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Brief Title: Behavioral Treatment of Adolescent Substance Use (SMART)

2/17/15

Design, procedures, materials and methods:
We will recruit adolescent male and females, who enroll in substance use treatment at Mountain Manor Treatment Center Treatment is 26 weeks in duration total, and half the participants will be randomly assigned to Treatment A and receive CM/WMT and the other half of participants will be randomly assigned to Treatment B and receive CM only. Weeks 1-14 involve once weekly sessions with a therapist. The individual sessions will involve a review of substance use, the incentive program, spending ideas, and clarify any questions. The individual sessions will last approximately 30 minutes. Weeks 1-14 also involve once-weekly drug testing. In Treatment A, WMT will be delivered, usually starting in week 2 at Mountain Manor. Weeks 15-26 involve drug testing only. Post-treatment assessment will occur at the end of treatment. There will be three follow up assessments: 14 weeks, 6 months, and 12 months after intake. The final study visit will be the 12 month follow up assessment.

Participants will be randomly assigned to one of two first-line interventions (CM or CM with active WMT). Then treatment response will be assessed at week 4, and non-responders will be randomly assigned to either continue with assigned intervention or to an intensive contingency management (ICM) intervention.

Clinical Site and Participant Recruitment: Participants will present for treatment at Mountain Manor Treatment Center in Baltimore, Maryland. Counselors are Master's level licensed Psychology Associates.

Youth who present for substance use treatment at Mountain Manor will be screened for eligibility and provided the opportunity to participate in the study. We expect to enroll at least 5 youth per month based on the census at Mountain Manor and their history of recruiting youth in their programs into clinical research protocols.

Treatment Components Delivered to all Participants

Clinic-delivered CM. All youth will receive our standard escalating CM incentive program. In weeks 1-2, participants receive $10 incentives for each urine specimen provided as scheduled, regardless of results to facilitate initial compliance with providing specimens. During weeks 3–14, the program targets abstinence from marijuana and other substances by awarding incentives for documented abstinence. Abstinence is defined as abstinence from all substances determined by: 1) urine and breath alcohol tests indicate no use, and 2) participant reports no alcohol or drug use since the last test. The escalating schedule has a maximum value of $570 (complete abstinence). Participants will receive a reloadable prepaid Mastercard (CTpayer, Inc.), and staff will remotely load earned incentives onto the card after each session. The card does not allow teens to withdraw cash. During Weeks 15–26, participants will attend weekly substance testing, and begin a renewed incentive schedule that starts with a $10 incentive and increases by $2 per week.

Working Memory Training. Usually beginning in Week 2, youth assigned to Treatment A will start WMT and will complete up to 5 WMT sessions per week at the clinic (30-45 min), with the goal of completing at least 25 sessions; this replicates or exceeds the number of WMT sessions from previous studies with adults and adolescents. Youth will be trained using Cogmed-RM (Pearson,Inc), which is a commercially available, program used successfully to train WM in youth samples (e.g., normal, ADHD, low birth weight history).(Gibson et al., 2011; Holmes et al., 2010; Klingberg et al., 2005; Klingberg et al., 2002; Lohaugen et al., 2011) The PI, Co-I and the RA have obtained administrative and coach training needed to ensure WMT fidelity. Mountain Manor is currently using WMT in a research protocol with the same population targeted for this study.

Each session will include 15 trials from each of 8 of a possible 12 different WM exercises. The program includes a series of verbal and visuospatial WM tasks with appropriately designed graphics and tasks for this age group. Each task involves the temporary storage and manipulation of visuospatial or verbal information, or both. In the adaptive version, an algorithm based on performance automatically adjusts task difficulty and promotes training at a participant's individual WM capacity. An algorithm also rotates exercises so that equal numbers of trials across each of the 12 exercises are completed. The program has built-in motivational features designed to promote effort and interest, including positive feedback, displays of best scores and earnings on an 'energy bar' that activate access to a robo-racing game.
We will use additional incentives to reinforce effort and improvement, a technique employed in many rehabilitation programs. Youth will get $10 on their reloadable card each time they complete a session. Average scores across each session that are equal to or greater than prior sessions earn a second $5. Youth will also earn a $20 bonus for either completing 3 or more sessions in a week or completing 1 or more sessions than the week before (minimum of 2 sessions). Participants who meet these criteria throughout the study would earn $470.

Intensified Contingency Management (ICM): After 4 weeks of treatment, response will be assessed. Early responders (those abstinent in Week 4) will continue in their assigned intervention. Non-responders (still using substances in Week 4) will be randomly assigned to either continue with the assigned intervention for weeks 5–14 or to begin the ICM intervention. Those assigned to ICM will discontinue their CM incentive program, and initiate a new 11-week incentive program of higher magnitude during Weeks 5-14. ICM differs from CM in that the magnitude of the incentives will increase by approximately three times the relative magnitude of the initial incentive system. This is consistent with a prior adult study, which yielded a 50% positive response rate with this level of increase.(Silverman et al., 1999) ICM during this period will have maximum earnings of $1225 for continuous abstinence across weeks 5-14.
Procedures:

Initial evaluation, informed consent/assent, treatment assignment. The youth must attend the intake evaluation, and sign consent/assent forms covering the intake process and trial participation. Participants will be randomly assigned to one of two first-line interventions (CM or CM with active WMT).

Regarding the WMT assignment: Participants will be told, “you will be assigned randomly to either receive 25 sessions of WMT or not.”

Regarding the potential reassignment to ICM, participants will be told: “at week 4, we will assess your treatment response. If you are doing well (not using substances), you will continue with your current treatment plan. If you are still using substances, you will be randomly assigned to either remain in your current treatment or to a treatment with a revised incentive plan. Details of the revised plan will be explained after reassignment.”

Random assignment to the first line intervention (CM or CM/WMT) will occur immediately prior to session 1. Randomizations will be made using minimum-likelihood allocation as done successfully in prior trials to ensure groups are balanced for variables that may correlate highly with outcome assessments. The first randomization will be balanced on 6 measures: 1) abstinence prior to treatment initiation, 2) clinically significant conduct problems at intake, 3) age > 16, 4) gender, 5) race (white vs. other), 6) receiving treatment for opioid use disorder. The second randomization of non-responders will occur in Week 4 and will be balanced on variables 2 through 5.

Substance monitoring. Participants provide specimens once-weekly during weeks 1–26. Staff are trained and receive ongoing supervision related to handling questions about urine test results. We will use rapid testing devices that provide qualitative results because of ease of use, low cost, and likely use in dissemination efforts. We will protect from invalid results by using test strips for creatinine levels and four indicators of adulteration. Participants with invalid specimens will be asked to provide another specimen within 4–24 hrs. The criteria for cannabis abstinence will be determined by a negative result on our cannabis rapid testing devices; the cutoff on these devices is 50ng/ml. This is the standard THC level set for establishing abstinence in clinical studies, which reflects the clinical standard for using urine results with abstinence-based contingency management intervention. We, and others, have used these procedures effectively in multiple clinical trials.

Staff contact participants who do not attend the clinic at scheduled times, and when necessary, offer to collect specimens away from the clinic. Outreach collection will occur only with permission from the participants. In prior trials, <3% of specimens were collected away from the clinic. Failure to submit a specimen without making alternative arrangements is treated as testing positive for CM implementation.

Statistical Methods.

The a priori, primary hypothesis of the study was that youth receiving CM _ WMT would have better substance use outcomes than those receiving CM. When comparing the two Phase 1 intervention conditions, such analyses are no different from those in a “standard” randomized controlled trial. Zero-inflated negative binomial (ZINB) models compared cannabis use (percent days used and WCA) between conditions during the intervention (Atkins, Baldwin, Zheng, Gallop, & Neighbors, 2013). ZINB models were used because both outcomes were zero inflated (_22% of youth had 0% of days used cannabis and 47% had zero WCA) and somewhat

overdispersed (estimated dispersion parameters: WCA _ .69, 95% CI [.25, 1.91]; percent days used _ .67, 95% CI [.36, 1.25]).

Exploratory analyses compared the four treatment strategies embedded in the trial (see Table 1). Analysis of the treatment strategies requires additional statistical considerations (e.g., weighting and the use of robust [sandwich] standard errors), which are described in detail in Nahum-Shani et al. (2012).

In addition, to compare the four strategies simultaneously, duplicate observations for each responder and for each participant who dropped out before the Phase 2 randomization were added to the data set and assigned to multiple strategies based on starting condition and response. For example, responders assigned to stay in STANDARD CM are included in Strategy 1 (all start in STANDARD CM, all stay in STANDARD CM) and Strategy 3 (all start in STANDARD CM, responders stay in STANDARD CM, and nonresponders switch to ENHANCED CM). In these analyses, the "lowest" level of treatment (start in STANDARD CM and stay in STANDARD) was the comparison condition. TLFB models adjusted for baseline TLFB values. A total of 37 of 59 (63%) participants provided TLFB data on at least 25% of the days during treatment. The percentage of nonmissing TLFB data did not differ significantly between treatment arms, age, race, intake use, tobacco use status, or CUD severity (data not shown).

There are no missing WCA data because missing specimens are considered not abstinent. A sensitivity analysis was performed using the number of negative samples, which treated missing specimens as missing. The same pattern of results was observed. All analyses were performed using SAS Version 9.4. All tests were conducted using a two-sided alpha threshold of .05.