

## **Assessing the feasibility and acceptability of comparing the Lightning Process® with specialist medical care for Chronic Fatigue Syndrome or Myalgic Encephalopathy (CFS/ME) - pilot Randomised Controlled Trial.**

### *SMILE – Specialist Medical Intervention & Lightning Evaluation*

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#### **Introduction:**

The Royal College of Paediatrics and Child Health in the UK has defined chronic fatigue syndrome or myalgic encephalopathy (CFS/ME) as “generalised fatigue, causing disruption of daily life, persisting after routine tests and investigations have failed to identify an obvious underlying ‘cause’”<sup>1</sup>. The NICE guidelines recommend a minimum time of 3 months of fatigue before making a diagnosis in children.

CFS/ME in children is a relatively common<sup>2-5</sup> and potentially serious condition with over 50% of children bed bound at some stage and a mean time off school of one academic year<sup>6</sup>.

There is a limited evidence base for the treatment for children with CFS/ME. There is one randomised controlled trial (RCT) investigating long term follow up comparing cognitive behavioral therapy (CBT) and waiting list (delayed CBT)<sup>7,8</sup> and one controlled trial investigating outpatient multidisciplinary rehabilitative treatment (graded activity/exercise and supportive care) compared to supportive care alone<sup>9</sup>.

The Phil Parker Lightning Process® is a trademarked intervention that is used for a variety of conditions including CFS/ME. It has been developed from osteopathy, life coaching and Neuro-linguistic programming (NLP). The intervention includes three group sessions on consecutive days where young people will be taught skills that they can try out for themselves including looking at their sitting and standing posture. Families currently pay approximately £620 to attend the Lightning Process course.

Even though over 250 children and young people a year use the Lightning Process as an intervention for their CFS/ME, there are currently no reported studies investigating the effectiveness or possible side effects of the Lightning Process in children. As with all interventions, proper evaluation is necessary if it is to be brought into mainstream practice.

#### **Aims and objectives:**

The overall aim of this study is to investigate the feasibility and acceptability of conducting a Randomised Controlled Trial (RCT) to investigate the effectiveness and cost-effectiveness of specialist medical care with specialist medical care plus the Lightning Process in treating CFS/ME in children. The specific objectives aim to inform the design of a full-scale, adequately powered randomised trial.

The specific objectives are:

1. To investigate the feasibility of assessing children with CFS/ME for eligibility for entry into the RCT.
2. To investigate the recruitment process, including the information provided to potential participants and its acceptability, and barriers to, and rates of, randomisation.
3. To explore prior exposure, beliefs, expectations and preferences about specialist medical care and the Lightning Process intervention in the early stages of the trial, and experiences and acceptability of interventions and outcome later on.
4. To observe the delivery of both specialist medical care and the Lightning Process to provide data on setting, implementation and acceptability.
5. To investigate appropriate patient-reported outcomes for the RCT, including views and experiences of completing existing measures of school attendance, mood, fatigue and function, and development of new measures if necessary.
6. To develop resource use questionnaires to assess the impact of care on health service use and productivity.
7. To use the information above to provide estimates of sample size required for a full-scale RCT.

8. To investigate issues of retention in the RCT, including the acceptability of the care provided in both arms, and reasons for any drop outs.

### **Anticipated outcomes**

1. At the end of this study, we will know whether it is feasible to recruit children with CFS/ME into a RCT comparing specialist medical care with specialist medical care plus the Lightning Process. If it is feasible we will have the necessary pilot data on rates of randomisation and retention as well as sufficient information on treatment effects to determine sample size. This will put us in a very strong position to obtain further funding for a large multicentre study.
2. Information collected on suitability of the outcome measures used will enable us to apply for funding for further outcome development.
3. This study incorporates the first study on health service use in paediatric CFS/ME. This is necessary for the future RCT and will also enable us to perform additional studies using these resource use inventories on paediatric services nationally.
4. We will have detailed qualitative information about what happens when families consider randomisation for treatment.
5. We will have detailed information on socio economic status and loss of earnings in families prior to assessment in a specialist clinic.
6. We will have detailed information on engagement: which families engage, why they engage and whether it determines outcome.

### **Method:**

#### Design

This is an exploratory study to test the feasibility and acceptability of conducting a pragmatic randomised trial with children comparing specialist medical care with specialist medical care plus the Lightning Process. Qualitative research methods have been integrated into the feasibility study to ensure clear understanding of the issues that relate to the successful design and implementation of a full-scale RCT.

#### Population

Children and young people aged 12-18 years inclusive will be recruited after assessment by the Bath/Bristol paediatric CFS/ME service. This is a large regional and national service that currently provides assessment and treatment for over 250 children a year. The majority of referrals are from South Gloucestershire, Bristol, Somerset and West Wiltshire. Referrals are made by paediatricians, General Practitioners and in some cases schools. The majority of children referred into the service have CFS/ME as other causes of fatigue are usually excluded prior to referral. Approximately 10% of children referred into the service are housebound and are assessed at home.

#### Inclusion/exclusion criteria

Children will be included if they have CFS/ME and are between 12 and 18 years old inclusive. Children will be excluded if: they are too severely affected to attend hospital appointments (defined as children and young people that do not regularly leave their house); or if they or their parents have insufficient English to either understand the Patient Information Sheet (PIS) and consent form to take part in the Lightning Process or take part in the interviews.

#### Recruitment

Eligible children and their families will be identified by the clinician conducting the assessment who will inform them about the study and give both the young person and their parents the relevant patient information sheets. The clinician will check that the young person and their family are willing to be contacted by the research nurse and the researcher and will obtain consent for contact and interview by the researcher and for contact from the research nurse. The research nurse will contact the family and arrange to visit them at a convenient location (usually at home) to discuss and provide further information about the study. The qualitative researcher may interview the family prior to randomisation for 20 minutes (see below) at a convenient location.

#### Randomisation

Research nurses will explain the rationale for the study and its design, the uncertainties about the effectiveness of either intervention, the known advantages/disadvantages of the interventions, the options available outside the RCT, and the right not to take part or withdraw at any time. Those willing to take part in the study will be asked to consent to randomisation and sign the consent form. The research nurse will ascertain willingness to participate and will check that both the young person and their family understand the study. The nurse will then telephone the Bristol Randomised Trials Collaboration (BRTC) for the intervention allocation, which will be conveyed to the participant. If for any reason the phone line is unobtainable, randomisation will be completed during the next working day and the participant will be told of the results by phone or in person.

### Interventions

- Specialist Medical Treatment: children and their families are offered a variety of treatment options that are recommended in NICE guidelines<sup>10</sup>. Typically this is centred around graded activity and involves a follow up phone call at 2 weeks followed by family based rehabilitation consultations at approximately 6 weeks (1 hour), 3 months (1 hour), and 4.5 months (1 hour). The number and timing of the sessions are agreed with the child and family and varies depending on the needs and goals of the child. Children who have high levels of anxiety are offered 3 individual sessions of CBT every 2 weeks over a 6 week period. Other interventions such as Graded Exercise Therapy (GET) are available for children and young people if needed.
- Specialist Medical Treatment plus the Lightning Process: In addition to the specialist Medical Care detailed above, young people and their parents will be asked to read the information about the Lightning Process on the website or using information sheets. If the young person is well enough, they will be asked to read a book about the Lightning Process. If they are unable to read the book, they will be asked to listen to an audio book. Children/young people and their parents will be asked to complete an assessment form (which will take about 10 minutes) where they are asked to identify their goals and describe what they learnt from reading the book. After this they will have a telephone call with a Lightning Process practitioner (LPP) (usually approximately 20 minutes). This is used to check that the young person and their parents are happy about attending the course, checks the goals identified by the young person and is an opportunity for the young person and their parents to ask further questions. If the young person and their family are happy to continue, the young person will be given a date to attend a course.
- The course is 3 sessions on 3 consecutive days. Each session is 3 hours 45 minutes long. Group sessions include 4 to 5 young people between 12 – 18 years of age who live within the region covered by the CFS/ME service. During the group, children and young people will have a theory session and a practical session.
  - The theory session will include taught elements on the stress response, how the mind-body interacts and how thought processes can be helpful and negative. The language used by young people will be discussed and in some cases challenged. Young people will be encouraged to think about what they may be able to take responsibility for and change. The taught sessions are followed by a group discussion.
  - The practical session is used to put some of the skills learnt into practise. Young people identify a goal they wish to achieve (such as standing for longer) and are then given alternative ways to think about and prepare for this. This involves using different cognitive (thinking) strategies before and during the goal is attempted. Young people are also asked to identify a goal in which they can practise the strategies in the afternoon or evening. This goal will usually be short but could be an activity that is up to 30 minutes long.
- The LPP will then arrange two follow up phone calls with the young person and parents within 2 weeks of the course and then approximately 6 to 8 weeks later.

### Inventories

*Inventories already completed by children/young people with CFS/ME*

The following inventories are routinely completed by children and young people: 11 item Chalder fatigue scale; pain visual analogue scale; physical function subscale of the SF36; the Spence

Childrens Anxiety Scale (SCAS); the Hospital Anxiety and Depression Scale (HADS) for children aged 14 and over, a single item inventory on school attendance and the EQ5D a five item quality of life inventory. Inventories are collected at assessment 6 months and 12 months. Inventories are sent to children and young people already as part of service evaluation and are self completed and returned in the stamped addressed envelope provided with a high return rate (over 70%).

#### *Extra inventories*

Children and young people who take part in the study will complete the whole SF-36 and not just the physical function subscale (26 additional questions) so that we can calculate a quality adjusted life year at the same time points. We will also ask young people to complete the Profile of Mood States (POMS) because we want to compare this with the Hospital Anxiety and Depression Scale. We estimate that these two extra inventories will take less than five minutes to complete. Children and young people will also complete the inventories at an extra time point at 3 months.

In addition, both parents will be asked to complete three inventories at baseline (just after randomisation). These include an inventory to measure socioeconomic status; an adapted 4 item Work Productivity and Activity Impairment Questionnaire: General Health V2.0 (WPAI:GH) and an adapted existing health resource use questionnaire which we will use to ask a parent and young people about the health service (e.g. GP or specialist care), educational service (e.g. school counsellor) and travel costs most relevant to the CFS/ME population (all included in appendix).

At each follow up time point (, 3 months, 6 months and 12 months), parents involved in the study will be asked to complete the Work Productivity and Activity Impairment Questionnaire and the Health Resource Use questionnaire which will be sent to families in the post with a stamped addressed envelope for self completion.

Those who have not replied within one week of each mailout will be sent a reminder letter requesting that the original set of questionnaires is completed and returned. A reduced set of questionnaires (comprising SF36, Chalder Fatigue scale and school attendance inventory) with a stamped addressed envelope will also be included in case the originals have been mislaid. After another two weeks, those not returning any questionnaires will be telephoned by a researcher who will request gently for respondent to complete the reduced questionnaire set over the telephone. The interviewer will have to know the participant's identity in order to make the phonecall. Please note that this would not affect our policy regarding confidentiality and privacy, as both would have already met for previous data collection. Any data resulting from the phonecall will be recorded anonymously, since all questionnaires will only have the study ID on them.

#### Outcome assessment

The primary outcome measure for the interventions will be school attendance/home tuition at 6 months. Secondary outcome measures will be school attendance at 3 months and 12 months; the SF36 (physical function) at 3 months, 6 months and 12 months and pain visual analogue scale at 6 months.

#### School attendance

Children and young people are asked about school attendance and home tuition in a two item inventory. We will ask for consent to check school attendance using school records and will do this at assessment, 3 months 6 months and 12 months.

#### Patient Reported Outcome Measures

There is currently no evidence on which patient reported outcome measures should be used and what change is clinically significant in the assessment of children with CFS/ME. The qualitative component of this study provides an ideal opportunity to look at this in more detail.

Part of the interviews undertaken with parents and children will include questions about the inventories used at assessment and follow up. In particular, parents and children will be asked to compare the HADS with the Profile of Mood States (POMS) and the SCAS. Observations of

individuals completing outcome assessments will be used to determine the most acceptable and sensitive outcome measures.

#### Data analysis

The feasibility and acceptability of doing an RCT will be assessed using the percentage recruited of those eligible for recruitment and the percentage who complete each intervention out of those randomised to each arm. Qualitative data will also be used to understand the acceptability of the randomisation process. This will inform estimates of sample size for the full RCT.

#### Health economic assessment

The economic evaluation will gather preliminary information on the costs to the NHS, other government agencies and wider society of the interventions in the two arms of the pilot RCT. These costs will be compared to incremental differences in the generic outcome measure (SF-36, EQ-5D). Information on the variance and covariance of costs and outcomes will be used to determine statistical precision of the full trial for economic outcomes. This feasibility study will also enable us to evaluate a resource use questionnaire for use in a definitive trial.

#### Qualitative research

Qualitative research methods will be integrated into this feasibility study. The Lightning Process has received extensive publicity and so it will be important to understand the knowledge and effect of this on participation.

##### *In-depth interviews:*

In-depth interviews will be undertaken with some parents of children on several occasions to form "case studies". Parents will be interviewed at three time points: 1. After assessment and prior to randomisation; 2. After randomisation and before any intervention; and 3. After the intervention. Children will be interviewed once at one of these points for no more than 20 minutes. Purposive sampling will ensure that interviews include a range of informants, in terms of socio-economic circumstances, age, sex, ethnicity and families from both intervention arms (maximum variation sampling), with the potential to target people with characteristics of interest to follow-up and develop emerging findings (theoretical sampling). The sample size will be determined by data saturation, i.e. when no new themes are being uncovered.

It is anticipated that up to 30 interviews (10 case studies) will be conducted. Informants will be interviewed at a location of their choice. Interviews will be semi-structured in that they will follow a checklist of topics to ensure consistency, but parents and children will be able to raise issues of importance. Interviews will explore the recruitment process, including views and experiences of the initial assessment and recruitment to trial appointments, the written and verbal information provided to potential participants and its acceptability, and reasons for accepting or declining participation; beliefs, expectations and preferences about interventions in the early stages of the trial, and experiences of interventions and outcome later on; and prior exposure and external influences to the intervention that might impact upon its implementation and effectiveness.

Part of the interviews will include questions about the inventories used at assessment and follow up. In particular, parents and children will be asked to compare the HADS with the POMS and the SCAS. All interviews will be audio-recorded with consent, transcribed verbatim, and anonymised.

##### *Recording of recruitment to trial consultations:*

All recruitment consultations will be audio-recorded to document the interaction between recruiter and potential participant to explore information provision, recruitment techniques, patient treatment preferences, and randomisation decisions to identify recruitment difficulties and support change. This novel method can provide essential information about the way the study and its interventions are perceived and optimum methods for recruitment and design. It has proved crucial in evaluating information exchange and improving informed consent and rates of randomisation/acceptance of allocation in previous studies<sup>11-13</sup>.

##### *Observations:*

A small number of interventions, specialist medical assessments and specialist medical treatment follow up sessions will be observed by the qualitative researcher. These will be alternate sessions in each arm in the early, mid and late stages of implementation, to assess the implementation, acceptability and setting of intervention/treatment provision. Detailed notes will be taken at the sessions, including the context, intensity and variability of intervention/treatment

delivery, to understand how intervention/treatment is delivered and received in practice and to help interpret outcome results (for example, variations of effects in subgroups). All intervention sessions will be audio-recorded, with consent, for monitoring purposes. Observations will also be made of young people and parents completing the outcome measures to observe for any difficulties or misunderstandings<sup>14</sup>. Participants will be encouraged to describe what they are thinking of when they read each question and how they interpret it, with minimal prompting to allow as close to real life completion as possible. This will be followed by semi-structured interviews to ascertain their views on the measures and to explore areas of misunderstanding and misinterpretation to determine the most acceptable and sensitive outcome measures. The number of observations and interviews will be determined by data saturation, although up to 20 observations and interviews are anticipated.

### *Qualitative data analysis*

Analysis will be an ongoing and iterative process commencing soon after data collection and will inform further sampling and data collection. Interview transcripts and observation notes will be imported into Atlas.ti where they will be systematically assigned codes and analysed thematically to identify themes using techniques of constant comparison.<sup>6</sup> Individuals exhibiting contrasting attitudes ('negative cases') will be studied in detail to understand reasons underlying such contrasts and to gain a deeper understanding of the data and findings. Throughout analysis, the perspectives of the individuals will be paramount, with careful account taken of the context within which the discussion takes place. Descriptive accounts will be produced, and theoretical explanations for behaviours, opinions and decisions will be developed.

A sample of recruitment appointments will also be examined for common or divergent themes. It is likely that the appointments will follow similar basic patterns, and so the analysis will be structured around these patterns. Content analytic methods will be used to describe in a structured manner what was said by whom and how often. More flexible grounded theory methods (as in the interviews above) will be applied to identify common or divergent themes, particularly focusing on the impact of statements by the recruiter on patients. Conversation analysis will be used to focus in great detail on certain sections of the transcripts, for example the interactions during which randomisation is offered.

### Ethical issues

The Lightning Process is popular with over 250 children with CFS/ME attending courses each year. There is therefore an urgent need to study this intervention properly.

CFS/ME is different in children and adults with different risk factors<sup>15-17</sup>, course and outcome<sup>18</sup>. It is therefore not possible to complete a study in adults and extrapolate the results to children.

Although the Lightning Process is a popular process, it currently only has anecdotal evidence to support its efficacy as no formal studies have as yet been carried out. In this study, the Lightning Process is being offered as an add on to specialist medical care which is the treatment currently offered to children with CFS/ME. Children and families will also be followed up closely during and after the Lightning Process intervention. The parental interviews at each stage will help us understand parental and young people's views at each stage of the process.

Because many of the participants will be young people, we have put in place rigorous procedures for informed consent from parents and guardians on behalf of their children. We will also ensure we have informed consent/assent from participating children and young people. In the clinic, the clinician will ask for consent/assent for contact by a research nurse and qualitative researcher. Consent/assent to the study and to randomisation will be obtained by the research nurse after a full explanation of the study when both the young person and the family have had sufficient opportunity to ask questions. Young people and their families will be given as long as they need before giving consent/assent within the confines of the study. We will then obtain further consent/assent prior to each interview to check that young people or their parents continue to be willing to participate. We will also obtain consent/assent prior to recording any interventions from all present.

### Data protection

Children and young people are allocated a unique 13 digit identification number made up of the centre number, the team number, an individual patient number, first 4 digits of the postcode, and patient initials. This number is assigned to the patient and is used on assessment forms prior to

transfer of data so they are anonymised at source. A list of names and corresponding identification numbers are kept separately and securely on a password protected NHS server.

Audio-recordings will be encrypted, password protected and stored on a secure university server for five years. This is to enable us to check recordings if necessary while reports are being written. Transcripts will be anonymised and secure password protected university server.

#### Team expertise

Esther Crawley runs the Bath/Bristol Paediatric CFS/ME service which is the largest UK paediatric service in the UK. She is also a Consultant Senior Lecturer at the University of Bristol funded by an NIHR Clinician Scientist Fellowship for research in Paediatric CFS/ME. She chaired the British Association of CFS/ME with over 600 clinicians and researchers in CFS/ME (2007-2010) and is on the MRC CFS/ME expert working group.

Jonathan Sterne is Professor of Medical Statistics and Epidemiology in the University of Bristol's Department of Social Medicine. He has a wide range of expertise in the analysis of medical research data. He has a particular research interest in the design of randomised controlled trials, and how flaws in trial conduct can bias their results.

Zuzana Deans' field of expertise is applied ethics in medicine, specifically prenatal testing and screening, professionalism and research ethics. She currently holds a position as Research Associate (Bristol) working on the RAPID project on non-invasive prenatal diagnosis (funded by NIHR). She sits on the Medicine and Dentistry Faculty Ethics Committee of the University of Bristol, and has carried out extensive training for members of research ethics committees across Great Britain in association with Keele University.

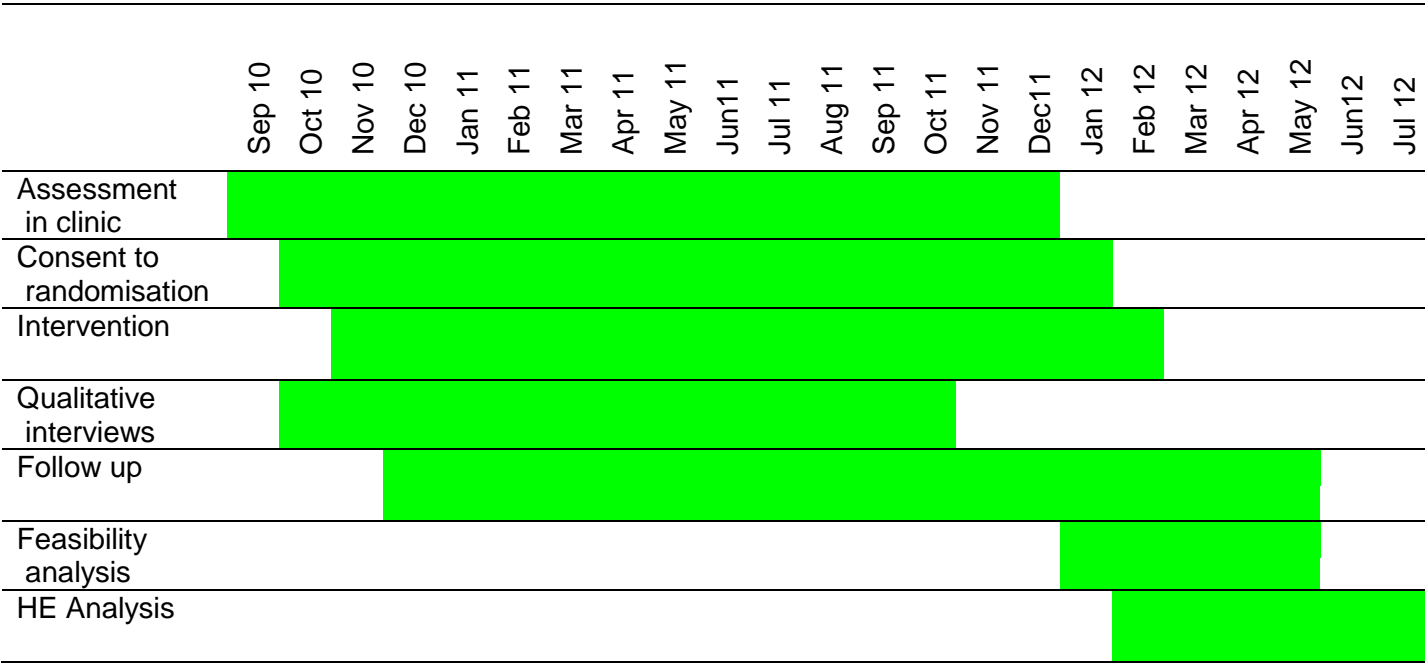
The MRC ConDuCT (COllaboration and iNnovation in DifficUlt and complex randomised Controlled Trials) methodology hub provides support for methodological development in RCTs, particularly potentially challenging feasibility studies. Jenny Donovan co-leads, and Nicola Mills is the primary researcher for the qualitative research aspect of the Hub, and so both will provide support for the integrated qualitative research. The **Bristol Randomised Trials Collaboration** (BRTC) is a collaboration between the University Departments of Community Based Medicine and Social Medicine in the design and conduct of high quality randomised trials. Alan Montgomery is Director of the BRTC and will provide methodological support. Will Hollingworth is a member of the ConDuCT Hub economic evaluation theme and will supervise the cost effectiveness methods and analysis of this feasibility trial.

#### Study management

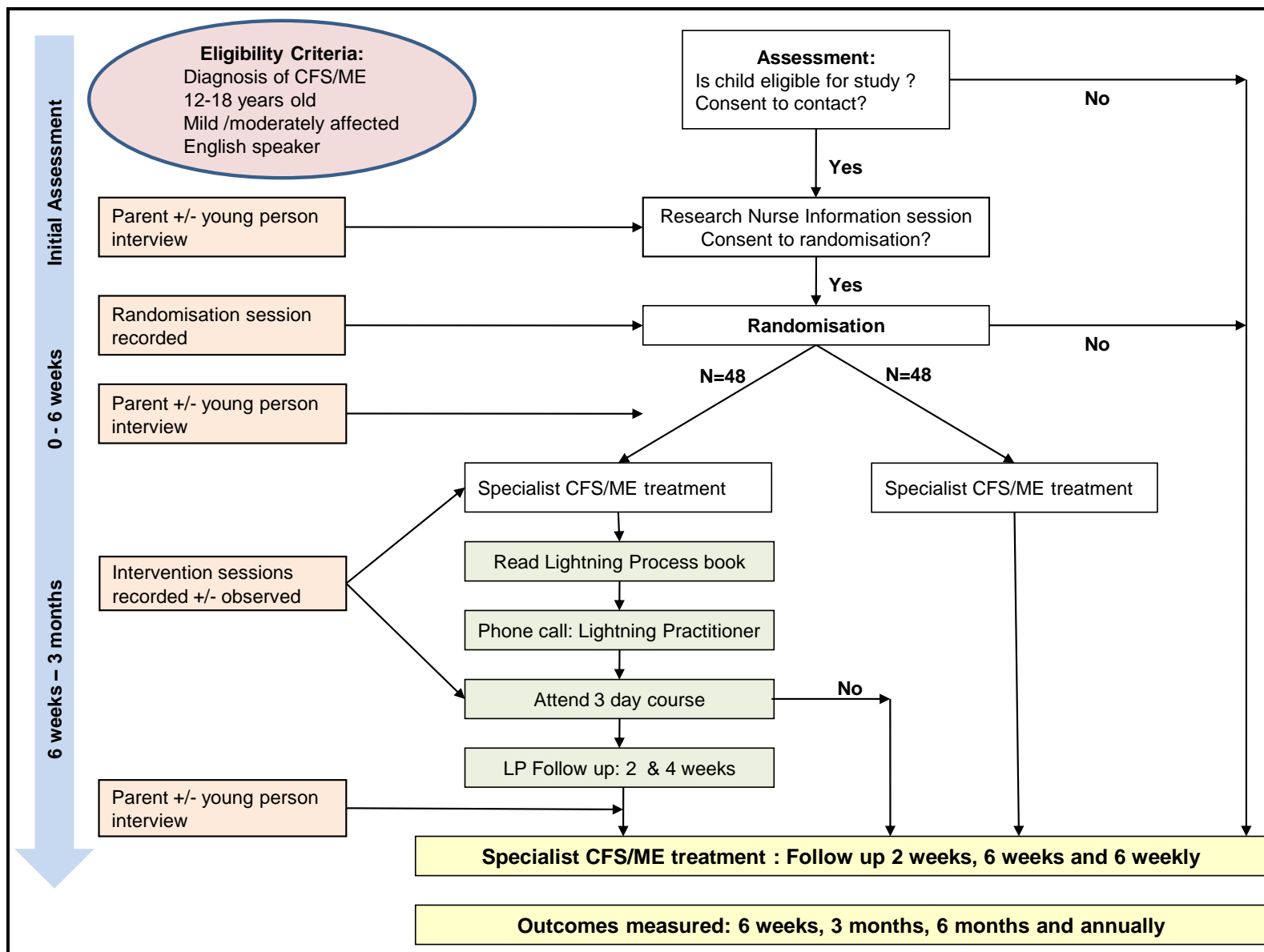
The study will be monitored by a Trial Monitoring Group which will meet every 4 to 6 weeks. The trial Monitoring Group will consist of: Dr Esther Crawley (PI), a member of the BRTC as well as applicants on the grant.

An External Advisory Group will also meet: prior to the study starting, by phone conference 6 monthly and at the end of the study. This will be an independent group and will include experts in CFS/ME, including a representative from the Association of Young people with ME (AYME) and the Lightning Process.

**Time plan for study**



50% participates followed up for 6 months



SMILE: Protocol Flow Chart

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