NOTTINGHAM CLINICAL TRIALS UNIT

ReMemBrIn
Rehabilitation of Memory in Brain Injuries

Rehabilitation of Memory following Traumatic Brain Injury – a Phase III Randomised Controlled Trial

Statistical Analysis Plan

Final version 1.0 (19th December 2016)

Based on Protocol version 5.0 (dated 22 January 2016)

The following people have reviewed the Statistical Analysis Plan and are in agreement with the contents			
Name	**Role**	**Signature**	**Date**
Lucy Bradshaw	Author	Lucy Bradshaw	19 Dec 2016
Alan Montgomery	NCTU Professor of Medical Statistics	A Montgomery	20 Dec 2016
ANDREW BATEMAN	DMC		3/Jan/2017
Prof Roshan Das Nair	Chief Investigator		06.01.2017
Prof Nadina Lincoln	Co-investigator	Nadina Lincoln	21 Dec 2016

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Abbreviations

Abbreviation	Description
AE	Adverse Event
AP	Assistant Psychologist
CI	Chief Investigator
Co-I	Co-investigator
CRF	Case Report Form
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
EBIQ	European Brain Injury Questionnaire
EMQ	Everyday Memory Questionnaire
GHQ	General Health Questionnaire
GMI	General Memory Index
HTA	Health Technology Assessment
NCTU	Nottingham Clinical Trials Unit
PI	Principal Investigator
PIL	Patient Information Leaflet
R&D	Research & Development
RA	Research Assistant
RBMT	Rivermead Behavioural Memory Test – 3rd edition
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
RN	Research Nurse
RSA	Research Sponsorship Agreement
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
TBI	Traumatic Brain Injury
TSC	Trial Steering Committee
QA	Quality Assurance

Amendments to versions

Version	Date	Change/comment	Statistician
1.0	19 Dec 2016	Final version 1.0	LB

1. INTRODUCTION & PURPOSE

This document details the rules proposed and the presentation that will be followed, as closely as possible, when analysing and reporting the main results from the Health Technology Assessment (HTA) funded randomised controlled trial of rehabilitation of memory following traumatic brain injury.

The purpose of the plan is to:

1. Ensure that the analysis is appropriate for the aims of the trial, reflects good statistical practice, and that interpretation of a priori and post hoc analyses are appropriate.
2. Explain in detail how the data will be handled and analysed to enable others to perform the actual analysis in the event of sickness or other absence.

Additional exploratory or auxiliary analyses of data not specified in the protocol or this plan are permitted but fall outside the scope of this analysis plan (although such analyses would be expected to follow Good Statistical Practice).

The analysis strategy will be made available if required by journal editors or referees when the main papers are submitted for publication. Additional analyses suggested by reviewers or editors will, if considered appropriate, be performed in accordance with the Analysis Plan, but if reported the source of such a post-hoc analysis will be declared.

Amendments to the statistical analysis plan will be described and justified in the final report of the trial.

2. SYNOPSIS OF STUDY DESIGN AND PROCEDURES

2.1. Trial aims and objectives

The purpose of this trial is to evaluate the clinical effectiveness and cost-effectiveness of a group-based memory rehabilitation programme for military personnel and civilians who have sustained a traumatic brain injury (TBI).

2.1.1. Primary objective

The primary objective is to determine whether attending a group memory rehabilitation programme is associated with improved management of memory in daily life, as measured on the Everyday Memory Questionnaire – patient version (EMQ-p) when compared to usual care.

2.1.2. Secondary objectives

The secondary objectives are to assess:

- cost-effectiveness of the intervention
- whether the intervention is associated with improvements in the participants':
    1. ability to achieve individually set goals
    2. 'objectively' assessed memory abilities
    3. cognitive, emotional, and social wellbeing
    4. health-related quality of life

2.2. Trial design and configuration

This is a multi-centre, parallel group, cluster randomised controlled trial comparing the effectiveness of a group-based memory rehabilitation programme to usual care for people who have sustained a traumatic brain injury. Outcomes will be assessed at six and twelve months after randomisation to assess immediate and long-term effects of the intervention. The primary time point of interest is six months after randomisation. Follow-up is by assessments included in questionnaire packs which are posted to participants and at clinic visits for assessments conducted by a research assistant.

2.3. Trial centres

Recruitment to the study began at 4 centres in the UK: Nottingham, Birmingham, Chester and Epsom. Liverpool was opened as an additional site, to replace Epsom, during the study. Sheffield was opened to replace Birmingham. Sites at Bristol, St Georges and South Tees were opened in 2015 meaning 9 centres recruited participants during the trial.

2.4. Eligibility criteria

2.4.1. Inclusion criteria

Eligible participants are those who:

- Were admitted to hospital with a TBI more than 3 months prior to recruitment.
- Report having memory problems as assessed at baseline. Defined as either a score of 24 or more on the EMQ patient version or a score below the 25th percentile on the Rivermead Behavioural Memory Test (RBMT-3)
- Are 18 to 69 years of age.
- Are able to travel to one of the study centres and attend group sessions.
- Give informed consent.

2.4.2. Exclusion criteria

Potential participants will be excluded if they:

- Are unable or unsuitable to engage in group treatment if allocated

- Are involved in other psychological intervention studies.
- Have impairment of language, as assessed on the Sheffield Screening Test for Acquired Language Disorders (cut-off score <17).

2.5. Description of interventions

Group memory rehabilitation
Participants will receive 10 group memory rehabilitation sessions (1.5 hours long, once a week for 10 weeks) in groups of between 4 and 6. Each group will be led by trained Assistant Psychologists (AP) following a treatment manual developed in a previous pilot study. The intervention will include restitution strategies to retrain memory functions, including attention retraining and strategies to improve encoding and retrieval. Compensation strategies will be taught, including internal mnemonics (such as chunking, use of first letter cues, rhymes), use of external devices (such as diaries, mobile phones, calendars) and ways of coping with memory problems. The importance of 'errorless learning' (not making errors while learning new material, and therefore preventing learning the errors) will also be taught. The emphasis will be on identifying the most appropriate strategies to help individuals overcome their memory problems, and in providing participants with a range of memory techniques which they can adapt and use according to their needs. This intervention provides an opportunity for revision of strategies taught during in-patient rehabilitation and discussion of their application in a community setting.

Usual care
Participants will receive their usual clinical care. This may include the provision of information on memory, and in some centres, participants are offered a few sessions of cognitive rehabilitation. The majority of participants will no longer be receiving any formal rehabilitation. They may be attending self-help groups or Headway services (a UK charity to improve life after brain injury).

All other clinical services will be provided as usual for both groups. This may include referral to employment rehabilitation services, self-help groups or support from specialist charities, such as Headway. Any additional input, including psychological or medical interventions, which participants receive during the study will be noted from the service use questionnaire.

2.6. Randomisation procedures

After the identification of potentially eligible participants, there is an initial screening assessment with the AP to give further details about the study and to confirm eligibility. For those patients who are eligible and still wish to participate in the study, there is a second assessment approximately 2 weeks after the first assessment to set some short and long term goals and complete the remaining baseline data collection. After this, participants will wait until a group of four to six are able to attend for treatment at the same time and venue and so can be randomly allocated as a cluster. APs will remain in regular contact with participants in the period between the second assessment and waiting for randomisation.

Participants will be randomly allocated in groups to intervention or usual care in a 1:1 ratio. The randomisation will be based on a computer generated pseudo-random code using random permuted blocks of randomly varying size, created by the Nottingham Clinical Trials Unit (NCTU) in accordance with their standard operating procedure (SOP) and held on a secure server. The randomisation will be stratified by study site. Access to the sequence will be confined to the NCTU IT Manager. Investigators will access the allocation for each group by means of a remote, internet-based randomisation system developed and maintained by the NCTU. The

sequence of treatment allocations will be concealed from the study statistician until all interventions have all been assigned and recruitment, data collection, and all other study-related assessments are complete.

2.7. Sample size and justification

The sample size calculation is based on the primary outcome measure, EMQ patient version, at six months post-randomisation. The main aim of the study is to detect a minimum clinically relevant difference in mean EMQ-p score of 12 between the memory intervention group and the usual care group. A 12-point difference is deemed to be a clinically significant change based on pilot data and clinical interviews. A common standard deviation of 21.9 from pilot data gives an effect size of 0.55. A type I error of 0.05 and power of 90% were used for the calculation. A fixed effects model at the level of the 4 centres is assumed, with 10% of the total variation due to between-centre variation. The participants are cluster randomised into groups of 6 at the second level and a random effects model will be used with a small intracluster correlation coefficient assumed (ICC=0.1). This ICC is likely to be small because within each centre the therapist, intervention, and delivery location do not vary. Using the 'Optimal Design' software with these parameters, the calculation gives 10 groups per centre (5 groups for each allocation). Data from the previous pilot study and taking account that the control group only receives usual care suggests a possible dropout rate of 20%, so 26 groups of each intervention will be required or 312 participants in total. Based on our pilot study, we estimate we will need to screen 400 participants to recruit the required 312. At the start of the trial, clinicians at the four centres indicated that this was an achievable target in the timeframe proposed (25 months).

2.8. Blinding and breaking of blind

Blinding participants and the APs is not logistically possible in the study. However, the assessment for the objective measure of memory (RBMT-3) and goal attainment will be conducted by research assistants (RA) blind to group allocation. At each visit, the RA will be asked if they have been unblinded and also their guess at the allocated treatment (probably control, definitely control, probably intervention, definitely intervention) to assess the success of keeping the RAs blind to treatment allocation.

2.9. Trial committees

A number of committees will be assembled to ensure the proper management and conduct of the trial, and to uphold the safety and well-being of participants. Each committee will develop its own rules and procedures which may evolve with time.

Trial Management Group:
The Trial Management Group (TMG) will oversee the operational aspects of the trial. The TMG will meet regularly to review the progress of the trial and address any issues arising.

Trial Steering Committee:
The Trial Steering Committee (TSC) will oversee the conduct of the study and will have an independent Chair. A service user representative and a member from one of the military charities will also be invited to join this group. It will advise on recruitment strategies, monitor progress with recruitment, and check adherence to the study protocol. Observers from the NIHR HTA programme (the funder) will be invited to TSC meetings.

Data Monitoring Committee:
The Data Monitoring Committee (DMC) will be an independent group, the members of which have no other involvement with the study. Members of this committee will include rehabilitation professionals and an experienced statistician. The DMC will safeguard the interests of trial participants, with particular reference to safety and the efficacy of the intervention, monitor the overall progress and conduct of the trial and assist and advise the Investigators so as to protect the validity and credibility of the trial.

2.10. Outcome measures

2.10.1. Primary outcome

The primary outcome, assessed at 6 months after randomisation, will be the EMQ-p, a subjective measure of memory failures in daily life, with good ecological validity. This is participant reported and is included in the questionnaire pack sent out at 6 and 12 months.

The questionnaire consists of 28 items asking about the frequency of memory failures in everyday life over the past month with 5 possible responses ranging from "once a week or less/never" to "once or more a day", scored 0 to 4 respectively. A total score is calculated from these 28 items ranging from 0 to 112, with higher scores indicating more frequent memory problems.

For this study, participants are also asked about the importance of these 28 items from "not at all important" (coded as 0) to "very important" (coded as 4). These will not be used for the primary outcome.

2.10.2. Secondary outcomes

The secondary outcomes, assessed at 6 and 12 months, after randomisation are described below.

Individual goal attainment
Participants set at least one and up to five short and long term goals that they would like to achieve by the end of the study. These are evaluated by the RA on a four point Likert scale: not met at all, met a little, mostly met, fully met (scored 0 to 3).

The average score for the goals set will be used as the secondary outcome for the study. Some goals were considered as not applicable at the follow-up timepoints, these goals will not be used in the calculation of the average score.

Rivermead Behavioural Memory Test – Third Edition (objective measure of memory)
This is a standardised objective measure of memory and is assessed by the RA. The test assesses aspects of visual, verbal, recall, recognition, immediate and delayed everyday memory. The subtests are scored by the RA using the instructions provided in the manual provided by Pearson Education who hold the copyright for the test. These subtest scores are converted into scaled scores based on the participant's age. A General Memory Index (GMI) score is then derived based on the sum of the scores to the 14 subtests to give an indication of overall memory performance. The GMI will be used as the secondary outcome for the study. This GMI has been standardised to have a mean of 100 and a standard deviation of 15 on a demographically representative sample from the UK and ranges between 52 and 174. Scores less than 85 indicate some memory impairment and scores less than 70 indicate significant memory impairment. All calculations are done by the RA and entered directly onto the database with reference to the scoring manual.

Everyday Memory Questionnaire
The total score of the 28 importance items will be used as a secondary outcome. Scores will range from 0 to 112, with higher scores indicating more important memory problems.

The participant completed version at 12 months is considered a secondary outcome to determine whether any benefits of the intervention observed at 6 months are maintained over time.

The EMQ is also completed by a relative or a friend at 6 and 12 months (if a relative or friend has agreed to participate in the study) to provide an independent rating of the memory problems that the participant experiences in daily life.

Secondary outcomes for the EMQ will be:

- Participant completed importance of problems at 6 months
- Participant completed frequency of problems at 12 months
- Participant completed importance of problems at 12 months
- Relative/friend completed frequency of problems at 6 and 12 months
- Relative/friend completed importance of problems at 6 and 12 months

European Brain Injury Questionnaire (EBIQ) (cognitive, emotional, and social wellbeing)
This is a 66-item self-report and relative/friend-report measure of the subjective experience of cognitive, emotional and social difficulties experienced by people with brain injury and is included in the questionnaire pack sent out to participants and their relative/friend (where applicable) at 6 and 12 months. There are 63 items which ask about problems and difficulties in the last month with possible responses of "not a lot", "a little" and "a lot" and scored 1 to 3 respectively. There are also 3 items asking about the impact of the participant's brain injury on their relative/friend.

Seven subscale scores can be derived from the questionnaires: cognitive (12 items), impulsivity (10 items), somatic (7 items), depression (5 items), communication (4 items), difficulties in social interaction (5 items) and fatigue (8 items) (Bateman, Teasdale et al. 2009). The questionnaire items included in these subscales are listed in the appendix. The average score is calculated for each subscale (range 1 to 3) with higher scores indicating increased difficulties.

The contents of the group memory intervention may have most impact on the cognitive, depression, communication and difficulties in social interaction subscales so these 4 will be used in a formal comparison between groups for the EBIQ. The other subscales will be summarised only.

General Health Questionnaire (GHQ 30) (mood)
This is a 30-item questionnaire that is commonly used to assess mood by comparing the participant's current state from his/her usual mood state. This is included in the participant questionnaire pack sent out at 6 and 12 months. Likert scoring will be used (0-1-2-3) and the total score from the 30 items will be used as the secondary outcome. The total score ranges from 0 to 90 with higher scores indicating increased psychological distress.

Health-related quality of life
This will be assessed using the EQ-5D-5L: a validated, generalised health profile questionnaire used to determine health-related quality of life. The EQ-5D-5L consists of a descriptive system with 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) each with 5 response levels and a visual analogue scale which asks participants to rate their current health status on a scale of 0 (worst health can imagine) to 100 (best health can imagine). This is included in the participant questionnaire pack at 6 and 12 months. Health related quality of life will be analysed as part of the health economics analysis by the team at the Swansea Centre for Health Economics, University of Swansea.

2.11. Interim analysis

No formal interim analyses are planned.

3. GENERAL ANALYSIS CONSIDERATIONS

3.1. Analysis populations

The main approach for the analysis will be to analyse participants as randomised regardless of the number of memory rehabilitation sessions attended (intention to treat) for all primary and secondary outcomes.

The main analysis populations for:

- the outcomes on the 6 month questionnaires will be all participants who complete the questionnaires within 9 months of randomisation (i.e. within 275 nights of randomisation)
- the outcomes on the 12 month questionnaires will be all participants who complete the questionnaires within 15 months of randomisation (i.e. within 456 nights of randomisation)
- the outcomes assessed at the 6 month visit will be all participants where the assessment is completed within 9 months of randomisation (i.e. within 275 nights of randomisation)
- the outcomes assessed at the 12 month visits will be all participants where the assessment is completed within 15 months of randomisation (i.e. within 456 nights of randomisation)

Outcomes completed/assessed outside of these windows will not be used, other than in a sensitivity analysis for the primary outcome (see section 6.2.1).

To explore the effect of actual attendance at the group memory rehabilitation sessions, the complier average causal effect (CACE) will be estimated for the primary EMQ outcome at 6 months. This will give an estimate of the treatment effect among participants who would comply with allocated treatment, whichever group they were randomised to receive.

3.2. Derived variables

The date of the TBI will be collected at the initial screening assessment and then later confirmed using information from medical notes, where possible. The time since TBI (in months) will then be calculated as (date of randomisation minus date of TBI) where the date of the TBI is taken from the medical notes as the most accurate source or the date recorded at the initial screening assessment if the date cannot be collected from the medical notes. If the month and year is recorded but the date is unknown (e.g. entered as "NK") then the date will assumed to be the 15th of the month. The number of participants where the time since TBI is based on an estimated date will be shown.

3.3. Procedures for missing data

Missing items in questionnaires

Missing items in questionnaires will be imputed by the participant/relative or friend specific mean of the completed responses if less than 10% of the items in the questionnaire have not been completed. Scores will therefore be calculable where:

- 25 or more of the 28 items are completed on the EMQ
- 27 or more of the 30 items are completed on the GHQ
- 11 or more of the 12 items in the EBIQ cognitive subscale have been completed and 9 or more of the 10 items in the EBIQ impulsivity subscale have been completed. Scores for all other EBIQ subscales will only be calculable for participants completing all items in the subscale.

The participant/relative or friend specific mean of the completed response will be calculated to 1 decimal place.

Outcomes will be treated as missing if more than 10% of items are missed.

Missing baseline data
If scores from the questionnaires remain missing at baseline after the process outlined above or other baseline information is missing, data will be imputed for the analysis using the mean score at each centre in order to be able to include all participants in the regression analysis of the outcome score. These simple imputation methods are superior to more complicated imputation methods when baseline variables are included in an adjusted analysis to improve the precision of the treatment effect (White and Thompson 2005).

Missing outcome data
The primary analysis will be based on participants with available data for the EMQ-p at 6 months (see above) with no imputation for participants with missing outcomes.

A sensitivity analysis will be performed to check the robustness of the conclusions to missing outcome data. The pattern of missing outcome data will be explored, overall and in the two groups. Multiple imputation using chained equations will be used to impute missing outcomes under the assumption that outcomes are missing at random (dependent on observed data but not the unobserved outcomes). Further sensitivity analyses will be used to explore the robustness of the conclusions if outcomes are assumed to be missing not at random.

3.4. Study centre effects

Study centre is used as a stratification variable in the randomisation. To take this part of the design into account, study centre will be included as a fixed effect in the regression models for all analyses. If models do not converge, centre will be included as a random effect or removed from the analysis model.

3.5. Outliers

All continuous variables in this study have fixed upper and lower values as they are derived from questionnaire responses or performances on tests. If outlying values are identified, a sensitivity analysis will be conducted in order to assess the robustness of the results with and without the outlier included.

4. DESCRIPTION OF PARTICIPANT CHARACTERISTICS

4.1. Disposition

A flow of patients through the trial will be summarised in a CONSORT diagram that will include the eligibility, reasons for exclusion, numbers (participants and clusters) randomised to the two treatment groups, numbers receiving the allocated treatment, losses to follow up and the numbers analysed. The number of participants and clusters randomised to the two treatment groups at each site will also be tabulated.

4.2. Baseline characteristics

We will summarise the baseline characteristics of the two groups with respect to age, gender, ethnicity, residential status, education, current or previous military status, and time since TBI. Information collected from medical notes on the type of head injury, the severity of the head injury and other neurological conditions will be summarised where available. In addition, scores from the memory, mood and health related quality of life scales taken at the screening assessments will also be summarised.

Continuous data will be summarised in terms of the mean, standard deviation, median, lower & upper quartiles, minimum, maximum and number of observations. Categorical data will be summarised in terms of frequency counts and percentages. The proportion of participants with missing values will also be given for each variable.

The internal consistency of the EMQ and GHQ will be evaluated using Cronbach's alpha.

5. ASSESSMENT OF STUDY QUALITY

5.1. Data validation

The data management plan and validation plan details all programmed validation checks including missing values, out of range values, illogical values, invalid responses and cross form checks. Additional data checks will be conducted by the statistician when preparing the data for analysis in Stata.

5.2. Adherence

The intervention consists of 10 group memory rehabilitation sessions over a 10 week period. The AP records attendance at each session and records the reason if a participant does not attend (the options for reason for non-attendance are: did not want to continue treatment, withdrew, lost to follow-up, forgot, unwell, holiday, work commitments or other). Attendance at each session will be tabulated. The number of group rehabilitation sessions attended by each participant will be summarised using the median, interquartile range and range. The reason for non-attendance at sessions will be summarised in two ways: using frequencies, for example the total number of sessions missed due to participants being unwell, and also at a participant level to show whether participants often missed sessions due to the same types of reason. Full details of sessions missed due to other reasons will be listed.

Participants who miss sessions can have a half hour catch up session prior to the next session. The frequency of participants catching up on sessions will be tabulated.

To assess the fidelity of the intervention, some treatment sessions were video recorded. The analysis of the content of these sessions will be described in a separate video analysis plan.

5.3. Visit attendance and questionnaire return.

Follow-up is at 6 and 12 months using a combination of participant reported outcomes, included in a questionnaire booklet to be returned by post, and objective assessments at a follow-up appointment with a RA. The questionnaire booklet is sent out to participants approximately 3 weeks before the follow-up visit due date. If the questionnaire has not been returned by the visit date the RA asks the participant to complete the questionnaire during the visit (implemented from December 2014). If the visit cannot be conducted or the participant does not want to complete the questionnaire at the visit the RA continues to follow-up the participant to complete the questionnaire over the phone if possible.

The number of participants returning the questionnaire booklet at 6 and 12 months will be summarised in the two groups with the number of days between randomisation and completion of the questionnaire booklets. The number of participants returning the 6 month questionnaire (which includes the primary outcome) within 9 months of randomisation will also be shown.

Similarly the number of participants completing the follow-up assessment visits will be summarised and the number of days between randomisation and these follow-up appointments will be calculated and summarised in the two groups.

The numbers (with percentages) of participants not completing the questionnaire booklet/visit will be shown with the reason for non-completion (death, withdrawal of consent, lost to follow-up). A listing of participants who do not complete the study will give further details on the reason for non-completion (if available).

5.4. Protocol deviations

A protocol deviation is an unanticipated or unintentional divergence or departure from the expected conduct of a study inconsistent with the protocol, consent documents or other study procedures. Of particular importance are major deviations (violations) which may expose participants to increased risk; compromise the integrity of the entire trial or affect participant eligibility.

The number of participants with protocol deviations will be summarised by treatment group along with the type of deviation (inclusion/exclusion criteria deviation, trial procedure not performed per protocol, etc) and whether the deviation was before or after randomisation. Full details of the protocol deviations will also be listed.

5.5. Blinding status of RAs throughout the study

At each visit, information is collected before and after the assessment of the participant's goals on whether the RA has been unblinded and their guess at the participant's treatment allocation (probably/definitely control/intervention). This will be summarised in the two groups at each timepoint. The Kappa statistic will be used to assess the agreement between a participant's actual treatment allocation and the RA's guess at treatment allocation (collapsing probably and definitely into one category to give two groups only – intervention and control). Kappa statistics values above 0.4 maybe considered as indicating that there is a moderate agreement between the actual treatment allocation and the RA's belief about the treatment allocation and so that there was a degree of unblinding during the study.

5.6. Questionnaire completion

The completion of each of the questionnaires (Everyday Memory Questionnaire, General Health Questionnaire, EQ-5D, European Brain Injury Questionnaire) included in the questionnaire booklet will be summarised at 6 and 12 months.

6. ANALYSIS OF EFFICACY

Analyses will be performed using Stata version 13 or above. All tests will be two-tailed with point estimates and 95% confidence intervals for the treatment effect presented. Participants will be analysed as randomised, regardless of adherence with allocation (ITT). No formal adjustment for multiple significance testing will be applied: secondary outcomes will be considered supportive to the primary analysis.

6.1. Primary analysis

The primary analysis will estimate the difference in mean score of the patient version of the Everyday Memory Questionnaire score at 6 months between the two groups, which will be presented with a 95% confidence interval and p-value, using all data returned by 9 months post randomisation. This will be estimated using a multi-level linear model with baseline EMQ score and centre as covariates. Although participants were randomly allocated in 'clusters', individuals in the usual care arm had no contact with each other and outcomes in this arm are therefore assumed to be independent. However participants in the intervention arm receive group therapy sessions together which must be taken into account in the analysis. Roberts and Roberts (2005) suggest using a fully heteroscedastic model for analysis of trials comparing group-based treatments with individual-based treatment as usual, when, as is the case here, there is adjustment for individual level covariates. This model estimates group-level residual variance in the intervention arm, and also permits

individual-level residual variance to differ between intervention and control arms. (Roberts and Roberts 2005, Bauer, Sterba et al. 2008).

The assumptions for the multi-level linear model will be checked. If there is strong evidence that they are violated an appropriate transformation will be used.

6.2 Sensitivity analysis

6.2.1 Sensitivity analysis including all questionnaires returned

The analysis will be repeated using all participants returning the 6 month questionnaire, including participants where these questionnaires were returned after the 9 months post-randomisation window.

6.2.2 Sensitivity analysis with adjustment for other baseline covariates

Baseline variables will be examined for imbalances between the two groups. Any characteristics where an imbalance is observed (based on comparison of summary statistics only, not statistical testing) will additionally be included as covariates in the multi-level model for the EMQ score at 6 months. The difference in means between the groups adjusted for these variables will be presented with a 95% confidence interval.

6.2.3 Sensitivity analysis for missing primary outcome data

The main analysis of the primary outcome will be using the available data with no imputation. Multiple imputation using chained equations will be used as a sensitivity analysis to include participants with missing data EMQ score at 6 months in order to explore their potential impact on the estimate of the treatment effect compared to the complete cases.

Variables used in the imputation model will be age and gender, baseline variables identified as predictive of drop-out (by examination only), prognostic baseline variables (EMQ, RBMT and GHQ), RBMT score assessed at the 6 and 12 month visit and EMQ score at 12 months. Imputations will be done using chained equations and separately for each allocated group if possible. The number of datasets imputed will be based on the proportion of participants with a missing outcome and will be at least 5. The results of the analyses on the imputed datasets will be combined using Rubin rules for multiply imputed data. This analysis will assume that unobserved outcomes are missing at random and depend on observed characteristics but not the unobserved outcomes. Methods of multiply imputing missing data that also take account of clustering in the intervention arm will be investigated.

The assumption that data are missing at random cannot be tested. Therefore further sensitivity analyses will also explore the robustness of the conclusion if missing data are missing not at random This will be done by assuming that participants with missing EMQ scores at 6 months have systematically different outcomes by subtracting or adding 3, 6, 9 and 12 points for these participants to the EMQ value imputed under the missing at random assumption. The analysis will be repeated to explore if the findings from this sensitivity analysis are similar to the main analysis and to inform how different the missing scores would need to be to alter conclusions from the main analysis.

6.2.4 Sensitivity analysis for adherence with allocation

To explore the effect of actual attendance at the group memory rehabilitation sessions, the complier average causal effect (CACE) will be estimated for the primary EMQ outcome at 6 months. This will give an estimate of

the treatment effect among participants who would comply with allocated treatment, whichever group they were randomised to receive.

Participants in the intervention group will be classified as adherent if they attend at least 4 memory rehabilitation sessions. It will be assumed that participants in the usual care group did not have any group memory rehabilitation for this analysis. . Our sensitivity analyses will investigate the use of principle stratification, simple instrumental variable regression, and more extended models to account for clustering in the intervention arm, baseline covariates, and missing data.

6.2.5 Subgroup analysis

An exploratory subgroup analysis for the primary outcome according to memory deficit at baseline (using the RBMT general memory index score, an objective measure of memory) will be performed by including an interaction term in the model for the primary analysis specified in 6.1.

The RBMT GMI at baseline will be split into three groups (based on classifications on the RBMT website): significant memory impairment (GMI ≤ 69), borderline/moderate memory impairment (70 to 84) and average range (GMI ≥ 85).

6.3. Secondary analyses

Secondary outcomes at 6 months

Where possible, the secondary outcomes listed above will be analysed using the same techniques as for the primary outcome (numbers of goals set will also be used a covariate in the model for goal attainment score) using appropriate regression models. The assumptions for the multi-level linear model will be checked. If there is strong evidence that they are violated an appropriate transformation will be used.

Analyses of outcomes at 12 months
The analyses for all the outcomes will be repeated with the 12 month follow-up data using the same techniques as specified above. The 6 month time point is however the primary time point of interest with the 12 month timepoint considered as exploratory to assess if any differences between treatments are maintained over time.

Sensitivity analyses for the secondary outcomes

Participants must set at least one short and long term goal but can set up to 5. An interaction term between the number of goals set (1 or more than 1) and treatment group will be included in the model for the goal attainment score to explore whether there is evidence of any differential effect of the intervention according to the number of goals set at baseline. It might be hypothesised that it may be harder for participants who set more than one goal to meet all their goals compared to the participants who set (and so focus) on one individual goal.

Goals set at the start of the trial should have had a measurable target to be assessed against at the 6 and 12 month follow-up visits. During the trial it became apparent that not all goals set by the assistant psychologist at baseline had such a measurable target. Each goal will therefore be classified as SMART (specific, measurable, assignable, realistic and time related) or not by one of the study APs and a sample will be checked by the chief investigator. The analysis for goal achievement will then be repeated including only SMART goals.

6.4. Exploratory analyses

A Rasch analysis of the Everyday Memory Questionnaire has been performed using an independent dataset. The EMQ scoring from this Rasch analysis will be used in an exploratory analysis comparing the primary outcome between the two groups using the methods specified in Section 6.1.

Further exploratory analysis will be conducted to explore:

- The relationship between the frequency and importance outcomes on the EMQ
- The relationship between participant and relative/friend reported measures of memory (EMQ) and objectives measures based on assessment (RBMT) as well as between measures of memory and mood (GHQ)

using correlation coefficients.

6.5. Other analyses

The health economic evaluation specified in the protocol will be conducted by Professor Deborah Fitzsimmons at the University of Swansea. Further details can be found in a separate Health Economics Analysis Plan.

7. ANALYSIS OF SAFETY

No adverse events or serious adverse events are recorded or reported for this trial as the risks of adverse events due to taking part in this trial were assessed as negligible.

Deaths during the study will be tabulated by group with the primary reason for death.

Incidents occurring during the group sessions that were recorded by the APs will be presented and classified according to type of incident (e.g. mood related, behaviour related, interpersonal). The chief investigators will agree on the classification of each incident.

8. FINAL REPORT TABLES AND FIGURES

The following rules may be adopted when creating the summary tables:

Number of decimal places (DP):

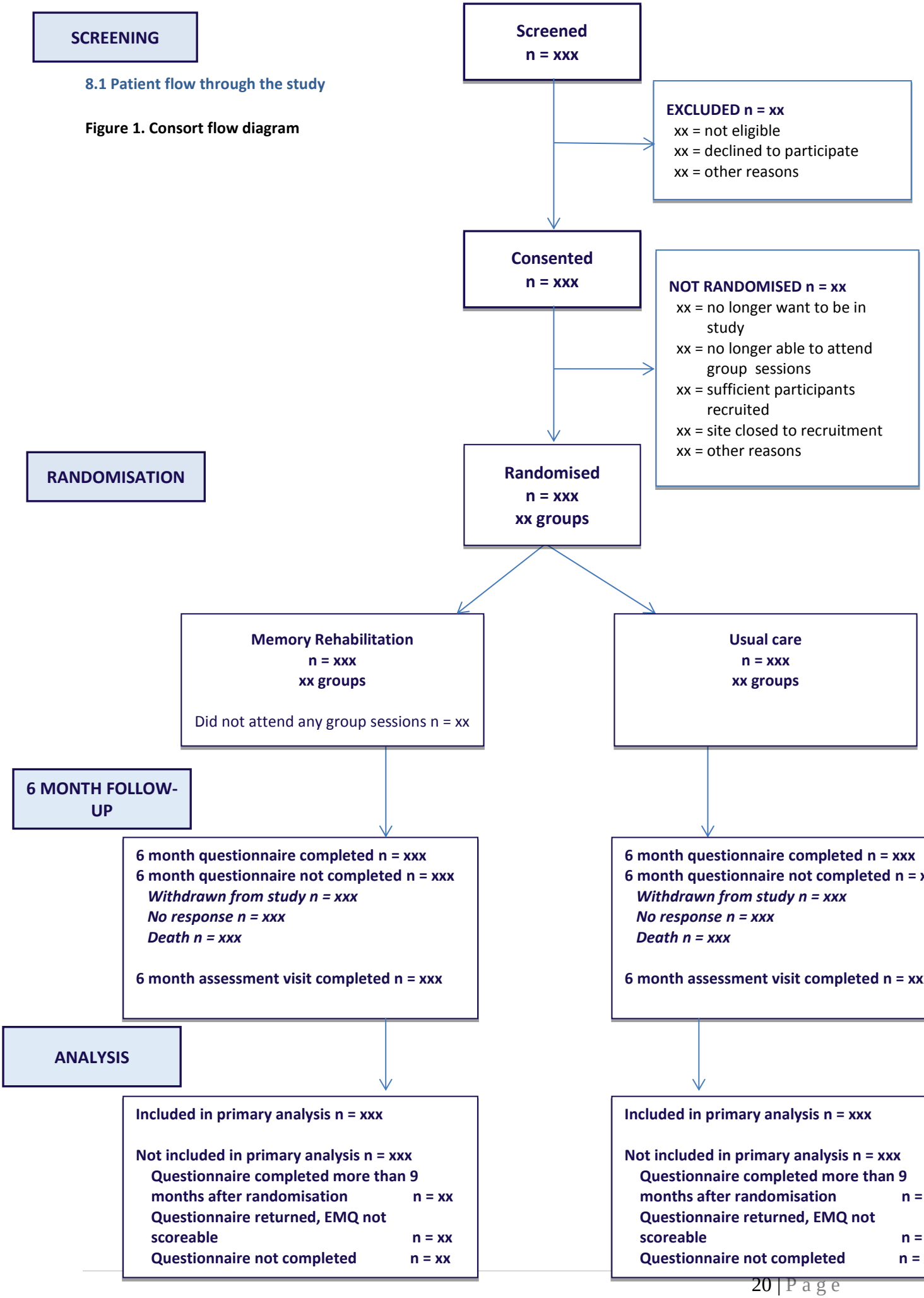
- For minimum and maximum the number of DPs will be the same as the raw data
- For mean, median and SD the number of DPs will be one more than the raw data
- Percentages will be rounded to the nearest whole number

Data Presentation:

- Treatment group will be in columns with the visits in rows
- Column headers in mixed case, with "(N=nn)" below treatments to denote the denominator
- Categories (ie in column 1) in sentence case, in the order on the CRF
- Ordering of statistics n, Mean, SD, Median, IQR, Minimum and Maximum

8.1 Patient flow through the study

Figure 1. Consort flow diagram



8.2. Participant characteristics

Table 1. Baseline Characteristics

	Memory Rehabilitation (n =)	Usual care (n =)	Total (n =)
Age (years)			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
Gender – n (%)			
Men			
Women			
Ethnicity – n (%)			
White			
Indian			
Etc…..			
Residential status – n (%)			
Lives alone			
Lives with others			
Living with informal care			
Living with formal care			
Living in care home			
Highest educational attainment – n (%)			
Below GCSE			
GCSE			
A-Level			
Degree			
Higher Degree			
Current military service – n (%)			
Military			
TA/reservist			
Non-military			
Previous military service – n (%)			
Military			
TA/reservist			
Non-military			
TBI in service if previously or currently in military service			
Time since TBI (months)[1]			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
Length of initial hospital stay for TBI (days)[2]			

	Memory Rehabilitation (n =)	Usual care (n =)	Total (n =)
Mean [sd]			
Median [25th, 75th centile]			
Min, max			

1 – Based on estimated date of TBI for XX participants in memory rehabilitation group and XX participants in usual care group. From clinical notes for all other participants.
2 – estimated for xx participants in the memory rehabilitation group and xx participants in the usual care group

Table 2. **Information on the head injury and other neurological conditions from clinical notes**

	Memory Rehabilitation (n =)	Usual care (n =)	Total (n =)
Clinical notes available			
Clinical notes not available			
Type of head injury			
Open			
Closed			
Unknown			
Severity of the head injury (Glasgow Coma Scale[1])			
Closest to admission			
Median [25th, 75th centile]			
Unknown			
Worst total score			
Median [25th, 75th centile]			
Unknown			
Other neurological conditions			
None			
Stroke			
Subarachnoid Haemorrhage			
Epilepsy			
Multiple Sclerosis			
Parkinson's			
Other			
Unknown			

1 – Glasgow Coma Scale scores range from 3 to 15 with lower scores indicating more severe brain injury

Table 3. Memory ability, mood and quality of life assessments prior to randomisation

	Memory Rehabilitation (n =)	Usual care (n =)	Total (n =)
Assessed at screening assessment			
Everyday Memory Questionnaire[1] – participant – frequency of problems			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
n			
Everyday Memory Questionnaire[1] – participant – importance of problems			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
n			
Rivermead Behavioural Memory test – version 3 (GMI[2])			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
n			
Level of memory impairment based on RBMT			
significant memory impairment			
borderline/moderate memory impairment			
score within average range or above average			
General Health Questionnaire 30[3]			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
n			
Estimated premorbid IQ (NART)			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
n			
Sheffield screening test total score[4]			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			

	Memory Rehabilitation (n =)	Usual care (n =)	Total (n =)
n			
Assessed at the second assessment			
Number of short term goals set[5]			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
Number of long term goals set[5]			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
Number of SMART short term goals set[5]			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
Number of SMART long term goals set[5]			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
EQ-5D health status VAS score[6]			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
n			
Relative/friend agreed to participate in trial – n (%)			
Everyday Memory Questionnaire[1] – relative/friend – frequency of problems			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
n			
Everyday Memory Questionnaire[1] – relative/friend – importance of problems			
Mean [sd]			
Median [25th, 75th centile]			
Min, max			
n			

	Memory Rehabilitation (n =)	Usual care (n =)	Total (n =)

1 - Everyday Memory Questionnaire scores range from 28 to 140 with higher scores indicating more frequent/important memory problems.
2 - The General Memory Index from the Rivermead Behavioural Memory Test ranges between 52 and 174 and has been standardised to have a mean of 100 and an SD of 15 on a demographically representative sample from the UK.
3 - General Health Questionnaire 30 score ranges from 0 to 90 (Likert scoring) with higher scores indicating increased psychological distress.
4 – A total SST score of 17 or more was required to participate in the trial. Maximum score 20.
5 - Participants should have at least one and can set up to five short and long term goals.
6 - EQ-5D health status scores are collected on a VAS scale from 0 to 100 where 0 is worst health state the participant can imagine and 100 is the best health state the participant can imagine.

8.3. Study quality summaries

Table 4. Cluster and participant randomisation by group and site

	Memory Rehabilitation (n =)	Usual care (n =)
Clusters randomised		
Nottingham		
Birmingham		
Chester		
Epsom		
Liverpool		
Sheffield		
St. Georges		
North Bristol		
South Tees		
Participants randomised		
Nottingham		
Birmingham		
Chester		
Epsom		
Liverpool		
Sheffield		
St. Georges		
North Bristol		
South Tees		
Days between baseline visit and randomisation		
Median [25th, 75th centile]		
Min, Max		
Size of group randomised		
Mean [sd]		
4		
5		
6		

Table 5. Information on number of groups delivered by assistant psychologists by site

	Number of assistant psychologists delivering group memory rehabilitation during trial	Number of groups run by first AP	Number of groups run by second AP	Number of groups run by third AP
Nottingham				
Birmingham				
Chester				
Epsom				
Liverpool				
Sheffield				
St. Georges				
North Bristol				
South Tees				

Table 6. Adherence – attendance at group memory rehabilitation sessions

(a) according to session

	Attendance at session – n(%)	Duration of session Mean [sd]
Session 1		
Session 2		
Session 3		
Session 4		
Session 5		
Session 6		
Session 7		
Session 8		
Session 9		
Session 10		

Group size at each session will also be presented e.g. 0, 1, 2, 3, 4, 5, 6.

(b) summary

Number of sessions attended	
Median [25th, 75th centile]	
n	
0 to 2	
3 to 7	
8 to 10	
Total number of sessions missed	
Reason sessions missed	
Did not want to continue	
Withdrew from study	
Lost to follow-up (unable to contact)	
Forgot to attend	
Unwell	
Holiday	
Work commitments	
Other[1]	
Reasons sessions missed- participant level median [min, max]	
Did not want to continue	
Withdrew from study	
Lost to follow-up (unable to contact)	
Forgot to attend	
Unwell	
Holiday	
Work commitments	
Other[1]	

1 – Other reasons given for participants missing group rehabilitation sessions are:

Attendance at catch up sessions will also be tabulated here.

Table 7. Visit and questionnaire booklet completion

(i) At 6 months

	Memory Rehabilitation (n =)	Usual care (n =)
6 month follow-up		
Face to face visit		
Attended		
Not done		
Death		
Withdrawal of consent		
Lost to follow-up		
Days to 6 month assessment visit from randomisation		
Median [25th, 75th centile]		
Min, Max		
Visit completed within 9 months of randomisation		
Participant questionnaire booklet		
Returned		
Not done		
Death		
Withdrawal of consent		
Lost to follow-up		
Not returned		
Days to completion from randomisation		
Median [25th, 75th centile]		
Min, Max		
Questionnaire completed within 9 months of randomisation		
Relative/friend questionnaire booklet		
Returned		
Not done		
Participant death		
Participant withdrew of consent		
Participant lost to follow-up		
Not returned		
Relative/friend did not agree to participate in the trial		

(ii) At 12 months

Repeat table 7(i) above for the 12 month follow-up timepoint

(iii) Cross tabulation of questionnaire completion and visit completion

Table 8. Listing of reasons for non-completion of the study

Participant number	Group	Rando-misation date	Date of discontinuation	Primary reason for discontinuation	Further details on discontinuation	EMQ completed at 6 months

Table 9. Questionnaire completion at baseline

	Memory Rehabilitation (n =)	Usual care (n =)
Primary outcome		
Everyday Memory Questionnaire – Participant – frequency		
Fully completed		
Partially completed & scoreable		
Partially completed & not scoreable		
Not completed		
Questionnaire booklet not returned		
Secondary outcomes		
Everyday Memory Questionnaire – Participant – importance		
Fully completed		
Partially completed & scoreable		
Partially completed & not scoreable		
Not completed		
Questionnaire booklet not returned		
General Health Questionnaire 30		
Fully completed		
Partially completed & scoreable		
Partially completed & not scoreable		
Not completed		
Questionnaire booklet not returned		
EQ-5D 5L		
Fully completed		
Partially completed		
Not completed		
Questionnaire booklet not returned		
Participant European Brain Injury Questionnaire		
Fully completed		
Partially completed		
Not completed		
Questionnaire booklet not returned		
Everyday Memory Questionnaire – Relative/friend – frequency		
Fully completed		
Partially completed & scoreable		
Partially completed & not scoreable		
Not completed		
Questionnaire booklet not returned		
Relative/friend did not agree to participate in trial		
Everyday Memory Questionnaire – Relative/friend – importance		
Fully completed		
Partially completed & scoreable		

	Memory Rehabilitation (n =)	Usual care (n =)
Partially completed & not scoreable		
Not completed		
Questionnaire booklet not returned		
Relative/friend did not agree to participate in trial		

Questionnaires are considered scoreable if 90% or more of items were completed

Table 10. Questionnaire completion at 6 months

Repeat Table 9 for outcomes at 6 months and add The European Brain Injury questionnaire to the table as below.

	Memory Rehabilitation (n =)	Usual care (n =)
Secondary outcomes		
European Brain Injury Questionnaire – participant		
Fully completed		
Partially completed & all subscales scoreable		
Partially completed & some subscales not scoreable		
Not completed		
Questionnaire booklet not returned		
European Brain Injury Questionnaire – relative		
Fully completed		
Partially completed & all subscales scoreable		
Partially completed & some subscales not scoreable		
Not completed		
Questionnaire booklet not returned		
Relative did not agree to participate in trial		

Table 11. Questionnaire completion at 12 months

Repeat table 10 for outcomes at 12 months

Table 12. Summary of protocol deviations

	Memory Rehabilitation (n =)	Usual care (n =)
Before randomisation		
Inclusion / Exclusion Criteria Deviation		
Trial procedure not performed per protocol		
Visit not performed within window		
Informed Consent Deviation		
Participant Non-Compliance		
Treatment Randomisation Error		
Other		
After randomisation		
Inclusion / Exclusion Criteria Deviation		
Trial procedure not performed per protocol		
Visit not performed within window		
Informed Consent Deviation		
Participant Non-Compliance		
Treatment Randomisation Error		
Other		

Note participants can have multiple protocol deviations

Table 13. List of protocol deviations

(a) Before randomisation

Site ID	Participant number	Group	Rando-misation date	Date of deviation	Deviation	Further details on deviation

(b) After randomisation

Repeat listing above

Table 14. Blinding status of Research Assistants throughout the trial

	Memory Rehabilitation (n =)	Usual care (n =)	Kappa statistic
6 month assessment			
Unblinded prior to the visit			
Unblinded during the visit			
Opinion of treatment allocation prior to goal assessment			0.xx
Definitely control			
Probably control			
Probably intervention			
Definitely intervention			
Opinion of treatment allocation after goal assessment			0.xx
Definitely control			
Probably control			
Probably intervention			
Definitely intervention			
12 month assessment			
Unblinded prior to the visit			
Unblinded during the visit			
Opinion of treatment allocation prior to the goal assessment			0.xx
Definitely control			
Probably control			
Probably intervention			
Definitely intervention			
Opinion of treatment allocation after the goal assessment			0.xx
Definitely control			
Probably control			
Probably intervention			
Definitely intervention			

Table 15. Baseline Characteristics by EMQ completion at 6 months and allocated group

Repeat **Table 1** also split by EMQ completed at 6 months (yes/no)

Table 16. Memory ability, mood and quality of life assessments prior to randomisation by EMQ completion at 6 months and allocated group

Repeat **Table 3** also split by EMQ completed at 6 months (yes/no)

8.4. Primary outcome

Table 17. Participant Everyday Memory Questionnaire at 6 months

	Baseline Mean [sd]	6 months Mean [sd]	Difference in means (95% CI)	p-value
Usual care (n =)	xx [xx]	xx [xx]		
Memory Rehabilitation (n =)	xx [xx]	xx [xx]	xx (xx, xx)	0.xx

Everyday Memory Questionnaire scores range from 28 to 140 with higher scores indicating more frequent memory problems (questionnaire booklets). Difference in means estimated using a multi-level linear model with a random effect for cluster in the intervention arm, allowing the participant level variance to vary between arms and baseline Everyday Memory Questionnaire score and centre included as covariates. The mean group size at follow-up was x.x in the intervention group and x.x in the control group. The estimated intracluster correlation coefficient for the participant EMQ is 0.xx in the intervention group.

8.5. Sensitivity Analysis for the primary outcome at 6 months

Table 18. Sensitivity analysis for Participant Everyday Memory Questionnaire at 6 months

	Baseline Mean [sd]	6 months Mean [sd]	Difference in means (95% CI)	p-value
Usual care (n =)	xx [xx]	xx [xx]		
Memory Rehabilitation (n =)	xx [xx]	xx [xx]	xx (xx, xx)	0.xx
		Additional adjustment for variables with baseline imbalance[1]		
			xx (xx, xx)	0.xx
Including participants completing the 6 month questionnaire booklet more than 9 months after randomisation				
Usual care (n =)	xx [xx]	xx [xx]		
Memory Rehabilitation (n =)	xx [xx]	xx [xx]	xx (xx, xx)	0.xx

1 – variable …. and variable …. also included as fixed effects in the model

Table 19. Sensitivity analysis for Participant Everyday Memory Questionnaire at 6 months using multiple imputation

Difference in means	Assuming missing outcomes missing at random	3 points	6 points	9 points	12 points
	xx (xx, xx)				
Assuming missing outcomes worse in intervention group		xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Assuming missing outcomes worse in usual care group		xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

Details of multiple imputation model will be included here.

Table 20. Estimated effect of group therapy sessions for memory rehabilitation if received as intended on the Participant Everyday Memory Questionnaire at 6 months

		Memory Rehabilitation (n =)	Usual care (n =)	
Attended at least 4 group therapy sessions				
	Yes			
	No			
Mean EMQ score [sd] at 6 months				
				Effect in adherers[1]
Where 4 or more group therapy sessions attended				xx (95% CI xx to xx, p =)
Where less than 4 group therapy sessions attended				

1 – attendance at 4 or more of the 10 group therapy sessions considered necessary for noticeable effect of sessions

Table 21. Subgroup analysis for participant Everyday Memory Questionnaire at 6 months according to memory impairment at baseline

	Baseline Mean [sd]	6 months Mean [sd]	Difference in means (95% CI)	Interaction effect (95% CI)
RBMT GMI score ≥ 85 (average range)				
Usual care (n =)	xx [xx]	xx [xx]		
Memory Rehabilitation (n =)	xx [xx]	xx [xx]	xx (xx, xx)	
RBMT GMI score 70 to 84 (borderline/moderate memory impairment)				xx (xx to xx)
Usual care (n =)	xx [xx]	xx [xx]		
Memory Rehabilitation (n =)	xx [xx]	xx [xx]	xx (xx, xx)	
RBMT GMI score ≤ 69 (significant memory impairment)				xx (xx to xx)
Usual care (n =)	xx [xx]	xx [xx]		
Memory Rehabilitation (n =)	xx [xx]	xx [xx]	xx (xx, xx)	

p-value for interaction effect: 0.xx

8.6. Secondary outcomes at 6 months

Table 22. Secondary outcomes at 6 months

(a) Assessed on participant questionnaire

	Baseline Mean [sd]	6 months Mean [sd]	Difference in means (95% CI)
Everyday Memory Questionnaire[1] – participant – importance of problems			
Usual care (n =)			
Memory Rehabilitation (n =)			
General Health Questionnaire 30[2]			
Usual care (n =)			
Memory Rehabilitation (n =)			

1 - Everyday Memory Questionnaire scores range from 28 to 140 with higher scores indicating more frequent/important memory problems (questionnaire booklets).
2 - General Health Questionnaire 30 score ranges from 0 to 90 (Likert scoring) with higher scores indicating increased psychological distress (questionnaire booklets).

(b) Assessed at visit

	Baseline Mean [sd]	6 months Mean [sd]	Difference in means (95% CI)
Rivermead Behavioural Memory test 3 (GMI[1])			
Usual care (n =)			
Memory Rehabilitation (n =)			
Short term goal achievement average score[2]			
Usual care (n =)			
Memory Rehabilitation (n =)			
Long term goal achievement average score[2]			
Usual care (n =)			
Memory Rehabilitation (n =)			

1 - The General Memory Index from the Rivermead Behavioural Memory Test ranges between 52 and 174 and has been standardised to have a mean of 100 and an SD of 15 on a demographically representative sample from the UK (RA assessment).
2 - Participants set at least one and can set up to five short and long term goals. At follow-up, each of these goals is assessed by the RA on a 4 point Likert scale of not met (0), met a little (1), mostly met (2) and fully met (3). The average achievement score across the goals set is calculated for each participant.

(c) Assessed on relative/friend questionnaire

	Baseline Mean [sd]	6 months Mean [sd]	Difference in means (95% CI)
Everyday Memory Questionnaire[1] – relative/friend – frequency of problems			
Usual care (n =)			
Memory Rehabilitation (n =)			
Everyday Memory Questionnaire[1] – relative/friend – importance of problems			
Usual care (n =)			
Memory Rehabilitation (n =)			

1 - Everyday Memory Questionnaire scores range from 28 to 140 with higher scores indicating more frequent/important memory problems (questionnaire booklets).

(d) European Brain Injury Questionnaire – participant completed

	Baseline Mean [sd]	6 months Mean [sd]	Difference in means (95% CI)
Cognitive subscale			
Usual care (n =)			
Memory Rehabilitation (n =)			xx (xx to xx)
Depression subscale			
Usual care (n =)			
Memory Rehabilitation (n =)			xx (xx to xx)
Communication subscale			
Usual care (n =)			
Memory Rehabilitation (n =)			xx (xx to xx)
Difficulties in social interaction subscale			
Usual care (n =)			
Memory Rehabilitation (n =)			xx (xx to xx)
Impulsivity subscale			
Usual care (n =)			
Memory Rehabilitation (n =)			
Somatic subscale			
Usual care (n =)			
Memory Rehabilitation (n =)			
Fatigue subscale			
Usual care (n =)			
Memory Rehabilitation (n =)			

Scores range between 1 and 3 with higher scores indicating increased difficulties.

(e) European Brain Injury Questionnaire – relative/friend completed

Repeat (d)

8.7. 12 month outcomes

Table 23. Outcomes at 12 months

Repeat Table 22 for outcomes at 12 months, also including results for the participant Everyday Memory Questionnaire – frequency of problems in (a)

8.8. Sensitivity analysis for secondary outcomes

Table 24. Sensitivity analysis for goal attainment at 6 months

	Memory Rehabilitation (n =)	Usual care (n =)	Interaction effect (95% CI)[1]
Short term goal achievement average score			
1 goal set at baseline			
Mean [sd]			
n			
			xx (95% CI xx to xx)
More than 1 goal set at baseline			
Mean [sd]			
n			
Long term goal achievement average score			
1 goal set at baseline			
Mean [sd]			
n			
			xx (95% CI xx to xx)
More than 1 goal set at baseline			
Mean [sd]			
n			

1 – The interaction effect shows the difference in the effect of intervention for the participants setting more than 1 goal at baseline compared to the participants setting only one goal at baseline.

Table 25. Sensitivity analysis for goal attainment at 12 months

	Memory Rehabilitation (n =)	Usual care (n =)	Interaction effect (95% CI)[1]
Short term goal achievement average score			
1 goal set at baseline			
Mean [sd]			
n			
			xx (95% CI xx to xx)
More than 1 goal set at baseline			
Mean [sd]			
n			
Long term goal achievement average score			
1 goal set at baseline			
Mean [sd]			
n			
			xx (95% CI xx to xx)
More than 1 goal set at baseline			
Mean [sd]			
n			

1 – The interaction effect shows the difference in the effect of intervention for the participants setting more than 1 goal at baseline compared to the participants setting only one goal at baseline.

Table 26. Sensitivity analysis for goal attainment including SMART goals only

(a) 6 months

	Baseline Mean [sd]	6 months Mean [sd]	Difference in means (95% CI)
Short term goal achievement average score			
Usual care (n =)			
Memory Rehabilitation (n =)			
Long term goal achievement average score			
Usual care (n =)			
Memory Rehabilitation (n =)			

Participants set at least one and can set up to five short and long term goals. At follow-up, each of these goals is assessed by the RA on a 4 point Likert scale of not met (0), met a little (1), mostly met (2) and fully met (3). The average achievement score across the goals set is calculated for each participant.

(b) 12 months

	Baseline Mean [sd]	12 months Mean [sd]	Difference in means (95% CI)
Short term goal achievement average score			
Usual care (n =)			
Memory Rehabilitation (n =)			
Long term goal achievement average score			
Usual care (n =)			
Memory Rehabilitation (n =)			

Participants set at least one and can set up to five short and long term goals. At follow-up, each of these goals is assessed by the RA on a 4 point Likert scale of not met (0), met a little (1), mostly met (2) and fully met (3). The average achievement score across the goals set is calculated for each participant.

8.9. Exploratory analyses

Table 27. Participant Everyday Memory Questionnaire at 6 months using Rasch scoring

	Baseline Mean [sd]	6 months Mean [sd]	Difference in means (95% CI)	p-value
Usual care (n =)	xx [xx]	xx [xx]		
Memory Rehabilitation (n =)	xx [xx]	xx [xx]	xx (xx, xx)	0.xx

Rasch scoring of Everyday Memory Questionnaire … *(details of the Rasch scoring system will be added here)*

Table 28. Correlation between memory assessments and mood

a) Baseline

	EMQ – frequency participant	**EMQ – frequency – relative/friend**	**RBMT - GMI**	**GHQ-30**
EMQ – frequency participant	0.xx (n = xx)	0.xx (n = xx)	0.xx (n = xx)	0.xx (n = xx)
EMQ – frequency – relative/friend	0.xx (n = xx)	0.xx (n = xx)	0.xx (n = xx)	0.xx (n = xx)
RBMT - GMI	0.xx (n = xx)	0.xx (n = xx)	0.xx (n = xx)	0.xx (n = xx)
GHQ-30	0.xx (n = xx)	0.xx (n = xx)	0.xx (n = xx)	0.xx (n = xx)

b) 6 months – intervention group

c) 6 months – usual care group

d) 12 months – intervention group

e) 12 months usual care group

8.10. Safety results

Table 29. Deaths during the trial

	Memory Rehabilitation (n =)	Usual care (n =)
Death during trial – n (%)		
Primary reason for death		
…..		
……..		

Primary reason for death based on MedDra preferred term.

Table 30. Incidents during group sessions

This information will come from logs kept by the assistant psychologists during the group sessions.

8.11 Table appendices

Table 31. Internal consistency of EMQ and GHQ assessed at the screening assessment

	n	Number of items	Cronbach's alpha
Everyday Memory Questionnaire – participant – frequency of problems			
Everyday Memory Questionnaire – participant – importance of problems			
Everyday Memory Questionnaire – relative/friend – frequency of problems			
Everyday Memory Questionnaire – relative/friend – importance of problems			
General Health Questionnaire 30			

Table 32. Intracluster correlation coefficient for secondary outcomes in memory rehabilitation group

	6 months	12 months
EMQ– participant – frequency of problems		
EMQ– participant – importance of problems		
GHQ 30		
RBMT-3 (GMI)		
Short term goal achievement average score		
Long term goal achievement average score		
EBIQ – participant - cognitive		
EBIQ – participant - impulsivity		
EBIQ – participant - somatic		
EBIQ – participant - depression		
EBIQ – participant - communication		
EBIQ – participant - difficulties in social interactions		
EBIQ – participant - fatigue		
EMQ– relative/friend – frequency of problems		
EMQ– relative/friend – importance of problems		
EBIQ – relative/friend - cognitive		
EBIQ – relative/friend - impulsivity		
EBIQ – relative/friend - somatic		
EBIQ – relative/friend - depression		
EBIQ – relative/friend - communication		
EBIQ – relative/friend - difficulties in social interactions		
EBIQ – relative/friend - fatigue		

ICC calculated using multi-level linear model *(add further details)*

9. APPENDICES

9.1. Derivation of EBIQ subscales scores

Using subscales in Table 2 in (Bateman, Teasdale et al. 2009)

Subscale	Number of items	Items number from questionnaire
Cognitive	12	2, 4, 8, 11, 15, 21, 22, 23, 36, 46, 54, 59
Impulsivity	10	3, 10, 13, 14, 19, 24, 37, 44, 57, 62
Somatic	7	1, 7, 16, 32, 45, 50, 51
Depression	5	9, 12, 30, 31, 53
Communication	4	5, 35, 55, 60
Difficulties in social interactions	5	3, 14, 19, 51, 57
Fatigue	8	2, 7, 15, 26, 29, 32, 45, 55

10. REFERENCES

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