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BEAT-IT: A randomised controlled trial comparing a behavioural activation treatment for depression in adults with learning disabilities with an attention control

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Signature Page for Investigators

Study Title: BEAT-IT: A randomised controlled trial comparing a behavioural activation treatment for depression in adults with learning disabilities with an attention control

I have read this protocol and agree to conduct this study in accordance with the stipulations of Good Clinical Practice (GCP) and all applicable regulatory requirements.

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Please contact the Trial Coordinator for general queries and supply of trial documentation

Queries:

Queries
All queries should be directed to the Trial Manager who will direct the query to the most appropriate person

Serious Adverse Events

SAE reporting
Where the adverse event meets one of the serious categories an SAE form should be completed by the clinical PI and faxed to the Trial Manager within 24 hours upon becoming aware of the event. (See Sections 10 for more details) **Fax number: 0141 2110356**

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Figure 1:Study flow chart

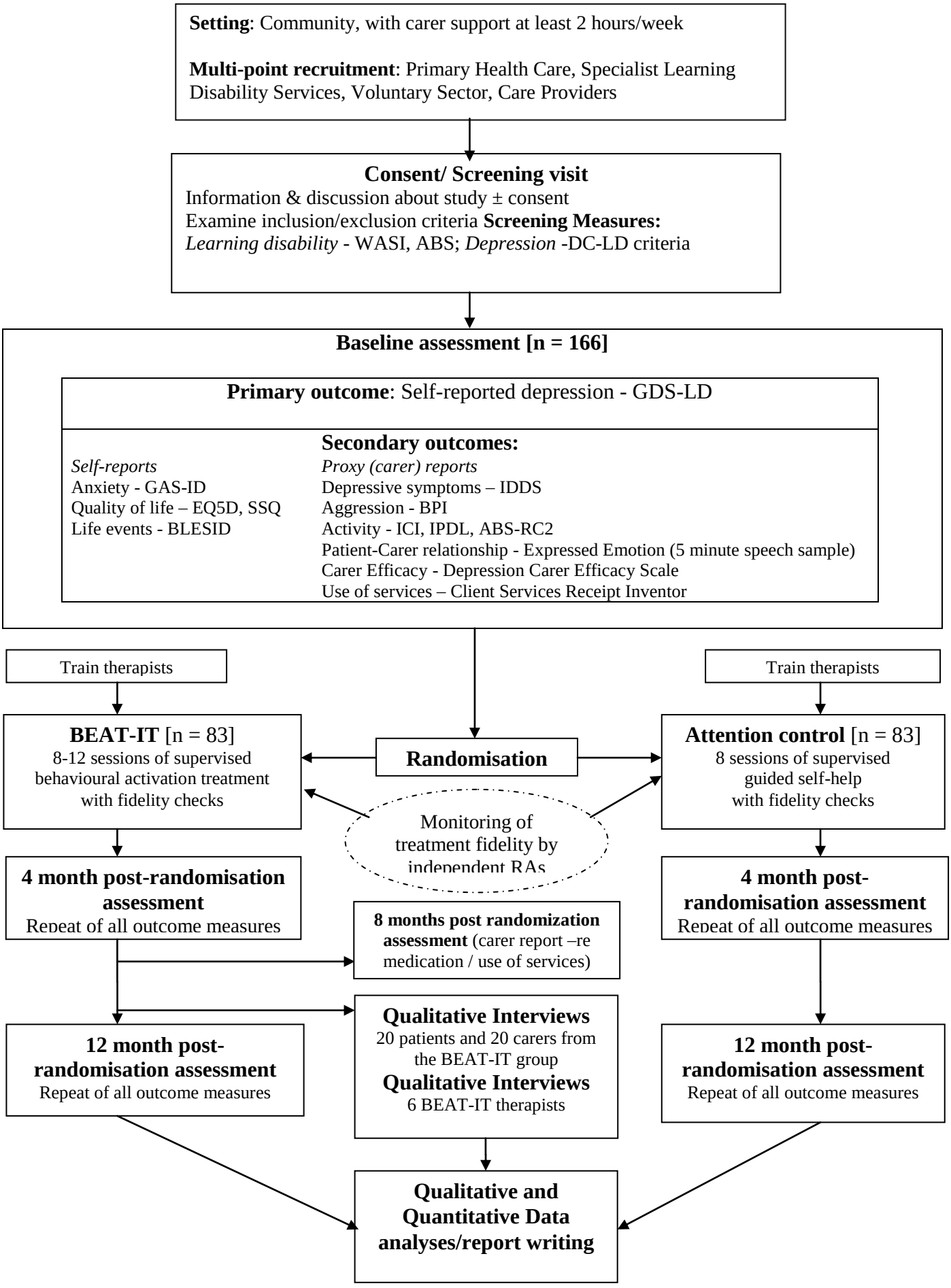

Table 1:Schedule of outcome measure assessments during trial (see section 10 for further details on outcome measures)

	Demographic & health questionnaire	**Self- report depressive & anxiety symptoms & aggressiveness**	**Proxy-report depressive symptoms**	**Carer efficacy questionnaire**	**Quality of life measures**	**Expressed emotion**	**Qualitative interview**
Baseline	x	x	x	x	x	x	
Time 1 (≈ 4 months from randomisation)		x	x	x	x	x	
Time 2 (≈ 12 months from randomisation)		x	x	x	x	x	X (sub sample only)

1 Trial Summary

Mental ill health is the biggest cause of disability in the UK. Depression is the most common type of severe mental ill-health experienced by adults. About half of all adults will experience at least one episode of depression in their lifetime. Depression has a negative effect on life expectancy, long-term health and quality of life. Adults with learning disabilities are as likely to have depression as adults who do not have learning disabilities. However, not much is known about what treatments help adults with learning disabilities and depression.

Psychological therapies, such as cognitive behavioural therapy (CBT), are recommended as the best treatment for most people with depression. Improving access to psychological therapies is an NHS priority. However, psychological therapies require good verbal communication. Studies have shown that adults with learning disabilities do not have the communication skills to participate in most available psychological therapies. Therefore, adults with learning disabilities and depression experience inequitable access to treatments for depression.

Behavioural Activation is a psychological therapy that has been shown to be as effective as CBT. The advantage for adults with learning disabilities is that Behavioural Activation is less dependent on verbal communication. Behavioural Activation gets people with depression involved in positive activities and helps them engage in everyday tasks which people with depression avoid. The proposed study would see if a Behavioural Activation treatment developed for adults with learning disabilities and depression is effective. This treatment is called BEAT-IT.

In the proposed study, half the participants will take part in the BEAT-IT treatment, and half will receive a control intervention. People who choose to take part will be involved for twelve months. The study will take place in Glasgow, North Wales and North West England. We need three centres to make sure we get enough people to take part in the study. Compared to participants in the control group, we will find out if the participants getting BEAT-IT are more likely to: i) show a reduction in symptoms of depression, ii) increase their activity iii) have an improved quality of life. We will also examine if the BEAT-IT treatment is cost effective. Participants with learning disabilities and their carers will be asked to tell us what they think about the BEAT-IT treatment.

The main ethical issue is ensuring that adults with learning disabilities make informed decisions about participating in the study. All information about the study will be made as accessible as possible, and researchers will be trained in communicating with people with learning disabilities. Some individuals we approach initially may not have the capacity to make a decision about whether to take part. If we find that any potential participants lack the capacity to consent to take part in the research, they will be excluded from the study and will continue to receive usual services locally.

Our team is made up of researchers with expertise in working with people with learning disabilities, experts on clinical therapeutic interventions, and experts in using statistics and health economics in research. In each of the three study centres we have strong links with the NHS and specialist learning disabilities services.

2 Background

2.1 The health need

A significant proportion of the UK population has learning disabilities. Approximately 2% of adults and 3.5% of children have an intelligence quotient <70 though this figure may be rising due to increasing life expectancy and birth rate (e.g. improving survival of very low birth weight babies, increasing maternal age) [2&3]. Individuals with learning disabilities experience health inequalities, with needs not well met by the NHS [4, 5&6].They have much higher levels of mental ill-health than the general population, with a point prevalence of 40% for adults [7]. This is a burden at the individual, family and societal level, including a cost burden. For example, England spends £3billion per annum on specialist support for persons with learning disabilities, with excess and poorly addressed mental health needs contributing to costs[8]. This is 50% of the equivalent amount spent on mental ill-health in the general population [9] despite being provided for only 2% of the population.

Depression is a major public health challenge, with unipolar depression alone being the third leading contributor to the global burden of disease, and also expected to rise [10]. Depression is highly prevalent amongst adults with learning disabilities and contributes to human misery as well as cost of daily care and support. Studies suggest a point prevalence of depression of 5% in adults with learning disabilities[11]. Depression is also more enduring when experienced by adults with learning disabilities than for the general population, suggesting it is either a more severe disorder, or more poorly managed. For example, a British cohort study found 15% of adults with learning disabilities compared with 3% of the general population met criteria for chronic depression [12].

2.2 Psychosocial interventions

Considerable work has been carried out to develop and study the efficacy of psychosocial interventions for depression in the general population. Such evidence is missing for people with learning disabilities. There is, therefore, a need to redress this inequity by identifying effective therapies for adults with learning disabilities. Recent efforts have focused on the adaptation of cognitive behavioural treatment (CBT) models for use with individuals with learning disabilities [13], but the efficacy of CBT has yet to be rigorously tested. Furthermore, studies have shown that CBT is not accessible for the majority of individuals with learning disabilities, due to the excessive cognitive and communicative demands[14, 15& 16].

2.3 Behavioural Activation

A recent meta-analysis of studies with the general population found that behavioural activation is as effective as CBT in the management of depression [17]. Models of behavioural activation interventions aim to increase overt behaviours that are likely to bring the individual into contact with positive environmental contingencies, with a corresponding improvement in mood, thoughts, and overall well-being. Because behavioural activation does not focus on monitoring the relationship between thoughts and other symptoms, the intervention is less reliant than CBT on verbal communication to access emotions and thoughts. Therefore, for adults with learning disabilities, behavioural activation treatment may be more accessible and effective in the management of depression.

Models of behavioural activation treatments[18&19] evolved from earlier behavioural approaches to take greater account of the context of an individual's life, and have a stronger focus on understanding the function of behaviour. Establishing the function of behaviour for the individual is crucial because the aim is not merely to increase activity, but to ensure that activities are purposeful and motivating for the individual.

Taking account of the context of a person's life is especially important when working with marginalised and more dependent individuals. People with learning disabilities may have limited opportunities to participate in a range of occupational or social activities [20]. By definition, they have problems with adaptive behaviour (day-to-day social, communication, and life skills) in addition to cognitive impairments [21]. Therefore, they are likely to rely on a degree of support to take advantage of opportunities for activity that do arise. Hence, the first step to increasing the levels of activity would be to ensure that the necessary opportunities and supports are in place. For a behavioural activation treatment to have ecological validity, in that it makes sense in the everyday context of the individuals' lives, it is necessary to work alongside families or paid carers who are already providing help. As a result, the BEAT-IT treatment adapted for use by people with learning disabilities works with dyads of individuals and their carers, to develop a structured programme of activities and strategies for increasing motivation. This more systemic approach is also designed to improve the generalisation and maintenance of the treatment's impact.

The proposed study would be the first large-scale RCT of an individually delivered psychological treatment for adults with mild to moderate learning disabilities and a mental

health problem. As such, the outcomes could also influence the design and delivery of other mental health treatments for this population.

2.4 BEAT-IT open trial results

An open trial of BEAT-IT for depressive symptoms demonstrated that there are eligible patients for a RCT, with 22 patients recruited in a 12 month period using limited resources, and recruiting from just one referral point: the specialist learning disabilities health service. A treatment manual was produced, and adherence and compliance rates were good for the 10-12 sessions, with only two patients failing to complete the intervention. Only two of the patients completing treatment were subsequently lost to follow-up at three months, demonstrating excellent overall retention. Outcomes show evidence of positive change on depressive symptoms, with strong effect sizes for those able to provide self-report on the Glasgow Depression Scale[22]pre and post intervention (r=.78) and at three months follow-up after completion (r=.84). Carer reports using the Intellectual Disabilities Depression Scale[23] also provided evidence of positive change pre to post intervention (r=.74) and at three months follow-up (r=.72).

A sub-set of participants who were able to talk about their experience of taking part in the trial were invited to take part in a semi-structured interview. Where possible, their carers were also interviewed. The participants expressed favourable views of the treatment, with key themes highlighting the importance of the therapeutic relationship, and finding new ways of achieving change at a time when they felt hopeless. This latter theme was echoed in the carer interviews. They also found the treatment motivating and that it galvanised a shared understanding and approach across groups of carers in the participant's life.

BEAT-IT is a complex intervention, which has to be adapted to particular individual and inter-personal contexts because the therapist is working with the client-carer dyad. For the open trial, the treatment manual was carefully developed with future delivery within learning disability service environments informing its design, and based on behavioural activation theory. In addition, the open trial provided evidence that:

1. A psychology assistant could be trained and supervised to deliver the treatment – a BEAT-IT training and supervision protocol has been developed
2. Sufficient numbers of suitable patients could be identified by referrers even with a limited referral route and limited research resources
3. Information and consent procedures, including the assessment of capacity, were robust

4. People with learning disabilities and depression, and both family and paid carers, were able to participate in the treatment
5. The BEAT-IT treatment can be delivered with a good level of fidelity to the manual
6. There were no adverse events experienced during treatment and follow-up
7. The treatment process was viewed positively by the patients and their carers
8. Retention in the treatment was good
9. Follow-up rates for those who completed the treatment were also excellent
10. Patient and carer dyads were able to complete the outcome measures (without missing data or lack of understanding of the measures)
11. The outcome data provided promising indications of a reduction in depressive symptoms as reported by both patients and carers

3 Trial objectives

3.1 Primary objective

To measure the clinical effectiveness of BEAT-IT for adults with learning disabilities and depression compared with an attention control intervention, in reducing self-report of depressive symptoms.

3.2 Secondary objectives

Secondary objectives, which address outcome issues, are to evaluate:

1) Does BEAT-IT lead to a greater reduction in carer-reported depressive symptoms compared to an attention control intervention?

2) Does BEAT-IT lead to a greater reduction in self-reported anxiety symptoms, compared to an attention control intervention?

3) Does BEAT-IT lead to a greater reduction in carer reported aggressiveness, compared to an attention control intervention?

4) Does BEAT-IT lead to more significant and sustainable changes in participants' activity levels, compared to an attention control intervention?

5) Does BEAT-IT lead to a significantly greater improvement in participants' quality of life compared to an attention control intervention?

6) Does BEAT-IT improve carers' sense of self-efficacy in supporting adults with learning disabilities who are depressed, compared to an attention control intervention?

7) Is BEAT-IT a cost-effective intervention for the management of depression experienced by adults with learning disabilities?

8) Does BEAT-IT improve carers' reported relationships with the adults with learning disabilities and depression they support?

Additionally, qualitative methods will be used to address process issues, which could help to inform the future uptake of BEAT-IT in practice. We will explore the perspectives of:

1) Participants receiving BEAT-IT

2) Carers supporting the participants

3) Therapists delivering BEAT-IT.

4 Trial design

The proposed study is a multi-centre single-blind randomised controlled trial (RCT) of BEAT-IT compared to an attention control treatment, plus a qualitative investigation of patients', carers' and therapists' perspectives on the treatment. The design of the study is illustrated in Figure 1, and the schedule of research assessments outlined in Table 1. The researchers collecting the outcome data will be blinded to which group participants have been allocated.

There are two phases:
Phase 1: Recruitment will begin at the Scottish centre and is expected to be slow initially whilst contacts are established/re-established. It will take time to educate potential referrers on appropriate patients to refer to the trial. However, recruitment should build up and be sustainable within five months.

Phase 2: If a minimum of 20 patients have been recruited at the end of the first phase or at least 16 patients recruited but with a recruitment rate of 4 per month in months five and six (month 7 is December when it is anticipated recruitment will be low), then the study will be also rolled out in the other two centres in England and Wales. Using the Phase 1 experiences, recruitment should reach the same rate more rapidly in England and Wales. Therefore, we expect to recruit 166 patients into the study within 18 months of active recruitment (Table 1):

there will additionally be a five month start-up period, and a four month period between pilot and full study where the HTA decide whether to fund the full scale study, and recruitment and training is undertaken in the English and Welsh centres.

5 Sample and recruitment

5.1 Recruitment strategy

The study aims to recruit 166 individuals with mild to moderate intellectual disabilities and clinical depression. A multi-point recruitment strategy[24] will be adopted, involving primary health care services, specialist learning disabilities services, relevant voluntary organisations, and social care provider organisations. Assistance will be sought from the mental health (the learning disability network in Wales) and primary care research networks at each of the centres, and recruitment strategies will include outreach work with voluntary provider organisations to help them to identify individuals with learning disabilities and depressive symptoms. Reviews will also be carried out with specialist health professionals to identify patients on caseloads who may be eligible. Finally, Primary Care electronic records will also be interrogated (which include both depression and learning disabilities as a part of their Quality and Outcome Framework). During Phase 1, a record will be kept of the numbers of potential patients, and individuals consenting to participate in the study, identified from each of these recruitment points.

5.2 Target Population

The research assistants will undertake consent/ screening visits and check inclusion/exclusion criteria, following which they will meet with the local clinical supervisor to review the collected data to determine whether or not the person meets inclusion criteria and does not have any exclusion criteria, using a structured decision protocol.

During screening, the presence of a learning disability will be assessed according to international criteria (ICD-10) that state the requirement for low intellectual ability and adaptive behaviour deficits. Intellectual ability will be assessed using the Weschler Abbreviated Scale of Intelligence[25] and adaptive behaviour skills using the Adaptive Behaviour Scale – RC2[26]. These data are also crucial to enable international dissemination of the research. It is important to be able to justify that all participants met international criteria for “learning disability”. The patient’s ability to provide informed consent, following an

assessment of capacity, is also an additional pragmatic way to distinguish individuals with mild to moderate learning disabilities from those with more severe disabilities. Requiring an IQ score of no higher than 75 for inclusion addresses the measurement error inherent in IQ assessment.

Clinically significant depression will be defined by the Diagnostic Criteria for Psychiatric Disorders for use with Adults with Learning Disabilities (DC-LD)[27].

To determine whether individuals are suicidal, they will first be asked about suicidal ideation. If they express suicidal ideation this will be followed up with a series of questions to both the individual and their carer. Those with current credible plans to commit suicide (a plan and available means) and who express intent to do so (explicit suicidal intent), will be excluded from the study. Individuals who have plans to commit suicide and have a past history of suicide attempts or are actively suicidal, will also be excluded from the study. This covers the same domains as structured questionnaires for the general population such as the Beck Depression Inventory II[28] .

Having the necessary receptive and expressive verbal ability to complete the screening and consent process will be taken as evidence of sufficient skill in English to participate in treatment. Any doubts in this area will be discussed with the clinical supervisor.

5.3 Inclusion criteria:

1. Mild/ moderate learning disabilities
2. 18 years old and over
3. Clinically significant unipolar depression
4. Is able to give informed consent to participate
5. A level of expressive and receptive communication skill in English (reading skills not required) to allow participation in the treatment
6. Has a family member or paid carer who has supported them for a minimum of six months, is available for weekly-fortnightly treatment sessions with the practitioner, and who currently provides a minimum of two hours support per week to the patient.

5.4 Exclusion criteria:

1. Suicidal
2. A measured IQ of >75

3. Factors that prevent the patient from interacting with the carer and therapist or retaining information from the therapy (e.g. dementia, significant agitation, withdrawal arising from psychosis)
4. Does not consent to her/his GP being contacted about their participation in the study.

6 Recruitment Process

Procedures for participant recruitment are outlined in the following sections.

6.1 Number of participants

A total of 166 participants will be required. Recruitment will be completed over two recruitment periods.

6.2 Informed consent

The Chief Investigator is responsible for ensuring informed consent is obtained before any protocol specific procedures are carried out. The decision of a participant to participate in the clinical research will be based on a clear understanding of what is involved. Research assistants employed on the study will be responsible for the process of seeking informed consent, under the supervision of the Chief Investigator. The researchers will receive training on assessing capacity to consent, based on current legislation and established best practice. The process of introducing the study to potential participants and carers, and seeking informed consent will take place in the home environment of potential participants. If the potential participant prefers this process will take place at appropriate NHS, provider organization or charity premises.

6.2.1 Patients

An information pack containing a letter, information sheets, and a FREEPOST return envelope will be given to potential participants by a member of staff known to the potential participant and working in primary health care services, specialist learning disabilities services, relevant voluntary organisations, and social care provider organisations. The member of staff will give a brief explanation to the individual about the study and ask the potential participant to discuss the information with a friend or carer. It will be explained to potential participants that they can return a tear off slip in the FREEPOST envelope if they are interested in finding out more about the study.

Adults with learning disabilities are often supported by several carers. For example, they may have paid carers working shifts, or different carers in their home and day centre environments. This means that the potential participant may not know who they should discuss the study with. This can create a situation where information sheets go missing before potential participants are able to discuss the study with carers, and make an informed decision about whether they would like to participate. To take account of this, as in previous studies, the member of staff who gives out the information sheet will be asked to notify an NHS secretary in learning disabilities who is independent of the research study that an information sheet has been handed out. After two weeks, if no tear off slip has been received, the NHS secretary will contact the individual once, by telephone, to check that they still have the information pack. If the information pack has gone missing a second information pack will be sent out.

Participant information sheets for use by adults with learning disabilities have been designed. These use language appropriate to the developmental level of individuals with a mild to moderate level of learning disabilities. A separate information sheet will be provided for family members and carers. Where an individual is interested in finding out more about a study a researcher will arrange to meet with them to discuss the study and answer any questions they have. It is anticipated that in the majority of cases a researcher will meet the potential participant at their home. However, if this is not convenient, or desirable, for a potential participant, then they will be invited to identify an alternative place to meet. At the time of the first meeting with the potential participant, the researcher will invite the person to discuss what would be involved in participation in the research study. The potential participant will be invited to choose whether they would like a carer to support them whilst discussing the research project. The researcher will read through the information sheet with the potential participant. There will be an opportunity to discuss the study, and the potential participant will be invited to ask any questions. When a potential participant, and where relevant their carer, are satisfied that all their questions have been adequately answered, he/she will be invited to choose whether or not they would like to participate.

The verbal explanation given to the potential participant will be given by a member of the research group identified on the delegation log, and will cover all the elements specified on the participant information sheets and consent forms. The participant will be given every opportunity to clarify points they do not understand and, if necessary ask for more

information. The participant will be given sufficient time to consider the information sheets provided. It will be emphasised that the participant may withdraw their consent to participate at any time without loss of benefits to which they otherwise would be entitled.

Individuals who chose to take part in the research study will be asked to complete a written consent form. This will include providing consent to take part in interviews to express their views about the intervention. The written consent form will use language appropriate to the developmental level of individuals with learning disabilities. The consent form will be read through with the individual with learning disabilities and they will be asked to sign it, witnessed by a carer or other individual independent of the study. A second copy of the consent form will be completed and given to the participant to keep. Individuals who do not have the capacity to consent to participation will be excluded from the research study.

A member of the research group and the participant will sign and date the consent form to confirm that consent has been obtained. A third party, independent of the research study, will be asked to witness the consent. The participant will receive one original consent form, the second original will be kept in the trial master file.

Only after an individual has consented to participate will screening data be collected.

Below lists the patient information sheets and consent forms for the service user:

Patient (main study)

1. Simplified accessible information sheet
2. General information sheet
3. Consent form

6.2.2. Carer

The main identified carer will be given the following information sheet and consent form:

Carer (main study)

1. General information sheet
2. Consent form

7 Withdrawal and loss to follow-up

Service users have the right to withdraw consent for participation in any aspect of the trial at any time. The service users' care will not be affected at any time by declining to participate or withdrawing from the trial. Data collected up to the point of withdrawal from the trial will still be used in the analysis.

8 Trial interventions

Patients will be randomised to either:

1) BEAT-IT for depression

2) The attention control intervention (guided self-help).

8.1 BEAT-IT

The treatment is designed to be delivered to individuals alongside a carer who provides regular support to them. It is a structured, time limited, manualised psychological therapy, developed to treat those with a learning disability and depressive symptoms. The manual was evaluated in our open trial (see above). There is an initial training session for carers regarding their role in the treatment, then 8-12 sessions held 1-2 weekly, spanning approximately 4 months.

The treatment is divided into two phases, starting with an assessment period (4 sessions), where the patient with learning disabilities and their carer are socialised into the model and an individual formulation is developed. Key components of this phase include: i) Identifying avoidant behaviours linked to depressive symptoms, and monitoring activity, ii) Identifying life goals, and iii) Psycho-education concerning the link between depression and activity. The assessment culminates in the presentation of a formulation to the patient and their carer (session 4). This provides a shared 'story' or common frame of reference for joint work between the patient, carer, and therapist. Maximum participation by the person with learning disabilities is achieved by flexibly implementing the sessions in accordance with the treatment manual, and the particular approach taken is based upon the psychological formulation. The shared agreement of the carer regarding the treatment goals is also essential, as otherwise they are unlikely to be properly supportive of the intervention or willing to motivate the patients to achieve change.

The subsequent 5-10 active treatment sessions focus on: (i) Recovering lost skills and interests, and new skills training, (ii) Graded exposure to reduce avoidant behaviours, and (iii) Targeting inherently reinforcing activity, and activity likely to increase access to other positive reinforcers in three life domains: domestic tasks, purposeful daytime activity, and social/recreational activity, iv) Addressing other emotional or inter-personal barriers to change, including anxiety and anger.

The final two sessions after the active treatment phase have a future focus, and are concerned with helping the patient and carer to maintain and build on progress they have made. A booklet is prepared for the patient and carer, reviewing progress and identifying changes that have been made, along with a plan for long-term maintenance and improvement.

Completion of the treatment is defined as attendance and participation in a minimum of eight sessions.

8.2 Guided self-help (attention control intervention)

The attention control intervention has been selected to be comparable to BEAT-IT in terms of carer and therapist attention, the use of a structured approach, and the support of a carer. Self-help materials were developed in Glasgow by co-applicant Melville and colleagues[29] for use with adults who have learning disabilities and depression. The self-help resources were designed to be used by patients with learning disabilities along with the support of a carer. There will be an initial meeting with the patient and carer to explain the materials and provide coaching in their use, then 8 sessions to support the dyads in their use of the self-help materials. Although the materials were designed to be accessible, carer support is essential for their delivery as the patients themselves are expected to have few, if any, literacy skills. The guided self-help model also meets the ethical criterion of being a meaningful comparison intervention in the absence of an alternative evidence-based treatment for people with learning disabilities who have depression. The patient and carer will be guided through a series of self-help materials by a therapist. The focus is psycho-educational and the first two sessions with the patient begin by looking at the nature of depression, before going on to outline how depressive symptoms can be tackled. The materials focus on key topics including feeling down, sleep, exercise, and problem solving.

8.3 Therapist adherence to the BEAT-IT and attention control protocols

To establish adherence in the delivery of the BEAT-IT treatment by therapists, two sessions will be audio recorded with the permission of the patients and their carers (total of 166 sessions). One will be from the initial assessment phase (1-3) and a second corresponding to the active treatment phase of the BEAT-IT treatment (sessions 4-12). The BEAT-IT session recordings will be reviewed by an independent rater against a checklist of core requirements for: i) Adherence to the manual, ii) Therapeutic process, and iii) Following the principles of BEAT-IT. This checklist has been adapted from the Manualised Group Intervention Check (MAGIC)[30] used in an earlier HTA funded trial with people with learning disabilities (Jahoda co-I), which takes into account the particular social and communication skills required when working with people who have learning disabilities. Twenty percent of the recordings will be double rated to ensure adequate examination of inter-rater reliability. Up to two recordings of the attention control intervention will also be reviewed, taken from sessions 1-3 and 4-8 (maximum total of 166 sessions). These session recordings will be reviewed to establish that the sessions last for the required time to ensure sufficient therapist and carer attention, and to ensure the materials provided are being used by the therapist as directed in the protocol.

9 Safety Reporting

9.1 Definition of adverse event

Adverse Event (AE) – Any unfavourable and unintended sign, symptom or disease temporarily associated with participation in the study.

9.2 Definition of Serious Adverse Event

Serious Adverse Event (SAE) - Any untoward occurrence that:

Results in death

Is life-threatening [refers to an event during which the participant was at risk of death at the time of the event; it does not refer to an event which might have caused death had it been more severe in nature]

Requires hospitalisation, or prolongation of existing hospitalisation

Results in persistent/significant disability or incapacity

Is a congenital abnormality or birth defect

Is otherwise considered medically significant by the investigator

9.3 Recording and Reporting of Adverse Events

AEs will be identified by observation and/or enquiry at study visits. AEs that do not meet the criteria for seriousness will be recorded in documentation on the CRF only. Details of SAEs will be added to the CRF and followed until resolution. Expected SAEs should be followed until resolution. The relationship with the study intervention will be assessed for any unexpected SAEs: if possible of definitely related, unexpected SAEs will be communicated to the CI for review and will be reported to the REC. Unexpected and unrelated SAEs will be followed until resolution.

9.4 Reporting to the Sponsor

All SAEs that arise during the BEAT-IT trial will be reported by the PI (or designee) to the CI and Sponsor by entering the details into the CRF as reasonable as practicable and in any event within 24 hours upon becoming aware of the event. Any follow up information should all be reported.

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9.5 Reporting to the Research Ethics Committee

Any SAE occurring to a research participant will be reported to REC (the REC that gave favourable opinion of the study) where in the opinion of the Chief Investigator, the event was

- related – that is, resulted from administration of any of the research procedures, **and**
- unexpected – that is, the type of event not listed in the protocol as an expected occurrence.

Reports of related and unexpected SAEs should be submitted to the REC within 15 days of the CI becoming aware of this event using the 'report of serious adverse event form' for non-CTIMPs published on NRES website.

9.6. Annual progress report

The CI is also responsible for providing an annual progress report to the REC using NRES 'Annual Progress Report form for all other research'. A section on the safety of participants is included in this report. DMC will be notified about unexpected and related SAEs.

10 Trial Outcomes

10.1 Measures/assessment instruments

As shown in Figure 1, outcome measure data will be collected at three time points:

- Baseline
- Time 1- four months post- randomisation (post intervention)
- Time 2- 12 months post-randomisation (follow-up/ maintenance)

There will be one additional data collection point at 8 months with the carer alone, to chart any changes in the participant's medication use and receipt of services.

The primary outcome measure will be self-rated depressive symptoms.

Secondary outcome measures include:

- Self-rated anxiety symptoms
- Carer rated depressive symptoms
- Carer self-efficacy
- Quality of life.

An outline of data collected at the three time points is shown in Table 4, below. Research interviews will take place in the home environment of participants. If participants prefer, these interviews will take place in appropriate clinical, provider organisation or charity premises. In addition to the assessments listed in Table 4, a purpose specific questionnaire to gather demographic and health data about participants will be completed at baseline only, the questionnaire will include questions about the participants' expectations of therapy. This questionnaire was used in the BEAT-IT open study and takes 20 minutes to complete.

Carers will also be given the option to complete assessments with the researcher by phone, if it proves to be more convenient for them or difficult to arrange a time to meet face to face.

Table 4: Outcome measure assessments

Outcome	Participant Measures	Carer Measures
Depressive and anxiety symptoms	Glasgow Depression Scale for People with Learning Disabilities (20 items: 10 minutes) Glasgow Anxiety Scale-ID(20 items: 10 minutes)	Intellectual Disabilities Depression Scale (38 items: 10 minutes)
Aggression		The Behaviour Problems Inventory for Individuals with Intellectual Disabilities; Aggressive Behaviour sub-scale (10 items: 5 minutes)
Carer Self-efficacy	Not applicable	Emotional Difficulties Self-Efficacy Scale (10 items: 5minutes)
Participant- carer relationship	Not applicable	Expressed Emotion: Five Minute Speech Sample (FMSS)
Activity measures and Quality of life	EQ-5D (5 items:5 minutes) Social Support Questionnaire (3 items: 10 minutes)	EQ-5D (5 items:5 minutes) Modified Index of Community Involvement (46 items: 10 minutes) Modified Index of Domestic Participation (13 items: 5 minutes) ABS-RC:2 (4 sub-scales; 48 items; 10 minutes)
Response to Life events	Bangor Life Events Schedule for Intellectual Disabilities (24 items: 10 minutes)	Not applicable
Health economics		Client Service Receipt Inventory (30 items: 10minutes) Medication inventory (10 items: 5 minutes)

10.2 Measures of depressive and anxiety symptoms; aggressiveness and perceived social support

Depressive symptoms (self-rating)

The Glasgow Depression Scale for People with Learning Disabilities (GDS-LD) [24]*:* This is a 20 item self rating scale that requires respondents to indicate how often a particular symptom has occurred using a 3 point scale (never/sometimes/always), during the previous week. The GDS-LD has good content and discriminant validity. The correlation between the GDS and the Beck Depression Inventory-II[28], when the two measures were completed by non-disabled individuals, indicates high criterion validity ($r = .94$, $P<0.001$). However, the Beck Depression Inventory-II does not use language or a response format that is accessible to most individuals with learning disabilities. There is also high short-term test-re-test reliability and high internal consistency (Cronbach'salpha = .90; n = 38). This was also the primary outcome measure in our open trial.

Depressive symptoms (carer rating)

Intellectual Disabilities Depression Scale (IDDS)[23]*:* This is a 38 item behavioural checklist derived from DSM-III-R criteria, designed to measure the frequency of identified depressive behaviours within a four week period. The IDDS has shown acceptable inter-rater agreement, and findings from the open trial have shown a high level of correlation between self-report on the GDS and carer report on the IDDS ($r=.77$, $p < .001$).

Anxiety symptoms (self-rating)

Glasgow Anxiety Scale-ID (GAS-ID)[31]*:*This scale has three sections dealing with worries, specific fears, and physiological symptoms. Items are rated on a 3-point scale, with potential responses of 'Never/No', 'Sometimes', and 'Always/A lot'. Before starting the assessment, an anchor event is identified with the participant from the previous week, and participants are questioned about their feelings with this time frame in mind. The scale has good discriminant validity, with a significant difference in scores observed between those with and without anxiety disorders. Correlations between the GAS-ID and Beck Anxiety Scale [32] indicated reasonable criterion validity

($r = .72$, $p < .001$). There is also good short-term test-retest reliability and high internal consistency (Cronbach's alpha = .96; n = 35).

Aggressiveness (carer rating)

The Behavior Problems Inventor[33] : The aggression sub-scale of the behaviour problems inventory will be used to examine the level of aggressiveness of the participants with learning disabilities. The informants will be asked to indicate the frequency with which the participants display different aggressive behaviours, if at all. The BPI-01 was found to have good test-retest reliability (r=.71) and the aggression sub-scale had good internal consistency (Cronbach's alpha = .82).

Social Support (Self-report)

Social Support Questionnaire (SSQ3)[34]*:* This three item questionnaire examines the participants' perceived level of social support. The language and scoring system has been simplified to make it more accessible for participants with learning disabilities. Research has shown that the measure has good internal consistency (Cronbach's alphas 0.75 - 0.79). Four week test-retest reliability was also good (r=.84-.85).

10.3 Activity measures

Where possible, two questionnaires will be administered jointly to the carers and patients with learning disabilities, to measure the level and types of activity in which the patients engage. Otherwise, the measures will be completed with the carers alone. These measures have been adapted on the basis of data obtained from the BEAT-IT open trial, to help ensure that they: i) Cover the range of activities in which individuals with learning disabilities might engage, and ii) Are sensitive to the changes in the frequency of participation in activity.

Index of Community Involvement (ICI)[35]*:* This scale provides a measure of participation in social and community based activities during the previous 4 weeks. The ICI has demonstrated good inter- rater agreement of 95% and good internal consistency (Cronbach's alpha = .79). The version adapted by Felce et al (1998) [36]would be used in this study as it records the frequency with which individuals take part in activities.

Index of Participation in Domestic Life (IPDL)[37]*:*This scale measures participation in 13 household tasks during the previous 4 weeks. The IPDL has been reported to have good inter-rater agreement (95% and 97%) and good internal consistency (Cronbach's alpha = .89). The version adapted by Felce et al (1998) will be used, as it provides frequency ratings.

The Adaptive Behavior Scale - Residential and Community: Second Edition (ABS-RC2)h[26:]*:* Four sub-scales of Part 1 of the ABS –RC2, concerning the motivation to engage in tasks and to take responsibility, will be used as a proxy measure of avoidance of activity, a key aspect of behavioural change targeted by the behavioural activation intervention. These sub-scales are 1) Domestic Activity (6 items); 2) Self-Direction (5 items); 3) Responsibility (3 items) and 4) Socialization (7 items). The ABS-RC2 was standardised on over 4,000 people with developmental disabilities living in community settings. The internal consistency of ABS-RC2 Part I domains and factors is reported to be high (Cronbach's alphas 0.82 - 0.99), with standard errors of measurement reported to be small (confidence intervals 0.42 - 2.60). Two-week test-retest reliability is also reported to be high (R_c 0.88 - 0.99), as is inter-scorer agreement (r 0.83 - 0.99). In terms of content validity, criterion-related validity and construct validity, the authors of the ABS-RC2 report a range of evidence to support the adequacy of the ABS-RC2 Part I items, domains and factors, including item analysis, correlations with other measures of adaptive behavior and mental ability tests and the ability of the ABS-RC2 to differentiate between different groups.

10.4 Patient – Carer relationship and Carer Self-Efficacy

Expressed Emotion: Five Minute Speech Sample (FMSS) [38]*:* The adapted format for staff will be used, which has been demonstrated to have 89.7% concordance for EE category with Camberwell Family Interview (CFI) [39]. Expressed Emotion (EE) has been widely used to capture the quality of relationships between family members where an individual has a high level of dependence on their parental carers and specifically in several studies in the field of learning disability [40].

Emotional Difficulties Self-Efficacy Scale (EDSE)[41&42]*:* This is a flexible five item

scale to assess carer (parents and paid carer) perceptions of their self-efficacy in specific support domains relating to children and adults with intellectual disability or autism. Most research to date has focused on self-efficacy in managing challenging behaviours, and reported internal consistency is good to excellent for mothers, fathers and paid carers (Cronbach's alpha range .81-.94) [41,42,43]

10.5 Life events

Although not a true outcome measure, life events will be measured at all data collection points using Bangor Life Events Schedule for Intellectual Disabilities (BLESID) Self-Report[44] version. This tool assesses exposure to life events that may be experienced by adults with a learning disability and also a rating of response to or impact of the life events (from negative to positive). Inclusion of the BLESID will allow analysis of the potential changes in response to life events over time (e.g., reduced negative impact of new life events experienced during the course of the study), and recent exposure to life events (prior to screening assessment) will be included as a potential moderator of outcome in exploratory analyses. As this questionnaire as been developed to allow individuals to report on life events that have occurred over the last 12 months, it will be administered at baseline and 12 month follow-up only.

10.6 Qualitative interviews and process evaluation

Patient, carer and therapist interviews will be conducted according to a semi-structured interview schedule. The questions will address the participants' views and experiences of the BEAT-IT therapy, to develop a better understanding of the change process. Design of the set of tools will take account of lessons learnt on our own and others' previous work, taking in the views of people with learning disabilities, including guidelines approved by the ESRC.

As a standard part of the BEAT-IT treatment protocol, therapists also complete written therapist logs at the end of each intervention session, noting their impressions of barriers to change, the successful therapy tasks, and ways they adapted the approach (in accordance with the manual) to individual need and circumstances.

Therapists will also collect routine data from the participants about their level of activity and their success in carrying out the homework tasks, along with reports from the participants about their mood that will provide evidence of the pattern of change across sessions.

10.7 Health economics measures

Client Socio-Demographic and Service Receipt Inventory - European Version (EQ-5D)[45]*:*To allow comparison with quality of life outcomes from depression studies that do not include adults with learning disabilities as participants, the *EQ-5D* [45]will be used. The EQ-5D has been shown to be reliable, valid and sensitive to change in depression studies and will provide information relevant to its use in health economics modeling. We will use a simplified version of the EQ-5D for the participants with learning disabilities. This version of the EQ-5D has more straightforward language aimed at young people aged seven years and older. However, the language is not actually "child like" and so is a good match for use with patients with learning disabilities.

Client Service Receipt Inventory (CSRI)[46]*:* CSRI is a validated tool to measure total package resource use and has been used in evaluations involving service users with psychiatric problems and service users with learning disabilities. It records items such as contacts with community-based primary care, other health or social services, educational services, and outpatient and inpatient attendances. Unit costs for most of these are available.

Medication Inventory: Medication use will be recorded, and any changes in use of medication over the course of the intervention and during follow-up will be noted to determine if there are treatment differences between the two arms of the study. In combination with the CSRI, medication use will also be costed.

11 Data collection and Blinding

The two interventions consume similar interaction time between dyads and therapists. This reduces the chance of the research assistants inadvertently having group

allocation revealed to them by virtue of patients' references to meeting with therapists.

The research assistants carrying out the assessments will be masked to intervention allocated and/or received. Masking will be maintained using a wide range of procedures, including separate offices for the therapists and research assistants carrying out assessments (where they are located in the same building), protocols for answering telephones, message taking and secretarial support, separate diaries and pigeonholes and data file security, and using passwords and encryption of randomisation information. The Chief Investigator will be informed of any unmasking by each centre and corrective action in terms of training and correctly following procedures would be instigated, if necessary. Treatment allocation would remain concealed until all participants have exited the trial.
Checking adherence to treatment protocols by rating the session audiotapes poses a potential threat to the integrity of blinding for the research assistants also collecting the outcome data. Research assistants rating recordings from their own study site would be unblinded. Therefore, these ratings will be completed by researchers at another one of the study sites, and reliability ratings by researchers at the second other study site. During the internal pilot phase, co-applicants at the England and Wales sites will carry out these ratings of session recordings.

12 Statistical considerations

12.1 Randomisation

After obtaining informed consent and the collection of baseline information, patients will be allocated to one of the two study groups, using a blocked randomisation within each study centre, using mixed block sizes of length 4 and 6, at random.

The design now carefully addresses and monitors possible confounding factors, most notably the use by participants of: a) Anti-depressants, St John's wort, and Lithium, and b) Other drugs which may have some mood stabilising properties and are commonly prescribed in this population (an estimated 25%, in view of comorbid epilepsy) - carbamazepine, sodium vaporate, lamotrigine, and pindolol. The randomisation process controls for these two drug categories and, given the

randomisation, changes in prescription over the duration of the study should be balanced in the two arms, but we will also monitor this.

The research assistant will telephone an interactive voice response system (IVRS) created and maintained by the Robertson Centre for Biostatistics (RCB). After logging onto the system with a user ID and PIN, they will provide the screening number, age and gender of the patient for identification. Study centre, determined by user ID, will be the only stratification variable. The IVRS will not reveal the random allocation to the researcher, but notify the study coordinator, who will contact the patient and clinicians to arrange subsequent study visits.

12.2 Sample size

In the open trial of BEAT-IT, the mean (standard deviation, SD) reduction in GDS-LD[22] scores at 3 month post-intervention follow-up was 8.50 (5.24). We have powered the study to detect a mean change of 3.14, or 0.6 SD units between study groups. This makes the conservative assumption that the 4 month post-randomisation change over that in the control group in the proposed design will be 60% of that observed from pre-test to follow-up in the intervention group during the open trial. To detect this effect size difference, the study requires 60 patients in each arm to provide outcome data at 12 months post randomisation (see below for a more detailed justification). The primary analysis will be an analysis of covariance adjusting for the baseline GDS score, which will have power to detect smaller intervention effects, depending on the level of correlation in scores over time.

There are no data to inform the effect of clustering of outcomes for patients seen by each therapist. Assuming each therapist works with an average of 9 participants (i.e. several part-time therapists at each site), and assuming an intraclass correlation of 0.025, the sample size must be increased by 20% to 72 per group, or 144 in total. Recruitment of 166 participants will allow for up to 13.3% loss to follow-up. The study would then be the largest behavioural activation evaluation to date (based on the studies included in recent reviews of the non-disability literature), despite targeting a difficult to reach population often excluded from research.

The meta-analysis of research with the non-LD population by Ekers, Richards and Gilbody[17] found a post-intervention effect size on self-reported depression symptoms of behavioural activation therapy vs. supportive therapy of 0.75. These designs are the equivalent to our own attention-control design. However, Ekers et al did not report data regarding longer-term follow-up in comparison to supportive therapy. The effects relative to brief psychotherapy were 0.56 post-intervention and 0.50 after an average follow-up of 4 months, suggesting that the effects of behavioural activation therapy might persist for some time. Our follow-up of 12 months post-randomisation will be approximately 9 months post-intervention so we will be able to detect differences between groups only if they persist over a longer time frame than usually studied. Therefore, we believe that an effect size for sample size estimation purposes of 0.60 is realistic given the results of this meta analysis for behavioural activation vs supportive therapy, and would be considered to be of "moderate" size and thus meaningful from a clinical perspective.

13 Data analysis

13.1 Main analysis

All outcome measures at each time point, and changes over baseline, will be summarised using appropriate statistics. The primary analysis will compare GDS-LD scores at 12 months post-randomisation between intervention groups, adjusting for baseline GDS-LD scores and study centre within a mixed effects linear regression model, including therapist as a random effect. Similar methods will be applied to the primary outcome measure at the immediate post-intervention assessment (4 months post-randomisation), and to secondary outcome measures at all assessment points. Where necessary, outcome measures will be transformed to satisfy modeling assumptions. Repeated measures analysis, adjusting for minimisation factors, will also be applied to each outcome measure. Models for the primary outcome will be extended to explore the effects of baseline characteristics, including the minimisation factors, chronicity of depressive symptoms, life events, and history of previous failed psychological intervention. The moderating effects of these factors will be explored using appropriately constructed interaction terms within linear regression models. These moderation analyses will be exploratory only and designed to inform future translation of intervention into clinical practice. Similarly, we will also carry out some

exploratory analyses focused on potential mediation effects. In particular, changes to 4 months post-randomisation can be explored as mediators of effects to follow-up at 12 months post-randomisation, and therapist rated session data can be used to explore potential mediators that may change within the therapeutic process.

13.2 Qualitative analysis

The interviews will be analysed using framework analysis. This is a highly structured form of qualitative data analysis initially developed by the National Centre for Social Research[47] and particularly suited for applied research. Rather than themes and sub-themes being wholly emergent from the data, framework analysis allows the researcher to start with a set of a priori themes which are used as an initial guide to the analysis, although in the analysis these themes can be altered and new themes can emerge from the data. Framework analysis is less labour-intensive than many other types of qualitative data analysis, and allows for the systematic examination of data from relatively large samples for qualitative analysis.

For this study, the major a priori themes to begin the framework analysis will concern a number of dimensions that may inform the future uptake of intervention in clinical practice. These will include: patients', carers', and therapists' perspectives on the process of change; helpful and unhelpful aspects of the interventions; factors relating to the three-way working relationship and the carer-patient relationship; and barriers and facilitative factors relating to the maintenance of the interventions after cessation of contact with the therapist.

This part of the research is not hypothesis driven. Instead, the main aim is to gain an 'insider's perspective' that will assist with the interpretation of the quantitative results and help with the translation of the research findings into everyday practice.

A focus group of the study therapists will be held after the cessation of all treatment to draw conclusions from the therapist logs about perceived barriers and successes, which they will keep at each session. Data from the focus group will be included in the framework analysis as additional evidence.

13.3 Relationship between qualitative and quantitative evaluation

We anticipate that the qualitative data will enhance the quantitative analyses in three distinct ways. First, while the quantitative data will provide answers to the question of the effectiveness and cost-effectiveness of the intervention, they will not provide detailed insights into the process or mechanisms of change. Initial data on this will, however, emerge from the participants' accounts (those of patients, carers, and therapists) of their experiences of BEAT-IT. Data from the therapists' session logs, adherence data and activity and mood data collected in session will offer further insights into the change process or, indeed, why change does not occur. Second, interviewing patients and carers may identify unanticipated outcomes of the group, either positive or negative, and barriers to change. Finally, if the study shows positive results, the qualitative data should provide insight into how the approach can be adapted to different individual needs, thereby assisting with the translation of the research findings into everyday practice.

13.4 Health economic analysis

In the initial pilot stage, the contribution of the health economics will be confined to ensuring that the appropriate data collection of resource use is made to support a full economic evaluation of the trial if the study proceeds to the second stage. The full economic analysis will compare the costs of the treatment with the quality of life benefits as measured by the EQ-5D in the 12 month post randomisation follow-up period. The estimation of benefits to participants will be based on the version of the EQ-5D that has been adapted for use with children, because the language is more accessible and straightforward (but not child-like) [48]. The difference between treatment and control will be adjusted for any baseline differences in EQ-5D.

In addition, consideration will be given to potential cost-offsets associated with the treatment in terms of both direct costs to health and personal social services and direct costs to the patient and their carer[49]. The base case perspective will be the NHS and personal social services supplemented by a broader analysis that considers patient/carer costs. There are two components to the estimation of direct health service costs. Firstly, the costing of the interventions (behavioural activation therapy and the attention control) where the principal cost for these will relate to the time required to deliver the intervention. The second part of the costing will be to establish

other service resource use and for that we will use the CSRI and the medication checklist. During the setup phase we will explore whether this format needs to be adapted for use with this patient population. Standard reference costs (e.g., from the PSSRU reference manual) will be used to cost resources. The societal perspective will be assessed very simply as the time burden associated with patients and their carers attending for contacts with the health/social services. Uncertainty in cost, QALY[50], and cost-per QALY estimates will be handled statistically through the use of non-parametric bootstrapping during the period of the trial. Extensive sensitivity analysis will be used to explore issues around whether unit costs might be somewhat different for patients with learning disabilities, the grade/salary of staff delivering the intervention and the number of sessions they can deliver per week, and the impact on cost-effectiveness of alternative assumptions concerning the durability of any treatment effect beyond the 12 months post-randomisation follow-up.

14 Good Clinical Practice (GCP)

14.1 Ethical conduct of the study

The study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki (version 9, 2008) and are consistent with Good Clinical Practice. The Research Governance Framework for Health and Community Care in Scotland (second edition, 2006), and the Department of Health Research Governance Framework for Health and Social Care will be adhered to.

A favourable ethical opinion will be obtained from an appropriate research ethics committee, and local NHS R&D approval will be obtained prior to commencement of the study in all study sites.

14.2 Investigator responsibilities

The Chief Investigator is responsible for the overall conduct of the study, compliance of the protocol and any protocol amendments. In accordance with the principles of GCP, the following areas listed in this section are also the responsibility of the Chief Investigator. The responsibilities may be delegated to an appropriate member of the

study staff. Delegated tasks will be documented in a delegation log and signed by all those named on the list.

14.3 Study site staff

The Chief Investigator will be familiar with the protocol and the study requirements, and will remain up to date with the principles of Good Clinical Practice. It is the Chief Investigator's responsibility to ensure that all study staff are adequately informed of the protocol and trial related duties.

The researchers and therapists involved in the study will follow the local University and NHS procedures and policies for lone workers.

14.4 Data recording

The Chief Investigator is responsible for the quality of the data recorded in the study databases affiliated documentation.

14.5 Confidentiality

All evaluation forms, reports and other records will be identified in a manner to maintain participant confidentiality. All records will be kept in a secure storage area with restricted access to research staff. Study information will not be released without the written permission of the participant, except as necessary for monitoring auditing by the sponsor, sponsor's designee, regulatory authorities or the research ethics committee.

The Chief Investigator and study staff will not disclose, or use for any other purpose other than performance of the study, any data, raw record or other unpublished, confidential information disclosed to those individuals for the purpose of the study. Prior written agreement from the sponsor, or the sponsor designee, will be obtained for the disclosure of any confidential information to other parties.

14.6 Data Protection

All study staff involved with this study will comply with the requirements of the Data Protection Act 1998[51] with regard to the collection, storage, processing and disclosure of personal information will uphold the Act's core principles. Access to collated participant data will be restricted to members of the Trial Management Group (TMG), and representatives of the Sponsor in specific circumstances.

Electronic data will be stored on firewalled University and NHS computers. Files will be password protected and only accessible to researchers responsible for the running of the study and the CI. All procedures for data storage, processing and management will be in compliance with the Data Protection Act 1998[51]. All participants will be given a unique study number and no personal details will be retained. All paper records will be stored in a locked filing cabinet, with keys available only to researchers and the chief investigator. The Trial Statistician will carry out analysis. All essential documents generated by the trial will be kept in the Trial Master File.

15 Study conduct responsibilities

15.1 Protocol amendments

Any changes in research activity except those necessary to remove an apparent immediate hazard to the participant must be reviewed and approved by the Chief Investigator. Amendments to the protocol must be submitted in writing to the sponsor for approval, and subsequently to the research ethics committee and local NHS Research and Development offices for approval prior to the participants being enrolled into an amended protocol.

15.2 Protocol violations and deviations

The Chief Investigator should not implement any deviation from the protocol without agreement from the sponsor, research ethics committee and with NHS R&D approval, except when necessary to eliminate an immediate hazard to trial participants.

In the event that the Chief Investigator needs to deviate from the protocol, the nature of and the reasons for the deviation should be recorded in the Trial Master File. If this necessitated a subsequent protocol amendment, this should be submitted to the

sponsor, research ethics committee and local NHS R&D for review and approval if appropriate.

15.3 Study record retention

All study documentation will be kept for at least five years after the end of the research, and will be archived in line with standard operating procedures on archiving.

15.4 End of study

The end of study is defined as the last participant's final visit from relevant research staff and will be reported to the sponsor, research ethics committee and NHS R&D.

Once the final report has been approved by the study funder, a copy will be sent to the sponsor, and NHS R&D offices. A summary report of the study will be provided to the research ethics committee within one year of the end of the study.

16 Trial management and oversight arrangements

16.1 Trial Management Group (TMG)

The TMG will consist of the Principal Investigator, Co-applicants, Research Staff, Trial Manager, Trial Statistician and Trial Secretary. The role of the TMG is to help set up the study by providing specialist advice, input to and comments on the Study procedures and documents (information sheets, protocol etc). They will also advise on the promotion and the running of the trial and deal with any issues that arise. The group will meet, either face to face or using audio-conferencing facilities, monthly throughout the course of the study.

16.2 Trial Steering Committee (TSC)

A TSC will be established and will meet at least annually after the internal pilot phase of the research. The TSC will include an independent chair, and six other independent members. All appropriate disciplines have been covered in choosing the TSC members. The TSC will be chaired by Professor David Felce (Director of The Welsh

Centre for Learning Disabilities, Cardiff University) who is an expert in interventions for people with learning disabilities, and has recent experience of helping to coordinate a RCT. Members will be a Consultant Clinical Psychologist with expertise on the delivery of psychological therapies to people with learning disabilities, a statistician, a learning disability key-worker, a family member, and two service users. Enable Scotland, the main voluntary organisation in Scotland representing the views of people with learning disabilities and their families, have agreed to identify service users who would be interested in joining the TSC. A supporter from Enable would also be in attendance to support the service users' participation. The first meeting will be before the recruitment commences to review the protocol and arrange the timelines for the subsequent meetings. If necessary, additional/more frequent meetings may occur. The Chief Investigator, trial manager and statistician will attend as observers. The Trial Steering Committee (TSC) will provide overall supervision for the trial and provide advice through its independent chair.

16.3 Data Monitoring Committee (DMC)

A DMC will be set up and will meet at least once a year during the trial. The DMC will comprise an independent chair and two other independent members with expertise in data management and clinical trials.

17 Reporting, publications and notifications of results

17.1 Authorship policy

Ownership of the data arising from this study resides with the study team. On completion of the study, the study data will be analysed, and a final report prepared.

17.2 Publication and presentations

All publications and presentations relating to the study will be authorized by the Trial Management Group.

The study report will be used for publication and presentation at scientific meetings. Investigators have the right to publish orally or in writing results of the study, subject to contract conditions with the NIHR. Published results will not contain any personal data that could allow identification of individual participants.

Summaries of results will be sent to participants and carers, after the findings have been accepted through the peer review process.

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