MANUAL FOR DOCTORS

STANDARDISED SPECIALIST MEDICAL CARE (SSMC)

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on behalf of the PACE Trial Management Group

NB This manual was used in the PACE trial by healthcare professionals to support Standardised Specialist Medical Care (SSMC) and is available free of charge for down-loading at www.pacetrial.org, so long as no changes are made. Any use of this manual should acknowledge the PACE trial (www.pacetrial.org). This treatment should only be delivered by appropriately qualified healthcare professionals, who have received appropriate training and continued supervision in the use of SSMC. The treatment described was not designed to be a stand-alone self-help approach. No responsibility is accepted by the authors for the application of SSMC described in this manual outside of the PACE trial.

The PACE trial team are unable to respond to queries or comments regarding the use of this manual or the treatment described.

Contents

Background to the PACE trial

The PACE trial is a randomised multi-centre clinical trial of four different treatments for patients with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis or Encephalopathy (CFS/ME). All participants in the trial will receive Standardised Specialist Medical Care (SSMC).

In addition, three of the four groups will receive fifteen sessions of one of the following supplementary therapies: Adaptive Pacing Therapy (APT), Cognitive Behaviour Therapy (CBT), or Graded Exercise Therapy (GET). For information on how these three therapies differ, please see Appendix 6.

Standardised Specialist Medical Care (SSMC)

SSMC is the standardised specialist medical care provided by the CFS/ME clinic doctor for patients who receive a diagnosis of CFS/ME.

SSMC includes:

- A positive diagnosis of CFS/ME and an explanation of the condition that is consistent with the Patient Clinic Leaflet (see Appendix 2).
- General advice on managing activity and stress and coping with the illness that is consistent with the Patient Clinic Leaflet (see Appendix 2).
- The prescription of medication for specific symptoms (such as simple analgesia, hypnotics, antihistamines and antidepressants) if indicated and agreed with the patient.
- Communication with and sharing of care with the participant's General Practitioner.
- Monitoring of the participant's progress and further assessment at the request of the participant, supplementary therapist, research nurse, or GP.
- A copy of the assessment letter will usually be sent to the participant, so long as they wish to receive it.

Patient Clinic Leaflet (PCL) – its use in SSMC

All trial participants will already have received this standardised patient clinic leaflet available to all patients with CFS/ME, whether they are participating in the trial or not, which gives general information about CFS/ME and a description of the different treatments (see Appendix 2). In addition, all participants will also have received the PACE trial Participant Information Sheet, as part of the consent process, which describes the nature of the PACE trial (Appendix 3).

General advice for participants

General advice on symptom and activity management should be given. This advice should be compatible with that in the Patient Clinic Leaflet.

It is important that this advice:

- Is as helpful as possible.
- Adequately reflects our uncertainly about aspects of management (the equipoise upon which the trial is based) – for example, whether it is better to try and increase activity or to focus pacing oneself to manage available energy most effectively.
- Does not contradict the principles of practice of any of the supplementary therapies, for example, does not argue against increasing activity or pacing.
- Is positive about the role of SSMC in advising and supporting the patient to create the best conditions for natural recovery.

Other SSMC treatments

It is expected that SSMC delivered by the specialist clinic doctor will be restricted to the care that is usually given and the doctor will not provide, or refer to providers of, a therapy which is being evaluated in another arm of the trial, or to a therapy with a similar rationale. **If in doubt the clinic doctor should speak with the centre leader.**

Timing of visits

The first SSMC appointment takes place a within one month of randomisation.

Participants will be seen by their SSMC doctor on a minimum of two further occasions in the 12 months after randomisation. Additional visits may be arranged by the clinic doctor on the basis of clinical need, to monitor pharmacotherapy, or to assess and manage a change or deterioration in the participant's condition. The participant, therapist, GP or research nurse may also ask for an extra appointment.

The last SSMC session should be held no less than one week before the last research assessment interview by the RN, which is held 12 months after randomisation. This is so that there is no immediate unintended influence on self-ratings by the participant.

A post-trial appointment may be scheduled, if thought necessary by the research nurse, after participation in the randomised trial treatment is complete to assess and discuss whether the participant requires additional post-trial therapy. This will be at the request of the Research Nurse after the final research assessment has been completed.

Each session with the SSMC doctor would commonly last about half an hour.

Additional post-trial therapy

Should a participant be referred by the Research Nurse for consideration of further treatment at the end of their involvement in the trial (twelve months after trial entry), then you should discuss supplementary therapy with the participant and the appropriate therapist, and a mutually agreed referral should be made.

Recording of SSMC

The doctor will keep the usual medical records of their interaction with the patient. To ensure standardisation of SSMC, to aid supervision, and to

ensure clinical equipoise, SSMC sessions will be audiorecorded. It is also essential that a clear and concise record is made in the medical notes. The duration of each session can be taken from the audiorecording machine display and should be recorded in the medical notes, so that the total time spent in SSMC can be recorded in the CRF at the end of the participant's SSMC.

Supervision of SSMC

SSMC will be supervised insofar as issues that might arise after review of audiorecordings will be discussed on an individual basis. In addition, telephone conferences for all those involved in providing SSMC will be arranged as necessary, but not less than twice in twelve months. Specific SSMC problems that might arise should be referred in the first instance to the centre leader, who can discuss the problem if necessary with the SSMC lead who is Gabrielle Murphy or if necessary the relevant PI who is Michael Sharpe.

Contact details for the SSMC lead

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Tel: 0131 537 6672, Fax: 0131 537 6641,

E-mail: michael.sharpe@ed.ac.uk

Missed Sessions

Telephone appointments may be considered if a participant has indicated that they are unable to attend a scheduled appointment but need advice relatively quickly. If a participant DNA's without warning, the SSMC doctor may establish the reason why by phoning then and there and providing clinical management advice if indicated. As an alternative, it is worth considering a future telephone appointment if further clinical input is thought necessary. (This will also happen with the supplementary therapies). If a participant drops out of SSMC it is essential that the Research Nurse is made aware of this immediately.

What SSMC is not

SSMC should be the medical care that one would reasonably expect clinic doctors experienced in the assessment and treatment of CFS/ME to provide.

- It does not involve advocacy of a particular form of management or therapy. During this trial it is also essential that any advice given should not strongly favour one particular illness management approach above another and such advice must also be compatible with any treatment that the participant is receiving (APT, CBT, GET or SSMC alone).
- SSMC does not involve seeing the patient on a frequent basis to deliver a version of one of the therapies in the trial (APT, CBT and GET). If however a participant receiving SSMC alone requests guidance on implementing a self-management approach themselves, appropriate general advice may be given about the approach they have chosen so long as it is consistent with the Patient Clinic Leaflet, whilst avoiding endorsing it as the best approach.
- Whilst SSMC may include referral to other doctors or therapists if there is a clear clinical need, it does not include the referral of the participant to other therapists for treatment of the CFS/ME, including those delivering therapies similar to those being evaluated in the trial (APT, CBT and GET).

*** If In Doubt Discuss With your Centre Leader ***

SSMC – FAQ

Q 1. The patient complains that SSMC alone is really no treatment - what do I say?

A. Explain that 'more is not necessarily better' and that we do not know if all the extra effort of doing a supplementary therapy would be worthwhile. People do recover naturally with the advice and support from an experienced doctor. The trial aims to establish whether the extra demands made on the participant by having a supplementary treatment are justified by an improved outcome.

Q 2. The patient seems to me to be depressed, can I prescribe an antidepressant drug within the trial setting.

A. Yes you can as per usual practice.

Q 3. The patient has been randomised to a supplementary therapy and tells me they would rather receive a different one - can I advise them?

A. Explain that we are running the trial because we do not know which therapy will be most helpful for which people and that is what the trial aims to find out. Participants should be encouraged to discuss questions about the supplementary therapy they are currently receiving with the appropriate therapist. It may be helpful to point out that research shows that some treatments may take some time to have a positive effect, and can be helpful after the face-to-face therapy has finished. They can also be reminded that twelve months after randomisation they will have an opportunity to receive a different trial therapy if that is deemed appropriate.

Other Questions

Q. The patient is treated with an antibiotic for an infection that has developed (as opposed to a previously undiagnosed chronic infection, e.g. chronic prostatitis) since entry into the trial and finds that their fatigue improves a little, goes onto the net and sees that there is evidence for use of antibiotics on an immune modulatory basis. They ask for a six -week course, pointing out that it is specialist medical care.

A. Some people find that their fatigue improves on antibiotics but there is no scientific evidence that this improvement is sustained, and extended courses of antibiotics may have adverse effects.

Q. A participant receiving SSMC alone has been talking to a fellow participant receiving CBT as well as SSMC, and learns that the fellow participant has been given specific advice about how to cope with possible relapse in the future. The patient asks for the same advice, ignoring the offer of extra appointments, saying they might be not be able to get there due to relapse. Do we offer telephone appointment as a future option or does this set a precedent.

A. Yes, offer a telephone appointment.

Q. What is my prognosis with SSMC alone?

A. We do not know for certain, although specialist medical care provided by a fatigue clinic specialist has previously been found to be helpful in a scientific trial. In addition, any prognosis will depend on the assessment of the individual's history and overall prognostic factors, but one of the aims of the trial is to establish the efficacy of SSMC alone.

Q. If SSMC alone can improve my symptoms how are you going to tell which therapy has helped in those receiving SSMC and another therapy?

A. A trial is designed to sort that out by comparing the number of participants who improve with each treatment. We expect that some people will improve with every therapy but not everyone will get better with any therapy. We will look to see if more people get better with supplementary therapy combined with SSMC compared to SSMC alone.

Q. If I am receiving no medication, what is it about the SSMC that may help improve my symptoms?

A. Advice and support of a doctor may be as good as any other treatment. The trial aims to assess this.

Appendix 1: General Therapy Skills

Knowledge and skills required

As well as a sound knowledge of the aetiology, epidemiology, consequences and available treatments of CFS/ME, a range of skills will also be necessary in order to help you to engage and work collaboratively with these people.

Engagement

In order to engage the participant in treatment, it is important that the doctor conveys belief in the reality of their symptoms, distress and limitations. The doctor should be able to demonstrate a sound knowledge of CFS/ME as participants will generally be well informed about their illness and may have had "difficult" experiences with other professionals who may have not taken their problems seriously. People with CFS/ME are often sensitive to the over-emphasis of psychological factors. In order to maintain participant's engagement throughout treatment, it will be important that you continue to use a medical approach and do not imply that the illness is non-biological, purely psychological or all in the mind.

Warmth and Empathy

Empathy is something that we will hopefully extend to all patients without thinking about it. However, with this patient group it is particularly important. Often they have had their health problems for a long time. Many of them will report at least one upsetting incident relating to a health professional, whether it is not being believed, not being taken seriously or being told it is all in their mind. They may have been given conflicting advice about how to deal with their problems, leading them to a state of confusion and frustration. Some participants will feel guilty about being ill and blame themselves for their predicament. Some participants will have had trauma in their background that may still provoke emotion.

It is therefore very important that you convey warmth and empathy at your first meeting. The assessment provides a wonderful opportunity for participants to

tell their story. Often it is the first time that they will have been able to go into detail about their problems. Allowing participants to elaborate on their illness often gives them the feeling that their illness is being taken seriously, often for the first time. Acknowledging the difficulties they have encountered along the way in terms of their illness, whether related to its impact on their life or response from other health professionals, etc, is important.

Sensitivity

Participants may not have had their illness taken seriously by previous professionals and may be concerned that you will be no different. They may think that you will be another "professional" who will tell them "to pull themselves together" etc. Participants may feel sensitive about the use of particular words; for example, asking them how often they feel *tired* can provoke anger in someone who differentiates strongly between the word *fatigue* and *tiredness*. Although you cannot forever be thinking about whether or not you are going to offend them, it is worthwhile listening to and trying to use language that is not going to be alienating. In general, it is best to use the language that the participant uses to describe their symptoms. For example if a participant calls their illness ME don't attempt to challenge this, ME or CFS is an appropriate term to use.

Collaboration

Collaboration is an essential skill in working with people with CFS/ME. Up to the point of meeting you, many participants will not have been included in the management of their illness. They may not have been asked their opinion about what is wrong with them and may feel rather helpless and out of control. Collaborating throughout treatment will help participants to feel more involved in their treatment and will help them to regain some sense of control.

Positive reinforcement

It is essential that you demonstrate positive reinforcement when you work with people with CFS/ME. Often, they will be very good at pointing out what they haven't achieved. It is therefore important that you emphasise and are very

positive about what they have achieved. Every session you should positively reinforce all of their achievements, however small they may seem.

Establishing confidence in you as a Specialist

Establishing the participant's confidence in you as a therapist is important. This is likely to occur if you have knowledge of research into CFS/ME and use the skills in the sections listed above. If you do not know the answer to a question, you are more likely to be respected for saying that you don't know the answer, rather than trying to answer it in a muddled way.

Encouraging optimism

Although it is important that you are realistic about the prognosis for participants, it is important that you encourage optimism about the progress that they may make. There is in fact some evidence that patients with symptomatic complaints are more likely to improve if you encourage a positive expectation of therapeutic outcome.

Engaging Participants in SSMC

Do's:

- Ask what the participant what they would like to be called when you first meet.
- Discuss the agenda for the appointment and ask the participant whether there is anything that they would like to add to it.
- Show empathy, warmth, sensitivity and understanding.
- Give a clear explanation of the diagnosis using the participant's own words where possible.
- Be very positive about participant's attempts to help themselves to overcome their CFS/ME.
- Give participants the opportunity to discuss any fears or worries in relation to treatment.
- Tell the participant that you will look forward to seeing them over the coming year.
- Use language that participants will understand.

Don'ts

- Get into an argument with the patient about their beliefs about the illness.
- Minimise symptoms by saying something like 'we all get tired'.
- Imply that the symptoms are imaginary.

Appendix 2: Patient Clinic Leaflet (PCL)

NOTES FOR PARTICIPATING CLINICS

PACE Trial
Clinic Leaflet

Version 8
11 November 2004

PACE queries to
Julia DeCesare

0207 601 8160
j.c.decesare@qmul.ac.uk

BEFORE PRINTING

Open up this PDF file

Type in therapies offered by your clinic
in the space provided on page six

WHEN PRINTING
print on HEADED PAPER from your CLINIC

Print page one on main letterhead
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please do not use UNHEADED PAPER

DO NOT GIVE THIS COVER SHEET TO PATIENTS

Basic information on your illness and the treatments we can offer you for

chronic fatigue syndrome (CFS)

also known as

myalgic encephalomyelitis or myalgic encephalopathy (ME)

Chronic fatigue syndrome (CFS) is an illness with a recognisable pattern of symptoms. The main symptom is fatigue – which you feel as tiredness, exhaustion or lack of energy. It is common to have muscle and joint pain, memory and concentration problems, disturbed sleep, headaches, and sore throats, and sometimes sufferers have tender lymph glands. Symptoms often get worse if you exert yourself.

This illness is also known as post-viral fatigue syndrome, myalgic encephalomyelitis (ME), and myalgic encephalopathy (ME).

Medical authorities are not certain that CFS is exactly the same illness as ME, but until scientific evidence shows they are different they have decided to treat CFS and ME as if they are one illness. We do the same at this clinic, and in this leaflet we will be calling this illness CFS/ME for short.

People with CFS/ME are sometimes afraid that people will not believe that their symptoms are real. In this clinic we believe CFS/ME is a real illness.

How is CFS/ME diagnosed?

There are several descriptions of the typical symptoms. Doctors call them case definitions, and all these definitions agree that people with CFS/ME:

- have the main symptom of fatigue that is often made worse by exertion
- often have other symptoms – including headaches, sleep disturbance, sore throat, muscle or joint aches and pain, and tender lymph glands
- have usually had these symptoms for more than six months
- cannot lead a normal life because of these symptoms.

When doctors recognise this pattern of symptoms, and when they can rule out all other causes, then they diagnose CFS/ME.

What causes CFS/ME?

We don't know what causes CFS/ME, although there are various theories – well-informed scientific ideas that have yet to be proved or disproved.

However, we do know that most illnesses have a number of causes that are often interlinked in complicated ways – and this is probably true for CFS/ME. This complexity means doctors prefer not to talk of causes in the everyday sense. They use the more accurate term 'factors', and they divide up factors into three types.

- Factors that make someone more likely to get the illness. An example might be their sex, as more women than men develop CFS/ME. Doctors call this a PREDISPOSITION
- Factors that bring on the illness in the first place. An example might be an infection. Doctors call this a TRIGGER
- Factors that stop people recovering from the illness. Sleep disturbance might be an example. Doctors call this a MAINTAINING factor.

What is a factor for one person may not be a factor for somebody else. For instance, sleep disturbance may be a maintaining factor in one person and not in another person.

What are these theories you mentioned?

These are the main theories about factors that trigger or maintain CFS/ME.

Infection

People often say their CFS/ME started after a flu-like illness. There is evidence that CFS/ME can be triggered by certain infections, most of them viral. There is no strong evidence that these infections are maintaining factors in CFS/ME.

The immune system

Minor abnormalities of the immune system are commonly found in people with CFS/ME. These abnormalities may be a factor in CFS/ME, or they may be an effect of having the illness. We don't know for sure.

Stress hormones and the hypothalamic-pituitary-adrenal (HPA) axis

The hypothalamus and the pituitary gland are organs at the lowest part of your brain that work with your adrenal glands as an 'axis' to control your reaction to stress. For instance, they control how much of the stress hormone cortisol is produced by your adrenal glands. Some research suggests that this axis works less well in people with CFS/ME. However, we don't know whether problems with the HPA axis predispose you to developing CFS/ME, maintain CFS/ME or are just an effect of the illness.

Stress

Stress may predispose you to all sorts of illness, and stress plus an acute infection can probably trigger CFS/ME. Once you have CFS/ME, this in itself will add to your stress, because you have to cope with disability, and other people may not understand or believe that you really are ill. Modern life doesn't give people much time to recover from illness, either, which may add to your stress.

Sleep disturbance

Many people with CFS/ME have problems sleeping. They may find it hard to fall asleep or stay asleep, and they can wake up unrefreshed. Poor sleep may delay your recovery from CFS/ME.

Doing too much and doing too little

People with CFS/ME often do too much and then feel ill – which forces them to do less. Alternating between too much and too little activity is called a 'boom-and-bust' pattern. This pattern may delay your recovery.

Loss of physical fitness and strength

After a period of being less physically active than usual, your body will become less fit. This can make it more difficult for you to do things you could once do easily. This loss of fitness may delay your recovery.

Food intolerance

Some people with CFS/ME say certain foods make them worse. But there is no good evidence that food intolerance triggers or maintains CFS/ME.

Other possible factors

Many other things are said to be linked to CFS/ME, and some get a lot of publicity – even though nobody has *proved* they are factors in CFS/ME. These include magnesium deficiency, overgrowth of the yeast *Candida* in the bowel, and low blood sugar (hypoglycaemia).

Is it true that CFS/ME leads to other illnesses?

Other illnesses often go together with CFS/ME – but we don't know that people get them *because* they've got CFS/ME. The main three such illnesses are described below.

Fibromyalgia

Fibromyalgia is like CFS/ME, but with more muscular pain and tenderness.

Irritable bowel syndrome

If you have bloating, cramps, and constipation alternating with diarrhoea you may be diagnosed as having irritable bowel syndrome (IBS).

Anxiety and depression

People with chronic illnesses such as CFS/ME often become understandably anxious or depressed.

How do you make or confirm a diagnosis?

We ask about your symptoms, how your illness started, and how it developed. We may give you a physical examination. We automatically do a set of standard blood and urine tests to make sure nothing else could be causing your symptoms – unless another doctor has done these tests recently. We also do specialist tests if they are necessary.

How soon will I get better?

Most people with CFS/ME improve over time with treatment, but we can't predict how long this will take.

What treatments are there for CFS/ME?

There is no agreed treatment for CFS/ME, and no drug has been found that is generally effective. There are various treatments that may help people to cope better, and they may help some people to recover. These treatments are usually given *as well as* specialist medical care. However, advice and support from a specialist CFS/ME doctor on its own may be just as good. Here are brief descriptions of the main treatments that are used in the NHS to treat CFS/ME.

Specialist Medical Care

Specialist medical care is the most usual treatment for CFS/ME, and it helps many people improve. You get a confirmed diagnosis, an explanation of why you are ill, and general advice about managing your illness. Your specialist might either prescribe medicine to help you manage troublesome symptoms such as insomnia and pain or advise your GP about what medicine is appropriate.

Here is some of the advice you may get as part of specialist medical care.

- *Avoid extremes of activity.* Many people with CFS/ME get into a pattern of being very active and then very inactive. It is better to give yourself a pattern of activity that you can keep going. This may be a lower level of activity you are used to.

- *Set a daily level of activity.* It will help to set a simple level of activity that you do every day. Stretching exercises, for example, will minimise the weakening effects that creep up if you don't use your muscles for a time.
- *Make only gradual changes to your activity level.* If you feel you can increase your level of activity, and not everyone does, make changes carefully and gradually. A sudden increase in activity may make your symptoms worse.
- *Try to reduce stress in your life.* When we are ill, stresses such as excessive work demands don't help us. If you can reduce these stresses, it will help you recover.

Pacing – Adaptive Pacing Therapy

This approach is about pacing yourself – matching your activity level very carefully to the amount of energy you have. Usually, an occupational therapist works with you, helping you monitor your activity and symptoms so that together you work out just how much activity you can manage without making your condition worse. The aim of this therapy is to improve your quality of life and give you the chance of a natural recovery.

Cognitive Behaviour Therapy

Cognitive behaviour therapy is about examining how your thoughts, behaviour and CFS/ME symptoms relate to one another. Usually you see a cognitive behaviour therapist, who helps you to understand your illness and change the way you manage it. In between sessions you would try out new ways of managing your CFS/ME. The aim of this therapy is to help you manage your symptoms more effectively and do more.

Graded Exercise Therapy

Graded exercise therapy is about gradually increasing your physical activity. Usually, you see a physiotherapist who helps you work out a basic activity routine, then together you plan to gradually increase the amount of physical activity or exercise you do. The gradual increase takes into account your symptoms, fitness, and current activity levels. The aim of this therapy is to help you do more and feel better.

Self-help guides

There are self-help guide books available that you might choose to read.

Complementary and alternative therapies

Some people take complementary or alternative therapies that are not available from the NHS – and some say they benefit from them. Yoga and aromatherapy are two examples. However, we cannot recommend these therapies, because there is no scientific evidence that they are effective.

Which treatments are available in this clinic?

We offer specialist medical care, as described above. We may also offer you these therapies as well as specialist medical care:

adaptive pacing therapy; cognitive behaviour therapy; graded exercise therapy; <<< *please add other available or subtract unavailable therapies to match what is on offer at your clinic* >>>

You also have the option in this clinic of putting yourself forward for the PACE Study, which is described below. This may increase your treatment options.

The PACE trial

This clinic is helping with a study of different treatments for CFS/ME called the PACE trial. The formal title of this trial is: *Pacing, graded Activity and Cognitive behaviour therapy – a randomised Evaluation.*

The PACE trial will tell us about the benefits and possible drawbacks of various treatments for CFS/ME. It could also tell us why successful treatments work and whether different people need different treatments. It may lead to a more effective treatment for CFS/ME.

Patients who join the PACE trial will get one of the following treatments.

- Specialist medical care
- Specialist medical care *plus* adaptive pacing therapy
- Specialist medical care *plus* cognitive behaviour therapy
- Specialist medical care *plus* graded exercise therapy

If you would like to know more, please ask your clinic doctor for a leaflet.

What if I have more questions?

If you have questions about this leaflet or your attendance at this clinic, we will be happy to answer them when we see you next.

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Appendix 3: Participant Information Sheet for PACE trial

NOTES FOR RESEARCHERS

PACE Trial
Patient Information Sheet

Version 15
22 November 2004

Researcher queries to
Julia DeCesare

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j.c.decesare@qmul.ac.uk

BEFORE PRINTING

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Research Nurse and Centre Leader

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UNHEADED PAPER IS NEVER ACCEPTABLE

DO NOT GIVE THIS COVER SHEET TO PATIENTS

invitation to join

the PACE trial

a randomised controlled trial of treatments for

chronic fatigue syndrome (CFS)

also known as

myalgic encephalomyelitis or myalgic encephalopathy (ME)

We are inviting you to help us with our research. But before you decide whether or not you want to join our study, you will want to know what we are doing, why we are doing it – and what we would be asking you to do.

This leaflet will answer most of your questions. Please take it away and read it carefully. Talk over your decision with other people if you want to. And if something in this leaflet isn't clear, or if you want to know more, you can ask us.

Take as much time as you need to decide whether or not you want to help us. If you don't want to join our study, this will not affect your NHS care.

Thank you for taking time to read about our work.

Research Nurse **Centre Leader**
[Insert contact details here]

Why are you asking me?
We have invited you to join our study because you have chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis or myalgic encephalopathy (ME).

In the rest of this leaflet we will be calling this condition CFS/ME for short.

What is your study for?
There are different treatments for CFS/ME, and we want to know which are the most helpful. To find this out, we are asking people like you who suffer from CFS/ME to join our study – which is a randomised controlled trial.

We hope our study will tell us about the benefits and possible drawbacks of each of these treatments. We also hope to learn why successful treatments work and whether different people need different treatments. Finally, the study will compare how much these treatments cost, to see if they are a good way of spending NHS money.

Whichever treatments are shown to be the best, we expect they will become more widely available across the country. This study may lead to a more effective treatment.

What are these different treatments you want to study?
Specialist medical care and three extra therapies are being tested in our study. Everyone joining our study will get specialist medical care from a hospital specialist. You might also get an extra therapy *as well as specialist medical care*. The specialist medical care and the three extra therapies being tested in our study are all described below.

Specialist Medical Care
Specialist medical care is the most usual treatment for CFS/ME, and it helps many people improve. In our study, you would get a confirmed diagnosis, an explanation of why you are ill, and general advice about managing your illness. Your specialist would either prescribe medicine to help you manage troublesome symptoms such as insomnia and pain or they would tell your GP what medicine is appropriate.

Adaptive Pacing Therapy (APT)
APT is about pacing yourself – matching your activity level very carefully to the amount of energy you have. In our study, an occupational therapist would work with you regularly, helping you monitor your activity and symptoms so that together you work out just how much activity you can manage without making your condition worse. The aim of this therapy is to improve your quality of life and give you the best chance of a natural recovery.

Cognitive Behaviour Therapy (CBT)

CBT is about examining how your thoughts, behaviour and CFS/ME symptoms relate to one another. With this treatment you would regularly see a CBT therapist, who would help you better understand your illness and change the way you cope with it. In CBT you would see a therapist, and in between sessions you would try out new ways of coping with your CFS/ME. The aim of this therapy is to help you find out which ways of coping work best for you.

Graded Exercise Therapy (GET)
GET is about gradually increasing your physical activity to make you fitter and get your body used to exercise again. In our study you would regularly see a physiotherapist. They would help you work out a basic activity routine then gradually increase the amount of exercise you do. The gradual increase would take into account your symptoms, fitness, and your normal activity levels. This therapy aims to help you do more, without making you worse.

Do I have to join your study?
No. You decide whether or not you want to help us. We ask you to go away and think about what you want to do. If you decide to help us, we will ask you to sign two consent forms and give you copies. Even if you sign the forms, you can still leave the trial at any time – and you won't even have to give us a reason if you don't want to.

If you decide not to join our study, or if you leave our study after you have joined, this will not affect the usual NHS care you get for your condition. Your clinic can tell you what the usual NHS care would be for you, as this does vary between clinics.

What will happen if I join your study?
If you agree to join our study, this is what will happen.

1. We ask you questions and measure your fitness
You will meet your local study nurse, who will explain our study to you in more detail and answer any questions you have. Then we ask you to sign the first consent form, to let us find out if you are eligible for our study. This involves you filling out some questionnaires about your symptoms and how CFS/ME affects your ability to do things. Your nurse will also ask you about any emotional or psychological symptoms you might have.

A six-minute walking test will tell us how physically able you are. Your nurse will give you a movement monitor – it looks a bit like a wristwatch – and ask you to wear it on your ankle for one week. This will tell us how physically active you are. You will also get some questionnaires to take away and complete in your own time.

2. You find out whether you are suited to our study
A week later, you will bring back the movement monitor and the questionnaires. Your nurse will ask you more questions, including how CFS/ME has affected you financially, and ask you to do a two-minute step test to tell us more about how fit you are. If we decide you should not be in our study, your nurse will refer you back to your clinic doctor. Otherwise, your

nurse will ask if you still want to help us. This is when we ask you to sign the second consent form – which says you agree to take one of the treatments in our study. You don't have to sign, and if you do you will still be free to leave our study at any time.

3. A computer randomly allocates a treatment for you
If you decide you still want to help us, you will be randomly allocated a treatment. We use a computer to do this, because it is important that your treatment is chosen *by chance*. This is the computer equivalent of tossing a coin to decide which treatment you will get. We have to decide at random because this is the only way to compare the treatments fairly. This means you won't know what treatment you will get until *after* your fitness is assessed and *after* you have decided to join our study.

You will get one of these four treatments:

- Specialist medical care
- Specialist medical care *plus* APT
- Specialist medical care *plus* CBT
- Specialist medical care *plus* GET

4. Everyone sees their research nurse three more times
You will see your research nurse three more times so we can see how you are doing. These meetings will be 12 weeks, 24 weeks and a year after you find out which treatment you will get. We will post you our questionnaires, so you can fill them in at home, at your own pace, and bring them with you. Filling them in will take about an hour. In the meetings, your nurse will ask you some questions and measure your fitness with the step and walking tests. You won't need to wear the movement monitor again.

5. If you get APT or CBT or GET you meet your therapist as well
If you get a treatment that includes APT or CBT or GET, then you will meet your therapist up to 15 times. The meetings will happen in the five months after you find out which treatment you are getting. At first they will be every week, then every fortnight. The first meeting will last an hour and a half so your therapist can explain the treatment to you, answer your queries, listen to any concerns you may have, and plan how the therapy will work for you. The rest of the sessions will last 50 minutes each. If you can't get to all of your sessions, some of them could be done over the phone.

You will still see the clinic doctor and get the normal care they would give, including any prescribed medicines that you need.

We record the interview with the nurse and the treatment sessions
We will audio- or video-record the interview when the nurse asks about your emotional and psychological symptoms. We do this to supervise the nurse and to make sure the interview is done properly and the right interpretations are made.

We will also audio- or video-record your treatment sessions. We do this to make sure your therapy sessions follow the manual we have written for our study, because that is the only fair way to compare these therapies. Only the

research team will listen to these recordings, which will be kept safe in computerised form at the hospital for 20 years. After that time, all files of the recordings will be permanently deleted and all CDs of recordings destroyed.

Will I have to do anything after the study?

We will ask if you mind us contacting you once a year after you leave our study, so we can find out how you are getting on. We may need follow-up information for up to five years after you leave our study.

If you join our study, we will ask if we can use your (English) NHS number or your (Scottish) CHI to register you with the (English) Office for National Statistics or the (Scottish) Information and Statistics Division. This will help us contact you, perhaps through your GP, if you move house after you leave our study.

How many appointments would that be altogether?

Here's a summary of all the things you would be asked to do.

Attend five research interviews over 12 months

• At the first interview you fill in some questionnaires, talk to your nurse, do the walking test, and take away the movement monitor and questionnaires
• At the second interview you bring back the questionnaires and movement monitor, talk to your nurse, do the step test, and decide whether to join
• For the other three interviews, we will post you questionnaires so you can fill them in at home and bring them with you. You will talk to your nurse, and there will be a two-minute step test and a six-minute walking test

Attend at least three appointments with your clinic doctor

• *You may get more if you and your clinic doctor feel they are needed*

Attend 15 therapy sessions IF your are getting APT or CBT or GET

• The first 14 of these therapy sessions will be in the first five months
• The final, 15th, therapy session will be after a three-month gap

Who will pay for my extra travel to these appointments?

We will pay for your travel to the hospital for the research interviews. We can also contribute to your travel costs for trips you make to see your clinic doctor or therapist.

Will I still be free to take other treatments?

If you already get other treatment, you may not be able to join our study.

Before you join our study, we will ask you not to start any other treatments for CFS/ME for the 12 months you are in our study – unless your clinic doctor or your GP advises you to take them. If you still decide to start another treatment we will understand, but we would like you to tell your research nurse so we know what is happening and can check to see whether your other treatment affects our study results.

Will my treatment suddenly stop at the end of the trial?

When you leave our study, you will see your clinic doctor to discuss whether

you need more treatment. If you do, your clinic doctor will discuss which of the three extra therapies would suit you best. The study therapists give you this treatment. This extra treatment is for patients who join our study; it may not be available outside our study. Your research nurse can give you more details.

How do I qualify for your study?

You must be diagnosed by us as having CFS/ME. Fatigue or lack of energy must be your main problem, and it must be sufficiently severe and disabling. You must be at least 18 years old and be able to read and understand English.

What could exclude me from your study?

You could have CFS/ME but still not qualify for our study. For instance, if:

- another condition, apart from CFS/ME, might also be causing your fatigue
- you have tried one of the treatments in another fatigue clinic
- you have another health problem that would not be helped in the trial
- you would not be able to get to the hospital regularly for your treatment.

Other reasons may make it sensible to exclude you from our study. For instance, pregnant women and women who are trying to get pregnant should not join our study. And we will be asking women who could get pregnant to use an effective contraceptive *and* to tell their GP and their clinic doctor if they do get pregnant. Our study would not harm a pregnant woman or her baby, but we would want to adjust their treatment and check whether they are taking any new medication.

If you think there may be a reason why you should not join our study, it is very important that you tell us. We will let you know if it is safe for you to join our study.

Will there be any disadvantages or risks if I join?

If you join us, then over one year you will need to go to the hospital five more times than you would have otherwise. And if you are given an extra therapy you will need to go to 15 therapy sessions over the year.

It is possible that a therapy we are studying may not be available at your clinic – for instance, if a therapist is sick for a long time. If this happens before you join us, we will tell you. And if this happens when you are already in our study, we will do our best to find you an alternative therapist.

Are there any benefits to joining your study?

We hope the treatment you get in our study will help you, even though this can't be guaranteed. And at the end of our study, you will get the chance to opt for one of the other treatments if you and your clinic doctor agree it could help you.

Our study should also lead to better treatment for people with CFS/ME, so you will be helping others who get the same condition you have now.

What treatments can I get if I don't *join your study?*

All the treatments we are testing are available *outside* our study in NHS centres in the UK. So you could get specialist medical care, pacing with an occupational therapist, cognitive behaviour therapy, or graded exercise therapy. However, your local NHS clinic may not offer all these therapies. There are also other, more general, treatments available for CFS/ME with clinical psychologists, physiotherapists and occupational therapists.

Could joining your study make my condition worse?

Patient surveys say APT helps many patients and does not cause harm. Research studies say CBT and GET appear to be safe when applied properly by trained staff, as will happen in our study. Some patient surveys suggest CBT and GET can make symptoms worse – but experts believe this happens when the therapy is not used properly or when there isn't good professional supervision.

Whatever treatment you get in our study, we will carefully monitor your progress. If you feel your condition is made worse by being in our study, we will give you a detailed reassessment and offer whatever help is appropriate.

The two-minute fitness test was designed for people of below average fitness. There is no evidence that it makes CFS/ME worse, but some people find that their legs ache for a day or so.

What about compensation if something goes wrong?

We will be monitoring your progress closely, so we don't expect to see any harmful effects caused by our study. However, you need to know that there are no special compensation arrangements if you are harmed because you have taken part. If you are harmed by someone's negligence you may be able to take legal action – but you may have to pay for it. The usual NHS complaints system will be available if you have any concerns about the way we have approached or treated you.

What if new information turns up while I'm in your study?

If we find any new information about the treatments we are studying, your research nurse or clinic doctor will tell you about it and ask if you want to stay in the study. If you want to leave our study, your clinic doctor will make sure your care continues. If you decide to stay in our study, we might ask you to sign an updated consent form that takes the new information into account. If your clinic doctor thinks the new information means that you should leave our study, they will tell you why and then make sure your care continues outside our study.

Will you keep my details confidential?

Yes. All your details and all recordings will be kept strictly confidential and held in a locked filing cabinet or on a secure computer. People on our research team will only see your records if they need to for the research.

Your GP and any other doctors you are consulting will be told you are joining our study. And occasionally, other researchers will need to see your notes so they can audit the quality of our work. An audit might be run by one of the universities helping with our study or hospital regulatory authorities, or by one

of the organisations funding our study.

The data and recordings we collect will be securely stored for 20 years after the end of the trial, for your protection and to follow good clinical practice (GCP). The same applies to other records gathered for our study, including your medical notes and the database holding the collected data for this trial.

Your name, address, and telephone number will be on only one database. This will be held securely at St Bartholomew's Hospital, in London, and it will be used only to monitor recruitment. You will not be named in any published results from our study.

What will happen to the results of your study?

Our results will be presented at national and international conferences and published in medical journals. Our study will run for five years, even though you will only be part of it for one year. This means you can expect to see the results around 2009.

The results won't say who took part or give any details that lead to people being recognised or identified.

Who is paying for your study?

Our study is funded by the Medical Research Council (MRC), the Scottish Chief Scientist's Office (CSO), the Department of Health (DH) and the Department of Work and Pensions (DWP).

Nobody gets paid a fee for signing you up with our study.

Has anybody reviewed your study?

The West Midland Multicentre Research Ethics Committee has given national approval for our study. Our study has also been reviewed by the Local Research Ethics Committee (LREC) for your local NHS Trust, and the local NHS Research and Development office.

Is this study local or across the country?

This is a national study. Here is a full list of the participating NHS centres.

The Astley Ainsley Hospital, Edinburgh, in collaboration with the
Regional Infectious Diseases Unit, Western General Hospital, Edinburgh, both of NHS Lothian

Bart's and the London NHS Trust, East London

East London and the City Mental Health NHS Trust

Oxfordshire Mental Healthcare NHS Trust
in collaboration with the Oxford Radcliffe Hospitals Trust

The Royal Free Hampstead NHS Trust

South London and the Maudsley Trust

Where can I get more information?

You can contact the research nurse or the centre leader listed below for more

information about our study. We have also listed an independent doctor who understands CFS/ME but has no connection with our study, in case you decide you need more independent advice.

Research Nurse **Centre Leader** **Independent Doctor**

. . . . . .

You can also read about joining research trials like ours at:
Consumers for Ethics in Research www.ceres.org.uk
National Electronic Library for Health www.nelh.nhs.uk/clinicaltrials

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Thank you for your interest in our work

Appendix 4: Managing Potential Difficulties

The participant has a fixed physical attribution of illness

If participants are insistent that there is an ongoing "physical" problem, it is rarely helpful to directly challenge them on this point. It is important that you acknowledge that their illness is real but its effects can be reduced by the way they manage it.

The patient feels that a cause has been missed and wants further investigations

Some patients may feel that despite adequate investigations, something has been missed. The value and limitation of investigations may be explained. It may also be explained that whilst we can never guarantee that the patient does not have an alternative explanation for their symptoms it is very unlikely. Clinical judgement is required in deciding to carry out any further tests. In general, such tests should be done for a clinical indication rather than in response to a patient's request.

Patient Deterioration

If you have a concern that a participant (in which ever therapy group) is deteriorating or there is evidence of suicide risk, deliberate self-harm, significant and prolonged illness progression, or a severe adverse event, this should be discussed with the centre leader immediately, so that the relevant course of action can take place. Please do this before the participant is given advice on what to do (whether continuing in or withdrawing from their therapy or from the trial).

Patient requests to withdraw from the trial

If a participant says that they no longer want to participate in the trial, i.e., they withdraw their consent, the centre leader should be informed on the same day, if possible. The centre leader or research nurse will then contact the participant to find out whether consent is withdrawn from further trial treatment only or further trial treatment and follow-up. The reason for dropout should be

ascertained if possible and passed on to the research nurse. The date of dropout and reason (if known) should be recorded in the participant's medical notes.

Cancellations, DNA s and missed appointments

If a patient does not attend it is worth considering a telephone appointment as an alternative. This will be done in the supplementary therapies. Cancellations or DNA's should be rearranged within five working days if possible.

Telephone calls from patients

Telephone contact between sessions should be handled on an individual basis. It is not banned, but should be discouraged.

Appendix 5: Information for participants about benefits

Work, Courses and Resources

If you are considering returning to work, doing a course or finding a new job, it can be difficult to know where to start. You may not know what opportunities are available to you.

Information for people who are in receipt of benefits

If you have been ill for some time you may be in receipt of benefits. However, some people are not aware that they are able to claim benefits. The information below summarises the most common benefits claimed by people with CFS/ME.

1. Invalidity benefit (IB) *can be claimed if*: -
   - *Statutory sick pay (SSP) has ended or you cannot claim SSP.*
   - *You have paid national insurance contributions*
   - *You have been incapable of work because of sickness or disability for at least 4 days in a row including weekends and public holidays*

2. Income Support (IS) can be claimed*: -*
   - *By people on a low income*
   - *By people who are between age 16-59*
   - *By people who are not working, or work less than 16 hours a week on average*

3. Severe Disablement Allowance (SDA) can be claimed: -
   - *By people who have been unable to work for at least 28 weeks in a row because of illness or disability*
   - *If you have never been able to work*
   - *By people aged 16-64*
   - *If you are unable to claim IB because you have not paid enough NI contributions*

If you are in receipt of benefits you may be aware that there are rules that determine how much work you can do without your benefits being affected. You may feel trapped, because on one hand you feel ready for some part time

work, but on the other hand may have concerns about how your income will be affected if you return to work. A useful way of bridging the 'benefit gap' of not being well enough to work, but being well enough to do some part-time work is to consider "permitted work". Below, is some information about work rules that have recently been introduced.

New Work rules for people on Incapacity Benefit (from 8th April 2002)

Any person receiving a benefit on the basis of incapacity, e.g. incapacity benefit, severe disablement allowance, national insurance credits, income support, housing benefit or council tax benefit, will be able to work for less than 16 hours a week and earn no more than £72 a week for 26 weeks.
In addition to this, a person may be able to do one of the following: -

- Extend the above for a further 26 weeks if they are working with a Job Broker, Disability Employment Adviser or Personal Adviser who agrees that an extension is likely to improve their capacity to move into full-time work (16 hours or more a week);
- Work and earn no more than £20 a week, at any time, without a time limit
- Do supported permitted work* and earn no more than £67.50 a week without time limit

*Under the new permitted work rules, the definition of "supported permitted work" is work that is supervised by someone who is employed by a public/local authority or a voluntary organisation, and it is their job to arrange work for disabled people. This work could be done in the community or in a sheltered workshop. It also includes work done as part of a hospital treatment programme.

Eligible people undertaking work under the permitted work rules will not need their doctor's approval to do so, but they should tell the office that pays their benefit before starting work. As long as the permitted work rules are observed, their earnings will not affect their incapacity benefit and/or severe disablement allowance. However, income support, housing benefit or council tax benefit could be reduced. It would therefore be advisable to seek advice

from the office that pays your benefit so that you are fully informed of your position before starting work. When permitted work is available you must apply to the benefits agency to get a permitted work form (PW1).

Income Protection (IP)

IP is an insurance scheme where usually, part of your salary is paid whilst you are unable to work. Usually, the policy is held between the employer and the insurance company. Many insurance companies are willing to negotiate a gradual return to work with part-payment until full-time work is achieved. Some insurers' are willing to pay for rehabilitation and cognitive behaviour therapy as a way of helping people to return to work. Some employer's will offer redundancy packages on health grounds.

Employment and educational schemes

Below, is a list of organisations for you to contact with regard to returning to work, finding new work, (voluntary or paid) or doing a training or educational course:

Disability employment advisors

Disability employment advisors may be able to give advice on the following: -

- Education and training opportunities
- The best way to find work
- How any sort of work will affect your benefit entitlement
- Other welfare and benefit questions

For enquires about services in your area phone the Disabilities Services Helpline on 0800 328 4933

Work Care

Work care is a new government research initiative that aims to help people who have been off sick to return to work.

It can provide:

- Free specialist treatment

- A boost to your existing NHS healthcare with no waiting time

These are available if you have been off work due to ill health for up to 6 months, have a job to go back to, or feel unable to return to your job in the near future.

For further information call 0800 052 1659 or visit their web site at: www.workcare.co.uk

Jobcentre Plus

Jobcentre plus is a new business within the department of work and pensions. In April 2002, it replaced the employment service (which previously ran jobcentres) and parts of the benefits agency which provided services to people of working age through social security offices. It offers help in both finding work and claiming benefits under one roof.

You can get details of the areas covered by Jobcentre Plus Offices from your local Jobcentre plus, Jobcentre or social security office.

For further information visit their web site at www.jobcentreplus.gov.uk

New Deal for disabled people

New deal for disabled people is a scheme that aims to give everyone on health-related disability benefits the chance to find rewarding work. If you are interested, Job brokers will be able to give you genuine support, tailored to your individual needs. The work will not affect your benefits.

For further information call the NDDP Helpline on 0800 137 177 or visit their website at www.newdeal.gov.uk/nddp

New Deal 50 plus

New deal 50 plus is a valuable package for people aged 50 or over to help them find work. It is for people who fulfil the following criteria:

- *Are aged 50 or over*

- *For the last six months or more:*
  - *have received Income support (IS), Jobseeker's allowance (JSA), Incapacity Benefit (IB) or Severe Disablement Allowance (SDA), or*
  - *have signed at the job centre for National Insurance Credits only, or have been in receipt of IB credits only; or*
  - *you have been the partner of someone who claims benefit for them.*

New Deal 50 plus offers the following:

- £60 per week employment credit, tax free, paid direct to you on top of your wage for the first year you are in full time work (30 hours or more per week), or £40 per week if you are in part time work (16 to 29 hours).
- Up to £750 for training that is relevant to your job and improves your skills in the long term.
- Personal advice and a wide range of support to improve your chances of finding the right sort of job
- Advice if you want to start your own business or become self-employed

For further information call 0845 606 2626 or visit their website at:

www.newdeal.gov.uk

NB: Contact your Benefits Agency or local Job centre to find out how it may affect any existing benefits that you are receiving.

Linkline

Linkline is a free telephone helpline service for adults. It provides information and advice on training, learning and work.

Linkline can help with the following:

- Information on local education courses
- Where and how to get the money you need
- How to get the right training for a new job
- Where to go to get your CV up to scratch
- Help with interview skills

- Information on training locally
- Help with job searching

For further information call 0800 0641 481

Learndirect courses and centres

Learndirect offer a variety of courses to do, either at home, if you have internet access, or at one of the many centres in the UK. They can take from 15 minutes to a few hours to complete, but because they are broken down into small chunks, you can work at your own pace.

There are over 750 courses to do in four key areas:-

Using information technology (IT)
Information technology (IT) professional
Skills for life
Business Management

For further information phone 0800 100 900 or visit the website at:
www.learndirect.co.uk

Voluntary work

There are a variety of organisations that may be contacted with a view to finding out about doing voluntary work.

Timebank *(020 7401 5420)*

- *is a national volunteering campaign.*
  - It offers a number of ways to get involved in your local community
  - Runs a number of targeted volunteer initiatives, e.g. in sport, the environment and the arts.

Volunteering.org.uk

- is an on-line resource for potential volunteers, volunteer managers and anyone
  seeking up to date information on volunteering.

NCVO *(National Council for Voluntary Organizations – 020 7713 6161 / www.ncvo-vol.org.uk))*

- Is the umbrella body for the voluntary sector in England

Citizens Advice Bureau (CAB)

The CAB is an organisation that gives free, confidential, impartial and independent advice on a wide range of subjects including employment, benefits and housing matters.

For further information contact your nearest CAB by telephoning or dropping-in during working hours Monday to Friday. They also have websites, e.g.: www.citizensadvice.co.uk

Please note that this section was correct and up to date in March 2004.

Appendix 6: Summary of Therapies

	SIMPLE ADAPTIVE PACING (APT)	INCREMENTAL PACING (GET)	COMPLEX INCREMENTAL PACING (CBT)
Model	Pathology	Physiology + behaviour	Physiology + behaviour + cognition
Ingredients of therapy	Balance activity and symptoms	Planned increases in activity on basis of physiological tolerance	Planned increases in activity with challenging of understanding of symptoms
Stabilise activity	Y	Y	Y
Planned increases in activity	N	Y	Y
Direct challenge of cognitions	N	N	Y
Specific encouragement of aerobic exercise	N	Y	N

Appendix 7: CGI for SSMC doctors

PIN		Participant Initials		Date completed			
						2 0	
Centre	Participant	Fore.	Midd. Sur.	Day	Month	Year	

The following is a global impression of change scale. Please rate this scale including all of the various therapeutic factors.

1. Overall, how much has the participant changed since the start of the study (please tick only one box)?	
Very much better	
Much better	
A little better	
No change	
A little worse	
Much Worse	
Very much worse	

2. How well has the participant adhered to both medical management and advice – did the participant actually implement what had been negotiated in the sessions (please tick only one box)?

Completely	Very well	Moderately well	Slightly	Not at all

3. To what extent did the participant accept the principles underlying the management advice they were given (please tick only one box)?

Completely	Very well	Moderately well	Slightly	Not at all

4. Sessions received

a. How many treatment sessions with you **in total** has the participant received (include face-to-face sessions and telephone sessions, but not administrative calls i.e. to re-arrange appointments)?

b. Of these, how many were conducted over the telephone (do not include administrative calls)?

☐☐

c. How many hours and minutes in total of treatment were given (do not include administrative calls)?

☐☐☐ Hours ☐☐ minutes

5. How many planned sessions did NOT occur?

☐☐

Of these:

d. How many were cancelled because of your being unable to attend?

☐☐

e. How many cancellations or DNAs were instigated by the participant (e.g. travel problems, sickness, family commitments)?

☐☐

f. How many sessions were cancelled by mutual consent (i.e. both you and the participant *agreed that the session was unnecessary*)?

☐☐

6. How many unplanned phone calls took place (phone calls regarding treatment issues, do not include administrative calls)?

☐☐

7. How many sessions were attended by a relative (not partner) **of the participant?**

☐☐

8. How many sessions were attended by a friend of the participant?

☐☐

9. How many sessions were attended by the participant's partner?

☐☐

Version 2, 26.11.2004

Appendix 8: Medical screening SOP

Assessment

All patients will be assessed by doctors experienced in the diagnosis and management of CFS/ME. The assessment process is intended to determine
Whether the diagnosis of CFS/ME is appropriate
Whether the patient is eligible for referral to the research nurse for screening for the PACE trial

Medical assessment will include:

History

Particular emphasis should be placed on:
History of present complaint
Current activity level/pattern
Mood disorder and illness beliefs
Sleep pattern
Severe personality disorder
Exclusion of patients in whom medical or psychiatric conditions are excluded by the Oxford criteria (see below and Oxford criteria) reference 2 in trial protocol

Examination

All patients will undergo a physical examination. The extent of this examination and the degree to which it includes a full neurological assessment is at the discretion of the examining physician, and will be influenced by the history and the extent to which physical examination has been performed by the referring doctor (See SOP9.).

All patients will undergo a mental state examination, (See SOP 10.)

Investigations

All patients will have the following investigations performed in the previous six months:

Full blood count, ESR or C-reactive protein, urea and electrolytes, liver function tests, calcium, albumin, creatine kinase, thyroid function (TSH and free T4), local coeliac screen (e.g. IgA endomysial autoantibodies), random blood glucose, urinalysis for blood, sugar and protein.

These tests must have been carried out no more than six months prior to assessment and the laboratory reports, or copies, must be reviewed by the assessing doctor.

The history may suggest the need for other tests (e.g. ANA, Lyme serology) but in the absence of a suggestive history no further tests are mandatory for trial entry. Medical exclusions are made from the history, relevant examination and investigations.

Common medical exclusions (taken from reference 1 in trial protocol)

Permanent medical exclusions include the following:

1) organ failure (e.g., emphysema, cirrhosis, cardiac failure, chronic renal failure);

2) chronic infections (e.g., AIDS, hepatitis B or C);

3) rheumatic and chronic inflammatory diseases (e.g., systemic lupus erythematosis, Sjogren's syndrome, rheumatoid arthritis, inflammatory bowel disease, chronic pancreatitis);

4) major neurologic diseases (e.g., multiple sclerosis, neuromuscular diseases, epilepsy or other diseases requiring ongoing medication that could cause fatigue, stroke, head injury with residual neurologic deficits);

5) diseases requiring systemic treatment (e.g., organ or bone marrow transplantation, systemic chemotherapy, radiation of brain, thorax, abdomen, or pelvis);

6) major endocrine diseases (e.g., hypopituitarism, adrenal insufficiency);

7) primary sleep disorders (e.g., sleep apnea, narcolepsy).

Temporary medical exclusions include treatable conditions that require evaluation over time to determine the extent to which they contribute to the fatiguing illness. These encompass four general categories:

1) conditions discovered at onset or initial evaluation (e.g., effects of medications, sleep deprivation, untreated hypothyroidism, untreated or unstable diabetes mellitus, active infection);

2) conditions that resolve (e.g., pregnancy until 3 months post-partum, breast feeding, major surgeries until 6 months post-operation, minor surgery until 3 months post-operation, and major infections such as sepsis or pneumonia until 3 months post-resolution; sleep disorders such as restless leg syndrome and periodic limb movement should be considered temporary exclusions for research criteria, if they are severe, but not if the degree of the sleep problem is insufficient to explain the severity of the fatigue);

3) major conditions whose resolution may be unclear for at least 5 years (e.g., myocardial infarction, heart failure);

4) morbid obesity (body mass index [BMI] > 40).

Psychiatric exclusions (taken from reference 2 in trial protocol)

A current diagnosis of:
Schizophrenia of any subtype,
Bipolar (manic depressive) mood disorder
An eating disorder
Alcohol or substance abuse
Proven organic brain disorder

Appendix 9: Contraindications and Cautions for Trial Treatments

Certain co-morbid medical or psychiatric conditions may either be a contraindication or require specialist assessment or advice from the centre leader before participating in the trial. These mainly concern GET, but some conditions may affect other treatment groups.

Absolute Contraindications to the PACE trial:

Oxford criteria will have excluded some of the following conditions. However, please note that the following conditions may either be definite clinical exclusions for a trial treatment, or else be excluded on the grounds of difficulty in participating in a manual derived, time-limited version of a therapy:

- Uncontrolled hypertension
- Poorly controlled/unstable respiratory conditions, e.g. asthma
- Unstable musculoskeletal conditions, e.g. recent or poorly healed fracture, recent or unstable back injury or current back disease/disorder
- Pregnancy: would usually not be contraindicated to exercise in particular. However, the time limitations of the trial would not allow for a suitable break prior to and after birth.

Potentially allowable conditions (To be discussed with Centre Leader and Physiotherapist)

Cardiac conditions

- Pacemakers may affect heart rate monitors and target heart rate, therefore needs highlighting and advice
- Those on beta-blockers/ other cardiovascular medication that may affect heart rate / BP: will need guidance from doctors re: target heart rate

Musculoskeletal disorders:
Conditions that may affect current exercise ability -

- Significant arthritic conditions
- Significant previous injury / fractures
- Significant previous surgery
- Significant loss of range of movement, especially lower limb

NB previous major injuries or surgery are only relevant if they currently exclude a participant from actively participating in exercise

Psychiatric conditions

- Psychiatric disorders that may affect engagement or attendance, e.g. severe depressive or anxiety disorders

Respiratory conditions:
Well controlled conditions can be considered, although may limit exercise capacity and progress.

Significant regional pain

Any other condition that is thought to affect the participant's current ability to engage or participate in exercise.

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