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Mental Imagery to Reduce Alcohol-related harm in patients with alcohol use disorder and alcohol-related liver damaGE: the MIRAGE randomised pilot trial results

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ABSTRACT

Objective The healthcare burden of alcohol-related liver disease (ARLD) is increasing. ARLD and alcohol use disorder (AUD) is best managed by reduction or cessation of alcohol use, but effective treatments are lacking. We tested whether people with ARLD and AUD admitted to hospital could be recruited to and retained in a trial of Functional Imagery Training (FIT), a psychological therapy that uses mental imagery to reduce alcohol craving. We conducted a multicentre randomised pilot trial of treatment as usual (TAU) versus FIT+TAU in people admitted to hospital with ARLD and AUD.

Design Participants were randomised to TAU (a single session of brief intervention) or FIT+TAU (TAU with one hospital-based FIT session then eight telephone sessions over 6 months). Pilot outcomes included recruitment rate and retention at day 180. Secondary outcomes included fidelity of FIT delivery, alcohol use, and severity of alcohol dependence.

Results Fifty-four participants (mean age 49; 63% male) were recruited and randomised, 28 to TAU and 26 to FIT+TAU. The retention rate at day 180 was 43%. FIT was delivered adequately by most alcohol nurses. 50% of intervention participants completed FIT sessions 1 and 2. There were no differences in alcohol use or severity of alcohol dependence between treatment groups at day 180.

Conclusion Participants with ARLD and AUD could be recruited to a trial of FIT versus FIT+TAU. However, retention at day 180 was suboptimal. Before conducting a definitive trial of FIT in this patient group, modifications in the intervention and recruitment/retention strategy must be tested.

Trial registration number ISRCTN41353774.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Functional Imagery Training (FIT) is a psychological therapy that aims to reduce alcohol craving.

WHAT THIS STUDY ADDS

⇒ Most people with alcohol-related liver disease who agreed to take part in this trial did not complete it.

⇒ The trial needs modification to improve FIT fidelity and retention before a definitive trial.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study demonstrates that better strategies are needed to support participant engagement with FIT.

INTRODUCTION

Globally, alcohol use is the leading cause of premature death or disability in adults younger than 50 years.[1] In the UK, alcohol contributed to almost 1 million unplanned hospital admissions in 2020/2021, of which 39 667 were due to alcohol-related liver disease (ARLD).[2 3] Alcohol-specific deaths increased by 20% in 2020/2021, of which 80.3% were due to ARLD.[4] Alcohol-related healthcare costs £3.5 billion to the NHS directly and up to £52 billion to the UK economy annually.[5] Management of patients with ARLD urgently needs improvement, including investment in alcohol services.[6]

ARLD is a spectrum of liver damage from steatosis to cirrhosis caused by long-term, high-risk alcohol consumption. Many people with ARLD are alcohol dependent, characterised by craving, tolerance and continued alcohol use despite harmful consequences.[7] Continued alcohol use increases the risk of progression of liver damage and increases

mortality risk in people with ARLD.[8 9] Conversely, reduction in consumption, even in those with late stage cirrhosis, results in improved survival.[10]

Reduction or cessation of alcohol use in people with ARLD is the cornerstone of management but there are few effective treatments and more than two-thirds relapse to alcohol after hospital admission.[9 11] Psychological interventions based on motivational interviewing (MI) techniques or cognitive behavioural therapy approaches are effective in reducing alcohol consumption and mortality rates in high-risk alcohol users admitted to hospital[12] but these require expertise, are expensive and time-consuming to deliver and have not been recommended for use in acute NHS settings. Multi-session MI is effective in people with ARLD in outpatient rather than inpatient settings.[13–15]

Pharmacological therapies are available but have limited effectiveness and are not licenced for use in people with ARLD.[16] Baclofen has been tested in people with chronic liver disease but results are conflicting[17–19] and a further definitive trial is underway.[20] However, results from drug trials to date suggest people receive the most benefit when psychological support is also provided.[21 22]

Current treatment as usual (TAU) in the UK for patients admitted to hospital with alcohol use disorder (AUD) and ARLD consists of a short (less than 20 min), single MI-based session of brief intervention and advice. It is delivered by a trained health professional, usually an Alcohol Liaison Nurse (ALN), in accordance with National Institute for Health and Care Excellence recommendations.[23] However, TAU has limited clinical benefit in secondary care compared with primary care or community settings.[24]

There is a need for a psychological intervention that effectively motivates sustained abstinence from alcohol. Ideally, this intervention would capitalise on receptiveness to change at the time of an unplanned hospital admission, as TAU does, and extend support beyond discharge, as multi-session MI does. Mental imagery amplifies emotion[25 26] and could be incorporated into such a new intervention.

Functional Imagery Training (FIT) combines MI with evidence-based imagery training to strengthen motivation, combat craving and train self-management skills.[25 27] Individuals are encouraged to create multi-sensory mental images of achieving their goal, taking the first steps needed to work towards their goal, and using previously successful strategies to work around potential obstacles to their goal. The individual is encouraged to practice this imagery frequently. FIT is effective for behaviour change in other contexts, including motivating dietary change and increasing athletes' resilience[27–29] and motivation.[30]

We plan to conduct a definitive trial to determine the clinical and cost-effectiveness of the addition of FIT to TAU in reducing alcohol-related harm over 6 months in patients with ARLD and AUD identified during an unplanned hospital admission. Before finalising the definitive trial design, we needed to determine whether patients with ARLD can be recruited and randomised to trials, whether they will engage with FIT treatment and how well ALNs can deliver FIT. In addition, we needed to collect information to (i) finalise the choice of outcome measures; (ii) test the cost-effectiveness framework; (iii) estimate the effect size of FIT on alcohol consumption and (iv) inform how many patients we would need to recruit in a definitive trial.

METHODS

Study design

Multicentre randomised pilot trial of FIT+TAU versus TAU alone in patients with unplanned hospital admissions with AUD and ARLD. The trial protocol has been reported in full.[31] The study was registered with ISRCTN on 12 March 2021 (https://doi.org/10.1186/ISRCTN41353774).

Participants

The study was initially conducted in three acute NHS Trusts in England (University Hospitals Plymouth, Leeds Teaching Hospitals and University Hospitals of Bristol and Weston). Due to slower than anticipated participant recruitment in the first 6 months, a fourth centre was opened (Royal Devon University Hospital) and the recruitment period extended by 3 months at all sites. Consecutive adult patients with an unplanned hospital admission with ARLD and AUD were invited to participate (table 1).

Table 1 Patient selection criteria

Inclusion criteria	Exclusion criteria
Adult patients ≥18 years	Any condition with an estimated life expectancy of less than 6 months
Able and willing to provide written informed consent	Patients participating in concurrent interventional research
Diagnosis of alcohol-related liver disease by radiological, histological or physical examination findings	Patients who have significant difficulties in adequate understanding of English
High risk alcohol consumption (>50 units/week for males and >35 units/week for females) within 4 weeks prior to hospital admission	Prisoners
Alcohol Use Disorder Identification Test (AUDIT) score[32] >15 during current hospital admission	Patients without access to a telephone
Diagnosis of alcohol dependence documented by clinician in medical records. This should be with reference to the ICD-10 definition[33]	

The site principal investigator or an authorised delegate, trained in the relevant principles of Good Clinical Practice and the requirements of the trial protocol, obtained written informed consent prior to the collection of any trial data.

Interventions

TAU comprised one brief MI-based session given in hospital by an ALN. A manualised FIT intervention was delivered by a member of the site's alcohol services team and comprised one session given face-to-face to participants before discharge from hospital, with a further eight sessions offered by telephone over a period of 6 months as previously described.[31] With participant consent, the first session was audio-recorded for fidelity assessment.

ALNs received two half-day remotely delivered training sessions in FIT, including practical exercises. During the trial, two of the first five audio-recorded FIT sessions from each ALN were reviewed by an experienced FIT practitioner, to assess fidelity (see below) and to provide individualised feedback to ALNs.

FIT and TAU fidelity

Fidelity to FIT was assessed using the FIT-QC 2.0.[31] In brief, global performance and nine items covering MI elements, functional imagery and training were rated between 0 and 4.

Procedures and follow-up

Follow-up was scheduled for telephone at 28 (±7) and 90 (±7) days and face-to-face (or telephone where participant preferred) at 180 (±14) days postbaseline. To incentivise retention, participants received a single payment of £20 (as cash or voucher) after completion of the final trial visit.

Outcomes

Pilot trial outcome measures

- Recruitment rate.
- Retention rate at 90 and 180 days.
- Fidelity of delivery of FIT and TAU.
- Number of successful FIT phone calls and visits.
- Completeness of data collection.

Patient-reported and other clinical outcomes

The primary focus of this trial was to assess the pilot measures listed above. The proposed primary outcome for a definitive trial would be self-reported alcohol use (grams of pure alcohol/week) between baseline and 180 days postbaseline. Alcohol use was assessed using the timeline follow-back technique,[32] which was used to determine an individual's alcohol use over the 7 days immediately prior to their hospital admission (baseline) and at 28, 90 and 180 days postbaseline.

Proposed participant reported secondary outcomes for a future definitive trial (table 2) were:

- Severity of Alcohol Dependence Questionnaire (SADQ).[33]
- EQ-5D-5L[34] to measure health-related quality of life.
- Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS)[35] and Short WEMWBS (SWEMWBS).[36]
- Health, social care and wider care services utilisation determined using a bespoke resource use questionnaire.
- Self-reported re-hospitalisation within 180 days postbaseline or, determined using hospital records at participating sites.
- Self-reported time to relapse to alcohol use (≥5 drinking days per week or ≥5 in a single day).[37]

Exploratory biochemical outcomes

Alcohol metabolites using urinary biomarkers (ethyl glucuronide/sulphate) at 180 days postbaseline.

Economic evaluation

This pilot study tested the methods for a subsequent, policy-relevant, cost-effectiveness analysis (CEA) of FIT and TAU, compared with TAU. Full details of the health economics methodology used in this trial are presented in online supplemental material.

Table 2 Summary of outcome measures

	Baseline	Day 28 (±7)	Day 90 (±7)	Day 180 (±14)
Current alcohol use*	X	X	X	X
SADQ score	X	X	X	X
EQ-5D-5L questionnaire	X	X	X	X
WEMWBS questionnaire†	X	X	X	X
Health and social care resource utilisation	X		X	X
Re-hospitalisation rate		X	X	X
Self-reported time to relapse		X	X	X
Urine sample for alcohol metabolites				X

*Self-reported alcohol use (units of alcohol) over a period of 7 days obtained using the timeline follow-back method. At baseline, this covers the 7 days prior to hospital admission. Post-allocation, this covers the 7 days prior to the data collection timepoint.
†Including Short WEMWBS.
SADQ, Severity of Alcohol Dependence Questionnaire; WEMWBS, Warwick-Edinburgh Mental Wellbeing Scale.

Qualitative study

Methods for the qualitative study are described in online supplemental material.

Study management

Study oversight and data management are described in online supplemental material.

Randomisation and blinding

Participants were allocated to receive TAU only or TAU+FIT, in a 1:1 ratio, using random permuted blocks, stratified by recruiting site and the participant's baseline SADQ total score, dichotomised as ≤30 (moderate) or >30 (severe). Web-based randomisation was managed by the Peninsula Clinical Trials Unit.

This trial was non-blinded to ALNs and participants, as it is not possible to conceal the active FIT intervention from them. The outcome assessors (ie, research team members conducting research visits) were blinded to treatment allocation. The trial statisticians were not blinded.

Sample size

We estimated that across all recruiting sites, 32 potentially eligible ARLD patients would be admitted per month. We anticipated screening ~180 patients; with a conservative recruitment rate of 50% of those screened, our total recruitment target was 90 participants. This would allow estimation of the overall retention rate with a 95% CI with precision of at least ±11%.

Statistical analysis

A detailed statistical analysis plan was developed and approved by an independent statistician prior to database lock and is publicly available at https://pearl.plymouth.ac.uk/handle/10026.1/21253. Primary analysis, in the form of summary statistics (mean and SD or median and IQR, where appropriate), was undertaken on a modified intention to treat basis, where participants were analysed according to their allocated group, regardless of adherence to the protocol. Missing outcome data was not imputed in this pilot study. The safety population included all participants who consented to partake in the study, with safety data collected from recruitment until completion or withdrawal and reported on an ITT basis.

As this is a pilot trial, no inferential between-group hypothesis testing was undertaken. Feasibility outcomes, such as recruitment rates, are presented with two-sided 95% CIs.

Safety reporting

Safety and tolerability of the trial intervention was monitored throughout the study by means of follow-up review of all participants. All serious adverse events (SAEs) were recorded and reported, whether they were deemed related to the trial intervention or not. Quarterly summaries of all SAEs were provided to the TSC and study sponsor.

RESULTS

Recruitment and retention

From 1 April 2021 to 28 February 2022, 121 patients were approached and provided with the participant information sheet (figure 1). Of these, 54 provided informed consent (recruitment rate 44.6%; 95% CI 35.6% to 53.9%) and all completed the baseline visit and were randomised, 28 to TAU and 26 to FIT+TAU. One participant was randomised to the control group but given the FIT intervention and one participant randomised to the intervention group but only offered TAU. Two participants in the TAU only arm did not receive TAU, one due to early hospital discharge and the other due to death.

Twenty-six participants (13 in the TAU and 10 in the FIT+TAU arm) completed the final day 180 visit (overall retention rate 42.6% (95% CI 29.2% to 56.8%), 46.4% (95% CI 27.5% to 66.1%) in the TAU arm and 38.5% (95% CI 20.2% to 59.4%) in the FIT+TAU arm). During follow-up, there were 14 withdrawals (8 in TAU and 6 in FIT+TAU) including 5 deaths (figure 1). Of the 26 participants randomised to FIT+TAU, there were 10 early discontinuations of the intervention. The trial was stopped after the pre-determined end date was reached.

Completion of FIT sessions

Twenty-one (80.6%) participants completed FIT session 1 and 7 (26.9%) session 2 within the specified timeframes (online supplemental table 1). One participant (3.8%) completed all nine FIT sessions. 13 (50.0%) participants completed both sessions 1 and 2, judged to provide an adequate dose of FIT (as they covered the key elements of the intervention from building motivation to developing an action plan and practising imagery associated with both). Four participants did not complete any FIT session: three were discharged before a FIT session could be delivered and then could not be contacted; one participant requested deferral of the first session until after discharge but could then not be contacted.

Participant characteristics at baseline

Mean age was 49.3 years (SD 11.0), 34 (63.0%) were male and all were of white ethnicity (table 3). Twenty-eight (51.9%) had cirrhosis, 22 (40.7%) fatty liver and 4 (7.4%) fibrosis. Of those with cirrhosis, the mean Child Pugh score was 8.3 (2.4) and mean Model for End-stage Liver Disease (MELD) score was 23.7 (6.5). Mean AUDIT score at baseline was 31.6 (5.6), higher than the threshold of 20 that is suggestive of moderate to severe AUD. Participant characteristics between allocated groups were mostly similar except for sex where there was a higher proportion of males in the TAU group in the FIT+TAU group (71.4% vs 53.8%).

Completeness of outcome measures

For participants who attended a visit, there was a high level of completeness of outcome measures (table 4). Completeness of alcohol use data was lower than anticipated at baseline due to incomplete data collection by

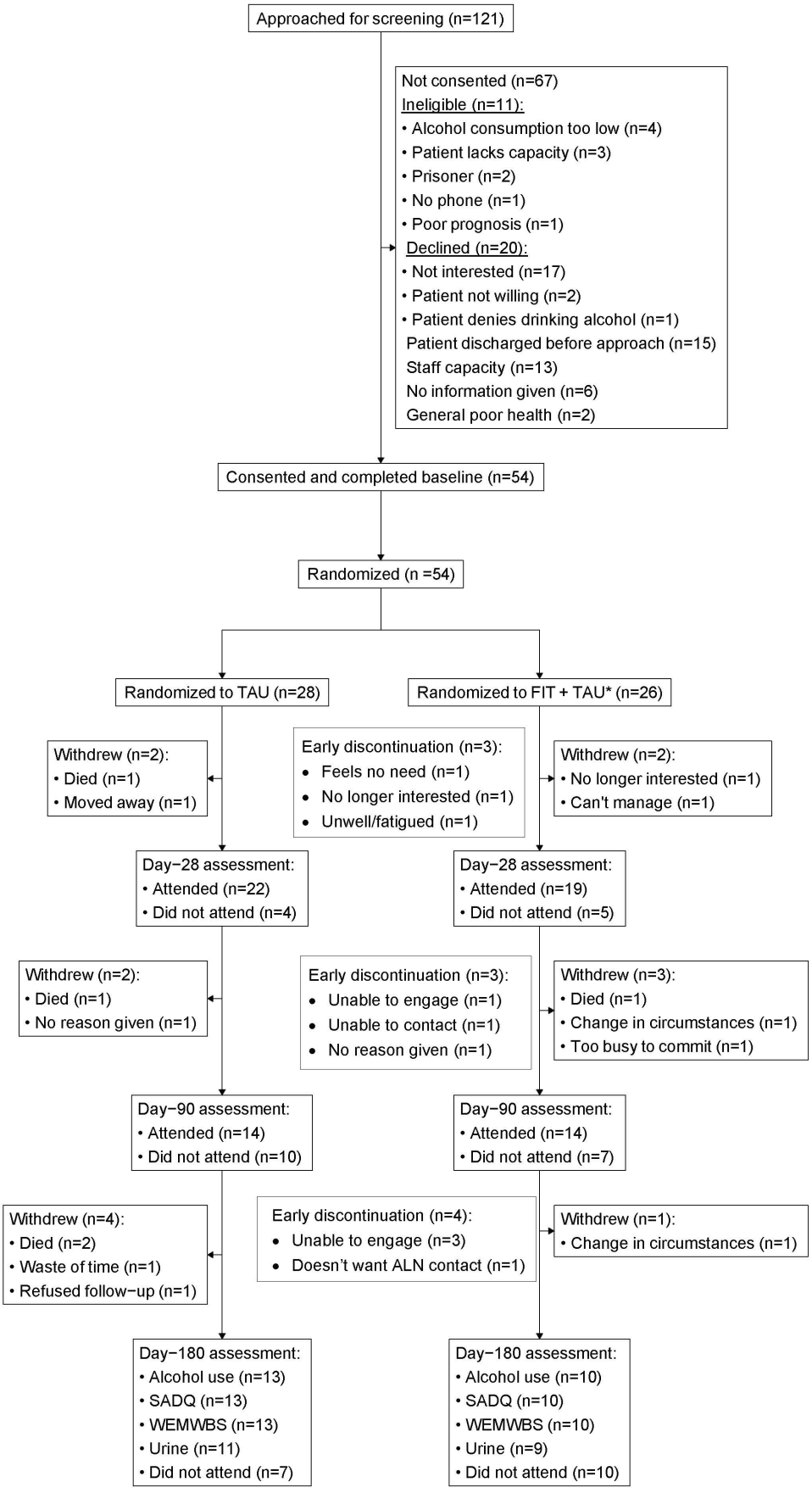

Figure 1 Consort diagram of participant screening, randomisation and follow-up. *TAU may be completed before recruitment, after recruitment or after baseline assessment. ALN, Alcohol Liaison Nurse; FIT, Functional Imagery Training; SADQ, Severity of Alcohol Dependence Questionnaire; TAU, treatment as usual; WEMBS, Warwick-Edinburgh Mental Wellbeing Scale.

Table 3 Summary statistics of baseline and demographic participant characteristics

	TAU (n=28)	FIT+TAU (n=26)	All (n=54)
Age			
Mean (SD) (range)	48.6 (9.4) (30, 65)	50.0 (12.63) (25, 73)	49.3 (11.0) (25, 73)
AUDIT score			
Mean (SD) (range)	30.9 (6.0) (17, 40)	32.3 (5.2) (21, 40)	31.6 (5.6) (17, 40)
Sex, n (%)			
Male	20 (71.4%)	14 (53.8%)	34 (63.0%)
Female	8 (28.6%)	12 (46.2%)	20 (37.0%)
Ethnicity, n (%)			
White	28 (100%)	26 (100%)	54 (100%)
Stage of liver disease, n (%)			
Fatty	10 (35.7%)	12 (46.2%)	22 (40.7%)
Fibrosis	3 (10.7%)	1 (3.8%)	4 (7.4%)
Cirrhosis	15 (53.6%)	13 (50.0%)	28 (51.9%)
Child-Pugh score			
Mean (SD) (range)	7.5 (1.8) (5, 11)	9.2 (2.6) (5, 12)	8.3 (2.4) (5, 12)
MELD score			
Mean (SD) (range)	22.7 (7.2) (14.9, 36.7)	24.8 (5.8) (13.2, 33.6)	23.7 (6.5) (13.2, 36.7)
Housing status, n (%)			
Owner occupier	6 (21.4%)	8 (30.8%)	14 (25.9%)
Tenant	17 (60.7%)	13 (50.0%)	30 (55.6%)
Free lodger	2 (7.1%)	3 (11.5%)	5 (9.3%)
Supported accommodation	2 (7.1%)	0	2 (3.7%)
Homeless	1 (3.6%)	2 (7.7%)	3 (5.6%)

AUDIT, Alcohol Use Disorder Identification Test; FIT, Functional Imagery Training; MELD, Model for End-stage Liver Disease; TAU, treatment as usual.

site teams. This was addressed by amendment of the electronic report form. Summary statistics of proposed primary and secondary outcomes of participants are presented in online supplemental table 2.

Alcohol use

Median alcohol use per week fell from 1568 g (range 788, 2128) of pure ethanol at baseline to 0 g (0, 180) at day 180 in the TAU group and from 1120 g (609.6, 1784) to 0 g (0, 196) in the FIT+TAU group (table 4). At day 28, 12 (43%) TAU and 14 (54%) FIT+TAU participants reported zero alcohol consumption. At day 180, these numbers fell to six (21%) and nine (19%) of the total number randomised to each group (TAU and FIT+TAU), respectively (table 5).

Summary measures of other patient-reported outcomes are presented in table 4 and urine alcohol metabolites in online supplemental table 3.

Self-reported time to relapse

The median (IQR) in the TAU group was 23 days (2, 165) based on data from nine participants, while in the FIT+TAU group it was 22.5 days[12 36] based on data from six participants.

Re-hospitalisation rate and SAEs

There were 34 hospital re-admissions in 17 unique participants, 16 in the TAU group and 18 in the FIT+TAU group (online supplemental table 4). Seventy-five SAEs were reported in 33 unique participants, 35 SAEs in the TAU group and 40 SAEs in the FIT+TAU group (online supplemental table 5). Most SAEs were related to complications of liver disease or AUD and none was considered to be related to the intervention or trial procedures.

Fidelity of FIT intervention delivery

Eleven audio recordings of FIT session 1 or 2 were evaluated for fidelity (online supplemental table 6). Four of the seven ALNs had two FIT sessions assessed, the remaining had one each assessed. The median global score was 2.1 (0.6, 3.0), with median scores of 2 for all components (online supplemental table 6). The range of scores shows that satisfactory ratings were not achieved on all aspects. Four recordings, belonging to three ALNs, were assessed as inadequate. Only one ALN delivered FIT to more than five participants; assessment of fidelity of two of the second set of five participants per ALN could not be completed.

Table 4 Completeness and summary measures of the participant-reported primary and secondary outcomes

Outcome	Time point	TAU (N=28)			FIT+TAU (N=26)		
		Attended visit	With valid score	Median (IQR)	Attended visit	With valid score	Median (IQR)
Alcohol use (grams of pure alcohol/ week)*	Baseline	28 (100.0%)	19 (67.9%)	1568 (788, 2128)	26 (100.0%)	20 (76.9%)	1120 (610, 1784)
	28 (±7) days	21 (75.0%)	18 (64.3%)	0 (0, 48)	19 (73.1%)	16 (61.5%)	0 (0, 0)
	90 (±7) days	14 (50.0%)	9 (32.1%)	0 (0, 0)	14 (53.4%)	13 (50.0%)	0 (0, 0)
	180 (±14) days	12 (42.9%)	11 (39.3%)	0 (0, 180)	10 (38.5%)	9 (34.6%)	0 (0, 196)
SADQ	Baseline	28 (100.0%)	28 (100.0%)	33 (22, 42)	26 (100.0%)	26 (100.0%), N=25*	30 (20, 41)
	28 (±7) days	22 (78.6%)	22 (78.6%), N=8*	37 (31, 52)	19 (73.1%)	17 (65.4%), N=4*	25 (10, 43)
	90 (±7) days	14 (50.0%)	11 (39.3%), N=4*	46 (39, 53)	14 (53.8%)	13 (50.0%), N=4*	40 (25, 51)
	180 (±14) days	13 (46.4%)	12 (42.9%), N=4*	47 (40, 50)	10 (38.5%)	9 (34.6%), N=3*	39 (15, 54)
WEMWBS†	Baseline	28 (100.0%)	28 (100.0%)	35 (20, 40)	26 (100.0%)	26 (100.0%)	32 (25, 39)
	28 (±7) days	22 (78.6%)	22 (78.6%)	42 (25, 56)	19 (73.1%)	17 (65.4%)	30 (26, 51)
	90 (±7) days	14 (50.0%)	11 (39.3%)	31 (20, 52)	14 (53.8%)	13 (50.0%)	41 (35, 47)
	180 (±14) days	13 (46.4%)	12 (42.9%)	39 (31, 43)	10 (38.5%)	9 (34.6%)	40 (32, 58)

*Participants who reported no alcohol consumption within the previous 28 days did not complete SADQ; N refers to number of participants for whom SADQ was calculated.
†Completeness rate of Short WEMWBS is the same as for WEMWBS.
FIT, Functional Imagery Training; SADQ, Severity of Alcohol Dependence Questionnaire; TAU, treatment as usual; WEMWBS, Warwick-Edinburgh Mental Wellbeing Scale.

Contamination between FIT and TAU

To evaluate potential contamination between FIT and TAU, the use of imagery in TAU was self-assessed by ALNs. There were no reported instances of imagery used in TAU sessions.

Economic evaluation

Of participants who undertook the follow-up assessments, there was a high degree of data completeness for these measures (online supplemental table 7).

Per-participant level contact and non-contact time data were available for 16 of the 26 participants allocated to the FIT intervention. The mean cost per participant of the intervention was £626. The resources required to deliver the intervention and their associated costs are provided in disaggregated form in online supplemental table 8.

Health state utility values, based on the EQ-5D-5L, and associated quality-adjusted life years (QALYs) are described in online supplemental table 9.

Qualitative study results

Participant interviews

Four control and two intervention participants participated in semi-structured virtual interviews. Reasons for participation included wanting to give something back following receipt of treatment and thinking it might help others. Participants found the recruitment process, documentation, follow-up visits and data collection acceptable, including providing a urine sample at the day 180 visit.

Table 5 Proportion of participants who completed each visit per protocol with no alcohol consumption as calculated from Timeline Follow Back (TLFB)

Variable	Time point	TAU: 28 randomised		FIT+TAU: 26 randomised	
		Number at visit	N (% with zero alcohol)	Number at visit	N (% with zero alcohol)
Participants with zero alcohol consumption	Baseline	28	0 (0%)	26	0 (0%)
	28 (±7) days	18	12 (66.7%)	16	14 (87.5%)
	90 (±7) days	9	8 (88.9%)	13	10 (76.9%)
	180 (±14) days	11	6 (54.5%)	9	5 (55.6%)

FIT, Functional Imagery Training; TAU, treatment as usual.

The two intervention participants spoke positively about their experiences. One participant liked the individual delivery of FIT rather than having to attend a group so that they did not need to listen to others' problems when they felt they had enough of their own. They said that they liked the phone sessions so that they didn't have to travel. This participant stated that they found '… the motivation that they gave me … to be abstaining' helpful and liked that they felt that they could contact the ALN if they needed to speak to someone. The second participant described FIT and working with the ALN as supporting them to take back control from alcohol.

ALN focus groups

Five ALNs from two sites participated in virtual focus groups about their experience of, preparation for and delivery of FIT. ALNs across both sites discussed the training positively overall and found it interesting. Opportunities to practice role-play were seen as beneficial. It was suggested that in person training would better support practicing delivery of FIT. They found the feedback session useful for supervision and appreciated being given guidance to enhance their delivery.

One of the greatest challenges faced by ALNs was in contacting participants. ALNs also spoke of the challenges of delivering FIT in the hospital setting, particularly the lack of privacy on the ward and the impact on engagement due to noise and sleep disturbance.

Although convenience of remote delivery was noted, this was viewed as challenging due to ALNs not being able to see patients' facial expressions and gauge the extent to which they were engaging with FIT. ALNs proposed that FIT would be better suited to being delivered in the community and only introduced in hospital rather than delivered in the hospital setting. Additionally, a dedicated room for delivery as well as video rather than phone sessions for remote delivery. They suggested that training could be enhanced through more relatable role-play and ongoing support through a supervision forum.

DISCUSSION

The MIRAGE pilot trial of FIT in addition to TAU, versus TAU alone, for people admitted to hospital with ARLD and AUD demonstrates the challenges of delivering a hospital-based trial in this patient population. It showed that FIT can be delivered by the existing acute hospital alcohol service workforce but further training and support is required to achieve consistent adequate fidelity. Recruitment and retention of the target population were lower than anticipated and most participants randomised to FIT+TAU failed to engage in the full therapy. This trial was not powered to detect differences between trial arms and low participant retention prevented evaluation for potential signals of clinical efficacy.

The recruitment rate of 45% of patients screened suggests there were barriers preventing eligible patients taking part in MIRAGE. Some of these were logistical (eg, lack of research workforce, discharge of potential participants before approach about the trial could be made), while others may be addressed by improved discussion or presentation of trial information. The key challenge identified in the trial was poor participant retention at the final trial visit, 6 months after randomisation, of only 43%. This is accounted for by 26% active withdrawal rate (including 9% mortality) and 31% lost to follow-up despite implementation of a strong retention strategy including a financial incentive at the final trial visit.

The retention rate was similar between arms: 46% in the TAU, 38% in the FIT+TAU groups. A single £20 incentive on completion of the final trial visit was not sufficient to encourage retention. Acknowledging the limitation of small numbers, there was no suggestion of differential loss to follow-up by baseline severity of AUD stratified by SADQ.

Few intervention trials have been conducted in this patient population. In a trial of baclofen in people with cirrhosis and AUD, recruitment rate was 57%[17] and in a trial of prednisolone or pentoxifylline in people with severe alcoholic hepatitis and AUD (STOPAH) the recruitment rate was only 21%.[11] However, the dropout rate in participants who were still alive was substantially lower than the current trial at 23% at 90 days in the baclofen trial and 32% at 1 year in the STOPAH trial. These trials cannot be directly compared with MIRAGE as they differed in terms of intervention (both pharmacological), target population and length of trial follow-up. The results of this feasibility study suggest that modification to the MIRAGE trial protocol may better enable participant engagement and retention in the trial. Strategies such as community based follow-up, offering alternative incentives throughout the trial and using participants' existing social networks to facilitate follow-up visits may be considered. However, it should be acknowledged that even with these approaches, retention may be lower than drug trials or studies in other populations. Sample size calculations for trials in similar target populations need to carefully consider the anticipated retention rates as well as other strategies for both maximising the data available for analyses, such as imputation of missing data, and minimising potential bias.

The sample of patients recruited to the trial is likely to be representative of the target population. The mean age of 49.3 years is comparable to data from English Hospital Episode Statistics in which mean age of ARLD patients ranged between 51 and 53 years over the last decade.[3] The proportion of males (63%) is similar to previously reported national (66%) and regional datasets (63%).[3 38] Additionally, participants were recruited from diverse social backgrounds including those experiencing homelessness or in supported accommodation. Although there was no evidence of increased loss to follow-up in this group, future studies including such participants should consider whether targeted extra support is needed to facilitate their participation. Participants with cirrhosis had a mean Child Pugh score of 8.3, similar to a UK

national audit in which patients admitted to hospital with ARLD cirrhosis had a mean score of 8.[3] The trial population consisted of only people of white ethnicity, despite the inclusion of sites serving more mixed communities. There is a paucity of data on ethnicity and ARLD in the UK; a Scottish study found that of over 50 000 hospital admissions with ARLD only 1.1% were non-white.[39] It is likely we have under-representation of minority ethnic groups in this trial. Given this caveat, the trial findings are otherwise broadly generalisable to the target population in the UK.

MIRAGE demonstrates the challenges for members of hospital alcohol services to deliver high-quality FIT. After two half-days of remote FIT training, four of seven ALNs provided FIT to participants with adequate fidelity while three missed a global rating of adequate. The fact that we did not achieve consistently satisfactory fidelity indicates a need for more training and feedback. ALNs were provided with individualised feedback after review of audio-recorded sessions and were offered further supervisory meetings with an experienced FIT practitioner but their workload limited engagement with further supervision. This drawback makes it hard to improve training in the ways suggested during ALN focus groups, such as additional role play. Overall, it was noted that ALNs had generally good MI skills and were able to incorporate imagery into their sessions although the latter could benefit from additional training.

Thirty-two of the 61 (52%) FIT sessions that took place occurred within the defined session windows suggesting that ALN workload and availability of participants may have affected per protocol timings. Eighty-five per cent of participants received the first FIT session and 50% received the first two FIT sessions. Future studies should ensure that the majority of FIT is delivered early in the trial but this must be balanced with the potential benefits of longer-term engagement with the technique over the full 6-month intervention period. Feedback from intervention participants was positive and acknowledged the benefit of regular contact with ALNs.

This pilot has demonstrated the feasibility of a policy-relevant, within-trial CEA alongside a definitive RCT of FIT+TAU. Completion rates of self-report resource use and the EQ-5D-5L, enabling the estimation of QALYs, were consistent with those of the other assessment measures in the trial. In addition, data were collected on FIT participant-level contact and non-contact time, training, supervision and other intervention-related resources, facilitating estimation of the cost per participant of FIT. A lower cost per participant would be anticipated across larger patient groups, as greater numbers could be treated per therapist and the investment of time in training and supervision could be realised across multiple recipients.

In conclusion, the MIRAGE pilot trial of the addition of FIT to TAU in patients with ARLD and AUD demonstrates that it would not be feasible to deliver a larger-scale definitive trial without modifying the study design. The fidelity assessments and qualitative interviews with ALNs suggest that FIT training requires improvement to obtain consistent quality. Furthermore, a robust recruitment and retention strategy must be developed for a future definitive trial to successfully assess effectiveness, and cost-effectiveness, of adding FIT to usual care, in this important patient group.

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