Measuring Outcome in the Treatment of Cocaine Dependence

Paul Crits-Christoph***, Robert Gallop†, Mary Beth Connolly Gibbons§, Jaclyn S Sadicario∥ and George Woody¶

1Department of Psychiatry, University of Pennsylvania, 3535 Market Street, Philadelphia, PA 19104, USA
2Applied Statistics Program, Department of Mathematics, West Chester University, 25 University Avenue, West Chester, PA 19383, USA

Abstract

**Background:** Little is known about the extent to which outcome measures used in studies of the treatment of cocaine dependence are associated with longer-term use and with broader measures of clinical improvement. The current study examined reductions in use, and abstinence-oriented measures, in relation to functioning and longer-term clinical benefits in the treatment of cocaine dependence.

**Methods:** Overall drug use, cocaine use, and functioning in a number of addiction-related domains for 487 patients diagnosed with DSM-IV cocaine dependence and treated with one of four psychosocial interventions in the NIDA Cocaine Collaborative Treatment Study were assessed monthly during 6 months of treatment and at 9, 12, 15, and 18 month follow-up.

**Results:** Measures of treatment-reduction in use were moderately correlated with drug and cocaine use measures 12 months, but showed non-significant or small correlations with measures of functioning at 12 months. Highest correlations were evident for abstinence measures (maximum consecutive days abstinence and completely abstinent) during treatment in relation to sustained (3 month) abstinence at 12 months. Latent class analysis of patterns of change over time revealed that most patients initially (months 1 to 4 of treatment) either became abstinent immediately or continued to use every month. Over the course of follow-up, patients either maintained abstinence or used regularly – intermittent use was less common.

**Conclusions:** There were generally small associations between various measures of cocaine use and long-term clinical benefits other than abstinence, was associated with continued abstinence. No one method of measuring outcome of treatment of cocaine dependence appears superior to others.

Keywords: Cocaine dependence; Psychosocial treatment; Patterns of change; Abstinence; Relapse

Introduction

The U.S. Food and Drug Administration (FDA) standard for evaluating medications for treating substance dependence has been the degree to which they achieve abstinence. Such an “all or none” criterion has not been used to approve medications for hypertension, depression, and many other disorders where a reduction in the target symptom, short of its absence, has been an acceptable endpoint. These FDA decisions appear to be based on data showing that a reduction in the target symptom is associated with clinically meaningful benefits. For example, a medication that lowers blood pressure from 220/110 to 145/95 reduces the risk of heart attacks and strokes even though it does not achieve the optimal level of 120/70.

The extent to which reductions in cocaine use are associated with clinically meaningful benefits has not been systematically evaluated. Part of the problem in evaluating the efficacy of treatment for cocaine dependence has been that, across the literature on psychosocial and pharmacological treatments, no consensual method for evaluating outcome in trials involving cocaine dependent individuals has emerged. Examples of how outcome has been evaluated in these studies include, among other approaches, the following: (1) percent of negative/positive (for cocaine) urines across all of treatment [1-4]; (2) number (or percent) of days using cocaine in the past 30 days [5,6] or 90 days [7]; (3) any cocaine reduction from baseline [5], (4) percent reduction in days using cocaine from baseline of 50% or greater [5,8] or 75% or greater [8,9], (5) binary outcome of whether or not abstinence has been achieved/maintained for the past 30 days [1,5] or 90 days [7], (6) single visit cocaine urine result at follow-up [1,5,10], (7) regular use (or not) of cocaine, defined as weekly (or more frequent) use of cocaine during a follow-up period [10,11], (8) maximum number of cocaine use days in a row over 3 months [7], (9) longest number of days or weeks of continuous abstinence [3,7,8,12,13] (10) binary variable for success, defined as 9 or more weeks of continuous abstinence over 12 weeks or 92% days or greater of abstinence from cocaine [12], (10) weekly urine quantitative concentrations of the cocaine metabolite benzoylecgonine [14-17], (11) urines (collected 2 or 3 times/week) coded as positive/negative based on benzoylecgonine concentrations of 300 ng/ml or greater and analyzed as a repeated measure over the course of treatment [1,18-21], (12) binary variable of achieving 3 or more weeks of consecutive abstinence from cocaine [8,9,13,21-25], (13) percent of days in past week not using cocaine measured weekly throughout treatment [8], (14) time to first cocaine use [6].

Recently, McCann and Li [26] suggested a new way of evaluating outcome in a study of methamphetamine dependence. This method involved focusing only on treatment success defined in terms of achieving multiple weeks of abstinence lasting through the end of the study, and quantified the degree of success by calculating the number of beyond-threshold weeks of success. For example, a threshold for...
success could be set at 1 week of end-of-study abstinence; variations in the degree of beyond-threshold success would then include values from 1 to 11, with 1 corresponding to 2 weeks end-of-study abstinence and 11 corresponding to abstinence throughout an entire 12-week trial. Using these methods, McCann and Li [26] found significant outcome differences between bupropion and placebo in the treatment of methamphetamine dependence, despite the fact that the original study [27] found no treatment differences using weekly methamphetamine-free urines over 12 weeks as the outcome measure. The extent to which such end-of-study abstinence measures are promising ways to examine outcome in the treatment of cocaine dependence has not been examined to date.

The criteria for evaluating outcome take on greater importance now that advances in the neuroscience of addiction pretend the advent of possibly successful pharmacological interventions for treating cocaine dependence [28,29]. Regulatory agencies such as the U.S. Food and Drug Administration will need to be able to set standards for companies requiring guidance about the design of cocaine treatment trials, and such standards will facilitate the comparison of results across studies.

The goal of the current study was to evaluate the relative merits of various methods for measuring outcomes, including end-of-study abstinence measures, during the active treatment of cocaine dependence. The relative merits of various methods for measuring outcome during active treatment were evaluated by examining their predictive validity in regard to other measures, including both longer-term measures of drug use and measures of functioning. Thus, we explored the associations between active treatment phase cocaine use outcomes and (1) measures of cocaine use across follow-up, and (2) broader measures of functioning during active treatment and follow-up. To further understand the nature of active treatment outcome in relation to longer-term outcome, we examined patterns of change in cocaine use during active treatment, using latent class analysis, in relation to longer-term drug use. These associations were examined using data from the National Institute on Drug Abuse Cocaine Collaborative Study [30].

Materials and Methods

Design and procedures

The design and procedures of the NIDA CCTS have already been detailed in other articles [30,31]. The NIDA CCTS was a multi-site randomized clinical trial that compared the efficacy of four psychosocial treatments for cocaine dependence. For two of the treatments, professional psychotherapy, either cognitive therapy (CT) [32] or supportive-expressive psychodynamic therapy (SE) [33,34], was provided in addition to group drug counseling (GDC) [35]. A third treatment combined individual drug counseling (IDC) [36] with GDC. The fourth treatment was GDC alone. Treatment consisted of 6 months of active phase treatment followed by a 3-month booster phase. For each of the three individual treatments, sessions were held twice per week during the first 12 weeks, weekly during weeks 13 to 24, and monthly during the booster phase. Group drug counseling sessions were held weekly during the active phase treatment. During the booster phase, patients in the GDC alone condition met with the group counselor individually once per month. Further details on therapies and therapists can be found in previous publications on the NIDA CCTS [30,31].

Patients

A total of 487 outpatients were randomly assigned to one of the four treatment conditions. To be eligible, patients needed to qualify for a principal diagnosis of cocaine dependence according to the Diagnostic and Statistical Manual of Mental Disorders (4th edition) (DSM-IV) [37] and have used cocaine during the past 30 days. Patients were excluded if they met diagnostic criteria for polysubstance dependence, opioid dependence (current or in early partial remission), principal diagnosis of alcohol dependence, dementia, or other irreversible organic brain syndrome. Individuals who were currently taking psychotrophic medications, displayed psychotic symptoms, had a history of Bipolar I disorder, or showed evidence of imminent suicide or homicide risk, were also excluded. Other details of inclusion/exclusion are given in Crits-Christoph et al. [30].

The randomized sample of patients (N=487) was 58% Caucasian, 40% African-American and 2% Hispanic, 33% women, and had an average age at intake of 34 years. Most participants lived alone (70%), were employed outside the home (60%), and had children (60%). The majority of patients smoked crack cocaine (79%); 2% used by injection, and the remaining 19% were intra-nasal users. At intake, patients on average used cocaine 10 days out of the past 30 and had been using cocaine for 7 years (SD=4.8). The most common co-occurring substance use disorders were alcohol dependence (33%), cannabis dependence (4%), and cannabis abuse (17%).

Instruments and data collection

Patient functioning in addiction-related domains was measured using the interview-based Addiction Severity Index (ASI) [38]. Specifically, composite scores in the domains of employment, family/social, psychiatric, medical, and legal were examined. Because of non-normal distributions, a shifted-logarithmic transformation with a shift of 0.001 was applied to the ASI subscale scores for analyses. The ASI was administered at baseline and monthly during the 6-month active phase treatment, and at quarterly follow-up assessments conducted at month 9, 12, 15, and 18 following randomization. ASI scores at the 12 month assessment are presented here (results for other follow-up assessments were very similar).

There were three sources of information about cocaine use. One was the specific ASI item asking about cocaine use during the last 30 days. A second measure was a self-report of cocaine use during the past week [13], administered weekly throughout the 6 month treatment period. A third measure of cocaine use was obtained from weekly observed urine samples. These samples were sent to a central laboratory and assayed for cocaine and other drugs. In addition to using these three measures separately, a composite cocaine outcome measure was constructed by pooling information from the three measures to code each month of treatment as abstinent versus any cocaine use. Concordance between these measures of substance use has been reported to be reasonably good [30]. Any indication of cocaine use across the three measures was used to score the month as “not abstinent”, regardless of whether the other measures indicated no use or were missing. If no information was available for a given month because all measures were missing (19% of the time), the month was coded as missing. The same composite cocaine measure, indicating use/non-use in the past month, was scored for data obtained at the 9, 12, 15, and 18-month follow-up assessments, however the time window for the follow-up ASI covered use during the previous 3 months. In addition to these measures of cocaine use, the ASI Drug Use composite score was used as a measure of overall drug use.
The above assessments were used to construct the following during-treatment measures of cocaine use: (1) average number of times using cocaine in the past week (from cocaine inventory), (2) maximum consecutive days abstinent from cocaine (from cocaine inventory), (3) binary variable of whether or not the patient achieved complete abstinence across all weeks in which they were in treatment (combining urines and cocaine inventory) (4) binary variables classifying patients as achieving or not achieving at least one week of abstinence (combining urines and cocaine inventory) (also scored for 2+, 3+, and 4+ weeks of abstinence), (5) percent reduction in cocaine use in past month from baseline to month 6 (from ASI), (6) binary variable classifying patients as achieving or not achieving a 50% or greater reduction in cocaine use in past month from baseline to month 6 (from ASI), (7) percent of available urines that were negative for cocaine, and (8) percent of scheduled urines that were negative for cocaine (i.e., for this measure, missing urines were coded as positive for cocaine). Following McCann and Li [26], these additional during-treatment cocaine use measures were scored: (1) binary variable classifying patients as achieving or not achieving one or more weeks of abstinence counting backwards from the point treatment was terminated (also scored for 2+, 3+, and 4+ weeks of end-of-study abstinence), and (2) count of number of beyond-threshold weeks of success (abstinence) at the end of study (scored for thresholds of 1+, 2+, 3+, and 4+ end-of-study weeks of abstinence). To these McCann and Li [26] end-of-study abstinence variables, we added a count of the number of consecutive weeks of abstinence from treatment endpoint going back in time.

Although missing data were not uncommon, the research teams had considerable success in continuing to obtain outcome data on patients even after they dropped out of treatment. For all randomized patients (N=487), the average number of post-baseline monthly assessments was 4.5 (of 6). At least one of the six active phase post-intake monthly assessments was obtained for 94% of the 487 patients randomized, and 85% had a 6-month assessment. The average number of follow-up assessments was 3.1 (of 4). At least one of the four follow-up assessments was obtained for 85% of the 487 patients randomized, and 72% had an 18-month assessment. Specific analyses had sample sizes varying from 337 to 363, depending on the measure.

**Data analysis**

The primary analyses consisted of partial correlations (controlling for treatment, site, and baseline scores, where appropriate) examining the associations between the various during-treatment measures and the 12-month follow-up outcome measures (results of correlations with other follow-up assessments, not reported here, were similar). With the partial correlations, the effective sample size varied measure-to-measure requiring both the during-treatment and follow-up measures to be available per patient.

Additionally, latent class analysis (LCA) was implemented to describe patterns of early cocaine usage and late cocaine usage. LCA is a statistical method used to identify unobserved (latent) classes of patients underlying the observed heterogeneity in a population. The latent class approach assumes that the cocaine usage represents a mixture of distinct subgroups that are not directly observed but can be determined based on variables of interest. Latent class models have been recently used in the substance abuse literature to identify various classes of cocaine usage [39-41]. The overall goal of this set of analyses was threefold. First, we defined clinically meaningful subgroups of cocaine usage within the first 4 months of active treatment through LCA. The input for these analyses was monthly scores of using or not using cocaine at any time during the month. The latent class model estimates the conditional probability of cocaine usage at each time point and the posterior probabilities of membership in each class for each patient based on his/her available data. Patients are assigned to the class to which they have the highest posterior probability of membership. Second, we defined clinically meaningful subgroups of cocaine usage over the remaining two months of treatment and follow-up assessments through LCA as previously done. Finally, but most importantly, we descriptively examined if any patterns of usage early in treatment (first four months) diverged from the subsequent patterns. To compare the two phases of usage, patients were required to have a grouping classification for both LCA models. Of the 487 randomized patients, 430 patients were classified into patterns of cocaine usage during both phases. We determined the number of latent classes per phase using the Bayesian information criterion (BIC), entropy, and the rule that each cluster must contain exceed 10% of the effective sample size [42-44].

All analyses were conducted in SAS 9.2 and implemented with the correlation coefficient algorithm (PROC CORR) and the SAS add-on LCA procedure developed at Penn State University (PROC LCA) [45].

**Results**

**Active phase cocaine use measures in relation to cocaine use at follow-up**

Descriptive information on each of the during-treatment cocaine use measures is presented in table 1. On average, patients used cocaine 0.75 times during the past week, and the typical patient achieved about 60 days of consecutive abstinence over the course of the 6 month treatment period. Although only 12% of the sample achieved complete abstinence for 6 months, 82% achieved at least one week of abstinence at some point. The average patient reduced their cocaine use by 68% from baseline to month 6; 78% had at least a 50% reduction in cocaine use. Of all available urines, 67% were negative for cocaine for the average patient, but only 49% of the scheduled urines were negative for cocaine (i.e., designating missing as positive for cocaine).

Table 1 also shows partial correlations (controlling for site and treatment modality) between the various cocaine outcome measures during the active phase (baseline to month 6) of treatment in relation to drug use outcomes at 12 month follow-up. In general, there were small to moderate sized correlations between the various during-treatment measures of cocaine use and measures of drug use at follow-up. The largest correlations were between measures of abstinence during treatment and measures of abstinence at follow-up: the partial correlation between maximum days of consecutive abstinence and complete abstinence in the prior 3 months at the 12 month follow-up was 0.40, and the partial correlation between achieving complete abstinence during treatment and complete abstinence during the prior 3 months during follow-up was 0.38. The percent of available negative urines for cocaine and the percent of scheduled urines negative for cocaine showed highly similar associations with the drug use measures at follow-up despite the relatively large mean difference between these two measures.

The McCann and Li measures of end-of-study abstinence and number of beyond-threshold weeks of success showed only relatively small partial correlations (highest=0.26) with the follow-up drug use measures (Table 2). A simple count of the number of consecutive weeks abstinent up until active treatment endpoint showed similar associations with the follow-up measures as did the McCann and Li measures.
Active phase cocaine use measures in relation to functional outcomes

Within-treatment measures of cocaine use showed little or no associations with the ASI scales measuring addiction-related problems (Table 3). An exception was that change in legal problems from baseline to month 12 was associated with most of the within-treatment measures of cocaine use. The McCann and Li measures also showed few significant associations with follow-up measures of functioning in addiction-related domains (Table 3).

Patterns of cocaine use during active treatment in relation to patterns across follow-up

Latent class analyses of patients’ scores on the binary cocaine composite measure across the first 4 months of active treatment revealed three distinct patterns of use. One pattern consisted of patients who continued to use cocaine every month ("continued users", N=215). A second pattern consisted of individuals who became immediately abstinent at month 1, with a small amount of relapse occurring in successive months ("immediate abstainers", N=125). A third pattern was a tendency for a steady decrease in use over time ("slower improvers"; N=90).

Individuals within each of the above 3 classifications of patterns of cocaine use during active treatment were then examined in terms of their pattern of use using both the data from the active treatment assessments (baseline, months 1 to 6) and the follow-up assessments (months 9, 12, 15, 18). Three class of response were evident: (1) "continued users" who were not abstinent almost every month, (2) "intermittent users" who showed a pattern of use in some months but not others, and (3) "continued abstainers" who maintained abstinence not only through active treatment but also through most months during follow-up. As seen in figure 1, the majority (67.4%; 145/215) of the "continued users" during active treatment showed a pattern of continued use across all follow-up visits. Very few (7.9% 17/215) of the "continued users" during active treatment became consistently abstinent across the follow-up visits. Of note is that those (N=17) who were abstinent during the follow-up visits, despite the fact that almost 100% of them had consistent usage during months 1 to 4, initiated abstinence during months 5 and 6 of the active treatment phase and then continued this abstinence throughout follow-up. The middle group (24.7%; 53/215) of "intermittent users" also began to show some degree of abstinence at month 5 (20% were abstinent) and month 6 (50% were abstinent), with some of these (about 50%) then showing abstinence at each follow-up visit.

Of those patients who were classified as immediately and...
Third, end-of-study measures, proposed by McCann and Li [26], were analyzed, did not appear to strongly influence the relation of during-treatment measures at follow-up. Second, whether missing urines were coded as oriented measures during active treatment in relation to abstinence follow-up. The highest associations were found between abstinence-in general, various measures of cocaine use during active treatment. The overall pattern of our results suggests that there is no easy way to summarize outcomes in one success/fail index, or continuous score, in the treatment of cocaine dependence. There was not one type of measure that stood out as clearly superior to other types of measures. There was some evidence, however, that measures that focus on abstinence may be the most appropriate for measuring outcome in the treatment of cocaine dependence. This conclusion is based on three aspects of our results. One relevant finding was that many patients are abstinent at a given point in time post-baseline. This was evident in the average number of days using cocaine per week (0.75 days/week) across all months of treatment. A second relevant finding was that the percentage of patients who achieved abstinence during active treatment tended to maintain abstinence over follow-up, and most patients who consistently continued to use cocaine during active treatment continued to use cocaine across follow-up.

Within-Treatment cocaine outcomes (months 1 to 6) predicting 12 month (after baseline) follow-up functioning.

Table 3: Within-treatment cocaine outcomes (months 1 to 6) predicting 12 month (after baseline) follow-up functioning.

<table>
<thead>
<tr>
<th>Within-Treatment Outcome</th>
<th>Psych</th>
<th>Family/Social</th>
<th>Medical</th>
<th>Legal</th>
<th>Employment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average times used cocaine past week</td>
<td>.13*</td>
<td>.09</td>
<td>.05</td>
<td>.15**</td>
<td>.14*</td>
</tr>
<tr>
<td>Max. consecutive days abstinent from cocaine from self-report</td>
<td>-.00</td>
<td>-.11</td>
<td>.04</td>
<td>-.10</td>
<td>-.05</td>
</tr>
<tr>
<td>Completely abstinent (urine + self-report)</td>
<td>-.02</td>
<td>-.10</td>
<td>.07</td>
<td>-.08</td>
<td>-.03</td>
</tr>
<tr>
<td>4+ weeks of abstinence (urine + self-report)</td>
<td>.02</td>
<td>-.05</td>
<td>-.05</td>
<td>-.14*</td>
<td>.09</td>
</tr>
<tr>
<td>3+ weeks of abstinence (urine + self-report)</td>
<td>-.03</td>
<td>-.03</td>
<td>-.09</td>
<td>-.16***</td>
<td>-.10</td>
</tr>
<tr>
<td>2+ weeks of abstinence (urine + self-report)</td>
<td>-.02</td>
<td>-.06</td>
<td>.10</td>
<td>-.17***</td>
<td>-.03</td>
</tr>
<tr>
<td>1+ weeks of abstinence (urine + self-report)</td>
<td>-.02</td>
<td>-.07</td>
<td>-.04</td>
<td>-.15**</td>
<td>-.05</td>
</tr>
<tr>
<td>Percent reduction in cocaine use from baseline to month 6 (self-report)</td>
<td>-.13*</td>
<td>-.07</td>
<td>-.01</td>
<td>-.14*</td>
<td>-.14*</td>
</tr>
<tr>
<td>50% reduction from baseline (yes/no)</td>
<td>-.16**</td>
<td>-.10</td>
<td>.00</td>
<td>-.17***</td>
<td>-.06</td>
</tr>
<tr>
<td>% (of available) Negative Urines for cocaine</td>
<td>-.04</td>
<td>-.06</td>
<td>-.01</td>
<td>-.12*</td>
<td>.07</td>
</tr>
<tr>
<td>% (scheduled) Negative Urines for cocaine</td>
<td>-.02</td>
<td>-.09</td>
<td>.04</td>
<td>-.15*</td>
<td>-.03</td>
</tr>
<tr>
<td>EOSA – 1+ wks</td>
<td>-.00</td>
<td>-.04</td>
<td>.09</td>
<td>.02</td>
<td>.07</td>
</tr>
<tr>
<td>EOSA -2+ wks</td>
<td>-.03</td>
<td>-.12</td>
<td>.08</td>
<td>-.05</td>
<td>-.01</td>
</tr>
<tr>
<td>EOSA -3+ wks</td>
<td>-.07</td>
<td>-.08</td>
<td>.02</td>
<td>-.04</td>
<td>-.12*</td>
</tr>
<tr>
<td>EOSA – 4+ wks</td>
<td>-.13*</td>
<td>-.06</td>
<td>.01</td>
<td>-.01</td>
<td>-.09</td>
</tr>
<tr>
<td>NOBWOS – 1+ wks</td>
<td>-.06</td>
<td>-.07</td>
<td>.03</td>
<td>-.02</td>
<td>-.08</td>
</tr>
<tr>
<td>NOBWOS – 2+ wks</td>
<td>-.06</td>
<td>-.06</td>
<td>.02</td>
<td>-.01</td>
<td>-.07</td>
</tr>
<tr>
<td>NOBWOS – 3+ wks</td>
<td>-.05</td>
<td>-.05</td>
<td>.02</td>
<td>-.01</td>
<td>-.07</td>
</tr>
<tr>
<td>NOBWOS – 4+ wks</td>
<td>-.04</td>
<td>-.05</td>
<td>.03</td>
<td>-.01</td>
<td>-.07</td>
</tr>
<tr>
<td>Number of consec. wks abstinent from endpoint</td>
<td>-.05</td>
<td>-.07</td>
<td>.04</td>
<td>-.01</td>
<td>-.06</td>
</tr>
</tbody>
</table>

Note. Partial correlations shown with treatment group, site, and baseline ASI scores as covariate. N's vary from 337 to 363. EOSA=end of study abstinence. NOBWOS=number of beyond-threshold weeks of success. Lower ASI scores=fewer problems. *p < .05. **p < .01.

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Discussion
Several clear findings were evident from the current study. First, in general, various measures of cocaine use during active treatment were all moderately associated with drug/cocaine use at 12-month follow-up. The highest associations were found between abstinence-oriented measures during active treatment in relation to abstinence measures at follow-up. Second, whether missing urines were coded as positive for cocaine use, or considered missing (i.e., only available data analyzed), did not appear to strongly influence the relation of during-treatment urine scores to follow-up drug/cocaine use outcomes. Third, end-of-study measures, proposed by McCann and Li [26], were not better predictors of drug/cocaine use during follow-up. Fourth, during-treatment cocaine use measures showed small correlations with measures of addiction-related problems across follow-up. Fifth, analyses of pattern of drug use revealed that most patients who achieved abstinence during active treatment tended to maintain abstinence over follow-up, and most patients who consistently continued to use cocaine during active treatment continued to use cocaine across follow-up.

The overall pattern of our results suggests that there is no easy way to summarize outcomes in one success/fail index, or continuous score, in the treatment of cocaine dependence. There was not one type of measure that stood out as clearly superior to other types of measures. There was some evidence, however, that measures that focus on abstinence may be the most appropriate for measuring outcome in the treatment of cocaine dependence. This conclusion is based on three aspects of our results. One relevant finding was that many patients are abstinent at a given point in time post-baseline. This was evident in the average number of days using cocaine per week (0.75 days/week) across all months of treatment. A second relevant finding was that the highest correlations between during-treatment measures and follow-up measures were apparent for abstinence-oriented measures (maximum consecutive days abstinent from cocaine from self-report and binary variable of completely abstinent during treatment in relation to binary variable of achieving/not achieving 3 months of abstinence at 12 month follow-up). A third relevant finding was that cluster analyses of patterns of use over the first 4 months of treatment revealed that the majority of patients fell into either a group of continued users (50%) who were never abstinent (although likely using at a relatively low level given the overall low mean number of days using cocaine/week), or a group who became immediately abstinent and stayed abstinent (29%), with a smaller group showing intermittent abstinence (21%).

This tendency to either become abstinent and stay abstinent, or never become abstinent, may be somewhat unique to stimulants like cocaine or methamphetamine. In the case of alcohol and marijuana, patterns of intermittent use may be more common; however, no
been associated in previous studies with a range of negative health and their relevance to patient functioning. Cocaine abuse/dependence has for buying cocaine, the strength of the association was insufficient to possibility of engagement in other illegal activities to raise money consistent with the illegal nature of cocaine possession, and the many of the cocaine use measures during treatment and the severity scale.

Moreover, the psychiatric symptoms commonly found with cocaine use when predicting 12-month follow-up from active (6 month) treatment. may be relatively short-lived and therefore be less likely to be evident variables. However, the influence of cocaine on psychiatric functioning (thinking) [47], one might expect a higher correlation between these psychiatric symptoms commonly found with cocaine use in naturalistic settings. In particular, it is unclear whether our findings would generalize to cocaine patients with more severe psychiatric comorbidity, given that current psychotropic medication was an exclusion criterion in the NIDA CCTS. Another limitation is that urine samples were collected weekly. Despite relatively good agreement between urine test results and self-reports of cocaine use, there is no way to validate cocaine use at times when no urine assessments were available. A further limitation is that the existence of a subset of patients who became completely abstinent resulted in somewhat restricted comparisons data on this issue exists. Direct comparisons among these various drugs of abuse in patterns of use over time, controlling for demographic and other factors that might be associated with use patterns, would be needed to fully determine if such patterns are particular to cocaine or stimulants in general. These patterns, however, do suggest that medications that lessen the cravings for cocaine among cocaine dependent individuals may be needed, as least in a subset of cocaine dependent individuals, to facilitate the difficult transition from using to abstinence.

The relative small correlations found here between measures of cocaine use and other addiction-related problems, as measured by ASI scales, reflects a longstanding finding of low associations between severity of alcohol/drug use and other ASI scales [46]. The one exception in the McLellan et al. [46] study was a higher association between severity of alcohol/drug use and the ASI psychiatric scale. Consistent with this previous finding, in the current study, small but statistically significant correlations between number of times using cocaine in the past week during active treatment and the ASI Psychiatric composite scale at 12 months (r=0.13), and achieving a 50% reduction in cocaine use over the course of treatment and the ASI Psychiatric scale at 12 months (r=−0.16), were found. Given the known effects of cocaine in producing psychiatric symptoms (i.e., agitation, paranoia, hallucinations, delusions, violence, suicidal and homicidal thinking) [47], one might expect a higher correlation between these variables. However, the influence of cocaine on psychiatric functioning may be relatively short-lived and therefore be less likely to be evident when predicting 12-month follow-up from active (6 month) treatment. Moreover, the psychiatric symptoms commonly found with cocaine use are touched upon in only one of the items within the ASI Psychiatric scale.

Significant, but small, associations were also found here between many of the cocaine use measures during treatment and the severity of legal problems at month 12. Although this connection is of course consistent with the illegal nature of cocaine possession, and the possibility of engagement in other illegal activities to raise money for buying cocaine, the strength of the association was insufficient to justify the use of such cocaine outcome measures based solely upon their relevance to patient functioning. Cocaine abuse/dependence has been associated in previous studies with a range of negative health and other patient outcomes including HIV transmission [48-53]. These relationships, however, may be primarily evident in comparisons between heavy cocaine users and non-users, rather than in comparisons across the range of amounts of cocaine usage, or reductions in usage, within a cocaine dependent sample. Although epidemiological associations between cocaine use and other measures of health and functioning are useful, in order to have greater confidence in the importance of an outcome measure used in treatment studies, evidence linking improvement on such a measure to clinically meaningful benefits within the target population (e.g., cocaine dependent individuals) is needed.

The current findings should be evaluated in terms of a number of limitations of the research. The NIDA CCTS was a controlled clinical trial that might have limited generalizability to the treatment of cocaine use in naturalistic settings. In particular, it is unclear whether our findings would generalize to cocaine patients with more severe psychiatric comorbidity, given that current psychotropic medication was an exclusion criterion in the NIDA CCTS. Another limitation is that urine samples were collected weekly. Despite relatively good agreement between urine test results and self-reports of cocaine use, there is no way to validate cocaine use at times when no urine assessments were available. A further limitation is that the existence of a subset of patients who became completely abstinent resulted in somewhat restricted comparisons data on this issue exists. Direct comparisons among these various drugs of abuse in patterns of use over time, controlling for demographic and other factors that might be associated with use patterns, would be needed to fully determine if such patterns are particular to cocaine or stimulants in general. These patterns, however, do suggest that medications that lessen the cravings for cocaine among cocaine dependent individuals may be needed, as least in a subset of cocaine dependent individuals, to facilitate the difficult transition from using to abstinence.
range in the cocaine use measures. Such restrictions in range would attenuate the relation of these predictors to the outcomes at 12 months. A final limitation is that measures of functioning were limited to the ASI subscales. Higher associations with cocaine use measures might be evident with other types of measures of functioning.

In summary, the results of the current study fail to provide compelling support for any of a variety of measures of cocaine dependence in terms of associations of such measures with longer-term clinical benefits. Further research with alternative types of treatments, particularly medications, should be conducted to see if this conclusion would hold with treatments that impact craving for cocaine or block the effects of cocaine.

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