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Psychiatric Disorders in Smokers Seeking Treatment for Tobacco Dependence: Relations With Tobacco Dependence and Cessation

Megan E. Piper, Stevens S. Smith, Tanya R. Schlam, and Michael F. Fleming
University of Wisconsin School of Medicine and Public Health

Amy A. Bittrich
Division of Public Health, Milwaukee, Wisconsin

Jennifer L. Brown
Medical College of Wisconsin

Cathlyn J. Leitzke
University of Wisconsin School of Medicine and Public Health

Mark E. Zehner
University of Wisconsin College of Engineering

Michael C. Fiore and Timothy B. Baker
University of Wisconsin School of Medicine and Public Health

Objective: The present research examined the relation of psychiatric disorders to tobacco dependence and cessation outcomes. ***Method:*** Data were collected from 1,504 smokers (58.2% women; 83.9% White; mean age = 44.67 years, *SD* = 11.08) making an aided smoking cessation attempt as part of a clinical trial. Psychiatric diagnoses were determined with the Composite International Diagnostic Interview structured clinical interview. Tobacco dependence was assessed with the Fagerström Test of Nicotine Dependence (FTND) and the Wisconsin Inventory of Smoking Dependence Motives (WISDM). ***Results:*** Diagnostic groups included those who were never diagnosed, those who had ever been diagnosed (at any time, including in the past year), and those with past-year diagnoses (with or without prior diagnosis). Some diagnostic groups had lower follow-up abstinence rates than did the never diagnosed group (*p*s < .05). At 8 weeks after quitting, strong associations were found between cessation outcome and both past-year mood disorder and ever diagnosed anxiety disorder. At 6 months after quitting, those ever diagnosed with an anxiety disorder (*OR* = .72, *p* = .02) and those ever diagnosed with more than one psychiatric diagnosis (*OR* = .74, *p* = .03) had lower abstinence rates. The diagnostic categories did not differ in smoking heaviness or the FTND, but they did differ in dependence motives assessed with the WISDM. ***Conclusion:*** Information on recent or lifetime psychiatric disorders may help clinicians gauge relapse risk and may suggest dependence motives that are particularly relevant to affected patients. These findings also illustrate the importance of using multidimensional tobacco dependence assessments.

Keywords: smoking cessation, psychiatric disorders, nicotine dependence, depression, anxiety

Smokers are more likely to have a psychiatric disorder than are nonsmokers; conversely, individuals with a psychiatric disorder are almost twice as likely to smoke as individuals without a psychiatric disorder (Grant, Hasin, Chou, Stinson, & Dawson, 2004; Gwynn et al., 2008; Kalman, Morissette, & George, 2005; Lasser et al., 2000; Wiesbeck, Kuhl, Yaldizli, & Wurst, 2008). As a group, smokers with psychiatric disorders consume a disproportionate number of cigarettes (Grant et al., 2004), and some data

Megan E. Piper, Stevens S. Smith, Tanya R. Schlam, Cathlyn J. Leitzke, Michael C. Fiore, and Timothy B. Baker, Center for Tobacco Research and Intervention, Department of Medicine, University of Wisconsin School of Medicine and Public Health; Michael F. Fleming, Department of Family Medicine, University of Wisconsin School of Medicine and Public Health; Amy A. Bittrich, Division of Public Health, Milwaukee, Wisconsin; Jennifer L. Brown, Department of Pediatric Oncology, Medical College of Wisconsin; Mark E. Zehner, Department of Industrial and Systems Engineering, University of Wisconsin College of Engineering. Cathlyn J. Leitzke is now at the Department of Medicine, University of Wisconsin School of Medicine and Public Health.

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Correspondence concerning this article should be addressed to Megan E. Piper, Center for Tobacco Research and Intervention, 1930 Monroe Street, Suite 200, Madison, WI 53711. E-mail: mep@ctri.medicine.wisc.edu

show that smokers with psychiatric disorders are less likely to quit smoking than are other smokers (Covey, 1999; Glassman, 1993; Glassman et al., 1990; Haas, Munoz, Humfleet, Reus, & Hall, 2004). These observations raise questions about whether psychiatric disorders are associated with severity or type of tobacco dependence. However, little is known about whether smokers with psychiatric disorders differ from other smokers (those without psychiatric comorbidity) in terms of the nature of their tobacco dependence.

Given that individuals with psychiatric disorders constitute such a large portion of the smoker population (in one study, 62% of smokers seeking treatment had a history of psychiatric disorders; Keuthen et al., 2000), it is critical to learn more about how psychiatric disorders may affect nicotine dependence and ability to quit (cf. Morissette et al., 2008; Ziedonis et al., 2008). The goal of this research is to answer two primary questions about smoking and comorbid psychiatric disorders: (a) whether smokers with psychiatric diagnoses (the *ever diagnosed*, who have ever been diagnosed in their lifetime, including in the past year, and those with *past-year diagnoses*, who were diagnosed in the past year and may or may not have been diagnosed previously) have less success with quitting smoking than smokers without such diagnoses and (b) whether smokers with psychiatric diagnoses report different levels of nicotine dependence motives than do smokers without such comorbid diagnoses.

At present, the literature is somewhat inconsistent regarding whether psychiatric disorders are, in fact, related to cessation success (Agrawal, Sartor, Pergadia, Huizink, & Lynskey, 2008; Breslau, Novak, & Kessler, 2004b; Lasser et al., 2000). Given the high prevalence of psychiatric disorders among smokers, there are important public health implications if certain types of psychiatric diagnoses hinder cessation. This research addresses several questions about the relation between psychiatric disorders and cessation. First, whereas much of the prior work has focused on depression, the current data set also contains diagnoses of anxiety disorders and substance use disorders (SUDs). Second, some prior research has suggested that vulnerability to relapse or cessation failure may be related to symptom recency, with only recent or current symptoms increasing risk (Breslau et al., 2004b; Burgess et al., 2002; Covey, Bomback, & Yan, 2006; Gilbert, Crauthers, Mooney, McClernon, & Jensen, 1999; Hitsman, Borrelli, McChargue, Spring, & Niaura, 2003; John, Meyer, Rumpf, & Hapke, 2004; Johnson & Breslau, 2006; Niaura et al., 2001). We used the Composite International Diagnostic Interview (CIDI; Kessler & Ustun, 2004; World Health Organization, 1990) in this research, which allowed us to compare ever qualifying for a diagnosis (ever being diagnosed) with having a recent (i.e., past-year) diagnosis.[1] Our goal was to determine the extent to which increased vulnerability to cessation failure is related to factors associated with ever receiving a comorbid diagnosis (e.g., genetic and personality factors) and/or to factors related to symptom recency (e.g., distress, acute stress). The former is indexed by the ever diagnosed category, whereas the latter is indexed by the past-year category. Third, previous research in this area comprises cessation trials that typically use symptom checklists to infer diagnoses, rather than formal diagnostic interviews (e.g., Niaura et al., 1999; Smith et al., 2003), and epidemiologic studies that use diagnostic interviews tend to use retrospective reports of cessation with no biochemical validation (Breslau et al., 2004b; John et al., 2004). In the current research, we used both structured psychiatric interviews for diagnosis and prospective biochemically confirmed cessation outcomes. In summary, this research combines the internal validity of a large randomized placebo-controlled comparative efficacy cessation trial with the use of structured interviews prior to a quit-smoking attempt to establish psychiatric diagnoses (ever in a lifetime and past year).

A second major question addressed in this article is whether smokers with and without psychiatric disorders (specifically, anxiety disorders, mood disorders, and/or SUDs) differ in severity or form of nicotine dependence. As discussed earlier, it is important to determine whether psychiatric comorbidity is related to dependence because dependence can affect cessation success and may have implications for treatment. Previous research in this area often used dependence measures such as the Fagerström Test of Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991) or the number of cigarettes smoked per day (Baker et al., 2007). These measures focus on smoking pattern and do not comprehensively assess the multiple dimensions of nicotine dependence (Hudmon et al., 2003; Piper et al., 2004; Shiffman, Waters, & Hickcox, 2004). Research with such measures suggests that, in general, smokers with psychiatric disorders are more dependent on nicotine than are other smokers (i.e., smokers without comorbidities; American Psychiatric Association, 1994; Breslau, Kilbey, & Andreski, 1994; Breslau, Novak, & Kessler, 2004a; Covey, 1999; Dierker & Donny, 2008; Heatherton et al., 1991; John et al., 2004). However, such research provides little insight into the nature of the differences in dependence beyond the fact that smokers with psychiatric comorbidity tend to smoke more than do smokers without such comorbidity. We used the Wisconsin Inventory of Smoking Dependence Motives (WISDM-68; Piper et al., 2004) to achieve a multidimensional assessment of nicotine dependence (Piper et al., 2004; Shiffman et al., 2004). The WISDM-68 targets 13 different dimensions of smoking dependence motives (i.e., the different influences that may cause people to smoke in a dependent manner). We examine five specific WISDM-68 motivation constructs that we predicted would differ on the basis of psychiatric diagnostic status.

Internalizing disorders, such as generalized anxiety disorder and depression, are linked by an underlying trait of neuroticism, which manifests as a tendency to experience negative affect (e.g., Watson, 2005). First, we hypothesized that smokers with internalizing disorders, relative to smokers without such disorders, would be especially likely to experience affective distress and would come to rely on smoking's perceived ability to ameliorate such distress. Thus, we hypothesized that smokers with internalizing disorders would report unusually strong negative reinforcement motives to smoke (i.e., a tendency to smoke to reduce distress), which would be assessed with the Negative Reinforcement subscale of the WISDM-68.

Second, we anticipated that smokers with internalizing disorders, relative to smokers without such disorders, would score especially highly on the Affiliative Attachment subscale of the WISDM-68, which elicits ratings of the extent to which the smoker

[1] The CIDI does not assess current symptomatology and therefore does not distinguish between current versus recent (past year) symptoms.

has developed an emotional attachment to the cigarette that resembles a close personal friendship. We hypothesized that these smokers would be especially emotionally attached to their cigarettes because these smokers tend to be high in social anxiety and experience social distress (Bifulco, Moran, Jacobs, & Bunn, 2009; Burnette, Davis, Green, Worthington, & Bradfield, 2009). Research has shown that nicotine effectively reduces social anxiety and distress by directly activating brain regions that mediate perceived social attachment (Sahley, Panksepp, & Zolovick, 1981). In addition, the alleviation of social distress has been implicated in the development of drug dependence motivation (i.e., the social attachment adheres to the cigarette; Nocjar & Panksepp, 2007; Panksepp, Knutson, & Burgdorf, 2002).

Third, we hypothesized that the cognitive enhancement produced by nicotine (see Heishman, Taylor, & Henningfield, 1994, for a review) might especially motivate smoking in smokers with internalizing disorders. This would occur if nicotine's cognitive actions were effective (or perceived to be effective) in ameliorating the repetitive and intrusive thoughts experienced by individuals with internalizing disorders. Therefore, smokers with internalizing disorders might endorse the Cognitive Enhancement WISDM-68 subscale more highly than smokers without internalizing disorders. Smokers with externalizing disorders (e.g., SUDs) might also endorse the Cognitive Enhancement subscale more highly than smokers without externalizing disorders given that an underlying dimension of externalizing disorders manifests as attention deficit (e.g., Krueger et al., 2002).

Fourth, we hypothesized that smoking among friends and family, assessed by the Social/Environmental Goads subscale, would be an especially important motivator of smoking for smokers with SUDs compared with those without SUDs. This hypothesis stems from research showing that (a) a high percentage of current and past substance abusers smoke (Dawson, 2000; Grant et al., 2004), (b) substance abusers tend to be concentrated in social networks (Buchanan & Latkin, 2008; Homish & Leonard, 2008), and (c) high rates of smoking in a social network expose members to smoking cues and sustain smoking (e.g., Christakis & Fowler, 2008).

Fifth, on the basis of past research (Breslau et al., 1994, 2004a; Covey, 1999; Dierker & Donny, 2008; Heatherton et al., 1991; John et al., 2004), we predicted that having a psychiatric diagnosis versus having no diagnosis would be associated with higher scores on dependence measures that primarily reflect smoking heaviness (e.g., the FTND and the Primary Dependence Motives subscales on the WISDM-68).

Against this backdrop, the current study used structured psychiatric diagnostic interviews to determine psychiatric diagnoses (ever diagnosed and past-year diagnoses) in smokers who volunteered for a formal cessation treatment study. The efficacy findings from this research are reported in a separate article (Piper et al., 2009) and revealed that all active treatments were significantly efficacious relative to placebo (*OR*s = 1.63–2.34, $p < .05$) but that nicotine patch plus nicotine lozenge appeared to be especially efficacious ($OR = 2.34$, $p < .001$). The analyses reported in this article focus on whether ever diagnosed or past-year psychiatric comorbidity is (a) related to cessation success and (b) related to level and type of nicotine dependence.

Method

Recruitment and Inclusion/Exclusion Criteria

Participants were recruited in Madison and Milwaukee, WI, to participate in the Wisconsin Smokers' Health Study. Recruitment methods included TV, radio, and newspaper advertisements, community flyers, and earned media (e.g., radio and TV interviews, press releases). Primary inclusion criteria included smoking at least 10 cigarettes per day on average for the past 6 months and being motivated to quit smoking (≥8 on a 1–10 scale where 10 is highly motivated to quit). Exclusion criteria included current use of any medications contraindicated for use with any of the study pharmacotherapies (this included monoamine oxidase inhibitors, bupropion, lithium, anticonvulsants, and antipsychotics); any history of psychosis, bipolar disorder, or an eating disorder (the latter was exclusionary because one of the study medications, bupropion, is contraindicated); consuming six or more alcoholic beverages daily 6 or 7 days a week (when drinking at this rate, bupropion may be contraindicated); pregnancy or breastfeeding; and serious health conditions that would prevent participation in or completion of the study. Women of childbearing age had to agree to take steps to prevent pregnancy during the medication treatment phase of the study. This study received human subjects approval from the University of Wisconsin Health Sciences Institutional Review Board.

Procedure

Participants who passed a phone screen were invited to an information session where written informed consent was obtained. Next, participants completed an individual orientation session where they underwent multiple screenings, including a medical history screening, vital signs measurements, and a carbon monoxide breath test. Participants also completed demographic, smoking history, and tobacco dependence questionnaires. If participants met the inclusion criteria assessed in this session, they then completed three baseline visits. At the first baseline visit, participants completed additional questionnaires and were interviewed with the World Mental Health Survey Initiative version of the CIDI (Kessler & Ustun, 2004; World Health Organization, 1990). At the second baseline visit, physical health (e.g., lipid profile, diabetes screen) measures were assessed. At the third baseline visit, participants completed additional questionnaires, and eligible participants were randomized to one of six treatment conditions: bupropion sustained release ($n = 264$); nicotine lozenge ($n = 260$); nicotine patch ($n = 262$); nicotine patch plus nicotine lozenge ($n = 267$); bupropion sustained release plus nicotine lozenge ($n = 262$), or placebo (five placebo conditions that matched the five active conditions; $n = 189$). At this visit, participants set a quit date for the following week. Participants had study visits on their quit day and at 1, 2, 4, and 8 weeks after quitting. All participants received individual counseling at the third baseline visit, on the quit day, and at each subsequent study visit. Each counseling session was 10–20 min and provided intratreatment social support and training in problem solving and coping skills, as recommended in the U.S. Public Health Service Guidelines (Fiore, Bailey, & Cohen, 2000; Fiore et al., 2008). Counselors were bachelor's-level case managers supervised by a licensed clinical psychologist. All medications

were provided for 8 weeks after quitting except the nicotine lozenge, which was provided for 12 weeks after quitting (consistent with prescribing instructions). Randomization was conducted in a double-blind fashion; we used a blocked randomization scheme with blocking on gender and race (White vs. non-White).

Measures

Carbon monoxide assessment. Participants provided a breath sample at all study visits to permit alveolar carbon monoxide analysis, using a Bedfont Smokerlyzer (Bedfont Scientific, Rochester, England). A carbon monoxide value of less than 10 ppm was considered to be confirmatory of self-reported abstinence from smoking.

Demographics and smoking history. A questionnaire assessed demographic characteristics, such as gender, ethnicity, age, education level, and employment. The smoking history questionnaire included items such as the number of cigarettes smoked per day, age at smoking initiation, number of prior quit attempts, and other smokers in the household.

Tobacco dependence measures. The FTND, a six-item scale, has fair internal consistency ($\alpha = .61$; Heatherton et al., 1991). The WISDM (Piper et al., 2004) comprises 68 items designed to assess 13 different theoretically derived motivational domains, with subscales possessing good internal consistency ($\alpha = .87$ or greater; Piper et al., 2004). We present data for selected WISDM subscales based on theorized relations between psychiatric diagnostic status and targeted constructs: for the Negative Reinforcement, Affiliative Attachment, Cognitive Enhancement, Social/Environmental Goads subscales and for the Primary Dependence Motives composite scale (a combination of the Automaticity, Craving, Loss of Control, and Tolerance subscales), which, like the FTND, appears to primarily reflect a heavy smoking motive (Piper et al., 2008).

World Mental Health Survey Initiative version of the CIDI. The CIDI (Kessler & Ustun, 2004; World Health Organization, 1990) is a structured clinical interview administered with Computer Assisted Personal Interviews (CAPI), Version 20 by trained study personnel who were certified by a CIDI trainer. The CIDI provides both past-year diagnoses (i.e., within the past 12 months) as well as lifetime diagnoses (i.e., ever in the participant's lifetime, which would include anyone with a past-year diagnosis) for the 12 modules administered: Screening, Depression, Mania, Panic Disorder, Social Phobia, Generalized Anxiety Disorder, Substance Use, Attention Deficit Disorder, Services, Chronic Conditions, 30-Day Functioning, and 30-Day Symptoms. Although other diagnostic interviews assess current psychiatric illness (e.g., occurring within the past 2 weeks; Structured Clinical Interview for *DSM–III–R*; Spitzer, Williams, Gibbon, & First, 1992), the CIDI used in this research did not allow this assessment. Therefore, a smoker with a past-year diagnosis may or may not have been experiencing clinically significant symptoms at the time of study participation.

We calculated the number of diagnoses (ever and past year) participants had that fit into three main diagnostic categories: mood disorders (primarily major depression), anxiety disorders (panic disorder, social phobia, generalized anxiety disorder), and alcohol and other nonnicotine SUDs. Other diagnoses, such as attention deficit disorder (5.2% of the sample), were too rare to analyze separately. The rates of diagnoses were evenly distributed across treatment conditions. Compared with participants without each specific diagnosis, rates of study withdrawal by 6 months after quitting were significantly higher for smokers who had ever (including in the past year) had a mood disorder or anxiety disorder but not for those who had ever had an SUD (see Figure 1).

Analytic Plan

All analyses were conducted with PASW Statistics 17.0. We used descriptive statistics to examine the rates of exclusions due to severe and chronic psychiatric disorders and use of exclusionary medications and to examine the rates of psychopathology in the eligible study sample. Cessation outcomes were defined as biochemically confirmed (carbon monoxide < 10) 7-day point-prevalence abstinence at 8 weeks and 6 months after quitting. We used the intent-to-treat principle such that smokers who did not provide outcome data were assumed to be smoking. To determine how psychiatric diagnoses are related to cessation outcome, we used cessation outcomes as the dependent variable and treatment, gender, race, and age as covariates. Psychiatric diagnoses (either ever diagnosed or past-year diagnosis) were used as predictors, and smokers with no psychiatric diagnosis were the reference condition. We did not control for all variables that differed significantly among diagnostic groups so that we would not partial out variance in the naturally occurring diagnostic groups that was intrinsic to the nature of the diagnoses examined (Cohen, Cohen, West, & Aiken, 2003). We also examined the role of ever having had a diagnosis with past-year diagnoses removed from the model to assess the impact of lifetime but not recent diagnosis. Relations between dependence and psychiatric disorders were examined through seven separate linear regression models in which one of the seven dependence measures (the FTND, one of the five WISDM subscales, or the WISDM total score) served as the dependent variable in a model; gender, race, and age served as covariates in each model. All three lifetime diagnoses (ever diagnosed mood, anxiety, and SUD disorders) were simultaneously entered into the regression models as predictors of the dependence facets.

Results

Participants

Of the 5,269 smokers who were phone screened to recruit this sample, 2,120 did not meet eligibility requirements. The most common reasons for exclusion on the phone screen were reporting insufficient motivation (<7 on a 10-point scale; 26%), smoking fewer than 10 cigarettes per day (13%), being unwilling to commit to the study (13%), and not planning to remain in the area for 12 months (13%). Of specific relevance to this study, 4.5% reported psychosis or bipolar disorder, 1.2% reported an eating disorder, and 1.7% reported currently drinking six or more drinks a day at least 6 days a week, all of which were exclusionary. In addition, 14.9% of the excluded smokers reported that they were currently taking exclusionary medications, including 87 (4.3%) who were taking bupropion for either smoking cessation or depression. Smokers may have met more than one exclusionary criterion (e.g.,

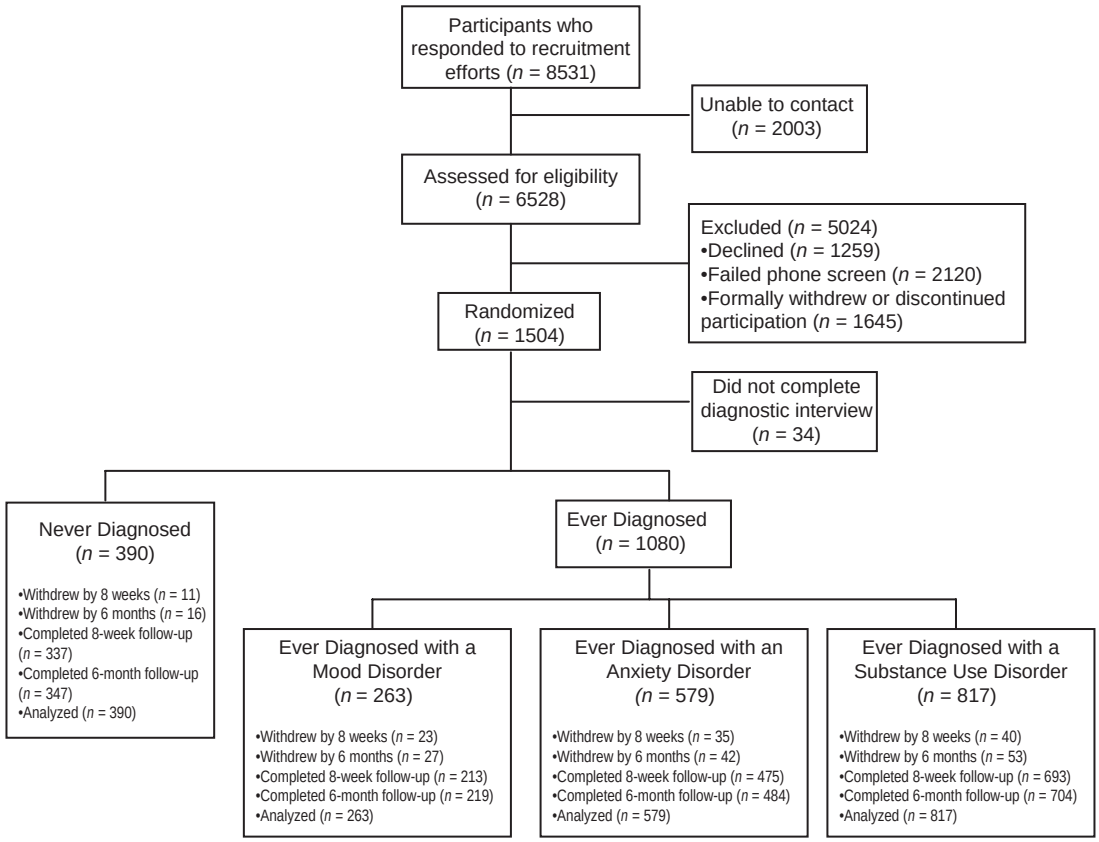


Figure 1. Study flow diagram. The numbers of mood disorder, anxiety disorder, and substance use disorder diagnoses do not sum to 1,080, the number of participants ever diagnosed, because there were 668 participants who received more than one diagnosis ever in their lifetime.

reporting both serious mental illness and taking exclusionary medication).

A total of 1,504 participants (876 of whom were women; 58.2%) were randomized into the study. The majority of participants were White (83.9%); 13.6% were African American, and 2.5% reported another race. In the entire sample, 2.8% reported that one of their parents was of Hispanic origin. In addition, 44.3% were married, and 23.6% had a high school education, but no more and 21.9% had a 4-year college degree. On average, participants were 44.67 ($SD = 11.08$) years old and smoked 21.43 ($SD = 8.93$) cigarettes per day. Study outcomes and additional study details are reported in a separate article (Piper et al., 2009). See Figure 1 for the study flow diagram.

Frequency of Psychiatric Diagnoses

Of the 1,504 study participants randomized, 34 did not complete the CIDI interview. Of the 1,080 who had ever received a diagnosis in their lifetime (including in the past year), the most common diagnosis was SUD (see Figure 1). With respect to diagnoses in the past year, 1,165 (77.5%) did not receive any past-year psychiatric diagnoses (other than tobacco dependence), 213 (14.2%) received one past-year diagnosis, 92 (6.1%) received two or more past-year diagnoses, and 34 did not complete the CIDI interview. With respect to specific diagnoses, 71 (27.0%) of the 263 smokers ever diagnosed with a mood disorder received a past-year mood disorder diagnosis. A total of 205 (35.4%) of the 579 smokers who ever had an anxiety disorder received a past-year anxiety disorder diagnosis. Finally, 87 (10.7%) of the 816 smokers who ever qualified for an SUD diagnosis qualified for an SUD diagnosis in the past year.

Cessation Outcomes

Logistic regression was used to predict 8-week and 6-month cessation outcomes with psychiatric disorders (the ever diagnosed and past-year diagnosis of mood disorders, anxiety disorders, and SUDs) as the primary predictors and with gender, race, age, and treatment condition as covariates. For all cessation analyses, smokers with no history of mental illness served as the comparison condition to provide the strongest contrast. Outcome variables were carbon monoxide confirmed 7-day point-prevalence intent-to-treat abstinence 8 weeks and 6 months after quitting in distinct analyses for each diagnosis.

Compared with smokers who had no history of psychiatric disorders, smokers who had ever had a mood disorder or an anxiety disorder (including those who had one in the past year) and those with a past-year mood or anxiety disorder were all less likely to be abstinent 8 weeks after quitting when controlling for treatment, age, gender, and ethnicity. Table 1 shows the percentage of

Table 1
Logistic Regression Comparing Participants With Diagnoses and Participants With No History of Psychiatric Disorders, Controlling for Treatment, Gender, and Race, and Percentage of Smokers Who Were Abstinent 8 Weeks and 6 Months After Quitting by Psychiatric Diagnosis (N = 1,470)[a]

Diagnosis and outcome assessment time	Percentage abstinent	Wald	*p*	*OR*	95% CI
No history of psychiatric disorders (*n* = 390; 26.5% of total sample)					
8 weeks	47.4				
6 months	35.4				
Ever diagnosed with a mood disorder (*n* = 263; 17.9% of total sample)					
8 weeks	39.5	4.87	.03[c]	0.69	[0.50, 0.96]
6 months	31.2	1.46	.23	0.81	[0.58, 1.14]
Past-year mood disorder (*n* = 71; 4.8% of total sample)					
8 weeks	28.2	7.61	.01	0.45	[0.25, 0.79]
6 months	23.9	2.37	.12	0.62	[0.34, 1.14]
Ever diagnosed with an anxiety disorder (*n* = 579; 39.4% of total sample)					
8 weeks	39.9	5.89	.02	0.72	[0.55, 0.94]
6 months	28.7	5.31	.02	0.72	[0.54, 0.95]
Past-year anxiety disorder (*n* = 205; 13.9% of total sample)					
8 weeks	37.6	3.79	.05	0.70	[0.49, 1.00]
6 months	29.8	1.21	.27	0.81	[0.55, 1.18]
Ever diagnosed with a substance use disorder (*n* = 816; 55.5% of total sample)					
8 weeks	43.4	2.62	.11	0.81	[0.63, 1.05]
6 months	32.8	1.43	.23	0.85	[0.65, 1.11]
Past-year substance use disorder (*n* = 87; 5.9% of total sample)					
8 weeks	46.0	0.004	.95	1.02	[0.62, 1.68]
6 months	34.5	0.01	.91	1.03	[0.61, 1.75]
Only one lifetime diagnosis (*n* = 410; 27.9% of total sample)					
8 weeks	43.9	1.08	.30	0.86	[0.64, 1.15]
6 months	36.2	0.08	.77	1.05	[0.77, 1.41]
Two or more lifetime diagnoses (*n* = 667; 45.4% of total sample)[b]					
8 weeks	41.9	3.97	.05	0.77	[0.59, 1.00]
6 months	29.9	4.52	.03	0.74	[0.57, 0.98]

[a] The percentages do not sum to 100% because some participants had more than one diagnosis. [b] Compared with smokers with only one lifetime diagnosis, smokers with two or more lifetime diagnoses were less likely to be abstinent at 6 months after quitting (Wald = 6.00, $p = .01$, $OR = .72$, 95% CI = 0.55–0.94), but the two groups were equally likely to be abstinent 8 weeks after quitting. [c] It should be noted that this effect is no longer significant if smokers with a diagnosis in the past year are removed from the analysis.

smokers with different types of psychiatric diagnoses who were abstinent at each measurement time. Ever having a diagnosis of an anxiety disorder was also related to a decreased likelihood of maintaining abstinence 6 months after quitting. Table 1 results were similar when no covariates were included.

To focus on residual risk due to lifetime diagnoses per se, we removed smokers with a past-year diagnosis from the ever diagnosed group. Results showed that having a history of an anxiety disorder without a past-year diagnosis continued to be a significant predictor of cessation outcome 8 weeks and 6 months after quitting ($OR = .73$, $p = .04$ and $OR = .68$, $p = .02$, respectively). When smokers with a past-year mood disorder ($n = 71$) were removed from the analyses for the participants ever diagnosed with a mood disorder, the effect on 8-week outcome was no longer statistically significant ($p = .25$), and the effect size decreased from $OR = .69$ to $OR = .81$.

To examine the relative effects of specific diagnoses on outcome, we included ever having a mood disorder, anxiety disorder, or SUD (including a past-year diagnosis) as three predictors in a logistic model, controlling for treatment, gender, age, and race. Results revealed that ever having an anxiety disorder remained a significant predictor of 8-week and 6-month abstinence (8 weeks: $OR = .78$, $p = .04$, 95% $CI = .62$–$.99$; 6 months: $OR = .72$, $p = .01$, 95% $CI = .57$–$.92$), whereas ever having a mood disorder and ever having an SUD diagnosis were not significant predictors. Specifically, ever having an anxiety disorder was related to poorer cessation outcome at 8 weeks and 6 months, independent of the effects of ever having a mood disorder or an SUD diagnosis.

We used logistic regression, controlling for gender, race, age, and treatment, to analyze the relation of number of diagnoses in a lifetime (coded as 0, 1, and 2 or more) with cessation outcome to model the cumulative impact of diagnoses. Number of diagnoses did not predict abstinence 8 weeks after quitting, but it did predict abstinence 6 months after quitting (see Table 1). Specifically, 6 months after quitting, smokers with no diagnoses or smokers with only one lifetime diagnosis were significantly more likely to be abstinent than were smokers ever diagnosed with two or more disorders.

Tobacco Dependence and Psychiatric Disorders

We examined the relation of different ever diagnosed categories (i.e., ever diagnosed with a mood disorder, anxiety disorder, or SUD, including past-year diagnoses) to the tobacco dependence measures (the FTND and selected WISDM subscales). We conducted a series of linear regression analyses with seven different dependence measures as the dependent variable (the five theoretically targeted WISDM subscales, the total WISDM score, and the

FTND score) and with gender, race, age, and ever being diagnosed with a mood disorder, anxiety disorder, or SUD as predictors (the three diagnoses were dummy coded as 0 = *no diagnosis* and 1 = *diagnosis*). For each disorder, smokers without that particular disorder served as the comparison group (e.g., smokers ever diagnosed with a mood disorder vs. smokers never diagnosed with a mood disorder). We chose to enter all the diagnostic categories into the same model to control for individuals who had more than one diagnosis. We did not use past-year disorder as a predictor because of the smaller sample sizes of the past-year groups.

Results indicated that diagnostic category was not related to the FTND—the dependence measure most heavily influenced by smoking heaviness per se (see Table 2). When dependence was analyzed with the multidimensional WISDM, results were fairly consistent with predictions. Smokers with any psychiatric diagnosis had higher WISDM total scores than smokers with no diagnoses. Smokers with a history of anxiety disorders and SUDs had significantly higher scores on the WISDM Primary Dependence Motives scale, which assesses heavy, automatic smoking that is out of control, than did smokers without such disorders. Smokers with a lifetime mood or anxiety disorder scored significantly higher on the WISDM Affiliative Attachment, Cognitive Enhancement, and Negative Reinforcement subscales than did smokers without those respective diagnoses (see Table 2). As predicted, smokers with a lifetime history of SUD had significantly higher scores than did smokers with no history of SUD on the Social/Environmental Goads subscale. We were surprised to find that smokers with a history of an anxiety disorder also had significantly higher scores on this subscale than did smokers with no history of an anxiety disorder.

Discussion

The first major question we addressed in this research was whether psychiatric disorder diagnosis was related to cessation success. The results suggest that smoking cessation outcome is related to internalizing (mood and anxiety) disorders, such that smokers who have ever had a mood or anxiety disorder were less likely to be abstinent 8 weeks after quitting. The influence of past-year mood disorder seemed especially important in this relation as reflected by the odds ratio magnitude and the fact that the ever diagnosed condition was no longer significantly related to cessation outcome once smokers with past-year diagnoses were removed from the sample (see Table 1). Past research has also found that recent depressive symptoms are especially predictive of cessation outcomes (Breslau et al., 2004b; Burgess et al., 2002; Covey et al., 2006; Gilbert et al., 1999; Hitsman et al., 2003; John et al., 2004; Johnson & Breslau, 2006; Niaura et al., 2001). In addition, in the current study, smokers who had ever had an anxiety disorder and those with two or more lifetime psychiatric diagnoses were less likely than smokers who had never had psychiatric diagnoses to be abstinent 6 months after quitting. These findings suggest that both mood and anxiety disorders place smokers at increased risk for tobacco cessation failure, although ever having had an anxiety disorder was unique in this study in that it was associated with differences in abstinence levels at both 8 weeks and 6 months after quitting. In addition, if psychiatric disorders are modeled as cumulative impact of the number of

Table 2
Linear Regressions, Controlling for Gender, Race, and Age, in Predicting Dependence Scores With All Three Ever Diagnosed Categories Included in the Analyses

Scale	Lifetime mood disorder versus no mood disorder					Lifetime anxiety disorder versus no anxiety disorder					Lifetime SUD versus no SUD				
	Disorder *M* (*SD*)	No disorder *M* (*SD*)	*B*	*p*	95% CI	Disorder *M* (*SD*)	No disorder *M* (*SD*)	*B*	*p*	95% CI	Disorder *M* (*SD*)	No disorder *M* (*SD*)	*B*	*p*	95% CI
WISDM Primary Dependence Motives	5.15 (1.17)	4.88 (1.17)	0.13	.11	[−0.03–0.29]	5.09 (1.15)	4.83 (1.19)	0.21	.001	[0.09–0.34]	4.97 (1.19)	4.88 (1.17)	0.14	.03	[0.01–0.26]
WISDM Affiliative Attachment	3.72 (1.81)	3.16 (1.69)	0.32	.006	[0.09–0.55]	3.58 (1.77)	3.05 (1.66)	0.43	<.001	[0.25–0.62]	3.28 (1.72)	3.23 (1.72)	0.12	.18	[−0.06–0.30]
WISDM Cognitive Enhancement	3.92 (1.81)	3.47 (1.65)	0.31	.01	[0.07–0.54]	3.81 (1.72)	3.38 (1.64)	0.35	<.001	[0.16–0.53]	3.59 (1.69)	3.50 (1.68)	0.08	.39	[−0.10–0.26]
WISDM Negative Reinforcement	4.96 (1.57)	4.44 (1.39)	0.35	<.001	[0.16–0.54]	4.79 (1.36)	4.36 (1.40)	0.28	<.001	[0.13–0.43]	4.56 (1.41)	4.50 (1.38)	0.12	.12	[−0.03–0.26]
WISDM Social/Environmental Goads	3.53 (1.79)	3.39 (1.83)	0.005	.97	[−0.25–0.26]	3.61 (1.81)	3.28 (1.82)	0.24	.02	[0.04–0.44]	3.60 (1.87)	3.18 (1.74)	0.38	<.001	[0.19–0.57]
WISDM Total	57.39 (13.70)	53.09 (12.84)	2.35	.01	[0.57–4.14]	56.46 (13.06)	52.18 (12.86)	3.25	<.001	[1.85–4.66]	54.30 (13.22)	53.32 (12.95)	1.54	.03	[0.17–2.91]
FTND Total	5.64 (2.25)	4.88 (1.17)	0.27	.07	[−0.03–0.57]	5.50 (2.19)	5.31 (2.11)	0.17	.15	[−0.06–0.41]	5.47 (2.20)	5.28 (2.07)	0.14	.22	[−0.09–0.37]

Note. SUD = substance use disorder; WISDM = Wisconsin Inventory of Smoking Dependence Motives; FTND = Fagerström Test of Nicotine Dependence.

diagnoses, the more psychiatric diagnoses ever assigned, the less likelihood there is of long-term cessation success.

It should be noted that the small size ($n = 71$) of the past-year mood disorder group reduced power to detect a significant effect (post hoc power = .45). Therefore—despite having the greatest effect size at 6 months after quitting on the basis of the odds ratio ($OR = .62$)—the effect was not statistically significant, whereas an effect of $OR = .72$ was statistically significant for the lifetime anxiety disorder group ($n = 579$). Modified post hoc power analyses revealed that significantly larger effect sizes (i.e., a difference of 15 percentage points in abstinence rates) would be needed to detect a significant effect with the current sample size of the past-year mood disorder group.

Psychiatric diagnosis (i.e., mood and anxiety disorders) was more consistently associated with early versus late cessation outcomes. These results raise the question of why the effect of psychiatric disorders decreased from the 8-week to the 6-month follow-up, as indicated by odds ratio magnitude (see Table 1). Reasons for this are unknown, but it may be that the high rates of relapse at 8 weeks in comorbid groups left relatively few participants with psychiatric disorders available to relapse over the next 4 months. This pattern of susceptibility to early relapse among smokers with psychiatric diagnoses replicates previous findings regarding depression history (Japuntich et al., 2007). These results suggest that smokers who have ever had internalizing psychiatric disorders may benefit from intensive treatment early in the cessation process.

Among the individual psychiatric diagnoses, ever having had an anxiety disorder was unique in that it significantly predicted smoking status 6 months after quitting, and this effect was not dependent on smokers with a past-year diagnosis. This relation was found after controlling for mood disorder and SUD diagnoses, suggesting that specific features of anxiety may impede cessation success. Multiple studies have focused on the role of depression in relapse, perhaps because negative mood and anhedonia are symptoms of both depression and nicotine withdrawal (Hughes & Hatsukami, 1986; Welsch et al., 1999). Few studies have examined the role of anxiety in cessation, although anxiety has been linked to smoking (e.g., Strine et al., 2008). Several theories address the role of anxiety in the maintenance of dependence, including the theory that smokers with anxiety disorders have increased anxiety sensitivity (Brown, Kahler, Zvolensky, Lejuez, & Ramsey, 2001; Zvolensky et al., 2005) and believe that their anxiety symptoms, which may be a product of withdrawal, will have profound negative physical, social, or psychological consequences (Reiss, 1991). Additional research is needed to understand factors and mechanisms that contribute most to the heightened relapse vulnerability of smokers with anxiety disorders.

Of interest, SUD diagnosis was not associated with smoking cessation failure in this population (i.e., treatment-seeking smokers with an SUD diagnosis who were not currently drinking more than six drinks on 6 or 7 days a week). Thus, a significant proportion of smokers who have a history of substance abuse and dependence are able to quit smoking; other research has suggested that quitting smoking does not cause relapse back to other substances (Bobo, McIlvain, Lando, Walker, & Leed-Kelly, 1998; Burling, Burling, & Latini, 2001; Hurt et al., 1994, 1995; Myers & Brown, 2005; Prochaska, Delucchi, & Hall, 2004; Shoptaw et al., 2002). An absence of heightened SUD-linked risk supports recommendations that those with SUD diagnoses be provided with evidence-based smoking cessation interventions (Fiore et al., 2008).

The second major question targeted in this research was whether smokers with and without psychiatric disorders differ on dimensions of nicotine dependence. In general, psychiatric diagnostic status was not significantly related to dependence measures that narrowly reflect smoking heaviness (i.e., cigarettes per day, the FTND). These findings stand in contrast to large sample epidemiological studies that have found such differences (e.g., Grant et al., 2004; cf. Breslau & Johnson, 2000). It may be that psychiatric disorders confer risk for especially heavy smoking when a large, population-based sample of smokers is studied. In other words, this effect may depend on the presence of light smokers in the analyzed sample; such smokers tend not to seek out formal cessation treatment (Pierce & Gilpin, 2002; Shiffman, Di Marino, & Sweeney, 2005), and smokers were excluded from this study if they smoked fewer than 10 cigarettes a day.

When dependence was measured with the multidimensional WISDM-68, psychiatric diagnostic status was associated with the Primary Dependence Motives composite scale and with theoretically relevant subscales. Psychiatric diagnosis may be associated with the Primary Dependence Motives scale because this composite assesses more than smoking heaviness per se (i.e., it assesses automatic smoking, strong urges, and a sense that smoking is out of control). Smokers with internalizing disorders also scored higher than smokers without internalizing disorders on negative reinforcement motives for smoking. As noted earlier, such smokers struggle to cope with affective distress, and smoking may constitute a more valued means of affective coping for these smokers. Smokers with lifetime anxiety disorders also reported a strong emotional bond with their cigarettes and reported that smoking enhanced their cognitive processing. Contrary to our hypothesis, however, smokers with lifetime mood disorders did not differ from smokers without lifetime mood disorders on the Affiliative Attachment and Cognitive Enhancement WISDM subscales. Compared with smokers who did not have a history of SUD, those with a history of SUD reported that social and environmental influences were especially likely to affect their smoking. In summary, these results suggest that particular smoking dependence motives may be especially influential for smokers with particular psychiatric disorders. These findings may be helpful in guiding the development of treatment for smokers with particular psychiatric diagnoses because these dependence motives can confer added risk of cessation failure.

Although these findings concerning psychiatric disorders and dependence motives are provocative, certain caveats must be borne in mind. One is that the self-report of a dependence motive may reflect only attributions or beliefs that are associated with the various psychiatric disorders. (Although recent research suggests that motives reported on the WISDM-68 do predict the behaviors and symptoms that smokers report with real-time experience sampling techniques; Japuntich, Piper, Schlam, Bolt, & Baker, in press). In addition, aspects of this work raise questions about sample representativeness. We found strikingly high levels of psychiatric diagnoses in this clinical sample of smokers. Although fewer than 25% of the sample received a past-year *DSM–IV* diagnosis, approximately 75% had a lifetime history of at least one *DSM–IV* diagnosis, and almost 50% had two or more lifetime diagnoses. These rates are higher than in other research (Keuthen

et al., 2000), which found that 62% of treatment-seeking smokers had a history of psychiatric disorders. Also, this research is based on smokers who were motivated to quit and eligible to participate in a formal smoking cessation trial, which included a willingness to complete numerous assessments. This study excluded smokers with schizophrenia, psychosis, or bipolar disorder. These individuals smoked at very high rates (de Leon & Diaz, 2005). Smokers were also excluded if they reported taking monoamine oxidase inhibitors, bupropion, lithium, anticonvulsants, or antipsychotics, and 87 smokers were excluded for taking bupropion, which may have been used to treat depression. Thus, depression diagnoses may be more common in a clinical sample of smokers who are not similarly screened. If more smokers with a depression diagnosis had been included in the sample, it may have resulted in stronger relations between a depression diagnosis and cessation outcomes. It is also important to note that smokers with internalizing disorders were more likely to withdraw from the study; therefore, they were counted as smoking in the intent-to-treat analyses. The results may have been different if such smokers had remained in the study. This study was conducted in the state of Wisconsin, which has the highest rate of binge drinking in the United States (23.4%; Centers for Disease Control and Prevention, 2007). Therefore, the rate of alcohol abuse and dependence may be relatively high in this sample. However, the exclusion criteria of consuming six or more alcoholic drinks daily on 6 or 7 days per week eliminated some of the heavily alcohol dependent smokers. Also, this sample was predominantly White (83.9%); only 13.6% of participants were African American, and less than 3% were of another race. Finally, this study did not assess current or ongoing psychiatric diagnoses at baseline or at the 6-month follow-up. Therefore, we were unable to address the relation between current or ongoing mental illness and cessation outcome.

Conclusions

Smokers who presented for smoking cessation treatment in the current study had significant levels of psychiatric disorders, both ever in their lifetime and past-year diagnoses. Internalizing disorders (anxiety and mood disorders) were related to poor cessation outcome 8 weeks after quitting. Ever having an anxiety disorder and having more than one lifetime psychiatric diagnosis predicted poorer cessation outcome 6 months after quitting. Smokers with and without histories of the different psychiatric disorders could not be distinguished on the basis of measures of nicotine dependence that primarily reflect heavy smoking (e.g., FTND), but they did differ on dependence motives, such as the importance of environmental cues as smoking triggers and the use of cigarettes to cope with negative affect. These findings may offer a basis for tailoring treatment to smokers with psychiatric comorbidities. In summary, the results show—in a relatively large clinical population of smokers—that certain psychiatric comorbidities (i.e., past-year mood disorder and past-year or lifetime anxiety disorder) are associated with especially poor cessation outcomes. The results also show that smokers diagnosed with such disorders report significantly higher smoking dependence motives than do smokers without such diagnoses.

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