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Pain-Related Anxiety as a Predictor of Early Lapse and Relapse to Cigarette Smoking

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Abstract

Pain-related anxiety has been positively associated with tobacco dependence, smoking motives, self-reported barriers to smoking cessation, and expectancies for negative affect reduction via smoking. Although emerging research suggests that pain-related anxiety may play a role in the maintenance of tobacco dependence, no previous work has examined pain-related anxiety as a predictor of smoking cessation outcomes. The goal of the current study was to test the hypothesis that pain-related anxiety would predict early lapse and relapse to cigarette smoking among a sample of 55 daily tobacco smokers who participated in an unaided cessation attempt (i.e., without psychosocial or pharmacological intervention). Pain-related anxiety was assessed at baseline using the PASS-20, which yields a total score that ranges from 0-100. Number of days to early lapse (i.e., any instance of smoking during the first 14 days post-quit) and early relapse (i.e., 7 consecutive days of smoking that began during the first 28 days post-quit) were assessed using timeline follow-back procedures. Cox regression analyses indicated that pain-related anxiety was a significant predictor of both early smoking lapse and relapse, such that for every one point increase on the PASS-20, the risk of early lapse increased by 3.7% and the risk of early relapse increased by 3.6%. These effects were evident above and beyond the variance accounted for by tobacco dependence, past four-week pain severity, anxiety sensitivity, and the presence of current Axis I psychopathology. Kaplan-Meier survival analyses further revealed that among early lapsers, greater pain-related anxiety predicted a more rapid trajectory to lapse. Pain-related anxiety was also shown to be a significant predictor of early lapse when the sample was limited to smokers who endorsed past four-week pain. These findings lend support to the notion that pain-related anxiety may contribute to the maintenance of tobacco dependence among smokers who experience varying levels of pain intensity.

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by

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Table of Contents

Page

List of Tables

Table Page

List of Figures

Figure Page

List of Appendices

Pain-Related Anxiety as a Predictor of Early Lapse and Relapse to Cigarette Smoking

Cigarette smoking remains the leading cause of preventable death worldwide (World Health Organization, 2008). Despite known health risks and an annual economic burden in excess of $300 billion in the United States, about 42 million Americans continue to smoke tobacco cigarettes (US Department of Health & Human Services, 2014). Although about half of all smokers attempt to quit each year, nearly 70% do not utilize recommended pharmacological or behavioral cessation aids (e.g., nicotine replacement, cognitive-behavioral counseling; CDC, 2011), and the vast majority (72-85%) who engage in an unaided quit attempt relapse within the first month (Hughes, Keely, & Naud, 2004). Whereas substantial progress has been made in the identification of reliable predictors of smoking cessation (e.g., nicotine dependence, withdrawal symptoms, self-efficacy for quitting; Ditre, Zale, & Brandon, 2015), additional work is needed to identify risk factors that can be addressed in the context of tailored interventions.

There is increasing empirical and clinical interest in the role of pain and related factors in the maintenance of tobacco dependence (e.g., Ditre, Heckman, Butts, & Brandon, 2010; Ditre, Langdon, Kosiba, Zale, & Zvolensky, 2015). Pain has been defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or defined in terms of such damage" (IASP, 1994), and pain complaints account for up to 80% of all annual U.S. physician visits (Mayo Clinic, 2001; Turk & Melzack, 1992). Although about 18% of U.S. adults smoke cigarettes, rates of smoking among persons in pain appear to be substantially higher. Indeed, an estimated 30-42% of persons with pain concurrently smoke tobacco cigarettes (Zvolensky, McMillan, Gonzalez, & Asmundson, 2009), and the prevalence of smoking among clinical pain patients may be as high as 68% (Michna et al., 2004).

A recently proposed reciprocal model suggests that smoking and pain interact in the manner of a positive feedback loop, resulting in greater pain and the maintenance of tobacco dependence (Ditre, Brandon, Zale, & Meagher, 2011b). Consistent with this perspective, cigarette smoking has been identified as a unique risk factor in the onset and progression of painful conditions (e.g., Aho & Heliovaara, 2004; Shiri, Karppinen, Leino-Arjas, Solovieva, & Viikari-Juntura, 2010), situational pain has been shown to motivate smoking urge and behavior (e.g., Ditre & Brandon, 2008), and pain patients have reliably endorsed smoking cigarettes to cope with pain (e.g., Jamison, Stetson, & Parris, 1991; Patterson et al., 2012).

To better inform the development of tailored interventions, researchers have recently turned their attention to the identification of anxiety-relevant transdiagnostic factors in the etiology, progression, and maintenance of both pain and smoking (Zale, Maisto, & Ditre, 2015). Indeed, various facets of anxiety (e.g., generalized anxiety, anxiety sensitivity) have been associated with greater pain and the maintenance of tobacco dependence (e.g., Assayag, Bernstein, Zvolensky, Steeves, & Stewart, 2012; Leventhal & Zvolensky, 2015; McCracken & Keogh, 2009). One factor that is of increasing clinical and empirical interest is the cognitive-affective construct termed pain-related anxiety (e.g., Ditre, Langdon, et al., 2015; Ditre, Zale, Kosiba, & Zvolensky, 2013). Pain-related anxiety reflects the tendency to respond to pain or pain-related events with anxiety or fear (McCracken, Zayfert, & Gross, 1992), and may be particularly important to understanding the maintenance and exacerbation of tobacco dependence due to its specificity to pain-related phenomena and incorporation of pain-relevant behavioral responses (i.e., responding with escape or avoidance). Pain-related anxiety has been identified as a risk factor in the transition from acute to chronic pain (Boersma & Linton, 2006; Vlaeyen & Linton, 2000), and greater pain-related anxiety has been related to greater pain intensity,

maladaptive approaches to pain coping, and increased somatic reactivity in anticipation of pain-eliciting physical activity (McCracken, Gross, Sorg, & Edmands, 1993). A growing body of evidence further suggests that pain-related anxiety can be experienced even in the absence of co-occurring pain (e.g., Abrams, Carleton, & Asmundson, 2007).

Pain-related anxiety has also been implicated in the maintenance of substance use in general (e.g., Hogan, Gonzalez, Howell, Bonn-Miller, & Zvolensky, 2010), and tobacco smoking in particular. Among individuals with chronic pain, higher levels of pain-related anxiety have been associated with current smoking (vs. non-smoking; Hooten et al., 2009; Hsu, Harden, & Houle, 2002) and the use of tobacco to cope with pain (Patterson et al., 2012). Pain-related anxiety has also been positively associated with both primary (i.e., central features of tobacco dependence, such as compulsion to smoke) and secondary (i.e., situational motivators of smoking, such as mood regulation) smoking dependence motives among smokers with chronic pain (Ditre et al., 2013), and those recruited from the local community (Ditre, Langdon, et al., 2015). Among community samples, pain-related anxiety has been positively associated with self-reported barriers to smoking cessation and expectations that smoking can alleviate negative mood (Ditre, Langdon, et al., 2015; Gonzalez, Hogan, McLeish, & Zvolensky, 2010). Collectively, these data suggest that pain-related anxiety should be considered in the maintenance of tobacco dependence among smokers with and without co-occurring pain.

An important next step in this line of research is to assess the extent to which pain-related anxiety may be associated with smoking cessation outcomes. The primary goal of the current study was to test whether pain-related anxiety would predict early cessation outcomes among a sample of daily tobacco smokers who were recruited from the local community to participate in a self-guided smoking cessation attempt (i.e., without psychosocial or pharmacological

intervention). Given evidence that pain-related anxiety may be particularly important among smokers with co-occurring pain (e.g., Ditre et al., 2013; Hooten et al., 2009), a secondary goal of this study was to examine the relationship between pain-related anxiety and cessation outcomes among a subsample of participants who endorsed past four-week pain. Specifically, we hypothesized that higher levels of pain-related anxiety would be associated with (a) an increased risk of *early lapse* (i.e., a lapse within 14 days post-quit) and *early relapse* (i.e., a relapse beginning within 28 days post-quit) to smoking, and (b) a more rapid trajectory to lapse among early-lapsers and to relapse among early-relapsers. Early abstinence outcomes were of particular interest given that participants engaged in an unaided quit attempt, and that duration of abstinence prior to the first lapse/relapse (e.g., < 1 month) is highly predictive of longer-term cessation outcomes (e.g., 6-12 months; Brown et al., 2001).

Method

Participants

Participants were recruited from the local community at two sites (Houston, TX and Burlington, VT) via advertisements for a smoking cessation study that consisted of a self-guided quit attempt (Langdon, Farris, Øverup, & Zvolensky, 2015). Participants were screened for the following inclusion criteria: between 18 and 65 years of age, smoke at least 8 cigarettes per day for at least one year (verified via expired carbon monoxide [CO] breath analysis; ≥ 8 ppm), have not decreased the number of daily cigarettes smoked by more than half in the past 6 months, and willing to engage in a self-guided quit attempt. Participants were also screened for the following exclusion criteria: current use of nicotine replacement or other tobacco products, current substance dependence (excluding nicotine dependence), current or past history of psychotic spectrum symptoms or disorders, and current use of psychotropic medication.

A total of 122 participants attended a baseline session, and 80 were deemed eligible to participate in the self-guided quit attempt and completed the measure of pain-related anxiety. Of these, 55 participants (69%) attended their quit day appointment and were included in the current analyses (see Figure 1)[1]. It is important to note that modest retention rates are expected in studies that ask daily tobacco smokers to engage in an unaided, non-incentivized quit attempt. For example, in a previous study that required a self-guided quit attempt, approximately 23% of the sample withdrew prior to the quit day (Zvolensky et al., 2008).

Measures

Pain-related anxiety. Pain-related anxiety was assessed using the Pain Anxiety Symptom Scale-20 item (PASS-20; McCracken & Dhingra, 2002). The PASS-20 uses a 6-point Likert scale ranging from *never* (0) to *always* (5) to assess how often participants engage in various thoughts (e.g., "When I feel pain, I am afraid that something terrible will happen") and behaviors (e.g., "I avoid important activities when I hurt"). PASS-20 total scores (range 0-100) have demonstrated utility as a both a continuous variable with higher scores reflecting greater pain-related anxiety (i.e., occurring along a latent continuum ranging from low to high; Asmundson, Collimore, Bernstein, Zvolensky, & Hadjistavropoulos, 2007), and as a taxonic variable for classifying individuals as either low or high (e.g., Evans, Seidman, Lung, Zeltzer, & Tsao, 2013). The PASS-20 has demonstrated excellent reliability and validity in a previous study of adults who did not report a history of chronic pain or endorse severe current pain ($\alpha = .91$; Abrams et al., 2007), thus supporting its utility among samples that were not recruited based on pain status. The PASS-20 demonstrated excellent internal consistency in the current sample ($\alpha = .91$), and the statistical distribution of total scores fell within the normal ranges suggested by Kim et al. (2013), with a skewness of 0.531 ($SE = 0.322$) and kurtosis of 0.104 ($SE = 0.634$).

Past Four-Week Pain Severity. The Short Form Health Survey-12 (SFHS; Ware, Kosinski, & Keller, 1996) is a widely used 12-item self-report measure of mental and physical health. Consistent with previous research (e.g., Ditre, Langdon, et al., 2015), a single item was used to assess the presence of past four-week bodily pain (i.e., "How much bodily pain have you had during the past four weeks?"; Ware et al., 1996). Response options consisted of *none*, *very mild*, *mild*, *moderate*, and *severe*. Given demonstrated associations between the presence of pain and numerous smoking-related factors and outcomes (e.g., Ditre, Brandon, Zale, & Meagher, 2011a; Zvolensky, McMillan, et al., 2009), past four-week bodily pain severity was selected as an a priori covariate for all statistical analyses.

Tobacco use and dependence. Historical and current tobacco use (e.g., number of cigarettes smoked per day) were assessed via self-report. Tobacco dependence was assessed using the Heaviness of Smoking Index (HSI; Heatherton, Kozlowski, Frecker, Rickert, & Robinson, 1989), which is comprised of two items (i.e., "How soon after you wake up do you smoke your first cigarette?" and "How many cigarettes per day do you smoke?"; Heatherton et al., 1989). HSI scores were identified as an a priori covariate, given that they have been shown to predict smoking abstinence outcomes (Courvoisier & Etter, 2010), especially during the early stages (i.e., 1 week to 1 month) of a cessation attempt (Yong et al., 2014).

Current Axis I Psychopathology. All participants were administered the Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Non-Patient Edition (SCID-IV-N/P) by a trained clinician to assess whether participants met criteria for past-month Axis I psychopathology. Interviews were audio-taped, the reliability of a random selection of 10% of interviews was checked for accuracy, and there were no diagnostic disagreements between the SCID interviewer and outsider raters. Consistent with previous work, a single dichotomous

variable was created to reflect the presence (1) or absence (0) of current Axis I psychopathology (e.g., Johnson, Farris, Schmidt, Smits, & Zvolensky, 2013). Given established associations between the presence of Axis I psychopathology and greater difficulty quitting (e.g., Lasser et al., 2000; Weinberger, Pilver, Desai, Mazure, & McKee, 2013; Weinberger, Pilver, Hoff, Mazure, & McKee, 2013; Zvolensky et al., 2008), this variable was identified as an a priori covariate.

Anxiety Sensitivity. The Anxiety Sensitivity Index-III is a well-established, 18-item measure of the fear that arousal-related sensations may result in adverse consequences such as death, insanity, or social rejection (ASI-3; Taylor et al., 2007). Given that anxiety sensitivity has been positively associated with affect-regulatory smoking motives (Farris, Leventhal, Schmidt, & Zvolensky, 2015), more severe nicotine withdrawal (e.g., Johnson, Stewart, Rosenfield, Steeves, & Zvolensky, 2012), and increased risk for lapse and relapse (Assayag et al., 2012; Zvolensky, Stewart, Vujanovic, Gavric, & Steeves, 2009), ASI-3 scores were selected as an a priori covariate. The ASI-3 demonstrated excellent internal consistency in the current sample (α = .93).

Time to Lapse/Relapse. Time to lapse and relapse were assessed via timeline follow-back procedures. The timeline follow-back is a widely used, interview-style assessment that incorporates calendar-guided recall and anchoring of dates to significant events (Sobell & Sobell, 1992). Timeline follow-back procedures for cigarette smoking have demonstrated high reliability and validity (as measured by correlations with daily monitored smoking, reports from significant others, and saliva cotinine levels; Brown et al., 1998). Participants were asked to recall and record the total number of cigarettes smoked each day prior to the follow-up session. Consistent with previous research, a lapse (i.e., any instance of smoking after a quit attempt) during the first

14 days post-quit was classified as an ‘early lapse’ (e.g., Brown et al., 2008; Holt, Litt, & Cooney, 2012; Zvolensky, Stewart, et al., 2009), and a relapse (i.e., 7 consecutive days of smoking following a quit attempt) beginning during the first 28 days post-quit was classified as an ‘early relapse’ (e.g., al'Absi, Hatsukami, & Davis, 2005; Nakajima & al'Absi, 2011). These classifications were also employed because they tend to capture the majority of early lapses/relapses and have demonstrated utility in predicting longer-term abstinence rates (e.g., Brown et al., 2001; Brown et al., 2009).

Procedure

Participants were recruited to take part in a larger study examining barriers to successful smoking cessation (Langdon et al., 2015). Upon arrival to the baseline session, smoking status was biochemically verified by expired CO, the SCID-IV/NP was administered, and self-report questionnaires were completed. Participants were compensated $20 for completion of the baseline session. Eligible respondents were then invited to participate in an unaided smoking cessation attempt. Each participant selected his/her own quit date, which typically occurred within two weeks of the baseline assessment (M = 12.8 days, SD = 5.7). In-person follow-up appointments were scheduled for the quit day, and days 3, 7, 14, 28, and 90 post-quit. Each follow-up visit consisted of self-report assessments and timeline follow-back procedures. Participants were compensated $10 for completing each follow-up assessment, and could earn an additional $20 for completing all of them. Participants were not incentivized to remain abstinent. Procedural details are depicted in Figure 2.

Data Analytic Plan

All analyses were conducted using SPSS Statistics 21 (IBM SPSS Statistics, 2012). First, we ran a series of bivariate correlations to test zero-order associations between PASS-20 total

scores (pain-related anxiety), number of days to lapse and relapse, HSI scores (tobacco dependence), severity of past four-week bodily pain, presence of current Axis I psychopathology, ASI-3 scores (anxiety sensitivity), and sociodemographic factors.

Next, we used the Cox proportional hazards model to estimate the risk of both early lapse and early relapse as a function of pain-related anxiety. The Cox model is a well-established statistical procedure that has frequently been used to examine predictors of lapse/relapse to cigarette smoking (e.g., Lemieux, Nakajima, Hatsukami, Allen, & al'Absi, 2015; Messer et al., 2015; Nakajima & al'Absi, 2011; Schepis, Tapscott, & Krishnan-Sarin, 2016; Zvolensky et al., 2008). This semiparametric model estimates hazard ratios by examining the pattern of covariation of predictor variables with the event of interest (e.g., lapse/relapse; Christensen, 1987; Cox & Oakes, 1984). Unlike ordinary regression models, the Cox proportional hazards model incorporates information from both censored (cases are 'censored' if the exact survival time is unknown; Christensen, 1987) and uncensored observations when estimating model parameters. Consistent with previous research, individuals who maintained abstinence during the given time period (i.e., did not report an early lapse or early relapse) or withdrew from the study before having lapsed/relapsed were censored (e.g., al'Absi, Nakajima, Allen, Lemieux, & Hatsukami, 2015). Established procedures for the Cox proportional hazards model indicate that a minimum of 5 events should be included per predictor variable to increase confidence interval coverage, and decrease relative bias and type I error (Vittinghoff & McCulloch, 2007). After ensuring that our models were consistent with this recommendation (our models included 5 predictor variables, and we observed 44 events for early lapse and 34 events for early relapse), covariates (i.e., ASI-3 total scores, past four-week pain severity, presence of current Axis I

psychopathology, and HSI scores) were entered into the first step of each model, and continuous PASS-20 scores were entered at the second step.

We used Kaplan Meier survival curves to compare the trajectories to early lapse and relapse between participants with high vs. low levels of pain-related anxiety. Consistent with previous research, PASS-20 scores were dichotomized via median split (e.g., Evans et al., 2013). The Kaplan Meier survival curve represents the probability of maintaining smoking abstinence for a given length of time while considering time in many small intervals (Goel, Khanna, & Kishore, 2010; Kaplan & Meier, 1958). Two survival curves can be compared statistically using a log-rank test to challenge the null hypothesis that the survival curves do not differ by group (Goel et al., 2010). If a significant log-rank result is observed ($p < .05$), then it can be concluded that the trajectory to lapse/relapse differs based on group status. These procedures are well-established and have been used in numerous studies examining differences in time to lapse/relapse to cigarette smoking (e.g., López-Torrecillas, Rueda, López-Quirantes, Santiago, & Tapioles, 2014; Walker et al., 2011; Wong, Chan, & Lam, 2015).

Results

Participant Characteristics

Participants included 55 current daily tobacco smokers (66% male; $M_{age} = 34.8$, $SD = 14.6$), who reported smoking approximately 16 cigarettes per day ($SD = 5.5$) for an average of 16 years ($SD = 14.0$). The mean HSI score was 2.6 ($SD = 1.4$), indicating a moderate level of tobacco dependence (e.g., Chaiton, Cohen, McDonald, & Bondy, 2007). The sample was predominantly white (87%) and fairly well-educated (27% completed four years of college). Structured clinical interviews (SCID-IV-N/P) revealed that 38% of the sample met criteria for current (past month) Axis I psychopathology. PASS-20 total scores ranged from 0 to 68 ($M =$

28.4, *SD* = 16.5, *median* = 28.0). The majority of participants (*n* = 44; 80%) endorsed an early *lapse* to smoking, and about 62% of the sample (*n* = 34) endorsed an early *relapse* to smoking. We observed a moderate correlation (*r* = .543) between early *lapse* and early *relapse*, which indicates that although there was some overlap between early *lapsers* and early *relapsers*, these outcomes were not redundant (e.g., 25% of participants who endorsed an early *lapse* to smoking did not subsequently endorse an early *relapse*). Approximately 73% (*n* = 40) of the sample endorsed at least *very mild* past four-week pain, and smokers who endorsed past four-week pain reported higher levels of pain-related anxiety (*M* = 31.68, *SD* = 16.06) than those who did not endorse past four-week pain (*M* = 19.60, *SD* = 14.68; *F* [1, 53] = 6.449, *p* = .014). Among smokers who reported past four-week pain, 82.5% (*n* = 33) endorsed an early lapse to smoking, and 65% (*n* = 26) endorsed an early relapse. Sociodemographic and clinical data are presented in Table 1.

Bivariate Correlations

PASS-20 total scores were positively correlated with past four-week pain severity (*r* = .37, *p* < .01), ASI-3 total scores (*r* = .70, *p* < .01), and the presence of current Axis I psychopathology (*r* = .30, *p* < .05). The presence of current Axis I psychopathology was negatively associated with number of days to first smoking lapse (*r* = -.29; *p* < .05). No additional covariates were identified via bivariate analyses (see Table 2).

Pain-Related Anxiety and Early Lapse and Early Relapse to Smoking

As hypothesized, Cox regression analysis revealed that pain-related anxiety was a significant predictor of early smoking *lapse* (*HR* = 1.037, *p* = .013; see Table 3). Examination of the hazard ratio revealed that for every one point increase on the PASS-20, the risk of early *lapse* increased by 3.7%. These effects were evident above and beyond the variance accounted for by

tobacco dependence scores, past four-week pain severity, anxiety sensitivity, and the presence of current Axis I psychopathology. Also as hypothesized, Cox regression analysis revealed that pain-related anxiety was a significant predictor of early smoking *relapse* after accounting for the same covariates, such that for every one point increase on the PASS-20, the risk of early *relapse* increased by 3.6% (*HR* = 1.036, *p* = .027; see Table 4).

Pain-Related Anxiety and Trajectories to Early Lapse and Early Relapse to Smoking

Kaplan Meier survival analysis further revealed that, among early-lapsers, greater pain-related anxiety predicted a more rapid trajectory to *lapse* (*p* = .037; Figure 3). All participants (100%) high in pain-related anxiety *lapsed* by day 7, compared to just 77.3% of those low in pain-related anxiety. Among early-relapsers, 84.2% of participants who reported high pain-related anxiety *relapsed* by day 7, compared to only 66.7% of those low in pain-related anxiety. However, no significant differences in *relapse* trajectories were observed as a function of pain-related anxiety (*p* = .322; Figure 4).

Pain-Related Anxiety and Early Lapse/Relapse among Smokers with Pain

To further explore relations between pain-related anxiety and early lapse/relapse, we replicated our analyses among the subsample of participants who endorsed past four-week pain. Similar to the primary findings, Cox regression analysis revealed that pain-related anxiety was a significant predictor of early smoking *lapse* among smokers who endorsed past four-week pain (*HR* = 1.050, *p* = .009; shown in Table 5), such that every one point increase on the PASS-20 was associated with a 5.0% increase in the risk of early lapse. Although 78.3% of smokers with high levels of pain-related anxiety endorsed an early relapse to smoking (vs. 47.1% of smokers with low levels of pain-related anxiety), pain-related anxiety was not found to be a significant predictor of early *relapse* among smokers with past four-week pain (*HR* = 1.036, *p* = .075; see

Table 6). Kaplan Meier survival analyses revealed no differences in trajectory to *lapse* among early-lapsers (p = .098) or to *relapse* among early-relapsers (p = .958) as a function of pain-related anxiety among participants with co-occurring pain.

Discussion

The current study is the first to examine pain-related anxiety as a predictor of lapse and relapse to smoking. As hypothesized, pain-related anxiety was observed to be a significant predictor of both early lapse and early relapse among a sample of smokers who were recruited from the local community to participate in a self-guided quit attempt. Importantly, these effects were evident above and beyond the variance accounted for by tobacco dependence, past four-week pain severity, anxiety sensitivity, and the presence of current Axis I psychopathology. Among early-lapsers, greater pain-related anxiety was also associated with a more rapid trajectory to lapse. Pain and anxiety have both been shown to motivate smoking behavior, and it is possible that these factors may be more likely to interfere with quit attempts among smokers who endorse higher levels of pain-related anxiety (e.g., Ditre & Brandon, 2008; Ditre et al., 2010; Kimbrel, Morissette, Gulliver, Langdon, & Zvolensky, 2014). Only recently have researchers begun to evaluate pain and anxiety-related cognitive-affective processes as potential mechanisms in the maintenance of tobacco dependence (e.g., Ditre et al., 2011a; Hooten, Shi, Gazelka, & Warner, 2011), and these findings are consistent with demonstrated positive associations between pain-related anxiety, smoking dependence motives (Ditre, Langdon, et al., 2015; Ditre et al., 2013), and perceived barriers to cessation (Ditre, Langdon, et al., 2015).

Analyses conducted among the subsample of participants who endorsed past four-week pain largely corroborated the primary findings, and suggest that pain-related anxiety may be associated with an even greater risk of *early lapse* among smokers with co-occurring pain (every

one-point increase on the PASS-20 was associated with a 5% increased risk in early lapse among smokers with co-occurring pain, compared to a 3.7% increased risk among the total sample). Pain-related anxiety was not associated with risk of *early relapse* when analyses were limited to smokers who endorsed past four-week pain, though this may have been a function of reduced statistical power (n = 40). Interestingly, we observed a wide range of PASS-20 scores among the subsample of smokers who reported no past four-week pain (M = 19.60, SD = 14.68, *range* = 55), demonstrating that smokers may endorse varying levels of pain-related anxiety, even in the absence of co-occurring pain.

Strengths of the current study include the prospective design and recruitment of daily tobacco smokers from the local community (such that the sample was not limited to persons with co-occurring pain). The utilization of diagnostic clinical interviews and in-person timeline follow-back assessments are additional methodological strengths. Finally, in examining early lapse/relapse outcomes, we were able to account for variance associated with tobacco dependence, past four-week pain severity, anxiety sensitivity, and the presence of current Axis I psychopathology.

Several limitations should also be noted, including the modest sample size. Although it is important that future work replicate these findings among a larger and more diverse sample of tobacco smokers, it can be beneficial to study smaller samples during the early stages of hypothesis testing (e.g., reduces time and cost, helps generate initial effect estimates), and we took steps to ensure that the Cox proportional hazards models were adequately powered. It is also important to consider that participants in this study volunteered to engage a self-guided quit attempt. Although an unaided quit approach confers several benefits (e.g., provides knowledge about self-quitters, prevents interpretive problems related to delivering an intervention, provides

a natural history of smoking cessation that can yield normative data against which treatment outcomes can be compared; e.g., Marlatt, Curry, & Gordon, 1988; Zvolensky et al., 2008), the extent to which these results may generalize to smokers receiving cessation treatment remains unclear. Finally, although duration of abstinence prior to first lapse and relapse has been shown to predict longer-term cessation outcomes (e.g., Brown et al., 2001; Garvey et al., 1992; Gilpin et al., 1997), this period of assessment does not adequately capture the dynamic process of quitting (e.g., Velicer, Prochaska, Rossi, & Snow, 1992). Future work should examine pain-related anxiety as a predictor of both prolonged and point prevalence cessation outcomes to better account for smokers who regain abstinence following an early lapse or relapse (e.g., Hughes et al., 2003; Velicer et al., 1992).

Clinical research has implicated pain-related anxiety in the onset and exacerbation of pain (e.g., Boersma & Linton, 2006), and these data contribute to an emerging literature which suggests that pain-related anxiety may also play a role in the maintenance of cigarette smoking. Thus, pain-related anxiety may warrant consideration as a transdiagnostic factor in the co-occurrence of pain and tobacco addiction. Pain-related anxiety can be reduced via cognitive behavioral intervention (e.g., Lami et al., 2016; Watt, Stewart, Lefaivre, & Uman, 2006), and treatments for smokers with and without co-occurring pain may benefit from addressing pain-related anxiety prior to smoking cessation.

In summary, results of the current study represent an initial, yet important step towards better understanding the role of pain-related anxiety in the maintenance of tobacco dependence. No previous research has examined associations between pain-related anxiety and attempts to abstain from smoking, and these findings provide the first evidence that high levels of pain-related anxiety may be associated with early lapse and relapse to smoking tobacco cigarettes.

This and future work has the potential to inform the development of tailored cessation interventions for smokers who experience varying levels of pain intensity and pain-related anxiety.

Footnotes

[1] Among participants who were eligible to participate in the quit attempt and completed the PASS-20, those who attended their quit day appointment smoked fewer cigarettes per day (M = 15.564, SD = 0.809) than those who did not attend their quit day appointment (M = 18.600, SD = 1.200), F (1, 78) = 4.399, p = .039. No differences in any other baseline sociodemographic, smoking, or pain variable were observed as a function of quit day attendance (all ps > .05).

Table 1

Sociodemographic, smoking, and pain characteristics

	Total Sample	Pain-Related Anxiety		Past Four-Week Pain Status	
		Low	High	No Pain	Pain
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Gender					
Male	36 (65.5%)	22 (78.6%)	14 (51.9%)	9 (60.0%)	27 (67.5%)
Race					
White	48 (87.3%)	25 (89.3%)	23 (85.2%)	14 (93.3%)	34 (85.0%)
Black	3 (5.5%)	0 (0.0%)	3 (11.1%)	0 (0.0%)	3 (7.5%)
Other	4 (7.3%)	3 (10.7%)	1 (3.7%)	1 (6.7%)	3 (7.5%)
Marital Status					
Single	30 (54.5%)	13 (46.4%)	17 (63.0%)	9 (60.0%)	21 (52.5%)
Married/Living with Someone	15 (27.3%)	10 (35.7%)	5 (18.5%)	3 (20.0%)	12 (30.0%)
Separated/Divorced/Annulled	10 (18.2%)	5 (17.9%)	5 (18.5%)	3 (20.0%)	7 (17.5%)
Education					
12 Years	6 (10.9%)	2 (7.1%)	4 (14.8%)	2 (13.3%)	4 (10.0%)
12 - 15 Years	33 (61.9%)	20 (71.4%)	14 (51.8%)	9 (60.0%)	25 (62.5%)
≥ 16 Years	15 (27.3%)	6 (21.4%)	9 (33.3%)	4 (26.7%)	11 (27.5%)
Current Axis I Psychopathology [a]	21 (38.2%)	8 (28.6%)	13 (48.1%)	5 (33.3%)	16 (40.0%)
Past Four-Week Pain Severity [b]					
None	15 (27.3%)	11 (39.3%)	4 (14.8%)	15 (100%)	0 (0.0%)
Very Mild	22 (40.0%)	10 (35.7%)	12 (44.4%)	0 (0.0%)	22 (55.0%)
Mild	9 (16.4%)	4 (14.3%)	5 (18.5%)	0 (0.0%)	9 (22.5%)
Moderate	6 (10.9%)	1 (3.6%)	5 (18.5%)	0 (0.0%)	6 (15.0%)
Severe	3 (5.5%)	2 (7.1%)	1 (3.7%)	0 (0.0%)	3 (7.5%)
	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
Age	34.78 (14.55)	34.46 (15.58)	35.11 (13.68)	29.87 (12.64)	36.63 (14.93)
Cigarettes per Day	15.56 (5.53)	16.32 (6.40)	14.78 (4.45)	16.27 (6.87)	15.30 (5.01)
Years of Smoking	16.25 (13.98)	15.75 (14.72)	16.78 (13.44)	12.80 (13.68)	17.55 (14.04)
Tobacco Dependence [c]	2.56 (1.40)	2.75 (1.48)	2.37 (1.31)	2.73 (1.44)	2.50 (1.40)
Anxiety Sensitivity [d1]	14.82 (12.44)	8.61 (6.15)	21.26 (14.05)	11.47 (8.53)	16.08 (13.50)
Pain-Related Anxiety [e12]	28.38 (16.48)	15.71 (8.16)	41.52 (11.95)	19.60 (14.68)	31.68 (16.06)
Days to First Lapse	12.92 (26.67)	18.48 (31.86)	6.92 (18.42)	17.14 (29.04)	11.37 (25.98)
Days to First Relapse	21.65 (31.29)	28.18 (35.91)	15.66 (25.69)	27.55 (33.49)	19.80 (30.84)

Note. [a] Structured Clinical Interview for DSM-IV Non-Patient Edition (SCID-IV-N/P); [b] Short Form Health Survey – 12; [c] Heaviness of Smoking Index; [d] Anxiety Sensitivity Index – III; [e] Pain Anxiety Symptoms Scale – 20 item. [1]Significant ($p < .05$) difference as a function of pain-related anxiety; [2]Significant ($p < .05$) difference as a function of past four-week pain status

Table 2

Bivariate correlations between variables of primary interest

Variable	1	2	3	4	5	6	7	8	9	10	11	12
1 Age	-	-.11	.01	.22	-.53**	.26	.01	-.12	.38**	-.09	.03	.14
2 Gender		-	.08	-.12	-.06	-.13	.18	-.02	-.07	-.20	-.06	.21
3 Race			-	.05	.00	-.06	.00	-.21	.06	-.14	-.16	.06
4 Education Level				-	-.06	-.09	-.09	-.10	.07	.00	-.16	.11
5 Marital Status					-	.01	-.00	.18	-.21	.07	.09	.02
6 Tobacco Dependence [a]						-	-.09	-.05	-.05	-.16	.21	-.12
7 Anxiety Sensitivity [b]							-	.41**	.35**	-.06	.03	.70**
8 Current Axis I Psychopathology [c]								-	.14	.21	.16	.30*
9 Past Four-Week Pain Severity [d]									-	.20	-.01	.37**
10 Early Lapse										-	.54**	-.17
11 Early Relapse											-	.17
12 Pain-Related Anxiety [e]												-

Note. Gender: 0 = female, 1 = male. [a] Heaviness of Smoking Index; [b] Anxiety Sensitivity Index – III; [c] Structured Clinical Interview for DSM-IV Non-Patient Edition (SCID-IV-N/P); [d] Short Form Health Survey – 12; [e] Pain Anxiety Symptoms Scale – 20; * $p < .05$; ** $p < .01$

Table 3

Cox Proportional Hazards Regressions

	Unadjusted Hazard Ratio 95% Confidence Interval	*p*	Adjusted Hazard Ratio 95% Confidence Interval	*p*
Early Lapse among Entire Sample [a]				
Past Four-Week Pain Severity [c]	1.160 (.915-1.469)	.219	1.172 (.901-1.525)	.238
Anxiety Sensitivity [d]	.999 (.976-1.022)	.938	.940 (.899-.982)	.005**
Current Axis I Psychopathology [e]	2.232 (1.183-4.210)	.013*	3.567 (1.641-7.755)	.001**
Tobacco Dependence [f]	.988 (.815-1.197)	.900	1.129 (.897-1.421)	.302
Pain-Related Anxiety [g]	1.011 (.995-1.028)	.174	1.037 (1.008-1.068)	.013*
Early Relapse among Entire Sample [b]				
Past Four-Week Pain Severity	1.066 (.804-1.412)	.658	1.041 (.748-1.449)	.812
Anxiety Sensitivity	1.007 (.981-1.033)	.597	.958 (.913-1.004)	.071
Current Axis I Psychopathology	1.895 (.947-3.789)	.071	3.033 (1.276-7.207)	.012*
Tobacco Dependence	1.175 (.926-1.492)	.185	1.379 (1.032-1.842)	.030*
Pain-Related Anxiety	1.014 (.995-1.033)	.154	1.036 (1.004-1.069)	.027*
Early Lapse among Participants with Pain				
Past Four-Week Pain Severity	1.043 (.748-1.453)	.804	.993 (.687-1.434)	.968
Anxiety Sensitivity	1.007 (.986-1.029)	.517	.944 (.898-.992)	.023*
Current Axis I Psychopathology	1.863 (.896-3.876)	.096	2.767 (.977-7.833)	.055
Tobacco Dependence	.965 (.772-1.205)	.752	1.055 (.820-1.357)	.677
Pain-Related Anxiety	1.019 (1.000-1.039)	.046*	1.050 (1.012-1.089)	.009**
Early Relapse among Participants with Pain				
Past Four-Week Pain Severity [b]	.884 (.583-1.340)	.562	.862 (.549-1.352)	.517
Anxiety Sensitivity [c]	1.010 (.985-1.036)	.443	.966 (.914-1.021)	.216
Current Axis I Psychopathology [d]	1.816 (.825-3.995)	.138	2.443 (.818-7.292)	.109
Tobacco Dependence [e]	1.141 (.866-1.503)	.350	1.234 (.910-1.673)	.176
Pain-Related Anxiety [f]	1.017 (.995-1.040)	.122	1.036 (.996-1.078)	.075

Note. [a] First lapse within 14 days; [b] relapse within 28 days; [c] Short Form Health Survey – 12; [d] Anxiety Sensitivity Index – III; [e] Structured Clinical Interview for DSM-IV Non-Patient Edition (SCID-IV-N/P); [f] Heaviness of Smoking Index; [g] Pain Anxiety Symptoms Scale – 20;
* $p < .05$; ** $p < .01$.

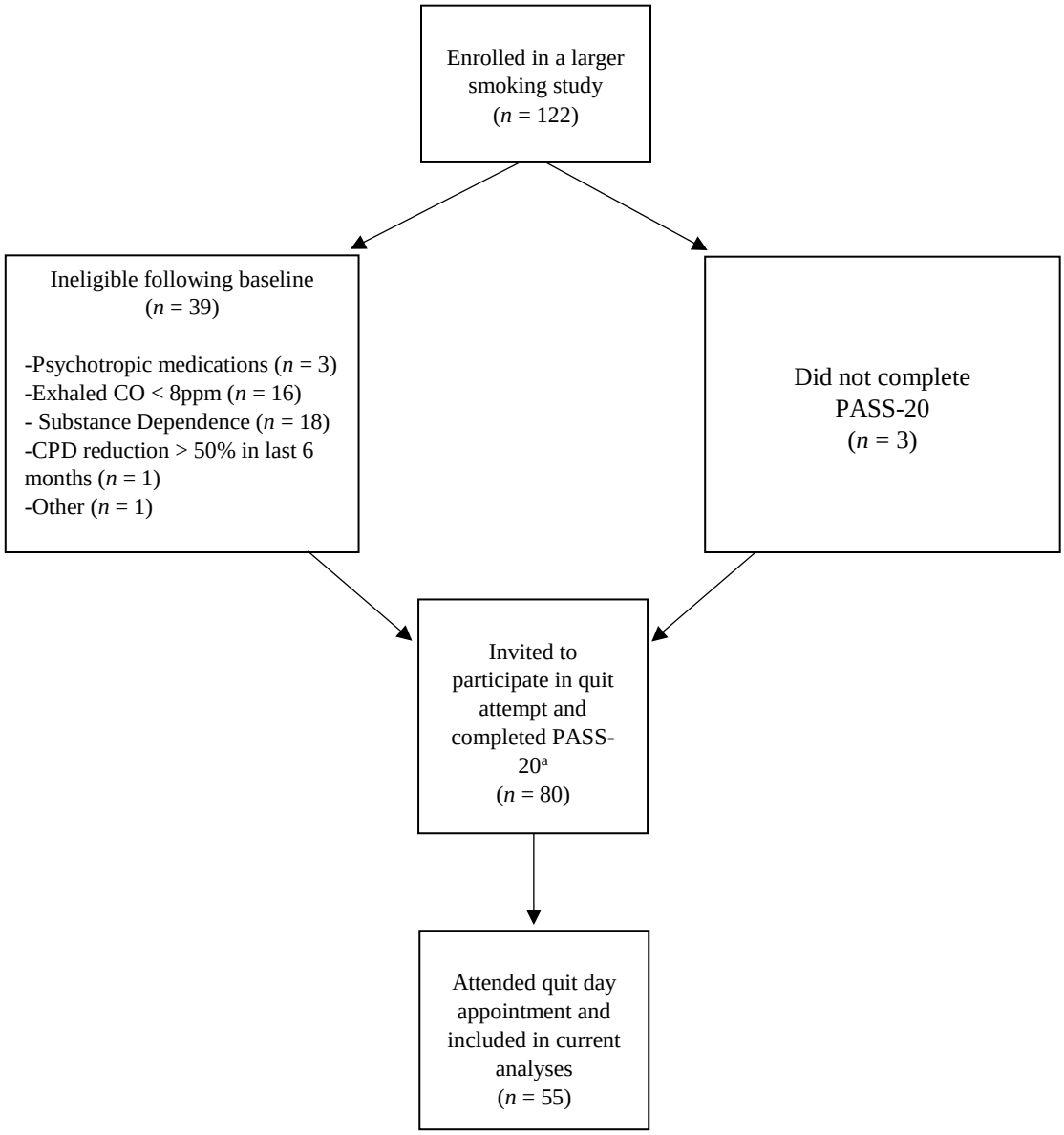

Figure 1. Inclusion of participants in the current study. [a] Pain Anxiety Symptoms Scale – 20 item.

Recruitment	Baseline		Self-Guided Quit Attempt					
			Quit Day	Day 3	Day 7	Day 14	Day 28	Day 90
Those who responded to an ad on 'quitting smoking' were scheduled for a baseline visit.	Biochemical verification of smoking status; self-report questionnaires (e.g., PASS-20[a], ASI-3[b], HSI[c], SCID-IV-N/P[d])	**Eligible Participants:** Each participant determined his or her own quit date.	TLFB[e]	TLFB	TLFB	TLFB	TLFB	TLFB

Figure 2. Study procedure. [a] Pain Anxiety Symptoms Scale – 20 item; [b] Anxiety Sensitivity Index – III; [c] Heaviness of Smoking Index; [d] Structured Clinical Interview for DSM-IV Non-Patient Edition (SCID-IV-N/P); [e] Timeline Follow Back Procedures.

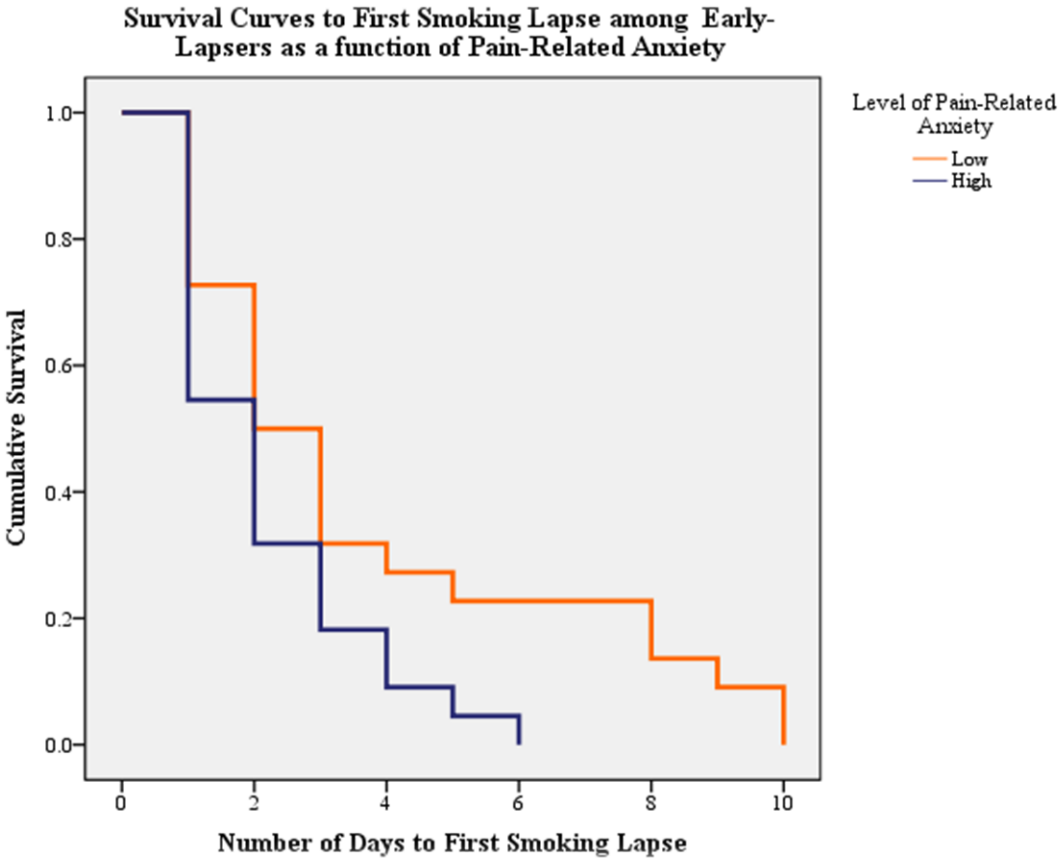

Figure 3. Kaplan-Meier survival curves to first smoking lapse among early-lapsers.

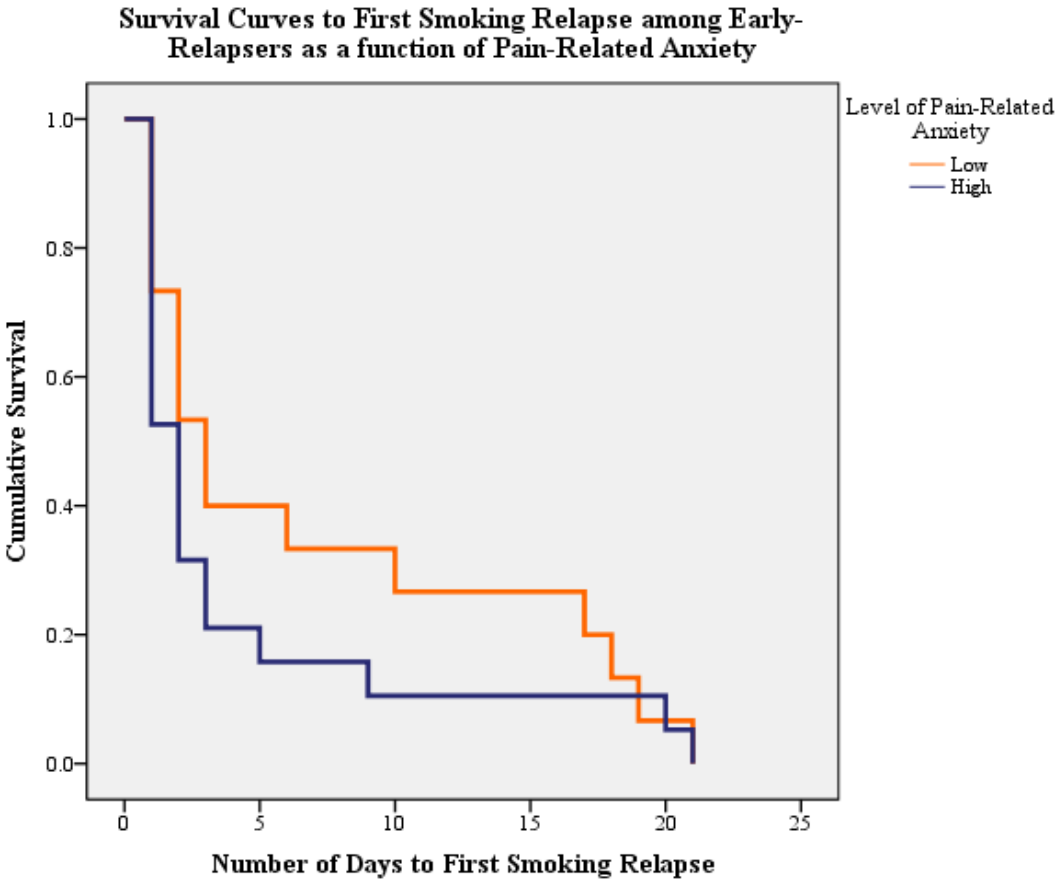

Figure 4. Kaplan-Meier survival curves to first smoking relapse among early-relapsers.

Appendix A

Pain-Anxiety Symptoms Scale (PASS-20)

INSTRUCTIONS: Individuals who experience pain develop different ways to respond to that pain. We would like to know what you do or what you think about when in pain. Please use the rating scale below to indicate how often you engage in each of the following thoughts or activities. Record your rating on the line next to each item.

Never **Always**

0 1 2 3 4 5

_____1. I think that if my pain gets too severe, it will never decrease.
_____2. When I feel pain, I am afraid that something terrible will happen.
_____3. I go immediately to bed when I feel severe pain.
_____4. I begin trembling when engaged in an activity that increases pain.
_____5. I can't think straight when in pain.
_____6. I will stop any activity as soon as I sense pain is coming on.
_____7. Pain seems to cause my heart to pound or race.
_____8. As soon as pain comes on I take medication to reduce it.
_____9. When I feel pain, I think that I might be seriously ill.
_____10. During painful episodes it is difficult for me to think of anything besides the pain.
_____11. I avoid important activities when I hurt.
_____12. When I sense pain, I feel dizzy or faint.
_____13. Pain sensations are terrifying.
_____14. When I hurt, I think about the pain constantly.
_____15. Pain makes me nauseous.
_____ 16. When pain comes on strong I think that I might become paralyzed or more disabled.
_____17. I find it hard to concentrate when I hurt.
_____18. I find it difficult to calm my body down after periods of pain.
_____19. I worry when I am in pain.
_____20. I try to avoid activities that cause pain.

Appendix B

Past Four-Week Pain Severity

How much bodily pain have you had during the past 4 weeks? (circle one)

None	Very Mild	Mild	Moderate	Severe

Appendix C

Heaviness of Smoking Index (HSI)

1. How soon after you wake up do you smoke your first cigarette?

- ☐ Within 5 minutes
- ☐ 6 - 30 minutes
- ☐ 31 - 60 minutes
- ☐ After 60 minutes

2. How many cigarettes per day do you smoke?

- ☐ 10 or less
- ☐ 11 - 20
- ☐ 21 - 30
- ☐ 31 or more

Appendix D

Timeline Follow-Back for Cigarette Use

Instructions for Filling Out the Timeline Cigarette Use Calendar

To help us evaluate your cigarette use, we need to get an idea of what your smoking was like in the past ____ days. To do this, we would like you to fill out the attached calendar.

- ✓ Filling out the calendar is not hard!
- ✓ Try to be as accurate as possible.
- ✓ We recognize you won't have perfect recall. That's OKAY.

✓ WHAT TO FILL IN

- The idea is to record how many cigarettes you smoked for **each day** on the calendar.
- On days when you **did not smoke cigarettes**, not even one, you should write a "0."

It's important that something is written for <u>every</u> day, even if it is a "0".

✓ YOUR BEST ESTIMATE

- We realize it isn't easy to recall things with 100% accuracy.
- If you are not sure whether you smoked 15 or 16 cigarettes or whether you smoked on a Thursday or a Friday, give it your best guess! What is important is that 15 or 16 cigarettes is very different from 1 cigarette. The goal is to get a sense of how frequently you smoked, how much you smoked, and your patterns of smoking.

✓ HELPFUL HINTS

- If you have an appointment book you can use it to help you recall your use.
- Holidays such as Thanksgiving and Christmas are marked on the calendar to help you recall your smoking. Also, think about how much you smoked on personal holidays & events such as birthdays, vacations, or parties.
- If you have **regular patterns to your smoking**, you can use these to help you recall your use. For example, some people may only smoke during social situations.

✓ COMPLETING THE CALENDAR

- A blank calendar is attached. Write in the number of cigarettes you smoked on **each day**.
- The time period we are talking about on the calendar is

from _____ to _____.

- In estimating the number of cigarettes you smoked, be as accurate as possible.
- **DOUBLE CHECK THAT <u>ALL</u> DAYS ARE FILLED IN BEFORE RETURNING THE CALENDAR.**
- Before you start look at the **SAMPLE CALENDAR**.

✓ SAMPLE CALENDAR

2000	SUN	MON	TUES	WED	THURS	FRI	SAT
						1 20	2 0
S	3 20	4 Labor Day 20	5 23	6 28	7 21	8 20	9 23
E	10 20	11 20	12 20	13 28	14 25	15 0	16 24
P	17 20	18 20	19 20	20 20	21 22	22 22	23 24
T	24 21	25 22	26 26	27 24	28 23	29 0	30 22

Appendix E

Anxiety Sensitivity Index – III (ASI-3)

Please select the number that best corresponds to how much you agree with each item. If any items concern something that you have never experienced (e.g. fainting in public) answer on the basis of how you think you might feel if you had such an experience. Otherwise, answer all items on the basis of your own experience. Be careful to select only one number for each item and please answer all items.

	Very little 0	A little 1	Some 2	Much 3	Very Much 4
1. It is important for me not to appear nervous.	❍	❍	❍	❍	❍
2. When I cannot keep my mind on task I worry I might be going crazy.	❍	❍	❍	❍	❍
3. It scares me when my heart beats rapidly.	❍	❍	❍	❍	❍
4. When my stomach is upset, I worry I may be seriously ill.	❍	❍	❍	❍	❍
5. It scares me when I am unable to keep my mind on a task.	❍	❍	❍	❍	❍
6. When I tremble in the presence of others, I fear what people might think of me.	❍	❍	❍	❍	❍
7. When my chest feels tight, I get scared that I won't be able to breathe properly.	❍	❍	❍	❍	❍
8. When I feel pain in my chest, I worry that I'm going to have a heart attack.	❍	❍	❍	❍	❍
9. I worry that other people will notice my anxiety.	❍	❍	❍	❍	❍
10. When I feel "spacey" or spaced out I worry I may be mentally ill.	❍	❍	❍	❍	❍
11. It scares me when I blush in front of people.	❍	❍	❍	❍	❍
12. When I notice my heart skipping a beat, I worry that there is something seriously wrong with me.	❍	❍	❍	❍	❍

13. When I begin to sweat in a social situation, I fear people will think negatively of me.	❍	❍	❍	❍	❍
14. When my thoughts seem to speed up, I worry that I might be going crazy.	❍	❍	❍	❍	❍
15. When my throat feels tight, I worry that I could choke to death.	❍	❍	❍	❍	❍
16. When I have trouble thinking clearly, I worry that there is something wrong with me.	❍	❍	❍	❍	❍
17. I think it would be horrible for me to faint in public.	❍	❍	❍	❍	❍
18. When my mind goes blank, I worry there is something terribly wrong with me.	❍	❍	❍	❍	❍

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