Smoking Characteristics of Veterans With Bipolar Disorder

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This study of smoking behaviors and smoking characteristics in veterans with bipolar disorder contributes useful data to continue research into smoking and its associated risk factors, such as homelessness, lower education, and cardiovascular disease.

In 2006, the prevalence of bipolar disorder among veterans who use VHA facilities and clinics was estimated at 4.4% of the treatment-seeking population.[1] This percentage compares with the estimated 1% to 5% of bipolar disorder prevalence in the general population.[2] Military service has been found to increase cigarette smoking over a lifespan, and there are estimates that more than 50% of veterans returning from Iraq and Afghanistan will return as smokers.[3-5] Furthermore, veterans with bipolar disorder who seek treatment from the VA may have greater rates of additional smoking-associated risk factors (eg, homelessness and lower education). People with bipolar disorder, particularly those with bipolar depression, have higher rates of cardiovascular disease, and smoking is a modifiable risk factor.[6,7]

The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) was a multicenter study funded by the National Institute of Mental Health and designed to evaluate the longitudinal outcome of patients with bipolar disorder. The overall study combined a large prospective naturalistic study and a series of randomized controlled trials.[8] Waxmonsky and colleagues performed comparisons between current smokers and nonsmokers on a wide array of variables available in the first 2,000 participants in STEP-BD and found several variables were associated in a univariate manner with current smoking, but they did not go on to develop logistic regression models.[9]

The goal of this study was to develop logistic regression models to predict current smoking and to differentiate current smokers from former smokers in a sample of veterans with bipolar disorder. For the variables found significant at the $P \leq .05$ level by Waxmonsky and colleagues, the study authors performed the same univariate comparisons between current smokers and current nonsmokers (never and former smokers) on the 121 U.S. veterans enrolled in the STEP-BD clinical trial at the Portland VAMC (PVAMC).[9] This study then extended the work of that paper (referred to as STEP 2,000) by developing logistic regression models using these candidate variables in a smaller sample of veterans with bipolar disorder. Finally, these analyses were repeated with the subset of former smokers, to determine which variables were predictive of continued smoking in this sample.

The study authors predicted that only a subset of risk factors found in STEP 2,000 would be associated with increased rates of smoking in the subsequent study, because STEP 2,000 had a large sample size, which increased the ability to detect significant univariate comparisons. The authors also predicted that some subsets of these risk factors would be significant predictors of current smoking in their logistic regression model. In particular, it was expected that variables such as current caffeine use, current substance abuse or dependence, lower income, lower education, and a history of suicide attempt would be associated with current smoking, as these variables are commonly associated with smoking.[10,11] Also predicted was a greater

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Table 1. Demographic data: Current smokers vs current nonsmokers in each sample

	VA (N = 121)		STEP (N = 1,904[a])			
	All	VA current smokers	All	STEP 2,000 current smokers	VA *P*[b]	STEP *P*[b]
Totals (%)	121	51/121 (42.1)	1,904	594/1,904 (31.2)		
Bipolar subtype						
Bipolar I disorder (%)[c]	85 (70.2)	37 (43.5)	1,337 (70.3)	444 (33.2)		
Bipolar II disorder (%)	34 (28.1)	13 (38.2)	443 (23.3)	117 (26.4)	= .597	= .2652
Bipolar NOS (%)	2 (1.7)	1 (50)	123 (6.4)	33 (26.6)	= .856	= .4721
Employment						
Part-time or unemployed	102 (84.3)	44 (43.1)	1,166 (66.3)	378 (32.4)	= .611	= .0343
Full-time	19 (15.7)	7 (36.8)	593 (33.7)	163 (27.5)		
Gender						
Female (%)	21 (17.4)	10 (47.6)	1,045 (58.1)	297 (28.4)	= .577	= .0063
Male (%)	100 (82.6)	41 (41.1)	753 (41.9)	259 (34.4)		
Race[d]						
Nonwhite (%)	7 (5.8)	3 (42.9)	131 (7.3)	35 (26.7)	= .984	= .2761
White (%)	113 (94.2)	48 (42.5)	1,668 (92.7)	522 (31.3)		

[a] Data were not available for all 1,904 subjects on all variables. See Waxmonsky (2005) for exact numbers.[9]
[b] Wald chi-square *P* value to test for association between specified variable and smoking in each sample.
[c] Reference category.
[d] Race data were not available for 1 subject in the VA sample (N = 120).
NOS = not otherwise specified; STEP = Systematic Treatment Enhancement Program for Bipolar Disorder.

smoking prevalence in this sample than that in the STEP 2,000 sample, due to the increased prevalence of smoking among veterans.

MATERIALS AND METHODS

Study participants were enrolled in STEP-BD at the PVAMC. STEP-BD required the participants be aged ≥ 15 years and meet the *Diagnostic and Statistical Manual of Mental Disorders* IV (DSM-IV) criteria for bipolar illness (bipolar I, bipolar II, cyclothymia, bipolar not otherwise specific [NOS], or schizoaffective manic or bipolar subtypes). A battery of clinical assessment tools were administered at study entry in order to determine clinical status, severity of illness, number of affective episodes, and presence of psychosis. The Clinical Monitoring Form (CMF) was the primary ongoing source of clinical status information.[12] All instruments were administered by trained raters.[8] Exclusion criteria were limited to the unwillingness or inability to comply with study assessments or inability to give informed consent.

At the PVAMC, 140 individuals met lifetime criteria of bipolar I, bipolar II, and bipolar NOS (including cyclothymia) and completed baseline diagnostic assessments indicating smoking status. As in the STEP 2,000 study, schizoaffective patients (N = 8; 2 of which were also nonveterans) were excluded from the sample as well as nonveterans (N = 13) for a total of 19 subjects excluded, leaving 121 patients in the sample of interest. The Institutional Review Board of the PVAMC gave its approval to conduct the STEP-BD study and to analyze the data presented in this article.

The authors examined the data on the 121 eligible patients enrolled in the STEP-BD clinical trial at the PVAMC and made comparisons to the first 2,000 participants in STEP-BD. Patients were classified as current smokers, former smokers, or never-smokers, using data collected from the initial clinical assessment

and the initial CMF. Consistent with the previous smoking study on this data set, patients were classified as current smokers at the start of the study if they smoked any number of cigarettes (recorded as packs per day) on entry into the STEP program for the 2 months prior to study entry. If participants had met the definition of current smokers at some time in their life but were not smoking at study entry, they were classified as former smokers; otherwise, they were considered never-smokers.

The STEP 2,000 sample examined current smokers vs current nonsmokers (former and never-smokers) in univariate comparisons and found the following 16 variables significant at the $P \leq .05$ level: gender, education, employment, history of suicide attempt, age at study entry, age at psychiatric illness onset, Affective Disorder Evaluation (ADE) depression score sum, ADE elevated mood sum, Montgomery-Asberg Depression Rating Scale (MADRS) total score, Global Assessment of Function (GAF) score, current caffeine use, current alcohol use, current illicit drug use, current anxiety disorder, past anxiety disorder, and atypical antipsychotic currently prescribed. Differences between current smokers and current nonsmokers for each of these variables were assessed using univariate statistical tests. In addition, the following 8 variables were found significant in the STEP 2,000 sample, but meaningful univariate tests in the manner of STEP 2,000 could not be made in the present study, because cell sizes were too small due in part to the number of categories used for the variables: clinical status, number of lifetime depression phases, number of lifetime manic phases, rapid cycling within the past year, current psychotic symptoms, current attention deficit-hyperactivity disorder (ADHD), past ADHD, and yearly income. Logistic regression techniques were used to develop models to predict current smoking as opposed to current nonsmoking.[13] These analyses were repeated with the subset of former and current smokers, to determine which variables were predictive of continued smoking in this sample. To narrow the number of variables out of the hundreds available in the STEP-BD data set, only the variables found significant in the STEP 2,000 sample were considered as candidate variables.

Although not considered for inclusion in the regression modeling, the authors also looked at current and past alcohol and drug dependence, rapid cycling, and history of a suicide attempt and examined whether these variables were independently related to current smoking.

Table 2. Variables found predictive of current smoking in STEP 2,000

Variable	STEP 2,000 current smokers *P*	VA current smokers *P*	VA former smokers *P*
ADE depression score sum	< .001	= .364	= .702
ADE elevated mood score sum	= .001	= .136	= .543
Age at study entry	< .001	= .104	= .111
Age of psychiatric illness onset	< .001	= .285	= .486
Alcohol use, current	= .012	= .149	= .259
Anxiety disorder, current	< .001	= .686	= .719
Anxiety disorder, past	= .031	= .944	= .872
Atypical antipsychotic prescribed	= .038	= .975	= .978
Caffeine use, current (cups per day)	< .001	= .005	= .010
Education	< .001	= .006	= .013
Employment	= .034	= .611	= .489
GAF	< .001	= .271	= .387
Gender	= .006	= .577	= .946
History of suicide attempts	< .001	= .030	= .022
Illicit drug use, current	< .001	= .084	= .065
MADRS total score	= .001	= .169	= .369

ADE = Affective Disorder Evaluation; GAF = Global Assessment of Functioning scale; MADRS = Montgomery-Asberg Depression Rating Scale; STEP = Systematic Treatment Enhancement Program for Bipolar Disorder.

RESULTS

There were a total of 121 persons

Table 3. Univariate logistic regression results for the candidate variables to predict current smoking

Variable[a]	Current smokers	Current nonsmokers	Odds ratio	95% CI (range)	Wald χ^2	*df*	*P*
ADE elevated mood score sum (%)	0.907 (1.317)	0.600 (0.894)	1.293	0.922-1.813	2.224	1	= .136
Age at STEP entry (%)[b]	47.060 (11.5)	50.700 (12.4)	0.975	0.945-1.005	2.651	1	= .104
Cups of caffeine per day (%)	4.410 (4.30)	2.500 (2.37)	1.199	1.057-1.361	7.897	1	= .005
Current alcohol use							
Current alcohol use (%)	16	14	1.849	0.802-4.261	2.080	1	= .149
No current alcohol use[c]	34	55					
Current illicit drug use							
Current illicit drug use (%)	11	7	2.475	0.886-6.913	2.990	1	= .084
No current illicit drug use[c]	40	63					
Education					10.237	2	= .006
High school or less	18	10	6.429	2.056-20.104	10.231	1	= .001
Some college/ technical/associate degree	26	35	2.653	0.996-7.067	3.810	1	= .051
College graduate/ professional[c]	7	25					
History of suicide attempts							
History of suicide attempts	31	28	2.270	1.083-4.755	4.719	1	= .030
No history of suicide attempts[c]	20	41					
MADRS total score (%)	15.4 (10.0)	13.100 (8.5)	1.028	0.988-1.070	1.889	1	= .169

[a] Continuous variable presented as mean +/- standard deviation, categorical as N (%).
[b] Data were not available for 5 subjects (N = 116).
[c] Reference category.
ADE = Affective Disorder Evaluation; CI = confidence interval; *df* = degrees of freedom; MADRS = Montgomery-Asberg Depression Rating Scale; STEP = Systematic Treatment Enhancement Program for Bipolar Disorder.

with bipolar disorder enrolled in STEP-BD at PVAMC (19 patients with schizoaffective disorder or who were nonveterans were excluded), and data on tobacco use was available for all participants. The mean age at study entry was 49.2 years (standard deviation = 12.1). Fifty-one participants (42.1%) reported that they were current smokers; 42 participants (34%) reported that they were former smokers; and 28 participants (23.1%) reported that they had never smoked (never-smokers). The lifetime prevalence of smoking (current and former smokers) was 76.9% (N = 93) (Table 1 shows comparisons of the VA current smokers and STEP 2,000 current smokers). Of the 51 current smokers in the study,

Table 4. Final logistic regression model for prediction of current smoking[a]

Variable	B	SE	Wald	*df*	*P*	Odds ratio	95% CI (range)
Cups of caffeine per day	0.203	0.07	8.321	1	= .004	1.225	1.067-1.406
Education			10.303	2	= .006		
High school or less	1.936	0.603	10.302	1	= .001	6.931	2.125-22.608
Some college/technical/associate degree	1.038	0.52	3.987	1	= .046	2.823	1.019-7.82
College graduate/professional[b]							
Constant	-1.966	0.505	15.129	1	= .001	0.14	

[a] Model $\chi^2(3) = 21.192$, $P < .001$; $R^2_{\text{Cox \& Snell}} = 0.164$, $R^2_{\text{Nagelkerke}} = 0.221$.
[b] Reference category.
CI = confidence interval; *df* = degrees of freedom; SE = standard error.

37.3% (n = 19) had current alcohol abuse or dependence, 19.6% (n = 10) had current drug abuse or dependence, and 60.8% (n = 31) had a history of a suicide attempt. Only 4% (n = 2) of the 50 current smokers with data exhibited rapid cycling. The VA sample had a significantly higher proportion of current smokers, a higher proportion of men, and a lower proportion of subjects in full-time employment than did those of the STEP-BD sample.

Current smokers. Of the 121 veterans, 100 (82.6%) were men (Table 1). Men were no more likely to be smokers than were women ($P = .577$).

Univariate analyses were run on the 16 variables identified as predictive of smoking in the STEP 2,000 data if cell sizes permitted (Table 2). Using $P \leq .25$ as a cutoff point for STEP 2,000 variables that could be considered for the logistic regression model, candidate variables for the model were determined to predict current smoking. Being a current smoker was significantly associated with lower education ($P = .006$), drinking more caffeine ($P = .005$), and having a history of a suicide attempt ($P = .030$). In addition, greater age at study entry, increased ADE elevated mood scores, increased MADRS total scores, current alcohol use, and current illicit drug use were predictive of current smoking at the $P \leq .25$ significance level and were considered as candidate variables (Table 3 shows the statistics of these 8 candidate variables).

The study goal was to develop the best predictive model possible, while keeping the model statistically significant. Model development proceeded by first forcing all these 8 variables into a forced model. From the forced model, 2 variables were able to be identified that were significant predictors of current smoking in the predictive model: cups of caffeine per day and level of education. The same model was obtained using a forward selection procedure (Table 4 shows the final logistic regression model, including these variables [$P < .001$]).

Additional analyses indicated that current smokers were more likely than current nonsmokers to have a history of alcohol dependence (smokers: 62.7%; nonsmokers: 40.0%, $\chi^2(1) = 6.106$, $P = .013$), be currently alcohol dependent (smokers: 17.6%; nonsmokers: 4.3%, $\chi^2(1) = 5.896$, $P = .015$), and have a history of drug dependence (smokers: 41.2%; nonsmokers: 18.6%, $\chi^2(1) = 7.462$, $P = .006$). Current drug dependence was not related to current smoking; however, few subjects were currently drug dependent (smokers: 5.9%; nonsmokers: 4.3%, $P > .05$).

Rates of rapid cycling were low and did not differ between current smokers and nonsmokers (smokers: 4.0%; nonsmokers: 10.6%, $\chi^2(1) = 1.734$, $P > .05$). However, history of suicide attempts was a significant predictor of current smoking (smokers: 60.8%; nonsmokers: 40.6%, $\chi^2(1) = 4.790$, $P = .029$). Finally, use of bupropion, a nonbupropion antidepressant, or any antidepressant was not associated with current smoking ($P > .05$).

Former smokers. Within the subset of 93 ever smokers, 42 were former smokers and 51 were current smokers. Demographic data for the 42 former smokers are presented in Table 5. Univariate analyses comparing former smokers and current smokers on the variables found significant in the STEP 2,000 sample are presented in Table 2. As before, using $P \leq .25$ as a cutoff point for variables to be considered in a logistic regression model, 5 candidate variables were identi-

Table 5. Demographic data: Current smokers vs former smokers

	VA (N = 93 ever smokers)		
	Current smokers	Former smokers	VA *P*[a]
Totals	51	42	
Bipolar subtype			
Bipolar I disorder	37	32	
Bipolar II disorder[b]	13	9	
Bipolar NOS[b]	1	1	
Employment			
Part-time or unemployed	44	34	= .489
Full-time	7	8	
Gender			
Female	10	8	= .946
Male	41	34	
Race			
Nonwhite (%)[b]	3	4	
White (%)	48	38	

[a] Wald chi-square *P* value to test for association between specified variable and smoking in each sample.
[b] Cell size too small to calculate.
NOS = not otherwise specified.

fied that were predictive of continued smoking: lower education (P = .006), history of a suicide attempts (P = .022), increased age (P = .111), current caffeine use (P = .010), and current illicit drug use (P = .065). Table 6 illustrates the details of the univariate analysis for each of these variables. Using the same variable selection methods described earlier, a model was obtained that included the number of cups of caffeine per day and level of education. Specifically, lower education and greater caffeine intake were associated with continued smoking (Model $\chi^2(3) = 19.749$, P = .001; $R^2_{\text{Cox \& Snell}} = 0.191$, $R^2_{\text{Nagelkerke}} = 0.256$).

Additional analyses indicated that current and past alcohol dependence were not related to continued smoking ($P > .05$), and whereas current rates of drug dependence were low in both groups and not related to continued smoking, past drug dependence was related to continued smoking (current smokers: 41.2%; former smokers: 21.4%, $\chi^2(1) = 4.110$, $P < .043$).

Similar to the earlier analysis comparing current smokers with current nonsmokers, rapid cycling was not related to continued smoking (current smokers: 4.0%; former smokers: 10.3%, $P > .05$). However, history of a suicide attempt was a significant predictor of continued smoking (current smokers: 60.8%; former smokers: 36.6%, $\chi^2(1) = 5.324$, P = .021). Finally, former smokers were more likely than continuing smokers to be on an antidepressant (either bupropion or nonbupropion) (current smokers: 41.2%; former smokers: 61.9%, $\chi^2(1) = 3.959$, $P < .047$).

DISCUSSION

A significantly higher proportion of the STEP-BD subjects enrolled through the PVAMC reported they were current smokers compared with those enrolled in the STEP 2,000 sample, indicating that veterans with bipolar disorder smoke at a higher rate than do nonveterans with bipolar disorder. This result was consistent with previous studies.[2] This study sample also included fewer women and those with less employment, likely reflective of the VA sample at large. Many factors that were found to be significant univariate predictors of current smoking in the STEP 2,000 sample were not found to be significant in this analysis. This is likely due in part to lower power because of the smaller sample size in the data set compared with the STEP 2,000 sample.

Level of education and cups of caffeine per day were significantly associated with current and continued smoking in the study logistic regression models. Increased caffeine use is significantly associated with increased odds of current smoking, which suggests that veterans should be encouraged to reduce or eliminate their use of caffeine as part of a successful smoking cessation intervention. This is consistent with the literature showing that quitting alcohol use at the same time as quitting smoking increases smoking abstinence and suggests that there may be a role for further research into how reduction in caffeine use may aid in smoking cessation.[5,14] This population is more likely to have multiple poor heath behaviors that need in-

Table 6. Univariate logistic regression results for the candidate variables to predict current smoking vs former smoking

Variable[a]	Current smokers	Former smokers	Odds ratio	95% CI (range)	Wald χ^2	*df*	*P*
Age at STEP entry (%)	47.06 (11.5)	51.24 (13.35)	0.973	0.940-1.006	2.540	1	= .111
Cups of caffeine per day (%)	4.41 (4.30)	2.30 (2.12)	1.241	1.054-1.461	6.714	1	= .010
Current illicit drug use							
Current illicit drug use	11	3	3.575	0.926-13.799	3.418	1	= .065
No current illicit drug use[b]	40	39					
Education					8.047	2	= .018
High school or less	18	6	6.429	1.773-23.303	8.020	1	= .005
Some college/technical/ associate degree	26	21	2.653	0.914-7.701	3.810	1	= .073
College graduate/ professional[b]	7	15					
History of suicide attempts							
History of suicide attempts	31	15	2.687	1.150-6.276	5.212	1	= .022
No history of suicide attempts[b]	20	26					

[a] Continuous variable presented as mean +/- SD, categorical as N.
[b] Reference category.
CI = confidence interval; *df* = degrees of freedom; SD = standard deviation; STEP = Systematic Treatment Enhancement Program for Bipolar Disorder.

tervention, and tailored programs to address caffeine use in this population would be beneficial. Success at an activity such as stopping or reducing caffeine use can build self-efficacy that may be useful when trying to stop a more addictive substance like tobacco.[15-17]

This study supports the already known association between low educational status and smoking. The study data also indicate that higher education is associated with smoking cessation among ever smokers (Table 6). This suggests that interventions for smoking cessation should be intensified for those with lower education, and educational level should be taken into account when counseling about smoking.[18,19]

In addition to the variables found to be significant in the STEP 2,000 paper, this study examined several other variables of potential interest. Of the current smokers, 32.0% used alcohol compared with 34.4% in the STEP 2,000 sample, and 21.6% used other illicit substances, compared with 54.0% in STEP 2,000.[9] The much lower rates of illicit substance use in this study sample likely reflect that this is an older group, and many of them are likely in recovery. Although STEP 2,000 did not examine the rates of current dependence, these data also showed significantly higher rates past drug dependence in current smokers and in continued smokers. This study also concluded that current and past alcohol were associated with current smoking ($P < .05$), suggesting that these may be risk factors for smoking in this population.

Rates of a history of suicide attempts were significantly higher in the study sample of current smokers than in current nonsmokers and among the subset of ever smokers that continue to smoke than in those who had quit smoking. Smoking has previously been shown to be associated with suicide, and this reconfirms that finding.[20] This also suggests that it may be particularly important to council returning veterans on smoking cessation as a means of decreasing their risk of suicide.

STRENGTHS AND LIMITATIONS

The strengths of this study included using data collected by a large Na-

tional Institute of Mental Health-funded naturalistic study of bipolar disorder, which used trained raters with rigorous techniques for data collection, entry, cleaning, and storage.[8] Limitations of the study included a small sample size and that the particular sample is mostly Vietnam-era veterans. Also, the models generated may not be generalizable to the veterans of more recent eras. There is a need for further study of more recent era veterans, particularly as smoking becomes less acceptable in the military and in the culture at large.

CONCLUSION

This study expanded on the STEP 2,000 study by using candidate variables derived from that study to characterize risk factors for current smoking in veterans with bipolar disorder. The authors believe that this study is the only one that looks at U.S. veterans that were enrolled in the STEP-BD study and that uses the results of the previous study (STEP 2,000). Using STEP 2,000 in this way guided data analyses and allowed the authors to suggest similarities and differences between the veteran population and general population, which might be useful in future treatment and future studies. The results suggested that reducing caffeine drinking may improve smoking cessation outcomes and replicates the association between level of education and smoking that has been seen in previous literature. Future research should look at the effect of antidepressants and other psychotropic medications on smoking and smoking cessation and whether specific health interventions that target reducing caffeine lead to better outcomes with eventual smoking cessation.

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