**Quality of life, alcohol detoxification and relapse: Is quality of life a predictor of relapse or only a secondary outcome measure?**

Quality of Life Research

# Quality of life, alcohol detoxification and relapse: Is quality of life a predictor of relapse or only a secondary outcome measure?

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| **Abstract:** | Purpose: To estimate variations in Overall Quality of Life (OQOL) within 12 months following alcohol detoxification, and to evaluate the predictive value of OQOL for relapse and alcohol use severity.<br>Methods: Alcohol use disorders and four OQOL domains (Physical health, Psychological health, Social relationships and Environment) were assessed in 199 patients entering in-patient alcohol detoxification. Follow-up assessments were performed at 6 and 12 months after discharge. Cross-sectional and longitudinal analyses explored the relationship between OQOL and alcohol use severity, examining differences between abstinent and relapsed patients. The predictive value of OQOL was analyzed by logistic and linear regression.<br>Results: Correlation between OQOL and Alcohol Use Disorders Identification Test (AUDIT) scores was confirmed at all stages of observation. Abstinent patients showed a significant improvement in all OQOL domains at 6 months after discharge, whereas OQOL domains did not undergo any significant change in relapsed patients. Baseline OQOL did not prove to be predictive of either relapse or alcohol use severity.<br>Conclusions: OQOL changed in parallel with alcohol use severity throughout the duration of the study, confirming it to be a useful and sensitive measure of secondary outcome for alcohol detoxification. Conversely, none of the OQOL baseline scores functioned as predictors of relapse within 12 months following discharge or alcohol use severity in relapsed patients. |

To the attention of the Editor
Quality of Life Research

February 24, 2014

Dear Editor,

Please consider for the publication the manuscript “Quality of life, alcohol detoxification and relapse. Is quality of life only a secondary outcome or may it be considered also a predictor of relapse?” by Rocco Luigi Picci, Francesco Oliva, Marco Zuffranieri, Paola Vizzuso, Luca Ostacoli, Alessandro Jaretti Sodano, and Pier Maria Furlan.

The paper concerns the cross-sectional and longitudinal evaluation of the change in quality of life among patients with alcohol use disorder during twelve months following inpatient alcohol detoxification. Both the comparison of quality of life trend between relapsed and non-relapsed patients and the estimation of baseline quality of life predicting value were also performed. The use of an overall quality of life assessment tool rather than a health-related one is a noteworthy feature of our study.

The article is original and it is not currently under consideration by other journals.

All authors have been personally and actively involved in substantive work leading to the report, they participated to the revision of the article, they approved the manuscript, and thus, they agreed on its submission to Quality of Life Research.

Yours sincerely,

Francesco Oliva

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Dear Ms. Carolyn Emily Schwartz,

We apologize for any inconvenience regarding the first submission. As you requested, we defined all acronyms before first use in the abstract and manuscript text.

Yours sincerely,

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**TITLE**

**Quality of life, alcohol detoxification and relapse: Is quality of life a predictor of relapse or only a secondary outcome measure?**

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**KEYWORDS**

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**ABSTRACT**

**Purpose:** To estimate variations in Overall Quality of Life (OQOL) within 12 months following alcohol detoxification, and to evaluate the predictive value of OQOL for relapse and alcohol use severity.

**Methods:** Alcohol use disorders and four OQOL domains (Physical health, Psychological health, Social relationships and Environment) were assessed in 199 patients entering in-patient alcohol detoxification. Follow-up assessments were performed at 6 and 12 months after discharge. Cross-sectional and longitudinal analyses explored the relationship between OQOL and alcohol use severity, examining differences between abstinent and relapsed patients. The predictive value of OQOL was analyzed by logistic and linear regression.

**Results:** Correlation between OQOL and Alcohol Use Disorders Identification Test (AUDIT) scores was confirmed at all stages of observation. Abstinent patients showed a significant improvement in all OQOL domains at 6 months after discharge, whereas OQOL domains did not undergo any significant change in relapsed patients. Baseline OQOL did not prove to be predictive of either relapse or alcohol use severity.

**Conclusions:** OQOL changed in parallel with alcohol use severity throughout the duration of the study, confirming it to be a useful and sensitive measure of secondary outcome for alcohol detoxification. Conversely, none of the OQOL baseline scores functioned as predictors of relapse within 12 months following discharge or alcohol use severity in relapsed patients.

## INTRODUCTION

Quality of Life (QOL) is determined by a range of parameters, including the ability to function in physical, familial, social, marital and professional contexts. The World Health Organization (WHO) has stated that the impairment of these same parameters is an integral component of alcoholism [1]. Moreover, some studies have confirmed that QOL is lower in alcoholics, and varies with the severity of alcohol dependence [2, 3]. Indeed, QOL tends to improve after detoxification and treatment [4–8] and worsen during relapse [6, 9–11].

Based on this evidence, several studies have included QOL assessment as a measure of secondary outcome of alcohol detoxification programs [7, 8, 10, 12–14]. However, as reported in two recent reviews [15, 16], two types of QOL assessment can be distinguished in addiction research: the Health-related Quality Of Life (HQOL) assessment focused on functional limitations due to illness and treatment; and the Overall Quality Of Life (OQOL) assessment, which takes into account both the objective well-being related to needs and desires common to most people and subjective satisfaction with life. Most studies reporting a poorer QOL have used Medical Outcome Study – Short Form healthy survey (MOS–SF)-based tools (e.g., SF-20, SF-36, SF-12), which are expressly designed to assess HQOL [3–5, 7, 8, 10]. Conversely, few studies have adopted the World Health Organization Quality of Life (WHOQOL) tools [17, 18], which are currently considered the gold standards for the assessment of OQOL [15]. In view of these different ways of assessing QOL, LoCastro et al. [17] included both SF-12 and WHOQOL – Brief version (WHOQOL-BREF) as secondary outcomes in the COMBINE treatment trial. Both tools found patients to have poor QOL at the beginning of the study, and only the psychological and physical domains of the WHOQOL showed improvement between 26 and 52 weeks of follow-up. The study concluded that the WHOQOL tool was more sensitive to variations in drinking patterns than the SF-12 [17]. Moreover, Laudet [15] reported that WHOQOL tools relate more directly to recovery goals than MOS-SF, and encouraged the use of OQOL assessment tools in future prospective studies.

In the field of treating Alcohol Use Disorders (AUD), the identification and estimation of outcome predictors is becoming increasingly relevant. To date, more than 30 baseline variables have been identified and clustered into socio-demographic, alcohol-related and clinical domains [19, 20]. Some studies have reported that certain variables that are commonly used as primary outcomes may have predictive value, including baseline alcohol consumption [21–24], dependence severity [24–27] and history of previous treatment or intervention [23, 28–30]. Only one such study has investigated whether relapse can be predicted by measuring baseline QOL, using the Life Situation Survey (LSS) in a small sample of alcohol-dependent patients, but this approach failed to identify any significant predictors [4].

The primary aims of the present study were 1) to confirm that alcoholics entering detoxification had poor OQOL and 2) to evaluate the role of OQOL as a secondary outcome measure of alcohol detoxification. These aims were achieved by assessing OQOL at admission, examining any correlation with the severity of alcohol use at different stages of the

observation period, and comparing longitudinal variations in post-discharge OQOL in abstinent patients and relapsed patients. Secondarily, the study aimed to evaluate whether baseline OQOL can be used to predict the likelihood of relapse and/or the severity of alcohol use.

## METHODS

### Sample and enrolment

All patients entering the Hospital Complex "Fatebenefratelli" in San Maurizio Canavese (Turin, Italy) for alcohol detoxification treatment between 1 September 2009 and 1 December 2010 were invited to participate in the study. This invitation was made seven days after admission and was accompanied by comprehensive information regarding the aims, methods, risks and benefits of the study. If accepted, the agreement was formalized by the patient signing a written informed consent form. A unique identification code was assigned to each patient, in order to maintain data anonymity and patient confidentiality.

Substance use was considered an exclusion criterion for this study. Indeed, all patients were screened by means of urinalysis prior to admission on to the study for the recent use of other drugs, including marijuana, cocaine, opiates, phencyclidine, amphetamine, and methamphetamine; any patient testing positive for a substance other than alcohol was hence excluded from the study population. However, a previous history of substance abuse/dependence was recorded and treated as a dichotomous variable.

The co-existence of alcoholism with psychiatric disorders and/or high levels of anxiety or depression were not considered as exclusion criteria; conversely, a thorough categorical and dimensional evaluation of psychopathologic variables was performed.

### Alcohol detoxification

All patients entering the hospital stopped drinking alcohol. Detoxification treatment consisted of a fixed-schedule regimen that included administration of lorazepam (8-10 mg/day), or oxazepam (120-180 mg/day), or the equivalent dose of another benzodiazepine, with subsequent gradual reduction of this dosage until the drug was discontinued. During hospitalization, other psycho-pharmacological treatments were administered according to evidence-based recommendations described in the American Psychiatric Association Practice Guidelines [31].

Several non-pharmacological treatments, such as parent-training intervention, short-term individual psychotherapy, group psychotherapy, motivational enhancement therapy, and nutrition education, were included at the discretion of the clinician. In accordance with the observational study design, the investigators were not actively engaged in providing

treatment. All additional therapeutic interventions were recorded as dichotomous variables in the study database.

**Study design**

The mixed cross-sectional and longitudinal design of the observational study consisted of three stages of observation and assessment: baseline assessment (T0); first follow-up at six months after discharge (T1); and second follow-up at 12 months after discharge (T2). The T0 assessment was made on the seventh day of hospitalization, and involved the collection of both socio-demographic information (date of birth, gender, marital status, education, living conditions, employment, etc.) and alcohol-related data (i.e. age at onset of alcohol use, age at onset of alcohol abuse, previous admission(s) for detoxification, and current pharmacological treatment). The assessment also included evaluation of alcohol use severity and QOL, using the Alcohol Use Disorders Identification Test (AUDIT) [32] and the WHOQOL-BREF [33]. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I) [34] was used to identify both AUD and psychiatric disorders, following the Diagnostic and Statistical Manual of Mental Disorders, Fourth edition, Revised (DSM-IV-TR) criteria. Baseline continuous measures of psychopathology were also estimated through the State-Trait Anxiety Inventory – Form Y (STAI-Y) [35] and Beck Depression Inventory (BDI) [36].

Both follow-ups included the assessment of alcohol use severity and QOL by AUDIT and WHOQOL-BREF, respectively.

Failure to sign the written informed consent form or to attend the follow-up appointments was considered as refusal. By contrast, patients who were no longer contactable at T1 and T2 were considered lost.

**Assessment tools**

The AUDIT consists of a ten-item core questionnaire and an eight-item clinical procedure. Total scores range from 0–40 and give a reliable estimate of the severity of alcohol use behavior in the preceding year [37]. This tool explores not only the alcohol dependence itself but also the risk of alcohol-related physical/mental harm arising from hazardous or harmful drinking conduct. The international and Italian versions of this tool have both been verified for their good psychometric properties [38, 39].

According to the AUDIT manual, three threshold values were used to identify four zones of risk and intervention. Abstinent patients have a total score of 0, so all patients with values above 0 at follow-up were considered to have relapsed. Since the study design included a six-month scheduled follow-up, the time reference of the questionnaire was reduced from twelve months to six months.

WHOQOL-BREF is an abbreviated (26 items) version of WHO Quality of Life questionnaire (WHOQOL-100), which enables a quick but thorough evaluation of OQOL domains, including Physical health, Psychological health, Social

relationships and Environment. WHOQOL-BREF is comparable to WHOQOL-100 in terms of discriminant validity and internal consistency [33] and it is superior to an array of other possible tools in its ability to identify subjective aspects of OQOL without becoming disorder-specific [15, 40]. Good reliability was also reported for both international and Italian version [41–43].

SCID-I is a semi-structured interview characterized by a modular structure, whose items are based on DSM-IV Axis I criteria. It is commonly used to make categorical diagnosis of DSM-IV Axis I disorders, providing good inter-rater reliability [44]. In this study, SCID-I was employed at T0 to formulate categorical diagnosis of AUD and psychiatric disorders.

STAI-Y and BDI were used to achieve continuous measurement of anxiety and of depressive symptoms, respectively. The STAI-Y inventory consists of 40 items, and is specifically designed to assess both trait and state anxiety. STAI-Y has been proven to have good psychometric properties among alcoholic populations [35, 45].

Similarly, the BDI index is a well-established 21-item tool for quantitative assessment of depressive symptoms and is widely used in psychological research [46]. Many studies have concluded that the BDI is a rational choice of screening tool for depression in an alcohol-dependent population [47, 48].

**Statistical analysis**

All computations were performed using the IBM SPSS Statistics for Windows package (Version 19.0. Armonk, NY: IBM Corporation).

Comparison of baseline data between responder and lost groups was carried out using Pearson's $\chi^2$ test or Fisher's exact test for categorical variables, depending on the expected frequencies in each group. Mean differences in continuous variables were evaluated either through the independent-samples t-test or by the Mann-Whitney U test, depending on whether the distribution of variables was normal or non-normal, as determined by the Shapiro-Wilk test.

To confirm the correlation between alcohol use severity and OQOL, cross-sectional data analysis was performed at three stages of assessment using either Pearson’s correlation or Kendall’s rank correlation, depending on the normality of the distribution of variables. A Generalized Linear Model (GLM) for repeated measures was applied to analyze differences in longitudinal variations of QOL between abstinent and relapsed patients. WHOQOL domains at the three assessment stages (T0, T1 and T2) were used as within-subject variables, and relapse outcome at T2 was used as a between-subject factor. The effect size of each factor is reported as a partial Eta-squared ($\eta^2_p$) value, with a Huynh–Feldt correction applied in cases where sphericity was violated. Pairwise comparisons of mean scores at different stages of assessment were made by repeated contrasts and are reported as mean differences ($\Delta$) with a Sidak-corrected 95% Confidence Interval (95%CI).

Logistic and linear regression analyses were also performed to evaluate the predictive value of QOL for relapse and for alcohol use severity, respectively. Logistic regression was carried out on the overall sample, using abstinence or relapse as a dichotomous outcome. Linear regression was applied only to relapsed patients, using AUDIT scores as a continuous outcome. All socio-demographic, alcohol-related, psychopathological, and treatment variables were compared initially by univariate analysis. Subsequently, those that were significantly different between abstinent and relapsed subjects were used as covariates in both logistic and linear regression models. Probability tests were considered bilaterally with a type I error set at 5% ($p$=0.05).

## RESULTS

The enrolled sample consisted of 199 patients, of which 146 attended both follow-ups. Several patients that had agreed to participate and had signed informed consent became non-contactable before attending follow-ups, with 31 (15.6%) patients disappearing before T1 and a further 22 (11.0%) before T2. These 53 lost patients were excluded from the longitudinal analysis. However, a comparison between responders and lost patients showed no statistically significant differences in baseline socio-demographic, alcohol-related, or other studied variables (Tables 1 and 2).

The mean sample values show that, on average, patients started drinking alcohol at age 18 (Table 2), began to abuse it 14 years later (age 32), and were admitted to a detoxification unit at around age 47 (Table 1). Half of our patient sample had never undergone detoxification, with a further third having been detoxified once and the remainder detoxifying at least twice before (Table 2).

According to baseline SCID results all patients had an AUD (Table 2), of which 181 (91%) were in the high risk zone of the AUDIT scoring range (zone IV). A further 11(5.5%) had a medium health risk (zone III), with the remaining 7 (3%) being at low risk (zone II). The mean AUDIT score was above 20, placing it in zone IV of the health risk range (mean±SD: 27.5±6.5; Table 2).

The mean scores of all QOL domains at T0 were below normative Italian values [42]. The Physical health domain mean score was 12.9±2.8 (*vs*. normative values of 16.8±3.3; t=15.19; $p$<0.001; N=379). The mean scores in the Psychological health, Social relationships and Environment domains were 12.7±1.7 (*vs.* 15.0±2.4; t=16.21; $p$<0.001), 12.2±3.1 (*vs.* 15.1±2.6; t=11.91; $p$<0.001) and 12.5±2.3 (*vs.* 14.3±2.0; t=9.75; $p$<0.001), respectively.

### Outcome of detoxification

At T1, 79 (47.0%) of the 168 patients remaining in the study relapsed to alcohol drinking, presenting scores indicating different health-risks. From the AUDIT scores, 55 (32.7%) had high health risk (zone 4), 6 (3.6%) were in risk zone 3, 12 (7.1%) in risk zone 2, and 6 (3.6%) had low health risk (zone 1). 89 (53.0%) patients maintained abstinence.

At T2, 64 (43.8%) of 146 patients remaining in the study had relapsed to alcohol drinking, 50 (34.2%) were in zone 4, with high health risk, while 5 (3.4%) and 6 (4.1%), respectively, were in zone 3 and zone 2 for health risk. Only 3 (2%) patients were in zone 1 for health risk. Furthermore, 14 (9.6%) patients who had relapsed at T1 become abstinent 6 months later, at T2; these patients had previously been considered as relapsed, and thus in all 68 patients (46.6%) were abstinent at T2. Only 11 (7.53%) patients who were abstinent at T1 returned to drinking 6 months later, and thus were counted as relapsed at T2.

**Longitudinal analysis**

The Huyny-Feldt epsilon correction for degrees of freedom was applied, because the sphericity assumption was not met for the main effects on any of the four WHOQOL domains.

Longitudinal analysis by GLM revealed a significant within-subject effect for stages of assessment in the domains of Physical health ($F(1.61,231.85)=31.07$, $p<0.001$, $\eta 2p =0.18$), Psychological health ($F(1.92,275.94)=9.68$, $p<0.001$, $\eta 2p =0.06$), Social relationships ($F(1.42,205.04)=20.46$, $p<0.001$, $\eta 2p =0.12$) and Environment ($F(1.79,257.42)=15.09$, $p<0.001$, $\eta 2p =0.09$).

The main between-subject effect of the relapse was also significant for all four QOL domains (Physical health, $F(1,144)=31.75$, $p<0.001$, $\eta 2p =0.18$; Psychological health, $F(1,144)=12.43$, $p=0.001$, $\eta 2p=0.08$; Social relationships, $F(1,144)=11.32$, $p=0.001$, $\eta 2p=0.07$; Environment, $F(1,144)=11.32$, $p=0.001$, $\eta 2p=0.07$).

At T0, there was no significant difference between the relapsed and abstinent groups in any of the WHOQOL domains (Table 4; Physical health, $\Delta=0.58$, 95%CI=-0.34/1.51, $p=0.216$; Psychological health, $\Delta=0.16$, 95%CI=-0.43/0.76, $p=0.587$; Environment, $\Delta=0.21$, 95%CI=-0.52/0.93, $p=0.573$; Social relationships, $\Delta=-0.39$, 95%CI=-1.40/0.63, $p=0.449$).

At T1, there was significant improvement in all WHOQOL domains in abstinent patients (Physical health, $\Delta=2.47$, 95%CI= 1.63/3.30, $p<0.001$; Psychological health, $\Delta=0.86$, 95%CI=0.32/1.40, $p<0.001$; Social relationships, $\Delta=2.45$, 95%CI=1.55/3.36, $p<0.001$; Environment, $\Delta=1.62$, 95%CI=1.01/2.24, $p<0.001$). In contrast, there was no improvement in any domain in the relapsed patients (Physical health, $\Delta=0.56$, 95%CI=-0.22/1.34, $p=0.229$; Psychological health, $\Delta=0.02$, 95%CI=-0.48/0.52, $p=0.999$; Social relationships, $\Delta=0.18$, 95%CI=-0.66/1.03, $p=0.935$; Environment, $\Delta=0.29$, 95%CI=-0.28/0.86, $p=0.538$). This distinction between the abstinent and relapsed groups at T1 was accompanied by significantly higher mean scores in the abstinent group in all QOL domains (Table 4).

Changes in mean QOL scores from T1 to T2 did not translate to any significant differences in either the relapse group (WHOQOL Physical health, $\Delta=-0.43$, 95%CI=-0.91/0.05, $p=0.096$; WHOQOL Psychological health, $\Delta=0.06$, 95%CI=-0.34/0.47, $p=0.973$; WHOQOL Social relationships, $\Delta=-0.23$, 95%CI=-0.67/0.20, $p=0.492$; WHOQOL Environment,

Δ=0.27, 95%CI=-0.40/0.94, p=0.702) or the abstinent group (WHOQOL Physical health, Δ=0.07, 95%CI=-0.45/0.59, p=0.982; WHOQOL Psychological health, Δ=0.27, 95%CI=-0.17/0.70, p=0.367; WHOQOL Social relationships, Δ=-0.11, 95%CI=-0.57/0.35, p=0.916; WHOQOL Environment, Δ=-0.15, 95%CI=-0.87/0.56, p=0.936).

At T2, there was a significant increase in values between the two groups in the Physical health, Psychological health and Social relationships domains. The Environment domain score decreased slightly in the abstinent group, but remained significantly higher than that of the relapsed group (Table 4).

**Cross-sectional correlations**

The alcohol use severity at each stage of AUDIT observation was significantly correlated with each QOL domain when measured at the same stage (Table 3). Baseline AUDIT scores of 199 enrolled patients were significantly correlated with baseline Physical health, Psychological health, Social relationships, and Environment QOL scores. AUDIT scores were more closely correlated with QOL domains at T1 than at T0 (Table 3). AUDIT scores were also significantly correlated with each QOL domain at T2. This correlation was weaker than at T1, but stronger than at T0 (Table 3). The only exception was the WHOQOL Environment score, which was lowest in T2 (Table 3).

**Regression analysis**

Univariate analysis estimation of baseline predictors revealed significant differences between the relapsed and abstinent groups in the context of two continuous variables (previous detoxifications (t(144)=4.63, p<0.001) and age at onset of alcohol abuse (t(144)=2.48, p=0.014)) and two categorical variables (living conditions ($\chi2(4)=11.00$, p=0.020) and SCID-I AUD ($\chi2(1)=7.51$, p=0.006)).

With regard to treatment, there were statistically-significant differences between the two groups in terms of the four non-pharmacological interventions (training intervention, $\chi2(1)=4.85$, p=0.037; group psychotherapy, $\chi2(1)=8.67$, p=0.003; motivational enhancement therapy, $\chi2(1)=3.93$, p=0.047; and nutrition education, $\chi2(1)=4.74$, p=0.029).

Four baseline variables and four interventions were thus used as covariates in the logistic and linear regression models, which were then used to evaluate the predictive value of QOL for relapse and for drinking behavior, respectively. The logistic regression model correctly predicted 72.6% of the responses (Nagelkerke's R2=0.40).

According to baseline scores, none of the four WHOQOL domains function adequately as predictors of relapse (Physical health: OR=0.97, 95%CI=-0.82/1.15, p=0.763; Psychological health: OR=0.78, 95%CI=0.60/1.00, p=0.055; Social relationships: OR=1.07, 95%CI=0.92/1.24, p=0.408; Environment: OR=1.14, 95%CI=0.91/1.43, p=0.253). In contrast, the number of previous detoxifications (OR=2.51, 95%CI=1.33/4.73, p=0.004) and SCID-I Alcohol Dependence Disorder (OR=0.12, 95%CI=0.02/0.83, p=0.032) were found to be positive predictors of relapse.

The linear regression model with covariates and WHOQOL domains failed to reliably predict the AUDIT score at T2 (Adjusted R2=0.09, F(12,65)=1.65, p=0.099) and had no predictive value for basal scores of WHOQOL domains (Physical health: β=0.150, t(12)=-1.05, p=0.297; Psychological health: β=-0.006, t(12)=-0.04, p=0.965; Social relationships: β=0.032, t(12)=0.25, p=0.800; Environment: β=-0.081, t(12)=-0.56, p=0.576). Conversely, the number of previous detoxifications and group psychotherapy worked, respectively, as positive (β=0.31, t(12)=2.59, p=0.012) and negative (β=-0.74, t(12)=-2.02, p=0.047) predictors for AUDIT scores at T2.

**DISCUSSION**

The present study found that patients with AUD entering in-patient detoxification treatment had poor OQOL. We also validated OQOL as a secondary outcome measure. The baseline QOL domain scores for Physical and Psychological health, Social relationships and Environment were statistically significantly lower than those of the reference population. These results are consistent with previous studies that used MOS-SF-based tools [2, 3, 10] and the LSS [49] to compare AUD patients entering detoxification against a reference population.

Furthermore, across the three assessment stages, the scores in all four QOL domains were significantly negatively correlated with alcohol use severity, as assessed by AUDIT. At admission, this correlation was weak, but increased dramatically at the 6-month follow-up before declining slightly by the time of the 12-month follow-up. Foster et al. [50] reported a similar weak baseline correlation between alcohol dependence severity and QOL using a more subjective assessment tool (i.e., LSS). LoCastro et al. [17] also found correlations at the 6- and 12-month follow-ups, but these were weaker than those described here. However, despite using the same QOL evaluation tool, the previous study employed a different alcohol use severity assessment. Their assessment included measurements of both drinking frequency and consumption but, unlike AUDIT, it did not consider the hazardous or harmful consequences of alcohol use. Thus, the stronger correlation found in the current study could be due to the possible overlap between the alcohol-related health risk assessed by AUDIT and the physical and psychological health domains of WHOQOL-BREF.

The longitudinal analysis performed here showed that only patients who maintained abstinence until the end of the study achieved a significant improvement in OQOL at 6 and 12 months after discharge. Conversely, patients who relapsed did not achieve a significant change in QOL in the months following discharge. Thus, maintenance of abstinence led to an improvement of OQOL that involved the patients' environment, social relationships, physical health and, to a lesser extent, psychological health. These findings were consistent with those of previous short-term studies [3–5, 7, 8, 10] and supported the findings of the long-term COMBINE study [17]. In the present study, OQOL among abstinent patients was particularly improved at 6 months after discharge, whereas OQOL was merely maintained at 12 months after discharge. The physical health and social relationships domains were the most improved in abstinent

patients when comparing the effect sizes in the relapsed and abstinent groups. Moreover, since AUDIT scores were strongly and negatively correlated with WHOQOL scores at two follow-up assessments, the present study also supports the finding of Frischknecht et al. that QOL is increased, not only in abstinent patients, but also in those who improved their drinking behavior [6]. Therefore both the cross-sectional and longitudinal appraisals of OQOL performed in the present study seem to confirm its role as a secondary outcome measure and a recovery goal in the treatment of AUD. This is because abstinence from alcohol and the reduction of hazardous and harmful drinking behaviors, as assessed by AUDIT, lead to objective improvement in well-being. Abstinence and behavior modification also increase satisfaction with the physical, psychological, familial, and professional aspects of life and with overall functioning, as assessed by WHOQOL-BREF.

The second aim of the study was to assess the predictive power of the WHOQOL domains. However, we found that none of the baseline QOL scores worked as predictors for either relapse within 12 months following discharge or alcohol use severity in relapsed patients. Foster et al. [4] reported a similarly poor performance of baseline QOL scores in predicting outcome at 12 weeks follow-up and implicated the lack of difference in baseline LSS scores between the relapsed and non-relapsed groups as being the reason for this failure. In this study, although a different QOL assessment was applied to a sample more than twice the size, we found neither significant predictive value for QOL domains nor significant differences in baseline QOL between the relapsed and abstinent groups. Further studies might explore the predictive value of QOL in a larger patient population, in which basal differences might be significant.

In contrast, two of the eight variables selected as covariates in our regression models had significant efficacy as predictors of both relapse and alcohol use severity. The most significant predictor was the number of previous detoxifications, which is an intuitive and influential outcome predictor [19, 20]. The baseline DSM-IV-TR diagnosis of Alcohol Dependence Disorder slightly increased the risk of relapse, though it should be recognized that almost all patients were alcohol-dependent. Although evaluation of individual treatments was not a goal of this study, our results did suggest that group psychotherapy was a significant negative predictor for alcohol use severity.

The present study has some potential limitations. First, although the detoxification treatment was fixed and scheduled, and all other treatments were taken into account, we cannot exclude some influence of treatment differentiation on QOL parameters. Secondly, a low response rate at follow-up (84.4% of 199 enrolled patients at 6 months; 73.4% at 12 months) might lead to a non-response bias. However, the response rates observed in this study are comparable to other studies, which range from 39.7% at 6 months [10] to 82.3% at 12 months [17]. Moreover, no patients refused the follow-up assessment; non-responders were instead lost patients that were no longer contactable *via* their given details. Furthermore, our comparison of the baseline socio-demographic, alcohol-related, and QOL variables between the responders and the lost patients revealed no significant differences between these groups.

**CONCLUSIONS**

The present study stresses the importance of OQOL assessment as a secondary outcome measure of alcohol detoxification. The study was a cross-sectional and longitudinal evaluation of QOL in patients with AUD during admission for detoxification and within 12 months after discharge. It revealed a significant correlation with severity of alcohol use across the entire patient population at all stages of assessment, and also a significant improvement in QOL in patients that maintained abstinence for the duration of the study. Combining a comprehensive primary outcome assessment tool (AUDIT) with the gold-standard OQOL assessment tool (i.e., WHOQOL-BREF) appears to improve the sensitivity of QOL assessment in evaluating alcohol use-related variations.

OQOL at admission could not predict either relapse or alcohol use severity in relapsed patients, but OQOL assessment remains a useful secondary treatment outcome measure in AUD patients.

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Table 1. Baseline socio-demographic characteristics in responders and lost patients.

| | Enrolled (n=199) | Lost (n=53) | Responders (n=146) | |
|---|---|---|---|---|
| | N (%) | N (%) | N (%) | *p* |
| Gender | | | | 0.743[a] |
| Male | 135 (67.8) | 35 (66.0) | 100 (68.5) | |
| Female | 64 (32.2) | 18 (34.0) | 46 (31.5) | |
| Education (years) | | | | 0.585[b] |
| <6 | 14 (7.0) | 5 (9.4) | 9 (6.2) | |
| 6–8 | 103 (51.8) | 26 (49.1) | 77 (52.7) | |
| 9–13 | 72 (36.2) | 18 (34.0) | 54 (37.0) | |
| >13 | 10 (5.0) | 4 (7.5) | 6 (4.1) | |
| Marital status | | | | 0.298[b] |
| Single | 66 (33.2) | 19 (35.8) | 47 (32.2) | |
| Married/partnered | 58 (29.1) | 13 (24.5) | 45 (30.8) | |
| Separated/divorced | 70 (35.2) | 18 (34.0) | 52 (35.6) | |
| Widowed | 5 (2.5) | 3 (5.7) | 2 (1.4) | |
| Living condition | | | | 0.407[b] |
| Alone | 54 (27.1) | 14 (27.5) | 40 (27.4) | |
| With partner | 64 (32.2) | 18 (35.3) | 46 (31.5) | |
| With parents | 62 (31.2) | 13 (24.5) | 49 (33.6) | |
| With children | 6 (3.0) | 2 (3.8) | 4 (2.7) | |
| With friends | 13 (6.5) | 6 (11.3) | 7 (4.8) | |
| Employment | | | | 0.290[b] |
| Employed | 94 (47.2) | 32 (60.4) | 62 (42.5) | |
| Unemployed | 71 (35.7) | 14 (26.4) | 57 (39.0) | |
| Disability pension | 13 (6.5) | 3 (5.7) | 10 (6.8) | |
| Retired | 16 (8.0) | 3 (5.7) | 13 (8.9) | |
| Housewife | 5 (2.5) | 1 (1.9) | 4 (2.7) | |
| | Mean (SD) | Mean (SD) | Mean (SD) | *p* |
| Age (years) | 46.5 (9.3) | 46.3 (8.7) | 46.6 (9.5) | 0.817[c] |

[a]Pearson's $\chi^2$ test

[b]Fisher's Exact test

[c]Student's t-test

Table2
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Table 2. Baseline alcohol-related characteristics and QOL domains of responders *vs.* lost patients.

| | Enrolled (n=199) | Lost (n=53) | Responders (n=146) | |
|---|---|---|---|---|
| | n (%) | n (%) | n (%) | *p* |
| SCID-I Alcohol Use Disorder | | | | 0.249[b] |
| Alcohol Abuse Disorder | 17 (8.5%) | 2 (3.9%) | 15 (10.3%) | |
| Alcohol Dependence Disorder | 182 (91.5%) | 51 (96.2%) | 131 (89.7%) | |
| Previous detoxifications | | | | 0.831[b] |
| 0 | 107 (53.8%) | 27 (50.9%) | 80 (54.8%) | |
| 1 | 64 (32.2%) | 19 (35.8%) | 45 (30.8%) | |
| 2 | 22 (11.1%) | 5 (9.4%) | 17 (11.6%) | |
| >2 | 6 (3.0%) | 2 (3.8%) | 4 (2.7%) | |
| | Mean (SD) | Mean (SD) | Mean (SD) | *p* |
| Age at onset of alcohol use (years) | 18.0 (6.3) | 17.9 (6.3) | 18.0 (6.3) | 0.924[c] |
| Age at onset of alcohol abuse (years) | 31.8 (11.3) | 30.4 (11.4) | 32.4 (11.3) | 0.276[c] |
| AUDIT total score | 27.5 (6.5) | 27.9 (5.8) | 27.3 (6.7) | 0.563[c] |
| WHOQOL Physical health | 12.9 (2.8 | 12.8 (2.9) | 12.9 (2.8) | 0.859[c] |
| WHOQOL Psychological health | 12.7 (1.7 | 12.7 (1.6) | 12.8 (1.8) | 0.847[c] |
| WHOQOL Social relationships | 12.2 (3.1 | 12.1 (3.4) | 12.2 (3.1) | 0.940[c] |
| WHOQOL Environment | 12.5 (2.3 | 12.8 (2.6) | 12.3 (2.2) | 0.161[c] |

[a]Pearson's $\chi^2$ test

[b]Fisher's Exact test

[c]Student's t-test

Table 3. Correlations between AUDIT and WHOQOL scores.

| | AUDIT | | | | | |
|---|---|---|---|---|---|---|
| | T0 (n=199) | | T1 (n=168) | | T2 (n=146) | |
| QOL domains at T0, T1, T2[a] | r | *p* | r | *p* | r | *p* |
| WHOQOL Physical health | -0.25 | <0.001 | -0.58 | <0.001 | -0.50 | <0.001 |
| WHOQOL Psychological health | -0.22 | 0.002 | -0.46 | <0.001 | -0.41 | <0.001 |
| WHOQOL Social relationships | -0.21 | 0.003 | -0.48 | <0.001 | -0.42 | <0.001 |
| WHOQOL Environment | -0.29 | <0.001 | -0.41 | <0.001 | -0.25 | 0.003 |

[a]i.e. QOL domain score at the corresponding stage of AUDIT (e.g. correlation between the AUDIT score at T0 with each WHOQOL domain at T0; correlation between the AUDIT score at T1 with each WHOQOL domain at T1, etc.)

Table4
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Table 4. Pairwise comparison of WHOQOL mean scores from abstinent and relapsed groups at three stages of assessment.

| | Stage of assessment | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | T0 | | | T1 | | | T2 | | |
| | Abstinent (n=68) | Relapsed (n=78) | | Abstinent (n=68) | Relapsed (n=78) | | Abstinent (n=68) | Relapsed (n=78) | |
| WHOQOL domain | M (SD) | M (SD) | F, $\eta^2_p$ | M (SD) | M (SD) | F, $\eta^2_p$ | M (SD) | M (SD) | F, $\eta^2_p$ |
| Physical health | 13.2 (2.91) | 12.6 (2.72) | 1.54, 0.01 | 15.7 (2.52) | 13.2 (2.61) | 34.11[b], 0.192 | 15.7 (2.41) | 12.7 (2.42) | 55.64[b], 0.279 |
| Psychological health | 12.9 (1.88) | 12.7 (1.76) | 0.30, 0.002 | 13.7 (1.41) | 12.7 (1.77) | 14.00[b], 0.089 | 14.0 (1.66) | 12.8 (1.52) | 20.81[b], 0.126 |
| Social relationships | 12.0 (3.30) | 12.4 (2.87) | 0.58, 0.004 | 14.4 (2.49) | 12.5 (2.42) | 21.30[b], 0.129 | 14.3 (2.43) | 12.3 (1.97) | 30.04[b], 0.173 |
| Environment | 12.4 (2.20) | 12.2 (2.24) | 0.32, 0.002 | 14.0 (1.70) | 12.5 (1.84) | 27.61[b], 0.161 | 13.9 (1.89) | 12.8 (3.16) | 6.51[b], 0.043 |

[a]$p < 0.05$; [b]$p < 0.01$