Behaviour Research and Therapy 63 (2014) 1–8

Contents lists available at ScienceDirect

Behaviour Research and Therapy

journal homepage: www.elsevier.com/locate/brat

Prevalence and predictors of recovery from chronic fatigue syndrome in a routine clinical practice

Elisabeth Flo [a, b, *], Trudie Chalder [c]

[a] Norwegian Competence Center for Sleep Disorders, Haukeland University Hospital, Bergen, Norway
[b] Centre for Elderly and Nursing Home Medicine, Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway
[c] Institute of Psychiatry, King's College London, London, United Kingdom

ARTICLE INFO

Article history:
Received 15 January 2013
Received in revised form
21 July 2014
Accepted 19 August 2014
Available online 26 August 2014

Keywords:
Chronic fatigue syndrome
Recovery
Cognitive behavioural therapy
Follow-up
Longitudinal

ABSTRACT

Cognitive behavioural therapy (CBT) is one of the treatments of choice for patients with chronic fatigue syndrome (CFS). However, the factors that predict recovery are unknown.

The objective of this study was to ascertain the recovery rate among CFS patients receiving CBT in routine practice and to explore possible predictors of recovery.

Recovery was defined as no longer meeting Oxford or CDC criteria for CFS measured at 6 months follow-up. A composite score representing full recovery additionally included the perception of improvement, and normal population levels of fatigue and of physical functioning. Logistic regression was used to examine predictors of recovery. Predictors included age, gender, cognitive and behavioural responses to symptoms, work and social adjustment, beliefs about emotions, perfectionism, anxiety and depression at baseline.

At 6 months follow-up 37.5% of the patients no longer met either the Oxford or the CDC criteria for CFS while 18.3% were fully recovered. Multivariate analyses showed that worse scores on the work and social adjustment scale, unhelpful beliefs about emotions, high levels of depression and older age were associated with *reduced* odds for recovery.

Recovery rates in this routine practice were comparable to previous RCTs. There was a wide spectrum of significant predictors for recovery.

Chronic fatigue syndrome (CFS) is a heterogeneous and multifactorial condition, characterised by fatigue and disability. Two commonly used criteria are; the Oxford criteria (Sharpe et al., 1991), and the US Center for Disease Control (CDC) criteria (Fukuda et al., 1994). While these two criteria are similar, there is not a complete overlap in terms of included symptoms. The CDC criteria necessitate the presence of several discrete symptoms. The Oxford criteria are less "detailed" in this respect but require the presence of both physical and mental fatigue for 6 months or more.

The aetiology is still much debated with some focused on finding a specific cause (Cairns & Hotopf, 2005). Since CFS does not have pathognomonic manifestations, the diagnostics of CFS remains a clinical endeavour, and suggests that the condition may be multi-factorial. Our original cognitive behavioural model of CFS suggested that an initial trigger such as a virus may contribute to a vicious cycle in which the individual avoids activity for fear of making symptoms worse (Butler, Chalder, Ron, & Wessely, 1991). In an effort to manage symptoms people become hypervigilant and this so called symptom focussing can exacerbate symptoms (Chalder, Butler, & Wessely, 1996). Surawy and colleagues subsequently added to the model by suggesting that pre-morbid characteristics such as conscientiousness and perfectionism contributed to individuals becoming vulnerable. In addition, patients with CFS were more likely to hold the belief that showing emotions was unacceptable (Surawy, Hackmann, Hawton, & Sharpe, 1995). Cognitive behavioural therapy (CBT) addresses these factors but in particular focuses on encouraging patients to become more consistent in engaging in activity before increasing activity thereby challenging fearful cognitions such as fear avoidance beliefs and catastrophising whilst simultaneously addressing symptom focussing. CBT and graded exercise therapy (GET) have proven to be the most effective treatments for CFS with significant improvements in fatigue and disability (Chambers, Bagnall, Hempel, & Forbes, 2006; White et al., 2011). However, reduction

* Corresponding author. Norwegian Competence Center for Sleep Disorders, Haukeland Universitetssjukehus, Jonas Lies vei 65, 5021 Bergen, Norway. Tel.: +47 55 97 07 86; fax: +47 55 97 46 10.
E-mail addresses: elisabeth.flo@psykp.uib.no, ellipropelli.florida@gmail.com (E. Flo).

http://dx.doi.org/10.1016/j.brat.2014.08.013

in symptoms and improvement from disability does not necessarily entail recovery.

Recovery as an outcome has rarely been investigated in CFS patients. Recovery involves several conditions such as perception of improvement, perception of symptom reduction and perception of improvement of fatigue impact. More objectively, recovery entails no longer meeting the Oxford and the CDC CFS criteria. To recover may represent a return to premorbid levels of health and wellbeing. When previously defining recovery from CFS, studies have used the normal population statistics as a guide. However, for some CFS patients recovery as defined by the population mean may entail a level of good health they did not have before their CFS started. Likewise, "healthy" individuals could regard themselves as fully functional and still be under the population mean on health questionnaires. Some studies have thus set the cut-off for recovery at 1 standard deviation (SD) from the population mean (Deale, Husain, Chalder, & Wessely, 2001; Knoop, Bleijenberg, Gielissen, van der Meer, & White, 2007).

Early studies found that up to a quarter of people with CFS who receive CBT in the context of a randomized controlled trial (RCT) make a full recovery (Deale et al., 2001; Knoop, Bleijenberg, et al., 2007). Although Deale and colleagues found that patients recovered there was a slight downward trajectory from the 1 to 5 year follow-up (Deale et al., 2001). More recently a large multi-centred four-arm RCT found that 22% of patients in secondary care recovered after CBT, 22% after GET, 8% after adaptive pacing therapy (APT) and 7% after specialist medical care (White, Goldsmith, Johnson, Chalder, & Sharpe, 2013). The odds for recovery after CBT or GET were 3.36 and 3.38 respectively when compared to APT. This study confirmed that recovery from CFS was possible.

Outside the confines of an RCT clinical follow-ups have found that between 0% and 31% of the CFS patients show full recovery depending on the setting (Cairns & Hotopf, 2005). In Cairns and Hotopf (2005) systematic review covering various clinical follow-ups, they found a median of 5% showing full recovery and 39.5% showing improvement (Cairns & Hotopf, 2005). However, the studies used different inclusion criteria. Some were conducted in primary care whereas others were secondary care studies. Some of the highest recovery rates were found in primary care settings, possibly involving lower levels of severity or chronicity than those treated in secondary care. In addition, the studies involved different types of treatment many of which were not recorded systematically.

The variation in recovery rates in different studies is likely to be affected by the inclusion criteria used. Furthermore, the recovery rate will be influenced by the operationalization of "full recovery" and the timing of follow-ups in the different studies.

Predictors of outcome after CBT

Several studies have examined predictors of outcomes after CBT. A recent study examined heterogeneity in terms of symptom clusters and their association with fatigue outcome. This study indicated that characteristics in CFS patients may affect responsiveness to CBT (Cella, Chalder, & White, 2011). They found that a higher frequency of weight fluctuation, physical shaking, pain and anxiety together with higher levels of symptom focussing were predictive of a negative outcome. Similarly, symptom focussing and a passive activity pattern had previously been found to predict less improvement in a randomised controlled trial of CBT (Prins et al., 2001).

Psychiatric disorders like depression and anxiety represent the most common co-morbid disorders among CFS patients, and have been linked to outcome after CBT (Kempke et al., 2010; Prins, Bleijenberg, & Rouweler, 2005; Sharpe, Hawton, Seagroatt, & Pasvol, 1992). An association between maltreatment and CFS (Nater et al., 2009) has been found and this may explain some of the co-morbid anxiety and depression seen in CFS. Interestingly though, only those people with CFS and childhood trauma had low cortisol (Nater et al., 2009). Although low cortisol showed a poor response to CBT in one study (Roberts et al., 2010) reassuringly the presence of maltreatment did not affect the outcome of CBT for people with CFS in another (Heins, Knoop, Lobbestael, & Bleijenberg, 2011).

A number of other factors have been associated with outcome after CBT. Patients who believe that their illness is primarily physical are more likely to have a poorer outcome after CBT (Butler et al., 1991). Older age has been associated with a poorer outcome (Quarmby, Rimes, Deale, Wessely, & Chalder, 2007) as has being in receipt of disablement insurance benefit (Bentall, Powell, Nye, & Edwards, 2002) or being involved in a legal procedure related to financial benefits (Prins, Bazelmans, Van der Werf, Van de Meer, & Bleijenberg, 2001). Focussing specifically on recovery, data from two randomized controlled trials were used to examine the association between pain and outcome from CBT. Recovered adult patients had fewer pain locations following treatment but higher pain severity at baseline was associated with a negative treatment outcome (Knoop, Stulemeijer, Prins, van der Meer, & Bleijenberg, 2007).

In the present study we aimed to investigate recovery rates in patients who received CBT at a secondary care CFS treatment unit in routine clinical practice. We looked at differences in recovery rates at the 6 month follow-up according to different indicators of recovery: i) the CDC and the oxford criteria, ii) levels of fatigue, iii) physical disability and iv) subjective experience of improvement. We furthermore aimed to investigate the association between the different indicators of recovery and the following predictors: age, gender, duration of CFS, anxiety, depression, perfectionism, symptom/illness acceptance, beliefs about emotions, work and social adjustment and cognitive and behavioural responses to symptoms. These variables were chosen as they represented aspects of the cognitive behavioural model of CFS and also took account of the previous research findings. Univariate associations were initially explored. However, subsequently variables included in the multivariable analysis were those that were significant at 0.1. We predicted that the presence of distress in the form of anxiety or depression, symptom focussing, more avoidance behaviour and unhelpful perfectionism would be associated with not recovering.

Method

Participants

The participants in this study were CFS patients who were treated with CBT at the Chronic Fatigue Syndrome Unit at South London and Maudsley, NHS Trust. Outcomes after CBT are measured routinely and audit approval was given by the Psychological Medicine Clinical Academic Group (CAG) at the South London and Maudsley Hospital to examine predictors of outcome.

All of the participants were diagnosed with CFS in accordance with the NICE guidelines (Turnbull et al., 2007) and assigned to CBT based on a clinical assessment. At pre-treatment assessment, all participants fulfilled the NICE guidelines for the CFS criteria (having fatigue for the last 4 months), 72.7% met the Oxford criteria and 52.6% of the participants met the CDC criteria. This non-randomized cohort included 200 CFS patients whose treatment was initiated before August of 2010.

In this study CBT was based on the illness model of fear avoidance, as described in the PACE protocol (White, Sharpe, Chalder, DeCesare, & Walwyn, 2007). The model involved these fundamental elements: (i) reviewing beliefs about the illness and coping strategies, (ii) re-establishing a stable baseline of general activities

and gradually returning to normal activity through organization of daily rest, sleep and activity, (iii) collaboration between therapist and patient in challenging unhelpful beliefs about symptoms and activity.

Instruments

At the pre-treatment assessment demographic information were obtained (age and gender), as well as information on the number of months the CFS had persisted. A checklist was used to ascertain whether patients fulfilled the CDC and the Oxford criteria. Self-report scales included the: Chalder fatigue questionnaire, short form-36 physical functioning scale, cognitive behavioural response questionnaire, work and social adjustment scale, beliefs about emotions scale, hospital anxiety and depression scale, acceptance scale, and the Frost multidimensional perfectionism scale. At the 6 month follow-up, patients were asked to report their subjective experience of improvement on the Global improvement scale (Shega et al., 2007; Guy, 1976) in addition to the aforementioned scales.

Oxford criteria for CFS

The Oxford inclusion criteria for CFS are defined as: i) fatigue is the main symptom, ii) fatigue symptoms show a definite onset i.e., the problem is not lifelong, iii) fatigue symptoms are severe, disabling and affect physical and mental function and iv) fatigue is present 50% of the time for a minimum of 6 months (Sharpe et al., 1991). Diagnostic exclusion criteria entail the presence of other medical conditions that are likely to cause fatigue (e.g., severe depression, anorexia or bulimia nervosa, neurological disorders).

CDC criteria for CFS

The present study employed participant ratings to assess the CDC inclusion criteria for CFS. The criteria were defined as: i) severe chronic fatigue for a minimum six months with no other known medical conditions explaining the symptoms; and ii) A minimum of four of the following symptoms: post-exertional malaise, impaired memory or concentration, non-refreshing sleep, muscle pain, multi-joint pain without redness or swelling, tender lymph nodes, sore throat, headache (Fukuda et al., 1994).

Chalder fatigue questionnaire (CFQ)

The CFQ measures symptoms of physical and mental fatigue (Chalder et al., 1993). Each of the 11-items have a response range 0–3, from 'less than usual' to 'much more than usual', with a maximum summed score of 33. The scale can also be scored using binary coding, yielding a maximum score of 11. The scale has good psychometric proprieties (Cella & Chalder, 2010). In this study, the Cronbach's alpha was 0.92.

The physical functioning subscale of the short form-36 (SF-36)

The level of disability i.e., physical functioning, was measured with the SF-36 (Jenkinson, Layte, Coulter, & Wright, 1996). The scores range from 0 (maximum physical limitations) to 100 (ability to do vigorous activity). A score of 65 or higher denotes being within 1SD of the UK population mean of 83 or higher (Deale et al., 2001). In the present study the Cronbach's alpha value was 0.92.

Hospital anxiety and depression scale (HADS)

The HADS (Zigmond & Snaith, 1983) measures symptoms of anxiety (HADS-A) and depression (HADS-D). Scores for each 14 items range from 0 to 3 and the maximum summed scores are 21 for both depression and anxiety subscales. Increased scores indicate higher symptom severity. In the present study the Cronbach's alpha values were 0.83 and 0.78 for HADS-A and HADS-D respectively.

Acceptance questionnaire

An adapted version of the Pain Acceptance Questionnaire (McCracken & Eccleston, 2003) was used to assess the level of fatigue acceptance. Pain was substituted for fatigue. The questionnaire was previously used in a study examining outcomes in a CFS service (Brooks, Rimes, & Chalder, 2011). The 9-item questionnaire is scored from 0 to 6 (never true to always true). The first item in this questionnaire reads: "I am getting on with the business of living no matter what my level of fatigue is". A high summed score indicates lack of acceptance of fatigue. In the present study, the Cronbach's alpha for this scale was 0.80.

Frost multi-dimensional perfectionism scale

The Frost Multi-dimensional Perfectionism Scale assesses facets of perfectionism using statements rated from 1 to 5 (strongly disagree to strongly agree) (Frost, Marten, Lahart, & Rosenblate, 1990). For the purpose of this study we used the questions pertaining to unhelpful aspects of perfectionism such as excessive concern with mistakes, doubt about the quality of personal accomplishments, and worrying about parents' expectations and evaluations. To provide an example the first item dealing with concerns over mistakes reads: "9. If I fail at work/school, I am a failure as a person". These issues are measured with four items (Cronbach's alpha in brackets): concern over mistakes (0.92), doubts about actions (0.79), parental expectations (0.89), parental criticism (0.88).

Beliefs about emotions scale (BES)

The BES is a 12-item scale that measures beliefs about emotional experience and expression. Items are rated on a Likert-type scale ranging from 0 to 6. A high summed score indicates less adaptive beliefs. The first item of this scale reads: "1. It is a sign of weakness if I have miserable thoughts". The BES has good psychometric properties (Rimes & Chalder, 2010). The Cronbach's alpha in this present study was 0.89.

Work and social adjustment scale

The work and social adjustment scale (WSAS) (Mundt, Marks, Shear, & Greist, 2002) measures impairment in work, home management, relationships, social and private life. This scale has been validated for patients with CFS (Cella, Sharpe, & Chalder, 2011). The 5 items are scored on an 8-point scale ranging from 'very severely impaired' to 'not impaired at all', with a maximum summed score of 40. The first item of this scale reads: "Because of my [problem] my ability to work is impaired. '0' means 'not at all impaired' and '8' means very severely impaired to the point I can't work". In the present study the Cronbach's alpha value was 0.84.

Cognitive behavioural response questionnaire (CBRQ)

The CBRQ (Skerrett & Moss-Morris, 2006) measures cognitive and behavioural responses to symptoms of health problems and illness. The questionnaire includes the following subscales (with Cronbach's alpha in brackets) i) symptom focussing (excessive symptoms focus [0.88]), ii) fear avoidance i.e., I am afraid that I will

make my symptoms worse if I exercise [0.78], iii) catastrophising i.e., If I push myself too hard I will collapse [0.73], iv) embarrassment avoidance i.e., I am ashamed of my symptoms [0.81], v) beliefs about damage i.e., Symptoms are a sign that I am damaging myself [0.81], vi) all-or-nothing behaviour (either being intensely active or resting extensively [0.89]), and vii) avoidance/resting (avoiding behaviour i.e., resting and inactivity [0.77]). All items are rated on a five-point Likert scale ranging from "strongly disagree" to "strongly agree" or "never" to "all the time". The scale has previously been used in patients with CFS (Knudsen, Henderson, Harvey, & Chalder, 2011).

Global improvement scale (GIS)

Patients were asked to rate their improvement on a 0–7 point scale ranging from very much better to very much worse (Guy, 1976). This self-report question has previously been used when assessing improvement and recovery in CFS patient's (Deale et al., 2001). For the purpose of this study the "much better" and "very much better" responses were combined, making a dichotomized measure of subjective improvement.

Defining recovery

Both the CDC and Oxford criteria are standards by which CFS can be operationalised. As there is not a complete overlap between these two criteria, both the CDC and Oxford criteria were chosen as primary conditions for recovery. Yet, not meeting the CDC or Oxford Criteria would not necessarily be indicative of a healthy *fully recovered* individual. Thus, in this study we also assessed other indicators of recovery such as the patients' subjective experience of actually feeling "much better" or "very much better" measured by the GIS at the 6 month follow-up assessment.

In addition, the CFQ and the SF-36 physical subscale were employed to indicate whether participants could be considered to be within normal levels of fatigue and physical functioning at follow-up. Previous studies have indicated a CFQ score of below 18 and an SF-36 physical function score of 65 or higher are both within 1 SD of the normal population mean score (Deale et al., 2001; Jenkinson, Coulter, & Wright, 1993). These values were used as cut-offs in the present study.

Recovery was defined as no longer meeting either the CDC-criteria *or* the Oxford criteria. A total recovery score was defined as no longer meeting the CDC- criteria *and* the Oxford criteria, *and* feeling much better/very much better *and* scoring below 18 on the CFQ *and* scoring 65 or higher on the SF-36.

Statistical analyses

In the present study SPSS 20 was used for all analyses. We provide the prevalence of the different indicators of recovery, and a total recovery composite score at 6 month follow up. Numbers and percentages are calculated for those who did and did not meet the criteria pre-treatment. Since not all participants fulfilled the CDC or Oxford criteria, or met the cut-offs for CFQ and SF-36 at pre-treatment assessment, follow-up figures were compared with baseline assessments, for those who at baseline met the corresponding criteria, by means of chi square analyses. We also calculated means and standard deviations for the predictor variables in the recovered and non-recovered CFS patients.

We performed univariate and multivariate logistic regression analyses with previously defined recovery indicators as dependent variables; i) recovery defined as "no longer meeting the CDC criteria *and* no longer meeting the oxford criteria", ii) "feeling much better or very much better" (GIS), iii) scoring below 18 on the CFQ, and iv) Scoring 65 or higher on the SF-36. Those not meeting the corresponding criteria or cut-off were excluded from both the univariate and multivariate analyses. The univariate analyses included pre-treatment assessment of the following: demographic variables (age, gender), duration of CFS before entering therapy, CBRQ, acceptance, WSAS, Frost perfectionism scale, BES, HADS-A and HADS-D. These variables were chosen as they were theoretically important and/or had been found previously to predict a poor outcome. In addition to significant predictors, variables showing *p*-values of 0.1 or less in an univariate analysis were also included in the corresponding multivariate analysis. We chose this method as a result of the sample size which could not accommodate a large number of predictor variables. Those meeting either CDC or Oxford criteria at pre-treatment assessment were included in the multivariate analyses related to feeling much better or better at the 6 month follow-up. We performed preliminary analyses to exclude the possibility of collinearity in the logistic regression analyses. Significance was set to $p < 0.05$.

Table 1
Differences in prevalence rates for CFS criteria and cut-offs at pre-treatment and 6 month follow-up (significance tested with chi square analyses), and prevalence for patients feeling much/better and total recovery[a] at 6 month follow-up.

	Pre-treatment	6 month Follow-up
	% (*n*)	% (*n*)
Meeting Oxford criteria***	72.7 (125)	53.1 (60)
Meeting CDC criteria***	52.6 (91)	37.5 (45)
Meeting *either* Oxford *or* CDC criteria***	83.2 (134)	62.7 (69)
>=18 CFQ*	83.9 (156)	51.4 (71)
<65 SF-36***	71.1 (133)	49.3 (66)
<83 SF-36***	87.7 (164)	67.9 (91)
Feeling much better or very much better		60.8 (79)
Total recovery	0 (0)[a]	18.3 (19)[b]

*$p < 0.05$, ***$p < 0.001$.
CFQ = Chalder fatigue questionnaire, SF-36 = medical outcomes short form physical functioning subscale.
[a] Total recovery defined as the combination of not meeting CDC and Oxford criteria, scoring less than 18 on the CFQ and more than 65 or higher on the SF-36.
[b] Total recovery defined as the combination of not meeting CDC and Oxford criteria, scoring less than 18 on the CFQ, more than 65 or higher on the SF-36 and feeling much better or better.

Missing data

For single missing data cells, we performed missing data substitution using the participant's mean score for that particular scale or subscale. This was only done where less than 30% of items in the scale/questionnaire were missing.

Results

There were in total 140 participants with 6 month follow-up data to be included in analyses (response rate: 72.2%). Five patients were excluded from analyses due to severe co-morbidity (cancer, seizures, bipolar disorder and eating disorder) and one for receiving alternative treatment which alleviated the fatigue symptoms. Of the remaining 194 patients, 185 (95.4%) completed the discharge assessment. If patients had not completed the 6-month follow-up, but had completed the 1 year follow-up, the 1 year assessment data replaced the missing 6 month assessment ($n = 5$). Between 6 and 20 sessions were attended, with a mean of 15.3 sessions (SD = 3.7). Preliminary analyses did not reveal any significant differences between patients completing and those not completing the 6-month follow-up assessment in terms of Oxford and CDC criteria (chi-square analyses; $p > 0.05$). Similarly, there were no differences in baseline cut-offs in fatigue and physical impairment, or any of the predictor variables that were explored in

the logistic regression analyses ($p > 0.05$ in all comparisons). All patients were 18 years or older (mean age of 38.3, SD = 11.6), and 72% were females.

The pre-treatment and 6-month follow-up assessments for each discrete outcome measure are shown in Table 1. Chi square analyses revealed significant change in prevalence rates for all recovery measures. While 72.2% met the oxford criteria for CFS at pre-treatment assessment, 53.1% did so at the 6-month follow-up (Pearson chi square = 19.5, df = 1, $p < 0.001$). Likewise, chi-square revealed a significant reduction in prevalence from 52.6% of the participants meeting the CDC criteria at the pre-treatment assessment to 37.5% at the 6-month follow-up (Pearson chi square = 16.8, df = 1, $p < 0.001$). With regard to the combined Oxford and CDC criteria, as many as 83.2% met either one of the criteria at pre-treatment, compared to 62.7% at the 6-month follow-up (Pearson chi square = 11.4, df = 1, $p < 0.001$). In other words, defining recovery as no longer meeting any of the criteria entailed a *recovery* rate of 37.3% at the 6-month follow-up.

In terms of fatigue symptoms, 83.9% scored 18 or higher on the CFQ at the pre-treatment assessment, compared to 51.4% at the 6-month follow-up (Pearson chi square = 4.9, df = 1, $p < 0.05$). As shown in Table 1, at pre-treatment assessment, 71.1% of the patients were below 1 SD of the normal population SF-36 mean score (i.e., below 65). At the 6-month follow up, 49.3% was below this cut-off (Pearson chi square = 5.5, df = 1, $p < 0.001$). Using the approximated population mean, 87.7% of the patients scored below the 83 point cut-off at pre-treatment assessment compared to 67.9% below the cut-off at follow-up (Pearson chi square = 32.9, df = 1, $p < 0.001$).

When combining the CDC and oxford criteria, the GIS score (much better/very much better) as well as the fatigue cut-off (<18) and the SF-36 cut-off (>=65) in one composite total recovery score, 18.3% showed total recovery at the 6-month follow-up. None of the patients met the criteria set for the total composite recovery score at pre-treatment.

As shown in Table 2, the means of predictor variables were somewhat different between those showing recovery at the 6-month follow-up assessment. The significance of these predictors was tested in the logistic regression analyses which now follow.

Recovery defined as not meeting either CDC or Oxford criteria

Firstly, recovery as defined by no longer meeting the Oxford and CDC criteria was used as dependent variable in the univariate analyses. As shown in Table 3, the following variables were associated with a *reduced* odds for recovery: disability in terms of work and social adjustment (WSAS), high levels of "catastrophizing" (CBRQ) and increased symptoms of depression (HADS-D). These significant predictors were included in the multivariate logistic regression analysis. Additionally, the CBRQ subscale "All or nothing behaviour" was included in the multivariate analysis as it had a *p*-value of below 0.1. None of these significant results from the univariate analysis remained significant in the multivariate analysis (see Table 4).

Feeling much better or better as indicator of recovery

The dichotomised GIS score, i.e., those who felt much better/better and those not experiencing such an improvement, were used as an indicator of recovery and as a dependent variable. In the univariate analyses we found an association between fear avoidance (CBRQ), disability in terms of work and social adjustment (WSAS) and increased symptoms of depression (HADS-D). In addition to the significant predictors, the variables "months with CFS" and unhelpful beliefs about emotions and expression of emotions (BES) were also included in the multivariate analysis, due to a *p*-value below 0.1 in the univariate analysis.

Table 2
Means and standard deviation of predictor scores in recovered and not recovered patients (no longer meeting either Oxford or CDC criteria for CFS) at 6 month follow up.

	Not recovered	Recovered
	Mean (SD)	Mean (SD)
Age	38.4 (11.9)	37.2 (10.1)
Time with CFS	89.9 (80.2)	68.7 (68.8)
HAD – Depression	8.6 (3.8)	7.0 (3.5)
HAD – Anxiety	10. 7 (4.6)	9.4 (4.8)
Beliefs about emotions	36.0 (13.4)	34.9 (12.9)
Acceptance	35.4 (8.6)	35.9 (8.2)
FMPS – Concerns about mistakes	22.6 (9.3)	20.6 (9.2)
FMPS – Doubts over actions	10.9 (3.7)	10.1 (4.5)
FMPS – Parental expectations	11.7 (5.5)	10.6 (5.0)
FMPS – Parental criticism	8.6 (4.4)	7.9 (4.5)
CBRQ – Damaging beliefs	10.3 (4.5)	10.4 (3.3)
CBRQ – Fear avoidance	14.2 (4.1)	13.1 (4.3)
CBRQ – Catastrophizing	8.1 (3.3)	6.5 (3.4)
CBRQ – Embarrassment	12.6 (5.6)	11.6 (5.5)
CBRQ – Avoidance/resting	13.8 (5.5)	12.2 (4.7)
CBRQ – Symptom focussing	13.7 (5.1)	13.4 (4.7)
CBRQ – All-or-nothing	10.9 (5.1)	8.9 (5.0)
Work and social adjustment scale	25.3 (7.7)	19.4 (9.4)

CFS = Chronic fatigue syndrome, HAD = Hospital anxiety and depression scale, FMPS = Frost multidimensional perfectionism scale, CBRQ = Cognitive and behavioural response questionnaire.

The variables unhealthy beliefs about emotions (BES) and high levels of depression symptoms (HADS-D) were associated with not feeling better at the 6-month follow-up in the multivariate analysis.

Scoring 18 or less on the CFQ as indicator of recovery

Reduced odds of recovery as measured by means of the CFQ cut-off (<18), was significantly associated with the following variables in the univariate analysis: being concerned about mistakes (perfectionism), high parental expectations (perfectionism), embarrassment avoidance (CBRQ) and disability in terms of work and social adjustment (WSAS). Additionally, lack of acceptance, doubts about actions (perfectionism), avoidance/resting (CBRQ) and increased symptoms of depression (HADS-D) were included as predictors in the multivariate analysis ($p < 0.1$).

In the multivariate analysis, WSAS was the only variable with a *reduced* odds of recovery as defined by the CFQ cut-off. The control variable (CFQ cut-off at pre-treatment), was not significantly related to recovery at 6 month follow-up.

Scoring 65 or higher on the SF-36 physical subscale as indicator of recovery

Using the SF-36 cut-off (>=65) as a recovery measure, the following variables were associated with a *reduced* odds for recovery in the univariate analysis: older age, months with CFS, lack of acceptance, and increased symptoms of depression (HADS-D). Furthermore the variables catastrophizing, more avoidance/resting behaviour (CBRQ), disability in terms of work and social adjustment (WSAS) and all-or-nothing behaviour (CBRQ) were included in the multivariate analysis ($p < 0.1$) in addition to the significant predictor variables.

In the multivariate analysis, the predictor variable older age remained associated with a *reduced* odds of recovery defined by SF-36.

Discussion

In this study we investigated recovery rates and examined predictors of recovery in patients who received CBT at a secondary

Table 3
Associations between predictor variables at baseline assessment and recovery at 6 month follow-up.

	Not meeting CDC and Oxford criteria			Feeling much better or better			Scoring <18 on the CFQ			Scoring >=65 on the SF-36		
	OR	95%	C.I.	OR	95%	C.I.	OR	95%	C.I.	OR	95%	C.I.
Gender (1)	0.98	0.42	2.31	0.98	0.93	1.03	0.77	0.37	1.60	0.65	0.31	1.37
Age	0.98	0.94	1.03	0.99	0.99	1.01	0.98	0.93	1.03	0.94**	0.90	0.98
Months with CFS	1.00	0.99	1.01	0.97^{+}	0.90	1.01	1.00	0.99	1.01	0.98*	0.98	0.99
Acceptance	0.96	0.91	1.02	0.97	0.91	1.03	0.95^{+}	0.88	1.02	1.02	0.97	1.08
FMPS – Concerns about mistakes	0.94	0.83	1.07	0.93	0.80	1.08	0.91**	0.84	0.98	1.01	0.96	1.06
FMPS – Doubts over actions	0.93	0.84	1.02	0.92	0.82	1.04	0.88^{+}	0.76	1.01	0.99	0.88	1.10
FMPS – Parental expectations	0.93	0.84	1.02	0.92	0.82	1.04	0.88*	0.78	1.00	0.98	0.91	1.07
FMPS – Parental criticism	0.91	0.80	1.04	0.92	0.80	1.07	0.84	0.72	1.01	0.98	0.91	1.07
CBRQ – Damaging beliefs	1.00	0.89	1.12	1.01	0.88	1.15	0.99	0.87	1.12	0.97	0.88	1.08
CBRQ – Fear avoidance	1.00	0.88	1.13	0.79*	0.65	0.97	0.91	0.80	1.04	0.99	0.89	1.10
CBRQ – Catastrophizing	0.83*	0.70	0.97	1.01	0.88	1.17	0.95	0.85	1.05	1.02^{+}	0.92	1.10
CBRQ – Embarrassment	0.95	0.88	1.04	0.96	0.87	1.05	0.90*	0.81	1.00	0.97	0.85	1.12
CBRQ – Avoidance/resting	0.96	0.87	1.05	0.96	0.86	1.06	0.84^{+}	0.70	1.01	1.04^{+}	0.96	1.11
CBRQ – Symptom focussing	0.99	0.90	1.09	0.99	0.89	1.10	0.96	0.85	1.07	1.00	0.92	1.01
CBRQ – All-or-nothing	0.98+	0.89	1.01	0.98	0.88	1.10	0.96	0.86	1.07	1.02^{+}	0.94	1.11
Beliefs about emotions	1.00	0.97	1.04	1.00^{+}	0.96	1.04	1.02	0.98	1.07	0.98	0.90	1.07
Work and social adjustment scale	0.92**	0.86	0.98	0.91**	0.84	0.98	0.90**	0.83	0.97	0.98^{+}	0.95	1.00
HAD – Depression	0.84*	0.72	0.97	0.80*	0.66	0.97	0.87^{+}	0.74	1.03	0.96*	0.91	0.99
HAD – Anxiety	0.92	0.83	1.03	0.96	0.84	1.08	0.92	0.81	1.04	0.97	0.87	1.09

$^{+}p < 0.1$, $^{*}p < 0.05$, $^{**}p < 0.01$, $p < 0.001$; CFQ = Chalder fatigue questionnaire, SF-36 = medical outcomes short form physical functioning subscale, HAD = Hospital anxiety and depression scale, FMPS = Frost multidimensional perfectionism scale, CBRQ = Cognitive and behavioural response questionnaire.

care CFS treatment unit in the UK. Significantly fewer patients met the Oxford and the CDC criteria, and more patients were within normal population levels of fatigue and physical functioning at 6 months follow-up compared to the pre-treatment assessment. Utilising a combined recovery score 18.3% was totally recovered.

Table 4
Four multivariate logistic regression analyses with measures of recovery at 6 month follow up as outcome variables (points 1–4) and predictor variables assessed before treatment.

	OR	95% C.I.	
1 Not meeting CDC and Oxford criteria – Follow-up			
CBRQ – Catastrophising	0.87	0.73	1.04
CBRQ – All-or-nothing	1.03	0.92	1.15
Work and social adjustment scale	0.94	0.88	1.02
HAD – Depression	0.92	0.76	1.11
2 Global improvement scale – Follow-up			
Months with CFS	1.00	0.99	1.00
CBRQ – Fear avoidance	0.92	0.81	1.05
Beliefs about emotions	0.95*	0.91	0.99
Work and social adjustment scale	1.01	0.94	1.08
HAD – Depression	0.79*	0.67	0.94
3 Scoring <18 on the CFQ – Follow-up			
Acceptance	1.05	0.98	1.12
FMPS – Concerns about mistakes	1.02	0.95	1.10
FMPS – Doubts over actions	1.08	0.94	1.24
FMPS – Parental expectations	1.03	0.92	1.15
CBRQ – Embarrassment	1.06	0.97	1.17
CBRQ – Avoidance/resting	0.96	0.87	1.08
Work and social adjustment scale	1.09*	1.02	1.17
HAD – Depression	0.94	0.81	1.08
4 Scoring >=65 on the SF-36 – Follow-up			
Months with CFS	1.00	0.99	1.00
Age	0.93*	0.88	0.98
CBRQ – Catastrophising	0.99	0.83	1.17
CBRQ – Avoidance/resting	1.09	0.96	1.24
CBRQ – All-or-nothing	0.97	0.86	1.08
Work and social adjustment scale	0.92	0.83	1.00
HAD – Depression	1.06	0.88	1.28

$p < 0.05$, $^{*}p < 0.01$, $p < 0.001$.
SF-36 = medical outcomes short form physical functioning subscale, CFQ = Chalder fatigue scale, HAD = Hospital anxiety and depression scale, FMPS = Frost multidimensional perfectionism scale, CBRQ = Cognitive and behavioural response questionnaire.

Similar measures of recovery have been employed in previous studies of CBT in the context of randomised controlled trials (see Deale et al., 2001; Knoop, Bleijenberg, et al., 2007; Knoop, Stulemeijer, et al., 2007; White et al., 2013). However, the timing of the final follow-up assessment varied in each study. The follow-up in the Knoop study occurred at discharge from treatment; the Deale study reported recovery at 12 months after randomisation (6 months follow up) and at 5-year follow-up. Finally, the White et al. study reported recovery rates at 12 months after randomisation. Nevertheless, to contextualise our descriptive results we will consider these studies comparatively. In relation to the operational criteria for CFS about half of the patients in the present study met the Oxford criteria at follow up. This rate is similar to previous studies carried out in the UK (Deale et al., 2001; White et al., 2013). More than 60% of patients no longer met the CDC criteria in this study, again, similar rates to those found in previous studies (Knoop, Bleijenberg, et al., 2007; Knoop, Stulemeijer, et al., 2007; White et al., 2013). Recovery defined as not meeting the CDC criteria yielded slightly higher recovery rates compared to the Oxford criteria.

Using a self-rated global measure of improvement 60.8% of the patients in the present study reported feeling better or much better. This percentage is very similar to the results of Quarmby et al. (2007) in which 57% of patients in routine care reported feeling better or much better. Overall this rate is lower than the 70% global improvement rates in the context of a randomised controlled trial (Deale et al., 2001). Self-rated improvement was also lower than the 78% self-rated improvement reported in the context of a randomised trial of therapist aided internet therapy for adolescents with CFS (Nijhof, Bleijenberg, Uiterwaal, Kimpen, & van de Putte, 2012). This sample was obviously younger and so is not directly comparable but it does suggest that a younger cohort may have better chances of recovery. Although the global measure does not pertain to symptom reduction, the high prevalence of subjectively experienced improvement attests to the benefit patients experienced when receiving CBT in the present study.

Knoop, Bleijenberg, et al. (2007) and Knoop, Stulemeijer, et al. (2007) found that 48% were within 1 SD of the normal population mean of fatigue, which is comparable to the prevalence of 48.6% found in the present study. Although different fatigue scales

were employed, recovery was based on normal population data in both studies. Although Deale et al. (2001) found that 63% of the participants were within normal range of fatigue at 6 months (Deale et al., 2001) the larger study carried out by White et al. (2013) found only 41% of those who received CBT were within the normal range which suggests that this figure is more accurate within a larger cohort.

Total Recovery was measured similarly in all previous studies. We found a total recovery rate of 18.3%, compared to 23% (Knoop, Bleijenberg, et al., 2007), 24% (Deale et al., 2001), and 22% (White et al., 2013) respectively. Factors such as patient selection and the use of manualised protocols may have affected the minor differences in outcomes between the present study and the randomised controlled trials. Nevertheless, all in all, the recovery rates found in these studies were comparable. Meanwhile, the study of total recovery remains problematic in this population, where the patients are rarely recovered or not recovered, but rather improving on a range of outcomes all of which are continuous.

We found differences in terms of what predictors were associated with the different recovery measures. Recovery in terms of no longer meeting CDC and Oxford criteria were related to catastrophizing, depression and work and social adjustment in the univariate analyses, but not at follow-up.

Believing that expression of emotions is unacceptable and depression were associated with worse outcome on the global improvement scale, in the multivariate analysis. Depression and dysthymia have previously been related to the prognosis of CFS patients (Cairns & Hotopf, 2005; Sharpe et al., 1992). Furthermore, the processing, expression and acceptance of emotions particularly distressing emotions has been found to be a predictor of improvement in chronic fatigue patients in primary care (Godfrey, Chalder, Ridsdale, Seed, & Ogden, 2007). It also adds weight to the cognitive model suggested by Surawy et al. (1995) in which it is suggested that holding the belief that showing emotions is unacceptable is characteristic of people who fulfil criteria for CFS.

Recovery from fatigue as measured by the CFQ was significantly related to degree of impairment (WSAS) at baseline.

Older age was related to poorer prognosis in terms of physical functioning. Noticeably, even though the odds ratio was low, age was a continuous variable. Thus, such an effect may be evident in the case of a 20 years old compared to a 60 years old CFS patient. Older age has in previous studies been related to poorer outcome/prognosis (Cairns & Hotopf, 2005). Somewhat surprisingly, more avoidance/resting at baseline was positively related to recovery as defined by physical functioning, while this association was negative in the univariate analysis (i.e., related to reduced odds for recovery). The relationship with recovery may indicate a difference in response to treatment among patients with this coping strategy at pre-treatment. Interestingly, Cella and Chadler (2010) found that patients characterised by avoidance and resting were less likely to show a reduction in level of fatigue symptoms (Cella, Chalder, et al., 2011). There may be different mechanisms at play with regard to recovery in physical function.

Strengths and limitations

This evaluation took place in routine clinical practice. While this adds to the study's ecological validity, the non-randomized nature of the study cannot exclude the importance of unmeasured confounding variables. However, issues such as patient and therapist selection are a recurring theme also in randomized controlled trials.

The number of participants in this study was acceptable but low resulting in limited statistical power. Some of the borderline significant findings could possibly have reached significance with more participants, thus we cannot exclude false negatives in this study. The number of participants meant that the multivariate analyses were only just within the limits of the ratio of number of participants to included variables (10 to 1). Thus, the selection of variables for the multivariate analyses was restricted to those which were significant or approaching significance in order to have a sound number of participants/number of predictor variables ratio. All of the variables were chosen as they are theoretically important.

There was a drop-out of 27.8% in the present study. However, this study was based on data from a routine clinical practice. There was no screening for eligibility for participation in a research study, as treatment was the primary focus. We did not find any significant differences between patients who completed and who did not complete the 6-month follow-up assessment in terms of baseline fatigue criteria. We believe that the retention rate was satisfactory, effectively reducing the likelihood of selection bias in terms of drop-outs from the study. Nevertheless, drop-out remains a potential bias in all follow-up studies.

Conclusion

In conclusion, we found recovery rates in line with previous studies on recovery from CFS. Different predictors were related to recovery in terms of official criteria, subjective improvement, reduced fatigue symptomatology and reduced physical impairment. This suggests that a broad therapeutic focus is necessary to improve all facets of CFS, and to facilitate total recovery. CBT has this broad focus but the number of sessions may need to be increased to facilitate a full recovery.

Acknowledgements

Trudie Chalder acknowledges financial support from the Biomedical Research Centre for Mental Health at the South London and Maudsley NHS Foundation Trust (SLaM) and the Institute of Psychiatry at King's College London. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. Elisabeth Flo received a PhD scholarship from the Western Norway Regional Health Authority. We thank Sheila Ali for her assistance with data management. We also thank the cognitive behavioural psychotherapists, Mary Burgess, Suzanne Roche, Sue Wilkins, Barbara Bowman and clinical psychologists Anna Hutchinson and Antonia Dittner.

References

Bentall, R. P., Powell, P., Nye, F. J., & Edwards, R. H. T. (2002). Predictors of response to treatment for chronic fatigue syndrome. *The British Journal of Psychiatry, 181*, 248–252.

Brooks, S. K., Rimes, K. A., & Chalder, T. (2011). The role of acceptance in chronic fatigue syndrome. *Journal of Psychosomatic Research, 71*, 411–415.

Butler, S., Chalder, T., Ron, M., & Wessely, S. (1991). Cognitive behaviour therapy in chronic fatigue syndrome. *Journal of Neurology, Neurosurgery & Psychiatry, 54*, 153–158.

Cairns, R., & Hotopf, M. (2005). A systematic review describing the prognosis of chronic fatigue syndrome. *Occupational Medicine, 55*, 20–31.

Cella, M., & Chalder, T. (2010). Measuring fatigue in clinical and community settings. *Journal of Psychosomatic Research, 69*, 17–22.

Cella, M., Chalder, T., & White, P. D. (2011). Does the heterogeneity of chronic fatigue syndrome moderate the response to cognitive behaviour therapy? An exploratory study. *Psychotherapy and Psychosomatics, 80*, 353–358.

Cella, M., Sharpe, M., & Chalder, T. (2011). Measuring disability in patients with chronic fatigue syndrome: reliability and validity of the Work and Social Adjustment Scale. *Journal of Psychosomatic Research, 71*, 124–128.

Chalder, T., Berelowitz, G., Pawlikowska, T., Watts, L., Wessely, S., Wright, D., et al. (1993). Development of a fatigue scale. *Journal of Psychosomatic Research, 3*, 147–153.

Chalder, T., Butler, S., & Wessely, S. (1996). In-patient treatment of chronic fatigue syndrome. *Behavioural and Cognitive Psychotherapy, 24*, 351–365.

Chambers, D., Bagnall, A. M., Hempel, S., & Forbes, C. (2006). Interventions for the treatment, management and rehabilitation of patients with chronic fatigue

syndrome/myalgic encephalomyelitis: an updated systematic review. *Journal of the Royal Society of Medicine, 99*, 506–520.
Deale, A., Husain, K., Chalder, T., & Wessely, S. (2001). Long-term outcome of cognitive behavior therapy versus relaxation therapy for chronic fatigue syndrome: a 5-year follow-up study. *American Journal of Psychiatry, 158*, 2038–2042.
Frost, R. O., Marten, P., Lahart, C., & Rosenblate, R. (1990). The dimensions of perfectionism. *Cognitive Therapy and Research, 14*, 449–468.
Fukuda, K., Straus, S. E., Hickie, I., Sharpe, M. C., Dobbins, J. G., & Komaroff, A. (1994). The chronic fatigue syndrome: a comprehensive approach to its definition and study. *Annals of Internal Medicine, 121*, 953–959.
Godfrey, E., Chalder, T., Ridsdale, L., Seed, P., & Ogden, J. (2007). Investigating the active ingredients of cognitive behaviour therapy and counselling for patients with chronic fatigue in primary care: developing a new process measure to assess treatment fidelity and predict outcome. *British Journal of Clinical Psychology, 46*, 253–272.
Guy, W. (1976). *Clinical global impressions, ECDEU assessment manual for psychopharmacology – revised*. Rockville, MD: National Institute of Mental Health.
Heins, M. J., Knoop, H., Lobbestael, J., & Bleijenberg, G. (2011). Childhood maltreatment and the response to cognitive behavior therapy for chronic fatigue syndrome. *Journal of Psychosomatic Research, 71*, 404–410.
Jenkinson, C., Coulter, A., & Wright, L. (1993). Short form 36 (SF36) health survey questionnaire: normative data for adults of working age. *British Medical Journal, 306*, 1437–1440.
Jenkinson, C., Layte, R., Coulter, A., & Wright, L. (1996). Evidence for the sensitivity of the SF-36 health status measure to inequalities in health: results from the Oxford healthy lifestyles survey. *Journal of Epidemiology & Community Health, 50*, 377–380.
Kempke, S., Goossens, L., Luyten, P., Bekaert, P., Van Houdenhove, B., & Van Wambeke, P. (2010). Predictors of outcome in a multi-component treatment program for chronic fatigue syndrome. *Journal of Affective Disorders, 126*, 174–179.
Knoop, H., Bleijenberg, G., Gielissen, M. F. M., van der Meer, J. W. M., & White, P. D. (2007a). Is a full recovery possible after cognitive behavioural therapy for chronic fatigue syndrome? *Psychotherapy and Psychosomatics, 76*, 171–176.
Knoop, H., Stulemeijer, M., Prins, J. B., van der Meer, J. W. M., & Bleijenberg, G. (2007). Is cognitive behaviour therapy for chronic fatigue syndrome also effective for pain symptoms? *Behaviour Research and Therapy, 45*, 2034–2043.
Knudsen, A. K., Henderson, M., Harvey, S. B., & Chalder, T. (2011). Long-term sickness absence among patients with chronic fatigue syndrome. *British Journal of Psychiatry, 199*, 430–431.
McCracken, L. M., & Eccleston, C. (2003). Coping or acceptance: what to do about chronic pain? *Pain, 105*, 197–204.
Mundt, J. C., Marks, I. M., Shear, M. K., & Greist, J. M. (2002). The Work and Social Adjustment Scale: a simple measure of impairment in functioning. *The British Journal of Psychiatry, 180*, 461–464.
Nater, U. M., Lin, J. S., Maloney, E. M., Jones, J. F., Tian, H., Boneva, R. S., et al. (2009). Psychiatric comorbidity in persons with chronic fatigue syndrome identified from the Georgia population. *Psychosomatic Medicine, 71*, 557–565.
Nijhof, S. L., Bleijenberg, G., Uiterwaal, C. S. P. M., Kimpen, J. L. L., & van de Putte, E. M. (2012). Effectiveness of internet-based cognitive behavioural treatment for adolescents with chronic fatigue syndrome (FITNET): a randomised controlled trial. *The Lancet, 379*, 1412–1418.
Prins, J. B., Bazelmans, E., Van der Werf, S. P., Van de Meer, J., & Bleijenberg, G. (2001). Cognitive-behaviour therapy for chronic fatigue syndrome: predictors of treatment outcome. In *Paper presented at the psycho-neuro-endocrino-immunology (PNEI): A common language for the whole human body: Proceedings of the 16th World Congress on Psychosomatic Medicine, Göteborg, Sweden*.
Prins, J. B., Bleijenberg, G., Bazelmans, E., Elving, L. D., de Boo, T. M., Severens, J. L., et al. (2001). Cognitive behaviour therapy for chronic fatigue syndrome: a multicentre randomised controlled trial. *The Lancet, 357*, 841–847.
Prins, J. B., Bleijenberg, G., & Rouweler, E. K. (2005). Effect of psychiatric disorders on outcome of cognitive-behavioural therapy for chronic fatigue syndrome. *The British Journal of Psychiatry, 187*, 184–185.
Quarmby, L., Rimes, K. A., Deale, A., Wessely, S., & Chalder, T. (2007). Cognitive-behaviour therapy for chronic fatigue syndrome: comparison of outcomes within and outside the confines of a randomised controlled trial. *Behaviour Research and Therapy, 45*, 1085–1094.
Rimes, K. A., & Chalder, T. (2010). The beliefs about emotions scale: validity, reliability and sensitivity to change. *Journal of Psychosomatic Research, 68*, 285–292.
Roberts, A. D. L., Charler, M. L., Papadopoulos, A., Wessely, S., Chalder, T., & Cleare, A. J. (2010). Does hypocortisolism predict a poor response to cognitive behavioural therapy in chronic fatigue syndrome? *Psychological Medicine, 40*, 515.
Sharpe, M. C., Archard, L. C., Banatvala, J. E., Borysiewicz, L. K., Clare, A. W., David, A., et al. (1991). A report–chronic fatigue syndrome: guidelines for research. *Journal of the Royal Society of Medicine, 84*, 118.
Sharpe, M. C., Hawton, K., Seagroatt, V., & Pasvol, G. (1992). Follow up of patients presenting with fatigue to an infectious diseases clinic. *British Medical Journal, 305*, 147–152.
Shega, J., Emanuel, L., Vargish, L., Levine, S. K., Bursch, H., Herr, K., et al. (2007). Pain in persons with dementia: complex, common, and challenging. *8*, 373–378.
Skerrett, T. N., & Moss-Morris, R. (2006). Fatigue and social impairment in multiple sclerosis: the role of patients' cognitive and behavioral responses to their symptoms. *Journal of Psychosomatic Research, 61*, 587–593.
Surawy, C., Hackmann, A., Hawton, K., & Sharpe, M. (1995). Chronic fatigue syndrome: a cognitive approach. *Behaviour Research and Therapy, 33*, 535–544.
Turnbull, N., Shaw, E. J., Baker, R., Dunsdon, S., Costin, N., Britton, G., et al. (2007). *Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy): Diagnosis and management of chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) in adults and children*. London: Royal College of General Practitioners.
White, P., Goldsmith, K., Johnson, A., Chalder, T., & Sharpe, M. (2013). Recovery from chronic fatigue syndrome after treatments given in the PACE trial. *Psychological Medicine, 43*, 2227–2235.
White, P., Sharpe, M., Chalder, T., DeCesare, J., & Walwyn, R. (2007). 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. *BMC Neurology, 7*, 6.
White, P. D., Goldsmith, K. A., Johnson, A. L., Potts, L., Walwyn, R., DeCesare, J. C., et al. (2011). Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. *The Lancet*, 823–836.
Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica, 67*, 361–370.