



Published in final edited form as:

*Am J Psychiatry*. 2014 June 1; 171(6): 683–690. doi:10.1176/appi.ajp.2014.13081055.

## Internet-delivered Treatment for Substance Abuse: A Multi-site Randomized Controlled Clinical Trial

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### Abstract

**Objective**—Drug and alcohol abuse constitutes a major public health problem. Computer-delivered interventions have potential to improve access to quality care. The objective of this

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**Author contributions:** Drs Campbell and Matthews had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Design and conduct of the study (Campbell, Nunes, Polsky); data collection (Campbell, Nunes); study management (Campbell, Nunes); analysis (Matthews, VanVeldhuisen, Wahle, Campbell, Nunes); interpretation of results (all authors); preparation (Campbell, Turrigiano, Matthews, Wahle, Miele, Nunes); review (all authors); and approval of the manuscript (all authors).

**Financial Disclosure:** Dr Nunes receives medication for research studies from Alkermes/Cephalon, Inc. and Reckitt-Benckiser and has previously received medication for a research study from Duramed Pharmaceuticals. The authors report no additional conflicts of interest. Dr Lisa Marsch is President of HealthSim Inc., the privately owned company that developed TES. Dr. Marsch provided scientific consultation on this study related to TES implementation, but did not take part in the conduct of the trial, data analysis and interpretation, or manuscript development (including the current manuscript).

**Previous Presentations:** Portions of this manuscript were presented at the Addiction Health Services Research conference in Portland, OR, October 25, 2013 and at the American Academy of Addiction Psychiatry conference in Scottsdale, AZ, December 7, 2013. This manuscript has not been published elsewhere and is not under consideration by another publication or electronic medium.

study was to evaluate the effectiveness of the Therapeutic Education System, an internet-delivered behavioral intervention that includes motivational incentives, as a clinician-extender in the treatment of substance use disorders.

**Method**—Adult men and women (N=507) entering 10 outpatient addiction treatment programs were randomly assigned to 12-weeks of treatment-as-usual (n=252) or treatment-as-usual + Therapeutic Education System, whereby the intervention substituted for 2 hours of standard care per week (n=255). Therapeutic Education System consists of 62 computer-interactive modules covering skills for achieving and maintaining abstinence, plus prize-based motivational incentives contingent on abstinence and treatment adherence. Treatment-as-usual consisted of individual and group counseling at the participating programs. Primary outcomes were (1) abstinence from drugs and heavy drinking measured by twice weekly urine drug screens and self-report, and (2) time to drop-out from treatment.

**Results**—Compared to treatment-as-usual, those receiving Therapeutic Education System reduced dropout from treatment (Hazard Ratio=0.72 [95% CI, 0.57-0.92], P=.010), and increased abstinence (Odds Ratio=1.62 [95% CI: 1.12-2.35], P=.010), an effect that was more pronounced among patients with a positive urine drug and/or breath alcohol screen at the point of study entry (n=228) (Odds Ratio=2.18 [95% CI: 1.30-3.68], P=.003).

**Conclusion**—Internet-delivered interventions, such as Therapeutic Education System, have the potential to expand access and improve addiction treatment outcomes; additional research is needed to assess effectiveness in non-specialty clinical systems and to differentiate the effect of Community Reinforcement Approach and Contingency Management.

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## INTRODUCTION

Drug and alcohol abuse is one of the costliest public health problems in the U.S., with illicit drug use accounting for an estimated economic cost of \$193 billion in 2007 (1) and excessive alcohol consumption exceeding \$223 billion in 2006 (2). Effective treatments for substance use disorders exist but face serious barriers to successful implementation, including lack of access to specialty care (3) and avoidance of treatment due to stigma. Individuals with substance use disorders often present to primary care, but primary care providers face many competing demands for services. Further, evidence-based behavioral treatments require that the clinicians delivering them receive adequate training and ongoing supervision, without which treatments tend to be implemented incorrectly or not at all (4-6).

Internet-delivered behavioral interventions have the potential to surmount these barriers by delivering treatment of high and consistent quality at low cost, and with limited burden on clinical staff (7, 8). Patients can interact with web-based interventions outside of traditional clinical settings, addressing problems of access and stigma. The past decade has seen the emergence of a number of technology-based interventions for substance abuse, primarily for alcohol, most of which have not been adequately tested for effectiveness (9-11). Several computer-delivered cognitive-behavioral and/or Contingency Management interventions for substance use disorders have shown efficacy in single site clinical trials (12-14).

Here we present one of the first large, multi-site effectiveness trials of a computer-delivered intervention for substance abuse, implemented across a diverse sample of community-based

addiction treatment programs. The Therapeutic Education System (12) is a web-based version of the Community Reinforcement Approach plus Contingency Management, a packaged approach with substantial demonstrated efficacy (15, 16). Effective treatments, particularly behavioral interventions, often consist of combinations of active ingredients likely to produce the largest effect and thus, the most benefit to treatment programs. The hypothesis was that the Therapeutic Education System, when substituted for some of usual, clinician-delivered treatment, would both improve substance use outcome and reduce dropout, compared to treatment-as-usual.

## METHODS

### Recruitment Sites

Patients seeking treatment for drug or alcohol problems at 10 community-based, outpatient treatment programs across the United States, and affiliated with the National Drug Abuse Clinical Trials Network, were enrolled between June 2010 and August 2011. Details of program selection and characteristics have been previously published (4). Outpatient addiction treatment programs were selected for geographic and patient diversity, and also varied in programming, consistent with the goals of an effectiveness trial to promote external validity. Programs had to offer at least two face-to-face therapeutic group or individual sessions per week, consisting of two or more hours, with most offering between 2-6 sessions per week. Each program was asked to enroll approximately 50 patients (range=38-60).

### Study Design

After completing a 2-3 hour baseline assessment, patients were randomized in a 1:1 ratio to receive 12 weeks of either: (1) treatment-as-usual; or (2) treatment-as-usual + the Therapeutic Education System, whereby the intervention was a substitute for approximately 2 hours of clinician time (the equivalent of 2 internet-delivered modules, twice per week; i.e. 4 modules/week or 48 over 12 weeks). All participants were asked to provide urine drug and breath alcohol screens twice per week. Randomization was conducted by an independent statistician at a centralized data center in randomly permuted blocks, stratified by: treatment site; patient's primary substance of abuse (dichotomized as stimulant vs. non-stimulant since Contingency Management has been tested most for cocaine dependence [17, 18]); and whether or not the patient was abstinent at point of baseline assessment and study entry based on urine drug and breath alcohol tests. Abstinence at the point of study entry is a strong predictor of outcome (19) and thus arguably an important covariate in primary outcome analyses (20). Patients and staff were not blind to treatment arm. Additional details of the study design and rationale were previously published (4).

### Participants

Patients were eligible if they were: (1) 18 or older; (2) self-reported use of illicit substances in the 30 days prior to study entry, or 60 days if the patient was exiting a controlled environment (alcohol could be the primary problem, but patients had to have used at least one illicit drug as well); (3) within 30 days of entering the treatment episode (randomization occurred on average 9.5 ( $SD=7.4$ ) days after entering treatment); (4) planning to remain in

the area and treatment program for 3 months; and 5) proficient in English. Patients were excluded if they were: (1) prescribed opioid replacement therapy (e.g. buprenorphine, methadone); or (2) unable to provide informed consent. The study was approved by the Institutional Review Boards of the New York State Psychiatric Institute and all participating clinical sites. After a complete description of the study to each patient, written informed consent was obtained.

### Internet-delivered Intervention

Therapeutic Education System (12) includes Contingency Management and 62 interactive, multimedia modules, based on the Community Reinforcement Approach, requiring approximately 20-30 minutes each to complete. The Community Reinforcement Approach is grounded in the premise that drugs compete with more delayed prosocial reinforcers; as such the treatment promotes skills training to teach, encourage, and increase satisfaction with drug-free sources of reinforcement (21). An initial training module teaches patients how to use the program, followed by modules on basic cognitive behavioral relapse prevention skills (e.g. drug refusal, managing thoughts about using, conducting functional analyses). Subsequent modules teach skills aimed at improving psychosocial functioning (e.g. communication, mood management, family/social relations, time management), as well as prevention of HIV, hepatitis and other sexually transmitted infections. Video clips show actors modeling the skills being taught. Short quizzes assess patient's grasp of material; the pace and level of repetition of material is adjusted accordingly to maximize individual mastery of the skills and information being taught.

Each clinic received computers for onsite intervention completion; patients could also access the intervention via the internet outside the clinic. Treatment program clinicians, who had patients in the internet-based condition, were asked to incorporate brief discussion of module completion into individual counseling sessions. An electronic reporting system allowed clinicians to view summaries of their patients' computer activity. According to clinicians' documentation, most individual treatment-as-usual sessions (85.3%) included discussion of the patient's participation in the computer intervention.

Therapeutic Education System includes a flexible system for delivering Contingency Management according to the prize-based incentive system developed by Petry and colleagues for delivering low cost Contingency Management in community-based treatment settings (17, 18). Incentives take the form of opportunities to draw vouchers from a virtual "fish bowl". Some vouchers yield congratulatory messages (e.g. "good job"), while others are exchangeable for prizes of mostly modest value (usually around \$1, occasionally around \$20, rarely \$80-\$100). In the present study, draws were awarded for abstinence based on negative urine or alcohol breathalyzer screens and for completion of modules (up to the recommended 4 per week although there was no cap on the number of modules that could be completed). Research staff entered target behaviors into the computer and oversaw prize distribution.

## Assessments

Twice per week during the 12 week treatment phase (i.e. 24 half-weeks), and again at 3 and 6 month follow-up points, urine was collected and screened for 10 drugs with standard lateral flow chromatographic immunoassays (QuickTox® dip card) and the use of temperature and adulterant test strips; and self-report drug and alcohol use data collected using the Timeline Follow-back calendar method (22). Each half-week of treatment was categorized as abstinent if the urine screen was negative and the self-report indicated no drug use/heavy drinking days (according to the National Institute on Alcohol Abuse and Alcoholism guidelines: > 4 drinks a day for men and > 3 drinks a day for women), and not abstinent otherwise. If self-report was missing, but urine screen was positive, the half-week was scored as not abstinent. Abstinance during a given half-week was considered missing if (a) self-report indicated no use but the urine screen was missing, (b) the urine screen was negative but self-report was missing, or (c) both urine and self-report were missing. Abstinance at the 3 and 6 month follow-up visits was scored similarly based on the urine screen and the last four days of self-report data.

Research staff tracked each patient's participation in the community-based treatment program. If a patient dropped out of treatment, the event of dropout was scored as the last week that a patient attended a face-to-face group or individual therapy session at the treatment program (range=0-11). Patients who attended treatment in week 12 were considered censored at that time.

## Sample Size, Power and Statistical Analysis

Means and standard deviations or frequencies and percentages were calculated for baseline characteristics of the randomized sample. Two co-primary outcomes, abstinence from drug/heavy alcohol use in the last four weeks of treatment and retention in treatment, were pre-specified in the study protocol, along with their respective data analysis plans (4). Sample size computations were based on a Bonferroni adjustment approach (i.e. each hypothesis test has a significance level of .025) with 80% power to detect an odds ratio of 1.5 for the abstinence outcome (12) and 90% power to detect 50% vs. 35% (internet-based intervention vs. treatment-as-usual) retention (17) with 500 participants. The dichotomous abstinence scores for each of the 24 half-weeks in the 12-week treatment phase were analyzed using a repeated measures, piece-wise logistic model, where a linear time-by-treatment interaction was allowed during the first 16 half-weeks (8 weeks), but a constant study intervention effect was assumed during the last 8 half-weeks (4 weeks). Generalized estimating equations (23) were utilized to adjust for the correlation of half-weeks within patients. Missing half-week data were excluded, however the median number of missing half-weeks during the last 8 was 1 (interquartile range=4) for both treatment arms. The stratification factors (treatment site, primary substance [stimulant vs. non-stimulant], and abstinence at point of baseline/study entry) were included in the model as main effects. During subsequent model building, the interaction of each covariate with treatment was tested, and significant if  $P < .100$ .

The primary retention outcome (time to dropout) was analyzed with survival methods stratified by site, using a log-rank test and a proportion hazards model to consider effects of

the stratification factors as covariates (24). Schoenfeld residuals were used to test the assumptions of proportional hazards (25).

Two summary outcome measures typically reported in other clinical trials – the total number of abstinent half-weeks and the greatest number of consecutive abstinent half-weeks – were pre-specified secondary outcomes and analyzed using a Wilcoxon rank-sum test. Missing half-weeks imputed as not abstinent. At the 3 and 6 month post treatment follow-up points, the log-odds of abstinence was modeled as a function of visit, treatment assignment, and stratification factors, using generalized estimating equations to adjust for the correlation within patients. Missing half-week data were excluded. All analyses utilized the intent-to-treat sample and were implemented using SAS version 9.2 statistical software.

## RESULTS

As seen in Figure 1, 1,781 patients entering outpatient addiction treatment were screened. Of these, 850 were not eligible, primarily because of no reported recent drug use. Of those who were eligible, 408 did not complete the baseline assessment, and 507 were ultimately randomized. Of note, of the 130 who were eligible but not interested, only 7.7% indicated that this was due to the computer delivery of the intervention. The randomized sample (see Table 1) was diverse (37.9% female, 44% ethnic/racial minorities), and presenting for a range of typical substance problems. 33.7% (n=171) were primary stimulant users (cocaine or other stimulants), and 54.2% (n=275) had negative urine drug and breath alcohol screens at the point of baseline/study entry. Patients with negative urine drug/breath alcohol screens at the point of baseline/study entry had fewer days of substance use in the prior 30 days (Mean=5.3, SD=6.7) compared to those with positive screens (Mean=15.2, SD=9.2).

### Treatment Adherence

Patients randomized to Therapeutic Education System completed a mean of 36.6 computer-delivered modules (SD=18.1) out of a recommended 48 (range=0-72). 22% of internet sessions were completed offsite. They earned a mean of 118 (SD=90) voucher draws (out of a possible 252 draws) contingent on abstinence or module completion, resulting in \$277 (SD=\$226) worth of prizes over 12 weeks. Patients in both conditions attended similar total numbers of treatment-as-usual therapy sessions at their treatment programs (Therapeutic Education System: Mean=21.2, SD=17.5; Treatment-as-Usual: Mean=20.4, SD=17.5), and similar numbers of sessions per week in the weeks prior to dropout (Therapeutic Education System: Mean=1.4, SD=0.9; Treatment-as-Usual: Mean=1.3, SD=0.9). Notably, these average sessions attended are lower than the 2 to 6 sessions per week typically recommended across the participating treatment programs.

### Effect of Treatment on Abstinence

Results of the logistic regression modeling abstinence are shown in Table 2. Model A includes the main effects of treatment and stratification factors. Compared to only treatment-as-usual, those receiving Therapeutic Education System increased the odds of abstinence at the end of treatment by a factor of 1.62 (P=.010). Main effects of abstinence at the point of baseline/study entry and treatment site were also significant. Abstinence at baseline/study

entry strongly predicted abstinence at the end of treatment. Sites varied in the overall rates of abstinence achieved by their patients. There was no significant main effect of primary stimulant use. Interactions of primary stimulant use by treatment and site by treatment did not near significance. The interaction of abstinence at baseline/study entry by treatment ( $P=.068$ ) was included in Model B, where the effects of each treatment condition are estimated separately in the abstinent and non-abstinent strata. Among patients who were not abstinent at baseline/study entry, Therapeutic Education System more than doubled the odds of abstinence compared to treatment-as-usual, whereas among those who were abstinent, there was no significant difference between conditions. Figure 2 shows the observed rates of abstinence by half-week across the 12-week trial, and at 3 and 6 month follow-up, stratified by abstinence at baseline/study entry.

Patients in Therapeutic Education System achieved significantly more total half-weeks of abstinence during the 12-week trial (Mean=11.1,  $SD=9.0$ ) compared to treatment-as-usual (Mean=8.8,  $SD=8.2$ ;  $P=.008$ ), and greater consecutive abstinent half-weeks (Mean=8.0,  $SD=8.1$  vs.  $M=5.1$ ,  $SD=6.1$ ;  $P=.001$ ).

At 3 and 6 month follow-up, abstinence at baseline/ study entry continued to significantly predict abstinence at follow-up (Odds Ratio=2.39 [95% CI, 1.67 to 3.42],  $P<.001$ ). The effect of Therapeutic Education System, compared to treatment-as-usual, was no longer significant (Odds Ratio=1.25 [95% CI, 0.90 to 1.74],  $P=.175$ ).

### Retention in Treatment

There was less dropout from outpatient treatment for those in Therapeutic Education System compared to treatment-as-usual (log-rank  $P=.017$ ) (see Figure 3). The proportional hazards model yielded a similar main effect of treatment (Hazard Ratio=0.72 [95% CI: 0.57 to 0.92],  $P=.010$ ), and an analogous effect of abstinence at baseline/ study entry to the primary abstinence outcome – patients who were abstinent were less likely to dropout (Hazard Ratio=0.66 [95% CI: 0.51 to 0.86],  $P=.002$ ). There was no main effect of the stratum of primary stimulant use, nor were there significant stratum by treatment interactions.

## DISCUSSION

An internet-delivered behavioral intervention, the Therapeutic Education System, consisting of a combination of skills-oriented counseling derived from the Community Reinforcement Approach and Contingency Management, was effective at improving treatment outcomes in a large, diverse sample of patients seeking care across 10 geographically disparate community-based addiction treatment programs. Compared to the control condition, where patients received standard care, the internet-delivered intervention improved retention in treatment, produced equivalent, high rates of abstinence among good prognosis patients (i.e. abstinent at baseline/study entry), and, most importantly, doubled the odds of abstinence among patients with an otherwise poor prognosis (i.e. not abstinent at baseline/study entry). Community-based effectiveness trials represent an important step in the Translational spectrum (26). Consistent with the emphasis of an effectiveness trial on external validity, the computerized intervention was integrated within community-based treatment programs with

typical patients seeking treatment. The results support the promise of the intervention for dissemination and adoption into the addiction treatment system.

Increasing recognition of the public health impact of addictions, as well as Affordable Care Act legislation, calls for the expansion of services for addicted patients (27, 28). However, both the specialty addiction and primary care systems face shortages of provider time and expertise with successful delivery of evidence-based interventions (29). Therapeutic Education System is a computerized version of two of the most effective and best-replicated treatments for substance dependence. Computerized versions of other effective treatments for substance abuse, such as Cognitive-Behavioral Relapse Prevention (CBT) (13, 14), have also shown promise in single site, randomized trials. Treatments such as Community Reinforcement Approach or CBT require substantial time and specialty training for clinicians to deliver them. In contrast, computer-assisted treatments can be prescribed by a clinician without specific intervention training, or even by a clinician with little training or experience in any form of addiction treatment, in less time than if a clinician were to directly deliver the treatments (12). The present study took place in community-based addiction specialty care settings. Future studies should test Therapeutic Education System and similar interventions in non-addiction treatment settings and as part of screening, brief intervention, and referral to treatment models.

The trial was designed so that patients in the Therapeutic Education System condition were assigned to attend fewer standard care sessions at their treatment programs, according to a clinician-extender model. However, those patients ended up attending a similar number of usual counseling sessions as the control patients. Consistent with the finding of improved retention in treatment, this suggests the Therapeutic Education System improved engagement in standard outpatient treatment. It also means the intervention condition experienced a higher overall dose of therapy. The relatively low overall attendance at treatment-as-usual sessions may reflect the difficulty engaging patients in addiction treatment, and the importance of efforts to improve engagement.

### Strengths and Limitations

Strengths of this effectiveness study include the randomized, controlled design, pre-specification of primary outcome measures and analyses, and the high follow-up rates and relatively low rates of missing outcome data. The outcomes chosen are germane in that abstinence is the primary goal of treatment, and dropout from treatment is a substantial problem that limits the effectiveness of outpatient addiction treatment (30). As befits an effectiveness trial, the study was conducted with a large, demographically and geographically diverse sample, and eligibility criteria were kept broad. These features suggest the sample is likely to be representative of patients seeking community-based treatment for substance abuse problems across the U.S., and the findings reflective of how the intervention performs when integrated into real-world treatment settings.

A main limitation is that the study tested the Therapeutic Education System as a package, compared to treatment-as-usual, in a two-arm design. Thus, it is not possible to disentangle the unique effects of computerized Community Reinforcement Approach and Contingency Management. The two-arm design has the advantage of simplicity, which is a consideration



in community-based effectiveness trials. Further, prior research with clinician- and computer-delivered Community Reinforcement Approach and Contingency Management have suggested both contribute to beneficial treatment effects (15, 31-34). However, future research should address disentangling of the effects of the two components in both community-based addiction and non-specialty settings.

The superiority of Therapeutic Education System over treatment-as-usual was not sustained at longer-term follow-up. The effects of Contingency Management interventions may diminish once the contingencies end (35). In contrast, some (36), though not all (37), studies of CBT for addictions have observed the benefits of the intervention to actually increase post treatment, suggesting, as one would hope, the patients have learned skills that they continue to practice and benefit from over time. This might indicate that the beneficial effect of the Therapeutic Education System observed during the active treatment phase was mainly attributable to the Contingency Management component of the intervention, although this was not tested in the current study. A diminishing intervention effect over time is consistent with the chronic, relapsing nature of addiction (38) and the need for ongoing monitoring and treatment. In the present study, the Therapeutic Education System was only available to patients during the 12-week trial, but, being internet-accessible, it could be made available to patients indefinitely, and this should be studied.

Finally, a number of patients were eligible for the study, but did not enroll. This raises questions about generalizability in terms of whether the un-enrolled patients might have responded differently to the intervention. Prior analysis of the screening data (39) showed that un-enrolled patients reported more drug use compared to their enrolled counterparts. The greater relative benefit of the Therapeutic Education System among patients not abstinent at the point of baseline/study entry (associated with more drug use), suggests those not enrolled might have benefited. Engaging patients at the outset of an episode of outpatient treatment remains a challenge that needs to be addressed.

## CONCLUSIONS

The present findings suggest that internet-based Therapeutic Education System, as well as other efficacious computer-assisted interventions now emerging (13, 14), have the potential to help bridge the gap between the enormous need for high quality, evidence-based treatment for addiction, and the capacity of the treatment system to deliver. Barriers to implementation of such interventions need to be addressed, including training clinicians to effectively prescribe and monitor computer-delivered interventions, and developing reimbursement systems to fund the costs. Effective computer-delivered interventions for addictions should be studied in a broader array of clinical settings, including primary care.

## Acknowledgments

We thank the patients who participated in this study and acknowledge the commitment and effort of the participating treatment programs and research staff.

**Funding/Support:** This work was supported by grants from the National Drug Abuse Treatment Clinical Trials Network (CTN), National Institute on Drug Abuse (NIDA): U10 DA013035 (Edward V. Nunes and John Rotrosen), U10 DA015831 (Kathleen M. Carroll and Roger D. Weiss), U10 DA013034 (Maxine L. Stitzer and

Robert P. Schwartz), U10 DA013720 (José Szapocznik and Lisa R. Metsch), U10 DA013732 (Eugene C. Somoza), U10 DA020024 (Madhukar H. Trivedi), U10 DA013714 (Dennis M. Donovan and John Roll), U10 DA015815 (James L. Sorensen and Dennis McCarty), and K24 DA022412 (Edward V. Nunes). The full trial protocol is available from the corresponding author.

**Trial Registration:** [clinicaltrials.gov](http://clinicaltrials.gov) Identifier: NCT01104805

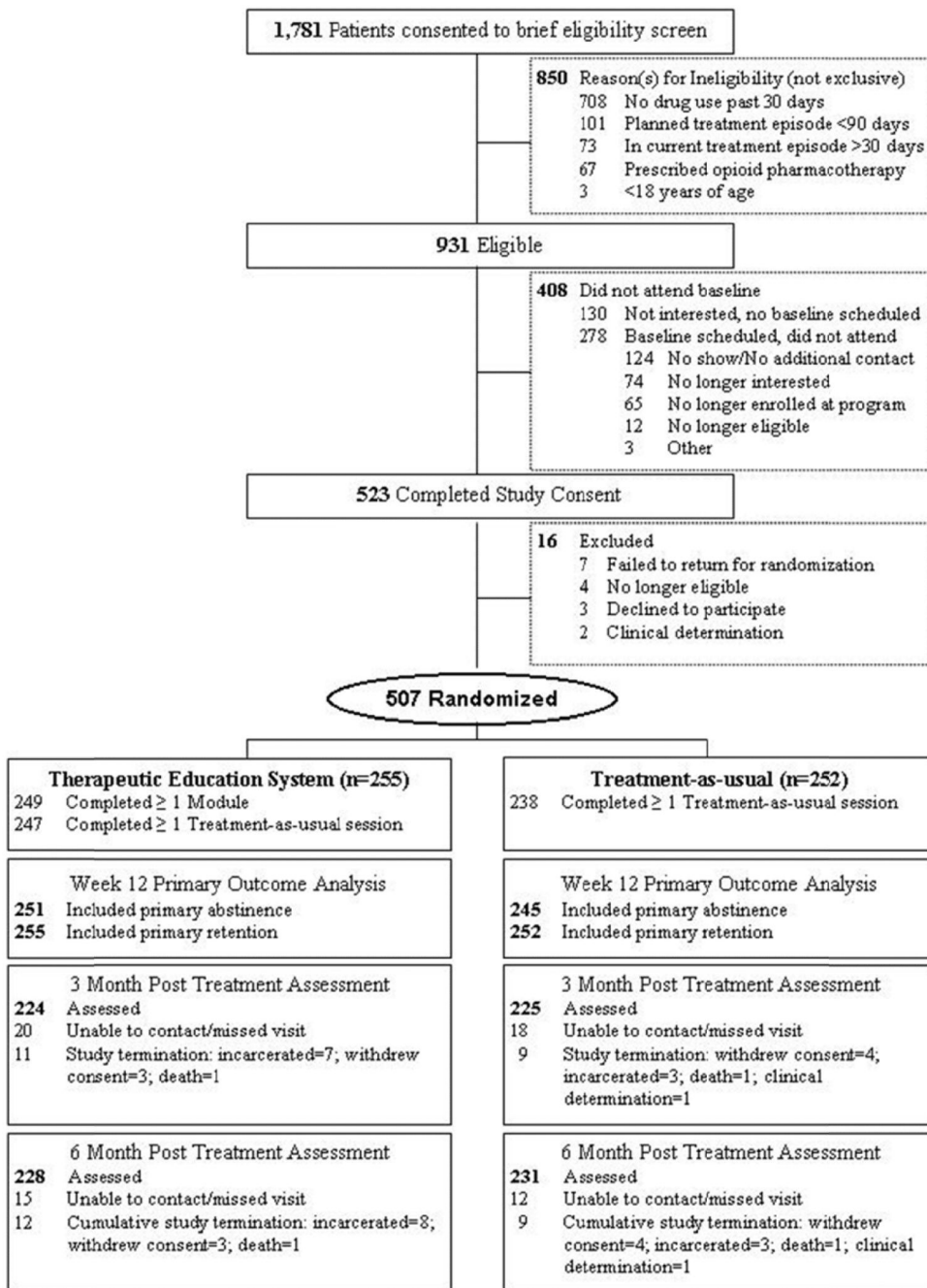
**Role of Sponsors:** The NIDA Center for the Clinical Trials Network (CCTN) participated in discussions of study design and reviewed study implementation metrics during the course of the trial. NIDA CCTN did not participate in the collection, management, or analysis of study data. Dr. U. E. Ghitza, a NIDA CCTN staff member, contributed to the writing of this manuscript and is a co-author.

## REFERENCES

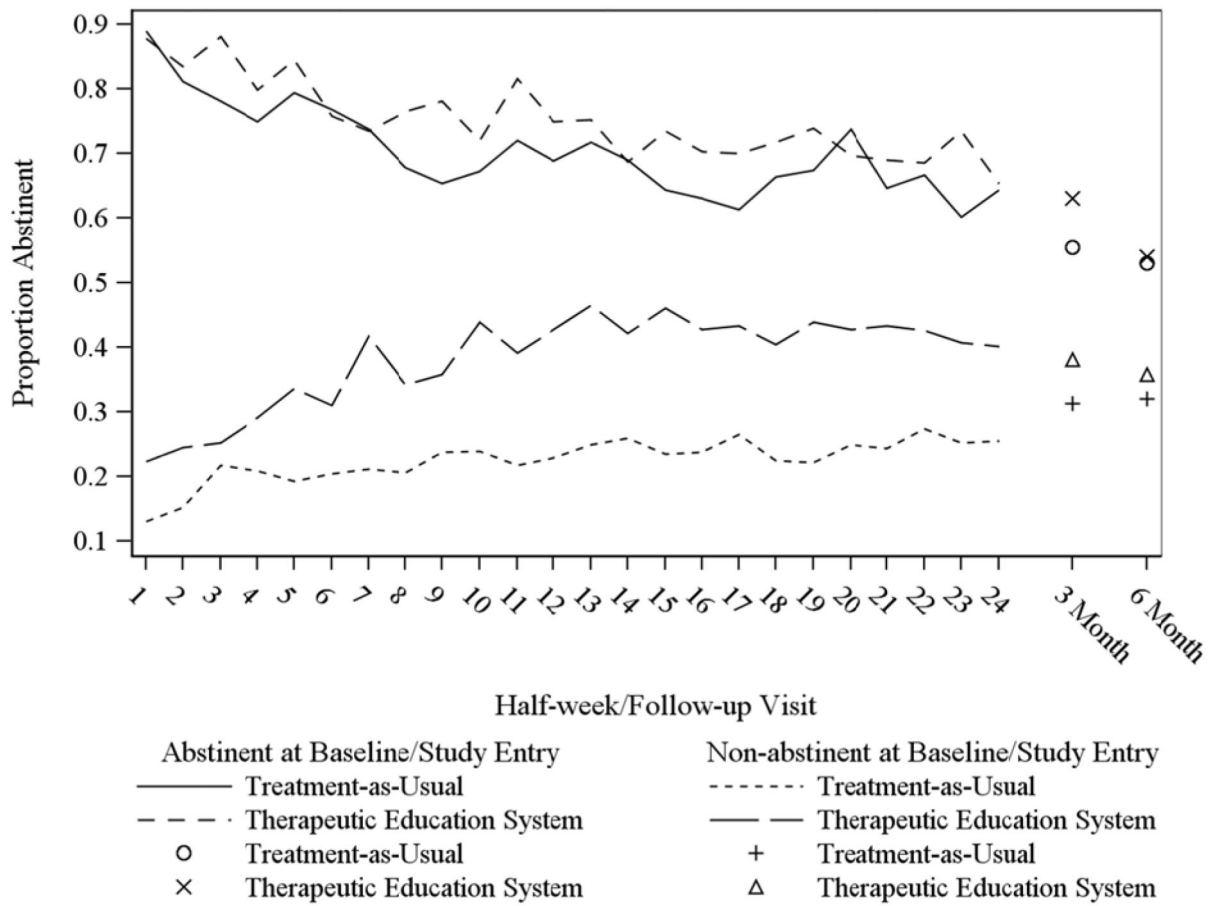
1. National Drug Intelligence Center. Economic impact of illicit drug use on American society. United States Department of Justice; Washington, DC: 2011.
2. Bouchery EE, Harwood HJ, Sacks JJ, Simon CJ, Brewer RD. Economic costs of excessive alcohol consumption in the U.S. 2006. *Am J Prev Med.* 2011; 41(5):516–524. [PubMed: 22011424]
3. Substance Abuse and Mental Health Services Administration. Results from the 2011 National Survey on Drug Use and Health: Summary of National Findings. Substance Abuse and Mental Health Services Administration; Rockville, MD: 2012. NSDUH Series H-44, HHS Publication No. (SMA) 12-4713
4. Campbell ANC, Nunes EV, Miele GM, Matthews A, Polsky D, Ghitza UE, Turrigiano E, Bailey GL, VanVeldhuisen P, Chapdelaine R, Froias A, Stitzer ML, Carroll KM, Winhusen T, Clingerman S, Perez L, McClure E, Goldman B, Crowell AR. Design and methodological considerations of an effectiveness trial of a computer-assisted intervention: an example from the NIDA Clinical Trials Network. *Contemp Clin Trials.* 2012; 33(2):386–395. [PubMed: 22085803]
5. Fichman RG, Kemerer C. The illusory diffusion of innovation: an examination of assimilation gaps. *Inform Syst Res.* 1999; 10(3):255–275.
6. Martino S, Ball SA, Nich C, Frankforter TL, Carroll KM. Informal discussions in substance abuse treatment sessions. *J Subst Abuse Treat.* 2009; 36(4):366–375. [PubMed: 18835679]
7. Bennett GG, Glasgow RE. The delivery of public health interventions via the internet: actualizing their potential. *Annu Rev Public Health.* 2009; 30:273–292. [PubMed: 19296777]
8. Carroll KM, Rounsaville BJ. Computer-assisted therapy in psychiatry: Be brave – it’s a new world. *Curr Psychiat Reports.* 2010; 2:426–43.
9. Moore BA, Fazzino T, Garnet B, Cutter CJ, Barry DT. Computer-based interventions for drug use disorders: a systematic review. *J Subst Abuse Treat.* 2011; 40(3):215–223. [PubMed: 21185683]
10. Bewick BM, Trusler K, Barkham M, Hill AJ, Cahill J, Mulhern B. The effectiveness of web-based interventions designed to decrease alcohol consumption – a systematic review. *Prev Med.* 2008; 47:17–26. [PubMed: 18302970]
11. Kiluk BD, Sugarman DE, Nich C, Gibbons CJ, Martino S, Rounsaville BJ, Carroll KM. A methodological analysis of randomized clinical trials of computer-assisted therapies for psychiatric disorders: toward improved standards for an emerging field. *Am J Psychiatry.* 2011; 168(8):790–799. [PubMed: 21536689]
12. Bickel WK, Marsch LA, Buchhalter A, Badger G. Computerized behavior therapy for opioid dependent outpatients: a randomized, controlled trial. *Exp Clin Psychopharm.* 2008; 16:132–143.
13. Carroll KM, Ball SA, Martino S, Nich C, Babuscio TA, Nuro KF, Gordon MA, Portnoy GA, Rounsaville BJ. Computer-assisted delivery of cognitive-behavioral therapy for addiction: a randomized trial of CBT4CBT. *Am J Psychiatry.* 2008; 165(7):881. [PubMed: 18450927]
14. Kay-Lambkin FJ, Baker AL, Lewin TJ, Carr VJ. Computer-based psychological treatment for comorbid depression and problematic alcohol and/or cannabis use: a randomized controlled trial of clinical efficacy. *Addiction.* 2008; 104:378–388. [PubMed: 19207345]
15. Higgins ST, Budney AJ, Bickel WK, Foerg F, Donham R, Badger GJ. Incentives improve outcome in outpatient behavioral treatment of cocaine dependence. *Arch Gen Psychiatry.* 1994; 51:568–576. [PubMed: 8031230]

16. Higgins ST, Sigmon SC, Wong CJ, Heil SH, Badger GJ, Donham R, Dantona RL, Anthony S. Community reinforcement therapy for cocaine-dependent outpatients. *Arch Gen Psychiatry*. 2003; 60:1043–1052. [PubMed: 14557150]
17. Petry NM, Peirce JM, Stitzer ML, Blaine J, Roll JM, Cohen A, Obert J, Killeen T, Saladin ME, Cowell M, Kirby KC, Sterling R, Royer-Malvestuto C, Hamilton J, Booth RE, Macdonald M, Liebert M, Rader L, Burns R, DiMaria J, Copersino M, Stabile PQ, Kolodner K, Li R. Effect of prize-based incentives on outcomes in stimulant abusers in outpatient psychosocial treatment programs: a National Drug Abuse Treatment Clinical Trials Network study. *Arch Gen Psychiatry*. 2005; 62:1148–1156. [PubMed: 16203960]
18. Stitzer ML, Petry NM, Peirce JM. Motivational incentives research in the National Drug Abuse Treatment Clinical Trials Network. *J Subst Abuse Treat*. 2010; 38(S1):S61–69. [PubMed: 20307797]
19. Kampman KM, Volpicelli JR, Mulvaney F, Rukstalis M, Alterman AI, Pettinati H, et al. Cocaine withdrawal severity and urine toxicology results from treatment entry predict outcome in medication trials for cocaine dependence. *Addict Behav*. 2002; 27(2):251–260. [PubMed: 11817766]
20. Nunes EV, Pavlicova M, Hu M, Campbell A, Miele G, Hien D, Klein D. Baseline matters: the importance of covariation for baseline severity in the analysis of clinical trials. *Am J Drug Alcohol Abuse*. 2011; 37(5):446–452. [PubMed: 21854289]
21. Budney, AJ.; Higgins, ST. Therapy manuals for drug addiction, a community reinforcement plus vouchers approach: treating cocaine addiction. National Institute on Drug Abuse; Rockville, MD: 1998.
22. Sobell, LC.; Sobell, MB. Timeline follow-back: a technique for assessing self-reported alcohol consumption. In: Allen, J.; Litten, RZ., editors. *Measuring Alcohol Consumption: Psychosocial and Biological Methods*. Humana Press; Totowa, NJ: 1992.
23. Liang K-Y, Zeger S. Longitudinal data analysis using generalized linear models. *Biometrika*. 1986; 73:13–22.
24. Cox DR. Regression models and life-tables. *J Roy Stat Soc B Met*. 1972; 34(2):187–220.
25. Schoenfeld D. Partial residuals for the proportional hazards regression model. *Biometrika*. 1982; 69(1):239–241.
26. Lamb, S.; Greenlick, MR.; McCarty, D., editors. *Committee on Community-based Drug Treatment, Institute of Medicine. National Academy Press; Washington, DC: 1998. Bridging the Gap Between Practice and Research: Forging Partnerships with Community-based Drug and Alcohol Treatment*.
27. Buck JA. The looming expansion and transformation of public substance abuse treatment under the Affordable Care Act. *Health Affairs*. 2011; 30(8):1402–1410. [PubMed: 21821557]
28. Office of National Drug Control Policy Substance abuse and the Affordable Care Act. [cited April 29, 2013]. Available from: <http://www.whitehouse.gov/ondcp/healthcare>
29. McLellan AT, Carise D, Kleber HD. Can the national addiction treatment infrastructure support the public's demand for quality care? *J Subst Abuse Treat*. 2003; 25:117–121. [PubMed: 14680015]
30. Nunes EV, Ball SA, Booth RE, Brigham G, Calsyn DA, Carroll K, Feaster DJ, Hien D, Hubbard RL, Ling W, Petry NM, Rotrosen J, Selzer J, Stitzer M, Tross S, Wakim P, Winhusen T, Woody G. Multisite effectiveness trials of treatments for substance abuse and co-occurring problems: have we chosen the best designs? *J Subst Abuse Treat*. 2010; 39(S1):S97–S112. [PubMed: 20307801]
31. Chaple M, Sacks S, McKendrick K, Marsch LA, Belenko S, Leukefeld C, Prendergast M, French M. Feasibility of a computerized intervention for offenders with substance use disorders: a research note. *J Exp Criminol*. 2013 doi:10.1007/s11292-013-9187-y.
32. Knapp WP, Soares B, Farrell M, Silva de Lima M. Psychosocial interventions for cocaine and psycho-stimulant amphetamines related disorders. *The Cochrane Library*. 2008 doi: 10.1002/14651858.CD003023.pub2.
33. Marsch LA, Guarino H, Acosta M, Aponte-Melendez Y, Cleland C, Grabinski M, Brady R, Edwards J. Web-based behavioral treatment for substance use disorders as a partial replacement of standard methadone maintenance treatment. *J Subst Abuse Treat*. 2014; 46(1):43–51. [PubMed: 24060350]

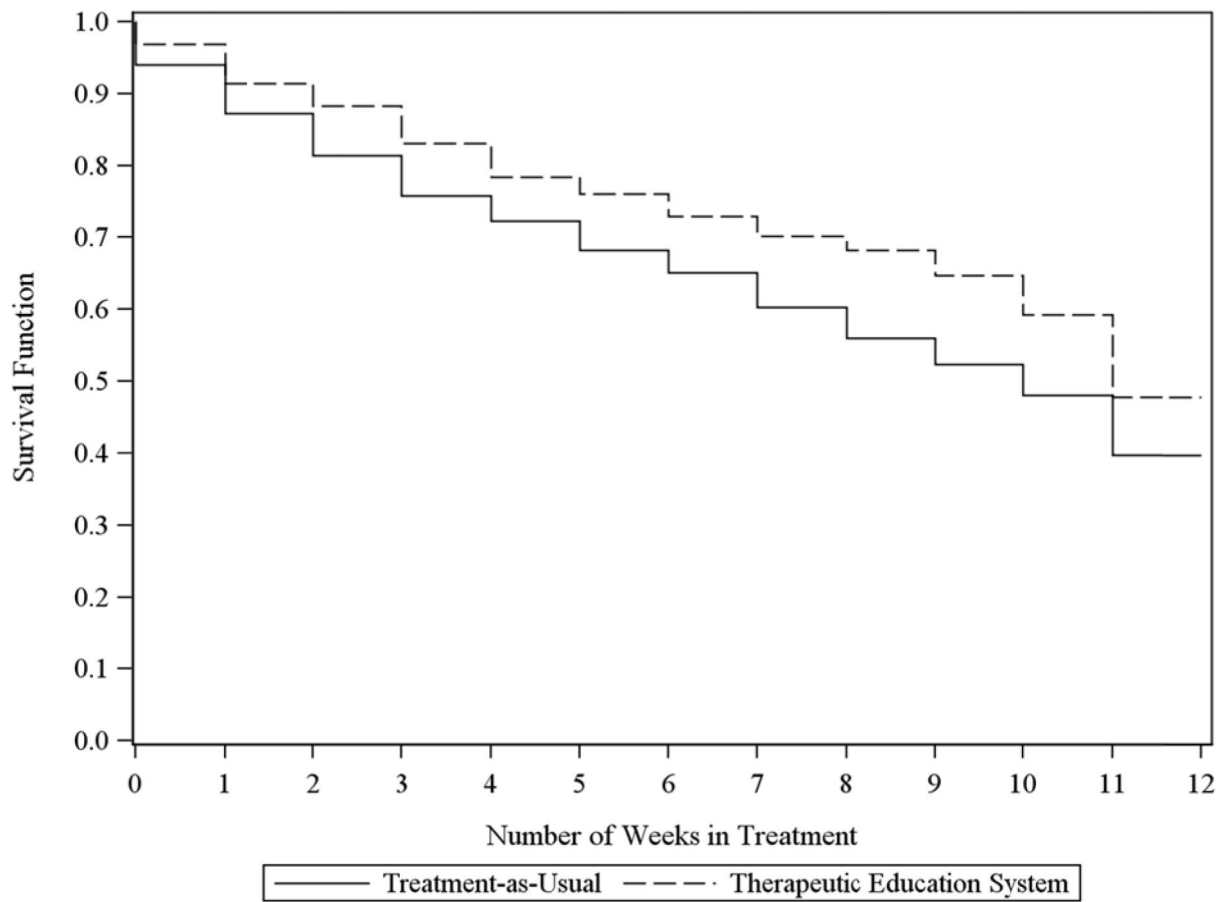
34. Roozen HG, Boulogne JJ, van Tulder MW, van den Brink W, De Jong CA, Kerkhof AJ. A systematic review of the effectiveness of the community reinforcement approach in alcohol, cocaine, and opioid addiction. *Drug Alcohol Depend.* 2004; 74:1–13. [PubMed: 15072802]
35. Stitzer ML, Petry NM, Peirce J. Motivational incentives research in the National Drug Abuse Treatment Clinical Trials Network. *J Subst Abuse Treat.* 2010; 38(S1):S61–S69. [PubMed: 20307797]
36. Carroll KM, Ball SA, Martino S, Nich C, Babuscio TA, Rounsaville BJ. Enduring effects of a computer-assisted training program for cognitive behavioral therapy: a 6-month follow-up of CBT4CBT. *Drug Alcohol Depend.* 2009; 100(1-2):178–181. [PubMed: 19041197]
37. Magill M, Ray LA. Cognitive-behavioral treatment with adult alcohol and illicit drug users: a meta-analysis of randomized controlled trials. *J Stud Alcohol Drugs.* 2009; 70(4):516. [PubMed: 19515291]
38. McLellan AT. Have we evaluated addiction treatment correctly? Implications from a chronic care perspective. *Addiction.* 2002; 97(3):249–252. [PubMed: 11964098]
39. Campbell ANC, Nunes EV, McClure E, Hu M, Turrigiano E, Goldman B, Stabile PQ. Characteristics of an outpatient treatment sample by primary substance of abuse. *Journal Addiction Medicine.* 2013; 7(5):363–371.
40. Hudziak JJ, Helzer JE, Wetzel WW, Kessel KB, McGee B, Janca A, Przybeck T. The use of the DSM-III-R Checklist for initial diagnostic assessment. *Compr Psychiatry.* 1993; 34(6):375–383. [PubMed: 8131381]



**Figure 1.**  
Study Enrollment and Patient Flow.



**Figure 2.** Proportion of patients abstinent by treatment half-week and at 3 month post treatment follow-up and 6 month post treatment follow-up as a function of treatment assignment (Therapeutic Education System vs. Treatment-as-Usual) and abstinence at baseline/study entry.



**Figure 3.** Kaplan-Meier Plot of time to treatment program drop-out by treatment assignment (Therapeutic Education System vs. Treatment-as-Usual).

**Table 1**

Baseline demographic and clinical characteristics by treatment assignment (Therapeutic Education System or Treatment-as-Usual) for all randomized patients (N=507)

Variable	TOTAL N=507		Therapeutic Education System <sup>a</sup> n=255		Treatment- as-Usual <sup>a</sup> n=252	
	n (%) or Mean (SD)					
<b>Age (years)</b>	34.9	(10.9)	35.6	(10.7)	34.2	(11.1)
<b>Female (%)<sup>b</sup></b>	192	(37.9)	91	(35.7)	101	(40.1)
<b>Race (%)<sup>c</sup></b>						
White	284	(56.0)	136	(53.3)	148	(58.7)
Black/African American	116	(22.9)	69	(27.1)	47	(18.7)
American Indian/Alaska Native	3	(0.6)	2	(0.8)	1	(0.4)
Asian	13	(2.6)	6	(2.4)	7	(2.8)
Native Hawaiian/Pacific Islander	12	(2.4)	7	(2.7)	5	(2.0)
Multi-racial	54	(10.7)	23	(9.0)	31	(12.3)
Other	23	(4.5)	10	(3.9)	13	(5.2)
<b>Hispanic/Latino (%)<sup>d</sup></b>	55	(10.8)	26	(10.2)	29	(11.5)
<b>Education (%)</b>						
< High School Degree	118	(23.3)	60	(23.5)	58	(23.0)
High School Degree/GED	310	(61.1)	161	(63.1)	149	(59.1)
> High School Degree	79	(15.6)	34	(13.3)	45	(17.9)
<b>Marital Status (%)</b>						
Single/Never Married	308	(60.7)	148	(58.0)	160	(63.5)
Married/Remarried	72	(14.2)	36	(14.1)	36	(14.3)
Separated/Divorced/Widowed	127	(25.0)	71	(27.8)	56	(22.2)
<b>Underemployed (%)</b>						
(unemployed/irregular part-time)	190	(37.5)	106	(41.6)	84	(33.3)
<b>Primary Substance (%)</b>						
Alcohol	104	(20.5)	58	(22.7)	46	(18.3)
Cocaine	102	(20.1)	53	(20.8)	49	(19.4)
Stimulants	69	(13.6)	33	(12.9)	36	(14.3)
Marijuana	114	(22.5)	54	(21.2)	60	(23.8)
Opiates	108	(21.3)	49	(19.2)	59	(23.4)
Other	10	(2.0)	8	(3.1)	2	(0.8)
<b>Substance Dependence (%)<sup>e</sup></b>						
Alcohol	224	(44.2)	119	(46.7)	105	(41.7)
Cocaine	177	(34.9)	90	(35.3)	87	(34.5)
Stimulants	100	(19.7)	47	(18.4)	53	(21.0)
Marijuana	146	(28.8)	68	(26.7)	78	(31.0)
Opiates	158	(31.2)	78	(30.6)	80	(31.7)



Variable	TOTAL N=507		Therapeutic Education System <sup>a</sup> n=255		Treatment- as-Usual <sup>a</sup> n=252	
	n (%) or Mean (SD)					
Other	41	(8.1)	21	(8.2)	20	(7.9)
<b>Alcohol/Drug Use (past 30 days)</b>	9.8	(9.4)	10.2	(8.9)	9.4	(9.8)
<b>Abstinent, Baseline/Study Entry</b>	275	(54.2)	136	(53.3)	139	(55.2)

<sup>a</sup>No statistically significant differences on demographic or clinical characteristics by intervention condition.

<sup>b</sup>One participant elected not to report their gender.

<sup>c</sup>Two participants elected not to report their race.

<sup>d</sup>Four participants elected not to report their ethnicity.

<sup>e</sup>Dependence was assessed using the DSM-IV Checklist, a semi-structured, interviewer-administered measure which provides a current (last year) substance use dependence diagnosis based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision criteria (40).

**Table 2**

Logistic regression model of abstinence from drug use or heavy drinking during a 12-week randomized trial of computer-delivered behavioral therapy (the Therapeutic Education System), vs. treatment-as-usual among patients (N=507) enrolled in treatment for substance abuse across 10 community-based treatment programs.

Variable	Odds Ratio <sup>a</sup>	95% C.I.	P Value
<b>Model A: Main Effects</b>			
Abstinent at Baseline/Study Entry	5.73	4.20 – 7.80	.0001
Primary Substance Stimulant	1.23	0.90 – 1.68	.193
Clinical Site <sup>b</sup>			.003
Treatment (Therapeutic Education System vs. Treatment-as-Usual)	1.62	1.12 – 2.35	.010
<b>Model B: Treatment Assignment by Abstinance at Baseline/Study Entry Interaction<sup>c</sup></b>			
Therapeutic Education System vs. Treatment-as-Usual, Non-abstinent at Baseline/Study Entry (n=228)	2.18	1.30 – 3.68	.003
Therapeutic Education System vs. Treatment-as-Usual, Abstinent at Baseline/Study Entry (n=268)	1.17	0.76 – 1.80	.489

Abbreviation: CI, Confidence Interval.

<sup>a</sup>The odds ratios reflect the last four weeks (weeks 9 through 12) of the treatment phase.

<sup>b</sup>Odds ratios for each site compared to the referent site ranged from 1.02 [95% CI: 0.55-1.90] to 0.31 [95% CI: 0.17 to 0.58] indicating that the odds of abstinence varied across sites.

<sup>c</sup>After fitting Model A, including the main effects of treatment and stratification factors, each of the stratum by treatment interactions was tested using a .100 significance level. Only the abstinence at baseline/study entry by treatment interaction (P=.068) met the threshold, and the effects of treatment (Therapeutic Education System vs. Treatment-as-Usual) are therefore shown separately in the non-abstinent and abstinent strata.