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Sliedrecht, Wilco; Seesink, Henk Jan; Vrijmoeth, Cis; de Waart, Ranne; Wiers, Reinout W.; Ostafin, Brian; Schaap-Jonker, Hanneke; Roozen, Hendrik; Witkiewitz, Katie; Dom, Geert

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Alcohol use disorder relapse factors: an exploratory investigation of craving, alcohol dependence severity, and meaning in life

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De Hoop GGZ, Dordrecht, The Netherlands; Centre for Research and Innovation in Christian Mental Health Care, Dordrecht, the Netherlands; Mentrum/Arkin, Amsterdam, The Netherlands; Vrije Universiteit, Amsterdam, The Netherlands; University of Groningen, Groningen, The Netherlands; Universiteit van Amsterdam, Amsterdam, The Netherlands; University of New Mexico, Albuquerque, US; Antwerp University, Antwerp, Belgium

ABSTRACT
For decades predictors of alcohol use disorder (AUD) relapse have been studied, and around 40 different clinical and demographic relapse determinants have been identified. This paper aims to investigate the relationship of two of these AUD relapse factors, namely craving and meaning in life (MiL). We hypothesized that greater meaning in life would be associated with lower cravings and lower relapse rates. An AUD subsample of 81 patients within a clinical population that participated in ongoing exploratory research on religious/spiritual factors related to substance use disorders was followed up to 1 year. Craving (as measured with the Penn Alcohol Craving Scale) and meaning in life (as measured with the Meaning in Life Questionnaire- presence subscale) measures were assessed at baseline and relapse was assessed at 6- and 12-month follow up. Main effects and the interaction between craving and meaning in life in predicting alcohol relapse (with relapse defined as ‘any alcohol use’ and ≥ 3 consecutive days of drinking) were calculated/subject of analyses. We also investigated the relationship between relapse and alcohol dependence severity as measured with the Leeds Dependence Questionnaire. Baseline craving and dependence severity were related to relapse, but there were no associations between meaning in life and levels of craving or alcohol relapse. Our findings suggest a need for additional research on characterizing the Meaning in Life concept.

Introduction
Alcohol use disorder and relapse
Alcohol use disorder (AUD) is highly prevalent (Grant et al. 2015, 2017; Rehm et al. 2015), and accountable for substantial morbidity and mortality (Rehm et al. 2017; Griswold et al., 2018; Leong et al. 2022). Most individuals with AUD do not seek treatment (Tuithof et al. 2016), and a majority of people with AUD recover without any formal treatment (Cutler and Fishbain 2005; Cohen et al. 2007; Grant et al. 2015; Fan et al. 2019; Tucker et al. 2020). Yet, for a sizeable number of patients, AUD encompasses a chronic, recurring condition (McKay and Hiller-Sturmhofel 2011). Recent epidemiologic research showed a 1-year persistence of AUD of 34.2% within a national US population survey (Fan et al. 2019). Within this group with AUD, eventually, 16% achieved abstinent recovery (Fan et al. 2019). Therefore, the prevention of relapse and promotion of recovery remain challenging and are the focus of most forms of psychological and pharmacological treatment (Ray et al. 2019).

Determinants frequently associated with relapse, as well as factors that are protective in preventing relapse, have already been well studied for several decades (Miller 1996; Witkiewitz and Marlatt, 2004; Sliedrecht et al. 2019). Several psychological and psychobiological models have been postulated and tested for their validity in predicting relapse (Connors et al. 1996; Witkiewitz and Marlatt, 2004, 2007; Hendershot et al. 2011; Witkiewitz 2011; Sliedrecht et al. 2019), and have generated therapeutic targets to prevent relapse (Donovan and Witkiewitz, 2012; Huebner and Kantor, 2010; Larimer et al. 1999). Craving is one of the most prominent targets for interventions (Donovan and Witkiewitz, 2012; Larimer et al. 1999) and a limited number of medications (Donoghue et al. 2015; Mann et al. 2018; Witkiewitz et al. 2019; Donoghue 2021) within many treatment settings. ‘Craving’, as well as other determinants like ‘severity of AUD’, ‘psychiatric comorbidity’, ‘emotions’ and several social and spiritual factors, have been identified as important factors in the achievement of remission or the occurrence of a relapse (Witkiewitz and Marlatt, 2004; Hendershot et al. 2011; Sliedrecht et al. 2019). Given the prominence of craving as risk factor in both AUD and substance use disorder (SUD), a recent meta- analysis suggested that in future research also examining mediating and
moderating roles of different other neurocognitive functions should be considered (Cavicchioli et al. 2020).

One such potential moderator of the association between craving and relapse could be purpose or meaning in life (Waisberg and Porter 1994; Lyons et al. 2010; Cranford et al. 2014; Roos et al. 2015). A recent paper stated that meaning in life "refers to the feeling that one’s life and experiences make sense and matter,” and purpose in life "is characterized by the extent to which one experiences life as being directed, organized, and motivated by important goals” (Salsman et al. 2020, p2299). It must be noted that the current concept of meaning in life is broader than the concept of purpose in life. A recent systematic review identified meaning to comprise of: comprehension/coherence, purpose, and existential mattering/significance (King and Hicks 2021). Our main study goal was to examine the roles of craving and meaning in life (MiL) in AUD relapse.

**Craving**

Craving refers to the phenomenon of intense longing for alcohol and is often seen as a multidimensional concept, consisting of emotional, cognitive, physiological and behavioral components (Rosenberg 2009). Craving is currently one of the symptoms in the DSM 5 definition of AUD (Casey et al. 2012; Hasin et al. 2013; Robinson and Adinoff 2016), as well as the description of Alcohol Dependence Syndrome in the International Classification of Diseases (ICD-11) (Saunders et al. 2019). A neurobiological underpinning of craving with the ‘incentive-sensitization theory’ was postulated (Robinson and Berridge 1993, 2008); such that alcohol-induced sensitization of mesocorticolimbic systems in the brain can lead to implicit ‘wanting’ or explicit cognitive craving (Kavanagh et al. 2005; Robinson and Berridge 2008). Skinner and Aubin (2010) identified four different types of craving, namely conditioning-based-, cognitive-, psychobiological-, and motivation models (Skinner and Aubin 2010). Recently, a metacognitive model of craving was postulated; integrating cognitive, automatic and physiological aspects of craving (Flaudias et al. 2019).

Although a number of behavioral tasks have been developed to measure craving (Kavanagh et al. 2013), craving is most commonly measured by various self-report questionnaires. The multi-item Penn Alcohol Craving Scale is one widely used measure, which has demonstrated excellent reliability, construct and concurrent validity (Kavanagh et al. 2013). Earlier research indicated that the Penn Alcohol Craving Scale (PACS) can be regarded as a reliable prognostic measurement instrument (Flannery et al. 1999). The PACS measures self-reported craving via five different items in which scores can vary between 0 and 6. The PACS has now been used in a growing body of research as a craving measurement instrument (Evren et al. 2012; Schneekloth et al. 2012; Hartwell and Ray 2018; Hartwell et al. 2019; Stohs et al. 2019). Higher PACS scores are associated with higher relapse risk during (Flannery et al. 2003) and within 12 months after treatment (Stohs et al. 2019). More specifically, after dichotomizing to identify predictive cut-off values, additional analysis showed that PACS scores of ≥6 were predictive of 12 months relapse (Stohs et al. 2019). This is in line with earlier research indicated PACS scores ≥7 measured at admission into an addiction clinic and PACS scores of ≥4 at discharge were predictive for relapse (Schneekloth et al. 2012).

**Meaning in life**

A number of MiL concepts have been used in previous research, with one well-known definition of MiL as “the sense made of, and significance felt regarding, the nature of one’s being and existence” (Steger et al. 2006, p.81). In contrast to the well-studied concept of craving, the effect of various MiL-related issues in relation to AUD relapse seems to have been relatively understudied. In a recent systematic review on AUD relapse factors the MiL-related concept of ‘purpose in life’ (PiL) and likewise denominators like finding purpose in e.g. ‘caringgiving’ were found mostly protective in relation to relapse (Sliedrecht et al. 2019), but it must be noted that in only two out of nine reviewed papers this factor had been assessed by using the Purpose in Life test as a standardized assessment instrument (Cranford et al. 2014; Roos et al. 2015). It must be noted that ‘purpose in life’(PiL) and ‘meaning in life’ (MiL) are related concepts, but are not synonyms (Steger et al. 2006; King and Hicks 2021). MiL refers to how one appraises the meaningfulness of the world (consisting of the beliefs about self, the world, and relationships between self and the world) or one’s life’s goals and purposes, whereas PiL seems to encompass only the narrower, goal-directed compound (Park and Folkman 1997; Czekierda et al. 2017). In line with this, recent theoretical overviews postulated that MiL consists of three subconstructs, namely: coherence/comprehension, purpose and significance/mattering (George and Park 2016; Martela and Steger 2016). MiL has been shown to be positively associated with health and mental well-being (Leamy et al. 2011; Steptoe et al. 2015; Czekierda et al. 2017; Aftab et al. 2019), and lower suicide risk (Costanza et al. 2020). Moreover, meaning in life interventions has a clinical benefit in patients with advanced disease (Rubio et al. 2018).

However, in more recent research a frequently used measurement instrument to assess MiL is the “Meaning in Life Questionnaire” (MLQ) (Steger et al. 2006), which consists of the subscales ‘presence of’ and ‘search for’ MiL. The MLQ has produced valid scores in different age groups, cultures and clinical populations (Schulenberg et al. 2011; Schutte et al. 2016; Rose et al. 2017; Halford et al. 2018; Chika Chukwuorji et al. 2019; Naghiyaee et al. 2020). The presence of meaning is associated with better health and mental well-being, but the search for meaning shows an inverse relationship (Aftab et al. 2019). Moreover, it was recently found, that a higher presence of meaning is associated with less alcohol use in a group of young adults (Csabonyi and Phillips 2020).
**Dependence, craving and meaning in life in association with AUD relapse**

One prior study has examined the association between PiL with craving as related to alcohol relapse and found craving and PiL were both associated with drinking outcomes (Roos et al. 2015). Higher PiL was related to lower craving and lower PiL was and higher craving were associated with more frequent and greater intensity drinking. In the same way, it seems plausible that the related concept of MiL could as well be related to drinking outcomes, and could potentially moderate the association between craving and relapse.

It was recently found that the presence of MiL as measured with the MLQ is associated with less harmful drinking (Copeland et al. 2020). Interestingly, the search for meaning showed an inverse relation (more harmful drinking). Moreover, these factors were mediated by trait self-control and how alcohol was valued, which however could be related to, but is not akin to craving. In line with this, other research within a group of undergraduate students suggested that a brief MiL intervention could lead to a reduction in the ‘incentive salience’ of alcohol, which could potentially facilitate less drinking behavior (Ostafin and Feyel 2019). As the presence of meaning is associated with better health and mental well-being (Aftab et al. 2019), and perceived stress (Pulopulos and Kozusznik 2018), it seems conceivable that the presence of meaning could lead to less craving, eventually leading to less proneness to relapse. However, the association and interaction between MiL and craving with relapse outcomes in patients with AUD have still not been thoroughly investigated. Given the importance of MiL in relation to other areas of mental and physical health and well-being, and being a potential therapeutic target, it may be the case that MiL may predict relapse outcomes and attenuate the association between craving and relapse.

In addition, ‘Severity of AUD’ or the level of ‘dependence’ has now been for decades been identified as a robust relapse factor (Sliedrecht et al. 2019). Measuring dependence levels over time, as for example often measured by the Leeds dependence questionnaire (LDQ), can be used to monitor the effects of treatment (Heather et al. 2008).

**The current study**

The objective of the current study was to conduct a prospective cohort study within a clinical AUD population, in which we tested the association between MiL and craving with relapse outcomes at 6- and 12-month follow-ups. We hypothesized that higher baseline MiL would be associated with lower craving levels, and lower relapse. We also tested if this effect would run via a moderation effect, namely in that higher levels of meaning would attenuate the craving-relapse relation. In addition, we tested the association between MiL, the severity of alcohol dependence (LDQ scores) and relapse.

**Methods**

**Participants**

The sample consisted of a clinical population that participated in an ongoing longitudinal research study examining religious/spiritual factors related to substance use disorder. For our study, we included the subgroup with a diagnosed primary AUD. From this sample of 81 participants, we had 6-month follow-up (FU) data from 78 patients (96%) available. In addition, from 51 participants (63%) 12-month FU data were available. In 3 patients the 6-month relapse data were not available, but nevertheless, we had 12-month FU data of these patients. All participants were already detoxified at the baseline inclusion, mostly hospitalized within a specialized clinical psychotherapeutic treatment setting at the Hoop GGGZ in Dordrecht, The Netherlands. This specific ward is predominantly overseen by psychologists, that are specialized in mental health, but also a psychiatrist and a doctor specialized in addiction medicine are part of the treatment staff. All patients received disorder-specific treatment, which consisted of cognitive-behavioral therapy for addiction as well as a ‘schema therapy based’ approach of comorbid personality disorders. Whenever needed, also additional pharmacotherapy or trauma therapy could be part of treatment. Besides the primary AUD, there were no other inclusion or exclusion criteria for our sample. However, the inpatient population consists of patients who despite their disorder can function within a group-therapy setting. Comorbid conditions were common in the inpatient population, including high rates of comorbid personality disorders, attention deficit hyperactivity disorder and posttraumatic stress disorder.

**Procedure**

Analyses were performed on data derived from patients who were included from February 2018 to December 2020. From the group of 81 patients, 68% were male (n = 55) and the mean age was 42.37 years (SD = 11.83). Most participants had one or more comorbid psychiatric disorders (78%). Comorbid substance use was rather common (38%; mostly cannabis- followed by cocaine use), and 45% were diagnosed with a tobacco use disorder. The smaller subgroup that provided the 12-month FU data was comparable to the total sample recruited at baseline (Table 1).

The ethical committee of the Universiteit van Amsterdam ethically approved the original larger research design (registration ID: 2017-DP-7969), and attested that as no

**Table 1. Background characteristics of the participants with 6- and 12-month FU data.**

<table>
<thead>
<tr>
<th></th>
<th>6-month FU (N = 81)</th>
<th>12-month FU (N = 51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>42.37 (11.83)</td>
<td>42.90 (12.69)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>55 (68%)</td>
<td>37 (72.5%)</td>
</tr>
<tr>
<td>Female</td>
<td>26 (32%)</td>
<td>14 (27.5%)</td>
</tr>
<tr>
<td>Co morbid smoking</td>
<td>36 (44%)</td>
<td>23 (45%)</td>
</tr>
<tr>
<td>Co morbid SUD</td>
<td>30 (37%)</td>
<td>21 (41%)</td>
</tr>
<tr>
<td>Co morbid psychiatric disorder</td>
<td>63 (78%)</td>
<td>38 (75%)</td>
</tr>
</tbody>
</table>
interventions were conducted, an extensive assay was not required. Participants could voluntarily participate after they were on admission informed of the ongoing survey on ‘spiritual and religious factors in treatment’.

A team of specialized clinicians clinically diagnosed the presence of substance use disorders or psychiatric comorbid disorders based on DSM 5 criteria. At the start of treatment, the ‘Measurements in the Addictions for Triage and Evaluation’ (MATE) (Schippers et al. 2010) was used to classify AUD and SUD’s, and on the indication, the ‘Structured Clinical Interview for DSM-5 Personality Disorders’ (SCID-5-PD) was used to classify co-morbid personality disorders. Trained psychologists did the assessment of craving and meaning in life at baseline. Baseline measurements were mostly done during the hospitalization phase; several weeks after detoxification. Furthermore, a telephone interview was used to obtain follow-up data at 1, 6, and 12 months. In addition, the LDQ was used at baseline and during follow-up to assess for dependence on a variety of substances (Raistrick et al. 1994). We pre-registered our research at the Open Science Framework (OSF) database website (https://osf.io/yt8q5).

Measurement instruments and definitions

Craving
The PACS is a self-report questionnaire reporting on different aspects of craving covering the last week. Total scores on this 5 item assessment instrument could range from 0 to 30 (Flannery et al. 1999). An example item is: “How often have you thought about drinking or about how good a drink would make you feel during this period?” In our reliability analysis, we found Cronbach’s alpha of 0.92, which is consistent with former research that found a very high-reliability value of 0.92 (Flannery et al. 1999).

Meaning in life
The MLQ (5-item presence subscale) functions as a gauge to assess how patients judge their present life as being meaningful. Patients can rate on a scale from 1 to 7 (“absolutely untrue” - “absolutely true”) how they experience present MiL. Consequently, total subscale scores could range from 5 to 35 (Steger et al. 2006). The statements are: ‘I understand my life’s meaning’, ‘My life has a clear sense of purpose’, ‘I have a good sense of what makes my life meaningful’, ‘I have discovered a satisfying life purpose’, and ‘My life has no clear purpose’ (reverse-coded) (Steger et al. 2006). Former research found Cronbach alpha’s varying from 0.81 to 0.93 (Schulenberg et al. 2011), and in our own reliability analysis, this value was .90 for the ‘presence’ subscale. In addition, we found Cronbach’s alpha of .80 for the MLQ ‘search’ subscale (which also consists of 5 items). Also, MLQ scores showed good (1 month) to moderate (13 months) test-retest reliability (Schulenberg et al. 2011). We only used the presence subscale and hypothesized that ‘presence’ of MiL, but not ‘search’ for meaning would moderate craving levels.

Dependence
Alcohol dependence severity levels at baseline, 6-month FU and 12-month FU were assessed with the LDQ. The LDQ is a 10-item, self-report questionnaire to assess dependence upon a variety of substances and monitor treatment outcomes. Items are scored from 0 to 3, with higher scores pointing at higher levels of dependence. Cronbach’s alpha was 0.94 and the test-retest reliability was found to be 0.95 (Raistrick et al. 1994). We found Cronbach alpha’s of .90 for baseline LDQ, .91 at 6 months- and .93 at 1 year FU.

AUD relapse
AUD relapse was conservatively defined as ‘any alcohol use’ at 6 and 12 months follow-up. This definition has been extensively used in AUD relapse research (Maisto et al. 2016; Sliedrecht et al. 2022). In addition, we examined ≥ 3 consecutive days of drinking as an alternative outcome measure, which has been used in former research (Wiers et al. 2011; Demirbas et al. 2012; Wiers et al. 2015).

Statistical analyses
In June 2020 (well before data analyses) we performed a power analysis (considering main and interaction effects) within G*Power alpha = 0.05, power = 0.8). Estimated relapse figures were conservatively set at 40% at six months and 75% at 12 months FU. The explaining variance for MiL was set at 0.09 for the 6 month FU (as Rubio et al. (2018) reported a 1-year coefficient of 0.17 (Rubio et al. 2018)). Based on these estimates we required 72 participants in assessing the relation between craving, MiL and relapse outcomes at 6-month FU. This matched with our inclusion of 81 patients with primary AUD from which we had 6 months and/or 1 year FU data. Statistical analyses were performed in SPSS v25. Moderation analyses were done by using Hayes’ PROCESS v3.5.3 (version 11 February 2021; http://www.processmacro.org/download.html).

Statistical significance was considered to be at the level of p < 0.05. Assessing the 6 months relapse outcomes showed that, for unknown reasons, the outcome data of 3 patients were missing, whereas their data at 12-month FU were present.

Additionally, the PACS and MLQ scores were plotted to assess a normal distribution and to identify potential outliers. Descriptive statistics were performed for both the 6- and 12-month FU groups (Table 1). To test the association of baseline presence of MiL with craving levels and eventually relapse, univariate-, and multivariate analyses in SPSS were estimated. To test if MiL moderated the association between craving and relapse, we conducted a moderation analysis. As a side note, out of interest we also tested the possible effect of ‘search for meaning’ on craving and relapse. Table 1 study participants.

Results

Descriptive statistics and correlational analyses
Percentages of relapse at 6- and 12-month FU and variables (craving, substance dependence and presence of MiL) for
the total group and the groups based on relapse (yes or no) can be found in Table 2. In this clinical sample, the 6- and 12-month ‘any alcohol use’ relapse rates were 54% (42 of 78) and 63% (32 of 51), in which relapse conservatively was defined as ‘any alcohol use’. When relapse was defined by ≥ 3 consecutive days of alcohol drinking, the relapse rates were 31% (24 of 78) and 39% (20 of 51), thus considerably lower. Mean baseline craving, baseline Mil, and consecutive dependence scores of the 6- and 12-month FU groups are tabulated in Table 2. Sample t-tests indicated craving and dependence baseline scores were notably higher in the group of relapsed patients, statistically, significant results are indicated in Table 2. Dependence scores at 6 months were generally lower than at baseline and 1 year follow-up (Table 2). Table 2 relapse percentages and variables.

Logistic regression analyses

To test our hypotheses, we performed univariate (see Supplemental Table 1) and multivariate (see Table 3) logistic regression analyses, to examine the association of craving, substance dependence and presence of Mil with relapse rates. In the univariate and multivariate analyses, there were no significant relations between craving, dependence, and Mil with relapse defined as any alcohol use at 6 months, and no interaction between Mil and craving. Similarly, univariate and multivariate analyses showed no significant effects of craving, dependence and Mil on the outcome ≥ 3 consecutive days of alcohol drinking at 6 months, and no interaction with craving. At 12 months no effects were found for all univariate analyses for ‘any alcohol use’ and univariate and multivariate analyses for ≥ 3 consecutive days of alcohol drinking. In multivariate analyses, there was a sig-

### Table 2. Percentages of relapse at 6- and 12-month FU and variables (craving, substance dependence and presence of Mil; mean & SD) for the total group and the groups based on relapse (yes or no).

<table>
<thead>
<tr>
<th></th>
<th>Total group</th>
<th>Relapse ‘any alcohol use’ at 6-month FU</th>
<th>Relapse ‘≥ 3 drinking days’ at 6-month FU</th>
<th>Relapse ‘any alcohol use’ at 12-month FU</th>
<th>Relapse ‘≥ 3 drinking days’ at 12-month FU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>6-month FU</td>
<td></td>
<td>12-month FU</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(N = 81)</td>
<td>(N = 51)</td>
<td>(N = 36)</td>
<td>(N = 32)</td>
</tr>
<tr>
<td>Baseline craving (Mean/SD)</td>
<td>7.37 (6.66)</td>
<td>7.18 (6.60)</td>
<td>8.24 (7.39)</td>
<td>6.08 (5.61)</td>
<td>8.25 (7.28)</td>
</tr>
<tr>
<td>Baseline presence of Mil (Mean/SD)</td>
<td>22.90 (7.82)</td>
<td>22.57 (8.07)</td>
<td>22.95 (7.29)</td>
<td>22.78 (8.62)</td>
<td>25.00 (6.45)</td>
</tr>
<tr>
<td>Baseline substance dependence (Mean/SD)</td>
<td>8.42 (7.64)</td>
<td>8.39 (7.42)</td>
<td>9.62 (7.67)</td>
<td>6.39 (6.70)</td>
<td>9.71 (7.95)</td>
</tr>
<tr>
<td>6-month FU Substance dependence</td>
<td>4.43 (6.19)</td>
<td>N/A</td>
<td>6.05 (7.15)</td>
<td>2.47 (4.07)</td>
<td>7.75 (8.46)</td>
</tr>
<tr>
<td>12-month FU Substance dependence</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*At 6-month FU 3 patients had missing relapse data.
**With 9 patients missing variables LDQ/PACS/MLQ meaning.
Craving > PACS at baseline, presence of Mil > MLQ presence at baseline, Substance Dependence > LDQ at baseline, 6-month FU & 12-month FU.
Bold: statistically significant difference in means (t-test) at the p < 0.05 level.

### Table 3. Multivariate logistic regression of craving or substance dependence with the presence of Mil associated with relapse.

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>SE</th>
<th>Z</th>
<th>p-value</th>
<th>Odds ratio</th>
<th>95% CI odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any use at 6-month FU</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Craving</td>
<td>.06</td>
<td>.039</td>
<td>2.28</td>
<td>.13</td>
<td>1.06</td>
<td>0.98–1.15</td>
</tr>
<tr>
<td>Presence of Mil</td>
<td>.02</td>
<td>.032</td>
<td>0.37</td>
<td>.54</td>
<td>1.02</td>
<td>0.96–1.09</td>
</tr>
<tr>
<td>Substance dependence</td>
<td>.06</td>
<td>.034</td>
<td>3.65</td>
<td>.06</td>
<td>1.07</td>
<td>1.00–1.14</td>
</tr>
<tr>
<td>Presence of Mil</td>
<td>.01</td>
<td>.030</td>
<td>0.10</td>
<td>.76</td>
<td>1.01</td>
<td>0.95–1.07</td>
</tr>
<tr>
<td>≥ 3 consecutive days use at 6-month FU</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Craving</td>
<td>.06</td>
<td>.041</td>
<td>2.15</td>
<td>.14</td>
<td>1.06</td>
<td>0.98–1.15</td>
</tr>
<tr>
<td>Presence of Mil</td>
<td>.07</td>
<td>.036</td>
<td>3.73</td>
<td>.05</td>
<td>1.07</td>
<td>1.00–1.15</td>
</tr>
<tr>
<td>Substance dependence</td>
<td>.05</td>
<td>.035</td>
<td>2.13</td>
<td>.15</td>
<td>1.05</td>
<td>0.98–1.13</td>
</tr>
<tr>
<td>Presence of Mil</td>
<td>.06</td>
<td>.035</td>
<td>3.01</td>
<td>.08</td>
<td>1.06</td>
<td>0.99–1.14</td>
</tr>
<tr>
<td>Any use at 12-month FU</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Craving</td>
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<td>.063</td>
<td>4.90</td>
<td>.03a</td>
<td>1.15</td>
<td>1.02–1.30</td>
</tr>
<tr>
<td>Presence of Mil</td>
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<td>.044</td>
<td>3.18</td>
<td>.07</td>
<td>1.08</td>
<td>0.99–1.18</td>
</tr>
<tr>
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<td>3.24</td>
<td>.07</td>
<td>1.09</td>
<td>0.99–1.19</td>
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<td>.039</td>
<td>1.58</td>
<td>.21</td>
<td>1.05</td>
<td>0.97–1.13</td>
</tr>
<tr>
<td>≥ 3 consecutive days use at 12-month FU</td>
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<td></td>
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<tr>
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<td>.051</td>
<td>2.94</td>
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<td>1.09</td>
<td>0.99–1.20</td>
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<td>.037</td>
<td>0.14</td>
<td>.71</td>
<td>1.01</td>
<td>0.94–1.09</td>
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*aSignificant at the p < 0.05 level.
nificant association between craving and relapse defined as any alcohol use at 12 months alcohol use \( (B=0.139, \text{Wald} \,(df=1) = 4.90, \, p=0.03; \, OR: 1.15) \), but there was no interaction with MiL. In addition, also no interaction effects of the search subscale of MiL on craving and relapse were found. Table 3 multivariate analyses.

**Discussion**

As most of the previous research has used cross-sectional designs, the prospective design of our study could be considered a strength. Our hypotheses, that higher baseline MiL would be associated with lower craving levels, and lower relapse, both directly and indirectly (moderation effect) via craving, were not confirmed within this research. However, although in most cases not statistically significant, the craving and dependence scores in the relapsed groups (both drinking outcomes) were higher as compared to the non-relapsed. This is in line with the findings in a recent systematic review that identified AUD severity and craving as robust relapse factors (Sliedrecht et al. 2019), and suggests a relation of these clinical parameters with our chosen relapse outcomes. Interestingly, dependence scores declined at 6-month FU; probably showing a treatment effect and indicating early recovery. At 12-month FU these scores were still lower than at baseline; but it must be noted that the sample size at 12-month FU was relatively small. In this relatively small clinical prospective cohort study, more than half of the patients had relapsed (outcome ‘any alcohol use’) at 6- and 12-months FU. This is in line with relapse rates mentioned in the literature, depending on how ‘relapse’ had been defined. However, when we defined relapse as ‘\( \geq 3 \) consecutive days of drinking’, which can be regarded as a less strict outcome, these figures were considerably lower. In our univariate-, multivariate-, and moderation logistic regression analyses, we found no statistically significant effect of craving, meaning in life (MiL), or dependence scores on relapse, nor a moderating effect of MiL. MiL has in earlier research been shown to positively influence health and mental well-being in prior research, but this was not found in relation to craving and relapse within our sample of individuals receiving treatment for AUD. Out of interest we also tested the possible effect of ‘search for meaning’ on craving and relapse, which outcomes however were also not statistically significant. The presence of and search for meaning are not one-to-one related concepts. Empirical research suggested that people lacking meaning search for it, and the search for meaning did not appear to lead to the presence of meaning (Steger et al. 2008). Moreover, understanding distinct meaning-related concepts and their interrelationship warrants more empirical research (Park 2010).

In this exploratory research, we examined craving, MiL, and drinking outcomes. Although the denominators MiL and PiL have been postulated to be equivalent (Steger et al. 2006), it seems that MiL is not synonymous with the more robust relapse factor ‘having a purpose in life’, which has been shown to predict alcohol relapse and be associated with craving (Roos et al. 2015; Sliedrecht et al. 2019). It could be debated if these denominators are indeed identical as has been postulated in the literature on this subject (Steger et al. 2006). MiL seems to point at a broader concept, whereas PiL refers to the goal-directed part of MiL, but also might fathom one’s affective state (Steger et al. 2006). Moreover, according to recent research, MiL also consists of the constructs ‘coherence/comprehension’ and ‘significance/mattering’, from which the ‘mattering’ component partly accounts for the protective effect recently found (Sliedrecht et al. 2019). Moreover, as MiL seems to conflate 3 related concepts, potential future purer measures of an overall judgment of meaning might provide more useful information and should be examined in future research. However, as far as we know there is no earlier research that has explicitly investigated MLQ- scores in relation to relapse. However, also research investigating the PiL/AUD relapse association, as measured with the Purpose in Life test, seems to be relatively scarce, but has shown such a relation (Waisberg and Porter 1994; Roos et al. 2015).

In our treatment settings, one of the goals should still be to alleviate ‘craving’, while its association with relapse has been consistently shown in literature and clinical practice. Consequently, further research at possible moderators (Cavicchioli et al. 2020) could be an area of additional future research.

**Limitations**

Our research has several limitations. It must be noted that our number of patients was relatively small and the outcome ‘any alcohol use’ can be regarded as somewhat strict. The less stringent relapse outcome \( \geq 3 \) consecutive days of drinking, however, was also not associated with craving or MiL. In future research, it would be worthwhile to examine continuous outcome measures, such as percent heavy drinking days or reductions in drinking, as well as non-consumption outcomes such as drinking consequences and well-being. Furthermore, it also must be noted, that still no uniform relapse definition exists (Maisto et al. 2016; Sliedrecht et al. 2022), which makes it difficult to compare research outcomes.

The small sample size and rather heterogeneous patient population with high comorbidity may have reduced our ability to detect effects of interest. Furthermore, given the design of the study, which was still ongoing, the results of the smaller 12 months follow-up group, might probably be underpowered. Especially for moderation analyses, larger samples would be required. We did not apply any correction for multiple testing, but given the small number of tests and lack of statistically significant outcomes do not think this would have led to other outcomes. An additional sensitivity power analysis indicated that an effect size of 0.15 would be detectable, given the current samples size.

Another limitation is the use of self-report data, which could for example have led to underreporting of relapse. However, the use of self-report data has been commonplace in former relapse literature, and the reliability can be regarded as acceptable (Whitford et al. 2009; Schneekloth
et al. 2012; Cherrier et al. 2020). Nevertheless, last decades, a growing area of research has evolved on the ‘near real time’ assessment of craving (also in relation to relapse) via ecological momentary assessment (EMA) (Shiffman et al. 2008) and alcohol use (McKay et al. 2006; Morgenstern et al. 2014; Serre et al. 2015; Treolar Padovano and Miranda 2021). Moreover, also EMA relies on self-report data.

Furthermore, it must be noted that craving and presence of MiL will fluctuate over time, although baseline MiL might be more stable over time and PACS measures craving over the last week period. However, higher PACS scores at admission have in earlier research indeed been related to higher relapses rates at 12 months (Stohs et al. 2019).

Finally, the Covid-19 pandemic may have influenced our research in several ways. The inpatient setting from 2020 on received fewer patients (Marsden et al. 2020), which led to fewer than expected participants in our study. Furthermore, the pandemic and resulting ‘lock downs’ and ‘social distancing’ may have influenced the levels of stress and craving (Sallie et al. 2020) and experiencing lower meaning in life, eventually leading to fewer moderation effects of MiL on relapse.

However, in real life ‘meaning’ might actually be an important factor in the process of relapse, which is a finding we expected to see in this study. We think that despite statistically non-significant outcomes, this kind of research still deserves a place within the literature and requires additional research.

Conclusions

Craving has in earlier research been shown to be a robust predictor of AUD relapse, whereas the role of meaning in life as a predictor of relapse and potential moderator remains unclear. In other research, experiencing a ‘purpose in life’ has been found to be a protective factor in AUD relapse as well, but this denominator does not seem to equal the broader concept of experiencing MiL. In the current study, craving and alcohol dependence were more prominent in the relapsed groups. However, we did not find a meaningful statistical relationship between craving/MiL and relapse in our study. As potential relapse determinants, the role of MiL and more specific religious factors might still be relevant to be investigated in future studies, which should encompass more participants.

Open Scholarship

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ORCID

Wilco Sliedrecht http://orcid.org/0000-0002-6675-8581
Henk Jan Seesink http://orcid.org/0000-0002-2817-8148
Cis Vrijmoeth http://orcid.org/0000-0003-3642-2072
Reinout W. Wiers http://orcid.org/0000-0002-4312-9766
Brian Ostafin http://orcid.org/0000-0001-9739-2757
Hanneke Schaap-Jonker http://orcid.org/0000-0002-0825-6188
Hendrik Roozen http://orcid.org/0000-0001-6412-4043
Katie Witkewitz http://orcid.org/0000-0002-1086-3067
Geert Dom http://orcid.org/0000-0001-6492-0429

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