Quality of Life Depends on the Drinking Pattern in Alcohol-Dependent Patients

Jean-Bernard Daeppen[1,*], Mohamed Faouzi[1], Nathalie Sanchez[1], Nora Rahhali[2], Sébastien Bineau[2] and Nicolas Bertholet[1]

[1]Alcohol Treatment Centre, Department of Community Medicine and Health, Lausanne University Hospital, Lausanne, Switzerland and [2]International Epidemiology Department, Lundbeck, Issy les Moulineaux, France

*Corresponding author: Alcohol Treatment Centre, CHUV, avenue de Beaumont 21 bis, 1011 Lausanne, Switzerland. Tel.: +41-21-314-73-51; Fax: +41-21-314-05-62; E-mail: jean-bernard.daeppen@chuv.ch

Abstract — Aims: In patients with alcohol dependence, health-related quality of life (QOL) is reduced compared with that of a normal healthy population. The objective of the current analysis was to describe the evolution of health-related QOL in adults with alcohol dependence during a 24-month period after initial assessment for alcohol-related treatment in a routine practice setting, and its relation to drinking pattern which was evaluated across clusters based on the predominant pattern of alcohol use, set against the influence of baseline variables **Methods:** The Medical Outcomes Study 36-Item Short-Form Survey (MOS-SF-36) was used to measure QOL at baseline and quarterly for 2 years among participants in CONTROL, a prospective observational study of patients initiating treatment for alcohol dependence. The sample consisted of 160 adults with alcohol dependence (65.6% males) with a mean (SD) age of 45.6 (12.0) years. Alcohol use data were collected using TimeLine Follow-Back. Based on the participant's reported alcohol use, three clusters were identified: 52 (32.5%) mostly abstainers, 64 (40.0%) mostly moderate drinkers and 44 (27.5%) mostly heavy drinkers. Mixed-effect linear regression analysis was used to identify factors that were potentially associated with the mental and physical summary MOS-SF-36 scores at each time point. **Results:** The mean (SD) MOS-SF-36 mental component summary score (range 0–100, norm 50) was 35.7 (13.6) at baseline [mostly abstainers: 40.4 (14.6); mostly moderate drinkers 35.6 (12.4); mostly heavy drinkers 30.1 (12.1)]. The score improved to 43.1 (13.4) at 3 months [mostly abstainers: 47.4 (12.3); mostly moderate drinkers 44.2 (12.7); mostly heavy drinkers 35.1 (12.9)], to 47.3 (11.4) at 12 months [mostly abstainers: 51.7 (9.7); mostly moderate drinkers 44.8 (11.9); mostly heavy drinkers 44.1 (11.3)], and to 46.6 (11.1) at 24 months [mostly abstainers: 49.2 (11.6); mostly moderate drinkers 45.7 (11.9); mostly heavy drinkers 43.7 (8.8)]. Mixed-effect linear regression multivariate analyses indicated that there was a significant association between a lower 2-year follow-up MOS-SF-36 mental score and being a mostly heavy drinker (-6.97, $P < 0.001$) or mostly moderate drinker (-3.34 points, $P = 0.018$) [compared to mostly abstainers], being female (-3.73, $P = 0.004$), and having a Beck Inventory scale score ≥ 8 (-6.54, $P < 0.001$), at baseline. The mean (SD) MOS-SF-36 physical component summary score was 48.8 (10.6) at baseline, remained stable over the follow-up and did not differ across the three clusters. Mixed-effect linear regression univariate analyses found that the average 2-year follow-up MOS-SF-36 physical score was increased (compared with mostly abstainers) in mostly heavy drinkers ($+4.44$, $P = 0.007$); no other variables tested influenced the MOS-SF-36 physical score. **Conclusion:** Among individuals with alcohol dependence, a rapid improvement was seen in the mental dimension of QOL following treatment initiation, which was maintained during 24 months. Improvement was associated with the pattern of alcohol use, becoming close to the general population norm in patients classified as mostly abstainers, improving substantially in mostly moderate drinkers and improving only slightly in mostly heavy drinkers. The physical dimension of QOL was generally in the normal range but was not associated with drinking patterns.

INTRODUCTION

Changes in health-related quality of life (QOL) are observed in a number of disease states and can be used as a measure of treatment efficacy (Lyons *et al.*, 1994; Jenkinson and McGee, 1998). The Medical Outcomes Study 36-item Short-Form Health Survey (MOS-SF-36) is a well-established method for assessing health-related QOL (Ware *et al.*, 1993; Ware and Gandek, 1998). The MOS-SF-36, which provides a generic measure of health status, has been validated extensively, and population-related normative data are available. It has been found to be reliable and valid for use in patients with alcohol dependence (Daeppen *et al.*, 1998; Stein *et al.*, 1998; Romeis *et al.*, 1999).

Studies have found significant impairment of QOL in individuals with alcohol dependence, particularly with respect to their mental health and social functioning (Gillet *et al.*, 1991; Welsh *et al.*, 1993; Longabaugh *et al.*, 1994; McKenna *et al.*, 1996; Volk *et al.*, 1997; Daeppen *et al.*, 1998; Foster *et al.*, 1998, 2000a,b; Stein *et al.*, 1998; Blow *et al.*, 2000).

Determinants of QOL in patients with alcohol dependence who undergo treatment have also been studied. Factors that predict baseline QOL in such studies include severity of alcohol dependence, intensity of alcohol use, employment status, age, gender and psychiatric history, including the presence of personality disorders and post-traumatic stress disorder (Morgan *et al.*, 2004; Colpaert *et al*, 2012; Goldstein *et al.*, 2012). However, only limited information is available about the effect that reduced alcohol intake due to treatment has on QOL, including the dynamics of QOL changes after treatment initiation, and whether such changes relate to drinking outcomes (Rather and Sherman, 1989; Gillet *et al.*, 1991; Amodeo *et al.*, 1992; McKenna *et al.*, 1996; Foster *et al.*, 1998, 2000a,b; Kraemer *et al.*, 2002; Bertholet and Daeppen, 2006).

A few studies have evaluated QOL as the primary measure in treatment trials of patients with alcohol dependence (Morgan *et al.*, 2004; Lahmek *et al.*, 2009; Martínez González *et al.*, 2011; Frischknecht *et al.*, 2013). These studies indicate that QOL, particularly the mental aspect, improves during treatment for alcohol dependence. In addition, changes in QOL during treatment are influenced by baseline QOL, the duration of abstinence from alcohol, the presence/absence of psychotic symptoms and use/non-use of illegal drugs (Morgan *et al.*, 2004; Lahmek *et al.*, 2009). However, these studies generally assessed QOL as part of a trial evaluating a specific treatment with abstinence as the treatment goal. It would also be helpful to observe the dynamics of QOL changes over an extended period in a more naturalistic, clinical practice, setting. Such an opportunity was provided by CONTROL, a prospective observational study evaluating the natural history of consecutive alcohol-dependent patients referred to a specialist treatment center (Daeppen *et al.*, 2013). The primary analysis, which identified three clusters of patients based on

their predominant pattern of alcohol use, has been reported previously (Daeppen *et al.*, 2013). The objective of the current analysis was to describe the evolution of health-related QOL in adults with alcohol dependence enrolled in CONTROL during a 24-month period after their initial assessment for alcohol-related treatment in a routine practice setting. Associations between QOL and drinking pattern were evaluated across clusters based on the predominant pattern of alcohol use, and the influence of baseline variables (including sociodemographic factors and the severity of dependence) on the dynamics of QOL changes was assessed.

METHODS

CONTROL was a single center, prospective, observational study evaluating consecutive adults with alcohol dependence, assessed for the first time at the alcohol treatment center (ATC) at Lausanne University Hospital, Lausanne, Switzerland.

Adult patients who sought treatment for alcohol dependence through the ATC outpatient clinic or inpatient program, or who were referred to the ATC after hospitalization at the general hospital, were eligible for inclusion. Patients were excluded if they did not meet the criteria for alcohol dependence based on the Mini International Neuropsychiatric Interview (MINI) questionnaire (Lecrubier *et al.*, 1997), were aged <18 years, were confused or delirious, did not speak French or had no contact address. Participants provided written informed consent. The study was approved by the Ethics Committee for clinical research at the Lausanne University Medical School (protocol 127/09). Enrolled patients were followed up by ATC research staff.

Participants included in the study were offered standard care, provided at ATC by physicians, nurses and/or psychologists. This included an initial assessment of their alcohol history, the severity and repercussions of their alcohol use disorder, and somatic and psychiatric assessments. Individuals were then invited to participate in the standard care program, and to choose their own objective with regard to their drinking. They received a combination of motivational interviews, relapse prevention measures and medication. If participants decided to abstain from alcohol, they were provided with an oxazepam-based withdrawal regimen (Daeppen *et al.*, 2002). ATC outpatients were offered the opportunity to attend weekly individual and/or group sessions, with the session frequency adjusted based on the needs of the patient as treatment progressed. ATC inpatients took part in a structured 3-week inpatient program including alcohol withdrawal, general medical evaluation and treatment, and individual and group psychotherapy sessions incorporating motivational interviewing and relapse prevention. On discharge, these patients were referred to an outpatient treatment program, an aftercare program, or to their general practitioner. Individuals referred to the ATC from the general hospital were offered 1–3 sessions of motivational interview counseling, after which they decided whether to continue with an inpatient or outpatient program or to decline further treatment.

Study assessments

Baseline and 3-, 6-, 9-, 12-, 15-, 18-, 21- and 24-month follow-up data were collected during face-to-face interviews with a trained psychologist.

Baseline sociodemographic information, family history of alcohol dependence, tobacco and drug-use data were collected using direct questions. Information on daily alcohol consumption was collected for each patient using the TimeLine Follow-Back (TLFB) method (Sobell and Sobell, 1992). At baseline and at monthly intervals during the first year and quarterly during the second year, patients provided a retrospective estimate of their daily drinking over the previous month. A consumption profile (curve) was generated for each patient that corresponded to the series of measurements of daily alcohol consumption. Health-related QOL was assessed prospectively using the MOS-SF-36 at baseline, 3, 6, 9, 12, 15, 18, 21 and 24 months.

The age of onset of alcohol dependence was based on subjects' estimate of occurrence of the first few criteria of dependence while they were invited to review their answers to the MINI. Severity of alcohol dependence was measured using the Alcohol Dependence Scale (ADS; Skinner and Horn, 1984), a self-administered questionnaire assessing alcohol withdrawal symptoms, impaired control over drinking, awareness of a compulsion to drink, increased tolerance to alcohol and awareness of drink-seeking behavior. Adverse consequences of alcohol dependence were measured using the Drinker Inventory of Consequences (Miller *et al.*, 1995), a self-administered questionnaire that results in an overall score based on five areas (physical, intrapersonal, social, interpersonal and impulse control), with scores interpreted according to the distribution described for project MATCH (Miller *et al.*, 1995). Depression was assessed using the Beck Depression Inventory-Short Form (Beck and Steer, 1987), a questionnaire evaluating depression symptoms (e.g. hopelessness and irritability), cognition (e.g. guilt or feelings of being punished) and physical symptoms (e.g. fatigue, weight loss and lack of interest in sex).

Statistical analyses

The association between drinking pattern and MOS-SF-36 summary scores in our cohort was described across three clusters of patients with different dominant alcohol use patterns, based on their consumption profile curves: (a) nearly abstinent patients hereafter referred to as 'mostly abstainers', (b) 'mostly moderate drinkers' and (c) 'mostly heavy drinkers', described in an earlier paper assessing the first 12-month follow-up (Daeppen *et al.*, 2013).

To properly address curve-clustering problems such as curve dependence on time, and to identify participants with the same alcohol consumption profile, a curve-clustering methodology based on a polynomial regression mixture model was used (Banfield and Raftery, 1993; Gaffney and Smyth, 1999; Gaffney, 2004). In this model, each individual trajectory is assumed to be generated from a finite mixture of polynomial regression model components. Model parameters and cluster membership are estimated using conditional mixture and an expectation maximization algorithm. Individual trajectories are assigned to each cluster with a certain probability. The model allowed the use of data for patients who did not complete all of the first 24 months. A similar method, applied to the first 12 months of follow-up, is described in an earlier paper (Daeppen *et al.*, 2013).

Mixed-effect linear regression analysis (Verbeke and Molenberghs, 2000; Diggle *et al.*, 2002) was used to identify

factors that are potentially associated with the mental and physical summary MOS-SF-36 scores at each time point of measurement. If Y_{ij} is the measured MOS-SF-36 score for subject i at visit j (visit$_{ij}$), and X_i is the covariate measured for subject i at the baseline, the mixed-effect linear model used is given by: $Y_{ij} = (\beta_0 + u_i) + \beta_1 \cdot \text{visit}_{ij} + \beta_2 \cdot (\text{visit}_{ij})^2 + \beta_3 \cdot (\text{visit}_{ij})^3 + \beta_4 \cdot (\text{visit}_{ij})^4 + \beta_x \cdot X_i + \varepsilon_{ij}$. The fixed part parameters are: β_0 the global mean, β_1, β_2, β_3 and β_4 the time effect, β_x the effect of the covariate X on the MOS-SF-36 score. The random effect u_i represents the individual deviation from the global intercept, and ε_{ij} represents the independent measurement errors with mean 0. The following factors were tested: age, gender, living alone, employment, age of onset of alcohol dependence, family history of alcoholism, alcohol dependence severity and consequences, tobacco use, drug use, depression, and 'drinking cluster' (mostly abstainers, mostly moderate drinkers, or mostly heavy drinkers). These variables were chosen based on available data in the literature regarding factors associated with QOL in alcohol-dependent individuals. The initial site of recruitment was also included as a variable in the analyses because it could possibly have an effect. The association between the outcome of each factor was tested in a univariate analysis. Significant predictors at a level of 5% were used in a forward procedure to fit a multivariate model.

To account for missing (imputed) data, sensitivity analyses were performed using two imputation techniques (Gaussian normal regression and Hotdeck imputation). For each technique, a total of 10 imputed data sets were generated. To combine results from imputed data sets, we used the mim stata command which allows for working with multiply imputed data sets and combining estimates using Rubin's rules (Rubin and Schenker, 1986).

RESULTS

Among the 160 patients who were enrolled into the study, 59 completed the entire study period up to 24 months. Forty-two patients had discontinued by Month 3, another 22 by Month 12, and 37 discontinued during the second year of the study.

The sociodemographic and baseline drinking characteristics of participants enrolled in the study are summarized in Table 1. The mean age of the participants was 45.6 years, two-thirds were male, just over half were unemployed and almost two-thirds were single or living alone. A family history

of alcohol dependence was common (66.9%), and patients' alcohol dependence started at a mean age of 32.4 years. At baseline, the mean ADS score was 16.5, indicating, on average, an intermediate level of severity of alcohol dependence, across a wider range. Patients reported on average 15 heavy drinking days (a day with alcohol consumption >60 g for males and >40 g for women) in the previous month, and reported consuming a mean of 7.7 drinks per drinking day. Almost three-quarters of patients smoked tobacco, while over a quarter reported using drugs; 50% of patients scored as 'depressed'.

When patients were divided into three clusters based on their dominant pattern of alcohol use over the 2 years of follow-up, 52 (32.5%) were classified as mostly abstainers, 64 (40.0%) as mostly moderate drinkers and 44 (27.5%) as mostly heavy drinkers.

Quality of life: MOS-SF-36 mental component summary score

Baseline MOS-SF-36 mental component summary scores are shown in Table 1. The mean (SD) baseline mental component summary score across the whole study population was 35.7 (13.6) points. Among the three patient clusters, the mean mental component summary score was highest, indicating better QOL, among those who were mostly abstainers [40.4 (14.6)], intermediate for moderate drinkers [35.6 (12.4)], and lowest among patients who were mostly heavy drinkers [30.2 (12.1)].

During the study, mean mental component summary scores improved in the study sample as a whole (Fig. 1) and in each individual cluster (Fig. 2). Improvements were seen by Month 3, and mental component summary scores were generally maintained or increased further during the rest of the study. The mean mental component summary score for the group of mostly abstainers reached the general population norm ~10 months after treatment initiation and remained around that level thereafter. Although mental component summary scores improved in the clusters of mostly moderate and mostly heavy drinkers, they remained below the population norm (Donovan et al., 2005; Lahmek et al., 2009) (Fig. 2). The mean (SD) mental component summary score for the whole population increased to 43.1 (13.4) points by Month 3 (an increase of 7.4 points from baseline), to 47.3 (11.4) at 12 months, and was 46.6 (11.1) at 24 months. The mean mental component summary score for the cluster of mostly abstainers increased to

Table 1. Baseline characteristics of the cohort by cluster

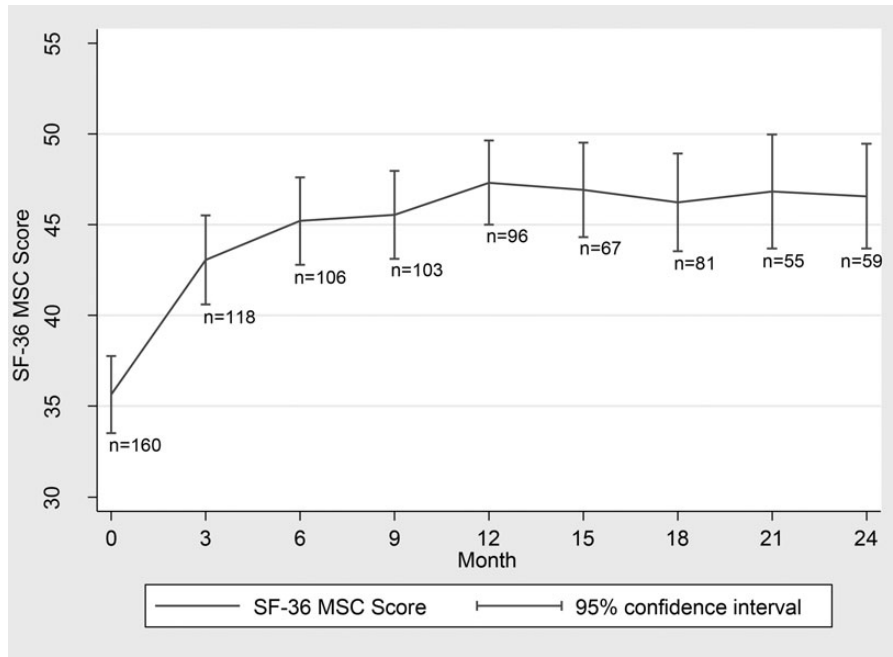|		Mostly abstainers	Mostly moderate drinkers	Mostly heavy drinkers	Total
N		52	64	44	160
Age (years)	Mean ± SD	48.9 ± 11.3	47.3 ± 12.2	39.4 ± 10.2	45.6 ± 12.0
Gender, n (%)	F	19 (36.5)	23 (35.9)	13 (29.6)	55 (34.4)
Family history of alcoholism, n (%)	Yes	31 (63.3)	44 (71)	28 (65.1)	103 (66.9)
Smoking status, n (%)	Yes	38 (73.1)	40 (62.5)	36 (83.7)	114 (71.7)
Drug use, n (%)	Yes	11 (21.2)	16 (25)	18 (40.9)	45 (28.1)
DrInC Total score	Mean ± SD	38.3 ± 28.4	40.8 ± 23.3	58.8 ± 22.6	44.9 ± 26.2
Alcohol Dependence Scale score	Mean ± SD	15.5 ± 6.7	15.1 ± 7.8	19.7 ± 7.8	16.5 ± 7.7
Beck Depression Inventory ≥ 8, n (%)	Yes	18 (34.6)	36 (56.3)	26 (59.1)	80 (50.0)
Employment, n (%)	Yes	22 (43.1)	31 (50.8)	19 (45.2)	72 (46.8)
Age of onset of alcohol dependence	Mean ± SD	33.6 ± 13.6	34.1 ± 13.3	28.9 ± 10.9	32.4 ± 12.9
MOS-SF-36 Mental Component Summary score	Mean ± SD	40.4 ± 14.6	35.6 ± 12.4	30.2 ± 12.1	35.7 ± 13.6
MOS-SF-36 Physical Component Summary score	Mean ± SD	45.5 ± 11.7	49.6 ± 10.7	51.6 ± 8	48.8 ± 10.6
Mean total drinks (10 g ethanol) over 30 days prior baseline	Mean ± SD	101 ± 210	170 ± 132	500 ± 275	238 ± 262

Fig. 1. Mean MOS-SF-36 mental component summary score by visit: all patients.
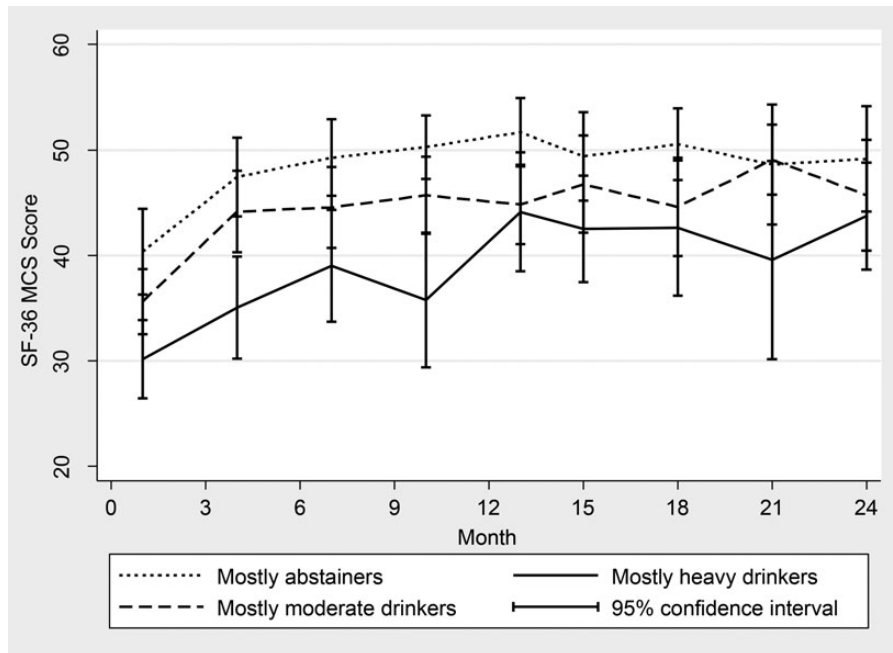

Fig. 2. Mean MOS-SF-36 mental component summary scores according to patient cluster (reporting raw data not including imputation of missing values).

47.4 (12.3) at 3 months, 51.7 (9.7) at 12 months, and was 49.1 (11.6) at 24 months. Mental component summary scores at 3, 12 and 24 months among mostly moderate drinkers were 44.2 (12.7), 44.8 (11.9) and 45.7 (11.9), respectively, and among mostly heavy drinkers were 35.1 (12.9), 44.1 (11.3) and 43.7 (8.8).

In univariate linear regression analysis, a number of parameters were associated with the mean mental component summary score (in the direction of a more severe mental score), including younger age, being female, younger age at onset of alcohol dependence, positive family history, higher ADS score, higher daily alcohol intake, having depression and being in the mostly moderate or mostly heavy drinking clusters (Table 2). There was no association between mental component summary score and marital status, employment status, smoking, or drug use.

Multivariate analysis (which included the following variables: age, gender, age at onset of alcohol dependence, depression, family history, severity of alcohol dependence, daily alcohol intake, drinking cluster) found a significant association

between a lower mental component summary score and being a mostly heavy drinker (coefficient −6.97, $P < 0.001$) or mostly moderate drinker (−3.34, $P = 0.018$) (versus mostly abstainers), being female (−3.73, $P = 0.004$), and having moderate to severe depression (−6.54, $P < 0.001$) A 5-point increase in ADS score was associated with a decrease in mental component summary score (−0.94, $P = 0.044$) (Table 3).

Data from the sensitivity analysis (Table 4) show that, when accounting for missing data, female gender, presence of depression at baseline corresponding to a Beck Inventory Scale score ≥ 8, an improvement in ADS score by 5 units, and being in the mostly heavy drinker cluster all retained statistical significance, across both imputation models, with regard to the association with mental component summary score.

Quality of life: MOS-SF-36 physical component summary score

Baseline MOS-SF-36 physical component summary scores are shown in Table 1. The mean (SD) baseline physical component summary score across the whole study population was 48.8 (10.6) [mostly abstainers: 45.5 (11.7), mostly moderate drinkers: 49.6 (10.7), mostly heavy drinkers: 51.6 (8.0)], and it remained relatively stable throughout the study, reaching a mean end-of-study value of 49.5 (9.5) (Fig. 3). Physical component summary scores did not differ substantially between the three clusters (Fig. 4).

Among all tested variables in the univariate analysis, only age (beta = −0.11, 95% CI = [−0.21, −0.004]; $P = 0.043$) and being in the mostly heavy drinkers cluster (beta = 4.44, 95% CI = [1.23–7.65]; $P = 0.007$) were significantly associated with the physical component summary score at 2 years. No subsequent multivariate modeling was performed.

DISCUSSION

This study indicates that mental health QOL, measured with the MOS-SF-36, improved in individuals with alcohol dependence during 24 months of follow-up after an initial assessment for an alcohol treatment program. An improvement was seen by 3 months, which was then maintained over time. The progression of mental health QOL appeared to be related to participants' predominant pattern of drinking and also to any

Table 2. Factors associated with MOS-SF-36 mental and physical component summary score at 2 years: univariate mixed-effects linear regression analysis

Variable	Mental score			Physical score		
	Regression coefficient (SE)	95% confidence interval	*P*-value	Regression coefficient (SE)	95% confidence interval	*P*-value
Age	0.25 (0.06)	0.13, 0.38	<0.001	−0.11 (0.05)	−0.21, −0.004	0.043
Sex (female; ref = male)	−5.32 (1.65)	−8.55, −2.09	0.001	−1.45 (1.35)	−4.11, 1.20	0.283
Marital status (married; ref = not married)	1.41 (1.65)	−1.84, 4.65	0.395	−0.78 (1.33)	−3.38, 1.82	0.555
Employment status (active; ref = not active)	−1.12 (1.63)	−4.32, 2.08	0.492	1.47 (1.29)	−1.07, 4.00	0.256
Age on onset of alcohol dependency	0.13 (0.06)	0.004, 0.25	0.043	0.02 (0.05)	−0.08, 0.12	0.750
Family history (yes; ref = no)	−4.44 (1.71)	−7.78, −1.09	0.009	0.73 (1.39)	−1.99, 3.45	0.599
ADS score[a]	−0.52 (0.10)	−0.71, −0.33	<0.001	0.07 (0.08)	−0.10, 0.24	0.410
Daily alcohol intake[b]	−0.82 (0.07)	−0.95, −0.69	<0.001	−0.06 (0.06)	−0.16, 0.05	0.306
Current tobacco smoker[c]	−1.80 (1.78)	−5.29, 1.69	0.311	−1.16 (1.42)	−3.93, 1.62	0.413
Drug use[d]	−0.42 (1.80)	−3.96, 3.11	0.815	1.15 (1.44)	−1.67, 3.97	0.423
Depression (Beck Inventory Scale score ≥ 8)[e]	−9.85 (1.41)	−12.61, −7.09	<0.001	−1.77 (1.28)	−4.28, 0.75	0.168
Being in the 'mostly moderate drinker' cluster	−5.19 (1.71)	−8.53, −1.85	0.002	2.22 (1.47)	−0.66, 5.10	0.132
Being in the 'mostly heavy drinker' cluster	−10.46 (1.91)	−14.21, −6.72	<0.001	4.44 (1.64)	1.23, 7.65	0.007

[a]Score 14–21 = intermediate level of dependence, score 22–30 = substantial level of dependence.
[b]Average number of standard drinks per day during the past 30 days.
[c]At least one cigarette/day over the last 3 months.
[d]Any drug use over lifetime.
[e]Beck Depression Inventory scale short-form score ≥8 indicates moderate to severe depression.

Table 3. Factors associated with MOS-SF-36 mental component summary score at 2 years: multivariate mixed-effects linear regression analysis

Variable	Regression coefficient (SE)	95% confidence interval	*P*-value
Age	0.06 (0.06)	−0.05, 0.18	0.252
Gender (female; ref = male)	−3.73 (1.28)	−6.24, −1.22	0.004
Increase in ADS score by 5 points[a]	−0.94 (0.46)	−1.85, −0.03	0.044
Depression (Beck Inventory Scale score ≥ 8)[b]	−6.54 (1.32)	−9.13, −3.94	<0.001
Mostly moderate drinker	−3.34 (1.41)	−6.09, −0.58	0.018
Mostly heavy drinker	−6.97 (1.64)	−10.18, −3.76	<0.001
Visit*	3.94 (0.85)	2.28, 5.60	<0.001
Visit^2*	−0.44 (0.15)	−0.73, −0.15	0.003
Visit^3*	0.022 (0.01)	0.003, 0.040	0.021
Visit^4*	−0.0004 (0.0002)	−0.0007, 1.64e-06	0.051

[a]Score 14–21 = intermediate level of dependence, score 22–30 = substantial level of dependence.
[b]Beck Depression Inventory scale short-form score ≥8 indicates moderate to severe depression.
*Coeff Beta1, Beta2, Beta3, Beta4, according to polynomial form for the time [equation reported in the Methods section (Statistical Analyses)].

Table 4. Factors associated with MOS-SF-36 mental component summary score at 2 years: sensitivity analysis, based on two imputation techniques (Gaussian regression and Hotdeck)

Variable	Regression imputation method		Hotdeck imputation method	
	Coefficient	*P*-value	Coefficient	*P*-value
Age	0.05	0.34	0.06	0.18
Gender(F, ref = M)	−2.28	0.05	−4.20	<0.0001
Baseline Depression (Beck > 8)	−5.17	<0.0001	−3.39	0.001
Improvement in ADS score by 5 units	−0.76	0.05	−0.53	0.16
Mostly heavy drinkers	−4.53	0.002	−7.72	<0.0001
Mostly moderate drinkers	−2.26	0.08	−4.27	<0.0001
Visit*	3.97	<0.0001	3.68	0.001
Visit^2*	−0.42	0.005	−0.388	0.04
Visit^3*	0.019	0.04	0.018	0.16
Visit^4*	−0.0003	0.09	−0.0003	0.27

*Coeff Beta1, Beta2, Beta3, Beta4, according to polynomial form for the time [equation reported in the Methods section (Statistical Analyses)].
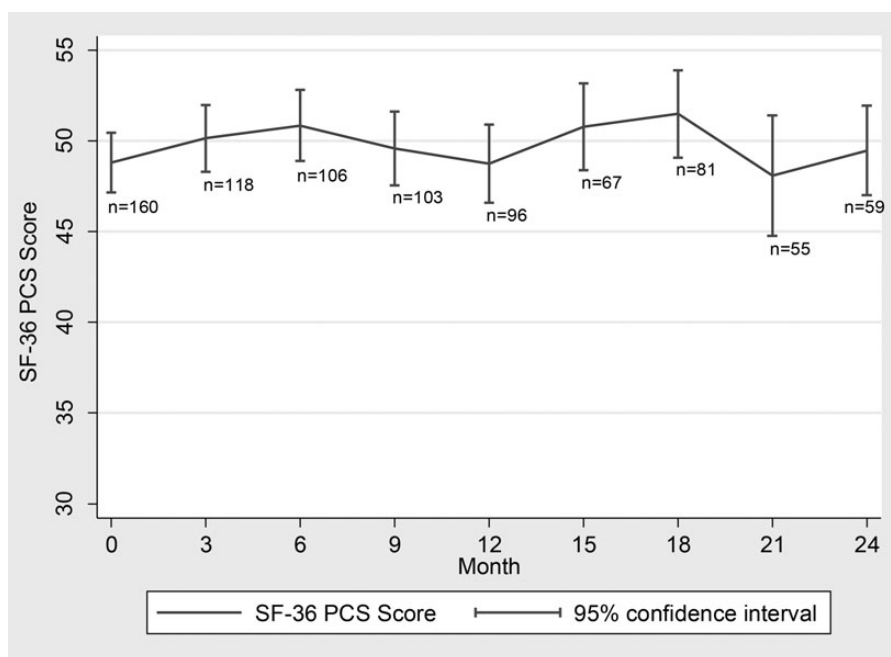

Fig. 3. Mean MOS-SF-36 physical component summary score by visit: all patients.

change in their level of alcohol dependence during treatment. In contrast to mental health QOL, physical QOL did not change during the study and did not differ substantially between individuals with different drinking patterns.

It is well established that QOL is impaired in individuals with alcohol dependence (Welsh *et al.*, 1993; McKenna *et al.*, 1996; Volk *et al.*, 1997; Daeppen *et al.*, 1998; Foster *et al.*, 2000b). Studies specifically evaluating QOL over time have shown that treatment for alcohol dependence is followed by improvements in mental health QOL after 3 weeks to 3 months (Morgan *et al.*, 2004; Lahmek *et al.*, 2009; Eshelman *et al.*, 2010; Martinez-Gonzalez *et al.*, 2011). The largest of these studies evaluated changes in QOL in >1200 patients with alcohol dependence during treatment with acamprosate and psychosocial support, and found that after 3 months the MOS-SF-36 mental component summary score had increased by 28.7 points from a baseline of 37.9 points (Morgan *et al.*, 2004). In our study, improvements in the MOS-SF-36 mental component summary score occurred in a similar timeframe,

with an improvement of 11.7 points seen after 3 months (from a baseline of 35.7 points). It should be noted that our study did not evaluate the effect of a specific treatment regimen on QOL, but rather changes in QOL in patients offered the opportunity to receive a standard care program at our center (irrespective of whether they accepted treatment or how well they complied with treatment); consequently, the design of our study does not allow one to draw any causal inferences regarding the effects of treatment for alcohol dependence on QOL.

Several of the studies mentioned also found that improvements in mental health QOL seen after 1 or 3 months were maintained (and in some cases improved slightly further) after 6–12 months (Morgan *et al.*, 2004; Eshelman *et al.*, 2010; Martinez-Gonzalez *et al.*, 2011). The results of our study are in agreement with this, and extend the data further, showing that improvements were maintained out to 24 months.

The current study also provides additional information, in terms of the effects seen in individuals according to their predominant pattern of alcohol use. Three clusters were
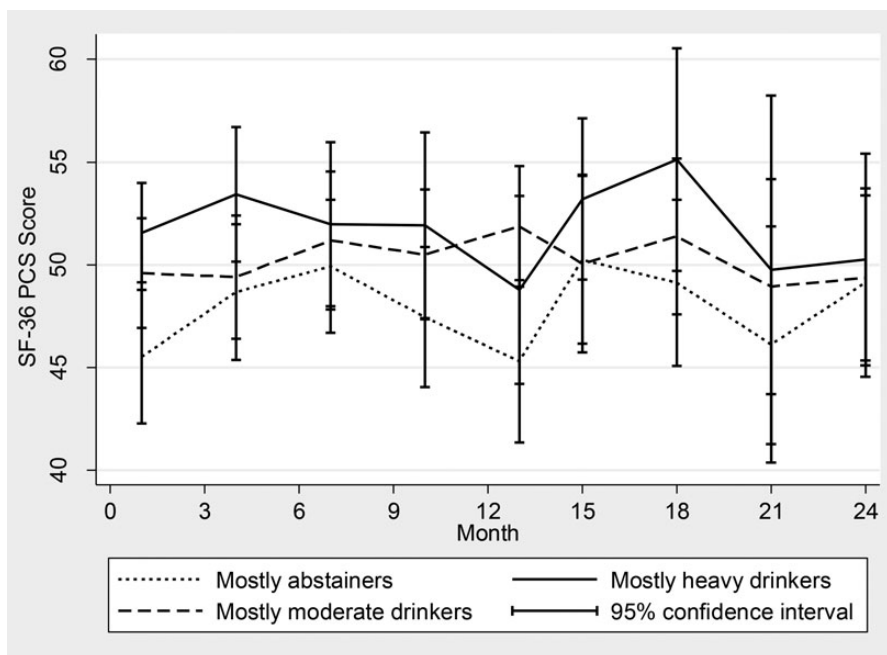
Fig. 4. Mean MOS-SF-36 physical component summary score according to patient cluster (reporting raw data not including imputation of missing values).

identified: mostly abstainers, mostly moderate drinkers and mostly heavy drinkers. Improvements in the mental score were seen in all three clusters; however, in patients classified as mostly abstainers, the score increased to the normative level seen in the general population, whereas among mostly moderate and mostly heavy drinkers, scores remained below the norm, particularly in those who were mostly heavy drinkers. With regard to the three clusters, sensitivity analysis showed that only the association between mental component summary score and being in the mostly heavy drinker cluster retained statistical significance when imputing data by two different imputation methods.

Previous studies have identified various factors as being predictive of changes in QOL after treatment for alcohol dependence, including baseline QOL, the duration of abstinence from alcohol, the presence/absence of psychotic symptoms and use/non-use of illegal drugs (Morgan *et al.*, 2004; Lahmek *et al.*, 2009). In our study, factors identified as being independently predictive of the MOS-SF-36 mental component summary score included being in the mostly heavy drinker cluster, being female, the presence of moderate to severe depression and having a high level of alcohol dependence. A study in Spain also found evidence of a relationship between QOL and drinking outcome; in that study, baseline QOL was predictive of the level of alcohol use during the first 3 months of cognitive-behavioral treatment (Martinez-Gonzalez *et al.*, 2011).

The relation between treatment for alcohol dependence and change in physical QOL is not as clear-cut in the literature as the change in mental QOL. Although some studies have found an improvement in physical QOL after treatment (Morgan *et al.*, 2004; Lahmek *et al.*, 2009), a study in liver transplant recipients found no significant improvement in patients with a history of alcohol-use disorder (Eshelman *et al.*, 2010). In our study, there was no significant difference between the mean MOS-SF-36 physical component summary scores at baseline and after 24 months. Nevertheless, it is interesting to note that univariate analysis showed that age and being in the mostly heavy drinking cluster were the only independent variables to be significantly associated with physical component summary score at 2 years.

An important limitation of our study was the attrition rate. Although the sensitivity analysis compensated for the effect of loss to follow-up, the 37% follow-up rate impacts on our ability to draw robust conclusions. However our sensitivity analyses suggest that missing data are missing at random, indicating that subjects lost to follow-up were similar to counterparts at baseline regarding age, gender, depression, severity of alcohol dependence and repartition in clusters. This means that higher follow-up rate would have resulted in similar findings, except if other baseline differences not included in the sensitivity analyses were considered, i.e. psychiatric conditions not assessed at baseline. Use of the MOS-SF-36 questionnaire represents another potential limitation. Although it is considered valid for use in alcohol-dependent subjects (Daeppen *et al.*, 1998; Stein *et al.*, 1998), it is nonetheless a generic health status measure, and is not based on specific symptoms associated with alcohol dependence. Thus, the information it collects may not be completely relevant or specific for individuals with alcohol dependence, and may not be the ideal quality-of-life measure in this group (Luquiens *et al.*, 2012). However, no specific instrument has yet been developed to assess changes in QOL in individuals with alcohol dependence (Luquiens *et al.*, 2012). The MOS-SF-36 questionnaire was administered every 3 months during the study. Due to no QOL assessment being performed within a 3-month time period, QOL may have deteriorated during the first few weeks of treatment, and this would have been missed in the current study; however, the main purpose of the study was to assess changes over a longer timeframe up to 24 months. There was also no control group in the study; nevertheless, the aim of the study was to obtain data in a naturalistic setting reflecting normal clinical

practice. Finally, as alcohol-dependent patients were recruited after initial evaluation for treatment in one center in Lausanne, Switzerland, and included in three different settings, our findings are limited in their generalizability to other patients in other countries, with different recruitment processes or settings.

In conclusion, MOS-SF-36 mental component summary scores improved in alcohol-dependent subjects during the 24 months after an initial evaluation for standard alcohol-related treatment. An early improvement in mental health QOL was observed that was maintained over time. The progression in MOS-SF-36 mental component summary score was related to the predominant pattern of alcohol usage and to drinking outcome.

REFERENCES

Amodeo M, Kurtz N, Cutter H. (1992) Abstinence, reasons for not drinking, and life satisfaction. *Int J Addict* **27**:707–16.

Banfield JD, Raftery AE. (1993) Model-based Gaussian and non-Gaussian clustering. *Biometrics* **49**:803–21.

Beck AT, Steer RA. (1987) *Manual for the Beck Depression Inventory*. San Antonio, Texas, USA: The Psychological Corp.

Bertholet N, Daeppen JB. (2006) A possible way to motivate ambivalent patients to undergo detoxification. *Alcohol Alcohol* **41**:205.

Blow FC, Walton MA, Barry KL *et al.* (2000) The relationship between alcohol problems and health functioning of older adults in primary care settings. *J Am Geriatr Soc* **49**:335–6.

Colpaert K, De Maeyer J, Broekaert E *et al.* (2012) Impact of addiction severity and psychiatric comorbidity on the quality of life of alcohol-, drug-and dual-dependent persons in residential treatment. *Eur Addict Res* **19**:173–83.

Daeppen JB, Kreig MA, Burnand B *et al.* (1998) MOS-SF-36 in evaluating health-related quality of life in alcohol-dependent patients. *Am J Drug Alcohol Abuse* **24**:685–94.

Daeppen JB, Gache P, Landry U *et al.* (2002) Symptom-triggered vs fixed-schedule doses of benzodiazepine for alcohol withdrawal: a randomized treatment trial. *Arch Intern Med* **162**:1117–21.

Daeppen JB, Faouzi M, Sanglier T *et al.* (2013) Drinking patterns and their predictive factors in CONTROL: a 12-month prospective study in a sample of alcohol-dependent patients initiating treatment. *Alcohol Alcohol* **48**:189–95.

Diggle PJ, Heagerty PJ, Liang K-Y *et al.* (2002) *Analysis of Longitudinal Data*, 2nd edn. New York, USA: Oxford University Press Inc.

Donovan D, Mattson ME, Cisler RA *et al.* (2005) Quality of life as an outcome measure in alcoholism treatment research. *J Stud Alcohol Suppl* (15):119–39.

Eshelman A, Paulson D, Meyer T *et al.* (2010) The influence of alcohol abuse history on the differential, longitudinal patterns of mental and physical quality of life following liver transplantation. *Transplant Proc* **42**:4145–7.

Foster JH, Marshall EJ, Hooper R *et al.* (1998) Quality of life measures in alcohol-dependent subjects and changes with abstinence and continued heavy drinking. *Addict Biol* **3**:321–32.

Foster JH, Marshall EJ, Peters TJ. (2000a) Application of a quality of life measure, the life situation survey (LSS), to alcohol-dependent subjects in relapse and remission. *Alcohol Clin Exp Res* **24**:1687–92.

Foster JH, Peters TJ, Marshall EJ. (2000b) Quality of life measures and outcome in alcohol-dependent men and women. *Alcohol* **22**:45–52.

Frischknecht U, Sabo T, Mann K. (2013) Improved drinking behaviour improves quality of life: a follow-up in alcohol-dependent subjects 7 years after treatment. *Alcohol Alcohol* **48**:579–84.

Gaffney S. (2004) Probabilistic Curve-Aligned Clustering and Prediction with Regression Mixture Models. Thesis Dissertation, University of California, Irvine, USA.

Gaffney S, Smyth P. (1999) Trajectory Clustering with Mixtures of Regression Model. Technical Reports N°99–15. Irvine, USA: Department of Information and Computer Science, University of California.

Gillet C, Paille F, Wahl D *et al.* (1991) Outcome of treatment in alcoholic women. *Drug Alcohol Depend* **29**:189–94.

Goldstein RB, Dawson DA, Smith SM *et al.* (2012) Antisocial behavioral syndromes and 3-year quality-of-life outcomes in United States adults. *Acta Psychiatr Scand* **126**:137–50.

Jenkinson C, McGee H. (1998) *Health Status Measurement: A Brief but Critical Introduction*. Oxfordshire, UK: Radcliffe Medical Press.

Kraemer KL, Maisto SA, Conigliaro J *et al.* (2002) Decreased alcohol consumption in outpatient drinkers is associated with improved quality of life and fewer alcohol-related consequences. *J Gen Intern Med* **17**:382–6.

Lahmek P, Berlin I, Michel L *et al.* (2009) Determinants of improvement in quality of life of alcohol-dependent patients during an inpatient withdrawal programme. *Int J Med Sci* **6**:160–7.

Lecrubier Y, Sheehan DV, Weiller E *et al.* (1997) The mini international neuropsychiatric interview (MINI). A short diagnostic structured interview: reliability and validity according to the CIDI. *Eur Psychiatry* **12**:224–31.

Longabaugh R, Mattson ME, Connors GJ *et al.* (1994) Quality of life as an outcome variable in alcoholism treatment research. *J Stud Alcohol (Suppl)* **12**:119–29.

Luquiens A, Reynaud M, Falissard B *et al.* (2012) Quality of life among alcohol-dependent patients: how satisfactory are the available instruments? A systematic review. *Drug Alcohol Depend* **125**:192–202.

Lyons RA, Lo SV, Littlepage NC. (1994) Comparative health status of patients with 11 common illnesses in Wales. *J Epidemiol Community Health* **48**:388–90.

Martínez González JM, Graña Gómez JL, Trujillo Mendoza H. (2011) [Longitudinal study on quality of life, craving and psychological adjustment in alcohol-dependent patients: variations depending on the personality disorders]. *Adicciones* **23**: 227–35.

McKenna M, Chick J, Buxton M *et al.* (1996) The SECCAT survey: I. The costs and consequences of alcoholism. *Alcohol Alcohol* **31**: 565–76.

Miller WR, Tonigan JS, Longabaugh R. (1995) *The Drinker Inventory of Consequences (DrInC): An Instrument for Assessing Adverse Consequences of Alcohol Abuse*. Project MATCH Monograph Series, **Vol. 4**. DHHS Publication No. 95–3911. Rockville, Maryland, USA: National Institute on Alcohol Abuse and Alcoholism.

Morgan MY, Landron F, Lehert P, for the New European Alcoholism Treatment Study Group. (2004) Improvement in quality of life after treatment for alcohol dependence with acamprosate and psychosocial support. *Alcohol Clin Exp Res* **28**:64–77.

Rather BC, Sherman MF. (1989) Relationship between alcohol expectancies and length of abstinence among Alcoholics Anonymous members. *Addict Behav* **14**:531–6.

Romeis JC, Waterman B, Scherrer JF *et al.* (1999) The impact of sociodemographics, comorbidity and symptom recency on health-related quality of life in alcoholics. *J Stud Alcohol* **60**:653–62.

Rubin DB, Schenker N. (1986) Multiple imputation for interval estimation from simple random samples with ignorable nonresponse. *J Am Stat Assoc* **81**:366–74.

Skinner HA, Horn JL. (1984) *Alcohol Dependence Scale: Users Guide*. Toronto, Canada: Addiction Research Foundation.

Sobell LC, Sobell MB. (1992) Timeline follow-back. A technique for assessing self-reported ethanol consumption. In Allen J, Litten RZ (eds). *Measuring Alcohol Consumption: Psychosocial and Biological Methods*. Totowa, NJ: Humana Press, 41–72.

Stein MD, Mulvey KP, Plough A *et al*. (1998) The functioning and well being of persons who seek treatment for drug and alcohol use. *J Subst Abuse* **10**:75–84.

Verbeke G, Molenberghs G. (2000) *Linear Mixed Models for Longitudinal Data*. New York, USA: Springer-Verlag.

Volk RJ, Cantor SB, Steinbauer JR *et al*. (1997) Alcohol use disorders, consumption patterns, and health-related quality of life of primary care patients. *Alcohol Clin Exp Res* **21**: 899–905.

Ware JE, Jr, Gandek B. (1998) Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) Project. *J Clin Epidemiol* **51**:903–12.

Ware JE, Jr, Snow KK, Kosinski M *et al*. (1993) *SF-36 Health Survey Manual and Interpretation Guide*. New England Medical Center, Boston, USA: The Health Institute.

Welsh JA, Buchsbaum DG, Kaplan CB. (1993) Quality of life of alcoholics and non-alcoholics: does excessive drinking make a difference in the urban setting? *Qual Life Res* **2**:335–40.