

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.

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. Specialist medical care will be given by an appropriately trained doctor in the hospital clinic.

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 appropriately trained 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. APT is usually given by an occupational therapist but may be given by an appropriately trained therapist of another appropriate healthcare discipline. You will be informed of the qualification and discipline of your therapist if you are randomised to receive APT.

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. CBT is given by an appropriately trained cognitive behavioural therapist, such as a nurse specialist, psychologist or occupational therapist. You will be informed of the qualification and discipline of your therapist if you are randomised to receive CBT.

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 an appropriately trained therapist. 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. GET is usually given by a physiotherapist but may be given by an appropriately trained therapist of another appropriate healthcare discipline. You will be informed of the qualification and discipline of your therapist if you are randomised to receive GET.

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 sessions follow the manual we have written for our study, because that is the only fair way to compare these treatments. 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 up to 15 therapy sessions IF you 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, your clinic doctor or therapist will discuss whether you need more treatment. If you do, your clinic doctor or therapist will discuss which of the three extra therapies would suit you best. The study therapists give you this treatment. 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 a PACE 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 the study, 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 (DoH) 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.

- Astley Ainsley Hospital, Edinburgh, working 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 working with the Oxford Radcliffe Hospitals Trust
- The Royal Free Hampstead NHS Trust
- Guy's, King's & St Thomas' School of Medicine

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.

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

Thank you for your interest in our work

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