challenge for researchers in preventive medicine.

Limitations. The most important limitation of this study is the small sample size. A larger sample size would provide more power and a more precise estimate of the key outcome measures. Similarly, this study was recruited from a single site, and as such its findings are not necessarily generalizable to full population for which the intervention is intended. The lack of requiring a detectable viral load could also be considered a study limitation. However, the results of this study suggest that individuals with undetectable viral loads do not necessarily engage in strict medication adherence, and that level of adherence is inconsistent over time for many people. Thus, ART medication adherence interventions may be worthwhile for patients who are currently adherent, especially if they are at risk for future non-adherence. Nevertheless, reengagement of patients who have completely stopped ART is a critical behavioral target that is not addressed by the approach developed as part of this study. A final limitation of this study is that the procedure for collecting biometric data used in this study was flawed. In this study, only individuals who submitted test results indicating undetectable viral load were provided with incentives. A better approach would be to incentivize submission of biometric data independent of the viral load. This would likely yield a much higher collection rate, and allow for a determination of the effect of the contingency management intervention on viral load. Nevertheless, the fact that participants in either group could receive incentives for undetectable viral load does not appear to have affected adherence. This suggests that process-oriented incentive interventions were more effective than outcome-oriented incentive interventions in the present study. However, extrapolating to other interventions is likely unwarranted.

7. Conclusion

Remote delivery of a contingency management intervention is effective in promoting adherence to ART in people with a history of drug use. The app used to deliver the intervention in this study showed high levels of usability and acceptability. As such, smartphone-based delivery of contingency management appears worthy of adoption by ART providers. Future studies should examine the generalizability and costeffectiveness of this approach.

8. Authors' notes

This research was supported by R34DA037130 from the National

Institute on Drug Abuse. The authors declare no conflicts of interest. Thanks to De'Lon Dixon and Rogelio J.F. Bates for their assistance preparing study materials.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This study was funded by the National Institute on Drug Abuse, part of the National Institutes of Health, (R34DA037130, DeFulio, PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The funders played no role in any aspect of the preparation of the manuscript or the decision to publish the data. The first author is a research consultant for DynamiCare Inc., who offer smartphone-based contingency management for people recovering from substance use disorders. No DynamiCare Inc. services or products were used in the present study. The second author is now at the National Institute of Drug Abuse, Technology and Translational Research Unit. The fourth author is now at Baylor University. This study is registered at clinicaltrials.gov, under the identifier NCT02317614. The study manual is available upon request to the corresponding author.

References

- Altice, F.L., Kamarulzaman, A., Soriano, V.V., Schechter, M., Friedland, G.H., 2010. Treatment of medical, psychiatric, and substance-use comorbidities in people infected with HIV who use drugs. Available at: Lancet 376 (9738), 367–387 http ://www.ncbi.nlm.nih.gov/pubmed/20650518.
- Bangsberg, D.R., 2006. Less than 95% adherence to nonnucleoside reverse-transcriptase inhibitor therapy can lead to viral suppression. Available at: Clinical Infectious Diseases 43 (7), 939–941 http://www.ncbi.nlm.nih.gov/pubmed/16941380.
- Binford, M.C., Kahana, S.Y., Altice, F.L., 2012. A systematic review of antiretroviral adherence interventions for HIV-infected people who use drugs. Available at: Current HIV/AIDS Reports 9 (4), 287–312 http://www.ncbi.nlm.nih.gov/pubmed /22936463.
- Buscher, A., Hartman, C., Kallen, M.A., Giordano, T.P., 2011. Validity of self-report measures in assessing antiretroviral adherence in newly diagnosed HAART-naïve patients. HIV Clinical Trials 12 (5), 244–254.
- Cohen, M.S., Chen, Y.Q., McCauley, M., et al., 2011. Prevention of HIV-1 infection with early antiretroviral therapy. N. Engl. J. Med. 365 (6), 493–505.
- Dallery, J., Glenn, I.M., Raiff, B.R., 2007. An Internet-based abstinence reinforcement treatment for cigarette smoking. Drug Alcohol Depend 86 (2–3), 230–238. https:// doi.org/10.1016/j.drugalcdep.2006.06.013.
- De Jongh, T., Gurol-Urganci, I., Vodopivec-Jamsek, V., Car, J., Atun, R., 2012. Mobile phone messaging for facilitating self-management of long-term illnesses. Cochrane Database of Systematic Reviews. 2012,12 Art. No.: CD007459. DOI: 10.1002/ 14651858.CD007459.pub2.
- DeFulio, A., Silverman, K., 2012. The use of incentives to reinforce medication adherence. Prev. Med. 55 (Suppl), S86–S94. https://doi.org/10.1016/j. vpmed.2012.04.017.
- DeFulio, A., Donlin, W.D., Wong, C.J., Silverman, K., 2009. Employment-based abstinence reinforcement as a maintenance intervention for the treatment of cocaine dependence: a randomized controlled trial. Addiction 104 (9), 1530–1538. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi? artid=2729763&tool=omcentrez&rendertvpe=abstract.
- DeFulio, A., Rzeszutek, M.J., Furgeson, J., Ryan, S., Rezania, S., 2021. A smartphonesmartcard platform for contingency management in an inner-city substance use disorder outpatient program. J. Subst. Abuse Treat. 120 (108188).
- Galassi, J.P., Schanberg, R., Ware, W.B., 1992. The Patient Reactions Assessment: a brief measure of the quality of the patient-provider medical relationship. Available at: Psychol. Assess. 4 (3), 346–351 http://doi.apa.org/getdoi.cfm?doi=10.1037/1040-3 590.4.3.346.
- HIV/AIDS and Drug Abuse: Intertwined Epidemics, 2012. NIDA Research Report Series. NIH Pub Number 10-3859. Bethesda, MD; 2012:1–3. Available at: www.drugabuse. gov/publications/research-reports/hivaids.
- Hull, M.W., Montaner, J., 2011. Antiretroviral therapy: a key component of a comprehensive HIV prevention strategy. Available at: Current HIV/AIDS Reports 8 (2), 85–93 http://www.ncbi.nlm.nih.gov/pubmed/21445551.
- Kalichman, S.C., Pope, H., White, D., et al., 2008. The association between health literacy and HIV treatment adherence: Further evidence from objectively measured medication adherence. J. Int. Assoc. Physic. AIDS Care 7 (6), 317–323.

A. DeFulio et al.

Kerr, S.J., Avihingsanon, A., Putcharoen, O., et al., 2012. Assessing adherence in Thai patients taking combination antiretroviral therapy. Available at: Int. J. STD AIDS 23 (3), 160–165.

King, M.S., Brun, S.C., Kempf, D.J., 2005. Relationship between adherence and the development of resistance in antiretroviral-naive, HIV-1-infected patients receiving lopinavir/ritonavir or nelfinavir. Available at: J. Infect. Dis. 191 (12), 2046–2052 http://www.ncbi.nlm.nih.gov/pubmed/15897990.

Kirakowski, J., Corbett, M., 1993. SUMI: the software usability measurement inventory. Br. J. Educ, Technol. 24 (3), 210–212.

Kirby, K.C., Benishek, L.A., Dugosh, K.L., Kerwin, M.E., 2006. Substance abuse treatment providers' beliefs and objections regarding contingency management: Implications for dissemination. Drug Alcohol Depend. 85 (1), 19–27.

- Koffarnus, M.N., Bickel, W.K., Kablinger, A.S., 2018. Remote alcohol monitoring to facilitate incentive-based treatment for alcohol use disorder: a randomized trial. Alcohol. Clin. Exp. Res. 42 (12), 2423–2431.
- Kuo, I., Greenberg, A.E., Magnus, M., et al., 2011. High prevalence of substance use among heterosexuals living in communities with high rates of AIDS and poverty in Washington, DC. Drug Alcohol Dependence 117 (2-3), 139–144. Available at: http:// www.ncbi.nlm.nih.gov/pubmed/21316871.

Kurti, A.N., Davis, D., Redner, R., et al., 2016. A review of the literature on remote monitoring technology in incentive-based interventions for health-related behavior change. Tranls. Issuses Psychol. Sci. 2 (2), 125–152.

Kurti, A.N., Tang, K., Bolivar, H.A., et al., in press. Smartphone-based financial incentives to promote smoking cessation during pregnancy: a pilot study. Prev. Med.

Lehane, E., McCarthy, G., 2007. Intentional and unintentional medication nonadherence: a comprehensive framework for clinical research and practice? A discussion paper. Int. J. Nurs. Stud. 44 (8), 1468–1477.

Lucas, G.M., 2005. Antiretroviral adherence, drug resistance, viral fitness and HIV disease progression: a tangled web is woven. Available at: J. Antimicrob. Chemother. 55 (4), 413–416 http://www.ncbi.nlm.nih.gov/pubmed/15722389.

McLellan, A.T., Luborsky, L., Cacciola, J., et al., 1985. New data from the Addiction Severity Index. Reliability and validity in three centers. J. Nerv. Ment. Dis. 173 (7), 412–423. Available at: http://www.ncbi.nlm.nih.gov/pubmed/4009158.

Moore, B.A., Rosen, M.I., Wang, Y., et al., 2015. A remotely delivered CBT and contingency management therapy for substance using people with HIV. AIDS Behav. 19, S156–S162. https://doi.org/10.1007/s10461-014-0990-x.

Parker, R.M., Baker, D.W., Williams, M.V., Nurss, J.R., 1995. The test of functional health literacy in adults: a new instrument for measuring patients' literacy skills. Available at: J. Gen. Intern. Med. 10 (10), 537–541 http://www.ncbi.nlm.nih.gov/pubme d/8576769.

Pham, P.A., 2009. Antiretroviral adherence and pharmacokinetics: review of their roles in sustained virologic suppression. Available at: AIDS Patient Care STDs 23 (10), 803–807 http://www.ncbi.nlm.nih.gov/pubmed/19795999.

Raffa, J.D., Tossonian, H.K., Grebely, J., Petkau, A.J., Devlaming, S., Conway, B., 2008. Intermediate highly active antiretroviral therapy adherence thresholds and empirical models for the development of drug resistance mutations. J. Acquir. Immune Deficiency Syndromes 47 (3), 397–399. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18398974.

- Raiff, B.R., Dallery, J., 2010. Internet-based contingency management to improve adherence with blood glucose testing recommendations for teens with type 1 diabetes. J. Appl. Behav. Anal. 43 (3), 487–491.
- Raiff, B.R., Jarvis, B.P., Dallery, J., 2016. Text message reminders plus incentives increase adherence to antidiabetic medication in adults with type 2 diabetes. J. Appl. Behav. Anal. 49 (4), 947–953.
- Rosen, M.I., Black, A.C., Arnsten, J.H., et al., 2013. Association between use of specific drugs and antiretroviral adherence: findings from MACH 14. AIDS Behavior 17 (1), 142–147. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22246513.
- Schmidt, H., Asch, D.A., Halpern, S.D., 2012. Fairness and wellness incentives: what is the relevance of the process-outcome distinction? Prev. Med. 55, S118–S123.
- Silverman, K., Svikis, D., Wong, C.J., Hampton, J., Stitzer, M.L., Bigelow, G.E., 2002. A reinforcement-based Therapeutic Workplace for the treatment of drug abuse: Three-year abstinence outcomes. Available at: Exp. Clin. Psychopharmacol. 10 (3), 228–240 http://doi.apa.org/getdoi.cfm?doi=10.1037/1064-1297.10.3.228.
- Silverman, K., Robles, E., Mudric, T., Bigelow, G.E., Stitzer, M.L., 2004. A randomized trial of long-term reinforcement of cocaine abstinence in methadone-maintained patients who inject drugs. J. Consult. Clin. Psychol. 72 (5), 839–854. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15482042.
- Silverman, K., DeFulio, A., Sigurdsson, S.O., 2007. Maintenance of reinforcement to address the chronic nature of drug addiction. Prevent. Medcine. 2012 (55 Suppl), S46–S53. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22668883. Accessed March 5, 2013.
- Silverman, K., DeFulio, A., Siggursson, S.O., 2012. Maintenance of reinforcement to address the chronic nature of drug addiction. Prev. Med. 55, S46–S53.
- Simoni, J.M., Amico, K.R., Smith, L., Nelson, K., 2010. Antiretroviral adherence interventions: translating research findings to the real world clinic. Available at: Current HIV/AIDS Reports 7 (1), 44–51 http://www.pubmedcentral.nih.gov/article render.fcgi?artid=3607373&tool=pmcentrez&rendertype=abstract.
- Springer, S.A., Dushaj, A., Azar, M.M., 2012. The impact of DSM-IV mental disorders on adherence to combination antiretroviral therapy among adult persons living with HIV/AIDS: a systematic review. AIDS Behav. 16 (8), 2119–2143.
- Van Velthoven, M.H., Bursamento, S., Majeed, A.C.J., 2013. Scope and effectiveness of mobile phone messaging for HIV/AIDS care: a systematic review. Psychol. Health Med. 18 (2), 1–2.
- Wilson, I.B., Bangsberg, D.R., Shen, J., et al., 2013. Multisite adherence collaboration in HIV. Heterogeneity among studies in rates of decline of ART adherence over time: Results from the MACH 14 study. J. Acquir. Immune Defic. Syndr. 64 (5), 448–454.
- Wu, A.W., Revicki, D.A., Jacobson, D., Malitz, F.E., 1997. Evidence for reliability, validity and usefulness of the Medical Outcomes Study HIV Health Survey (MOS-HIV). Available at: Quality of Life Research 6 (6), 481–493 http://www.ncbi.nlm.nih .gov/pubmed/9330549.
- Zeger, S.L., Liang, K.Y., Albert, P.S., 1988. Models for longitudinal data: a generalized estimating equation approach. Biometrics 44 (4), 1049–1060.