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Guided self-help for patients with chronic fatigue syndrome prior to starting cognitive behavioural therapy: a cohort study

Short title: Self-help CBT for CFS

Key words: Chronic fatigue syndrome, self-help, CBT, fatigue

Authors:

Sheila Ali^a,

Dr Kimberley Goldsmith^b,

Dr Mary Burgess^a,

Professor Trudie Chalder^{c*},

^a Chronic Fatigue Research and Treatment Unit, South London and Maudsley NHS Foundation Trust, UK.

^b Biostatistics and Health Informatics Department, Division of Psychology and Systems Sciences, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK.

^c Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK.

***Corresponding author: Professor Trudie Chalder.** Email address:

trudie.chalder@kcl.ac.uk

Address: Department of Psychological Medicine, King's College London, Weston Education Centre, Cutcombe Road, London SE5 9RJ, UK. Phone: (+44) 02078480406. Fax: (+44) 02078485408.

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Abstract

Background

Previous research suggests that minimal interventions such as self-help guidance can improve outcomes in patients with fatigue or chronic fatigue syndrome (CFS).

Aims

The aim of the current study was to investigate whether self-help guidance could improve physical functioning, social adjustment and fatigue in a group of patients with CFS who were awaiting CBT at a clinic in secondary care.

Method

Patients completed questionnaires at their initial assessment (baseline); immediately before beginning CBT (pre-treatment); and after their last session of CBT (end of treatment). The primary outcome was physical functioning, and the secondary outcomes were social adjustment and fatigue. Multilevel linear models were used to assess change over time after adjustment for gender and age.

Results

Multilevel models revealed that from baseline to pre-treatment, patients showed statistically significant improvements in physical functioning, but there were no statistically significant improvements in fatigue or social adjustment. However, all the primary and secondary outcomes showed statistically significant changes after CBT.

Conclusions

The findings of this study indicate that self-help guidance may be beneficial for patients with CFS who are awaiting CBT treatment or those who are unable to access specialist treatment in their local area.

Keywords: chronic fatigue syndrome, self-help, CBT, CFS, fatigue, minimal intervention.

Introduction

Fatigue is a common symptom which is prevalent in the general population (Wessely, Chalder, Hirsch, Wallace, and Wright, 1997; Pawlikowska et al., 1994). It is described in the literature using a variety of terminology including fatigue, chronic fatigue, unexplained chronic fatigue, and idiopathic chronic fatigue. There is a general consensus in the literature that in order to be considered chronic, the fatigue must be of at least six months' duration, not attributable to activity, and not alleviated by rest (Jorgensen, 2008). Fatigue can be thought of on a continuum, with acute fatigue at one end and CFS at the other (Lewis and Wessely, 1992).

Fatigue is also the primary symptom of chronic fatigue syndrome (CFS), which is also referred to as ME (myalgic encephalomyelitis or myalgic encephalopathy), or CFS/ME. CFS is characterised by persistent fatigue and symptoms such as pain and sleep disturbance (Fukuda et al., 1994). The illness can be extremely disabling and has impacts on social and occupational functioning and health-related quality of life (Cella, Sharpe and Chalder, 2011; Hardt et al., 2001). It affects approximately 2.6% of the population, and is more prevalent in women than in men (Wessely et al., 1997; Jason et al., 1999; Kroenke, Wood, Mangelsdorff, Meier, and Powell, 1988).

There are few evidence-based treatments recommended for CFS. In the UK, cognitive behaviour therapy (CBT) and graded exercise therapy (GET) are the only treatments recommended by the National Institute for Health and Care Excellence for CFS (National Institute for Health and Care Excellence, 2007). There is evidence from systematic reviews, meta-analyses and a large randomised controlled trial (RCT) that these treatments can reduce fatigue and improve functioning in patients with CFS (Castell, Kazantzis, and Moss-Morris,

2011; Edmonds, McGuire, and Price, 2004; Larun, Brurberg, Odgaard-Jensen and Price, 2016; Malouff, Thorsteinsson, Rooke, Bhullar, and Schutte, 2008; White et al., 2011). There is also preliminary evidence that CBT is effective in routine clinical practice (Flo and Chalder, 2014; Quarmby, Rimes, Deale, Wessely, and Chalder, 2007; Stahl, Rimes and Chalder, 2014).

Minimal interventions for fatigue and CFS in the context of primary care

Often, the demand for psychological therapies in the population outweighs the available resources. This situation applies to psychological therapies generally, but it is also true for the treatment of fatigue and CFS, where resources are limited and demand for psychological therapies is high. Provision of specialist CFS services in the UK is varied and inconsistent, which results in many people with CFS not being able to access the treatment they need (Collin, Sterne, Hollingworth, May, and Crawley, 2012). A potential solution to the problem of high demand and low supply in psychological therapies is offering minimal interventions in the context of stepped care (Bower and Gilbody, 2005). Minimal interventions are brief patient-led or therapist-supported interventions that a patient can use at his or her own pace. When this approach is applied to fatigue and/or CFS, minimal interventions might include information about maintaining factors of fatigue, as well as guidance about gradually increasing activity levels, establishing a routine, creating a consistent sleep schedule, and challenging unhelpful thoughts about fatigue.

There is evidence from RCTs that minimal interventions such as self-help guidance can be effective for the reduction of fatigue and for CFS in primary care. In the UK, one RCT showed that a self-help booklet and guidance from a nurse led to reduced fatigue, reduced

psychological distress and improved physical functioning in patients with chronic fatigue lasting more than six months (Chalder, 1995; Chalder, Wallace, and Wessely, 1997). Subsequent RCTs in the UK have shown that therapist delivered, brief interventions of CBT, GET or counselling reduced fatigue and improved functioning in patients with unexplained fatigue (Ridsdale, Darbishire, and Seed, 2004; Ridsdale et al., 2001).

Similarly, in the USA an RCT demonstrated that a brief nurse-led self-help intervention reduced the impact of fatigue in patients in primary care who had a diagnosis of either unexplained chronic fatigue (UCF) or CFS (Friedberg et al., 2013). A more recent study showed that a patient-directed self-help intervention was effective in reducing fatigue severity and depression, and improving physical functioning in patients with UCF or CFS (Friedberg, Ngan, and Chang, 2014), which suggests that self-help can be beneficial even without guidance from a health professional.

Minimal interventions for fatigue and CFS in secondary care

There is also increasing evidence from RCTs that guided self-help can be effective for the treatment of fatigue and CFS in secondary care, where patients are more disabled and thought to require more intense treatment. In a specialist clinic for CFS in the Netherlands, Knoop et al. (Knoop, van der Meer, and Bleijenberg, 2008) compared a group of patients with CFS who received self-help, in combination with fortnightly email/ telephone-based support from a therapist, to a group of patients with CFS who were randomised to a waiting list condition. The group who received self-help showed reduced levels of fatigue and increased physical functioning, compared to the waiting list group. In a follow up study (Tummers, Knoop, and Bleijenberg, 2010) all patients went on to receive CBT. Both groups, i.e. those who received

guided self-help and those who did not, showed reduced fatigue and improved functioning. However the group of patients who received guided self-help in addition to CBT (stepped care) required fewer CBT sessions than those who received care as usual (CBT after a waiting period).

Another RCT carried out in a community mental health centre showed that guided self-help with input from psychiatric nurses led to a reduction in fatigue in patients with CFS (Tummers, Knoop, van Dam, and Bleijenberg, 2012). Similarly, a recent study showed that guided self-help from a therapist led to reductions in fatigue in people with idiopathic chronic fatigue in an outpatient facility in secondary care (Janse, Wiborg, Bleijenberg, Tummers, and Knoop, 2016).

Taken together, these findings suggest that minimal interventions for fatigue and CFS in both primary and secondary care can be implemented by nurses or other healthcare professionals and patients may not always require treatment from a psychotherapist or clinical psychologist. These minimal interventions could help people with fatigue who may not otherwise be able to access treatment.

Factors affecting response to minimal interventions

Research in primary care suggests that there may be several factors which affect response to minimal interventions for fatigue, including negative illness perceptions, worse social adjustment, stronger physical illness attributions and a greater degree of fatigue severity (Chalder, Godfrey, Ridsdale, King, and Wessely, 2003; Darbishire, Seed, and Ridsdale, 2005).

Factors such as mood, avoidance of activity and age may also moderate treatment response.

A secondary analysis of the two aforementioned RCTs of guided self-help for CFS (Knoop et al., 2008; Tummers et al., 2012), showed that patients who were younger, had low avoidance of activity, or lower levels of depression, were more likely to benefit from the guided self-help intervention (Tummers, Knoop, van Dam, and Bleijenberg, 2013).

The current study

Although there are a number of studies on minimal interventions for fatigue and CFS, most research on minimal interventions has taken place in primary care settings or in the context of RCTs. Despite RCTs being accepted as the gold standard in research, there are some shortcomings, such as the participants being drawn from a highly selected sample. Moreover, the effect sizes for fatigue in primary care are quite variable, ranging from trivial to large (Chalder et al., 1997; Friedberg et al., 2013; Friedberg et al., 2014; Malouff et al., 2008; Ridsdale et al., 2001). In secondary care settings, the effect sizes for fatigue are moderate to large, whereas effect sizes for physical functioning range from trivial to large (Janse et al., 2016; Knoop et al., 2008; Tummers et al., 2010; Tummers et al., 2012). Overall this suggests that more evidence is needed about the effectiveness of this type of intervention for improving fatigue and physical functioning.

There is especially a dearth of information about the effect of self-help materials in routine clinical settings in secondary care for patients who are awaiting treatment. The main aim of the current study was to assess whether self-help materials, focused on physical activity, could improve physical functioning in patients with CFS who were waiting for CBT in secondary care. Patients were given self-help materials while on a waiting list for CBT. We also wanted to examine the outcomes of patients once they had received their full course of

CBT. It was hypothesised that patients would show improvements in their physical functioning after receiving self-help. We were not expecting change in fatigue or social adjustment early in the treatment trajectory as clinical experience suggests there is usually a lag between behaviour change and symptom change. After a full course of CBT we hypothesised that patients would show increased physical functioning, improved social adjustment and also reduced fatigue.

Methods

Participants

This study was carried out as an evaluation of routine clinical practice. This clinical evaluation received audit approval from the Audit committee of the Psychological Medicine Clinical Academic Group at South London and Maudsley NHS Foundation Trust.

All patients in the current study were recruited consecutively from an outpatient clinic for CFS between November 2009 and April 2013. Patients who were referred to the service received a thorough medical assessment (Sharpe et al., 1991). The assessment was done according to NICE guidelines (National Institute for Health and Care Excellence, 2007), which included assessment of the patient's symptoms, taking the patient's history, as well as a physical examination and blood and urine tests. These tests were done to exclude other causes of fatigue and to assess whether the patient met clinical criteria for a diagnosis of CFS.

Inclusion and exclusion criteria.

All patients with CFS were eligible to take part in the self-help programme. Patients were included in the analysis if they had a diagnosis of CFS, had been given a self-help pack, and

had been referred for CBT treatment (see Figure 1 and the results section for information about exclusions). Patients could withdraw from treatment at any time, and declining to take part did not impact on the care that patients received.

Patients were asked whether they were willing to complete questionnaires at their initial assessment (baseline), immediately before starting their CBT treatment (pre-CBT), and at the end of active treatment (post-CBT).

Procedure

At baseline, all patients who met eligibility criteria received a self-help pack. This was given to them by the assessing doctor. Assessors were asked to go through the self-help pack with patients and inform them that a therapist would be calling them in several weeks' time to discuss their progress with the self-help materials and any problems they may be having with them. Patients were also told that they could call the unit to speak to a therapist if they had any questions about the information they had received.

The self-help pack consisted of a self-help manual (19 pages; Flesch reading ease score = 65.9; Flesch-Kincaid Grade level = 9.8) and a self-help book (70 pages) based on cognitive behavioural approaches to chronic fatigue (Chalder, 1995). The self-help materials were developed by two of the authors, who are clinicians experienced in the treatment of fatigue and chronic fatigue syndrome within a specialist treatment centre for chronic fatigue and CFS. This material was primarily behavioural, focusing on self-monitoring of activity and sleep, gradually increasing activity, setting targets, and reviewing progress with targets.

Patients were encouraged to complete sleep and activity diaries for 2 weeks, to set targets related to behaviour change and to plan a programme of activity. Patients were asked to schedule time for breaks and rests as well as physical activities such as walking. They were also encouraged to adjust their activity levels and make them more consistent, with the aim of

avoiding a 'boom and bust' pattern of activity. Finally, participants were asked to review their own progress with the activity programme and to make changes as necessary.

During the waiting period (approximately 4-10 weeks after the initial assessment), the therapist or clinical psychologist attempted to contact the participant by phone. The therapist asked the participant about their use of the self-help materials and a discussion was had about how to overcome any problems they may have encountered while following the self-help guidance. Patients were encouraged to monitor their activity, establish a routine, and set goals. If a patient was not available at the time of the phone call, a message was left and further attempts were made to contact the participant. Some participants did not receive a phone call (for example, if the waiting period was very short or they were not contactable and did not respond to messages).

Subsequently, patients who went on to treatment had face to face CBT which was delivered by cognitive behaviour therapists and clinical psychologists, who were experienced in delivering CBT for CFS. Treatment was based on a cognitive behavioural model of understanding CFS which assumes that unhelpful beliefs and behaviours contribute to the perpetuation of fatigue and disability (Burgess, Andiappan, and Chalder, 2012). Specific interventions included self-monitoring, sleep and activity scheduling, goal setting and cognitive restructuring. The CBT treatment and the self-help pack were both based on the same model, but the latter was much briefer and focused more on the behavioural aspects of CBT. It gave patients an introduction to the types of tasks that would be done during CBT treatment.

Questionnaires

Primary outcome.

SF-36 Physical functioning scale(McHorney, Ware Jr and Raczek, 1993; Ware Jr and Sherbourne, 1992)

This scale measures physical functioning; the ability to carry out daily physical activities such as carrying groceries and climbing stairs. There are 10 items, each scored out of 10, giving a total score out of 100, with a higher score indicating higher levels of physical functioning. It is reliable and valid (Cronbach's alpha: 0.92).

Secondary outcomes.

Work and social adjustment scale (Cella et al., 2011; Mundt, Marks, Shear and Greist, 2002).

This scale measures the degree to which an individual's problem affects their ability to manage the home, private and social leisure activities, work and relationships. It has been validated in CFS patients and has good reliability (Cella et al., 2011; Mundt et al., 2002). Each item is scored out of 8, and the 5 items are summed together to give a maximum possible score of 40. A higher score indicates a greater degree of impairment (Cronbach's alpha: 0.89).

Chalder Fatigue Scale (Cella and Chalder, 2010; Chalder et al., 1993) .

This scale measures physical and mental fatigue and has been validated in clinical and community settings. It consists of 11 Likert-scored items, which are rated from 0-3. The 11 items are summed to get a maximum possible total score of 33. The scale has good reliability and is valid (Cronbach's alpha: 0.88).

Data Analysis

Data were analysed using SPSS Statistics Version 21(IBM Corp, 2012).

Management of missing data.

Missing data were pro-rated. Pro-rating is a method for imputation of missing data whereby the missing items of a scale are replaced with the mean of the non-missing items of the scale for that particular individual. The number of missing items must be below a given threshold in order for the missing data to be pro-rated. In our study this threshold was 20%. Pro-rating was carried out at all time-points for all three of the outcome measures.

In addition, a next observation carried backward (NOCB) imputation method was used for the post-CBT (end of treatment) scores, whereby if a participant's post-CBT score was missing, it was replaced by the next available score from the same individual (for further information about this method see Engels and Diehr, 2003). This score was taken from a questionnaire administered approximately three months after the end of active treatment, at the patient's first follow up appointment (median number of months between post-CBT and three month follow up questionnaire=3.2 months IQR=1.0). There were 24 scores imputed for fatigue, 27 for social adjustment and 22 for physical functioning. The NOCB imputation method was implemented at the post-CBT time point only.

Analysis of change over time and mixed models analysis.

The data were summarised using the mean and standard deviation, median and interquartile range (IQR) or frequency and percentage as appropriate. In addition, profile plots were constructed in order to show change in means over the three time-points for each outcome. These profile plots show unadjusted means (i.e. without controlling for any variables).

The Mixed Models procedure in SPSS was used to fit a multilevel model to total scores of each outcome in turn (physical functioning, social adjustment, fatigue) in order to assess change over time. Age, gender and time were added into the model as fixed effect covariates. A random intercept for participants was included in the model to account for repeated measures on individuals. Despite imputation, there were still some missing data; the use of multilevel models and maximum likelihood methods to fit these models accounts for missing data under plausible statistical assumptions (Carpenter and Kenward, 2008).

The time that each of the assessments was made varied from individual to individual based on the time CBT appointments had been scheduled. Time was therefore entered into models as a categorical variable to represent the three important time points for patients during their course of treatment: baseline, pre-CBT and post-CBT. The time-points were coded as categorical variables in SPSS. The multilevel models were used to make comparisons between pre-CBT and baseline, and subsequently between post-CBT and pre-CBT. This was in order to firstly assess the impact of self-help before beginning full CBT, and then the change in outcomes over the period of receipt of full CBT.

A sensitivity analysis was performed in order to examine the impact of the NOCB imputation on the mixed models analysis. This involved comparing the analysis with and without the NOCB-imputed data.

For the main mixed models analysis and the sensitivity analysis, the only patients excluded were those with no data for all time-points of the outcome variable in question.

Analysis of data on implementation of self-help guidance.

Although we did not systematically examine adherence or compliance to the self-help programme, we collected some data from therapists and patients about whether patients had used the self-help materials and to what extent they had implemented the guidance within. This information was gathered from records made by therapists during discussions with the patient at the time of the self-help phone call and at the start of treatment. The information was also gathered from patients, who were asked about implementation of self-help at the start of their CBT treatment. This data was compiled together and sorted into categories based on the degree of engagement with the programme and the extent to which the self-help had been implemented.

Post-hoc sub-group analysis: impact of self-help phone call.

Post-hoc independent (two-tailed) t-tests were conducted using the pro-rated imputed data to examine differences in outcome between participants who had received a phone call and participants who had not. Groups were compared at pre-CBT and post-CBT in turn.

Participants were automatically dropped from the analysis if they were missing the dependent variable that was being analysed at the time.

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Results

Participant characteristics

Figure 1 shows the flow of participants through the study. Participants were excluded from the analysis if they: did not have a diagnosis of CFS; were not eligible for treatment; did not receive a self-help guide, received GET or both CBT and GET treatments; were housebound and received home-based CBT treatment, or had previously received treatment in the clinic. 294 participants were included in the analysis.

[Insert Figure 1 here]

Table A.1 in the supplementary material details completeness of data and numbers recovered through prorating and NOCB imputation. For the main mixed models analysis, there were 272 (93% out of 294) participants included for physical functioning, 275(94%) for social adjustment and 272 (93%) for fatigue.

Table A2 in the supplementary material shows the baseline characteristics of responders and non-responders (people who did not complete a measure at the end of CBT or at 3-month follow-up). Non-responders were significantly more fatigued at baseline.

[Insert links to supplementary material: tables A1 and A2]

Participants were aged between 18 and 78 years old with a mean age of 38 (SD 12). Of those who were eligible for inclusion in the analysis, 219 (75%) were female and 75 (25%) were

male. Of the eligible patients who responded to self-report questions about CFS diagnostic criteria, 159 (78%) met Oxford criteria for CFS (Sharpe et al., 1991) and 119 (61%) met CDC criteria (Fukuda et al., 1994) for CFS.

The median waiting time for CBT was 2.9 months (IQR=2.3, minimum = 0.5; maximum = 22.5). Sessions were one hour long and participants were seen approximately every 2-4 weeks during the active stage of treatment. The number of sessions depended on the needs of the patient but the standard treatment package that was offered consisted of 12-16 active treatment sessions with 4 sessions of follow-up. The patients had a median of approximately 12 active treatment sessions (IQR= 5) with a maximum of 29 sessions. The median number of months between pre-CBT and post-CBT was 8.5 months, (minimum = 2.9, maximum = 27.2, IQR= 3).

Multilevel models of change over time

Change over time.

Figures 2 to 4 show profile plots of the changes in physical functioning, work and social adjustment and fatigue over time. These plots show the unadjusted means (i.e. without adjustment for age and illness duration). However the main mixed models analysis (described below) is adjusted for both age and illness duration.

[Insert figures 2 to 4 here]

Primary outcome.

There was a statistically significant improvement in physical functioning scores at pre-CBT compared to baseline, with an increase of 2.7 points (95% CI 0.1 to 5.3, $p=.044$). Also, compared to pre-CBT, post-CBT physical functioning scores were 9.6 points higher: (95% CI

6.9 to 12.4, $p<.001$). These comparisons were both adjusted for gender and age and both covariates were found to significantly influence the outcome (both $p<.001$).

Secondary outcomes.

Results for social adjustment showed that the change between baseline and pre-CBT scores on the work and social adjustment scale did not reach statistical significance, (decrease of 1.0 points, 95% CI -2.1 to 0.1; $p=.075$). However, post-CBT scores were 7.1 points lower than pre-CBT (95% CI -6.0 to -8.3, $p<.001$), indicating that patients were less impaired after CBT treatment. These comparisons were adjusted for gender and age and both covariates were found to significantly influence the outcome ($p=.006$ and $p<.001$).

The model examining change in fatigue over time, adjusted for gender and age, found no statistically significant difference in fatigue between baseline and pre-CBT (decrease of 0.7 points, 95% CI -1.7 to 0.3, $p=.196$). However, fatigue showed a statistically significant improvement (decrease) of 8.0 points at post-CBT as compared to pre-CBT (95% CI -6.9 to -9.1, $p<.001$). Both comparisons were adjusted for age and gender and the results showed that neither gender ($p=.058$) nor age ($p=.135$) had any statistically significant influence on the outcome.

Examination of the residuals suggested that the normality of residuals assumption was met for the models. This suggested that the data were normally distributed and that multilevel model analysis was appropriate for this data.

Sensitivity analysis.

The sensitivity analysis indicated that the approaches (using NOCB imputed data versus non-imputed data) gave similar results, lending credence to the findings. Significance levels and directions of effect did not differ greatly between the two types of analysis (see supplement A3).

[Insert link to supplementary material: supplement A3]

Pairwise comparisons between baseline and pre-CBT and between pre-CBT and post-CBT

We also made pairwise comparisons between baseline and pre-CBT (Table A4 in the supplementary material) and from Pre-CBT to Post-CBT (Table A5 in the supplementary material). These tables show unadjusted means and standard deviations for the three main outcomes.

[Insert link to supplementary materials here – Table A4 and Table A5]

Implementation of self-help materials

This information can be found in table 1. Over half of the patients (58%) included in the analysis reported that they made some use of the self-help pack, either by reading the material, completing self-monitoring activities, changing their behaviour, setting targets, reviewing progress, or a combination of some or all of the above. Many of the patients found the self-help materials and or phone call to be useful. One patient commented: “I found self-help treatment and the call from a therapist very valuable, and importantly, I feel that I have

achieved a lot while on the waiting list. The ‘homework’ and link with the [clinic] meant that I didn’t feel abandoned, and could usefully work on my treatment”. Some patients stated that they were not able to implement the self-help materials because they did not have enough time, or were prevented by personal circumstances. Others reported that they would prefer to wait until the treatment had started, or that they lacked motivation. Some stated that they felt like they required support from a therapist to implement the materials.

[Insert table 1 here]

Post-hoc analysis: impact of self-help phone call

Of the 294 participants who met eligibility criteria for the study, for 44 (15%) participants, there was no record of whether or not they had received a phone call, and therefore they were not included in the analysis. 146 (51%) participants received a phone call and spoke to a therapist about the self-help materials. 97 (34%) participants did not receive a phone call or speak with a therapist. Phone calls were between 2 and 45 minutes long with a median of 17 minutes (IQR=14). As seen in Table 2, there were no statistically significant differences in outcome between patients who received a phone call and those who did not.

[Insert Table 2 here]

Discussion

This study examined the effect of self-help guidance for participants with CFS in a specialist outpatient clinic in secondary care. In line with hypotheses, participants reported a statistically significant improvement in the primary outcome of physical functioning in the short period after receiving self-help guidance, and before beginning CBT. Moreover,

statistically significant improvements in physical functioning, fatigue and social adjustment were seen after completion of full CBT treatment. Gender was a statistically significant covariate, with females showing worse social adjustment and lower levels of physical functioning than males. In addition, being older was associated with worse social adjustment and physical functioning.

There were no statistically significant differences in outcome between participants who received a phone call and those who did not, which suggests that the self-help materials may have been useful to the patients even without the extra support from a therapist. It can be argued that specific advice about activity scheduling, sleep monitoring and goal setting contained in the written self-help materials may have helped patients to gradually increase their activity levels and this in turn may have positively impacted upon their perceived level of physical functioning. Self-help may have served as an introduction to the cognitive behavioural approach to fatigue and allowed patients to engage more effectively with treatment. The self-help materials may have also benefitted those who did not go on to have a full course of CBT. However, it is important to emphasise that this was not a controlled study and that the results require replication within the context of a RCT.

Our findings are in line with previous research which suggests that self-help guidance leads to improved physical functioning in patients with CFS (Knoop et al., 2008; Tummers et al., 2010).

Patients in the current study did not show an improvement in social adjustment or fatigue directly after receiving self-help guidance and before beginning CBT. However, after a full course of CBT, improvement in social adjustment and decreases in fatigue were observed

despite this being in a 'real life' routine clinical setting. This suggests that in patients with CFS, brief self-help, which is not supported by input from a therapist, is not sufficient to reduce fatigue and improve social adjustment. A full course of CBT is needed in order to show changes in these outcomes. On the other hand, the early change in physical functioning suggests that this specific outcome may be more amenable to change with a minimal intervention such as self-help. Although the changes in physical functioning were small and not likely to be clinically significant, the results suggest that patients were able to benefit from some input while waiting to start CBT treatment.

In the current study, improvements in functioning may have been facilitated by behavioural changes as suggested in the self-help materials. It may take time for the effects of behavioural change to impact on the experience of fatigue. In addition, it may take longer for other aspects of people's work, social and private life to improve.

Minimal interventions may be beneficial for those with fatigue or CFS who are unable to access specialist treatment in secondary or tertiary care. For example, patients may find it difficult to attend appointments at an outpatient clinic because of the disabling nature of their fatigue. They may also be unable to access treatment due to a shortage of specialist services in their area. Patients in primary care could be prescribed a self-help book and given guidance from their GP. This could prevent a downward spiral into worsening disability that can happen to people with fatigue over time, and may reduce referrals to secondary care.

However, it is important to note that minimal interventions such as self-help cannot replace a full course of CBT for those who need it. Self-help often lacks key elements of face to face therapy, such as a strong therapeutic relationship (Gega, Smith and Reynolds, 2013).

Although self-help may be more economical, CBT has been found to have better outcomes (McCrone, Ridsdale, Darbishire and Seed, 2004). Moreover, CBT for CFS has a dose-response effect, with more sessions leading to better outcomes (Castell et al., 2011; Malouff et al., 2008). Patients with more severe symptoms may require a greater 'dose' of treatment (Chambers, Bagnall, Hempel, and Forbes, 2006).

This study has some limitations that should be noted. Firstly, as this was a clinical evaluation carried out within routine clinical practice, it lacked some of the control of confounding variables that would be possible in a randomised controlled trial. For example, there was no control group, and participants were not randomised. Without randomisation and a control group, it is not possible to say definitively that the self-help guidance led to the change in physical functioning. Another limitation is that despite imputation, there were still a number of non-responders at the end of CBT. Therefore the findings of this study should be interpreted with caution.

The waiting period for CBT was variable which meant that some patients had more time than others to engage with self-help materials. Overall, 58% of the patients made some use of the self-help materials, but a sizeable proportion of patients did not, with several patients only reading the self-help materials and not making any behavioural changes or setting targets. Our analysis included all patients who were given a self-help guide, regardless of their adherence to the self-help programme. This may have impacted upon the findings and requires further investigation. A qualitative study using semi-structured interviews would allow for a more in-depth exploration of the acceptability of the intervention, reasons for non-engagement with the self-help programme, and patients' experience of implementing the self-help guidance.

It is possible that improvements after self-help were seen because patients' expectations about treatment led to them feeling better before treatment started. Previous research has shown that expectations can influence treatment outcomes of people who have CFS (Heins, Knoop and Bleijenberg, 2013; Vos Vromans et al., 2016). However since we did not measure treatment expectations in this study, these conclusions cannot be drawn from our data.

Future studies could evaluate whether self-help interventions could be used as a form of early intervention for people with fatigue in primary care. A randomised controlled study design could also be used to investigate whether self-help given before the commencement of CBT improves outcomes at the end of treatment and whether these gains are maintained into follow up. Furthermore, preliminary research findings suggest that subgroups of CFS may exist, and that people sharing certain demographic characteristics may respond differently to CBT (Cella, Chalder and White, 2011). The impact of heterogeneity could potentially affect the response to self-help. This could be investigated further.

In summary, minimal interventions such as self-help may assist patients in managing their physical functioning and help them to manage their symptoms while they are waiting for treatment within secondary care. However as noted in the literature, self-help interventions may not be suitable for all patients, and those with more severe symptoms are likely to require more intensive treatment.

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Conflict of interest statement:

Two of the authors (MB and TC) have published self-help books relating to chronic fatigue and chronic fatigue syndrome.

Ethical approval

The authors have abided by the Ethical Principles of Psychologists and Code of Conduct as set out by the APA(American Psychological Association). This study did not require ethical approval because it was an audit of routine clinical practice. The study received audit approval from the Clinical Audit Committee of the Psychological Medicine Clinical Academic Group at the South London and Maudsley NHS Foundation Trust.

Figure captions

Figure 1: Consort flow diagram showing flow of participants through the study

Figure 2: Profile plot of change in Physical functioning over time showing unadjusted means (SD) for the three time points (Error bars show 95% confidence intervals).

Figure 3: Profile plot of change in Social Adjustment scores over time showing unadjusted means (SD) for the three time points (Error bars show 95% confidence intervals).

Figure 4: Profile plot of change in fatigue over time showing unadjusted means (SD) for the three time points (Error bars show 95% confidence intervals).

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ACCEPTED MANUSCRIPT

Table 1

Table describing usage and implementation of self-help materials

Description of level of usage of self-help materials	N	%
Level 0 No change		
Did not use self-help pack	23	7.8
Already using strategies	4	1.4
Level 1 Education		
Read self-help pack	24	8.2
Level 2 Monitoring and identifying areas to change		
Target setting	5	1.7
Monitoring (sleep diary, activity diary or both)	33	11.2
Monitoring and target setting	19	6.5
Level 3 Changing behaviour		
Monitoring and behaviour change	11	3.7
Behaviour change	10	3.4
Behaviour change and target setting	14	4.8
Level 4 Integration of self-help principles into everyday life		
Monitoring and target setting and behaviour change	33	11.2
Monitoring and target setting and review of progress	3	1.0
Monitoring and target setting and behaviour change and review of progress	8	2.7
Target setting and behaviour change and review of progress	2	0.7
Other		
Generic use of self-help pack (not specified)	9	3.1
Unknown	96	32.7

Note: Total percentages add to more than 100 due to rounding.

Table 2 Outcomes compared between participants who received a phone call and participants who did not receive a phone call (pre and post CBT)

	N	Phone call group Mean (SD)	N	No phone call group Mean (SD)	T test	Mean difference	95% confidence interval for mean difference	
Physical functioning at pre-CBT	113	49.5 (26.2)	74	50.2 (27.3)	$t(185)=0.18, p=.86$	0.7	-7.2	8.6
Physical functioning at post-CBT	90	59.6 (28.3)	56	63.1 (28.4)	$t(144)=0.72, p=.48$	3.5	-6.1	13.0
Social adjustment at pre-CBT	116	25.3 (9.3)	72	25.2 (9.0)	$t(186)=-.08, p=.94$	0.11	-2.8	2.6
Social adjustment at post-CBT	88	17.4 (11.5)	59	17.9 (11.3)	$t(145)=0.28, p=.78$	0.54	-3.3	4.3
Fatigue at pre- CBT	117	25.2 (6.1)	74	24.1 (6.8)	$t(189)=-1.2, p=.23$	-1.1	-3.0	0.7
Fatigue at post- CBT	90	17.3 (8.0)	58	16.2 (9.3)	$t(146)=-0.8, p=.42$	-1.2	-4.0	1.7

Figure 1

Figure 2

Figure 3

Figure 4

SUPPLEMENTARY MATERIAL:

Table A1 Complete and missing data for all stages of the study

Measure	Time point (number of cases)			
	Baseline	Pre-CBT	Post-CBT	
Physical functioning				
	Complete data	189	192	138
	≤20% of scale missing (data pro-rated)	34	24	8
	Number of cases with complete data after pro-rating	223	216	146
	Number of cases imputed using NOCB	-	-	22
	Complete data after imputation and pro-rating	223	216	168
Social adjustment				
	Complete data	224	204	133
	≤20% missing (data pro-rated)	4	13	8
	Number of cases with complete data after pro-rating	228	217	141
	Number of cases imputed using NOCB	-	-	27
	Complete data after imputation and pro-rating	228	217	168
Fatigue				
	Complete data	209	205	140
	≤20% of scale missing (data pro-rated)	19	16	6
	Number of cases with complete data after pro-rating	228	221	146
	Number of cases imputed using NOCB	-	-	24
	Complete data after imputation and pro-rating	228	221	170

Table A2

	Responders (171)	Non-responders(123)
Female gender (N)	127	92
Mean Age	38.02(11.50)	38.89(12.02)
Mean baseline Fatigue	25.07(5.20)	26.54(4.71)*
Mean baseline Physical functioning	50.97(24.79)	44.08(26.22)
Mean baseline Social adjustment	25.76 (8.16)	26.43 (10.02)

* $p < .05$

Note: Differences between responders and non-responders were compared using independent (two-tailed) t-tests, apart from gender, which was analysed using a Chi-square test.

Supplement A3

Sensitivity analysis: mixed model analyses using prorated data only (no imputation)

Primary outcome:

Physical functioning scores showed a statistically significant improvement at pre- CBT compared to baseline, with an increase of 2.7 points (95% CI 0.1 to 5.2, $p=.039$). Also, compared to pre-CBT, post-CBT physical functioning scores were 10.0 points higher: (95% CI 7.2 to 12.8, $p<.001$). These comparisons were both adjusted for gender and age and both covariates were found to significantly influence the outcome (both $p<.001$).

Secondary outcomes:

Results for social adjustment showed that the change between baseline and pre- CBT scores on the Work and social adjustment scale was not statistically significant, (decrease of 0.9 points, 95% CI -2.0 to 0.2; $p=.093$). However, post-CBT scores were 7.4 points lower than pre-CBT (95% CI -6.2 to -8.6, $p<.001$), indicating that patients were less impaired after CBT treatment. These comparisons were both adjusted for gender and age and both covariates were found to significantly influence the outcome ($p=.007$ and $p<.001$).

The model examining change in fatigue over time, adjusted for gender and age, showed no statistically significant difference in fatigue between baseline and pre-CBT (decrease of 0.7 points, 95% CI -1.6 to 0.3, $p=.189$). However, fatigue showed an improvement (decrease) of 8.4 points at post-CBT as compared to pre-CBT (95% CI -7.3 to -9.6, $p<.001$). Results showed that neither gender ($p=.084$) nor age ($p=.152$) had any statistically significant influence on the outcome.

Table A4 Comparison between baseline and pre-CBT for physical functioning, social adjustment and fatigue

	N	Mean at initial assessment (SD)	Mean at pre- CBT(SD)	T test	95% confidence interval for mean difference	
Physical functioning	171	48.00 (24.24)	51.18 (25.92)	$t(170)=-2.91, p=.004$	-5.33	-1.02
Social adjustment	174	26.42 (8.37)	25.35 (8.67)	$t(173)=2.44, p=.016$	.20	1.92
Fatigue	180	25.61 (5.16)	24.74 (6.42)	$t(179)=2.19, p=.030$	.09	1.64

Table A5 Comparison between pre-CBT and post- CBT scores for physical functioning, social adjustment and fatigue

	N	Mean at pre- CBT (SD)	Mean at post- CBT (SD)	T test	95% confidence interval for mean difference	
Physical functioning	156	52.99 (26.02)	62.14(27.64)	$t(155)=-6.42, p=.000$	-11.97	-6.33
Social adjustment	160	24.61(9.33)	17.90(11.08)	$t(159)=10.57, p=.000$	5.46	7.97
Fatigue	162	24.39(6.25)	16.73(8.57)	$t(161)=11.19, p=.000$	6.31	9.01