Behavioural activation for depression (Beat-D) in adolescents with mild to moderate learning disabilities. A feasibility randomised controlled study of Beat-D versus treatment as usual

Sponsor:	University of Warwick
Address:	University of Warwick, University Road, Coventry, CV4 7AL
Named Contact:	
Tel. No:	
E-mail:	

Chief Investigator	Professor Kylie Gray CEDAR University of Warwick
Funder and reference number	Monash Warwick Alliance
REC number	
UKCRN number	
Version number and date	Version 1.4 16.03.2023
Sponsor R&D number	

Signature Page for Investigators

Study Title: Behavioural activation (Beat-D) for depression in adolescents with mild to moderate learning disabilities. A feasibility randomised controlled study of Beat-D versus treatment as usual

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.

Chief Investigator

Professor Kylie Gray

Signature	Date
	16.01.2022

Chief Investigator:

Professor Kylie Gray

CEDAR
Westwood Campus
University of Warwick
Coventry
CV4 7AL

Tel No: 024 765 73147
E-mail: k.gray.1@warwick.ac.uk

Co-Investigators:

Professor Richard Hastings
Professor of Psychology

Centre for Educational Development Appraisal and Research (CEDAR)
University of Warwick
Coventry
CV4 7AL
UK

Email: R.Hastings@warwick.ac.uk

Andreas Paris
Research Assistant

Centre for Educational Development Appraisal and Research (CEDAR)
University of Warwick
Coventry
CV4 7AL
UK

Email: andreas.paris.1@warwick.ac.uk

Professor Andrew Jahoda
Professor

Institute of Health and Wellbeing,
University of Glasgow
1 Lilybank Gardens
Glasgow
G12 8RZ

Email: Andrew.Jahoda@glasgow.ac.uk

Dr Ashley Liew

Centre for Educational Development Appraisal and Research (CEDAR)
University of Warwick
Coventry
CV4 7AL
UK

Figure 1: Study flow chart

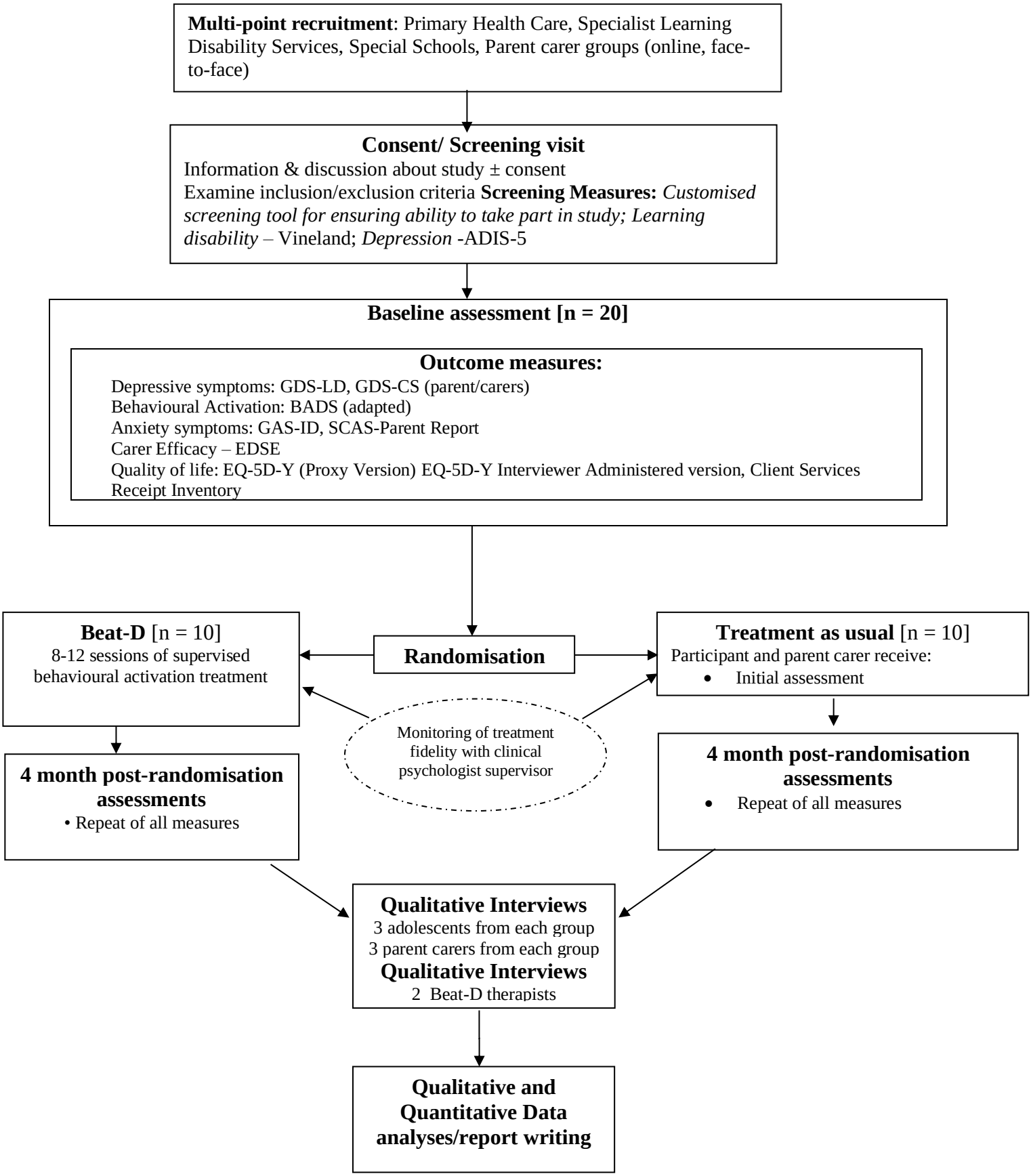

Table 1: Schedule of outcome measure assessments during trial (see section 10 for further details on outcome measures)

	Demographic & health questionnaire	**Self-report depressive symptoms**	**Proxy- report depressive symptoms**	**Activity questions**	**Carer efficacy questionnaire**	**Behaviour and emotional problems**	**Quality of life and well-being measures**	**Qualitative interview**
Baseline	x	x	x	x	x	x	x	
Time 2 (≈ 4 months from randomisation)		x	x	x	x	x	x	X (sub sample)

1.0 Study Summary

Adolescents with learning disability (LD) face significant mental health inequalities. Children and adolescents with LD are 4-5 times more likely to have mental health problems compared to children and adolescents without LD. The inequalities include a lack of tested effective treatments. We aim to address this neglected area of mental health research, establishing a platform internationally for developing/adapting and evaluating psychological treatments. A working method will be developed via a feasibility study of a psychological treatment for depression in adolescents with LD.

Depression is the third leading contributor to the global burden of disease, and the World Health Organization predicts it will be the second leading contributor to global burden by 2020. Young people with LD are 1.7 times more likely to experience depression than other young people. Depression causes avoidable human suffering for people with ID, their families and local communities.

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 people with LD do not have the communication skills to participate in most available psychological therapies.

Clinical guidelines recommend the provision of individual psychological therapy for children and adolescents with moderate-severe depression. However, recent international reviews have established that there is no quality evidence for psychological therapies for children and adolescents with ID. To date, studies of the treatment of depression in children and adolescents have not included children with LD.

Behavioural Activation is a psychological therapy that has been shown to be as effective as CBT. The advantage for people with LD 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. We have shown that Behavioural Activation is effective for adults with mild/moderate LD (Beat-It-A). The proposed study will examine the effectiveness of the Behavioural Activation intervention that has been slightly adapted for adolescents with mild to moderate LD and depression (Beat-D).

In the proposed study, half the participants will take part in the Beat-D (behavioural

activation) treatment, and half will receive usual NHS treatment. People who choose to take part will be involved for a maximum of six months. The study will take place in Birmingham. We would like to find out: i) if we can recruit participants to the study, ii) if we can collect the outcome measures iii) what people think about the treatment and research study design.

Our team is made up of researchers with expertise in working with people with LD, experts on clinical therapeutic interventions, and experts in using statistics in research. In the study centre, we have strong links with the NHS and specialist learning disabilities service.

2.0 Background

2.1 The health need

A significant proportion of the UK population has LD. Approximately 2% of adults and 3.5% of children have an intelligence quotient <70, although 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) [1&2]. Individuals with LD experience health inequalities, with needs not well met by the NHS [3-5]. They have much higher levels of mental ill-health than the general population, with a point prevalence of 40% for adults [6]. This is a burden at the individual, family and societal level, including a cost burden. For example, England spends £3 billion per annum on specialist support for persons with LD, with the prevalence of their poorly addressed mental health needs contributing to costs[7]. This is 50% of the equivalent amount spent on mental ill-health in the general population [8], despite being provided for only 2% of the population.

Depression is a major public health challenge. Unipolar depression alone is the third leading contributor to the global burden of disease and its prevalence is expected to rise [9]. Depression is highly prevalent amongst adolescents with LD and contributes to human misery, as well as cost of daily care and support.

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 LD. There is, therefore, a need to redress this inequity by identifying effective therapies for adolescents with LD. Recent efforts have focused on the adaptation of cognitive behavioural treatment (CBT) models for use with individuals with LD [10], 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 LD, due to the cognitive and communicative demands[5].

2.3 Behavioural Activation

A meta-analysis of studies with the general population found that behavioural activation is as effective as CBT in the management of depression [11]. 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 adolescents with LD, behavioural activation treatment may be more accessible and effective in the management of depression.

Models of behavioural activation treatments[12-13] have evolved from earlier behavioural approaches and take greater account of the context of an individual's life. They have a focus on understanding the function of an individual's 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 LD may have limited opportunities to participate in a range of occupational or social activities [14]. By definition, they have problems with adaptive behaviour (day-to-day social, communication, and life skills), in addition to cognitive impairments [15]. 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-A treatment adapted for use by adults with LD works with dyads of individuals and their carers to develop a structured programme of activities and strategies for increasing motivation[16]. This systemic approach is also designed to improve the generalisation and maintenance of the treatment's impact. This approach has been further adapted for use with adolescents with LD and depression.

2.4 Beat-D clinical trial

For this feasibility RCT, the Beat-It-A treatment manual has been carefully tailored to take account the needs of adolescents with mild to moderate LD. The adapted treatment manual has been named ‘’Beat-D’’.

This is a randomised controlled trial of Beat-D for depressive symptoms experienced by adults with mild-moderate LD demonstrated positive change on depressive symptoms at 4 and 12 months post-treatment [16], with strong effect sizes on the Glasgow Depression Scale[17] and carer report using the Intellectual Disabilities Depression Scale[18].

3.0 Study objectives

3.1 Primary objective

To comprehensively evaluate the feasibility of a treatment trial for depression in adolescents with mild to moderate LD.

3.2 Secondary objectives

1. How acceptable is the treatment to the adolescents with LD, their parents/carers, and therapists? Do therapists feel the therapeutic processes were appropriate for adolescents and their parents/carers?
2. What is the rate of recruitment of adolescents with depression and mild-moderate LD to the study over a 10-month period?
3. What is the retention rate of the recruited adolescents with LD six-months post-randomisation?
4. Which outcome measures (potential primary and secondary outcome measures) have greatest utility to detect meaningful change in the participants with LD, and their parents/carers?
5. Are adverse events associated with the treatment in this study population?
6. What are the reasons for study non-completion?
7. Is behavioural activation delivered with fidelity to the manual/model, and what is the adherence of participants to the treatment?
8. What is treatment as usual for adolescents with LD and depression?

4.0 Study design

The proposed study is a single-centre, single-blind, feasibility randomised controlled trial (RCT) of Beat-D compared to treatment as usual, plus a qualitative investigation of adolescents', 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.

5.0 Sample and recruitment

5.1 Recruitment strategy

The study aims to recruit 20 adolescents with mild to moderate LD and clinical depression. A multi-point recruitment strategy[19] will be adopted, involving primary health care services, specialist LD services, relevant voluntary organisations, local special schools, and parent carer groups (online and face-to-face). Self-referrals will also be accepted, as potential participants and carers may find out about the study through this multi-point recruitment strategy. Recruitment strategies will include outreach work with voluntary provider organisations to help them to identify adolescents with LD and depressive symptoms. Reviews will also be carried out with specialist health professionals to identify potential participants on caseloads who may be eligible. A record will be kept of the numbers of potential participants 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. During screening, the presence of a learning disability will be assessed using the Vineland Adaptive Behaviour Scale[20]. The diagnosis of mild-moderate learning disability will be based on international criteria (ICD-10) that includes both low intellectual ability and adaptive behaviour deficits. Clinically significant depression will be defined by the Anxiety Disorders Interview Schedule for DSM-IV (Parent Interview Schedule)[21].

5.3 Inclusion criteria:

1. Learning disability – a standard score in the range of 75 or below for the Adaptive Behaviour Composite score on the Vineland Adaptive Behaviour Scales 3rd edition

2. Adolescents identified administratively with a Learning Disability (LD), or with diagnostic information (IQ score below 70, assessed by a standardised test, and having deficits in adaptive functioning) age), and/or administratively defined as having LD (e.g., enrolled in a special school for children/adolescents with mild LD or in a SEN setting in a mainstream school, day centre etc)
3. Participants with LD may also have other conditions or developmental disabilities such as Autism Spectrum Disorder (ASD) or Attention deficit hyperactivity disorder (ADHD).
4. Participants with LD have capacity to assent/consent to take part in the research (and thus would then also have sufficient communication and understanding to take part in the treatment)
5. Aged 12-17 years
6. Clinically significant unipolar depression as determined using information gathered through clinical interview (ADIS).
7. Has support from a family member, or paid carer who can support them throughout the treatment.

5.4 Exclusion criteria:

1. A suicide attempt in the past six months; or require intensive (inpatient) treatment for mental illness
2. Intensive inpatient treatment for mental illness in the past 6 months
3. Anti-depressive medication initiated or changed dose in the past 4 weeks
4. Factors that prevent the young person from interacting with the supporter and therapist or retaining information from the therapy (e.g. severe psychosis, degenerative condition). Consent not given to contact the participant's GP about their participation in the study.
5. Currently receiving any psychological therapy for a mental health problem
6. Insufficient English language skills to complete the measures or participate in the treatment.

6.0 Recruitment Process

Procedures for participant recruitment are outlined in the following sections.

6.1 Informed consent

6.1.1 Participants

A study information leaflet will be given to potential participants, supported by a parent carer, by a member of staff known to the potential participant and working in primary health care services, specialist LD services, relevant voluntary organisations, special schools or directly to parent carer groups (online/face to face). The member of staff will give a brief explanation to the individual and their carer about the study and explain that they can contact the research team if they are interested in finding out more about the study.

Participant information sheets for use by adolescents with LD have been designed. These use language appropriate to the developmental level of individuals with a mild to moderate level of LD. A separate information sheet will be provided for their parent carer. When an individual is interested in finding out more about the 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 and their parent carer at their home. However, if this is not convenient or desirable for a potential participant and their parent carer, then they will be invited to identify an alternative place to meet. At the time of the first meeting with the potential participant and their parent carer, the researcher will invite the person and their parent carer to discuss what would be involved in participation in the research study. The researcher will read through the information sheet with the potential participant and their parent carer.

The verbal explanation given to the potential participant and their parent carer 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. There will be an opportunity to discuss the study and the potential participant and their parent carer will be given every opportunity to clarify points they do not understand and, if necessary, ask for more information. The participant and their parent carer 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. When a potential participant, and their parent 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.

During the process of obtaining consent, procedures in keeping with the Adults with Incapacity Act, 2000, will be used. The written consent form will use language appropriate to the developmental level of individuals with LD. Where participants are under 16, their parent carer will be required to provide their consent for them to participate in the research. Parent carers will also be providing their own consent to participate in the study. The consent form will be read through with the individual with LD and they will be asked to sign it, witnessed by a carer or other individual independent of the study. A member of the research group and the participant will sign and date the consent form to confirm that consent has been obtained. 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 participant information sheets and consent forms for the participant:
1. Simplified and accessible easy read information sheet
2. General information sheet
3. Simplified and accessible easy read consent form
4. General consent form

6.1.2. Carer

The main identified carer will be given the following information sheet and consent form:
1. General information sheet
2. Consent form

7.0 Withdrawal and loss to follow-up

Participants have the right to withdraw consent for participation in any aspect of the trial at any time. The participant's 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, unless the participant or their parent carer, requests for their data to be removed prior to analysis taking place (date to be specified in information sheets).

8.0 Study interventions

Participants will be randomised to either:

1) Beat-D for depression
2) Treatment as usual

8.1 Beat-D

The treatment is designed to be delivered to individuals alongside a parent carer. It is a structured, time limited, manualised psychological therapy, developed to treat those with an LD and depressive symptoms. 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 can be delivered in person, or using video conferencing.

The treatment is divided into two phases, starting with an assessment period (4 sessions), where the participant with LD 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 participant and their carer (session 4). This provides a shared 'story' or common frame of reference for joint work between the participant, carer and therapist. Maximum participation by the person with LD 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 participants 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, (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, and 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 participant and carer to maintain and build on progress they have made. A booklet is prepared for the participant 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 Treatment as usual

This will include the existing treatments available in NHS and social care for adolescents with LD with depression, including anti-depressants, mood stabilizers, and any available psychological interventions. Information will be collected from both groups about service supports and treatments they receive during the course of the study, to help describe treatment as usual and to inform the data collection methods for the economic element of a future trial.

8.3 Therapist adherence to the Beat-D protocols

To establish adherence in the delivery of the Beat-D treatment by therapists, fidelity checklists will be completed after every session by the therapists and provided to the research team for analysis.

8.4 Risk Assessment

Risk information regarding visiting participants at home will be communicated to researchers and therapists by the referring individual/organisation. The participant should be informed of this. If the allocated participant is not previously known to services, the therapist should follow their service's standard procedure for seeing new clients safely.

8.4.1 Lone Working Policy

A Lone Working Protocol has been created for Research Assistants carrying out home visits/assessments (Appendix A)

8.4.2 COVID-19 Mitigation

There are risks associated with the COVID-19 pandemic for this study. For the Recruitment and Consent/Screening phases, risk to either participants or the study team because of taking part in this study or carrying our any procedure associated with this study is minimal. The reason is that these phases will take place via the phone or online using video-conferencing and online survey methods.

The assessment, intervention and post intervention phases pose greater risk as there is likely to be planned contact between members of the study team, health care professionals, and parents/carers/participants. However, as this study will take place in the NHS, and will be delivered by NHS clinicians, any wider COVID-related risk mitigation strategies in operation within NHS Trusts will apply to this study, the study team, and any therapist working as part of the study. This is likely to involve the use of Personal Protective Equipment and/or increased use of video conferencing or telephone calls.

9.0 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 Case Report Form (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 unexpected SAEs are possibly or definitely related to the study intervention, these unexpected SAEs will be communicated to the CI for review and will be reported to the Research Ethics Committee. Unexpected and unrelated SAEs will be

followed until resolution.

9.4 Reporting to the Sponsor

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

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.

10.0 Study Outcomes

10.1 Measures/assessment instruments

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

- Baseline
- Time 1 – four months post-randomisation (post intervention)

Data collection interviews should take place as close to the scheduled data collection point as possible and always within the period of between two weeks before and four weeks after the due date (based on date of randomisation).

Outcome measures for the feasibility study include:

1. Depressive and anxiety symptoms
2. Behavioural Activation and coping ability
3. Participant activity levels
4. Quality of life
5. Carer efficacy
6. Service use (information about service supports and treatments)

An outline of data collected at the two time points is shown in Table 2, 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 2, a purpose specific questionnaire to gather demographic and health data about participants will be completed at baseline only. This will include questions about the participants' expectations of therapy. This questionnaire was used in the initial Beat-It-A (for adults) clinical trial 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 2: Outcome measure assessments

Outcome	Measures
Depressive symptoms	Glasgow Depression Scale for Intellectual Disabilities (20 items: 10 minutes) Glasgow Depression Scale for Intellectual Disabilities – Caregivers Supplement (16 items: 10 minutes)
Behavioural Activation	BADS (8 items: 10 minutes)
Anxiety symptoms	Glasgow Anxiety Scale for Intellectual Disabilities (27 items: 10 minutes) Spence Children's Anxiety Scale – Parent Report (45 items: 15 minutes)
Carer Self-efficacy	Emotional Difficulties Self-Efficacy Scale (10 items: 5minutes)
Quality of life	EQ-5D-Y Proxy version (5 dimensions: 5 minutes) EQ-5D-Y Interviewer Administered version (5 dimensions: 10 minutes)
Health economics	Client Service Receipt Inventory (30 items: 10 minutes)

10.2 Measures of depressive and anxiety symptoms

Depression symptoms

Glasgow Depression Scale[17]: The Glasgow Depression Scale is a self-report measure designed to assess depressive symptoms in people with LD. It consists of 20 questions assessing depressive symptoms over the past week and is designed to be easily understood and completed by individuals with mild to moderate LD. Participants (adolescents) will complete this measure at baseline and 4 months. It takes approximately 10-15 minutes to complete.

Glasgow Depression Scale – Caregiver Supplement[17]: The Glasgow Depression Scale – Caregiver Supplement (GDS—CS) consists of 16 items and was designed to assess carers' views and report of their direct observations and concerns about the prevalence of depressive symptomatology of the person with LD. The scale can assess symptom level across a 1-week period and can be used both as a process and an outcome measure.

Children's Depression Rating Scale Revised: The CDRS-R is a brief rating scale based on a semi-structured interview with children and adolescents. The clinician rates 17 symptom areas that are used to aide in diagnosis of depression. Each item is rated on a 7point scale, with a final Summary Score obtained. It takes approximately 15-20 minutes to complete, and will be administered at both baseline and 4 months to gather information on change in depression symptomatology.

Anxiety symptoms (self-report)

Glasgow Anxiety Scale for people with ID (GAS-ID): Self-reported measure designed to measure the intensity of anxiety symptomatology in people with an intellectual disability and has been shown to discriminate between anxious and non-anxious participants. It consists of 27 items. Takes approximately 10 mins to complete and will be completed by the adolescent themselves at baseline and 4 months.

10.3 Behavioural Activation and functional engagement with activities

Behavioural Activation for Depression Scale: The BADS is an 8-item clinician or self-administered questionnaire, designed to track changes weekly in behaviours

hypothesised to underlie depression and specifically targeted for change by behavioural activation. Has been previously used with neurotypical participants and has been adapted for adolescents with LD. It will be administered at baseline and at 4 months

10.4 Qualitative interviews and process evaluation

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-D therapy and attention control 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 LD, including guidelines approved by the ESRC.

As a standard part of the Beat-D 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 needs 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.

10.5 Quality of Life and Health economics measures

Client Service Receipt Inventory (CSRI)[23]*:* 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 LD. 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. EQ-5D-Y Proxy version 1 (EuroQol, 2009): The EQ-5D -Y is a standardised measure of health status for clinical and economic appraisal, and will be completed by parents to assess their children's' health-related quality of life in their (the proxy's) opinion, as well as to explore the feasibility of measures to be used in a future health economics evaluation. It takes approximately 5 minutes to complete.

EQ-5D-Y Interviewer Administered version (EuroQol, 2009): The EQ-5D-Y is a standardised online measure of health status for clinical and economic appraisal and will be completed by adolescents (youth version) to assess their health-related quality of life, in the areas of mobility, looking after oneself, doing usual activities, having pain or discomfort and feeling worried, sad or unhappy). It will also be used to explore the feasibility of measures to be used in a future health economics evaluation.

11.0 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 participants' references to meeting with therapists.

The research assistants carrying out the assessments will be masked to intervention allocated and/or received. The Chief Investigator will be informed of any unmasking and corrective action in terms of training and correctly following procedures will be instigated if necessary. Treatment allocation will remain concealed until all participants have exited the trial.

12.0 Statistical considerations

12.1 Randomisation

Participants will be allocated to one of two study groups using random permuted blocks. The randomisation lists will be developed by the trial statistician, who will not be involved in recruitment, data collection, or statistical analysis. The final lists will be passed to the study coordinator, who will save them in a restricted folder (i.e. not accessible by those who are to remain blind to allocation for the duration of the study period).

After obtaining informed consent and the collection of baseline information, participants will be allocated to one of the two study groups.

The research assistant will e-mail the study coordinator with the participant's screening number, age, and gender (for verification). The study coordinator will access the list corresponding to the participant's centre and assign the next available allocation to the participant. The allocation will not be revealed to the research assistant. Following this, the study coordinator will contact the clinicians to arrange subsequent study visits.

12.2 Data analysis

12.2.1 Quantitative analysis

All outcome and demographic variables will be presented descriptively using appropriate summary statistics. In addition, variables with baseline and post-intervention measurements will be analysed using mixed effects linear regression to explore potential intervention effects. Although this feasibility study is not powered to explore efficacy, the outcome data will be used to estimate the standard deviation of the data for the different outcomes and will be used to inform the sample size calculations for the next phase of this study.

12.2.2 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[24] 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 the intervention in clinical practice. These will include: 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-participant 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 results and inform decision making about whether a full scale clinical trial is warranted.

13.0 Good Clinical Practice (GCP)

13.1 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.

13.2 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.

13.3 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.

13.4 Data recording

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

13.5 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.

13.6 Data Protection

All study staff involved with this study will comply with the requirements of the GDPR regulations with regard to the collection, storage, processing and disclosure of personal information.

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 GDPR regulations. 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.

14.0 Study conduct responsibilities

14.1 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.

14.2 Study record retention

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

14.3 End of study

The end of the 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.

15.0 Reporting, publications and notifications of results

15.1 Authorship policy

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

15.2 Publication and presentations

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. 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.

16.0 References

1. Bittles AH, Petterson BA, Sullivan SG, Hussain R, Glasson EJ, Montgomery PD. The influence of intellectual disability on life expectancy. Journal of Gerontology 2002; 57A:470-472.

2. Morris JK. The National Down Syndrome Cytogenetic Register 2007/8 Annual Report. Barts and The London School of Medicine and Dentistry.Queen Mary University of London 2009.

3. Scheepers M, Kerr M, O'Hara D, Bainbridge D, Cooper S-A, Davis R, Fujiura G, Heller T, Holland AJ, Krahn G, Lennox N, Meaney J, Wehmeyer M. Reducing health disparity in people with intellectual disabilities: A report from the Health Issues Special Interest Research Group of the International Association for the Scientific Study of Intellectual Disabilities. Journal of Policy and Practice in Intellectual Disabilities 2005; 2:249-55.

4. Mencap. Death By Indifference.http://www.mencap.org.uk/document.asp?id=284 2007.

5. Disability Rights Commission. Equal Treatment: Closing the Gap. A Formal Investigation into the Health Inequalities Experienced by People with Learning Disabilities and/or Mental Health Problems 2006.

6. Cooper S-A, Smiley E, Morrison J, Williamson A, Allan L. Mental ill-health in adults with intellectual disabilities: prevalence and associated factors. British Journal of Psychiatry 2007; 190:27-35.

7. Department of Health. Valuing People: A New Strategy for the 21st Century. London: The Stationery Office 2001.

8. Sainsbury Centre for Mental Health. The Economic and Social Costs of Mental Illness. Policy Paper 3. London: Sainsbury Centre for Mental Health 2003.

9. Collins PY, Patel V, Joestl S, et al. Grand Challenges in global mental health. Nature 2011; 475:27-30.

10. Hassiotis A, Serfaty M, Azam K, Strydom A, Martin S, Parkes C, Blizard R, King M. Cognitive behaviour therapy (CBT) for anxiety and depression in adults with mild intellectual disabilities (ID): a pilot randomised controlled trial. Trials 2011; 12:95 doi:10.1186/1745-6215-12-9.

11. Jahoda A, Dagnan D, StenfertKroese B, Pert C. Trower P. Cognitive behavioural therapy: From face to face interaction to a broader contextual understanding of change. Journal of Intellectual Disability Research (Invited review) 2009; 53:758-771.

12. Stancliffe RJ, McVilly KR, Radler G, MountfordL,Tomaszewski P. Active support, participation and depression. Journal of Applied Research in Intellectual Disabilities 2010; 23:312-321.

13. EkersD, Richards D. Gilbody S. A meta-analysis of randomized trials of behavioural treatment of depression. Psychological Medicine 2007; 1-13.

14. Lejuez CW, HopkoDR,Hopko SD. A brief behavioral activation treatment for depression. Treatment manual. Behaviour Modification 2001; 25:255-86.

15. Dimidjian S, Hollon SD, Dobson KS, Schmaling KB, Kohlenberg RJ, Addis ME, Gallop R, McGlinchey JB, Markley DK, Gollan JK, Atkins DC, DunnerDL,Jacobson NS. Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the acute treatment of adults with major depression. Journal of Consulting and Clinical.Psychology2006; 74:658-70.

16. Jahoda, A., Hastings, R., Hatton, C., Cooper, S. A., Dagnan, D., Zhang, R., ... & Melville, C.A. (2017). Comparison of behavioural activation with guided self-help for treatment of depression in adults with intellectual disabilities: a randomised controlled trial. *The Lancet Psychiatry*, *4*, 909-919.

17. Cuthill FM, Espie CA, Cooper SA. Development and psychometric properties of the Glasgow Depression Scale for people with a Learning Disability. Individual and carer supplement versions. British Journal of Psychiatry 2003; 182:347-53.

18. Evans KM, Cotton MM, Einfeld SL, Florio T. Assessment of depression in adults with severe or profound intellectual disability. Journal of Intellectual and Developmental Disability 1999; 24:147-160.

19. Woodford J, Farranda P, Bessant M, Williams C. Recruitment into a guided internet based CBT (iCBT) intervention for depression: Lesson learnt from the failure of a prevalence recruitment strategy. Contemporary Clinical Trials 2011; 32(5):641-648.

20. Sparrow, S. S., Cicchetti, D. V., Balla, D. A., & Doll, E. A. (2005). *Vineland adaptive behavior scales: Survey forms manual*. American Guidance Service.

21. Silverman, W.K & Albano, A.M. (1996). *Anxiety Disorders Interview Schedule for DSM-IV: Child Version (Parent Interview Schedule).* USA: Graywind Publications Incorporated.

22. Gray, K.M., Tonge, B., Einfeld, S., Gruber, C., & Klein, A. (2018). *Developmental Behavior Checklist Second Edition: DBC2*. Torrance, California: Western Psychological Services.

23. Chisholm D, Knapp MRJ, Knudsen HC, Amaddeo F, GaiteL,VanWijngaarden B. Client Socio-Demographic and Service Receipt Inventory - European Version: development of an instrument for international2000.

24. Ritchie, J. & Spencer, L. (1994). Qualitative data analysis for applied policy research. In A.Bryman and R. G. Burgess (Eds.). Analyzing qualitative data (pp.173-194). London: Routledge.

APPENDIX A - Lone Working Protocol for BEAT-D

Lone Working:

Lone workers should ensure that their team/line manager have their personal contact number, their In Case of Emergency (ICE) details and details of their car make/model and registration number (if applicable) or other travel details. It is the lone worker's responsibility to ensure that all contact details are maintained and updated.

All lone workers that are issued with mobile phones are expected to keep them charged and turned on whilst at work. Lone workers should consider putting the phone number for their CEDAR admin staff/ RA buddy in the phone so that they have quick access if required. There are a number of personal safety mobile apps which could also be considered: https://www.suzylamplugh.org/Pages/Category/app-directory

Protocol for attending a site/home visit alone:

The RAs on the BEAT-D project have shared access to their Outlook calendar so that appointment details (including the time, participant name and visit location) can be viewed by their Line Manager, admin staff and other RAs if needed.

Before a site/home visit, the RA who is completing the visit shares information with their RA buddy and LM about which participant (Participant ID) they are going to visit and where they are meeting them, whether this is in a public place or at a family home, the date and time of the meeting, and how long they anticipate that this will last. Both LM and buddy RA at the Warwick site have access to the participant databases, within which are all participant data (including home address).

On the day of the site/home visit, the RA who is completing the visit calls the other RA to confirm that they have arrived at the meeting location. If possible, the RA completing the visit can share their location with the other RA on their mobile 'phone. The RAs agree a time to call after the visit and if the RA completing the visit does not call at the agreed time then the other RA will call them to confirm that they are OK. If necessary, this can be completed when the RA completing the visit arrives home after the visit.

If the RA who is completing the visit answers the phone, then the other RA will ask if they are OK and if they need to arrange for another call to take place (if the visit has overrun). The process above is then completed at the newly arranged time.

If the RA who is completing the visit does not answer the phone after a couple of attempts, then the other RA can try to call the person/place they were visiting to establish if they are there or when they left. If no contact can be made, then the other RA must report this to their line manager or a senior member of staff who will then escalate the procedure. If there is concern then the police should be contacted.

University security should also be informed of the situation by calling 02476 522222. University security will then respond to the incident and will liaise with emergency services as required.

If the RA completing the visit feels unsafe but cannot leave the situation, a phrase must be agreed which will be used and understood by the other RA. This phrase means that they are in difficulty and requires help, for example, “I need the red folder”. This should prompt the other RA to alert a line manager who will escalate to a senior member of staff who should consider phoning the police.

Principles of Lone Working from the Warwick Clinical Trials Unit:

When lone working, staff should:

- Be alert to warning signs (body language, tone of voice)
- Carry out a ’10 second risk assessment’, if staff feel unsafe they should leave
- Check for evidence of pets
- On arrival assess the layout and quickest/safest exit route
- Be aware of entrances and exits
- Place themselves near an exit
- Be aware of the positioning of items which could be potential weapons
- In multi-storey buildings consider safety when choosing lifts or staircases
- Remain calm and focussed under no circumstances put themselves at risk
- Consider the distance that they are travelling each day. Staff should liaise with their line managers about reasonable distances to travel in a day.
- **Remember that if they are in any doubt about their safety, to leave the situation**