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A Randomized Controlled Trial of Extended Brief Intervention for Alcohol-Dependent Patients in an Acute Hospital Setting

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Abstract

Aims: To determine whether alcohol-dependent patients in a hospital setting benefit from extended brief interventions (EBI) delivered by an Alcohol Specialist Nurse.
Methods: Alcohol-dependent patients recruited via screening at the emergency department (ED) (n = 267), whether or not admitted to hospital, were randomized to EBI (up to six counselling sessions offered) or control. At 6 months, 84.2% of patients were assessed by a researcher blinded to the intervention. The primary outcome was a fall in Severity of Alcohol Dependence Questionnaire.
Results: There was no difference between groups in the primary outcome [odds ratio (OR) 1.02; 95% confidence interval (CI): 0.38, 2.75, P = 0.97]. Secondary outcomes including alcohol consumption and readiness to change did not show a significant difference between groups. However, all secondary outcome measures improved, on average, in both arms.
Conclusions: Although EBI can be delivered in an ED or inpatient setting, it was not shown to be an advantage over screening and usual management (which included advice on alternative services), with patients in both groups showing an average improvement.
Trial Registration: ISRCTN78062794

INTRODUCTION

Alcohol dependence, as determined by DSM-IV alcohol abuse and dependence criteria (APA, 1994), affects ~3% of the English population, and accounts for significant medical and psychiatric morbidity (Anderson *et al.*, 2012). Only a small percentage of these individuals ever seek treatment for their alcohol use disorder (AUD),

and for those who do, it is estimated that only 6% ever get access to a specialist treatment service (HM Government, 2012). A range of harms ensue from alcohol consumption, many of which are managed by general hospitals. In 2011/2012, alcohol-related problems accounted for 1.1 million hospital admissions in England, an increase of 12% compared with 2008/2009 (NWPHO, 2011). This figure does not include the 12% of emergency department (ED) attendances that are attributed to alcohol, a figure that increases to 70% at peak times (Pirmohamed *et al.*, 2000). Screening to identify alcohol-related harm has been deemed inadequate in English acute hospitals (Patton *et al.*, 2005; Coulton *et al.*, 2009; Drummond *et al.*, 2014) and might be a missed opportunity if early identification and treatment of AUD and co-morbid conditions can reduce subsequent harm and disease progression and ultimately reduce the overall burden of alcohol to society including the health service. It is deemed sensible and practical to ensure that acute hospitals are utilized as an access point for delivery of interventions and referral for specialist treatment (Owens, 2010; Moriarty *et al.*, 2012).

The ED has been shown to be an environment in which to identify non-treatment seeking individuals with AUDs (Ryder *et al.*, 2010), and is potentially an appropriate setting to deliver brief interventions (BIs; Emmen *et al.*, 2004). It has become common, but not universal, to refer to structured BIs delivered on more than two occasions as extended brief interventions (EBIs). BIs are defined as structured motivational sessions, delivered by healthcare professionals on 1–6 occasions, typically one session per week aimed at helping individuals reduce their alcohol consumption (Bien *et al.*, 1993). Although BIs are effective for non-dependent drinkers, they may also have some efficacy for reduction in alcohol consumption in dependent drinkers (Cobain *et al.*, 2011).

BI as a treatment option in acute hospitals has yet to be systematically studied in a randomized control trial (RCT) in patients showing features of alcohol dependence (Touquet and Paton, 2006). However, an observational study of BIs by Alcohol Specialist Nurses (ASNs) showed that 30% of alcohol-dependent patients maintained abstinence for 6 months post-intervention (Owens, 2010). Other studies have shown that structured interventions significantly reduce length of stay in hospital and produce a significant reduction in alcohol consumption and dependence at 6 months (Cobain *et al.*, 2011; Hughes *et al.*, 2013). This is consistent with a recent retrospective evaluation, which showed that alcohol-dependent and non-dependent patients realized comparable benefit from BIs delivered by an ASN in acute care (Ryder *et al.*, 2010). BIs were effective in alcohol-dependent patients suffering alcohol-related injury (Smith *et al.*, 1998). BIs have been shown to be a valued by patients, with as many as 93% of patients accepting an intervention whilst in the ED (Hungerford *et al.*, 2000).

For EBIs, it seems that the duration and intensity of intervention does not predict effectiveness (MATCH, 1997; UKATT, 2005; Saitz *et al.*, 2007). Interventions of low duration and intensity may be as effective as more intensive interventions, and may be more amenable for implementation in busy acute hospital settings. Although BIs were not designed for patients with alcohol dependence, and therefore have not been evaluated in randomized trials in this group, there appears to be some evidence that they might have some utility and effectiveness in hospital settings (Crawford *et al.*, 2004; Cobain *et al.*, 2011). Given the prevalence of alcohol dependence, the high use of hospitals by this group of patients, and the fact that this is a missed opportunity for intervening (Touquet and Paton, 2006), we investigated the effectiveness of EBIs for reducing the severity of alcohol dependence in an acute care setting using a randomized design.

METHODS

Design

Alcohol-dependent patients in an acute hospital setting (ADPAC) were an RCT to determine if EBIs delivered in an ED were (a) effective in reducing alcohol dependence, (b) cost effective and (c) valued by patients. The trial was approved by the research ethics committee in Liverpool, England (ref: 09/H1005/61) and compliant with the Declaration of Helsinki 2008; patients gave written informed consent. Oversight was provided by an independent trial steering group.

At an acute general hospital in the North West of England, consecutive patients attending the ED irrespective of index cause of attendance or subsequent admission were screened using the Alcohol Use Disorders Identification Test (AUDIT) set at a score >15 (Saunders *et al.*, 1993), and possible cases referred to the research nurse for assessment of eligibility. Eligible patients, following consent, were randomized using sequentially numbered opaque sealed envelopes prepared according to a computer-generated randomization allocation sequence. Research nurses who conducted follow-up assessments at 3 and 6 months were blinded to treatment allocation. The trial protocol was published (Owens *et al.*, 2011).

The nurse delivering the interventions was an experienced general nurse who prior to commencement of the study received dedicated training in delivery of EBI. She received monthly clinical supervision throughout the study. This nurse delivered all interventions.

Patients randomized to the control arm were given usual clinical care, which included advice on alternative treatment options. For the EBI arm, the first of a maximum of six interventions was delivered followed by an invitation to further interventions at 1–2-week intervals. Follow-up for both groups was planned for 3 and 6 months.

The primary outcome measure was reduction (binary outcome) in alcohol dependence indexed by the Severity of Alcohol Dependence Questionnaire (SADQ) at 6 months (Stockwell *et al.*, 1979). Secondary outcome measures included: reduction in alcohol consumption; the actual score change in the SADQ; reduction in AUDIT score, analysed both dichotomized at a value of 16 and as a continuous measure; Leeds Dependency Questionnaire (LDQ) (Raistrick *et al.*, 1994); quantity of alcohol consumption in UK units per drinking day; Readiness to Change Questionnaire (RTCQ) (Heather *et al.*, 1993); number of ED attendances, length of stay in hospital and number of hospital admissions, all measured 6 months pre- and 6 months post-treatment/control; length of stay for initial treatment in days; and biochemical markers [gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT) and mean corpuscular volume (MCV)] when available. EuroQoL EQ-5D (Rabin and de Charro, 2001) data were collected to provide utility measurement for cost-effectiveness analysis. We also undertook a qualitative substudy to investigate patients' experiences and perceptions of both their clinical journey and their involvement in research; this will be reported in a separate paper.

Baseline data were collected by the ASN performing the screening and consent process. The nature of delivery of EBI precluded blinding of participants and the nurse delivering the interventions. However, the nurses conducting the follow-up assessments at 3 and 6 months remained blinded to treatment allocation, as did the investigators and statisticians who performed the data analyses: the research nurses undertaking the follow-up interview did not have access to trial report forms, and had a script for the patients that included the phrase '…please do not tell me if you visited the hospital nurse for support….'

Sample size

Based on a previous study of dependent drinkers receiving interventions from an ASN (Cobain *et al.*, 2011), it was expected that 55% of such patients would display a fall in SADQ score between baseline and 3-month follow-up. Another confounder in this area of research is the phenomenon of natural recovery (NR). The NR rate expected in the control group over this time period was deemed to be 25% [the literature ranges from 12% with a treatment population up to 35% within a general lifetime population (Stockwell *et al.*, 1979; Bischof *et al.*, 2003; Weisner *et al.*, 2003)]. In order to detect a difference between the groups (55% vs. 25%) with 90% power at the 5% significance level, 65 patients were therefore required in each group. In order to allow for an estimated 50% drop-out rate (observed in previous studies in similar patients), it was calculated that 130 patients would need to be recruited per group.

Statistical analysis

Standard statistical software SAS version 9.3 (SAS Institute, Inc., Cary, NC, USA) was used. Baseline characteristics are presented by treatment group and overall, with continuous variables summarized in terms of means [standard deviations (SD)] or medians [interquartile range (IQR)] depending on the degree of skewness, and categorical variables presented in terms of numbers (%) per category. The intention-to-treat principle was followed with a two-sided *P*-value of 0.05 (5% level) for statistical significance testing and 95% CIs for the estimated relative treatment effect reported throughout. To assess the appropriateness of the event rates used in our sample-size calculation, an internal pilot was planned when 160 patients had been randomized. The two main reasons for performing the internal pilot were to (a) estimate the overall proportion of patients displaying a fall in SADQ score to allow comparison with the estimates used in the original sample-size calculation and (b) monitor the study recruitment rate and amount of missing data for all primary and secondary outcomes.

The primary outcome of fall in SADQ score at 6 months post-randomization is presented with count and percentage for each group. The fall in SADQ score (binary outcome) was analysed using logistic regression, and the corresponding ORs estimated to quantify the treatment effect of EBI against the control. The reasons for missing primary outcome data are provided with the results of the sensitivity analyses, which were used to investigate the robustness of the primary outcome results to missing data.

Continuous secondary outcomes that were normally distributed were analysed using paired *t*-test, while continuous secondary outcomes that were non-normally distributed were summarized in terms of medians and IQR for each treatment group and compared using the Mann–Whitney *U*-test. When a secondary outcome was binary, logistic regression was used to estimate the OR between EBI and control. Comparisons between the two groups were made for all outcomes at both 3 and 6 months.

RESULTS

Participants

From January 2010 to January 2011, 390 patients with a suspected AUD were referred for assessment of eligibility to participate (Fig. 1). Following assessment including alcohol history and baseline demographics, 267 patients consented and were randomly assigned to either the EBI (n = 134) or control (n = 133). Follow-up was offered according to randomized group, EBI arm at every 2 weeks and control at 12 weeks.

A first intervention was received as an inpatient by 177 patients, while the remaining 87 patients received their first intervention in the ED. Setting was not recorded for 3 (1%) of the first interventions. All follow-up interventions were delivered in the outpatient clinic setting.

Three-month follow-up was completed in 234 patients (87.6%) and in 225 patients (84.2%) at 6 months. All in the EBI arm received at least 1 EBI, and 98 (73%) attended at least one further session. The mean number of interventions delivered was 3.0 (range 1–6), with mean duration of 19.6 minutes per session (range 18–22).

Internal pilot and baseline imbalance

For patients recruited after the internal pilot, it was noted that there was an imbalance in the baseline primary outcome measure (SADQ) (Table 1). Since the probability of this occurring by chance was calculated to be 3×10^{-9}, failure of randomization was independently investigated, and no definite cause could be determined. Given these findings, it was agreed between the trial management group and the independent trial steering committee that pooling of the pre- and post-pilot data would be based on the following criterion:

The primary analysis was to be the difference between the two treatment groups (intervention and control) in the rate of fall in SADQ at 6 months. This difference (plus 95% CIs) would be calculated for the pre- and post-pilot data. If the difference in rate of pre- and post-pilots was >10%, then the pre- and post-pilot results would not be pooled, but if it was ≤10%, the pre- and post-pilot results would be pooled in a meta-analysis.

The difference in proportions between the pre- and post-pilot data was 12% (95% CI, 11%, 14%), and thus no pooling was conducted. Therefore, the results for only the pre-pilot data are shown (n = 160) (Table 1).

Analysis of the primary outcome

One hundred and sixty patients were randomly allocated to treatment (n = 79) or control (n = 81) arms before the internal pilot (Table 2). The fall in SADQ at 6 months was similar between the two groups, with an OR 1.02 (95% CI: 0.38–2.75).

Sensitivity analysis of missing primary outcome

Sensitivity analysis was carried out to investigate the robustness of the conclusions concerning the analysis of the primary outcome to assumptions about the missing data. In the cases of 6 alcohol-related deaths, 4 withdrawn consents and 17 un-contactable patients, no fall in SADQ was assumed, whereas for two patients entering long-term rehabilitation, a fall in SADQ was assumed. The estimated OR for the treatment difference in this sensitivity analysis was 1.03 (95% CI: 0.52–2.05), a negligible change from the primary analysis.

Analysis of secondary outcomes

A statistically significant difference between the two groups at 6 months was not observed for any of the secondary outcomes (Table 2). A reduction in alcohol consumption was observed in both groups, which continued to decrease between 3 and 6 months. The difference between the two groups was statistically significant at 3 months but not by 6 months. Similarly, the LDQ showed a statistically significant difference between the two groups at 3 months, but not at 6 months.

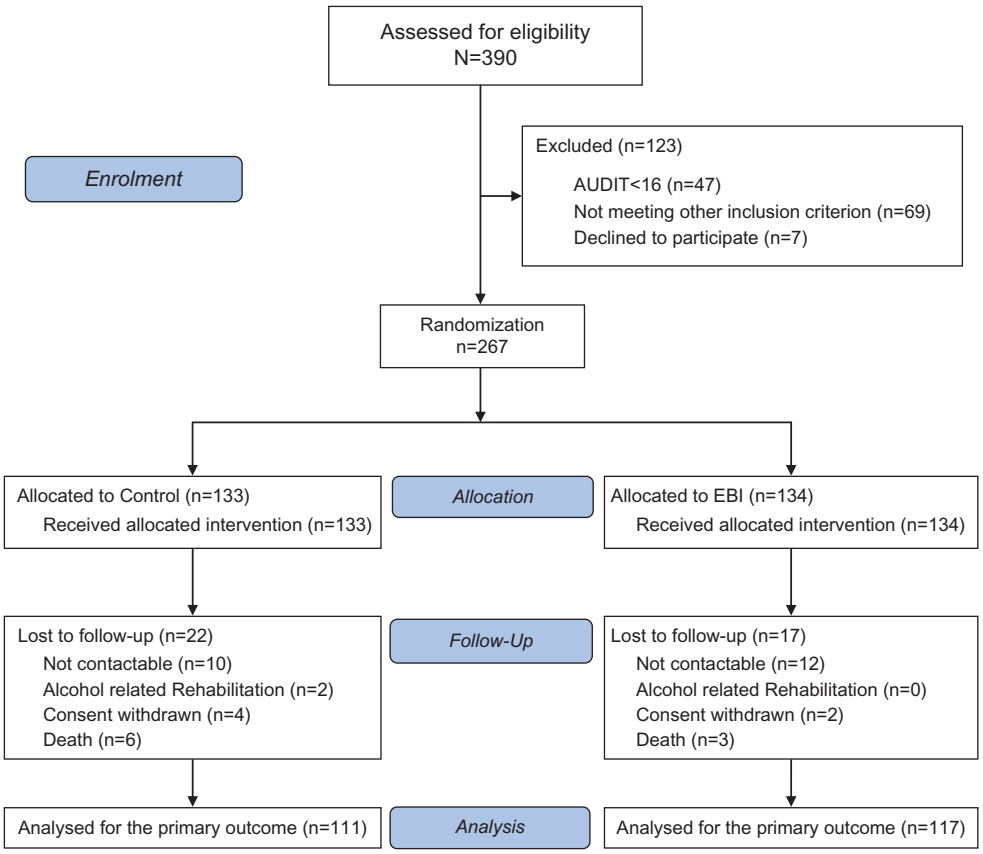

Fig. 1. ADPAC Trial CONSORT Flow diagram.

Economic assessment

The number of general practitioner contacts, hospital admissions, emergency attendances and total length of hospital stay in the 6 months prior to study entry showed no important differences between the two groups. In addition, the baseline quality of life scores was not statistically different. In the 6 months following study entry, the total length of hospital stays fell for both groups but the fall was larger for the EBI arm such that the mean difference between the EBI arm (3.46 days) and the control arm (7.37 days) was statistically significant ($P = 0.02$). For the other economic outcomes, including EQ-5D measures, there was no difference between the groups at 6-month post-study entry. Whilst there is some evidence that there was a reduction in healthcare utilization from EBIs, with no differences in the primary outcomes or utility, there was insufficient evidence to state that EBIs are cost effective.

DISCUSSION

Given the UK epidemic of alcohol-related harm, and evidence that interventions in an acute hospital setting can have a positive impact on a range of measures from decreased alcohol consumption to reduced readmission (Patton *et al.*, 2005; Nilsen *et al.*, 2008; Hughes *et al.*, 2013; Wei *et al.*, 2015), we must consider the possibility that patients presenting to acute hospitals may benefit from intervention (Moriarty *et al.*, 2012; Patton and O'Hara, 2013). In contrast to some studies (Cherpitel, 2007; Drummond *et al.*, 2014) and in concordance with others (D'Onofrio and Degutis, 2002; Désy and Perhats, 2008; Cunningham *et al.*, 2010; Désy *et al.*, 2010), our research did not identify problems using ED as a gateway for identification of AUD. Therefore, we should use alcohol-related presentation as an opportunity to (a) identify non-treatment seeking individuals (Crawford *et al.*, 2004), (b) remind patients about the harms of alcohol misuse, (c) provide patients with support during their hospital stay, and most importantly, (d) as our control group perhaps benefitted from a single session with advice only, provide advice on where and how to access support following hospital discharge.

The only systematic review examining the effects of BIs in 'heavy drinkers' demonstrated clear benefits (McQueen *et al.*, 2011), and Mdege *et al.* (2014) found that patients admitted with AUD associated with gastroenterology or emergency presentation responded well; however, Daeppen *et al.* (2007) failed to demonstrate benefit.

In our trial, the ASN gave advice as needed or requested, irrespective of allocation to treatment, which could constitute an intervention in itself. It was interesting that at baseline, although half of the patients had previous treatment for AUD, almost all showed awareness of and planning toward addressing their AUD on measures of RTCQ (Heather *et al.*, 1993). This may suggest that the act of being assessed by the ASN was important in motivating non-treatment seeking patients to seek treatment (Cobain *et al.*, 2011).

Although systematic testing of interventions for *dependent* drinkers in hospital settings is scarce, there are promising results from three studies (Chick *et al.*, 1985; Owens, 2010; Ryder *et al.*, 2010). However, both the mode of intervention and categorization of patient groups varied, and none used patient by patient randomization. To avoid crossover between AUD of lower severity of dependence seen in previous trials (Guth *et al.*, 2008), we chose SADQ as

Table 1. Baseline characteristics for EBI patients and controls before and after the internal pilot

	Pre-internal pilot		Post-internal pilot	
	Control *N* = 81	EBI *N* = 79	Control *N* = 52	EBI *N* = 55
Gender, *n* (%): male	56 (69.1)	51 (64.6)	32 (61.5)	33 (60.0)
Age (years) mean (SD), range	49.9 (11.9), 25.3–75.8	50.8 (11.2), 20.8–83.7	48.2 (16.1), 19.0–87.7	47.1 (14.6), 19.4–74.2
Ethnicity, *n* (%)				
White	80 (98.8)	79 (100.0)	52 (100.0)	55 (100.0)
Black or Black British	1 (1.2)	0	0	0
Employment status, *n* (%)				
Employed	15 (18.8)	12 (15.2)	6 (11.8)	15 (27.3)
Unemployed	65 (80.2)	67 (84.8)	45 (88.2)	40 (73.7)
Missing	1 (1.2)	0 (0)	1 (2.0)	0
Marital status, *n* (%)				
Married/cohabiting	25 (30.0)	26 (32.9)	18 (34.6)	22 (40.0)
Divorced/single/widow/widower	52 (64.1)	51 (64.5)	34 (65.3)	33 (60.0)
Missing	4 (4.9)	2 (2.5)	0	0
Accommodation, *n* (%)				
Owner/rented	31 (38.7)/45 (56.3)	27 (35.5)/46 (60.5)	17 (32.7)/34 (65.4)	20 (37.0)/32 (59.3)
Homeless	4 (5.0)	3 (4.0)	1 (1.9)	2 (3.7)
Missing	1 (1.2)	3 (3.8)	0	1 (1.8)
Live alone, *n* (%)	49 (63.6)	43 (57.3)	23 (45.1)	17 (31.5)
Drinking measures				
Previous treatment of alcohol dependence, *n* (%) yes	55 (67.9)	51 (64.6)	24 (46.2)	23 (41.8)
Primary care prescribing for acute alcohol withdrawal	9 (9.7)	15 (16.8)	3 (12.5)	5 (21.7)
Counselling	27 (29.0)	20 (22.5)	8 (33.3)	13 (56.5)
Admissions for alcohol dependence	34 (36.6)	32 (36.0)	8 (33.3)	8 (34.8)
Admissions/outpatient support from a tertiary centre	23 (24.7)	22 (24.7)	9 (37.5)	9 (39.1)
SADQ				
Mean (SD)	36.1 (13.8)	35.5 (15.2)	20.4 (15.0)	39.6 (13.8)
Range	10.0–57.0	5.0–56.0	3.0–56.0	9.0–60.0
Median (IQR)	39.0 (26.0, 49.0)	40.0 (22.0, 49.0)	13.5 (8.5, 33.5)	43.0 (30.0, 52.0)
AUDIT				
Mean (SD)	34.7 (6.8)	33.6 (7.0)	29.1 (7.3)	35.6 (5.4)
Range	16.0–40.0	18.0–40.0	18.0–40.0	20.0–40.0
Median (IQR)	38.0 (31.0, 40.0)	36.0 (29.0, 40.0)	29.5 (22.0, 35.5)	38.0 (31.0, 40.0)
AUDIT-C				
Mean (SD)	11.9 (0.5)	11.7 (0.7)	11.6 (0.7)	12.0 (0.2)
Range	9.0–12.0	9.0–12.0	9.0–12.0	11.0–12.0
Median (IQR)	12.0 (12.0, 12.0)	12.0 (12.0, 12.0)	12.0 (11.0, 12.0)	12.0 (12.0, 12.0)
LDQ				
Mean (SD)	23.8 (7.7)	25.0 (6.3)	14.0 (9.1)	25.0 (7.3)
Range	0.0–30.0	8.0–30.0	2.0–30.0	7.0–30.0
Median (IQR)	27.0 (17.0, 30.0)	29.0 (20.0, 30.0)	11.0 (6.5, 21.0)	30.0 (20.0, 30.0)
Missing, *n* (%)	5 (6.2)	2 (2.5)	0	0
RCTQ, *n* (%)				
Action (A)	19 (23.5)	16 (20.3)	22 (42.3)	13 (23.6)
Contemplation (C)	58 (71.6)	61 (77.2)	28 (53.8)	42 (76.4)
Pre-contemplation (PC)	4 (4.9)	2 (2.5)	2 (3.8)	0
Duration of alcohol dependence (years) median (IQR), range	10.0 (4–16), 0–50	10.0 (4–20), 0–60	10.0 (3.0, 17.0), 0–40	6.0 (2.0, 10.0), 0–50
Number of alcohol-drinking days per week				
Mean (SD)	6.7 (0.8)	6.7 (1.0)	6.2 (1.5)	6.7 (0.8)
Range	3.0–7.0	3.0–7.0	3.0–7.0	3.0–7.0
Median (IQR)	7.0 (7.0, 7.0)	7.0 (7.0, 7.0)	7.0 (5.0, 7.0)	7.0 (7.0, 7.0)
Number of units (1 unit = 8 g) of alcohol per day				
Mean (SD)	30.4 (14.2)	32.4 (19.1)	21.1 (13.7)	37.2 (16.2)
Range	7.0–80.0	8.0–120.0	8.0–70.0	14.0–80.0
Median (IQR)	30.0 (20.0, 40.0)	30.0 (18.0–40.0)	15.0 (12.5, 30.0)	30.0 (25.0, 50.0)
Alcohol consumption per week				
Mean (SD)	204.3 (101.0)	216.4 (129.5)	135.3 (100.1)	252.7 (118.5)
Range	49.0–560.0	42.0–840.0	24.0–490.0	45.0–560.0
Median (IQR)	210.0 (126.0, 280.0)	210.0 (120.0, 280.0)	98.0 (66.5, 210.0)	210.0 (168.0, 350.0)

Continued

Table 1. Continued

	Pre-internal pilot		Post-internal pilot	
	Control $N = 81$	EBI $N = 79$	Control $N = 52$	EBI $N = 55$
Current and previous ED/hospital admissions				
Number of ED attendances in the past 6 months				
Patients with data	76 (93.8%)	75 (94.9%)	50 (96.2%)	54 (98.2%)
Mean (SD)	1.84 (1.67)	1.83 (1.84)	1.42 (0.93)	1.69 (1.46)
Range	0–10	0–14	0–5	0–8
Median (IQR)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 1.8)	1.0 (1.0, 2.0)
Length of stay sum days in hospital in the past 6 months				
Patients with data	76 (93.8%)	75 (94.9%)	50 (96.2%)	54 (98.2%)
Mean (SD)	9.29 (11.05)	10.33 (12.48)	7.52 (15.01)	7.76 (8.30)
Range	0–64	0–70	0–99	0–32
Median (IQR)	7.0 (3.0, 12.0)	6.0 (2.0, 14.0)	4.0 (2.0, 6.8)	5.0 (2.0, 9.8)
Number of hospital admissions in the past 6 months				
Patients with data	76 (93.8%)	75 (94.9%)	50 (96.2%)	54 (98.2%)
Mean (SD)	2.37 (4.28)	2.15 (2.41)	1.76 (1.81)	1.57 (1.52)
Range	0–32	0–16	0–8	0–7
Median (IQR)	1.0 (1.0, 2.0)	1.0 (1.0, 3.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)
Euroqol EQ-5D				
Mean (SD)	0.72 (0.29)	0.73 (0.26)	0.62 (0.35)	0.64 (0.31)
Range	−0.26 to 1	−0.19 to 1	−0.32 to 1	−0.22 to 1
Median (IQR)	0.81 (0.52, 1)	0.78 (0.59, 1)	0.73 (0.41, 0.85)	0.73 (0.52, 0.85)
Biochemical indicators of co-morbid conditions[a]				
GGT				
Mean (SD)	309.0 (274.9)	284.4 (295.8)	201.0 (242.5)	261.6 (349.3)
Range	14.0–999.0	17.0–999.0	5.0–999.0	12.0–2014.0
Median (IQR)	221.0 (94.0, 456.0)	126.0 (65.0, 535.0)	75.5 (33.0, 298.0)	137.0 (54.0, 301.0)
Missing, *n* (%)	23 (28.4)	28 (35.4)	14 (26.9)	9 (16.4)
ALT				
Mean (SD)	61.6 (60.1)	72.2 (80.9)	49.0 (45.5)	77.7 (97.8)
Range	6.0–348.0	10.0–516.0	9.0–199.0	9.0–483.0
Median (IQR)	38.0 (26.0, 84.0)	46.0 (26.0, 80.0)	35.5 (19.0, 62.0)	42.5 (24.5, 85.5)
Missing, *n* (%)	22 (27.2)	22 (27.8)	10 (19.2)	3 (5.5)
MCV				
Mean (SD)	97.7 (7.5)	95.8 (8.3)	96.0 (7.3)	125.2 (145.2)
Range	82.0–122.0	79.0–113.0	83.0–114.0	83.0–943.0
Median (IQR)	98.0 (92.0, 102.0)	96.0 (92.0,103.0)	96.0 (90.0, 100.0)	99.0 (93.0, 103.0)
Missing, *n* (%)	38 (46.9)	34 (43.0)	21 (40.4)	21 (38.2)

[a]Biochemical indicators of co-morbid conditions measures (GGT, ALT and MCV) were available only if a patient was admitted to a hospital with a more serious status. As a result, the measurements are available only for a sub-group who had a more severe condition, and not for everyone randomized, hence the high missing %.

the primary outcome measure to ensure that we had accurately described and categorized the patients severity of dependence. Although we were unable to demonstrate an effect on the primary outcome, we did observe significant short-term (3 months) reduction in LDQ and alcohol consumption in the EBI arm, but this significant difference was lost by 6 months.

Strengths and weaknesses

During the final analysis, an imbalance in the primary outcome measure was identified for patients recruited after the internal pilot. The investigators sought advice from the independent trial steering committee. A full independent investigation identified no errors, and a subsequent examination confirmed research protocol compliance. Since the imbalance could not be explained, but the comparative results of pre- and post-pilots differed by more than an amount specified in advance, we have reported findings in only those patients randomized prior to the internal pilot. This reduced the total number of patients in the trial, and our trial is therefore under-powered to detect the target difference originally specified. Furthermore, although the trial was designed to limit bias by blinding research nurses collecting outcome measures at follow-up, we relied on patients not to reveal their allocation. The strengths of the trial included the high recruitment conversion rate from screening to eligibility (68.4%) and follow-up rate (86%), which compares favourably with similar studies (Patton *et al.*, 2005; Daeppen *et al.*, 2007). Furthermore, as the first intervention was delivered at the time of assessment, all patients in the intervention group received at least one EBI.

Explaining the 'negative' result

Although we failed to establish a significant difference between the treatment and control groups, it is interesting that both groups improved on all measures between baseline and the 6 months. This

Table 2. Primary and secondary outcome analyses for all alcohol consumption measures

Outcome	Control *N* = 81	EBI *N* = 79	Treatment effect: EBI vs Control (95% CI), *P*-value
Fall in SADQ at 6 months			
Yes, *n* (%)	56 (86.2)	57 (86.4)	1.02 (0.38, 2.75), 0.9722[b]
No	9	9	
Missing, *n* (%)	16 (20)	13 (16)	29 (18)
Fall in SADQ in 12 weeks			
Yes, *n* (%)	49 (74.2)	59 (84.3)	1.86 (0.80, 4.34), 0.1511[b]
No	17	11	
Missing, *n* (%)	15 (18)	9 (11)	24 (15)
SADQ continuous score at 12 weeks			
Median (IQR)	19.5 (3.0, 43.0)	11.5 (0.0, 32.0)	−3.00 (−11.00, 0.00), 0.1807[c]
Missing, *n* (%)	15 (18)	9 (11)	24 (15)
SADQ continuous score at 6 months			
Median (IQR)	14.0 (3.0, 32.0)	7.0 (0.0, 30.0)	−1.00 (−7.00, 1.00), 0.2874[c]
Missing, *n* (%)	16 (20)	13 (16)	29 (18)
AUDIT at 12 weeks			
<16, *n* (%)	23 (35.4)	36 (51.4)	1.93 (0.97, 3.86), 0.0617[b]
≥16	42	34	
Missing, *n* (%)	16 (20)	9 (11)	25 (16)
AUDIT at 6 months			
<16, *n* (%)	25 (39.7)	30 (44.8)	1.23 (0.61, 2.48), 0.5571[b]
≥16	38	37	
Missing, *n* (%)	18 (22)	12 (15)	30 (19)
AUDIT continuous score at 12 weeks			
Median (IQR)	30 (8, 36)	15 (8, 36)	−2.00 (−8.00, 2.00), 0.3327[c]
Missing, *n* (%)	16 (20)	9 (11)	25 (16)
AUDIT continuous score at 6 months			
Median (IQR)	24 (8, 35)	16 (5, 36)	−1.00 (−7.00, 2.00), 0.5057[c]
Missing, *n* (%)	18 (22)	12 (15)	30 (19)
RTCQ at 12 weeks			
A, *n* (%)	45 (68.2)	52 (74.3)	1.35 (0.64, 2.84), 0.4322[d]
C, *n* (%)	21 (31.8)	17 (24.3)	
PC, *n* (%)	0	1 (1.4)	
C/PC, *n* (%)	21 (31.8)	18 (25.7)	
Missing, *n* (%)	15 (19)	9 (11)	24 (15)
RTCQ at 6 months			
A, *n* (%)	45 (71.4)	49 (74.2)	1.15 (0.53, 2.51), 0.7195[d]
C, *n* (%)	18 (28.6)	16 (24.2)	
PC, *n* (%)	0	1 (1.5)	
C/PC, *n* (%)	18 (28.6)	17 (25.8)	
Missing, *n* (%)	18 (22)	13 (16)	31 (19)
LDQ at 12 weeks			
Median (IQR)	14 (0, 26)	2 (0, 18)	−1.00 (−8.00, 0.00), 0.0384[c]
Missing, *n* (%)	16 (20)	9 (11)	25 (16)
LDQ at 6 months			
Median (IQR)	9 (0, 19)	1.5 (0, 18)	0.00 (−4.00, 0.00), 0.2262[c]
Missing, *n* (%)	18 (22)	13 (16)	25 (16)
Alcohol consumption at 12 weeks[a]			
Median (IQR)	126 (4, 210)	42 (0, 126)	−28.00 (−84.00, 0.00), 0.0267[c]
Missing, n(%)	17 (21)	9 (11)	26 (16)
Alcohol consumption at 6 months[a]			
Median (IQR)	84 (9, 154)	36 (0, 126)	−14.00 (−48.00, 0.00), 0.1098[c]
Missing, *n* (%)	18 (22)	16 (20)	34 (21)

Note: Biochemical indicators of co-morbid conditions measures (GGT, ALT and MCV) were not routinely done during follow-up. These were available only if a patient was admitted to a hospital with a more serious status. As a result, follow-up measurements are available only for a sub-group who had a more severe condition, and not for everyone randomized. The average number of missing was about 70% at 12 weeks and 6 months, and therefore, comparison between the two treatment groups was not performed.

[a]Alcohol consumption was calculated as number of units per drinking day × number of drinking days per week.

[b]Logistic regression (OR).

[c]Wilcoxon Two-Sample Test (mean difference).

[d]Logistic regression for binary (A, C/PC) RTCQ.

finding has been seen in other alcohol treatment research studies, which often fail to find differences either between different treatment groups (UKATT, 2005) or treatments compared with controls (Saitz *et al.*, 2007). A systematic review and meta-analysis of studies in this population and similar to this trial design explained this failure by concluding that exposure of controls to assessments introduces bias, which results in the effectiveness of BIs being underestimated (McCambridge and Kypri, 2011; McCambridge *et al.*, 2011). Described as 'assessment reactivity' (Clifford *et al.*, 2007; Maisto *et al.*, 2007; Bernstein *et al.*, 2010) or Hawthorne-like effects (Feil *et al.*, 2002), it is likely that interest and care shown to patients during the initial assessment had a positive impact (Nilsen *et al.*, 2008). An additional consideration for changes in controls could be the phenomenon of 'natural recovery' (Sobell *et al.*, 2000; Bischof *et al.*, 2003) where between 12% and 35% of alcohol-dependent individuals 'recover' with little or no specialist intervention. A meta-analysis of BIs across a variety of settings (Jenkins *et al.*, 2009) demonstrated heterogeneity amongst studies, but nevertheless showed a reduction in alcohol consumption in control groups, especially in trials conducted in Anglophone countries. Furthermore, in 16 studies where controls received some form of alcohol advice, there was a reduction in consumption (Bernstein *et al.*, 2010). It is possible that this has also been the case in our trial, particularly, since the control group received three assessments; at baseline, 3 and 6 months, which may have a potential cumulative effect.

Finally, regression to the mean has been postulated to be an artefact of the heterogeneity and extremes observed within this rather complex and unhealthy patient group, who are detected by definition when they have attended for medical attention (Cunningham, 2004; Bernstein *et al.*, 2010).

CONCLUSIONS

We must never underestimate the significance of a hospital visit as a motivator for behaviour change. Thus, although we were unable to establish the effectiveness of EBI, we noted that patients valued the opportunity to talk about their drinking and identify their personal risks. Not being allocated to the treatment group seemed to motivate non-treatment seekers to seek treatment, which was confirmed in a qualitative analysis of the interview data (unpublished data). Further research is required but perhaps alternative randomization methods (Zelen, 1979; Bernstein *et al.*, 2010) to control for bias described above (McCambridge *et al.*, 2014), and demonstrated in our findings should be considered.

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CONFLICT OF INTEREST STATEMENT

None declared.

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