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What a Difference a Day Makes: Differences in Initial Abstinence Response During a Smoking Cessation Attempt

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Abstract

Aims—To 1) identify distinct classes of smokers based on quit day withdrawal symptoms and 2) explore the relations between withdrawal classes and demographics, tobacco dependence, treatment, and smoking outcomes.

Design—Secondary data analysis of participants (N=1504) in a randomized double-blind placebo-controlled multi-site smoking cessation trial who provided ecological momentary assessments of withdrawal symptoms on their quit day. Participants received smoking cessation counseling and were randomized to receive placebo or one of five active pharmacotherapies.

Setting—Research offices in Madison and Milwaukee, Wisconsin, USA.

Participants—Adult smokers (N=1236; 58% female, 86% white), recruited from the community via advertisements, who abstained on their quit day.

Measurements—Demographics and tobacco dependence were assessed at baseline and participants carried palmtop computers to record withdrawal symptoms (craving, negative affect, difficulty concentrating, hunger, and anhedonia) on their quit day. Point-prevalence abstinence and latency to relapse were assessed at Weeks 8 and 26.

Findings—Latent class analysis identified four withdrawal classes (AIC=70.09): Moderate Withdrawal (64% of sample), High Craving-Anhedonia (8% of sample), Affective Withdrawal (13% of sample) and Hunger (15% of sample). The High Craving-Anhedonia class reported significantly higher dependence ($p<0.01$), were less likely to have received combination nicotine

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replacement, reported lower Week 8 abstinence rates, and relapsed sooner than those in the Moderate Withdrawal class ($p<0.05$). The Affective Withdrawal class reported higher levels of baseline negative affect and lifetime psychopathology ($p<0.05$) and relapsed more quickly than the Moderate Withdrawal class ($p<0.01$).

Conclusions—While the majority of smokers report typical levels of withdrawal symptoms on their quit day, more than one-third report extreme craving or extreme negative affective or extreme hunger responses to initial abstinence. These distinct quit-day withdrawal symptom patterns are related to baseline characteristics, treatment, and cessation success.

Keywords

Withdrawal; Smoking Cessation; Latent Class Analysis

Introduction

Nearly 1 billion people in the world continue to smoke cigarettes despite the health risks posed by tobacco smoke [1]. Theory, empirical evidence, and clinical experience all point to withdrawal—the cluster of symptoms resulting from smoking cessation or reduction—as a primary determinant of smoking persistence (see [2] for review). Tobacco withdrawal includes a range of physical and affective symptoms including hunger, craving, negative affect (i.e., sadness, anger, anxiety), difficulty concentrating, and sleep disturbance [3–5]. In addition, emerging evidence suggests that anhedonia (i.e., reduced pleasure in response to reward) is a unique component of the tobacco withdrawal syndrome [6]. Craving and negative affect are the two withdrawal symptoms most robustly associated with tobacco dependence and abstinence (e.g., [7–9]); anhedonia has also been linked with dependence and failure to quit [6].

According to classical addiction theory, initial abstinence should result in a precipitous rise in withdrawal symptoms among dependent smokers (see [2] for review). Research has demonstrated that withdrawal symptoms tend to spike during the first few days of abstinence, then decline in the following days (e.g., [10–12]). Research has also demonstrated the importance of the first day of abstinence, linking quit day lapses to ultimate relapse [13, 14]. However, while we know that smoking on the first day of a quit attempt may set the stage for ultimate cessation failure and that withdrawal plays a critical role in achieving and maintaining abstinence, little is known about how withdrawal symptoms on the in first day of abstinence affect ultimate cessation success. Moreover, few, if any, studies have examined quit day withdrawal symptom patterns among treatment-seeking smokers, although some studies have examined quit day withdrawal in the context of studying the jump in withdrawal symptoms from pre-quit to post-quit [15–17]; also cf [18, 19].

In addition to a limited understanding of the effects of initial quit day abstinence on withdrawal symptoms, heterogeneity across individuals in their initial reaction to abstinence has not been sufficiently explored (cf. [20]). Research suggests that withdrawal, though a syndrome, is not a homogenous experience; rather, the timing and severity of different symptoms vary [11]. Person-centered analyses, such as cluster analysis or latent class

analysis (LCA), hold potential as an innovative method for examining patterns of quit day withdrawal symptoms during an aided quit attempt. In contrast to more traditional variable-centered approaches, which might examine each component of withdrawal separately or combined as a latent construct, a person-centered approach examines patterns or profiles among various withdrawal symptoms and their interactions as well as the predictors and outcomes associated with different withdrawal symptom patterns [21].

To date, person-centered withdrawal analyses have focused exclusively on retrospective reports of lifetime symptoms (i.e., those that ever occurred during a quit attempt assessed via a structured clinical interview) or withdrawal during the days or weeks following the quit day (e.g., [22–25]). Latent class analyses of retrospective symptoms found withdrawal classes that differ only by severity [26–28]. Conversely, cluster analyses of prospective longitudinal data have shown that distinct withdrawal profiles can emerge over time during an aided quit attempt (e.g., withdrawal that improves, remains elevated or increases over time [29]). This research will conduct person-centered analyses on real-time reports of quit-day withdrawal symptoms that occurred as part of an aided quit attempt.

Using a person-centered approach to identify distinct symptom patterns of quit-day withdrawal could be used as an index of early treatment response and relapse risk. Effective treatments (both pharmacotherapeutic and behavioral) have been shown to more than double quit rates, but the effectiveness of such treatments appear to have stalled at 20–35% [30, 31]. Although there are no compelling data suggesting that tailoring treatment to individual baseline characteristics (e.g., gender, socioeconomic status, psychiatric diagnosis) other than dependence (e.g., nicotine replacement dose is based on cigarettes per day or time to first cigarette) is helpful [30], adapting treatment based on initial response to that treatment may improve clinical outcomes.

Rose and colleagues have conducted research on adapting smoking cessation interventions based on treatment response prior to the target quit date [32, 33]. These studies showed that participants were less likely to quit smoking if they failed to achieve a 50% prequit reduction while using prequit nicotine patch. However, abstinence rates in the group not able to reduce with the prequit nicotine patch were bolstered if participants received additional and/or different medication rather than continuing on the nicotine patch alone. Thus, treatment adaptation may be more successful if done early in the cessation process, before a smoker has started down the slippery slope of lapsing and relapse.

Examination of the current literature reveals important questions that need to be answered. What profiles of withdrawal symptoms are present on the first day of quitting smoking? Are there demographic or dependence characteristics that predict response to initial abstinence? How does treatment assignment relate to withdrawal class membership? Are quit-day withdrawal profiles associated with abstinence? The aims of the current research are to use real-time data from a large, placebo-controlled smoking cessation trial to: 1) identify distinct classes of smokers based on quit-day withdrawal symptoms and 2) explore the relations between withdrawal classes and baseline characteristics (e.g., demographics, tobacco dependence, psychopathology), treatment, and smoking outcomes. The answers to these questions may improve understanding of the cessation process and help inform the

development and provision of treatment, including the development of treatment strategies designed to adapt to comprehensive profiles of withdrawal experienced in response to quit-day abstinence.

Methods

Study Design and Participants

This secondary data analysis used data from 1236 participants (58% female, 86% white) of the 1504 who participated in a placebo-controlled, double-blind smoking cessation clinical trial (see [34] for details). All participants were offered 6 individual counseling sessions conducted by trained health counselors and were randomized to receive nicotine patch (n = 216), nicotine lozenge (n = 211), bupropion (n = 213), patch + lozenge (n = 228), bupropion + lozenge (n = 221), or placebo (n = 147).

Participants completed baseline assessments of demographics, psychiatric history [35], and tobacco dependence [36–38]. Participants used palmtop computers to complete ecological momentary assessments (EMAs) 4 times per day (morning, evening and 2 random prompts) for 2 weeks pre-quit and 2 weeks post-quit. Each prompt assessed participants' experiences of withdrawal symptoms (hunger [Hungry; Thinking about food a lot], poor concentration [Hard to pay attention; Difficult to think clearly], anxiety [Tense or anxious; Impatient], sadness [Sad or depressed; Hopeless or discouraged], anger [Bothered by negative moods such as anger, frustration, and irritability; Irritable or easily angered], and craving [Bothered by desire to smoke a cigarette; Urge to smoke]) in the previous 15 minutes on a scale of 1=not at all to 5=extremely. Anxiety, sadness, and anger were combined into a single negative affect withdrawal variable (e.g., [39]). The evening prompt also assessed anhedonia (lack of pleasure) during the day (mean of items assessing pleasure in contact with others, recreation, and work/school/chores on a 1–10 scale). Seven-day point-prevalence abstinence and daily smoking status were assessed at 8 weeks (the end of all treatment except lozenge, which ended at 12 weeks) and 6 months post quit day.

Participants from the initial trial were included in the analyses if they provided EMA data and were abstinent on their quit day. There were no significant differences in age, gender, total FTND score, or cigarettes smoked per day between those who were and were not included in the analyses. However, white participants were more likely to quit and provide quit-day EMA data, and therefore be included in the analyses, than non-white participants.

Measures

Indicators of Class Membership—EMA data on five withdrawal dimensions—hunger, poor concentration, negative affect (mean of anxiety, sadness, and anger), craving, and anhedonia—from the quit day were used to create five latent class indicators. Measures of hunger, poor concentration, negative affect, and craving were each averaged across all EMA occasions on the quit day. The five withdrawal indicators were then coded to reflect high (the most severe 20% for that variable) vs. not high (the remaining 80%) mean responses. Therefore, classes were created based on a reasonable proportion of participants who reported extremely elevated levels of a specific symptom.

Baseline Factors Related to Class Membership—We examined how individuals in each latent class differed on a the following baseline factors: 1) demographics (gender, age); 2) smoking history (age at first cigarette, number of cigarettes, and years smoked cigarettes); 3) nicotine dependence (Fagerström Test for Nicotine Dependence; FTND [36] and Wisconsin Inventory for Smoking Dependence Motives; WISDM [37]); 4) baseline positive and negative affect (Positive and Negative Affect Schedule; PANAS [40]); and 5) lifetime clinical depression, anxiety or substance use disorders (DSM-IV aligned Composite International Diagnostic Interview structured clinical interview; CIDI [35, 41]).

Outcomes—Seven-day point-prevalence abstinence was assessed at 8 weeks and 6 months post-quit. Participants reported smoking status for each day of the study using timeline-follow-back [42, 43]. These data were used to calculate the number of days to relapse (i.e., smoke for 7 consecutive days).

Analytic Plan

First, models with different numbers of classes were estimated with SAS PROC LCA [44]. Model selection was based on minimizing the Akaike Information Criteria (AIC; [45]) and Bayesian Information Criteria (BIC; [46]). Once the number of latent classes was determined, we assigned individuals to the best-fitting class based on their probability of class membership. We chose the classify-analyze approach in which we assigned participants to a class based on the probability of being in that class, to enable us to perform all subsequent analyses including survival analyses and pairwise tests, which are not possible within PROC LCA. We explored the latent classes by examining mean scores within each class on baseline factors (demographic, affective, and smoking-related variables), as well as the relation between class membership and treatment group using multinomial logistic regression. We also conducted a multivariable multinomial logistic regression that included all baseline factors and treatment to identify the factors most strongly, independently related to class membership. Variables that had significant omnibus tests in the multinomial regressions were then analyzed to determine which classes were significantly different from the Moderate Withdrawal class. Finally, we calculated the association between withdrawal class membership and cessation outcome to further validate the classes. This analysis was designed to answer the exploratory question of whether initial cessation experience was related to long-term outcome. We did not attempt to determine whether quit-day withdrawal experience predicts long-term outcome over and above other variables or explore possible mediation (e.g., does quit-day withdrawal class mediate the relation between a baseline factor and long-term outcome), given the exploratory nature of this research. Point-prevalence abstinence at 8 weeks and 6 months was analyzed using logistic regression and latency to relapse was analyzed using Cox regression.

Results

Model fit information was compared across models with varying numbers of latent classes. The BIC suggested a 2-class model and the AIC suggested a 4-class model (see Table 1). Thus, we considered models with 2–4 latent classes. Based on the fit indices, the BIC's tendency to underextract latent classes [47], and the clarity of class interpretation, we

selected the 4-class model of quit-day withdrawal. Sensitivity analyses were conducted using the top 15% and 25% of scores as the “severe” category and those analyses also supported a 4-class model with consistent interpretation of the 4 classes.

The parameter estimates from the LCA model shown in Table 2 indicate the relative class sizes and the probability of scoring high (the most severe 20% for that variable) on each withdrawal symptom given membership in each class. The Moderate Withdrawal class was the most common, comprising 64% of the sample. Participants in this class were the least likely to report high levels of any individual symptom, with probabilities ranging from 0.01 for hunger to 0.17 for anhedonia. The High Craving-Anhedonia class was the smallest class, comprising only 8% of the participants. In this class, participants had greater than 0.7 probability of reporting high levels of both anhedonia and craving, as well as 0.6 probability of reporting high negative affect. The Affective Withdrawal class, comprising 13% of the sample, had elevated probabilities of scoring in the high range on poor concentration and negative affect (0.85 and 0.96, respectively). Finally, the Hunger class (15%) was marked by a relatively high probability (0.63) of reporting high quit-day hunger, but low probabilities of scoring high on the other indicators.

We examined baseline demographic, affect and dependence-related factor differences among the four classes by classifying participants into the latent class to which they had the highest probability of belonging. Among individuals assigned to a specific class, the mean probability of being in that class was 0.89, representing low classification error [48]. The series of univariate multinomial regression analyses for each baseline covariate revealed that relative to the Moderate Withdrawal class, participants in the High Craving-Anhedonia class had higher scores on dependence measures (i.e., FTND, and WISDM Total, Primary, and Secondary Motives) and had higher negative affect, lower positive affect, and a greater likelihood of lifetime anxiety or substance use disorder (see Table 3). Those in the Affective Withdrawal class, compared to the Moderate class, reported smoking fewer years, higher scores on most dependence measures, higher negative and lower positive affect, and higher rates of lifetime mood, anxiety, and substance use disorders. Smokers in the Hunger class reported smoking fewer years, higher WSDM Total scores, more negative affect, and a higher rate of lifetime substance use disorder compared to those in the Moderate class. Participants in the Moderate Withdrawal class were older, on average, than those in all other classes.

We also examined the association between treatment and quit-day withdrawal profiles (see Table 3). The emergence of the High Craving-Anhedonia group led us to hypothesize that this class would be less common in the Patch + Lozenge group, given our prior results that combination nicotine replacement (NRT) significantly suppresses craving compared to monotherapy [49]. The omnibus test was not significant at the $p<0.05$ level for any of the 5 treatment conditions compared to the placebo, although the p-values for Patch and Patch + Lozenge were $p=0.09$ and $p=0.06$ respectively. When we conducted the specific post-hoc test of our hypothesis [50, 51] we found that participants in the Patch + Lozenge group were less likely to be in the High Craving-Anhedonia class than the Moderate class ($p=0.04$).

In the multivariate multinomial regression, positive affect, negative affect, WISDM Total, lifetime substance use disorder, and receiving nicotine patch + nicotine lozenge remained significant predictors of class membership in the full model (see Table 4). Specifically, compared to participants in the Moderate class, participants in the High Craving-Anhedonia class reported lower positive affect, higher negative affect, higher WISDM Total scores, and higher lifetime substance use disorder rates. The Affective Withdrawal class was predicted by higher negative affect and WISDM Total scores, and the Hunger class was predicted by higher WISDM Total scores and lifetime substance use disorders compared to the Moderate class.

Finally, we explored the associations between quit-day withdrawal latent class and cessation outcome through a series of logistic regression and survival (Cox regression) models, with the Moderate Withdrawal class serving as the reference group (Table 5). Participants in the High Craving-Anhedonia class were more likely to have smoked at 8 weeks and relapsed more quickly compared to the Moderate Withdrawal class. In addition, participants in the Affective Withdrawal class relapsed more quickly compared to the Moderate Withdrawal class. There were no significant differences in abstinence rates for the Hunger compared to Moderate Withdrawal group.

Discussion

This research identified four distinct types of quit-day withdrawal experiences that were characterized by: 1) high levels of craving and anhedonia; 2) high levels of negative affect and concentration difficulties; 3) high levels of hunger, and; 4) moderate levels of all withdrawal symptoms. These findings differ from retrospective research suggesting that, with the exception of severity ratings, withdrawal experience is largely similar across individuals [26–28]. These person-centered analyses using prospective data support the notion that withdrawal is a heterogeneous construct, that symptoms covary in different ways among different people, and that this variability appears to have theoretical and clinical significance. Further, this research demonstrates that meaningful heterogeneity in the withdrawal experience can be detected on the very first day of abstinence (cf. [9]).

Research has shown that higher baseline nicotine dependence is related to higher levels of quit-day withdrawal [19, 52, 53] and that early withdrawal predicts long-term cessation [22, 54, 55]. This is consistent with the High Craving-Anhedonia group that, though small (n=72), reported significantly greater dependence and a reduced likelihood of point-prevalent abstinence at 8 weeks and reduced relapse latency, relative to the Moderate Withdrawal class. Other EMA research also shows that craving and anhedonia predict smoking following a quit attempt [6, 56, 57]. Interestingly, combination NRT reduced the number of participants classified in the High Craving-Anhedonia withdrawal class, illustrating the importance of nicotine agonists to mitigate relapse risk among those with severe post-quit urges and reward deficits.

The emergence of a High Craving-Anhedonia group has theoretical implications as well as it suggests an important connection between post-quit deficits in reward responsivity and the urge to smoke. Previous research has shown that anhedonic smokers experience

disproportionate losses in positive mood during early nicotine deprivation, which in turn, mediates elevated craving for cigarettes [39]. These results suggest that, for some smokers, the role of craving in smoking motivation may be linked with blunted reward functioning following quitting. In other words, smokers who experience significant losses in reward function following quitting may especially crave smoking for its ability to restore pleasurable response to rewarding stimuli [6]. It is also important to note that members of the High Craving-Anhedonia group had a 0.60 probability of reporting elevated negative affect. Perhaps those who experience elevated post-quit anhedonia have fewer positive emotional resources with which to buffer the stress of nicotine deprivation, leading to increased post-quit negative affect. Future research is needed to better understand the interaction between anhedonia, craving and negative affect.

High negative affect emerged in combination with concentration difficulties in the Affective Withdrawal class. This cluster of symptoms is consistent with symptoms comprised by affective disorders such as major depression. Smokers who primarily reacted with high levels of affective and cognitive distress to quit-day abstinence (13% of the sample) had significantly higher levels of baseline negative affect and dependence scores and were more likely to report a lifetime history of major depression, anxiety, or substance use disorders than the Moderate Withdrawal group. It is possible that smokers with a history of psychopathology, who were more likely to be in the Affective Withdrawal group, are more vulnerable to affective distress during a stressor such as quitting smoking. However, it may be that such smokers are more sensitized to increases in negative affect and concentration difficulties and therefore more likely to note and report them. Thus, baseline affective vulnerability, in combination with high levels of dependence, may manifest as extremely high levels of quit day negative affect. Treatment assignment did not appear to reduce the likelihood of experiencing such symptoms.

Smokers in the Affective Withdrawal group returned to regular smoking more quickly than the Moderate Withdrawal group; however, there were no significant differences in point-prevalence abstinence rates. This lack of an effect of quit-day negative affect on abstinence illustrates the complexity of the role of negative affect in smoking motivation. Although extant theory and research suggest that negative affect motivates smoking (e.g., [11, 17, 58–60]), including negative affect elicited during a laboratory deprivation [54], studies using EMA data have failed to show an association between negative affect and smoking (e.g., [57, 59]). However, one EMA study that examined individual differences in response to negative affect, rather than mean responses, found that high negative affect was related to lapsing [61]. The variability in these findings may be related to differences in analytic approach, type of data used (i.e., EMA vs. retrospective reports), and timing of assessments. The current research presents evidence that although extreme quit-day negative affect, especially when combined with high levels of concentration difficulties, shortens the duration of abstinence, it does not appear to influence long-term cessation.

The presence of a Hunger class was surprising. This group reported higher levels of WISDM Secondary Dependence Motives and were more likely to have a history of substance use disorders. These findings suggest that the endorsement of smoking for instrumental goals, such as reducing hunger, may be related to withdrawal suppression in addition to weight

control. It may also be that such participants have learned to use smoking as a way to cope with abstaining from other substances. This increase in appetitive motivation for other rewards may be a specific concern for such smokers. However, it is important to note that members of the Hunger class were not more likely to relapse, consistent with prior research suggesting that hunger is not strongly related to cessation outcome [62, 63].

The results from this research are preliminary and should be considered hypothesis generating. If replicated, they could be used to inform clinical practice. For instance, it may be important to understand whether high levels of quit-day negative affect are associated with feelings of anhedonia and strong cravings or concentration difficulties. If a smoker's severe negative affect is associated with high cravings and anhedonia, combination NRT might help mitigate these symptoms. However, if a smoker is experiencing extreme negative affect and cognitive difficulties, there is no evidence to suggest that one cessation medication is better than another. Furthermore, smoking cessation counseling could educate smokers about the possibility of experiencing extreme levels of specific symptoms on their quit day, to work with such smokers to develop coping strategies for these emerging symptoms, and to enhance motivation to stay smoke-free. Future research is needed to examine the impact of tailoring treatment to pre-quit variables as well as adapting treatment in response to initial quit-day abstinence.

It is important to acknowledge the limitations of the current research. First, participants in this study were highly motivated to quit smoking and agreed to participate in a longitudinal treatment study with intensive counseling and pharamcotherapy; therefore, these results may not generalize to all smokers attempting to quit. Second, we examined symptoms on the quit day, rather than changes in symptoms from pre- to post-quit. The quit-day symptoms undoubtedly reflect multiple factors, including prior mental state, but previous research illustrates that abstinence contributes significantly to these ratings and that post-quit withdrawal symptoms (i.e., current levels of distress) may be more important than changes in ratings from pre- to post-quit [6, 11]. Future research is needed to investigate person-centered differences in changes in symptoms on the quit day. Finally, these results focused only on the first day of abstinence and did not assess all identified withdrawal symptoms (e.g., restlessness, difficulty sleeping). Future research is needed to understand the relation of quit-day withdrawal to all withdrawal symptoms on subsequent days, treatment response, and cessation success. Further, we need to understand whether individual differences in response to initial abstinence are consistent across quit attempts. Examining differences in initial withdrawal profiles over repeated quit attempts may provide insight into the mechanisms that underlie dependence and relapse.

In sum, this research illustrates that although withdrawal symptoms may be correlated, a distinct pattern of findings emerges when the symptoms are examined using person-centered analyses to identify profiles of response to initial abstinence. These findings suggest that on the quit day, the majority of smokers (64%) report coping with typical levels of withdrawal symptoms. However, more than one-third had extreme craving and anhedonia (8%), negative affective (13%), or hunger (15%) responses to initial abstinence. These distinct quit-day withdrawal symptom patterns are related to baseline characteristics, treatment response, and ultimate cessation success.

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Table 1

Fit statistics for LCA models of withdrawal

# of Classes	AIC	BIC
1	609.40	635.00
2	84.94	**141.25**
3	76.06	163.09
4	**70.09**	187.84
5	71.75	220.22

Note. AIC=Akaike Information Criteria, BIC=Bayesian Information Criteria

Table 2

Estimated probability of scoring high on each of the withdrawal indices by latent class

	Moderate Withdrawal	High Craving-Anhedonia	Affective Withdrawal	Hunger
Estimated Proportion	**(64%)**	**(8%)**	**(13%)**	**(15%)**
Anhedonia	0.17	**0.71**	0.14	0.00
Hunger	0.01	0.51	0.41	**0.63**
Poor concentration	0.45	0.40	**0.85**	0.14
Negative Affect	0.04	**0.60**	**0.96**	0.01
Craving	0.09	**0.70**	0.41	0.22

Note. Bolded values indicate probabilities >.60 to facilitate interpretation

Table 3

Descriptive statistics for each withdrawal latent class

	Moderate Withdrawal (N=877)	High Craving-Anhedonia (N=72)	Affective Withdrawal (N=154)	Hunger (N=133)	X^2
	M(SD)	M(SD)	M(SD)	M(SD)	
Baseline Covariates					
% Female	57.8	62.5	61.7	54.9	1.98
Age	45.8 (10.9)	42.7 (10.3)*	42.3 (11.1)***	42.6 (11.5)**	23.32***
Age at first cigarette	14.7 (3.8)	13.87 (3.06)	14.1 (3.7)	14.5 (4.0)	238.0
Years smoked	31.1 (11.0)	28.9 (10.6)	28.1 (11.1)**	28.1 (11.5)*	14.06**
Cigarettes per day	21.4 (9.0)	23.82 (9.96)***	20.9 (7.6)	21.1 (10.3)	5.23
Positive affect	33.4 (7.5)	30.0 (6.36)***	32.2 (7.5)	33.3 (7.8)	15.70**
Negative affect	17.0 (6.5)	20.6 (7.5)***	22.0 (7.9)***	18.3 (6.9)*	71.17***
WISDM Total	51.9 (12.4)	58.7 (13.25)***	59.3 (11.8)***	55.1 (14.4)***	60.13***
WISDM Primary	4.8 (1.2)	5.4 (1.1)***	5.2 (1.0)***	4.9 (1.2)	36.36***
WISDM Secondary	3.6 (1.0)	4.1 (1.1)***	4.3 (1.0)***	3.9 (1.2)**	58.72***
FTND total	5.3 (2.1)	6.2 (1.9)***	5.9 (2.0)**	5.2 (2.4)	22.54***
% Lifetime Depression	15.4	22.5	26.7**	20.0	12.15**
% Lifetime Anxiety	35.8	47.9*	50.7**	43.8	15.58**
% Lifetime SUD	52.2	69.0**	61.3*	66.9**	18.36***
Treatment Group					
Placebo	10.9%	16.7%	14.9%	12.0%	REF
Bupropion	15.8%	23.6%	23.4%	15.8%	.18
Lozenge	16.6%	19.4%	15.6%	20.3%	1.92
Patch	18.5%	12.5%$^{+}$	13.0%*	18.8%	6.51^{+}
Bupropion + Lozenge	18.6%	16.7%	18.8%	12.8%	3.27

	Moderate Withdrawal (N=877)	High Craving-Anhedonia (N=72)	Affective Withdrawal (N=154)	Hunger (N=133)	X^2
	M(SD)	M(SD)	M(SD)	M(SD)	
Baseline Covariates					
Patch + Lozenge	19.5%	11.1%*	14.3%$^{+}$	20.3%	7.39^{+}

Note.

$^{+}$ $p < .10$,

* $p < .05$,

** $p < .01$,

*** $p < .001$; all mean comparisons are relative to the Moderate Withdrawal class.

LL = log likelihood. WISDM = Wisconsin Inventory of Smoking Dependence Motives. FTND = Fagerström Test of Nicotine Dependence. SUD = Substance Use Disorder.

Table 4

Multivariate multinomial logistic regression including all baseline covariates and treatment conditions to predict withdrawal latent class membership (Odds Ratio [95% confidence interval])

	Moderate Withdrawal (N=877)	High Craving-Anhedonia (N=72)	Affective Withdrawal (N=154)	Hunger (N=133)	X^2
Female	1.00	1.4 [.78–2.50]	.89 [.59–1.33]	.89 [.59–1.99]	2.26
Age	1.00	1.01 [.96–1.06]	.98 [.94–1.02]	.98 [.94–1.02]	2.44
Age at first cigarette	1.00	.95 [.88–1.03]	.98 [.93–1.04]	1.01 [.95–1.06]	1.97
Years smoked	1.00	1.02 [.91–1.01]	.98 [.95–1.03]	.99 [.95–1.03]	2.51
Cigarettes per day	1.00	.91 [.98–1.05]	.97+ [.95–1.00]	1.00 [.97–1.03]	5.19
Positive affect	1.00	.95** [.92–.98]	.99 [.96–1.01]	1.00 [.98–1.03]	9.56*
Negative affect	1.00	1.05*** [1.01–1.09]	1.07*** [1.04–1.09]	1.01 [.98–1.04]	27.2***
WISDM Total	1.00	1.03* [1.01–1.05]	1.04*** [1.02–1.06]	1.02* [1.01–1.04]	26.14***
FTND total	1.00	1.12 [.95–1.3]	1.13* [1.01–1.27]	.95 [.85–1.07]	7.29+
Lifetime Depression	1.00	1.02 [.52–2.00]	1.43 [.90–2.27]	1.23 [.74–2.02]	2.54
Lifetime Anxiety	1.00	1.25 [.72–2.17]	1.14 [.77–1.70]	1.18 [.79–1.77]	1.28
Lifetime SUD	1.00	1.90* [1.07–3.37]	1.17 [.79–1.73]	1.75** [1.17–2.63]	11.36*
Placebo	1.00				
Bupropion	1.00	1.21 [.53–2.8]	1.37 [.73–2.6]	1.03 [.50–2.10]	1.05
Lozenge	1.00	.78 [.53–1.77]	.79 [.40–1.55]	1.07 [.53–2.14]	.79
Patch	1.00	.49 [.32–1.88]	.48* [.23–.99]	1.02 [.51–2.03]	5.66

	Moderate Withdrawal (N=877)	High Craving-Anhedonia (N=72)	Affective Withdrawal (N=154)	Hunger (N=133)	X^2
Bupropion + Lozenge	1.00	.59 9.24–1.45]	.78 [.41–1.50]	.65 [.31–1.37]	2.47
Patch + Lozenge	1.00	.31* [.11–.83]	.55+ [.28–1.07]	1.01 [.59–1.34]	7.88*

Note:

+ $p < .10$,

* $p<.05$,

** $p<.01$,

*** $p<.001$; all odds ratio comparisons are relative to the Moderate Withdrawal class.

X^2 = difference in −2 log likelihood. WISDM = Wisconsin Inventory of Smoking Dependence Motives. FTND = Fagerström Test of Nicotine Dependence. SUD = Substance Use Disorder.

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Table 5

Point-prevalence abstinence rates and logistic regressions and latency to relapse and cox regression by withdrawal latent class

	8 weeks		6 months		Days to Relapse	
	% abst	OR [95% CI]	% abst	OR [95% CI]	M	OR [95% CI]
Moderate Withdrawal	50%	1.00	37%	1.00	153.19	1.00
High Craving-Anhedonia	35%	0.53* [.32–.88]	31%	0.74 [.44–1.25]	105.89	0.74* [.57–.96]
Affective Withdrawal	43%	0.75 [.53–1.06]	33%	0.81 [.56–1.16]	118.29	0.81* [.67–.97]
Hunger	48%	1.08 [.75–1.56]	41%	1.15 [.79–1.67]	153.19	1.07 [.86–1.33]

Note.

* $p<.05$.

OR = Odds Ratio. CI = confidence interval. % abst = percent abstinence at each point in time. M = mean number of days to relapse among individuals who relapsed.