

## TREATMENT

# Treatment for Alcohol Dependence in Catalonia: Health Outcomes and Stability of Drinking Patterns over 20 Years in 850 Patients

Antoni Gual<sup>1,\*</sup>, Fabián Bravo<sup>1</sup>, Anna Lligoña<sup>1</sup> and Joan Colom<sup>2</sup>

<sup>1</sup>Alcohol Unit, Psychiatry Department, Clinical Institute of Neurosciences, Hospital Clínic, IDIBAPS, Barcelona, Spain and <sup>2</sup>Program on Substance Abuse, General Directorate of Public Health, Department of Health, Generalitat de Catalunya, Barcelona, Spain

\*Corresponding author: Alcohol Unit, Psychiatry Department, Clinical Institute of Neurosciences, Hospital Clínic, IDIBAPS, Villarroel 170, 08036 Barcelona, Spain. Tel: +34-932279923; Fax: +34-932277300; E-mail: tgual@clinic.ub.es

(Received 23 April 2009; in revised form 23 April 2009; accepted 6 May 2009; advance access publication 2 June 2009)

**Abstract — Aims:** The aim of this study was to evaluate long-term outcomes in alcohol-dependent patients following outpatient treatment and gender differences in drinking outcome and mortality. **Methods:** A 20-year longitudinal prospective study was done with interim analyses at 1, 5 and 10 years. Of the original sample of 850 patients, 767 (90%) were located 20 years later and 393 of these were interviewed. 273 (32%) patients died during the intervening period and 101 (12%) no longer wished to participate in the study. Drinking status was assigned based on the 12 months prior to the follow-up interview. **Results:** At the 20-year follow-up, 277 (32.6%) of the 393 patients for whom drinking status could be assigned were abstinent (defined never drinking or drinking on less than occasion per month and never more than four drinks/drinking occasion.), 29 (3.4%) were controlled drinkers and 87 (10.2%) were heavy drinkers. Controlled drinking was the least stable category, with 23% continuing from year 5 to year 10 in that category, and 10% continuing in that category from year 10 to year 20. Mortality was higher (39.1%) in those who had been categorized at year 5 as heavy drinkers compared to those who had been categorized as controlled drinkers or abstinent. Abstinent patients reported fewer alcohol-related problems and better psychosocial functioning than heavy drinkers. Women achieved higher abstinence rates (47.2% versus 29.0%,  $P = 0.005$ ) and had lower mortality (22.4% versus 34.5%,  $P = 0.03$ ) than men. **Conclusions:** Over the long-term, abstinence is the most frequent and stable drinking outcome achieved and is associated with fewer problems and better psychosocial functioning. Controlled drinking is rarely achieved and sustained. Women appear to do better than men in the long term.

## INTRODUCTION

Alcohol dependence is a chronic condition and thus needs to be considered from a long-term perspective. Longitudinal cohort studies have shown that the consequences of alcohol dependence can be observed over long periods, evolve over time and have an impact on multiple dimensions of quality of life (Edwards, 1984; Longabaugh *et al.*, 1994). However, relatively few prospective studies have followed the course of the disease over long periods and even fewer have assessed the long-term impact of treatment.

Over the last decades, a limited number of studies have reported treatment outcome in alcohol-dependent patients with follow-up periods extending beyond 15 years (Hyman, 1976; O'Connor and Daly, 1985; McCabe, 1986; Nordström *et al.*, 2004; Mann *et al.*, 2005; Moos *et al.*, 2006). Most of these have been conducted in English-speaking countries (Hyman, 1976; O'Connor and Daly, 1985; McCabe, 1986; Moos *et al.*, 2006) and have followed cohorts in which relatively few women, if any, were included (McCabe, 1986; Mann *et al.*, 2005), with the exception of one American study that followed up a sample of 232 women for 16 years (Moos *et al.*, 2006). The limited representation of women in such studies explains the lack of gender-specific data on drinking outcome and our ignorance of potential gender differences in the long-term course of the illness following treatment. It is important that future studies evaluate long-term outcome in more diverse populations in which different ethnic groups are represented adequately and in which a sufficient number of women are included.

From a methodological point of view, it is generally accepted that interim analyses are required in long-term follow-up studies, together with the evaluation of multiple endpoints in addition to drinking outcome *per se* (Duckitt *et al.*, 1985; Edwards

*et al.*, 1988), notably with respect to social outcomes. In contrast, no consensus has been reached on other aspects of the design of such studies, for example with respect to the definition of treatment success, to the minimum time required to establish stable remission (6 months, 1 year or 3 years) and to how patients who no longer wish to participate should be handled in the data analysis (Vaillant, 1988; Mann *et al.*, 2005; Moos and Moos, 2005). Differences in the criteria used to assess outcome hamper comparisons between available long-term studies.

For all these reasons, we have performed a prospective study of long-term outcome in a large sample of patients treated for alcohol dependence in Catalonia that attempts to meet these different challenges. The goals of the study were firstly to assess long-term outcome in terms of drinking behaviour, morbidity, alcohol-related socio-legal problems and psychosocial functioning, and secondly to evaluate potential gender differences in drinking outcome and mortality.

## METHODS

### Sample and procedure

This longitudinal, prospective study was initiated in 1987 in eight Addiction Centres in Catalonia (Spain). The study originally included 850 patients who have now been followed up for 20 years. The study centres were chosen to cover the sociodemographic and territorial diversity of Catalonia. In accordance with the distribution of the Catalan population, two-thirds of the patients were recruited in the metropolitan area of Barcelona and one-third in the rest of Catalonia. The sample size was planned to correspond to all patients entering treatment during

Table 1. Definition of drinking status

Definition	Quantity consumed <sup>a</sup>	And/Or	Drinking frequency <sup>b</sup>
Abstinent	None or <5 drinks/drinking occasion	And	Never or <1 drinking occasion per month
Controlled drinker	<5 drinks/drinking occasion	And	≥1 drinking occasion per month but <7 days per week
Heavy drinker	≥5 drinks/drinking occasion	Or	Daily drinking

<sup>a</sup>One drink = 10 g of pure alcohol.

<sup>b</sup>Last 12 months: never, <1 occasion/month, ≥1 occasion/month, ≥1 occasion/week, daily.

1 year, based on the number of patients who had been treated for the first time in each of the participating centres in the year preceding the start of the study. The study included all patients aged between 18 and 55 years who fulfilled DSM-III criteria for alcohol dependence (American Psychiatric Association, 1980) and who had accepted to enter a treatment programme. Patients were expected to have a stable home with at least one other family member.

All patients in the study entered a similar treatment programme lasting approximately 2 years. The overall aim of the programme was to achieve abstinence and set three specific goals. These were to build awareness of alcohol dependence as an illness, to acquire new lifestyle habits facilitating abstinence and to improve quality of life. The treatment programme began with acute detoxification of the patient, including medication when needed, followed by a rehabilitation programme involving medication, medical management and group therapy led by a clinical psychologist. All treatments were delivered by health professionals in the facilities of the eight participating addiction centres.

The study cohort was evaluated at inclusion and after 1, 5 (Gual *et al.*, 1999a), 10 (Gual *et al.*, 2004) and 20 years using a protocol that included information on drinking behaviour, morbidity, mortality, alcohol-related problems, psychosocial stress and global functioning (Axes IV and V; DSM-III-R). At each time-point, data were collected during interviews with psychiatrists or clinical psychologists from the study centres. The assessment protocol was designed to allow interviews in three different settings: study centre, patients' home and by telephone. Wherever possible, the patient and family member were interviewed. In the case of discrepancy between the patient and the family member, data reporting a worse outcome were taken into account. All patients lost to follow-up at each evaluation time-point were systematically searched for at the Civil Records Office of Mortality at the Health Department.

### Measures

**Drinking patterns.** Drinking behaviour was evaluated at the 5-, 10- and 20-year horizons by scoring the quantity and frequency of alcohol consumption according to the information provided by the patient and/or his relative. This approach, based on the patient as a main source of information, has been used in previous long-term studies (Mann *et al.*, 2005) since self-reports are widely accepted as a main source of data on alcohol consumption (Babor *et al.*, 2000; Del Boca and Darkes, 2003). No biological markers were used. At each evaluation point, patients were asked about their alcohol consumption during the previous 12 months concerning the frequency of drinking (never, <1 occasion/month, ≥1 occasion/month, ≥1 occasion/week, daily), and amounts drunk per drinking day expressed in standard drinks (one standard drink = 10 g of pure

alcohol) (Gual *et al.*, 1999b). According to this information, patients were assigned to one of three drinking status categories (abstinent, controlled drinking or heavy drinking) on the basis of the consumption criteria listed in Table 1. It was necessary to have maintained these consumption patterns continually over the last 12 months in order to meet the criteria. Where consumption patterns had changed during this period, the patient was assigned to the worst drinking status category.

### Morbidity and mortality

At each time-point, data were collected in the presence of chronic illnesses and use of medication during the previous 3 years. Visits to emergency units and hospital admissions during the previous 12 months were also registered. If the family member reported that the patient had died, the cause of death was sought, and the date of death was verified from the Civil Records Office at the Health Department.

### Alcohol-related problems

We assessed accidents (home, work, traffic), unemployment, long-term disability, and financial and legal problems over the previous 12 months. Unemployment was estimated excluding those retired or with permanent disability. Patients were considered to have financial problems if they were marginalized or reported insufficient income to cover basic needs.

### Psychosocial stress and social functioning

Psychosocial stress was assessed with DSM-III-R Axis IV criteria (American Psychiatric Association, 1987) with a score ranging from 1 (absence of stress) to 6 (maximum stress). Social functioning was assessed with the GAF scale (DSM-III-R Axis V) with scores ranging from 0 to 100. Both assessments referred to the situation of the patient at the time of the interview.

### Statistical analysis

Percentages in each follow-up status, drinking category and mortality were calculated with respect to the initial sample of 850 subjects at each time-point analysis. Potential differences in the distribution of categorical variables between groups were assessed using the two-tailed  $\chi^2$  test. Potential between-group differences for ordinal and quantitative variables were evaluated using the Kruskal–Wallis test and ANOVA, respectively. Multiple comparison tests using Bonferroni's correction were used for both qualitative and quantitative data (Dawson and Trapp, 2001). A probability level of <0.05 was taken to be statistically significant. Data were analysed using SPSS statistical software version 14.0 (SPSS, Inc, Chicago, IL, USA).

Table 2. Baseline sociodemographic and clinical features of the sample

	N = 850
Male/female (n, %)	685 (81)/165 (19)
Age (years ± SD)	39 ± 9
Married (n, %)	570 (67)
Single (n, %)	170 (20)
Primary school (n, %)	595 (70)
High school (n, %)	161 (19)
Employed (n, %)	527 (62)
Unemployed (n, %)	162 (19)
DSM-III-R criteria (mean ± SD) <sup>a</sup> (range 0–9)	7.2 ± 1.4
Years of dependence (years ± SD)	9.6 ± 7
Use of other drugs (n, %)	170 (20)
Psychiatric comorbidity (n, %)	87 (10.2)

<sup>a</sup>Each criterion was scored as 0 = not present; 1 = present.

Table 3. Follow-up status at 5, 10 and 20 years

Drinking status	Year 5 (n = 850)	Year 10 (n = 850)	Year 20 (n = 850)
Abstinent (n, %)	426 (50.1)	356 (41.9)	277 (32.6)
Controlled drinker (n, %)	69 (8.1)	57 (6.7)	29 (3.4)
Heavy drinker (n, %)	254 (29.9)	189 (22.2)	87 (10.2)
Refused to answer (n, %)	3 (0.4)	54 (6.4)	101 (11.9)
Lost to follow-up (n, %)	33 (3.9)	63 (7.4)	83 (9.8)
Death (n, %)	65 (7.6)	131 (15.4)	273 (32.1)

## RESULTS

### Patients

Of the 1113 subjects who consulted a participating centre for the first time during 1987–1988 and fulfilled the inclusion criteria, 850 (76.3%) agreed to participate in the study and provided written informed consent. Sociodemographic and clinical features of the initial cohort are shown in Table 2. The drinking behaviour of the cohort before they entered treatment, notably with respect to alcohol consumption patterns, the type of alcohol consumed and the duration of the dependence were reported in a publication describing the 5-year follow-up data from this study (Gual *et al.*, 1999a). Initial detoxification was undergone by 660 patients (77.7% of the sample) and during the first 12 months of follow-up, patients attended 6.7 (±4.3) clinical appointments and remained in treatment for 7.2 (±4.5) months. At 1 year, 46.2% of the sample (n = 393) reported continuous abstinence during the first 12 months.

### Status follow-up

Twenty years after inclusion, it was possible to locate 767 (90%) patients of the original cohort, the remaining 83 patients being lost to follow-up. According to family members, 15 of these individuals had disappeared or were living in the street. Of the patients with known outcome, 273 (32%) had died. It was possible to interview 393 (46%) patients after 20 years. The remaining 101 (12%) patients refused to be interviewed at this stage of the study (see Table 3).

### Drinking outcome

The drinking behaviour status at each of the three time horizons during the follow-up period is presented in Table 3. After 20 years of follow-up, 32.6% of the original cohort was abstinent, 10.2% were still classified as heavy drinkers and 3.4% fulfilled

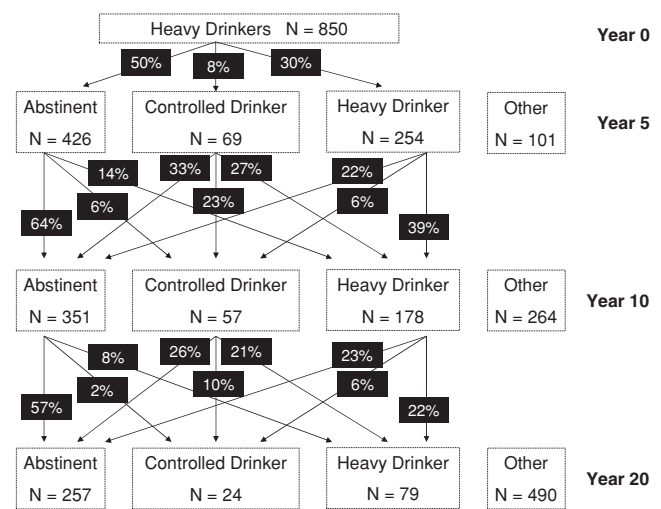


Fig. 1. Stability of drinking patterns over 20 years. 'Other' means dead, not contacted and refused to answer. At each time point, patients were not included if their drinking status had not been established at previous evaluations. Thus, no arrows go from the category 'other' at 5 years to the evaluation of drinking status at 10 years, and the same between 10 and 20. Instead, in Table 5, we include those patients who were not followed at any intermediate evaluation but were traced at the 20-year follow-up.

the criteria for controlled drinking. Abstinence remained the most common outcome over the course of the follow-up period: 50.1% at year 5, 41.9% at year 10 and 32.6% at year 20. Heavy drinking fell from 29.8% to 22.2% and 10.2% over the same periods of time. The number of controlled drinkers remained low throughout the study. Abstinence appears to be the most stable drinking pattern (see Fig. 1). Of abstainers, 64% at year 5 remain abstinent at 10 years, and 57% of abstinent patients at year 10 remain in the same drinking category at 20 years. The figures are much lower for heavy drinkers (39% and 22%, respectively), and even lower for controlled drinkers, since only 23% of those who comply criteria at year 5 remain controlled drinkers at year 10, and just 10% of them remain in the same category 10 years later.

### Gender differences in the drinking behaviour status and mortality

The distribution of drinking behaviour categories at the 20-year follow-up differed markedly between genders ( $\chi^2 = 10.6$ ,  $df = 2$ ,  $P = 0.05$ ). Of the 93 women interviewed at this time-point, 78 (83.9%) were abstinent, 12 (12.9%) were heavy drinkers and only 3 (3.2%) were controlled drinkers. In contrast, for the 300 men, 199 (66.3%) were abstinent, 75 (25%) were heavy drinkers and 26 (8.7%) were controlled drinkers. Gender differences were also observed in mortality rates ( $\chi^2 = 8.4$ ,  $df = 1$ ,  $P = 0.03$ ), with 236 men (34.5% of the original cohort) having died over the 20-year period compared with only 37 women (22.4% of the original cohort).

### Drinking status and mortality

Drinking outcome at 5 years predicted mortality at the 10- and 20-year follow-up points (see Table 4). At the 10-year follow-up, heavy drinkers showed higher mortality rates than

Table 4. Drinking behaviour at year 5 and mortality at 10 and 20 years

Drinking behaviour	Drinking status at year 5 (n)	Mean age at year 5 (m ± SD)	Mortality at year 10 (n, %)	Mortality at year 20 (n, %)
Abstinent	426	43.6 ± 11.0	22 (5.3)	84 (19.7)
Controlled drinker	69	41.3 ± 9.6	5 (7.5)	15 (21.7)
Heavy drinker	253	43.1 ± 8.8	37 (15.0) <sup>a</sup>	99 (39.1) <sup>a</sup>

Multiple comparison tests were performed using Bonferroni's correction.

<sup>a</sup>Significantly different from abstinent and controlled drinkers ( $P < 0.01$ ).

controlled drinkers and abstainers (15.0%, 7.5%, 5.3%;  $\chi^2 = 18.3$ ,  $df = 2$ ,  $P < 0.01$ ).

The figures were very similar 10 years later, at the 20-year follow-up, where mortality in the heavy drinking group still doubles that of controlled drinkers and abstainers (39.1%, 21.7%, 19.7%;  $\chi^2 = 31.6$ ,  $df = 2$ ,  $P < 0.01$ ). No age differences between the three drinking categories were found at the 5-year follow-up ( $F = 1.21$ ,  $df = 2$ ,  $P = 0.297$ ).

#### Drinking status and morbidity

Data on morbidity and hospitalization according to the drinking status are presented in Table 5. At 20 years, no differences were observed in the proportion of patients with chronic illnesses, rate of hospitalization or visits to emergency units between the three drinking categories. However, when individual morbidities were considered, the prevalence of respiratory illnesses was significantly higher in the heavy drinker category ( $\chi^2 = 7.7$ ,  $df = 2$ ,  $P = 0.02$ ) compared to abstainers.

#### Drinking status and sociolegal problems

The number of subjects reporting social or legal problems over the follow-up period is presented in Table 5. In the heavy drinker group, a higher proportion of subjects reported accidents ( $\chi^2 = 6.1$ ,  $df = 2$ ,  $P = 0.04$ ), financial difficulties ( $\chi^2 = 10.5$ ,  $df = 2$ ,  $P = 0.05$ ) and legal problems ( $\chi^2 = 22.4$ ,  $df = 2$ ,  $P < 0.01$ ) compared with abstainers.

**Drinking status and psychosocial functioning.** Data on psychosocial functioning are presented in Table 5. At the 20-year follow-up point, significantly more psychosocial distress (Axis IV of the DSM-III-R) was observed in the heavy drinker group ( $\chi^2 = 20.8$ ,  $df = 2$ ,  $P < 0.01$ ). Data obtained with the GAF scale (Axis V of the DSM-III-R) also revealed a worse social functioning in the heavy drinker group compared to the abstinent and controlled drinker groups ( $F = 32.7$ ,  $df = 2$ ,  $P < 0.01$ ).

#### Refusals to answer

Patients who refused to answer at the end of follow-up were compared with the rest of the cohort in terms of baseline and intermediate variables. No significant differences were found in age, gender, marital status, employment status, age at drinking onset, length of dependence or dependence symptoms. As for treatment compliance, a higher percentage of these patients had abandoned treatment by the 1-year point in comparison with the rest of the cohort (63.4% versus 52.2%, respectively,  $\chi^2 = 4.47$ ,  $df = 2$ ,  $P = 0.034$ ), although no differences were found in the duration of delivered treatment or the number of appointments during the first year. Those who refused to answer at year 20 were not more likely to be heavy drinkers at any of the previous assessments (34.4% versus 33.7% at year 5; 30.2% versus 29.5% at year 10).

## DISCUSSION

Twenty years after the treatment for alcohol dependence was initiated, we were able to locate 767 (90%) of the original cohort of 850 patients, the remaining 83 being lost to follow-up. The overall rate of final ascertainment was thus high, with an attrition rate of 0.5% of subjects per year. Such an attrition rate is low compared to previous long-term studies (O'Connor and Daly, 1985; Nordström *et al.*, 2004) and below the threshold of 1% per year that has been proposed as the acceptable limit to ensure the validity of data collected from this type of

Table 5. Morbidity, sociolegal problems, psychosocial stress, global functioning and alcohol consumption in patients contacted at 20 years (includes some patients not seen at intermediate years)

	Abstinent (n = 277)	Controlled drinker (n = 29)	Heavy drinker (n = 87)	$\chi^2/F$	P
<b>Morbidity</b>					
Chronic illness (%)	53.4	65.4	59.8	2.15	0.341
Digestive system (%)	22.4	23.1	25.6	0.37	0.828
Cardiovascular system (%)	17.3	30.8	17.2	2.95	0.228
Respiratory system (%)	13.4	11.5	25.6 <sup>a</sup>	7.72	0.021
Nervous system (%)	5.4	11.5	2.3	3.62	0.163
Hospitalization (%)	50.2	50	50.6	0.00	0.998
Emergency department visits (%)	41.7	53.8	50.6	3.11	0.210
<b>Problems</b>					
Accidents (%)	27.1	37.9	40.2 <sup>a</sup>	6.12	0.047
Job loss (%)	8.2	21.4	17.6	4.91	0.086
Long-term incapacity (%)	13.1	7.7	22.1	5.32	0.070
Financial problems (%)	16.8	20	32.9 <sup>a</sup>	9.82	<0.01
Legal problems (%)	4.3	3.8	12.6 <sup>a</sup>	8.17	0.017
<b>Axis IV and V DSM III-R</b>					
Psychosocial stress (mean ± SD, 95% CI)	2.8 ± 1.6 2.6 – 3.0	2.8 ± 1.8 2.1 – 3.5	3.7 ± 1.7 <sup>b</sup> 3.4 – 4.1	20.80	<0.01
GAF scale (mean ± SD, 95% CI)	74.7 ± 15.9 72.8 – 76.7	71.5 ± 16.8 64.7 – 78.3	57.4 ± 21.0 <sup>b</sup> 52.8 – 61.9	32.72	<0.01

Multiple comparison tests were performed using Bonferroni's correction.

<sup>a</sup>Significantly different from abstinent ( $P < 0.05$ ).

<sup>b</sup>Significantly different from abstinent and controlled drinkers ( $P < 0.05$ ).

longitudinal study (Vaillant and Milofsky, 1984). Of the 767 identified patients, we managed to interview 393. Of the remainder, 273 had died and 101 no longer wished to participate. The latter patients who refused to be interviewed at the 20-year time horizon were excluded from the analysis of drinking status. In contrast to other authors (Mann *et al.*, 2005), we did not consider refusals to be exclusively a surrogate marker of treatment failure or relapse. In fact, being in stable remission for a number of years, the wish to put their drinking past behind them or other alcohol-independent factors such as a changed family situation or professional constraints could be valid reasons for patients no longer wishing to participate in the study. Data on refusals are scarce, but there is some evidence that this group also includes patients with good outcomes when intermediate evaluations are taken into account (Mackenzie *et al.*, 1987). Our data seem to confirm this previous evidence; patients who refused were not different from the rest of the cohort in terms of baseline variables or intermediate drinking outcomes. However, we did observe that a higher number of these patients abandoned treatment, which may result in lower commitment with the follow-up assessments.

In order to avoid over-estimating abstinence rates, we used conservative criteria of drinking behaviour to classify the drinking status. At each time horizon (5, 10 and 20 years), the frequency and quantity of alcohol consumed was reported for the previous year, and the patient assigned to the most severe drinking category entered during this period. The 'controlled drinking' category was limited to patients drinking less than five drinks per session on less than 7 days a week and the abstinence category included also patients drinking less than five drinks less than once a month. These criteria correspond to the treatment goals for abstinence used in everyday practice in our Addiction Network clinics.

Drinking status could be assigned in 393 patients interviewed after 20 years. At this time, 32.6% of the original cohort were abstinent, 3.4% were classified as controlled drinkers and 10.2% as heavy drinkers. Three patients achieved the treatment goal of abstinence for each one that continued to drink. This distribution of long-term drinking outcome at 20 years was not observed in the interim analyses at 5 or 10 years, and can be accounted for principally by a progressive loss of subjects from the heavy drinking and controlled drinking groups over time. From the 5th to the 20th year, those groups experienced a reduction in their size of 65.6% and 58%, respectively. The abstinence group experienced a 35% reduction during the same period of time. As expected, those reductions mirror the increase in mortality, lost to follow-up and refusal to answer categories (see Table 3). Other authors have suggested that the heavy drinkers' reduction may be attributed to their excess mortality (Gerdner and Berglund, 1997). However, further analyses are being conducted to evaluate the impact of mortality, refusals to answer and loss to follow-up on the dynamics of changes in drinking status distribution over time.

The analysis of movements between drinking patterns shows relevant evidence of the superior stability over the time of abstinence outcomes in front of heavy drinking and specially controlled drinking. Controlled drinking appears as a small and transitional category where it is difficult to stay. This finding has clear clinical implications and supports abstinence-oriented treatment approaches.

It is difficult to compare longitudinal studies with clinical populations, since there are crucial differences in sampling, setting, outcome measures and length of the evaluation. Nevertheless, our mortality rates (32.1%) were close to those found by Mann (27% at 16 years). Abstinence rates in Mann's study (39.6%) were higher than ours (32.6%) but his criteria were different, since they allowed up to 60 g of ethanol occasional consumption and even a relapse shorter than 1 week.

A major finding of the study was that long-term outcome in women treated for alcohol dependence was better than that in men. Of the original sample of 165 women and 685 men, 47.2% of women achieved abstinence at 20 years compared with only 29% of men. This beneficial outcome was associated with lower mortality (22.4% in women and 34.5% in men). Our data are quite similar to those presented by Moos *et al.* (2006) and Timko *et al.* (2006) who found higher rates of stable remission (60% versus 49%) and lower mortality rates (16.6% versus 21.7%) among women. It is interesting to note that gender differences are very similar even though our sample comes from a 'wet culture' (traditional wine drinking culture) and Moos's sample can be taken as representative of a 'dry culture'. Alcohol-related mortality in the Spanish general population is 3-fold higher in men and 60% of those deaths are related to chronic diseases (Fierro *et al.*, 2008). Higher mortality rates among men have already been described in clinical samples in the medium (Feuerlein *et al.*, 1995) and long term (Hurt *et al.*, 1996). Our data show that excess mortality in alcoholics was mostly due to those who continued drinking heavily. In our sample, heavy drinkers at year 5 show a 3-fold increase in their mortality rate at year 10 compared to abstainers (15% versus 5%), and at year 20 their mortality still doubles that of abstainers (39.1% versus 19.7%).

In addition to the drinking behaviour, we also evaluated a number of other outcome variables pertinent to the quality of life of our patients over the follow-up period. As previously reported (Duckitt *et al.*, 1985), we were unable to identify any long-term association between drinking status and chronic illness in general, even though at the 5-year time horizon abstinent patients had reported significantly less chronic illnesses (Gual *et al.*, 1999a). This difference could be explained by the accrual over longer periods of time of new chronic illnesses that were not related to alcohol but a consequence of ageing of the sample (the mean age of the sample was 56 years at the end of the study). In order to throw more light on this unexpected finding, we intend in a future step to compare the information available from patient interview with data on the same patient recorded in the Catalan regional hospital admissions registry. Such data from the Catalan registry will also be of interest to throw light on morbidities in patients who were not interviewed at 20 years.

The residual association observed between drinking status and chronic respiratory diseases may be related to the possibility that heavy drinkers might also smoke more heavily than abstainers. The interaction between alcohol and tobacco in clinical samples of alcoholics is not yet clear. In the short term, contradictory results have been published (Toneatto *et al.*, 1995; Gulliver *et al.*, 2000; Friend and Pagano, 2005a; Friend and Pagano, 2005b). In the long term, it would be reasonable to expect that, as in the general population, alcohol and smoking should reinforce each other. Surprisingly this was not the case in the 16-year follow-up of Mann (Mann *et al.*, 2005),

and even though 76.8% of our patients were smokers at baseline, unfortunately the smoking status was not collected in the follow-up.

We observed an association between alcohol-related problems and drinking status throughout the follow-up period, which has also been consistently found in other studies (Vaillant, 1983; McCabe, 1986; Finney and Moos, 1991). Accidents, financial difficulties and legal problems were significantly higher in the heavy drinker group compared to abstinent patients. It is worth to mention that at 20 years, the controlled drinking group performs closer to heavy drinkers than to abstainers in terms of alcohol-related problems.

With respect to psychosocial distress, this was less marked in abstinent and controlled drinkers than in heavy drinkers at the end of the follow-up period. Social functioning measured with the GAF scale was also better in abstinent patients and in controlled drinkers than that in heavy drinkers. These findings are consistent with what had been observed at the 5 and 10-year time horizons (Gual *et al.*, 1999a, 2004).

#### Strengths and limitations

The context, length and size of our sample represent important strengths of our study, since it covers a wide Mediterranean region and provides data that extend our knowledge of long-term treatment outcomes beyond English-speaking countries, where treatment modalities and the drinking patterns may be different. Inclusion of a large proportion of female patients into the cohort enabled potential gender differences in treatment outcome to be assessed and revealed that long-term outcome is in fact better in women.

With respect to the study design, evaluation of drinking behaviour over the previous year with conservative criteria minimizes the risk of over-estimating the rate of abstinence, which was estimated at 32.6%. This methodological feature limits comparison with long-term abstinence rates determined in other studies that used different criteria. Moreover, exclusion of patients who declined to be interviewed after 20 years limits comparisons that can be made with other studies in which such patients were considered to be treatment failures.

The study presents a number of limitations. In particular, the relatively large proportion of subjects (11.8%) who declined to be interviewed at 20 years introduces a possible source of bias (see above). Moreover, although psychiatric comorbidity was not an exclusion criterion, it is possible that patients with such comorbidity were under-represented due to inadequate coordination between conventional psychiatric services and the addiction centres at the time when the study was initiated, resulting in such patients not being seen in the participating centres. Also, the study excluded at the outset patients who did not have a stable home and at least one other family member, and such individuals may have a poorer outcome than the sample depicted here.

Finally, it is important to point out that the present results need to be completed with further analyses in order to understand more clearly the interplay between drinking measures and other outcomes over time. The identification of drinking phenotypes, of risk factors for remission and relapse, of changes in mortality over time and of the evolution of drinking behaviour in women represent important challenges for future research.

**Acknowledgements** — We thank all the professionals from the eight Addiction Centres of the Catalan Addiction Network [Unitat d'Alcoholologia de la Generalitat, Hospital Clínic; Programa DROSS (Centre d'Atenció i Seguiment Garbí-Vent; Centre d'Atenció i Seguiment de Sarrià-Sant Gervasi; Centre d'Atenció i Seguiment de Sants); Centre d'Atenció i Seguiment de Girona. Fundació Teresa Ferrer; Centre d'Atenció a les Drogodependències d'Osona CADO, Hospital General de Vic; Centre d'Atenció i Seguiment Joan XXIII-IMSS CAP Tarragonès; Dispensari d'Alcoholisme i altres Toxicomanies, Hospital Santa Maria de Lleida] for their continuous support to the project and for their help in keeping track of patients. We also thank Anna Sanahuja and Cecilia Garcia for their participation in the follow-up interviews with patients and relatives. Data on mortality were provided by the Registre de Mortalitat de Catalunya, Barcelona, and the Instituto de Información Sanitaria from the Ministerio de Sanidad, Madrid, Spain. Funding for this study was provided by a grant from the Department of Health, Government of Catalonia, Spain.

#### REFERENCES

- American Psychiatric Association. (1980) *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edn. Washington, DC: American Psychiatric Association.
- American Psychiatric Association. (1987) *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edn revised. Washington, DC: American Psychiatric Association.
- Babor TF, Steinberg K, Anton R *et al.* (2000) Talk is cheap: measuring drinking outcomes in clinical trials. *J Stud Alcohol* **61**: 55–63.
- Dawson B, Trapp RG. (2001) *Basic and Clinical Biostatistics*, 3rd edn. New York: McGraw-Hill.
- Del Boca FK, Darkes J. (2003) The validity of self-reports of alcohol consumption: state of the science and challenges for research. *Addiction* **98**(Suppl 2):1–12.
- Duckitt A, Brown D, Edwards G *et al.* (1985) Alcoholism and the nature of outcome. *Br J Addict* **80**:153–62.
- Edwards G. (1984) Drinking in a longitudinal perspective: career and natural history. *Br J Addict* **79**:175–83.
- Edwards G, Brown D, Oppenheimer E *et al.* (1988) Long term outcome for patients with drinking problems: the search for predictors. *Br J Addict* **83**:917–27.
- Feuerlein W, Küfner H, Flohrschütz T. (1995) The mortality rate of alcoholic patients 4 years after inpatient treatment. *Ver-sicherungsmedizin* **47**:10–4.
- Fierro I, Ochoa R, Yáñez JL, Valderrama JC *et al.* (2008) Mortalidad y mortalidad prematura relacionadas con el consumo de alcohol en España entre 1999 y 2004. Alcohol-related mortality and premature death in Spain between 1999 and 2004. *Med Clin (Barc)* **131**: 10–3.
- Finney JW, Moos RH. (1991) The long-term course of treated alcoholism: I. Mortality, relapse and remission rates and comparisons with community controls. *J Stud Alcohol* **52**:44–54.
- Friend KB, Pagano ME. (2005a) Smoking cessation and alcohol consumption in individuals in treatment for alcohol use disorders. *J Addict Dis* **24**:61–75.
- Friend KB, Pagano ME. (2005b) Changes in cigarette consumption and drinking outcomes: findings from Project MATCH. *J Subs Abuse Treat* **29**:221–9.
- Gerdner A, Berglund M. (1997) Mortality of treated alcoholics after eight years in relation to short-term outcome. *Alcohol Alcohol* **32**:573–9.
- Gual A, Lligoña A, Colom J. (1999a) Five-year outcome in alcohol dependence. A naturalistic study of 850 patients in Catalonia. *Alcohol Alcohol* **34**:183–92.
- Gual A, Martos AR, Lligoña A *et al.* (1999b) Does the concept of a standard drink apply to viticultural societies? *Alcohol Alcohol* **34**:153–60.
- Gual A, Lligoña A, Costa S *et al.* (2004) Tratamiento del alcoholismo y su impacto a largo plazo. Resultados a 10 años de un estudio longitudinal prospectivo de 850 pacientes. Long-term impact of treatment in alcoholics. Results from a 10-year longitudinal follow-up study of 850 patients. *Med Clin (Barc)* **123**:364–9.
- Gulliver SB, Kalman D, Rohsenow DJ *et al.* (2000) Smoking and drinking among alcoholics in treatment: cross-sectional and longitudinal relationships. *J Stud Alcohol* **61**:157–63.

- Hurt RD, Offord KP, Croghan IT *et al.* (1996) Mortality following inpatient addictions treatment. Role of tobacco use in a community-based cohort. *JAMA* **275**:1097–103.
- Hyman MM. (1976) Alcoholics 15 years later. *Ann N Y Acad Sci* **273**:613–23.
- 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.
- Mackenzie A, Funderburk FR, Allen RP *et al.* (1987) The characteristics of alcoholics frequently lost to follow-up. *J Stud Alcohol* **48**:119–23.
- Mann K, Schäfer DR, Längle G *et al.* (2005) The long-term course of alcoholism, 5, 10 and 16 years after treatment. *Addiction* **100**:797–805.
- McCabe RJR. (1986) Alcohol-dependent individuals sixteen years on. *Alcohol Alcohol* **21**:85–91.
- Moos RH, Moos BS. (2005) Sixteen-year changes and stable remission among treated and untreated individuals with alcohol use disorders. *Drug Alcohol Depend* **80**:337–47.
- Moos RH, Moos BS, Timko C. (2006) Gender, treatment and self-help in remission from alcohol use disorders. *Clin Med Res* **4**:163–74.
- Nordström G, Berglund M, Frank A. (2004) Stability of successful long-term adjustment in alcohol dependence: a follow-up study 15 years after the first long-term follow-up. *Eur Addict Res* **10**:126–32.
- O'Connor A, Daly J. (1985) Alcoholics a twenty year follow-up study. *Br J Psychiatry* **146**:645–7.
- Timko C, Debenedetti A, Moos BS *et al.* (2006) Predictors of 16-year mortality among individuals initiating help-seeking for an alcoholic use disorder. *Alcohol Clin Exp Res* **30**:1711–20.
- Toneatto A, Sobell LC, Sobell MB *et al.* (1995) Effect of cigarette smoking on alcohol treatment outcome. *J Subst Abuse* **7**:245–52.
- Vaillant G. (1983) *The Natural History of Alcoholism*. Cambridge, MA: Harvard University Press.
- Vaillant GE. (1988) What can long-term follow-up teach us about relapse and prevention of relapse in addiction? *Br J Addict* **83**:1147–57.
- Vaillant G, Milofsky ES. (1984) Natural history of male alcoholism: paths to recovery. In Goodwin DW, Van Dusen KT, Mednick SA (eds). *Longitudinal Research in Alcoholism*. Boston: Kluwer-Nijhoff Publishing 53–71.