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Psychiatric Comorbidities in a Comparative Effectiveness Smoking Cessation Trial: Relations with Cessation Success, Treatment Response, and Relapse Risk Factors

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Abstract

BACKGROUND: Comorbid psychiatric diagnoses have been shown to predict cessation failure. The relative impact of various diagnoses on cessation *and* other cessation processes is rarely studied, particularly among a general population. The impact of psychiatric history among primary care patients seeking cessation services on nicotine dependence, cessation outcomes, treatment effects and adherence, and withdrawal symptoms was examined.

METHODS: Secondary data analysis of a multi-site comparative effectiveness smoking cessation trial was conducted. Adult smokers ($n=1051$; 52.5% Female, 68.1% white) completed a structured clinical interview at baseline to assess psychiatric diagnostic history (past-year and lifetime). Nicotine dependence was assessed via self-report measures at baseline. Point-prevalence abstinence was assessed at 8 weeks and 6 months post-quit. Withdrawal symptoms were assessed for one week pre- and post-quit using ecological momentary assessment. Treatment adherence was self-reported at 1, 4, 8, and 12 weeks post-quit.

RESULTS: Past-year substance use disorder, lifetime mood disorder, and > one lifetime diagnosis, were related to lower rates of short-term, but not long-term, cessation. Lifetime psychiatric diagnosis was related to elevated nicotine dependence, particularly to secondary dependence motives associated with instrumental tobacco use. History of psychiatric diagnosis

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was associated with increased withdrawal-related craving. There was little evidence that psychiatric diagnostic status moderated the effects of the tested pharmacotherapies on long-term abstinence.

CONCLUSIONS: Psychiatric diagnoses affect risk factors that exert their effects early in the post-quit process and highlight the potential utility of examining transdiagnostic risk factors to better understand the relations between psychiatric vulnerabilities and the smoking cessation process.

Keywords

cessation; cigarette; nicotine dependence; psychiatric comorbidity; smoking

1. Introduction

Despite a historic low in smoking prevalence in the US (13.9%; National Health Interview Survey, 2019), cigarette use remains elevated in certain populations. More than 35% of people with severe psychiatric disorders smoke, leading to an increased disease burden and a substantial health inequity (National Health Interview Survey, 2019; Streck, et al, 2018). Psychiatric diagnosis and greater psychiatric symptom severity have been associated with increased nicotine dependence and smoking heaviness, greater withdrawal symptoms, and limited cessation success (Breslau, et al, 2004b; Goodwin, et al., 2012; Piper, et al., 2010; Smith, et al., 2014; Streck et al., 2018; Weinberger, et al., 2010). Ample work examines smoking in psychiatric populations, especially those with severe mental illness (Banham and Gilbody, 2010; Cook et al., 2014; Tidey and Miller, 2015). Mood, anxiety, and substance use disorders (SUD) commonly predict cessation failure (Hitsman et al., 2013; Lawrence, et al., 2010; Piper, et al., 2010; 2011; Stepankova et al., 2017; Weinberger, 2012). However, the relative effects of these diagnoses on cessation *and* other cessation processes is rarely studied (Breslau et al., 2004b; Piper, Smith, et al., 2010; Smith, Homish, et al., 2014; Weinberger et al., 2010), particularly among a general population with a broad distribution of mental health histories. This study examines the role of psychiatric history among primary care patients seeking cessation services.

Methodological limitations in the extant research limit our understanding of the effects of psychiatric comorbidity on the smoking cessation process and how to effectively treat such at-risk smokers. These limitations include: 1) outdated samples; 2) nonspecific, varying, or global measurement of psychiatric disorder; 3) varying diagnostic time frames (current, past-year, lifetime history); and 4) lack of evaluation of comorbid diagnoses.

1.1. Outdated samples

Most seminal articles on the relations between smoking and comorbid psychiatric disorders used samples that were gathered over 15 years ago (Breslau et al., 2004b; Brown, et al., 1996; Grant, et al., 2004; Lasser et al., 2000), prior to large shifts in smoking prevalence and demographics (National Health Interview Survey, 2019). A recent large, multi-country trial, demonstrated that smokers with any current and/or lifetime mood, anxiety, or psychotic disorder as identified using a diagnostic interview, achieved lower long-term (6-months)

abstinence rates than did smokers without such diagnoses (West et al., 2018). However, this study excluded individuals with other current SUDs and did not report analyses of cessation-related constructs (e.g., dependence or withdrawal symptoms) among these diagnostic groups.

1.2. Diagnostic specificity

Semi-structured comprehensive clinical interviews such as the Composite International Diagnostic Interview [CIDI] (Kessler and Uston, 2006) remain the “gold standard” for psychiatric diagnosis, but such interviews are both costly and time consuming (Stuart et al., 2014). Many researchers have shifted to using brief, validated self-report scales of single disorders (i.e., Beck Depression Inventory – II [BDI-II], Generalized Anxiety Disorders 7 Item Scale [GAD-7] (Beck, et al., 1996; Spitzer, et al., 2006; Stuart et al., 2014) or assessing psychological distress as a proxy for psychiatric diagnosis (Hagman, et al., 2008; Kulik and Glantz, 2017; Pratt, et al., 2007; Streck et al., 2018; Sung, et al., 2011). However, measures of psychological distress do not provide information on specific diagnoses (e.g., SUD; Kessler et al., 2003), preventing analysis of relations of specific diagnostic categories (i.e., mood or anxiety disorders) or comorbidity with outcome.

1.3. Diagnostic time frame

Research on mood and SUDs highlight the discrepant relations of past (vs. current) psychiatric diagnosis on cessation success. A recent meta-analysis found a negative association between past depression diagnosis and short- and long-term cessation success (Hitsman et al., 2013). However, other studies failed to find significant associations between past mood disorder and long-term cessation success (Japuntich et al., 2007; Piper, et al., 2010) or found that current mood disorder is most strongly predictive of cessation success (Piper, et al., 2010). Studies examining SUDs also rarely cast results in terms of diagnostic timeframe (Leeman, et al., 2007), which limits the ability to relate diagnostic timeframe to cessation success and related processes such as withdrawal.

1.4. Comorbid psychiatric diagnoses

Comorbid diagnoses, a marker of severity of psychiatric status have been linked to cessation failure in some, but not all, studies (Breslau, et al., 2004a; Mykletun, et al., 2008; Piper, et al., 2010; Weinberger et al., 2010). Almost no research has documented examining the prevalence of overlap between specific diagnostic categories (e.g., depression and anxiety vs. depression and SUD) and their relations with cessation. Understanding whether distinct diagnostic constructs represent unique risk factors and/or whether comorbid diagnoses indicates an increase in a general vulnerability (e.g., greater difficulty with affective regulation and cessation) may be important to understanding the cessation process and identifying effective treatments (Leventhal et al., 2012).

1.5. Current Study

The current exploratory study aimed to provide additional insight into the relations of psychiatric diagnoses with cessation success and related processes using data from a large comparative effectiveness trial, the Wisconsin Smokers Health Study 2 (see Baker et al.,

2016 for primary results), among smokers seeking cessation treatment in a primary care setting. The current research attempted to address limitations in the extant research literature via: (1) assessing the prevalence of specific and comorbid psychiatric diagnostic groups in a recent sample of smokers trying to quit and (2) systematically evaluating the relations of current and lifetime psychiatric diagnosis with nicotine dependence, cessation success, treatment effects, withdrawal symptoms, and treatment adherence.

2. Method

2.1. Participants

Participants were recruited from the community via advertisements and earned media ($n = 917$) and from the Wisconsin Smokers Health Study ($n = 169$; Piper et al., 2009; Stein et al., 2014), which followed smokers longitudinally. Potential participants were recruited between May 2012 and June 2014 and screened for eligibility including: smoking 5 cigarettes/day, wanting to quit smoking, willing and able to use study medications and not use e-cigarettes, not reporting moderately severe or severe depression on the Patient Health Questionnaire (PHQ-9; Kroenke, et al., 2001), no current suicidal ideation or suicide attempts in the past 5 years, and no diagnosis/treatment for psychosis in the past 10 years (see Baker et al., 2016). Only 1.5%, of the total 6462 smokers originally screened (not necessarily deemed eligible) for the study were excluded for depression symptom elevation (Baker et al., 2016). The local Institutional Review Board approved this study. Only those who completed the CIDI at baseline ($N = 1051$) were included in subsequent analyses.

2.2. Study Design

Participants were randomized to receive 12 weeks of varenicline, combination nicotine replacement therapy (C-NRT; nicotine patch + nicotine lozenge), or the nicotine patch (39.0%, 38.8%, and 22.2% of the sample, respectively). Participants started the patch or C-NRT on the target quit date (TQD), or started varenicline 1-week pre-TQD followed by 11 weeks post-TQD (see Baker et al., 2016). All participants were offered six cessation counseling sessions (five in-person sessions and one phone call).

2.3. Assessments

At baseline, participants completed assessments of basic demographic characteristics, smoking history, and current smoking behavior. Participants also completed the Fagerström Test for Nicotine Dependence (FTND; Heatherton, et al., 1991) and the Brief Wisconsin Inventory of Smoking Dependence (Brief WISDM; Smith et al., 2010). The FTND is a six-item measure commonly used to assess nicotine dependence. The Brief WISDM is a 37-item nicotine dependence measure with a total scale, 11 subscales, and two higher order subscales: Primary Dependence Motives (WISDM-PDM; Automaticity, Craving, Loss of Control, and Tolerance) and Secondary Dependence Motives (WISDM-SDM; e.g., Affiliative Attachment, Affective Enhancement, Cognitive Enhancement, Cue Exposure, Social/Environmental Goals, Taste/Sensory Properties, Weight Control).

2.3.1 Psychiatric assessment.—At baseline, participants completed the CIDI (Kessler and Uston, 2006), a structured clinical interview delivered by bachelors-level

trained research assistants. The CIDI provided lifetime and past-year diagnosis for multiple disorders based on DSM-IV-TR criteria: Alcohol Abuse, Alcohol Dependence, Bipolar I Disorder, Bipolar II Disorder, Drug Abuse (excluding tobacco), Drug Dependence (excluding tobacco), Dysthymic Disorder, Generalized Anxiety Disorder, Major Depressive Disorder, Panic Disorder, Panic Attacks, Social Phobia, and Specific Phobia. Diagnoses were categorized via three overarching groups: anxiety disorders (Generalized Anxiety Disorder, Panic Disorder, Panic Attacks, Social Phobia), mood disorders (Dysthymia, Bipolar I Disorder, Bipolar II Disorder, or Major Depressive Disorder), and SUDs (Alcohol Abuse, Alcohol Dependence, Drug Abuse, or Drug Dependence). For group inclusion, a participant needed to have at least one of the listed diagnoses present for the time period selected (past year or lifetime). Participants could have > one diagnosis within a group (e.g., lifetime Panic Attacks and lifetime Social Phobia) and have diagnoses in multiple groups (e.g., past-year Panic Disorder and past-year Major Depressive Disorder).

2.3.2 Nicotine withdrawal.—During the week prior to the TQD and for two weeks post-quit participants completed ecological momentary assessments (EMA), including items from the Wisconsin Smokers Withdrawal Scale (WSWS; Welsch et al., 1999), every evening via interactive voice response. EMA data on the WSWS Craving and WSWS Negative Affect scales were averaged for the week pre-quit and for the first week post-quit to create measures of pre-quit and post-quit measures of craving and negative affect.

2.3.3 Treatment adherence.—Medication use was assessed using self-reported 7-day time-line follow back methods at 1, 4, 8 and 12 weeks post-quit. Participants were defined as adherent if they reported use of a medication at least once per day for 6 or 7 days in the past week (e.g., at least 1 pill used on 6 or 7 days in the past week). Participation in smoking cessation counseling sessions was also documented.

2.3.4 Smoking cessation.—Participants reported 7-day point-prevalence abstinence at every study visit (Weeks 1, 4, 12) and follow-up call (Weeks 8, 26 and 52). At each visit, participants also provided a breath sample for a carbon monoxide (CO) assay using a Bedfont Smokerlyzer (Bedfont Scientific, Rochester, England). Participants reporting abstinence during phone follow-ups at weeks 26 and 52 were asked to attend a visit to biochemically confirm abstinence (i.e., CO < 5 ppm). Participants also reported smoking or abstinence for each day, via a timeline follow back interview (Brown et al., 1998; Robinson, et al., 2014). These data were used to determine latency to relapse (i.e., the first of 7 consecutive days of smoking).

2.4. Data Analytic Plan

We determined the overall frequency of lifetime and past-year diagnosis as well as comorbidity across diagnostic categories. We also used independent sample *t*-tests to examine differences in nicotine dependence levels between diagnostic groups. Residual scores were calculated for both WISDM PDM and SDM and used as dependent variables in reported dependence analyses to ensure findings were not due to the overlapping variance between the PDM and SDM scales. We examined cessation success, treatment response, withdrawal, and adherence to gain insight into potential mechanisms via which diagnoses

might affect the cessation process. We used logistic regression to examine the relations of diagnoses with dichotomous cessation outcomes (initial cessation, 8-week and 26-week biochemically confirmed cessation) and Cox-regression survival analyses to examine latency to relapse for diagnostic groups. We included treatment by diagnosis interaction terms in the cessation logistic regression models to examine differential response to treatment. Hierarchical linear regression analyses, with pre-quit withdrawal symptoms entered as a covariate at step one and presence or absence of psychiatric diagnosis entered at step two, were used to examine the relations between diagnostic group and post-quit withdrawal (i.e., withdrawal symptoms that worsened as a result of abstinence). Chi-square tests of independence and independent samples *t*-tests were used to examine differences between diagnoses in terms of treatment adherence. For all analyses, relations of specific diagnoses were modeled via independent comparisons of each diagnostic category versus no lifetime psychiatric history. Benjamini-Hochberg corrections, which are less susceptible to type II error than other forms of statistical corrections, subsequently controlled for false discovery rate for covariate-corrected analyses involving cessation outcomes, nicotine dependence, and withdrawal symptoms (Benjamini and Hochberg, 1995; Glickman, et al., 2014).

Following initial analyses, logistic and linear regression analyses were conducted to ensure findings were not due to the presence of confounding variables. Consistent with the recommendations of Kraemer (Kraemer, 2015), gender and race were chosen as *a priori* additive covariates for all analyses due to their known associations with cigarette smoking and psychiatric disorders (Leventhal et al., 2017; McLean, et al., 2011; Piper, et al., 2010; Wetter et al., 1999) as well as the demonstrated impact of race on cessation in this sample (Baker et al., 2016). Treatment condition was used as a covariate in analyses involving cessation success to control for treatment effects.

3. Results

Of 1051 participants, 68.1% were White, 27.4% were African American, 4.5% Other, and 52.5% were female. Participants had a mean age of 48.0 ($SD = 11.7$) and smoked 17.0 ($SD = 8.3$) cigarettes per day. There were differences (p 's < .05) in diagnostic rate by gender, age, and menthol smoking. Specifically, women had higher rates of past-year and lifetime anxiety and lifetime mood disorders and lower rates of past-year and lifetime SUDs, consistent with epidemiological findings. Participants who had smoked menthol cigarettes had higher rates of past-year SUD, past-year and lifetime anxiety diagnoses and lifetime mood diagnoses. Finally, smokers with past-year SUD, past-year anxiety diagnoses, and past-year and lifetime mood disorders were significantly younger than those without such diagnoses (see Supplemental Table 1 for data). There were no differences in race or cigarettes smoked per day by diagnosis. With respect to treatment, 230 (21.9%) were randomized to patch, 410 (39.0%) to C-NRT, and 411 (39.1%) to varenicline.

3.1. Frequency of Psychiatric Diagnosis

A total of 764 (72.7%) participants met criteria for at least one lifetime psychiatric diagnosis; 46.6% ($n = 490$) met criteria for > one lifetime diagnosis (see Table 1). Only 21.5% ($n = 204$) participants received a past-year diagnosis and 4.3% ($n = 45$) received >

one past-year diagnosis. Of those with lifetime mood diagnosis ($n = 149$), 30.1% had a past-year mood disorder diagnosis. Figures 1 and 2 illustrate the diagnostic comorbidities within the past-year and lifetime. In the past year, co-occurrence of anxiety and depression was the most common comorbidity; anxiety and SUD was the most common comorbidity with respect to lifetime diagnoses.

3.2. Nicotine Dependence

Participants with lifetime and past-year psychiatric diagnoses generally reported higher levels of nicotine dependence compared to participants with no history of psychiatric diagnosis except on the WISDM-PDM (see Table 2). Results did not differ after including race and gender as covariates or accounting for false-discovery rates.

3.3. Cessation Outcomes

3.3.1 Lifetime history.—Compared to smokers with no history of lifetime mental illness, smokers with a history of mood disorder and multiple lifetime psychiatric disorders (i.e., at least 2 different diagnoses during the participant's lifetime, not 2 occurrences of the same diagnosis) were significantly less likely to be abstinent at 8 weeks ($OR = 0.61$, $p = .02$, 95% CI = 0.41–0.91; $OR = 0.74$, $p = .04$, 95% CI = 0.55–0.99), but not at 6 months post-quit ($p > .05$). Relations between any lifetime diagnosis and initial cessation were not significant. Results did not differ after race, gender, and treatment were added as covariates, but were no longer significant after correcting for false discovery rate.

3.3.2 Past year.—SUD was the only past-year diagnostic category that predicted abstinence at any of the three time points; smokers with past-year SUD were less likely to achieve initial and 8-week abstinence compared to smokers with no lifetime psychiatric history (initial: $OR = 0.55$, $p = .03$, 95% CI = 0.32–0.95; 8 weeks: $OR = 0.55$, $p = .02$, 95% CI = 0.34–0.91). However, these relations were no longer statistically significant when covariates were added to the model (initial: $OR = 0.62$, $p = .11$, 95% CI = 0.34–1.12; 8 weeks: $OR = 0.62$, $p = .08$, 95% CI = 0.37–1.06).

3.3.3 Comorbidity.—We examined the 8-week and 6-month abstinence rates of participants with no diagnosis, a single diagnosis, and the various diagnostic comorbidities for both past-year and lifetime diagnoses (Figures 1 & 2). Due to small sample sizes, the relations of specific comorbidities with long-term abstinence were not evaluated with inferential tests. Descriptive data, however, suggested that individuals with some types of comorbidity had relatively low rates of abstinence relative to individuals with no psychiatric history (e.g., 50.5% 8-week abstinence for no lifetime diagnosis vs. 16.7% for lifetime mood disorder or 29.0% for lifetime mood and SUD).

3.3.4 Latency to relapse.—Cox-regression analyses revealed that participants with lifetime SUD and those with > one lifetime psychiatric diagnosis, tended to relapse sooner than those with no lifetime psychiatric history ($HR = 1.20$; $p = .04$, 95% CI = 1.01–1.43; $HR = 1.25$; $p = .02$, 95% CI = 1.04–1.49; see Figures 3 & 4). Similarly, individuals with past-year SUD tended to relapse more quickly than participants with no lifetime psychiatric

history ($HR = 1.52$; $p = .004$, 95% $CI = 1.15$ – 2.01). Results remained unchanged when covariates were added to the model.

3.4. Treatment Effects

Logistic regression analyses revealed that lifetime or past-year diagnosis did not significantly moderate the effect of treatment on either early or late cessation. Figures 5 and 6 depict the 8-week and 6-month abstinence rates by diagnosis and treatment condition. However, inspection of the graphs led us to conduct exploratory analyses to determine whether varenicline and the nicotine patch were differentially effective in patients with a history of a mood disorder. Among participants with a lifetime mood disorder diagnosis, participants using varenicline were significantly more likely to be abstinent at 8 weeks than those using the patch ($OR = 2.91$, $p = .02$, 95% $CI = 1.18$ – 7.20); this difference did not remain statistically significant at 6-months post quit ($OR = 1.22$, $p = .72$, 95% $CI = 0.41$ – 3.64). Moreover, C-NRT produced the highest abstinence rates at 6-months post-TQD. Results did not differ after adding race and gender to the model.

3.5. Withdrawal symptoms

Lifetime and past-year diagnosis significantly predicted higher post-quit negative affect and craving. However, hierarchical linear regression analyses showed that participants with any lifetime diagnosis reported greater post-quit craving, but not negative affect, after controlling for pre-quit craving and negative affect, compared to participants with no psychiatric comorbidity (Table 3). No past-year diagnoses significantly predicted post-quit withdrawal symptoms. Results did not differ after including covariates in the models or correcting for false-discovery rate.

3.6. Treatment Adherence

All participants demonstrated a steady decline in nicotine patch adherence and excellent counseling attendance (full results presented in Appendix 1).

4. Discussion

This study examined the relations of psychiatric diagnoses with smoking cessation and related processes by (1) assessing the prevalence of specific and comorbid psychiatric diagnostic groups in a recent sample of smokers trying to quit and (2) evaluating the relations of current and lifetime psychiatric diagnosis with nicotine dependence, cessation success, treatment effects, withdrawal symptoms, and treatment adherence. Findings revealed that even after excluding those with severe mental illness, a history of psychiatric diagnosis was common amongst smokers trying to quit, with 75% of the sample qualifying for diagnosis. Consistent with prior research (e.g., Piper, et al., 2010; Weinberger, et al., 2016), lifetime SUD was particularly common, occurring in about 65% of the sample. There was also considerable psychiatric comorbidity amongst smokers seeking cessation treatment. Almost half of the sample met diagnostic criteria for > one diagnosis, with lifetime anxiety and SUD being the most common comorbidity.

Both measures of nicotine dependence (FTND and WISDM-Total) were elevated across all diagnostic categories, with the exception of the non-significant relation between lifetime mood disorder and FTND. However, upon closer examination it appeared that secondary, rather than primary, dependence motives were especially sensitive to differences across all diagnostic categories. The SDM subscale was significantly different across diagnostic groups while the PDM subscale showed no significant differences by diagnostic status. This suggests that smokers with psychiatric diagnoses tend to differ from other smokers not in core dependence processes such as automatized smoking processes, craving, loss of control, and tolerance, but rather in the instrumental and contextually bound use of cigarettes. Thus, it may be that individuals with psychiatric diagnoses are especially likely to use smoking for relief of affective distress or to counter diagnostically related conditions such as anhedonia (Cook et al., 2015).

Psychiatric diagnosis was significantly related to short- but not long-term cessation likelihood. Compared to smokers with no psychiatric diagnoses, 8-week abstinence was less likely among those with past-year SUD, lifetime mood disorder, or > one lifetime psychiatric diagnosis. Participants also relapsed sooner if they had a past-year or lifetime SUD or > one lifetime psychiatric diagnosis. It is unclear whether the association between SUD and cessation failure is related to individual characteristics or person factors (e.g., impulsivity), or to lifestyle factors correlated with that diagnosis (e.g., social network, density of smoking cues, life stress, and poor adherence). It is also unclear why smokers with > one diagnosis are especially likely to fail early in the cessation attempt. This may be due to their greater lability or level of diagnostically related symptoms.

The finding that psychiatric comorbidity was significantly related to short- vs. long-term cessation suggests that psychiatric diagnoses may affect risk factors that exert their effects early in the post-quit process—such as abstinence-related craving. While there was no difference among psychiatric comorbidity groups in the degree to which cravings motivate smoking (i.e., the WISDM PDM subscale), those with psychiatric diagnoses tended to report greater real-time craving during the first week of the cessation attempt than did other participants, and craving in the first week post-quit predicted 8-week abstinence ($\beta = -0.14$, $p = .001$). Additionally, this lack of a significant long-term relation may be partly attributable to a lack of power. Table 1 shows that some comorbidities were associated with potentially meaningful differences in 6-month abstinence. Of those with no history of psychiatric diagnosis, 27.5% were abstinent, compared to 20.8% of participants with a lifetime history of mood disorder or 17.4% of those with a past-year SUD.

Results provided no clear basis for tailoring pharmacotherapy to psychiatric diagnosis. Treatments were similarly effective across diagnostic categories. While participants with a lifetime history of mood disorder demonstrated a substantial difference in 8-week cessation success with regard to patch versus varenicline (23.7 vs. 47.5%, respectively), this effect dissipated by 6 months. In fact, at 6-months C-NRT produced the highest abstinence rates (albeit, nonsignificantly higher). It may be that smokers with a lifetime history of mood disorder could benefit from longer-term varenicline treatment and this should be further explored in future research. It is clear that all smokers could benefit from interventions to improve medication adherence.

The results suggest that increased severity of abstinence-induced craving might account for some risk conferred by history of psychiatric diagnosis, more so than other vulnerabilities (e.g., negative affect). Those with lifetime psychiatric diagnoses tended to report especially large increases in abstinence-related increase in craving. They also reported high levels of negative affect, but such levels did not increase significantly with abstinence. This increase in craving occurred while participants were using pharmacotherapy, suggesting that non-pharmacotherapeutic interventions may be needed to help such smokers manage their cravings and to reduce their exposure to cues that may trigger such cravings. Although participants in this study were offered 6 smoking cessation counseling sessions over the course of 12 weeks, optimal counseling for smokers with psychiatric diagnoses might need to be modified in terms of frequency, timing, or duration (e.g., more frequent smoking cessation counseling early in the quit attempt). Another option might be a mobile intervention that provides additional support for coping with craving in real time. The potential utility of such interventions is also consistent with the idea that smokers are reporting smoking for instrumental and environmental reasons (versus primary dependence), which could be addressed via smoking cessation counseling and skill-building.

The lack of strong, robust relations between specific diagnoses and long-term smoking outcomes suggest that researchers should consider greater focus on broader trait-like, transdiagnostic risk factors in their efforts to understand relapse risk (Leventhal et al., 2012). This is also supported by the fairly consistent relations between cessation outcomes and counts of diagnoses or measures of general distress (Kulik and Glantz, 2017; Leventhal et al., 2012; Leventhal and Zvolensky, 2015). Such transdiagnostic factors might be associated with symptoms such as affective distress or with distress intolerance that undermine cessation and that spur the instrumental uses of smoking to mitigate such factors. This could account, in part, for the association of secondary motives with smoking.

Findings must be viewed within the context of the certain limitations and caveats. First, the parent study (Baker et al., 2016) did not find a significant benefit for varenicline or C-NRT, when each was compared to the patch alone, in terms of short- or long-term cessation success. This lack of effect and lack of a placebo control may contribute to the lack of differential treatment effects on cessation success among smokers with and without a psychiatric diagnosis. Second, all participants were offered intensive smoking cessation counseling. It is possible that psychiatric comorbidity vulnerabilities were mitigated to some extent by this support and pharmacotherapy treatment differences would be more evident had participants received less intense counseling. Third, the inclusion/exclusion criteria for this study (i.e., volunteers for a treatment research study, no presence of psychosis in the past year, no current moderate to severe depression, and smoking rate of < 5 cigarettes per day) limits the generalizability of findings. Fourth, relatively few participants had past-year diagnoses, which likely reduced power for such comparisons. In addition, the sample sizes within each overlapping diagnostic group were too small to examine with inferential tests. Finally, short-term cessation differences in outcomes were not robust with regard to correction for false-detection rate (i.e., Benjamini-Hochberg correction).

5. Conclusion

This study found that past-year SUD, lifetime mood disorder, and > one lifetime diagnosis, were related to short-term, but not long-term, cessation. Lifetime psychiatric diagnosis was related to elevated nicotine dependence, particularly to secondary dependence motives associated with instrumental use of tobacco. History of psychiatric diagnosis was also associated with increased withdrawal-related craving. Finally, there was little evidence that psychiatric diagnostic status moderated the effects of the tested pharmacotherapies on long-term abstinence. Findings suggest that psychiatric diagnoses affect risk factors that exert their effects early in the post-quit process and highlight the potential utility of examining transdiagnostic risk factors to better understand the relations between psychiatric vulnerabilities and the smoking cessation process.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Psychiatric diagnosis was significantly related to lower likelihood of short-term cessation
- Psychiatric diagnosis was not significantly related to long-term cessation likelihood
- Lifetime psychiatric diagnosis was related to elevated nicotine dependence
- History of psychiatric diagnosis related to increased withdrawal-related craving

Figure 1.

Past-year psychiatric diagnosis distribution and 8-week and 6-month abstinence rates.

^aNumbers do not add up to total because participants could have more than one specific diagnosis (e.g., a diagnosis of both Generalized Anxiety Disorder and Panic Disorder in the past year).

Figure 2.

Lifetime psychiatric diagnosis distribution and 8-week and 6-month abstinence rates.

aNumbers do not add up to total because participants could have more than one specific diagnosis (e.g., a diagnosis of both Generalized Anxiety Disorder and Panic Disorder in their lifetime)

Figure 3.

Latency to relapse for participants with a lifetime history of SUD compared to those with no lifetime psychiatric history. Cox-regression survival curves illustrate that participants with lifetime SUD relapse sooner than those with no lifetime psychiatric history (HR = 1.20; $p = .04$, 95% CI = 1.01–1.43).

Figure 4.

Latency to relapse for participants with a lifetime history of more than one psychiatric diagnosis compared to those with no lifetime psychiatric history. Cox-regression survival curves show that participants with more than one lifetime psychiatric diagnosis relapse sooner than those with no lifetime psychiatric history (HR = 1.25; $p = .02$, 95% CI = 1.04–1.49).

Figure 5.

8-week abstinence rates by treatment condition for lifetime psychiatric diagnoses. * $p < .05$.

^aResults remained unchanged after race and gender were added as covariates to the model.

Figure 6. 6-month abstinence rates by treatment condition for lifetime psychiatric diagnosis. None of these abstinence rates were statistically significant across diagnostic condition.

Table 1.

Logistic regression of impact of psychiatric diagnosis on initial, 8-weeks and 6 month post quit cessation success and sample distribution by diagnosis.

Diagnosis and Outcome Assessment Time	Percentage Abstinent	Wald	<i>p</i>	OR	95% CI
All Participants (<i>n</i> = 1051; 100%) ^a					
Initial	77.7				
8 weeks	47.4				
6 months	24.7				
No Psychiatric Diagnosis (<i>n</i> = 287; 27.3%) ^b					
Initial	79.0				
8 weeks	50.5				
6 months	27.5				
Past-year Anxiety Disorder (<i>n</i> = 123; 11.7%)					
Initial	76.3	0.36	0.55	0.86	[0.51–1.43]
8 weeks	44.7	1.16	0.28	0.79	[0.52–1.21]
6 months	22.8	1.01	0.32	0.78	[0.47–1.27]
Lifetime Anxiety Disorder (<i>n</i> = 358; 34.1%)					
Initial	77.9	0.11	0.75	0.94	[0.64–1.38]
8 weeks	45.8	1.42	0.23	0.83	[0.61–1.13]
6 months	25.7	0.27	0.60	0.91	[0.64–1.29]
Past-year Mood Disorder (<i>n</i> = 46; 4.4%)					
Initial	75.0	0.36	0.55	0.80	[0.38–1.68]
8 weeks	45.7	0.38	0.54	0.82	[0.44–1.54]
6 months	30.4	0.17	0.68	1.15	[0.58–2.27]
Lifetime Mood Disorder (<i>n</i> = 149; 14.2%)					
Initial	77.5	0.13	0.72	0.92	[0.56–1.49]
8 weeks	38.3	5.89	0.02^c	0.61	[0.41–0.91]
6 months	20.8	2.34	0.13	0.69	[0.43–1.11]
Past-year Substance Use Disorder (<i>n</i> = 86; 8.2%)					
Initial	67.5	4.61	0.03^d	0.55	[0.32–0.95]
8 weeks	36.0	5.49	0.02^d	0.55	[0.34–0.91]
6 months	17.4	3.50	0.06	0.55	[0.30–1.03]
Lifetime Substance Use Disorder (<i>n</i> = 646; 61.5%)					
Initial	77.3	0.32	0.57	0.91	[0.64–1.28]
8 weeks	45.7	1.88	0.17	0.82	[0.62–1.09]
6 months	23.4	1.84	0.18	0.80	[0.59–1.10]
More than One Lifetime Diagnosis (<i>n</i> = 490; 46.6%)					
Initial	78.1	0.08	0.78	0.95	[0.66–1.37]

Diagnosis and Outcome Assessment Time	Percentage Abstinent	Wald	<i>p</i>	OR	95% CI
8 weeks	43.1	4.05	0.04 ^e	0.74	[0.55–0.99]
6 months	21.6	3.45	0.06	0.73	[0.52–1.02]

Note. Bolded text indicates statistically significant effects. Smoking status coded as 0 = smoking, 1 = abstinent. Initial smoking status defined as achieving abstinence for 24 hours at any time during the first seven days after quit date.

^aPercentages of diagnoses do not add up to 100 because some participants have more than one diagnosis.

^bNo history of any psychiatric diagnosis was used as the comparison group for all analyses.

^cResults remain significant even after individuals with past year mood disorder diagnosis were removed from analyses.

^dResults become not significant when covariates of race, gender, and treatment condition are included in the model.

^eResults remain significant when comparing participants with more than one lifetime diagnosis to those with only one lifetime diagnosis. All significant results become not significant when using the Benjamini-Hochberg correction.

Table 2.

Linear regression analyses examining the relations between psychiatric diagnostic category and nicotine dependence.

Diagnosis and Outcome Dependence Measure	Mean (SD)	<i>t</i>	df	<i>p</i>	95% CI
No Lifetime Psychiatric Disorder					
FTND	4.46 (2.03)				
WISDM-Total	40.65 (12.71)				
WISDM-PDM	4.39 (1.33)				
WISMD-SDM	3.30 (1.20)				
Past-year Anxiety Disorder					
FTND	5.08 (2.15)	2.77	404	0.006	[0.18–1.06]
WISDM-Total	47.52 (12.92)	4.97	403	<0.001	[4.16–9.60]
WISDM-PDM	4.98 (1.28)	1.18	395	0.24	[−0.09–0.35]
WISMD-SDM	3.89 (1.24)	2.44	395	0.02	[0.05–0.49]
Lifetime Anxiety Disorder					
FTND	4.88 (2.14)	2.52	638	0.01	[0.09–0.75]
WISDM-Total	46.11 (12.24)	5.50	636	<0.001	[3.51–7.41]
WISDM-PDM	4.83 (1.29)	0.73	626	0.47	[−0.10–0.22]
WISMD-SDM	3.81 (1.16)	3.30	626	0.001	[0.11–0.43]
Past-year Mood Disorder					
FTND	5.17 (2.32)	2.15	328	0.03	[0.06–1.36]
WISDM-Total	53.19 (12.24)	6.23	327	<0.001	[8.59–16.50]
WISDM-PDM	5.22 (1.27)	−0.89	322	0.37	[−0.47–0.18]
WISMD-SDM	4.58 (1.17)	5.45	322	<0.001	[0.56–1.19]
Lifetime Mood Disorder					
FTND	4.83 (2.27)	1.72	431	0.09	[−0.05–0.80]
WISDM-Total	47.61 (12.41)	5.46	430	<0.001	[4.45–9.47]
WISDM-PDM	4.83 (1.32)	−0.97	424	0.33	[−0.31–0.11]
WISMD-SDM	4.03 (1.17)	5.01	424	<0.001	[0.31–0.72]
Past-year Substance Use Disorder					
FTND	5.11 (2.01)	2.56	367	0.02	[0.15–1.13]
WISDM-Total	47.49 (13.12)	4.29	364	<0.001	[3.70–9.99]
WISDM-PDM	4.85 (1.24)	−0.63	360	0.55	[−0.32–0.17]
WISMD-SDM	4.02 (1.31)	3.80	360	<0.001	[0.23–0.74]
Lifetime Substance Use Disorder					
FTND	4.88 (2.08)	2.79	927	0.005	[0.12–0.70]
WISDM-Total	44.83 (12.44)	4.68	923	<0.001	[2.42–5.93]
WISDM-PDM	4.72 (1.28)	0.41	914	0.68	[−0.11–0.17]
WISMD-SDM	3.71 (1.20)	3.19	530.81	0.002	[0.09–0.37]

Diagnosis and Outcome Dependence Measure	Mean (SD)	<i>t</i>	df	<i>p</i>	95% CI
More than One Lifetime Diagnosis					
FTND	4.98 (2.08)	0.12	771	0.001	[0.21–0.82]
WISDM-Total	46.26 (12.19)	6.06	768	<0.001	[3.79–7.42]
WISDM-PDM	4.85 (1.27)	0.86	761	0.39	[−0.08–0.21]
WISMD-SDM	3.83 (1.17)	3.71	761	<0.001	[0.13–0.43]

Note. Bolded text indicates statistically significant effects. Comparison group for all analyses was participants with no history of psychiatric diagnosis. All results remained the same after including gender and race as covariates in the model. FTND: Fagerström Test of Nicotine Dependence [37]. WISDM-Total: Brief Wisconsin Inventory of Smoking Dependence Motives [38]. WISDM-PDM: Brief Wisconsin Inventory of Smoking Dependence Motives, Primary Dependence Motives Scale; raw scores are presented here. WISDM-SDM: Brief Wisconsin Inventory of Smoking Dependence Motives, Secondary Dependence Motives Scale; raw scores are presented here. All results remain unchanged following Benjamini-Hochberg corrections.

Table 3.

Linear regression analyses examining the relations between psychiatric diagnostic category and average withdrawal symptoms for the first week following the target quit date after controlling for pre-quit withdrawal scores.

Diagnosis and Outcome Withdrawal Scale	Mean (SD)	<i>t</i>	β	R^2	<i>p</i>	95% CI
No Lifetime Psychiatric Disorder						
WSWS-Negative Mood	1.76 (1.06)					
WSWS-Craving	2.90 (1.70)					
Past-year Anxiety Disorder						
WSWS-Negative Mood	2.32 (1.30)	1.74	0.07	0.00	0.08	[-0.02–0.36]
WSWS-Craving	3.57 (1.82)	1.38	0.06	0.00	0.17	[-0.10–0.54]
Lifetime Anxiety Disorder						
WSWS-Negative Mood	3.10 (1.73)	0.73	0.02	0.00	0.47	[-0.08–0.18]
WSWS-Craving	3.54 (1.73)	2.81	0.10	0.01	<0.01	[0.11–0.60]
Past-year Mood Disorder						
WSWS-Negative Mood	2.45 (1.29)	1.65	0.07	0.01	0.10	[-0.05–0.51]
WSWS-Craving	3.89 (1.75)	1.58	0.07	0.01	0.12	[-0.09–0.82]
Lifetime Mood Disorder						
WSWS-Negative Mood	2.13 (1.17)	0.81	0.00	0.00	0.42	[-0.10–0.25]
WSWS-Craving	3.68 (1.72)	2.68	0.12	0.01	<0.01	[0.42–1.13]
Past-year Substance Use Disorder						
WSWS-Negative Mood	2.08 (1.25)	1.73	0.08	0.01	0.09	[-0.03–0.43]
WSWS-Craving	3.47 (1.87)	1.06	0.05	0.00	0.29	[-0.02–0.57]
Lifetime Substance Use Disorder						
WSWS-Negative Mood	1.95 (1.06)	0.59	0.02	0.00	0.56	[-0.09–0.16]
WSWS-Craving	3.32 (1.74)	2.22	0.07	0.00	0.03	[0.03–0.46]
More than One Lifetime Diagnosis						
WSWS-Negative Mood	2.01 (1.05)	1.09	0.03	0.00	0.28	[-0.06–0.20]
WSWS-Craving	3.41 (1.71)	2.49	0.08	0.01	0.01	[0.06–0.53]

Note. Bolded text indicates statistically significant effects. Comparison group for all analyses was participants with no history of psychiatric diagnosis. All results remained the same after including treatment, gender, and race as covariates in the model. WSWS-Negative Mood: Wisconsin Smoking Withdrawal Scale, Negative Mood Subscale [39]. WSWS-Craving: Wisconsin Smoking Withdrawal Scale, Craving Subscale [39]. All results remain unchanged following Benjamini-Hochberg correction.