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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	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 22/05/2003	**Overall study status** Completed	
Last Edited 03/11/2015	**Condition category** Mental and Behavioural Disorders	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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 theraphy (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

Study design
Multicentre randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet
Available on http://www.pacetrial.org/TrialInfo.pdf

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 measure
1. Is APT and SSMC more effective than SSMC alone in reducing (i) fatigue, (ii) disability, or (iii) both?
2. Is CBT and SSMC more effective than APT and SSMC in reducing (i) fatigue, (ii) disability or (iii) both?
3. Is GET and SSMC more effective than APT and SSMC 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 SSMC, in reducing fatigue, in reducing physical disability?
5. What are the relative cost-effectiveness and cost-utility of these treatments?

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

Overall study start date
14/06/2004

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
600

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
England

United Kingdom

Study participating centre
St Bartholomew's Hospital
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Sponsor type
University/education

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, 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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Protocol article	protocol	08/03/2007		Yes	No
Results article	results	05/03/2011		Yes	No
Results article	results	01/10/2013		Yes	No
Statistical Analysis Plan	statistical analysis plan	13/11/2013		No	No
Results article	results	01/05/2014		Yes	No
Results article	results	01/12/2015		Yes	No