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Predicting Relapse After Alcohol Use Disorder Treatment in a High-Risk Cohort: The Roles of Anhedonia and Smoking

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Abstract

On average, two-thirds of individuals treated for alcohol use disorder (AUD) relapse within six months. There is a critical need to identify modifiable risk factors associated with relapse that can be addressed during AUD treatment. Candidate factors include mood disorders and cigarette smoking, which frequently co-occur with AUD. We predicted that co-occurrence of mood disorders, cigarette smoking, and other modifiable conditions will predict relapse within six months of AUD treatment. Ninety-five Veterans, 23–91 years old, completed assessments of multiple characteristics including demographic information, co-occurring psychiatric disorders, and medical conditions during residential treatment for AUD. Participants' alcohol consumption was monitored over six months after participation. Logistic regression was used to determine if, mood disorders, cigarette smoking status, alcohol consumption, educational level, and comorbid general medical conditions are associated with relapse after AUD treatment. Sixty-nine percent of Veterans (n = 66) relapsed within six months of study while 31% remained abstinent (n = 29). While education, comorbid general medical conditions, and mood disorder diagnoses were not predictors of relapse, Veterans with greater symptoms of anhedonia, active smokers, and fewer days of abstinence prior to treatment showed significantly greater odds for relapse within six months. Anhedonia and cigarette smoking are modifiable risk factors, and effective treatment

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Author Statement

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No conflict declared.

of underlying anhedonic symptoms and implementation of smoking cessation concurrent with AUD-focused interventions may decrease risk of relapse.

Keywords

alcohol use disorders; relapse; anhedonia; cigarette smoking; Veterans

1. Introduction

Alcohol use disorder (AUD) is the most prevalent and costly of substance use disorders, with an incidence rate of 13.9% across the U.S. population (Grant et al., 2015). In addition, current AUD diagnosis is estimated at 16% in recently deployed Veterans and is approximately four times as common among combat Veterans than in the general population (Kessler et al., 2005; Office of Public Health DoVA, 2017; Wilk et al., 2010). For many individuals, AUD is a chronic, relapsing-remitting disorder (Witkiewitz, 2011; Witkiewitz and Marlatt, 2007). Despite the ongoing development and refinement of pharmacological and psychosocial treatments, at least 60% of those with AUD will relapse to hazardous drinking within 6 months following treatment (Durazzo and Meyerhoff, 2017; Kirshenbaum et al., 2009; Maisto et al., 2006a; Meyerhoff and Durazzo, 2010). Furthermore, relapse within 6 months of treatment is associated with extended periods of hazardous drinking and adverse psychosocial consequences (Durazzo et al., 2008; Maisto et al., 2006a; Maisto et al., 2006b), marking a critical need to understand factors related to relapse.

Multiple biopsychosocial characteristics have been implicated in the chronic addiction cycle experienced by many individuals with AUD (Florez et al., 2015; Meyerhoff and Durazzo, 2010; Meyerhoff et al., 2013; Seo and Sinha, 2015; Seo et al., 2015; Witkiewitz, 2011). Depression and cigarette smoking are the most commonly co-occurring conditions in those with AUD (Durazzo et al., 2007; Durazzo and Meyerhoff, 2017; Grant et al., 2015; Tolliver and Anton, 2015; Weinberger et al., 2016). Comorbid major depressive disorder (Durazzo and Meyerhoff, 2017; Hobbs et al., 2011; Suter et al., 2011) or depressive symptoms (Bottlender and Soyka, 2005; Kodl et al., 2008) in Veterans and civilians with AUD is associated with increased risk of relapse following treatment. Prior work from our group has demonstrated that depression is comprised of multiple distinct symptom features, including anhedonia (loss of pleasure) and anxious arousal (Grisanzio et al., 2018). These unique symptom features may influence treatment outcome; for example, anhedonia is commonly associated with poor psychosocial outcomes in those treated for depression (Vinckier et al., 2017). In the context of AUD, anhedonia shares several characteristics with hyperkatifia, which is often experienced by those with AUD during abstinence (Shurman et al., 2010), and a motivating factor to return to drinking which may increase risk of relapse. Taken together, this highlights the potential utility of considering transdiagnostic factors like the Research Domain Criteria (RDoC) positive valence construct in addition to diagnoses.

Cigarette smoking is another relevant comorbid substance use issue to AUD, particularly in Veterans. Although cigarette smoking within the general population has decreased over time, the smoking prevalence is at least twice as high among individuals with an AUD

compared to the national average (Weinberger et al., 2019). Specifically, the prevalence of smoking ranges from 50% to at least 75% among individuals seeking treatment for AUD in the United States, depending on geographic region (Daeppen et al., 2000; Durazzo, T. C. et al., 2014b). Veteran cigarette smoking rates are also significantly higher than the national average (Durazzo, Timothy C et al., 2014; Weinberger et al., 2015a). In those with AUD, smoking is associated with increased alcohol consumption severity (Durazzo, T. C. et al., 2014a; Meyerhoff et al., 2013), greater symptoms of alcohol withdrawal, and increased likelihood of relapse (Chiappetta et al., 2014; Satre et al., 2007; Weinberger et al., 2015b), or earlier relapse in individuals who resumed hazardous drinking after treatment (Durazzo and Meyerhoff, 2017).

It is also important to consider biopsychosocial characteristics that have previously been associated with treatment outcomes in those with AUD. These include age, education, marital status, employment, and socioeconomic status (Adamson et al., 2009; Al Abeiat et al., 2016; Durazzo and Meyerhoff, 2017; Greenfield et al., 2003). Alcohol consumption severity, co-occurring substance use, depressive symptomology, mood disorders, and other comorbid psychiatric conditions are also related to resumption of hazardous alcohol use following treatment (Bradizza et al., 2006; Durazzo and Meyerhoff, 2017; Moos and Moos, 2006; Sugarman et al., 2014). In addition, individuals with AUD and co-existing medical conditions (e.g. hypertension, hepatitis C, hyperlipidemia) relapse significantly earlier than those without medical conditions following treatment (Durazzo and Meyerhoff, 2017).

These findings highlight the adverse associations between depressive disorders, cigarette smoking, and biopsychosocial characteristics and AUD treatment outcome. To the best of our knowledge, no previous study has undertaken a multipronged approach to identify the sociodemographic, psychiatric, and concurrent substance factors associated with treatment outcomes (Adamson et al., 2009; Greenfield et al., 2003; Kirshenbaum et al., 2009; Witkiewitz, 2011) in one sample of Veterans in residential treatment for AUD. We improve on prior studies by expanding on and refining definitions of these predictors of relapse. We refine on depression by examining transdiagnostic and dimensional factors of depression that may contribute to treatment outcome. We expand on the definition of smoking status by further classifying participants into three groups (i.e. active-smokers, former-smokers, and non-smokers) as opposed to previous studies that only compared active daily or non-daily smoking to non-smokers; in these studies, former smokers were likely subsumed within non-smokers. Based on prior research, we hypothesized that history of major depressive disorder (MDD), smoking status, level of alcohol consumption, educational level, and co-existing general medical conditions would significantly predict posttreatment drinking status 6 months following study participation.

2. Methods

2.1. Participants

Veterans with a diagnosis of AUD (n = 95; 18 females) were recruited from residential treatment programs for AUD at the VA Palo Alto Health Care System (VAPAHCS). Treatment programs ranged from 28 to 90 days. Participants were between 23 and 91 years of age and met DSM-5 criteria for Alcohol Use Disorder (American Psychiatric Association,

2013). Consistent with the patient populations who seeks AUD treatment at the VA, 96% percent of the sample was classified as having severe AUD (per DSM-5 criteria). Study procedures were approved by the VAPAHCS and Stanford University institutional review boards and were in accordance with the ethical standards of the Declaration of Helsinki.

2.2. Inclusion/exclusion criteria

The inclusion and exclusion criteria are consistent with a larger, parent study examining the neural correlates of AUD in Veterans. Primary inclusion criteria were adults aged 18 years and older, fluency and literacy in English, endorsement of at least two DSM-5 criteria for AUD and were seeking treatment for AUD at the VA. Exclusion criteria were: i) general medical conditions, diseases, or neurological disorders that are known to affect the primary outcome measures of the study (i.e., space occupying cerebral lesion, cerebrovascular accident, multiple sclerosis, Parkinson disease, etc.), ii) moderate or severe traumatic brain injury (history of mechanical/blast injury to the head resulting in loss of consciousness greater than 10 minutes), iii) severe impediment to visual and/or auditory acuity or motor skills, likely to interfere with ability to complete the assessments, and iv) MRI contraindications due to the aims of the parent study (e.g., metal in the body, claustrophobia, pregnancy). Psychiatric exclusions were any history of primary bipolar disorder, schizophrenia spectrum and other psychotic disorders, and/or other current substance use disorders, except nicotine and cannabis use disorders. Participants were breathalyzed and urine-tested for illicit substances prior to the assessments and no participants tested positive for illicit or non-prescribed substances, except cannabinoids. Participants with uncontrolled diabetes were not excluded.

2.3. Baseline Clinical Measures

Current and past psychiatric symptomatology, including major depressive disorder diagnosis, was assessed via the Mini-International Neuropsychiatric Interview [MINI (Sheehan, 2014; Sheehan et al., 1998)]. Participants also completed the Clinical Interview for DSM-5 Alcohol Use Disorder and structured questionnaires assessing demographics (to determine age, gender, and education), psychosocial factors (employment, marital, and socioeconomic status), biomedical history (general medical conditions and medications), and other substance use (nicotine, cannabis, and any other illicit substance use). Smoking status was defined categorically into three groups: active-smokers, former-smokers, and non-smokers. Active-smokers were engaged in cigarette smoking at the time of participation. Former-smokers were defined as individuals who used cigarettes on a regular basis prior to study enrollment but were not actively smoking at the time of participation; any duration of smoking cessation greater than 7 days prior to study qualified as former-smoking status, and former-smokers were abstinent from cigarettes for 9 ± 12 years (median 5 years). Non-smokers were operationalized as participants who never used cigarettes or endorsed smoking cigarettes “only a few times” in their lives. All participants provided written informed consent prior to the study. The Timeline Follow-back [TLFB (Sobell and Sobell, 1992)] was used to assess alcohol consumption over the three months prior to study participation. Dimensional depressive symptomatology was assessed with the Mood and Anxiety Symptom Questionnaire 30-item version [MASQ (Watson et al., 1995a; Watson et al., 1995b)].

2.4. Follow-Up Assessments

Participants were monitored for 6 months following participation in the study to assess treatment outcomes. Specifically, participants were contacted at 1-month, 3-months, and 6-months following study participation via telephone. Participants were directly interviewed via telephone to determine relapse status, date of initial relapse, and given the Brief Addiction Monitor (BAM) and TLFB. Available medical records were reviewed to determine relapse status for the remaining participants who were unable to be reached after three failed phone call attempts. Date of relapse and level of alcohol consumption post-treatment was acquired from records, when possible. When indicated, two independent study personnel reviewed the available medical records to determine relapse status and, if possible, level of alcohol consumption and date of relapse; there was 100% agreement between independent raters on relapse status and date of relapse.

2.5. Definition of Abstainers and Relapsers

Abstainers.—Participants were designated as abstainers (n = 29) if they met any of the following criteria: i) they self-reported no alcohol consumption between the baseline and 6-month follow-up assessments (n=9), ii) there was an actual report confirming abstinence in available medical records during the 6-month follow-up period (n=19), or iii) abstinence was reported by a relative or close friend via telephone interview (n=1). A lack of confirmation of alcohol consumption in the medical records post-treatment was not considered an indicator of abstinence.

Relapsers.—Participants were designated as relapsers (n = 66) if they met any of the following criteria: i) self-report of any alcohol consumption after their participation in the study at follow-up assessments via telephone or in-person interview (n=24), ii) alcohol consumption or relapse was indicated in available medical records (n=41), or iii) alcohol use was reported by a relative or close friend via telephone interview (n=1). Any alcohol consumption was used as the criteria for relapse given prior studies showing that any level of alcohol consumption following treatment was associated with poorer psychosocial functioning (Durazzo et al., 2008). Where possible, date of initial relapse was reported or recorded via the above methods.

Lost to Follow Up.—A total of 4 individuals did not have 6 month follow up data available and were excluded from the analyses.

2.6. Statistical Analyses

2.6.1. Demographic and Clinical Variables—Biopsychosocial characteristics at baseline were compared between those who maintained their abstinence (abstainers) and those who consumed alcohol within 6 months of participation (relapsers) with independent-samples t-tests and Fisher’s Exact Test, where indicated.

2.6.2. Prediction of Post-Treatment Relapse—Binary logistic regression was used to evaluate predictors of relapse and p-values < .05 were considered statistically significant for individual predictors in the model. Given our a priori hypotheses, the initial binary logistic regression model included the following predictors: mood disorders (current or

past history of major depressive episode or alcohol/substance induced mood disorder vs no history), smoking status (non-smoker, former-smoker, active-smoker), education, general medical conditions (history of one or more general medical conditions vs. no history; most common conditions were diabetes, hypertension, and hepatitis C seropositivity). All categorical variables were dummy coded (e.g., 0 = no history of mood disorder, 1 = positive history of mood disorder; 0 = never-smoker, 1 = former-smoker, 2 = active-smoker). Models used positive history of a mood disorder and medical conditions as the reference group. Models also used active-smoker status as the reference group, but additional models using never-smoker as the reference group were conducted to determine if there were differences in odds of relapse between never-and-former-smokers. MASQ anhedonic depression score and days since last drink prior to study were added to the model given the significant difference between abstainers and relapsers on these variables. All continuous variables were converted to z-scores to place all measures in a common metric, so that one unit change in the all continuous predictors is equivalent to one unit change the logit of the outcome variable.

3. Results

3.1. Participant Demographics and Clinical Variables

Abstainers and relapsers were equivalent on all demographic and clinical variables obtained in this study, except that relapsers had a lower number of days since last drink prior to study, and higher MASQ anhedonic depression scores than abstainers (all $p < .05$). See Table 1.

3.2. Predictors of Post-Treatment Relapse

The binary logistic regression model, with the following predictors, was significant and demonstrated the best fit [$\chi 2$ (4) = 24.4, $p < .001$, r^2 (Nagelkerke) = 0.32], MASQ anhedonic depression score [b = 0.70, SE = 0.26, p = .008, Exp(b) = 2.02 (95% CI = 1.21 – 3.38)], non-smoker status [b = −0.94, SE = 0.72, p = .18, Exp(b) = 0.39 (95% CI = 0.01 – 1.56)], former-smoker status [b = −1.90, SE = 0.63, p = .003, Exp(b) = 0.15 (95% CI = 0.04 – 0.52)], and days since last alcohol consumption [b = −0.68, standard error of the estimate (SE) = 0.26, p = .010, Exp(b) = 0.51 (95% CI = 0.30 – 0.85)]. See Table 2. The model accurately classified 55% (16 of 29) of abstainers and 89% (59 of 66) of relapsers, with an overall classification accuracy of 79% (75 of 95). Contrary to hypotheses, MDD, comorbid general medical conditions, level of alcohol consumption variables and education were not significant predictors (all $p > .30$) when included with above variables. Additionally, the model fit was statistically superior and classification accuracy was improved when the foregoing variables were removed from the model. With each standard deviation unit decrease in days since last alcohol consumption prior to treatment, the odds of relapse within 6 months post-treatment were increased by 2.0. Each standard deviation unit increase in MASQ anhedonic depression score was associated with 2.0 greater odds of relapse. Active-smokers had 6.6 times greater odds of relapse than former-smokers. Active smokers were 2.6 times more likely to relapse than non-smokers, but this odds ratio was not statistically significant (p = .18)

4. Discussion

Anhedonic depression symptoms, cigarette smoking status, and days since last alcohol use prior to treatment were significant predictors of relapse in Veterans 6 months following residential treatment for AUD. Of the 95 participants, 69% relapsed following treatment, which is generally consistent with previous research on relapse rates in AUD (Durazzo and Meyerhoff, 2017; Kirshenbaum et al., 2009; Maisto et al., 2006a; Maisto et al., 2006b).

Prior studies have reported diagnosis of depression, or level of depressive symptomatology, at treatment entry (Bottlender and Soyka, 2005; Kodl et al., 2008; Miller et al., 1996; Parsons et al., 1990), and/or post-treatment (Curran et al., 2000; Glenn and Parsons, 1991; Kodl et al., 2008), as significant predictors of relapse in AUD treatment-seeking samples. These studies utilized versions of the Beck Depression Inventory to assess depressive symptomatology, which reflects the overall magnitude of depressive symptoms severity, but does not capture the multidimensional facets of depression. The tripartite model of depression, as assessed by the MASQ, categorizes depressive symptomatology into three subtypes: anhedonic depression, general distress, and anxious arousal (Wardenaar et al., 2010; Watson et al., 1995a; Watson et al., 1995b). MASQ anhedonia is operationalized as the diminished ability to experience positive affect, and is consistent with the notion of hyperkatifia in individuals with AUD that initiate abstinence. Hyperkatifia is described as general dysphoria, irritability, or simply a not hedonically normal state, and a strong motivation to drink in order to provide relief from these symptoms (Shurman et al., 2010). Contrary to our a priori hypothesis, a diagnosis of MDD was not predictive of relapse; however, relapsers had significantly greater MASQ anhedonic depression scores at baseline and higher anhedonic depression scores were associated with increased odds of relapse. Of note, abstainers and relapsers were not different on MASQ general distress and anxious arousal, showed no differences on the frequency of lifetime MDD, and MASQ subscales were not associated with lifetime MDD diagnosis (data not shown). Furthermore, at the time of study, abstainers and relapsers were not significantly different on use of psychiatric medications, including antidepressants. Prior studies have demonstrated associations between anhedonia in non-AUD samples and reward system dysfunction. These observations are consistent with the reward system dysfunction observed in chronic AUD. These brain-based transdiagnostic associations are evident in brain structure, metabolites, functional connectivity, and task-based activation (Der-Avakian and Markou, 2012; Durazzo and Meyerhoff, 2017; Durazzo et al., 2010; Durazzo et al., 2011; Harvey et al., 2007; Heinz et al., 2007; Moeller and Paulus, 2018; Seo et al., 2015; Williams, 2016), suggesting a pervasive and multimodal commonality of reward system dysfunction. Consequently, resumption of alcohol use following treatment in those with anhedonic symptoms and AUD may be an attempt to regulate reward system dysfunction.

With respect to cigarette smoking status, individuals who were active-smokers were significantly more likely to relapse relative to former-smokers. Our findings are novel as previous studies have reported that active-smokers versus non-smokers with AUD was associated with greater likelihood of relapse (Hufnagel et al., 2017; Satre et al., 2007; Weinberger et al., 2015b), but these studies did not specifically distinguish between non-smokers, former-smokers, and active-smokers. In addition, the results expand on earlier,

predominantly Veteran research, which found that individuals with AUD and co-occurring active cigarette smoking relapsed significantly earlier relative to non-smokers (Durazzo and Meyerhoff, 2017). There are several possible explanations for the increased likelihood of relapse in smokers. In rodent models, nicotine consumption is related to increased alcohol self-administration and reinstatement of extinguished alcohol-seeking behavior (McKee and Weinberger, 2013). In treatment-seeking individuals with AUD, smoking is related to increased alcohol use urges, and alcohol relapse is associated with high urges to use cigarettes (Cooney et al., 2007; Piasecki et al., 2011). Chronic pairing of alcohol and tobacco use can promote the development of one substance serving as a conditioned stimulus for the other, thereby increasing probability of concurrent consumption, which is supported by human and animal studies indicating cross-substance craving for alcohol and nicotine (McKee and Weinberger, 2013).

An additional predictor of relapse at 6 months was shorter number of days of abstinence prior to treatment entry. A combination of psychosocial factors may be protective for maintaining a longer period of abstinence prior to seeking treatment for AUD, including current employment, prior treatment history, and/or court-ordered sobriety following incarceration. Additionally, the greater length of sobriety prior to treatment demonstrated by abstainers may reflect greater levels of self-efficacy, coping skills and resource utilization, and stronger social support systems (Moos and Moos, 2006, 2007).

This study focused on demographic and clinical variables in a predominantly male, White sample of Veterans, which may limit the generalizability of the results to women, racial and ethnic minorities, and civilians. A larger sample size of female Veterans is required to better examine gender effects, although a preliminary investigation suggests gender does not predict relapse. We defined relapse as any level of alcohol consumption posttreatment, which may limit the generalizability of our results to studies with a different operational definition of relapse, like Project MATCH (1997). Although any level of relapse at six-months is associated with poorer psychosocial outcomes (Durazzo et al., 2008), future studies that examine relapse beyond six-months can better capture treatment outcomes. Treatment outcome data was collected via multiple methods (i.e., telephone interview, rigorous medical record review, and report from close family or friends), possibly adding variability to our data. In addition, we were not able to obtain objective biological measures (i.e., breathalyzer or urine toxicology) of alcohol consumption following treatment. The variability in duration of smoking cessation in the former-smokers was substantial; larger scale studies are required to better understand the impact of smoking cessation duration on relapse in former-smokers. The present study also did not examine alcohol use disorder with comorbid substance use disorders or co-occurring behavioral addictions such as gambling, which previously has been demonstrated to worsen clinical outcomes and should be more carefully examined in future studies (Ahmadi et al., 2009; Di Nicola et al., 2015). While this study expands on prior research by including individuals with depression, anxiety, and PTSD, future studies should include individuals with severe mental illness and other substance use disorders to predict treatment outcome. Other psychological constructs that could have influenced the outcome, including empathy ability, impulsivity, self-efficacy, or social support, were not investigated (Bountress et al., 2017; Martinotti et al., 2009). In addition, the length of treatment program was not examined. Alcohol drinking patterns (e.g.

binge versus daily use) are important to consider when predicting relapse (Martinotti et al., 2017) and will be included in future studies.

The association of greater anhedonic symptoms with greater likelihood of relapse, and former-smoking status with lower odds of relapse, significantly expands upon and refines previous research on the biopsychosocial factors associated with the chronic relapse-remit cycle that affects many individuals with AUD (Durazzo and Meyerhoff, 2017; Florez et al., 2015; Satre et al., 2007; Seo and Sinha, 2015; Witkiewitz, 2011). The findings also reinforce that AUD recovery is a dynamic, temporal process that is influenced by a multidimensional system that are operative before, during, and after treatment (Durazzo and Meyerhoff, 2017; Witkiewitz, 2011; Witkiewitz and Marlatt, 2007). Given the heterogeneity of depressive symptomology that constitute MDD, assessment of anhedonic symptoms using more specific instruments for anhedonia (e.g. SHAPS, TEPS) in those seeking treatment for AUD may allow for greater precision in identifying mood disorder phenotypes associated with AUD relapse (Gard et al., 2006; Snaith et al., 1995). Additional research is necessary to determine if an anhedonic subtype of depression and/or persistent post-acute withdrawal symptoms represent transdiagnostic symptoms that are associated with relapse risk. Our results highlight the modifiable risk factors that can be targeted during AUD treatment. For example, pharmacological interventions that target anhedonia include agomelatine for patients with MDD or intravenous Acetyl-l-Carnitine to improve anhedonia in individuals with AUD (Cao et al., 2019; Di Giannantonio and Martinotti, 2012; Martinotti et al., 2011). Aripiprazole may promote abstinence in individuals with alcohol use disorder via dopaminergic and serotoninergic pathways linked to modulating reward, craving, and alcohol-related anhedonic symptoms (Martinotti et al., 2016). Moreover, repetitive transcranial magnetic stimulation (rTMS) techniques may be efficacious in treating addiction related anhedonia, as seen in a pilot study of cocaine use disorder (Pettorruso et al., 2019; Pettorruso et al., 2018). In those with AUD, cigarette smoking is prevalent and poses increased risk for relapse following treatment. Historically, providers have assumed that concurrent implementation of AUD treatment and smoking cessation programs is too challenging for patients, smoking is not as harmful as AUD or cigarettes facilitate abstinence of other substances (McKee and Weinberger, 2013; Prochaska, 2010; Satre et al., 2007). However, multiple studies have demonstrated that integrating smoking cessation programs into AUD treatment does not interfere with treatment and/or is associated with decreased likelihood of relapse to hazardous drinking (Baca and Yahne, 2009; Cooney et al., 2015; Kalman et al., 2010; Prochaska, 2010; Satre et al., 2007). In addition, our smoking status results underscore the need to include individuals with alcohol use disorders in smoking cessation research (Lembke and Humphreys, 2016; Schroeder and Morris, 2010), and the importance of investigating the relationship between never, former and active smoking status on relapse risk. Anhedonic symptoms and cigarette smoking are modifiable risk factors and their effective treatment concurrent with AUD-focused interventions may lead to a clinically meaningfully decrease in relapse risk. Findings from this study emphasize the importance of developing precise and individualized treatment plans for those with AUD in light of risk factors, both during and following treatment.

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- Greater anhedonic symptoms significantly increased the odds of relapse in AUD.
- Active cigarette smokers showed significantly higher risk of relapse in AUD.
- Treatment of anhedonic symptoms and cigarette smoking may decrease risk of relapse.

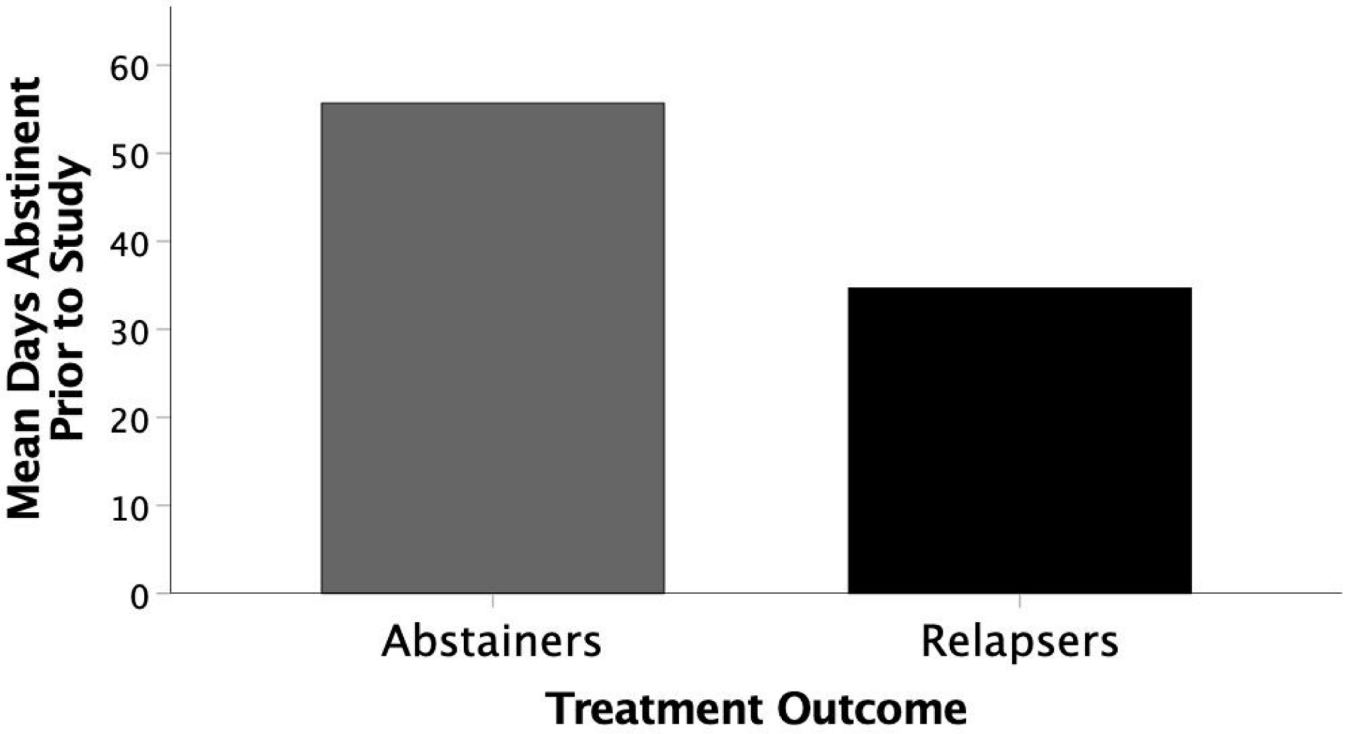

Figure 1a.
Mean MASQ Anhedonic Depression Scores for Abstainers versus Relapsers.

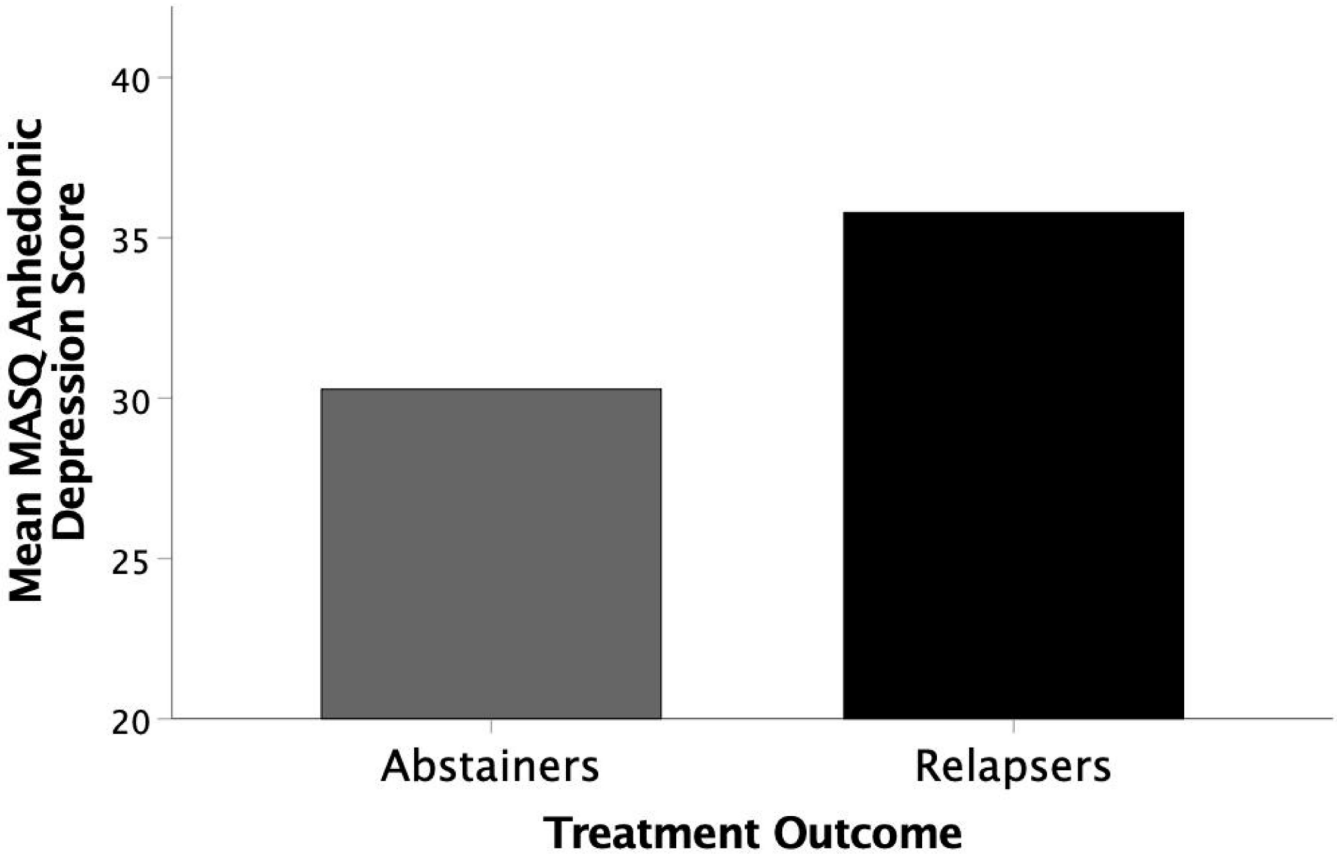

Figure 1b.
Proportion of self-reported cigarette smoking status (never, former, and active-smokers) for Abstainers versus Relapsers.

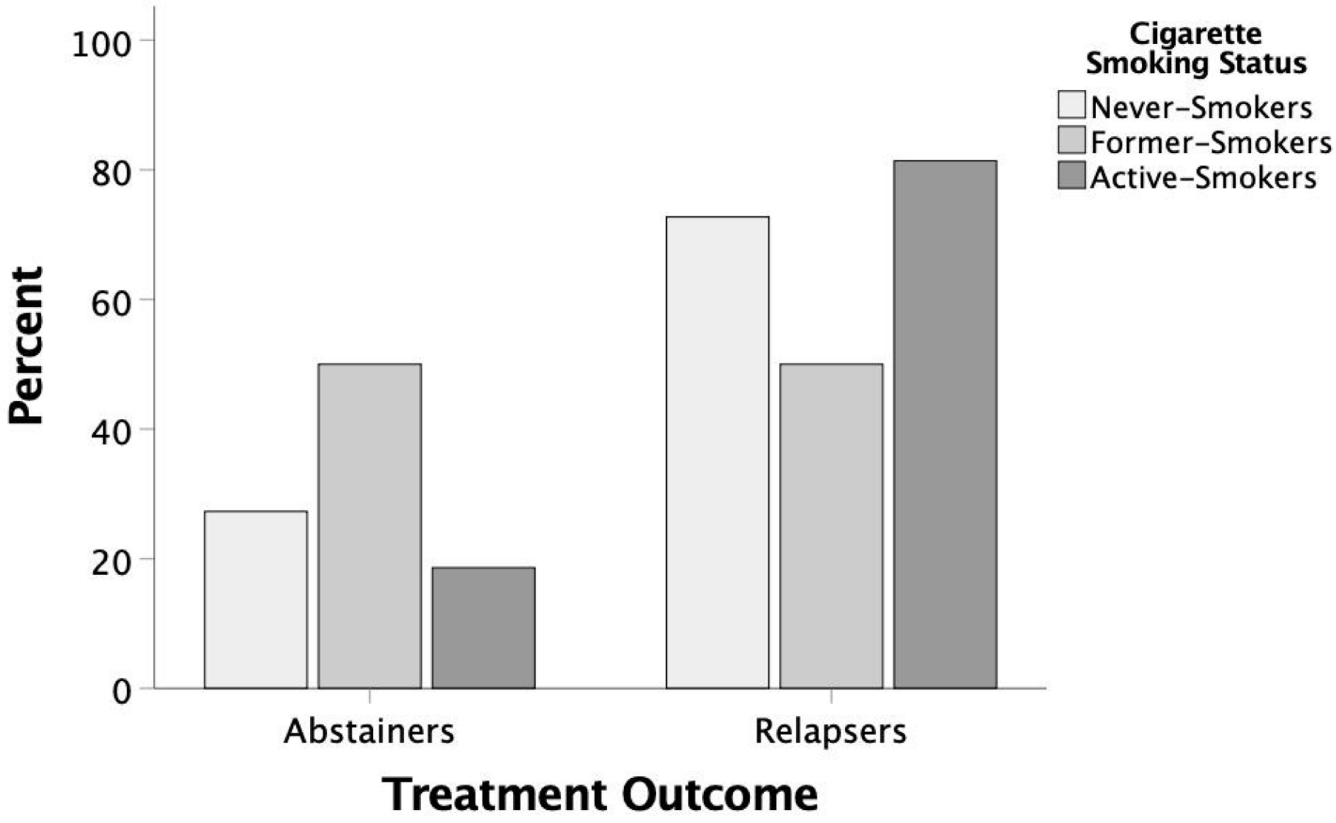

Figure 1c.
Mean days of abstinence prior to study enrollment for Abstainers versus Relapsers.

Table 1.

Group Demographics, Alcohol and Cigarette Use Histories, Self-Report Questionnaires, and Comorbidity Frequency

Measure	Abstainers (n=29)	Relapsers (n=66)	Group Differences*
Age (years)	45 (15)	48 (14)	
Education (years)	14 (2)	14 (2)	
White (%)	72	89	
Female (%)	14	21	
DSM 5 Alcohol Total Number of Criteria	10 (2)	10 (2)	
AUDIT	30 (8)	27 (8)	
Days abstinent prior to study enrollment	56 (57)	34 (29)	Abstainers > Relapsers
Total drinking days within 3 months prior to study enrollment	42 (29)	41 (29)	
Total drinks within 3 months prior to study enrollment	660 (632)	605 (675)	
Average drinks per day within 3 months prior to study enrollment	12 (10)	14 (11)	
Max drinks per day within 3 months prior	16 (12)	19 (14)	
to study enrollment			
Duration of abstinence post-treatment [mean (SD) median]	N/A	64 (47) 59	
Non-smokers (%)	24	21	
Former-smokers (%)	52	23	Abstainers > Relapsers
Active-smoker (%)	18	53	Abstainers < Relapsers
Pack-years	15 (11)	14 (21)	
Any psychiatric comorbidity (%)	73	69	
Major Depressive Disorder (%)	54	46	
PTSD (%)	45	55	
Using psychiatric medications (%)	62	55	
General medical condition (%)	66	64	
History of Traumatic Brain Injury (%)	21	36	
History of other substance use disorder (%)	31	29	
MASQ General	25 (10)	25 (9)	
Distress			
MASQ Anhedonic Depression	30 (7)	36 (9)	Abstainers < Relapsers
MASQ Anxious Arousal	20 (7)	18 (6)	
PCL-5	54 (17)	55 (18)	
Beck Anxiety Inventory	12 (11)	15 (12)	

AUDIT: Alcohol Use Disorders Identification Test; FTND: Fagerstrom Tolerance Test for Nicotine Dependence; MASQ: Mood and Anxiety Symptom Questionnaire; PCL-5: PTSD Checklist for DSM-5

*All listed group differences $p < 0.05$. Mean (SD), except where indicated.

Table 2.

Logistic Regression Analysis of Treatment Outcome.

					95% CI	
Predictor	**β**	**SE**	**p**	**Exp(β)**	**Lower**	**Upper**
Days since last alcohol consumption	−0.68	0.26	.010	0.51	0.30	0.85
MASQ anhedonic depression score	0.70	0.26	.008	2.02	1.21	3.38
Non-smoker status	−0.94	0.72	0.18	0.39	0.01	1.56
Former-smoker status	−1.90	0.63	.003	0.15	0.04	0.52