Statistical and Health Economic Analysis Plan (SHEAP)

Full/ Long title of the Trial: Care Coordinator Delivered Method of Levels Therapy to Improve Engagement and other Outcomes in Early Psychosis (CAMEO): Feasibility Cluster Randomised Controlled Trial

Short Study title/ Acronym: CAMEO

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ABBREVIATIONS

CC	Care Coordinator
SU	Service User
EIP-T	Early Intervention in Psychosis Team

GLOSSARY

C-RCT	Cluster Randomised Controlled Trial
EIP	Early Intervention in Psychosis
GMMH	Greater Manchester Mental Health NHS Foundation Trust
MBI-HSS	Maslach Burnout Inventory: Human Services Survey
MOL	Method of Levels
QPR	Questionnaire about the Process of Recovery
RoC	Reorganisation of Conflict Scale
WAI-SR	Working Alliance Inventory-Short Revised
“3 month”	13-week post-randomisation appointment: this will normally be scheduled between 11-weeks and 17-weeks post-baseline, but exceptionally can be held up to 22-weeks post-baseline
“6 month”	26-week post-randomisation appointment: this will normally be scheduled between 24-weeks and 30-weeks post-baseline, but exceptionally can be held up to 35-weeks post-baseline.

1. INTRODUCTION

1.1 Background and rationale

Psychosis refers to a range of distressing mental health difficulties. Common symptoms of psychosis include hearing and seeing things others do not (hallucinations), persecutory or grandiose beliefs (delusions), feelings of paranoia, and reduced motivation, apathy, or self-neglect (negative symptoms). Without effective and timely support, psychosis can lead to a range of poor psychological, physical, social, and vocational outcomes for individuals affected and their relatives. Specialist early intervention in psychosis (EIP) teams have, therefore, been established to provide rapid access to evidence based biopsychosocial interventions for individuals experiencing a first episode of psychosis.

EIP services aim to work with people for up to three years following a first episode of psychosis. Rates of disengagement prior to the planned three years, however, are estimated to be between 12% and 54%. The therapeutic benefits of EIP are dependent upon service users' continued engagement with these services. If a service user (SU) does not remain in contact with EIP services, it is not possible to provide the biopsychosocial interventions which NICE (2014) recommend should be offered.

Care coordinators make up the largest staff group working within EIP teams and generally have a core professional qualification in either mental health nursing, social work, or occupational therapy. The role of the care coordinator (CC) is to take a lead role in care planning and the promotion of personal recovery. They work flexibly to support the individual with a range of health and social care needs and are central to the functioning of EIP teams.

The Method of Levels (MOL) is a transdiagnostic psychological intervention that aims to help people resolve distressing problems and regain control over important aspects of their life. MOL directly applies principles from a theory of human behaviour called Perceptual Control Theory (PCT), which argues that psychological distress arises when people are unable to maintain control over important aspects of their life. MOL aims to support the resolution of internal conflicts that are believed to disrupt people's capacity to maintain control.

Practitioners delivering MOL have two primary goals: (1) encourage the person to talk freely about their problems, and (2) pay attention for signs that the person is experiencing background thoughts while they are talking and then ask about these. Once a relevant background thought has been identified, the practitioner shifts back to the first goal of encouraging the person to explore this new thought in more detail.

Previous research has demonstrated that it is feasible and acceptable to deliver MOL for people experiencing psychosis. Because CCs are the staff group with the most contact with SUs, however, it could be more practical and effective to train them in the approach, rather than rely on the use of specialist psychological therapists who are in contact with service-users for a comparatively short time.

This study aims to assess the feasibility of training CCs to deliver MOL, to understand whether this approach might improve service-user engagement and recovery from psychosis compared to routine care, and to assess the feasibility of conducting a cluster-randomised controlled trial (C-RCT) with clustering at the level of teams.

1.2 Objectives

1. To determine the feasibility of recruiting and retaining participants (CCs and SUs) in a C-RCT comparing the effects of MOL-trained CCs versus treatment as usual on outcomes (engagement and recovery) for people experiencing first episode psychosis.
2. Establish the acceptability of the MOL training programme amongst CCs and of MOL delivered by CCs amongst SUs.
3. Identify barriers and facilitators to MOL delivered by CCs.
   Assessed via the study's qualitative component only – this is therefore not subject to further coverage in this SAP.
4. Refine the MOL training programme and implementation plan based on participant feedback.
5. Establish the most appropriate primary outcome measure for a definitive (i.e. evaluation) trial.
6. Generate further evidence on the promise of the intervention via estimates of effectiveness on key outcome measures.
7. Estimate key parameters to inform a sample size calculation for a definitive (evaluation) trial.
8. To determine the feasibility of conducting an economic evaluation of MOL as part of a definitive (evaluation) RCT.

1.3 Feasibility trial success criteria

The following pre-specified success criteria will be used to determine whether progression to a larger study is indicated:

1. **Recruitment:** Successful recruitment of CC and service-user participants within 8 months (for CC: ≥75% = green; 60%-<75% = amber; <60% = red; for service-user participants: average ≥3 per CC = green; 2-<3 = amber; <2=red).

2. **Retention:** Successful retention of CC and service-user participants at final follow up (for both groups: ≥80% = green; 60%-<80% = amber; <60% = red).

3. **Engagement with MOL training and supervision:** Attendance at initial MOL training (≥80% = green; 60%-<80% = amber; <60% = red) and monthly MOL supervision sessions (average of ≥4 sessions per CC = green; 2-<4 = amber; <2=red).

4. **Implementation:** Evidence that CCs believe that they can deliver the MOL intervention in clinical practice.

5. **Acceptability:** Evidence that MOL delivered by CCs is perceived to be acceptable and helpful by service-users.

2 TRIAL METHODS

2.1 Trial design

A two-arm 2:1 cluster-randomised feasibility trial to either: TAU + MOL (i.e. support from a CC who has received training in Method of Levels therapy) versus TAU alone.

2.2 Randomisation

Permuted-block randomisation stratified by NHS Trust (GMMH, Lancashire and South Cumbria, Mersey Care) was used within the Sealed Envelope system. Randomisation was carried out for all recruited EIP teams within a Trust only after all care-coordinators and service-users had been recruited. The order that all the teams within a Trust would be randomised was to be pre-specified prior to any allocations being revealed to help preserve allocation concealment.

2.3 Sample size

The plan was to recruit and randomise 12 EIP teams, each including 2 CCs, resulting in 24 CCs total. Each CC was then expected to recruit up to 4 SUs, resulting recruitment of up to 96 SUs. Whilst there was no formal sample size calculation for this feasibility trial, the trial was premised on there being good precision in the estimation of retention (95% confidence interval [CI] of width 16.9% if retention is ≥80%) but was otherwise chosen on pragmatic grounds to collect sufficient data at each level (team, CC, SU) to assess the feasibility and acceptability of the intervention and the feasibility of the cluster-randomised controlled trial.

2.4 Framework

Not applicable, although the underlying framework for an effectiveness trial would be superiority.

2.5 Statistical interim analysis and stopping guidance

There are no planned interim analyses.

Interim Analysis

Not applicable.

Guidelines for stopping a trial early

Not applicable.

2.6 Timing of final analysis

A single analysis is planned i.e. all outcomes will be analysed collectively on completion of all outcome assessments.

2.7 Timing of outcome assessments

Outcome measures are collected on three occasions:

- Baseline (9-week window prior to randomisation, or, exceptionally, for SUs, between randomisation and commencement of intervention delivery)
- “3 months” (normally scheduled between 11-weeks and 17-weeks post-baseline, but exceptionally can up to 22-weeks post-baseline);
- “6 months” (normally be scheduled between 24-weeks and 30 weeks post-baseline, but exceptionally can be held up to 35-weeks post-baseline).

Feasibility outcomes will be assessed throughout the study, at time-points appropriate for the specific feasibility outcome.

3 STATISTICAL PRINCIPLES

3.1 Confidence intervals (CI) and level of statistical significance

A 95% confidence level will be used throughout, where relevant, unless otherwise specified in this document. No adjustment for multiplicity will be used and no formal testing will be performed.

3.2 Adherence and protocol deviations

Adherence

Given the nature of the intervention, there is no specific service-user adherence measure. For CCs, adherence relates to attendance at training and supervision sessions and usage of MOL: this will be assessed and is included in the main analysis (see Section 5.2).

Non-compliances (Protocol deviations)

Prospective, planned deviations or waivers to the protocol are not permitted and will not be used (e.g. it is not acceptable to enrol a participant if they do not meet the trial's eligibility criteria). Accidental protocol breaches will be reported to the CI and Sponsor and discussed at TMG meetings to develop a plan to reduce the likelihood of their recurrence. The following potential accidental protocol deviations will be recorded and reported in the Statistical Analysis Report:

1. Any care-coordinator or service-user baseline data expected but not collected prior to randomisation of the corresponding EIP team.
2. Any incidents of outcome data being collected from participants outside of the planned timeframe.
3. Any incidents of researchers failing to collect outcome data from participants. This will not include situations where outcome data is not collected for appropriate reasons (e.g., where the participant declines to provide this data).
4. Incidents where Method of Levels training and supervision sessions could not be delivered as planned.

3.3 Analysis populations

The primary analysis population for the statistical and economic analyses to address Objectives 1,2 and 4-8 is “intention to treat” (“as randomised”), based on the SU and CC populations of study participants remaining in the trial at the point of randomisation. The trial safety population will be all service-user participants who provided consent to take part.

4 TRIAL POPULATION

Numbers approached/screened, numbers eligible and numbers consented (as described in 4.1-4.3 below) will be presented in CONSORT diagrams (Figures 1-3). Although numbers of EIP Teams and their CCs, and SUs will be presented in the same CONSORT diagram, (Fig. 1) details of those approached/screened and those eligible will be presented in separate CONSORT diagrams, one for EIP Teams and their CCs (Fig. 2) and one for SUs (Fig. 3).

4.1 Screening data

We will report the:

1. total number of EIP teams within each participating NHS Trust;
2. number of EIP teams approached by the study team within each participating NHS Trust;
3. number of CCs who were members of teams for which the EIT Lead agreed for their team to participate, and the number of CCs who subsequently expressed an interest in taking part in the study;
4. number of SUs who gave their CC consent for the study team to contact them;

4.2 Eligibility

Inclusion criteria for CCs

- Working within EIP services based within participating NHS Trusts
- Likely to remain in their current post for the duration of the study
- Have organisational support from their employer to engage with MOL training and supervision
- Be willing and able to engage with MOL training and supervision

We will report the number of CCs who were eligible to participate as members of the teams for which the Team Lead agreed that their CCs could be approached, the number of CCs

who expressed an interest in taking part in the study (and percentage of the total number in the teams for which the Team Lead agreed that their CCs could be approached) , and the number of CCs who consented (and the percentage of the number who expressed an interest in taking part. We will also report the number of CCs who remained in the study at the point of randomisation (and the percentage of the number who were members of the teams for which the Team Lead agreed that their CCs could be approached), We will also report any reasons for non-eligibility (e.g. not likely to remain in their current post for the duration of the study).

Inclusion criteria for SUs:

- Current users of an EIP service that is included in the study
- Have an allocated CC who is participating in the study
- Due to remain under the care of their EIP service until the end of the study
- Have capacity to provide informed consent to participate in the study
- Have sufficient written and verbal English language skills to complete outcome measures and engage with the MOL intervention
- Be aged 18 years or older.

We will report the number of SUs who were deemed potentially eligible to participate and approached, and the number of SUs who agreed to be contacted about the study (and the percentage out of those who were approached).

4.3 Recruitment

Numbers of EI Teams, CCs and SUs recruited into the trial will be presented in a CONSORT diagram (see **Error! Reference source not found.**).

For CCs, we will define 'recruited' (also referred to as 'included at time of randomisation') as 'consented, completed baseline MBI-HSS, recruited at least one SU and not having withdrawn prior to randomisation of their team'. We will present:

- the number of CCs recruited;
- the number of CCs who agreed to participate but were not 'recruited', with reasons for non-recruitment as follows:
    - did not complete baseline MBI-HSS;
    - did not recruit at least one SU;
    - withdrew pre-randomisation (with reasons for withdrawal, as appropriate);
    - other reasons (sub-classified as appropriate).

For SUs, we will define ‘recruited’ (also referred to as ‘included at time of randomisation’ as ‘consented, completed the QPR, and CC remaining in the trial at the time of randomisation of their team’. We will present:

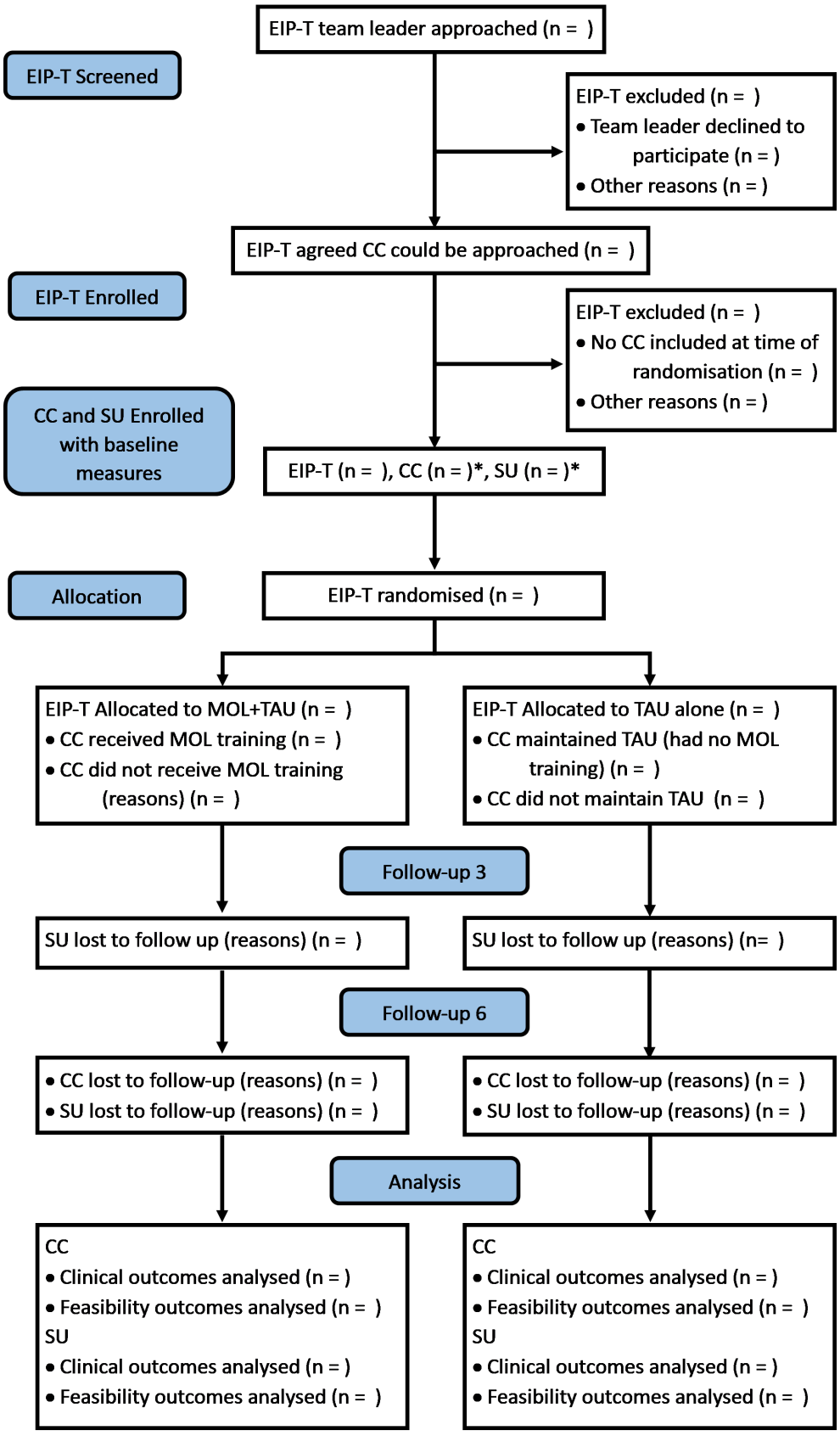
- the number of SUs recruited;
- the number of SUs who agreed to be contacted about the trial but were not ‘recruited’, with reasons for non-recruitment as follows:
    - did not consent to participate;
    - did not complete QPR;
    - withdrew pre-randomisation (with reasons for withdrawal, as appropriate);
    - excluded post-consent but pre-randomisation (with reasons for exclusion, as appropriate).

Percentages of each, based on denominators of:

- for EI Teams, the total number of EI Teams across the three participating services;
- for CCs, the number of CCs who expressed an interest in participating; number of CCs in teams approached;
- for SUs, the number of SUs who agreed to be contacted about the trial; number of SUs approached;

respectively, will also be presented.

Figure 1: Main CONSORT Diagram



* Details provided in Figures 2 and 3 below
EIP-T = Early Intervention in Psychosis Team
SU = Service User
CC = Care Coordinator
MOL = Method of Levels (CC
TAU = Treatment as usual

Figure 2: CONSORT flow diagram for Care Coordinators

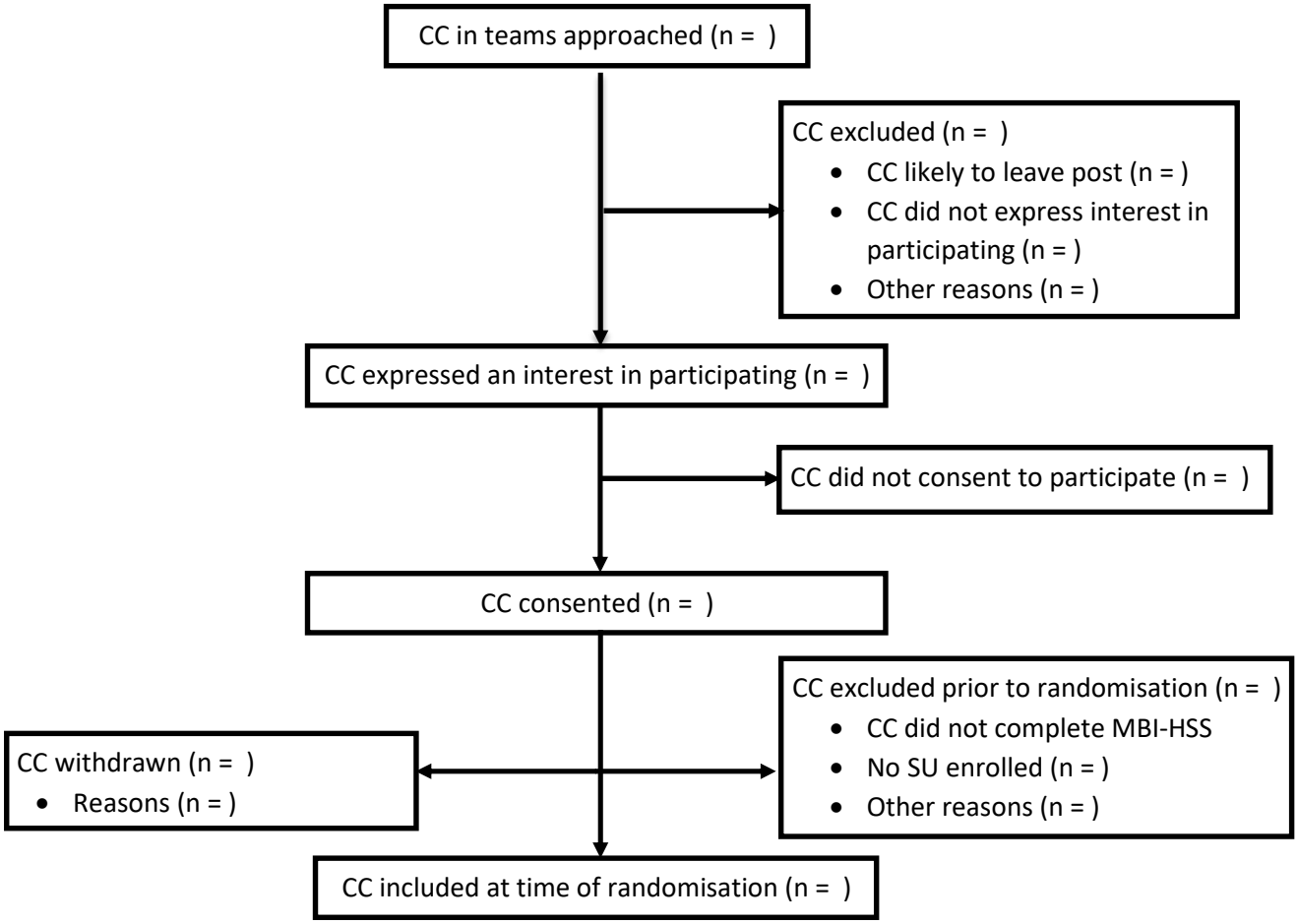
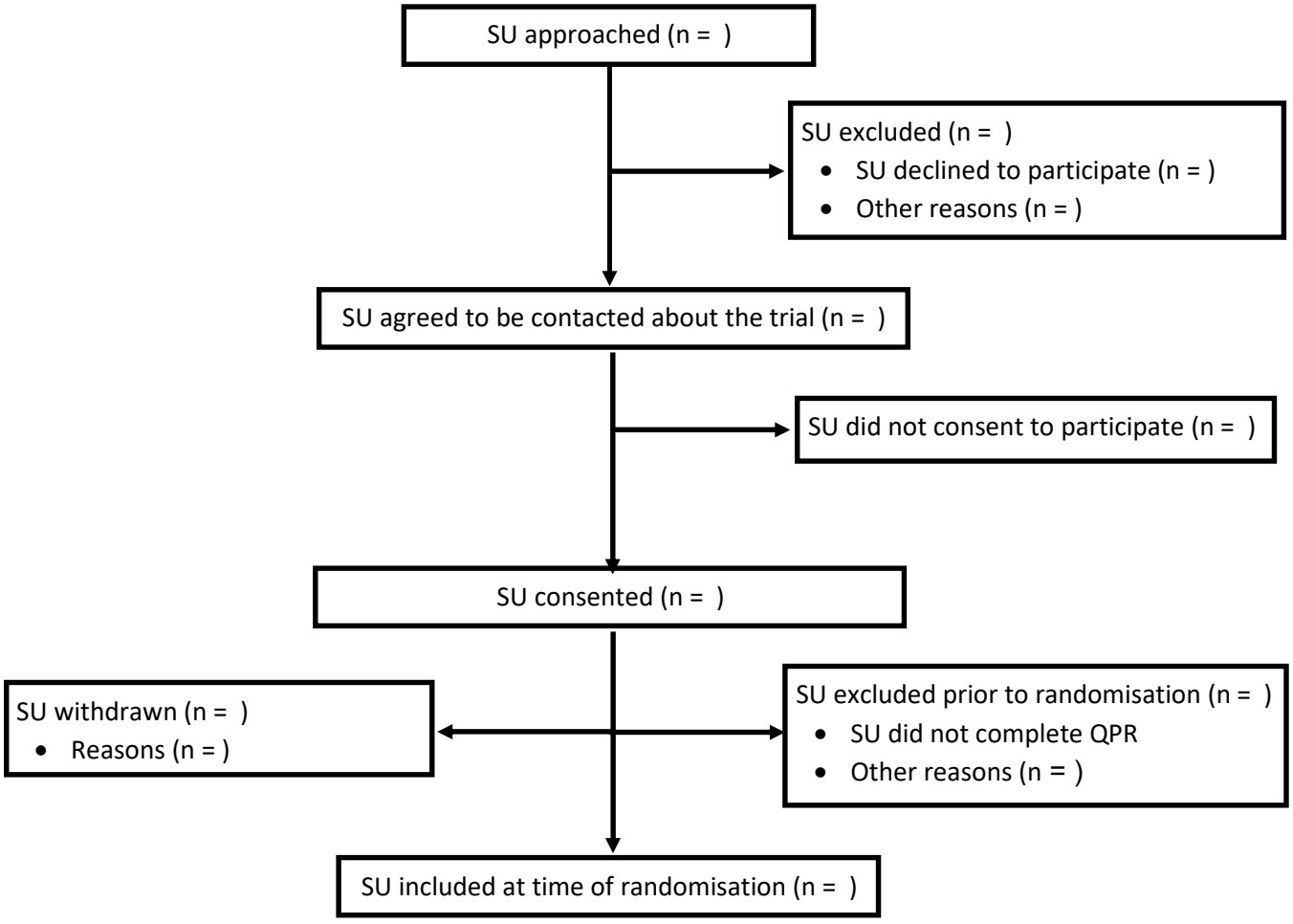


Figure 3: CONSORT flow diagram for Service Users



4.4 Withdrawal/follow-up

This will be presented in a CONSORT diagram (see Figure 1), with numbers and reasons for withdrawal and/or exclusion from analysis for EIP-T, CCs and SUs each given at each stage: 3-month follow up; 6-month follow-up.

4.5 Baseline participant characteristics

Baseline characteristics will be summarised for SUs and CCs 'recruited' (i.e. 'included at the time of randomisation').

A number of the following items (preceded by an asterisk [*]) permit free-text entries and the research team will undertake an exercise at the end of data collection to group the terms that were used into "categories". This mapping will be provided to the statistician and used to recode the items when summarising. For these and other categorical characteristics (e.g. ethnicity, gender etc.) which are found to contain small frequencies (<3), appropriate merging of categories will be performed to ensure a balance between disclosure control and the usefulness of important participant characteristic data.

All the variables in the baseline CRF will be summarised, both overall and by trial arm, using mean, standard deviation (sd), median, minimum, lower quartile, median, upper quartile, maximum (as appropriate) for interval variables, and frequency and percentage for categorical variables. These will include:

<u>Service users</u>

Age

Gender (Female; Male; Non-binary; F to M transgender; M to F transgender; Other).

Ethnicity (Arab; Asian/Asian British; Black African; Black Caribbean; Black British; Irish Gypsy or Traveller; White British; White and Black Caribbean; White and Black African; White and Asian; White other; Other Mixed / Multiple Ethnic Background; Any other ethnic group).

*Mental health diagnoses (Y; N), up to 3 may be recorded as free text.

*Physical health diagnoses (Y; N), up to 3 may be recorded as free text.

Months since acceptance to EIP team services.

*Receiving psychological or talking therapies (Y; N), up to 3 may be recorded as free text.

Number of admissions to hospital because of mental health.

*Prescribed medication (Y; N), up to 5 may be recorded as free text.

Relationship Status (Single; Married/Co-habiting; Divorced/Separated).

Accommodation status (Mainstream Housing; Supported Accommodation; Homeless).

Employment Status (Unemployed; Paid Employment; Unpaid Employment; Education/Training).

Care coordinators

Age

Gender (Female; Male; Non-binary; F to M transgender; M to F transgender; Other).

Ethnicity (Arab; Asian/Asian British; Black African; Black Caribbean; Black British; Irish Gypsy or Traveller; White British; White and Black Caribbean; White and Black African; White and Asian; White other; Other Mixed / Multiple Ethnic Background; Any other ethnic group).

Professional Background (Mental Health Nursing; Occupational Therapy; Social Work; Other)

Length of time professional qualification held (years)

Length of time working as a CC (years)

Length of time working in EIP services (years)

*Completed formal training in psychological interventions or talking therapies (Y, N), up to 3 may be recorded as free text.

a) The scales and subscales for the following questionnaires will be calculated and summarised by trial arm (mean, sd, median, minimum, lower quartile, median, upper quartile, maximum).

Service users

QPR (Questionnaire about the Process of Recovery) (total recovery score: range 0 to 60).

- This tool is comprised of 15 items; e.g. item 1 “I feel better about myself”
- Each item is scored on the same five-point scale (0 = disagree strongly, 1 = disagree, 2 = neither agree nor disagree, 3 = agree, 4 = agree strongly).
- The 15 items are summed to give a total recovery score.

- As there is no guidance on handling item missing, mean imputation will be used to calculate the scale score provided no more than 3 items (≤20%) are missing, otherwise it will be set to missing.
- Higher scores indicate improved recovery.

DIALOG (subjective satisfaction score and treatment satisfaction score: each has range 1 to 7)

- This tool is comprised of 11 items; e.g. item 1 “How satisfied are you with your mental health?”
- Each item is scored on the same seven-point scale (1 = totally dissatisfied, 2 = very dissatisfied, 3 = fairly dissatisfied, 4 = in the middle, 5 = fairly satisfied, 6 = very satisfied, 7 = totally satisfied).
- Mean of ítems 1 to 8 gives a subjective satisfaction score.
- Mean of ítems 9 to 11 gives a treatment satisfaction score.
- As there is no guidance on handling item missing, mean imputation will be used to calculate the subjective satisfaction score provided no more than 1 item (≤20%) is missing, otherwise it will be set to missing. No imputation will be used for the treatment satisfaction score as it is only comprised of 3 items.
- Higher scores indicate greater satisfaction.

RoC (Reorganisation of Conflict) (Mean score: range 0-100)

- This tool is comprised of 11 items.
- e.g. item 1 “Talking through my problems helps me to feel different about them”.
- Each item is on a 0 to 100 scale with marks at 0, 10, 20, …, 100. 0 is labelled “I don’t believe this at all” and 100 “I believe this completely”.
- The mean score is computed as the mean across the 11 items
- As there is no guidance on handling item missing, mean imputation will be used to calculate the ROC (mean-item) score provided no more than 2 items (≤20%) are missing, otherwise it will be set to missing.

WAI-SR (Working Alliance Inventory – Short Revised) (Goal, Bond and Task subscales: each has range 4 to 20).

- This tool is comprised of 12 items; e.g. item 1 “As a result of these sessions I am clearer as to how I might be able to change”.
- Each item is scored 1 = “Seldom, 2 = “Sometimes”, 3 = “Fairly Often”, 4 = “Very Often”, 5 = “Always”.

- There is no overall score but there are three subscales:
    - Goal: Agreement on the goals of therapy (sum of scores from ítems 4, 6, 8, 11);
    - Bond: Development of an affective bond (sum of scores from ítems 3, 5, 7, 9);
    - Task: Agreement on the tasks of therapy (sum of scores from ítems 1, 2, 10, 12).
- No imputation will be used for the subscale scores as each only comprises 4 items.

EQ-5D-5L (Utility values: range essentially 0 to 1 but small negative values are possible, indicating health utility worse than death)

- This instrument comprises 5 items representing domains of health (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).
- Each item is scored on a 5-point scale (1 = no problems, 2 = slight problems, 3 = moderate problems, 4 = severe problems, 5 = unable to do) with a higher score indicating worse health.
- Utility index values will be calculated using the approach recommended by NICE at the time of analysis.
- No imputation will be used.

Service-use questionnaire

- This is a questionnaire designed to capture use of health and social care services.
- Researchers will talk participants through the questionnaire.
- Categories of service use included are: mental health, accident and emergency (A&E), hospital, primary/community/social care.
- No imputation will be used.

Care coordinators

MBI-HSS for Medical Personnel (Emotional Exhaustion subscale: range 0 to 54; Depersonalisation subscale: range 0 to 30; Personal Accomplishment subscale range 0 to 48)

- This tool comprises 22 items; e.g. item 1 “I feel emotionally drained from my work”.
- Each item is scored on the same seven-point scale (“0 = Never”, “1 = A few times a year or less”, “2 = Once a month or less”, “3 = A few times a month”, “4 = Once a week”, “5 = A few times a week”, “6 = Every day”)

- There is no overall score but there are three subscales:
    - Emotional Exhaustion (9 items: 1, 2, 3, 6, 8, 13, 14, 16, 20)
    - Depersonalisation (5 items: 5, 10, 11, 15, 22)
    - Personal Accomplishment (8 items: 4, 7, 9, 12, 17, 18, 19, 21)
- Subscales are each formed by summing the respective ítems
- As there is no guidance on handling item missing, mean imputation will be used to calculate subscale scores provided no more than 1 item (≤20%) is missing for a given subscale, otherwise it will be set to missing.

5 ANALYSIS

The analysis in this document is focused on **objectives** addressed using quantitative data.

5.1 Objective 1 - To determine the feasibility of recruiting and retaining participants (CCs and SUs) in a C-RCT comparing the effects of MOL-trained CCs versus treatment as usual on outcomes (engagement and recovery) for people experiencing first episode psychosis

Feasibility outcome (1A)

CC recruitment: the number of CCs 'recruited' (see Section 4.3) and having valid scores for each of the MBI-HSS subscales at baseline will be expressed as a percentage (x_A) of the target of 24.

Analysis:

Feasibility trial success "traffic lights" criteria: Green: $x_A \geq 75\%$; Amber; $60\% \leq x_A < 75\%$; Red: $x_A < 60\%$.

Feasibility outcome (1B)

CC retention: the percentage (x_B) of recruited CCs retained in the study at "6 months" post randomisation and having valid scores for each of the MBI-HSS subscales at "6-months".

Analysis:

Feasibility trial success “traffic lights” criteria: Green: $x_B \geq 80\%$; Amber: $60\% \leq x_B < 80\%$; Red: $x_B < 60\%$.

Feasibility outcome (1C)

Average number of SUs recruited per CC (x_C): the total number of SUs recruited and having a valid QPR total recovery score at “baseline”, divided by the total number of CCs recruited (as defined for Feasibility outcome 1A).

Analysis:

Feasibility trial success “traffic lights” criteria: Green: $x_C \geq 3$; Amber: $2 \leq x_C < 3$; Red: $x_C < 2$.

Feasibility outcome (1D)

SU retention: the percentage (x_D) of recruited SUs retained in the study at “6 months” and having a valid QPR total recovery score at “6 months”.

Analysis:

Feasibility trial success “traffic lights” criteria: Green: $x_D \geq 80\%$; Amber; $60\% \leq x_D < 80\%$; Red: $x_D < 60\%$.

5.2 Objective 2- Establish the acceptability of the MOL training programme amongst CCs and of MOL delivered by CCs amongst SUs

Whilst this objective will primarily be assessed using the qualitative data, the CC attendance at the initial training and the monthly MOL supervision sessions will also be used to inform the assessment of acceptability of the MOL training programme and ‘success’ of the feasibility trial with respect to the MOL training programme to inform an evaluation trial. Data from the short questionnaire, sent weekly to a small sample of CCs, will inform acceptability but is not linked to the specific progression criteria detailed in Section 1.3.

Feasibility outcome (2A)

Percentage (y_a) of CCs (denominator number of CCs recruited, as defined for Feasibility outcome 1A – see Section 5.1) attending all 3 sessions of initial MOL training.

Analysis:

Feasibility trial success "traffic lights" criteria: Green: $y_a \geq 80\%$; Amber: $60\% \leq y_a \leq 79\%$; Red: $y_a < 60\%$).

Feasibility outcome (2B)

Average number (y_{b1}) of monthly MOL supervision sessions completed (denominator number of CCs recruited, as defined for Feasibility outcome 1A – see Section 5.1).

Although not linked to a set of direct progression criteria, we will also present the number (y_{b2}) and percentage (y_{b3}) of CCs who complete at least 4 (out of the 6) of monthly MOL supervision sessions to aid interpretation.

Analysis:

Feasibility trial success "traffic lights" criteria: Green; $y_{b1} \geq 4$ Sessions;
Amber: 2 Sessions $\leq y_{b1} < 4$ Sessions; Red: $y_{b1} < 2$ Sessions.

Feasibility outcome (2C)

Percentage (y_c) of CC reports of acceptability (defined as responding 'strongly agree' or 'agree' to the question "To what extent do you agree with … Method of Levels is a helpful approach for people using Early Intervention in Psychosis services)) in the weekly questionnaires (based on the last questionnaire completed for any CC who completes more than one questionnaire).

Analysis:

No specific feasibility trial success criteria have been set for this outcome.

Feasibility outcome (2D)

Percentage (y_d) of CC reports of acceptability (defined as responding 'strongly agree' or 'agree' to the question "To what extent do you agree with … Method of Levels training and supervision has improved the support I am able to provide to SUs) in the weekly questionnaires (based on the last questionnaire completed for any CC who completes more than one questionnaire).

Analysis:

No specific feasibility trial success criteria have been set for this outcome.

5.3 Objective 4 - Refine the MOL training programme and implementation plan based on participant feedback.

Whilst this objective will primarily be addressed using qualitative methods, including analysis of the open questions from the weekly CC questionnaires, the following quantitative outcomes will also be used to help address this objective.

Feasibility outcomes:

Whilst this objective will be primarily address using qualitative methods, the following outcomes will be assessed to inform future refinement and implementation of MOL in clinical practice:

1. Percentage of CC reports indicating use of MOL in their clinical practice at any point in the last seven days;
2. Average number of clinical contacts in which CC report using MOL to some extent in the past seven days
3. Percentage of clinical contacts seen in the past 7 days in which CC report using MOL to some extent
4. Percentage of CC reports indicating use of MOL in their clinical practice at any point in the last seven days
5. Percentage of CC reports indicating that MOL principles have informed their clinical practice in the last seven days;
6. Percentage of CC reports of use of MOL over the past 7 days (defined as responding 'strongly agree' or 'agree' to the question *"In the last seven days, I have been able to use Method of Levels in my clinical practice"* in the weekly questionnaires).

As there will be multiple CC reports for most CCs, we will also use alternative definitions for these outcomes based on the:

a. *First* report for each CC (to reflect their application of MOL early in the study);
b. *Last* report for each CC (to reflect their application of MOL later in the study).

So, for example, outcome 1. above will have alternative definitions:

1b. For each CC the percentage of their *first* weekly questionnaire report indicating use of MOL in their clinical practice at any point in the last seven days;
1c. For each CC the percentage of their *last* weekly questionnaire report indicating use of MOL in their clinical practice at any point in the last seven days;

Analysis:
Whilst no feasibility trial success criteria have been set for outcomes, they will be summarised using appropriate descriptive statistics. The summary statistics will be numbers and percentages (as detailed above) for outcomes 1. and 3.-6. and mean (with SD) for outcome 2.

The outcomes described in relation to Objective 2 will also be used to help meet this objective.

5.4 Objective 5 - Establish the most appropriate primary outcome measure for a definitive trial

Candidate outcomes

A number of participant-completed outcome questionnaires are in use in the study. However, it is felt that only the QPR is a candidate primary outcome measure and that the most relevant time-point would probably be the 6-month time-point.

Analysis

There are no specific feasibility trial success criteria linked to this objective. Exploratory multi-level models will be fitted to the QPR outcome data at each time-point separately, including the baseline value as a level 1 covariate (level 1 = “SU”, level 2 = “CC”, level 3 = “EIP team”). Interest will focus on the level 3 trial-arm effect estimate and whether this may demonstrate ‘promise’ of the intervention (See Section 5.5). For the QPR (at each of the 3-month and 6-month timepoints), in addition to 95% confidence interval estimates, 75%, 80% and 85% confidence interval estimates will be extracted from the model, to help address Objective 6 below.

5.5 Objective 6 - Generate further evidence on the promise of the intervention via estimates of effectiveness on key outcome measures.

Outcomes

In addition to putative primary outcome for a future evaluation trial, namely the QPR (see Section 5.4 above), promise will be assessed in terms of other key outcome measures. These are the scales and subscales of the DIALOG, RoC and WAI-SR tools.

Analysis

Analysis along similar lines to that previously described in section 5.4 for QPR and interest will, again, focus on the level 3 trial-arm effect estimates. All models will be fitted separately to 3-month and 6-month outcome data and will be adjusted for site (as a fixed factor) and the baseline value of the corresponding outcome measure.

For each of the 3 subscales of the MBI-HSS tool, 2-level models (level 1 = "CC", level 2 = "EIP team") will be fitted for the 6-month timepoint only (as this tool is not collected at the 3-month timepoint. Interest will focus on the level 2 trial-arm effect estimate. All models will be adjusted for site (as a fixed factor) and the baseline value for the corresponding MBI-HSS subscale score.

For the QPR, a minimally important difference between groups of 4 points has been determined[1]. Consideration of the 75% - 95% confidence intervals will be made to help the assessment of the degree of 'promise' of the intervention, with particular attention on the 75% and 80% confidence intervals (given the expected limited precision of the estimation).

5.6 Objective 7 – Estimate key parameters to inform a sample size calculation for a definitive trial.

Analysis

No additional statistical analyses will be performed to address this objective. As indicated in Section 5.4, it is anticipated that the QPR at 6 months will be the primary outcome in a definitive trial. Estimates of the residual variance from the 3-level model outlined in Section 5.4 will be used to inform a sample size calculation for such a trial. The estimates of the Level 2 and Level 3 variances will be used, together with values presented in the literature, to form plausible estimates of those parameters. Retention rate (Feasibility outcome 1D - see Section 5.1) will also be used here to inform the inflation necessary to allow for withdrawal and non-completion of the putative primary outcome measure.

5.7 Objective 8 - To determine the feasibility of conducting an economic evaluation of MOL as part of a full RCT

EQ-5D-5L

Summary statistics will be reported for the EQ-5D-5L responses namely the proportion of people reporting problems for each domain and the profile of responses across all domains will be summarised graphically using the *eq5dds* command in STATA. The proportion of participants with missing EQ-5D-5L data will be reported. Health utility values will be estimated using the method recommended by NICE at the time of the analysis. Mean utility values will be reported at each time point and quality-adjusted life years (QALYs) estimated across the whole study period. These will be reported by treatment allocation group. No formal statistical tests will be conducted.

Service use questionnaire

The number and proportion of participants reporting use of different health and social care services (and quantity of services used) will be summarised by treatment allocation group. The extent of missing data will also be reported.

Estimating the cost of the intervention

The resources required to deliver the intervention will be summarised in terms of the number of therapists trained, time required for training, and number (and duration) of CC sessions delivered to each participant. Unit costs will be attached to the quantity of resources used to estimate the cost. Unit costs will be obtained from freely available, published sources namely the 'PSSRU Unit Costs of Health and Social Care' (https://www.pssru.ac.uk/project-pages/unit-costs/) and 'NHS Schedule of Reference Costs' (https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/).

5.8 Sensitivity analyses

Sensitivity analysis will include the estimation of effectiveness for the QPR (see Section 5.4) but excluding any responses collected outside the normal time-window (i.e. treating 6-month QPR data collected outside the interval 24-30 weeks post-baseline as ‘missing data’).

5.9 Subgroup analyses

There are no planned subgroup analyses.

5.10 Missing data

Missing data will be reported for each outcome measure but there is no planned imputation for missing values in the multi-level modelling. Item missing data will be imputed for the various scales as described in Section 4.5.

5.11 Additional analyses

For all scales and subscales (putative outcome measures for a future evaluation trial) described in Section 4.5 b), means and standard deviations will be tabulated by trial arm and timepoint (3 months, 6 months). Change from baseline scores will also be calculated and means and standard deviations tabulated by trial arm and timepoint (3 months, 6 months).

5.12 Harms

Adverse events for SUs in CAMEO are coded as follows:

Category

- Death
- Life threatening
- Hospitalisation or prolongation of existing hospitalisation
- Persistent or significant disability or incapacity
- Other

Type: Non suicidal self-injury; Suicide attempt; Other.

Severity: Mild; Moderate; Severe; Unknown.

Related to trial: Yes; No; Unsure.

Analysis

Analysis of safety data will be descriptive in nature:

- The number of AEs will be tabulated by trial arm and severity both overall and for each category.

- The number of participants with at least one AE will be tabulated by trial arm and greatest severity both overall and for each category.
- SAEs will be line-listed separately for each trial arm including at a minimum category, type, severity and relatedness to trial.
- The number of SAEs will be tabulated by trial arm and severity both overall and for each category.
- The number of participants with at least one SAE will be tabulated by trial arm and greatest severity both overall and for each category.

5.13 Statistical software

Analysis will primarily be performed using Stata V18[3], although graphs may be created using other software (e.g. R)[4].

6 REFERENCES

1. Dehmahdi N, Law H, Pyle M, et al. Estimating the minimum important difference for the questionnaire about the Process of Recovery (QPR): an anchor-based approach. *Psychosis*. 2021;00(00):1-11. doi:10.1080/17522439.2021.1883726.

2. E. C. Lee, A. L. Whitehead, R. M. Jacques and S. A. Julious. The statistical interpretation of pilot trials: should significance thresholds be reconsidered? *BMC Medical Research Methodology.* 2014;14:41. doi: 10.1186/1471-2288-14-41.

3. StataCorp. 2023. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC.

4. R Core Team (2023). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/