

# The Interaction of Depressive Symptoms and Hazardous Drinking in Relation to Tobacco Craving Among Treatment Seeking Depressed Smokers: Sex Differences

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**Objectives:** The present study sought to address whether there is sex effect in the interactive effect between depressive symptoms and hazardous drinking in the prediction of smoking craving after cognitive-behavioral smoking cessation treatment among those with at least mild depression.

**Methods:** Participants ( $n = 114$ , mean age 42.0,  $SD = 9.73$ , 64% women) were treatment-seeking smokers who attended 6 weekly 1-hour sessions involving psychological treatment for cessation. Participants reported depressive symptoms and alcohol use at baseline and reported craving at baseline and after treatment.

**Results:** Results indicated that there was a statistically significant 3-way interaction (depression by alcohol use by sex) for smoking craving ( $B = -0.30$ , standard error [SE] = 0.14,  $P = 0.042$ ) and appetitive craving ( $B = -.21$ ,  $SE = 0.09$ ,  $P = 0.031$ ), but not negative reinforcement craving. The form of the significant interactions indicated that higher levels of depressive symptoms and alcohol use were related to greater levels of craving at the end of treatment only among men.

**Conclusions:** The current findings provide novel empirical evidence suggesting that there is a clinically relevant interplay between depressive symptoms and alcohol use regarding general craving

and appetitive craving among male treatment-seeking smokers. Although the present results should be replicated in larger samples, this type of research can inform the development of sex-specific interventions for smoking cessation.

**Key Words:** craving, depression, hazardous drinking, sex, smoking (*J Addict Med* 2017;xx: xxx–xxx)

Tobacco use remains the leading preventable cause of death and disability in developed countries (Lim et al., 2012). More than 1 billion people smoke tobacco (World Health Organization [WHO], 2017). Despite the reduction in smoking incidence in certain areas of the world (United States Department of Health and Human Services, 2014), smoking relapse remains highly common. For example, nearly 70% of smokers report a desire to quit smoking (USDHHS, 2014), but more than 60% who receive smoking-cessation treatment relapse within a year (Bauld et al., 2010).

Theory and research suggest craving, denoting the subjective experience of desiring to smoke (Tiffany and Wray, 2012), is a core construct involved in the maintenance and relapse of smoking. Craving is related to an increased likelihood of smoking (Shiffman et al., 2013), cigarette dependence (Carpenter et al., 2014), reduced likelihood of quitting (Piñero et al., 2014), and an increased likelihood of relapse (Allen et al., 2008). Past work also indicates that craving is a multidimensional construct, including the intention and desire to smoke based on the anticipation pleasure derived from cigarettes; and the anticipation of reduced negative affect (Cox et al., 2001). Given the broad-based prominence of craving in smoking maintenance and relapse (Wray et al., 2013), there is a need to better understand factors that may help identify variables associated with craving as a global and multidimensional construct.

Depressed affect is 1 common and important public health factor to consider in craving-tobacco relations. People with compared to without clinical depression tend to smoke more cigarettes on a daily basis (Ziedonis et al., 2008), have greater cigarette dependence (Dierker and Donny, 2008), and are more likely to relapse (Cooper et al., 2016). A recent systematic review concluded that depressed smokers struggle with smoking cessation and evince a greater appetitive value to smoke in comparison to nondepressive smokers (Mathew

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et al., 2017). Therefore, it is important to better understand smoking processes, such as craving, among smokers with elevated depressive symptoms. Previous studies have reported that smokers with greater depressive symptoms have higher levels of craving than smokers with lower depressive symptoms (Reid and Ledgerwood, 2016). In addition, craving partially explains the effect of depressive symptoms in terms of smoking lapse (Brodbeck et al., 2014). Yet, because not all smokers with depressive symptoms demonstrate greater craving (Leventhal et al., 2009), there is a need to identify the other factors that explain why some smokers demonstrate greater craving, whereas others do not (Brodbeck et al., 2014); such for whom and under what conditions depressive symptoms are related to craving.

Importantly, alcohol use is highly common among smokers (Kahler et al., 2008) and may be 1 factor involved in the depression-craving association among smokers. For example, in the context of an integrated alcohol and smoking treatment, Holt et al. (2012) found that participants with lower positive mood and greater craving had greater likelihood of smoking during the first days after quitting. Also, smokers with higher depressive symptoms are more likely to engage in hazardous drinking even when compared with nonsmokers with similarly high levels of depressive symptoms (Lombardero et al., 2014). Other research among older adult smokers who were largely men (67%) suggests that alcohol problems were a moderator of the relationship between depressive symptoms and smoking cessation (Kenney et al., 2009). Collectively, available work suggests clinically relevant, but complex, relations may be evident between depressed affect, craving, and alcohol use among smokers with elevated depressive symptoms.

Negative-reinforcement motivational models of substance use (Baker et al., 2004) provide a useful conceptual framework for better understanding craving in the context of depressed affect and alcohol use. Specifically, greater depressed affect may be related to more intense craving (Leventhal et al., 2009), which, in turn, could be influenced by alcohol use used to modulate such cognitive-affective experiences (Bolton et al., 2009). Such a perspective would lead to the prediction that the interaction of depressive symptoms and alcohol use would be associated with smoking craving severity among smokers with elevated depressive symptoms. Given that smokers with higher depressive symptoms present greater craving (Reid and Ledgerwood, 2016), exploring this interaction among smokers with higher depressive symptoms would help to better understand the interplay effect of depression and alcohol use in smoking craving.

Sex differences may help explain the relationship between depressive symptoms, alcohol, and craving. Past work has found that depressive symptoms and smoking co-occurrence is more likely in women (Husky et al., 2008). Furthermore, some work suggests depressive symptoms among women relative to men may have a more detrimental impact on smoking processes cessation (Weinberger et al., 2013). Alcohol use also has been found to evince differences among smokers in terms of sex. For example, alcohol use is related to increased smoking urge and behavior in men, but only urge among women (King et al., 2009). Likewise,

hazardous alcohol use has been found to have a greater effect on relapse among men relative to women (Rodríguez-Cano et al., 2016). Consistent with this work, research has found that men demonstrate greater craving compared with women after quitting (Pomerleau et al., 2005; Collins et al., 2011). In another investigation, depressive symptoms and craving severity interacted to predict relapse among women relative to men (Rodríguez-Cano et al., 2017).

Together, the present study sought to address whether there is a synergic effect of depressive symptoms and alcohol use (pretreatment) in the prediction of smoking craving at post-treatment among those reporting at least mild depressive symptoms. We modeled the data as a function of sex, given past work that suggests differences among women and men in terms of smoking, depression, and alcohol use. We hypothesized that among women with at least mild depressive symptoms, the interactive effect of depressive symptoms and alcohol use would be related to greater post-treatment craving. We also hypothesized that among men, this craving effect would be less intense (ie, statistically smaller), as theoretically there is lesser impact of depressive symptoms in smoking among men (Weinberger et al., 2013).

## METHODS

### Participants

Individuals were 114 adult treatment-seeking smokers who scored 14 and above on the Beck Depression Inventory (BDI)-II at pretreatment (Beck et al., 1996) (mean age 42.0, SD = 9.73, 64.0% women). They were selected from initial sample of 493 smokers who received a group format cognitive-behavioral treatment for smoking cessation and attended to the end of treatment assessment. Excluded participants ( $n = 379$ ) did not show differences in covariates (age, marital status, years of smoking, number of cigarette at pretreatment, cigarette dependence) or predictors (sex and alcohol use). By design, the study sample had higher depressive symptoms and craving before treatment (general and appetitive craving) and after treatment (general, appetitive craving, and negative reinforcement craving).

Smokers were excluded if they were aged under 18, participated in the same treatment or received pharmacological treatment to quit smoking (nicotine replacement therapy, varenicline, and/or bupropion) during the past year, presented with psychosis or bipolar disorder, were dependent on a substance other than cigarettes (determined via clinical interview), or suffered a high-risk physical disease (eg, recent cancer diagnosis).

### Procedure

The research was approved and authorized by Bioethics Committee of the University of Santiago de Compostela. Participants were informed by written consent before starting the study procedure. Next, they completed self-questionnaires at pretreatment and participated in a pretreatment clinical interview. They also completed Questionnaire Smoking Urges (QSU)-brief at posttreatment. A 6-session cognitive-behavioral smoking-cessation treatment (Becona, 2007) was administered in a group format (6–8 participants). This treatment

was applied in Spain during several years (Becoña et al., 2014). Sessions occurred weekly. The treatment components included tobacco use and general health information, nicotine fading, strategies for craving, and nicotine withdrawal (eg, reducing alcohol and coffee consumption), cigarette consumption feedback by carbon monoxide (CO) in expired air, and relapse prevention skills (eg, not accepting cigarettes when others offer them). Treatment was delivered by Master level psychologists. Abstinence at the end of treatment (sixth session of treatment) was determined by self-report of not having smoked, even a puff, in the 24 hours before the session, and assessment of CO <5 (Perkins et al., 2013). Sixty-nine participants (60.5% of the sample) quit smoking at the end of treatment.

## Measures

### Smoking Habit Questionnaire

The Smoking Habit Questionnaire (SHQ) is a self-report questionnaire that measures information about sex, age, marital status, educational background, and smoking history. The SHQ was administered before treatment (Becoña, 1994).

### Fagerström Test for Cigarette Dependence, Spanish version

The Fagerström Test for Cigarette Dependence (FTCD; Fagerström, 2012 and its Spanish version Becoña and Vázquez, 1998) is a 6-item self-report assessment of cigarette dependence. Scores range from 0 to 10 (Heatherton et al., 1991). Higher scores correspond to higher levels of physiological cigarette dependence. In the current sample, the FTCD demonstrated a Cronbach  $\alpha$  of 0.56. The FTCD was administered at pretreatment.

### Beck Depression Inventory-II, Spanish Version

The BDI-II (Beck et al., 1996 and its Spanish version Sanz and Vázquez, 2011) is a multiple-choice 21-item self-report questionnaire. Scores range from 0 to 63, with higher scores reflecting greater depressive symptomatology in the previous 2 weeks. Scores of 14 and above were used as cut-off to indicate the presence of mild or greater depressive symptoms, as in past work with North American (Beck et al., 1996) and Spanish (Sanz and Vázquez, 2011; Sanz et al., 2014) samples. The BDI-II demonstrated excellent internal consistency in a prior study with Spanish population (Cronbach  $\alpha$  = 0.91; Sanz and Vázquez, 2011). The BDI-II was administered before treatment.

### Alcohol Use Disorder Identification Test, Spanish Version

The Alcohol Use Disorder Identification Test (AUDIT) (Saunders et al., 1993, Spanish version Contel et al., 1999) is a 10-item self-report scale that assesses hazardous alcohol drinking. Scores range from 0 to 40. Items assess frequency, quantity, symptoms of dependence, and harmful drinking. In the current report, we used the term “hazardous drinking” to refer to the AUDIT total score. This instrument has demonstrated sound psychometric properties among Spanish

samples (Cronbach  $\alpha$  = 0.88) (Contel et al., 1999). The AUDIT was administered before treatment.

### Questionnaire Smoking Urges-brief, Spanish Version

The QSU-brief (Cox et al., 2001 and its Spanish version Cepeda-Benito and Reigh-Ferrer, 2004) is a multidimensional measure of current smoking craving. It is comprised of 10 self-report items with total scores ranging from 7 to 70. Higher scores correspond to greater levels of craving. The instrument produces a global craving score (QSU-Total) and 2 subfactors tapping appetite craving (QSU-Factor 1) (eg, “I want to smoke right now”) and negative reinforcement craving (QSU-Factor 2) (eg, “I will feel less depressed if I smoke”). This instrument has good reliability (Cox et al., 2001), which has been replicated among Spanish samples (Cepeda-Benito and Reigh-Ferrer, 2004). The QSU was administered at pre and post-treatment. In the current study, the QSU-brief demonstrated good internal consistency (pre-Cronbachs  $\alpha$  = 0.85; post-Cronbach  $\alpha$  = 0.90).

Micro+ Smokerlyzer (Bedfont Scientific Ltd, Sittingbourne, UK) was used to measure carbon monoxide (CO) in expired air. CO was used to validate smoking.

## Data Analyses

Variables in the study were normally distributed (skewness |0.11–2.54| and kurtosis |0.17–7.71|). Multivariate outliers were identified with Mahalanobis test ( $n=2$ ) and removed from analysis.

First, descriptive statistics and 0-order correlation were calculated to examine the association between study variables (sex, age, marital status, years smoking, number of cigarettes per day at pretreatment, cigarette dependence, depressive symptoms, hazardous drinking, and craving pre and post-treatment). Then, the interactive effects of sex, depressive symptoms, and hazardous drinking were tested using 3 hierarchical regression models to study the change in variance (measured by the increasing of R square), one for each smoking post-treatment craving-dependent variable. Analyses were conducted with the PROCESS Macro (Hayes and Preacher, 2014), using IBM SPSS version 23.0. In step 1, age, marital status, years smoking, number of cigarettes per day at pretreatment, cigarette dependence, and pretreatment levels of the smoking craving were included. The second step included the main effects of sex, depressive symptoms, and hazardous drinking entered simultaneously. The third step included three 2-way interaction terms (depressive symptoms  $\times$  sex, depressive symptoms  $\times$  hazardous drinking, hazardous drinking  $\times$  sex). Finally, the 3-way interaction term was added in the fourth step.

When the 3-way interaction was statistically significant, follow-up tests were conducted to evaluate whether the interaction of depressive symptoms (X) and hazardous drinking (M) was significantly different between men ( $W=0$ ) and women ( $W=1$ ). Then, post hoc analyses were run separately in men and women for significant interactions using simple slopes to examine the effect of depressive symptoms on craving at high versus low ( $\pm 1$  SD from the mean) levels of alcohol use (M). Furthermore, the Johnson-Neyman

technique (Johnson and Neyman, 1936) was used to identify regions of significance (ie, levels of hazardous drinking), where depressive symptoms are associated with smoking craving. This technique was selected because is more specific than selected an arbitrary value (as in “pick-a-point” method used for simple slopes; Hayes, 2013). Regression weights and standard errors were reported.

## RESULTS

### Descriptive Statistics and Zero-order Associations

Slightly more than half of the participants were married ( $n = 58$ , 50.9%). Less than half reported completing more than high school ( $n = 44$ ; 38.6%), with 41.2% ( $n = 47$ ) completing high school and 20.2% ( $n = 23$ ) completing less than high school. The sample included regular smokers who smoked for 24.2 years ( $SD = 10.33$ ), smoked an average of 21.6 ( $SD = 8.8$ ) cigarettes per day, scored an average of 25.12 ( $SD = 12.12$ ) in CO in expired air, and presented with moderate cigarette dependence, scoring an average of 5.36 ( $SD = 2.16$ ) on the FTCD (Heatherton et al., 1991) pretreatment.

Descriptive statistics and differences by sex are displayed in Table 1. Men were less likely to quit (68.0% women vs 46.3% men) and reported significantly greater pretreatment number of cigarettes, less pretreatment depressive symptoms, and higher hazardous drinking than women.

Correlations indicated a positive relation between being women and negative reinforcement craving (pretreatment),

depression, and alcohol use. Depressive symptoms were negatively related to hazardous drinking. Craving (pretreatment) was positively related to all post-treatment craving variables (see Table 2).

### Interactive Effect Analyses

Results from hierarchical regression analyses are reported in Table 3.

#### Global Craving (QSU-Total)

For the model estimating post-treatment global craving, the 3-way interaction of sex by depression by hazardous drinking was significant ( $B = -0.30$ , standard error [SE] = 0.14,  $P = 0.042$ ). The effect of depressive symptoms in relation to global craving was moderated by hazardous drinking in men ( $B = 0.28$ ,  $SE = 0.11$ ,  $P = 0.009$ ), but not in women ( $B = -0.01$ ,  $SE = 0.10$ ,  $P = 0.879$ ) (Fig. 1). Follow-up analyses among men ( $n = 41$ ) showed that depressive symptoms were only related to craving at higher levels of hazardous drinking ( $B = 1.99$ ,  $SE = 0.49$ ,  $P < 0.001$ ). Finally, the Johnson-Neyman technique revealed that depressive symptoms were positively associated with craving ( $B = 0.46$ ,  $SE = 0.23$ ,  $P < 0.05$ ) for AUDIT scores of 2.62 or higher (representing 51.22% of the sample; Fig. 2).

#### Appetitive Craving (QSU-Factor 1)

Regarding posttreatment craving for appetitive reasons, the 3-way interaction of sex by depression by hazardous drinking was significant ( $B = -0.21$ ,  $SE = 0.09$ ,  $P = 0.031$ ).

**TABLE 1.** Demographics, Smoking History, and Study Variables By Sex (N = 114)

	Total (N = 114)		Female (n = 73)		Male (n = 41)		$\chi^2$	P	Cramer V
	n	%	n	%	N	%			
Marital status							0.003	0.956	0.005
Single	56	49.1	36	49.1	20	48.8			
Married	58	50.9	37	63.8	21	51.2			
Educational level							4.161	0.125	0.191
Lower high school	23	20.2	17	23.3	6	14.6			
High school	47	41.2	25	34.2	22	53.7			
More high school	44	38.6	31	42.5	13	31.7			
Smoking status end of treatment							5.392	0.020	0.217
Abstinent	69	60.5	50	68.5	19	46.3			
Smokers	45	39.5	23	31.5	22	53.7			
	M	SD	M	SD	M	SD	t	P	Cohen d
Age	42.03	9.7	42.56	9.6	41.07	10.0	-0.782	0.436	0.153
CO level	25.12	12.1	25.00	12.5	25.34	11.6	0.144	0.886	0.028
Years smoking	24.18	10.3	24.26	10.2	24.05	10.6	-0.104	0.917	0.020
CPD	21.63	8.8	20.29	7.5	24.02	10.5	2.208	0.029	0.431
FTCD	5.36	2.2	5.30	2.2	5.46	2.1	0.383	0.702	0.075
BDI-II	21.9	7.3	23.63	7.7	18.83	5.2	-3.964	<0.001	0.774
AUDIT	3.17	3.8	2.26	2.7	4.78	4.8	3.113	0.003	0.608
QSU-Total pretreatment	32.98	12.8	34.21	14.0	30.80	9.9	-1.502	0.136	0.293
QSU-Factor 1 pretreatment	21.22	8.1	21.30	8.5	21.07	7.48	-0.576	0.566	0.112
QSU-Factor 2 pretreatment	11.76	6.7	12.90	7.6	9.73	4.3	-0.189	0.850	0.037
QSU-Total post-treat.	19.68	11.7	20.05	11.8	19.00	11.6	-0.460	0.645	0.090
QSU-Factor 1 post-treat.	11.73	7.8	12.04	7.9	11.17	7.7	-0.571	0.569	0.111
QSU-Factor 2 post-treat.	7.95	5.0	8.01	5.2	7.83	4.7	-0.462	0.645	0.090

AUDIT, Alcohol Use Disorders Identification Test total pretreatment score; BDI-II, Beck Depression Inventory second version pretreatment score; CO, carbon monoxide; CPD, cigarettes per day at pretreatment; FTCD, Fagerström Test for Cigarette Dependence pretreatment score; QSU-Factor 1, appetitive craving; QSU-Factor 2, negative reinforcement craving; QSU-Total score, Questionnaire Smoking Urges.

**TABLE 2.** Descriptive Statistics and Bivariate Correlations Among Study Variables (N = 114)

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Age <sup>a</sup>	—												
2. Marital status <sup>a</sup>	0.35*	—											
3. Years smoking <sup>a</sup>	0.86*	0.35†	—										
4. CPD <sup>a</sup>	0.18	0.08	0.22†	—									
5. FTCD <sup>a</sup>	0.13	0.09	0.20†	0.67*	—								
6. Sex <sup>b</sup>	0.07	-0.01	0.01	-0.20†	-0.04	—							
7. BDI-II <sup>b</sup>	0.23†	0.06	0.22†	0.03	0.18	0.32*	—						
8. AUDIT <sup>b</sup>	-0.16	-0.10	-0.12	0.03	-0.07	0.32*	-0.26*	—					
9. QSU-Total score-pretreatment <sup>a</sup>	0.07	-0.01	0.10	0.20*	0.19†	0.13	0.19†	-0.07	—				
10. QSU-Factor 1 pretreatment <sup>a</sup>	0.01	0.00	0.10	0.17	0.14	0.01	0.08	-0.01	0.89*	—			
11. QSU-Factor 2 pretreatment <sup>a</sup>	0.12	-0.01	0.07	0.17	0.20†	0.23†	0.26*	-0.12	0.83*	0.47*	—		
12. QSU-Total score post-treatment <sup>c</sup>	0.07	0.07	0.01	0.06	0.07	0.04	-0.10	0.13	0.31*	0.27*	0.27*	—	
13. QSU-Factor 1 post-treatment <sup>c</sup>	0.13	0.10	0.09	0.08	0.12	0.05	-0.03	0.10	0.30*	0.28*	0.23†	0.95*	—
14. QSU-Factor 2 post-treatment <sup>c</sup>	-0.03	0.01	-0.10	0.02	-0.25	0.18	-0.18	0.15	0.27*	0.20†	0.28*	0.87*	0.67*

Note: Superscript alphabet ‘a’ denotes covariates; ‘b’ predictors; and ‘c’ dependent variables.

Marital status, coded as single = 0, married = 1.

Numbers across on the top correspond with variables numbered 1–13.

AUDIT, Alcohol Use Disorders Identification Test total pretreatment score; BDI-II, Beck Depression Inventory second version pretreatment score; CPD, cigarettes per day at pretreatment; FTCD, Fagerström Test for Cigarette Dependence pretreatment score; Sex, coded female as 1; QSU-Factor 1, appetitive craving; QSU-Factor 2, negative reinforcement craving; QSU-Total score, Questionnaire Smoking Urges.

\*P < 0.01.

†P < 0.05.

**TABLE 3.** Hierarchical Regression Analysis (Main and Interactive Effects of Depressive Symptoms, Alcohol Use, and Sex in Relation to Post-treatment Craving (N = 114))

Step	Predictor	B	SE	t	P	R <sup>2</sup> Change
QSU-Total score						
1	Age	0.284	0.22	1.315	0.191	0.120*
	Marital status	1.798	2.27	0.792	0.430	
	Years smoking	-0.283	0.21	-1.376	0.172	
	CPD	-0.013	0.16	-0.077	0.938	
	FTCD	0.130	0.67	0.194	0.846	
	QSU-TS pretreatment	0.292	0.09	3.435	0.001	0.056
2	Sex	2.036	2.46	0.827	0.410	
	BDI-II	-0.281	0.16	-1.745	0.084	
	AUDIT	0.518	0.30	1.725	0.088	
	BDI-II × sex	-0.833	0.40	-2.067	0.041	
3	AUDIT × sex	-1.069	0.69	-1.547	0.125	0.067*
	BDI-II × AUDIT	0.119	0.07	1.641	0.104	
	BDI-II × AUDIT × sex	-0.295	0.14	-2.062	0.042	
QSU-Factor 1						
1	Age	0.224	0.15	1.536	0.127	0.112*
	Marital status	1.108	1.52	0.731	0.466	
	Years smoking	-0.164	0.14	-1.182	0.240	
	CPD	-0.046	0.11	-0.415	0.679	
	FTCD	0.409	0.45	0.918	0.361	
	QSU-F1 pretreatment	0.275	0.09	3.074	0.003	0.145
2	Sex	1.688	1.66	1.019	0.310	
	BDI-II	-0.107	0.11	-0.988	0.326	
	AUDIT	0.321	0.20	1.581	0.117	
	BDI-II × sex	-0.491	0.27	-1.787	0.077	
3	AUDIT × sex	-0.698	0.46	-1.502	0.136	0.203*
	BDI-II × AUDIT	0.076	0.05	1.544	0.126	
	BDI-II × AUDIT × sex	-0.213	0.09	-2.186	0.031	
QSU-Factor 2						
1	Age	0.071	0.09	0.759	0.450	0.108
	Marital status	0.620	0.97	0.637	0.525	
	Years smoking	-0.124	0.09	-1.409	0.162	
	CPD	0.038	0.07	0.547	0.586	
	FTCD	-0.235	0.29	-0.815	0.417	
	QSU-F2 pretreatment	0.213	0.07	3.063	0.003	0.074*
2	Sex	0.541	1.05	0.514	0.608	
	BDI-II	-0.161	0.07	-2.344	0.021	
	AUDIT	0.196	0.13	1.541	0.126	
	BDI-II × sex	-0.339	0.17	-1.980	0.050	
3	AUDIT × sex	-0.453	0.30	-1.521	0.131	0.061*
	BDI-II × AUDIT	0.048	0.03	1.561	0.122	
	BDI-II × AUDIT × sex	-0.080	0.06	-1.302	0.196	

Note: Marital status coded as single = 0, married = 1.

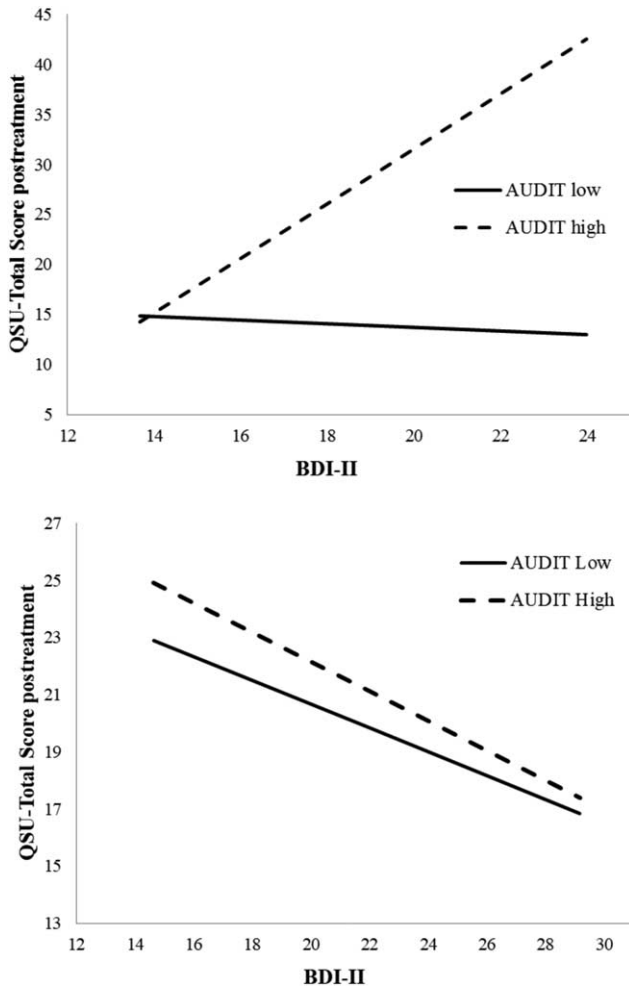
AUDIT, Alcohol Use Disorders Identification Test total pretreatment score; BDI-II, Beck Depression Inventory second version pretreatment score; CPD, cigarettes per day at pretreatment; FTCD, Fagerström Test for Cigarette Dependence pretreatment score; sex, female coded by 1; QSU-Factor 1, appetitive craving; QSU-Factor 2, negative reinforcement craving; QSU-Total score, Questionnaire Smoking Urges. Three-way interaction = BDI-II × AUDIT × sex.

\*P < 0.05.

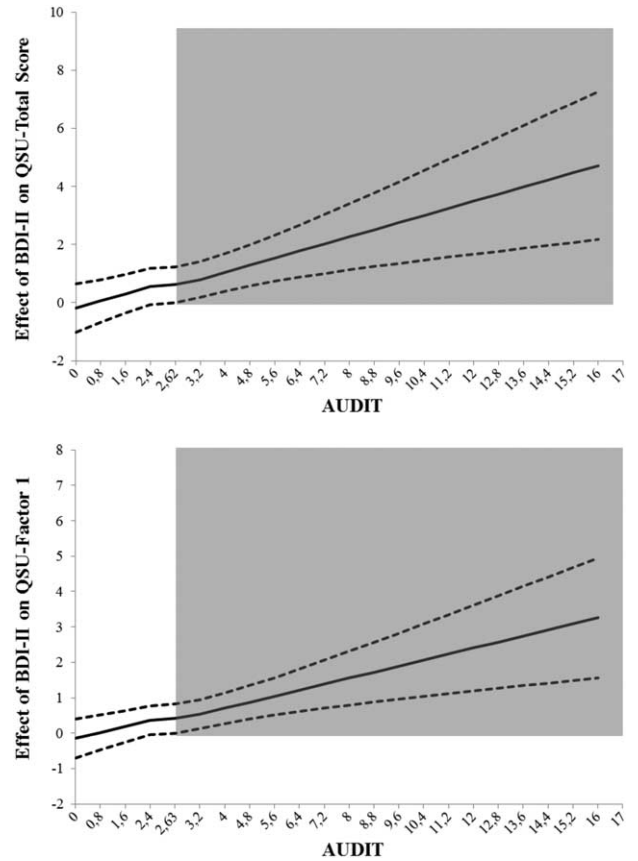
The effect of depressive symptoms in relation to appetitive smoking craving was moderated by hazardous drinking in men ( $B=0.19$ ,  $SE=0.07$ ,  $P=0.009$ ), but not in women ( $B=-0.02$ ,  $SE=0.07$ ,  $P=0.759$ ) (see Fig. 3). Follow-up analyses among men ( $n=41$ ) showed that depressive symptoms were related to appetitive craving at higher hazardous drinking scores ( $B=2.00$ ,  $SE=0.49$ ,  $P<0.001$ ). Johnson-Neyman technique results indicated that depressive symptoms were positively associated with appetitive craving ( $B=0.46$ ,  $SE=0.23$ ,  $P<0.05$ ) for AUDIT scores of 2.63 or higher (representing 51.22% of the sample; Fig. 2).

**Negative Reinforcement (QSU-Factor 2)**

For post-treatment negative reinforcement craving, the 3-way interaction was not significant ( $B=-0.08$ ,  $SE=0.06$ ,  $P=0.196$ ). Only pretreatment negative reinforcement craving



**FIGURE 1.** Conditional effect of depressive symptoms (BDI-II) on general craving (QSU-Total scores) in terms of levels of alcohol use (AUDIT). The male interaction is represented in upper chart. The female interaction is represented in lower chart. AUDIT, Alcohol Use Disorders Identification Test total pretreatment score; BDI-II, Beck Depression Inventory 2nd version pretreatment score; QSU, Questionnaire Smoking Urges post-treatment scores.

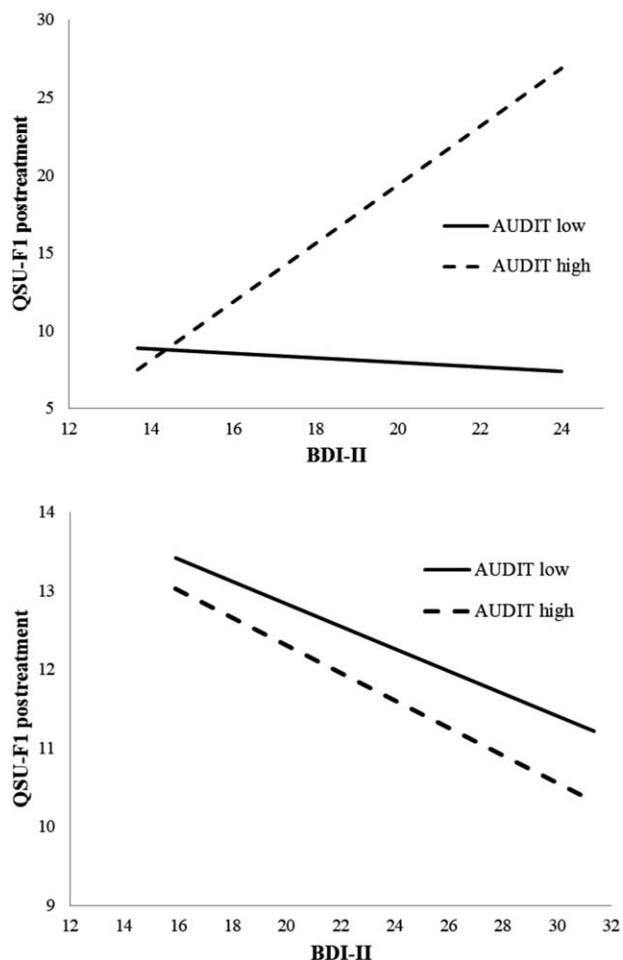


**FIGURE 2.** Area of significant conditional effect of pretreatment depressive symptoms (BDI-II) on general (QSU-Total scores; upper chart) and appetitive posttreatment smoking craving (QSU-Factor 1; lower chart) by pretreatment alcohol use scores (AUDIT) in males with at least mild depressive symptoms ( $n=41$ ). Note: Solid black line displays the conditional effect at AUDIT scores. Dot lines display 95% confidence interval for the effect. Shaded area displays the significant association of BDI-II and QSU at AUDIT scores. AUDIT, Alcohol Use Disorders Identification Test total pretreatment score; BDI-II, Beck Depression Inventory 2nd version pretreatment score; QSU, Questionnaire Smoking Urges post-treatment scores.

accounted for significant variance ( $B=0.21$ ,  $SE=0.07$ ,  $P=0.003$ ). Finally, lower depression ( $B=-0.16$ ,  $SE=0.13$ ,  $P=0.021$ ) was the only main effect significantly related to post-treatment negative reinforcement craving.

**DISCUSSION**

The present study examined the interactive effects of depressive symptoms and hazardous drinking in relation to craving among treatment-seeking smokers with heightened depressive symptoms in the context of sex. Results were partially in accord with a priori prediction. The interactive effect of depressive symptoms and hazardous drinking at pretreatment was related to craving at post-treatment only among men. These findings extend past work that has focused in the individual effects of depressive symptoms (Reid and Ledgerwood, 2016) and hazardous drinking (Kahler et al.,



**FIGURE 3.** Conditional effect of depressive symptoms (BDI-II) on appetitive craving (QSU-Factor 1) in terms of levels of alcohol use (AUDIT). The male interaction is represented in upper chart. The female interaction is represented in lower chart. AUDIT, Alcohol Use Disorders Identification Test total pretreatment score; BDI-II, Beck Depression Inventory 2nd version pretreatment score; QSU, Questionnaire Smoking Urges post-treatment scores.

2014) in relation to craving. The form of the interactions showed that higher depressive symptoms were positively related to greater global craving and appetitive craving among men with greater hazardous drinking. Specifically, this interactive relationship was evident when mild depressed smokers scored over 2 on alcohol use problems. Despite the low overall level of hazardous drinking in the sample, our results are in line with past work that has found that low level hazardous drinking is related to greater craving (Oliver et al., 2013). Clinically, the results suggest that hazardous drinking is a possibly important variable to consider in relation to craving among male treatment-seeking smokers with at least mild depressive symptoms.

Interestingly, there was no interactive effect for negative reinforcement craving among men. Such results are consistent with other research that has found depressive symptoms were not related to negative reinforcement craving (Leventhal et al.,

2009). Theoretically, these findings might be explained by incentive learning (Mathew et al., 2017), wherein depressive smokers anticipate the positive effect of nicotine on their mood (Cook et al., 2007). The present results expand past work showing that alcohol use may be related to increased appetitive craving (Shiffman et al., 2013) and may be more relevant in men than in women (Rodríguez-Cano et al., 2016).

There was no interactive effect of depressive symptoms and hazardous drinking on craving among women. Previous work suggests depressive symptoms generally have a greater influence on smoking maintenance and relapse among women (Weinberger et al., 2013). However, given that past work has documented that hazardous drinking has a greater effect on smoking among men than in women in Spanish-speaking populations from Europe (Rodríguez-Cano et al., 2016), it is possible that alcohol does not operate as a moderator among women universally (ie, across countries/cultures). Future research may benefit from exploring the interaction of depressive symptoms and hazardous drinking in relation to craving among male smokers from other countries. Such work also could examine other moderator variables such as social context and social support (King et al., 2009).

There are several study limitations. First, there was a relatively small sample of men in the study. Thus, future work should replicate and extend the present findings to larger treatment-seeking smoking samples balanced by sex. Second, participants with mild depressive symptoms included in the current analyses represented 23% of the total sample. Future research may benefit from exploring more severe samples, including smokers with clinical depression. Third, we did not assess the nature of depression and hazardous drinking during smoking-cessation treatment. Future research should therefore explore how these factors interplay with one another during smoking-cessation treatment. Finally, although the present study evaluated pretreatment depression and alcohol in relation to post-treatment craving and controlled for pretreatment levels of craving, causal inferences cannot be drawn. Future work should evaluate the present model with multiple observations.

### CONCLUSIONS

The present findings suggest that there may be clinical utility to better understanding sex differences in the context of depressive symptoms, hazardous drinking, and craving among treatment-seeking smokers with at least mild depressive symptoms. Future research may benefit from developing sex-specific intervention programming for smoking cessation to help in the clinical management of craving.

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