

# Short-Term Naturalistic Treatment Outcomes in Cigarette Smokers With Substance Abuse and/or Mental Illness

Risa B. Gershon Grand, M.D.; Sun Hwang, M.S.; Juliette Han, B.S.; Tony George, M.D.; and Arthur L. Brody, M.D.

**Objective:** The majority of cigarette smokers have a lifetime diagnosis of substance abuse and/or mental illness, and treatment outcomes for smokers with these comorbidities are generally reported to be worse than for smokers without comorbidities. We sought to examine the effect of specific substance abuse/mental illness diagnoses compared to one another on treatment outcomes.

Method: A retrospective chart review of naturalistic treatment for nicotine dependence was performed on male smokers (N = 231) who enrolled in the Greater Los Angeles Veterans Affairs Mental Health Clinic Smoking Cessation Program (Los Angeles, Calif.) over a 1.5-year period (January 2004 to June 2005). Subjects in this program, who were diagnosed with nicotine dependence on the basis of a DSM-IV-based interview and a Fagerström Test for Nicotine Dependence score of  $\geq 3$ , underwent comprehensive treatment for nicotine dependence (including, but not limited to, group psychotherapy, nicotine replacement therapy, and bupropion hydrochloride). Quitting smoking was defined as a report of at least 1 week of abstinence and an exhaled carbon monoxide less than or equal to 8 parts per million at the final clinic visit.

**Results:** Of the total group, 36.4% (84/231) quit smoking at the end of treatment. Quit rates were affected by the presence of specific diagnoses, with smokers with a history of alcohol abuse/dependence or schizophrenia/ schizoaffective disorder having poorer response rates than smokers without such diagnoses. Other substance abuse and mental illness diagnoses did not affect quit rates.

*Conclusion:* Lower quit rates among patients with alcohol abuse/dependence or schizophrenia/ schizoaffective disorder may be due to the severity of these conditions and suggest that specialized treatment is needed for these populations of smokers. Smokers with most comorbid diagnoses are successfully treated with standard treatment methods.

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Corresponding author and reprints: Arthur L. Brody, M.D., UCLA Department of Psychiatry and Biobehavioral Sciences, 300 UCLA Medical Plaza, Suite 2200, Los Angeles, CA 90095 (e-mail: abrody@ucla.edu).

**C** igarette smoking is common among people with a lifetime history of substance abuse/dependence and/or mental illness as assessed in both clinical<sup>1</sup> and population-based<sup>2,3</sup> samples. For substance abuse/ dependence, tobacco use rates are reported to be as high as 90% among active alcoholics,<sup>4</sup> 80% among cocaine abusers,<sup>5</sup> 92% among methamphetamine abusers,<sup>6</sup> and 82% to 94% among opiate addicts<sup>6-8</sup> (compared to the general U.S. population rate of tobacco use of 23%<sup>9</sup>). In addition, marijuana smokers are 5 times more likely than marijuana nonusers to smoke tobacco cigarettes.<sup>10</sup> Cigarette smoking contributes greatly to morbidity and mortality among patients with alcohol<sup>11</sup> and drug<sup>12</sup> dependencies, making it vital to understand better the complex relationship between alcohol/drug dependence, mental illness, and response to smoking cessation treatments.

In general, substance abusers are less likely than nonabusers to quit smoking with standardized treatment.<sup>13</sup> Specifically, both nicotine gum<sup>14</sup> and patch<sup>15</sup> have been found to be less effective in alcoholic than non-alcoholic

## **TAKE-HOME POINTS**

- Comprehensive treatment for nicotine dependence is effective in populations with considerable psychiatric and substance abuse comorbidity.
- In a population of smokers with much psychiatric and substance abuse comorbidity, the presence of either alcohol abuse/dependence or schizophrenia is associated with poorer smoking-cessation treatment outcomes (compared with smokers without a history of these conditions).

smokers, especially for long-term outcomes. Although worse outcomes for substance abusers are fairly consistently reported, there are 3 studies utilizing the nicotine patch for smoking cessation that demonstrate similar outcomes for patients with and without alcohol abuse/ dependence histories. Two studies showed similar outcomes for alcoholics in treatment compared to nonalcoholic controls,<sup>16,17</sup> while a high rate of smoking abstinence (51%) was achieved in alcohol-dependent smokers in sustained full remission with a specialized tailored patch treatment program.<sup>18</sup> Patients with opiatedependence histories have been reported to have been treated with nicotine patch in combination with cognitive behavioral therapy or contingency management<sup>19,20</sup> with moderate success. We are aware of no prior studies that specifically examined outcomes of smoking cessation treatment (including nicotine replacement therapy, bupropion hydrochloride [HCl], and group psychotherapy) among cocaine-, methamphetamine-, or marijuana-dependent cigarette smokers.

Cigarette smoking is also common among patients with mental illnesses other than substance abuse/ dependence. Prevalence rates for tobacco use in clinical samples approach 90% in schizophrenics,  $^{21-23}$  are 43% to 82% in bipolar patients,  $^{2,3,22,24,25}$  and are 45% to 60% in patients with posttraumatic stress disorder.  $^{2,26}$  Patients with a history of depression are at increased risk for nicotine dependence (about 50%),  $^{2,3,27}$  and it is reported that a history of regular smoking occurs more frequently among individuals who have experienced a major depressive episode at some time in their lives.<sup>28</sup>

Treatment courses for smokers with mental illness have proved challenging.<sup>29</sup> Patients with severe mental illnesses been shown to have low rates of smoking cessation in a large naturalistic study.<sup>30</sup> Schizophrenic smokers represent one subset of mentally ill smokers that have been particularly difficult to treat,<sup>31</sup> though treatment with bupropion HCl has been shown to improve smoking abstinence rates in schizophrenic smokers.<sup>32–34</sup> Patients with major depressive disorder have also shown lower success rates with treatment,<sup>35</sup> though bupropion HCl has been found to be efficacious in smokers with this illness as well.<sup>36</sup> Bupropion has been demonstrated to be more effective than placebo in treatment of veterans with both posttraumatic stress disorder and nicotine dependence.<sup>37</sup> We are aware of no studies that have examined efficacy of smoking cessation treatment among bipolar patients.

While standardized treatments (as described above) have been well studied in the substance-abusing population, less is known about treatment for nicotine dependence in a naturalistic setting, where first-line treatments (such as nicotine replacement therapy, bupropion HCl, and group psychotherapy) are used alone or in combination. While it is known that substance abuse and mental illness generally predict worse outcomes in treatment, a comparison of treatment outcomes between specific substance abuse and mental illness conditions has not yet been reported. Based on the scientific literature and knowledge of the individual conditions, we hypothesized that patients with more severe drug dependencies (e.g., polysubstance dependencies) and more pervasive mental illnesses (e.g., schizophrenia-spectrum disorders) would have more difficulty quitting smoking during naturalistic treatment than those without these conditions. Our aim in conducting this research was to understand better the specific substance abuse/dependence and mental illness diagnoses, and their interactions, that affect quit rates among cigarette smokers in a naturalistic setting.

#### **METHOD**

## Subjects, Treatment, and Data Collected

A retrospective chart review of naturalistic treatment for nicotine dependence was performed on a convenience sample of 231 male cigarette smokers who enrolled in the Greater Los Angeles Veterans Affairs Mental Health Clinic Smoking Cessation Program (Los Angeles, Calif.) over a 1.5-year period (January 2004 to June 2005). This smoking cessation program enrolls only smokers with current or a history of substance abuse/dependence and/or mental illness. Charts were reviewed in July 2005 by R.B.G., J.H., and A.L.B.

All patients in this chart review were diagnosed with nicotine dependence during their participation in the smoking cessation program, based on a semistructured interview using DSM-IV criteria<sup>38</sup> and a score of 3 or greater on the Fagerström Test for Nicotine Dependence (FTND).<sup>39,40</sup> All subjects were treated with practical group

counseling (45 minutes per week) based on the relapse prevention model<sup>41</sup> for a standard 6- to 12-week course, in combination with nicotine replacement therapy, bupropion HCl, or both (based on patient preference in consultation with a clinic physician [R.B.G. or A.L.B.]). In the practical group counseling, subjects received education about tobacco and the treatment of nicotine dependence, monitoring of exhaled carbon monoxide (CO) levels, practical advice on smoking cessation techniques, problem-solving exercises, social support, and co-mentoring. Medication treatments were individualized based on patient preference, and subjects received the nicotine patch alone, bupropion HCl alone, a combination of the nicotine patch and bupropion, or no pharmacologic treatment. Exhaled CO measurements were monitored on all patients on a weekly basis with the commonly used Bedfont EC-50 Microsmokerlyzer II device, as a rough measure of recent cigarette usage.

Subjects were considered to have quit smoking at the end of program participation, if they reported at least 1 week of smoking abstinence and had a final exhaled CO level of  $\leq 8$  parts per million. These criteria are similar or identical to other treatment studies of nicotine dependence.<sup>42,43</sup>

The following information was collected from the initial treatment visit and from a review of the patient's history prior to coming to treatment: age, gender, number of cigarettes smoked, number of years smoking, number of quit attempts, longest quit period, FTND<sup>39,40</sup> and Beck Depression Inventory<sup>44</sup> scores, previous mental illness and substance abuse/dependence diagnoses, length of substance abuse/dependence, length of substance abstinence, medications used at the onset of treatment, and comorbid medical conditions. Information collected from the treatment itself included number of clinic visits, medication received (nicotine replacement therapy [usually with the nicotine patch] vs. bupropion HCl vs. both vs. neither), exhaled CO levels throughout treatment, and number of cigarettes reported per day for the last week of treatment.

## **Statistical Analysis**

To explore the central question of this study (namely, which mental illness or substance abuse/dependence diagnoses predict treatment outcome in a naturalistic setting), we performed logistic regression (SPSS version 13.0; Chicago, Ill.) using the fewest possible variables based on what is known about prediction of treatment response in smokers. Quit status at the end of treatment was the dependent variable. Independent variables were 4 mental illness diagnoses (major depressive disorder, bipolar disorder, posttraumatic stress disorder, and schizophrenia/schizoaffective disorder) and 5 substance abuse/dependence diagnoses (alcohol, marijuana, cocaine, methamphetamine, and opiates). Age and number

of cigarettes smoked per day were used as confounding independent variables in all logistic regression models because these variables are known to affect treatment outcome.<sup>45</sup> Diagnoses that were seen in fewer than 5% of the subjects (e.g., panic disorder, generalized anxiety disorder, and hallucinogen abuse) were excluded from the analysis. The bipolar disorder group included patients diagnosed with either bipolar I or II disorder. Demographic and treatment variables are presented as mean ± SD. We first evaluated each predictor in a separate logistic regression analysis, controlling for age and cigarettes smoked per day. Then, we evaluated all the diagnostic variables in a single multiple logistic regression model. We report the significance tests from both the separate and multiple models and odds ratios. In all cases, the  $\chi^2$  tests are for the increment over and above the covariates. The Hosmer-Lemeshow test was used for global goodness-of-fit testing.

#### RESULTS

The 231 subjects were middle-aged  $(49.1 \pm 8.3 \text{ years})$ old), smoked moderately at the time of treatment initiation  $(17.6 \pm 9.9 \text{ cigarettes per day})$ , and had lengthy smoking histories  $(30.9 \pm 9.9 \text{ years})$ , few quit attempts  $(2.4 \pm 2.6)$ , moderately long prior periods of smoking abstinence  $(1.7 \pm 3.6 \text{ years})$ , moderate nicotine dependence (FTND scores  $5.1 \pm 2.2$ ), and mild depressive symptoms (Beck Depression Inventory scores  $5.1 \pm 3.8$ ). For the substance abuse diagnoses studied here, more than half of the subjects had been diagnosed with alcohol abuse/dependence (N = 184, 80%) or cocaine abuse/dependence (N = 133,58%), while fewer were diagnosed with marijuana (N =78, 34%), methamphetamine (N = 50, 22%), and opiate abuse/dependence (N = 47, 20%). For the mental illness diagnoses, more than half of the sample had been diagnosed with major depressive disorder (N = 131, 57%), while smaller numbers were diagnosed with bipolar disorder (N = 28, 12%), posttraumatic stress disorder (N = 50, 22%), and schizophrenia/schizoaffective disorder (N = 39, 17%). The most common patterns of co-occurring mental illness and addiction were alcohol abuse/ dependence, cocaine abuse/dependence, and major depressive disorder (N = 17, 7.4%); alcohol abuse/dependence, cocaine abuse/dependence, marijuana abuse/dependence, and major depressive disorder (N = 13, 5.6%); and alcohol abuse/dependence and cocaine abuse/dependence (N = 11, 4.8%).

Eighty-four (36.4%) of 231 participants met criteria for having quit smoking at the end of treatment. Table 1 summarizes the separate logistic regression analyses, and Table 2 summarizes the multiple regression analysis. The overall multiple regression model yielded a likelihood ratio  $\chi^2 = 16.83$ , df = 9, p = .05 for the increment of the 9 predictors over and above the 2 covariates. Two of the substance abuse diagnoses were significant in the multiple

Table 1.	Separate	Logistic	Regression	Analyses	for Each	) Diagnosis <sup>a</sup>
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	В	SE	$\chi^2$	р	Odds Ratio	95% CI for OR	
Diagnosis						Lower	Upper
Depression	0.04	0.28	0.02	.90	1.04	0.60	1.79
Posttraumatic stress disorder	0.16	0.34	0.23	.63	1.18	0.61	2.28
Bipolar disorder	-0.11	0.42	0.07	.79	0.89	0.39	2.03
Schizophrenia/schizoaffective disorder	1.04	0.44	5.74	.02	2.84	1.21	6.66
Substance abuse/dependence							
Alcohol	0.63	0.33	3.60	.06	1.88	0.98	3.62
Marijuana	-0.42	0.29	2.05	.15	0.66	0.37	1.17
Cocaine	-0.02	0.28	0.01	.94	0.98	0.56	1.70
Methamphetamine	0.26	0.35	0.54	.46	1.29	0.66	2.55
Opiates	0.12	0.35	0.12	.72	1.13	0.57	2.22
<sup>a</sup> All degrees of freedom for Wold $x^2$ test s	ra 1						

Table 2	Multiple	Logistic	Regression	Including All	Diagnoses <sup>a</sup>

						95% CI for OR	
Diagnosis	В	SE	$\chi^2$	р	Odds Ratio	Lower	Upper
Depression	0.34	0.31	1.22	.27	1.41	0.77	2.60
Posttraumatic stress disorder	0.26	0.36	0.53	.47	1.30	0.65	2.61
Bipolar disorder	0.02	0.45	0.002	.97	1.02	0.42	2.46
Schizophrenia/schizoaffective disorder	1.33	0.49	7.40	.01	3.80	1.45	9.92
Substance abuse/dependence							
Alcohol	0.72	0.36	4.03	.05	2.06	1.02	4.16
Marijuana	-0.67	0.33	4.07	.04	0.51	0.27	0.98
Cocaine	0.14	0.32	0.20	.65	1.15	0.62	2.14
Methamphetamine	0.43	0.37	1.33	.25	1.53	0.74	3.15
Opiates	0.14	0.37	0.15	.70	1.16	0.56	2.38
<sup>a</sup> All degrees of freedom for Wald $\gamma^2$ test a	re 1. p Valu	e for Hosm	er-Lemesh	ow good	ness-of-fit test is .	.37.	

regression analysis: alcohol abuse/dependence (Wald  $\chi^2 = 4.03$ , df = 1, p = .05, OR = 2.06) (associated with a worse quit rate) and marijuana abuse/dependence (associated with a better quit rate) (Wald  $\chi^2 = 4.07$ , df = 1, p = .04, OR = 0.51) (Figure 1). The diagnoses of schizophrenia/schizoaffective disorder were significant in both the separate logistic regression ( $\chi^2 = 5.74$ , p = .02, OR = 2.84) and multiple logistic regression models ( $\chi^2 = 7.40$ , p = .01, OR = 3.80, both df = 1) (Figure 2). Individuals in this diagnostic category were less likely to quit successfully. The Hosmer-Lemeshow goodness-of-fit test indicated that the model prediction did not significantly differ from the observed values (p = .37). The total number of substance abuse/dependence diagnoses did not have a linear relationship with the chance of quitting smoking  $(\chi^2 = 0.32, df = 1, p = .57)$ , indicating that specific diagnoses, rather than more diagnoses, were associated with treatment responsiveness.

The pharmacologic treatment used in the study varied with patient preference. The majority of the subjects were treated with the nicotine patch alone (N = 140), while many used bupropion HCl alone (N = 53) and fewer used the combination of nicotine patch plus bupropion HCl (N = 30). Treatment with both nicotine patch and bupropion HCl together resulted in a quit rate of 33%, which was not higher than the quit rates of subjects treated with monotherapy.

## DISCUSSION

Results of this retrospective chart review demonstrate that the overall smoking cessation rates for patients with mental illness and/or substance abuse/dependence treated in a naturalistic setting are similar to those in published reports of controlled treatment in more general populations of smokers.<sup>15,20,46,47</sup> For specific diagnoses associated with treatment responsiveness, our data demonstrate that the absence of an alcohol dependence history predicts better response to treatment, while the presence of schizophrenia/schizoaffective disorder predicts poorer outcome to treatment. The presence of marijuana abuse also predicts better response to treatment.

A history of alcohol dependence might lead to lower quit rates than the absence of this history for several reasons. There is considerable evidence that chronic alcohol use leads to structural, physiologic, and functional brain changes,<sup>48–50</sup> along with neuropsychological impairment.<sup>51</sup> Chronic alcohol use leads to atrophy of the frontal lobes,<sup>48</sup> hypofrontal brain metabolism,<sup>52</sup> and electrophysiologic abnormalities.<sup>53</sup> Such frontal lobe damage is associated with impulsivity, impaired planning, poor problem solving, and impaired insight and judgment.<sup>54</sup> This type of brain damage (even in a subtle form) could account for the lower quit rates in smokers with a history of alcohol dependence, since behavioral modification (part of the treat-





Figure 2. Percentage of Subjects With or Without Specific Mental Illnesses Who Had Quit Smoking at the End of Acute Treatment



Abbreviation: PTSD = posttraumatic stress disorder.

ment program here) might be more challenging in an impulsive subject with impaired coping and planning skills.

Cognitive deficits associated with alcohol dependence are well documented. It has been shown that between one half and two thirds of newly abstinent alcoholics exhibit cognitive impairment in the first few months of sobriety.<sup>51</sup> These deficits may persist for years or indefinitely after detoxification in some patients and include impairment in new learning, executive functioning, visual spatial abilities, and perceptual-motor integration.55 Specifically, verbal learning<sup>56,57</sup> and retention,<sup>58</sup> as well as abstract reasoning,<sup>58–61</sup> have been shown to be impaired in patients with a history of alcoholism. These specific deficits may lead to suboptimal participation in treatment, where verbally acquired directions for treatment and abstract reasoning are important for such components of treatment as medication instructions, suggestions for behavioral modification from group therapy, training in coping with stress, and the identification of triggers.

Our data also support prior work<sup>31</sup> that points to schizophrenia and schizoaffective disorders as illnesses that are particularly resistant to smoking cessation treatment. A central feature of these illnesses may be negative symptoms, such as avolition, alogia, and blunted affect.<sup>38</sup> Also, similar to alcohol abuse/dependence, structural, physiologic, and functional deficits are seen in the schizophrenic brain, such as lower frontal lobe volumes<sup>62</sup> and frontal electrophysiologic abnormalities.<sup>63</sup> As noted above, structural and functional impairments of the frontal lobes are associated with impulsivity, poor planning, and limited problem solving. Additionally, schizophrenic subjects have been identified as having moderately impaired executive functioning and more severely impaired verbal learning and memory when compared with controls.<sup>64</sup> Consistent with the functional consequences for such cognitive dysfunction, one study demonstrated that the presence of prefrontal executive function deficits in spatial working memory and Wisconsin Card Sorting Test performance, prior to a quit attempt, was associated with smoking cessation treatment failure in smokers with schizophrenia, but not controls.65 They also have low Global Assessment of Functioning scores,<sup>66</sup> a measure that includes social functioning, and a higher level of social support has been shown to be a positive predictor for smoking cessation.<sup>67</sup> Taken together, these features (negative symptoms, frontal lobe dysfunction, and low global functioning scores) all point to potential mediating factors in the poor response people with schizophrenia/schizoaffective disorder show to comprehensive treatment.

In this study, a history of marijuana abuse/dependence was associated with slightly higher tobacco abstinence rates when compared to other substance abuse and mental illness diagnoses. Many of the subjects were currently in treatment or had a history of treatment for substance abuse/dependence. Having a history of successful abstinence from a drug of abuse that was experienced through smoking (rather than intravenous or intranasal use) may have conferred a slight advantage in this group of tobacco users. Since they had been able to discontinue smoking marijuana in the past, perhaps this led to successful discontinuance of tobacco use due to higher confidence in their own abilities to overcome a similar habit.

One limitation of this study stems from the sample of male veteran subjects. It is known that the rates of substance abuse<sup>68,69</sup> and affective disorders<sup>68</sup> are higher in the veteran population when compared with similar genderand age-matched patients in the private sector. Furthermore, male veterans with severe mental illnesses, such as schizophrenia, tend to be older and to have had more inpatient hospitalizations,<sup>70</sup> which suggests that the sample used in this study may have been older and more ill than patients who might be found in other types of health care systems. A second limitation of the study is that long-term follow-up data (6 months to 1 year) were not available. A

third limitation of the study is its retrospective design. The retrospective set-up of the study was the most reasonable and practical design for a naturalistic investigation of the data. While we are aware that such study designs may introduce incomplete study groups and interpretive bias during the chart review, we attempted to minimize these limitations by remaining cognizant of them.<sup>71,72</sup> Another limitation of this study is the same as that of most naturalistic treatment studies, namely that subjects were not randomly assigned to treatments and clinicians were not blinded to the treatments administered. This lack of random assignment may have led to subjects being assigned to particular treatments that may have altered their possibility of quitting (e.g., it is probable that patients with bipolar disorder were less likely to receive bupropion HCl because mania is a potential side effect of this antidepressant). However, our data reflect treatment in a naturalistic setting, which may prove informative for real-life treatment scenarios.

In summary, this study identified several predictors of the success of smoking cessation in this naturalistic setting. While prior initial work has been done to tailor treatments to schizophrenic smokers,<sup>73</sup> our data indicate that further research is needed to optimize treatments for smokers with psychotic illnesses and/or alcohol dependence. Both schizophrenic and alcohol-dependent smokers may be better served with modified treatments<sup>15</sup> that are specialized to take into account the needs of these specific populations.

*Drug names:* bupropion (Zyban and others), clonidine (Catapres and others).

*Disclosure of off-label usage:* The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside U.S. Food and Drug Administration–approved labeling has been presented in this article.

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