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Examining longitudinal stimulant use and treatment attendance as parallel outcomes in two contingency management randomized clinical trials

Sterling McPherson^{1,2,3,4,6}, Olivia Brooks^{1,2,3}, Celestina Barbosa-Leiker^{1,2,3}, Crystal Lederhos^{1,2,3}, Amanda Lamp^{2,5}, Sean Murphy^{2,3,4}, Matthew Layton^{2,3,5}, and John Roll^{1,2,3,4}

¹Washington State University, College of Nursing

²Washington State University, Program of Excellence in Addictions Research

³Washington State University, Translational Addictions Research Center

⁴Washington State University, Department of Health Policy and Administration

⁵Washington State University, College of Medical Sciences

Abstract

The primary aim of this study was to examine stimulant use and longitudinal treatment attendance in one ‘parallel outcomes’ model in order to determine how these two outcomes are related to one another during treatment, and to quantify how the intervention impacts these two on- and off-target outcomes differently. Data came from two multi-site randomized clinical trials (RCTs) of contingency management (CM) that targeted stimulant use. We used parallel multilevel modeling to examine the impact of multiple pre-specified covariates, including selected Addiction Severity Index (ASI) scores, age and sex, in addition to CM on concurrent attendance and stimulant use in two separate analyses, i.e., one per trial. In one trial, CM was positively associated with attending treatment throughout the trial ($\beta = 0.060$, $p < 0.05$). In the second trial, CM predicted negative urinalysis (¬UA) over the 12-week treatment period ($\beta = 0.069$, $p < 0.05$). In both trials, there was a significant, positive relationship between attendance and ¬UA submission, but in the first trial a ¬UA at both baseline and over time was related to attendance over time ($r = 0.117$; $r = 0.013$, respectively) and in the second trial, a ¬UA submission at baseline was associated with increased attendance over time ($r = 0.055$). These findings indicate that stimulant use and treatment attendance over time are related but distinct outcomes that, when analyzed simultaneously, portray

⁶Corresponding author: Please address all requests for reprints to Dr. Sterling McPherson, PhD, College of Nursing, PO 1495, SNRS 314D, Washington State University, Spokane, WA, 99210-1495, U.S.A.; Phone: (509) 324-7459; Fax: (509) 324-7341; smcpherson05@wsu.edu.

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a more informative picture of their predictors and the separate trajectories of each. This ‘indirect reinforcement’ between two clinically meaningful on-target (directly reinforced behavior) and off-target (indirectly reinforced behavior) outcomes is in need of further examination in order to fully exploit the potential clinical benefits that could be realized in substance use disorder treatment trials.

Keywords

contingency management; clinical trials; treatment attendance; stimulant use; parallel growth modeling

1. Introduction

Substance use disorder (SUD) treatment researchers are usually interested in participants’ use of a targeted substance (e.g., stimulants, opioids) throughout the treatment period (Donovan, 2012; Donovan et al., 2012; Peirce et al., 2006; Petry, Peirce, et al., 2005; J. M. Roll et al., 2006a). Often they are also interested in treatment attendance as an important outcome because of its high correlation with a variety of use-based treatment outcomes (Chi, Campbell, Sterling, & Weisner, 2012; Collins, Malone, & Larimer, 2012; Donovan, 2012; Donovan et al., 2012; Gossop, Stewart, & Marsden, 2008; Petry, Alessi, & Ledgerwood, 2012; J. M. Roll, Chudzynski, Cameron, Howell, & McPherson, 2013; Walker et al., 2010). However, primary analyses for randomized clinical trials (RCTs) examine urinalyses (UAs; e.g., UAs over time, total number of positive UA submissions, etc.) as a separate and independent outcome from treatment attendance (e.g., total number of sessions attended, sessions attended over time, etc.) even though these two outcomes are often necessarily related to one another (Little & Rubin, 2002; McPherson, Barbosa-Leiker, Burns, Howell, & Roll, 2012; Peirce et al., 2006; Petry, Peirce, et al., 2005; J. M. Roll et al., 2013; J. M. Roll et al., 2006a).

In many RCTs, increased attendance is associated with an increase in drug or alcohol abstinence (Manning et al., 2012; Milward, Lynskey, & Strang, 2014; Petry, 2000). When investigating more nuanced change in use while receiving treatment, recent advanced analytic models have demonstrated a more complex relationship if attendance is factored into an analysis (e.g., latent class growth modeling). This evidence suggests that more attendance is not always better, and that it is important to consider the ‘quality of dose received’ or more ‘active involvement’ as the marker of alcohol and drug abstinence during treatment (Hien et al., 2012; Kelly, Stout, & Slaymaker, 2013). Other analyses have found that *any* treatment attendance is consistently better for predicting long-term abstinence (Witbrodt, Kaskutas, Bond, & Delucchi, 2012; Witbrodt, Mertens, et al., 2012). In some (usually non-randomized) investigations, treatment attendance has been used as a predictor of relevant clinical outcomes (e.g., total quantity of alcohol consumed, total heavy drinking days, narcotics anonymous attendance) rather than an independent outcome (Collins et al., 2012; Gossop et al., 2008). Other investigations have found a direct association between attendance or level of treatment exposure and better outcomes across-the-board (Wells et al., 2014). This work points to the need for increased research efforts to define the complicated

relationship between attendance and substance use during drug and alcohol addiction treatment.

CM is based on a strong basic science research literature which has consistently demonstrated that substance use is, at least in part, a type of operant behavior (Bigelow & Silverman, 1999). Therefore, if alternative non-drug reinforcers (e.g., money, prizes) are available, such reinforcement should increase abstinence or attendance (Higgins, Bickel, & Hughes, 1994; Petry, 2000; Petry et al., 2006; Rosen et al., 2007). CM has been consistently demonstrated to increase drug abstinence and/or treatment attendance (Peirce et al., 2006; Petry, Alessi, Marx, Austin, & Tardif, 2005; Petry, Martin, Cooney, & Kranzler, 2000; Petry, Peirce, et al., 2005; J. M. Roll et al., 2006c) across virtually all abused substances including: benzodiazepines (Stitzer, Bigelow, & Liebson, 1979), cocaine (Higgins, Budney, et al., 1994), nicotine (McPherson, Packer, Cameron, Howell, & Roll, 2014; Packer, Howell, McPherson, & Roll, 2012; Stitzer, Rand, Bigelow, & Mead, 1986), opiates (Higgins, Stitzer, Bigelow, & Liebson, 1986; Robles, Stitzer, Strain, Bigelow, & Silverman, 2002), marijuana (Budney, Higgins, Radonovich, & Novy, 2000; Kadden, Litt, Kabela-Cormier, & Petry, 2007), and methamphetamine (J. M. Roll, 2007; J. M. Roll et al., 2013; John M Roll, Rawson, Ling, & Shoptaw, 2009). Dutra et al. (Dutra et al., 2008) reported that CM caused the *largest increase in abstinence* compared to several other types of treatment, and another meta-analysis found that CM interventions produced a treatment episode that was successful 61% of the time, while other comparison treatments did the same only 39% of the time (Prendergast, Podus, Finney, Greenwell, & Roll, 2006).

CM has consistently improved treatment retention (Higgins, Budney, et al., 1994; Petry, 2000; Petry et al., 2000) even though most CM trials have reinforced drug abstinence. CM often results in a plethora of ‘off-target’, positive treatment outcomes (M. McDonell et al., 2014; M. G. McDonell et al., 2013). Petry et al. (2006) found that reinforcing abstinence directly results in better treatment outcomes (including both increased submission of negative UAs and increased treatment attendance) compared to either standard care or reinforcement of treatment attendance. However, a currently under-recognized potential problem with analyzing UAs and attendance separately within a CM trial is that they are intrinsically linked. When abstinence is being reinforced, participants must first be present in order to be considered for abstinence. This creates a situation wherein treatment attendance can be ‘indirectly reinforced’ because being present to submit a UA for analysis first requires a secondary, related but distinct behavior occurrence (i.e., attending the visit). As far as our research team is aware, the potential for a reciprocal relationship between treatment attendance and the primary outcome of UAs has not been modeled in a longitudinal multivariate framework, leaving a significant gap in the current literature.

The primary aim of this study was to begin to fill this gap by examining treatment attendance and UAs throughout the treatment period in two multi-site RCTs of CM using multilevel parallel growth modeling in order to understand the longitudinal relationship between treatment, attendance and abstinence. This will help to elucidate how treatment may have an impact on off-target attendance through its impact on the primary on-target outcome of UA status (i.e., abstinence). In addition, our analysis also included several pre-specified covariates in an attempt to further explicate differences in association between

these covariates and their respective on-target (i.e., substance use) and off-target (i.e., treatment attendance) outcomes which could drive future design considerations when deciding what specifically to target with CM and when (e.g., in the context of being combined with a pharmacotherapy versus combined with psychosocial treatment).

2. Methods

2.1 Secondary Data Source

Data for this investigation come from two previously published RCTs conducted through the National Drug Abuse Treatment Clinical Trials Network (CTN) and through a publicly available database (<http://datashare.nida.nih.gov>). Below we summarize the RCT methodology descriptions that can be found in the original publications (Peirce et al., 2006; Petry, Peirce, et al., 2005) and other secondary analyses that have been published (Brooks et al., 2013; Defulio et al., 2013; Wu et al., 2013). Both of these RCTs evaluated stimulant use among participants enrolled in an abstinence-based CM intervention while also receiving treatment as usual for a stimulant use disorder in either a psychosocial (i.e., non-opioid agonist; CTN 0006) treatment program (Petry, Peirce, et al., 2005) or in the context of a methadone maintenance treatment program (CTN 0007) (Peirce et al., 2006).

Importantly, both of the original investigations examined the impact of CM on both treatment attendance and stimulant use over time, but did so using generalized estimating equations (GEE) and ran separate models for attendance and stimulant use. Our intent is to build on those analyses by understanding the direct effects of CM on stimulant use at baseline (i.e., intercept) and over time (i.e., linear slope), along with attendance over time using a linear slope, within the same model since the outcomes are inherently related to one another. In addition, our modeling strategy will build on the previously reported findings by estimating the relationship between baseline stimulant use and attendance and stimulant use over time using random effects to capture inter- and intra-individual variation (Muthen & Muthen, 1998–2010). Because attendance to a baseline visit was required in both RCTs, we include an intercept growth factor for attendance in each RCT model, but we do not associate this random effect with any other variable because it has no variance. Lastly, we examine whether a set of pre-specified covariates are related to both of these outcomes (i.e., treatment attendance and stimulant use) over time and to stimulant use at baseline, and how such covariate relationships differ by outcome and trial.

The comparison of these two RCTs provides a unique opportunity to examine the on-target outcome (i.e., stimulant UA) and the off-target outcome (i.e., treatment attendance) simultaneously. This is of interest because CM targeted the same outcome in both trials, but with divergent results. The primary findings from CTN 0006 were that CM had a significant impact on retention, attendance and provision of urine samples (Petry, Peirce, et al., 2005). However, for the CTN 0007 trial CM had a significant impact on stimulant use, but not attendance (Peirce et al., 2006).

2.2 Participants

Participants in the psychosocial treatment study (CTN 0006) were recruited from 8 different treatment programs across the US that did not administer any type of opioid agonist therapy

(Petry, Peirce, et al., 2005). Participants who were eligible for this study: 1) self-reported use of stimulants within a 2-week period of entering the study, 2) used stimulants within a 2-week period of entering a type of controlled environment (e.g., hospital, correctional facility, or an inpatient detoxification unit) and left the controlled facility within a 2-week period of enrolling in the study, or 3) submitted a stimulant positive UA (⁺UA) at treatment intake (Petry, Peirce, et al., 2005; Wu et al., 2013).

Participants in the methadone maintenance treatment study (CTN 0007) came from 6 different programs across the US (Peirce et al., 2006), all of which utilized methadone as part of their treatment regimen for opioid-dependent patients (Peirce et al., 2006; Wu et al., 2013). Participants who were eligible for this study: 1) submitted a cocaine or amphetamine stimulant ⁺UA during treatment or, within 2-weeks of study enrollment, 2) used stimulants within a 2-week period of entering a type of controlled environment (e.g., hospital, correctional facility, or an inpatient detoxification unit) and left the controlled facility within a 2-week period of enrolling in the study, 3) self-reported that they were not currently in recovery from a gambling disorder, and 4) correctly answered 80% or more of quiz questions about study procedures that covered risks, benefits, and requirements during study involvement (Peirce et al., 2006; Wu et al., 2013).

2.3 Procedure

As is standard procedure for collecting demographic information across CTN investigations, upon study entry participants provided their age, sex, race/ethnicity and several other variables. All participants were assessed for alcohol and substance use disorders (i.e., marijuana, cocaine, amphetamines, methamphetamine, and opioids) (Forman, Svikis, Montoya, & Blaine, 2004; Hudziak et al., 1993; Wu et al., 2013) using the DSM-IV checklist. Upon completion of the intake assessment, participants were randomized to either the CM arm or the control arm of the study. Importantly, study participation did not interfere with the receipt of usual care (Peirce et al., 2006; Petry, Peirce, et al., 2005).

Each participant in both of these trials was expected to attend a clinical research visit twice weekly (non-consecutive days) during a 12-week treatment period (24 total visits) to submit a urine sample for analysis. Visits were individualized to coincide with attendance to treatment as usual, making participation in either of the trials part of the visits to receive standard care. In fact, every effort was made to ensure that the research visits coincided with the many different treatment as usual visits that participants attended while enrolled in one of the two RCTs. Participants in the CM arm in either trial received chances, or 'draws', to earn prizes in exchange for a stimulant negative urine (⁻UA) sample and an alcohol negative breath sample. Prizes ranged in value from a chip that said 'Good Job', to 'Jumbo' prizes that were worth \$80–\$100. Participants received escalating reinforcement the longer they remained abstinent from stimulants (i.e., an increase of 1 draw for each week of complete abstinence with a maximum of 12 draws). If a stimulant ⁺UA sample or an alcohol positive breath sample was submitted (or the participant missed an unexcused visit) the participant was 'reset' to receive only one chance to draw a prize. The full details of the abstinence incentive algorithm for determining the number of possible draws per participant based on stimulant and alcohol abstinence can be found in the originally reported clinical trials and/or

other recent secondary analyses of these trials (Brooks et al., 2013; Defulio et al., 2013; Peirce et al., 2006; Petry, Peirce, et al., 2005; Wu et al., 2013).

2.4 Statistical Analysis

Initially, we conducted chi-square and t-test analyses (for categorical and continuous data, respectively) in order to examine basic differences and similarities in demographics and ASI composite among participants enrolled in one of the two RCTs (CTN 0006: n=442; CTN 0007: n=394). Next, we examined the impact of CM on attendance and stimulant $\bar{U}$ As among participants in each of the two trials. While the trials are very similar in procedure, the nature of the clinics included in both of these trials was substantially different, and the type of patients recruited differed across the trials as well. For this investigation we were interested in understanding the simultaneous impact of CM on stimulant use and attendance to inform future treatment development and analytic methods, but importantly, our populations within the two RCTs differ substantially and as such the models were estimated and discussed separately.

For each model, we also included a number of pre-specified covariates for inclusion in our analysis of attendance and stimulant $\bar{U}$ As over time. These covariates included baseline Addiction Severity Index (ASI) composite scores on both longitudinal outcomes. We selected all of the ASI composite scores in addition to age, sex, and race/ethnicity.

We utilized parallel multi-level growth modeling for this analysis (Muthen & Muthen, 1998–2010) wherein stimulant $\bar{U}$ As (but not attendance) was modeled with a random intercept (i.e., baseline status), and both stimulant use and attendance was modeled with a random linear slope (i.e., change over time) growth factor at the between-level across 24 visits that included submission of a urine sample. No within-individual covariates were modeled. An overview of our parallel multi-level model of stimulant use and treatment attendance is presented in Figure 1. The ovals represent the random effects for the intercepts and the slopes, while the variables listed in the box represent fixed effect predictors of the two outcomes under investigation. Importantly, and as noted above, the attendance intercept is included as a placeholder in order to correctly specify the growth model. It is not associated with any other random effects or covariates. Each of the relationships (i.e., either single-headed regression paths or double-headed association paths) in the schematic are broken down in detail in the Results.

Missing data was addressed using maximum likelihood, which is a method consistent with current expert recommendations (Enders, 2010; Little & Rubin, 2002; McPherson et al., 2012; McPherson, Barbosa-Leiker, McDonell, Howell, & Roll, 2013). Unfortunately, while we would ordinarily account for the potential site effects that could be present in this analysis, the policy concerning the release of publically available data through the CTN disallows the inclusion of site in the dataset in order to avoid the potential identification of participants who were involved in the investigation. We set our alpha threshold at $p < 0.05$ in order to determine statistical significance. All analyses were conducted in Mplus 7.2 (Muthen & Muthen, 1998–2010) and we used robust maximum likelihood in order to estimate our model.

3. Results

3.1 Demographics Across CTN 0006 and CTN 0007

As shown in Table 1, participants differed significantly across the two clinical trials on all demographics and all of the ASI composite scores, with the exception of the psychiatric dimension. However, in most instances, the differences were not large. Participants enrolled in CTN 0007 were approximately 3 years younger, had 10% more females and 4% fewer African Americans. CTN 0006 had, on average, lower ASI composite scores on the alcohol, legal, and family indices; but higher scores on the medical, drug, and employment dimensions.

3.2 CTN 0006: Predictors of Stimulant Use and Attendance Over Time

In the context of the trial with outpatient psychosocial drug-free clinics, CM was not associated with UA submission status at baseline or over time (see Table 2). However, the ASI Employment score was inversely associated with stimulant use throughout the 12-week trial ($\beta = -0.137, p < 0.05$; see Table 2; Outcomes = UA Slope), such that a higher ASI Employment score was indicative of more stimulant use during treatment. The ASI Drug score was associated with a significantly lower likelihood of a –UA submission at baseline ($\beta = -6.263, p < 0.05$) and with fewer –UA submissions throughout the treatment period ($\beta = -0.359, p < 0.05$).

CM was associated with a higher likelihood of attending treatment visits throughout the trial ($\beta = 0.060, p < 0.05$; see Table 3; Outcomes = AT Slope). The ASI Legal score ($\beta = 0.123, p < 0.05$) and the ASI Employment score ($\beta = -0.075, p < 0.05$) were both associated with attendance over time, indicating that a higher legal score predicted higher levels of attendance over time while a higher employment score was associated with lower levels of attendance during treatment. Lastly, the ASI Drug score was associated with attending significantly fewer treatment visits throughout the treatment period ($\beta = -0.343, p < 0.05$).

3.3 CTN 0007: Predictors of Stimulant Use and Attendance Over Time

In the context of the trial with methadone maintenance clinics, age ($\beta = -0.032, p < 0.05$; see Table 4; Outcomes = UA Intercept) and ASI Drug score ($\beta = -6.417, p < 0.05$) were negatively associated with submitting a stimulant –UA sample at baseline. ASI Psychiatric score ($\beta = 2.191, p < 0.05$; see Table 4; Outcomes = UA Intercept) was positively associated with submitting a stimulant –UA sample at baseline. CM was a significant predictor of –UA for stimulant use over the 12-week treatment period ($\beta = 0.069, p < 0.05$), such that those in the CM group provided more –UA stimulant samples over time. Similar to CTN 0006, the ASI Employment score was inversely associated with stimulant use throughout the 12-week trial ($\beta = -0.117, p < 0.05$; see Table 4; Outcomes = UA Slope), such that a higher ASI Employment score was indicative of more stimulant use during treatment.

Age was associated with greater attendance throughout the treatment period ($\beta = 0.002, p < 0.05$; see Table 5), while both being white (relative to all other racial/ethnic categories; $\beta = -0.040, p < 0.05$) and the ASI Legal composite ($\beta = -0.096, p < 0.05$) score were associated with less treatment attendance over time.

3.4 Associations Between Stimulant Use and Attendance Random Effects

As indicated in Figure 1, all of the random effects, with the exception of baseline attendance, were tested for significant associations amongst one another. For CTN 0006 there was a significant, positive association between the stimulant $\neg$ UA slope ($r = 0.117, p < 0.05$) and the $\neg$ UA intercept ($r = 0.013, p < 0.05$) with the attendance slope (see Table 6) indicating that less stimulant use at baseline and over time was associated with more treatment attendance throughout the trial. A similar pattern emerged for the CTN 007 random effects covariance analysis such that the $\neg$ UA intercept ($r = 0.055, p < 0.05$) was positively associated with more treatment attendance over time during the trial.

4. Discussion

4.1 Main Findings

The impact of CM on the primary outcome of stimulant $\neg$ UA and treatment attendance, both at trial baseline and throughout the 12-week treatment regimen, varied significantly between trial but in both trials there were off-target (i.e., significant associations with attendance) effects. In addition, both trials evidenced significant relationships between stimulant $\neg$ UA (i.e., either intercept, slope, or both) and treatment attendance over time. This is a signal of indirect reinforcement and off-target effects in both trials, but to varying degrees based on the differences in type and magnitude of association. Age, sex, race/ethnicity, and ASI composite scores also varied in their associations with the primary outcome of stimulant $\neg$ UA and treatment attendance. This provides evidence for a need to tailor future treatment trials to different populations perhaps based on these characteristics, but also on the type of clinical context and existing co-addiction (i.e., outpatient psychosocial clinics versus methadone maintenance clinics).

The reason for the different degrees of indirect reinforcement are likely multi-faceted, but our initial analyses could indicate that patients who are already receiving methadone are more conditioned to attend treatment. This may remove a potential barrier to a successful treatment episode thus allowing patients already receiving methadone to focus more clearly on their co-morbid stimulant use disorder. For the drug-free clinic patients, attendance was lower overall compared to the methadone patients. Interestingly, attendance over time was associated with both $\neg$ UA at baseline and over time, whereas only the slopes were related amongst the methadone patients. This could be indicative of a stronger off-target effect in this trial because attendance was a barrier needing to be overcome before being able to significantly decrease their stimulant use. When combined with the drug-free clinic patients' increased disease burden (i.e., higher baseline ASI Drug and ASI Medical scores), this could have resulted in an imbalance such that the low-cost incentives were too low to reinforce both the requisite attendance and stimulant abstinence.

These findings also build upon and replicate the original analyses reported for both of these trials. While we observed the same basic findings related to attendance for CTN 0006 and stimulant $\neg$ UA for CTN 0007, this investigation further documented the effects of CM on baseline use, and the relationship between stimulant $\neg$ UA and attendance over time, which could be leveraged for clinical benefit in future treatment protocols. Moreover, our analyses

provide a potential template for future investigations wherein there is an inherent reinforcement dependency due to the nature of reinforced delivery that requires another observable behavior, such as treatment attendance.

4.2 Unique Contributions of Findings

To our knowledge, this is the first investigation of two large CM trials utilizing a parallel outcomes analysis that simultaneously evaluates the impact of CM on both attendance and the primary outcome of UAs over time. Such an analysis is the first to examine the indirect reinforcement between the primary targeted outcome (i.e., stimulant use) and an off-target outcome (i.e., attendance) in detail. This investigation helps elucidate both the separation and the overlap between the trajectories of both outcomes, and provides a framework for future investigations that examine two parallel outcomes of interest simultaneously. We have demonstrated that while there is a significant indirect reinforcement between these two outcomes, there is also a difference in the impact of multiple pre-specified covariates across the two outcomes (i.e., covariates of one outcome are not necessarily covariates of the other, closely related but distinct outcome). This should inform future clinical trial development when the research team is deciding how best to target the intervention and what, if any, off-target clinical benefits may be realized.

Elsewhere, we have reported on other off-target substance use changes when participants are receiving CM for a targeted substance (e.g., decreased tobacco smoking when stimulant use was the targeted substance) (M. McDonell et al., 2014; M. G. McDonell et al., 2013). In both of the trials reported here, participants were eligible to receive additional prizes if they provided urine samples that were free of opioids and marijuana (Peirce et al., 2006; Petry, Peirce, et al., 2005), which suggests additional off-target effects that could be examined using a parallel outcomes analysis. Such a procedure is not uncommon in several types of clinical trial investigations, including those that have utilized CM. It is likely that additional indirect reinforcement effects exist in previously conducted trials. Additional research attention should be focused on these indirect reinforcement effects in order to better understand the potential ‘secondary effects’ of CM on attendance, off-target substances, and other outcomes of interest that may share, to varying extents, a level of dependency with the primary outcome.

4.3 Limitations

There are several limitations with this project. First, only CM interventions were included in the analysis. It would be beneficial to analyze other RCTs to understand whether there are similar indirect off-target effects. Second, we did not conduct advanced classification modeling techniques (e.g., latent class analysis) wherein the primary outcome is modeled in such a way as to account for the direct and indirect influence of another outcome such as attendance. While we believe such work is important to further inform the literature on this topic, we view the current study as a critical first step in understanding how stimulant use is related to attendance over time in a ‘single class model’. Future studies may want to build on this methodology by examining potential classification schemes that may help explore separate but related questions pertaining to the existence of sub-groups based on change in two or more outcomes. Lastly, our inability to control for site differences across the two

trials due to the CTN data use agreements represents a limitation of the current set of analyses and should be taken under consideration when evaluating our findings.

4.4 Conclusions

These findings indicate that stimulant use and attendance to treatment over time are related but distinct outcomes that should be analyzed in concert with one another in order to better understand their predictors and trajectories. Future clinical trials might consider evaluating these outcomes simultaneously in the random effects context as we have done here, in order to recognize potential covariate effects and the impact of treatment on multiple primary outcomes simultaneously, such as attendance and substance use.

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Highlights

- The primary aim of this study was to examine treatment attendance and stimulant use in one ‘parallel outcomes’ model in order to determine how these two related outcomes impact one another during stimulant use disorder treatment.
- In one trial, contingency management (CM) was positively associated with attending treatment throughout the trial ($\beta = 0.060, p < 0.05$), but it was not related to urinalysis (UA) status during the trial.
- In the second trial, CM positively predicted $\neg$ UA over the 12-week treatment period ($\beta = 0.069, p < 0.05$), and CM was not associated with attendance during the treatment period.
- In both trials, there was a significant, positive relationship between attendance and $\neg$ UA submission. In the first trial a $\neg$ UA at both baseline and over time was related to attendance over time ($r = 0.117; r = 0.013$, respectively, $p < 0.05$), but in the second trial only baseline $\neg$ UA submission was related to attendance over time ($r = 0.055, p < 0.05$).
- These findings indicate that stimulant use and treatment attendance over time are related but distinct outcomes that, when analyzed simultaneously, portray a more informative picture of their predictors and the separate trajectories of each.

Figure 1.

Parallel multi-level growth model of substance use and treatment attendance across two contingency management clinical trials. (Note: Between-level only shown; UA = stimulant urine analysis, AT = treatment attendance.)

Table 1

Participant characteristics across two CTN contingency management clinical trials.

	CTN 006 & CTN 007	Psychosocial Drug-Free Outpatient Clinics (CTN 006)	Methadone Maintenance Clinics (CTN 007)	p Value
Age ¹	38.73 (9.10)	35.86 (8.67)	41.95 (8.47)	< 0.001 [*]
Female ²	50.2 (418)	55.2 (243)	44.6 (175)	0.002 [*]
Race/Ethnicity				0.008 [*]
African American ²	45.9 (382)	42.0 (185)	50.3 (197)	
White ²	31.0 (258)	35.7 (157)	25.8 (101)	
Hispanic ²	14.7 (122)	13.2 (58)	16.3 (64)	
Other ²	8.3 (69)	9.1 (40)	7.4 (29)	
ASI Alcohol ¹	0.13 (0.36)	0.17 (0.24)	0.08 (0.15)	< 0.001 [*]
ASI Medical ¹	0.29 (0.34)	0.25 (0.34)	0.32 (0.37)	0.004 [*]
ASI Drug ¹	0.23 (0.13)	0.17 (0.11)	0.29 (0.12)	< 0.001 [*]
ASI Psychiatric ¹	0.26 (0.25)	0.28 (0.26)	0.24 (0.23)	0.052
ASI Legal ¹	0.11 (0.19)	0.13 (0.20)	0.09 (0.17)	0.003 [*]
ASI Employment ¹	0.72 (0.30)	0.67 (0.31)	0.78 (0.28)	< 0.001 [*]
ASI Family ¹	0.18 (0.23)	0.22 (0.25)	0.14 (0.20)	< 0.001 [*]

* = $p < 0.05$;¹ M (SD);² = % (N).

Table 2

Parallel multi-level growth model of UAs across 12-week contingency management clinical trial (CTN 006).

Covariates	Outcomes	Unstandardized Estimate (β)	Standard Error	p Value
Trial Arm →	UA Intercept	0.542	0.287	0.059
Age →	UA Intercept	0.014	0.021	0.495
Sex →	UA Intercept	0.076	0.334	0.819
African American* →	UA Intercept	− 0.420	0.416	0.312
White* →	UA Intercept	0.522	0.379	0.168
ASI Alcohol →	UA Intercept	0.139	0.683	0.839
ASI Medical →	UA Intercept	− 0.457	0.436	0.295
ASI Drug →	UA Intercept	− 6.263	1.387	< 0.001
ASI Psychiatric →	UA Intercept	0.389	0.689	0.577
ASI Legal →	UA Intercept	− 0.222	0.762	0.770
ASI Employment →	UA Intercept	0.858	0.479	0.074
ASI Family →	UA Intercept	1.300	0.671	0.053
Trial Arm →	UA Slope	− 0.006	0.026	0.826
Age →	UA Slope	− 0.001	0.002	0.727
Sex →	UA Slope	0.030	0.031	0.342
African American* →	UA Slope	0.061	0.037	0.096
White* →	UA Slope	0.023	0.034	0.500
ASI Alcohol →	UA Slope	− 0.002	0.057	0.975
ASI Medical →	UA Slope	− 0.017	0.040	0.675
ASI Drug →	UA Slope	− 0.359	0.143	0.012
ASI Psychiatric →	UA Slope	0.006	0.063	0.928
ASI Legal →	UA Slope	0.074	0.064	0.248
ASI Employment →	UA Slope	− 0.137	0.045	0.002
ASI Family →	UA Slope	−0.006	0.057	0.913

UA Intercept = stimulant urinalysis at baseline (0 = negative UA; 1 = positive UA); UA Slope = stimulant urinalysis across the 12-week treatment period (0 = negative UA; 1 = positive UA); Trial Arm = clinical trial group assignment (0 = Control Group; 1 = CM Group); Sex = patient gender (0 = females; 1 = male).

* All remaining categories = comparison group. $p < 0.05$ = bold text.

Table 3

Parallel multi-level growth model of attendance across 12-week contingency management clinical trial (CTN 006).

Covariates	Outcomes	Unstandardized Estimate (β)	Standard Error	p Value
Trial Arm →	AT Slope	0.060	0.020	0.003
Age →	AT Slope	0.002	0.001	0.200
Sex →	AT Slope	– 0.026	0.022	0.241
African American* →	AT Slope	0.016	0.028	0.569
White* →	AT Slope	0.014	0.027	0.618
ASI Alcohol →	AT Slope	– 0.026	0.046	0.576
ASI Medical →	AT Slope	– 0.024	0.031	0.452
ASI Drug →	AT Slope	– 0.343	0.104	0.001
ASI Psychiatric →	AT Slope	– 0.012	0.049	0.810
ASI Legal →	AT Slope	0.123	0.051	0.016
ASI Employment →	AT Slope	– 0.075	0.035	0.031
ASI Family →	AT Slope	0.039	0.044	0.379

AT Slope = treatment attendance across the 12-week treatment period (0 = did not attend; 1 = attended); Trial Arm = clinical trial group assignment (0 = Control Group; 1 = CM Group); Sex = patient gender (0 = females; 1 = male).

* All remaining categories = comparison group. $p < 0.05$ = bold text.

Table 4

Parallel multi-level growth model of UAs across 12-week contingency management clinical trial (CTN 007).

Covariates	Outcomes	Unstandardized Estimate (β)	Standard Error	p Value
Trial Arm →	UA Intercept	0.317	0.339	0.350
Age →	UA Intercept	− 0.032	0.015	0.035
Sex →	UA Intercept	0.563	0.355	0.112
African American* →	UA Intercept	− 0.061	0.437	0.890
White* →	UA Intercept	0.195	0.452	0.666
ASI Alcohol →	UA Intercept	1.273	1.187	0.283
ASI Medical →	UA Intercept	0.409	0.497	0.410
ASI Drug →	UA Intercept	− 6.417	1.355	< 0.001
ASI Psychiatric →	UA Intercept	2.191	0.813	0.007
ASI Legal →	UA Intercept	0.112	1.020	0.913
ASI Employment →	UA Intercept	0.618	0.630	0.327
ASI Family →	UA Intercept	0.364	0.909	0.689
Trial Arm →	UA Slope	0.069	0.024	0.004
Age →	UA Slope	− 0.001	0.001	0.576
Sex →	UA Slope	0.031	0.025	0.206
African American* →	UA Slope	0.008	0.030	0.783
White* →	UA Slope	− 0.017	0.034	0.617
ASI Alcohol →	UA Slope	− 0.103	0.083	0.218
ASI Medical →	UA Slope	0.039	0.036	0.274
ASI Drug →	UA Slope	− 0.158	0.106	0.139
ASI Psychiatric →	UA Slope	0.024	0.058	0.676
ASI Legal →	UA Slope	0.093	0.072	0.198
ASI Employment →	UA Slope	− 0.117	0.046	0.012
ASI Family →	UA Slope	0.007	0.065	0.916

UA Intercept = stimulant urinalysis at baseline (0 = negative UA; 1 = positive UA); UA Slope = stimulant urinalysis across the 12-week treatment period (0 = negative UA; 1 = positive UA); Trial Arm = clinical trial group assignment (0 = Control Group; 1 = CM Group); Sex = patient gender (0 = females; 1 = male).

* All remaining categories = comparison group. $p < 0.05$ = bold text.

Table 5

Parallel multi-level growth model of attendance across 12-week contingency management clinical trial (CTN 007).

Covariates	Outcomes	Unstandardized Estimate (β)	Standard Error	p Value
Trial Arm →	AT Slope	0.007	0.013	0.589
Age →	AT Slope	0.002	0.001	0.029
Sex →	AT Slope	0.018	0.014	0.172
African American* →	AT Slope	– 0.014	0.018	0.440
White* →	AT Slope	– 0.040	0.020	0.042
ASI Alcohol →	AT Slope	0.011	0.043	0.788
ASI Medical →	AT Slope	– 0.024	0.019	0.206
ASI Drug →	AT Slope	– 0.092	0.056	0.103
ASI Psychiatric →	AT Slope	– 0.056	0.031	0.072
ASI Legal →	AT Slope	– 0.087	0.040	0.028
ASI Employment →	AT Slope	0.032	0.024	0.194
ASI Family →	AT Slope	0.067	0.034	0.050

AT Slope = treatment attendance across the 12-week treatment period (0 = did not attend; 1 = attended); Trial Arm = clinical trial group assignment (0 = Control Group; 1 = CM Group); Sex = patient gender (0 = females; 1 = male).

* All remaining categories = comparison group. $p < 0.05$ = bold text.

Table 6

Parallel growth random effect model of attendance and UAs across 2 12-week contingency management clinical trials.

Random Effect	Random Effect	Covariance	Standard Error	p Value
<i>Psychosocial Drug-Free Outpatient Clinics (CTN 006)</i>				
UA Intercept $\leftarrow \rightarrow$	UA Slope	0.015	0.028	0.585
UA Intercept $\leftarrow \rightarrow$	AT Slope	0.117	0.034	0.001
UA Slope $\leftarrow \rightarrow$	AT Slope	0.013	0.004	< 0.001
<i>Methadone Maintenance Clinics (CTN 007)</i>				
UA Intercept $\leftarrow \rightarrow$	UA Slope	0.033	0.037	0.363
UA Intercept $\leftarrow \rightarrow$	AT Slope	0.055	0.022	0.013
UA Slope $\leftarrow \rightarrow$	AT Slope	0.003	0.002	0.061

AT Slope = treatment attendance across the 12-week treatment period (0 = did not attend; 1 = attended); UA Intercept = stimulant urinalysis at baseline (0 = negative UA; 1 = positive UA); UA Slope = stimulant urinalysis across the 12-week treatment period (0 = negative UA; 1 = positive UA). $p < 0.05$ = bold text.