Clinical Trials IV

Case Studies

Nuno Sepúlveda

Recap

Course content

1. Basic concepts related to CTs
2. Designing/Reporting CTs/Mendelian Randomisation/Survival Analysis
3. Reporting CTs (CONSORT guidelines)
4. Discussion on the controversial PACE trial
5. Project’s Presentations/Course Summary

Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial

P D White, K A Goldsmith, A L Johnson, L Potts, R Walwyn, J C DeCesare, H L Baber, M Burgess, L V Clark, D L Cox, J Bavinton, B J Angus, G Murphy, M Murphy, H O'Dowd, D Wilks, P McCrone, T Chalder, M Sharpe*, on behalf of the PACE trial management group†*

Summary

Background Trial findings show cognitive behaviour therapy (CBT) and graded exercise therapy (GET) can be effective treatments for chronic fatigue syndrome, but patients' organisations have reported that these treatments can be harmful and favour pacing and specialist health care. We aimed to assess effectiveness and safety of all four treatments.

Methods In our parallel-group randomised trial, patients meeting Oxford criteria for chronic fatigue syndrome were

Lancet 2011; 377: 823–

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See Comment page 78

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Editorial

JHP

'PACE-Gate': When clinical trial evidence meets open data access

Journal of Health Psychology
2017, Vol. 22(9) 1106–1112
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Keith J Geraghty

Abstract
Science is not always plain sailing and sometimes the voyage is across an angry sea. A recent clinical trial of treatments for chronic fatigue syndrome (the PACE trial) has whipped up a storm of controversy. Patients claim the lead authors overstated the effectiveness of cognitive behavioural therapy and graded exercise therapy by lowering the thresholds they used to determine improvement. In this extraordinary case, patients discovered that the treatments tested had much lower efficacy after an information tribunal ordered the release of data from the PACE trial to a patient who had requested access using a freedom of information request.

Commentary

JHP

PACE trial authors continue to ignore their own null effect

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SAGE

Mark Vink

Abstract
Protocols and outcomes for the PACE trial were changed after the start of the trial. These changes made substantial differences, leading to exaggerated claims for the efficacy of cognitive behavior therapy and graded exercise therapy in myalgic encephalomyelitis/chronic fatigue syndrome. The small, self-reported improvements in subjective measures cannot be used to say the interventions are effective, particularly in light of the absence of objective improvement. Geraghty's criticism of the trial was reasonable and supported by the evidence.

Wilshire and Kindlon *BMC Psychology* (2019) 7:19
https://doi.org/10.1186/s40359-019-0296-x

BMC Psychology

CORRESPONDENCE Open Access

Response: Sharpe, Goldsmith and Chalder fail to restore confidence in the PACE trial findings

Carolyn E. Wilshire[1*] and Tom Kindlon[2]

(10.1186/s40359-018-0218-3) The original article was published in BMC Psychology 2018 6:6
(10.1186/s40359-019-0288-x) This correspondence to this article has been published in BMC Psychology 2019 7:15

Open Peer Commentary Article

JHP

Response to the editorial by Dr Geraghty

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DOI: 10.1177/1359105316688953
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Peter D White[1,2], Trudie Chalder[3], Michael Sharpe[4], Brian J Angus[5], Hannah L Baber[1], Jessica Bavinton[6], Mary Burgess[7], Lucy V Clark[1], Diane L Cox[8], Julia C DeCesare[1], Kimberley A Goldsmith[3], Anthony L Johnson[9], Paul McCrone[3], Gabrielle Murphy[10], Maurice Murphy[6], Hazel O'Dowd[11], Laura Potts[3], Rebecca Walwyn[9] and David Wilks[12]

Abstract
This article is written in response to the linked editorial by Dr Geraghty about the adaptive Pacing, graded Activity and Cognitive behaviour therapy; a randomised Evaluation (PACE) trial, which we led, implemented and published. The PACE trial compared four treatments for people diagnosed with chronic fatigue syndrome. All participants in the trial received specialist medical care. The trial found that adding cognitive behaviour therapy or graded exercise therapy to specialist medical care was as safe as, and more effective than, adding adaptive pacing therapy or specialist medical care alone. Dr Geraghty has challenged these findings. In this article, we suggest that Dr Geraghty's views are based on misunderstandings and misrepresentations of the PACE trial; these are corrected.

Commentary

JHP

PACE trial claims for recovery in myalgic encephalomyelitis/chronic fatigue syndrome – true or false? It's time for an independent review of the methodology and results

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Charles Bernard Shepherd

Commentary

JHP

Once again, the PACE authors respond to concerns with empty answers

Journal of Health Psychology
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David Tuller

Abstract
In their response to Geraghty, the PACE investigators state that they have "repeatedly addressed" the various methodological concerns raised about the trial. While this is true, these responses have repeatedly failed to provide satisfactory explanations for the trial's very serious flaws. This commentary examines how the current response once again demonstrates the ways in which the investigators avoid acknowledging the obvious problems with PACE and offer non-answers instead—arguments that fall apart quickly under scrutiny.

BMC Neurology

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Study protocol

Open Access

Protocol for the PACE trial: 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

Peter D White*[1], Michael C Sharpe[2], Trudie Chalder[3], Julia C DeCesare[4], Rebecca Walwyn[5] and the PACE trial group[4]

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Email: Peter D White* - p.d.white@qmul.ac.uk; Michael C Sharpe - michael.sharpe@ed.ac.uk; Trudie Chalder - t.chalder@iop.kcl.ac.uk; Julia C DeCesare - j.c.decesare@qmul.ac.uk; Rebecca Walwyn - R.Walwyn@iop.kcl.ac.uk; the PACE trial group - pace@qmul.ac.uk

* Corresponding author

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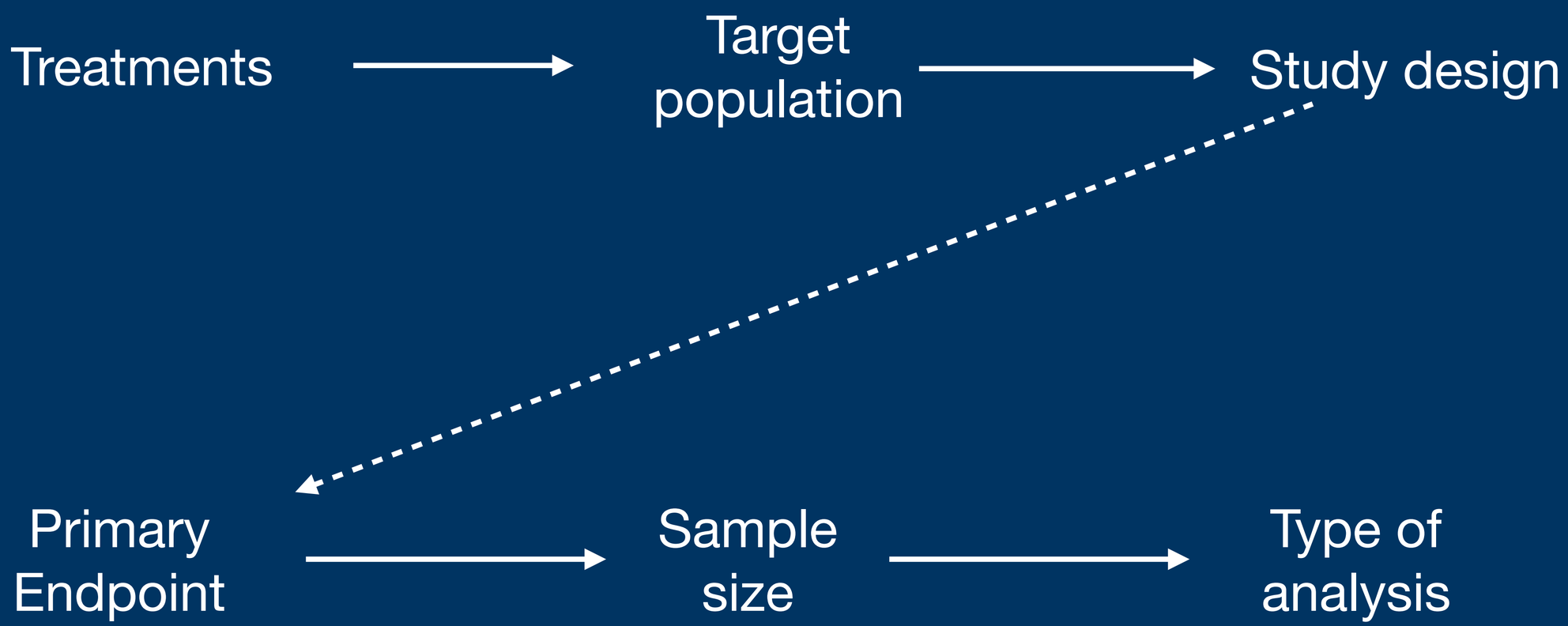
Key Elements in Clinical Trial



Treatments under comparison

Adaptive Pacing Therapy (APT)

Specialized Medical Care (SMC)

Graded exercise therapy (GET)

Cognitive behavioural therapy (CBT)

Specialized Medical Care

All participants were given a leaflet explaining the illness and the nature of this treatment. The manual was consistent with good medical practice, as presently recommended. Treatment consisted of an explanation of chronic fatigue syndrome, generic advice, such as to avoid extremes of activity and rest, specific advice on self-help, according to the particular approach chosen by the participant (if receiving SMC alone), and symptomatic pharmacotherapy (especially for insomnia, pain, and mood).

https://www.equator-network.org/reporting-guidelines/consort/

Adaptive Pacing Therapy

APT was based on the envelope theory of chronic fatigue syndrome. This theory regards chronic fatigue syndrome as an organic disease process that is not reversible by changes in behaviour and which results in a reduced and finite amount (envelope) of available energy. The aim of therapy was to achieve optimum adaptation to the illness, hence APT. This adaptation was achieved by helping the participant to plan and pace activity to reduce or avoid fatigue, achieve prioritised activities and provide the best conditions for natural recovery

Cognitive Behaviour Therapy

The aim of treatment was to change the behavioural and cognitive factors assumed to be responsible for perpetuation of the participant's symptoms and disability. Therapeutic strategies guided participants to address unhelpful cognitions, including fears about symptoms or activity by testing them in behavioural experiments.

https://www.equator-network.org/reporting-guidelines/consort/

Graded Exercise Therapy

GET was done on the basis of deconditioning and exercise intolerance theories of chronic fatigue syndrome. These theories assume that the syndrome is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. The aim of treatment was to help the participant gradually return to appropriate physical activities, reverse the deconditioning, and thereby reduce fatigue and disability.

https://www.equator-network.org/reporting-guidelines/consort/

Target population

Inclusion criteria

1. Both participant and clinician agree that randomisation is acceptable.

2. The participant has given written informed consent.

3. The participant meets operationalised Oxford research diagnostic criteria for CFS [2].

4. The participant's Chalder Fatigue Questionnaire score is 6 or more [27].

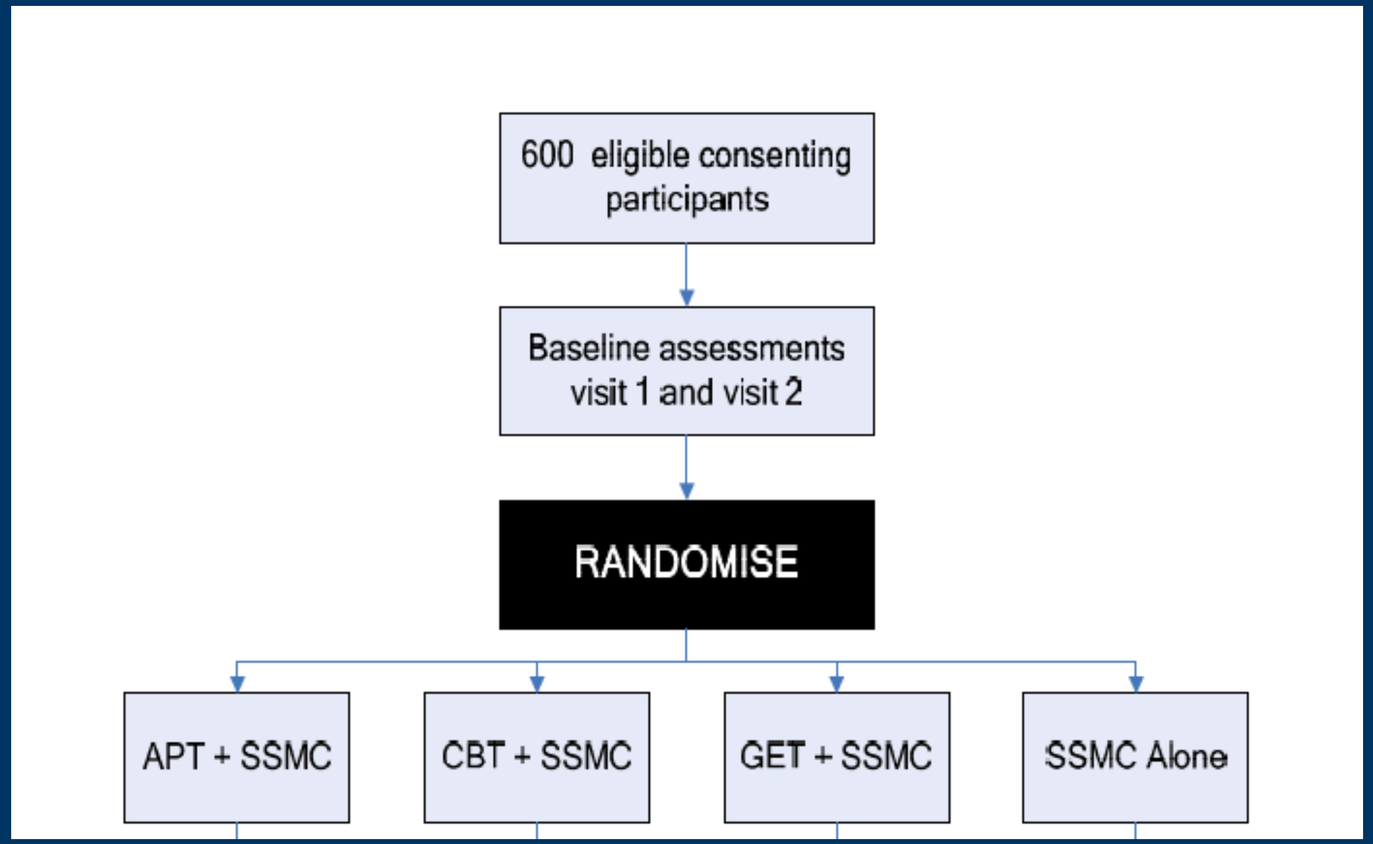
5. The participant's SF-36 physical function sub-scale score [28] is 65 or less.

6. The participant is aged at least 18 years old.

Exclusion criteria

Participation in previous PACE trials
Psychological disorders

Study design



Primary Endpoint

The 11 item Chalder Fatigue Questionnaire measures the severity of symptomatic fatigue [27], and has been the most frequently used measure of fatigue in most previous trials of these interventions. We will use the 0,0,1,1 item scores to allow a possible score of between 0 and 11. A positive outcome will be a 50% reduction in fatigue score, *or* a score of 3 or less, this threshold having been previously shown to indicate normal fatigue [27].

The SF-36 physical function sub-scale [29] measures physical function, and has often been used as a primary outcome measure in trials of CBT and GET. We will count a score of 75 (out of a maximum of 100) or more, *or* a 50% increase from baseline in SF-36 sub-scale score as a positive outcome. A score of 70 is about one standard deviation below the mean score (about 85, depending on the study) for the UK adult population [51,52].

Secondary outcome measures – Secondary efficacy measures

1. The Chalder Fatigue Questionnaire Likert scoring (0,1,2,3) will be used to compare responses to treatment [27].

Sample Size/Power Calculation

Power analyses

Our planned intention to treat analyses will compare APT against SSMC alone, and both CBT and GET against APT. Assuming $\alpha = 5\%$ and a power of 90%, we require a minimum of 135 participants in the SSMC alone and APT groups, 80 participants in the GET group and 40 in the CBT group [57]. However these last two numbers are insufficient to study predictors, process, or cost-effectiveness. We will not be able to get a precise estimate of the difference between CBT and GET, though our estimates will be useful in planning future trials. As an example, to detect a difference in response rates of 50% and 60%, with 90% power, would require 520 participants per group; numbers beyond a realistic two-arm trial. Therefore, we will study equal numbers of 135 participants in each of the four arms, which gives us greater than 90% power to study differences in efficacy between APT and both CBT and GET. We will adjust our numbers for dropouts, at the same time as designing the trial and its management to minimise dropouts. Dropout rates were 12 and 33% in

Statistical analysis

We calculated sample sizes assuming 60% response to CBT at 52 weeks, 50% response to GET, 25% response to APT, and 10% response to SMC.[10] We assumed APT to be at least as effective as in previous trials of relaxation and flexibility therapies.[20,22] For a two-sided test with 5% significance level and 90% power, we calculated that the number of participants needed to compare SMC with APT was 135, SMC with GET was 80, and SMC with CBT was 40. We increased group size to 150 per group to allow for 10% dropout, to provide equality between groups, and for secondary analyses. The

Is there any problem with these calculations?

Let’s redo sample size calculation

SMC - 10%

APT - 25%

GET - 50%

CBT - 60%

SMC vs APT

SMC vs GET

SMC vs CBT

time!!!!

Package pwr

Type of analysis

Intention-to-treat

Primary analyses of efficacy

The primary analysis will be pragmatic, based on intention to treat, and will utilise all available follow-up data from all randomised participants. The primary binary out-

What actually happened?

Target population

Other eligibility criteria consisted of a bimodal score of 6 of 11 or more on the Chalder fatigue questionnaire[15] and a score of 60 of 100 or less on the short form-36 physical function subscale.[16] 11 months after the trial began, this requirement was changed from a score of 60 to a score of 65 to increase recruitment.

Study design

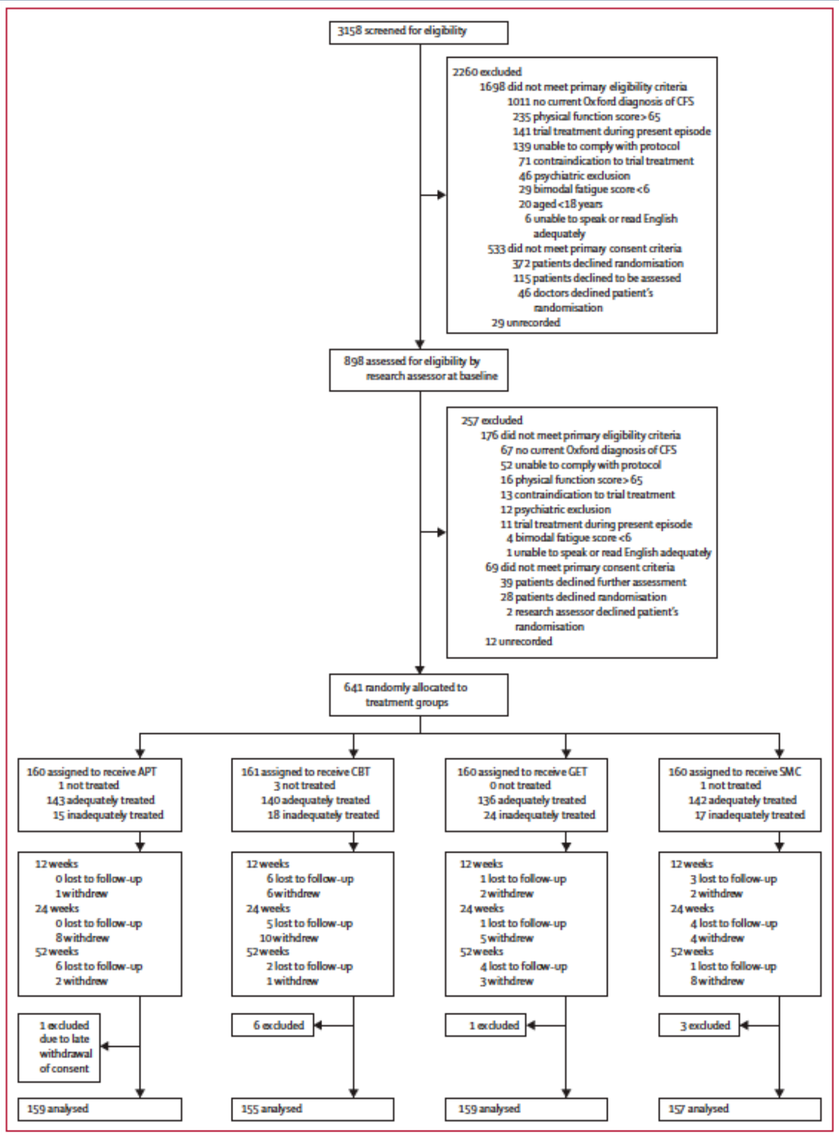


Figure 1: **CONSORT trial profile**
CFS=chronic fatigue syndrome. APT=adaptive pacing therapy. CBT=cognitive behaviour therapy. GET=graded exercise therapy. SMC=specialist medical care alone. The numbers of participants per centre ranged from 63 to 135.

Primary Endpoint

	Trial protocol	Final publication
Fatigue (bimodal Chalder scale)	50% reduction or score ≤3	7% reduction* or score ≤4†
Physical functioning (SF-36 subscale)	50% increase or score ≥75	21% increase‡ or score ≥60

*Clinically useful difference of 2 points (0·5 SD) and mean baseline Likert score of 28·2. †Likert score of ≤18 used by the authors implies bimodal score of ≤4. ‡Clinically useful difference of 8 points (0·5 SD) and mean baseline short-form 36 (SF-36) physical function subscale score of 38·0.

Table: **Definition of positive outcome/improvement in the trial protocol and the final publication**

Is this a case of "outcome reporting bias"?[4]

We declare that we have no conflicts of interest.

Bart Stouten, Ellen M Goudsmit, Neil Riley

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Primary Endpoint

Outcomes

The two participant-rated primary outcome measures were the Chalder fatigue questionnaire (Likert scoring 0, 1, 2, 3; range 0–33; lowest score is least fatigue)[15] and the short form-36 physical function subscale (version 2; range 0–100; highest score is best function).[16] Before outcome data were examined, we changed the original bimodal scoring of the Chalder fatigue questionnaire (range 0–11) to Likert scoring to more sensitively test our hypotheses of effectiveness. The two primary outcome measures[15, 16] are valid and reliable and have been used in previous trials.[4, 5, 6, 7]

Recovery: $CFQ \leq 18$

However…

ELSEVIER

Journal of Psychosomatic Research 69 (2010) 17–22

Journal of Psychosomatic Research

Measuring fatigue in clinical and community settings

Matteo Cella*, Trudie Chalder

Institute of Psychiatry, King's College London, London, United Kingdom

Received 11 June 2009; received in revised form 8 October 2009; accepted 13 October 2009

Abstract

Objective: The Chalder Fatigue Scale (CFQ) is a widely used instrument to assess fatigue in both clinical and nonclinical settings. Psychometric properties of the scale and discriminative abilities were examined. **Methods:** A total of 361 patients with CFS and 1615 individuals in the community were assessed with the CFQ. Principal component analysis (PCA) was used to explore the structure of the scale. Receiver-operating characteristic curve (ROC) was used to investigate the discriminative properties. **Results:** Two components, physical and mental fatigue, were identified in the CFS patient group and in the general population samples. Area under the curve for ROC was .91. The fatigue scale effectively discriminates, at high scores, between CFS patients and the general population. **Conclusion:** Physical and mental fatigue are clearly separable components of fatigue. The CFQ can discriminate reliably between clinical and nonclinical conditions.

Keywords: CFS; Chalder fatigue scale; Chronic fatigue syndrome; Fatigue; ROC

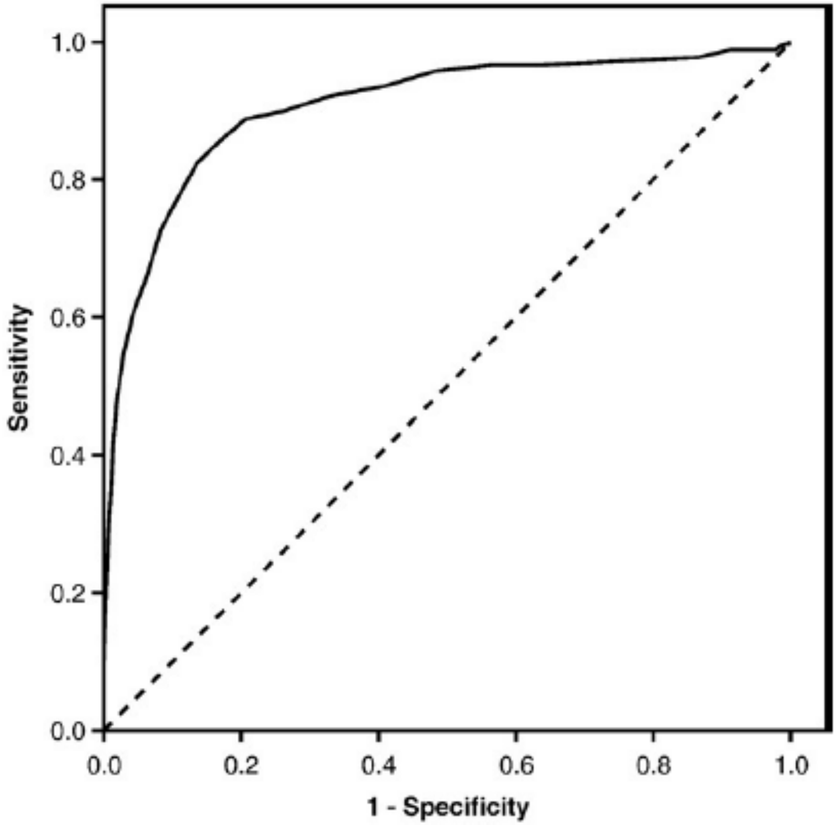

Fig. 1. Fatigue scale ROC plot.

However…

Table 3
Sensitivity and 1−specificity for the fatigue scales scores

CFQ Score	Sensitivity	1−Specificity
0	1.000	1.000
1	1.000	.999
2	.997	.998
3	.997	.997
4	.997	.993
5	.994	.985
6	.989	.979
7	.989	.964
8	.989	.940
9	.989	.913
10	.978	.866
11	.966	.637
12	.966	.565
13	.958	.484
14	.936	.408
15	.922	.330
16	.899	.260
17	.888	.207
18	.854	.167
19	.824	.136
20	.773	.107
21	.728	.084
22	.658	.062
23	.605	.043
24	.546	.029
25	.473	.018
26	.415	.014
27	.339	.010
28	.286	.007
29	.202	.004
30	.151	.000
31	.095	.000
32	.062	.000
33	.000	.000

What is the best CFQ score for discriminating CFS from healthy controls?

time!!!!

Results of primary endpoint

	Fatigue*				Physical function†			
	Adaptive pacing therapy	Cognitive behaviour therapy	Graded exercise therapy	Specialist medical care alone	Adaptive pacing therapy	Cognitive behaviour therapy	Graded exercise therapy	Specialist medical care alone
Baseline	28·5 (4·0); n=159	27·7 (3·7); n=161	28·2 (3·8); n=160	28·3 (3·6); n=160	37·2 (16·9); n=159	39·0 (15·3); n=161	36·7 (15·4); n=160	39·2 (15·4); n=160
12 weeks	24·2 (6·4); n=153	23·6 (6·5); n=153	22·8 (7·5); n=153	24·3 (6·5); n=154	41·7 (19·9); n=153	51·0 (20·7); n=153	48·1 (21·6); n=153	46·6 (20·4); n=154
24 weeks	23·7 (6·9); n=155	21·5 (7·8); n=148	21·7 (7·1); n=150	24·0 (6·9); n=152	43·2 (21·4); n=155	54·2 (21·6); n=148	55·4 (23·3); n=150	48·4 (23·1); n=152
52 weeks	23·1 (7·3); n=153	20·3 (8·0); n=148	20·6 (7·5); n=154	23·8 (6·6); n=152	45·9 (24·9); n=153	58·2 (24·1); n=148	57·7 (26·5); n=154	50·8 (24·7); n=152
Mean difference (95% CI) from SMC (52 weeks)	−0·7 (−2·3 to 0·9)	−3·4 (−5·0 to −1·8)	−3·2 (−4·8 to −1·7)	–	−3·4 (−8·4 to 1·6)	7·1 (2·0 to 12·1)	9·4 (4·4 to 14·4)	–
Unadjusted p values	0·38	0·0001	0·0003	–	0·18	0·0068	0·0005	–
Bonferroni adjusted p values	0·99	0·0006	0·0013	–	0·89	0·0342	0·0025	–
Mean difference (95% CI) from APT (52 weeks)	–	−2·7 (−4·4 to −1·1)	−2·5 (−4·2 to −0·9)	–	–	10·5 (5·4 to 15·6)	12·8 (7·7 to 17·9)	–
Unadjusted p values	–	0·0027	0·0059	–	–	0·0002	<0·0001	–
Bonferroni adjusted p values	–	0·0136	0·0294	–	–	0·0012	0·0002	–
Number improved from baseline‡	99 (65%)	113 (76%)	123 (80%)	98 (65%)	75 (49%)	105 (71%)	108 (70%)	88 (58%)

Data are mean scores (SD) or n (%), unless otherwise stated. Comparisons of differences across groups made at 52 weeks are from the final adjusted models, so are slightly different from unadjusted values. p values for comparisons are unadjusted, with Bonferroni values adjusted for five comparisons for every primary outcome. *Chalder fatigue questionnaire (range 0–33, 0=best).[15] †Short form-36 physical function subscale score (range 0–100, 100=best).[16] ‡Participants improved from baseline by two or more points for fatigue and eight or more for physical function.

Table 3: Primary outcomes of fatigue and physical function

Was intention-to-treat actually followed?

	Fatigue*				Physical function†			
	Adaptive pacing therapy	Cognitive behaviour therapy	Graded exercise therapy	Specialist medical care alone	Adaptive pacing therapy	Cognitive behaviour therapy	Graded exercise therapy	Specialist medical care alone
Baseline	28·5 (4·0); n=159	27·7 (3·7); n=161	28·2 (3·8); n=160	28·3 (3·6); n=160	37·2 (16·9); n=159	39·0 (15·3); n=161	36·7 (15·4); n=160	39·2 (15·4); n=160
12 weeks	24·2 (6·4); n=153	23·6 (6·5); n=153	22·8 (7·5); n=153	24·3 (6·5); n=154	41·7 (19·9); n=153	51·0 (20·7); n=153	48·1 (21·6); n=153	46·6 (20·4); n=154
24 weeks	23·7 (6·9); n=155	21·5 (7·8); n=148	21·7 (7·1); n=150	24·0 (6·9); n=152	43·2 (21·4); n=155	54·2 (21·6); n=148	55·4 (23·3); n=150	48·4 (23·1); n=152
52 weeks	23·1 (7·3); n=153	20·3 (8·0); n=148	20·6 (7·5); n=154	23·8 (6·6); n=152	45·9 (24·9); n=153	58·2 (24·1); n=148	57·7 (26·5); n=154	50·8 (24·7); n=152
Mean difference (95% CI) from SMC (52 weeks)	−0·7 (−2·3 to 0·9)	−3·4 (−5·0 to −1·8)	−3·2 (−4·8 to −1·7)	–	−3·4 (−8·4 to 1·6)	7·1 (2·0 to 12·1)	9·4 (4·4 to 14·4)	..
Unadjusted p values	0·38	0·0001	0·0003	–	0·18	0·0068	0·0005	..
Bonferroni adjusted p values	0·99	0·0006	0·0013	–	0·89	0·0342	0·0025	..
Mean difference (95% CI) from APT (52 weeks)	–	−2·7 (−4·4 to −1·1)	−2·5 (−4·2 to −0·9)	–	–	10·5 (5·4 to 15·6)	12·8 (7·7 to 17·9)	..
Unadjusted p values	–	0·0027	0·0059	–	–	0·0002	<0·0001	..
Bonferroni adjusted p values	–	0·0136	0·0294	–	..	0·0012	0·0002	..
Number improved from baseline‡	99 (65%)	113 (76%)	123 (80%)	98 (65%)	75 (49%)	105 (71%)	108 (70%)	88 (58%)

Data are mean scores (SD) or n (%), unless otherwise stated. Comparisons of differences across groups made at 52 weeks are from the final adjusted models, so are slightly different from unadjusted values. p values for comparisons are unadjusted, with Bonferroni values adjusted for five comparisons for every primary outcome. * Chalder fatigue questionnaire (range 0–33, 0=best).[35] †Short form-36 physical function subscale score (range 0–100, 100=best).[36] ‡Participants improved from baseline by two or more points for fatigue and eight or more for physical function.

Table 3: Primary outcomes of fatigue and physical function

Any comments?

Treatnent	Expected by the Published Protocol	Observed (changed protocol) - CFQ	Power (SMC vs Other Groups)	Observed (Changed protocol)- SF36	Power (SMC vs Other Groups)
SMC	10%	65%	NA	58%	NA
APT	25%	65%	?	49%	?
GET	50%	80%	?	70%	?
CBT	60%	76%	?	71%	?

An interesting detail in “Views before treatment”

	Adaptive pacing therapy (n=159)	Cognitive behaviour therapy (n=161)	Graded exercise therapy (n=160)	Specialist medical care alone (n=160)	p value*
Treatment received					
Therapy sessions attended†	13 (12–15)	14 (12–15)	13 (12–14)	–	0·17
Specialist medical care sessions attended‡	3 (3–4)	3 (3–4)	3 (3–4)	5 (3–6)	0·0001
Adequate treatment§	143 (90%)	140 (87%)	136 (85%)	142 (89%)	0·56
Antidepressant at baseline	63 (40%)	57 (35%)	74 (46%)	66 (41%)	..
Antidepressant at 24 weeks¶	53 (34%)	45 (29%)	61 (40%)	60 (39%)	0·19
Antidepressant at 52 weeks¶	41 (27%)	47 (31%)	48 (31%)	61 (39%)	0·11
Hypnotic at baseline	6 (4%)	9 (6%)	6 (4%)	5 (3%)	..
Hypnotic at 24 weeks¶	3 (2%)	7 (5%)	5 (3%)	6 (4%)	0·61
Hypnotic at 52 weeks¶	5 (3%)	4 (3%)	3 (2%)	7 (5%)	0·62
Non-allocated treatment	8 (5%)	4 (3%)	7 (4%)	22 (14%)	0·0005
Dropouts from treatment	11 (7%)	17 (11%)	10 (6%)	14 (9%)	0·50
Views before treatment					
Treatment is logical	134 (84%)	115 (71%)	135 (84%)	79 (49%)	<0·0001
Confident about treatment	114 (72%)	91 (57%)	112 (70%)	65 (41%)	<0·0001
Views after treatment					
Satisfied with treatment¶	128 (85%)	117 (82%)	126 (88%)	76 (50%)	<0·0001
Dissatisfied with treatment¶	4 (3%)	7 (5%)	2 (1%)	17 (11%)	0·0010
Therapeutic alliance‖	6·5 (6·0–6·5)	6·5 (5·5–6·8)	6·5 (5·5–7·0)	–	0·96
Adherence to manual**	6·0 (6·0–6·5)	6·0 (5·0–6·5)	6·5 (6·0–6·5)	–	0·35

Data are median (IQR) or n (%). *p values across all groups. †86% of sessions were received face-to-face and 14% by telephone. ‡94% of sessions were received face-to-face and 6% by telephone. §Adequate treatment was ten or more sessions of therapy or three or more sessions of specialist medical care alone. ¶Percentages exclude missing data. ‖Scored 1–7 (1=poor, 7=excellent). **Scored 1–7 (1=not at all, 7=very much so).

Table 2: Treatment details

Where is the sin?

We estimated differences between treatment groups for both primary outcomes with mixed linear regression models with Kenward-Roger adjusted standard errors. Covariates were treatment group, baseline value of outcome, time, and stratification factors (centre, present depressive disorder, and alternative criteria for chronic fatigue syndrome and myalgic encephalomyelitis; all as stratified at entry). Time by treatment interaction terms

Two interesting details in “Views after treatment”

	Adaptive pacing therapy (n=159)	Cognitive behaviour therapy (n=161)	Graded exercise therapy (n=160)	Specialist medical care alone (n=160)	p value*
Treatment received					
Therapy sessions attended†	13 (12–15)	14 (12–15)	13 (12–14)	–	0·17
Specialist medical care sessions attended‡	3 (3–4)	3 (3–4)	3 (3–4)	5 (3–6)	0·0001
Adequate treatment§	143 (90%)	140 (87%)	136 (85%)	142 (89%)	0·56
Antidepressant at baseline	63 (40%)	57 (35%)	74 (46%)	66 (41%)	..
Antidepressant at 24 weeks¶	53 (34%)	45 (29%)	61 (40%)	60 (39%)	0·19
Antidepressant at 52 weeks¶	41 (27%)	47 (31%)	48 (31%)	61 (39%)	0·11
Hypnotic at baseline	6 (4%)	9 (6%)	6 (4%)	5 (3%)	..
Hypnotic at 24 weeks¶	3 (2%)	7 (5%)	5 (3%)	6 (4%)	0·61
Hypnotic at 52 weeks¶	5 (3%)	4 (3%)	3 (2%)	7 (5%)	0·62
Non-allocated treatment	8 (5%)	4 (3%)	7 (4%)	22 (14%)	0·0005
Dropouts from treatment	11 (7%)	17 (11%)	10 (6%)	14 (9%)	0·50
Views before treatment					
Treatment is logical	134 (84%)	115 (71%)	135 (84%)	79 (49%)	<0·0001
Confident about treatment	114 (72%)	91 (57%)	112 (70%)	65 (41%)	<0·0001
Views after treatment					
Satisfied with treatment¶	128 (85%)	117 (82%)	126 (88%)	76 (50%)	<0·0001
Dissatisfied with treatment¶	4 (3%)	7 (5%)	2 (1%)	17 (11%)	0·0010
Therapeutic alliance‖	6·5 (6·0–6·5)	6·5 (5·5–6·8)	6·5 (5·5–7·0)	–	0·96
Adherence to manual**	6·0 (6·0–6·5)	6·0 (5·0–6·5)	6·5 (6·0–6·5)	–	0·35

Data are median (IQR) or n (%). *p values across all groups. †86% of sessions were received face-to-face and 14% by telephone. ‡94% of sessions were received face-to-face and 6% by telephone. §Adequate treatment was ten or more sessions of therapy or three or more sessions of specialist medical care alone. ¶Percentages exclude missing data. ‖Scored 1–7 (1=poor, 7=excellent). **Scored 1–7 (1=not at all, 7=very much so).

Table 2: Treatment details

What do you conclude from this story?

What if you were the statistician/data scientist working with these data?