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BRIEF COMMUNICATION

Smokers With Pain Are More Likely to Report Use of E-Cigarettes and Other Nicotine Products

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Pain and tobacco cigarette smoking frequently co-occur, and smokers report using cigarettes to self-medicate pain. Despite the growing popularity of e-cigarettes and alternative nicotine products, no research has examined their use as a function of pain status. The goal of this study was to test cross-sectional relations between the presence of pain and current use of e-cigarettes, lifetime polynicotine use, and lifetime use of individual nicotine products. The sample was comprised of current daily smokers ($N = 301$) who were recruited to participate in a web-based longitudinal study examining predictors of cessation milestones. Results indicated that smokers who endorsed past-2-week significant pain (vs. no past-2-week pain) were 3 times more likely to endorse current e-cigarette use, reported having used a greater number of nicotine products in their lifetime, and were nearly 3 times more likely to endorse lifetime polynicotine use. In terms of individual products, smokers with pain were approximately 4 times as likely to have tried e-cigarettes and 7 times more likely to have tried cigars. This is the first study to demonstrate that smokers who endorse significant pain are also more likely to endorse use of e-cigarettes and other combustible nicotine products. Future research is needed to examine polynicotine use in relation to pain reporting among more varied samples of smokers and nonsmokers.




Public Health Significance

This is the first study to demonstrate that tobacco cigarette smokers with co-occurring pain are more likely to also use e-cigarettes and other nicotine products (relative to smokers without co-occurring pain). Smokers with pain may use additional nicotine products to help manage painful symptoms. Concurrent use of multiple nicotine products among smokers with pain may impede smoking cessation and contribute to the maintenance of addiction.

Keywords: e-cigarettes, nicotine, tobacco, pain

Pain and tobacco cigarette smoking are highly prevalent and frequently comorbid conditions that engender a combined economic burden of more than \$800 billion in health care costs and lost productivity in the United States each year (Gaskin & Richard, 2012; U.S. Department of Health and Human Services, 2014; Xu, Bishop, Kennedy, Simpson, & Pechacek, 2015). Prevalence data indicate that rates of smoking among individuals with co-occurring

pain are approximately 2 to 3 times greater than those observed in the general population (Michna et al., 2004; Orhurhu, Pittelkow, & Hooten, 2015; Zvolensky, McMillan, Gonzalez, & Asmundson, 2009). There is also evidence that smokers experience greater frequency and intensity of pain and greater pain-related functional impairment (Palmer, Syddall, Cooper, & Coggon, 2003; Weingarten et al., 2008).

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A reciprocal model of pain and smoking posits that these conditions interact in a bidirectional manner, resulting in greater pain and the maintenance of cigarette dependence (Ditre, Brandon, Zale, & Meagher, 2011; Ditre, Zale, & LaRowe, 2019; Zale, Maisto, & Ditre, 2016). Consistent with this framework, regular smoking has been identified as a risk factor in the onset and progression of painful conditions (Shiri, Karppinen, Leino-Arjas, Solovieva, & Viikari-Juntura, 2010; Sugiyama et al., 2010; Weingarten et al., 2009), and there is evidence that pain is a potent motivator of smoking urge and behavior (Dhingra et al., 2014; Ditre & Brandon, 2008; Ditre, Heckman, Butts, & Brandon, 2010; Kosiba, Zale, & Ditre, 2018). Nicotine has also been shown to confer acute analgesia (Ditre, Heckman, Zale, Kosiba, & Maisto, 2016), and smokers report using cigarettes to cope with pain (e.g., Jamison, Stetson, & Parris, 1991; Patterson et al., 2012).

Despite growing empirical focus on interrelations between pain and cigarette use, surprisingly limited work has examined covariation between pain and the use of other nicotine/tobacco products. The use of electronic cigarettes (e-cigarettes), cigars, smokeless tobacco, and hookah have risen sharply over the past decade (Corey et al., 2014; Delnevo et al., 2014; King, Patel, Nguyen, & Dube, 2014; Lee, Hebert, Nonnemaker, & Kim, 2014), and almost half of nicotine users report concurrent use of multiple nicotine products (Kasza et al., 2017). Polynicotine use (vs. single product use) is also associated with greater nicotine exposure (Bombard, Pederson, Nelson, & Malarcher, 2007; Bombard, Rock, Pederson, & Asman, 2008) and more severe nicotine dependence (Soule, Pomeranz, Moorhouse, & Barnett, 2015).

The increased prevalence of polynicotine use has spurred interest in identifying individual difference factors that may promote such use (Cummins, Zhu, Tedeschi, Gamst, & Myers, 2014; Hartwell, Thomas, Egan, Gilmore, & Petticrew, 2017; Jones, Popova, Weaver, Pechacek, & Eriksen, 2018). One recently published study showed that e-cigarette users with co-occurring pain (vs. no pain) were more dependent on e-cigarettes and perceived a greater number of barriers to quitting e-cigarettes (Zvolensky et al., 2019). Acute nicotine deprivation among cigarette smokers has been shown to increase pain intensity and sensitivity to experimental pain (Ditre, Zale, LaRowe, Kosiba, & De Vita, 2018), and e-cigarette users with co-occurring pain may endorse greater perceived difficulty quitting due to the exacerbation of pain during a quit attempt. Additionally, the acute pain-reducing effects of nicotine (Ditre et al., 2016) may negatively reinforce e-cigarette use and strengthen beliefs regarding the utility of e-cigarettes and other nicotine products for pain reduction. Greater lifetime nicotine exposure has further been shown to increase risk for the worsening of pain over time (De Vita, Maisto, Ansell, Zale, & Ditre, 2019). Although these findings provide evidence of a positive relation between pain and e-cigarette use/dependence, the degree to which such associations extend to concurrent traditional cigarette smokers or individuals who use other types of nicotine products remains unclear. The goal of the current study was to examine the use of e-cigarettes and other nicotine products as a function of pain status among current smokers. We hypothesized that smokers who endorsed past-2-week significant pain (vs. no past-2-week pain) would be more likely to report current use of e-cigarettes, lifetime polynicotine use, and lifetime use of individual nicotine products (i.e., e-cigarettes, cigars, cigarillos, pipes, hookah, chewing tobacco, dip, snus, and snuff).

Method

All study procedures were approved by the institutional review board at the Medical University of South Carolina. The current sample was comprised of cigarette smokers ($N = 301$) recruited via ads posted on Craigslist and ResearchMatch for a longitudinal study examining cessation fatigue as a predictor of cessation milestones (Heckman et al., 2018). Participants were required to smoke at least 10 cigarettes per day on at least 25 of the last 30 days and endorse strong intention to quit smoking in the next month (score of at least 7 out of 10) using a single-item Contemplation Ladder (Biener & Abrams, 1991). These data were collected at baseline prior to initiation of a quit attempt, using RED-Cap (Harris et al., 2009).

Measures

Cigarette dependence. Cigarette dependence was assessed using the Heaviness of Smoking Index (HSI; Heatherton, Kozlowski, Frecker, Rickert, & Robinson, 1989). The HSI 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?”). Previous work supports the total score as a valid and reliable measure of cigarette dependence (Borland, Yong, O'Connor, Hyland, & Thompson, 2010).

E-cigarette and other nicotine product use. Participants were asked, “Over the past week (including today), on how many days have you used an e-cigarette (even a puff)?” Those who endorsed using an e-cigarette over the past 7 days were coded as current e-cigarette users. The use of a single item for past-7-day use has shown high concordance with more detailed assessments of use (e.g., timeline follow-back; Bernstein, Rosner, & Toll, 2016). Participants were also queried regarding lifetime use (“Have you EVER tried any of the following products?”) of e-cigarettes, cigars, cigarillos, pipes, hookah, chewing tobacco, dip, snus, and snuff. Lifetime polynicotine use was determined based on whether current cigarette smokers endorsed having tried at least one additional nicotine product. Total number of nicotine products used and lifetime use of individual products were also tabulated.

Pain status. Past-2-week pain status was determined using a single yes/no item (i.e., “Have you had any significant pain in the past two weeks?”). The presence of past-2-week pain has predicted greater scores on more comprehensive measures of pain severity (Von Korff, Ormel, Keefe, & Dworkin, 1992). Additionally, past-1- and 2-week pain status has been associated with smoking rates and nicotine dependence (Aigner et al., 2016; Ditre, Gonzalez, et al., 2011; Hahn, Rayens, Kirsh, & Passik, 2006).

Data Analytic Plan

All analyses were conducted using SPSS Version 24. First, t tests and χ^2 tests were used to examine differences in participant characteristics as a function of pain. Variables that differed by pain status were included as covariates in adjusted models (Pocock, Assmann, Enos, & Kasten, 2002). Adjusted models also covaried for participant sex and age, as prior research has shown these factors to be strong predictors of e-cigarette and polynicotine use (Jones et al., 2018; Stanton & Halenar, 2018). Second, unadjusted

and adjusted logistic regression models were used to examine likelihood of current e-cigarette use and lifetime polynicotine use as a function of pain. Third, analysis of covariance assessed differences in total number of lifetime nicotine products as a function of pain. Finally, logistic regressions models tested differences in lifetime use of individual nicotine products (i.e., e-cigarettes, chewing tobacco, snuff, dip, snus, cigars, cigarillos, pipes, and hookah) as a function of pain. We examined unadjusted and adjusted results to determine if associations changed after the inclusion of relevant covariates.

Results

Participant Characteristics

Participant characteristics as a function of pain status are presented in Table 1. Participants were approximately 34 years old ($M = 34.39$, $SD = 8.67$), smoked nearly a pack of cigarettes per day ($M = 19.44$, $SD = 6.74$), and reported moderate levels ($M = 3.18$, $SD = 1.09$) of cigarette dependence (Heatherton et al., 1989). Over half of the total sample endorsed lifetime polynicotine use (65.1%), with an average of 1.58 products overall ($SD = 1.67$). Approximately 35% of participants reported lifetime use of e-cigarettes and 24% endorsed past-week e-cigarette use.

One quarter of participants ($n = 70$) endorsed past-2-week significant pain. Consistent with the extant literature, participants with pain smoked a greater number of cigarettes per day ($M = 22.90$, $SD = 6.66$ vs. $M = 17.30$, $SD = 4.87$, $p < .001$) and endorsed greater cigarette dependence ($M = 3.70$, $SD = .82$ vs. $M = 2.65$, $SD = 1.06$, $p < .001$). Smokers with pain were more

likely to be White, to be unemployed, and to endorse higher levels of depression (p 's $< .05$); thus, race, employment status, and depression were included as covariates in adjusted models.

Current E-Cigarette Use

Unadjusted logistic regression analyses revealed that participants with co-occurring pain were almost 4 times more likely to report current use of e-cigarettes ($OR = 4.78$, 95% CI [2.67, 8.52], $p < .001$). Results remained the same after adjusting for covariates ($OR = 4.39$, 95% CI [2.18, 8.83], $p < .001$). The percentage of participants who endorsed current e-cigarette use as a function of pain status is presented in Figure 1.

Lifetime Polynicotine Use

Approximately 90% of smokers with pain were lifetime polynicotine users, compared to 57% without pain (see Figure 1). Unadjusted models revealed that participants with significant pain were 7 times more likely to report lifetime polynicotine use ($OR = 8.00$, 95% CI [3.33, 19.22], $p < .001$), which decreased after adjusting for covariates ($OR = 3.83$, 95% CI [1.47, 9.95], $p < .01$). Regarding number of lifetime nicotine products, smokers with pain used a greater number of products ($M = 2.01$, $SE = .22$) compared to smokers without pain ($M = 1.44$, $SE = .21$; $F[1, 300] = 5.90$, $p = .016$).

Lifetime Use of Individual Nicotine Products

Unadjusted models revealed that smokers with pain were over 3 times more likely to have tried e-cigarettes ($OR = 4.61$,

Table 1
Participant Characteristics as a Function of Past-2-Week Pain

Participant characteristics	No pain ($n = 231$)	Pain ($n = 70$)	Total sample ($n = 301$)
	n (%)	n (%)	n (%)
Sociodemographic variables			
Sex			
Male	158 (68.4)	49 (70.0)	207 (68.7)
Female	73 (31.6)	21 (30.0)	94 (31.3)
Race*			
White	159 (68.8)	57 (81.4)	216 (71.8)
Non-White	72 (31.2)	13 (18.6)	85 (28.2)
Employment*			
Employed	206 (89.2)	54 (77.1)	260 (86.4)
Unemployed	25 (10.8)	16 (22.9)	41 (13.6)
Education			
High school or less	58 (25.1)	10 (14.3)	68 (22.6)
Some college or more	173 (74.9)	60 (85.7)	233 (77.4)
Relationship status			
Single	78 (33.8)	19 (27.1)	97 (32.2)
In a relationship	153 (66.2)	51 (72.9)	204 (67.8)
	M (SD)	M (SD)	M (SD)
Age	34.65 (8.56)	36.64 (11.93)	34.39 (8.67)
# Drinks past 2 weeks	20.36 (19.24)	24.55 (15.17)	22.70 (17.06)
Depression*	7.94 (4.49)	13.38 (5.33)	9.15 (1.86)
Cigarettes per day*	17.30 (4.87)	22.90 (6.66)	19.44 (6.74)
HSI*	2.65 (1.06)	3.70 (.82)	3.18 (1.09)

Note. Depression assessed via Patient Health Questionnaire—9. HSI = Heaviness of Smoking Index.

* $p < .05$.

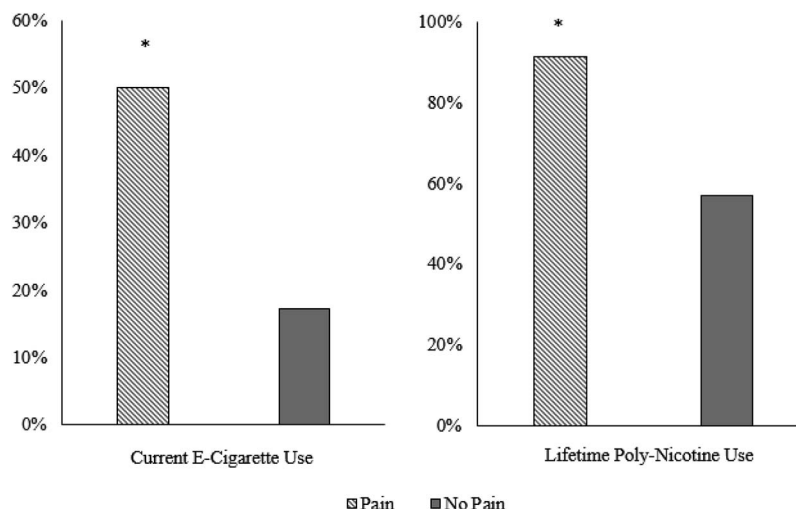


Figure 1. Percentage of participants as a function of past two-week pain (yes/no) who reported current e-cigarette use and lifetime polynicotine use. * $p < .05$.

95% CI [2.61, 8.12], $p < .001$), almost 9 times more likely to have tried cigars ($OR = 9.44$, 95% CI [5.17, 17.22], $p < .001$), and over twice as likely to have tried pipes ($OR = 3.26$, 95% CI [1.27, 8.38], $p = .014$), hookah ($OR = 2.79$, 95% CI [1.17, 6.68], $p = .021$), and cigarillos ($OR = 2.12$, 95% CI [1.16, 3.90], $p = .015$). There was no significant association between pain and use of chewing tobacco, snuff, snus, and dip (all p 's $> .05$). In the adjusted models, smokers with significant pain were almost 3 times more likely to have tried e-cigarettes ($OR = 3.78$, 95% CI [1.95, 7.35], $p < .001$), almost 7 times more likely to have tried cigars ($OR = 7.82$, 95% CI [3.80, 16.09], $p < .001$), over 2 times more likely to have tried pipes ($OR = 3.66$, 95% CI [1.07, 12.55], $p = .039$), and over 4 times more likely to have tried hookah ($OR = 4.48$, 95% CI [1.35, 14.82], $p = .014$). Conversely, smokers with pain were less likely to have tried snuff ($OR = .15$, 95% CI [.03, .68], $p = .015$), and all adjusted logistic regression models examining lifetime use of cigarillos, chew, snus, and dip were not statistically significant (all p 's $> .05$; Table 2). Because running multiple models increases the likelihood of a Type I error (Chen, Feng, & Yi, 2017), a Bonferroni correction was employed to reduce the false discovery rate and increase statistical power (Benjamini & Hochberg, 1995; Bland & Altman, 1995). After correcting for multiple models, both adjusted models examining lifetime e-cigarette and cigar use remained significant (p 's $< .005$).

Discussion

This is the first study to examine current e-cigarette use and lifetime polynicotine product use among cigarette smokers as a function of co-occurring pain. Results indicated that smokers with past-2-week significant pain (vs. no past-2-week pain) were over 3 times more likely to endorse concurrent use of e-cigarettes. In addition, smokers with co-occurring pain reported having used a greater number of nicotine products in their lifetime and were almost 3 times more likely to endorse lifetime polynicotine use (i.e., use of any nicotine product in

addition to traditional combustible cigarettes). Specifically, smokers with pain were more likely to have tried e-cigarettes, cigars, hookah, and pipes. Smokers with pain were less likely to have tried snuff. After correcting for multiple models (Benjamini & Hochberg, 1995; Bland & Altman, 1995), smokers with pain were still more likely to endorse lifetime use of e-cigarettes and cigars. No differences were observed regarding lifetime use of cigarillos, chew, snus, or dip.

Given the acute analgesic effects of nicotine (Ditre et al., 2016), one possible explanation for these findings is that smokers with co-occurring pain may also use e-cigarettes and other nicotine products in an effort to extend/supplement exposure to nicotine (e.g., between traditional cigarettes or during times when smoking is not permitted). Indeed, smokers report using cigarettes for pain coping (Hooten, Shi, Gazelka, & Warner, 2011) and may thus be more likely to also use e-cigarettes and other nicotine products to self-medicate pain symptoms. An alternative explanation is that smoking more cigarettes per day (smokers with pain in this study consumed approximately 32% more cigarettes per day than those without pain) while concurrently using a greater number of other nicotine products could increase lifetime nicotine exposure, which in turn may facilitate pain and elevate risk for developing painful conditions (De Vita et al., 2019). Collectively, these initial findings support the utility of assessing e-cigarette and other nicotine product use among smokers with pain. Additional research is needed to elucidate potentially bidirectional effects between polynicotine use and the experience of pain (e.g., Ditre, Brandon, et al., 2011; Ditre et al., 2019).

E-cigarette use has increased sevenfold over the past decade (McMillen, Gottlieb, Shaefer, Winickoff, & Klein, 2014), and empirical interest in the dual use of e-cigarettes and traditional cigarettes has increased in commensurate fashion (e.g., Jones et al., 2018; Stanton & Halenar, 2018). Despite previous work showing pain to be associated with greater e-cigarette dependence (Zvolensky et al., 2019), we are not aware of any work examining pain and dual use of e-cigarettes and cigarettes. There has been some

Table 2

Adjusted Logistic Regression Models Examining Pain as a Predictor of Lifetime Use of Individual Nicotine Products

Variables	E-cigarettes			Cigars			Cigarillos		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Age	.99	[.96, 1.02]	.506	.97	[.93, 1.00]	.055	.98	[.95, 1.01]	.253
Race ^a	.94	[.52, 1.72]	.851	.97	[.49, 1.94]	.936	1.43	[.70, 2.91]	.325
Sex ^b	2.07	[1.13, 3.82]	.019	.75	[.36, 1.55]	.433	2.86	[1.44, 5.70]	.003*
Employment status ^c	.38	[.17, .83]	.136	.79	[.31, 2.01]	.623	.79	[.33, 1.88]	.595
Depression ^d	1.05	[.99, 1.11]	.136	1.07	[1.00, 1.14]	.046*	1.07	[1.00, 1.14]	.030*
Pain status ^e	3.78	[1.95, 7.35]	<.001**	7.83	[3.80, 16.10]	<.001**	1.47	[.71, 3.03]	.301
	Pipes			Hookah			Chewing tobacco		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Age	.90	[.835, .98]	.013*	.88	[.82, .95]	.001*	1.01	[.97, 1.04]	.682
Race ^a	.86	[.24, 3.00]	.807	.52	[.18, 1.54]	.238	.33	[.18, .64]	.001*
Sex ^b	.79	[.29, 2.85]	.715	3.81	[1.26, 11.44]	.017*	.57	[.28, 1.16]	.122
Employment status ^c	.20	[.06, .73]	.015*	.30	[.09, .94]	.039*	3.24	[1.00, 10.48]	.049*
Depression ^d	.98	[.88, 1.09]	.681	.98	[.89, 1.08]	.660	1.09	[1.02, 1.17]	.011*
Pain status ^e	3.66	[1.07, 12.55]	.039*	4.48	[1.36, 14.82]	.014*	.56	[.25, 1.24]	.154
	Dip			Snus			Snuff		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Age	1.02	[.99, 1.06]	.232	1.04	[.99, 1.08]	.077	1.07	[1.02, 1.12]	.005*
Race ^a	.65	[.32, 1.32]	.234	1.37	[.62, 3.04]	.441	1.23	[.49, 3.08]	.661
Sex ^b	.74	[.34, 1.62]	.451	.83	[.38, 1.90]	.659	.88	[.34, 2.28]	.785
Employment status ^c	1.26	[.42, 3.79]	.676	1.78	[.53, 6.02]	.355	2.9	[.57, 15.44]	.194
Depression ^d	1.03	[.96, 1.11]	.370	1.06	[.98, 1.14]	.169	1.08	[.98, 1.19]	.118
Pain status ^e	.50	[.19, 1.30]	.154	.54	[.21, 1.36]	.191	.14	[.03, .69]	.015*

^a Coded as 0 = non-White, 1 = White. ^b Coded as 0 = male, 1 = female. ^c Coded as 0 = unemployed, 1 = employed. ^d Assessed via Patient Health Questionnaire—9. ^e Coded as 0 = no pain, 1 = pain.

* $p < .05$. ** $p < .001$, and p values significant after Bonferroni correction.

question in this line of research as to whether dual users may decrease their consumption of combustible cigarettes in the context of e-cigarette uptake (Rahman, Hann, Wilson, Mnatzaganian, & Worrall-Carter, 2015). There is also growing interest in identifying individual factors that contribute to e-cigarette use (e.g., Hartwell et al., 2017). The present findings suggest that daily cigarette smokers with pain may be more likely to initiate and continue use of e-cigarettes. However, patterns of e-cigarette use among smokers with co-occurring pain remain unclear, including whether smokers titrate their cigarette consumption following initiation of e-cigarette use. Future research is needed to examine interplay between pain and dual use of e-cigarettes and traditional cigarettes.

Although smokers with co-occurring pain were more likely to use e-cigarettes and other combustible nicotine products (e.g., cigars), there was no association between significant pain and lifetime use of cigarillos, chewing tobacco, dip, and snus. One potential explanation for these findings is that smokers with pain may prefer inhaled/combustible nicotine delivery systems. In e-cigarettes and combustible nicotine products, nicotine smoke or vapor is taken in through the mouth, throat, and lungs and can reach the brain in as little as seven seconds (Henningfield & Keenan, 1993; Russell & Feyerabend, 1978). In comparison, smokeless tobacco products vary in nicotine content (Henningfield, Radzisz, & Cone, 1995) and take longer to reach peak blood levels (Henningfield & Keenan, 1993), and smokers report feeling

less confident in their ability to control nicotine intake when using these products (Sami et al., 2012). Additionally, the route of administration in e-cigarettes and combustible nicotine products more closely resembles that of traditional tobacco cigarettes. Indeed, current smokers report that they are more likely to consider switching to an inhaled product, like e-cigarettes, relative to a smokeless tobacco product (Anic et al., 2018).

Several important limitations should be noted. First, cross-sectional assessment of polynicotine use and pain status prohibits inferences regarding temporal or causal effects. Second, although previous studies observed interplay between cigarette use/dependence and the presence of recent pain (e.g., Hahn et al., 2006), this study was limited to a single item assessing past-2-week significant pain. In addition, whereas past-2-week pain could indicate the presence of a persistently painful condition, chronic pain status was not assessed, and it is not possible to determine from these data whether past use of nicotine products covaried with pain experience. Future research should examine e-cigarette and polynicotine use in relation to clinical pain characteristics (e.g., persistence, intensity, impairment) over the same period of time (e.g., Turk & Melzack, 2011). Third, although binary variables are useful for estimating odds ratios, future work would benefit from incorporating more granular assessment of nicotine product use (e.g., frequency/duration, current polynicotine use, time since last use), along with biological assays of nicotine exposure (e.g., Marsot & Simon, 2016; Benowitz et al., 2002). Fourth, comorbid

psychopathology and several candidate transdiagnostic factors (e.g., pain-related anxiety, anxiety sensitivity, distress intolerance) have been proposed as potential mechanisms in bidirectional pain-smoking associations (Ditre et al., 2019). Consistent with prior research (Holmes et al., 2010), we covaried for relevant factors (e.g., depression) in the present analysis; however, prospective research should examine these variables as mediators of pain-smoking relations. Finally, the current sample was comprised of daily smokers who were motivated to quit in the next 30 days, and the extent to which these findings may generalize to lighter smokers or those not intending to quit remains unclear.

In summary, these data suggest that use of e-cigarettes and other nicotine products is highly prevalent among tobacco cigarette smokers with co-occurring pain. Despite preliminary findings showing associations between pain and e-cigarette dependence (Zvolensky et al., 2019) and literature documenting interrelations between pain and smoking (Ditre, Brandon, et al., 2011; Ditre et al., 2019), this is the first study that examined e-cigarette and polynicotine use as a function of significant pain. Future research is needed to elucidate prevalence and patterns of alternative nicotine product use among smokers and nonsmokers with varying levels of pain.

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