

A randomised controlled trial of adaptive pacing, cognitive behaviour therapy, and graded exercise, as supplements to standardised specialist medical care versus standardised specialist medical care alone for patients with the chronic fatigue syndrome /myalgic encephalomyelitis or encephalopathy

Submission date 22/05/2003	Recruitment status No longer recruiting	☒ Prospectively registered
Registration date 22/05/2003	Overall study status Completed	☒ Protocol
Last Edited 03/11/2015	Condition category Mental and Behavioural Disorders	☒ Statistical analysis plan
		☒ Results
		☐ Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number

G0200434

Study information

Scientific Title

A randomised controlled trial of adaptive pacing, cognitive behaviour therapy, and graded exercise, as supplements to standardised specialist medical care versus standardised specialist medical care alone for patients with the chronic fatigue syndrome/myalgic encephalomyelitis or encephalopathy

Acronym

PACE: Pacing, Activity, and Cognitive behaviour therapy: a randomised Evaluation

Study objectives

1. Are cognitive behaviour therapy (CBT) and/or graded exercise therapy (GET) more effective than pacing in reducing both fatigue and disability?
2. Is pacing more effective than usual medical care?
3. Are there differential predictors of response to CBT and GET and does the mechanism of change differ?
4. Do different treatments have differential effects on outcomes (i.e. disability versus symptoms)?
5. What factors predict a favourable response to treatment in general and with specific treatments?
6. What are the mechanisms of change with successful treatment?
7. What are the relative cost-effectiveness and cost-utility of these treatments?

As of 16/02/09 this record was updated to reflect an amendment to the anticipated end date. The initial information at the time of registration was 13/06/2009.

Ethics approval required

Old ethics approval format

Ethics approval(s)

UK West Midlands Multicentre Research Ethics Committee, 31/03/2003

Primary study design

Interventional

Study design

Multicentre randomised controlled trial

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Symptoms and general pathology

Interventions

PACE is a multicentre randomised controlled trial. The group assignment is parallel group.

1. Standardised Specialist Medical Care alone (SSMC) - manual guided advice from a secondary care clinic specialist in chronic fatigue
2. Standardised Specialist Medical Care plus adaptive pacing therapy (APT)
3. Standardised Specialist Medical Care plus graded exercise therapy (GET)
4. Standardised Specialist Medical Care plus cognitive behaviour therapy (CBT)

There is no masking as the supplementary treatments being trialled are delivered by therapists and maintaining any blind would be very difficult. Even though treatment allocation is not blinded, staff are encouraged not to discuss randomisations or any subject that might inadvertently lead to bias.

Intervention Type

Other

Phase

Not Applicable

Primary outcome(s)

1. Is APT and SSMD more effective than SSMD alone in reducing (i) fatigue, (ii) disability, or (iii) both?
2. Is CBT and SSMD more effective than APT and SSMD in reducing (i) fatigue, (ii) disability or (iii) both?
3. Is GET and SSMD more effective than APT and SSMD in reducing (i) fatigue, (ii) disability, or (iii) both?
4. Are the active rehabilitation therapies (of either CBT or GET) more effective than the adaptive approach of APT when each is added to SSMD, in reducing fatigue, in reducing physical disability?
5. What are the relative cost-effectiveness and cost-utility of these treatments?

Key secondary outcome(s)

The secondary analyses are exploratory but we will be guided by previously published findings.

1. Do different treatments have differential effects on outcomes (i.e. fatigue versus physical disability)?
2. What baseline factors (other than randomised treatment) predict a reduction in (i) fatigue, (ii) disability in all participants?
3. Are there differential predictors of response to APT, CBT, GET, and SSMD (i.e. treatment-covariate interactions)?
4. Are there changes in factors (time-dependent covariates) during the earlier stages of treatment that (after controlling for baseline overall and differential predictors) are associated with outcome at 1 year from randomisation?
5. Are the differences across treatment groups in the primary outcomes associated with similar differences in secondary outcomes (e.g. in global change, mood, quality of life and objective measures of physical activity)?

Hypotheses of efficacy:

1. APT plus SSMD is more effective than SSMD alone in reducing (i) fatigue, (ii) reducing physical disability and in reducing (iii) both
2. CBT plus SSMD is more effective than APT and SSMD in reducing (i) fatigue, (ii) disability and in reducing (iii) both
3. GET plus SSMD is more effective than APT and SSMD in reducing (i) fatigue, (ii) disability and in reducing (iii) both

4. The active rehabilitation therapies (of either CBT or GET) are more effective than the adaptive approach of APT when each is added to SSMC, in reducing fatigue, in reducing physical disability and both
5. CBT plus SSMC is more effective than SSMC in reducing (i) fatigue, (ii) disability and in reducing (iii) both
6. GET plus SSMC is more effective than SSMC in reducing (i) fatigue, (ii) disability and in reducing (iii) both

Completion date

01/07/2011

Eligibility

Key inclusion criteria

Consent:

1. Both participant and clinician agree that randomisation is acceptable
2. The participant has given written informed consent

Eligibility:

3. The participant meets operationalised Oxford research diagnostic criteria for CFS
4. The participant's Chalder Fatigue Questionnaire score is 6 or more
5. The participant's SF-36 physical function sub-scale score is 65 or less (changed from '60 or less' in April 2006)
6. The participant will be aged at least 18 years old, either sex

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

Key exclusion criteria

1. All potential participants will be screened for medical exclusions, by history and physical examination. Appropriate investigations will be undertaken by either the referring doctor or the centre doctors (checked by the RN). Patients with a relevant alternative medical diagnosis will be excluded. Investigations will be those recommended by the Royal Colleges' Report on CFS /ME and the CMO's working group report. These results will be collated by the RN, and will have been undertaken within six months of the baseline assessment.
2. The Research Nurse (RN) will use a standardised psychiatric interview (the Structured Clinical Interview for DSM-IV - SCID), under supervision by a participating centre PI or nominated deputy, to exclude those who are at significant risk of self-harm and those with psychiatric exclusions

listed in the Oxford diagnostic criteria for CFS.

3. Patients who are considered by the RN in discussion with their centre leader to be unable to do one or more of the trial therapies or to complete all trial measures or for whom participation in the PACE trial would be inappropriate to their clinical needs (e.g. someone with significant post traumatic stress disorder or borderline personality disorder).

4. Patients who have previously received one of the trial treatments before from a centre participating in PACE (rather than any secondary care clinic for Chronic Fatigue Syndrome) and received a course of any of the supplementary therapies of CBT, GET or pacing therapy from a therapist will be excluded from taking part in the trial, or of advice from a PACE doctor that is judged to have been similar to SSMC (changed from 'Patients who have previously attended a specialist fatigue clinic and received a course of any of the supplementary therapies of CBT, GET or pacing therapy from a therapist will be excluded from taking part in the trial' in April 2006).

Date of first enrolment

14/06/2004

Date of final enrolment

28/11/2008

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

St Bartholomew's Hospital

London

United Kingdom

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Sponsor information

Organisation

Queen Mary University of London (UK)

ROR

<https://ror.org/026zzn846>

Funder(s)

Funder type

Government

Funder Name

Medical Research Council (MRC) (UK)

Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Funder Name

The Scottish Chief Scientist's Office (UK)

Funder Name

Department of Health in England and Wales (UK)

Funder Name

Department for Work and Pensions (UK)

Results and Publications

Individual participant data (IPD) sharing plan**IPD sharing plan summary**

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	05/03/2011		Yes	No
Results article	results	01/10/2013		Yes	No
Results article	results	01/05/2014		Yes	No

Results article	results	01/12/2015	Yes	No	
Protocol article	protocol	08/03/2007	Yes	No	
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan	statistical analysis plan	13/11/2013	No	No	