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Panic Attacks and Smoking Cessation among Cancer Patients Receiving Smoking Cessation Treatment

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Abstract

Objective—Little is known about factors associated with smoking cessation in cancer patients. This study examined the impact of panic attacks on smoking abstinence likelihood among cancer patients receiving tobacco cessation treatment.

Method—The relationship of panic attacks to 7-day point-prevalence abstinence at mid-treatment, end of treatment, and 6-month post-end of treatment were examined among cancer patients ($N = 2,255$ patients; 50.1% female; $M_{age} = 54.9$, $SD = 11.0$) who received counseling and pharmacotherapy for smoking cessation. Panic attack history indexed by two questions from the Patient Health Questionnaire (PHQ). Post-prevalence abstinence was assessed via the Timeline Follow-Back.

Results—Cancer patients with a history of panic attacks, ($n = 493$, 21.9%) relative to those without, were less likely to be abstinent at mid-treatment ($OR = 0.79$, $CI_{95\%} = 0.64–0.98$) and end of treatment ($OR = 0.72$, $CI_{95\%} = 0.58–0.89$). After adjusting for significant covariates, panic attack history remained predictive of decreased abstinence likelihood at end of treatment ($OR = 0.78$, $CI_{95\%} = 0.62–0.99$).

Conclusions—Panic attacks may be related to poorer cessation outcome during smoking treatment among cancer patients, and may be usefully assessed and targeted for intervention.

Keywords

tobacco; panic attacks; abstinence; varenicline; nicotine replacement; cancer

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1. Introduction

It is estimated that 14–58% of smokers continue to smoke after receiving a cancer diagnosis (Cox *et al.*, 2003). Continued smoking among individuals who have been diagnosed with cancer is associated with cancer progression and treatment complications (Gritz, Dresler, & Sarna, 2005), while quitting smoking is associated with better cancer treatment outcomes and improved quality of life (Chen *et al.*, 2012; Cox, Africano, Tercyak, & Taylor, 2003; Gritz *et al.*, 2005; Toll, Brandon, Gritz, Warren, & Herbst, 2013), in addition to the typical health benefits of smoking cessation (e.g., decreased risk of tobacco-related disease, improved lung functioning). The National Cancer Institute and the American Association for Cancer Research guidelines recommend universal assessment and documentation of tobacco use among cancer patients, availability of tobacco treatment programs in comprehensive cancer centers (Morgan *et al.*, 2011; Toll *et al.*, 2013), and call for more research on the process of smoking cessation among cancer patients (Cox *et al.*, 2003).

Psychiatric disorders are a notable risk factor associated with the initiation and maintenance of smoking (CDCP, 2013; Lasser *et al.*, 2000; Piper *et al.*, 2010; Ziedonis *et al.*, 2008), and thus may be informative for understanding the nature of smoking among cancer patients. While relatively little scholarly work has examined the role of psychopathology in cancer patients seeking treatment to quit smoking, the presence of psychological disorders in cancer patients has been extensively reported (see reviews: Grassi, Biancosino, Marmai, Rossi, & Sabato, 2007; Kangas, Henry, & Bryant, 2002; Miovic & Block, 2007; Montel, 2010). One specific area of inquiry has addressed the presence of panic attacks among cancer patients, which is, in part, contextualized with the high prevalence of somatic worries and illness anxiety among cancer patients (Chaturvedi, Maguire, & Somashekar, 2006; Noyes *et al.*, 2005). Panic attacks, which reflect a discrete sense of extreme fear or impending doom accompanied by a massive autonomic surge and strong flight-or-fight action tendency (APA, 2000), are a risk marker for a relatively broad range of psychopathological conditions (e.g., Baillie & Rapee, 2005; Goodwin, Brook, & Cohen, 2005; Goodwin *et al.*, 2004) and are associated with physical illness, poorer quality of life, and disability (e.g., Goodwin, Pine, & Hoven, 2003; Kinley, Cox, Clara, Goodwin, & Sareen, 2009).

Clinical data suggest that approximately one-fifth of cancer patients presented with a current past-month history of panic attacks (Slaughter *et al.*, 2000). Case studies indicate that panic attacks may occur prior to cancer diagnosis (Griffeth & Mehra, 2008; Passik & Roth, 1999). Data also suggest that a cancer diagnosis, especially among younger patients (ages 15–54), is associated with increased odds of panic attacks (Rasic, Belik, Bolton, Chochinov, & Sareen, 2008), and that roughly 55% of cancer patients report a history of panic attacks following a cancer diagnosis (Slaughter *et al.*, 2000). Panic attacks may result in early termination of cancer treatment due to avoidance of uncomfortable bodily sensations experienced during treatment (Slaughter *et al.*, 2000). For example, one case series documented the presence of first-episode panic attacks in patients with head/neck cancers following head or neck surgery (Shimizu, Kinoshita, Akechi, Uchitomi, & Andoh, 2007). Here, patients reported distinct panic-relevant fears (e.g., neck stiffness indicative of feelings of being strangled), which were exacerbated by pain following surgical procedures (Shimizu *et al.*, 2007). Additionally, certain types of panic attack symptoms (e.g., respiratory) appear

to be more strongly associated with physical illness and cancer than other symptoms (e.g., cardiac or derealization symptoms; Bovasso & Eaton, 1999). It is of course worth noting that medical conditions should be ruled out as an explanation for panic attacks in this population (e.g., cancer tumors may cause panic attack symptoms; Tamburin, Cacciatori, Bonato, & Zanette, 2008; Wilcox, 1991). While specific mechanisms linking panic attacks to psychological and physical symptoms are not fully clear, panic attacks may enhance negative emotional learning in relation to various sources of interoceptive and exteroceptive cues and stressors, especially physical sensations (Bouton, Mineka, & Barlow, 2001). Collectively, these data illustrate the complex nature of panic attack symptoms in cancer patients.

There is growing evidence to suggest that panic attacks can also contribute to the maintenance of smoking (e.g., Cosci, Knuts, Abrams, Griez, & Schruers, 2010; Zvolensky, Feldner, Leen-Feldner, & McLeish, 2005). For example, smokers with a history of panic attacks relative to those without report higher levels of tobacco dependence (Piper, Cook, Schlam, Jorenby, & Baker, 2011; Vujanovic, Marshall, Gibson, & Zvolensky, 2010) and increased affect-regulatory smoking motivations (e.g., Farris, Zvolensky, Blalock, & Schmidt, 2014). Panic sensations/attacks are also associated with more severe subjective nicotine withdrawal symptom severity (Farris, Zvolensky, Otto, & Leyro, 2015), and lower success rates in quitting (Piper et al., 2011). Yet, there is no knowledge about the role of panic attacks in quit success among smokers with cancer. One prior study from our group examined the predictive role of anxiety disorders (in addition to depressive disorders, and probable alcohol abuse/dependence) in terms of abstinence likelihood at end-of treatment and six-months post-smoking cessation treatment among cancer patients (Blalock et al., 2011). Results indicated that cancer patients with depressive disorders and probable alcohol use disorders, but not anxiety disorders, were at a decreased likelihood of smoking abstinence at post-treatment and 6-months post-treatment, and that the comorbidity of psychopathology (depression, alcohol, and anxiety disorder) was associated with lesser odds of abstinence. This study did not examine the nature of panic attacks specifically; thus we are aware of no empirical data that have examined the interplay between panic attacks and smoking among cancer patients.

In the current study, we examined the role of panic attack history in relation to pre-treatment tobacco dependence and prediction of smoking abstinence following treatment, among cancer patients enrolled in a smoking cessation treatment program that included counseling and pharmacotherapy. We hypothesized that cancer patients with a history of panic attacks, relative to those patients with no history of panic attacks, would report higher levels of tobacco dependence, and a lower likelihood of smoking abstinence at the end of treatment and during long-term follow-up (three- and six-months post-end of treatment) than cancer patients without a history of panic attacks.

2. Method

2.1. Participants

The participants were 2,255 patients (50.1% female; $M_{age} = 54.9$, $SD = 11.0$) treated by the University of Texas MD Anderson Cancer Center Tobacco Treatment Program (TTP) from

2006 to 2013. See footnote 1 for additional information. The TTP provides assessment, counseling, and medication services free of charge and is available to all tobacco-using cancer patients at MD Anderson. The majority of patients (approximately 88%) were automatically electronically referred to the TTP if they self-reported using tobacco in the last 12 months. Approximately 10% of patients were referred directly from their treatment providers to the TTP, and about 2% of patients were self-referred. The patients comprising the current sample were diagnosed with head/neck (14.0%), lung (13.3%), lymphoma/hematological (9.2%), breast (8.8%), genitourinary (8.2%), colorectal/other gastrointestinal (7.4%), melanoma/other skin (4.9%), prostate (3.6%), carcinoma in situ (5.2%) or other cancers (10.4%), while 16.5% were being followed for cancer prevention (e.g., with benign neoplasm, lesions, nodule). Patients self-identified race as White (82.7%), Black (10.4%), Hispanic (3.7%), Asian (0.8%), and other (0.6%), with 1.5% not reported.

2.2. Procedure

The MD Anderson TTP treatment protocol included an initial in-person consultation followed by approximately 6–10 weeks of pharmacotherapy combined with smoking cessation counseling. The timing and duration of treatment was flexibly tailored to meet the needs of patients (i.e., patients were offered additional treatment as needed). Figure 1 illustrates the flow of treatment and follow-up assessment points. Follow-up assessments were conducted at approximately mid-treatment (Mid-TX: 45 days after initial consultation), 45 days post mid-treatment (here, termed ‘end of treatment’ [EOT]; 90 days after initial consultation and 6 months post-EOT (180 days after initial consultation). Patients are allowed to re-enroll in the TTP if desired, which is captured as an extension of treatment if within 15 months of their initial consult. If re-enrollment occurs more than 15 months after the initial consult, it is captured as a new treatment ‘episode’. The first treatment episode in the database was utilized for this sample. The average number of episodes was 1.3 ($SD = 0.7$) with a range from 1–8 episodes.

2.2.1. Initial Consultation—Patients were referred to the initial consultation through automatic electronic health record (EHR) referral, direct provider referral, or self-referral (Mallen, Blalock, & Cinciripini, 2006; Rabi, Karam-Hage, Blalock, & Cinciripini, 2014). At the initial consultation, information was obtained regarding smoking and cessation history, tobacco dependence, cancer treatment, psychosocial history, anxiety and depression symptoms, sleep, substance use, as well as other factors used in treatment planning. All consultations were completed by a Ph.D. or masters-level counselor. The counselor that conducted the initial assessment was assigned to the patient as the treating counselor. In addition, a medical consultation was conducted by medical staff (psychiatrist, physician assistant or advanced practice nurse) to determine the appropriateness of specific smoking cessation medications. A review of patient EHRs was conducted by the clinic research nurse prior to the initial consultation and initial medication contraindications were noted. During the medication consultation, the psychiatrist or physician assistant discussed medication

¹This sample partially overlaps with the sample evaluated in Blalock et al. (2011). The current sample differs by excluding patients being followed for cancer prevention (i.e., those without cancer tumors) and by including patients who completed follow-up assessments following publication of the prior study. Additionally, data from the first documented treatment episode was utilized for patients who had data available for more than one treatment episode ($n = 205$ cases).

options with patients. Medication recommendations were determined based on a clinical protocol, which included consideration of (a) past use and success with various pharmacotherapies for smoking cessation, (b) possible contraindications, and (c) patient preference. Initial consultation sessions were typically 1.5–2.5 hours in length.

2.2.2. Smoking Cessation Counseling—The MD Anderson Tobacco Treatment Program treatment protocol was designed in accordance with recommendations of the United States Department of Health and Human Services' *Treating Tobacco Use and Dependence: Clinical Practice Guideline* (Fiore *et al.*, 2008). Counseling sessions were conducted weekly over 6 to 10 weeks following consultation, occurred either in-person, via telephone or web-camera, and were approximately 30 to 45 minutes in duration. Counseling sessions were motivational interviewing-based (Miller & Rollnick, 2012) and included cognitive-behavioral strategies for smoking cessation, aligned with the clinical practice guidelines for treating tobacco dependence. Patients were able to approach quitting by setting a formal quit day or by gradual smoking reduction. Patients could initiate quitting/reduction at any point during treatment (i.e., this was not standardized). Broadly, treatment included problem-solving skills training, facilitation of intra-treatment social support, and strategies to address motivational factors related to cessation goals, as needed (e.g., express empathy, foster autonomy, develop discrepancy, roll with resistance, support self-efficacy). The treatment protocol was flexible, based on clinical need, patient's location, treatment schedule, individual preferences, and level of progress (Blalock *et al.*, 2011). In the current sample, the average number of treatment sessions attended was 8.6 ($SD = 6.5$). Treatment was most commonly delivered via telephone ($M = 79.6\%$ of sessions), with less common in-person sessions ($M = 20.1\%$) and a very small percentage of web-camera sessions ($M = 0.3\%$).

2.2.3. Pharmacotherapy—Patients were offered an initial 3 months of smoking cessation medication free of charge, including varenicline, bupropion, and nicotine replacement therapy (NRT; including patch, gum, lozenge, inhaler, and spray) or a combination of medications, per the recommended guidelines (Fiore *et al.*, 2008). Most patients filled their medication prescription on the same day as their initial consultation visit at the MD Anderson pharmacy (80.6%), which was free of charge. The clinic nurse contacted patients two weeks following the initial consultation to review progress with smoking cessation, any possible side effects of medication, and answer questions about dosing/use of treatment. If clinically warranted, treatment augmentation of original pharmacotherapy (e.g., strong craving not attenuated by use of behavioral strategies) or treatment switching (e.g., if due to side effects or no change in smoking behavior, despite behavioral strategies) were considered, typically around 45 days post-consultation visit. During each treatment session, counselors reviewed use of medication. If side effects were reported or refills of medication were requested, the treating psychiatrist, advanced practice nurse or physician assistant was consulted. In the event that patients changed pharmacotherapy treatment during the treatment episode, a new course of 12-week pharmacotherapy was provided free of charge, to ensure an adequate medication trial.

In the current study, the initial ‘base’ medication treatment phase lasted from days 1–45 post-consultation visit and continuation phase lasted from 46–145 days after the initial medication fill. See Figure 1 for illustration of the treatment protocol. Patients’ pharmacotherapy was re-assessed after approximately 45 days, and medication adjustments were made if clinically indicated in the second ‘continuation’ phase. Fifty percent of patients received mono-pharmacotherapy (i.e., only one medication; 50.2%) during the base treatment phase, and 41.0% received extended mono-pharmacotherapy that spanned into the continuation phase. The initial (‘base’) treatments included varenicline (44.1%), NRT (35.8% [14.7% episodic, 31.6% patch]), bupropion (XL or SR; 7.5%), combination varenicline and NRT (4.9%), combination bupropion and NRT (4.8%), or other medication/ combinations (2.8%). A minority of patients received treatment augmentation (increased dose of base medication; 4.9%) or switched to another medication (3.9%) after the base medication trial.

2.2.4. Follow-Up Assessments—Follow-up assessments of self-reported 7-day point prevalence abstinence (PPA) were conducted via telephone or in person by trained Tobacco Treatment Program research assistants at mid-TX, EOT, and 6-months post-EOT. The majority of follow-up assessments occurred via telephone ($M = 94.6\%$).

2.3. Measures

Demographic information and cancer tumor type was extracted from the patients’ EHRs. For descriptive purposes, tumor type was classified as being smoking-related or not, based on a pre-defined definition (based on USHDDS, 2014). Specifically, tobacco-related cancers were considered lung, head/neck, colorectal/other gastrointestinal, and genitourinary tumors.

Panic attack history was assessed at the consultation visit with the *Patient Health Questionnaire* a self-report assessment derived from the Primary Care Evaluation of Mental Disorders (PRIME-MD; Spitzer et al., 1994) that assesses common DSM-IV Axis I disorders seen in primary care. The PHQ has diagnostic validity comparable to the original clinician-administered PRIME-MD including in cancer patient populations (Spitzer, Kroenke, & Williams, 1999; Spitzer, Williams, Kroenke, Hornyak, & McMurray, 2000). Specifically, patients who endorsed both of the following questions from the PHQ were considered to have a panic attack history: (1) *In the last 4 weeks, have you had an anxiety attack —suddenly feeling fear or panic?*; and (2) *[IF YES] Has this ever happened before?* Use of modified/abbreviated screening algorithm versus traditional panic disorder scoring algorithm has been used before in medical samples with strong operating characteristics. Specifically, the modified/abbreviated screening algorithm has stronger sensitivity with lower specificity (93% and 78%, respectively) relative to the traditional scoring algorithm (greater specificity relative to sensitivity; 75% versus 96%, respectively; Löwe et al., 2003). The modified/abbreviated screening algorithm also has increased practicality due to brevity of assessment relative to full measure administration (Löwe et al., 2003). In addition, the PHQ was used to index the presence of probable psychiatric disorders, including depressive disorders, alcohol abuse/dependence, panic disorder, and other anxiety disorders. A dichotomous variable was computed to index the presence of any probable psychiatric disorder (0 = no disorder; 1 = one or more probable disorders).

The *Fagerström Test of Nicotine Dependence* (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991) is a 6-item scale that was used to assess gradations in tobacco dependence, with higher scores indicating more severe physiological dependence (possible range 0–10). In addition, a single item from the FTND was used to assess daily smoking rate at the consultation visit. The FTND has adequate internal consistency and test-retest reliability and is associated with key smoking variables (e.g., saliva cotinine; Heatherton et al., 1991; Pomerleau, Carton, Lutzke, Flessland, & Pomerleau, 1994).

Abstinence was assessed using the *Timeline Follow-Back procedure* (TLFB; Sobell & Sobell, 1996). Self-reported 7-day PPA (no smoking, not even a puff) was assessed during the previous 7-days at mid-TX, EOT, and 6-months post-EOT.

2.4. Data Analytic Strategy

Analyses were conducted in SPSS (version 22.0). First, differences between cancer patients with and without a panic attack history (0 = no panic attack history, 1 = panic attack history) were explored in relation to demographic (gender, age, race), smoking (level of tobacco dependence, cigarettes per day), and treatment variables (number of sessions completed, number of TTP episodes, session format, medication treatment). Next, a series of univariate logistic regression models were used to examine the effect of baseline characteristics and panic attack history in terms of 7-day PPA (0 = non-abstinent, 1 = abstinent) at the mid-TX, EOT, and 6-month post-EOT. For abstinence outcomes, intent-to-treat analyses were conducted, counting all individuals with missing data as non-abstinent, consistent with our prior work in this area (Blalock et al., 2011) and recommended by West et al. (2005). First, for each outcome time point, abstinence status was regressed on the baselined predictor variable (unadjusted univariate models). Second, stepwise multivariate logistic regression models were conducted for each abstinence outcome to examine the adjusted effects of panic attack history. Specifically, any significant baseline characteristics in the univariate model were included as covariates in the first step of each predictive model. Panic attack history was entered in the second step. Significant results were determined based on a standard criterion of $\alpha = .05$. We also report a Bonferroni corrected alpha, which offers a more conservative significance test ($\alpha = .05 \div 3$ [number of outcome timepoints/sets of analyses] = .0167).

3. Results

3.1. Descriptive Characteristics

Table 1 includes the descriptive characteristics of the sample, and by panic attack status. At consultation, participants smoked an average of 17.2 ($SD = 10.9$) cigarettes per day and reported moderate levels of tobacco dependence on the FTND ($M = 4.5$, $SD = 2.2$). A total of 21.9% ($n = 493$) of the sample reported a history of panic attacks, and 51.9% ($n = 1,171$) indicated having one or more probable Axis I disorder per the PHQ. The panic attack group, relative to those with no history of panic attacks, was significantly more likely to be female (70.4% versus 44.4%, $p < .001$) and younger in age ($M = 50.6$ versus $M = 56.0$, $p < .001$). Patients with a history of panic attacks did not differ from those without in terms of race, cigarettes per day, or level of tobacco dependence. Those with a history of panic attacks

were significantly more likely to have a probable psychiatric disorder including depressive disorder (55.8% versus 24.3%) and anxiety disorder (28.4% versus 18.8%, p 's < .001), but not alcohol use disorder. Per the PHQ, 38.7% of the patients with a history of panic attacks met criteria for probable panic disorder.

Regarding treatment characteristics, patients with panic attacks, relative to those without, did not differ in terms of number of treatment sessions completed or medication approach (e.g., solo-pharmacotherapy, extended solo-pharmacotherapy, augmented or switched medication), although they had significantly more treatment episodes at the TTP. Regarding the type of medication prescribed, relative to patients with no history of panic attacks, patients with a history of panic attacks were significantly more likely to receive NRT alone (43.2% versus 33.8%) and significantly less likely to receive varenicline (34.7% versus 46.8%). Patients with a history of panic attacks, relative to those without, were also significantly more likely to receive NRT as a treatment in the continuation phase (20.7% versus 16.8%), but did not differ in terms of likelihood of receiving varenicline during this phase (18.3% versus 21.4%).

3.2. Abstinence Outcomes

Results from the univariate and adjusted logistic regression models are presented in Table 2. At mid-TX (i.e., 45 days after initial medication fill), results indicated that cancer patients with a history of panic attacks were less likely to be abstinent (29.8%) relative to patients with no panic attack history (35.0%; Wald $\chi^2 = 4.54$, $df = 1$, $p = .033$; classification accuracy = 66.2%); although this effect is non-significant at the Bonferroni-corrected alpha level. In the adjusted model, controlling for FTND and presence to tobacco-related cancer, the effect of panic attack history on abstinence was non-significant (Wald $\chi^2 = 3.50$, $df = 1$, $p = .061$). Higher FTND scores at the consultation visit was significantly predictive of decreased abstinence likelihood at mid-TX (Wald $\chi^2 = 40.43$, $df = 1$, $p < .0001$) and having a tobacco-related cancer was significantly associated with increased likelihood of abstinence at mid-TX (Wald $\chi^2 = 9.06$, $df = 1$, $p = .003$).

At EOT, cancer patients with a history of panic attacks had a decreased likelihood of abstinence (32.0%) relative to those with no history of panic attacks (39.7%; Wald $\chi^2 = 9.45$, $df = 1$, $p = .002$; classification accuracy = 62.0%), which remained significant although a weaker effect, in the adjusted model (Wald $\chi^2 = 4.00$, $df = 1$, $p = .045$); this effect is non-significant at the Bonferroni-corrected alpha level. The FTND (Wald $\chi^2 = 38.14$, $df = 1$, $p < .0001$) was the only significant covariate that was predictive of decreased likelihood of abstinence at EOT.

At 6-months post-EOT, cancer patients with a panic attack history did not statistically differ from those with no history of panic attacks in abstinence (33.0% versus 36.5%, respectively). The univariate model of panic attack history predicting abstinence at 6-month post-EOT was non-significant (Wald $\chi^2 = 1.20$, $df = 1$, $p = .274$; classification accuracy = 64.0%). The adjusted model was significant, driven exclusively by the effect of the FTND in predicting decreased likelihood of abstinence at 6-months post-EOT (Wald $\chi^2 = 35.20$, $df = 1$, $p < .001$).²

3.3. Post Hoc Analyses

Based on group differences in prescription of NRT and varenicline at the consultation visit, we conducted post-hoc exploratory analyses on abstinence by panic attack status for those who received NRT versus varenicline (see Table 3). FTND scores at the consultation visit were entered as the model covariate based on its significant and consistent prediction of abstinence outcomes in the abovementioned analyses. A subset of patients who received mono-pharmacotherapy were included in these analyses ($n = 944$). The lower order constituent factors and interaction term between panic attack status (0 = no, 1 = yes) and medication status (0 = NRT, 1 = varenicline) were entered into a stepwise logistic regression model to test this model in predicting abstinence at mid-treatment, EOT, and 6-months post-EOT. Groups included NRT+No Panic ($n = 329$; 29.1%), varenicline+No panic ($n = 416$; 36.7%), NRT+Panic ($n = 119$; 10.5%) and varenicline+Panic ($n = 80$; 7.1%).

Controlling for the significant effect of FTND, the prediction model was significant at mid-TX (Wald $\chi^2 = 36.01$, $df = 4$, $p < .001$; classification accuracy = 64.8%). There was a significant main effect of medication status in the prediction of abstinence, such that cancer patients who received varenicline were at an increased likelihood of being abstinent at mid-TX (Wald $\chi^2 = 13.35$, $df = 1$, $p < .001$) and a non-significant effect for panic attack status (Wald $\chi^2 = 3.71$, $df = 1$, $p = .054$). In the second step, the interaction term was non-significant (Wald $\chi^2 = 0.06$, $df = 1$, $p = .807$). At EOT, the model was significant (Wald $\chi^2 = 31.16$, $df = 4$, $p < .001$; classification accuracy = 62.7%). There was a significant main effect of medication status and panic attack history predicting abstinence. Specifically, varenicline was significantly related to increased likelihood of abstinence at EOT (Wald $\chi^2 = 10.57$, $df = 1$, $p = .001$), whereas panic attack status was related to decreased likelihood of abstinence at EOT (Wald $\chi^2 = 5.04$, $df = 1$, $p = .025$), although this effect is non-significant at the Bonferroni-corrected alpha level. The interaction term was non-significant (Wald $\chi^2 = 0.09$, $df = 1$, $p = .760$). Lastly, at 6-months post-EOT, the model was significant (Wald $\chi^2 = 25.78$, $df = 4$, $p < .001$; classification accuracy = 68.4%). There was a significant effect for varenicline predicting increased likelihood of abstinence (Wald $\chi^2 = 8.52$, $df = 1$, $p = .004$); however, the main effect of panic attack status was non-significant (Wald $\chi^2 = 2.96$, $df = 1$, $p = .085$) as was the interaction term (Wald $\chi^2 = 0.07$, $df = 1$, $p = .791$).

4. Discussion

Approximately one-fifth (21.9%) of the cancer patients in this clinical sample reported having experienced a lifetime history of panic attacks. The prevalence of panic attacks in this sample of cancer patients is comparable to other documented estimates in nationally-representative samples of smokers (19.0%) and higher than estimates among former smokers (12.0%) and never-smokers (10.1%; e.g., Goodwin et al., 2014). Contrary to predictions, we found that cancer patients with panic attacks did not differ from those without panic attacks in level of tobacco dependence or cigarettes smoked per day. These data suggest that among cancer patients receiving treatment, panic attacks are not related to smoking severity.

²Subsequent analyses were conducted to test whether any of the baseline characteristics were significant moderators of the effect of panic attack history on smoking abstinence at Mid-TX or EOT. There were no significant interactions with panic attack history and any examined baseline characteristics.

However, cancer patients with a history of panic attacks had more treatment episodes at the TTP relative to cancer patients without a panic attack history, perhaps indicating motivation for smoking cessation, coupled with difficulties maintaining abstinence. Additionally, partially consistent with our hypotheses, panic attacks were associated with reduced rates of abstinence at mid-treatment and EOT, but not 6-months EOT. These findings should be qualified by the non-significant or weaker observed effects after adjusting for model covariates and considering the Bonferroni-corrected alpha level. These initial findings extend empirical work that found panic attacks were associated with early smoking cessation failure among non-cancer specific treatment-seeking smokers (Piper et al., 2011) and quit failure in epidemiologic samples (Bakhshaie, Zvolensky, & Goodwin, 2016), and uniquely adds to the literature by linking panic attacks to end of treatment quit failure. The finding that panic attacks had a non-significant effect on longer-term smoking cessation outcomes is comparable with other smoking cessation trials that have failed to find that psychiatric disorders are consistently predictive of smoking abstinence at long-term follow-ups (e.g., Piper et al., 2010).

Post hoc analyses indicated that cancer patients with panic attacks compared to those without were more likely to receive NRT and less likely to receive varenicline. While it is unknown why this difference was observed, decisions about medication prescriptions were impacted in part by patient preference, in addition to recommendations by the medical treatment team. It is possible that patients with a history of panic attacks may have had increased fear of taking varenicline due to concerns about potential side effects. It is also possible that prescribing practice was impacted by the potential for increased psychiatric events as adverse side effects of varenicline use (Wippold, Karam-Hage, Blalock, & Cinciripini, 2015). More recent evidence suggests that psychiatric side effects are largely no different than what is observed with placebo (based on a pooled analysis of 18 double-blinded, randomized placebo-controlled clinical trials; Pfizer, 2014). It would be important to explicitly examine these factors in future work. However, it is important to note that relative to NRT, varenicline was associated with increased likelihood of smoking abstinence at all time points, in patients with and without a history of panic attacks. Certainly, in light of these findings, it is possible that cancer patients with a history of panic attacks, relative to those with no history of panic attacks, had poorer abstinence rates due to greater use of NRT versus varenicline. The naturalistic (uncontrolled) nature of these data preclude systematic investigation of this hypothesis; however other non-cancer data suggest that even after adjusting for type of medication/therapeutic intervention, smokers with a history of panic attacks are significantly less likely to be abstinent after smoking cessation treatment relative to those without such history (Piper et al., 2011).

While not the primary focus of the current investigation, it is interesting to note that the majority of these cancer patients reported symptoms consistent with at least one or more probable psychiatric disorder on the PHQ (51.9%), which is higher than estimates in the general population of smokers (CDCP, 2013; Lasser et al., 2000; Morris, Burns, Waxmonsky, & Levinson, 2014). This is perhaps not surprising, given high rates (estimated 50%) of psychiatric disorders in cancer patients (Miovic & Block, 2007). Moreover, comorbid probable psychiatric disorders were common in cancer patients with a panic attack

history (81.7%) *and* those without (43.6%) suggesting that panic attacks were not simply redundant with comorbid psychopathology (i.e., distinct constructs).

The study has a number of limitations. First, patients were provided smoking cessation treatment based on individual need, within general TTP guidelines. That is, treatment was not standardized in terms of number of psychotherapy sessions, modality of intervention (telephone versus in-person), or type of pharmacological treatment. Additionally, while all clinicians utilized motivational enhancement and cognitive-behavioral intervention strategies, patients presented with varying treatment goals (e.g., smoking reduction only, complete abstinence, short-term abstinence during cancer treatment), which influenced the target of treatment. In addition, patients presented to the clinic in various stages of cancer progression and treatment, which likely influenced cessation goals, motivation, and treatment selection. As an illustration, a breast cancer patient presenting to the TTP for smoking cessation treatment four weeks prior to a planned mastectomy might be more strongly motivated for brief smoking abstinence given that abstinence is frequently required by surgical oncologists prior to this surgery. As a result, pre-surgery smoking cessation treatment sessions may focus on assessing reasons for smoking, barriers to cessation, adherence to pharmacotherapy, and developing short-term strategies for coping with smoking urges, and validating anxiety/worry related to cancer treatment. Re-assessment of willingness/motivation for maintaining smoking abstinence during post-surgery smoking cessation sessions may become the primary focus of treatment. This example illustrates the extent of potential variability in clinical treatment. Given that data were collected naturalistically in the context of clinical treatment, and systematic information regarding cancer characteristics or treatment was not available, the present analyses were unable to capture the nuances in smoking cessation that exist in this sample.

Moreover, given that the prevalence of panic attacks (and other psychopathology) is often associated with cancer diagnosis stage, status pre/post treatment, and uncertainty about the future (Pandey et al., 2006; Jacobsen & Jim, 2008), the lack of specific cancer treatment data limits the specificity of these findings. Relatedly, data were not available on the onset of panic attacks (pre- or post-cancer diagnosis), current use of psychotropic medications, or additional patient characteristics (e.g., socioeconomic status). Second, medication compliance was not measured. Third, self-report data were exclusively used to assess smoking abstinence status. Biochemical corroboration of self-reported smoking status would be a useful next research step. Fourth, past work has indicated that structured clinical interviews are the most valid method for measuring panic attack history, as many persons can misinterpret other negative mood states (e.g., worry) as panic attacks. Indeed, while the PHQ as scored here has strong sensitivity to detect presence of panic attacks in medical populations (when compared to a diagnostic assessment), the specificity is lower. Last, approximately 70% of cancer patients with a panic attack history were Caucasian females. Thus, the relative generalizability of findings may be limited.

Overall, the current findings add to the scholarly literature documenting the link between panic attacks and smoking maintenance, and uniquely extend this work to cancer patients. Given the notable risk that psychiatric disorders present for the initiation and maintenance of smoking (Ziedonis et al., 2008), and the high rates of psychiatric comorbidity within the

current sample, findings may, in part, support the important role that panic attacks may play in terms of achieving abstinence during the initial stages of early quit attempts. To further understand the nature of the panic attack-smoking treatment effect, future mechanistic work is needed to identify the processes underlying this association (e.g., heightened negative mood, nicotine withdrawal). While the effect sizes and classification accuracy of the current results were modest, these data suggest that there may be utility in assessing panic attacks and integrating interventions (targeted) to reduce panic attacks among cancer patients in the context of smoking cessation treatment. Empirically-derived cognitive-behavioral strategies for anxiety and panic (Craske & Barlow, 2007) are aimed at decreasing emotional sensitivity and reactivity to feared bodily sensations, to help individuals learn (or re-learn) a sense of tolerance, control, and safety in the presence of anxiety-related sensations. Through planned, controlled exposures to internal somatic sensations (i.e., interoceptive exposure), individuals experience feared sensations directly and corrective emotional and cognitive outcomes are facilitated, rather than in the naturally-occurring context where catastrophic misinterpretation of these symptoms likely to occur. For smokers, misinterpretation of internal bodily sensations may occur during cessation or smoking abstinence. Accordingly, smoking-panic interventions have aimed to integrate cognitive-restructuring with interoceptive and situational exposure to nicotine deprivation, in order to facilitate reduction in panic arousal (Schmidt, Raines, Allan, & Zvolensky, 2016) and smoking quit success (see Zvolensky et al., 2003, for non-cancer specific example of intervention). For cancer patients, smoking cessation treatment programs could be tailored to specifically provide psychoeducation about the cyclical nature of somatic arousal and smoking, and how physical health symptoms/concerns may further contribute to smoking maintenance and concerns about physiological arousal. It may also be important for treatment providers to increase patients' awareness to physical sensations that might be expected during the process of quitting smoking (e.g., due to nicotine withdrawal), and differentiate this from potential cancer symptoms and panic attack symptoms.

References

- American Psychiatric Association. Diagnostic and statistical manual of mental disorders – (4th ed. text revision). Arlington, VA: American Psychiatric Publishing; 2000.
- Baillie AJ, Rapee RM. Panic attacks as risk markers for mental disorders. *Social Psychiatry and Psychiatric Epidemiology*. 2005; 40(3):240–244. DOI: 10.1007/s00127-005-0892-3 [PubMed: 15742230]
- Bakhshaie J, Zvolensky MJ, Goodwin RD. Cigarette smoking and the onset and persistence of panic attacks during mid-adulthood in the United States: 1994–2005. *Journal of Clinical Psychiatry*. 2016; 77(1):e21–e24. DOI: 10.4088/JCP.14m09290 [PubMed: 26845274]
- Blalock JA, Lam C, Minnix JA, Karam-Hage M, Gritz ER, Robinson JD, Cinciripini PM. The effect of mood, anxiety, and alcohol use disorders on smoking cessation in cancer patients. *Journal of Cognitive Psychotherapy*. 2011; 25(1):82–96.
- Bovasso G, Eaton W. Types of panic attacks and their association with psychiatric disorder and physical illness. *Comprehensive Psychiatry*. 1999; 40(6):469–477. DOI: 10.1016/S0010-440X(99)90092-5 [PubMed: 10579380]
- Bouton ME, Mineka S, Barlow DH. A modern learning theory perspective on the etiology of panic disorder. *Psychological Review*. 2001; 108(1):4–32. DOI: 10.1037/0033-295X.108.1.4 [PubMed: 11212632]

- Center for Disease Control and Prevention. Smoking-attributable mortality, years of potential life lost, and productivity losses--United States, 2000--2004. *MMWR: Morbidity and Mortality Weekly Report*. 2008; 57(45):1226--1228. [PubMed: 19008791]
- Center for Disease Control and Prevention. Vital Signs: Current Cigarette Smoking Among Adults Aged 18 Years with Mental Illness — United States, 2009–2011. *Morbidity and Mortality Weekly Report*. 2013; 62(5):77–80. [PubMed: 23388550]
- Chaturvedi SK, Maguire GP, Somashekar BS. Somatization in cancer. *International Review of Psychiatry*. 2006; 18(1):49–54. DOI: 10.1080/09540260500466881 [PubMed: 16451880]
- Chen J, Qi Y, Wampfler JA, Jatoi A, Garces YI, Busta AJ, ... Yang P. Effect of cigarette smoking on quality of life in small cell lung cancer patients. *European Journal of Cancer*. 2012; 48(11):1593–1601. DOI: 10.1016/j.ejca.2011.12.002 [PubMed: 22244802]
- Cosci F, Knuts IJE, Abrams K, Griez EJJ, Schruers KRJ. Cigarette smoking and panic: A critical review of the literature. *Journal of Clinical Psychiatry*. 2010; 71(5):606–615. [PubMed: 19961810]
- Cox LS, Africano NL, Tercyak KP, Taylor KL. Nicotine dependence treatment for patients with cancer. *Cancer*. 2003; 98(3):632–644. DOI: 10.1002/cncr.11538 [PubMed: 12879483]
- Craske, MG., Barlow, DH. *Treatments that Work. 4.* Oxford University Press Inc; New York, NY: 2007. *Mastery of your anxiety and panic: Therapist Guide.*
- Farris SG, Zvolensky MJ, Blalock JA, Schmidt NB. Negative affect and smoking motives sequentially mediate the effect of panic attacks on tobacco-relevant processes. *American Journal of Drug and Alcohol Abuse*. 2014; 40(3):230–239. DOI: 10.3109/00952990.2014.891038 [PubMed: 24720260]
- Farris SG, Zvolensky MJ, Otto MW, Leyro TM. The role of distress intolerance for panic and nicotine withdrawal symptoms during a biological challenge. *Journal of Psychopharmacology*. 2015; 29(7):783–791. DOI: 10.1177/0269881115575536 [PubMed: 25762651]
- Fiore, MC., Jaen, CR., Baker, TB., Bailey, WC., Benowitz, N., Curry, SJ. *Clinical Practice Guideline. Rockville, MD: U. S. Department of Health and Human Services. Public Health Service; 2008. Treating Tobacco Use and Dependence: 2008 Update.*
- Goodwin RD, Brook JS, Cohen P. Panic attacks and the risk of personality disorder. *Psychological Medicine*. 2005; 35(2):227–235. DOI: 10.1017/S0033291704003319 [PubMed: 15841680]
- Goodwin RD, Lieb R, Hoefler M, Pfister H, Bittner A, Beesdo K, Wittchen HU. Panic attack as a risk factor for severe psychopathology. *The American Journal of Psychiatry*. 2004; 161(12):2207–2214. DOI: 10.1176/appi.ajp.161.12.2207 [PubMed: 15569891]
- Goodwin RD, Pine DS, Hoven CW. Asthma and panic attacks among youth in the community. *Journal of Asthma*. 2003; 40(2):139–145. DOI: 10.1081/JAS-120017984 [PubMed: 12765315]
- Goodwin RD, Wall MM, Choo T, Galea S, Horowitz J, Nomura Y, ... Hasin DS. Changes in the prevalence of mood and anxiety disorders among male and female current smokers in the United States: 1990–2001. *Annals of Epidemiology*. 2014; 24(7):493–497. DOI: 10.1016/j.annepidem.2014.01.014 [PubMed: 24935462]
- Grassi L, Biancosino B, Marmai L, Rossi E, Sabato S. Psychological factors affecting oncology conditions. *Advances in Psychosomatic Medicine*. 2007; 28:57–71. DOI: 10.1159/0000106797 [PubMed: 17684320]
- Griffeth BT, Mehra A. Panic as a harbinger of pancreatic cancer. *Psychosomatics: Journal Of Consultation And Liaison Psychiatry*. 2008; 49(6):538–539. DOI: 10.1176/appi.psy.49.6.538
- Gritz ER, Dresler C, Sarna L. Smoking, the missing drug interaction in clinical trials: ignoring the obvious. *Cancer Epidemiol Biomarkers Prev*. 2005; 14(10):2287–2293. DOI: 10.1158/1055-9965.epi-05-0224 [PubMed: 16214906]
- Heatherton TF, Kozlowski LT, Frecker RC, Fagerström K. The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire. *British Journal of Addiction*. 1991; 86(9):1119–1127. DOI: 10.1111/j.1360-0443.1991.tb01879.x [PubMed: 1932883]
- Jacobsen PB, Jim HS. Psychosocial interventions for anxiety and depression in adult cancer patients: achievements and challenges. *CA: A Cancer Journal of Clinicians*. 2008; 58(4):214–30.
- Kangas M, Henry JL, Bryant RA. Posttraumatic stress disorder following cancer: A conceptual and empirical review. *Clinical Psychology Review*. 2002; 22(4):499–524. [PubMed: 12094509]

- Kinley DJ, Cox BJ, Clara I, Goodwin RD, Sareen J. Panic attacks and their relation to psychological and physical functioning in Canadians: Results from a nationally representative sample. *The Canadian Journal of Psychiatry/La Revue canadienne de psychiatrie*. 2009; 54(2):113–122.
- Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: A population-based prevalence study. *Journal of the American Medical Association*. 2000; 284(20):2606–2610. [PubMed: 11086367]
- Löwe B, Gräfe K, Zipfel S, Spitzer RL, Herrmann-Lingen C, Witte S, Herzog W. Detecting panic disorder in medical and psychosomatic outpatients: Comparative validation of the Hospital Anxiety and Depression Scale, the Patient Health Questionnaire, a screening question, and physicians' diagnosis. *Journal Of Psychosomatic Research*. 2003; 55(6):515–519. DOI: 10.1016/S0022-3999(03)00072-2 [PubMed: 14642981]
- Mallen MJ, Blalock JA, Cinciripini PM. Using technology to serve patients and practitioners: A comprehensive tobacco-cessation program for cancer patients. *Counselling & Psychotherapy Research*. 2006; 6(3):196–201.
- Miller, WR., Rollnick, S. *Motivational interviewing: Helping people change* (3rd edition). New York, NY, US: Guilford Press; 2013.
- Miovic M, Block S. Psychiatric disorders in advanced cancer. *Cancer*. 2007; 110(8):1665–1676. [PubMed: 17847017]
- Montel S. Mood and anxiety disorders in breast cancer: An update. *Current Psychiatry Reviews*. 2010; 6(1):56–63.
- Morgan G, Schnoll RA, Alfano CM, Evans SE, Goldstein A, Ostroff J, ... Cox LS. National cancer institute conference on treating tobacco dependence at cancer centers. *Journal of Oncology Practice*. 2011; 7(3):178–182. DOI: 10.1200/jop.2010.000175 [PubMed: 21886500]
- Morris CD, Burns EK, Waxmonsky JA, Levinson AH. Smoking cessation behaviors among persons with psychiatric diagnoses: Results from a population-level state survey. *Drug and Alcohol Dependence*. 2014; 136:63–68. DOI: 10.1016/j.drugalcdep.2013.12.010 [PubMed: 24417963]
- Noyes RJ, Carney CP, Hillis SL, Jones LE, Langbehn DR. Prevalence and correlates of illness worry in the general population. *Psychosomatics: Journal Of Consultation And Liaison Psychiatry*. 2005; 46(6):529–539. DOI: 10.1176/appi.psy.46.6.529
- Passik SD, Roth AJ. Anxiety symptoms and panic attacks preceding pancreatic cancer diagnosis. *Psycho-Oncology*. 1999; 8(3):268–272. DOI: 10.1002/(SICI)1099-1611(199905/06)8:3<268::AID-PON369>3.0.CO;2-W [PubMed: 10390740]
- Pandey M, Sarita GP, Devi N, Thomas BC, Mussain BM, Krishnan R. Distress, anxiety, and depression in cancer patients undergoing chemotherapy. *World Journal of Surgical Oncology*. 2006; 4:68.doi: 10.1186/1477-7819-4-68 [PubMed: 17002797]
- Pfizer. Chantix® (varenicline) tablets: Highlights of prescribing information. 2014. Retrieved from http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/021928s032s036s038lbl.pdf
- Piper ME, Cook JW, Schlam TR, Jorenby DE, Baker TB. Anxiety diagnoses in smokers seeking cessation treatment: relations with tobacco dependence, withdrawal, outcome and response to treatment. *Addiction*. 2011; 106(2):418–427. DOI: 10.1111/j.1360-0443.2010.03173.x [PubMed: 20973856]
- Piper ME, Smith SS, Schlam TR, Fleming MF, Bittrich AA, Brown JL, ... Baker TB. Psychiatric disorders in smokers seeking treatment for tobacco dependence: relations with tobacco dependence and cessation. *Journal of Consulting and Clinical Psychology*. 2010; 78(1):13–23. DOI: 10.1037/a0018065 [PubMed: 20099946]
- Pomerleau CS, Carton SM, Lutzke ML, Flessland KA, Pomerleau OF. Reliability of the Fagerstrom Tolerance Questionnaire and the Fagerstrom Test for Nicotine Dependence. *Addictive Behaviors*. 1994; 19(1):33–39. DOI: 10.1016/0306-4603(94)90049-3 [PubMed: 8197891]
- Rabius V, Karam-Hage M, Blalock JA, Cinciripini PM. "Meaningful use" provides a meaningful opportunity. *Cancer*. 2014; 120(4):464–468. [PubMed: 24496865]
- Rasic DT, Belik S, Bolton JM, Chochinov HM, Sareen J. Cancer, mental disorders, suicidal ideation and attempts in a large community sample. *Psycho-Oncology*. 2008; 17(7):660–667. DOI: 10.1002/pon.1292 [PubMed: 18050260]

- Schmidt NB, Raines AM, Allan NP, Zvolensky MJ. Anxiety sensitivity risk reduction in smokers: A randomized control trial examining effects on panic. *Behaviour Research and Therapy*. 2016; 77:138–146. DOI: 10.1016/j.brat.2015.12.011 [PubMed: 26752327]
- Shimizu K, Kinoshita H, Akechi T, Uchitomi Y, Andoh M. First panic attack episodes in head and neck cancer patients who have undergone radical neck surgery. *Journal of Pain and Symptom Management*. 2007; 34(6):575–578. DOI: 10.1016/j.jpainsymman.2007.08.007 [PubMed: 17959346]
- Slaughter JR, Jain A, Holmes S, Reid JC, Bobo W, Sherrod NB. Panic disorder in hospitalized cancer patients. *Psycho-Oncology*. 2000; 9(3):253–258. [PubMed: 10871721]
- Sobell, LC., Sobell, MB. *Timeline FollowBack user's guide: A calendar method for assessing alcohol and drug use*. Toronto: Addiction Research Foundation; 1996.
- Spitzer RL, Kroenke K, Williams JBW. Validation and utility of a self-report version of PRIME-MD: The PHQ Primary Care Study. *JAMA: Journal of the American Medical Association*. 1999; 282(18):1737–1744. [PubMed: 10568646]
- Spitzer RL, Williams JB, Kroenke K, Hornyak R, McMurray J. Validity and utility of the PRIME-MD patient health questionnaire in assessment of 3000 obstetric-gynecologic patients: the PRIME-MD Patient Health Questionnaire Obstetrics-Gynecology Study. *American Journal of Obstetrics and Gynecology*. 2000; 183(3):759–769. [PubMed: 10992206]
- Spitzer RL, Williams JBW, Kroenke K, Linzer M, deGruy FV, Hahn SR, ... Johnson JG. Utility of a new procedure for diagnosing mental disorders in primary care: The PRIME-MD 1000 study. *JAMA: Journal of the American Medical Association*. 1994; 272(22):1749–1756. [PubMed: 7966923]
- Tamburin S, Cacciatori C, Bonato C, Zanette G. Cingulate gyrus tumor presenting as panic attacks. *The American Journal of Psychiatry*. 2008; 165(5):651–652. DOI: 10.1176/appi.ajp.2007.07061005
- Toll BA, Brandon TH, Gritz ER, Warren GW, Herbst RS. Assessing tobacco use by cancer patients and facilitating cessation: an American Association for Cancer Research policy statement. *Clinical Cancer Research*. 2013; 19(8):1941–1948. DOI: 10.1158/1078-0432.ccr-13-0666 [PubMed: 23570694]
- US Department of Health and Human Services. *The health consequences of smoking - 50 years of progress: A report of the Surgeon General*. Atlanta, GA: 2014.
- Vujanovic AA, Marshall EC, Gibson LE, Zvolensky MJ. Cognitive-affective characteristics of smokers with and without posttraumatic stress disorder and panic psychopathology. *Addictive Behaviors*. 2010; 35(5):419–425. [PubMed: 20060228]
- West R, Hajek P, Stead L, Stapleton J. Outcome criteria in smoking cessation trials: Proposal for a common standard. *Addiction*. 2005; 100(3):299–303. [PubMed: 15733243]
- Wilcox JA. Pituitary microadenoma presenting as panic attacks. *The British Journal of Psychiatry*. 1991; 158:426–427. DOI: 10.1192/bjp.158.3.426 [PubMed: 1645208]
- Wippold R, Karam-Hage M, Blalock JA, Cinciripini PM. Selection of optimal tobacco cessation medication treatment in patients with cancer. *Clinical Journal of Oncology Nursing*. 2015; 19(2): 170–175. DOI: 10.1188/15.CJON.170-175 [PubMed: 25840382]
- Ziedonis D, Hitsman B, Beckham JC, Zvolensky M, Adler LE, Audrain-McGovern J, ... Riley WT. Tobacco use and cessation in psychiatric disorders: National Institute of Mental Health report. *Nicotine Tob Res*. 2008; 10(12):1691–1715. DOI: 10.1080/14622200802443569 [PubMed: 19023823]
- Zvolensky MJ, Feldner MT, Leen-Feldner EW, McLeish AC. Smoking and panic attacks, panic disorder, and agoraphobia: A review of the empirical literature. *Clinical Psychology Review*. 2005; 25(6):761–789. [PubMed: 15975699]
- Zvolensky MJ, Lejuez CW, Kahler CW, Brown RA. Integrating an interoceptive exposure-based smoking cessation program into the cognitive-behavioral treatment of panic disorder: Theoretical relevance and case demonstration. *Cognitive and Behavioral Practice*. 2003; 10(4):347–357. DOI: 10.1016/S1077-7229(03)80052-4

Figure 1.
Timeline of treatment course

Table 1

Descriptive Characteristics among Cancer Patients with and without Panic Attack History

Variable	Total Sample (n = 2255)	Panic Attack History (n = 493)	No Panic Attack History (n = 1962)	X ² or t
Gender (n, % Female)	1129 (50.1%)	347 (70.4%)	782 (44.4%)	104.20 ***
Race (n, % White)	1866 (82.7%)	404 (81.9%)	1458 (83.0%)	0.28
Age (<i>M, SD</i>)	54.9 (11.0)	50.6 (10.7)	56.0 (10.8)	9.83 ***
Tobacco-Related Cancer (n, % Y) ^a	953 (42.3%)	196 (39.8%)	757 (43.0%)	1.62
Any Probable Psychiatric Disorder	1171 (51.9%)	403 (81.7%)	768 (43.6%)	224.66 ***
# Probable Psychiatric Disorders	0.7 (0.8)	1.3 (0.9)	0.5 (0.7)	-18.38 ***
Depressive Disorder (<i>n, % Y</i>)	704 (31.2%)	275 (55.8%)	429 (24.3%)	177.26 ***
Alcohol Abuse/Dependence (<i>n, % Y</i>)	210 (9.3%)	56 (11.4%)	154 (8.7%)	3.13
Panic Disorder (<i>n, % Y</i>)	191 (8.5%)	191 (38.7%)	--	--
Other Anxiety Disorder (<i>n, % Y</i>)	471 (20.9%)	140 (28.4%)	331 (18.8%)	21.54 ***
Tobacco dependence (<i>M, SD</i>)	4.5 (2.2)	4.7 (2.3)	4.5 (2.2)	-1.61
Cigarettes per day (<i>M, SD</i>)	17.2 (10.9)	16.7 (10.7)	17.3 (10.9)	1.12
Treatment Sessions attended (<i>M, SD</i>)	8.6 (6.5)	9.1 (7.1)	8.5 (6.3)	-1.63
% Telephone sessions	79.6%	78.1%	80.1%	1.31
% In-Person session	20.1%	21.4%	19.7%	-1.13
% Web-Cam session	0.3%	0.5%	0.2%	-1.02
# Treatment Episodes at TTP (<i>M, SD</i>)	1.3 (0.7)	1.4 (0.8)	1.3 (0.7)	-2.30 *
Medication Approach				
Solo medication (<i>n, % Y</i>)	1132 (50.2%)	247 (50.1%)	885 (50.2%)	0.57
Extended mediation (<i>n, % Y</i>)	924 (41.0%)	205 (41.6%)	719 (40.8%)	
Augmented mediation (<i>n, % Y</i>)	110 (4.9%)	21 (4.3%)	89 (5.1%)	
Switched medication (<i>n, % Y</i>)	89 (3.9%)	20 (4.1%)	69 (3.9%)	

* $p < .05$,** $p < .01$,*** $p < .001$;^a Tobacco-related cancers were considered lung, head/neck, colorectal/other gastrointestinal, and genitourinary tumors.

Table 2

Logistic regression models

Predictor	Abstinence at Mid-TX			Abstinence at EOT			Abstinence at Post- EOT		
	Univariate Model		Adjusted Model	Univariate Model		Adjusted Model	Univariate Model		Adjusted Model
	OR (95% CI)		AOR (95% CI)	OR (95% CI)		AOR (95% CI)	OR (95% CI)		AOR (95% CI)
Tobacco Dependence ^a	0.88 (0.84–0.92)	**	0.88 (0.84–0.91)	**	0.88 (0.85–0.92)	**	0.88 (0.85–0.92)	**	0.89 (0.85–0.92)
Cancer Type ^b	1.28 (1.07–1.53)	**	1.31 (1.31–1.57)	**	1.14 (0.96–1.35)		1.14 (0.96–1.35)		--
Gender ^c	0.88 (0.74–1.05)		--		0.87 (0.74–1.04)		0.86 (0.72–1.02)		--
Age	1.01 (0.99–1.02)		--		1.01 (1.00–1.02)	*	1.00 (0.99–1.01)		--
% In-Person sessions	1.00 (0.99–1.01)		--		0.99 (0.99–1.00)		1.00 (0.99–1.00)		--
Any PHQ diagnosis ^d	0.90 (0.76–1.07)		--		0.82 (0.69–0.97)	*	0.86 (0.72–1.02)		--
# PHQ diagnoses	0.90 (0.81–1.01)		--		0.87 (0.78–0.97)	*	0.83 (0.75–1.14)		0.90 (0.80–1.00)
# TTP Episodes	0.89 (0.78–1.00)		--		0.88 (0.78–0.99)	*	0.92 (0.81–1.03)		0.92 (0.82–1.04)
Panic attack history	0.79 (0.64–0.98)	*	0.81 (0.65–1.01)		0.72 (0.58–0.89)	**	0.78 (0.62–0.99)	*	0.99 (0.78–1.25)

*
p < .05,**
p < .01;

Univariate models include crude ORs; Adjusted model include only significant covariates from univariate models.

^aFTND;^bTobacco-related cancer (0=no, 1=yes),^cGender (0=male, 1=female);^dAny PHQ diagnosis (0 = none, 1 = at least one disorder per PHQ).

Table 3

Post-hoc logistic regression models (n = 944)

Predictor	Abstinence at Mid-TX		Abstinence at EOT		Abstinence at Post- EOT	
	AOR (95% CI)		AOR (95% CI)		AOR (95% CI)	
Tobacco Dependence ^a	0.87 (0.81–0.93)	**	0.88 (0.83–0.94)	**	0.88 (0.83–0.94)	**
Medication ^b	1.67 (1.27–2.21)	**	1.58 (1.20–2.07)	**	1.53 (1.15–2.03)	*
Panic attack ^c	0.71 (0.50–1.00)		0.67 (0.48–0.95)	*	0.73 (0.51–1.05)	
Panic x Medication ^d	0.92 (0.46–1.84)		1.12 (0.56–2.24)		0.91 (0.44–1.87)	

Note:

*
p < .05,**
p < .01;^aFTND;^bMedication type (0=NRT, 1=varenicline),^cPanic attack history (0=no, 1=yes).^dInteraction term.