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Cognitive Behaviour Therapy for Chronic Fatigue Syndrome in Adults: Face to Face versus Telephone Treatment - A Randomized Controlled Trial

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Background: Previous research has shown that face to face cognitive behaviour therapy (CBT) is an effective treatment for chronic fatigue syndrome (CFS)/Myalgic Encephalomyelitis (ME). However, some patients are unable to travel to the hospital for a number of reasons. **Aims:** The aim of this study was to assess whether face to face CBT was more effective than telephone CBT (with face to face assessment and discharge appointment) for patients with CFS. **Method:** Patients aged 18–65 were recruited from consecutive referrals to the Chronic Fatigue Syndrome (CFS) Research and Treatment Unit at The South London and Maudsley NHS Trust in London . Participants were randomly allocated to either face to face CBT or telephone CBT by a departmental administrator. Blinding of participants and care givers was inappropriate for this trial. A parallel-groups randomised controlled trial was used to compare the two treatments. The primary outcomes were physical functioning and fatigue. **Results:** Significant improvements in the primary outcomes of physical functioning and fatigue occurred and were maintained to one year follow-up after discharge from treatment. Improvements in social adjustment and global outcome were noted and patient satisfaction was similar in both groups. **Conclusions:** Results from this study indicate that telephone CBT with two face to face appointments is a mild to moderately effective treatment for CFS and may be offered to patients where face to face treatment is not a viable option. Despite these encouraging conclusions, dropout was relatively high and therapists should be aware of this potential problem.

Keywords: Cognitive behaviour therapy, chronic fatigue syndrome, telephone, face to face.

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Introduction

Chronic Fatigue Syndrome (CFS), often referred to as myalgic encephalomyelitis (ME), is an illness that has a definite onset and is characterized by severe unexplained physical and mental fatigue that lasts at least 6 months. At present the two most widely accepted operational criteria for CFS are the Oxford criteria (Sharpe et al., 1991) and the Centres for Disease Control (CDC) Fukuda criteria (Fukuda et al., 1994). The illness is associated with profound fatigue and disability. Other symptoms may be present, particularly myalgia, mood and sleep disturbance, concentration and memory problems (Sharpe et al., 1991).

National Institute for Health and Clinical Excellence (NICE) (2007) recommends that either cognitive behaviour therapy (CBT) or graded exercise therapy (GET) should be offered as a treatment to patients with mild to moderate CFS, as these are the two interventions for which there is currently the clearest research evidence of benefit (NICE, 2007; Whiting, Bagnall, Snowdon, Cornell and Mulrow, 2001; Chambers, Bagnall, Hempel and Forbes, 2006). A recent large randomized trial adds further support to these findings (White et al., 2011). A Cochrane review has shown that CBT improves fatigue and physical functioning in about 40% of patients (Price, Mitchell, Tidy and Hunot, 2008).

Despite these encouraging results, several problems remain. It has proved impossible to keep pace with demand for treatment. The number of therapists with the necessary skills is limited and many patients are unable to travel to specialist units for treatment. To overcome these problems we piloted a telephone treatment package of CBT, consisting of 13 telephone and 2 face to face sessions, which reduced the demand on patients in terms of travel time. Nine consecutive patients with a diagnosis of CFS who were unable to attend regular out-patient appointments had a face to face assessment with MB. They were given a self-help manual and were phoned fortnightly for up to half an hour to discuss progress, problem-solve any difficulties, review diaries sent by post to the therapist, and discuss plans for the coming fortnight. Patients attended a discharge appointment. Eight patients completed treatment; one dropped out after 6 weeks as she felt too ill to continue with the programme or complete records due to the severity of her symptoms. Improvement was seen on all measures at discharge; fatigue had improved by 75%. At 6-month follow-up, levels of functioning had continued to improve although fatigue had slightly risen due to one patient having influenza at this time point. This pilot study demonstrated that telephone CBT resulted in a reduction in fatigue and improvement in disability (Burgess and Chalder, 2001). The advantage of a telephone-based approach is that it is less time consuming for the therapist, therefore allowing more patients to be treated. The advantages for the patient are that it is less time consuming and less disruptive to their life.

Given the promising results of the pilot study, the next obvious step was to compare telephone CBT plus two face to face sessions with face to face CBT, which has already been shown to be efficacious in randomized controlled trials (Deale, Chalder, Marks and Wessely, 1997; Prins et al., 2001; Sharpe et al., 1996). Although telephone-based interventions are becoming more popular, a systematic review of the literature was unable to draw firm conclusions about its efficacy due to small sample sizes and a lack of randomized controlled trial methodology in many of the studies (Leach and Christensen, 2006).

Method

Design, objectives and randomization

We carried out a parallel-groups randomized controlled trial to compare CBT either delivered face to face or primarily by telephone. We decided to omit a "no treatment" or "placebo" group because of the potential ethical objections of leaving patients untreated and the fact that we hypothesized that one approach, face to face CBT, would be superior to telephone CBT in reducing fatigue and improving physical functioning.

Participants

The study was conducted at the Chronic Fatigue Syndrome (CFS) Research and Treatment Unit at the South London and Maudsley NHS Trust in London, which is part of the Academic Health Sciences Centre (AHSC) at King's College London. The protocol was approved by the local ethics committee. Patients aged 18–65 years were recruited from consecutive referrals to the unit. All patients were assessed by a psychiatrist and were invited to participate in the trial if they fulfilled both the CDC (Fukuda et al., 1994) and Oxford criteria (Sharpe et al., 1991) for CFS. They also had to have had CFS for less than 10 years, as a longer duration raised concerns over the accuracy of the diagnosis and the possibility that telephone treatment would be inappropriate. Additional inclusion criteria were being able to attend the hospital or have telephone sessions fortnightly. Patients were excluded from the trial if they had any medical condition that may have accounted for their fatigue, had started or changed medication within 3 months to ensure stability of additional treatments, were pregnant, had psychosis, drug abuse, a somatoform disorder or melancholic depression, a subtype of major depression with specific features including anhedonia, severe weight loss, psychomotor agitation or retardation, insomnia with early morning waking, and guilt.

Procedure

An explanation of the trial was given to patients who fulfilled trial criteria at the end of the assessment by the psychiatrist. Some patients gave written consent to participate at the end of their assessment; other patients who wanted time to think about their decision were contacted by phone by MB within two weeks of the assessment. Informed written consent was obtained from those wishing to participate prior to randomization.

Eligible patients were randomly allocated to either face to face or telephone CBT just prior to starting treatment. A clinic administrator kept a random list of numbers. The list was prepared using a table of random numbers (Pocock, 1995). Randomization was started at the first number on the list. The administrator was informed by phone or in person by the assessing psychiatrist or by MB when a patient had consented for the trial. She then randomized the patient using the prepared list and wrote the treatment group to which the patient had been assigned in their medical notes as well as keeping a separate record.

Treatment procedures

Once participants had consented and had been randomized, an initial detailed face to face cognitive behavioural assessment took place with their assigned therapist. Participants in

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the face to face group had their assessment split into two 1½ hour appointments whereas participants in the telephone group had one long appointment of up to 3 hours.

Interventions

Cognitive behavioural models suggest that a combination of physiological, behavioural, cognitive, emotional and social factors contribute to the perpetuation of symptoms and disability associated with CFS (Wessely, David, Butler and Chalder, 1989; Sharpe and Chalder, 1994). The essence of CBT is to help patients to change behavioural and cognitive factors, focusing specifically on changing avoidance behaviour, unhealthy sleep patterns and unhelpful beliefs in order to improve levels of fatigue and disability.

Participants were socialized to the model of treatment and a rationale for the approach was discussed collaboratively. Long term goals were negotiated. Participants allocated to telephone treatment had all subsequent sessions over the telephone, apart from the discharge session which was carried out face to face. The structure of the treatment was otherwise similar in both groups.

Early treatment sessions involved a combination of collaborative agenda setting, homework reviewing, planning of future homework, discussion about how to manage sleep problems and ways to gradually increase activity without overdoing it. Subsequent sessions involved discussion around identifying and challenging unhelpful cognitions that were standing in the way of behavioural change. Social factors, for example work, relationship or child care issues, were addressed if they were identified as being important in perpetuating the symptoms and disability associated with their CFS. Management of setbacks was discussed in the final few treatment sessions and goals agreed for participants to work towards during follow-up. Participants were offered follow-up sessions 3 months, 6 months and 12 months after the end of treatment, by phone if in the telephone group and face to face if in that group.

Face to face CBT consisted of up to 15 sessions. The number of sessions was agreed collaboratively with the participant. The first two sessions lasted up to 1½ hours in order to complete a detailed assessment. Subsequent sessions were between 50 minutes and 1 hour. Handouts containing relevant material to the session were given at the therapist's discretion; these were not standardized.

Telephone CBT consisted of one face to face session of up to 3 hours with their assigned therapist. The long session allowed adequate time for a detailed assessment and socialization to the model. In addition, participants were given a folder containing a treatment manual, activity, sleep and thought diaries to complete, and stamped addressed envelopes in which to return them. Thereafter, participants were offered 13 fortnightly phone appointments of half an hour's duration. Participants returned completed homework diaries by post, fax or e-mail for the therapist to look at before and during their phone appointment.

Some participants felt confident in using their self-help manual independently and required minimal input from the therapist who acted in a supportive role. Others required more specific help with setting a realistic programme of planned activity and rest, overcoming sleep problems and identifying and challenging unhelpful thoughts. Therapists encouraged participants to find solutions to their difficulties in order to build their confidence in using the manual. Some participants also used part of the telephone session to discuss other issues that were affecting their ability to maintain their programme; the therapist would

problem-solve with them to identify the best way forward. Aside from the discharge appointment, which was carried out face to face, the follow-up appointments were carried out over the phone.

Therapists

Both treatments were delivered by eight trained cognitive behavioural nurse therapists all of whom had worked in the department for at least 6 months. The therapists had all received rigorous training involving live observation of sessions, feedback on recorded sessions, as well as close supervision of their cases. Fortnightly face to face clinical supervision was provided to ensure adherence to protocol and to problem solve clinical and protocol issues relating to trial participants.

Outcomes

Evaluations consisted of self-rated questionnaires. Participants completed questionnaires before treatment, after treatment, and 3, 6 and 12 months after completing treatment. Information was collected on demographic information, namely age, sex, marital status, social class.

Primary outcome measures

Medical Outcomes Survey: short form (physical functioning subscale) (MOS; Stewart, Hays and Ware, 1988). Items relating to limitation of activities caused by ill-health were assessed on a scale of 1 (limited for more than 6 months) to 3 (not limited at all). Scores from the 6 items were then summed and converted into a percentage rating; 100% = no limitation to 0% = limited for more than 6 months. This questionnaire has been shown to be reliable and valid and has been used in other CFS/ME trials, (Deale et al., 1997).

Chalder Fatigue Scale (Chalder et al., 1993). This 11-item questionnaire measures the severity of fatigue. Four response options range from "less than usual" to "much more than usual". Bimodal scoring gives a range of 0–11 and yields a cut-off for "caseness" or excessive fatigue at 4 or over. This questionnaire has been used in previous CFS/ME intervention trials and is reliable and valid (Cella and Chalder, 2010).

Secondary outcome measures

Social Adjustment Scale (Mundt, Marks, Shear and Griest, 2002). This 5-item questionnaire measures impairment in occupational, social, private leisure, domestic activities and relationships. Impairment in each area is measured on a Likert scale from 0 indicating "not at all impaired" to 8 "very severely impaired". The scale has been shown to be reliable (Cronbach's alpha 0.7–0.9), has good face validity, correlates with symptom severity in depression and obsessive compulsive disorder and is sensitive to change. It has recently been shown to be reliable and valid in a CFS population (Cella, Sharpe and Chalder, 2011).

Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983). This is a 14-item scale that measures anxiety and depression. It was designed specifically for the liaison setting and has good reliability and validity. Each item has 4 possible responses.

Self-rated global improvement was rated on a 6-item scale from "very much better" to "very much worse". Scores were dichotomized for the analysis by grouping together participants who scored very much better and much better (1 or 2) with those who scored a little better to very much worse (3 to 6). Satisfaction with treatment was rated on a 7-point scale from "very satisfied" to "very dissatisfied". Scores were dichotomized for the analysis by grouping together participants who were very satisfied or moderately satisfied (1 or 2) compared respectively with those who were slightly satisfied to very dissatisfied (3 to 7).

Sample size and statistical methods

A power-calculation based on the actual number of dropouts was calculated to ensure that an effect size between the two groups could be detected. A sample size of 50 with 80% power and a significance level of 0.05 for a two-tailed test will be able to detect an effect size of 0.35 using a two groups and three time points repeated measures of ANOVA. Allowing a maximum dropout rate of 50%, the sample size required was calculated to be 75. The power calculations were carried out using G power 3.0.8.

The baseline demographic and clinical variables namely gender, marital status, ME association, has a job to return to, age, duration of illness, number of sessions, anxiety and depression and the outcome variables fatigue, social adjustment and physical function (MOS) were summarized using descriptive statistics. Since there was an overall attrition rate of 46.25% from baseline to 12-month follow-up, the dropout mechanism was investigated. Logistic regression was used to assess whether the subject characteristics, namely gender, marital status, ME association, has a job to return to, age, duration of illness, number of sessions, anxiety and depression, were predictive of the probability of dropouts. In addition, to assess whether earlier values of an outcome variable predicted later dropouts, subjects at time 't' were divided into those who supplied data (non-dropout) on the outcome variable and those who have not, at time '$t+1$' (dropout). The emerging patterns were assessed by plotting means and 95% confidence intervals for dropout and non-dropout groups at various time points.

From logistic regression (significant coefficient value for subject characteristics in the logistic regression model) and Figure 2 (the non-overlapping confidence intervals for dropouts and non-dropouts groups at baseline and later time points), it was observed that baseline characteristics and earlier values appeared to predict absence of data and hence it was concluded that dropping out in this study was not completely at random (MCAR), but predicted by observed data. Hence, random effects models were used for the analysis of outcome variables since the inferences drawn from this model is valid under less restrictive missing at random (MAR) assumptions, provided all the variables involved are included in the model. An intention to treat analysis was carried out for the dropouts.

A random intercept model was fitted using the 'xtmixed' command in Stata 10 for each outcome variable. The varying intercept in this model accounted for the correlation between repeated temporal measures for the subject and the fixed part contained contrasts for the time factor, main effect of group and group by time interactions. The interaction between group and time was tested initially to assess whether any group effects differed significantly between

different time points and was removed from the model if it was not statistically significant. The final model contained only the main effects of group, time points, baseline scores and the subject characteristics that were predictive of dropouts. To decide whether any of the subject characteristics such as gender, marital status, belonging to the CFS/ME organization, has a job to return to, age, duration of illness, number of sessions, anxiety and depression to be included in the final analysis model as predictors, each variable was included separately in the model and tested for its significant contribution to the post-treatment variability along with the baseline scores and effects of group and time. If any such variables explained significant variability at a liberal 10% level, then they were included in the final model.

Results

Subject flow

Four hundred and ten consecutive patients referred to the clinic were assessed for suitability for the trial; 300 of these did not meet inclusion criteria; 30 did not wish to participate and 80 did (see Figure 1). Reasons for ineligibility of the 300 patients included: not meeting Oxford and Fukuda criteria (37%), onset of over 10 years (20%), would not be able to attend regular appointments, did not have a phone (14%) or were offered group CBT in the clinic (7%). Other reasons for ineligibility included 7% being referred back to local services and 6% having started or changed medication within the previous 3 months. No reason was given or there were missing data in 9% of patients. Eighty participants were randomized to either face to face CBT ($n = 35$, 43.75%) or telephone CBT ($n = 45$, 56.25%). The participants were predominantly female (78.8%); 39.7% were married and the remaining 60.3% were single, widowed, divorced or co-habiting.

The average age of participants was 37.4 (*SD* 10.1). Only 35.5% of the participants had a job to return to. The mean depression score of participants at the start of the study was 9.1 (*SD* 1.7). The mean anxiety score of the participants was 11.2 (*SD* 3.2). Ninety percent of the participants were white. The mean duration of illness for the study group was 4.0 years (*SD* 2.1). Participants attended an average of 11.3 sessions (*SD* 5.2). The large variability of session attendance is accounted for by dropouts at different stages of treatment as well as some participants feeling better and not requiring the full amount of sessions. Twenty-eight of the 35 participants allocated to face to face CBT and 30 of the 45 participants allocated to telephone CBT received treatment. Six participants allocated to telephone treatment did not start; 2 felt better, 1 wanted face to face treatment, 1 had local treatment and 3 gave no reason. One participant allocated to face to face treatment no longer wished to participate as she felt better. Reasons for dropping out during treatment included being unable to commit to sessions due to personal circumstances, moving abroad, starting another treatment for pain, or no reason was given.

Table 1 summarizes the group-wise baseline characteristics. There was no evidence of a significant difference (p values $> .05$ for all the variables) between the groups with respect to sex, marital status, ME association and jobs to return to. Similarly, the mean age, duration of illness, average number of sessions attended and the depression scores did not differ between the two groups ($p > .05$ for all these variables). However, the two groups differed significantly ($p = .046$) with respect to the anxiety scores. The anxiety score was higher in the face to face therapy group compared to the telephone CBT group.

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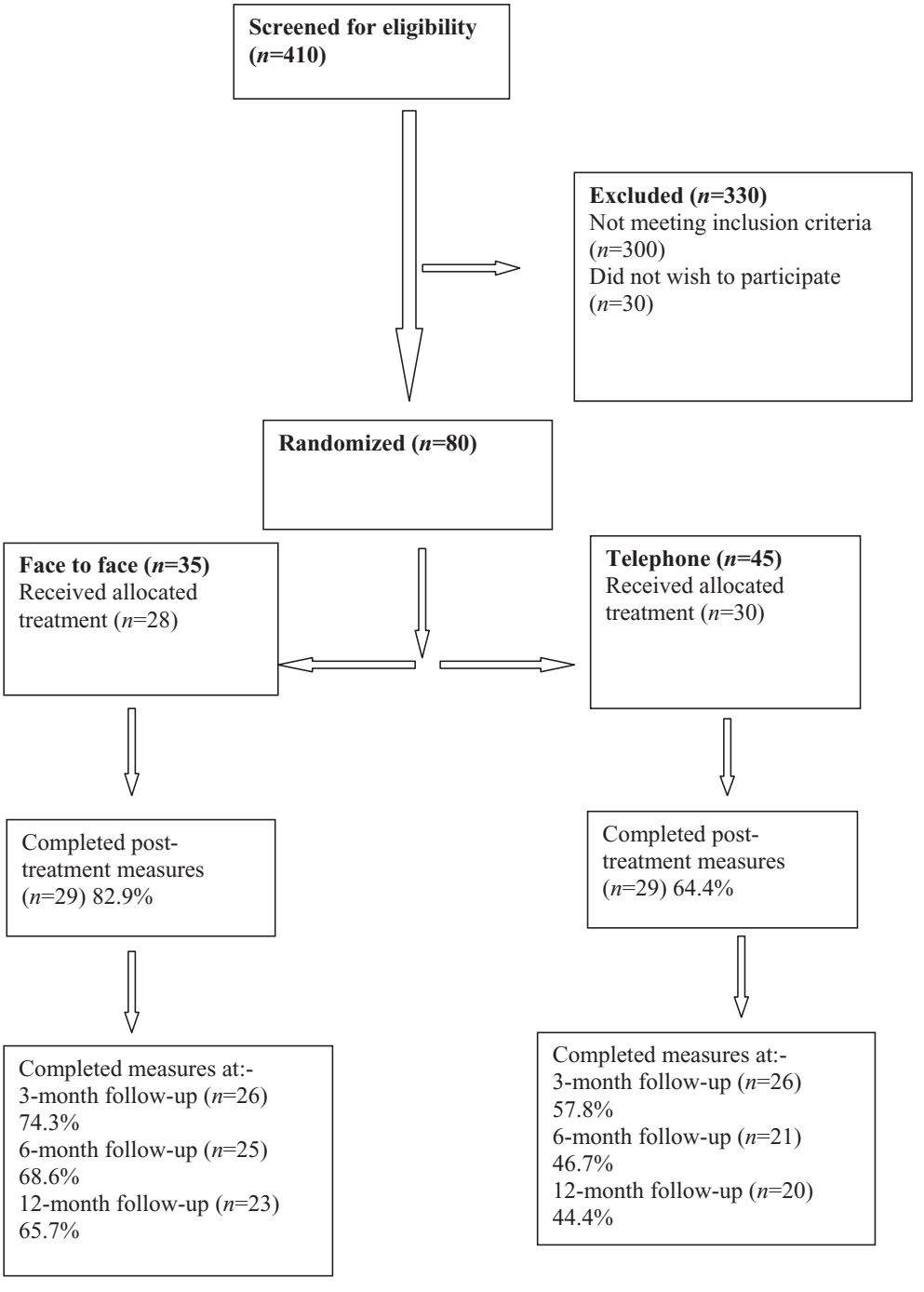

Figure 1. Consort statement

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Table 1. Descriptive summaries of baseline variables and tests for group differences

Variable	Telephone CBT ($N = 45$) n (%)	Face to Face CBT ($N = 35$) n (%)	Overall ($N = 80$) n (%)	Group comparison (Mann-Whitney or Fisher's exact test) p value
Gender:				
Male	8 (17.78)	9 (25.71)	17 (21.25)	0.421
Female	37 (82.22)	26 (74.29)	63 (78.75)	
Status:				
Married	14 (31.82)	17 (50.00)	31 (39.74)	0.161
Single/ Others	30 (68.18)	17 (50.00)	47 (60.26)	
Member of ME association:				
Yes	9 (20.45)	7 (21.21)	16 (20.78)	1.000
No	35 (79.55)	26 (78.79)	61 (79.22)	
Job to return to:				
Yes	20 (45.45)	7 (21.88)	27 (35.53)	0.052
No	24 (54.55)	25 (78.13)	49 (64.47)	
Age:	36.66 (10.49)	38.41 (9.74)	37.42 (10.14)	0.468
	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	
Duration	3.80 (2.09)	4.20 (2.21)	3.97 (2.13)	0.423
No. of sessions	11.54 (5.64)	11.03 (4.72)	11.31 (5.22)	0.110
Anxiety	10.35 (2.55)	12.15 (3.65)	11.20 (3.22)	0.046
Depression	9.19 (1.73)	8.91 (1.67)	9.05 (1.69)	0.686

Outcome measures

Group-wise mean and standard deviation of fatigue, social adjustment and physical function are depicted in Table 2. Fatigue scores showed a decline from baseline to post-treatment time points and maintained the score for the rest of the follow-ups for both telephone CBT and face to face groups. A similar trend was observed in social adjustment scores. The physical function (MOS) scores showed an increase from baseline to post treatment time points for both the groups. The increased score was maintained in the rest of the follow-up time points.

Dropout mechanism

The comparison of dropout rates between groups showed no significant difference between telephone CBT and face to face CBT ($p > .05$) with respect to the proportion of dropouts from base line to 12-month follow-up. To find out whether the baseline variables predicted the later dropout, logistic regression analysis was carried out. The results of the logistic regression analysis showed job status as a significant ($p = .003$) predictor of dropouts; participants who were in employment were more likely to drop out at the post treatment and follow-up time points. The means and 95% confidence interval of the outcome measure fatigue for the two groups, namely the dropouts in the later time points and the non-dropouts, are shown in Figure 2. Although the mean values for dropout cases are slightly higher than the non-dropout cases at baseline and 6-month time points, there was no evidence to conclude that dropping

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Table 2. Mean and standard deviations (*SD*) of outcome variables by groups and time points

	Telephone CBT			Face to Face CBT		
Time points	*N*	Mean (*SD*)	ES (95% CI)	*N*	Mean (*SD*)	ES (95% CI)
Fatigue						
Baseline	41	10.41 (1.58)		34	10.06 (2.27)	
Post	29	7.55 (4.19)	1.81 (−0.15 to 3.77)	29	7.41 (3.73)	1.17 (−0.79 to 3.13)
3 months	24	7.08 (3.56)	2.11 (0.15 to 4.07)	25	7.08 (3.97)	1.31 (−0.65 to 3.27)
6 months	20	7.75 (3.77)	1.69 (−0.27 to 3.65)	24	5.75 (4.49)	1.90 (−0.06 to 3.86)
12 months	19	7.89 (3.75)	1.60 (−0.36 to 3.56)	23	6.83 (4.57)	1.42 (−0.54 to 3.38)
Social adjustment						
Baseline	44	29.02 (6.28)		34	27.26 (7.58)	
Post	29	21.86 (7.35)	1.14 (−0.82 to 3.10)	29	21.45 (8.24)	0.77 (−1.19 to 2.73)
3 months	26	21.65 (7.42)	1.17 (−0.79 to 3.13)	26	23.35 (8.54)	0.52 (−1.44 to 2.48)
6 months	21	23.43 (8.06)	1.21 (−0.75 to 3.17)	25	19.40 (10.77)	1.04 (−0.92 to 3.00)
12 months	20	19.40 (8.73)	1.53 (−0.43 to 3.49)	23	20.83 (12.25)	0.85 (−1.11 to 2.81)
Physical function (MOS)						
Baseline	37	51.80 (15.77)		31	50.90 (17.34)	
Post	28	66.47 (17.14)	−0.93 (−2.89 to 1.03)	28	58.53 (20.59)	−0.44 (−2.40 to 1.52)
3 months	25	62.89 (20.33)	−0.70 (−2.66 to 1.26)	26	58.97 (19.38)	−0.47 (−2.43 to 1.49)
6 months	21	62.96 (20.36)	−0.71 (−2.67 to 1.25)	25	65.78 (23.61)	−0.86 (−2.82 to 1.10)
12 months	18	65.83 (21.73)	−0.89 (−2.85 to 1.07)	23	62.32 (24.96)	−0.66 (−2.62 to 1.30)

Effect sizes are calculated by subtracting the mean scores at post treatment time points from the mean scores at baseline time points and divided by the baseline standard deviation for Telephone CBT and Face to Face CBT separately.

out depended on previous fatigue scores since the confidence intervals for dropout and non-dropout overlap at various time points. A similar trend was noted for social adjustment scores. However, for physical functioning, participants with very low scores at baseline tended to drop out in the post treatment period; this suggests that job status and earlier values predicted the later dropout and hence in the random effects model, the analysis of which assumes only that the data are Missing At Random (MAR), these were included in the model to assess group differences.

Group comparisons

The results of the random effects model fitted to three different outcome measures, namely fatigue, social adjustment and physical functioning, are summarized in Table 3. For fatigue, the explanatory variables sex and number of sessions were included in the model as they were significantly predicting the fatigue scores at a liberal 10% level in addition to job status, which was a predictor of dropouts. The interaction between group and time was not statistically significant (chi-squared = 3.29, $df = 3$, $p = .35$) and hence it was removed from the original model and only the main effects of group and time were tested along with the baseline variables in the final model. The telephone CBT group and face to face CBT group did not differ significantly ($z = -1.31$, $p = .19$) with respect to fatigue scores. Also, there was

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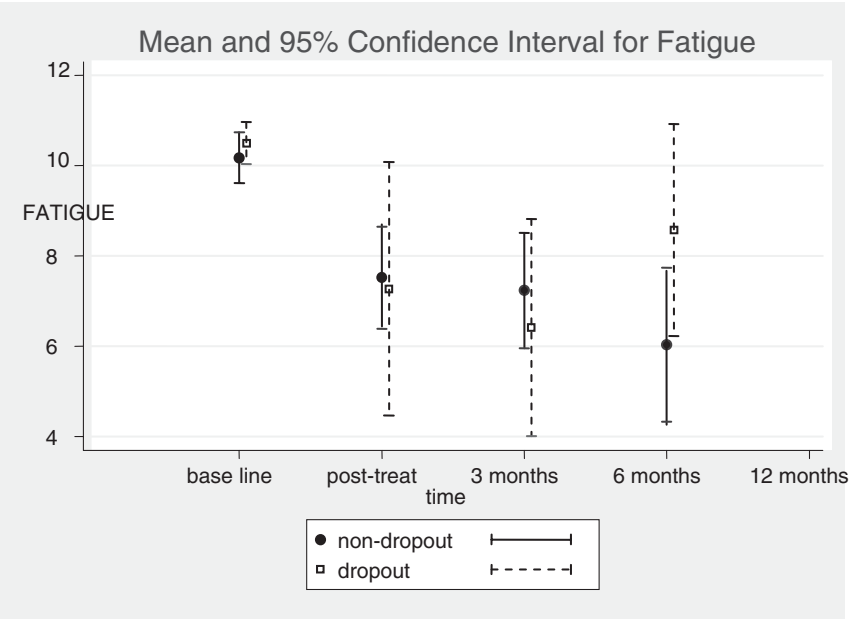

Figure 2. Mean and confidence interval of fatigue scores for dropout and non-dropout groups at various time points

no evidence for the predictive effect of baseline scores on later scores ($p > .05$). The fatigue scores at 3 months, 6 months and 12 months after treatment did not differ significantly (all p values $> .05$) when compared to the fatigue scores at post treatment. The predicted mean and 95% confidence intervals for the two groups at all time points are shown in Figure 3.

The model for social adjustment included age, sex, marital status and baseline scores as explanatory variables along with job status as predictors of dropout. Since the interaction between time and group was not significant (chi-squared $= 3.39$, $df = 3$, $p = .34$), this term was removed from the model and the final model contained the main effects of group, time and predictor variables. No significant difference ($z = -1.57$, $p = .117$) between telephone CBT and face to face CBT groups were observed. As expected, the baseline social adjustment scores significantly ($z = -6.57$, $p<.001$) predicted the later scores at various time points. The social adjustment scores at 3 months and 6 months after treatment did not differ significantly (all p values $> .05$) when compared to the scores at post treatment time point. However, the social adjustment score at 12 months after treatment significantly reduced when compared to the score post treatment (p value $= .013$; see Table 3).

For physical function, none of the baseline variables were significantly predictive of MOS scores at a liberal 10% level. Hence the analysis model included baseline scores and job status in addition to group and time. Since the interaction between group and time was not significant (chi-squared $= 5.91$, $df = 3$, $p = .12$), the interaction term was removed from the final model and only the main effects of group and time were tested along with job and baseline score. The baseline score significantly predicted ($p<.001$) the later physical function scores. The

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Table 3. Comparison of post-treatment with different time points

Time points	Effec size*t	Time diff.**	z	p value	95% confidence interval	Group by time interaction
Fatigue						
3 months	−0.10	−0.84	−1.38	0.168	−2.04 to 0.36	$\chi^2 = 3.29$, $df = 3$
6 months	−0.21	−1.02	−1.59	0.112	−2.28 to 0.24	$p = .349$
12 months	−0.04	−0.47	−0.72	0.469	−1.75 to 0.81	
Social adjustment						
3 months	0.11	−0.32	−0.37	0.711	−2.00 to 1.36	$\chi^2 = 3.39$, $df = 3$
6 months	−0.05	−0.39	−0.44	0.663	−2.17 to 1.38	$p = .336$
12 months	−0.19	−2.29	−2.49	0.013	−4.10 to − 0.49	
Physical function						
3 months	−0.08	0.32	0.15	0.878	−3.78 to 4.42	$\chi^2 = 5.91$, $df = 3$
6 months	0.10	3.55	1.62	0.104	−0.73 to 7.84	$p = .120$
12 months	0.07	4.62	2.02	0.043	0.14 to 9.09	

*Effect sizes are calculated by subtracting mean scores at 3, 6 and 12 months after treatment time points from the mean score immediately after treatment (comparison group) and divided by the standard deviation of the comparison group. ** Time difference refers to the estimated difference in out come measures between post treatment and various time points (3 months, 6 months and 12 months) accordingly.

physical function scores did not differ significantly ($z = 0.56$, $p = .576$) between participants who received telephone CBT and face to face CBT. A significant increase (p value = .043) in physical function score was observed at 12 months after treatment when compared to the score at post treatment. However, there was no evidence for a significant increase (all p values $> .05$) at 3 months and 6 months after treatment compared to post treatment scores (see Table 3).

For self-rated global scores, no significant difference was found between groups on global improvement post-treatment (chi-squared = 0.16, $p = .689$), at 6 months (chi-squared = 1.78, $p = .182$) or 12 months after treatment (chi-squared = 0.1, $p = .982$). There was no significant difference between groups on their satisfaction with outcome of treatment post-treatment (chi-squared = 0.29, $p = .589$), at 6-months (chi-squared = 0.16, $p = .688$) or 12 months after treatment (chi-squared = 0.2, $p = .889$). Most participants reported being moderately satisfied or very satisfied with the outcome of treatment at each time point, with ranges between 78% to 80% in the face to face group and 72% and 80% in the telephone group (see Table 4).

Discussion

Significant reductions in scores of fatigue, social adjustment and physical functioning occurred post-treatment in both the face to face CBT group and telephone CBT group and were maintained throughout the follow-up period of one year. There were no significant differences on any primary outcomes between subjects in the two groups, which indicate that

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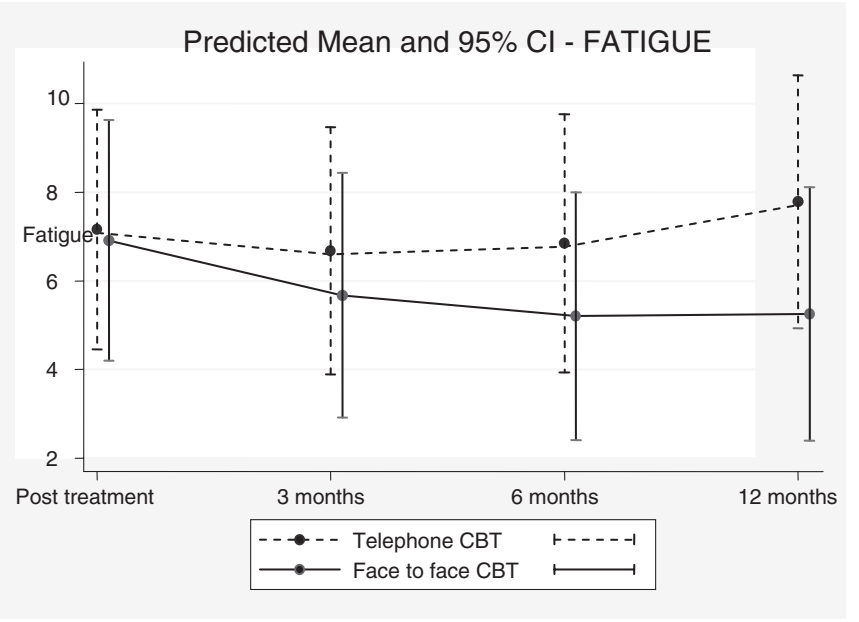

Figure 3. Predicted mean and 95% confidence interval of fatigue scores for telephone CBT and face to face CBT groups at various time points (graph adjusted for sex = female, job = yes and anxiety = 11.2 (mean value))

our hypothesis that face to face CBT was more effective than telephone CBT for patients with CFS was not confirmed. The fact that a significant difference was not seen between treatment groups on primary outcome measures is not disappointing. Telephone treatments were shorter in length and therefore less costly. However, it is difficult to be precise about specific savings as we did not carry out an economic analysis in this study. The results from this study are in keeping with a well designed randomized controlled study by Lovell et al. (2006), where telephone CBT was as effective as face to face CBT in patients with obsessive compulsive disorder. Both of these conditions are severely disabling and it is encouraging to note that significant improvements can be made with this mode of delivery. Another factor that cannot be ignored in terms of explaining the changes associated with telephone treatment is the face to face contact on two occasions. The initial assessment was carried out face to face and this may have helped the therapeutic alliance at the start.

The considerable number of dropouts may question the findings of this study. However, the post hoc power calculation showed a sample of 50 (25 in each group) had a mild to moderate effect size of 0.35, which confirms that the results obtained are reliable. One may have assumed that there would have been more dropouts from the face to face arm because of the increased accessibility afforded by telephone sessions. However, this was not the case; a variety of reasons were given by participants in both groups and accessibility was not one of them.

This study showed smaller changes in mean scores on our main outcomes than our previous randomized controlled trial in which we compared CBT with relaxation for patients with CFS

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Table 4. Self-rated Global Improvement scores

		Telephone CBT		Face to Face CBT		Chi-square analysis ($df = 1$)	
Time points	Rating	*N*	%	*N*	%	χ^2	*p*
Post-treatment	*Global improvement* v.much better/much better	14	48	15	54	0.16	.689
	Little better-v.much worse	15	52	13	46		
	Satisfied with outcome Moderately/very satisfied	21	72	22	79	0.29	.589
	Slighty satisfied-v. dissatisfied	8	28	6	21		
6-month follow-up	*Global improvement* v.much better/much better	8	40	15	60	1.78	.182
	Little better-v.much worse	12	60	10	40		
	S*atisfied with outcome* Moderately/very satisfied	15	75	20	80	0.002	.964*
	Slighty satisfied-v. dissatisfied	5	25	5	20		
12 month follow-up	*Global improvement* v.much better/much better	11	55	13	57	0.01	.92
	Little better-v.much worse	9	45	10	43		
	S*atisfied with outcome*	16	80	18	78	0.06	.813*
	Moderately/very satisfied Slightly satisfied-v. dissatisfied	4	20	5	22		

*with yate's correction.

(Deale et al., 1997). Although a higher percentage of patients in the Deale et al. (1997) trial reported feeling very much better or much better, satisfaction with treatment was similar in both studies. It is important to consider why results from this trial were not as impressive as our earlier RCT. Participants in this study had a longer duration of illness and were older, factors that have been noted in other studies to have an association with symptom persistence (Joyce, Hotopf and Wessely, 1997). There was only one therapist in the Deale et al. trial whereas eight therapists treated participants in this trial which is more indicative of real life. Therapists may have had diverse treatment outcomes. However, when using a different but much larger sample of consecutive patients receiving CBT in the same setting we did not find any evidence of therapist effects (Cella**,** Stahl, Reme and Chalder, 2011). It is of course possible that some of the participants who did not complete questionnaires had improved and therefore decided to disengage with the service.

We also compared the results from the present study to results from routine clinic practice at this clinic (Quarmby, Rimes, Deale, Wessely and Chalder, 2007). Fatigue and social adjustment scores at 6 months follow-up in the face to face group in this study were slightly better than the outcomes from our study of routine clinical practice (Quarmby et al., 2007). The results from this study (0.35) suggest mild to moderate clinical effectiveness based on estimations by Cohen (1988).

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Limitations of this study include the high dropout rate and non-completion of measures. However, there were no differences in the dropout rate between the groups and this trial was more representative of normal clinical practice as seen in Quarmby et al.'s (2007) examination of outcomes outside the confines of a randomized controlled trial. One could argue that it is difficult to accurately draw the conclusion that the interventions are effective as we did not find a difference between them and therefore change over time could be due to chance. However, evidence from previous trials, as already mentioned, have demonstrated the efficacy of face to face CBT for patients with CFS (Deale et al., 1997; Prins et al., 2001; Sharpe et al., 1996). Independent therapist ratings would ideally have been carried out. Methodologically, it would have been better to have randomized participants in blocks to ensure even numbers in both groups. One of our inclusion criteria was having CFS for less than 10 years as we were concerned that a longer duration raised concerns over the accuracy of the diagnosis. However, this may have meant that some patients were excluded who could have benefited. The absence of recording participants' sessions to ensure treatment fidelity was a limitation but regular supervision, detailed discussion of the content of sessions, and observation of notes partially overcame this.

In summary, notwithstanding the several limitations to this study, the results highlight that telephone treatment can bring about meaningful change in patients with CFS. For those patients who cannot travel to the hospital because of excessive fatigue or because they live a long way from the hospital or have child care or work commitments, it is a credible alternative to face to face treatment. Both treatments were acceptable to the majority of participants who completed treatment, given that 72%–80% of participants in the telephone group and 78%–80% of participants in the face to face group reported being moderately or very satisfied with the outcome of treatment. Although there was an average of 25% dropout during treatment, no participant suggested that the reason for them dropping out was dissatisfaction with the treatment. It is interesting to note that participants who were working and did not have a job to return to were significantly more likely to drop out during treatment or follow-up than those who were not working. This issue is a complex one, potentially involving social reinforcers such as benefits (Bentall, Powell, Nye and Edwards, 2002) and significant others (Schmaling, Smith and Buchwald, 2000), making change on the patients part very difficult.

We suggest that the results of this study are generalizable to other secondary care CFS populations. The new mode of delivery comprising mainly of telephone sessions plus two face to face sessions was highly structured and manuals were adhered to by therapists, therefore making the treatment easy to replicate.

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