

Variables involved in the long-term alcohol abstinence: Which variables are involved and at what point of time?

Variables implicadas en la abstinencia de alcohol a largo plazo: cuáles son y cuándo juegan un papel más importante

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Abstract

Several psychological variables have been associated with the prognosis during alcohol dependence treatment and after discharge. However, we still do not know the role that these variables play in the achievement of abstinence and if they modify throughout time. Method: Longitudinal survey data related to anxiety, depression, impulsivity, coping, meaning in life (MiL) and attendance to mutual-help groups were collected from outpatients with alcohol dependence (N= 159, 66% male, mean age=42.54 years). Assessment points were the following: baseline, at discharge (after 2-years of treatment), and 2-years and 4-years follow-up after discharge. Drinking outcomes were evaluated with the Timeline Followback Method Assessment. Results: At baseline, levels of avoidance coping and impulsivity were associated with months of accumulated abstinence at 4-years follow-up, higher scores in MiL were consistently associated with months of accumulated abstinence at 4-years of follow-up. Mediation models showed that MiL increased accumulated abstinence at 4 years-follow-up by increasing avoidance coping and reducing levels of depression. Conclusions: MiL is a determining component in the long-term sustained abstinence. Our results support the key role of MiL and point to a new mechanism through which it influences the maintenance of sobriety. Because mutual-help groups have consistently demonstrated to promote MiL, they should be implemented and recommended as an essential part of an integrated treatment of alcohol dependence.

Keywords Avoidant coping style; meaning in life;	alcohol dependence; anxiety-depression; mutual-help groups.
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Resumen

Diversas variables psicológicas están implicadas en el pronóstico de los pacientes con dependencia de alcohol, durante el tratamiento y después del alta. Sin embargo, aún no conocemos el papel que juegan estas variables en la consecución y mantenimiento de la abstinencia y, si éstas, se modifican a lo largo del tiempo. Metodología: Se recogieron datos longitudinalmente relacionados con ansiedad, depresión. impulsividad, estrategias de afrontamiento, sentido de la vida (SV) y asistencia a las asociaciones de ayuda-mutua (AM) de pacientes ambulatorios con dependencia de alcohol (N=159, 66% varones, edad media=42.54 años). Se realizaron evaluaciones basalmente, al alta (después de 2 años de tratamiento), a los 2 y a los 4 años después del alta. Las variables relacionadas con el consumo de alcohol fueron evaluadas con el método Timeline Followback. Resultados: En la evaluación basal, el estilo de afrontamiento evitativo y la impulsividad se asociaron con los meses de abstinencia acumulada a los 4 años. Al alta, y a los 2 años de seguimiento, las puntuaciones altas en el SV se asociaron con los meses de abstinencia acumulada a los 4 años. Los modelos de mediación encontraron que el SV incrementaba los meses de abstinencia acumulada a los 4 años a través del estilo de afrontamiento evitativo y una reducción de los niveles de depresión. Conclusiones: El SV es un componente determinante en la abstinencia a largo plazo. Dado que las asociaciones de AM promueven el SV, éstas deberían ser recomendadas como una parte esencial de un tratamiento integrado de la dependencia de alcohol.

Palabras clave

Estilo de afrontamiento evitativo; sentido de la vida; dependencia de alcohol; ansiedad-depresión; asociaciones de ayuda-mutua.

INTRODUCTION

Europe is one of the continents with the highest alcohol use disorder (AUD) costs (GBD, 2015). AUD is defined by the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as a chronic, relapsing, psychopathological clinical condition (APA, 2013). Several strategies have been developed for the treatment of AUD, ranging from behavioral treatments to pharmacotherapies (Morgenstern and Longabaugh, 2000; Anton et al. 2014).

One of the main objectives of clinical studies has been determining which variables are associated, in the short and the long-term, with the maintenance of abstinence (Sliedrecht et al., 2019). Thus, it is well known that

the severity of anxiety, depression, and impulsivity at the beginning of alcohol treatment are associated with higher relapse rates (Bartrés-Faz et al., 2018; Khazanov & Ruscio, 2016; Kleftaras & Psarra, 2012; Stevens et al., 2014). In addition, coping strategies used by the patients during the treatment period are also a predictive factor for achieving abstinence (Sliedrecht et al., 2019). Follow-up studies in the context of 12-step programs point out that variables such attending to group sessions, and purpose and meaning in life must also been considered (Carroll, 1993; Krentzman et al., 2017; Robinson et al., 2007).

However, not only being aware of the association between these variables and the prognosis of alcohol-dependence eases the



way in which clinicians treat patients that seek treatment. This could be due, among several reasons, to the fact that certain variables, such as achieving abstinence, could be more determinant for the prognosis in the first stages of treatment, whereas others, such as spirituality, could play a more important role in the medium and long-term (Krentzman et al., 2017). The other issue is that these variables have not been frequently assessed in real-world settings, so they are hardly useful for clinicians in order to improve the efficacy of treatments.

Taking into account these considerations it would be of advantage knowing which variables are associated, in the same sample, with the prognosis during the treatment period, and which of those continue to be determinant during the medium and long-term follow-up. In this way, we could implement effective strategies in order to improve the recovery of patients during the treatment period and after discharge.

With this objective in mind, we have performed an additional statistical analysis of a previous study which aimed to demonstrate the additional effect of integrating mutual-help groups to an intensive outpatient treatment program (Rubio et al., 2018). Treatment lasted 24 months, and after discharge patients were followed-up for 4 years during which they were interviewed during the second and fourth year. The goal of this second analysis was to determine which baseline (assessed before the beginning of treatment), at discharge and during the second year of follow-up variables were implicated in achieving and maintaining abstinence at the end of the follow-up period.

METHOD

Participants

For more information regarding the included population, therapeutic strategies applied and follow-up periods see are previous work (Rubio et al., 2018). The final sample analyzed included 159 patients (n=68 received the usual treatment and n=91 received the usual treatment + Mutual-Help groups; MH groups). Table I shows socio-demographic and clinical characteristics of participants at baseline. The mean age of onset of alcohol consumption was 17.6 years (SD=6.24). The mean age at which participants met diagnostic criteria for alcohol dependence was 29.8 years (SD=9.33). Before initiating treatment, the mean number of years of alcohol use was 12.8 years (SD=10.07). The mean score of the Alcohol Dependence Severity Scale was 30.18 (SD=14.1), which indicates a severe dependence. Regarding the use of other substances. 81.2% had a tobacco dependence and 18.9% reported a cocaine dependence.

Design and procedure

Participants in this study came from two cohorts of patients who received treatment for their alcohol dependence at a public center, and after its completion they were followed up for 4 years, during which data were obtained by telephone or personal interviews. In this study, patients were assessed at different time points (baseline, at discharge, at 2-years follow-up and at 4-years follow-up). We also explored the role of each of these variables in explaining cumulative abstinence after 4 years of follow-up.



Table 1. Demographic and Clinics Characteristics of Sample

	PARTICIPANTS, n= 159
Age, Mean (SD)	42.54 (± 8.39)
Marital Status, n (%) Single Married Separated/Divorced Widow	56 (35.2) 68 (42.7) 33 (20.7) 2 (1.2)
Education, n (%) Primary school Secondary school College education	29 (18.2) 79 (49.6) 51 (32.1)
Employment, n (%) Active Unemployed Others	81 (50.9) 32 (20.1) 46 (28.9)
Treatment Group, n (%) TAU Combined with Mutual-help groups	68 (42.8) 91 (57.2)
Age onset of alcohol use, Mean (SD)	17.68 (± 6.24)
Age of diagnosis of alcohol dependence, Mean (SD)	29.79 (± 9.33)
Years of alcohol use, Mean (SD)	12.82 (± 10.07)
Alcohol dependence scale, Mean (SD)	30.18 (± 14.11)
Tobacco dependence, n (%)	129 (81.1)
Cocaine Use, n (%)	52 (32.7)
Months of attendance to Mutual-help group sessions (relatives), Mean (SD)	8.21 (± 12.78)
Number of Mutual-help group sessions (patients), Mean (SD)	224.89 (303.78)

Note: TAU: treatment as usual

The <u>dependent variable</u> was **months** of accumulated abstinence at 4-years follow-up, and it was correlated with the <u>independent variables</u> (demographic variables, avoidance coping, impulsivity, anxiety and depression levels, Meaning in Life (MiL), number of sessions attended by the patient to a MH program, and months during which patients' relatives attended to a MH program) at the different assessment points: baseline, at discharge and at 2-years follow-up.

Continuity of care therapy program

The explanation of the treatment program can be found in other publications (Rubio et al., 2018; Rubio et al., 2020), but in summary, it is a 24-months, multimodal, intensive, cognitive-behavioral treatment, divided into the following 5 phases: (a) Detoxification and motivation towards abstinence (2–3 months); (b) Relapse prevention, which was based on the cognitive-behavioral model of Marlatt and Gordon (1985); (c) Social skills program,



which was based on the one developed in the MATCH Project (Kadden et al., 1992); (d) Consolidation of behavior and lifestyle changes (10-12 months). After completing the Therapeutic Intervention Program (TIP), patients were referred to the Continuing Care Program carried out by the Primary Care team (Rubio et al., 2020). Data from the follow-up period gathered by general practitioners (GPs) were obtained from electronic medical records. If a patient had been moved to another healthcare provider, it was discussed with the GP responsible for the case. Every 2 years, all participants were interviewed in order to fill out psychological scales and gather information regarding months of abstinence and attendance to follow-up appointments.

Patients and families could attend mutual-help groups (MH group) free of charge. This has allowed us to include as variables for the study the Number of sessions attended by the patient to MH groups (224.89, SD=303.7) and the number of Months of attendance of relatives to MH groups (32.23, SD= 12.7).

Measures and Instruments

Patients were interviewed and diagnosed according to criteria of statistical manual of mental disorders (American Psychiatric Association (APA, 2000).

The following variables were determined during the assessment periods: Baseline, at discharge, at 2-years-follow-up and at 4-years-follow-up.

MiL: The Meaning in Life Questionnaire (MiLQ) is an instrument that assesses the meaning of life, defined as the meaning and

significance that a subject has of the nature of one's being and existence (Steger et al., 2006). The questionnaire evaluates two aspects of meaning through the following subscales with 5 items each: Presence and Search. Presence refers to the extent to which people understand, give, or see meaning in their lives accompanied by the degree to which they perceive themselves as having a purpose, mission, or ulterior objective. The validated Spanish version had a Cronbach alpha of 0.80 for the total scores (Góngora & Solano, 2011) and for this study was 0.87. The measure included in this study was the total MiL score.

Impulsivity: The Barrat Impulsivity Scale (BIS-11) (Patton et al., 1995) is a 30 item self-report scale that determines the cognitive, motor, and unplanned components found in impulsivity. The Spanish version (Oquendo et al., 2001) has a good alpha coefficient and maintains the three initial factors. Cronbach's alpha in this study was 0.79.

Anxiety and depression levels: The Hamilton Anxiety Scale (HADS-A) (Hamilton, 1959) and the Hamilton Depression Scale (HADS-D) (Hamilton, 1967) were used to determine the symptoms of anxiety and depression, respectively, with Cronbach's alphas of 0.78 and 0.82 for this study.

Avoidance coping: The Coping behavior Inventory (CBI) Scale (Litman et al., 1983) adapted to the Spanish population (García González & Alonso Suárez, 2002) is a self-administered questionnaire consisting of 36 items developed to identify the frequency with which they use coping skills to remain abstinent in risky situations. Cronbach's alpha of the Spanish validation was 0.78 and for this study 0.76. Taking into account that one of



the most frequently used strategies by Spanish patients is avoiding risky situations and its relevance in a country with our culture, we have included for this study 5 items of the avoidance subscale (items 3, 8, 18, 20 and 30).

Severity of alcohol dependence: The Severity of Alcohol Dependence Scale (SADS) (Rubio, Urosa, & Santo Domingo, 1998). It consists of 30 Likert-type questions with four alternative answers. The total score differentiates between mild (score <20), moderate (21-37) and severe (>37) alcohol dependence. Cronbach's alpha in the original version was 0.91 and, 0.87 in this study.

Months of accumulated abstinence during the 4-years-follow-up period: Assessment of alcohol consumption during the follow-up: the Alcohol Timeline Followback (TLFB) interview designed by Sobell and Sobell (Sobell et al., 1988) was used to retrospectively determine daily alcohol consumption. Through this interview, the presence of relapse, extension of consumption and periods of accumulated abstinence were determined. These data were compared with GGT serum levels, which were also obtained annually.

Number of sessions attended by the patient to MH groups and number of months of attendance of family members to MH group sessions. These data were obtained from the attendance register recorded on a weekly or fortnightly basis by our team members coordinated with the associations to which patients and families attended to.

Statistical analyses

Pearson's correlation analyses were performed to explore the association between gender, age, and psychological variables (avoidance coping, impulsivity, anxiety and depression, and MiL), measured at different assessment points (baseline, at discharge, 2-year follow-up), and variables associated with attendance of patients and relatives to mutual-help groups (number of sessions attended by the patients to MH groups, number of months of attendance of family members to MH group sessions), with the months of accumulated abstinence at 4-years follow-up. In addition, several stepwise linear regression analyses were also performed, to study which variables significantly predicted the number of months of abstinence at 4-years of follow-up. Finally, we observed at 2-years-follow-up significant relationships between avoidance coping, depression, MiL and months of accumulated abstinence at 4-years followup, so we decided to explore if avoidance coping, and depression levels measured at 2-years follow-up could constitute mediators of the relationship between MiL (2-years follow-up) and months of accumulated abstinence at 4-years followup. Statistical significance of the mediating effects of the model tested in the current research was examined by Ordinary Least Squares Regression Method and Bootstrap Method through the software developed by Hayes (2013; 2012). Bootstrap analyses were conducted through PROCESS Macro and "Multiple Mediation Model 4" for parallel multiple mediation. Statistical significance of the mediating variables was examined on 10000 Bootstrap samples. Significance level was set as 0.05. Research data analysis was conducted through IBM SPSS 22.0 software.

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RESULTS

In the following sections we firstly show the correlations between the assessed variables in each period and the prognosis related to abstinence at 4-years of followup, and their respective regression models. Secondly, we show the results regarding the parallel-multiple-mediated analysis.

Correlations and regression models

Baseline assessments and accumulated abstinence at 4 years-follow-up. Table 2 shows that age, avoidance coping, and MH-attendance by patients and by relatives positively correlated with months of accumulated abstinence, and negatively with impulsivity.

A stepwise linear regression model was carried out introducing those variables that had been statistically significant in the correlations. Firstly, age was introduced to control for the effect of this variable on the dependent variable. Next, avoi-

dance coping and impulsivity, and number of months and number of sessions that family members and patients attended to MH-groups, respectively, were introduced. The program added variables and it created 3 models. The models are shown in Table 3. The final model reflected that the significant predictors that explained 16% $(R^2=0.16)$ of the variance of the months of accumulated abstinence were avoidance coping and lower levels of impulsivity $(\Delta R^2 = 0.02, (\Delta F(1,155) = 5.20, p=0.02),$ with which the model reached significance (F(3,158)=10.05, p=0.0001). It was the avoidance coping the variable that presented a higher beta (0.29) (see Table 3).

At Discharge assessments and accumulated abstinence at 4-years-follow-up. Table 4 shows that there were statistically significant relationships between the avoidance coping subscales, lower levels of anxiety and higher levels of MiL with months of accumulated abstinence at 4-years follow-up.

Table 2. Correlations between Baseline measures and months of accumulated abstinence at 4 years follow-up

		I	2	3	4	5	6	7	8	9
N° Abstinence Months	Ι									
I. Gender	-0.09	Ι							ĺ	
2. Age	0.16*	-0.14*	I							
3. Avoidance Coping	0.34**	0.03	0.11	1						
4. Impulsivity	-0.24**	-0.04	-001	-0.22**	I					
5. Anxiety	0.008	-0.01	0	-0.12	0.15*	I				
6. Depression	0.03	-0.04	-0.09	-0.11	0.18*	0.34**	I			
7. MiL	-0.02	-0.19**	-0.22**	0.07	-0.18**	-0.15*	-0.09	ı		
8. Attendance rela-tives	0.42**	-0.06	0.10	0.19*	0.16*	0.08	0.16*	-0.12	ı	
9. Attendance pa-tients	0.59**	-0.07	0.03	0.26**	0.10	0.09	0.12	-0.12	0.77**	1

Note: MiL: Meaning in life; Attendance relatives: Number of months of attendance regarding relatives; Attendance patients: Number of mutual-help group sessions attended by patients.



Table 3. Baseline predictors of months of accumulated abstinence at 4 years follow-up

Predictors	R^2	ΔR^2	b	β	t	p
Model I	0.02	0.02				
Age			0.06	0.16	2.02	0.04*
Model 2	R^2	ΔR^2	b	β	t	p
	0.13	0.11				
Age			0.04	0.12	1.60	0.11
Avoidance Coping (baseline)			0.67	0.33	4.44	0.001**
Model 3	R^2	ΔR^2	b	β	t	p
	0.16	0.02				
Age			0.04	0.12	1.61	0.10
Avoidance Coping (baseline)			0.59	0.29	3.89	0.001**
Impulsivity (baseline)			-0.04	-0.17	-2.28	0.02*

Note: *p<0.05;**p<0.001

Stepwise linear regression models were carried out with these variables. Avoidance coping, anxiety, MiL, and family and patient's attendance to MH-group sessions were then introduced. The program added variables and it created 4 models. The models are shown in Table 5. The final model reflected that significant predictors that explained 44% (R^2 =0.44) of the variance of months of ac-

cumulated abstinence were: age, avoidance coping, MiL and the number of sessions that patients attended to FACOMA (ΔR^2 =0.07, ($\Delta F(2,153)$ =9.42, p=0.0001), reaching the model statistical significance (F(5,158)=24.08, p=0.0001). The total number of sessions to which patients attended to MH-group was the variable that presented a higher beta (0.38) (see Table 5).

Table 4. Correlations between AT discharge Assessments and months of accumulated abstinence at 4 years follow-up

		1	2	3	4	5	6	7	8	9
N° Abstinence Months	1									
I. Gender	-0,09	1								
2. Age	0,16*	-0,14*	1							
3. Avoidance Coping	0,55**	-0,005	0,11	ı						
4. Impulsivity	-0,13	-0,05	-0,02	-0,11	I					
5. Anxiety	-0,16*	0,02	-0,01	-0,21**	0,28**	1				
6. Depression	-0,07	0,02	-0,11	-0,10	0,25**	0,43**	l I			
7. MiL	0,32**	-0,14*	-0,05	0,17*	-0,05	-0,13*	-0,16*	I		
8. Attendance relatives	0,42**	-0,06	0,10	0,44**	0,15*	0,08	0,14*	0,22**	1	
9. Attendance Patients	0,59**	-0,07	0,03	0,58**	0,08	-0,2	0,05	0,32**	0,77**	I

Note: MiL: Meaning in life; Attendance relatives: Number of months of attendance regarding relatives; Attendance patients: Number of mutual-help group sessions attended by patients.



Table 5. Assessments at Discharge as predictors of months of accumulated abstinence at 4 years follow-up

Predictors	R^2	ΔR^2	b	β	t	p
Model I	0.02	0.02				
Age			0.06	0.16	2.02	0.04*
Model 2	R^2	ΔR^2	b	$ \beta $	t	p
	0.31	0.28				
Age			0.04	0.10	1.50	0.13
Avoidance Coping (after treat-ment)			1.25	0.53	8.05	0.001**
Model 3	R^2	ΔR^2	b	β	t	p
	0.37	0.06	1			
Age			0.05	0.13	2.06	0.04*
Avoidance Coping (after treat-ment)			1.15	0.49	7.55	0.001**
MiL (after treatment)			0.12	0.25	3.85	0.001**
Model 4	R^2	ΔR^2	b	β	t	p
	0.44	0.07	1			
Age			0.05	0.12	2.00	0.04*
Avoidance Coping (after treat-ment)			0.72	0.31	4.10	0.001**
MiL (after treatment)	İ		0.07	0.14	2.20	0.03*
Number of mutual-help group			0.004	0.38	3.65	0.001**
sessions						
Months attendance of relatives			-0.01	-0.05	-0.53	0.56

Note: *p<0.05;**p<0.001

2-years follow-up assessments and accumulated abstinence at 4-years-follow-up

Table 6 shows that there were statistically significant relationships between the avoidance coping subscale, lower levels of depression, lower levels of impulsivity and MiL with months of accumulated abstinence during the 4-years of follow-up.

The regression models are presented in Table 7. The final model reflected that significant predictors which explained 51.5% (R^2 =0.51) of the variance of months of accumulated abstinence were avoidance coping, lower levels of depression and MiL (ΔR^2 =0.01, (ΔF (1,154)=4.84, p=0.03), with the model reaching significance (F(4,158)= 40.89; p=0.0001). It was MiL

that presented the highest beta (0.42) (see table 7).

In summary, in Figure I we can see how significant predictors for the number of months of accumulated abstinence at 4-years follow-up were changing throughout time. At baseline, levels of avoidance coping and levels of impulsivity (inverse) seemed relevant to predict a higher number of months of accumulated abstinence at the end of the follow-up period. However, at discharge, avoidance coping, MiL and number of sessions to which patients attended to MH-groups were significant predictors of accumulated abstinence at 4-years followup. Finally, at 2-years follow-up, MiL was especially the best predictor of abstinence, surpassing avoidance coping.



Table 6. Correlations between assessments at 2 years follow-up and months of accumulated abstinence at 4 years follow-up

		I	2	3	4	5	6	7	8	9
N° Abstinence Months	I									
I. Gender	-0.09	ı								
2. Age	0.16*	-0.14*	ı							
3. Avoidance Coping	0.56**	-0.06	0.08	I						
4. Impulsivity	-0.22	-0.02	-0.02	-0.25**	I					
5. Anxiety	-0.08	0.06	-0.05	-0.19*	0.22**	ı				
6. Depression	-0.37*	-0.008	-0.12	-0.25**	0.21**	0.29**	I			
7. MiL	0.62**	-0.06	0.07	0.46**	-0.04	-0.20*	-0,21**	I		
8. Attendance relatives	0.42**	-0.06	0.10	0.47**	0.08	-0.08	-0,07	0.36**	I	
9. Attendance patients	0.59**	-0.07	0.03	0.61**	0.02	-0.16*	-0,16*	0.52**	0.77**	I

Note: MiL: Meaning in life; Attendance relatives: Number of months of attendance regarding relatives; Attendance patients: Number of mutual-help group sessions attended by patients.

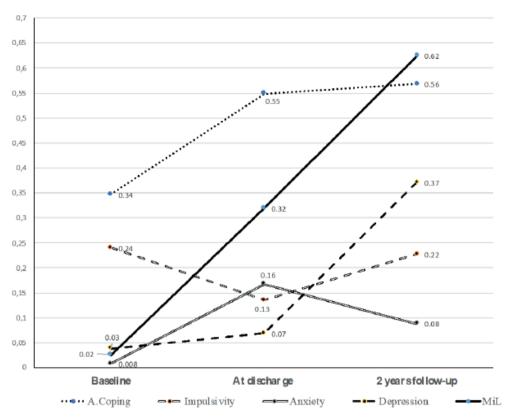
Table 7. 2 years follow-up measures as predictors of months of accumulated abstinence at 4 years follow-up

Predictors	R^2	ΔR^2	b	β	t	p
Model I	0.02	0.02	ĺ			
Age			0.06	0.16	2.02	0.04*
Model 2	R^2	ΔR^2	b	β	t	p
	0.40	0.38				ĺ
Age			0.04	0.12	1.94	0.05
MiL (2 years After Treatment)			0.29	0.61	9.96	0.001**
Model 3	R^2	ΔR^2	b	β	t	p
	0.50	0.09				
Age			0.04	0.10	1.77	0.07
MiL (2 years After Treatment)			0.21	0.45	7.15	0.001**
Avoidance Coping (2 years			0.89	0.35	5.43	0.001**
Af-ter Treatment) `						
Model 4	R^2	ΔR^2	b	β	t	p
	0.51	0.01				
Age			0.03	0.09	1.63	0.10
MiL (2 years After Treatment)			0.20	0.42	6.37	0.001**
Avoidance Coping (2 years			0.85	0.33	5.24	0.001**
Af-ter Treatment)						
Depression (2 years After			-0.11	-0.13	-2.20	0.02*
Treatment)						

Note: *p<0.05;**p<0.001

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Figure 1. Correlations between psychological variables (at baseline, at discharge and at 2 years follow-up) and months of accumulated abstinence assessed at 4 years follow-up



Parallel multiple mediation

The above results indicated that among the measures taken at 2-years follow-up, MiL was the best to predict the number of months of accumulated abstinence at 4-years follow-up, with a higher weight in the linear regression model. Thus, we decided to explore specific mechanisms in these relationships by means of a parallel multiple-mediated analysis using the principal component analysis (see Table 8).

The results showed that MiL, both directly and indirectly, increased the number of months of accumulated abstinence at 4-years follow-up by increasing avoidance coping and reducing levels of depression (see Figure 2).

As it can be seen in Figure 2, total effect (c=0.29, SE=0.03, t=10.01, p<0.001) of MiL over the months of accumulated abstinence 4 years after treatment was on a significant level (Step 1). In addition, direct effects of MiL on



Table 8. The Comparison of Indirect Effects of MiL (2 years follow-up) on months of accumulated abstinence at 4 years follow-up, through avoidance coping and depression levels and its specific indirect effects

Booststrapping										
	Prod	95%BCa Confidence Interval								
Effects	Point Estimate	SE	Z	Þ	Lower	Upper				
Total indirect effects	.0980	.0194			.0643	.1406				
Avoidance Coping	.0747	.0189	4.08	.00001	.0425	.1168				
Depression	.0233	.0087	2.03	.022	.0083	.0432				
Contrasts										
СІ	.0514	.0221			.0112	.0975				

Note: N= 159, k= 10000, *p<.05, **p<.01, ***p<.001, Level, BCa: Bias Corrected and Accelerated 10000 bootstrap samples.

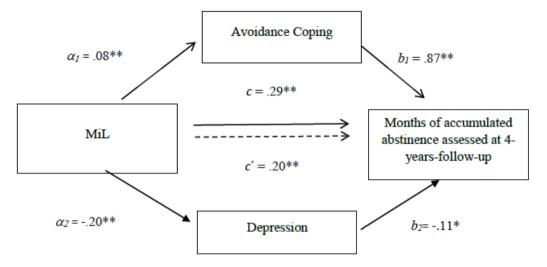
avoidance coping (B α_i = 0.08, SE= 0.01, t= -6.49, p<0.001), and depression levels (B α_2 = -0.20, SE= 0.04, t= -4.65, p<0.001) as mediating variables, were on a significant level (Step 2). When the direct effects of mediating variables on months of accumulated abstinence were examined, the effects of avoidance coping (B $b_1 = 0.87$, SE= 0.16, t = 5.31, p < 0.001) and depression levels ($Bb_2 = -0.11$, SE = 0.05, t = -2.31, p<0.05) were found to be significant. When MiL and all mediating variables were entered in the equation simultaneously (Step 3), in regard to the direct effect, the relationship between MiL and abstinence decreased, and significant values were found on the same level (c'=0.20, SE=0.03, t= 6.35, p<0.001). Based on this result, two mediating variables were found to mediate between MiL and abstinence. In addition, it was observed that the overall model was on a significant level (F(3,155) = 53.06, p < 0.001) and it explained 50% of the total variance on months of abstinence 4 years after treatment.

Statistical significance of indirect effects within the tested model was examined on

10000 bootstrap samples. Estimations were tested within the 95% confidence interval. Biascorrected and accelerated results are included in Table 8. As seen in Table 8. indirect total effect of MiL, through the avoidance coping and depression (namely, the difference between the total and direct effect /c-c') was statistically significant (point estimation= 0.09 and 95% BCa CI [0.0643, 0.1406]). When the two mediating variables were separately considered in regard to the mediation for indirect effects of MiL on abstinence 4 years after treatment within the tested model, the mediations of avoidance coping (point estimate = 0.07 and 95% BCa CI [0.0425, 0.1168]), and depression (point estimate=0.02 and 95% BCa CI [0.0083, 0.0432]) were found statistically significant. Paired comparisons were conducted in order to define the powers of mediating variables. Two statistically significant comparisons with point estimates outside the zero interval, based on 95% confidence interval, were included in Table 8. Based on the paired comparisons of certain indirect effects, avoidance coping was found to be a more powerful mediator than depression levels (C2).



Figure 2. Parallel-Multiple Mediation of avoidance coping and depression level (2-years follow-up) between MiL (2-years follow-up) and months of accumulated abstinence assessed at 4-years-follow-up and Non-Standardized Beta Values



DISCUSSION

Our results suggest that in a sample of severe alcohol-dependent patients who underwent a 24-months intensive treatment and were then followed-up for 4 years, the variables that predicted a larger number of months of accumulated abstinence varied depending on the assessment period. Before the beginning of the treatment, impulsivity and avoidance coping predicted the prognosis at 4 years of follow-up; at discharge, the predicting variables were avoidance coping, MiL, age, and patient's attendance to MH groups sessions; during the assessment carried out at the second year of follow-up predicting variables were MiL, avoidance coping and depression. In this last period, mediating analyses showed that MiL, directly, or indirectly through avoidance coping and reduction of depression levels, predicted

an achievement of more months of accumulated abstinence. In conclusion, our data indicate that MiL is an especially important variable involved in the achievement of abstinence in the long-term after completing an intensive treatment.

Other studies (see references mentioned above in the Introduction section) have found that these same variables, individually, are associated with achieving abstinence. However, until now, it has not been considered how and why certain variables such as impulsivity and avoidance coping, throughout time, lose weight in favor of MiL. In the following sections we will firstly tackle why avoidance coping could be the most relevant mechanism for the maintenance of long-term abstinence, especially during the treatment period, and why after discharge MiL is the variable which plays a more prominent role.



Coping skills as a mechanism involved in the maintenance of abstinence during the treatment period

Regarding coping skills our results support the idea that an intensive cognitive-behavioral treatment improves coping resources, especially in severe patients as those of our sample (Roos et al 2017). Several analyses performed in the MATCH Project indicated that coping skills mediated the positive treatment effects of cognitive-behavioral therapy (CBT) on drinking outcomes at oneyear post-treatment, specifically in subjects with severe alcohol dependence (Roos et al., 2017). These results are consistent with the social-cognitive theory, which considers that CBT enhances abstinence by improving coping skills (Morgenstern & Longabaugh, 2000). The fact that patients included in our study, in addition to having a severe illness condition, had also a history of previous therapeutic failures, and an elevated percentage of them belonged to the cohort which have attended to MH groups could explain why these patients could have learnt to avoid risky situations as the main coping skill during the treatment period (Arias et al., 2021).

Role of MiL after discharge as a variable implicated in the maintenance of abstinence in the long-term

Our results support the idea that MiL is a key component in the recovery of substance dependent subjects. They highlight that having a higher MiL significantly predicts achieving a longer long-term cumulative abstinence, at 4-years follow-up. Moreover, the predictive power increases as a function of time since

the subject enters to treatment. This variable, either directly, or indirectly through mediating variables such as avoidance coping and the reduction of depressive symptoms, was found to be the one that most robustly predicted the months of accumulated abstinence at the end of the follow-up.

Overall, our results are in line with those of other studies that have also pointed out the importance of MiL in the recovery of subjects with alcohol dependence (Kelly et al., 2011; Witkiewitz et al., 2019), so it can be considered as a core dimension for the recovery of these subjects (Slade et al., 2012; Substance Abuse and Mental Services Administration (SAMHSA), 2011). The fact that, in our analyses, unlike results of other studies (Kelly et al., 2011; White & Laudet, 2006; Zemore, 2007), MiL had a higher weight in the regression model than other variables, such as patient's attendance to MH groups, can be explained by the different points at which assessments were performed (Cranford et al., 2014; Kelly et al., 2011; Krentzman et al., 2017; Waisberg & Porter, 1994; Witkiewitz et al., 2019). In all these studies, MiL evaluations were conducted at baseline and upon discharge from treatment (at I week and 3 months), and follow-up periods ranged from 12 to 15 months, so these studies reflected only the early stages of the recovery process. In fact, in our data, we can observe the progress of MiL, so that among the variables with a predictive power at the baseline assessment we cannot find MiL as determinant, and instead, the variables involved during this treatment stage are higher levels of avoidance coping or less impulsivity. However, the weight of MiL at discharge progressively increases and has already a significant predictive power, although it is not until 2 years after discharge



that it reaches its greatest explanatory power. These follow-up measures demonstrate how the recovery process of patients is longer than that reflected by cross-sectional or prepost treatment studies, showing as well that variables that are implicated in the maintenance of abstinence evolve as the treatment progresses, and while in the initial stages avoiding risky situations is especially relevant, in the middle and later stages MiL plays a more important role in the recovery process.

On the other hand, according to our results there are other variables that clearly influence the maintenance of abstinence such as the reduction of negative emotions, specifically anxiety and depression, avoidance coping or attendance to treatment sessions at Mutual-Help groups. This last variable is of particular importance, firstly because of the type of treatment. It is common for intervention programs to include different components, but they are not usually described in a standardized way. With the exception of the study by Kelly et al. (2011) where treatments were standardized - for patients included in the MATCH Project - it is not clear from the literature which type of therapeutic approaches have been used and whether or not they could be compatible with improving MiL (Waisberg & Porter, 1994). However, improvements in MiL are considered a consequence of treatment adherence and a recovery measure.

In our study, there is also a correlation between MiL scores, the number of MH group sessions to which the patient attended to and the number of months of abstinence. It is therefore likely that at discharge, although attendance to MH-group sessions is still relevant for alcohol outcomes, it has a ceiling effect, with MiL variables beginning to play

a greater role in explaining the maintenance of abstinence. This interpretation is in line with the opinion of clinicians who claim that spirituality, perhaps through MiL, is especially relevant in the recovery of severe alcoholic patients (Kelly, 2017).

These findings have led us to consider that maintaining or increasing MiL can be the thread through which recovery is achieved in severe alcohol dependent patients who request treatment. It is possible that, initially, recovery depends on the adherence to the treatment program, attendance and involvement in tasks of MH groups (Kaskutas et al., 2003; Pagano et al., 2004) or changes in lifestyle (learning to cope with risky situations and emotional management) (Marlatt & Gordon, 1985), but afterwards, MiL could be the guiding thread that drives the maintenance of recovery. It has been pointed out that purposeful individuals have a predisposition that guides their actions towards future achievements. This way of orienting their lives leads them to limit their perceived value of a forthcoming opportunity (drinking again, for example) in order to take advantage over those of a greater reward value (Burrow & Spreng, 2016).

MiL as a modulating variable of coping skills and depressive symptomatology

Regarding the data presented in this study, in the case of patients suffering from an alcohol dependence, a successful management of negative emotions and using more adaptative coping strategies are related to the maintenance of abstinence from alcohol. Specifically, we have found that MiL has not only a direct effect on the maintenance of abstinence



but has also an indirect effect through the improvement of avoidance coping strategies.

Many patients have learnt to use alcohol as a behaviour that ameliorates anxiousdepressive states (Anker et al., 2019; Gamble et al., 2010). From this point of view, subjects opt for immediate rewards against delayed rewards of greater value (for example health or sobriety) (Song et al., 2018). However, it is possible that in subjects who score highly in Engagement with life, this is, on MiL, the feeling of well-being linked to non-drinking choices, following their own values (what patients call to go from "I cannot stop drinking" to "I do not want to drink"), could constitute an adequate coping strategy (Miller et al., 1996) which could favour the avoidance of risky situations (Tonigan et al., 2001) and the maintenance of sobriety.

Our results regarding the role of MiL in the achievement of alcohol abstinence through the reduction of depressive symptoms and the maintenance of avoidance coping strategies are in line with other researches that have demonstrated, on the one hand, that MiL is associated with greater reductions in anxiety, depressive, and general emotionally negative symptoms, in both, non-substance dependent populations (Khazanov & Ruscio, 2016; Kleftaras & Psarra, 2012), and addictive populations (Shorey et al., 2015; Song et al., 2018; Yek et al., 2017), and, on the other, the relationship between these types of symptoms and an increased risk of alcohol relapse (Anker et al., 2019; Curran et al., 2007; Gamble et al., 2010).

In this way, our results support the role of MiL as a modulating element of emotionally negative states in patients who suffer from an alcohol dependence. Until now, this role

had nearly exclusively been linked to the involvement in 12-step groups (Wilcox & Tonigan, 2018). However, our findings are suitable within the context of the models of addiction. Lower levels of MiL. associated with an emotionally negative state, would involve less effective emotional regulation strategies which could lead to an increased risk to relapse (Roos et al., 2015; Tiffany, 1999). According to the dynamic model of relapse, several factors interact in order to predict relapse in highly risky situations (Witkiewitz & Marlatt, 2004). In this case, the feeling of a low MiL could modulate the influence of proximal risk factors (negative affect) in these situations. In summarize, MiL could help to maintain an appropriate motivational state so as to achieve goals and live in accordance to them, but it could also reduce the impact of adverse experiences through biological mechanisms underlying stress management.

Applicability of our results

With that in mind, we should then ask ourselves about which type of strategies could be offered to our patients to improve their MiL. Strategies based on motivational interviewing (MI) involve values clarification (Miller & Rollnick, 2013). The mindfulnessbased relapse prevention strategies have been shown to be effective in reducing substance use; they use mindfulness-based practices to teach alternative responses to emotional distress and to lessen the conditioned response of craving in the presence of depressive symptoms (Witkiewitz & Bowen, 2010). One of the most promising strategies in this area is the acceptance and commitment therapy (Hernández-López et al., 2009). And, indeed, 12-step programmes and others such as those developed in Europe, for example



"Help yourself-Help us" (FACOMA, 2016), constitute undeniable tools, firstly because of their efficacy, and secondly because they are free-of-charge.

Limitations

Despite our promising results, we must consider several limitations. Firstly, this study was carried out with a sample that included severe alcohol dependent patients seeking treatment, in which the decline of quality of life and social support was significant, and thus, their motivation towards change was high. It is possible that in less severe patients, our findings related to MiL could differ, or that the influence of negative emotions and coping skills could be modulated in a different way. For this reason, it would be necessary to assess the progression of MiL and abstinence over time in other types of alcohol dependent patients. In addition, we must consider that some of the result variables were obtained through self-reports. However, to partially avoid this limitation we used a structured interview and determined GGT levels. Another possible limitation refers to the type of coordination done with the Associations. In our case, the closeness to associations allowed us to attend them with a fortnightly frequency, but it is possible that in other places, where the distance between the treatment centre and associations is bigger, it would be necessary to design other coordination strategies. Because FA-COMA has a therapeutic programme available (www.facoma.org), the heterogeneity of group interventions can be reduced, and consequently we recommend developing the same programme if our study wants to be replicated.

In conclusion, to the best of our knowledge, this is the first study that has explored the role of MiL in a cohort of alcohol dependent patients treated with standardised cognitivebehavioural techniques and followed-up for 4 years within a continuing care programme carried out by Primary Care teams. In addition, this is the first study in which the philosophy of the mutual-help groups to which most of the patients attended to (57% of the total of our sample) was not based on the 12-step principles. The follow-up strategy designed in our study implies a characterization of the course of recovery, and it manages to reflect how, as a patient progresses in his/her therapeutic process, psychological variables which define the maintenance of abstinence also change, until it demonstrates that recovery in the MiL determines changes in lifestyle which are necessary to achieve patient's recovery.

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Conflicts of Interest

None of the authors have conflicts of interest with public or private entities.

Ethics Approval

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation, "12 de Octubre Biomedical Research



Institute" and with the Helsinki Declaration of 1975. Informed consent was obtained from all patients for being included in the study.

Data availability

The datasets generated during and/ or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contribution statements

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Rosa Jurado Barba, Marta Marín, Ana Sion, Regina and Gabriel Rubio. The manuscript was written by Rosa Jurado, Regina Espinosa and Gabriel Rubio and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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