

Behavioral responses in people affected by alcohol use disorder and psychiatric comorbidity: correlations with addiction severity

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Abstract

Aim. In this study, we investigated in people suffering from alcohol use disorder (AUD) with or without dual diagnosis (concomitant psychiatric disability) how they feel their dependence condition. We predicted that AUD people with a dual diagnosis could feel potentiated their addiction.

Methods. Alcohol habits and psychiatric conditions of 183 AUD men and 62 AUD women were measured by using the DSM-5, the severity of alcohol dependence questionnaire (SADQ), the alcohol anamnesis and psychiatric examination by the symptom check list 90-R (SCL-90-R).

Results. We have shown that alcohol drinking does not correlate with both psychiatric examination and self-reported psychopathology. SADQ shows that severe alcohol dependence correlates with highest psychiatric symptoms and with the levels of alcohol consumption.

Conclusions. This finding suggests that high SADQ scores may represent a tool to early disclose only patients with dual diagnosis. SADQ may provide information to address pharmacological interventions because revealing aspects of the dark side of addiction potentiated by AUD associated psychopathology.

Key words

- alcohol use disorders
- dual diagnosis
- addiction
- psychiatric comorbidity
- symptom check list 90-R

INTRODUCTION

People suffering from Alcohol Use Disorder (AUD) frequently show behavioral impairments and related psychiatric disruptions (dual diagnosis) [1-12]. In the early studies of the Cloninger group, two subtypes of alcoholism have been described. The type I, affecting both men and women, could have genetic or environmental bases, usually starting at an early age, and causing either mild or severe alcohol dependence [13]. The type I was characterized by loss of control over drinking, binge drinking, guilt about drinking and progressive severity of alcohol abuse. The personality traits of type I were high harm avoidance and low novelty seeking, the person drinks to relieve anxiety. Instead, the type

II is primarily genetic [5] affects men more often than women, and mainly sons of male alcoholics, the alcohol problems appear before age 25 and often begins during adolescence or early adulthood. Type II is characterized by the inability to abstain from alcohol. Type II is also associated with criminal behavior and with a history of antisocial acts. Relatively to personality traits, type II is characterized by high novelty seeking, person drinks to induce euphoria. Psychopathological dysfunction and sociopathy and often coexist in type II. In fact, type II alcoholism has more emotional regulation difficulties and a lot of social problems, than type I alcoholism, that can contribute to developing psychiatric disorders [14].

Depression, anxiety and personality disorders are of-

ten associated with alcoholism and contribute to craving and relapse [2, 6, 15-21]. AUD people with dual diagnosis are reported to be high users of the health care system [22] and to have a more severe course of alcohol dependence [23, 24] than AUD people without a dual diagnosis [17, 25]. Indeed, the comorbid condition of psychiatric impairments and AUD may predict both relapsing shorter time and increasing treatment drop-out [26-28]. Dual diagnosis and alcohol addiction severity are crucial at-risk factors for relapse and drop-out events [29-31], but only a few studies concurrently investigated their related conditions. Such studies used self-administered questionnaires as the symptom check list 90-R (SCL-90-R) [32] and the severity of alcohol dependence questionnaire (SADQ) [33] to assess psychiatric condition and alcohol addiction magnitude. However, for assessing the levels of alcohol addiction previous studies [34-36] mostly investigated only the SADQ total score but without considering the analysis of the questionnaire subscales. Such analyses may provide subtle indications to disclose that certain drinking problem domains are closely related to crucial aspects of dependence [37, 38]. Thus, the aim and novelty of this study was to analyze in a cohort of about 250 AUD people the relationship between psychiatric diseases and the severity of alcohol dependence using not only the behavioral responses to self-administered questionnaires (SADQ and SCL-90-R) but also the clinical examinations carried out by psychiatrists and physicians with long-lasting expertise in psychiatry and alcohol addiction by using the DSM-5 criteria and ad hoc tools for measuring real drinking habits as life drink history (LDH) and time line follow back (TLFB) according to the standardized methodology of the Italian guidelines for the treatment of alcohol addiction [39, 40]. We predict that AUD people with dual diagnosis could feel potentiated their addiction. Potential gender differences were also investigated.

MATERIALS AND METHODS

AUD people recruitment

AUD participants were recruited in the Latium Region Alcohol Referral Center at Policlinico Umberto I, Sapienza University Hospital, in Rome, Italy during a 15 days-long day-hospital period. All participants met the DSM-5 criteria for AUD. According to the indications of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) we considered “at-risk” drinkers people drinking up to 4 drinks per day or 14 per week for men (in Italy 1 drink = 12 g), more than 3 drinks per day or 7 drinks per week for women (in Italy 1 drink = 12 g). NIAAA defines heavy drinking as 5 or more standard drinks in a day for a man and 4 or more standard drinks in a day for a woman [41]. AUD people enrolled in the study were 245 (Table 1), 74.6% (n = 183) of them were men and their mean age was 47.20 ± 10.8 years and 62 (25.4%) women (48.15 ± 10.28 age in years). The 81.6% of AUD people were Italians, the 39.8% were married and 31% were single. The mean age of onset of alcohol problems was 28.99 ± 10.96 years. The AUD group reported an average of 17.95 ± 12.88 years of problem drinking and an average of 13.99 ± 10.86 drinks per day during the month prior to the admission to the treatment unit. 40% of the cases had completed at least 8 years of schooling.

Patients were divided into two groups: AUD patients without a dual diagnosis as referred to the SCL-90-R and as evaluated by the psychiatrist examination (n = 74; 58 men and 16 women) and AUD patients with a dual diagnosis (n = 171; 125 men and 46 women). Such differences between the number of recruited men and women may be explained to the fact that AUD men tend to ask for help more often than AUD women [42] even though the same women could show a more serious psychiatric condition [43].

The 171 AUD patients with dual diagnosis present-

Table 1
Description of the two groups of AUD patients with and without dual diagnosis divided for gender, enrolled in the study. Data are expressed as means ± SD, as median or as percentage. CAD = cumulative abstinence duration; SES = socio-economic status (1 up to 5000 euro per year; 2 from 5000 to 10 000 euro; 3 from 10 000 to 20 000; 4 over 20 000). According to NIAAA for men alcohol risk consumption begins with more than 4 drinks on any single day and more than 14 drinks per week. 1 drink = 12 g of alcohol in Italy. For the Educational Level, 1 represents no scholastic degree, 2 Primary School (8 years of compulsory formal education), 3 Secondary School (5 years of formal education), 4 University degree

	AUD patient without dual diagnoses		AUD patient with dual diagnoses	
	Men (n = 58)	Women (n = 16)	Men (n = 125)	Women (n = 46)
Age	48.40 ± 9.76	49.79 ± 10.25	46.65 ± 11.25	47.61 ± 10.35
Educational level [1 low – 4 high]	2.11 ± 0.49	2.33 ± 0.62	2.30 ± 0.69	2.44 ± 0.62
SES [1 low – 4 high]	2.24 ± 0.31	2.43 ± 0.18	2.34 ± 0.35	2.28 ± 0.28
Age of first consumption	28.97 ± 10.78	31.38 ± 9.26	26.89 ± 10.68	32.93 ± 11.58
Years of critical consumption	19.52 ± 14.01	16.50 ± 10.98	19.20 ± 13.26	14.23 ± 11.09
Alcohol preference (%)				
wine	50.3	44.1	52.6	44.6
beer	30.9	28.5	31.6	29.4
spirit	15.8	25.8	16.4	27.4
Abstinence days before the test [CAD]	5.63 ± 8.976	9.33 ± 11.672	5.11 ± 7.964	5.64 ± 7.312
Previous use of psychoactive substances [%]	30.9	17.1	32.1	16.3
Smoking [daily number of cigarettes]	17.8 ± 11.76	16.43 ± 11.98	17.1 ± 11.95	16.75 ± 12.78

ed different psychiatric conditions: most of them, the 49.7%, present a bipolar disorder followed by the 28.8% that present a mood disorder, the 8.9% present an anxiety disorder, the 8.8% present a personality disorder. Only the 2.3% present psychotic symptomatology and the 1.5% present adjustment disorders.

Table 1 shows also the differences in the sociodemographic and alcohol variables between the two groups of AUD patients with and without a dual diagnosis for gender.

Exclusion criteria for all participants included history of head injury, loss of consciousness, history of organic mental disorder, present assumption of psychoactive drugs as cocaine, opioids, amphetamine, other recreational drugs, anxiolytics, euphorants, antipsychotics, barbiturates, antidepressants, hallucinogens-data based on urine toxicology), seizure disorder or central nervous system diseases and no sign of hypertension at the time of recruitment. Breath alcohol level was measured by using Alcoscan AL7000. During the 15-day long hospitalization period, alcohol consumption was also analyzed by the presence of Ethylglucuronide in the urine [44]. Psychiatric examination and self-administered interviews were carried out between day 7 and day 8 of the two weeks day-hospital period. The study was approved by the University Hospital ethical committee and informed consent was signed by each participant and all the study procedures were in accordance with the Helsinki Declaration of 1975, as revised in 1983, for human experimentation. The clinical diagnosis for dual diagnosis and the clinical diagnosis for alcohol addiction were carried out by different specialists unaware of the final group assignment of the patients according to the psychological and cognitive assessments by self-report questionnaires (see below).

Clinical assessment for a dual diagnosis

Psychiatric examination by DSM-5 criteria for dimensional assessment and diagnosis of mental disorders (based on descriptions, symptoms and other criteria for diagnosing mental disorders) [45] in AUD people was carried out to assess the presence of psychiatric disorders. A psychiatric examination was carried out between day 7 and day 8 of the 15-day long day-hospital period for a first diagnostic orienting as stated before. Then, the psychiatrist, when the patients concluded the detox period, performs a second evaluation to confirm or modify the diagnosis (between day 15 and 20 after the end of the day-hospital). The last diagnosis was used to confirm the classification of the two groups of AUD patients without and with dual diagnosis.

Clinical assessment for alcohol dependence

AUD magnitude and the lifetime alcohol consumption were assessed by clinicians by using LDH, TLFB and the DSM-5 Severity Scale for Alcohol Use Disorder.

LDH [46] is a retrospective, interview-based procedure, used to identify patterns of alcohol use, abuse, and dependence beginning with the onset of regular drinking and ending with the individual's current drinking pattern [46-48].

TLFB [49, 50] is used as a clinical and research tool

to obtain a variety of quantitative estimates of alcohol and other drugs' use in the last month.

Both LDH and TLFB were administered by physicians with a long-lasting experience on alcohol addiction after the disappearing of the withdrawal symptoms according to a set of specific evidence, such as elevated blood pressure, tachycardia, tremor, sweating and no alcohol presence (see also the above-described methods).

The DSM-5 diagnostic criteria for alcohol use disorder [45] is used to designate mild (2-3), moderate (4-5), and severe (≥ 6) dependence. The AUD diagnosis was determined by analysing the number of AUD criteria of the past 12 months. DSM-5 defined AUD symptoms included: 1) tolerance, 2) withdrawal, 3) substance taken in larger amounts/longer period than intended, 4) persistent desire or unsuccessful attempts to decrease/control use, 5) a great deal of time spent obtaining, using or recovering from effects of alcohol, 6) social, occupational, or recreational activities given up or reduced because of use, 7) use despite knowledge of physical or psychological problems caused or exacerbated by use, 8) recurrent failure to fulfil major role obligations, 9) recurrent use in hazardous situations, 10) craving/strong desire to use the substance, 11) continued use despite social/interpersonal problems.

Psychological and cognitive assessments by self-report questionnaires

Self-report measures were carried out to investigate the psychological and cognitive functioning and the severity of the dependence. AUD people provided different self-report assessments under the supervision of a psychologist with a long-lasting training in alcohol addiction. In particular, we analysed the mini-mental state examination (MMSE), the vocabulary subtest of the WAIS-R, the SCL-90-R and the SADQ.

The MMSE [51] is a brief 30-point questionnaire, the most frequently used assessment methods for the estimation of cognitive function, and it has been shown to have adequate reliability and validity to screen for cognitive impairment. The raw score needs to be corrected for educational attainment and age [52].

The vocabulary subtest of the WAIS-R [53] is considered to be one of the best indicators of general intelligence and is used to assess the verbal intellectual functioning in clinical practice. The WAIS-R vocabulary subtest consists of the meaning definition of 40 words.

The SCL-90-R [54] is a 90-item self-report symptom inventory designed to reflect psychological symptom patterns of psychiatric and medical patients. Each item of the questionnaire is rated on a 5-point scale of distress from 0 (none) to 4 (extreme). The SCL-90-R used in the present investigation consists of the following nine primary symptom dimensions and a global severity index (GSI): somatization (SOM, which reflects distress arising from bodily perceptions), obsessive-compulsive (OC, which reflects obsessions-compulsions symptoms), interpersonal sensitivity (IS, which reflects feelings of personal inadequacy and inferiority in comparison with others), depression (DEP, which reflects depressive symptoms, as well as lack of motivation), anxiety (ANX, which reflects anxiety symptoms and ten-

sion), hostility (HOS, which reflects thoughts, feelings, or actions that are characteristic of negative affective states of anger, aggression, irritability, rage, and resentment), phobic anxiety (PHO, which reflects symptoms of persistent fears as responses to specific conditions), paranoid ideation (PAR, which reflects symptoms of projective thinking, hostility, suspiciousness, and fear of loss of autonomy), and psychoticism (PSY, which reflects a broad range of symptoms from mild interpersonal alienation to dramatic evidence of psychosis) [32, 55, 56]. The SCL-90-R presents three global indices: global severity index (GSI) designed to measure overall psychological distress; positive symptom distress index (PSDI) designed to measure the intensity of symptoms and positive symptom total (PST) reporting the number of self-reported symptoms. However, the GSI is the single best indicator of the current level or depth of an individual's disorder. It combines information concerning the number of symptoms reported with the intensity of perceived distress. The SCL-90-R takes between 12 and 20 min to complete. The internal consistency coefficient α values for the nine symptom dimensions ranged from a low of 0.77 for psychoticism to a high of 0.90 for depression. In an Italian study, the internal coherence for all subscales showed alpha values ranging between 0.70 and 0.96 [57]. Based on the Italian version of the SCL-90-R [58] the *T* cut-off level used in the present study to discriminate AUD people with dual diagnosis vs AUD without dual diagnosis people was set to $T \geq 55$ in the GSI score. The SCL-90-R was completed in the presence of psychologists who provided clarifications when necessary.

The SADQ [33, 59, 60] is a short, easy-to-complete, self-administered, 20-items questionnaire designed to measure the severity of dependence on alcohol as formulated by Edwards & Gross [61]. There are five subscales each including four items: physical withdrawal, affective withdrawal, withdrawal relief drinking, alcohol consumption, and rapidity of reinstatement. The physical withdrawal, withdrawal relief drinking, alcohol consumption, and rapidity of reinstatement subscales are specially focused on the physical aspects of alcohol dependence while the affective withdrawal subscales refers to affective aspects of alcohol dependence. Each item is scored on a 4-point scale, ranging from almost never to nearly always, resulting in a corresponding score of 0 to 3. Thus, the total maximum score possible is 60 and the minimum is 0 [33, 62]. A score greater than 30 indicates severe alcohol dependence; scores ranging from 16 and 30 indicate the presence of moderate alcohol dependence. Above 16 a mild dependence was assessed [63].

Statistical analysis

Data were analyzed using SPSS. Descriptive analyses were conducted to evaluate the characteristics of the enrolled participants. TLFB, LDH, SCL-90-R, SADQ and DSM-5 data were analyzed by two-way ANOVA to determine differences between AUD people with or without a dual diagnosis. Gender differences were also considered as a main factor. Post-hoc comparisons were carried out by using the LSD testing. Pearson bivar-

ate correlations were calculated between SADQ scores and psychopathological indicators and alcohol variables (years of alcohol abuse, the age of onset, total alcoholic units in the last month, the daily alcoholic units in the last month).

RESULTS

Sample characteristics

AUD people characteristics are described in Table 1. All recruited AUD people fulfilled the criteria for severe alcohol dependence (8.84 ± 1.99 – mean number of DSM-5 positive criteria) as assessed by using DSM-5 criteria and resulting heavy drinkers according to NIAAA (14.38 ± 11.16 – mean number of daily alcohol units).

AUD people were compared for gender in all investigated parameters (see Table 2). Since no statistical differences were found between males and females in the analysed factors, except, as expected, for the drunk alcoholic units (higher in men) and the depression dimension of the SCL-90-R (elevated in women), the gender factor was not considered in the other reported results.

Dual diagnosis and drinking parameters

AUD with dual diagnosis and AUD people without dual diagnosis did not differ in alcohol consumption habits resulting, however, both groups heavy drinkers according to the NIAAA criteria (daily alcohol units: 15.06 ± 11.57 vs 12.79 ± 10.06 and monthly alcohol units consumed: 425.94 ± 322.95 vs 365.97 ± 279.43 respectively). Moreover, AUD with dual diagnosis and AUD people without dual diagnosis displayed comparable addiction severity (9.09 ± 2.07 vs 8.18 ± 1.59 – mean number of DSM-5 positive criteria).

SCL-90-R scores and SADQ

Table 3 shows the relationship between the levels of dependence measured by SADQ (mild, moderate and severe) and the SCL-90-R primary symptoms and the GSI. AUD patients with severe dependence had significantly higher mean scores in the psychopathological SCL-90-R domains.

Post-hoc tests show that somatization, depression, hostility, paranoid ideation, psychoticism, obsessive-compulsive, interpersonal sensitivity, anxiety and the GSI were significantly higher in AUD people with severe and moderate dependence when compared with mild dependence ($ps < 0.05$). Post-hocs also reveal differences between moderate and mild addiction in somatization, obsessive-compulsive, interpersonal sensitivity, anxiety, hostility and the GSI ($ps < 0.05$).

SCL-90-R scores and psychiatric examination

Table 4 shows the ANOVA data between SCL-90-R scores, as dependent variables, and the psychiatric examination by a specialist in order to disclose AUD people with dual diagnosis and AUD people without a dual diagnosis. The results evidence significant differences between the two groups for each dimension ($ps < 0.01$ in the ANOVA) with the highest values in AUD patients with dual diagnosis.

Table 2

Differences between AUD patients without and with dual diagnosis for gender in self report measures

	AUD patient without dual diagnoses		AUD patient with dual diagnoses	
	Men (n = 58)	Women (n = 16)	Men (n = 125)	Women (n = 46)
DSM 5 severity criteria	8.40 ± 1.45	6.50 ± 2.12	9.09 ± 1.77	9.08 ± 2.78
MMSE	15.25 ± 4.74	14.68 ± 3.98	15.56 ± 3.99	15.45 ± 2.63
WAIS	29.80 ± 17.18	32.68 ± 20.35	35.47 ± 14.50	41.98 ± 14.53
SCL-90-R somatization	0.44 ± 0.45	0.50 ± 0.54	0.74 ± 0.67	0.85 ± 0.68
SCL-90-R obsessive compulsive	0.66 ± 0.55	0.58 ± 0.43	1.13 ± 0.72	1.23 ± 0.81
SCL-90-R interpersonal sensitivity	0.44 ± 0.44	0.45 ± 0.54	0.75 ± 0.64	0.90 ± 0.65
SCL-90-R depression	0.56 ± 0.46	0.59 ± 0.56*	0.95 ± 0.63	1.29 ± 0.83*
SCL-90-R anxiety	0.43 ± 0.47	0.54 ± 0.52	0.89 ± 0.64	0.91 ± 0.66
SCL-90-R hostility	0.28 ± 0.40	0.36 ± 0.38	0.63 ± 0.66	0.66 ± 0.77
SCL-90-R phobic anxiety	0.21 ± 0.28	0.23 ± 0.25	0.42 ± 0.51	0.38 ± 0.46
SCL-90-R paranoid ideation	0.52 ± 0.48	0.68 ± 0.68	0.86 ± 0.64	1.07 ± 0.79
SCL-90-R psychoticism	0.38 ± 0.40	0.45 ± 0.47	0.70 ± 0.66	0.89 ± 0.75
SCL-90-R GSI	0.48 ± 0.36	0.52 ± 0.42	0.84 ± 0.53	0.96 ± 0.58
SADQ physical withdrawal	3.89 ± 3.27	2.87 ± 3.36	4.83 ± 3.26	5.35 ± 3.40
SADQ affective withdrawal	1.86 ± 2.01	2.81 ± 3.82	3.78 ± 3.37	5.00 ± 4.16
SADQ withdrawal relief drinking	3.62 ± 4.29	2.19 ± 3.85	5.75 ± 4.41	5.24 ± 5.03
SADQ alcohol consumption	4.29 ± 2.31	3.94 ± 2.46	5.60 ± 3.38	4.89 ± 3.34
SADQ rapidity of reinstatement	3.24 ± 2.92	2.63 ± 2.83	5.03 ± 3.46	5.59 ± 3.80
SADQ total	16.93 ± 11.23	14.44 ± 9.58	14.44 ± 9.58	26.04 ± 15.95

SCL-90-R: symptom check list 90-R.

Table 3

SCL-90-R primary symptom dimensions and SADQ dependence levels (mean ± SD). # p < 0.05 Severe vs moderate/mild; § p < 0.05 moderate vs mild

SCL-90-R	Total SADQ n = 245	SADQ Mild dependence (Score range 0-15) n = 93	SADQ Moderate dependence (Score range 16-30) n = 88	SADQ Severe dependence (Score > 30) n = 64	F(df)	p
Somatization	0.68 ± 0.64	0.49 ± 0.48	0.81 ± 0.70§	0.76 ± 0.68	6.479(2,244)	= 0.002
Obsessive compulsive	1.00 ± 0.72	0.78 ± 0.62	1.10 ± 0.77§	1.18 ± 0.73	7.316(2,244)	= 0.001
Interpersonal sensitivity	0.68 ± 0.61	0.50 ± 0.49	0.75 ± 0.66§	0.86 ± 0.65	7.693(2,244)	= 0.001
Depression	0.90 ± 0.68	0.73 ± 0.65	0.97 ± 0.72	1.06 ± 0.62	5.431(2,244)	= 0.005
Anxiety	0.76 ± 0.63	0.52 ± 0.53	0.86 ± 0.66§	0.97 ± 0.64	12.007(2,244)	< 0.001
Hostility	0.54 ± 0.63	0.41 ± 0.55	0.65 ± 0.70§	0.55 ± 0.63	3.445(2,244)	= 0.033
Phobic anxiety	0.35 ± 0.45	0.23 ± 0.35	0.35 ± 0.39	0.52 ± 0.58#	8.414(2,244)	< 0.001
Paranoid ideation	0.81 ± 0.67	0.68 ± 0.61	0.83 ± 0.67	0.96 ± 0.72	3.682(2,244)	= 0.027
Psychoticism	0.65 ± 0.64	0.50 ± 0.57	0.71 ± 0.62	0.78 ± 0.72	4.485(2,244)	= 0.012
GSI	0.76 ± 0.53	0.58 ± 0.46	0.84 ± 0.56§	0.91 ± 0.53	9.748(2,244)	< 0.001

SADQ: severity of alcohol dependence questionnaire; SCL-90-R: symptom check list 90-R.

Psychiatric examination and SADQ scores

ANOVA considering AUD people with dual diagnosis vs AUD people without dual diagnosis and the SADQ total score as dependent variable shows that

AUD patients with dual diagnosis had significantly ($F(1,244) = 23.101$; $p < 0.001$) higher mean scores of total SADQ (25.30 ± 14.25) compared to AUD people without dual diagnosis (16.39 ± 10.88 respectively).

Table 4
SCL- 90-R Scores and Psychiatric Examination (mean \pm SD)

SCL-90-R	Psychiatric examination		F	p
	Non-psychiatric AUD patients n = 74	Psychiatric AUD patients n = 171		
Somatization	0.46 \pm 0.47	0.77 \pm 0.67	13.599	< 0.001
Obsessive compulsive	0.65 \pm 0.52	1.15 \pm 0.75	28.758	< 0.001
Interpersonal sensitivity	0.45 \pm 0.46	0.79 \pm 0.64	17.212	< 0.001
Depression	0.57 \pm 0.48	1.04 \pm 0.70	27.720	< 0.001
Anxiety	0.45 \pm 0.48	0.90 \pm 0.65	27.815	< 0.001
Hostility	0.30 \pm 0.40	0.64 \pm 0.69	15.855	< 0.001
Phobic anxiety	0.21 \pm 0.27	0.41 \pm 0.49	9.935	= 0.002
Paranoid ideation	0.55 \pm 0.53	0.92 \pm 0.69	16.011	< 0.001
Psychoticism	0.40 \pm 0.41	0.75 \pm 0.69	16.877	< 0.001
GSI	0.49 \pm 0.37	0.88 \pm 0.54	30.975	< 0.001

SCL-90-R: symptom check list 90-R.

The emerging finding from the SADQ scales and the psychiatric evaluation clearly demonstrates that AUD people with dual diagnosis describe themselves affected by a more severe alcohol dependence than AUD people without a dual diagnosis.

Comparable results were found in the SADQ subscales: patients with dual diagnosis referred to higher levels of physical withdrawal (4.97 ± 3.29 vs 3.68 ± 3.29), affective withdrawal (4.11 ± 3.63 vs 2.07 ± 2.51), withdrawal relief drinking (5.61 ± 4.58 vs 3.31 ± 4.23), alcohol consumption (5.41 ± 3.38 vs 4.22 ± 2.33), and rapidity of reinstatement (5.18 ± 3.55 vs 3.11 ± 2.89) compared to AUD patients without dual diagnosis ($p < 0.05$).

SADQ/SCL-90-R and drinking parameters (TLFB/LDH)

Figure 1 shows the relationships between the SCL-90-R, the SADQ and the drinking parameters measured by TLFB. Indeed, correlations reveal that the total score of SADQ positively correlates in all AUD patients with the alcoholic units totally consumed ($r = 0.301$; $p \leq 0.001$) and the daily alcoholic units consumed in the last month ($r = 0.284$; $p \leq 0.001$) when

measured by TLFB. No correlations were found with the drinking parameters evaluated by LDH.

Relatively to the SADQ subscales (Figure 2) the correlations demonstrate that the Withdrawal Relief Drinking and Alcohol Consumption subscales were significantly and positively associated with the alcoholic units totally consumed and the alcoholic units consumed daily in the last month. No relationship was found between total and daily alcoholic units and Affective Withdrawal and Rapidity of Reinstatement subscales. Significant negative correlations were observed between SADQ total scores, physical withdrawal, alcohol consumption and the age of onset of alcohol problems (see plots of Figure 2). No relationship was found between SADQ total scores/SADQ subscales with the years of at-risk drinking.

Quite interestingly, no correlations were found between SCL-90-R and the drinking parameters of the TLFB/LDH (alcohol unit/daily, alcohol unit/monthly, age of alcohol onset and years of at risk drinking). Furthermore, no evidence was found between psychiatric examination and the drinking parameters of the TLFB/LDH.

SCL-90-R and SADQ subscales

Table 5 indicates the correlation between the symptoms' scales of SCL-90-R and the SADQ subscales. Data shows that affective withdrawal, physical withdrawal and rapidity of reinstatement subscales of SADQ were significantly and positively associated with the GSI of the SCL-90-R. No relationship was found between SADQ alcohol consumption and withdrawal relief drinking subscales and GSI.

DISCUSSION

In the present study, we evaluated the relationship between the AUD severity and the presence of psychiatric comorbidity. Serious AUD patients with dual diagnosis are more at-risk of relapse and abandonment of treatment. The psychometric tools used to assess the magnitude of addiction are mainly self-reported interviews,

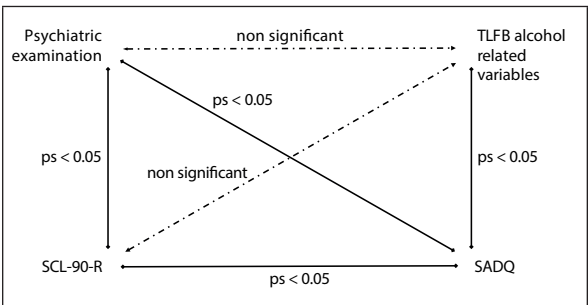


Figure 1
Picture illustrating the connections and statistical significance between SCL-90-R, SADQ, TLFB alcohol related variables and psychiatric examination.

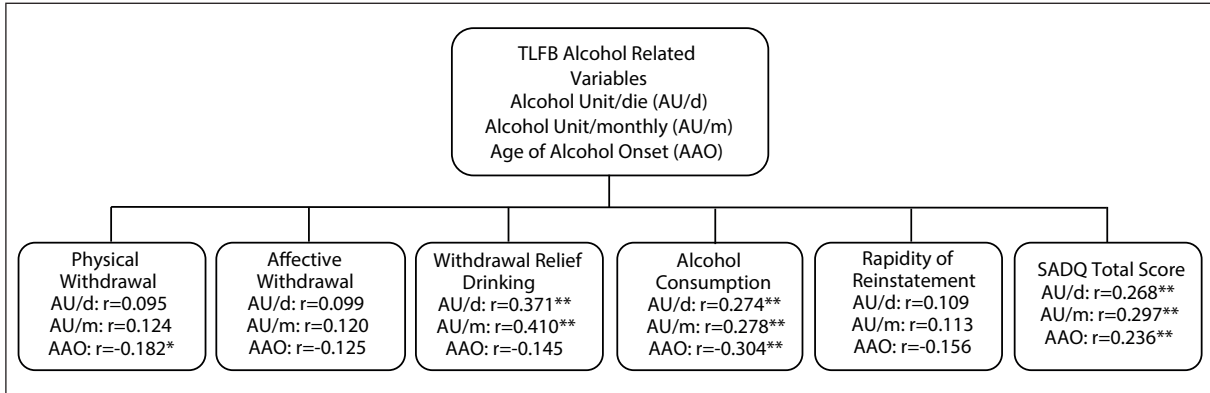


Figure 2
The figure shows the relationship between TLFB alcohol drinking variables and SADQ subscales.
** = $p < 0.01$; * = $p < 0.05$

Table 5
The table shows the correlation between SCL-90-R and SADQ by Pearson's analysis. Asterisks indicates correlation at 0.05 (*) and 0.01 (**)

	SADQ physical withdrawal	SADQ affective withdrawal	SADQ withdrawal relief drinking	SADQ alcohol consumption	SADQ rapidity of reinstatement	SADQ total score
SCL-90-R Somatization	0.204**	0.170**	0.131*	0.187**	0.210**	0.229**
SCL-90-R Obsessive compulsive	0.238**	0.274**	0.141*	0.130*	0.281**	0.270**
SCL-90-R Interpersonal sensitivity	0.183**	0.279**	0.157*	0.133*	0.234**	0.253**
SCL-90-R Depression	0.171**	0.241**	0.131*	0.085	0.222**	0.218**
SCL-90-R Anxiety	0.243**	0.285**	0.232**	0.136*	0.315**	0.314**
SCL-90-R Hostility	0.091	0.073	0.069	0.031	0.160*	0.108
SCL-90-R Phobic anxiety	0.210**	0.232**	0.198**	0.179**	0.230**	0.271**
SCL-90-R Paranoid ideation	0.141*	0.191**	0.116	0.105	0.159*	0.182**
SCL-90-R Psychoticism	0.160*	0.272**	0.103	0.085	0.180**	0.203**
SCL-90-R GSI	0.234**	0.277**	0.177**	0.156*	0.283**	0.288**

SADQ: severity of alcohol dependence questionnaire; SCL-90-R: symptom check list 90-R

with the exception of the severity scale of DSM-5 and of the anamnestic instruments based on the frequency and the quantities of alcohol consumption, which are instead detected by the clinician. In the present investigation, we found that there are no differences between AUD people with dual diagnosis and AUD people without dual diagnosis based on the amount of alcohol drunk and on the severity highlighted by DSM-5. Indeed, our patients were all heavy drinkers, however, is that despite the dual and non-dual AUD patients do not show differences in the alcohol parameters or even in the observation of the clinician, dual AUD patients report a higher gravity of SADQ dependence.

As highlighted in the results section, we evaluated the presence of a psychiatric disorder either through a self-report tool, the SCL-90-R, or through a psychiatric examination and in both cases AUD patients describe themselves as more severe at SADQ. We used the two methods because the SCL-90-R, despite being used in other studies previously conducted [56, 57], is a screening questionnaire that identifies the presence of psycho-

logical distress, while obviously, the psychiatric interview conducted on the criteria of the DSM-5 allows to the clinician to be able to make an affordable diagnosis.

Although self-report instruments may offer a rapid method to collect information, their use also reveals certain disadvantages [64]. One is that they are vulnerable to the consequences of social desirability biases. Patients tend to present themselves in a favorable way, especially when they are asked to make judgments about attitudes and traits that are negatively valued [64]. Another self-report instruments' limit is that they necessarily rely on information that is consciously accessible to the person. This problem, known as the introspective restriction, has a significant impact on the information reliability obtained using self-report instruments [65]. Based on these biases, to investigate the association between alcohol addiction and psychiatric associated diseases, we used other tools as the DSM-5 criteria by a specialist examination, to further assess psychiatric associated disorders and LDH and TLFB to assess alcohol consumption. These latest semi-struc-

tured tools have the highest quality to assess alcohol consumption using several memory aids to enhance recall in which the clinicians have a facilitator role [46, 66]. Obviously, information on alcohol drinking behavior obtained using TLFB and LDH are not a specific measure of dependence severity, but they certainly offer crucial information on the nature of patient alcohol behavioral relationship [67].

In particular, we found that, by using DSM-5 criteria, AUD people with a positive psychiatrist diagnosis, as shown by psychiatrist examination, had higher SADQ subscales mean scores compared with AUD patients negative to psychopathology. Intriguingly, when analyzing the alcohol consumption measured by the clinicians (TLFB and LDH), no correlations were found between SCL-90-R and alcohol drinking, as emerged by TLFB and LDH, and no differences were found in drinking habits between patients with or without psychiatric associated disorders assessed by psychiatrist examination because the values of alcohol consumption are in AUD people with or without dual diagnosis comparable. Data analyzing SADQ and alcoholic units totally consumed and the daily alcoholic units consumed in the last month by TLFB disclosed significant correlations.

Investigating the different dimensions of the dependence levels by SADQ we found that the dimensions most closely related to the physical size of addiction (physical withdrawal, withdrawal relief drinking and alcohol consumption) correlate with the quantities of alcohol consumed. However, when we aimed to evaluate the relationship between the SADQ subscales and the SCL-90-R scales correlations with the affective withdrawal, physical withdrawal and rapidity of reinstatement scales were revealed. Finally, the association between the psychiatric examination and the SADQ subscales clearly demonstrates that AUD patients with dual diagnosis describe themselves as more affected in all dimensions.

To further investigate the relationship between psychiatry, the severity of dependence and alcohol variables, we considered how the five SADQ subscales (physical withdrawal, affective withdrawal, withdrawal relief drinking, alcohol consumption, and rapidity of reinstatement) were related to SCL-90-R and alcohol drinking variables. We found that alcohol drinking behavioral variables were significantly and positively associated with physical withdrawal and alcohol consumption SADQ subscales and the total SADQ score whereas no relationships were found with affective withdrawal, withdrawal relief drinking and rapidity of reinstatement SADQ subscales. By contrast, affective withdrawal, physical withdrawal and relief rapidity of reinstatement SADQ subscales correlated with SCL-90-R GSI while no relationship was found between alcohol consumption and withdrawal relief drinking SADQ subscales and SCL-90-R GSI.

These findings clearly show that *i*) the GSI of SCL-90-R correlates mainly with the affective behavior subscales of SADQ and less with the physical aspects of SADQ subscales; *ii*) intriguingly, the alcoholic units consumed by AUD people are mainly linked with the

physical aspects of SADQ subscales and less with the affective behavior subscales; *iii*) SADQ, although is one of the most widely used questionnaires and recommended by the guidelines, suffers a bias due to the patient's psychiatric conditions. The SADQ specifically captures the perception of the severity of addiction that in patients with dual diagnosis such perception is emphasized and considered more disabling and suffering. However, it should be noted that AUD patients with a dual diagnosis perceiving a greater amount of stress due to their psychopathology feel more dramatically the compulsive phase of dependence, while the SADQ self-responses differs from the measures obtained by the specialist examination where the operator discloses the data on consumption without considering the emotional part related to consumption.

Although many environmental, social, genetic, physiological and neurobiological factors have been shown to contribute to the gender difference in response to alcohol induced damage [68, 69], our study did not disclose gross sex differences in behavioral responses. Nonetheless, the subject of drinking abuse in women is quite significant since women are more sensitive compared to men to the harm induced by ethanol [70, 71] and because women who drink during gestation may stimulate a variety of damaging effects to the fetus named Fetal Alcohol Spectrum Disorders (FASD) [42, 70-82 as also shown in 73, 78, 83-86].

CONCLUSION

In conclusion, the strength of the present study is that by analyzing 245 AUD patients with or without a dual diagnosis, those with dual diagnosis appear to emphasize the emotional aspects of their addiction based on the SADQ results. Psychiatric comorbidity is a crucial issue among patients suffering AUD because increases the risk of relapse [87, 88] making more arduous the therapeutic intervention [89-97]. Our data suggest that an overestimated self-perception of addiction for alcohol, as measured by SADQ, may represent a useful prognostic index to relapse but only for patients with dual diagnosis. A careful analysis of the SADQ affective subscales could reveal in AUD people with a dual diagnosis a disrupted addiction self-perception, information that could be used as a warning signal for treating not only dependence per se but, particularly, the psychopathological associated diseases to properly address pharmacological intervention [98, 99].

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Conflict of interest statement

Authors do declare that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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REFERENCES

- Coriale G, Bilotta E, Leone L, Cosimi F, Porrari R, De Rosa F, et al. Avoidance coping strategies, alexithymia and alcohol abuse: A mediation analysis. *Addict Behav.* 2012;37:1224-9. doi:10.1016/j.addbeh.2012.05.018
- Grant B, Stinson F, Dawson D, Chou S, Dufour M, Compton W, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: Results from the national epidemiologic survey on alcohol and related conditions. *Alcohol Res Heal.* 2004;29:807-16. doi:10.1001/archpsyc.61.8.807
- Ledda R, Battagliese G, Attilia F, Rotondo C, Pisciotto F, Gencarelli S, et al. Drop-out, relapse and abstinence in a cohort of alcoholic people under detoxification. *Physiol Behav.* 2019;198:67-75. doi:10.1016/j.physbeh.2018.10.009
- Iannitelli A, Castra R, Antenucci M. Doppia diagnosi o comorbidità? Definizioni e osservazioni cliniche. *Ann Ist Super Sanità.* 2002;38:233-9.
- Ciafrè S, Carito V, Ferraguti G, Greco A, Chaldakov GN, Fiore M. How Alcohol drinking affects our genes: an epigenetic point of view. *Biochem Cell Biol. Press n.d.* doi:10.1139/bcb-2018-0248
- Grant BF, Stinson FS, Dawson DA, Chou SP, Ruan WJ, Pickering RP. Co-occurrence of 12-month alcohol and drug use disorders and personality disorders in the United States. *Arch Gen Psychiatry.* 2004;61:361-8. doi:10.1001/archpsyc.61.4.361
- Helzer JE, Pryzbeck TR. The co-occurrence of alcoholism with other psychiatric disorders in the general population and its impact on treatment. *J Stud Alcohol.* 1988;49:219-24. doi:10.15288/jsa.1988.49.219
- Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. *Arch Gen Psychiatry.* 1994;51:8-19. doi:10.1001/archpsyc.1994.03950010008002
- Kessler RC, Crum RM, Warner LA, Nelson CB, Schulenberg J, Anthony JC. Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comorbidity Survey. *Arch Gen Psychiatry.* 1997;54:313-21. doi:10.1001/archpsyc.1997.01830160031005
- Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. *JAMA.* 1990;264:2511-8. doi:10.1001/jama.1990.03450190043026
- Rich SD, Riley LJ. Neurodevelopmental Disorder Associated with Prenatal Alcohol Exposure: Consumer Protection and the Industry's Duty to Warn. *Cham: Springer;* 2016. p. 39-47. doi:10.1007/978-3-319-20866-4_3
- Stewart SH. Alcoholics in acute medical settings have increased risk for other drug, mood, and personality disorders. *Int J Psychiatry Med.* 2007;37:59-67. doi:10.2190/E075-04TK-2N6J-1RH5.
- Cloninger CR. Neurogenetic adaptive mechanisms in alcoholism. *Science.* 1987;236:410-6. doi:10.1126/science.2882604
- Gulec Oyekcin D, Gurgun A. Is cloninger type 1 and type 2 alcoholism differ in terms of emotion regulation? *Eur Psychiatry.* 2017;41:S863-4. doi:10.1016/j.EURPSY.2017.01.1727
- Driessen M, Veltrup C, Wetterling T, John U, Dilling H. Axis I and axis II comorbidity in alcohol dependence and the two types of alcoholism. *Alcohol Clin Exp Res.* 1998;22:77-86. doi:10.1097/00000374-199802000-00009
- Echeburúa E, De Medina BR, Aizpiri J. Alcoholism and personality disorders: an exploratory study. *Alcohol Alcohol.* 2005;40:323-6. doi:10.1093/alcalc/agh158
- Ipser JC, Wilson D, Akindipe TO, Sager C, Stein DJ. Pharmacotherapy for anxiety and comorbid alcohol use disorders. In: Ipser JC (Ed). *Cochrane Database Syst. Rev., Vol. 1.* Chichester, UK: John Wiley & Sons, Ltd; 2015. p. CD007505. doi:10.1002/14651858.CD007505.pub2
- Karpyak VM, Biernacka JM, Geske JR, Abulseoud OA, Brunner MD, Chauhan M, et al. Gender-specific effects of comorbid depression and anxiety on the propensity to drink in negative emotional states. *Addiction.* 2016;111:1366-75. doi:10.1111/add.13386
- Swendsen JD, Merikangas KR. The comorbidity of depression and substance use disorders. *Clin Psychol Rev.* 2000;20:173-89. doi:10.1016/S0272-7358(99)00026-4
- Tragesser SL, Trull TJ, Sher KJ, Park A. Drinking motives as mediators in the relation between personality disorder symptoms and alcohol use disorder. *J Pers Disord.* 2008;22:525-37. doi:10.1521/pedi.2008.22.5.525
- Verheul R. Co-morbidity of personality disorders in individuals with substance use disorders. *Eur Psychiatry.* 2001;16:274-82. doi:10.1016/S0924-9338(01)00578-8
- Stewart SH. Alcoholics in acute medical settings have increased risk for other drug, mood, and personality disorders. *Int J Psychiatry Med.* 2007;37:59-67. doi:10.2190/E075-04TK-2N6J-1RH5
- Ciafrè S, Carito V, Tirassa P, Ferraguti G, Attilia ML, Ciolli P, et al. Ethanol consumption and innate neuro-immunity. *Biomed Rev.* 2018;28:49-61. doi:10.147848/bmw.v28.4451
- Ciafrè S, Fiore M, Ceccanti M, Messina MP, Tirassa P, Carito V. Role of neuropeptide tyrosine (NPY) in ethanol addiction. *Biomed Rev.* 2017;27:27-40. doi:10.147848/bmw.v27.2110
- Di Sclafani V, Finn P, Fein G. Psychiatric comorbidity in long-term abstinent alcoholic individuals. *Alcohol Clin Exp Res.* 2007;31:795-803. doi:10.1111/j.1530-0277.2007.00361.x
- Bischof G, Rumpf H-J, Meyer C, Hapke U, John U. Influence of psychiatric comorbidity in alcohol-dependent subjects in a representative population survey on treatment utilization and natural recovery. *Addiction.* 2005;100:405-13. doi:10.1111/j.1360-0443.2005.01008.x
- Greenfield SF, Weiss RD, Muenz LR, Vagge LM, Kelly JF, Bello LR, et al. The effect of depression on return to drinking: a prospective study. *Arch Gen Psychiatry.* 1998;55:259-65. doi:10.1001/archpsyc.55.3.259
- Morley KC, Baillie A, Sannibale C, Teesson M, Haber PS. Integrated care for comorbid alcohol dependence and anxiety and/or depressive disorder: study protocol for an assessor-blind, randomized controlled trial. *Addict Sci Clin Pract.* 2013;8:19. doi:10.1186/1940-0640-8-19
- Booth PG. Maintained controlled drinking following severe alcohol dependence--a case study. *Br J Addict.* 1990;85:315-22; discussion 323-8. doi:10.1111/j.1360-0443.1990.tb00641.x
- Langenbucher J, Sulesund D, Chung T, Morgenstern J. Illness severity and self-efficacy as course predictors of DSM-IV alcohol dependence in a multisite clinical sample. *Addict Behav.* 1996;21:543-53. doi:10.1016/0306-4603(95)00085-2
- Quartini A, Pacitti F, Bersani G, Iannitelli A. From adolescent neurogenesis to schizophrenia: opportunities,

- challenges and promising interventions. *Biomed Rev*. 2018;28:62. doi:10.14748/bmr.v28.4452
32. Derogatis L. SCL-90-R: symptom checklist-90-R: administration, scoring & procedures manual. 3rd ed. Minneapolis Minn: National Computer Systems Inc.; 1994.
 33. Stockwell T, Murphy D, Hodgson R. The severity of alcohol dependence questionnaire: its use, reliability and validity. *Br J Addict*. 1983;78:145-55. doi:10.1111/j.1360-0443.1983.tb05502.x
 34. Ceccanti M, Sasso GF, Nocente R, Balducci G, Prastaro A, Ticchi C, et al. Hypertension in early alcohol withdrawal in chronic alcoholics. *Alcohol Alcohol*. 2006;41:5-10. doi:10.1093/alcac/agh221
 35. Ewusi-Mensah I, Saunders JB, Johnson RD, Williams R. Alcohol dependence and psychopathology in alcoholic liver disease. *Addiction*. 1986;81:231-5. doi:10.1111/j.1360-0443.1986.tb00321.x
 36. Pradeep RJ, Dhilip AM, Mysore A. Do SADQ and AUDIT identify independent impacts of alcohol abuse - clinical and biochemical markers respectively? *Indian J Psychiatry*. 2015;57:278-83. doi:10.4103/0019-5545.166629
 37. Drummond DC. The relationship between alcohol dependence and alcohol-related problems in a clinical population. *Br J Addict*. 1990;85:357-66. doi:10.1111/j.1360-0443.1990.tb00652.x
 38. Stockwell T, Hodgson R, Edwards G, Taylor C, Rankin H. The development of a questionnaire to measure severity of alcohol dependence. *Br J Addict Alcohol Other Drugs*. 1979;74:79-87.
 39. Ceccanti M, Hamilton D, Coriale G, Carito V, Aloe L, Chaldakov G, et al. Spatial learning in men undergoing alcohol detoxification. *Physiol Behav*. 2015;149:324-30. doi:10.1016/j.physbeh.2015.06.034
 40. Ceccanti M, Coriale G, Hamilton DA, Carito V, Coccorello R, Scalese B, et al. Virtual Morris task responses in individuals in an abstinence phase from alcohol. *Can J Physiol Pharmacol*. 2018;96:128-36. doi:10.1139/cjpp-2017-0013
 41. National Institute on Alcohol Abuse and Alcoholism. Alcohol facts and statistics fact sheet. n.d.
 42. Mangrum LF, Spence RT, Steinley-Bumgarner MD. Gender differences in substance-abuse treatment clients with co-occurring psychiatric and substance-use disorders. *Br Treat Cris Interv*. 2006;6:255-67. doi:10.1093/brief-treatment/mhl006
 43. Frem Y, Torrens M, Domingo-Salvany A, Gilchrist G. Gender differences in lifetime psychiatric and substance use disorders among people who use substances in Barcelona, Spain. *Adv Dual Diagn*. 2017;10:45-56. doi:10.1108/ADD-01-2017-0002
 44. Ferraguti G, Ciolli P, Carito V, Battagliese G, Mancinelli R, Ciafrè S, et al. Ethylglucuronide in the urine as a marker of alcohol consumption during pregnancy: Comparison with four alcohol screening questionnaires. *Toxicol Lett*. 2017;275:49-56. doi:10.1016/j.toxlet.2017.04.016
 45. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. American Psychiatric Association; 2013. doi:10.1176/appi.books.9780890425596
 46. Skinner HA, Sheu WJ. Reliability of alcohol use indices. The Lifetime Drinking History and the MAST. *J Stud Alcohol*. 1982;43:1157-70. doi:10.15288/jsa.1982.43.1157
 47. Jacob T, Seilhamer RA, Bargeil K, Howell DN. Reliability of lifetime drinking history among alcohol dependent men. *Psychol Addict Behav*. 2006;20:333-7. doi:10.1037/0893-164X.20.3.333
 48. Koenig LB, Jacob T, Haber JR. Validity of the lifetime drinking history: a comparison of retrospective and prospective quantity-frequency measures. *J Stud Alcohol Drugs*. 2009;70:296-303. doi:10.15288/jsad.2009.70.296
 49. Sobell LC, Ellingstad TP, Sobell MB. Natural recovery from alcohol and drug problems: methodological review of the research with suggestions for future directions. *Addiction*. 2000;95:749-64.
 50. Sobell MB, Sobell LC. Controlled drinking after 25 years: how important was the great debate? *Addiction*. 1995;90:1149-53; discussion 1157-77.
 51. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189-98. doi:10.1016/0022-3956(75)90026-6
 52. Crum RM, Anthony JC, Bassett SS, Folstein MF. Population-based norms for the mini-mental state examination by age and educational level. *JAMA J Am Med Assoc*. 1993;269:2386. doi:10.1001/jama.1993.03500180078038
 53. Wechsler D. Manual for the Wechsler adult intelligence scale-revised (WAIS-R). San Antonio: TX Psychol Corp; 1981.
 54. Derogatis LR. SCL-90-R: symptom checklist-90-R: administration, scoring & procedures manual. 3rd ed. Minneapolis: National Computer Systems; 1994.
 55. Moussas G, Fanouraki I, Pachi A, Asomatou A, Drylli O, Paschalakis G, et al. Comorbid psychopathology and alcohol use patterns among methadone maintenance treatment patients. *J Addict*. 2015;2015:1-10. doi:10.1155/2015/197652
 56. Derogatis LR, Cleary PA. Confirmation of the dimensional structure of the scl-90: A study in construct validation. *J Clin Psychol*. 1977;33:981-9. doi:10.1002/1097-4679(197710)33:4<981::AID-JCLP2270330412>3.0.CO;2-0
 57. Prunas A, Sarno I, Preti E, Madeddu F, Perugini M. Psychometric properties of the Italian version of the SCL-90-R: a study on a large community sample. *Eur Psychiatry*. 2012;27:591-7. doi:10.1016/j.eurpsy.2010.12.006
 58. Sarno I, Preti E, Prunas A, Madeddu F. SCL-90-R Symptom checklist-90-R Adattamento italiano. Firenze: Giunti, Organizzazioni Speciali; 2011.
 59. Stockwell T, Bolt L, Milner I, Russell G, Bolderston H, Pugh P. Home detoxification from alcohol: its safety and efficacy in comparison with inpatient care. *Alcohol Alcohol*. 1991;26:645-50.
 60. Stockwell T, Bolt L, Milner I, Pugh P, Young I. Home detoxification for problem drinkers: acceptability to clients, relatives, general practitioners and outcome after 60 days. *Addiction*. 1990;85:61-70. doi:10.1111/j.1360-0443.1990.tb00624.x
 61. Edwards G, Gross MM. Alcohol dependence: provisional description of a clinical syndrome. *Br Med J*. 1976;1:1058-61. doi:10.1136/bmj.1.6017.1058
 62. Raistrick D, Dunbar G, Davidson R. Development of a questionnaire to measure alcohol dependence. *Br J Addict*. 1983;78:89-95.
 63. Doyle SR, Donovan DM. A validation study of the alcohol dependence scale. *J Stud Alcohol Drugs*. 2009;70:689-99.
 64. Okada M, Oltmanns TF. Comparison of three self-report measures of personality pathology. *J Psychopathol Behav Assess*. 2009;31:358-67. doi:10.1007/s10862-009-9130-8
 65. Greenwald AG, Pickrell JE, Farnham SD. Implicit partisanship: taking sides for no reason. *J Pers Soc Psychol*. 2002;83:367-379. doi:10.1037/0022-3514.83.2.367
 66. Sobell LC, Sobell MB. Timeline follow-back. In: Lit-

- ten RZ, Allen JP (Eds). *Measuring alcohol consumption*. Totowa, NJ: Humana Press; 1992. p. 41-72. doi:10.1007/978-1-4612-0357-5_3
67. Witkiewitz K, Horn BP. Reductions in healthcare costs following alcohol treatment: moving toward low-risk drinking end points in alcohol clinical trials. *Alcohol Clin Exp Res*. 2016;40:1415-7. doi:10.1111/acer.13092
 68. Koyejo OM, Kliewer W, Gbiri CAO, Svikis DS. Sex differences in alcohol-related problems among a sample of HIV-positive Nigerians. *Int Perspect Psychol Res Pract Consult*. 2018;7:231-9. doi:10.1037/ipp0000096
 69. Holmila M, Raitasalo K. Gender differences in drinking: why do they still exist? *Addiction*. 2005;100:1763-9. doi:10.1111/j.1360-0443.2005.01249.x
 70. Mancinelli R, Vitali M, Ceccanti M. Women, alcohol and the environment: an update and perspectives in neuroscience. *Funct Neurol*. 2009;24:77-81.
 71. Mancinelli R, Binetti R, Ceccanti M. Woman, alcohol and environment: Emerging risks for health. *Neurosci Biobehav Rev*. 2007;31:246-53. doi:10.1016/j.neubio-rev.2006.06.017
 72. Coriale G, Fiorentino D, Di Lauro F, Marchitelli R, Scalese B, Fiore M, et al. Fetal Alcohol Spectrum Disorder (FASD): neurobehavioral profile, indications for diagnosis and treatment. *Riv Psichiatri*. 2018;48:359-69. doi:10.1708/1356.15062
 73. Ceccanti M, De Nicolò S, Mancinelli R, Chaldakov G, Carito V, Ceccanti M, et al. NGF and BDNF long-term variations in the thyroid, testis and adrenal glands of a mouse model of fetal alcohol spectrum disorders. *Ann Ist Super Sanità*. 2013;49:383-90. doi:10.4415/ANN_13_04_11
 74. Ceccanti M, Coccurello R, Carito V, Ciafrè S, Ferraguti G, Giacobazzo G, et al. Paternal alcohol exposure in mice alters brain NGF and BDNF and increases ethanol-elicited preference in male offspring. *Addict Biol*. 2016;21:776-87. doi:10.1111/adb.12255
 75. Tarani L, Micangeli G, Rasio D, Ottombrino S, Liberati N, Angelis D De, et al. Clinical and genetic approach to the dysmorphic child. *Biomed Rev* 2018;29:37-46. doi:10.14748/bmr.v29.5848.
 76. Carito V, Parlapiano G, Rasio D, Paparella R, Paolucci V, Ferraguti G, et al. Fetal alcohol spectrum disorders in pediatrics. FASD and the pediatrician. *Biomed Rev*. 2018;29:27-35. doi:10.14748/bmr.v29.5847
 77. Carito V, Ceccanti M, Ferraguti G, Coccurello R, Ciafrè S, Tirassa P, et al. NGF and BDNF Alterations by Prenatal Alcohol Exposure. *Curr Neuropharmacol*. 2019;17:308-17. doi:10.2174/1570159X15666170825101308
 78. De Nicolò S, Carito V, Fiore M, Laviola G. Aberrant Behavioral and Neurobiologic Profiles in Rodents Exposed to Ethanol or Red Wine Early in Development. *Curr Dev Disord Reports* 2014;1:173-80. doi:10.1007/s40474-014-0023-5
 79. Ferraguti G, Merlino L, Battagliese G, Piccioni MG, Barbaro G, Carito V, et al. Fetus morphology changes by second-trimester ultrasound in pregnant women drinking alcohol. *Addict Biol* 2019. doi:10.1111/adb.12724
 80. Ceccanti M, Fiorentino D, Coriale G, Kalberg WO, Buckley D, Hoyme HE, et al. Maternal risk factors for fetal alcohol spectrum disorders in a province in Italy. *Drug Alcohol Depend*. 2014;145:201-8. doi:10.1016/j.drugalcdep.2014.0.017
 81. Kodituwakku P, Coriale G, Fiorentino D, Aragon AS, Kalberg WO, Buckley D, et al. Neurobehavioral Characteristics of children with fetal alcohol spectrum disorders in communities from Italy: preliminary results. *Alcohol Clin Exp Res*. 2006;30:1551-61. doi:10.1111/j.1530-0277.2006.00187.x
 82. Coriale G, Fiorentino D, Kodituwakku PW, Tarani L, Parlapiano G, Scalese B, et al. Identification of Children With Prenatal Alcohol Exposure. *Curr Dev Disord Reports*. 2014;1:141-8. doi:10.1007/s40474-014-0018-2
 83. Ceccanti M, Mancinelli R, Tirassa P, Laviola G, Rossi S, Romeo M, et al. Early exposure to ethanol or red wine and long-lasting effects in aged mice. A study on nerve growth factor, brain-derived neurotrophic factor, hepatocyte growth factor, and vascular endothelial growth factor. *Neurobiol Aging*. 2012;33:359-67. doi:10.1016/j.neurobiolaging.2010.03.005
 84. Angelucci F, Fiore M, Cozzari C, Aloe L. Prenatal ethanol effects on NGF level, NPY and ChAT immunoreactivity in mouse entorhinal cortex: a preliminary study. *Neurotoxicol Teratol*. 1999;21:415-25. doi:10.1016/S0892-0362(99)00005-7
 85. Fiore M, Mancinelli R, Aloe L, Laviola G, Sornelli F, Vitali M, et al. Hepatocyte growth factor, vascular endothelial growth factor, glial cell-derived neurotrophic factor and nerve growth factor are differentially affected by early chronic ethanol or red wine intake. *Toxicol Lett*. 2009;188:208-13. doi:10.1016/j.toxlet.2009.04.013
 86. Fiore M, Laviola G, Aloe L, di Fausto V, Mancinelli R, Ceccanti M. Early exposure to ethanol but not red wine at the same alcohol concentration induces behavioral and brain neurotrophin alterations in young and adult mice. *Neurotoxicology*. 2009;30:59-71. doi:10.1016/j.neuro.2008.11.009
 87. Bradizza CM, Stasiewicz PR, Paas ND. Relapse to alcohol and drug use among individuals diagnosed with co-occurring mental health and substance use disorders: A review. *Clin Psychol Rev*. 2006;26:162-78. doi:10.1016/j.cpr.2005.11.005
 88. Smith JP, Randall CL. Anxiety and alcohol use disorders: comorbidity and treatment considerations. *Alcohol Res*. 2012;34:414-31.
 89. Ceccanti M, Iannitelli A, Fiore M. Italian Guidelines for the treatment of alcohol dependence. *Riv Psichiatri*. 2018;53:105-6. doi:10.1708/2925.29410
 90. Daley DC, Moss H. Dual disorders : counseling clients with chemical dependency and mental illness. Hazelden; 2002.
 91. Sterling S, Chi F, Hinman A. Integrating care for people with co-occurring alcohol and other drug, medical, and mental health conditions. *Alcohol Res Health*. 2011;33:338-49.
 92. Vitali M, Sorbo F, Mistretta M, Coriale G, Messina MP, Alessandrini G, et al. Drafting a dual diagnosis program: a tailored intervention for patients with complex clinical needs. *Riv Psichiatri*. 2018;53:149-53. doi:10.1708/2925.29417
 93. Coriale G, Fiorentino D, De Rosa F, Solombrino S, Scalese B, Ciccarelli R, et al. Treatment of alcohol use disorder from a psychological point of view. *Riv Psichiatri*. 2018;53:141-8. doi:10.1708/2925.29416
 94. Coriale G, Fiorentino D, Porrari R, Battagliese G, Caprigione I, Cereatti F, et al. Diagnosis of alcohol use disorder from a psychological point of view. *Riv Psichiatri*. 2018;53:128-40. doi:10.1708/2925.29415
 95. Vitali M, Sorbo F, Mistretta M, Scalese B, Porrari R, Galli D, et al. Dual diagnosis: an intriguing and actual nosographic issue too long neglected. *Riv Psichiatri* 2018;53:154-9. doi:10.1708/2925.29418.
 96. Attilia F, Perciballi R, Rotondo C, Capriglione I, Iannuzzi S, Attilia ML, et al. Pharmacological treatment of alcohol use disorder. Scientific evidence. *Riv Psichiatri*. 2018;53:123-7. doi:10.1708/2925.29414



97. Attilia F, Perciballi R, Rotondo C, Capriglione I, Iannuzzi S, Attilia ML, et al. Alcohol withdrawal syndrome: diagnostic and therapeutic methods. *Riv Psichiatr.* 2018;53:118-22. doi:10.1708/2925.29413
98. Kelly TM, Daley DC. Integrated treatment of substance use and psychiatric disorders. *Soc Work Public Health.* 2013;28:388-406. doi:10.1080/19371918.2013.774673
99. Orford J. [Commentary] Joining the queue of dissenters. *Addiction.* 2008;103:706-7. doi:10.1111/j.1360-0443.2007.02128.x