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## Cigarette smoking during substance use disorder treatment: Secondary outcomes from a National Drug Abuse Treatment Clinical Trials Network study

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### Abstract

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**Conflict of Interest.** Dr. Nunes has received medication from research studies from Alkermes/Cephalon, Inc. and Reckitt-Benckiser and has received from Brainsway devices under investigation and reimbursement for travel expenses for investigators' meeting; he has previously received medication for a research study from Duramed Pharmaceuticals. He was paid an honorarium and received reimbursement for travel expenses for attendance at a Lilly Advisory Board Meeting in January 2012 and received educational materials from Otsuka America Pharmaceutical, Inc. in 2013. The authors have no additional conflicts of interest to report.

**Introduction**—The majority of patients enrolled in treatment for substance use disorders (SUDs) also use tobacco. Many will continue to use tobacco even during abstinence from other drugs and alcohol, often leading to smoking-related illnesses. Despite this, little research has been conducted to assess the influence of being a smoker on SUD treatment outcomes and changes in smoking during a treatment episode.

**Methods**—In this secondary analysis, cigarette smoking was evaluated in participants completing outpatient SUD treatment as part of a multi-site study conducted by the National Drug Abuse Treatment Clinical Trials Network. Analyses included the assessment of changes in smoking and nicotine dependence via the Fagerström Test for Nicotine Dependence during the 12-week study among all smokers (Aim #1), specifically among those in the experimental treatment group (Aim #2), and the moderating effect of being a smoker on treatment outcomes (Aim #3).

**Results**—Participants generally did not reduce or quit smoking throughout the course of the study. Among a sub-set of participants with higher baseline nicotine dependence scores randomized to the control arm, scores at the end of treatment were lower compared to the experimental arm, though measures of smoking quantity did not appear to decrease. Further, being a smoker was associated with poorer treatment outcomes compared to non-smokers enrolled in the trial.

**Conclusions**—This study provides evidence that patients enrolled in community-based SUD treatment continue to smoke, even when abstaining from drugs and alcohol. These results add to the growing literature encouraging the implementation of targeted, evidence-based interventions to promote abstinence from tobacco among SUD treatment patients.

### Keywords

substance use disorders; smoking; tobacco; cessation; internet-delivered treatment; Therapeutic Education System

## 1. Introduction

The majority of patients enrolled in treatment for substance use disorders (SUDs) also use tobacco with reported rates as high as 97% (Bobo, 1989; Guydish et al., 2011; Kalman, 1998; McClure, Acquavita, Dunn, Stoller, & Stitzer, 2014; Nahvi, Richter, Li, Modali, & Arnsten, 2006; Pajusco et al., 2012). This is significantly higher than the smoking rate in the general population, which is currently 19.3% in the United States (Centers for Disease Control and Prevention, 2012). Those enrolled in treatment for SUDs are more likely to die due to smoking-related illnesses than from complications from their primary drug of choice (Baca & Yahne, 2009; Hser, McCarthy, & Anglin, 1994; Hurt et al., 1996). Attempts to explain the relationship between nicotine and the use of other substances have involved conceptual models including, biological vulnerabilities due to nicotine during adolescents (Kelley & Rowan, 2004; Lydon, Wilson, Child, & Geier, 2014; Santos, Marin, Cruz, Delucia, & Planeta, 2009), common neural pathways, substrates, and dysregulation contributing to addiction (Kalivas, Lalumiere, Knackstedt, & Shen, 2009), and pharmacological interactions between drugs potentially increasing their reinforcing properties (Mello, Lukas, & Mendelson, 1985; Mello, Mendelson, Sellers, & Kuehnle, 1980; Mutschler, Stephen, Teoh, Mendelson, & Mello, 2002). Additional conceptual models, not

specific to nicotine, have focused on reinforcer pathology (Bickel, Johnson, Koffarnus, MacKillop, & Murphy, 2014) and reward seeking (Arias-Carrion & Salama, 2012), to name only a few.

Despite high rates of smoking among SUD treatment patients and the well-known negative health effects of smoking, the majority who enter SUD treatment as cigarette smokers will not contact resources to assist them in quitting and tobacco cessation services are not always available onsite for those who might be interested. Several studies administered across treatment settings have reported low levels of both availability and use of smoking cessation services in participating SUD programs (Eby & Laschober, 2013; Friedmann, Jiang, & Richter, 2008; Fuller et al., 2007; Knudsen & Studts, 2011; Laschober & Eby, 2013; Richter, Choi, McCool, Harris, & Ahluwalia, 2004), though services are becoming more common with the introduction of state mandates and smoking cessation guidelines for SUD treatment clinics (Gyudish et al., 2012; Williams et al., 2005).

Recent evidence appears to suggest that non-smokers or former smokers may have better drug abstinence outcomes or proxies of outcomes compared to smokers. This is concerning given that the majority of SUD patients are smokers, and they may be starting treatment episodes already at a disadvantage. Among users of both tobacco and cannabis, a recent review showed poorer cannabis cessation outcomes compared to cannabis only users (Peters, Budney, & Carroll, 2012), and a human laboratory-based study showed that co-users of tobacco and cannabis were more likely to relapse (to cannabis) compared to non-smoking cannabis users (Haney et al., 2013). Smoking during opioid detoxification was shown to increase opioid craving (Mannelli, Wu, Peindl, & Gorelick, 2013). It has also been found that cocaine-dependent patients who stopped smoking in response to smoking cessation treatment provided concurrently with SUD treatment had improved cocaine-use outcomes relative to those who continued to smoke (Winhusen, Kropp, Theobald, & Lewis, 2014). The aforementioned results suggest that there is a potentially important relationship between tobacco use and SUD treatment outcomes. Studies to this point have been substance-specific, and may be limited in generalizability. The current report, however, includes data from a large, geographically diverse outpatient SUD treatment population, and may provide additional insight, generalizability, and support for the previous findings that smokers appear to have poorer SUD treatment outcomes.

Additionally, little is known about changes in smoking during a SUD treatment episode and published evaluations have been limited to adolescent populations. One study found that smoking persisted throughout SUD treatment and increased at the 12-month follow-up visit (Coleman-Cowger & Catlin, 2013). Another study showed that among adolescents in treatment for cannabis use disorders, moderate and heavy cigarette smokers decreased their cigarettes per day only slightly during treatment, but showed similar smoking rates at follow-up, while mild smokers decreased their cigarettes per day during treatment and follow-up (Shelef, Diamond, Diamond, & Myers, 2009). Among adolescents enrolled in a cannabis cessation pharmacotherapeutic clinical trial, there were no changes in cigarette smoking during treatment (McClure, Baker, & Gray, 2014), while another report showed that adolescent cannabis users with attention-deficit/hyperactivity disorder who reduced their cannabis use by at least 50% following treatment also significantly decreased their

cigarette smoking (Gray et al., 2011). The scarcity of data on this topic suggests that the majority of treatment trials among SUD populations do not assess or do not report the impact of SUD treatment on cigarette smoking and other tobacco use, presenting a missed opportunity for future trials and intervention improvement.

In order to contribute to the literature on the complex issue of cigarette smoking among SUD treatment patients, the current report explored cigarette smoking within the context of a randomized controlled effectiveness trial of a web-delivered psychosocial treatment (WEB-TX) conducted within the National Drug Abuse Treatment Clinical Trials Network (NIDA CTN) (Campbell et al., 2014; Campbell et al., 2012). This secondary analysis had three main aims; 1) assess if smoking and nicotine dependence changed over the course of the 12-week study, 2) explore if the treatment group (Therapeutic Education System [TES]) showed reductions in smoking and changes in nicotine dependence over the treatment period compared to the control group (treatment as usual [TAU]), and 3) determine if being a smoker moderated the effect of treatment with TES (versus TAU) on abstinence from drugs and alcohol.

Though TES as a treatment intervention for drugs and alcohol does not target cigarette smoking specifically, the content material of TES focuses on skills-based learning for achieving and maintaining abstinence from drugs (e.g., drug refusal, coping with craving and withdrawal, avoiding triggers, etc.). It follows that interventions of this sort targeting SUDs may extend to cigarette smoking through knowledge and acquired skills that may prove useful in cessation efforts. In a broader sense, it is also possible that the improvement of SUD symptomology is associated with reductions in tobacco use or cessation. Evaluation of the relations between smoking and substance use is valuable for the continued improvement of treatment strategies to address both concurrently.

## 2. Methods

### 2.1 Participants and Procedures

The parent trial (WEB-TX; CTN-0044) was conducted within 10 outpatient, geographically-diverse, community-based SUD treatment programs (Campbell et al., 2014; Campbell et al., 2012). Enrolled participants were adult men and women (N=507) who were within the first 30 days of their current treatment episode. After screening and baseline assessment, participants were randomized to receive 12 weeks of either standard TAU (n=252) or TAU + TES (n=255), whereby TES replaced two hours of standard care per week. TES (Bickel, Marsch, Buchhalter, & Badger, 2008; Marsch et al., 2014) consisted of a web-delivered version of the Community Reinforcement Approach (Onken, 1997) that incorporated voucher-based contingency management (Higgins et al., 1994; Peirce et al., 2006; Petry et al., 2005; Stitzer, Petry, & Peirce, 2010) to promote abstinence from drugs and alcohol. TES has 62 computer-delivered, interactive, multimedia modules, which covered skills for achieving and maintaining abstinence. Participants made two weekly research assessment visits for 12 weeks and completed 3- and 6-month follow-up visits. Primary outcomes for this study (Campbell et al., 2014) and further study details (Campbell et al., 2013; Campbell et al., 2012) are described elsewhere, but briefly, participants randomized to TES had greater abstinence rates and lower treatment dropout rates compared to a standard outpatient

treatment control condition (Campbell et al., 2014). The trial was registered with Clinicaltrials.gov (NCT01104805).

## 2.2 Measures

**Smoking**—Cigarette smoking was self-reported during the trial. Smoking status and nicotine dependence were assessed at the baseline visit, weeks 4, 8, and 12 during treatment, and at the 3- and 6-month follow-up visits. Participants were asked if they currently smoked cigarettes and if they were using any smoking cessation medication (i.e., nicotine replacement, bupropion, varenicline, or other). If participants endorsed smoking, they completed the six-item Fagerström Test for Nicotine Dependence (FTND, range 0–10) (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991). Responses on the FTND were summed resulting in a score of nicotine dependence, with 10 indicating the most severe level of dependence. Two specific items, often referred to as the Heaviness of Smoking Index (HSI) (Heatherton, Kozlowski, Frecker, Rickert, & Robinson, 1989; Kozlowski, Porter, Orleans, Pope, & Heatherton, 1994), from the FTND were examined in a separate analysis. The first item was number of cigarettes per day, which was categorized into four levels based on the standard response categories used in the FTND questionnaire: 10 or less, 11–20, 20–30, and 31+. The second item was time to first cigarette after waking, also categorized into four levels: within 5 min, 6–30 min, 31–60, and after 60 min.

**Substance Use**—Abstinence from drugs and alcohol was assessed twice per week during the treatment phase. Abstinence was defined as: 1) a negative urine drug test (for 10 substances), and 2) self-reported abstinence from drugs and alcohol based on the Timeline Follow Back method (Sobell, Sobel, Bogardis, Leo, & Skinner, 1992). Abstinence data were considered missing if: 1) the urine screen was missing or; 2) the urine screen was negative and the self-report was missing. The outcome for the purposes of this analysis was a binary measure of abstinence (yes or no). Treatment responders were defined as participants who were abstinent from all drugs and drinking days during the final four weeks of treatment (weeks 9–12) with no missing data points. The last four weeks of active treatment was the pre-specified indicator of treatment success and consistent with the primary outcome publication (Campbell et al., 2014).

## 2.3 Statistical Analyses

Demographic and clinical characteristics were described for the total sample (N=507) and by smoking status at baseline using means, standard deviations, and frequencies; chi-square and t-tests were used to test differences between baseline smokers and non-smokers on these variables. Additionally, the categorical variables of cigarettes per day and time to first cigarette after waking were analyzed for changes from baseline to week 12 (Aim #1). The proportion of participants endorsing each category and change in category was assessed using chi-square tests.

Four outcome variables were analyzed: smoking status at the end of treatment (EOT; week 12) (binary; among N=507 enrolled participants, n=448 cases with smoking status data at EOT) (Aim #2); number of cigarettes per day at EOT (categorical; among n=391 baseline smokers, n=344 with smoking data available at EOT) (Aim #2); FTND scores at week 4, 8,

and 12 (continuous longitudinal; among n=391 baseline smokers, n=366 with 1 FTND assessment) (Aim #2), and weekly abstinence from drugs and alcohol during the last four weeks of treatment (binary longitudinal; among N=507 enrolled participants, n=469 with 1 observation during the last 4 weeks of treatment) (Aim #3). Treatment arm, baseline drug use status (positive vs. negative assessed by urine drug and breath alcohol screen) and baseline smoking status or baseline FTND score, as appropriate, were included as predictors in statistical models. Generalized linear models were applied for the outcomes with appropriate link functions (logit for binary outcome, cumulative logit for categorical outcome, and identity for continuous outcome). Interactions were tested (between treatment arm, baseline drug use status, and baseline smoking status or baseline FTND scores) and included in the final models only if significant ( $p < .05$ ). In addition, for the model testing smoking status at week 12, treatment response (i.e., participants who were completely abstinent during this time with no missing data) was also tested in an attempt to replicate prior research (i.e., Gray et al., 2011). This was not significant ( $p < .05$ ) and therefore not included in the final model. Time was included in the models testing the longitudinal outcomes: FTND and abstinence. Site and subject were treated as random effects. The correlation between the repeated measurements over time within subject was modeled using the first-order autoregressive structure. Missing data were assumed missing at random. SAS version 9.3 was utilized for all analyses.

### 3. Results

#### 3.1 Demographic and Smoking Characteristics

Demographic and smoking characteristics are shown in Table 1 for the entire study sample (N=507) and for self-reported cigarette smokers (n=391; 77%) and non-smokers (n=116; 23%) at baseline. Participants who were cigarette smokers at baseline tended to be younger, more likely to be female, less educated, and unemployed. No significant difference was found in baseline drug use status by smoking status. Smokers and non-smokers were equally likely to be randomized to each treatment arm. When separated by primary substance of abuse, the proportion of smokers to non-smokers was generally consistent with overall averages, with the exception of the opioid group, which had a higher rate of smokers compared to other substances of abuse, while the stimulant group had a lower rate of smokers. At baseline, only 16 smokers (4.1%) reported current use of a smoking cessation medication, and even fewer reported currently using a medication at the end of 12 weeks (12; 3.5%). During the 12 weeks of active treatment and participation in SUD treatment, approximately 19 (5% out of 344 reporting) baseline smokers reported being non-smokers at week 12. However, 11 (11% out of 104 reporting) baseline non-smokers reported being smokers at week 12.

#### 3.2 Changes in Smoking during Treatment (Aim #1)

The categorical variables of cigarettes per day and time to first cigarette were assessed via individual items on the FTND and were examined among baseline smokers. At week 12, responses to these items were categorized as an improvement or decrement in severity, or no change from baseline. Improvements or decrements were defined as participants changing categories during treatment to reflect changes in nicotine dependence (e.g., fewer cigarettes



per day and/or more time to first cigarette). Table 2 shows the proportions of participants who showed either categorical decrease, increase, or no changes on cigarettes per day, and also in time to first cigarette at EOT. Decreases in cigarettes per day and longer time to first cigarette occurred for approximately 22% and 26% of participants, respectively. Increases in cigarettes per day and less time to first cigarette (considered detrimental) occurred in 12% and 17% of participants, respectively. The majority of the sample did not change their number of cigarettes smoked per day (66%) or time to first cigarette (57%). The only significant predictor of cigarettes smoked per day at EOT was baseline cigarettes smoked per day ( $X^2(1)=107.27$ ,  $p<.001$ ).

### 3.3 Smoking Changes between Treatment Groups (Aim #2)

**3.3.1 Smoking Status**—Smoking at EOT was modeled by treatment arm, baseline drug use status, and baseline smoking status. A significant two-way interaction of treatment assignment and baseline drug use status ( $X^2(1)=4.34$ ,  $p=.04$ ) was observed on self-reported smoking status at EOT (Figure 1). EOT smoking appeared to be lower among participants who were drug positive at baseline and assigned to TES compared to participants receiving TAU, but this observed treatment effect did not reach statistical significance (OR=0.40, 95% CI: 0.13, 1.28,  $p=.12$ ). There was also no significant difference between TES and TAU among baseline drug negative participants (OR=2.18, 95% CI: 0.77, 6.14,  $p=.14$ ). As expected, baseline smoking status (i.e., being a smoker) was significantly associated with continued smoking at EOT ( $X^2(1)=147.55$ ,  $p<.001$ ).

**3.3.2 Nicotine Dependence**—Average FTND nicotine dependence scores for smokers at baseline showed that participants were moderately nicotine dependent ( $3.49 \pm 2.3$ ). Dependence severity did not differ significantly by treatment arm at baseline or throughout treatment. There was no significant change over time in nicotine dependence scores among all cigarette smokers, and average FTND scores at EOT were 3.30 (SD=2.4).

The model testing the outcome of FTND scores during treatment included a three-way interaction between treatment arm, baseline drug use status, and baseline FTND ( $F(1, 661)=4.73$ ,  $p=.03$ ). To illustrate this significant interaction, FTND baseline scores were split into four categories (quartiles) to demonstrate the observed interaction between treatment arm and baseline drug use status for the lowest quartile (1, bottom 24% of scores; Figure 2A) and the highest quartile (6, top 23% of scores; Figure 2B). There were no significant differences by treatment arm or baseline drug use status for those with lower baseline FTND scores. Participants with higher baseline FTND demonstrated lower EOT FTND scores in TAU compared to TES, but only among those who were drug negative at baseline. There were no significant differences by treatment arm among baseline drug positive participants in the top quartile for baseline FTND.

### 3.4 Abstinence from Drugs and Alcohol (Aim #3)

Smoking was assessed as a possible moderator of treatment on the outcome of abstinence in the last four weeks of treatment. The final model yielded one significant two-way interaction: treatment and baseline smoking status ( $F(1, 2450)=3.76$ ,  $p=.053$ ). To illustrate this interaction, Figure 3 shows the proportion of participants who were abstinent from

drugs and alcohol in the last four weeks of treatment, separated by treatment arm and baseline smoking status. There was a significant treatment difference favoring TES over TAU among non-smokers (OR=6.61, 95% CI: 1.85, 23.59,  $p=.004$ ), but no differences by treatment arm among baseline smokers (OR=1.56, 95% CI: 0.77, 3.16,  $p=.21$ ). Baseline drug use status was also associated with the abstinence outcome ( $F(1, 2450)=62.20$ ,  $p<.001$ ); those who were drug negative at baseline were more likely to be abstinent in the last four weeks of treatment.

#### 4. Discussion

This secondary analysis examined cigarette smoking during outpatient SUD treatment among a large and geographically diverse sample of patients enrolled in community treatment clinics across the United States. Some study results were confirmatory of previous literature, including the high rates of smoking prevalence among the study sample (77%) (Bobo, 1989; Guydish et al., 2011; Kalman, 1998; McClure, Acquavita, et al., 2014; Nahvi et al., 2006; Pajusco et al., 2012). Unfortunately, the vast majority of participants (96%) were not using smoking cessation medications at treatment entry and this did not change during the 12-week study. Among baseline smokers, only 19 participants reported being non-smokers at week 12 (5%), and perhaps more troubling, 11 baseline non-smokers reported being smokers at week 12 (11%). These results serve to further justify the need to target smoking cessation during SUD treatment as the majority of patients smoke and few are using smoking cessation medications.

Study results revealed that nicotine dependence severity and cigarettes per day generally did not change over the course of the 12-week study. Upon further inspection, however, results showed that participants randomized to TES with greater nicotine dependence and who were also drug negative at baseline had higher FTND scores compared to their TAU counterparts at EOT. Given a treatment effect of TES on drug and alcohol abstinence, one possible conclusion that could be drawn is that participants in TES were substituting more tobacco in place of drugs and alcohol as a potential coping strategy for their abstinence. We did not find a change in cigarettes per day among this sub-set of participants, however, so this potential behavioral link and drug substitution hypothesis requires further study and more sensitive assessments to measure increases in smoking. It should also be noted that the higher FTND scores may reflect changes in other smoking-related behavior captured by this assessment, and not specific to quantity of tobacco being used. This difference in FTND at EOT among baseline drug negative participants is of interest, especially since increases in tobacco use represent very serious health-related concerns, and requires further study and increased attention, if reliably present.

While the TES intervention was efficacious for treating drug and alcohol use (Campbell et al., 2014), it did not specifically address cigarette smoking and, not surprisingly, intervention effects did not appear to extend to cigarette smoking. This supports the need for specialized interventions that target cessation from cigarettes and tobacco for use in SUD treatment patients. These interventions are desperately needed in SUD treatment and there is ample evidence to suggest that smoking cessation interventions delivered during SUD treatment episodes do not jeopardize abstinence and may even enhance long-term abstinence



from drugs and alcohol (Bobo, McIlvain, Lando, Walker, & Leed-Kelly, 1998; Frosch, Shoptaw, Nahom, & Jarvik, 2000; Hughes, 1993; Joseph, Nichol, & Anderson, 1993; Prochaska, Delucchi, & Hall, 2004; Richter & Arnsten, 2006; Tsoh, Chi, Mertens, & Weisner, 2011; Winhusen et al., 2013).

The results from the current study also suggest that being a cigarette smoker may be adversely related to SUD treatment outcomes. Among participants who were non-smokers at baseline, there was a significant difference in abstinence outcomes at EOT favoring TES over TAU. This difference was not present among baseline smokers. This result is consistent with the literature suggesting better drug abstinence outcomes (or proxies of outcomes) in non-smokers or former smokers (Haney et al., 2013; Mannelli et al., 2013; Peters et al., 2012; Winhusen et al., 2014), but demonstrates this relationship in a large, geographically diverse outpatient SUD (non-opioid) adult population. This relationship appears to be robust, and it may be possible that reducing smoking early in the SUD treatment may serve to improve treatment response. This represents an interesting avenue for future work to explore.

This secondary analysis had several limitations. First, biochemical verification of smoking status was not confirmed as part of study procedures. All smoking data were based on self-report and we cannot determine if non-smokers were former smokers and when they had quit. Second, tobacco policies and smoking cessation services and resources at the participating treatment facilities were not systematically assessed. While TES did not directly address tobacco, it is possible that study sites had different smoking cessation services and education available to participants, which may have influenced results. Also, sites most likely differed in terms of tobacco restrictions, policies, and cultures surrounding tobacco use while in SUD treatment, that were not accounted for in the current analysis. Third, demographic findings from our sample are descriptive and may not be generalizable to other SUD patients and treatment clinics. Finally, FTND was the primary measure to capture and quantify smoking, which is not ideal as an outcome measure of smoking. Cigarettes per day via Timeline Follow-Back methods were not collected as part of study procedures, which may have provided a more sensitive measure of reductions or increases in smoking during the trial.

#### 4.1 Conclusions

TES appeared to exert a greater effect on the outcome of drug and alcohol use for non-smokers compared to smokers in the current report. Also, for a sub-set of participants randomized to TES, FTND scores were higher compared to participants in TAU at EOT. This suggests that although participants were abstinent from drugs and alcohol, they were still using tobacco and may even be increasing their tobacco use as way to cope with or manage reductions in substance use, though this statement is speculative and requires further investigation. It is also possible that other smoking-related behavior is changing, contributing to higher FTND scores without an increase in tobacco use. Cigarette smoking was not targeted by the treatment intervention and may not have been addressed in the usual care received by participants in the treatment programs. Therefore, it is not surprising that participants generally did not quit smoking during the trial. Prior research suggests that

individuals enrolled in treatment for SUDs are receptive to smoking cessation interventions (McClure, Acquavita, et al., 2014; Nahvi et al., 2006; Richter, Gibson, Ahluwalia, & Schmelzle, 2001), and the results from the current study provide further evidence that patients enrolled in outpatient SUD treatment are in need of targeted smoking cessation interventions.

A logical next step for intervention development and refinement may be the incorporation of modules targeting smoking cessation within web-delivered programs, such as TES. There are several promising internet-delivered interventions for smoking cessation (Civljak, Stead, Hartmann-Boyce, Sheikh, & Car, 2013), which may hold the potential for use in outpatient SUD treatment settings as part of a comprehensive treatment plan. Future research should continue to work to incorporate evidence-based smoking cessation into comprehensive SUD treatment, and web-based interventions should be explored given their potential to deliver effective treatments in a cost-effective manner. SUD treatment patients are continuing to smoke during a treatment episode and resources to promote abstinence from tobacco should be encouraged among community treatment programs to avoid the almost inevitable smoking-related illnesses that these participants will likely encounter.

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### Highlights

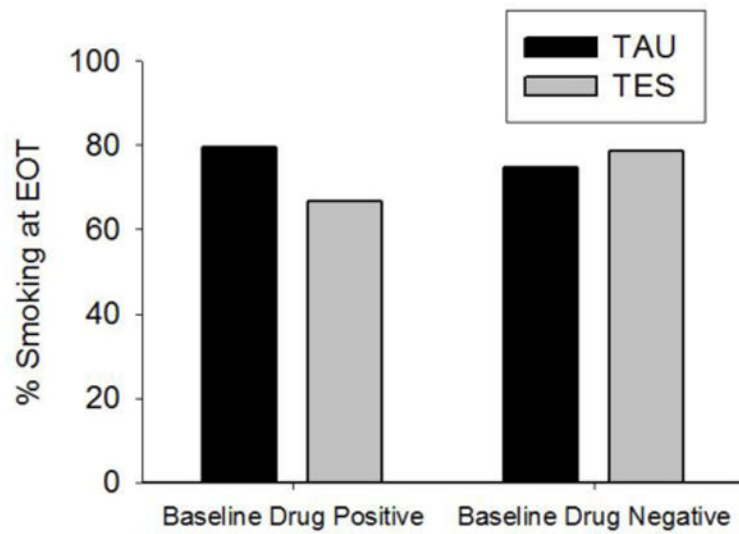
- The majority of those with substance use disorders are also tobacco users.
- Little is known about the influence of smoking on treatment outcomes.
- Smokers had poorer treatment outcomes compared to non-smokers.
- Participants did not reduce their smoking throughout the course of the study.
- Evidence-based tobacco interventions are needed among SUD patients.

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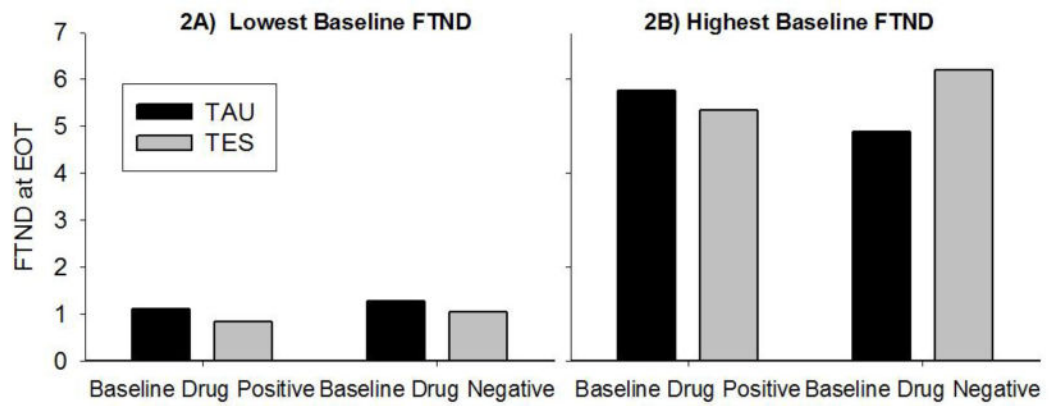
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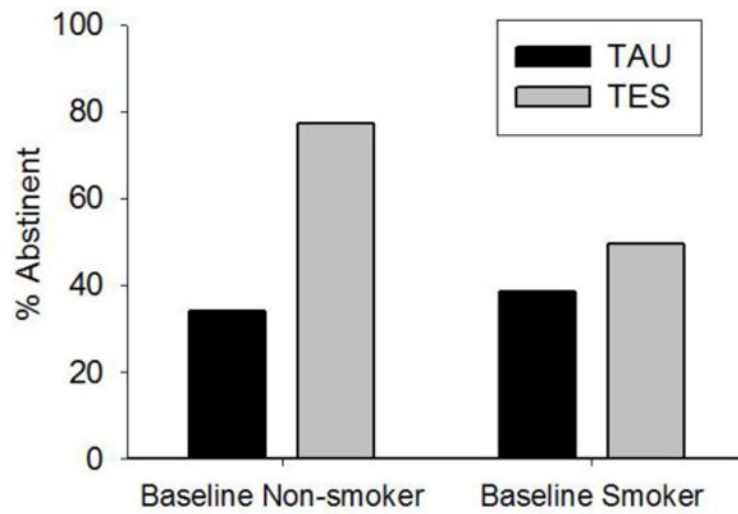
	(N=200)	(N=248)
	% (n/N)	
TAU	79.6 (78/98)	74.6 (94/126)
TES	66.7 (68/102)	78.7 (96/122)

**Figure 1.** Observed smoking proportions at week 12 (end of treatment [EOT]) by baseline drug use status (positive vs. negative assessed via urine drug and breath alcohol screen) and treatment arm (Therapeutic Education System [TES] vs. treatment as usual [TAU] (n=448). A significant two-way interaction of treatment arm and baseline drug use status ( $X^2(1)=4.34$ ,  $p=.04$ ) was observed on the proportion of participants who self-reported smoking at EOT.



	(N=36)	(N=47)	(N=42)	(N=32)
	Lowest Baseline FTND (Bottom 24% of participants, $\leq 1$ )		Highest Baseline FTND (Top 23% of participants, $\geq 6$ )	
TAU	1.11	1.27	5.75	4.88
TES	0.83	1.05	5.35	6.20

**Figure 2.** Nicotine dependence scores at week 12 (end of treatment [EOT]) by bottom ( $\leq 1$  FTND) and top ( $\geq 6$  FTND) quartiles of baseline nicotine dependence severity, baseline drug use status (positive vs. negative), and treatment arm (Therapeutic Education System [TES] vs. treatment as usual [TAU]) (n=366). Statistical analyses found a significant three-way interaction between treatment arm, baseline drug use status, and baseline FTND ( $F(1, 661)=4.73, p=.03$ ).



	N=104	N=344
TAU	34.1%	38.5%
TES	77.2%	49.5%

**Figure 3.** The observed proportion of participants abstinent from drugs and alcohol use days in the last 4 weeks of treatment (weeks 9–12) by baseline smoking status and treatment arm (Therapeutic Education System [TES] vs. treatment as usual [TAU]) (n=469). The final model yielded one significant two-way interaction: treatment and baseline smoking status ( $F(1, 2450)=3.76, p=.053$ ).

**Table 1**

Baseline characteristics by cigarette smoking status (N=507).

Variables	Total Sample (N=507)	Smokers (n=391)	Non-smokers (n=116)	t/χ <sup>2</sup>	p-value
	<b>Mean(SD)/n(%)</b>				
Age (years)	34.89 (10.89)	33.89 (10.14)	38.28 (12.58)	3.45	<.001
Female (%)	192 (37.9)	168 (43.1)	24 (20.7)	19.03	<.001
Race/Ethnicity (%)				4.37	.22
White	267 (52.7)	213 (54.5)	54 (46.6)		
Black/African American	112 (22.1)	87 (22.3)	25 (21.6)		
Hispanic/Latino	55 (10.9)	41 (10.5)	14 (12.1)		
Multi-racial/Other	73 (14.4)	50 (12.8)	23 (19.8)		
Education (%)				23.11	<.001
< High School	118 (23.3)	108 (27.6)	10 (8.6)		
High School/GED	310 (61.1)	233 (59.6)	77 (66.4)		
> High School	79 (15.6)	50 (12.8)	29 (25.0)		
Single/Never Married (%)	308 (60.8)	244 (62.4)	64 (55.2)	1.96	.16
Unemployed (%)	298 (58.8)	240 (61.4)	58 (50.0)	4.78	.03
Primary Substance (%)				11.12	.049
Alcohol	104 (20.5)	80 (20.5)	24 (20.7)		
Cocaine	102 (20.1)	83 (21.2)	19 (16.4)		
Stimulants	69 (13.6)	46 (11.8)	23 (19.8)		
Marijuana	114 (22.5)	82 (21.0)	32 (27.6)		
Opioids	108 (21.3)	91 (23.3)	17 (14.7)		
Other	10 (2.0)	9 (2.3)	1 (0.9)		
Negative Baseline Drug Use Status (%)	275 (54.2)	217 (55.5)	58 (50.0)	1.09	.30
Smoking medication (%)				4.90	.03
Baseline	16 (3.2)	16 (4.1)	0 (0.0)		
Week 12 (N=448)	13 (2.9)	12 (3.5)	1 (1.0)	1.81	.18
Smoking at week 12 (%)				299.8	<.001
(N=448)	336 (75.0)	325 (94.5)	11 (10.6)		
Treatment Assignment (%)				0.97	.32
TAU	252 (49.7)	199 (50.9)	53 (45.7)		
TES	255 (50.3)	192 (49.1)	63 (54.3)		
Baseline Abstinence Status and Treatment Assignment (%)				3.82	.28
Drug Negative + TES	136 (26.8)	108 (27.6)	28 (24.1)		
Drug Negative + TAU	139 (27.4)	109 (27.9)	30 (25.9)		
Drug Positive + TES	119 (23.5)	84 (21.5)	35 (30.2)		
Drug Positive + TAU	113 (22.3)	90 (23.0)	23 (19.8)		

**Table 2**

Changes in cigarettes per day and time to first cigarette from baseline to week 12 (end of treatment [EOT]) among baseline smokers (n=391) with an EOT observation (n=344). Categories were based on FTND responses during baseline and changes in categories were based on responses at week 12.

Cigarettes per Day				
Baseline Categories	N	% – Decreased	% – Same level	% – Increased
1–10	194	8.3	73.7	18.0
11–20	131	35.1	59.5	5.4
21–30	14	85.7	14.3	0.0
31+	5	40.0	60.0	0.0
Total	344	22.1	65.7	12.1
Time to First Cigarette				
Baseline Categories	N	% – More time	% – Same time	% – Less time
< 5 min	70	34.2	65.8	0.0
6–30 min	63	24.1	55.2	20.7
31–60 min	87	22.2	39.7	38.1
60+ min	123	18.6	60.0	21.4
Total	343	26.2	57.2	16.6