Greater Manchester Mental Health
NHS Foundation Trust

A mixed methods pilot study exploring the feasibility, acceptability and potential benefits to Mentalisation Based Treatment for Older Adults with Complex Emotional Needs

MBT for socially isolated older adults with personality disorder

This protocol has regard for the HRA guidance and order of content

A mixed methods pilot study exploring the feasibility, acceptability and potential benefits to Mentalisation Based Treatment for Older Adults with Complex Emotional Needs

Overall Aim: To enhance our understanding of whether MBT is an acceptable and feasible intervention for older adults with personality disorders. In addition, the aim of the study is to determine any potential benefits to MBT in older adults.

Hypothesis: MBT is acceptable and feasible as an intervention for OAs with CEN. It has potential cost saving, quality of life improving and risk reducing benefits. Some adaptations are required.

SHORT TRIAL TITLE – MBT for socially isolated older adults with personality disorder

PROTOCOL VERSION NUMBER AND DATE V 1.4 07.08.25

RESEARCH REFERENCE NUMBERS

IRAS Number: **341968**

SPONSORS Number: x750

SPONSOR

Greater Manchester Mental Health
NHS Foundation Trust

Collaborators

University of Tilburg

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles outlined in the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), amended regulations (SI 2006/1928) and any subsequent amendments of the clinical trial regulations, GCP guidelines, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as amended.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the trial publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies and serious breaches of GCP from the trial as planned in this protocol will be explained.

For and on behalf of the Trial Sponsor:

Signature:
.....

Date:
...../...../.....

Name (please print):
.....

Position:
.....

Chief Investigator:

Signature: 

Date:
02/07/2025

Name: (please print):

Luke Jordan

(Optional)

Statistician:

Signature: 

Name: (please print):

Samantha Bouwmeester

Position:

Statistician and researcher Tilburg University, owner - out of the Boxlot,

KEY TRIAL CONTACTS

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Sponsor	Greater Manchester Mental Health Research and Innovation Department
Joint-sponsor(s)/co-sponsor(s)	N/A
Funder(s)	N/A
Clinical Trials Unit	N/A
Key Protocol Contributors	Luke Jordan, luke.jordan@gmmh.nhs.uk, 07384248526 Arjan Videler Machteld Ouwens Peter Fonagy Emma Georgeson Uzma Meraj Vanessa Shaw Ross Dunne
Statistician	Samantha Bouwmeester
Trials Pharmacist	N/A
Committees	N/A

i. LIST of CONTENTS

ii. LIST OF ABBREVIATIONS

Define all unusual or 'technical' terms related to the trial. Add or delete as appropriate to your trial. Maintain alphabetical order for ease of reference.

AE	Adverse Event
CMHT	Community Mental Health Team
CI	Chief Investigator
CRF	Case Report Form
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
GMMH R&I	Greater Manchester Research and Innovation
ICF	Informed Consent Form
MBT	Mentalisation Based Treatment
PI	Principal Investigator
PIS	Participant Information Sheet
QA	Quality Assurance
QC	Quality Control
QP	Qualified Person
REC	Research Ethics Committee
SAE	Serious Adverse Event
SCED	Single Case Experimental Design
SOP	Standard Operating Procedure
TSC	Trial Steering Committee

iii. TRIAL SUMMARY

Trial Title	Multiple Single Case Series Design study into the efficacy of Mentalisation Based Treatment for treating personality functioning and social isolation in Older Adults with a diagnosis of Personality Disorder	
Internal ref. no. (or short title)	MBT for socially isolated older adults with personality disorder	
Clinical Phase		
Trial Design	Multiple Single Case Series Design	
Trial Participants	Older adults (65+) Personality disorders	
Planned Sample Size	10-14	
Treatment duration	24 months	
Follow up duration	6 months	
Planned Trial Period	3 years	
	Objectives	Outcome Measures
Primary	Measure change in personality functioning and social isolation	LPFS 2.0 Social Isolation 4.0
Secondary	Quality of life Satisfaction Suicidality	ReQoL Dialogue CSRSS
Investigational Medicinal Product(s)	N/A	
Formulation, Dose, Route of Administration	N/A	

iv. FUNDING AND SUPPORT IN KIND

Support in Kind	FINANCIAL AND NON FINANCIALSUPPORT GIVEN
NHS - Greater Manchester Foundation Mental Health Trust	Nonfinancial: time of Vanessa Shaw, Uzma Meraj, Luke Jordan,
Tilburg University/GGz Breburg	Nonfinancial: time of Ajan Videler and Machteld Ouwens
Greater Manchester Mental Health Research and Innovation Team	Nonfinancial: time of Research and Innovation team

v. ROLE OF TRIAL SPONSOR

Greater Manchester Mental Health Foundation Trust Research and Innovation Team. The role of this sponsor is to provide assurances that the study design accords with HRA processes, that the research is sustainable and achievable, and that it is safe and effective for participants.

vi. ROLES AND RESPONSIBILITIES OF TRIAL MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Trial Management Committees

- Trial Management Group

  The Trial Management Group should meets monthly. It is comprised of the academic sponsors at Tilburg University, and the members of the treatment and research team. It's function is to ensure all practical details of the trial are progressing well and working well and everyone within the trial understands them. The team also considers the ethical concerns of the trial, and the overall design.

vii. Protocol contributors

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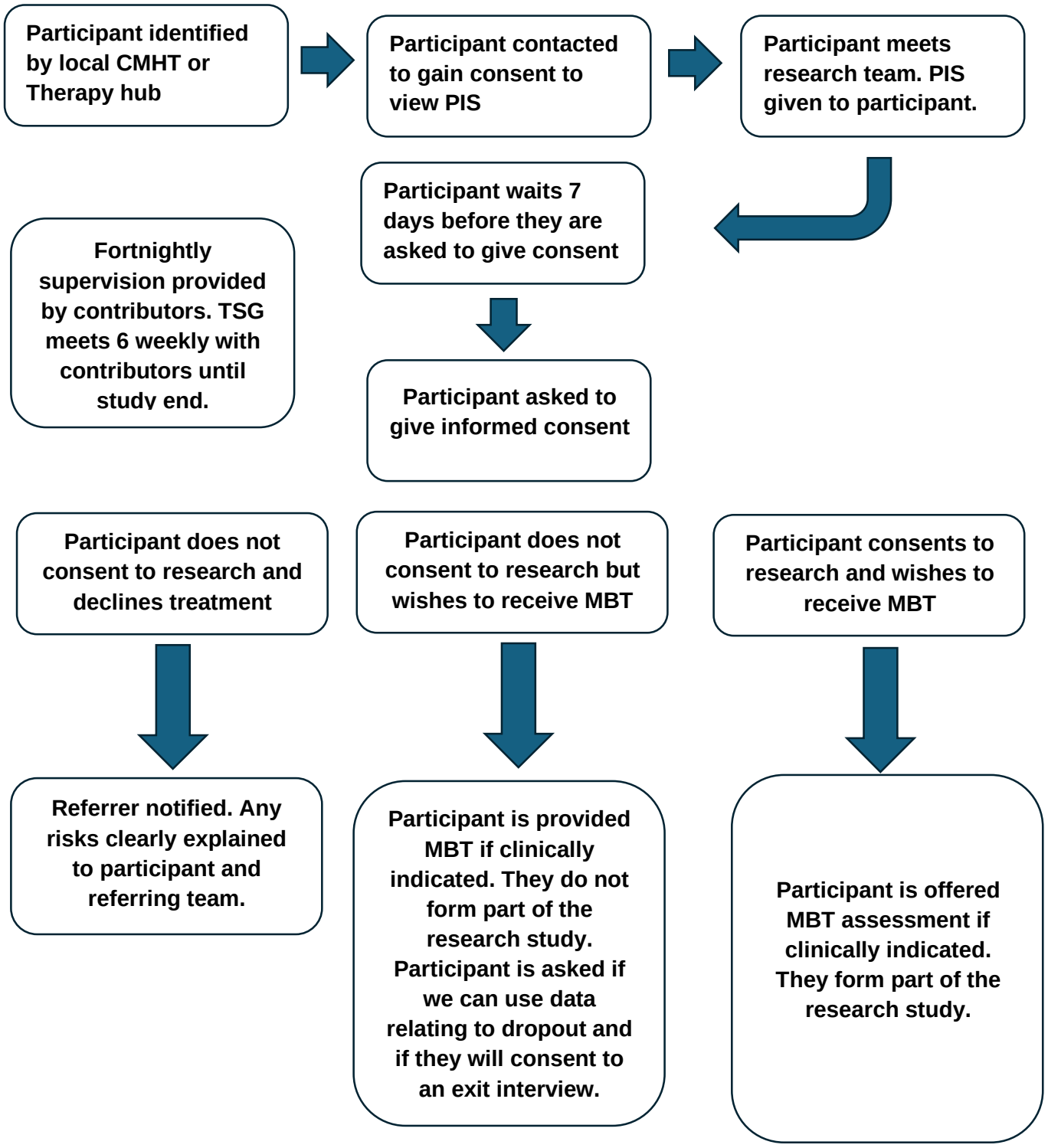
The above contributors have supported the planning of the project. All members excluding Peter Fonagy are members of the trial steering committee. All members excluding Peter Fonagy will also support the writing, dissemination and analysis of final anonymised data.

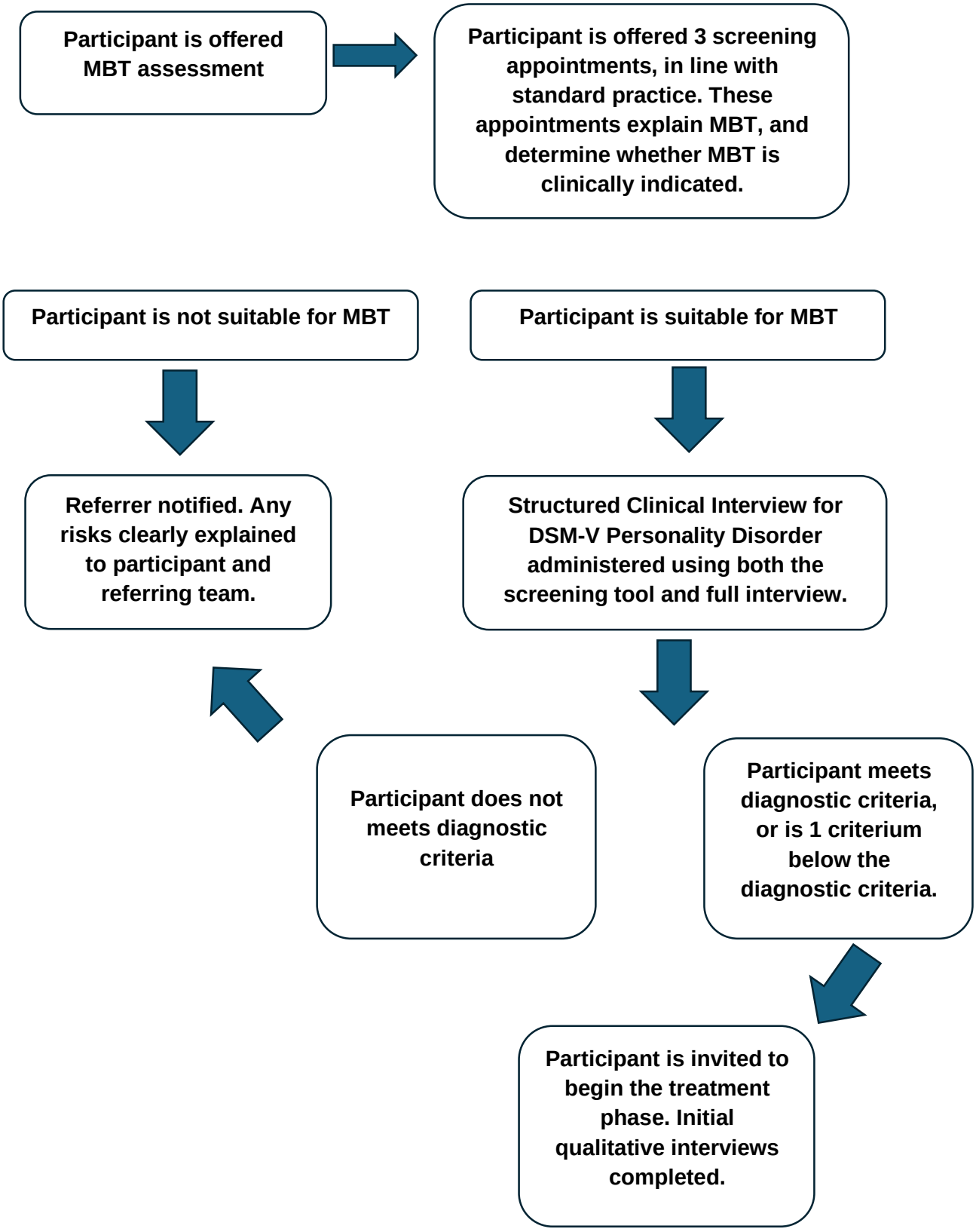
viii. KEY WORDS: **Older adults, personality disorder, social isolation, complex emotional needs, social isolation**

ix. TRIAL FLOW CHART

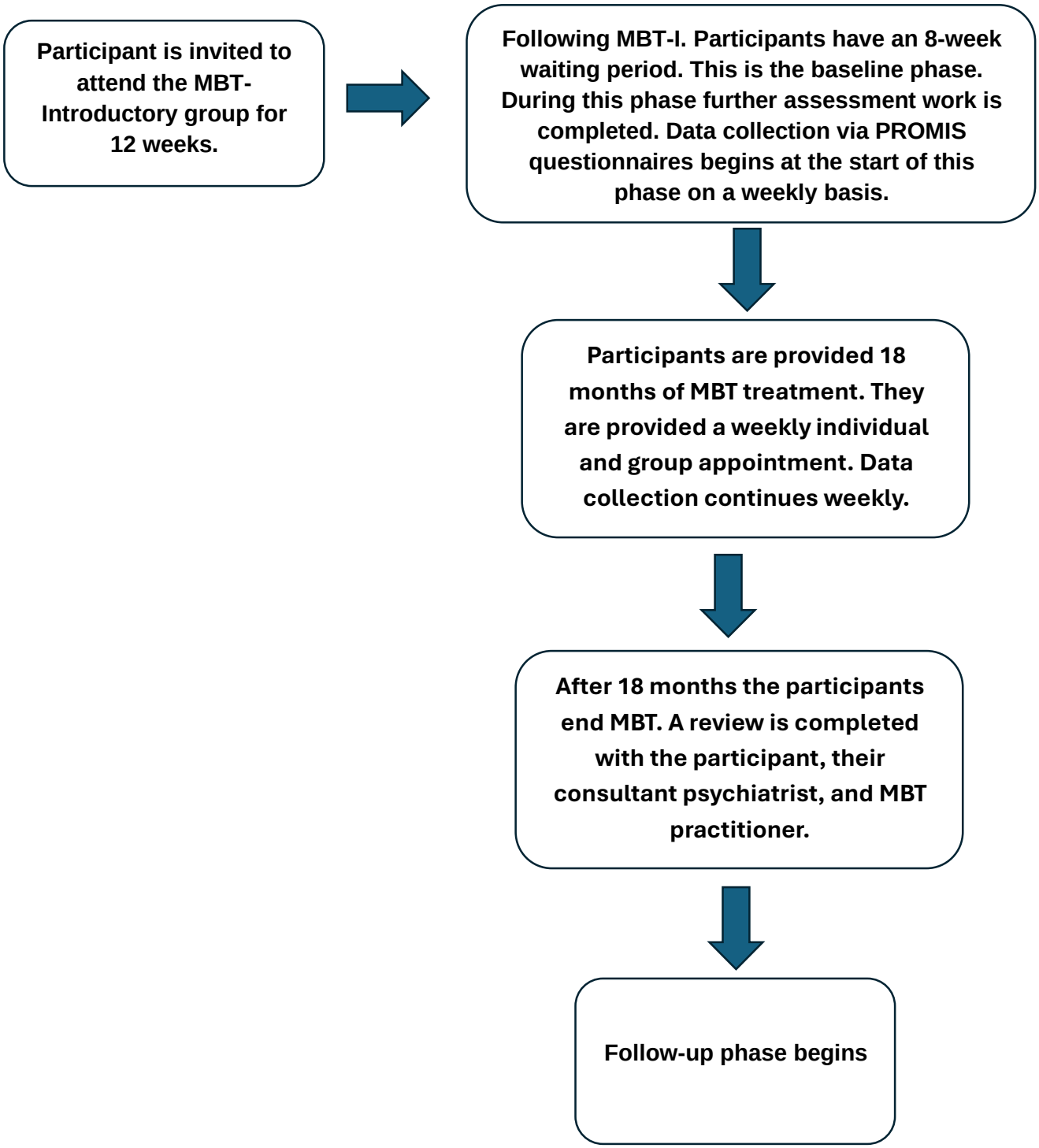
Phase 1 – consent.



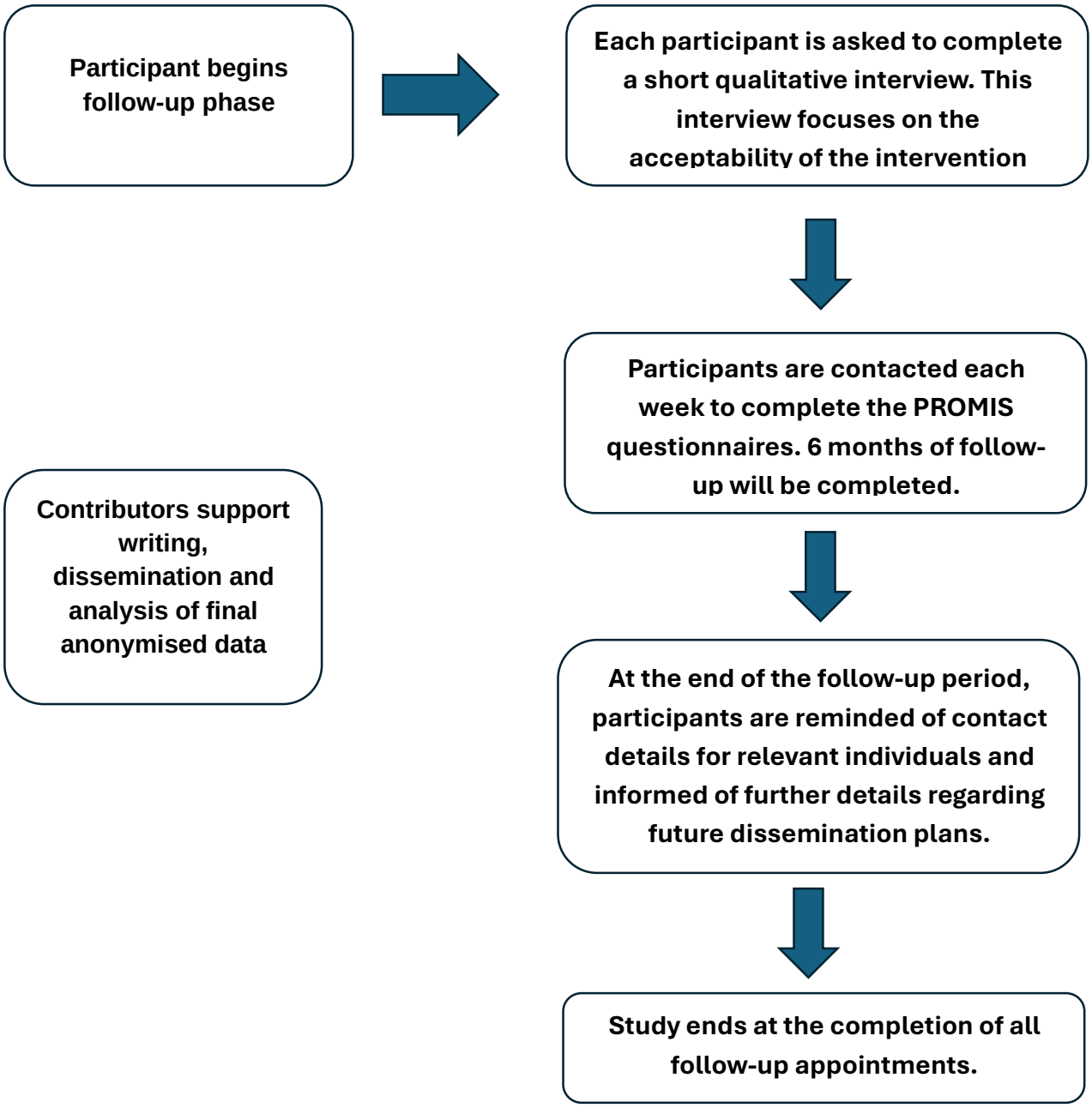
Phase 2 - Assessment



Phase 3 – Treatment



Phase 4 – Follow-up



1 BACKGROUND

Mentalisation Based Treatment (MBT) is an evidence-based approach for treating Borderline Personality Disorder in adults (Bateman and & Fonagy, 2009). It emphasizes building a therapeutic alliance, fostering epistemic trust, and nurturing the mentalizing process (Bateman & Fonagy, 2016). MBT is a structured psychological therapy program that includes weekly individual and group sessions.

Individuals with personality disorder often exhibit challenges in the mentalizing process (Bateman & Fonagy, 2010). Older adults, when assessed using the Mentalization Questionnaire, appear to have mentalizing strengths and weaknesses similar to younger adults, but with slightly more pronounced deficits in theory of mind (Brewer, et al, 2007)

Clinical populations of older adults also show significant mentalizing deficits compared to non-clinical older adult groups (Meinolf & Schulz, 2022). Given MBT's proven efficacy in enhancing mentalizing in younger populations and the observed mentalizing deficits in older clinical groups, MBT is a pertinent research area. While older adults seem to have broadly similar mentalizing deficits as younger adults, there's no evidence indicating they benefit from the same treatments. Anecdotal evidence suggests older adults may have distinct mentalizing needs, including increased suppression (Brummer et al., 2013), a higher prevalence of obsessive, avoidant, or dependent traits (Brudley, 2021), and potential physical or cognitive decline (Penders et al., 2020).

2 RATIONALE

To date, there have been no studies assessing the efficacy of MBT in older populations. Research on treatments for older adults with personality disorder is limited (van Alphen et al., 2015). While there is a growing interest in studying older adults with personality disorder, much of the research primarily focuses on assessment (Penders et al., 2020). However, studies on the effectiveness of Dialectical Behaviour Therapy (Lynch et al., 2007) and Schema Therapy (Videler et al., 2018; Videler et al., 2021; Khasho et al, 2023, Veenstra-Spruit et al., 2024) for older adults with personality disorder have been conducted and show potential.

The cost per person of outpatient treatment and prescribing is significantly higher per OA with CEN than any other age group with the same condition (King's Fund, 2008) Effective treatment of CENs in later life represents potential cost savings (Le, 2021), due to the burden associated with service use (King's fund, 2008), the prevalence of suicide (ONS, 2021), self-neglect (Sanders, 2022), and abuse (WHO, 2023).

The aims of this project accord with the NHS long term plan (NHS, 2019), which has clearly set out targets to increase the access for evidence-based treatment for OAs. This study will widen the access to research and treatment for OAs, develop an adapted model of care for OAs, and inform the design of a future RCT. Following this study, I plan to research the efficacy of a shortened version of MBT, which would be more cost effective, and feasible for use in primary care. This work, and future related projects will help to shape policy as well as NICE guidelines pertaining to treatment of CEN in OAs.

Interventions for OAs with CEN require significant adaptation, but there is no literature exploring systematically what sorts of adaptations OAs with CEN require. This study will provide necessary insight into how MBT, and CEN treatments more broadly, should be adapted for OAs..

When the research was discussed with our PPIE group, they said, “we are often forgotten about”, “I think its good that NHS is looking more into our problems”, "this is relevant to my wife who I care for", "this is relevant to me", and “I definitely think this is a good project”. With regards to MBT, one group member said that he feels more “useful” to society and his family as his functioning has improved following treatment. Another said he felt “less of a burden” and “more content with life” after receiving MBT.

2.1 Assessment and management of risk

The service which is being used for the study is an existing MBT service. No risks have been associated with participants being part of the programme. The treatment is a talking therapy, with no medical intervention. A large RCT which investigated the efficacy of MBT in working age adults found no adverse effects, or risks to participants. The intervention reduced incidents of self-harm, suicidal behaviour and hospital admission, and as such was risk reducing in that population (Bateman & Fonagy 2009).

Preliminary service evaluation data of the service which is to be studied indicated improvements in quality of life, personality functioning, social isolation, satisfaction, and suicidality (Jordan, 2023).

If risk incidents do arise, then the process of the therapy will be followed. This involved discussing and managing the cause of the risk in the treatment. Additionally the team will follow the NICE guidelines on the management of self-harm, which include

- Consideration to lethal means
- Problem solving cause of the crisis
- Increasing external support
- Validating and generating hope
- Ensuring timely follow up by team or wider care team
- Troubleshooting
- Adhering to care plan

Following any risk event, the participants care coordinator will be contacted, with the participant’s consent. Where consent is withdrawn, the team will take advice by the GMMH safeguarding service as to whether there is grounds to break confidentiality. This will be communicated to the participant, care team and study sponsor.

3 OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

3.1 Primary Outcomes:

<u>To evaluate the feasibility of MBT in older adults</u>

Feasibility of the study will be assessed by examining recruitment rate, consent rate, proportion of participants lost to follow-up, number of sessions attended, and drop out rate. The detailed table in the

upload section of this application illustrates the feasibility aims. This table shows the aims for the study with regard to above metrics.

To evaluate the acceptability of MBT in older adults

Acceptability will be evaluated by using Semi-structured qualitative interviews. These interviews will be delivered by 2-3 lived-experience researchers. I aim to determine what adaptations are indicated, integrating findings from qualitative and quantitative analysis to assess the feasibility of MBT. This will result in a fully adapted intervention.

I will use the Theoretical Framework for Acceptability to ensure the interviews assess acceptability. The interviews will focus on the seven constructs of acceptability (Paynter et al 2023):

To evaluate the change in personality functioning and social isolation in older adults undergoing MBT.

Changes in Personality Functioning Using the Level of Personality Functioning Scale Brief Form (LPFS-BF 2.0)

The LPFS 2.0 is a 12-item questionnaire that assesses personality functioning on a 4-point scale (Bender et al., 2011). This tool offers insights into the severity of personality pathology and sheds light on self and interpersonal functioning (Hutsebaut et al., 2016). The LPFS 2.0 has been empirically validated for older adults and has proven valuable in assessing personality functioning in this demographic (Stone et al., 2021).

To ensure adequate statistical power, the LPFS-BF will be administered weekly, following each individual therapy session. This frequent data collection will enhance the reliability of observed changes.

Loneliness Measured by the Social Isolation Short Form 4a

The Social Isolation Short Form 4a, derived from the more extensive UCLA Loneliness Scale, is a globally recognized tool for measuring loneliness. It aligns with the UK's Office for National Statistics recommendations for assessing loneliness (ONS, 2018) and has demonstrated reliability in gauging social isolation. Although a more detailed version, the Social Isolation Short Form 8a, is available and offers increased reliability, its length might be burdensome for weekly assessments. Therefore, this study proposes using the shorter form as a primary outcome. It will be administered weekly, following each individual therapy session.

Service use

To determine if there is any potential cost saving for the NHS, we will ask participants to consent to the research team to take a record of:

- Unplanned contact with the service
- A and E attendances
- Crisis line contacts
- Days in psychiatric hospital
- Days spent in general hospital

Self harm and suicidal behaviour

To determine if there has been any reduction in self-harm and suicidal behaviour, we will ask participants to consent to the research team to take a record of:

- Incidents of self-harm recorded in the clinical record

- Incidents where the participant has engaged in self-injury or self-neglect where their intent was to cause life threatening injury.

3.2 Secondary Outcome:

Other Routine Outcome Measures: Quality of Life, Patient Satisfaction, and Suicidality

In addition to the weekly assessments, participants will complete three other questionnaires at start of baseline, start of treatment, 6 months, 12 months, 18 months into the treatment and at the end of follow-up. These scales evaluate quality of life (ReQol), patient satisfaction (Dialogue), and suicidality (Columbia Scale).

***ReQol**: The Recovering Quality of Life (ReQol-10) scale tracks perceived changes in 'quality of life' over time. This 10-item scale is validated for individuals aged 16 and above. Scores range between 1 and 5, and a shift of 5 points on the scale indicates 'significant improvements' (Keetharuth et al., 2018).

Dialog The Dialog Satisfaction Scale gauges 'patient satisfaction' concerning their quality of life and the treatment they receive. This 11-item scale can be analysed item-wise or by calculating a mean score across all items. In this study, an overall mean score will be used, which ranges from 1 to 7. Scores above 5 suggest high satisfaction, potentially indicating that secondary mental health care might no longer be necessary. Conversely, scores below 4 highlight explicit dissatisfaction, warranting "particular attention" (Mosler et al., 2020).

Columbia Scale: The Columbia Suicidality Response Severity Scale (CSRSS) offers a preliminary indication of an individual's suicide risk. It contains 6 items and total or mean scores range from 0 to 1. While it should be used alongside other risk assessment tools, it serves as an initial screening tool for potential suicide risk in adults. The scale has shown sensitivity to changes in suicidality over time (Posner et al., 2011).

3.3 Outcome measures/endpoints

The endpoint for the study's outcome will be at 24 months. This will include 18 months of treatment, and 6 months of follow up.

3.4 Primary endpoint/outcome

Reductions in the LPFS 2.0 and Social Isolation short form 4.0 constitute a potential benefit. We have chosen these outcome measurements as they are used internationally, recommended by ICHOM, and have been validated for use in older adults. We are measuring personality functioning and social isolation as our primary measures. We are making comparisons between baseline functioning, and across participants to power the study. Measurements are taken weekly from start of the waiting period, for the duration of the treatment phase, and at follow up.

The primary endpoint will be whether personality function (as measured by the LPFS 2.0) and social isolation (as measured by the social isolation short form 4.0) have changed during 24 months. Significant decreases in both measures will indicate that MBT is effective at improving personality functioning and decreasing social isolation.

Additionally, if participants had any incidents of suicidal behaviour or self-harm, then a reduction in frequency of these events will constitute a potential benefit. As older people may keep suicidal behaviour and self-harm hidden, there is an expectation that participants may not make disclosures around these issues at baseline.

Taking data pertaining to service use may provide a limited indication as to whether any potential cost savings are associated with the intervention. Due to the limited number of participants, there is a recognition that statistical test on these findings may not reach statistical significance.

Any reduction in self-harm, suicidality, or service use may also represent efficacy.

3.5 Secondary endpoints/outcomes

Other endpoints include measures of ‘quality of life’, satisfaction, and suicidality. These measures will be taken at 6 monthly intervals.

3.6 Exploratory endpoints/outcomes

Qualitative interviews will be conducted to determine acceptability. See section on qualitative methods.

3.7 Table of endpoints/outcomes

Objectives	Outcome Measures	Timepoint(s) of evaluation of this outcome measure (if applicable)
Primary Objective Personality Functioning Social isolation Service use Self injury and suicidal behaviour Feasibility Acceptability	 LPFS 2.0. Social Isolation Short Form 4.0 Service use Suicidal behaviour Comparison of recruitment rate, drop out, and completion Thematic analysis of qualitative interview	Both questionnaires are given from day 0 till the end of data collection period at 24 months. Patients are requested to fill out these two questionnaires on a weekly basis during waiting period, treatment and follow up. Data to be taken from clinical records at 0,6,12,18, and 24 months Data to be taken at 0, 6, 12, 18, 24 months Analysis of data at 24 months
Secondary Objectives To evaluate quality of life (ReQol), patient satisfaction (Dialogue), and suicidality (Columbia Scale).	 ReQoL 10 Dialogue CSRSS (Columbia Scale)	Measures provided at 6 month intervals, at 0,6,12,18, and 24 months.

4 TRIAL DESIGN

Design:

This study uses a multiple single case series design, a form of Single Case Design (SCD). It will employ quantitative methods to track changes in personality functioning over time using the LPFS 2.0 scale and changes in loneliness using the Social Isolation Short Form 4a. Data from a participant will be compared within the participant between treatment phases (baseline, treatment and follow up), so participants serve as their own controls. Initial data collection will take place at an outpatient clinic in Manchester, United Kingdom. Data will be gathered weekly away from the MBT clinic. The research team, primarily involved in clinical practice, will utilize an established older adult MBT service in Manchester for the sample. This approach mitigates some challenges of assessing multi-modal

psychological treatments, as there's no need for the research team to establish a new therapy program.

A multiple single case series design will enhance experimental control since participants serve as their own control. In order to get a stable and representative estimate of the baseline state all participants will have a waiting period of 8 weeks before starting treatment. Participants who drop out of the research completely during this phase won't have any further data collected We will ask anyone who drops out of the therapy to consent to providing data relating to their reason for drop out.

The strength of a SCD study is that it produces statistical power by taking a large number of data points with a small number of participants. Due to the high number of data points per participant, change to outcome measurements can accurately be described. Additionally, due to the low number of participants, there is a lower cost to the intervention, which means that it is more feasible to carry out long term studies of psychological treatments for personality disorder, which often span multiple years.

Therapists providing MBT will not know the outcome scores provided by participants. Participants will complete these measures independently away from the clinic each session. These measures will be placed in an envelope and sent to a research assistant who will input the data into an anonymized database inaccessible to therapists. If participants need assistance with the measures, the research assistant will help in person before the session starts. Each participant will receive an anonymous participant number, unknown to the clinical team. There is increasing interest in adaptive designs for clinical trials, defined as the use of accumulating data to decide how to modify aspects of a trial as it continues, without undermining the validity and integrity of the trial. Examples of potential adaptations include stopping the trial early, modifying the allocation ratio, re-estimating the sample size, and changing the eligibility criteria. The most valid adaptive designs are those in which the opportunity to make adaptations is based on pre-specified decision rules that are fully documented in the protocol.

Qualitative interviews will be conducted at the beginning and end of the study using the theoretical framework of acceptability. Thematic analysis of these interviews will provide insight into the acceptability of MBT for older adults, as well as required adaptations.

Data relating to the recruitment rate, participation, drop-out, and completion of the intervention will be analysed to determine feasibility.

5 TRIAL SETTING

The trial will take place in one centre in an extant MBT for older adults service. The service is already operational, and as such local policies and procedures will be adhered to except where explicitly mentioned.

The treatment team will comprise of psychotherapists who have completed their basic and follow-up MBT training.

The patient population will be older people (over 65) in Manchester, who meet the criteria for personality disorder, or who are sub threshold to a diagnosis (score one point lower than the cutoff point in DSM-5). Participants will be recruited from later life CMHTs in Greater Manchester.

6 PARTICIPANT ELIGIBILITY CRITERIA

6.1 Inclusion criteria

- Resident of Manchester, England.

- Aged 65 or over.

- Confirmed Personality Disorder diagnosis via the Structured Clinical Interview for DSM 5 Personality Disorders (SCID-5-PD) or significant associated traits (Personality Disorder trait specified according to DSM-5). If individuals don't fully meet the criteria, their sub-threshold presentation will be explicitly noted (one criterium less than the cut off point for the personality disorder).

- Ability to provide informed consent.

- Under the care of a local community mental health team.

6.2 Exclusion criteria

- Primary issues related to psychosis, dementia, or mild cognitive impairment.

- Primary concerns associated with anti-social personality disorder or significant violent/aggressive traits.

- Ability to attend the outpatient clinic (free transport provided).

A diagnosis of autism won't be an exclusion criterion if all other inclusion criteria are met. The study's service site has seen referrals for individuals with autism over the past 18 months, and they've shown improvement in their outcome measures.

7 TRIAL PROCEDURES

Process	Time
Community Mental Health Teams, and Therapy Hub Teams are notified of recruitment by poster, visits to team meetings, and email.	Prior to commencement of study
CMHT or Therapy Hub staff to discuss the trial with existing patients of the CMHT service. CMHT staff will gain consent for the trial team to contact the participant.	Prior to the commencement of study
Participant contacted by trial team. Brief information about trial provided. If participant is provisionally interested in joining the study, then they will be offered an initial appointment to be given the full participation information leaflet.	Prior to the commencement of study
Following the initial meeting, the participant will be given 7 days to decide if they want to be part of the trial.	0 days

After 7 days, the participant will be invited back to sign informed consent forms or withdraw from the study.	At 7 days
Participant contacted to advise them of the date of the introductory group.	At 1 months
Participants that complete the introductory group will become part of the baseline phase of the study.	At 4 months
Participants will have a baseline waiting period of 8 weeks. Outcome data will be collected during this phase. The participant will also start producing their MBT passport, and assessment collaboratively with a member of the treatment team.	At 8 months
Participants will begin MBT treatment for a period of 18 months. Outcome data taken weekly. Secondary outcomes and review of service use/self-harm taken every 6 months.	At 24-26 months
Follow up period will begin. Primary outcome data taken weekly.	Between 24-26 and 30-32 months
Qualitative interviews take place.	Between 30-34 months
Study end point. Data analysis and publication phase begins.	30-36 months
Dissemination of findings, publication.	Within 12 months following the last follow up data point of the final participant.

7.1 Recruitment

Participants will come from a Later Life MBT service in Manchester, which exclusively serves older adults and offers a comprehensive MBT program. The study aims to collect data from 10 older adults for an 18-month treatment duration. As the population is likely to have multiple physical comorbidities, the study will aim to recruit 14 participants, with the expectation that there will be some attrition in the screening and introductory phases.

Single Case Experimental Design studies consider several factors for power, including participant count, observations, inter-participant correlation, and the likelihood of false positives (Shadish et al., 2014). To ensure adequate power, we'll collect weekly outcome data on personality functioning using the LPFS 2.0 and data on loneliness using the Social Isolation Short Form 4a before, during and after the 18 months treatment from the participants.

Participants will be sourced from an existing later life MBT service. All will have a confirmed personality disorder diagnosis based on the DSM-5 structured clinical interview (SCID-5-PD) or sub-threshold. Those not meeting this criteria will not be excluded from the service if MBT is clinically indicated. When participants fulfil only one criterium under the cutoff point at the SCID5-PD interview, they will also be included in the study, but it will be clearly indicated that they are ‘sub-threshold’ to a full diagnosis of personality disorder.

Typically, referrals to the later life MBT service come from older adult community-based mental health teams in England, overseen by the NHS. All study participants will receive standard treatment, including regular meetings with a mental health professional and periodic reviews with a consultant psychiatrist. No restrictions will be placed on participants seeking other treatments, though concurrent psychological treatments might be contraindicated.

All participants will be aged 65 or older, with no upper age limit. The study won't control for other demographics, except that participants must reside in Manchester. Free transport can be arranged for participants, and in rare cases, treatment can be provided at home or in hospital wards due to frequent treatment disruptions from physical ailments or illnesses in older adults.

7.1.1 Participant identification

To guarantee confidentiality, participants will receive both written and verbal information detailing the scope and limitations of confidentiality within the study. Information shared by participants will remain confidential and will not be disclosed to anyone outside the clinical or research team, barring urgent, life-saving circumstances. Outcome measure data will be securely stored, and participants will be allocated a unique identification number to safeguard their identities.

Identification of potential participants will be completed by members of the participants usual clinical team. No further recruitment will take place outside of later life community mental health teams.

Members of the research team will not have prior access to potential participants, who will be referred to the study by the community mental health teams. During the study, the therapists delivering the study intervention will record clinical information on the participants PARIS record, which is the local recording system used by the NHS trust. Outcome measurement data will be pseudonymized and will not be identifiable to members of the clinical team.

7.1.2 Screening

Before starting the program, participants undergo screening to assess their suitability for MBT. This stage addresses practical issues like attendance, transportation, and necessary adjustments for disabilities. Participants also receive an overview of MBT, its duration, and the existing evidence supporting its efficacy.

All participants will be assessed before commencing the study as to whether they meet the criteria for personality disorder. This will be confirmed on the DSM-5 structured clinical interview (SCID-5-PD). When participants fulfil only one criterium under the cutoff point, they will also be included in the study, but it will be clearly indicated that they are 'sub-threshold' to a full diagnosis of personality disorder.

Those not meeting these criteria will not be excluded from the service if MBT is clinically indicated, but they will not be included in the data collection, or wider research study. If MBT is not clinically indicated, then the clinical team will discuss appropriate care following the assessment process with the local CMHT.

7.1.3 Payment

If the NIHR bid is successful, participants will be provided a voucher for their participation in the study.

7.2 Consent

The Chief Investigator (CI) retains overall responsibility for the conduct of the research, this includes the taking of informed consent of participants at their site. They must ensure that any person delegated responsibility to participate in the informed consent process is duly authorised, trained and competent to participate according to the ethically approved protocol, principles of Good Clinical Practice (GCP) and Declaration of Helsinki. If delegation of consent is acceptable then details should be provided.

Informed consent must be obtained prior to the participant undergoing procedures that are specifically for the purposes of the trial and are out-with standard routine care (including the collection of identifiable participant data unless the trial has prior approval from the Confidentiality Advisory Group (CAG) and the Research Ethics Committee (REC)).

The right of a participant to refuse participation without giving reasons must be respected.

The participant must remain free to withdraw at any time from the trial without giving reasons and without prejudicing his/her further treatment and must be provided with a contact point where he/she may obtain further information about the trial. Data and samples collected up to the point of withdrawal can only be used after withdrawal if the participant has consented for this. Any intention to utilise such data should be outlined in the consent literature. Where a participant is required to re-consent or new information is required to be provided to a participant it is the responsibility of the PI to ensure this is done in a timely manner.

The CI takes responsibility for ensuring that all vulnerable participants are protected and participate voluntarily in an environment free from coercion or undue influence.

If a participant cannot read or write, or will require a translator, or has a cognitive impairment, appropriate alternative methods for supporting the informed consent process will be employed. This

may include allowing a witness to sign on a participant's behalf (in the case of problems with reading or writing), or allowing someone to date the form on behalf of the participant, or providing Participant Information Sheets in other languages or in a format easily understood by the participant population (in the case of minors or cognitive impairment).

Translation should be conducted by an NHS interpreter from the local interpretation service. The interpreter should be present in person for the duration of the consent process. Written information must be translated by an independent service that is able to back translate the document independently.

Regardless as to participant background, language, or cognitive impairment, they should be able to discuss the research with a member of the team knowledgeable about the research about the nature and objectives of the trial and possible risks associated with their participation, as well as a competent individual that can translate or support the communication needs of the participant.

Written material, including the participation information sheet and consent forms will be sent to the REC for approval.

Following the onboarding process, participants will have 7 days to consider the information, and a further appointment to ask any questions, before giving informed consent.

All participants must have capacity to decide whether or not to consent to being a participant of the study. Individuals that do not have capacity to make this decision will not be able to participate in the study, due to the nature of the intervention.

A capable person will:

- understand the purpose and nature of the research
- understand what the research involves, its benefits (or lack of benefits), risks and burdens
- understand the alternatives to taking part
- be able to retain the information long enough to make an effective decision
- be able to make a free choice
- be capable of making this particular decision at the time it needs to be made (though their capacity may fluctuate, and they may be capable of making some decisions but not others depending on their complexity)
- where participants are capable of consenting for themselves but are particularly susceptible to coercion, it is important to explain how their interests will be protected

A person is assumed to have the mental capacity to make a decision unless it is shown to be absent. Mental capacity is considered to be lacking if, in a specific circumstance, a person is unable to make a decision for him or herself because of impairment or a disturbance in the functioning of their mind or brain. In practice for participants with mental incapacity this means that they should not be included in clinical trials if the same results can be obtained using persons capable of giving consent and should only be included where there are grounds for expecting that their taking part will be of direct benefit to that participant, thereby outweighing the risks. The Mental Capacity Act 2005 does not apply to CTIMPs.

All these procedures will be taken into consideration in this study.

7.2.1 Consent Process

Participants that are referred to the study will be asked for consent to be contacted by a member of the community mental health team. If they consent to be contacted, a member of the MBT clincal team will contact them to arrange a face to face appointment. In this appointment the researcher will explain the participant information sheet to the participant, and answer any questions that the participant has about the study. They will be given 7 days to think about whether they would like to take part in the study. After this time, the team will contact them to determine whether they would like to consent to the study. The participant will be asked to read and sign the consent form, if they wish to be part of the study. They will be advised that they can withdraw consent at any time of the study without any risk to their clinical treatment. The consent forms will be scanned and stored securely on NHS servers, and the paper copy will be stored under lock and key until the end of the study. Both documents will be destroyed following the study.

7.3 Baseline data

Participants will be asked to provide demographic information about gender, age, and ethnicity at baseline. This will help the trial determine whether the study has been inclusive of a demographic representative of the local population.

Baseline data will also be taken for each of the 5 questionnaires used as outcome measures, and for data relating to service use, self-harm, and suicidality. This will enable the research study to sufficiently detect meaningful change.

Diagnostic data will also be taken – particularly pertaining to the results of each participant scores on the DSM-5 interview, SCID-5-PD, which will be used to determine whether the participant meets the inclusion criteria for the study.

7.4 Trial assessments

The timing of filling out the questionnaires will be:

- Weekly - LPFS 2.0. and Social Isolation Short Form 4.0.
- Every six months - ReQoL,10, Dialogue and CSRSS. Review of medical records to indicate changes to service use, self-harm, and suicidal behaviour.

All five questionnaires are taken as routine measures every 6 months in clinical treatment within the MBT service. The major change to the data collection is that the LPFS 2.0 and the Social Isolation Short Form 4.0 will be taken weekly.

7.5 Long term follow-up assessments

In the 6 months after the treatment phase the participant will be asked to fill out the primary outcome questionnaires (LPFS 2.0. and Social Isolation Short Form 4.0.) on a weekly basis and the secondary outcome questionnaires (ReQoL,10, Dialogue and CSRSS) at the end of the follow up period for the purpose of the scientific research.

7.6 Qualitative assessments

At the end of the follow up period, each participant will be asked to participate in a brief semi-structured interview. The purpose of this qualitative assessment will be two-fold. The first set of questions will be designed to determine the participants experience of being part of a long term research study, their experience of filling out weekly questionnaires, and their experience of adhering to the trial protocol. The second set of questions will be focused on the intervention, and will aim to understand the participants experience of the MBT programme generally, how relevant they felt MBT was to them as an older adult, their view on the impact MBT has had upon their mental health, as well as any adaptations or changes they think might be important to consider in future developments of MBT.

The qualitative assessments will be conducted by the CI, another member of the team or a person with lived experience at the end of the follow up period, in order to reduce any bias, or impact on participant's treatment. Clinicians will not interview participants that they have seen for individual therapy.

7.7 Withdrawal criteria

Participants can withdraw from the trial at any time, for any reason. They may choose to withdraw from different elements of the trial including:

- Withdrawal from MBT treatment only.
- Withdrawal from data collection.
- Withdrawal from the qualitative interviews.
- Withdrawal from any analysis of data from the participant's medical records.

If the participant wishes to withdraw, then they can do so at any time. If it is made clear, their rationale for withdrawing will be recorded and stored securely, and this will be made clear in the final report of the study. Participants may be replaced if the dropout rate is such that the statistical power of the study will be negatively impacted. This will increase the length of the trial, and as such an amendment from the REC will need to be sought, if the anticipated length of the trial will exceed 3 years.

Any participants that withdraw from the trial will be asked if they would like to continue to be involved in data collection, and follow up. They can withdraw from this aspect of the study.

If there are multiple severe adverse events, the trial may be stopped, if there is a direct link between the study and the adverse event.

In the event of a participant withdrawing from the study, they will be asked if the data collected to that point can be continued to be used in the data analysis. If they withdraw consent for their data to be used, it will be destroyed. All participants that withdraw will be offered an exit interview, using the theoretical framework of acceptability. Participants can refuse this interview with no impact to their clinical care. Participants can withdraw from the study but continue to access the treatment.

7.8 Storage and analysis of clinical samples

Not applicable.

7.9 End of trial

The trial will be considered complete when all participants have completed 18 months of treatment, and have completed 6 months of follow-up. The total length of the study may be up to 3 years.

8 TRIAL INTERVENTION

8.1

All participants will undergo a comprehensive Mentalisation Based Treatment (MBT) program.

This includes a weekly individual session lasting 50 minutes and a weekly group session of 75 minutes. The treatment will last for 18 months, as per the time specified in the treatment manual. The four clinicians delivering the treatment will participate in a weekly 90-minute peer supervision and receive bi-weekly group supervision of 60 minutes from an MBT expert, who is an accredited MBT supervisor. All these clinicians either have 'practitioner level status in MBT' or are in a program working towards this status.

9 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

9.1 Definitions

Term	Definition
Adverse Event (AE)	Any untoward occurrence in a participant to whom an intervention has been administered, including occurrences which are not necessarily caused by or related to that product.
Serious Adverse Event (SAE)	A serious adverse event is any untoward that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

9.2 Operational definitions for (S)AEs

1) Suicide

In the event that participant dies as the result of suicide, or the cause of a participant's death is suspected to be suicide, then this will be reported to the sponsor using the case report form.

The research team will report the event to the Sponsor, including the participant number, date of incident, as well as any information contained in an investigation that demonstrates any causative link between the study and the severe adverse event.

Life-threatening suicidal behaviour will be recorded throughout the study if it takes place.

9.3 Safety of intervention

There is no evidence to suggest that MBT causes serious or severe adverse events such as suicide. An RCT examining the impact that MBT has upon suicidal adults (including 168 participants) found a significant reduction in life threatening suicide attempts, serious self-harm incidents and hospitalisation (Bateman & Fonagy 2009). At baseline, all participants had engaged in self-harm, suicide attempts or had been admitted to hospital. At 8 year follow up, 75% of the follow up group had no incidents of self-harm, suicidal behaviour or hospital admission. As such, it is likely that MBT is protective against suicide and self-harm in adults.

9.4 Endpoints for the intervention

If participants end their life due to suicide which is linked to the intervention, the study will be stopped.

9.5 Recording and reporting of SAEs

Serious adverse events relating to suicide will be reported immediately to the sponsor. If a participant dies by suicide 6 months after the stud has ended, this will not be reported to the sponsor.

All SAEs occurring from the time of written informed consent until 6 months post cessation of trial treatment must be recorded on the CRF, and sent to the Sponsor **within 24 hours** of the research staff becoming aware of the event. Once all resulting queries have been resolved, the Sponsor will request the original form should also be posted to the Sponsor and a copy to be retained on site.

For each SAEs the following information will be collected:

- full details in medical terms and case description
- event duration (start and end dates, if applicable)
- action taken
- outcome
- seriousness criteria
- causality (i.e. relatedness to trial drug / investigation), in the opinion of the investigator
- whether the event would be considered anticipated.

Any change of condition or other follow-up information should be faxed to the Sponsor as soon as it is available or at least within 24 hours of the information becoming available. Events will be followed up until the event has resolved or a final outcome has been reached."

9.6 Responsibilities

Chief Investigator (CI):

Checking for AEs and ARs when participants attend for treatment / follow-up.

1. Using judgement in assigning seriousness, causality and whether the event/reaction was anticipated
2. Using judgement in assigning seriousness and causality and providing an opinion on whether the event/reaction was anticipated
3. Ensuring that all SAEs are recorded and reported to the sponsor within 24 hours of becoming aware of the event and provide further follow-up information as soon as available. Ensuring that SAEs are chased with Sponsor if a record of receipt is not received within 2 working days of initial reporting.
4. Ensuring that AEs are recorded and reported to the sponsor in line with the requirements of the protocol.
5. Clinical oversight of the safety of patients participating in the trial, including an ongoing review of the risk / benefit.
6. Review of specific SAEs in accordance with the trial risk assessment and protocol as detailed in the Trial Monitoring Plan.
7. Preparing the clinical sections and final sign off of the Development Safety Update Report (DSUR).

Sponsor:

1. Central data collection and verification of AEs, SAEs according to the trial protocol onto a database.
2. Reporting safety information to the CI for the ongoing assessment of the risk according to the Trial Monitoring Plan.
3. Reporting safety information to the Trial Steering Committee (TSC)) according to the Trial Monitoring Plan.

Trial Steering Committee (TSC):

In accordance with the Trial Terms of Reference for the TSC, periodically reviewing safety data and liaising with the DMC regarding safety issues. This meeting reoccurs every 4 weeks, reducing to every 8 weeks once data collection has commenced.

In accordance with the Trial Terms of Reference, periodically reviewing overall safety data to determine patterns and trends of events, or to identify safety issues, which would not be apparent on an individual case basis.

9.7 Notification of deaths

All deaths will be reported to the sponsor irrespective of whether the death is related to disease progression, the IMP, or an unrelated event". As above, any death that occurs after the follow up period of the study will not be reported to the sponsor.

10 STATISTICS AND DATA ANALYSIS

10.1 Sample size calculation

We used an app that was designed to calculate power in multiple single case series studies (Single Case Designs (architecta.shinyapps.io/SingleCaseDesigns_v3/)). A permutation distance test, which is useful in this design because it corrects for auto-correlation, showed that with sample size of 10 and Cohen's d of 1 the power is close to 1. We are expecting some participants may drop out of the study, and so aim to recruit 14 potential participants.

10.2 Planned recruitment rate

The older adult MBT service in Manchester receives on average 2 applications of new patients per month and runs one group of MBT treatment of 8 patients. Each year, the service runs on average 2 introductory groups of 6 patients each. We are planning to start a second MBT treatment group in 2025. The sample size of 10-14 participants should be possible to achieve when the data collection of this study runs for a period of 3 years.

10.3 Statistical analysis plan

10.3.1 Summary of baseline data and flow of patients

This study uses a multiple single case series design, a form of Single Case Design (SCD). It will employ quantitative methods to track changes in personality functioning over time using the LPFS 2.0 scale and changes in loneliness using the Social Isolation Short Form 4a. Data from a participant will be compared within the participant between treatment phases (baseline, treatment and follow up), so participants serve as their own controls.

There is no comparison between groups possible nor necessary in this design.

10.3.2 Primary outcome analysis

Primary outcome measures are personality functioning, using the LPFS 2.0 scale, and changes in loneliness, using the Social Isolation Short Form 4a. These measures will be filled out on a weekly basis. The line graphs of the data will be inspected visually first, to see the pattern of observations. We will analyse for trend (progress over time), level of change and stability (variability) within the three phases using within-condition and between-condition visual inspection analyses. The median, median regression, stability envelope of the regression and TAU-U (Parker et al. 2011) will be calculated for each phase, with the median level of change chosen to mitigate the influence of outliers in the data. We will test the hypothesis that the median in the baseline phase exceeds the medians of the treatment and follow-up phase. In addition, non-parametric randomisation tests will be used to statistically evaluate the difference in mean and median scores of the phases statistically. The permutation distance test (Vroegindeweij et al. 2023) will be used since this randomisation test corrects for autocorrelation before the permutation test takes place. In this test a p-value is calculated

for every participant. Moreover, a p-value for the group will also be calculated using the property of p-values that they are uniformly distributed under the null-hypothesis. Using this property, the p-value of the group effect is the probability of a series of individual p-values given the null hypothesis (Onghena et all. 2005). In this test a range of baseline lengths, i.e. the number of baseline measurements, is determined and participants are randomly assigned to one of these baseline lengths. In this test a null distribution of 1000 mean differences is calculated and it is counted how many of the random mean differences is as extreme or more extreme than the observed mean difference (Bouwmeester, 2021).

Service use and self-harm data will be compared between the treatment phases with nonparametric test for repeated measures (Friedman Test), depending on the fulfilment of the requirements for parametric test.

10.3.3 Secondary outcome analysis

Participants will complete three questionnaires at start of baseline, at start of treatment, 6 months, 12 months, and 18 months into the treatment and at the end of follow up. These scales evaluate quality of life (ReQol), patient satisfaction (Dialogue), and suicidality (Columbia Scale). Data from these questionnaires will be compared between the treatment phases with nonparametric test for repeated measures (Friedman Test). To evaluate whether change over time of the individuals scores on the ReQol-10, Dialogue and Columbia Scale a Reliable Change Index will be used.

Data from the qualitative interviews will be analysed through thematic analysis.

10.4 Subgroup analyses

Not applicable

10.5 Adjusted analysis

Not applicable

10.6 Interim analysis and criteria for the premature termination of the trial

In the event that an SAE occurs which is linked to the intervention, the study will be stopped.

10.7 Participant population

Data of patients who agree to participate in the study will be used for data-analysis. If the patient wants to stop participating in the study the patient will be asked if we can use the collected data up to and including that point in time.

10.8 Procedure(s) to account for missing or spurious data

The primary outcome data will be gathered weekly before each participant's individual MBT session, either by the therapist or via phone if the participant is absent. The secondary outcome measures will be collected by the research assistant. Patients will be attending at least weekly sessions at the location, so the research assistant and therapists will have regular contact with the participants to remind them to fill out the questionnaires.

In case of missing data we will try to find the reason that the participant did not fill out the questionnaire. In case of random missing data the data analysis contain an implicit imputation. In case of drop-out we will try to describe the reason for drop-out, because we are interested whether this treatment is feasible for older patients with personality disorders.

10.9 Other statistical considerations.

In case of slow recruitment rate an amendment to this protocol will be submitted to request for extension the recruitment period of 3 years.

10.10 Economic evaluation

Not applicable

11 DATA MANAGEMENT

11.1 Data collection tools and source document identification

Source documents obtained standardised tools

All source documents below are validated tools used to measure outcomes, or to in the use of establishing diagnostic criteria for inclusion.

Primary outcome tools:

Changes in Personality Functioning Using the Level of Personality Functioning Scale Brief Form (LPFS-BF 2.0)

The main objective of this study is to evaluate the change in personality functioning and social isolation in older adults undergoing MBT.

The LPFS 2.0 is a 12-item questionnaire that assesses personality functioning on a 4-point scale (Bender et al., 2011). This tool offers insights into the severity of personality pathology and sheds light on self and interpersonal functioning (Hutsebaut et al., 2016). The LPFS 2.0 has been empirically validated for older adults and has proven valuable in assessing personality functioning in this demographic (Stone et al., 2021).

To ensure adequate statistical power, the LPFS-BF will be administered weekly, following each individual therapy session. This frequent data collection will enhance the reliability of observed changes.

Loneliness Measured by the Social Isolation Short Form 4a

The Social Isolation Short Form 4a, derived from the more extensive UCLA Loneliness Scale, is a globally recognized tool for measuring loneliness. It aligns with the UK's Office for National Statistics recommendations for assessing loneliness (ONS, 2018) and has demonstrated reliability in gauging social isolation. Although a more detailed version, the Social Isolation Short Form 8a, is available and offers increased reliability, its length might be burdensome for weekly assessments. Therefore, this study proposes using the shorter form as a primary outcome. It will be administered weekly too.

Secondary Outcome:

Other Routine Outcome Measures: Quality of Life, Patient Satisfaction, and Suicidality

In addition to the weekly assessments, participants will complete three other questionnaires at start of baseline, start of treatment, 6 months, 12 months, and 18 months into the treatment and at end of follow up. These scales evaluate quality of life (ReQol), patient satisfaction (Dialogue), and suicidality (Columbia Scale).

**ReQol*: The Recovering Quality of Life (ReQol-10) scale tracks perceived changes in 'quality of life' over time. This 10-item scale is validated for individuals aged 16 and above. Scores range between 1 and 5, and a shift of 5 points on the scale indicates 'significant improvements' (Keetharuth et al., 2018).

Dialogue: The Dialogue Satisfaction Scale gauges 'patient satisfaction' concerning their quality of life and the treatment they receive. This 11-item scale can be analysed item-wise or by calculating a mean score across all items. In this study, an overall mean score will be used, which ranges from 1 to 7. Scores above 5 suggest high satisfaction, potentially indicating that secondary mental health care might no longer be necessary. Conversely, scores below 4 highlight explicit dissatisfaction, warranting "particular attention" (Mosler et al., 2020).

Columbia Scale: The Columbia Suicidality Response Severity Scale (CSRSS) offers a preliminary indication of an individual's suicide risk. It contains xx items and total or mean scores range from 0 to 1. While it should be used alongside other risk assessment tools, it serves as an initial screening tool for potential suicide risk in adults. The scale has shown sensitivity to changes in suicidality over time (Posner et al., 2011).

Initial screen and evaluation:

Structured Clinical Interview for DSM-5 Personality Disorders

This measure is a validated tool for assessing DSM-5 personality disorders. It has been used with both younger and older adults. There is a procedure for delivering the interview and scoring it. All three members of the team that will deliver this interview have been trained in its use.

Additional processes

To ensure adequate data collection, all outcome measurement forms will be provided to each participant weekly, at their face to face appointment. If the participant does not attend a session, then they will be asked to complete the questionnaire at the next available appointment. Data will be securely stored on a database that will not be accessible by the treatment team, and will only be accessible by the data management and collection team.

11.2 Data handling and record keeping

Four systems will be used to manage data. The PARIS system for clinical data, a secure database for outcome measures, SPSS software to manage statistics, and the Single Case Designs app to managed data relating to SCD portion of the study.

For clinical data, including records of appointments, and clinical communication, this will be recorded on PARIS, which is the local NHS trust’s recording software. Standard local processes will be followed, and adhered to.

Outcome data will be securely stored on a database, validated by the research and development team. The SOPs for the use of the system will be followed, and an audit trail of data changes will be maintained to ensure that there is no deletion of entered data. The system will be secure to protect against unauthorized access. Upon the commencement of the trial, a list of the individuals authorized to make data changes will be compiled. They will be responsible for data entry, maintain adequate backups of the data, and safeguarding the blinding of the trial to the clinical team. Source data will be archived. If data are transformed during processing, it should always be possible to compare the original data and observations with the processed data. Participant identification codes will be used to ensure identification of all the data reported for each participant.

11.3 Access to Data

Direct access will be granted to authorised representatives from the Sponsor, host institution and the regulatory authorities to permit trial-related monitoring, audits and inspections- in line with participant consent.

11.4 Archiving

Outcome data will be archived for 5 years following the end of the study. They will be stored under lock and key at The Therapy Hub, 70 Daisy Bank Road, Longsight, Manchester. Signed consent forms, participant information sheets, will also be stored for 5 years following the end of the study, in the event that any issues arise following the end of the study. Destruction of essential documents will require authorisation from the Sponsor, GMMH research and development.

12 MONITORING, AUDIT & INSPECTION

Three areas of the study require monitoring. These include:

a) Consent, participant information onboarding process,

All initial appointments will be video recorded using MS Teams and stored. The video recordings will be reviewed for adherence to the protocol by the CI at the beginning of the study. All participants must be given all information in the participant information sheet verbally, as well as additional written copies to review following the first contact. Signed consent forms will be reviewed by the CI once at the beginning of the study for all participants. The CI will be based on site, where all of the initial contacts will occur.

b) Adherence to MBT treatment manual

All MBT individual and group sessions will be recorded. A sample of these recordings will be reviewed every 4 weeks by an accredited MBT supervisor. The research team will review tapes as peers throughout the programme, using the adherence checklist, as part of the weekly MBT clinical team meeting.

c) Data input, management, and storage.

The data collection team will be responsible for ensuring that the data collection, management, and storage accords with the study protocol. The CI for the study is part of the clinical team, and so will be unable to access the database containing outcome scores. As such the data collection team will peer review their adherence. The CI will supervise the members of the data collection team, ensuring that they are aware of the processes and procedures required. A named person external to the data collection team will monitor the database every 6 weeks for adherence to the protocol, and reporting any deviations to the CI.

d) GMMH R & I audit and monitoring

This study will be subject to audit and monitoring by GMMH's R and I team. This monitoring will occur in line with the relevant SOP (RDSOP11)

13 ETHICAL AND REGULATORY CONSIDERATIONS

13.1 Research Ethics Committee (REC) review & reports

Before the start of the trial, approval will be sought from a REC for the trial protocol, informed consent forms and outcome measurement forms.

If amendments to the trial protocol are required, they will not be implemented until approval by the REC. All correspondence regarding the ethical review process will be stored in a secure folder on an NHS sever.

A progress report will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the trial is declared ended. At the end of the trial, the CI will notify the REC of the end of the trial.

At the end of the trial, a final report, with results and notes of any publications will be prepared within one year following the end of the trial.

13.2 Peer review

This protocol has been reviewed by the academic sponsor, Tilburg University, and the NHS trust sponsoring the study, Greater Manchester Mental Health Trust Research and Development Department.

13.3 Public and Patient Involvement

Patients have been involved in the design of the research. Early drafts of the design were shared with the Manchester Expert by Experience group, who gave comments on design of the participant information sheet, support processes afforded to participants, and views on making the data collection processes less onerous to participants. The research proposal has been discussed a total of three times with the group, who have received draft copies of the abridged protocol. The trial progress will be regularly reviewed by the group at each monthly meeting.

13.4 Regulatory Compliance

The trial will not commence until a Clinical Trial Authorisation (CTA) is obtained from the REC

Approval to undertake the research has been sought from both the management team at Later Life Community Mental Health Services at GMMH, as well as the Research and Innovation Team at GMMG.

For any amendment to the study, the Chief Investigator or designee, in agreement with the sponsor will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (R&D departments at NHS sites as well as the study delivery team) so they can put the necessary arrangements in place to implement the amendment to confirm their support for the study as amended.

13.5 Protocol compliance

Prospective, planned deviations or waivers to the protocol are not allowed under the UK regulations on Clinical Trials and must not be use. Accidental protocol deviations can happen at any time. They must be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately. Deviations from the protocol which are found to frequently recur are not acceptable, will require immediate action and could potentially be classified as a serious breach.

13.6 Notification of Serious Breaches to GCP and/or the protocol

A “serious breach” is a breach which is likely to effect to a significant degree –

(a) the safety or physical or mental integrity of the participants of the trial; or
(b) the scientific value of the trial

Should a serious breach occur:

- the sponsor will be notified immediately of any case where the above definition applies during the trial conduct phase
- the sponsor of a clinical trial will notify the licensing authority in writing of any serious breach of

  (a) the conditions and principles of GCP in connection with that trial; or
  (b) the protocol relating to that trial, as amended from time to time, within 7 days of becoming aware of that breach

13.7 Data protection and patient confidentiality

All investigators and trial site staff must comply with the requirements of the Data Protection Act 1998 with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act’s core principles.

Personal information is collected by members of the research team. Hardcopies of information will be kept secure under lock and key. Digitalised date will be managed by:

  - the creation of coded, depersonalised data where the participant’s identifying information is replaced by an unrelated sequence of characters
  - secure maintenance of the data and the linking code in separate locations using encrypted digital files within password protected folders and storage media
  - limiting access to the minimum number of individuals necessary for quality control, audit, and analysis

- how the confidentiality of data will be preserved when the data are transmitted to sponsors and co-investigators

No identifiable data will be shared with sponsors or co-investigators. For data analysis at the end of the study, raw data will be used only, and participant numbers will be used rather than any identifier that could be used to identify the participant. The data will be stored for 2 years. The CI, Luke Jordan, is ultimately responsible for the management of the data.

13.8 Financial and other competing interests for the chief investigator, PIs at each site and committee members for the overall trial management

No financial or other competing interests have been identified.

13.9 Indemnity

The trial is studying an extant NHS service, which already sees patients accessing MBT. All participants will be NHS patients, and as such existing arrangements surrounding indemnity in the NHS will be used.

13.10 Post trial care

Following the end of the trial, all participants will remain under the care of the local community mental health team, until they their care is reviewed by that service, and the responsible clinician in charge of that person's care is satisfied that they no longer need further care.

In addition to this, all participants of the MBT programme can be referred back to the service for further treatment should it be required.

13.11 Access to the final trial dataset

All members of the steering group will have access to the final dataset. Those individuals are named at the beginning of this protocol.

14 DISSEMINIATION POLICY

14.1 Dissemination policy

The data is owned by GMMH. On completion of the trial, the data will be analysed and tabulated and a Final Trial Report prepared. The full trial report can be accessed at the end of the treatment and will be prepared for publication. Both the CI and the research team at Tilburg University will have rights to publish the trial data.

The participants will be notified of the outcome of the trial and the publication will be provided to them personally.

The trial protocol will be made publicly available; and published on the HRA publication website.

14.2 Authorship eligibility guidelines and any intended use of professional writers

No professional writers will be employed. The CI, members of the research team, and the academic sponsors at Tilburg University will be involved in the writing of the study at completion.

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16. APPENDICIES

16.1 Appendix 1-Risk

Risks associated with trial interventions

X A ≡ Comparable to the risk of standard medical care

☐ B ≡ Somewhat higher than the risk of standard medical care

☐ C ≡ Markedly higher than the risk of standard medical care

Justification: The service that is being studied has been running for 2 years. The study protocol is to research this treatment. The major alterations for the study involve introduction of a baseline period of 8 weeks, frequency of data collection, the use of the structured clinical interview and the qualitative interview. None of these measures are known to cause any adverse reactions.

What are the key risks related to therapeutic interventions you plan to monitor in this trial?		How will these risks be minimised?		
IMP/Intervention	Body system/Hazard	Activity	Frequency	Comments
MBT programme	Suicide Risk	Participants cared for by local CMHT.	Monthly at least	
MBT programme	Suicide Risk	Participants will be offered MBT, which has shown promise at reducing suicide attempts in adults	Twice weekly	

The other processes that have been put in place to mitigate risks to participant safety:

- All participants will be reviewed by a consultant psychiatrist in their local care team
- All participants will have a named care coordinator
- All participants will have a care plan, and crisis care plan in line with local policy

Outline any processes (e.g. IMP labelling +/- accountability +/- trial specific temperature monitoring) that have been simplified based on the risk adapted approach. N/A

16.2 Appendix 2 - Trial management / responsibilities

(For multi-centre trials only)

N/A

16.2.1 Patient registration/randomisation procedure

Patients will be registered under the local later life CMHT. For the purposes of the trial, they will be registered in the trial record, which will be securely stored on an NHS server, accessible only by members of the data team.

16.2.2 Data management

The CI will be responsible for checking CRFs, responding to data queries, and clarifying any data management concerns by participants and external parties.

16.2.3 Preparation and submission of amendments

The CI will be responsible for making any amendments, in the event that they occur.

16.2.4 Preparation and submission of Annual Safety Report/Annual

The CI will be responsible for any progress reports.

16.2.5 Data protection/confidentiality

The CI is responsible for ensuring data protection and confidentiality.

16.2.6 Trial documentation and archiving

Trial documentation will be stored under lock and key at the Therapy Hub, 70 Daisy Bank Road, Longsight, Manchester. The data management team will be responsible for archiving.

16.3 Appendix 3 – Authorisation of participating sites

N/A

16.4 Appendix 4 – Schedule of Procedures

Procedures	Visits (insert visit numbers as appropriate)				
	Screening	Baseline	Treatment Phase		Follow Up
Informed consent	2				
Demographics	1				
Medical history		1			
Assessment 1 (SCID-PD screen)	1				1
Assessment 2 (SCID PD full interview)	1				
Assessment 3 (Primary outcomes)		8	72		24
Assessment 4 (Secondary outcomes)		1	4		1
Assessment 5 (Qualitative interview)					1
Adverse event assessments		1			1

16.5 Appendix 5 – Safety Reporting Flow Chart

Not applicable

16.6 Appendix 6 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC committee.