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Association Between Physical Pain and Alcohol Treatment Outcomes: The Mediating Role of Negative Affect

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Objective: Physical pain and negative affect have been described as risk factors for alcohol use following alcohol treatment. The current study was a secondary analysis of 2 clinical trials for alcohol use disorder (AUD) to examine the associations between pain, negative affect and AUD treatment outcomes. **Method:** Participants included 1,383 individuals from the COMBINE Study (COMBINE Study Research Group, 2003; 31% female, 23% ethnic minorities, average age = 44.4 [$SD = 10.2$]), a multisite combination pharmacotherapy and behavioral intervention study for AUD in the United States, and 742 individuals from the United Kingdom Alcohol Treatment Trial (UKATT Research Team, 2001; 25.9% female, 4.4% ethnic minorities, average age = 41.6 [$SD = 10.1$]) a multisite behavioral intervention study for AUD in the United Kingdom. The Form-90 was used to collect alcohol use data, the Short Form Health Survey and Quality of Life measures were used to assess pain, and negative affect was assessed using the Brief Symptom Inventory (COMBINE) and the General Health Questionnaire (UKATT). **Results:** Pain scores were significantly associated with drinking outcomes in both datasets. Greater pain scores were associated with greater negative affect and increases in pain were associated with increases in negative affect. Negative affect significantly mediated the association between pain and drinking outcomes and this effect was moderated by social behavior network therapy (SBNT) in the UKATT study, with SBNT attenuating the association between pain and drinking. **Conclusion:** Findings suggest pain and negative affect are associated among individuals in AUD treatment and that negative affect mediated pain may be a risk factor for alcohol relapse.

What is the public health significance of this article?

This study highlights the important associations between physical pain interference and intensity, negative affect, and alcohol use following treatment for an alcohol use disorder. Social network behavior therapy, which is one type of behavioral intervention for alcohol use disorders, may be particularly useful for preventing alcohol use in response to physical pain and negative affect.

Keywords: alcohol use disorder (AUD) treatment, pain interference, pain intensity, negative affect, alcohol relapse

Alcohol relapse, defined as the process of returning to heavy drinking (often defined as 4+/5+ drinks per occasion for women/men) after a period of abstinence or reduced alcohol use, is common in those with a history of alcohol use disorder (AUD), a

diagnosis often associated with periods of heavy drinking and consequent negative impacts of drinking on functioning (Leshner, 1997; Sutton, 1979). The accurate identification of factors that increase the risk of relapse is of crucial importance and there have

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been widespread efforts to identify the relevant risk factors in order to improve relapse prevention interventions (Connors, Maisto, & Donovan, 1996; Moos & Moos, 2006; Witkiewitz & Marlatt, 2004).

Nearly all models of the relapse process have proposed an interaction between biological, psychological, environmental, and social factors, with an emphasis on more stable risk factors (i.e., distal or tonic risk; Shiffman, 1989; Witkiewitz & Marlatt, 2004) creating heightened vulnerability for relapse in the presence of more immediate risk factors (i.e., proximal or phasic risk; Shiffman, 1989; Witkiewitz & Marlatt, 2004). For example, a recent analysis by Chow, Witkiewitz, Grasman, Hutton, and Maisto (2013) found that individuals who were high in distal risk were significantly more likely to experience a lapse if proximal risk (characterized by negative emotions, perceived stress, and craving) was heightened within the first 2 weeks of treatment. Similar studies of proximal risks such as dependence severity, emotional distress, and social support and recovery resources provide further support for proximal risks' potential role in increasing or decreasing the probability of relapse to problematic alcohol use (e.g., Garland, Franken, & Howard, 2012; Moos & Moos, 2006; Witkiewitz & Villarroel, 2009; Witkiewitz, 2011). Despite the identification of multiple risk factors, very few studies—and few theoretical models—have acknowledged the common experience of physical pain and pain interference as potential predictors of alcohol treatment outcomes (Booker, Haig, Geisser, & Yamakawa, 2003; Witkiewitz et al., 2015). This gap in the literature is surprising given evidence supporting the relationship between pain and negative affect (e.g., Davis, Zautra, & Smith, 2004), as well as the association between negative affect and alcohol use (Witkiewitz & Villarroel, 2009). Furthermore, alcohol has historically been used for its analgesic affect (Trafton, Oliva, Horst, Minkel, & Humphreys, 2004; Woodrow & Eltherington, 1988), and individuals with AUD have identified pain as both a common experience and as a primary reason for alcohol use (Caldeiro et al., 2008). Given these findings, it is plausible that an important association may be present between the experience of pain and AUD treatment outcomes (Witkiewitz et al., 2015). The relation between pain and AUD treatment outcomes may also be explained by experiences of negative affect.

Exploring this possibility was the primary objective of the present analyses. Specifically, the association between pain, negative affect, and alcohol treatment outcomes was examined via secondary analyses of data from two randomized clinical trials for alcohol dependence: the COMBINE Study (COMBINE Study Research Group, 2003), a large multisite randomized clinical trial for alcohol dependence conducted in the United States, and the United Kingdom Alcohol Treatment Trial (UKATT Research Team, 2001), a large randomized clinical trial for alcohol problems conducted in the United Kingdom (U.K.). It was hypothesized that pain would be associated with alcohol treatment outcomes (Hypothesis 1) and negative affect (Hypothesis 2) and that negative affect would mediate the association between pain and drinking outcomes (Hypothesis 3). Additional exploratory analyses were conducted to determine whether the treatments received in the COMBINE or UKATT studies had any influence on pain, as well as whether treatment moderated any of the associations between pain, negative affect, and alcohol treatment outcomes.

Method

COMBINE Participants and Procedures

The COMBINE study (Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence; COMBINE Study Research Group, 2003) randomized 1,383 subjects across 11 research sites into nine treatment groups, consisting of a combination of medical management (MM) or combined behavioral intervention (CBI) and medications (acamprosate, naltrexone, or placebo versions of each drug). Subjects received treatment for a total of 4 months; participants were offered nine MM visits and a maximum of 20 CBI sessions. Participants completed assessments at 2.5 months, 9 months, and 12 months following treatment.

The sample was recruited from treatment referrals at the study sites and throughout the community, as described previously (Anton et al., 2006). Individuals were excluded from participation if they were dependent on another drug besides alcohol, nicotine, or cannabis, had recently used opioids, had a serious mental illness, or any other medical condition that could disrupt study participation, had taken one of the study medications 30 days prior to baseline, or took medication that could raise the potential risks of the study. Inclusion criteria required participants have a minimum of 14 drinks (females) or 21 drinks (males) on average per week over a successive 30 days in the 90-day period prior to beginning abstinence, having 2 or more days of heavy drinking (defined as 4+ drinks for females and 5+ drinks for males) in the 90-day period with the last drink being within 21 days of enrollment.

Of the 1,383 participants in COMBINE, 31% were female and 69% were male, 23% of the study patients were ethnic minorities (76.3% non-Hispanic White, 11.6% Hispanic American, 7.8% African American, and 4.1% "other"). The participants' mean age was 44.4 years ($SD = 10.2$), 71% had at least 12 years of education, and 42% were married.

UKATT Participants and Procedures

For UKATT (UKATT Research Team, 2001), 742 subjects across seven treatment sites in Birmingham, Cardiff, and Leeds were randomized into two treatment groups: either motivation enhancement therapy (MET) or social behavior and network therapy (SBNT; UKATT Research Team, 2005). Subjects received treatment for a total of 2 to 3 months; participants receiving SBNT received up to eight sessions and those who received MET received up to three sessions. Participants completed assessments at 3 and 12 months after entry into the trial.

Participants were recruited into the study if they were seeking alcohol treatment from one of the treatment sites (UKATT Research Team, 2001, 2005). Individuals were excluded from participation if abuse or dependence of other drugs besides alcohol was a more serious problem, had uncontrolled psychotic symptoms or severe cognitive impairment, could not name a contact person, were planning to leave the area, were under 16 years old, or were illiterate.

Of the 742 participants in UKATT, 25.9% were female and 74.1% were male, 95.6% of the participants were White and 4.4% of the study patients were ethnic minorities (1.2% Black, 2.0% Indian or other Asian, 0.1 Pakistani, and 0.9% "other"). The mean age was 41.6 years ($SD = 10.1$), 10% had a secondary degree or equivalent training, and 44% were married.

Measures

Alcohol use. In both COMBINE and UKATT, alcohol consumption was assessed using a calendar method via the Form-90 Interview (Miller, 1996). In COMBINE daily alcohol consumption, measured in U.S. standard drink units (unit of alcohol = 11.358 g), was assessed for 485 days (120 days during treatment and 365 days following treatment). In UKATT daily alcohol consumption, measured in U.K. standard drink units (unit of alcohol = 8 g of ethanol), was assessed for the prior 90 days at baseline, 3-month follow-up (corresponding to the posttreatment assessment), and the 12-month follow-up. Four outcome variables were derived from the Form-90 data in each of the studies: percent drinking days (PDD; a measure of drinking frequency), drinks per drinking day (DDD; a measure of drinking intensity), percent heavy drinking days (PHDD; defined as percentage of days with 4+/5+ drinks for women/men), and the maximum number of drinks on the peak drinking occasion (MXD, a measure of peak drinking).

Pain. In COMBINE, pain was assessed via two items. One item was from the 26-item World Health Quality of Life (WHO-QOL) assessment (World Health Organization, 1998): "To what extent do you feel that physical pain prevents you from doing what you need to do?" with response options ranging from 1 *not at all* to 5 *an extreme amount*. The second item was from the 12-item Short Form Health Survey (SF-12; Ware, Kosinski, & Keller, 1996): "During the past 4 weeks, how much did pain interfere with your normal work including both work outside the home and housework?" with response options ranging from 1 *not at all* to 5 *extremely*. The WHO-QOL measure was administered at baseline, 6.5 months postbaseline, and 12 months postbaseline. The SF-12 was administered at baseline, 4 months postbaseline, and 12 months postbaseline. For both items we found that the greatest pain interference categories of *an extreme amount* (WHO-QOL) and *extremely* (SF-12) had very low response rates (less than 1% indicated this level of pain interference). To address this, we recoded the response options for the WHO-QOL to be from 1 *not at all* to 4 *very much or an extreme amount* and the response options for the SF-12 to be from 1 *not at all* to 4 *quite a bit or extremely*. Internal consistency reliability of the two items exceeded $\alpha = .81$ at all assessment time points.

In UKATT, pain was assessed via three items including one item from the European Quality of Life Group EQ-5D (European Quality of Life Group, 1990), a general measure of health status on five dimensions, and two items from the 36-item Short Form Health Survey (SF-36, Ruta, Garratt, Abdalla, Buckingham, & Russell, 1993). One item, the same item that was included in the SF-12 from COMBINE, measured pain interference: "During the past 4 weeks, how much did pain interfere with your normal work including both work outside the home and housework?" with response options ranging from *not at all* to *extremely*. Two items assessed pain intensity, one from the EQ-5D: "Please indicate which statement best describes your health today" with response options of *I have no pain or discomfort*, *I have moderate pain or discomfort*, or *I have extreme pain or discomfort* and one from the SF-36: "How much bodily pain have you had during the past 4 weeks" with response options ranging from *none* to *very severe*. The EQ-5D and SF-36 were administered at baseline, 3 months, and 12-month follow-ups. Internal consistency reliability of the

three items was $\alpha = .77$ at baseline and exceeded $\alpha = .81$ at 3- and 12-month time points.

Negative affect. In COMBINE, negative affect was measured by the Depression and Anxiety domains of the 53-item Brief Symptom Inventory (BSI; Derogatis & Melisaratos, 1983), which assesses self-reported psychiatric symptomatology across nine domains via ratings on a 5-point scale (0 = *not at all*, 4 = *extremely*). The BSI was administered at baseline as well as postbaseline months 4 (end of treatment), 6.5 (2.5 months posttreatment), 12 (9 months posttreatment) and 16 (12 months posttreatment). Scores on the Depression and Anxiety domains were used as indicators of a negative affect latent variable at each time point. Internal consistency reliability of the BSI exceeded $\alpha = .97$ at all assessment time points.

In UKATT, negative affect was measured by the Depression and Anxiety/Insomnia domains of the 28 item General Health Questionnaire (GHQ-28; Goldberg, 1972), which is a measure of psychiatric disturbance in four domains: Somatic Symptoms, Anxiety/Insomnia, Social Dysfunction, and Depression. The GHQ was administered at baseline, 3 months, and 12-month follow-ups. Scores on the Anxiety/Insomnia and Depression domains were used as indicators of a negative affect latent variable assessed at baseline, 3 months (posttreatment), and 12-month follow-up. Internal consistency reliability of the GHQ exceeded $\alpha = .96$ at all assessments time points.

Covariates. Acknowledging that other factors are often associated with pain, negative affect, and alcohol treatment outcomes; we included a number of covariates in the final mediation models. Covariates were not included in the models of associations between pain and drinking outcomes or in the models of associations between pain and negative affect because we were primarily interested in the bivariate associations among these constructs, without the additional influence of covariates. Covariates in both the COMBINE and UKATT studies included: demographic variables (gender, marital status, employment, income, and minority status), baseline dependence severity [assessed via the Alcohol Dependence Scale (ADS; Skinner & Horn, 1984) in COMBINE and the Leeds Dependence Questionnaire (LDQ; Raistrick et al., 1994) in UKATT], number of alcohol dependence symptoms based on the *Diagnostic and Statistical Manual for Mental Disorders—4th Edition Text Revision (DSM-IV-TR; American Psychiatric Association, 1995)*, readiness to change [assessed using the University of Rhode Island Change Assessment scale (URICA; DiClemente & Hughes, 1990) in COMBINE and the Readiness to Change Questionnaire—Treatment Version (RTCQ; Heather & Honekopp, 2008) in UKATT], and self-efficacy was assessed using the Alcohol Abstinence Self-Efficacy Scale (AASE; DiClemente, Carbonari, Montgomery, & Hughes, 1994). In UKATT, which did not exclude opiate users ($n = 67$, 9.0% of the UKATT sample), we included opiate use as a covariate.

Statistical Analyses

Analyses were conducted to test the three hypotheses listed above regarding the association between pain, negative affect, and alcohol treatment outcomes. Models were estimated in the COMBINE and UKATT datasets using Mplus version 7.2 (Muthén & Muthén, 2012) with maximum likelihood estimation, which is a preferred method for estimation when some data are

missing (Schafer & Graham, 2002). These models were considered to provide a reasonable fit to the data with a Root Mean Square Error of Approximation (RMSEA; Browne & Cudeck, 1993) <0.08 and the Comparative Fit Index (CFI; Bentler, 1990) >0.90 . There are varying opinions on the best cut-offs for the RMSEA and CFI for evaluating model fit, with some arguing for RMSEA <0.06 and CFI >0.95 as indicative of good fit (Hu & Bentler, 1999). We believed it was important not to focus exclusively on fit indices (although model fit is important) and to consider the replication of models across two samples as the ultimate goal.

Measurement models of pain and negative affect. First, we created longitudinal measurement models of the pain and negative affect constructs within each dataset. The underlying measurement model for each construct was selected based on the distributions of the data available, with graded response models used for ordered categorical items and confirmatory factor analysis used for continuous scale scores.

For the pain items, which were ordered categorical, we used longitudinal graded response models (Samejima, 1969, 1997) to create individual graded response scores at each time point using the expected a posteriori approach. Separate graded response models were estimated in the COMBINE and UKATT studies in order to generate graded response scores (similar to factor scores) for the pain latent factors at each time point (COMBINE: baseline, 4-, 6.5-, and 12 months postbaseline; UKATT: baseline, 3-, and 12 months postbaseline).

For negative affect variables, which were continuous scale scores, we used longitudinal confirmatory factor analyses (Little, Preacher, Selig, & Card, 2007; Little, 2013) to create study-independent latent factor scores at each time point. Longitudinal confirmatory factor analysis is a repeated measures extension of the confirmatory factor analysis model, whereby factor loadings and item intercepts are constrained to equality across time. First, we estimated latent factor models of negative affect at each time point (COMBINE: baseline, and 4-, 6.5-, 12-, and 16 months postbaseline; UKATT: baseline and 3-, and 12 months postbaseline) and then combined them into a longitudinal model with constraints placed on the item loadings, intercepts, and variance-covariance matrix to test for measurement invariance of the latent factor across time (Byrne, Shavelson, & Muthén, 1989). Models were estimated separately in the COMBINE and UKATT studies in order to generate factor scores for the negative affect latent factors at each time point.

For each dataset we used the pain graded response scores and negative affect latent factor scores as indicators in latent growth curve models of changes in pain and negative affect, respectively, over time. Parameters derived from a latent growth model provide information about a construct's average level (mean intercept) and average change over time (mean slope), as well as the individual variance around the intercept and slope. A significant intercept would indicate an average level that is significantly different from zero, whereas a significant slope would indicate an increase or decrease in either pain or negative affect score that was significantly different from no change. In both datasets we set the intercept for the growth models at the end of treatment (COMBINE: 4-month assessment; UKATT: 3-month assessment) and we examined the fit of models using varying parameterizations of the growth process (linear, quadratic, nonlinear). Linear growth represents the average rate of change in pain and negative affect

scores over time, quadratic growth represents acceleration or deceleration in the rate of change (e.g., the change is more rapid or slowed, introducing a parabolic change pattern), and nonlinear growth models could be used to identify other functional forms of growth (e.g., exponential growth).

Hypothesis 1: Association between pain and alcohol treatment outcomes. The association between pain and alcohol treatment outcomes was assessed by extending the latent growth model of pain to predict 12-month alcohol treatment outcomes. Specifically, we tested the association between the intercept and slope parameters of the pain latent growth curve models and 12-month drinking outcomes (PDD, DDD, PHDD, MXD), while controlling for baseline levels of the outcomes. For COMBINE the 12-month outcomes represented outcomes 1 year following treatment (16 months following baseline assessment), whereas for UKATT the 12-month outcome represented drinking outcomes 9 months following completion of treatment (12 months following baseline assessment).

Hypothesis 2: Association between pain and negative affect. The association between pain and negative affect scores over time was assessed using parallel process latent growth models. In COMBINE, we examined changes in negative latent factors across months 4 (intercept), 6.5, 12, and 16 as associated with changes in pain graded response scores across months 4 (intercept), 6.5, and 12. In UKATT we examined changes in negative latent factors across baseline to Month 3 (intercept) to Month 12 as associated with changes in pain graded response scores across baseline to Month 3 (intercept) to Month 12. In both the COMBINE and UKATT datasets we covaried the growth parameters (i.e., intercept parameters and slope parameters) across the pain and negative affect growth processes.

Hypothesis 3: Pain and alcohol treatment outcomes mediated by negative affect. Next, we extended the parallel process growth models of pain and negative affect to include covariates and the 12-month drinking indices as outcomes of the pain and negative affect latent growth parameters, with the negative affect growth process tested as mediating the effect of the pain growth process on 12-month drinking outcomes, as shown in Figure 1a (COMBINE) and b (UKATT). Mediation models were estimated using the product of coefficients approach (MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002), which provides an estimate of the mediated effect by multiplying two regression coefficients: (a) the regression of the mediator on the independent variable (the "a-path"), and (b) the regression of the outcome on the mediator (the "b-path"), with the independent variable included in the model (MacKinnon, 2008). The mediation models tested in the current paper examined negative affect growth (the mediator) regressed on pain growth (the independent variable), and the drinking outcomes (outcome) regressed on negative affect growth, with the inclusion of pain growth in the model. The 95% confidence intervals for the mediated effects were estimated using bootstrapping with 1,000 bootstrap samples.

Exploratory analyses: Effects of treatment assignment. In the final set of analyses we examined two questions regarding the effects of treatment on pain, negative affect, and alcohol treatment outcomes. First, we examined whether randomly assigned treatment condition in COMBINE (naltrexone, acamprosate, or placebo in combination with MM or CBI) or UKATT (MET or SBNT) significantly predicted pain scores by including fixed ef-

PHYSICAL PAIN AND ALCOHOL TREATMENT

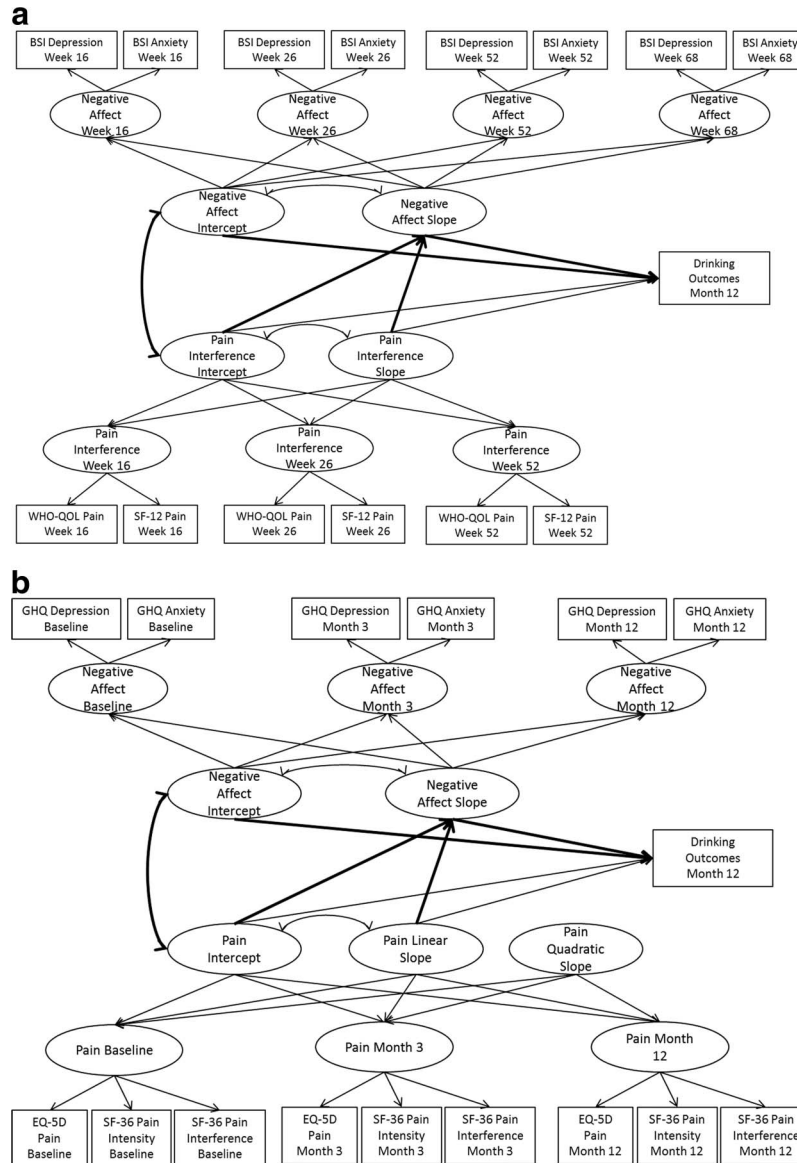


Figure 1. a. Parallel process growth mediation model in COMBINE. BSI = Brief Symptom Inventory; WHO-QOL = World Health Organization Quality of Life measure of pain interference; SF-12 = Short Form 12 measure of pain interference. b. Parallel process growth mediation model in UKATT. GHQ = General Health Questionnaire; EQ-5D = European Quality of Life measure of pain intensity; SF-36 = Short Form 36 Health Survey measure of pain intensity and pain interference.

fects of treatment in the pain latent growth curve models. Second, we examined whether treatment condition moderated the association between pain, negative affect, and alcohol treatment outcomes by including moderating effects of treatment (i.e., an interaction term for centered pain scores by treatment condition) in each set of analyses described above. For both studies we created dummy-coded variables for treatment effects. In COMBINE we examined three contrasts: naltrexone (coded 1) versus no naltrexone (coded 0); acamprosate (coded 1) versus no acamprosate (coded 0); and CBI (coded 1) versus MM + CBI (coded 0). In UKATT, we examined one contrast: SBNT (coded 1) versus MET (coded 0).

Results

Descriptive Statistics

Means (standard deviations) of all continuous measures (e.g., BSI, GHQ, Form 90 drinking outcomes) and the frequency (%) of item responses on the WHO-QOL and SF-12 items (COMBINE study) and EQ-5D and SF-36 items (UKATT study) are provided in Tables 1 (COMBINE) and 2 (UKATT). In both studies, we observed reductions in pain (defined as interference in COMBINE and both pain interference and pain intensity in UKATT), depres-

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Table 1
Descriptive Statistics, N (%) or Mean (Standard Deviation), for COMBINE Study Variables

	Baseline	4 months	6.5 months	12 months	16 months
WHO-QOL pain interference					
1-Not at all	845 (62%)	—	705 (66%)	608 (64%)	—
2-A little	335 (25%)	—	221 (21%)	220 (23%)	—
3-A moderate amount	120 (9%)	—	95 (9%)	90 (9%)	—
4-Very much/extremely	51 (4%)	—	40 (4%)	37 (4%)	—
SF-12 pain interference					
1-Not at all	796 (59%)	762 (69%)	—	577 (61%)	—
2-A little bit	342 (25%)	237 (22%)	—	234 (24%)	—
3-Moderately	137 (10%)	70 (6%)	—	93 (10%)	—
4-Quite a bit/extremely	81 (6%)	33 (3%)	—	47 (5%)	—
BSI-Depression (range 42–80)	61.6 (10.6)	55.1 (10.6)	55.5 (11.3)	55.3 (11.0)	55.2 (11.1)
BSI-Anxiety (range 38–80)	58.4 (11.5)	51.3 (11.1)	51.5 (11.7)	50.9 (11.1)	51.1 (11.4)
Percent drinking days	78.6 (22.5)	27.3 (33.5)	36.2 (37.8)	38.0 (38.7)	37.4 (39.1)
Drinks per drinking day	12.9 (8.1)	4.7 (5.8)	5.6 (6.7)	5.4 (6.4)	5.3 (6.3)
Percent heavy drinking days	73.7 (24.7)	19.8 (29.9)	27.7 (35.3)	29.4 (36.7)	29.3 (37.3)
Maximum drinks per day	22.2 (14.0)	6.7 (8.3)	7.3 (8.5)	7.1 (8.1)	5.9 (8.1)
Pain scores (range -0.5–2.5)	0.13 (0.73)	0.11 (0.64)	0.13 (0.77)	0.15 (0.70)	—
Affect scores (range -2.7–2.5)	0.01 (0.94)	0.01 (0.89)	0.00 (0.92)	0.01 (0.95)	0.01 (0.95)

Note. WHO-QOL = World Health Organization Quality of Life survey; SF-12 = Short Form Health Survey; BSI = Brief Symptom Inventory.

sion and anxiety scores, and drinking frequency and intensity from baseline to the follow-up assessments.

Measurement and Latent Growth Models of Pain and Negative Affect

Pain graded response model. The longitudinal graded response models of pain provided an adequate fit to the observed data in the COMBINE data ($\chi^2(13) = 70.04$, RMSEA = 0.06

(90% CI: 0.044, 0.070), CFI = 0.99) and the longitudinal graded response model of pain provided a reasonable fit to the observed data in UKATT ($\chi^2(43) = 279.97$, RMSEA = 0.08 (90% CI: 0.077, 0.096), CFI = 0.99). Means (standard deviations) for model-generated pain scores are provided in Tables 1 and 2.

Negative affect factor model. The longitudinal confirmatory factor analyses of the negative affect scales also provided an

Table 2
Descriptive Statistics, N (%) or Mean (Standard Deviation), for UKATT Study Variables

	Baseline	3 months	12 months
EQ-5D pain intensity			
1-No pain or discomfort	265 (36%)	284 (44%)	227 (40%)
2-Some pain or discomfort	419 (57%)	332 (51%)	293 (52%)
3-Extreme pain or discomfort	47 (7%)	34 (5%)	43 (8%)
SF-36 pain interference			
1-Not at all	207 (28%)	273 (42%)	194 (35%)
2-A little bit	178 (24%)	150 (23%)	129 (23%)
3-Moderately	152 (21%)	92 (14%)	91 (16%)
4-Quite a bit	122 (17%)	93 (15%)	93 (17%)
5-Extremely	72 (10%)	39 (6%)	54 (10%)
SF-36 pain intensity			
1-None	109 (14.9%)	169 (26%)	137 (24%)
2-Very mild	95 (13.0%)	105 (16%)	83 (15%)
3-Mild	133 (18.2%)	102 (16%)	96 (17%)
4-Moderate	241 (32.9%)	174 (27%)	132 (23%)
5-Severe	110 (15.0%)	74 (11%)	78 (14%)
6-Very severe	44 (6.0%)	24 (4%)	38 (7%)
GHQ-Depression (range 0–21)	7.92 (6.20)	5.61 (6.02)	5.24 (6.10)
GHQ-Anxiety (range 0–21)	10.97 (5.38)	8.37 (5.57)	7.96 (5.85)
Percent drinking days	78.1 (24.96)	50.36 (38.3)	49.59 (39.6)
Drinks per drinking day	24.64 (14.73)	14.40 (13.26)	13.70 (13.43)
Percent heavy drinking days	76.51 (25.95)	46.78 (38.56)	45.44 (39.91)
Maximum drinks per day	35.28 (19.76)	20.08 (17.89)	18.95 (18.39)
Pain scores (range -1.49–2.49)	0.06 (0.81)	-0.05 (0.82)	-0.0004 (.82)
Affect scores (range -1.74–2.79)	0.001 (0.90)	0.01 (0.90)	-0.01 (0.89)

Note. EQ-5D = European Quality of Life survey; SF-36 = Short Form Health Survey; GHQ = General Health Questionnaire.

adequate fit to the observed data in COMBINE ($\chi^2(25) = 53.41$, RMSEA = 0.03 (90% CI: 0.019, 0.041), CFI = 0.996) and a reasonable fit to the observed data in UKATT ($\chi^2(24) = 69.90$, RMSEA = 0.05 (90% CI: 0.037, 0.065), CFI = 0.99). All factor loadings exceeded 0.80 in both studies. Finally, in both studies, the longitudinal confirmatory factor models were found to display strong invariance across time (item loadings and item intercepts constrained to equality). From these models we generated negative affect scores using the modal posterior estimator approach. Descriptive statistics for the negative affect scores are provided in Tables 1 (COMBINE) and 2 (UKATT).

Pain and negative affect latent growth models. The pain graded response scores and negative affect scores at each time point were then entered into separate latent growth curve models. For COMBINE, the final pain model with the intercept at Month 4 and linear slope provided an excellent fit to the data ($\chi^2(2) = 11.23$, RMSEA = 0.06 (90% CI: 0.028, 0.093), CFI = 0.99) and the final negative affect model with the intercept at Month 4 and both linear and quadratic slopes provided an excellent fit to the data ($\chi^2(3) = 3.09$, RMSEA = 0.005 (90% CI: 0.000, 0.048), CFI = 1.00). For the UKATT data, the final pain model and the final negative affect model included the intercept centered at the 3-month follow-up (end of treatment) with linear and quadratic slopes. Both models were just-identified (e.g., the model degrees of freedom equal zero) with a random linear slope and fixed quadratic slope ($\chi^2(0) = 0.00$, RMSEA = 0.00), CFI = 1.00).

Hypotheses 1: Pain and Alcohol Treatment Outcomes

In order to test the association between pain and drinking outcomes, we examined the association between the intercept and slope parameters from the pain latent growth models and the 12-month drinking outcomes (PDD, DDD, PHDD, and MXD), while also controlling for baseline levels of the outcomes. All models provided an acceptable fit to the observed data. As shown in Table 3, results indicated that the end-of-treatment pain scores (intercepts in the latent growth models) were significantly associated with all four drinking outcomes in both COMBINE and UKATT. Thus, Hypothesis 1 was supported given that pain was significantly associated with drinking outcomes. Change in pain scores over time (slope) did not significantly predict 12-month outcomes, above and beyond the intercept and baseline levels of the outcomes. Across all models, including baseline drinking as a predictor, 5–10% of the variance in 12-month drinking outcomes was explained by the model. With baseline drinking excluded from the model (results not shown), pain independently explained 1–5% of the variance in drinking outcomes.

Hypothesis 2: Association Between Pain and Negative Affect

The parallel process growth models of pain and negative affect scores provided a reasonable fit to the data for COMBINE ($\chi^2(14) = 120.08$, RMSEA = 0.07 (90% CI: 0.062, 0.087), CFI = 0.989) and a slightly less than adequate fit based on RMSEA in the UKATT dataset ($\chi^2(6) = 63.10$, RMSEA = 0.11 (90% CI: 0.08, 0.14), CFI = 0.98). In both datasets the associations between the growth processes of pain and negative affect were significant, such that the intercepts were significantly positively associated

(COMBINE: B (*SE*) = 0.19 (0.02), $p < .001$; UKATT: B (*SE*) = 0.28 (0.02), $p < .001$) and the slopes were positively associated (COMBINE: B (*SE*) = 0.001 (0.00), $p < .001$; UKATT: B (*SE*) = 0.05 (0.01), $p < .001$). Thus a higher level of pain was associated with a higher level of negative affect (intercept) and increases in pain were associated with increases in negative affect (slope), providing support for Hypothesis 2. In both datasets, the intercept of pain was not significantly associated with the slope of negative affect and the intercept of negative affect was not significantly associated with the slope of pain.

Hypothesis 3: Pain and Alcohol Treatment Outcomes Mediated by Negative Affect

The parallel process growth models of pain and negative affect scores were extended to include covariates and 12-month drinking outcomes with negative affect as a mediator of the association between pain scores and drinking outcomes. All models provided an adequate fit to the data based on RMSEA and CFI. Results from the analyses were largely consistent across the COMBINE and UKATT datasets, such that in all models the negative affect growth factors (intercept and/or slope) significantly mediated the association between pain and drinking outcomes, providing support for Hypothesis 3.

In COMBINE (see Table 4), when negative affect was included in the model, the association between the pain growth factors in predicting drinking outcomes (Hypothesis 1) was no longer significant, and there were significant mediation effects of both the negative affect intercept and the negative affect slope. Numerous significant covariate effects were noted across all drinking outcome models. Males and individuals with higher ADS scores had significantly higher 12-month PDD and greater readiness to change at baseline was associated with significantly lower 12-month DDD and MXD. Across all four drinking outcomes, being female, unmarried, non-Hispanic White, more severe dependence severity (as measured by ADS and *DSM-IV*), and reporting lower self-efficacy were significantly associated with higher negative affect (intercept), and racial minority status predicted an increase in negative affect over time (slope). Being married, unemployed, with a lower income, and more severe dependence severity were associated with greater pain (intercept). None of the covariates were significantly associated with changes in pain over time.

In UKATT (see Table 5), the negative affect intercept did not mediate the association between the pain intercept and DDD, PHDD, or MXD outcomes. In other words, Hypothesis 3 was not supported for the intercept of negative affect mediating the intercept of pain in predicting PDD, PHDD, and MXD. On the contrary, Hypothesis 3 was supported for the intercept of negative affect mediating the association between the pain intercept and frequency of drinking (PDD). Hypothesis 3 was also supported for the slope of negative affect. The negative affect slope (change in negative affect over time) significantly mediated the association between the pain slope (change in pain over time) and all four drinking outcomes. As with COMBINE, we found several significant covariate effects. Males, individuals with higher LDQ scores, those with lower readiness to change, and lower self-efficacy had significantly higher 12-month PDD and PHD. Greater self-efficacy at baseline and employment were also associated with significantly lower 12-month DDD and MXD. Across all four drinking out-

T3

T4

T5

Table 3
Results From Analyses of Pain Growth Factors Predicting 12-Month Drinking Outcomes

	β	B (SE)	R ²
COMBINE			
12-month Percent Drinking Days (PDD)			0.09
Baseline PDD	0.30	0.52 (0.05)**	
Pain interference intercept	0.06	0.04 (0.02)*	
Pain interference slope	0.001	0.01 (0.13)	
12-month Drinks per Drinking Day (DDD)			0.07
Baseline DDD	0.22	0.17 (0.02)**	
Pain interference intercept	0.11	0.01 (0.003)**	
Pain interference slope	0.01	0.01 (0.02)	
12-month Percent Heavy Drinking Days (PHDD)			0.06
Baseline PHDD	0.22	0.33 (0.05)**	
Pain interference intercept	0.08	0.05 (0.02)*	
Pain interference slope	-0.001	-0.006 (0.13)	
12-month Maximum Drinks per Day (MXD)			0.05
Baseline MXD	0.18	0.10 (0.02)**	
Pain interference intercept	0.12	0.02 (0.004)**	
Pain interference slope	0.01	0.01 (0.03)	
UKATT			
12-month Percent Drinking Days (PDD)			0.10
Baseline PDD	0.25	0.40 (0.07)**	
Pain interference and intensity intercept	0.08	0.04 (0.02)*	
Pain interference and intensity slope	0.15	0.35 (0.50)	
12-month Drinks per Drinking Day (DDD)			0.16
Baseline DDD	0.38	0.34 (0.01)**	
Pain interference and intensity intercept	0.09	0.02 (0.007)*	
Pain interference and intensity slope	0.11	0.09 (0.14)	
12-month Percent Heavy Drinking Days (PHDD)			0.09
Baseline PHDD	0.25	0.38 (0.06)**	
Pain interference and intensity intercept	0.09	0.05 (0.02)*	
Pain interference and intensity slope	0.13	0.30 (0.44)	
12-month Maximum Drinks per Day (MXD)			0.15
Baseline MXD	0.36	0.33 (0.04)**	
Pain interference and intensity intercept	0.10	0.02 (0.01)*	
Pain interference and intensity slope	0.11	0.13 (0.24)	

Note. β = standardized regression coefficient; B = unstandardized regression coefficient; SE = Standard Error.

* $p < .05$. ** $p < .01$.

comes, being unemployed, with more severe dependence severity (as measured by LDQ and DSM-IV), lower self-efficacy, and opiate use were significantly associated with higher negative affect (intercept) and being unemployed with greater dependence severity (measured by LDQ) predicted an increase in negative affect over time (slope). Being unemployed, greater dependence severity (measured by DSM-IV), lower self-efficacy, and opiate use were associated with greater pain (intercept). Covariates were not significantly associated with changes in pain (slope).

Effects of Treatment Assignment

Results from conditional latent growth curve models indicated that none of the treatment contrasts in either COMBINE or UKATT had a significant effect on the intercept or slope of pain scores over time. Treatment condition also did not moderate the associations between pain and drinking outcomes or associations between pain and negative affect in COMBINE (all $p > 0.10$).

In UKATT, treatment significantly moderated the association between the pain intercept (end of treatment pain scores) and percent heavy drinking days (PHDD) at the 12-month follow-up (B (SE) = -0.01 (0.004), $p = .045$). As shown in Figure 2, the

association between the pain intercept and 12-month PHDD was significant for the MET condition (B (SE) = .14 (.04), $p < .001$), but was nonsignificant for the SBNT condition (B (SE) = .007 (0.04), $p = .87$). Treatment also significantly moderated the association between the pain intercept and the negative affect intercept (B (SE) = -0.01(0.006), $p = .028$); however, the simple slope analysis revealed that pain and negative affect were significantly positively associated in both treatment conditions, with a stronger association in MET (standardized $\beta = 0.46$), as compared to SBNT (standardized $\beta = 0.37$).

Results from the moderated mediation analyses were also significantly different by treatment condition in UKATT for the DDD outcome. The mediating effect of the negative affect slope was only significant in the association between pain slopes and DDD for the MET condition (indirect effect B (SE) = 0.002 (0.001), 95% CI: 0.001, 0.004), while the mediating effects were not significant for the SBNT condition (indirect effect B (SE) = .002 (0.002), 95% CI: -0.001, 0.004). Treatment condition moderated the effect of the “b-path” (i.e., negative affect slope in predicting DDD), with the association between negative affect slope and DDD significantly positive in the MET condition and nonsignifi-

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Table 4
Results From Analyses of Pain Growth Factors Predicting 12-Month Drinking Outcomes Mediated by Negative Affect in COMBINE

COMBINE	B (SE; 95% CI)	R ²
12-month Percent Drinking Days (PDD) (RMSEA = .05 (90% CI: 0.04, 0.06), CFI = .98)		.28
Baseline PDD	0.48 (0.04)**	
Pain interference intercept	0.02 (0.03)	
Pain interference slope	−0.71 (0.77)	
Negative affect intercept	0.10 (0.02)**	
Negative affect slope	2.89 (1.50)	
Pain intercept → Affect intercept → PDD Mediation	.01 (.003; 95% CI: .01, .02)**	
Pain slope → Affect slope → PDD Mediation	.97 (.71; 95% CI: 0.33, 3.23)*	
12-month Drinks/Drinking Day (DDD) (RMSEA = .05 (90% CI: 0.04, 0.06), CFI = .98)		.23
Baseline DDD	0.14 (0.04)**	
Pain interference intercept	0.004 (0.004)	
Pain interference slope	−0.07 (0.12)	
Negative affect intercept	0.02 (0.003)**	
Negative affect slope	0.40 (0.22)	
Pain intercept → Affect intercept → DDD Mediation	.003 (.001; 95% CI: .002, .004)**	
Pain slope → Affect slope → DDD Mediation	.13 (.10; 95% CI: .04, .45)*	
12-month % Heavy Drinking Days (PHDD) (RMSEA = .05 (90% CI: 0.04, 0.06), CFI = .98)		.28
Baseline PHDD	0.33 (0.04)**	
Pain interference intercept	0.02 (0.03)	
Pain interference slope	−0.69 (0.79)	
Negative affect intercept	0.11 (0.02)**	
Negative affect slope	3.19 (1.56)*	
Pain intercept → Affect intercept → PHDD Mediation	.02 (.003; 95% CI: .01, .02)**	
Pain slope → Affect slope → PHDD Mediation	1.07 (.76; 95% CI: .41, 3.43)*	
12-month Maximum Drinks/ Day (MXD) (RMSEA = .05 (90% CI: 0.04, 0.06), CFI = .98)		.23
Baseline MXD	0.07 (0.04)**	
Pain interference intercept	0.007 (0.01)	
Pain interference slope	−0.11 (0.16)	
Negative affect intercept	0.02 (0.004)**	
Negative affect slope	0.59 (0.28)*	
Pain intercept → Affect intercept → MXD Mediation	.003 (.001; 95% CI: .002, .01)**	
Pain slope → Affect slope → MXD Mediation	0.20 (.14; 95% CI: 0.07, 0.64)*	

Note. B = unstandardized regression coefficient; SE = Standard Error; 95% CI = 95% confidence interval of mediated effect.

* $p < .05$. ** $p < .01$.

cant in the SBNT condition. Thus, the SBNT intervention attenuated the mediating effect of negative affect on DDD in UKATT.

Discussion

The findings from current study suggest that pain and negative affect are closely associated among individuals who received treatment for AUD and that negative affect significantly mediated the association between pain and drinking outcomes. This suggests that negative affect-mediated pain may be an important risk factor in the alcohol relapse process. These results support all three hypotheses regarding the associations between pain, negative affect, and drinking outcomes. Specifically, the level of pain at the end of treatment (i.e., pain intercept) significantly predicted drinking frequency and intensity at 12 months posttreatment (COMBINE) and 9 months posttreatment (UKATT), supporting the first hypothesis that pain and drinking outcomes would be significantly associated. Interestingly, the slopes of the pain growth factors were not significantly associated with drinking outcomes, after controlling for baseline drinking outcomes and pain intercepts. Thus, it may be most important to assess the level of pain at the end of treatment and changes in pain following treatment may be less predictive of ultimate drinking outcomes.

The results also indicated that pain and negative affect were significantly associated (supporting Hypothesis 2) and that negative affect significantly mediated the association between pain and drinking outcomes (supporting Hypothesis 3).

The finding that negative affect significantly mediated the association between pain and drinking outcomes is consistent with a growing literature on the importance of negative affect as a mediator of drinking outcomes (Allan, Albanese, Norr, Zvolensky, & Schmidt, 2015; Black et al., 2012; Kelly, Hoepfner, Stout, & Pagano, 2012). Targeting negative affect in the treatment of AUDs has been described previously (Lowman, Allen, Stout, & The Relapse Research Group, 1996; Witkiewitz & Villarroel, 2009), and the current results would suggest that interventions to reduce negative affect might be particularly important among individuals with chronic pain. The results from the current study are also consistent with a growing literature on the association between pain and addiction treatment outcomes (Brennan, Schutte, SooHoo, & Moos, 2011; Caldeiro et al., 2008; Sheu et al., 2008). To our knowledge, this is the first study to examine the association between pain and alcohol treatment outcomes as mediated by negative affect. Moreover, the results were largely replicated across two different randomized clinical trials conducted in two

Table 5
Results From Analyses of Pain Growth Factors Predicting 12-Month Drinking Outcomes Mediated by Negative Affect in UKATT

UKATT	B (SE; 95% CI)	R ²
12-month % Drinking Days (PDD) (RMSEA = .08 (90% CI: 0.06, 0.09), CFI = .96)		.19
Baseline PDD	0.30 (0.07)**	
Pain interference and intensity intercept	0.09 (0.03)*	
Pain interference and intensity slope	−0.03 (0.16)	
Negative affect intercept	−0.08 (0.04)*	
Negative affect slope	0.19 (0.04)**	
Pain intercept → Affect intercept → PDD Mediation	−.01 (.01; 95% CI: −.03, −.001)*	
Pain slope → Affect slope → PDD Mediation	.008 (.002; 95% CI: .004, .012)*	
12-month Drinks/Drinking Day (DDD) (RMSEA = .08 (90% CI: 0.06, 0.09), CFI = .96)		.29
Baseline DDD	0.28 (0.06)**	
Pain interference and intensity intercept	0.004 (0.01)	
Pain interference and intensity slope	0.002 (0.05)	
Negative affect intercept	0.02 (0.02)	
Negative affect slope	0.06 (0.02)**	
Pain intercept → Affect intercept → DDD Mediation	.004 (.003; 95% CI: −.001, .01)	
Pain slope → Affect slope → DDD Mediation	.002 (.001; 95% CI: .001, .004)*	
12-month % Heavy Drinking Days (PHDD) (RMSEA = .08 (90% CI: 0.06, 0.09), CFI = .96)		.23
Baseline PHDD	0.28 (0.07)**	
Pain interference and intensity intercept	0.07 (0.03)**	
Pain interference and intensity slope	0.01 (0.12)	
Negative affect intercept	−0.05 (0.04)	
Negative affect slope	0.21 (0.04)**	
Pain intercept → Affect intercept → PHDD Mediation	−.009 (.01; 95% CI: −.02, .004)	
Pain slope → Affect slope → PHDD Mediation	.009 (.002; 95% CI: .005, .01)**	
12-month Maximum Drinks/Day (MXD) (RMSEA = .08 (90% CI: 0.06, 0.09), CFI = .96)		.27
Baseline MXD	0.30 (0.05)**	
Pain interference and intensity intercept	0.005 (0.01)	
Pain interference and intensity slope	0.00 (0.07)	
Negative affect intercept	0.03 (0.02)	
Negative affect slope	0.07 (0.02)**	
Pain intercept → Affect intercept → MXD Mediation	.01 (.004; 95% CI: −.002, .01)	
Pain slope → Affect slope → MXD Mediation	.003 (.001; 95% CI: .001, .01)**	

Note. B = unstandardized regression coefficient; SE = Standard Error; 95% CI = 95% confidence interval of mediated effect.

* $p < .05$. ** $p < .01$.

different countries (U.S. and U.K.) that included patients at very different levels of physical health severity and disparate drinking rates at baseline (as seen in Tables 1 and 2).

The differential findings by treatment conditions in UKATT, but not COMBINE, were particularly intriguing and deserve further exploration and replication. In UKATT, the associations between pain and drinking outcomes, pain and negative affect, and the full mediational model were moderated by treatment condition. The SBNT condition attenuated the associations, such that greater pain did not predict significantly greater PHDD and greater pain did not predict as strong of an association with negative affect, as compared to the MET condition. COMBINE included a comparison of medications (naltrexone, acamprosate, or placebo) to one behavioral intervention (CBI), whereas UKATT compared a lower intensity behavioral intervention (MET) with a higher intensity behavioral intervention (SBNT). Thus, it could be the intensity of the behavioral intervention or the content of the SBNT intervention was important for attenuating the associations between pain, negative affect, and drinking outcomes. Given the fairly well-established efficacy of behavioral interventions for persistent pain (e.g., Ehde, Dillworth, & Turner, 2014; Gatchel, Peng, Peters, Fuchs, & Turk, 2007), a possibility is that the SBNT helpfully

altered participants' responses to their pain experiences, as well as in relation to alcohol use.

SBNT also attenuated the association between changes in negative affect and DDD, suggesting that individuals who experienced greater negative affect did not show corresponding increases in DDD at the 12-month follow-up. Previous research has found behavioral treatments for addiction, including cognitive-behavioral treatment, may be partially effective by changing individual responses to negative affect such that individuals tend not to drink or use drugs in response to negative affect (Hunter, Witkiewicz, Watkins, Paddock, & Hepner, 2012). The SBNT intervention of UKATT utilized cognitive and behavioral strategies to build social support networks that were supportive of reduced drinking or abstinence and it is possible that increasing social support also provided an avenue for attenuating the reaction of frequent heavy drinking in response to both pain and negative affect. Numerous studies have found social support networks to be important in the recovery process following treatment for AUD (e.g., Havassy, Hall, & Wasserman, 1991; Timko, Finney, & Moos, 2005; Walter et al., 2006). Consistent with these correlational studies, a recent experimental study found that social partners reduced alcohol relapse-like behavior in prairie voles (Hostetler & Ryabinin,

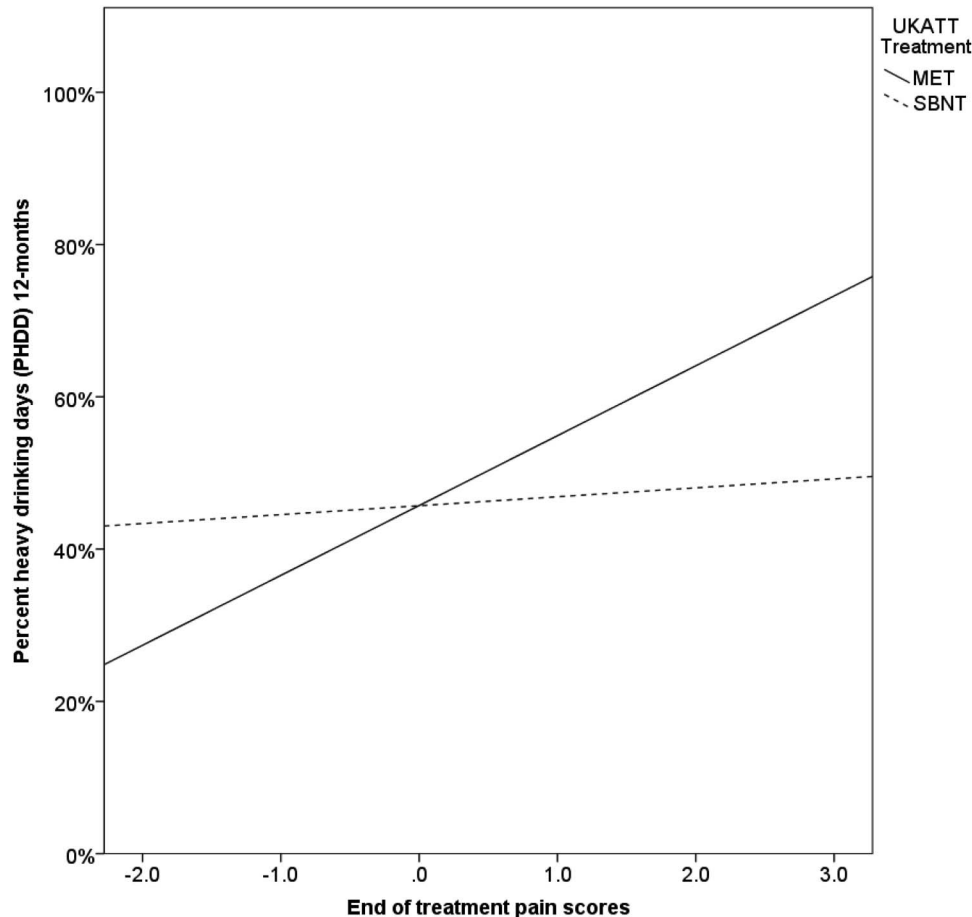


Figure 2. Association between pain scores at the end of treatment and percent heavy drinking days by treatment condition in UKATT. MET = Motivation enhancement therapy; SBNT = Social behavior and network therapy.

2014). Research on chronic pain has also found social support to predict better pain outcomes in correlational studies (Montoya, Larbig, Braun, Preissl, & Birbaumer, 2004) and experimental animal studies (Gabriel, Marcus, Honig, & Joosten, 2010; Vachon et al., 2013). In addition, there is research to suggest that individuals with chronic pain who indicate satisfaction with social support show decreased levels of depressed mood and pain intensity (López-Martínez, Esteve-Zarazaga, & Ramírez-Maestre, 2008) as well as pain interference (Kerns, Rosenberg, & Otis, 2002). Future research should be conducted to examine whether SBNT may be an effective treatment for comorbid pain and AUD.

Strengths and Limitations

The strengths of the current study include the replication of findings across two large datasets and the careful statistical approach to both datasets. Statistical procedures included the replication of longitudinal latent variable models to study the associations between constructs over time, while also controlling for multiple covariates and handling missing data using maximum likelihood estimation (Hallgren & Witkiewitz, 2013). The fact that the two clinical trials represent different samples with regard to

severity and nationality is an additional strength. Further, the findings were replicated using different measures of pain and negative affect in each of the datasets.

The limitations include the lack of a measure of pain intensity in COMBINE and the lack of a multidimensional pain measure in either study. The COMBINE study assessed pain interference only and UKATT assessed both pain intensity and interference. We elected to combine these into a single latent factor, simply labeled as *pain* in the present analyses, partially because the pattern of findings across the two studies was similar and partially due to the practical fact that no other measures were available to us. However, variability in responses to pain intensity and pain interference may have influenced the pattern of results in some way, and future studies in this area would benefit from more uniform and thorough assessment of both pain intensity and interference. The use of single measures for negative affect in each dataset is also a limitation. Finally, the current study was limited by looking at drinking outcomes only at a single follow-up time point (12 months posttreatment in COMBINE, 12 months postbaseline in UKATT), rather than examining time-varying associations between pain, negative affect, and drinking outcomes.

Conclusions and Future Directions

This study was the first to identify a longitudinal association between indicators of pain, negative affect, and drinking outcomes following AUD treatment. Chronic pain and AUD are both chronic conditions that often require years of maintenance therapies. It is critical to gain a better understanding of the association between pain and AUD treatment outcomes, including potential mechanisms of the association (e.g., negative affect). Studying the associations between pain, negative affect, and AUD treatment outcomes at self-report, behavioral, and neurobiological levels may also be critical for the development of behavioral treatment options for individuals with comorbid pain and AUD. The correlational nature of the longitudinal panel data used in the current study prevents any inferences regarding the directionality of the associations between pain, negative affect, and alcohol use; however, future research employing ecological momentary assessment design could potentially disentangle temporal ordering of the associations in real time.

The current study also holds numerous implications for intervention research. Targeting negative affect in treatment might be particularly useful among individuals with comorbid chronic pain and AUD. There has been a growing focus on the utility of mindfulness-based interventions in the treatment of chronic pain and separately in the treatment of AUD and other substance use disorders (Garland et al., 2014; Bowen et al., 2014), with some studies finding that mindfulness-based interventions may be particularly beneficial for individuals with comorbid mood disorders (Witkiewitz & Bowen, 2010; Zautra et al., 2008). Future treatment research may also consider the findings from the current study with regard to the attenuation of the pain–negative affect–drinking associations via the social behavior and network therapy utilized in UKATT.

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