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Medication Adherence Monitoring Using Smartphone Video Dosing in an Open-label Pilot Study of Monthly Naltrexone plus Once-daily Bupropion for Methamphetamine Use Disorder: Feasibility and Acceptability

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Abstract

Objectives: This paper describes how smartphones were used to monitor and encourage medication adherence in a pilot study evaluating the potential efficacy of a combination pharmacotherapy for methamphetamine use disorder. We examine the feasibility, utility, and acceptability of using smartphones to capture dosing videos from the perspectives of participants and staff.

Methods: The study was an 8 week, open-label evaluation of extended-release injectable naltrexone plus once-daily oral extended-release bupropion (BRP, Welbutrin XL, 450 mg/day). Participants attended visits twice-weekly for observed BRP dosing, assessments, and medical management. BRP was dispensed once weekly for dosing on non-clinic days. Medication adherence was assessed objectively (by observation in the clinic and smartphone videos for dosing at home) and subjectively (self-reports of dosing). Surveys assessing the smartphone component were completed by participants and study staff.

Results: Participants (N=49) reported taking 93.6% of the dispensed BRP doses while 86.6% of dispensed doses were confirmed via dosing video and in-person observations. Most participants who completed the survey agreed that the smartphone was easy to use (92.6%) and that taking the dosing videos helped to remember to take the study medication (80.5%). Staff agreed that the smartphone helped collect accurate dosing data for most (77.5%) participants.

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Conflicts of Interest

Dr. Ling has served as a consultant for Reckitt Benckiser Pharmaceuticals. No other financial or other conflicts of interest exist for authors.

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Conclusions: The use of smartphones for video-based oral medication dosing in this study provided a feasible and acceptable mechanism to encourage, monitor, and confirm medication adherence. Video-confirmed dosing adherence provides an objective numerical indicator of the lowest medication adherence rate participants achieve, allowing investigators to more confidently interpret results.

Keywords

directly observed therapy; medication adherence; methamphetamine; smartphone; video

Introduction

A universal problem in healthcare continues to be patient non-adherence with medication regimens (Haynes et al., 2002; Osterberg & Blaschke, 2005). In pharmacological research settings, high adherence rates are required to properly evaluate the targeted outcomes and to draw appropriate conclusions about medication effectiveness. Similar to findings from studies of other medical conditions (Julius et al. 2009; Brown & Bussell, 2011; Gadkari & McHorney, 2012), efforts to evaluate pharmacotherapies specifically for people with substance use disorders are negatively impacted by patient non-adherence with medication regimens (Stein et al., 2004; Magura et al., 2014). When there are no currently approved pharmacological treatments for a condition, as is the case with stimulant use disorder (methamphetamine type), the impact of low medication adherence in studies is particularly concerning. Interpreting the results of studies with poor medication adherence is difficult; one does not know if the lack of a treatment effect is because the medication is truly ineffective (and, therefore, should not be studied further) or if too little medication was taken to elicit a treatment response.

There are various ways to measure, assess, improve, and encourage medication adherence (Haynes et al., 2002; McDonald et al., 2002; Julius et al., 2009; Brown & Bussell, 2011; Nieuwlaat et al., 2014), all of which impact the conclusions that can be drawn from pharmacological research studies. The common use of self-reported adherence may not be reliable, especially when lacking corroborating measures (Osterberg & Blaschke, 2005; Garfield et al., 2011). For example, a study of mirtazapine for methamphetamine dependence revealed that medication adherence was self-reported at 74%, but adherence was 48% at best according to a medication event monitoring system (MEMS) cap technique (Colfax et al., 2011). In a trial of modafinil for methamphetamine dependence, researchers compared MEMS cap technology to cellphone-acquired photos of medication in the participant's hand and to pill count in clinic, finding that photographs of the capsules allowed more accurate time measures and more frequent adherence assessment than MEMS or capsule count (Galloway et al., 2011). These examples underscore how medication adherence, as well as the accurate assessment of it, continues to be problematic. A recent Cochrane Review (Nieuwlaat et al., 2014) on adherence to prescribed medications concluded the current methods of improving adherence are complex yet not very effective, and that medication adherence research needs to advance in the use of objective adherence measures.

Pharmacological research must include medication adherence components to avoid conducting expensive, time-consuming studies that produce findings of questionable validity. There are numerous recommendations to leverage technology to improve medication adherence (e.g., Hatch et al., 2017; Osterberg & Blaschke, 2005; Tsoli et al., 2018) and technology has been implemented in various ways. For example, given the travel required for directly observed therapy (either in the clinic or the field) that is recommended in tuberculosis (TB) treatment (World Health Organization, 2010), video directly observed therapy (DOT) for TB has been developed. Typically, patients record and upload videos for manual review and verification of adherence by staff (usually within 1-3 days). Various studies of video DOT for TB have demonstrated the feasibility and acceptability of video DOT (Hoffman et al., 2010; Garfein et al., 2015; Nguyen et al., 2017) and found it is as effective as in-person DOT (Chuck et al., 2016). While the TB field has led the way in video DOT to remotely monitor medication adherence, other fields have also begun to capitalize on this idea (Shields et al., 2018). We found only one instance of video DOT in the substance use treatment literature (DeWorsop et al., 2016), whereby daily video calls were made by staff to research participants to observe medication ingestion in real-time in a trial for cannabis dependence. Methamphetamine use in particular is associated with reduced medication adherence (Hermanstynne et al., 2014) and could benefit from methods that encourage and objectively monitor medication adherence. The aim of the current paper is to describe a smartphone video-based variation on directly observed therapy that was used in a study evaluating a pharmacotherapy for methamphetamine use disorder.

Use of mobile technology was a key component of the multi-site Accelerated Development of Addictive Pharmacotherapy Treatment (ADAPT) for Methamphetamine Use Disorder trial, sponsored by the National Drug Abuse Treatment Clinical Trials Network (Mooney et al., 2016). The aim of ADAPT was to evaluate the safety and potential efficacy of a new pharmacotherapy in a brief period with few participants. Consequently, high medication adherence was crucial for properly evaluating potential efficacy. Timely monitoring and correction of non-adherent medication related behaviors was extremely important. This paper describes the methods used to monitor participants' medication-taking behaviors and presents results from a secondary analysis of medication adherence data. Finally, patient and staff survey results regarding the feasibility and acceptability of the smartphone video procedures are presented.

Methods

Design

The ADAPT pilot study was an 8 week, uncontrolled, open-label pharmacotherapy trial evaluating the combination of extended-release oral bupropion (BRP) and extended-release naltrexone (XR-NTX) by monthly injection. Eligibility criteria included being 18 to 65 years old, meeting Diagnostic and Statistical Manual of Mental Disorders, 5th edition criteria for severe stimulant use disorder (methamphetamine type), self-reporting 20 days methamphetamine use in the 30 days prior to consent via Timeline Followback, and submitting 3 methamphetamine-positive urines collected at least 3 days apart in a 14-day period during screening. Remaining eligibility criteria were designed to ensure safe

participation. The study was approved by local IRBs and registered with clinicaltrials.gov (NCT01982643). All participants provided signed informed consent.

Procedures

Upon signing consent, a maximum of 30 days was allowed for screening to establish eligibility before participants received their first injection of 380 mg extended-release injectable naltrexone (XR-NTX; as Vivitrol[®]), followed by the first dose of oral extended-release bupropion tablets (BRP; as Wellbutrin XL[®]). The XR-NTX injections were provided at weeks 1 and 5. The dose of BRP was titrated over the first 4 days to reach 450 mg (3 pills) by day 5. To address any side effects, ancillary medications and/or dose reduction to 300mg BRP (allowed once in the first three weeks) were used. If intolerable side effects continued, participants were withdrawn from both medications. A taper from BRP occurred during the first 4 days of week 9 for participants who had not been withdrawn from medications.

Evaluation of the primary outcome of methamphetamine use required collecting urine samples twice weekly; drug testing was conducted by a central laboratory to blind study staff to results. Visits also included directly observed BRP dosing, safety and secondary outcome assessments, medication dispensation (once weekly), and medical management (once per week). Participants could receive up to \$980 for screening visits, clinic attendance, and dosing adherence (verified by smartphone dosing videos).

Medication Adherence Procedures via Smartphone Videos

One of the final eligibility criteria required participants to read and sign a smartphone agreement that described the rationale for the use of dosing videos for oral medication and established rules for keeping and properly using the study-provided device. All participants were provided a smartphone with phone, text, and internet service to ensure all had consistent service for the duration of the study. Participants were instructed on how to record videos (using the smartphone's front-facing camera) of oral medication ingestion on non-clinic days. Staff and participants established an individualized daily dosing time to accommodate the participant's schedule and medical needs. Dosing reminders were created using the native calendar on the smartphone.

Upon recording each video and when the phone was connected to cellular or Wi-Fi, dosing videos were automatically transmitted from the smartphone's native video files to the central study server by a Mobile Device Management System (MDMS), including a time and date stamp to ensure accurate dose monitoring. The MDMS provided an automated, secure, and encrypted dosing video transmission environment that provided daily transmission from the participants to the study administrators. Dosing videos were saved in separate folders only accessible to study administrators. Once saved on the study server, the MDMS automatically downloaded the videos to study-provided administrator smartphones for staff viewing to evaluate dosing validity. The study-provided smartphones for staff were used for study purposes only (e.g., viewing dosing videos, texting participants). Staff were required to password protect their study smartphone (i.e., password was required to unlock the phone) to further ensure participant confidentiality if the staff phone was accessed by non-staff members.

Valid dosing videos required that the participant present the pills clearly for identification, clearly show putting the pill(s) in his/her mouth followed by a drink of water from a clear container, and then showing an empty mouth including lifting the tongue. Site staff viewed each submitted video to ensure the correct dose was taken and all steps were completed correctly. Videos of questionable validity were reviewed by more than one staff member to determine by consensus if the video was valid. Videos were deemed invalid, for example, when the lighting was too dark to clearly observe behavior or if the participant moved out of the video frame. When deemed invalid, staff retrained participants how to correctly dose at the next clinic visit. If a daily dosing video had not been received by the expected time, staff contacted participants (e.g., by text, phone call) to remind them to dose but did not systematically record participant-reported reasons for not completing a dosing video. These reminder contacts were individualized per participant throughout the study.

Participants were compensated \$10 for each valid dosing video submitted, with compensation (e.g., cash or gift card per the site's IRB approval) provided at the next research visit attended. Participants who completed the study were allowed to keep the smartphone (service was discontinued at the end of month three) or return it and receive an additional \$30. Smartphones that were lost or stolen during the study were replaced and study staff retrained participants on the importance of safely maintaining the phone.

Measures and Analyses

Medication Adherence.—XR-NTX injections were administered and logged in the clinic. Staff documented on dosing logs the weekly BRP dose dispensed and participant-reported oral dosing adherence reported during the twice weekly visits. Staff further documented which doses were directly observed in-clinic and which were confirmed via valid smartphone video. Video-based monitoring of dosing was not expected to diminish side effects or prevent discontinuation from medication. Therefore, oral medication adherence is reported as mean percent of doses taken for all participants and for participants who were not withdrawn from medications.

Technology Feedback.—Participants who attended the final study visit after the 8 week medication phase completed a survey about their perspectives about the smartphone video-dosing component. For each participant, study staff collectively completed a similar survey that assessed staff members' impressions about how the technology component impacted the participant. Staff were asked to collaborate and complete one survey per participant. No additional instructions (i.e., how to resolve disagreements) were provided, and how staff completed the surveys were not systematically assessed or monitored during the study. The number of staff interacting with a specific participant over the course of the study ranged from approximately three to six medical (e.g., nurse, physician) and research staff members. Staff most responsible for managing and witnessing the technology components were likely the ones who completed the survey. For example, at one site, the two research coordinators completed the survey side-by-side, discussing each item until they reached consensus. Participants completed 13 items and staff completed 14 items, each using a 5-point Likert scale with responses ranging from "strongly agree" to "strongly disagree." Survey results are presented as frequencies for each item response.

Results

Participant Characteristics

Participants (N=49; 53% male) were enrolled and inducted onto study medications at 3 study sites (California, Hawaii, and Texas). Participants were on average 39.9 (± 10.76) years old and the majority (40%) were White. Almost all participants had a cellphone at baseline (85.7%) but fewer had a smartphone (63.3%). See Table 1 for baseline characteristics of the sample.

Medication Adherence

All participants received the first XR-NTX injection on the day of enrollment, and 83.7% (41/49 participants) received the second injection at week 5. Participants (N=49) reported taking 74.6% (6142/8232 pills) of the oral medication expected per protocol. This percentage does not take into consideration dose reductions (n=7) or early withdrawals (n=8) from medication. When evaluating adherence to oral medication that was dispensed, participants (N=49) self-reported taking 93.6% of the dispensed doses while 86.6% of the dispensed doses were objectively confirmed as taken (via dosing videos plus direct observation on clinic days). Specifically, 60.7% of dispensed doses were confirmed by video while 25.9% of doses were confirmed in clinic. Per the study design, for a fully adherent participant, approximately 73% of doses were expected to be confirmed by video while approximately 27% of doses were expected to be confirmed in clinic. The majority of submitted dosing videos demonstrated medication adherence. Of the videos submitted from all 49 participants, 97% were deemed valid. Of the dosing videos submitted from the 41 participants who were not withdrawn from medication, 83% of the expected videos were deemed valid. Videos containing content in addition to dosing behavior (e.g., talking to staff via the video) was received from 17 participants. Of all 49 participants, 11 reported a “lost or stolen” phone during the course of the study. Staff-recorded comments for 7 of those indicated 4 were broken, 2 were stolen, and 1 was lost. Staff took the phone away from one additional participant who had attempted to hack into the study software.

Technology Feedback

Responses from participants who attended the final study visit when the survey was administered (n=40) are shown in Table 2. Responses from staff members are shown in Table 3. Responses to these surveys demonstrate the feasibility, perceived usefulness, and low burden of the smartphone video medication adherence component from both the participant’s perspective as well as the staff’s perspective of the impact on the participant. In terms of feasibility of using a smartphone for confirming medication adherence, 92.6% of participants *agreed to strongly agreed* that it was easy to record the dosing video and 80.5% *agreed to strongly agreed* that the dosing videos helped them remember to take the study medication. Staff *agreed to strongly agreed* that the smartphone helped to collect accurate dosing data for 77.5% of the participants and *agreed to strongly agreed* that the smartphone helped to improve attendance for 47.3% of participants.

Discussion

Recognizing medication non-adherence as a source of serious confound and seeking to optimize oral medication adherence for a trial evaluating a promising combination pharmacotherapy for methamphetamine use disorder, we implemented a technology-assisted medication adherence component. To our knowledge, the ADAPT pilot study (Mooney et al., 2016) was the first trial that utilized a smartphone-enabled, video-confirmation strategy to remotely monitor and encourage oral medication adherence among people who use methamphetamine. The smartphone video dosing procedure was reported as feasible and well accepted by participants and staff. The technology surveys for participants and staff did not contain identical items and, thus, we did not report how well staff and participant survey responses agree with each other. Participant-level buy-in of the video dosing component is clearly an important factor to adherence. Staff-level assessment of *staff* impressions of how useful the technology is to participants is also important but for slightly different reasons. The staff survey results indicate that staff similarly saw benefit from and ease of use of the technology. Unless and until technology assisted medication adherence monitoring completely removes the need for human interaction outside of the technology platform, staff buy-in will continue to be an important factor to consider. For example, staff who are more enthusiastic about the technology likely convey that enthusiasm and may have more adherent participants as compared to staff who are less enthusiastic.

Oral medication adherence was high, and yet adherence indicated by smartphone videos was 7 percentage points lower than participant-reported medication adherence. These results are better understood when examined in conjunction with the data presented in the primary outcome manuscript. Mooney and colleagues (2016) showed that participants who responded to the medication (n=11) had high adherence rates and the self-reported (97.6%) and video-confirmed (95.2%) dosing adherence rates were very similar. In contrast, while participants who were medication non-responders (n=38, including early withdrawals) also had high self-reported rates of adherence (92.1%), fewer doses were corroborated by video confirmation (83.4%). It is impossible to determine which adherence rate most accurately represents dosing behavior. For example, perhaps all doses were taken as self-reported, but logistical, technical, or motivational issues interfered with submitting dosing videos. Perhaps only those doses confirmed by videos were taken, but participants self-reported higher adherence due to, for example, faulty memories or desire to please investigators. Considering the video-confirmed and self-reported dosing adherence rates together, they provide a low to high range of adherence rates within which we can be confident that participants took the study medications. Nevertheless, in this study, it appears as though video confirmation is likely the more accurate indicator of medication adherence since those with higher video-documented adherence had better methamphetamine use outcomes while those with lower video-documented adherence had worse outcomes.

A major strength of this study was that all participants were provided a smartphone to ensure equal access to reliable cellular services through the duration of the study, and participants received replacement phones if needed. Provision of phones to all participants allowed recruitment of the target sample of people who use methamphetamine at a high frequency without regard to their financial ability, which would have limited recruitment and

generalizability. Anecdotally, there were only a few instances of participants losing, selling, or having phones stolen. Despite being a relatively small, open-label pilot study, the inclusion of three study sites broadens the generalizability of study findings that indicate the feasibility and acceptability of implementing novel, smartphone-based medication adherence procedures. Staff were able to view the received videos at a time convenient to their daily schedule, which likely contributed to the feasibility and acceptability of it from the staff perspective. Finally, the ADAPT study was designed to include several of the best adherence practices (Haynes et al., 2002; Osterberg & Blaschke, 2005; Julius et al., 2009) to optimize medication adherence so medication efficacy could be confidently evaluated. It was not designed to test the effectiveness of various medication adherence procedures. Thus, given these collective design elements (e.g., \$10 for each dosing video, texting reminders when dosing video was late, medication management to problem-solve adherence barriers, twice weekly visits, use of extended-release formulation requiring only once-daily dosing), we cannot determine the extent to which the smartphone video dosing procedures independently contributed to the high adherence rates.

The conduct of this trial identified issues to be addressed in future efforts involving video-based medication adherence components. One issue that was of significant concern during the study was in the area of privacy and confidentiality. Although the smartphone procedures were designed to maximize privacy and confidentiality, a glitch in the MDMS programming during the manufacturer's software upgrade corrupted a programming script, which allowed two participants access to videos submitted by the other participant. One participant mistakenly viewed the other's video, and reported it to study staff. The second participant did not access the other participant's videos. The problem was recognized and corrected, and future MDMS software upgrades were prevented. The UCLA IRB was notified and provided guidance to the study team. Both participants were notified about the breach and opted to remain in the study. A second issue was the content of videos made by participants. A few participants used the videos to "talk" to study staff. At times, this included reports of adverse events that would have been best reported directly to staff in person or by phone. In these cases, participants were reminded what should and should not be included in the video because there was not a technological mechanism to limit video length or content, or to ensure immediate viewing and response. Finally, since technology feedback was solicited only from those participants who attended the final study visit, the results indicating high acceptance of the smartphone procedure may be biased if technology perceptions were associated with reasons for non-attendance.

A smartphone-enabled video dosing adherence procedure, like that used in the ADAPT pilot study, is a potential tool to objectively monitor and encourage medication adherence, enhancing investigators' ability to evaluate outcomes of medication treatment studies. The use of smartphones with video confirmation of pill-taking is a step toward simpler yet sophisticated approaches that directly monitor medication-taking behavior and can facilitate behavioral change, which may help address the criticism (Nieuwlaat et al., 2014) of current adherence methods being complicated with limited effectiveness. Similar to recommendations made for further developing video directly observed therapy in tuberculosis treatment (Story et al., 2016), the use of video-based medication adherence

appears to be feasible and acceptable, and more research is needed to fully understand how best to leverage this technology in persons with substance use disorders.

Conclusion

The use of smartphones for video-based oral medication dosing in this study provided a feasible and acceptable mechanism to encourage, monitor, and confirm medication adherence. Video-confirmed dosing adherence provides an objective numerical indicator of the lowest possible medication adherence rate participants achieve. This objective data allows investigators to more confidently interpret results of medication trials. The use of smartphones also addressed other logistical concerns typically encountered in substance use disorder research. The smartphone component: 1) was a reliable method of contact with participants; 2) served as a tangible reminder of study participation; 3) provided a means to incentivize valid dosing videos; 4) allowed participants to set reminders for clinic appointments in the smartphone calendar; and 5) may have fostered retention by allowing participants to keep smartphones at study completion.

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References

- Brown M, & Bussell J Medical Adherence: WHO Cares? *Mayo Clinic Proceedings* 2011; 86(4):304–314. doi:10.4065/mcp.2010.0575PMCID: PMC3068890 [PubMed: 21389250]
- Chuck C, Robinson E, Macaraig M, Alexander M, & Burzynski J Enhancing management of tuberculosis treatment with video directly observed therapy in New York City. *International Journal of Tuberculosis and Lung Disease* 2016;20(5):588–593. [PubMed: 27084810]
- Colfax G, Santos G, Das M, Santos D, Matheson T, Gasper J, et al. Mirtazapine to reduce methamphetamine use: A randomized controlled trial. *Archives of General Psychiatry* 2011;68(11):1168–1175. [PubMed: 22065532]
- DeWorsop D, Creatura G, Bluez G, Thurnauer H, Forselius-Bielen K, Ranganathan M, et al. Feasibility and success of cell-phone assisted remote observation of medication adherence (CAROMA) in clinical trials. *Drug and Alcohol Dependence* 2016;163:24–30. [PubMed: 27068252]
- Gadkari A, & McHorney C Unintentional non-adherence to chronic prescription medications: How unintentional is it really? *BMC Health Services Research*, 2012;12(98). doi: 10.1186/1472-6963-12-98

- Galloway G, Coyle J, Guillen J, Flower K, Mendelson J A simple, novel method for assessing medication adherence: capsule photographs taken with cellular telephones. *Journal of Addiction Medicine* 2011;5(3): 170–174. [PubMed: 21844832]
- Garfein RS, Collins K, Munoz F, Moser K, Cerecer-Callu P, Raab F, et al. Feasibility of tuberculosis treatment monitoring by video directly observed therapy: a binational pilot study. *International Journal of Tuberculosis and Lung Disease* 2015;19(9):1057–1064. [PubMed: 26260824]
- Garfield S, Clifford S, Eliasson L, Barber N, Wilson A Suitability of measures of self-reported medication adherence for routine clinical use: a systematic review. *BMC Medicine Research Methodology* 2011;3(11):149.
- Hatch. A, Docherty JP, Carpenter D, Ross R, Weiden PJ Expert consensus survey on medication adherence in psychiatric patients and use of a digital medicine system. *J Clin Psychiatry* 2017;78(7):e803–e812. doi: 10.4088/JCP.16m11252. [PubMed: 28541648]
- Haynes R, McDonald H, Garg A Helping patients follow prescribed treatment: clinical applications. *Journal of American Medical Association* 2002;288(22):2880–2883.
- Hermansteyne KA, Santos GM, Vittinghoff E, Santos D, Colfax G, Coffin P Event-level relationship between methamphetamine use significantly associated with non-adherence to pharmacologic trial medications in event-level analyses. *Drug and Alcohol Dependence* 2014;143:277–280. doi: 10.1016/j.drugalcdep.2014.07.031 [PubMed: 25156227]
- Hoffman JA, Cunningham JR, Suleh AJ, Sundsmo A, Dekker D, Vago F, et al. Mobile direct observation treatment for tuberculosis patients: a technical feasibility pilot using mobile phones in Nairobi, Kenya. *American Journal of Preventive Medicine* 2010;39(1):78–80. [PubMed: 20537846]
- Julius R, Novitsky M Jr., Dubin W Medication adherence: a review of the literature and implication for clinical practice. *Journal of Psychiatric Practice* 2009;15(1):34–44 [PubMed: 19182563]
- Magura S, Mateu P, Rosenblum A, Matusow H, Fong C Risk factors for medication non-adherence among psychiatric patients with substance misuse histories. *Mental health and substance use: dual diagnosis* 2014;7(4):381–390. [PubMed: 25309623]
- McDonald H, Garg A, & Haynes R Interventions to enhance patient adherence to medication prescriptions: scientific review. *Journal of American Medical Association* 2002;288(22):2868–2879.
- Mooney LJ, Hillhouse MP, Thomas C, Ang A, Sharma G, Terry G, et al. Utilizing a Two-stage Design to Investigate the Safety and Potential Efficacy of Monthly Naltrexone Plus Once-daily Bupropion as a Treatment for Methamphetamine Use Disorder. *Journal of Addiction Medicine* 2016;10(4): 236–243. doi:10.1097/adm.0000000000000218 [PubMed: 27379819]
- Nguyen TA, Pham MT, Nguyen TL, Nguyen VN, Pham DC, Nguyen BH, et al. Video Directly Observed Therapy to support adherence with treatment for tuberculosis in Vietnam: A prospective cohort study. *International Journal of Infectious Diseases* 2017;65:85–89. [PubMed: 29030137]
- Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, et al. Interventions for enhancing medication adherence (Review). *Cochrane Database Systematic Reviews* 2014; (11):Cd000011. doi:10.1002/14651858.CD000011.pub4
- Osterberg L, Blaschke T Adherence to medication. *New England Journal of Medicine* 2005;353(5): 487–497. doi:10.1056/NEJMr050100 [PubMed: 16079372]
- Shields MD, ALQahtani F, Rivey MP, McElnay JC Mobile direct observation of therapy (MDOT) - A rapid systematic review and pilot study in children with asthma. *PLoS ONE [Electronic Resource]* 2018;13(2):e0190031.
- Stein M, Herman D, Solomon D, Anthony J, Anderson B, Ramsey S, et al. Adherence to treatment of depression in active injection drug users: The Minerva Study. *Journal of Substance Abuse Treatment* 2004;26:87–93. [PubMed: 15050085]
- Story A, Garfein RS, Hayward A, Rusovich V, Dadu A, Soltan V, et al. Monitoring therapy compliance of tuberculosis patients by using video-enabled electronic devices. *Emerging Infectious Diseases* 2016;22(3):538–540. [PubMed: 26891363]
- Tsoli S, Sutton S, Kassavou A Interactive voice response interventions targeting behaviour change: A systematic literature review with meta-analysis and meta-regression. *BMJ Open* 2018;8(e018974). doi:10.1136/bmjopen-2017-018974

World Health Organization. Treatment of Tuberculosis: Guidelines, 4th *edition* 2010 Available at:
http://apps.who.int/iris/bitstream/handle/10665/44165/9789241547833_eng.pdf?sequence=1

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Table 1.

Baseline Participant Characteristics (N = 49)

	% or Mean	n or SD
Gender, % (n)		
Male	53.1	26
Female	46.9	23
Age, mean (SD)	39.9	10.76
Race/Ethnicity, % (n) *		
White	49.0	24
Hispanic or Latino	30.6	15
Multiracial	16.3	8
Black or African American	10.2	5
Asian	4.1	2
Native Hawaiian or Pacific Islander	2.0	1
Other	18.4	9
Education Completed, % (n)		
Less than high school diploma	14.3	7
High school graduate, or GED	28.6	14
Some college, no degree	34.7	17
Associate degree	12.3	6
Bachelor degree	6.1	3
Graduate degree	4.1	2
Cell Phone Use, % (n)		
Have a cellphone	85.7	42
Have a smartphone	63.3	31
Familiar with use of cellphones for health-related purpose **	34.7	17
Comfortable using cellphone **	93.9	46

* Sums to greater than n=49 because participants could select more than one race.

** Participants were asked these items in question format: Are you familiar with the use of cellphones for health related purposes? Are you comfortable using a cellphone? Response options were 'yes' or 'no.' Data shown is the percent responding 'yes.'

Table 2.

Participant Smartphone Survey Results*

Item	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
1. The cellphone reminders helped me to remember to take study drug as directed**	8 (20.0%)	9 (22.5%)	17 (42.5%)	5 (12.5%)	1 (2.5%)
2. I liked the fact that study staff could monitor my medication dosing and I didn't have to come to the clinic	22 (53.7%)	10 (24.4%)	8 (19.5%)	1 (2.4%)	0 (0.0%)
3. I used the study cellphone for personal calls	11 (26.8%)	13 (31.7%)	6 (14.6%)	6 (14.6%)	5 (12.2%)
4. I was confident that my privacy was protected when using the cell phone and sending the dosing video	19 (46.3%)	13 (31.7%)	8 (19.5%)	1 (2.4%)	0 (0.0%)
5. It was easy to record the dosing video	24 (58.5%)	14 (34.1%)	1 (2.4%)	1 (2.4%)	1 (2.4%)
6. The reminders to record and send the dosing video were helpful**	13 (31.7%)	7 (17.1%)	17 (41.5%)	2 (4.9%)	2 (4.9%)
7. It was easy to send the dosing video	22 (55.0%)	12 (30.0%)	5 (12.5%)	0 (0.0%)	1 (2.5%)
8. There was sufficient technical support when I ran into problems using the cellphone	15 (36.6%)	13 (31.7%)	10 (24.4%)	3 (7.3%)	0 (0.0%)
9. I received enough training so that I could use the cell phone	21 (51.2%)	14 (34.1%)	5 (12.2%)	0 (0.0%)	1 (2.4%)
10. If applicable, having both a study cell phone and personal cell phone was cumbersome	4 (10.0%)	7 (17.5%)	14 (35.0%)	8 (20.0%)	7 (17.5%)
11. I am better able to use a smartphone now than I was at the beginning of the study	5 (12.2%)	8 (19.5%)	16 (39.0%)	6 (14.6%)	6 (14.6%)
12. The compensation I received for sending the videos was important	14 (34.1%)	13 (31.7%)	8 (19.5%)	4 (9.8%)	2 (4.9%)
13. Having to take videos of my dosing helped me to take my study drug	20 (48.8%)	13 (31.7%)	5 (12.2%)	3 (7.3%)	0 (0.0%)

* N=40 or 41 per item. 40 participants completed the entire survey; 1 participant partially completed the survey; 8 participants missed the final study visit and were not surveyed.

** Participants were texted dosing reminders on an as-needed basis. Not all participants received reminders.

Table 3.

Staff Smartphone Survey Results*

Item	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
1. Using cellphone technology helped to collect accurate study data on this participant	23 (46.9%)	15 (30.6%)	6 (12.2%)	3 (6.1%)	2 (4.1%)
2. The participant needed additional assistance after training to troubleshoot a problem with the cellphone	4 (8.2%)	16 (32.7%)	2 (4.1%)	18 (36.7%)	9 (18.4%)
3. Using cellphone technology helped to improve attendance at study visits for this participant	9 (18.4%)	14 (28.6%)	16 (32.7%)	5 (10.2%)	5 (10.2%)
4. The study cellphone procedures were burdensome for study staff	2 (4.1%)	2 (4.1%)	12 (24.5%)	18 (36.7%)	15 (30.6%)
5. The participant was able to learn the cellphone procedures in 1-2 training sessions	16 (32.7%)	21 (42.9%)	5 (10.2%)	7 (14.3%)	0 (0.0%)
6. The study cellphone was useful in documenting the participant's compliance with study dosing	22 (44.9%)	17 (34.7%)	5 (10.2%)	3 (6.1%)	2 (4.1%)
7. The study cellphone was useful in promoting/increasing the participant's compliance with study dosing	14 (28.6%)	19 (38.8%)	8 (16.3%)	6 (12.2%)	2 (4.1%)
8. This participant seemed to like using the cellphone in this study	17 (34.7%)	15 (30.6%)	11 (22.4%)	6 (12.2%)	0 (0.0%)
9. Using cellphone technology helped to improve medication adherence for this participant	15 (30.6%)	16 (32.7%)	9 (18.4%)	5 (10.2%)	4 (8.2%)
10. The participant seemed to be overwhelmed by the cellphone components like the dosing videos or sending the videos	2 (4.1%)	2 (4.1%)	5 (10.2%)	26 (53.1%)	14 (28.6%)
11. Using cellphone technology helped to foster a strong relationship with this participant	9 (18.4%)	14 (28.6%)	17 (34.7%)	4 (8.2%)	5 (10.2%)
12. This participant was very tech-savvy at the beginning of the study	17 (34.7%)	15 (30.6%)	11 (22.4%)	5 (10.2%)	1 (2.0%)
13. This participant was very tech-savvy at the end of the study	18 (36.7%)	19 (38.8%)	12 (24.5%)	0 (0.0%)	0 (0.0%)
14. The study cellphone procedures were unnecessary/not useful	0 (0.0%)	1 (2.0%)	2 (4.1%)	21 (42.9%)	25 (51.0%)

*Site staff collaborated on a single survey for each of the 49 participants.