A Long Term Follow-up of a Multi-Disciplinary Approach to Chronic Fatigue Syndrome

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2012

Doctorate in Clinical Psychology

Declaration

I, Amalia Houlton, confirm that the research reported within this document for the award of Doctorate in Clinical Psychology, is entirely my own and has not been submitted for any other award.

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Abstract

Literature Review

A critical review of the literature investigated the question 'what is the strength of the evidence base for Cognitive Behavioural Therapy (CBT) for Chronic Fatigue Syndrome (CFS) on fatigue and physical functioning?' The studies reviewed included nine group based CBT studies, and six individually based CBT interventions. The evidence base was found to be weak, study designs complex making comparison difficult. There was some positive evidence for efficacy of CBT on fatigue and physical functioning in CFS sufferers, but it was found that some alternative interventions used as comparators such as Graded Exercise Therapy and Counselling showed similar results. There was no clear difference between the efficacy in individual or group based CBT approaches and long-term outcomes for both approaches were inconclusive.

Research Report

The current study evaluated the long-term effectiveness of a multi-disciplinary approach to CFS and explored patients' experience of service use through a longitudinal questionnaire based survey of patients who used a British multi-disciplinary secondary care specialist service. Measures were taken pre and post intervention, and at follow up (average 34 months post intervention). Telephone interviews with 10 participants based on a semi-structured interview schedule were used to explore in-depth information about experience of using the service.

Gains made in outcome measures were mostly maintained and continued to improve at follow up. A thematic analysis of interviews found that patients felt positively about the service, and gained validation, education and management skills from the intervention. Areas highlighted to be developed were improving access, reducing gate-keeping by primary care medical services, and offering all patients both group and individual interventions.

Critical Appraisal

A summary of the researcher's reflections on the research process can be found in the critical appraisal

Acknowledgements

For their assistance and support in producing this research I would like to thank:

Marilyn Christie
Eric Gardiner
2009-2012 Leicester DclinPsy cohort and staff
Bozena Smith
Maxine Webster
Alex Gasson
My family and friends

Word Counts

Thesis Abstract: 298
Literature Review (excluding abstract, tables, figures and appendices): 6954
Literature Review Abstract: 295
Main Report: (excluding abstract, tables, figures and appendices): 12,500
Main Report Abstract: 300
Critical Appraisal: 2907
Appendices (excluding mandatory appendices): 6302
Total word count (excluding mandatory appendices): 28,961

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What is the Strength of the Evidence Base for Cognitive Behavioural Therapy for Chronic Fatigue Syndrome on Fatigue and Physical Functioning?

Amalia Houlton

Background
Chronic Fatigue Syndrome (CFS) is a highly debilitating illness without a known cause and with symptoms spanning physical, neurological and psychological domains. UK treatment guidelines recommend the use of Cognitive Behavioural Therapy (CBT) for patients suffering mild to moderate CFS, although this has a relatively small research base.
Aims
The current review aimed to determine the strength of the evidence base for CBT for CFS on fatigue and physical functioning, with the goal of updating the evidence base from a meta analysis carried out in 2008 (Price et al.)
Method
Computer aided literature searches of bibliographic databases and hand searches of selected articles were carried out. The author consulted with a local CFS team to determine other relevant research. A data extraction form was created and piloted.
Results
Fifteen studies were reviewed. The evidence base for CBT for CFS was found to be weak, and study designs made comparison difficult. There was some positive evidence for efficacy of CBT on fatigue and physical functioning in CFS sufferers, but some alternative interventions used as comparators such as Graded Exercise Therapy and Counselling showed similar results. There was no clear difference between the efficacy in individual or group based CBT approaches and long-term outcomes for both approaches were inconclusive.
Conclusions
Future research is needed to look at alternative interventions for CFS. Research should aim to use a smaller number of outcomes and simplify its methodology in order to be more comparable, ethical, and add to the evidence base. The current trend found in some of the research of separating out components of CBT to determine their individual efficacy does not seem clinically important.

Introduction

What is Chronic Fatigue Syndrome?

Chronic Fatigue Syndrome (CFS)/Myalgic Encephalopathy (ME), is characterised by a wide range of symptoms, including physical and cognitive impairment, such as continual exhaustion, problems with body temperature regulation, and difficulty with concentration and memory. No discrete “physical or psychological disorder” (Price et al., 2008) has been found underlying these symptoms. Due to the heterogeneity of symptoms, there has historically been much debate around diagnostic criteria, and, whether CFS/ME is a distinct disorder at all. There is no diagnostic test that can be carried out, and people are usually diagnosed when certain symptoms have been exhibited over a period of time, and other conditions have been excluded. Although both CFS and ME are used to describe this condition, for the purpose of this report it will be referred to as CFS.

Diagnostic criteria developed in parallel in the UK and the USA, and differ slightly in their approach. The United States Centre for Disease Control (CDC) specifies that a diagnosis should be considered if sufferers experience: unexplained fatigue lasting for a minimum of six months, as well as at least four symptoms from: impaired memory; post exertional malaise; unrefreshing sleep; muscle pain; multi joint pain; headaches; sore throat; tender cervical or axillary lymph nodes, (Fukuda et al. 1994), and other disorders have been excluded. Hickie et al. (2009) carried out a cross-

cultural study investigating patients' views of the key features of their illness. They identified: prolonged fatigue and musculoskeletal pain; impaired neurocognitive function; symptoms of inflammation; disturbed sleep; and disturbed mood. A notable difference between these findings and the CDC criteria is the inclusion of disturbed mood by patients, which was not included by the CDC. Hickie et al. argued that historically, depressive symptoms have been attributed as a by-product of the illness, but claimed that their findings suggested it is a key component, independent of other precipitating factors or risk factors. The UK Oxford diagnostic criteria (Sharpe et al., 1991) were developed to assist recruitment of participants to research on CFS, and they do incorporate mood disorder. They specify, a six-month or more period of fatigue, with a definite onset, affecting both physical and mental functioning, which is present for more than 50% of the time. They also state "other symptoms may be present, particularly myalgia (muscle pain), mood and sleep disturbance" (Sharpe et al., 1991, pp119). The incorporation of mental fatigue and mood disturbance by the UK and not the US criteria, creates difficulties for researchers in participant recruitment. Although debate still remains, the CDC criteria tend to be used in American and European studies and the Oxford criteria are more commonly applied in UK based research.

Prevalence and prognosis

The general population prevalence for CFS is estimated to range between 0.2 and 2.2% in community samples (Malouff et al., 2008). Cairns and Hotopf (2005) reviewed studies about the prognosis of CFS, and found that full recovery was rare but improvement in symptoms was likely (Cairns & Hotopf, 2005). Much of the prevalence research is based on data from North America and the Netherlands and extrapolated to the UK. Due to this, the interim report of the All Party Parliamentary Group on ME (2009) recommended as a top guideline to the Department of Health that research to determine accurately the number of patients with CFS/ME in the UK is required.

Treatment and service provision in the UK

Due to the lack of understanding about aetiology, and the wide variation of symptoms in sufferers, the illness of Chronic Fatigue Syndrome (CFS) was not included in the World Health organisation (WHO), International Classification of Diseases (ICD) until 1998. In 1990, a recommendation was made to create a code for CFS, which did not happen due to lack of agreement on causes, a requirement for code creation. There was a long delay between the ICD classification and guidelines for treatment being

recommended. In the UK, the first National Institute for Clinical Excellence (NICE) guidance was not published until 2007 (Turnbull et al., 2007).

The NICE guidelines are based on research into treatment efficacy, and on input from specialists working in the area. They recommend diagnosis if symptoms have been persistent for four months or more in adults. The list of symptoms leading to diagnosis can be found in Appendix A.

Research on CBT for CFS

Some large reviews of the literature on CBT for CFS have been carried out. Malouff et al. (2008) carried out a meta-analysis of effect sizes from 13 studies, finding a mean effect size of 0.48 suggesting moderate efficacy for fatigue reduction. However, this ranged widely, and two studies showed 0 effect size for CBT. The results showed a higher effect size for physical fatigue compared to mental fatigue.

In 2008, Price et al. carried out a meta-analysis of 15 studies of CBT for CFS. As well as CBT in its pure form, they also included the 'third wave' approach, incorporating aspects of mindfulness, compassion focused, and acceptance and commitment therapy. The findings were that, on most measures of fatigue and physical functioning, the CBT group showed significant improvement compared to non-CBT groups. At a longer term

follow up, these findings were not all maintained, and the medium and long-term effectiveness of CBT was inconclusive.

Aim of the Current Review

The current literature review aimed to investigate the strength of the evidence base for CBT for CFS on fatigue and physical functioning, in terms of updating the evidence base since the 2008 reviews were published.

Method

Inclusion Criteria

Participants

Studies were included in the current review that used participants with a diagnosis of Chronic Fatigue Syndrome (CFS), who were aged 18 and above. The majority of outcome measures used in CFS research are validated on adults, and for the purposes of the current review, it was felt that studies using adolescents or children were not comparable with those using adults.

Studies explicitly using participants with CFS plus a co-morbid condition were included in the current review and the co-morbid exclusion criteria of each study were evaluated. A high level of co-morbidity has been found with CFS and other psychiatric disorders, in particular major depressive disorder, however many research studies exclude participants who have a co-morbid diagnosis. Matsuda et al. (2009) conducted a study into treatment of patients with just a CFS diagnosis and those with co-morbid psychiatric disorders and concluded that the co-morbidity was not significant in illness outcome, and was therefore a questionable cause for exclusion from research.

Interventions

Studies were included that used Cognitive Behavioural Therapy (CBT), alone or in combination with another intervention. This incorporated Graded Exercise Therapy (GET), Activity Management and Pacing. The specific aspects of each CBT intervention were reviewed to assess differences. Studies that used interventions not including both cognitive and behavioural elements were excluded. Although it has been found that interventions such as Rational Emotive Behaviour Therapy (REBT) (Balter, 1997) and GET (Moss-Morris et al., 2005) alone have shown effectiveness for CFS, the current review was concerned with the strength of evidence for CBT interventions. The mode of delivery, characteristics of those involved in the delivery, and setting of the intervention were also explored in the current review. Comparator studies were included and the comparator clearly defined. Wittkowski et al. (2004) highlighted that, to date, the research base for individual CBT was stronger than for group CBT. To explore this further, both approaches were incorporated into the current review.

Outcomes

Studies with outcome measures assessing fatigue and physical functioning were used in the current review. The length of follow up was compared for each study. Several new studies have been published using data from original trials. These were explored and related to the reviewed studies, however only the original study was critiqued in the current review.

Study Designs

The Downs and Black (1998) criteria for measuring study quality was used in the current review (Appendix B), as it is applicable to both randomised and non randomised studies. Studies were rated numerically on 27 variables, providing an overall global rating as well as a list of scores for internal and external validity, quality of reporting and power. The higher the score, the better the methodological quality of the study, with a maximum achievable score of 32. Table 3 (Appendix C) describes each study by design and scoring on the quality measure. The hierarchy of design quality from the York Centre for Reviews and Dissemination CRD (2009) was also utilised to assess study design. This ranks design in order of methodological superiority in order to minimise bias. (See Appendix B)

Due to the limited number of Randomised Controlled Trials (RCT's), studies with designs further down the hierarchy were incorporated into the current review, with design limitations discussed. Case series, case reports and purely qualitative studies were excluded due to bias in these study designs, however, where appropriate, they were used to inform the discussion of the quantitative literature. Economic evaluations were also excluded from the study, as they did not address the review question. Studies must have been published in English and searches were done between 2000 and 2011.

Search results

Computer assisted literature searches of bibliographic databases were carried out between August and November 2011. The references of selected articles were also hand searched to identify any further relevant studies. The author consulted with a local CFS team to gain information on relevant and current studies of which they were aware.

Price et al. (2008) highlighted the heterogeneity of CBT for CFS, which often incorporates activity management, graded exercise therapy and pacing. To ensure as comprehensive a search as possible, these were incorporated into the search criteria. Keywords used were: Chronic Fatigue Syndrome, CFS, myalgic encephalomyelitis, cognitive behavioural therapy, CBT, cognitive therapy, behaviour therapy, graded exercise therapy, activity management, pacing. Search findings are listed in Appendix D.

In total, 15 studies were reviewed using a data extraction form adapted to fit the research question. This was piloted and revised at the start of data extraction. (Appendix E).

Results

Due to the heterogeneity of what is meant by a CBT intervention, and the small sample size of some studies, a meta-analysis approach was not considered possible. A narrative data synthesis is therefore provided below.

Narrative Synthesis

Of the 15 studies reviewed, nine used group based CBT interventions, and six used individual CBT interventions. It was felt helpful to compare the studies within these subgroups. Tables referred to throughout the narrative synthesis can be found in Appendix C. Table 1 summarises each study.

Group Based Cognitive Behavioural Therapy

The strength of the evidence base for CBT for CFS was assessed by reviewing the studies on: design; outcome measures; the characteristics of the CBT approach used; the comparator groups used; and length of follow up.

Study design

Six studies were randomised controlled trials (RCT's) (Jason et al., 2007, Nunez et al., 2011, O'Dowd et al., 2006, Prins et al., 2001, Stubhaug et al., 2008, and Schreurs et al., 2011), and one was a non-randomised controlled trial (Bazelmans et al., 2005). These are at the top of the CRD hierarchy, and scored highest on the Downs and Black measure.

Table 2 in Appendix C shows the results of the Downs and Black scoring. No studies listed characteristics of participants lost to follow up, and only Stubhaug et al. (2008), listed adverse events occurring due to the

intervention. Due to studies often having varying length of times for participants between pre-study measures and follow up, it is important that analysis carried out takes this into account. This was done by Jason et al. (2007); Prins et al. (2001); Schreurs et al. (2011), and Stubhaug et al. (2008). All studies except Saxty and Hansen (2005) and Wittowski et al. (2004), had sample sizes large enough to carry out statistical tests for significance.

All group studies used the Fukuda (1994) criteria for diagnosing CFS, making results more comparable across studies. In addition, Stubhaug et al., (2008) primarily used the ICD 10 criteria for neurasthenia, and analysed how many of these participants met the Fukuda or Oxford (Sharpe et al., 1991) criteria. The study did not however analyse the results by these groups to determine if there was a difference in efficacy of CBT.

Sample sizes ranged from 6 to 278 participants and dropout rates from 3% to 25%. Interestingly, one of the studies with a high dropout (Jason et al., 2007), offered monetary incentive to participants to complete both the trial and the follow up data, suggesting this did not assist with dropout reduction. Where stated, group size ranged from 6 to 16, and did not seem to be related to efficacy of CBT.

All group CBT studies stated gender and age of participants, although not all described these characteristics of the dropouts or non-responders. Across the nine group CBT studies, 194 out of 996 participants were male (19%)

and the mean age of participants ranged from 34-46 years. None of the studies compared efficacy of CBT by gender or age.

Exclusion criteria were discussed in all group CBT studies to various degrees except Saxty et al. (2005). Although not always explicitly stated, by their very nature, participants would have to be able attend the sessions, excluding those who may be very unwell or disabled by the condition. Table 1 shows all exclusion criteria, the key ones being concurrent: major psychiatric disorder; past major depressive disorder; and ongoing legal procedures. The range of exclusions suggests that in studies finding CBT effective, this can be said only for the specific selected sample. Due to the commonality of co-morbid psychiatric disorders, this may constitute exclusion of a significant minority of CFS sufferers, making generalisability of results questionable.

The length of time for which a participant had been diagnosed with CFS ranged between 2.7 and 6.8 years. Jason et al., (2007) did not state the average but commented that it was 'about five years longer than many previous studies' and used this as an explanation for findings not being as efficacious as expected. However, Schreurs et al. (2011), who had the longest average illness duration found efficacy for CBT on both fatigue and physical functioning.

When considering research findings and quality of study, the most well designed and described studies were: Stubhaug et al., 2008; Prins et al.,

2001; O'Dowd et al., 2006; Nunez et al., 2011, and Schreurs et al., 2011. Of these studies, four measured fatigue and all found significant improvement in the CBT group. All measured physical functioning, and three found significant improvement, whereas Nunez et al. (2011) found significant worsening of physical functioning in the CBT group and O'Dowd et al. (2006) found no significant change.

CBT Characteristics

All studies except Stubhaug et al. (2008), provided enough information about the elements of the CBT approach used to compare across studies. There was wide variation in what was incorporated into CBT, the only common element being 'cognitive challenging' (Table 3, Appendix C).

Graded exercise was incorporated into nearly all studies, either explicitly, or as part of the CBT intervention. Bazelmans et al. (2005) was the only study of suitable methodological quality which did not incorporate some form of graded exercise into their CBT group intervention. They found a non-significant trend in fatigue reduction, and that participants in the waiting list control had better improved physical functioning than the CBT group.

Jason et al. (2007) attempted to specifically deconstruct efficacy of elements of CBT by comparing with a cognitive therapy group and an anaerobic exercise group intervention. They found that both the CBT and cognitive therapy group had significantly better physical functioning outcomes than

the exercise group, with the cognitive group being superior. However they found no difference between the groups on fatigue reduction.

The number of sessions delivered ranged from 8-75, where stated group sessions lasted from 45 minutes to two hours and were delivered between twice a week and fortnightly, over a time period of between 8 weeks and 8 months.

The characteristics of therapist delivering the group CBT were described in all studies and consisted of a combination of nurses, physiotherapists, psychologists, social workers and occupational therapists. (Table 1, Appendix C)

When considering dosage of CBT, Schreurs et al. (2011) and Prins et al. (2001) provided the highest number of sessions and both found significant improvement in fatigue and physical functioning, however the inverse was not true; studies with the lowest number of sessions also found significant improvements in one or the other domain. Therefore, the number of sessions and period of time delivered did not seem to have an impact on findings.

Table 1 (Appendix C), illustrates the outcome measures used across the studies, which ranged in number per study from three to 14 and were mostly self-report questionnaires. Despite the large range of outcome measures,

for primary outcomes of fatigue and physical functioning, the measures used were valid and reliable and comparable across studies.

Comparator Groups

To reduce bias, comparator groups and controls should be of a similar 'dose', in terms of contact time, to the CBT intervention. In the nine Group CBT studies, this was only controlled for by O'Dowd et al. (2006). A similar potentially confounding variable in intervention, is the therapists delivering to each comparator group. Only Jason et al. (2007) used the same therapists to deliver interventions and comparator groups.

Table 1 in Appendix C shows the comparator groups used across studies. These included: Education and Support Groups; Guided Support Groups; No Treatment group; standard medical care; antidepressant medication and exercise counselling. Saxty and Hansen (2005), Schreurs et al. (2011) and Wittowski et al. (2004) used no comparator groups or control, meaning they could only compare their approach with previous studies.

Table 1 in Appendix C provides a summary of the findings for fatigue and physical functioning for all studies. In the group CBT studies controlling for 'dose' and therapist factors, O'Dowd et al. (2006) found CBT to have a significantly positive impact on fatigue but not on physical functioning. Jason et al. (2007), conversely, found a significant improvement in physical

functioning in the CBT group, but not fatigue. For physical functioning, the CBT group was less efficacious than the cognitive group comparator.

Both studies using support group comparators (Prins et al., 2001, O'Dowd et al., 2006) found the CBT group significantly improved on fatigue scores when compared to comparators. Physical functioning was significantly improved in Prins et al's CBT group, but this was not true of O'Dowd et al's findings. Neither study found differences between the support group and non-intervention group. In Stubhaug et al.'s 2008 study comparing CBT with an antidepressant and a placebo, a significant improvement was found in the CBT group for fatigue but not physical functioning. They found that the improvement was highest if CBT was delivered prior to medication.

In studies which used a CBT group and comparison non-CBT groups, some showed CBT to be superior to comparators, but not all, and the results were not consistent across fatigue and physical functioning measures.

Long term Outcomes

Studies varied in the length of follow up period post intervention (Table 1, Appendix C), with few measuring over a year post treatment. Physical functioning was found to be significantly improved at 12-month follow up by Bazelmans et al. (2005), and Nunez et al. (2011). Prins et al. (2001) found that their CBT group had significantly reduced fatigue and physical functioning when compared to control groups at six month follow up, but the

difference between groups was reducing over time. O'Dowd et al. (2006) measured at six and 12 months, finding no improvement on physical functioning at either point, and a trend in fatigue reduction, favouring the CBT group over comparators.

Overall, improvements found following intervention seem to be maintained at follow up assessments, but with the differences between comparators reducing over time. However, the variability of follow up time points makes this a very small amount of data to compare.

Summary

The results of the current review of group based CBT for CFS showed few studies of good methodological quality, and a mixed picture for the efficacy of this intervention. The four studies of highest methodological quality measuring fatigue, found significant improvements in the CBT group, and this was more efficacious than comparators where used. (O'Dowd et al., 2006; Prins et al., 2001; Schreurs et al., 2011; & Stubhaug et al., 2008).

For physical functioning, three methodologically superior studies found significant improvements in the CBT group (Prins et al., 2001, Schreurs et al., 2011; and Stubhaug et al., 2008) but two of the best-designed studies (O'Dowd et al., 2006, and Nunez et al., 2011) found either no difference in physical functioning (the former), or a worsening in physical functioning in the CBT group (the latter). Only Prins et al., and Nunez et al. found CBT to be significantly more effective than comparators for physical functioning

improvement. In the studies comparing post intervention with a follow up period, improvements were maintained but showed reductions over time in positive change.

The findings from the current review suggest that, although there is some evidence that CBT can improve symptoms of sufferers for CFS, both for fatigue and physical functioning, the evidence base is not strong, and few studies to date, are of a good methodological quality.

Individual CBT

Study design

Of the six studies using individual CBT as an intervention for CFS, two were RCT's (White et al., 2011, Ridsdale et al., 2009) and a randomised non-inferiority study (Tummers et al., 2010), which ranks similarly to RCT's on the CRD hierarchy.

The findings from the Downs and Black (1998) assessment can be found in Table 4, Appendix C. White et al. (2011) was the only study to describe unexpected negative consequences from the research, and only Ridsdale et al. (2001) described the characteristics of those lost to follow up. No studies attempted participant blinding, and only White et al. (2011) blinded those measuring outcomes.

Of the three most methodologically sound studies, White et al. (2011) found significant improvements in fatigue and physical functioning in the CBT group on pre and post measures, but this was not superior to the Graded Exercise comparator group. Tummers et al. (2010) did not find significant improvements in either domain compared to Care As Usual, although when looking at clinically significant improvement, there was a positive trend in the CBT group. Ridsdale et al. (2001) only described between-group, not within-group differences, and found no difference between CBT and Counselling comparator groups for fatigue reduction, with a trend in favour of the Counselling group.

Table 1 in Appendix C shows the diagnostic criteria used by each study. White et al. (2011) used both the Oxford (Sharpe et al., 1991) and Fukuda criteria, finding no significant differences in treatment efficacy by diagnostic tool.

Sample sizes ranged from 30 to 640, and dropout rates, when comparing initial sample to completers, ranged from 2% to 63%. Friedberg and Sohl (2009) had the highest dropout rate, attributing this partially to having a sample that was mostly employed and high functioning.

Gender was clearly stated in all studies except Akagi et al. (2001). 63% of their sample were female, but they did not clarify if this was of the original sample or the respondents. Of the remaining studies, there were a total of 1091 participants, 830 (76%) were female and 261 (24%) male. The mean

age of participants ranged from 37.4 to 45.8 years. Only Tummers et al. (2010) compared efficacy of CBT by gender or by age, finding no significant difference.

The average length of time for which a participant had been diagnosed with CFS ranged between 2.7 and 8.4 years. The study with the longest fatigue duration (Friedberg and Sohl, 2009) found a moderate effect size for fatigue reduction, and the study with the smallest mean fatigue (White et al., 2011) found significant improvement in fatigue and physical functioning in the CBT group, suggesting duration of fatigue may not be a significant factor in CBT efficacy.

The same un-stated exclusionary criteria as discussed for the CBT group studies can be applied to individual interventions. Notable differences were exclusions of people with a risk of self-harm, and those undergoing procedures relating to disability benefit (see Table 1 Appendix C).

Outcome measures used across the studies, which ranged from two to eight and were mostly self-report questionnaires (Table 1, Appendix C). As with the group CBT studies, all of these measures have been shown to be valid and reliable in a CFS population.

CBT Characteristics

All studies provided enough information about the elements of the CBT approach used to compare them (Table 5, Appendix C). As in the group studies, the only common element was ‘cognitive challenging’, and graded exercise was incorporated into some of the studies. Of the three studies not incorporating graded exercise, Tummers et al. (2010) found no significant improvement in fatigue or functioning in the CBT intervention participants, White et al. (2011) found significant improvements on both domains, but this improvement was also shown in their purely Graded Exercise Therapy comparator group, and Ridsdale et al. (2001) found no difference in efficacy between CBT and Counselling on fatigue reduction.

The number of sessions delivered ranged from six to 32, with the average number provided ranging from six to 14, across a time period of seven to 35 weeks. Length of sessions varied within interventions, ranging from up to 30 minutes at shortest, and up to 90 minutes at longest.

The characteristics of therapists delivering the group CBT were described in all studies (Table 1, Appendix C). Friedberg and Sohl’s (2009) intervention was provided by one of the authors, which may introduce bias. White et al. (2011) and Scheeres et al. (2008) were the only studies explicitly stating that specialists in CBT trained therapists involved in the intervention for CFS. Of these studies, Scheeres et al. found moderate effect size for fatigue reduction for their CBT intervention and low effects size for improvement in physical functioning. White et al. (2011) found significant improvement in both domains, but CBT was not superior to Graded Exercise Therapy.

Comparators

Comparator groups are shown in Table 1, Appendix C, and included Specialist Medical Care (SMC), Graded Exercise Therapy (GET), Adaptive Pacing, and Psychodynamic Counselling. Scheeres et al. (2008) benchmarked their study against historic research findings, Akagi et al. (2001) compared their findings with a naturalistic outcome study, that is No Treatment Control, at the same institution. Tummers et al. (2010) used a Stepped Care approach, with a comparison group having received a minimal intervention based on elements of CBT administered by telephone and email in a previous research trial. The intervention group had this minimal intervention with additional face-to-face CBT, with the same CBT therapists used for each group. They found no significant differences between the two groups, suggesting that a control group could have been used to draw conclusions regarding differences in intervention.

Of the two studies controlling for therapy dosage, Ridsdale et al. (2011) found no differences between their Counselling or CBT interventions. White et al. (2011) found significant improvement in fatigue and physical functioning in both the CBT and Graded Exercise group, but, contrary to expectations, not in the Pacing group. As so many of the other studies used pacing techniques as part of their CBT intervention, it is not possible to draw useful comparisons between studies with this finding.

Long term Outcomes

White et al. (2011) and Ridsdale et al. (2001) incorporated long term follow up in their studies of up to one year, and six months respectively. Ridsdale et al. found CBT and Counselling to be comparable in fatigue reduction, with a positive trend in favour of Counselling at six months. White et al. found improvement in fatigue and physical functioning to be significant and increasing at 52 weeks for both the CBT and the Graded Exercise Group when compared to Specialist Medical Care and Adaptive Pacing.

Akagi et al.'s (2001) long-term follow-up of an intervention found functional impairment significantly reduced at all time points (6-12 months, 1-2 years, and 2-4 years) when comparing self report for illness at its worst, and self report over the month prior to outcome measure completion.

Summary

It proved difficult to compare studies using an individual based CBT intervention for CFS due to the variation in the interventions offered, the type of comparator group, and the analysis used in the studies.

Of the three methodologically superior studies, White et al. (2011) found significant improvement on fatigue and physical functioning within the

individual CBT sample, this was not more efficacious than a Graded Exercise comparator. Ridsdale et al. (2001) compared between-group fatigue measures and found a trend in favour of the sample receiving Counselling. Tummers et al. (2010) did not find any significant differences between their sample receiving individual CBT, and those receiving Care as Usual, although a trend in favour of the CBT group for clinically significant improvement was evident.

As in the group CBT studies, positive differences were maintained at follow up (maximum 12 months), for individualised CBT. In White et al.'s study (2011), this trend was increasing, which was contrary to the group based intervention results.

Of the studies in the current review, the majority attempted to reduce bias and improve quality by their methodology. However the current review has demonstrated that strict exclusionary criteria, gender bias in samples and the wide variety of what is incorporated into a ‘CBT’ intervention, means the results are not easily generalisable, and conclusions difficult to draw.

Discussion

The current review aimed to assess the strength of the evidence base of Cognitive Behavioural Therapy for fatigue and physical functioning in Chronic Fatigue Syndrome (CFS). An electronic database search was carried out, and 15 articles were selected for review: nine studies of group based CBT and six studies of individual face-to-face CBT.

All three methodologically superior individual based CBT studies found improvement in the CBT group on fatigue and physical functioning. However, White et al. (2011) found more improvement in a graded exercise comparator than in the individual CBT sample, Ridsdale et al. (2001) found most improvement in a counselling comparator, and Tummers et al. (2010) found a non significant trend for improvement in the stepped care CBT intervention (guided self instruction followed by CBT) when compared to Care as Usual, (waiting list followed by CBT).

For group based CBT, the four studies of highest methodological quality measuring fatigue, found significant improvements in the CBT group, and that it was more efficacious than comparators where used. (O'Dowd et al., 2006; Prins et al., 2001; Schreurs et al., 2011; and Stubhaug et al., 2008). For physical functioning, Three methodologically superior studies found significant improvements in the CBT group (Prins et al., 2001, Schreurs et al., 2011; and Stubhaug et al., 2008) but two of the best-designed studies (O'Dowd et al., 2006, and Nunez et al., 2011) found either no difference in

physical functioning (the former), or a worsening in physical functioning in the CBT group (the latter). Only Prins et al., and Nunez et al. found CBT to be significantly more effective than comparators. In the studies comparing post intervention with a follow up period, improvements were maintained but showed reductions over time in positive change.

A critical review of the literature highlighted the complexities of research into CBT for CFS, with multiple outcome measures and approaches to CBT being used. The complexity of some studies may have negatively impacted on result quality. For example Stubhaug et al. (2008) stated "some of the findings can be questioned in view of both the complex combination of interventions and the small number in each treatment group" (Stubhaug et al., 2008,p.221). There is scope for many more elements of this type of research to be reviewed, for example setting of the service, language and cross-cultural comparisons. The current review found that in several studies, CBT was not superior to comparator groups for fatigue and/or physical functioning, in particular, Graded Exercise Therapy, Cognitive Therapy and Counselling comparators. Ridsdale et al. (2001) concluded from their CBT versus counselling study, that other considerations such as cost and how easy access is to intervention should be taken into account when considering treatment. Training and supervision of staff for different interventions is a cost which may vary with intervention offered.

Developing the Evidence Base

The Price et al. (2008) meta-analysis found CBT to be significantly better than Care As Usual for fatigue, with CBT showing a trend for being better

than other interventions for fatigue and physical functioning as well. Findings at longer-term follow up in the studies reviewed by Price et al. were inconclusive. The current review included four of the 15 studies used in the Price et al. analysis and findings were similar in that individual based CBT studies found improvement in the CBT group for both physical functioning and fatigue. A difference however, with the Price et al. results was that this improvement was no more, and sometimes worse, than shown in comparator groups of Graded Exercise Therapy and counselling. Group based CBT was found in the current review to be more consistent with the Price et al. report: improvements were shown most in fatigue measures, and these improvements tended to be better than comparator groups. Consistent with Price et al's. (2008) findings, long term results were not conclusive across studies appraised in the current review, and the length of follow up was varied, mostly no longer than a year post intervention. All of the currently reviewed studies except for White et al. (2011) had follow up results where post treatment improvements were reducing over time. Other research for CBT for CFS has found mixed results at longer term follow up, with positive results maintained found by Knoop et al. (2008), and Marlin et al., (1998), but Deale et al., 2001, found positive outcomes were not maintained at five year follow up.

Theoretical implications

The results of the current literature review suggest some benefit from both group and individual CBT interventions for CFS**.** Although there is no distinct

cause found for CFS, several studies have proposed contributing and perpetuating factors which form the basis for therapeutic intervention. Van Houdenhove and Luyten (2003) summarised a biopsychosocial approach, and suggested that interventions should be individualised, and therapy should incorporate treatment of co-morbid depression and anxiety and sleep disturbance. Patients should be offered a theory of the illness which incorporates the link between physical and psychological elements. The rationale of understanding CFS from a CBT viewpoint is that key perpetuating factors of the illness are: fear of activity making the illness worse; activity avoidance; boom and bust activity cycles; disturbed sleep, symptom focus; perfectionist personality traits; life stressors and low mood (Burgess and Chalder, 2004). This rationale was used in the training of therapists in the 2011 PACE trial (White et al., 2011). These two approaches have a similar understanding of aetiology, but differ in their approach that a standardised treatment can be used versus individualising the therapy. Interestingly, Wallman et al. (2004), compared GET with relaxation for CFS, and found significant improvements in fatigue and physical functioning in the GET group. One explanation they gave for this was participants altering their beliefs about exercise following the positive outcome of the intervention. This is similar to the rationale used for a CBT approach.

Critique of studies

It is important to highlight, that when critiquing studies on methodology, and particularly using measures such as Downs and Black (1998), which rely on what is reported in the study, that all studies will have stringent criteria for publication leading them to have to be selective over what information they can include.

The current review found studies difficult to compare, due to the high number and range of outcome measures. Samples were biased in favour of ambulatory patients, and interventions being set up in a way likely to exclude people who are employed.

A range of explanations were given in the reviewed studies as to why predicted results were not found. Participants being less severely affected by the condition was suggested by Jason et al. (2007) and Friedberg and Sohl (2009). Bazelmans et al. (2005), however felt that the least severely affected participants benefited most from their CBT group. Cella et al. (2011) investigated subgroups of CFS patients given CBT including severity of different symptoms, and concluded that CBT should be offered to all patients irrespective of what severity category they fell into. Jason et al. (2007) felt the comparator groups were too similar, and Bazelmans et al. (2005) felt there was too much emphasis on rest and relaxation and not enough on activity management. Prins et al. (2001) and Bazelmans et al. (2005) both suggested inexperienced therapists may have affected the

results, although the findings of the current review suggest that training of therapists does not seem to affect outcomes of studies.

Ethical Issues

Issues highlighted by the current review include the ethics of administering large batteries of self-report outcome measures to patients with Chronic Fatigue Syndrome, characterised by cognitive problems and mental fatigue. Some studies had very small sample groups, failing to reach power calculations, suggesting the questionable utility of carrying out the research. In addition, the wide variety of interventions used as comparators brings into question the power dynamics involved in studying patients suffering a condition with such a lack of clarity over cause, and such a range of symptoms. Patients are likely to be desperate for assistance and perhaps feel lack of agency over treatment options. As with all research studies, funding needs to be assessed. Some of the CFS research is done in collaboration with charities for the condition. The motivation behind such funding should be considered, and the impact this may have on reporting of results.

Future research

Some of the currently reviewed literature has attempted to separate the exact elements of CBT and the difference between this and other therapies. It may, perhaps, be more clinically beneficial to continue researching the

models that seem most effective, to increase the robustness of the evidence base. The findings of the current review were that many of the studies incorporating GET into their CBT approach had positive results for fatigue and physical functioning, and White et al. (2011) found no difference between the GET and the CBT group. This suggests that GET can have some benefit for sufferers of CFS and is therefore useful to incorporate into future research interventions.

The long-term outcomes of CBT for CFS are inconsistent and not well researched, and further research to understand these inconsistencies is needed. There is scope to include elements of continued intervention at longer time points to determine if this has a positive impact on results, such as ongoing contact with a therapist or group members.

There is a question to debate as to whether it is helpful for some studies to stringently manualise their CBT approach, when other studies seem to individualise the approach, especially when NICE guidance recommends individualisation of treatment. Research by Van Houdenhove and Luyten (2008) suggested that effectiveness and acceptability of CBT may depend on customizing the approach to take heterogeneity of symptoms into account.

Critique of Current Review

The main limitation of this review was the constraint of using the Downs and Black (1998) tool for assessing study methodology. The measure scores weakly studies which do not explicitly state all of their methodology. This meant that some studies may have been classed as methodologically inferior, and therefore less focus given to their results, when they may have not had space to state all the relevant information.

The current review can be critiqued in terms of exclusion criteria for studies. Studies using adolescents, and using interventions incorporating 'third wave' elements of CBT as well as those applying CBT in more creative ways such as via the telephone and email were excluded, as it was felt by the author these were not helpful to compare with studies offering face to face CBT. The current review included studies which used co-morbidity as an exclusion criteria, which may have weakened the strength of the evidence.

The comparison used to structure this review could have been done in many ways. It was felt that comparing group versus individual interventions was a useful distinction to draw, however studies could have also been compared on those using explicitly GET in their CBT intervention versus those that did not, or comparing studies from different countries.

Conclusion

The current review found that the evidence base for Cognitive Behavioural Therapy for Chronic Fatigue Syndrome was not strong, and the designs of studies made them difficult to compare with one another. There was some positive evidence for efficacy of CBT on fatigue and physical functioning in CFS sufferers, but it was found that some alternative interventions used as comparators such as Graded Exercise Therapy and Counselling showed similar results. There was no clear difference between the efficacy in individual or group based CBT approaches and long-term outcomes for both approaches were inconclusive.

A key theoretical implication of this review is that an intervention based on the CBT assumption that people suffering CFS symptoms may be avoiding activity due to fear of exacerbating the condition, is not always relevant and a more biopsychosocial theoretical approach may be more helpful for some clients. The findings of the current review suggest that a wider range of psychological interventions may be beneficial for this client group.

Future research is needed to look at other interventions for CFS as opposed to CBT, particularly the comparator groups which showed unexpectedly positive findings. Research should aim to use a smaller number of outcomes and simplify its methodology in order to be more comparable, ethical, and add to the evidence base. The current trend found in some of the research

of separating out components of CBT to determine their individual efficacy does not seem clinically relevant.

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A Long term Follow-up of a Multi-Disciplinary Approach to Chronic Fatigue Syndrome

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2012

Doctorate in Clinical Psychology

A Long term Follow-up of a Multi-Disciplinary Approach to Chronic Fatigue Syndrome

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Aims

The current study evaluated the long-term effectiveness of a multi-disciplinary approach to Chronic Fatigue Syndrome and explored patients' experience of service use.

Methods

A longitudinal questionnaire based survey of patients who used a British multi-disciplinary secondary care specialist service. Measures were taken at pre, post and follow up to intervention (average 34 months post intervention). Telephone interviews with 10 participants based on a semi-structured interview schedule were used to explore in-depth information about experience of using the service.

Results

A linear mixed model statistical analysis found that most outcome gains were maintained or improving at follow-up. Employment had a significant positive impact on levels of fatigue, physical functioning, depression and pain. Increasing age had a negative impact on symptoms experienced and physical functioning. A multiple regression analysis found anxiety and depression results made a significant unique impact on self-efficacy.

A thematic analysis of interviews found that patients were positive about the service, gaining validation, education and management skills from the intervention. They appreciated the flexible approach used by the service. Areas to be developed were improving access, reducing gate-keeping by primary care medical services, and offering all patients both group and individual interventions.

Conclusions

The approach offered by the targeted service was efficacious long term, and highly acceptable to patients. The 364-day open appointment and flexible contact arrangements of email and telephone should continue. Interventions should be individualised and offer both individual and group approaches, combine Cognitive Behavioural Therapy, Graded Exercise Therapy and Pacing as well as alternative psychological interventions to meet individual need. A focus on assisting paid and unpaid employment would be beneficial. Further research incorporating long-term outcomes and alternative interventions is essential in order to best direct service provision and clinical guidance.

Introduction

Chronic Fatigue Syndrome (CFS)/Myalgic Encephalopathy (ME), is characterised by a wide range of symptoms, including physical and cognitive impairment, such as continual exhaustion, problems with body temperature regulation, and difficulty with concentration and memory. No discrete “physical or psychological disorder” (Price et al., 2008) has been found underlying these symptoms. Due to the heterogeneity of symptoms, there has historically been much debate around diagnostic criteria, and, whether CFS/ME is a distinct disorder at all. There is no specific diagnostic test that can be carried out, diagnosis usually occurs when certain symptoms have been exhibited over a period of time, and other conditions have been excluded. Although both CFS and ME are used to describe this condition, for the purpose of this report it will be referred to as CFS. In the UK, current treatment guidelines recommended by the National Institute for Clinical Excellence (NICE), suggest that an individualized Cognitive Behavioural Therapy (CBT) and/or Graded Exercise Therapy (GET) approach should be offered to patients with mild to moderate CFS (Turnbull et al., 2007).

A recent critical literature review by the author (unpublished manuscript, 2012), found that the majority of research exploring outcomes of CBT interventions for CFS patients, used outcome measures pre and post intervention, and at one year follow up. The findings for both group and individual CBT were that the CBT intervention was, overall, effective for

improving scores on fatigue and physical functioning measures, but often it was not more effective than comparator groups. Any gains made on fatigue and physical functioning measures post intervention, were often not maintained at follow up stage. Very few studies looked at outcomes over a year post intervention, and studies that have done this have mixed findings. Knoop et al. (2008) found that adolescents, at an average follow up of 2.1 years following a CBT group for CFS, had maintained the significant post treatment improvement in fatigue and functioning at follow up when compared to a non CBT treatment group. Similarly, Marlin et al. (1998) found at a 33-month follow up, patients receiving individual CBT maintained positive gains. However, Deale et al. (2001) carried out a five year follow up of patients who participated in a CBT versus relaxation study. At the six month stage, the participants receiving CBT had significantly better scores on the outcome measures than the relaxation group, however at 5 year follow up these differences were not maintained. One of the problems with research trials for CFS patients, is that they often have small sample sizes, and they also tend to have strict exclusionary criteria, making it more difficult to generalise results to a wider population. Interestingly, Quamrby et al. (2007), found that CFS patients involved in a randomised controlled trial of CBT had better outcomes than those provided with the same treatment outside of the trial, suggesting a treatment effect provided by being within a trial.

A further finding of the review of the literature was that the majority of research into outcomes for patients with CFS, used purely quantitative

designs and did not incorporate more in-depth, qualitative analysis. To address these issues of short follow up periods and limitations of designs based purely on statistical analysis, the current research aimed to investigate longer term outcomes using a multi-method design incorporating a thematic analysis of semi-structured telephone interviews carried out with some of the participants.

Service History in United Kingdom

Service provision for patients with CFS in the UK has traditionally been inconsistent in terms of availability and interventions offered. In 1998, the UK Chief Medical Officer (CMO) established a working group on CFS/ME to determine best practice guidelines for treatment in the NHS. The report was published in 2002 (Department of Health), and subsequently led to government investment to cover service provision gaps in the UK and create centres of expertise for CFS patients. A National co-ordinating centre was established and 13 regional networks were formed which incorporated 36 adult and 11 children's specialist services. The role of these centres was to provide expert services to patients, and the Department of Health provided training to clinicians to ensure they provided the best possible care to the patient groups. The networks also aimed to share best practice between clinicians and develop services appropriately. The teams that developed from these initiatives were multi-disciplinary and comprised of: occupational therapists, physiotherapists, rehabilitation consultants and cognitive behavioural psychotherapists. The investment ended in 2006 and services

were required to be supported by local commissioning. (NHS: *The Improvement Network*, East Midlands, 2012).

The multi disciplinary services for CFS in the UK assisted in development of the NICE Guidelines (Turnbull et al., 2007), which stated that specialist ME/CFS care should be available nationally and include CBT, Graded Exercise Therapy (GET), and activity management. A meta analysis of research by Price et al. (2008) found some evidence for CBT being an effective treatment for symptoms of CFS, however the evidence base was small and follow up results were inconsistent. This was used to inform the NICE guidance and CBT became a recommended treatment, with the need for further research being highlighted. The guidelines emphasised the importance of an individualised approach to treatment, with the aim to "sustain or gradually extend, if possible, the person's physical, emotional and cognitive capacity." (Turnbull et al., 2007, p.9) as well as management of the physical and emotional impact of the condition

Much of the prevalence research into Chronic Fatigue Syndrome was based on non-UK community samples, for example Malouff et al. (2008). Several centres of expertise on CFS have become established in countries apart from the UK, and therefore much of the research base is from non-UK studies. Because of likely cultural and attitudinal differences towards health and healthcare, it was felt important to carry out a UK based study in order to compare with outcomes found in non UK samples. In addition, using a

service which offered a CBT approach that was not part of a research trial, may add validity to the results.

Rationale for Present Study

Current research into interventions for CFS is limited to having follow up periods of generally no more than a year, and much of the literature is based on Randomised Controlled Trials, with little research on existing UK services. The current study aimed to address these limitations by having a longer follow up period, and conducting research within an existing service using interventions based on NICE guidance. The research base shows mixed results for outcomes at follow up periods, and there is very little evidence as to what impact the length of time since ending treatment has on outcome measures. The current research aimed to address this gap in the evidence base. In addition, the majority of current research uses quantitative methodology. The author feels that due to the lack of understanding of CFS within health professionals, a multi method approach incorporating interviews with patients analysed qualitatively, would assist in the understanding of results from quantitative findings.

Research Questions and Hypotheses

The current study aims were two-fold: (1) to evaluate the long term effectiveness of a multi-disciplinary team approach taken by the specialist

services set up following the CMO report (2002); and (2) to explore which aspects of the target service were viewed by the patients as most useful.

The research questions were:

1. What are the long term health outcomes for people who have used a CFS service which is part of the clinical network; and
2. What are patients' views of the CFS service post discharge

The hypotheses were:

1. After using the service, the length of time between treatment and follow up will be negatively correlated with maintenance of positive gains on outcome measures;
2. Gender, age, time since diagnosis and gainful employment will impact on gains made on outcome measures.

Benefits of Research

In addition to adding to the research base for CFS, it is anticipated the current research will help to determine whether the current UK national clinical recommendations (Turnbull, 2007), which have been shown to be effective in the short term, are having a continued positive impact on patients at a longer term follow up. The research will explore factors which

may be impacting on outcome measure results, and the findings of this will inform recommendations for how this may be applied clinically.

As a key aim of this research was to determine patients' views of the service they used, it is anticipated that the research will provide practical suggestions for CFS services nationally to adapt their approach in response to this feedback. As well as impacting at a local level, as the service is part of the clinical network for CFS, it is intended that these changes will be communicated at a wider level in order to maximise impact on service development nationally.

Method

Study Design

The current study used a multi-method design involving a longitudinal repeated measures postal survey followed by semi-structured telephone interviews on a self-selecting sub-sample of participants. The quantitative aspect of the design was best suited to explore the research question of long-term health outcomes of participants and investigate factors which may impact on outcomes. The qualitative part of the design was appropriate to gain more in-depth information about patients' views of the service. To explore the impact that time since using the service has on outcome measures, the researcher posted a questionnaire pack to participants who had been discharged from the service. These were questionnaires that participants were given to complete by the service prior to service use, and on discharge. There were therefore three time-points where outcome measures were completed by each participant. It was anticipated the time since discharge from the service for participants would range between two and five years.

Choice of Statistical Analysis

To analyse the impact that time since discharge had on outcome measure results, a mixed linear model was determined to be the most appropriate statistical test. Alternative tests such as repeated measures ANCOVA would

exclude participants that did not have data at all time points, an expectation of the dataset for the research. Mixed Linear models do not assume homogeneity of regression, that the relationship between dependent variable and covariate is the same for all treatment groups, which is an assumption made by ANCOVA (Tabachnick & Fiddell, 2007). In addition an ANCOVA is more appropriate if the time interval between the three time points was the same for each participant which was not the case, and a mixed linear model does not make this assumption.

Research Service

The site used for the current research was a specialist adult Chronic Fatigue Syndrome/Myalgic Encephalitis (CFS/ME) service in the East Midlands, commissioned by two local Primary Care Trusts. Referrals came from General Practitioners and Consultant Psychiatrists. Patients had to meet the diagnostic criteria for CFS/ME specified by NICE guidance (Turnbull et al., 2007) See Appendix A.

Intervention

The treatment approach offered by the targeted CFS service was in line with NICE recommendations for CFS/ME, and the National Service Framework

for long-term conditions and Occupational Aspects of the management of CFS/ME (Department of Health, *A National Guideline*, 2008). The targeted service offered both group and one-to-one treatment, with the majority of patients receiving the latter. Interventions were tailored to meet patients' needs, perpetuating factors contributing to the condition were identified and informed the treatment approach. The approach was based on cognitive behavioural principles, incorporating graded exercise and pacing. Appendix F describes the treatment approach in more detail. On average, groups lasted nine sessions, and contained a maximum of 10 patients. The number of individual sessions varied, depending on patients' needs. The service also offered telephone and email support for patients when required, and patients were offered a 364-day open appointment following treatment. The service routinely collected questionnaire assessment data for patients prior to commencement of treatment (pre treatment measures) and again after treatment (post treatment measures), usually between 9 and 15 months after completing the pre-treatment measures.

Therapist Characteristics

The targeted service was headed by an Occupational Therapist who led a multi-disciplinary team comprising: an Occupational Therapist, two Physiotherapists, a Cognitive Behavioural Therapist and two Medical Consultants in Rehabilitation Medicine. The group was facilitated by an Occupational Therapist, Physiotherapist and CBT therapist. The medical consultants assisted in triaging the paper referrals to the service and offered

sessions to patients where there was a diagnostic query, medical query, atypical presentation or a psychiatric history. All staff in the service were trained in Cognitive Behavioural Therapy (CBT), and the CBT therapist supervised staff.

Participants

Inclusion Criteria

Inclusion criteria were restricted to the criteria used by the targeted service themselves:

- Age 18 years or over. (note: a specialist child CFS service was also available and patients under 18 were referred to this service). As the current outcome measures had mostly been standardized on a population over 18 years, it was decided to restrict recruitment to the current study to the adult services.
- Anyone who had used the service since its establishment and been discharged following the 364 day open appointment.

Exclusion Criteria

- Patients in current contact with the service for treatment.
- Major psychiatric illness.
- Concurrent rehabilitation for CFS/ME from another service.
- Patients aged under 18.
- Patients who opted out of the research.

Sample size

To determine the number of participants required to provide appropriate statistical power, Cohen's (1988) use of a minimum 0.80 power statistic was applied (Table 2.3.2). The effect size used to calculate power was 0.48, based on Malouff et al. (2007) meta analysis of 13 studies offering CBT for CFS, with a total of 1371 participants. Mean effect size for each outcome variable was calculated using means and standard deviations and a mixed effects model (Method of Moments Random Effects) analysis was used. $p<0.001$, CI +/-95%, 0.27, 0.69.

Using this criteria, 80 participants would provide power of 0.81. The targeted CFS service estimated they had 680 referrals since their establishment. They suggested a conservative 'Did Not Attend' rate of 40% which would remove 272 patients, an exclusion of 10% patients re-referred to the service (68 patients), leaving an estimated 340 potential participants. The targeted service was actually able to provide a database of 495 participants from which to recruit. Due to cost constraints of the postal survey, the entire database could not be used for recruitment. A 30% return rate assumption was made and 300 participants were randomly selected from the database, which would provide a predicted response rate of 90, adequate to meet the power needs.

Measures

Stage I

The repeated measures element of the design used pre and post treatment outcome data routinely collected by the targeted CFS service as well as new data collected for the current research at longer term follow up.

Independent variables were retrieved from patients case notes and a demographic information sheet attached to the questionnaire (Appendix G) as follows:

- Time since diagnosis
- Gainful employment (paid, unpaid and other activities)
- Gender
- Age

The **dependent variables** were the outcome scores on each questionnaire measure as described below. The same measures with an additional demographic information questionnaire and self-efficacy measure were sent together by the researcher as a postal questionnaire to participants. The measures can be found in Appendices G-M.

Medical Outcomes Study, Short Form-36, Physical Functioning Scale (Ware & Sherbourne, 1992) (Appendix H)

A 36-item self- rated measure that provides results on eight different general health areas. The 10 item physical functioning subscale has been used as an outcome in much of the research with CFS patients. The scale measures Physical Health on a scale of 0-100, with 0 being “limitation in all activities” and 100 being “no limitation”. Internal consistency has been found across scales (reliability coefficients 0.65-0.94, median 50.85) (Friedberg & Sohl, 2009).

Chalder Fatigue Scale (Chalder at al., 1993) (Appendix I)

This measures physical and mental fatigue and has been validated with patients suffering with CFS. It contains 11 self-rated items with a four-point Likert scale ranging from ‘less than usual’ to ‘much more than usual’. The scale can be scored on a 0-3 scale, ranging 0-33 and a cut off of 12 indicating fatigue. Reliability (Cronbach’s alpha 0.88-0.90) and validity (sensitivity 75.5 and specificity 74.5) (Chalder et al., 1993).

12-Month Clinical Global Improvement Scale (Guy, 1976)

This measure (Appendix M) was used by the targeted service in their follow up questionnaire and was included in the research questionnaire pack. The dimensions of Severity of Illness (CGI-S) and Improvement (CGI-I) domains of this scale are used to determine a patient’s self reported improvement over a period of time. This utilises a seven point Likert scale from 1, “very much improved” to 7, “very much worse”. The scale has been found to have

good validity and reliability and has been applied to Chronic Fatigue Syndrome patients by several studies, for example Stubhaug et al. (2008).

Symptom Checklist-Created by Service (Appendix J)

A self rated questionnaire of a list of 29 symptoms typical of Chronic Fatigue Syndrome. Patients circle “yes” or “no” to the symptoms, with space to add any other symptoms experienced. The measure was used by the target service to assess the number and type of symptoms experienced by patients.

Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983).

A 14-item scale measuring anxiety and depression (Appendix K). Scores of 0-7 are classed as normal, 8-10 borderline and 11-21 indicative of a mood disorder. Morriss and Wearden (1998) found that using a cut off score of 9-10 on the HADS was a “valid and efficient measure of psychiatric disorder, with high sensitivity, specificity and positive predictive value” in a sample of patients with CFS.

Pain Visual Analogue Scale

Visual analogue scales for pain are a simple measure for patients to rate their level of pain. Patients have a 100mm line with 0mm being ‘no pain at all’ and 100mm being ‘severe pain’, and are asked to mark where they feel their level is pain is at the time of completing the questionnaire. Appendix M shows an example of such a scale. Although a subjective measure, validity

has been demonstrated in the use of the scale when applied to pain (Price et al.1983).

Self-efficacy Scale (Schwarzer & Jerusalem, 1995)

A self-rating 10-item measure (Appendix L) to determine perceived self-agency. It uses a four point Likert scale: 1 (“not at all true”) to 4 (“exactly true”). The scale was developed in Germany and translated into 26 languages. It has been widely used and has a Chronbach’s alpha ranging from 0.76-0.90. (Scholz et al. 2002). The targeted service was planning on incorporating this as a standard measure, but had not done this when the current research was carried out. This scale therefore cannot be compared across the three time points but its correlation with the other outcome measures was deemed a useful area of investigation.

Epworth Sleepiness Scale (Johns, 1991)

The targeted service also used the Epworth Sleepiness Scale (Appendix N), which assesses daytime ‘sleepiness’. The scale consists of eight questions about situations in every day life, and the rather scores themselves on a scale of 0 ‘no chance of dozing’, to 3 ‘high chance of dozing’. Scores for each question are totalled giving a maximum score of 24, the higher the score, the higher the level of daytime sleepiness. To reduce participant burden, this measure was not incorporated in the current research questionnaire pack. A visual analogue scale to assess quality of sleep was used instead and this was compared with the sleepiness scale responses.

Fatigue Severity Scale (Krupp et al., 1989)

Some patients accessed the service prior to the standardised questionnaire packs being used. These patients however, often had a Fatigue Severity Scale score in their case file, which was used to compare with the Chalder Fatigue Scale measure in the current research questionnaire pack. As shown in Appendix P, this is a nine item self-report Likert scale measuring severity of Fatigue and Functioning. Patients score 1 – 7 depending on how much they agree with a statement. Higher scores suggest a higher level of Fatigue-related impairment. In the original study, Chronbach's alpha was .81-.89 and the measure was found to have test-retest and concurrent validity. Jason et al. (2011) compared several fatigue measures and found the FSS to have the highest specificity in differentiating patients with CFS and those without.

Questions to investigate mediating factors were also included on a separate sheet in the current questionnaire pack (Appendix G). These asked about: length of time since diagnosis; length of time the patient felt they had been suffering with CFS; gainful employment (paid or unpaid); confidence in managing the condition; other support received for CFS; and whether the patient had referred to information provided by the service.

Stage II

A semi-structured interview schedule was developed (Appendix Q) with the aim of gaining more in depth information about patients' experience of using

the targeted CFS service. Questions investigated patients' experience of the group or individual approaches, and if there was anything they would change. Due to the time constraints of the research, it was felt that ten telephone interviews would be able to be conducted. Guest et al. (2006) found that six interviews were enough to find basic elements for metathemes in a thematic analysis sample, and saturation occurred in 12 interviews.

Procedure

A pilot study was carried out on the current questionnaire pack. Two people known to the researcher who had been diagnosed with Chronic Fatigue Syndrome were sent the questionnaire pack and asked for feedback about length of time it took to complete and any areas they felt needed changing. Only one person responded to this and they took between 20 and 25 minutes to complete the pack and felt it was not too difficult or tiring. They suggested some changes to the sleep question for clarity, which led to changing the wording of this question to provide participants with an example.

The study was submitted to the Integrated Research Application System (IRAS), and reviewed by an Ethics Committee, following their favourable opinion, it was submitted to the local Research and Development Department of the host NHS Trust (IRAS approval letters can be found in Appendix R).

Prior to the postal survey, a member of administration staff at the CFS service used the hospital patient information system (PAS) to determine if any of the patients who had been through the service had since died or relocated. No one was excluded through this process.

The data of all potential participants was provided to the Researcher by the targeted CFS service on an Excel database. To ensure there was a random range of date from discharge, the list was put in alphabetical order by surname and the first 300 selected. They were assigned random numeric codes by the Researcher in order to anonymise the information and be able to link up pre- and post-treatment measures.

Patients were sent a postal research pack (see Appendix S) which included:

- Information Letter about the study from the targeted service on hospital headed paper with an opt-out slip
- A letter from the Researcher on University of Leicester headed paper with further details about their role and the study
- Participant Information Sheet
- Consent Form for access by the Researcher to patient data stored by the targeted service with a section to complete if they wished to be involved in the telephone interviews
- questionnaire pack which included their anonymised code (Appendix S).

- A stamped addressed envelope was included with the return address of the academic base of the researcher.

After four weeks, a reminder pack was sent to all those who did not respond and did not opt-out of the study. This included a covering letter from the Researcher (see Appendix S) as well as the original information in the research pack.

There was space provided on the questionnaire packs for participants to request if they wanted to receive a summary of the final research results.

Stage II-Interviews

Interview participants were selected randomly from all patients who opted in to the interview stage by signing the interview part of the consent form (see Appendix Q). The interviews carried out by the researcher lasted a maximum of 41 minutes and were recorded by hand-written notes by the researcher who carried out all of the interviews. Previous studies such as Orford et al. (2006) have used note taking in telephone interviews and argued it to be a valid alternative to transcribing of interviews.

Criteria were set as to how much information to disclose to people who answered the telephone who were not the participant and can be found in Appendix Q.

Data Analysis

The quantitative data of outcome measures was analysed using PASW statistics 18.0 to determine whether improvements made on outcome measures by patients during their use of the service were maintained at long term follow up. A Mixed linear model was the most appropriate statistical analysis to carry out, due to each participant having a different period of time between research time points, and because this method accounts for missing data at different time points, thereby reducing potential for bias and maintaining power. Gender, employment, age, time since diagnosis, and time since completing pre intervention assessment were fixed factors. The estimation method used was Maximum Likelihood, 95% confidence intervals were computed.

The interview data notes were analysed using thematic analysis (Braun & Clarke, 2006). This provided an overview of themes that came out of the interviews about the targeted CFS service and the factors that patients felt had impacted on their illness progression. It was most appropriate to take a theoretical approach to the analysis by conducting coding on the responses given to each question. A semantic approach grounded in starting with description of semantic content, and moving towards interpretation of these for significance, in order to inform theme identification was applied.

Ethical considerations

CFS is a condition characterised by both physical and cognitive fatigue and there is high co-morbidity with depression and anxiety. It was felt important in the current study to ensure that patients did not feel pressurised to participate in the study or that it was creating extra stressors for them.

The longest response time possible was allowed with flexibility around interview dates and times. On the Consent information to take part in the interviews (Appendix S), there was space provided for participants to write the best day and time to be telephoned. Due of the symptoms of CFS, take-up may have been lower for those patients who were most unwell. All efforts to encourage people to respond were made, based on Edwards et al. (2007). This included: giving response times felt appropriate by the targeted CFS service; sending reminder questionnaire packs; and making telephone interviews as flexible and suitable for the patient as possible.

It was not anticipated that participating in the questionnaire study or the telephone interview would raise levels of distress for participants. However information was given on the questionnaire cover letter (Appendix S) advising participants that if they felt the need for more assistance, then we advised them to contact their GP. The details of the Patient Advice and Liaison Service (PALS) at the host hospital were also provided.

Demographic Characteristics of Participants

Table 7 below states the baseline demographic information for all participants, and a randomly selected sample of 20 non-responders. This suggests the baseline scores, age and gender were comparable for participants and non-respondents. The anxiety score for responders was in the 'mild' clinical range, whereas for non-responders was in the non-clinical range. When compared to other studies, the average age and proportion of females was slightly higher than found by Price et al. (2008). The outcome measures at baseline were similar to those found in other studies (Stubhaug et al., 2008, Schreurs et al. 2011).

Table 7. Demographic information of responders and non-respondents

Measure	Participants Average Range Standard deviation Number of participants	Non responder Sample
Age (at follow up)	47 years 21-78 years 13 years 95	48 years 29-81 years 13 years 20
Gender	82 female (84%) 16 male (16%)	16 female (80%) 4 male (20%)
HADS Anxiety	9 0-21 5 87	7 1-15 4.4 19
HADS Depression	7.8 0-19 4.5 87	7.7 1-18 4.6 19
Chalder fatigue Scale	25.2 3-33 6.2 86	25.6 17-33 5.1 20
SF 36 Physical Functioning	43.8 0-95 24.7 78	49.4 0-100 31.1 17

Results

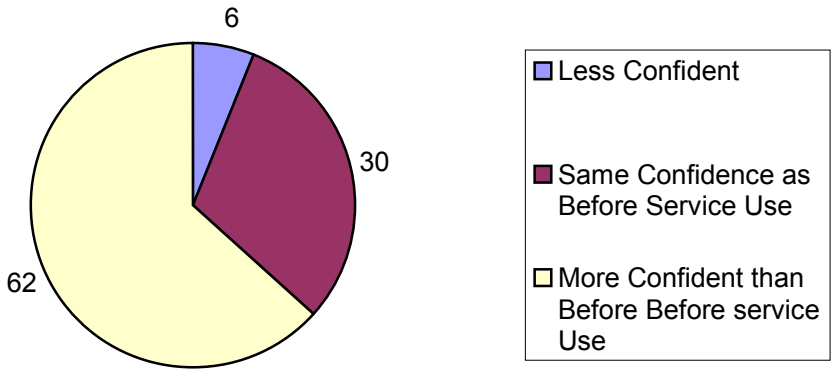
Stage I Questionnaire Measures

The following results describe the findings from the quantitative analysis of the questionnaire responses at the follow up time point, and the data gathered from participant case files for outcome measures pre and post service use. The sample size at follow up was 98 questionnaires returned. At pre and post assessment points, sample sizes differed depending on what measures had been completed, not all participants had completed post intervention assessments. Mixed Linear Modelling requires certain statistical assumptions to be met. More cases than independent variables are required, and an absence of outliers in both independent and dependent variables. Violation of collinearity assumptions were investigated using tests of tolerance and VIF, which showed, according to figures suggested by Pallant (2011) of tolerance less than .10, and VIF over 10, that collinearity was not a concern. Assumptions of normality, outliers, linearity, homoscedasticity and independence of residuals were checked using multiple regression plots within SPSS 18.0, and assumptions were found to be met.

Figures 2-3 below show the findings of the questions about service use completed by participants on the follow up assessment (*n*=98). 74 respondents (76%) had individual input, 3 (3%) were part of a group, and 21

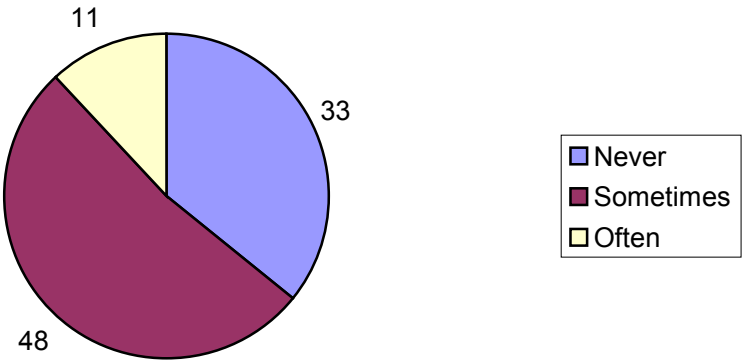
(21%) had both group and individual input. 31 participants (31%) had used the service more than once.

Figure 2. Confidence in Condition Management (*n* =98)



63% of the sample said they felt more confident in managing their condition following use of the service.

Figure 3. Referral to leaflets (*n* =92)

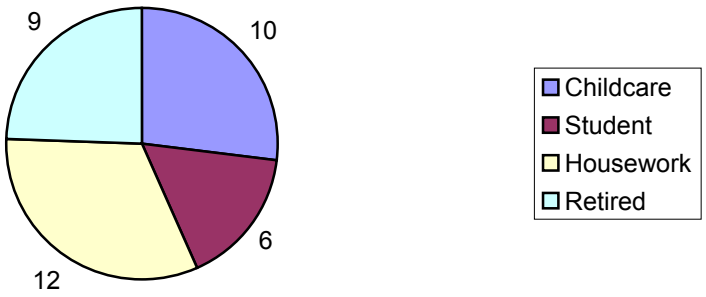


52% of respondents said they sometimes referred back to the handouts provided by the service.

Employment Information

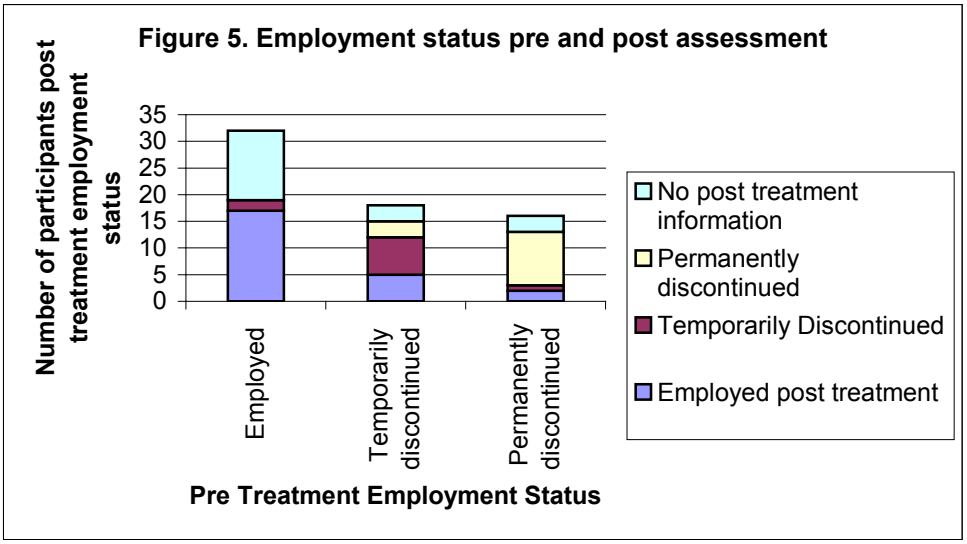
Gainful employment (paid or unpaid working) was hypothesised to have an impact on outcome measures, and was assessed in the follow up questionnaire. At follow up assessment (*n*=98), 56 respondents were in paid or unpaid employment, (50 paid, 11 unpaid). 47 respondents stated they were involved in other activities. Where stated, these are presented in Figure 4 below.

Figure 4. Other Activities (*n* =37)



Many participants had completed more detailed information about employment in the pre and post assessment measures, which looked at whether they were employed, temporarily unemployed due to fatigue, or permanently unemployed due to fatigue. Figure 5 below illustrates how this changed for participants between the pre and post assessment points.

Figure 5. Employment status pre and post assessment



Outcome Measures

Table 8 illustrates the straightforward mean scores (not corrected for influence of covariates), range and standard deviation for outcome measures at pre, post and follow up assessment

The average time between pre and post assessment was 15.9 months, (*n*=69, range 4-46, *SD* 7), between pre assessment and follow up 48.3

months (*n*=96, range 13-97, *SD* 17.9), and between post assessment and follow up was 34 months (*n*=69, range 0-77, *SD* 18,5).

Table 8. Mean scores, range and standard deviation for outcome measures at each assessment.

	Pre Assessment Average score Sample size Range Standard deviation	**Post Assessment**	**Follow up**
Chalder Fatigue Scale (max 33, higher score equals higher fatigue, suggested cut off of 12 indicating fatigue)	25.23 86 3-33 6.16	19.74 65 0-33 8.26	19.93 98 0-33 8.24
SF36 Physical Functioning (max 100, higher score equals better functioning)	43.85 78 0-95 24.69	52.06 66 0-100, 30.10	55.97 98 0-100 34.53
HADS Anxiety (Max 21, higher score equals higher anxiety, score 8-11 suggests mild disorder)	8.95 87 0-21 5	9 65, 0-21 5.45	7.80 98 0-21 4.90
HADS Depression (maximum 21, higher score equals higher anxiety, score 8-11 suggests mild disorder)	7.77 87 0-19 4.53	6.97 65 0-20 4.66)	6.31 98 0-19 4.82
Epworth Sleepiness scale (Max 24, higher score equals higher daytime sleepiness)	11 95 0-24 5.65	8.74 68 0-24 6.04	N/a
Pain Measure (0-100mm)	46.28 85 0-100 28.64	39.55 67 0-100 30.22	39.01 97 0-100 34.3
Symptom Checklist (range 0-29, higher score equals more symptoms)	13.80 84 9-22 2.66	12.75 64 9-18 2.02	13.05 92, 8-21 2.33

Table 8 illustrates that average fatigue score at all assessment points was above the clinical cut off of 12. In the SF36 Physical Functioning scale, a

score over 65 suggests absence of severe disability, at all time points the mean score for participants was within the clinical range. The Epworth Sleepiness Scale has a suggested clinical cut off of 10 indicating daytime sleepiness to be problematic enough to suggest a sleep disorder, the sample mean was above this cut off at pre assessment and below at post assessment. The depression scores were in the non-clinical range at all time points. The anxiety scores were in the mild range at pre and post assessment, but in the non-clinical range at follow up. The changes over time were not large but suggested improvement on all measures, except the symptom checklist, which changed very little.

Results from the study will be discussed in terms of what extent they support or refute the hypotheses. There is ongoing debate about the appropriateness of reporting effect sizes when undertaking mixed model analyses (Tabachnick & Fidell, 2007), and so for the purposes of the current report, the confidence intervals have been reported instead.

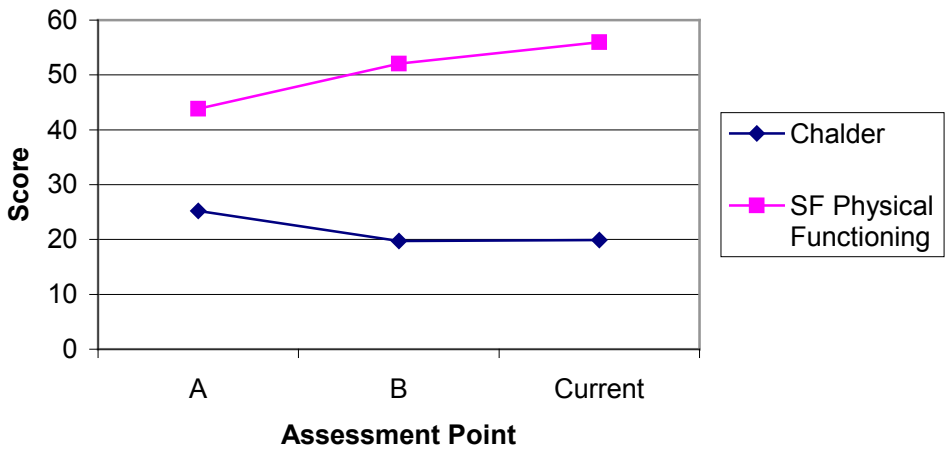
Hypothesis 1. After using the service, the length of time between treatment and follow up will be negatively correlated with maintenance of positive gains on outcome measures. Mixed model analysis using the PASW 18 statistical package was applied to determine which outcome measures were predicted to change with the length of time since completing the pre service assessment measures, when gender, age, time since diagnosis and gainful

employment were controlled for. It was hypothesised as length of time increased, any gains made would reduce.

a) Fatigue and Physical Functioning Measures

Figure 6 below, illustrates the changes in the Chalder Fatigue Score and the SF36 Physical Functioning scale across the three assessment points.

Figure 6. Fatigue and Physical Functioning mean scores across assessments



The mixed model analysis found that fatigue scores decreased significantly over time, representing reduced fatigue (estimated effects = .069, CI -.104 - -.036, p<.001). The mean score reduced between pre and post assessment, and increased by 0.19 at follow up.

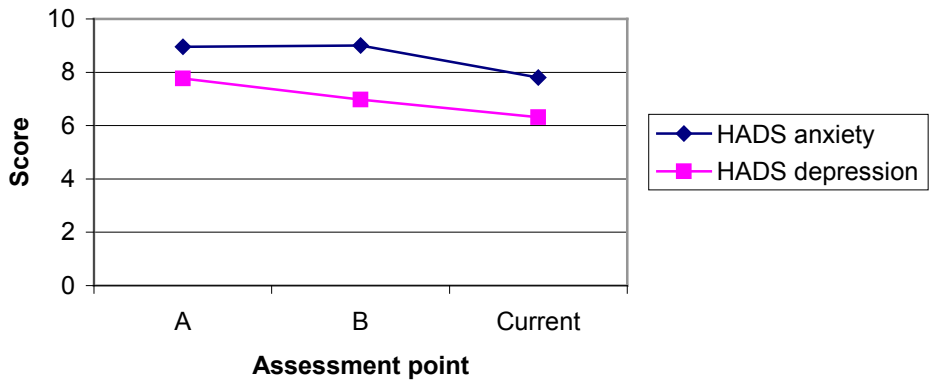
As shown in Figure 6 above, the SF36 Physical Functioning score increased across all time points, representing improvement in functioning and was statistically significant (estimated effects = .253, CI .154 - .352, *p*= <.001). From pre to post assessment, physical functioning in the sample improved,

and continued to improve to the current time point, on average 34 months after post treatment assessment.

b) Hospital Anxiety and Depression measure

Figure 7 below illustrates the mean scores on the anxiety and depression subscales of the HADS for each assessment.

Figure 7. Hospital Anxiety and Depression Scale means across assessments



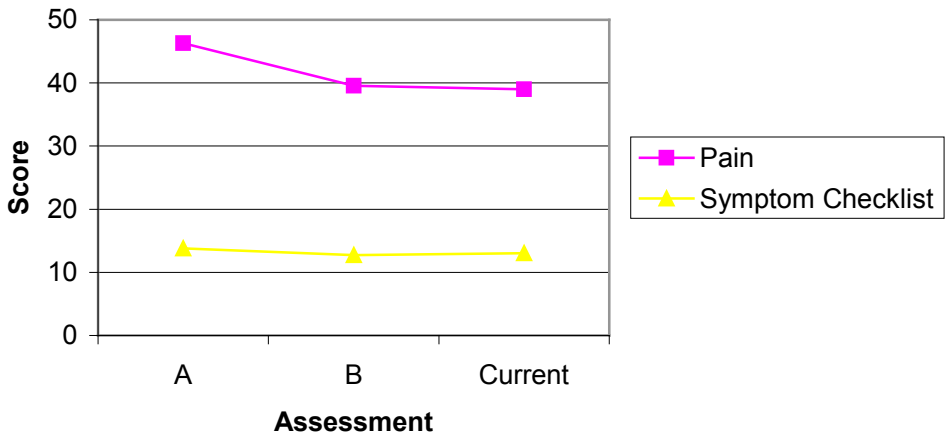
The mean scores show results for the depression subscale reducing at all three assessment points, suggesting improvement in symptoms. The anxiety score increased slightly (.05) between pre and post assessment, but reduced between post assessment and follow up. The mixed model analysis found that the HADS anxiety score significantly reduced over time, (estimated effects = -.019, CI -.033 - -.004, *p*=.012). The depression subscale score also significantly reduced over time, (estimated effects = -.023, CI -.040 - -.011, *p*=.001). These results suggest that patients' symptoms of depression reduced while using the service and continued to reduce after service use. The anxiety scores however, increased very

slightly during service use and since ending treatment were reducing to the follow up assessment.

c) Pain and Symptom scores.

Figure 8 below illustrates the means of the 0-100 visual analogue pain scale and the symptom checklist scores for each assessment point.

Figure 8. Pain and Symptom Checklist Scores over assessments



The mean scores on the 0-100mm pain visual analogue scale reduced over each assessment point, with the biggest reduction between pre and post treatment. The mixed model analysis found that there was a non-significant trend in pain score reduction over time (estimated effects = -.099, CI -.205 - .007, *p*=.068).

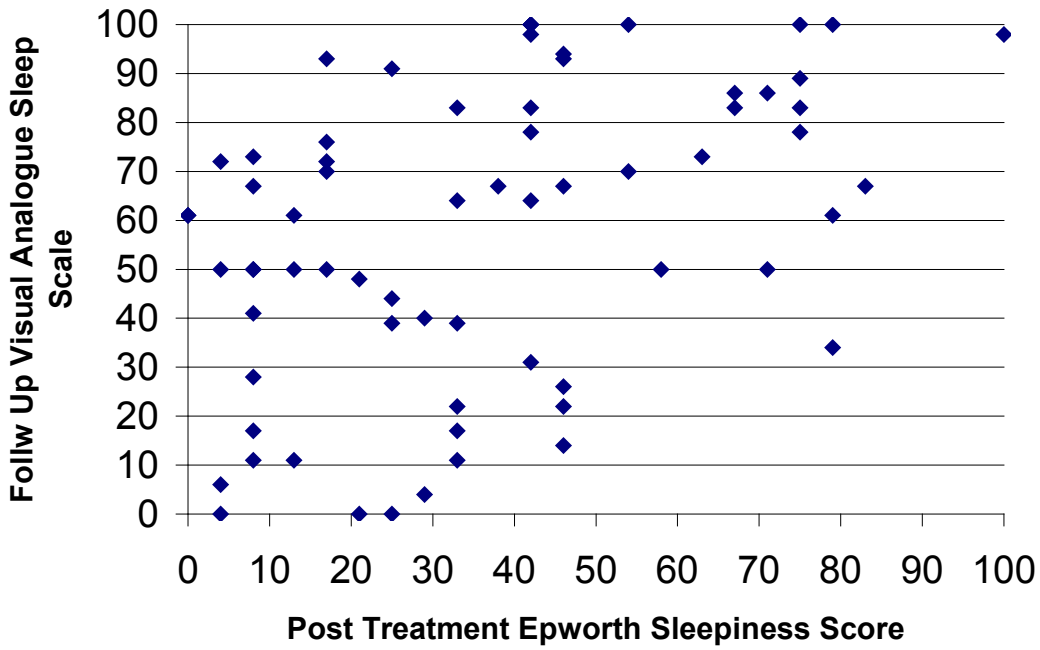
The number of symptoms experienced by patients was measured using the Symptom Checklist. The mean scores showed that symptom numbers reduced slightly pre to post treatment, and increased slightly post treatment

to follow up. The mixed model analysis showed a non-significant trend in symptoms reducing over time (estimated effects = -.004, CI -.015 - .006, *p*= .457).

d) Epworth Sleepiness Scale

The Epworth Sleepiness Scale was used by the service for pre and post treatment measures. In the current assessment measure, to reduce participant burden, it was changed to a 0-100mm visual analogue scale of sleep. The average Sleepiness score reduced from 11 to 8 from pre to post assessment, representing a reduction in symptoms of daytime sleepiness. A Pearson correlation of the post treatment Sleepiness scores (converted to a percentage score in order to compare with the visual analogue scale), and the follow up assessment visual analogue Sleep Scale found a small significant correlation, (*n*=68, r=.424, *p*= <.001). This is illustrated in Figure 9 below.

Figure 9. Correlation between Epworth Sleepiness Scores and Visual Analogue Sleep Scale



Findings from the analysis of outcome measures did not support Hypothesis one, that positive gains made during treatment will be negatively correlated with time since leaving the service. The results for fatigue, physical functioning, anxiety, depression and pain all improved over time and were either continuing to improve or reductions maintained at the follow up. The only outcome measure that did not fit this pattern was the Symptom Checklist where the average number of reported symptoms stayed the same across assessments.

Hypothesis 2. Gender, age, time since diagnosis and gainful employment will impact on gains made on outcome measures.

A mixed model analysis was used to assess whether these predictor variables were associated with any of the outcome measure results. Gainful employment was assessed by whether people reported to be working “paid” or “unpaid” in the follow up assessment questionnaire. 56 of the 98 respondents (57%) were in paid or unpaid employment.

a) Chalder Fatigue Score

Of the four variables hypothesized to have an impact on fatigue score, employment was significantly correlated with the Chalder Fatigue Score. The score was significantly lower for those who were employed in either paid or unpaid work (estimated effects = –3.58, CI –5.85 - -1.30, *p*= .002). The mixed models analysis found non-statistically significant predictions that increase in time since diagnosis and age would have a negative impact on fatigue, and that fatigue scores would be lower for females than males.

b) SF36 Physical Functioning

The physical functioning score was significantly higher (functioning improved) for those who were employed in either paid or unpaid work. (estimated effects = 24.81, CI 15.90 – 33.73, *p*= <.001). The analysis showed that the physical functioning score was predicted to reduce with age in years (estimated effects = -.376 CI -.732 - -.019, *p*=.039). There were non-significant trends that the physical functioning scores would reduce with time since diagnosis, and be more reduced for females than males.

c) HADS Anxiety and Depression measure

None of the predictor variables were significantly associated with the anxiety subscale score. There was a non-significant prediction that the anxiety score would reduce with time since diagnosis, age and gainful employment, and that females would have reduced scores compared to males.

The depression scores were, however, significantly associated with gainful employment, with a prediction that those who were employed, paid or unpaid, would have a lower score than those who were not, (estimated effects = –1.84, CI –3.58 - -.097, *p*=.039). There were non-significant trends that depression scores would decrease with time since diagnosis, and scores for females were lower than males. There was a non-significant trend that scores were predicted to increase (that is depression symptoms worsen) with age.

d) Pain Scores

The pain score was significantly lower for those who were employed in either paid or unpaid work (estimated effects = –23.99, CI –34.67 - -13.30, *p*= <.001). There were non-significant predictions that the pain scores would increase as time since diagnosis and age increased, and a non-significant prediction that scores would be higher for females as opposed to males.

e) Symptom Checklist

Of the four predictors, age was significantly associated with the Symptom Checklist scores. The score was predicted to increase with age, that is number of symptoms experienced to increase (estimated effects = .042, CI

.013 - .071, *p*=.005). There were non-significant predictions that the number of symptoms would reduce with employment, and increase with time since diagnosis. It was predicted the scores would be lower for females than males.

The results of the mixed model analysis of outcome measures partially support the hypothesis that age, gender, time since diagnosis and gainful employment impact on outcome measures. When the other variables were controlled for, employment had a significant positive impact on levels of fatigue, physical functioning, depression and pain. As age increased, the number of symptoms experienced increased and physical functioning scores worsened.

f) Additional measures

Self Efficacy Measure

The Self-Efficacy Measure was administered at the follow up assessment point. The average score was 29.41, with a range of 11-40. (Maximum range for measure 10-40) *SD* 6.62. A post hoc multiple regression was carried out to determine how much variance on self-efficacy scores was explained by fatigue, physical functioning and mental health measures. All variables entered into the regression were significantly correlated with the self-efficacy score. Collininearity for the Chalder Scale was on the borderline of being a concern (-.7). To further check the violation of collinearity assumptions, statistical tests of tolerance and VIF were used. These

showed that, according to figures suggested by Pallant, (2011) of tolerance less than .10, and VIF over 10, collinearity was not a cause for concern. Assumptions of normality were checked with the plot of regression.

The model incorporated Chalder Fatigue Scores, SF36 Physical Functioning scores and HADS anxiety and depression scores and explained 57.8% of the variance in the self-efficacy score. The significant variables making a unique impact on the self efficacy score with $p<.05$ were HADS Anxiety and Depression. (-.473, and -.288 respectively). HADS anxiety explained 10% and depression 3% of the variance in self-efficacy scores.

Clinical Global Improvement Scores

Figure 10 illustrates the responses on the Clinical Global Improvement measure post treatment and at follow up. This shows that post treatment scores were better, and had a smaller range than the follow up scores. Lower scores represent better outcome. Of the 62 respondents who had CGI data at post treatment and follow up, 15 had scores which were higher at follow up, 22 had scores lower at follow up, and 25 had scores the same as at post assessment. A paired sample t test was used to determine if the difference in mean scores post treatment and at follow up was significant. Normal distribution was checked using scatter plots in PASW 18.0. The mean CGI score post treatment (M= 3.16, SD = 1.70) was higher than at follow up (M = 2.76, SD = 1.26). This result was significant at the 95 % level, t (61) = 2.20; p =.032. Suggesting that subjective improvement scores were significantly better at follow up than post treatment.

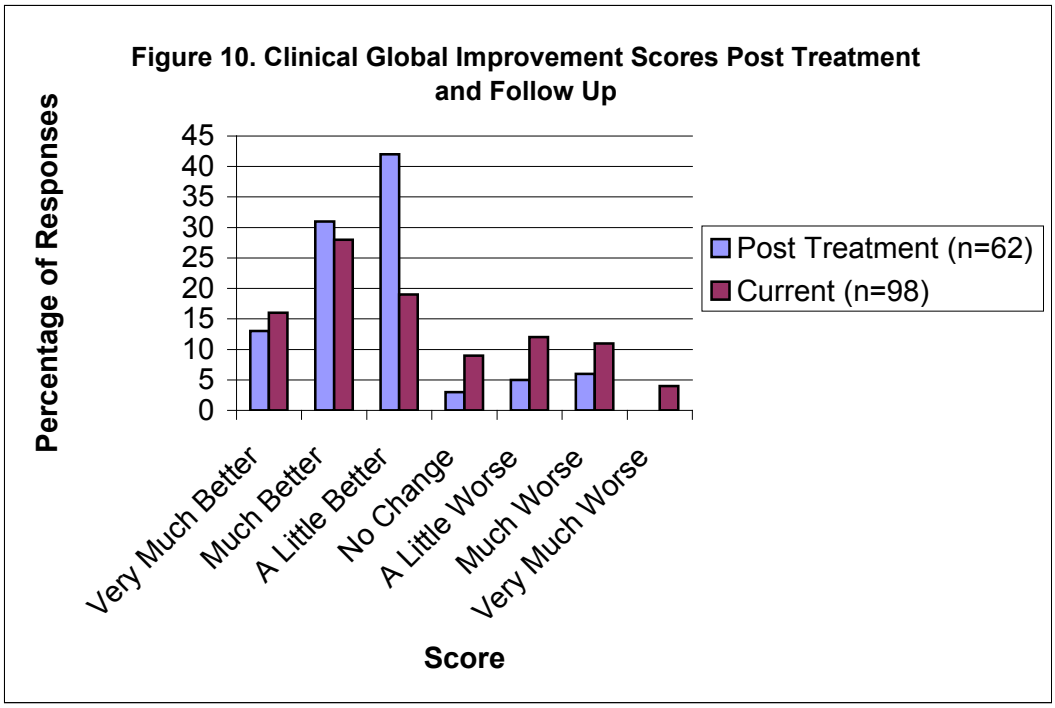


Figure 10. Clinical Global Improvement Scores Post Treatment and Follow Up
Percentage of Responses
45
40
35
30
25
20
15
10
5
0
Very Much Better
Much Better
A Little Better
No Change
A Little Worse
Much Worse
Very Much Worse
Score
Post Treatment (n=62)
Current (n=98)

Stage II Telephone Interviews

Ten telephone interviews were carried out in order to explore patients' experience of using the service. Of the 98 respondents at follow up stage, 65 consented to being contacted for telephone interview.

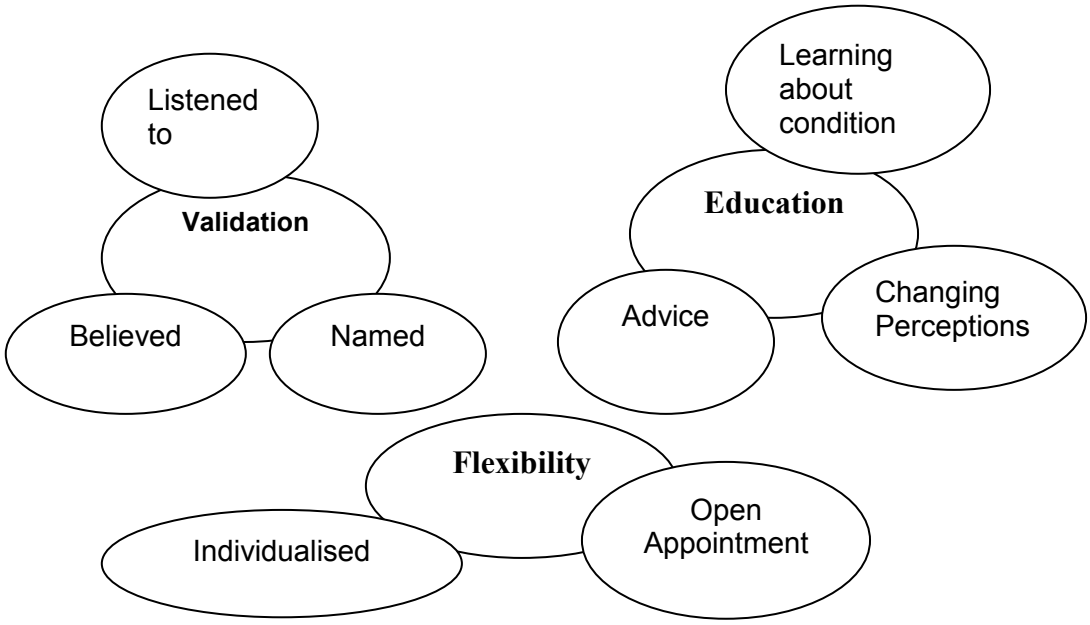
Of the ten interviewees, nine (90%) were female, the average age was 50 years (range 23-78 years), both slightly higher than the overall sample. In order to determine if there was a difference in the interviewees to the overall sample, fatigue, physical functioning and HADS scores were compared. The mean fatigue score of the interviewees went from was 28.6 at baseline to 16.7 (slightly higher than the whole sample average at baseline, and slightly lower at follow up, SF Physical functioning score went from 43.8 to 70.6 (similar at baseline but higher a follow up), HADS anxiety from 10.8 to7.5 (interviewees average higher at baseline but similar at follow up), and HADS depression from 8.3 to 4.9 (higher than average at baseline but lower at follow up). 8 out of 10 interviewees (80%) were in paid or unpaid employment, substantially higher than the 57% of the overall sample. Respondents who were interviewed were perhaps doing slightly better on outcome measures than the overall sample. However this is a sample of 10 out of 68 people, the majority of respondents, who consented to interview, suggesting that how well people are feeling is not necessarily a source of bias.

Appendix T provides an example of the codes identified from the interviews by question, and how they were incorporated into themes. Due to the small data set, a theme was identified if it recurred across more than one interview, or it was deemed by the Researcher to be a key aspect for the participant about their experience of service use. If a respondent provided answers in one question that answered another interview question, the code was listed under the question answered in italics, signposting into which question it was incorporated.

Question One: What aspects of the service were most helpful?

Figure 11 below illustrates the themes and sub-themes emerging from this question.

Figure 11. Question One: Most helpful aspects of service



The codes for question 1 were collated into three themes: Validation, Education and Flexibility. Validation was categorised into sub-themes of:

being listened to, being believed and having the condition named. One participant described being called ‘lazy’ by her husband, illustrating a lack of understanding and belief about the symptoms of CFS. Another felt like they were “going nuts” before having the condition named (Participant 6). Across several interviews, participants commented on how understanding and empathic the therapists in the service were, and the importance of being listened to, “I never felt alone” (Participant 9).

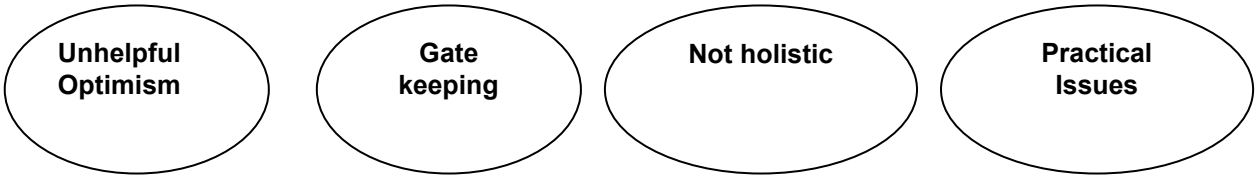
The theme of Education was subdivided into: Advice, Learning about the condition, and Changing Perceptions. Several participants talked about benefiting from condition management advice, in particular, the idea of pacing. The benefit of being able to discuss the advice with the therapists recurred in several interviews, “on your own, you can’t see the wood for the trees” (Participant 4). The theme of advice also incorporated skill development, and feeling equipped with tools to manage the condition. Participant 10 described learning about ways to manage the condition as “depressing and frustrating”, but that by doing so, “the service gave me my life back.” Changing Perceptions was a theme arising out of one interview, where the participant discussed the service helping her see things in a different light. It was felt by the researcher that this was key to the participant’s experience of service use, and so was classed as a theme.

Flexibility incorporated individualised approaches, and the 364-day open appointment. Frequency of appointments and the tailoring of the service to individual needs seemed key to some participants’ positive experience. The

open appointment allowed patients to contact the service directly within 364 days of ending treatment, as opposed to being re-referred via the GP. Participant 3 talked about experience of other services when she had tried to “do it on her own” but when she felt she needed more support after ending other service use, “you feel they shut the door and you are back to the beginning”

Question two: What aspects were less helpful/is there anything you would like to change?

Figure 12. Question two: Less helpful aspects of service



Several participants described no downsides, and did not want to criticise the service. Of these, some did go on to suggest aspects of the service they would like to be different. The codes for this question were categorised into four themes shown in Figure 12 above. Gate keeping by GPs seemed a key concern across several interviews. Participants described experiences of being told they could not be referred as they were too stressed, inappropriate referrals due to lack of GP understanding of the condition, and having a locum GP who had received training from the service, and so facilitated the referral. The practical factors discussed in interviews included difficulty in parking and distance to walk to the service, although the service had moved location since some of the participants attended. One participant discussed being given a relaxation CD towards the end of a group, but felt this would have been more useful to be provided with earlier. Limited appointment time, and the focus on psychological elements rather

than a holistic approach were also seen as problematic, “A cocktail of causes needs a cocktail of cures” (Participant 5). The theme of unhelpful optimism came from one interview, where the participant described a medical consultant at the service being positive about her condition. She felt this was unrealistic, and unhelpful for her personally, it “maybe gave me the confidence I was doing well when I wasn’t.”

Question three: Experience of the group or one to one approach

Figure 13. Question three: group or one to one approach

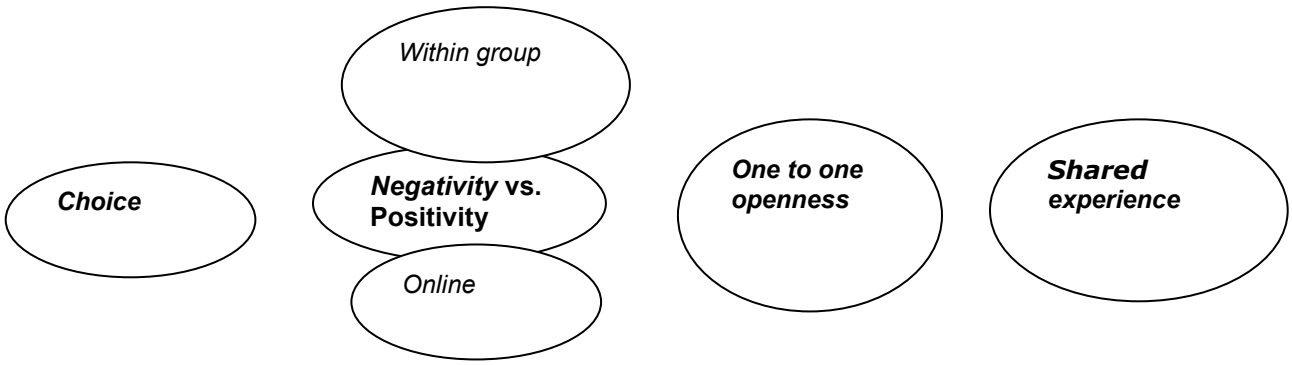


Figure 13 above illustrates the themes and sub themes developed responses about the type of intervention. Some participants discussed not being given the choice of a group, for one this was a negative, as they would have liked to attend a group; another interviewee described being glad there was not a group, as she was young at the time and would not “want to sit with people in a group discussing it.” (Participant 7). Several participants described feeling it was most helpful for them to have both the group and individual interventions. The group “normalises and gives good

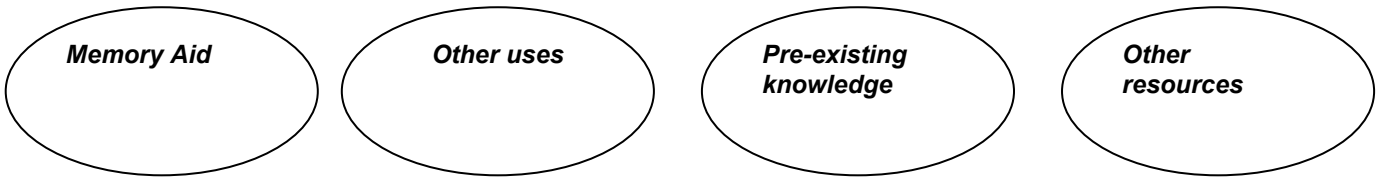
ideas, empathy and support." (Participant 6), but one-to-one sessions offer the ability to be more open and honest.

The overarching theme of Negativity versus positivity was divided into sub-themes of within the group and online. One participant described the benefit of the positive approach of the service, contrasting with negativity in many web-pages about CFS. One group attendee described some group members as being pessimistic about their future prognosis, and others wanting to recover, describing her own view as a middle ground, "I accept it's something I've got and it comes back to bite me when I do too much" (Participant 9).

Choice was a theme that incorporated practical issues: one respondent could not commit to attending all group sessions, and was advised she would not be able to attend the rest of the group, but was offered one to one sessions. She described this as a mixed experience, that it was difficult with the condition to commit to regular attendance, and being stopped from attending was "unhelpful", but that it was useful to be given an individual intervention alternative straight away.

Question four: How helpful were the leaflets provided

Figure 14. Question four: Leaflets provided

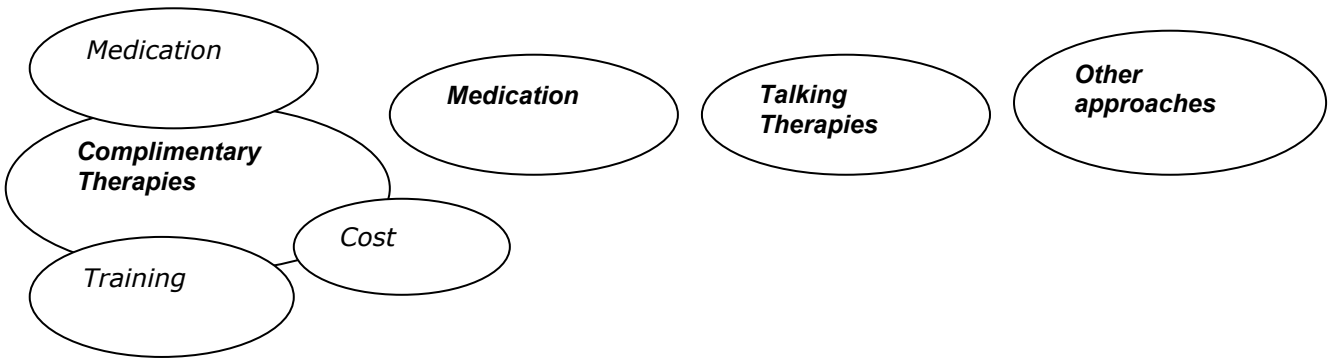


Several participants described referring back to the leaflets: one described "being sceptical at first" but referring back to them, particularly in the two years following service use (Participant 10). Leaflets were discussed in terms of being helpful for those with memory problems, offering useful metaphors and additional information to what could be found online. Some participants discussed feeling they already knew the information in the leaflets, leading to development of Pre-existing knowledge as a theme.

Other Uses was a theme incorporating responses given about using the leaflets to assist in completing benefit forms, and a tool to educate others. Some respondents felt that they already knew the information provided in the leaflets, they are "not that helpful if you have been suffering for a while" (Participant 7). One participant discussed being given CD's and books by the service which she found helpful and still referred back to now which led to the development of Other Resources as a theme.

Question five: Use of other interventions

Figure 15. Question five: Other interventions



The themes from the questions on the use of other interventions are shown in Figure 15 above. Complimentary therapies discussed in interviews included: massage, reflexology, acupuncture, iodine and vitamins. Although helpful, one participant felt complimentary medicines may be offering a placebo effect. The cost of complimentary approaches was a barrier; one interviewee thought the service could offer a model similar to a hospice where the alternative medications were offered for what you could afford. Training incorporated the response of one interviewee who described training in hypnotherapy and using self- hypnosis, and that they wanted the service to encourage self-help approaches.

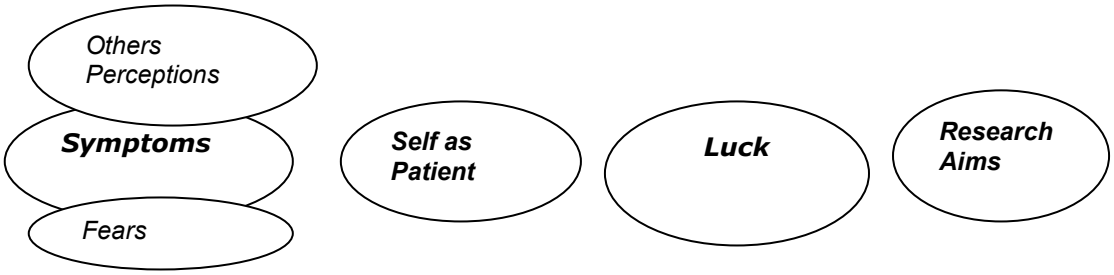
Medication was a theme that emerged across several interviews in different contexts. In some cases medication to aid symptoms was seen as a positive; one participant funded their own medication from America and used with the supervision of their GP. In contrast to this, another respondent discussed feeling that their GP forced medication on them, which she did not want to take, but felt compelled to in order to prove the medication did not help.

Participants had used talking therapies detached from the service of CBT and counselling. Some participants found these approaches helpful and others not so. One respondent had CBT offered as part of other research, they found this “helped me amazingly, and use everyday of my life” (Participant 9).

Other Approaches was a theme that encompassed respondents who described participating in research: one a study on brain trauma, and another schema focused CBT. One respondent had been sent on a condition management course by the Jobcentre, describing it as “dreadful and a waste of time” (Participant 9). The same respondent also tried to access an ME support group, but found the group members very negative and would not go back.

Question six: Is there anything else you would like to say about the service?

Figure 16. Question six: Other information



Several participants discussed their current symptoms in response to the question on general feedback, as well as some talking about their views on what caused their condition. A part of the theme of Symptoms was fear: one participant describing being “scared of things I shouldn’t be scared of” when discussing feeling that although CFS did not have a major impact on her life anymore, this was one way it did affect her. Multiple diagnoses were also described by some participants, and the impact this had, “when you tell people you have ME, you don’t get as supportive a response as if you say you have ME and Fibromyalgia” (Participant 1).

Luck was an unexpected theme to arise out of several interviews. Participants described being lucky in their diagnosis, in order to access the service, being lucky at the support of relatives, being lucky at the support of their workplace and, being lucky that a friend had been diagnosed previously as they were able to get advice from them.

The Self as Patient was a theme across several of the interviews. Being a CFS patient had benefits of being more compassionate to others, and being able to be involved in expert patient initiatives to educate others. One participant described feeling they were a challenging patient as they were a health service professional. A theme of Research was created as some participants asked the Researcher about the current study. One respondent thanked the current Researcher for carrying out the current project, as they felt it was an area that was under researched.

Interviewees were incredibly positive about the service, several respondents said they had recommended the service to others, and one prompted a friend to talk to their GP about the service. A participant who was in one of the first groups run by the service felt they had taken feedback and developed the group appropriately. One respondent described feeling fully recovered and able to work full time, which she attributed to having a supportive spouse and using the service. One respondent wanted to highlight her positive experiences of the health service locally. A response

which seemed to summarise the positive views of the CFS service was, “I generally have to live my life within the guidance given by the service to get quality of life, but I get a better quality of life than I ever expected” (Participant 10).

The findings from the thematic analysis of the telephone interviews provided areas that the service could develop on. They do offer training to GP’s, and extending this and trying to educate other healthcare providers about the service would help reduce some of the problems with gate keeping that participants faced. Signposting to local holistic or complimentary therapy practitioners may be a role the service could offer, enabling patients to make a choice about whether this would be suitable for them.

At the time of writing, the service offered a flexible patient focused approach, which seemed to be a unique experience of health services for some participants. Continuing to offer the 364-day appointment, and contact of telephone and email seemed key. Also providing patients with the choice of a group or one-to-one approach was important. Continuing to offer leaflets, books and resources in the service would be helpful. Interviewees discussed the agency provided to them by being able to inform others about the condition as a positive aspect to the patient role. A service user panel to assist with this and help steer the future direction of the service may be one way in which the service could facilitate this positive aspect of the patient role.

Discussion

The current study aimed to evaluate the long-term effectiveness of a multi-disciplinary approach to Chronic Fatigue Syndrome, determine which variables impacted on outcomes, and to explore patients' experience of using the service. A mixed model statistical analysis was carried out on outcome data pre and post service use, and at follow up (an average of 34 months post intervention). The findings were that: fatigue, physical functioning, pain, anxiety and depression measures improved significantly as time increased, with improvements being maintained or increasing at the follow up point. When other variables were controlled for, employment had a significant positive impact on levels of fatigue, physical functioning, depression and pain. As age increased, the number of symptoms experienced increased and physical functioning scores reduced. Multiple regression analysis showed that physical functioning, fatigue and anxiety and depression measures combined, contributed to over 50% of variance in self efficacy scores, with the HADS anxiety score having the most impact on self efficacy. The findings of a thematic analysis of 10 telephone interviews were that the CFS service was seen overall as incredibly positive and beneficial, with key themes of offering validation of the condition, flexibility of appointments and education about condition management. Areas that participants felt had created barriers for them were: negotiating service access; practically finding it difficult to attend appointments; and the service not offering as holistic an approach as some participants would have liked.

Participants highlighted the importance of being offered both group and individual input, often being viewed as complementary to one another.

Research Base

The current research helps to reduce a deficit in research of long-term follow up measures of interventions for CFS. It was anticipated that increasing time since leaving the service would have a negative impact on outcomes. This was based on findings showing mixed results in follow up outcomes of up to one year in both group based CBT interventions (Bazelmans et al., 2005, Nunez et al., 2011 & O'Dowd et al., 2006), and individual interventions (Ridsdale et al., 2001, Akagi et al., 2001). The current study found that on physical functioning, fatigue, and mental health outcome measures, scores were maintained or improving over time. A recent study with similar findings was White et al. (2011), who found outcomes were improving at one-year follow up for both the CBT and Graded Exercise Therapy comparator groups.

The findings of the current study are comparable to Price et al's. (2008) meta-analysis, that CBT had a positive impact on fatigue and physical functioning, although they found that CBT tended to be overall more efficacious than comparator groups, which was not found in a critical review of the literature by the current author (unpublished).

The mental health measures of anxiety and depression were found to be reducing over time in the current study. This is similar to findings by

Ridsdale et al. (2001) who found scores for both the CBT and counselling group comparator reduced. O'Dowd et al. (2006) found their CBT group to have significantly improved mental health scores post treatment than an education and support comparator or standard medical care, and a trend over time for reduced HADS depression and anxiety scores in the CBT group, but this was not significantly different to the comparator groups.

Other findings in the current study were that out of the variables: age, gender, time since diagnosis and employment status, outcome measures for patients were most impacted on by employment status, with those being employed in paid or unpaid work, having significantly better results on fatigue, physical functioning, depression and pain scores. Little research has been carried out into the impact of employment on CFS, however findings from research into Fibromyalgia, a condition often seen as similar in its chronicity to CFS, show that being employed had a significantly positive impact on physical quality of life in these patients (Reisine et al. 2004).

Theoretical Implications

Understanding of the aetiology and prognosis of CFS continues to develop. Symptoms are perpetuated by: number of severe life events, unhelpful coping responses of excessive activity or excessive rest, psychological morbidity, perfectionist traits, cognitive and interpersonal factors (Rimes & Chalder, 2005). A purely CBT based approach to CFS focuses most directly

on the cognitive elements, attempting to break cycles of phobic avoidance of exercise, and the behavioural elements of introducing pacing. Graded Exercise Therapy approaches focus just on the behavioural elements of the condition. Several studies have attempted to investigate efficacy of a 'pure' approach by different therapies, Jason et al. (2007) compared CBT with Cognitive Therapy, Anaerobic Activity and Relaxation groups. They found very similar results for the CBT and cognitive therapy group, results favouring the Cognitive Therapy intervention. The utility of offering interventions based on one specific theoretical understanding of CFS is questionable. Wallman et al. (2004) found GET to be effective for some CFS symptoms in an RCT, and concluded it may be partly due to patients abandoning previously held beliefs about the condition, linking the behavioural GET approach to impacting on the same theoretical understanding suggested by CBT approaches. Interestingly, other factors found to perpetuate symptoms and predict negative outcomes, such as depression, are often not specifically targeted in CFS interventions (Rimes & Chalder, 2005). The findings of the current study were unexpectedly positive, one explanation for this emerging from the interviews was the targeted service offered an individually tailored approach incorporating elements of CBT, GET and pacing, rather than being constrained to one specific framework. A similar multi-component approach was researched by Goudsmit et al. (2009) who aimed to offer "an alternative to graded activity-based programmes for individuals operating at their maximum level of functioning and those with no or little evidence of phobic avoidance" with positive outcomes post intervention.

Van Houdenhove and Luyten (2003) developed a biopsychosocial approach to CFS, suggesting individualising interventions, and incorporating treatment of co-morbid depression, anxiety and sleep disturbance. Patients should be offered a theory of the illness which incorporated the link between physical and psychological elements, as they felt patients were often wedded to one or other view, which is usually seen as likely to have a negative impact on outcome. This is supported by the thematic analysis in the current study finding that a key factor in the acceptability of the intervention to patients was that it offered validation of the illness and education on the condition and its management incorporating psychological and physical elements. Interestingly, Darbishire et al. (2005), and Kempke et al. (2010) investigated this illness attribution as an outcome predictor, finding it did not have an affect on patients' outcome measures.

Linking with illness beliefs is confidence in condition management, and self-efficacy. In the current study, the majority of participants felt that they had more confidence in managing their condition after attending the service. It might be expected this increased confidence impacts on self efficacy, and the self efficacy measure was correlated with fatigue, physical functioning and mental health, with HADS anxiety having the biggest impact on the correlation. Further research into self-efficacy and its impact on symptoms and other variables affecting this may be relevant, as well as an exploration of the relationship between employment and self efficacy.

Clinical Implications

To explore why the results of the current study were more positive for a long term follow up than in other research findings, it may be useful to compare the target research service and interventions used in other studies. One key difference was the 364-day open appointment offered by the research service. This was discussed in the interviews as being beneficial as it reduced the barriers of GP gate keeping, and participants described feeling less isolated knowing they could contact the service directly. Research from services offering health care and immunizations to children, found that offering 'open access' appointments, where patients called when care was needed and were offered appointments within one or two days, found a reduction in missed appointments and more on-time immunization (O'Conner et al., 2006). In addition, the targeted service offered less formal appointments, with the ability to talk to people on the phone, and respond to emails. Burgess and Chalder (2001) similarly found positive outcome in their telephone based study approach to CFS with implications for healthcare providers to meet the needs of those unable to attend appointments, a subgroup likely to be excluded from much of the research base. If these types of approaches were adopted by other services for CFS patients, it would be interesting to compare results and attrition rates pre and post the changes.

Depression and anxiety have often been viewed as a by-product of CFS, whereas Matsuda et al. (2009) found them to be independent of the condition. Integrating this with the findings of the predictors of outcome that pre-intervention depression was a negative predictor of outcome, suggests that interventions focused on depression may be helpful as a precursor to treatment for other CFS symptoms. Interestingly, in the current study, anxiety and depression scores were in the non-clinical and mild range at all time points, suggesting that for the respondents, this was not a significant concern. This is similar to other research with CFS patients (Goudsmit et al., 2009) and perhaps represents a bias in those suffering lower anxiety and depression symptoms being more likely to participate in research.

When considering clinical relevance, the findings in the current study, were that as time since service used increase, many outcome measures were also found to be improving. However, often the increases in outcomes were small, questioning their clinical significance. It is vital to individualise interventions, as well as outcome measures, to ensure that patient centred care is used and outcomes most important to the patient are targeted. In working age adults, employment prospects may be a key concern for CFS sufferers. The findings that gainful employment, paid or unpaid, had a positive impact on outcome measures, suggests that where relevant, this could be an area to be focused on by the service, most appropriately addressed in individual sessions.

The measures used as outcomes within the current study, were dictated by the targeted service. Due to the high symptom range, patients are often given a battery or outcome questionnaires, which try to capture change across a variety of difficulties. The client group suffer from mental fatigue and often have problems with concentration, making completion of this battery a challenge. It would be pertinent to reduce the measures used and aim to make them as tailored to the individual and condition as possible. The Chalder Fatigue Scale and SF36 Physical Functioning scale both seem highly relevant, and are both concise tools. The Symptom Checklist is, however, long and non specific, and it may be more relevant to ask patients to list some of their key symptoms, and rate how these have changed over time to make it more specific. The Sleepiness Scale seems to provide similar information to fatigue measures, and the current research has illustrated some correlation between the Epworth Sleepiness Scale, and a single question on quality of sleep using a visual analogue scale, the latter of which would be less burden on the participant. It is also important for services to focus on what their core aims are, and ensure outcome measures provide information on this. Pain as an outcome measure did not seem particularly relevant, and in the current study, many participants did not experience pain at any time point. This could be incorporated on a patient's list of key symptoms if relevant. The wording of some questionnaires may need to be altered to fit better with the client group. The Clinical Global Improvement measure has been found in some research not to reflect the results of outcome measures (Friedberg & Sohl, 2009). In the current study, the CGI scores do seem to partially reflect outcome measure

results, but the utility of this measure may also need to be evaluated, to determine if it could be adapted and made more relevant to the patient group, perhaps incorporating a question about why patients have chosen the answer they have, this would provide important information about patients views of what has helped or hindered their condition.

Overall, the current service intervention programme helped some clients on some outcomes. Malouff et al. (2007) summarised from their meta-analysis of CBT for CFS, that the average effect size found of 0.47 meant that “CBT for Chronic Fatigue Disorders has about the same efficacy as diverse psychological treatments for a variety of psychological disorders” (Malouff et al., 2007, p742). This highlights that, although CBT has some efficacy, other interventions may also offer similar findings. Traditionally CBT has been widely researched as an intervention, partially as it is relatively easy to standardise and control. In an unpublished review by the current author, it was found that the type of intervention, therapist delivery and duration, seemed not to lead to major differences in outcomes, implying that there are a lot of potential treatment options. A fascinating finding by Stubhaug et al. (2008) was that drug effect was more positive when preceded by CBT, which led the authors to conclude timing, and sequence is an important factor in treatment. The telephone interviews and the additional information section in the questionnaire of the current study echoed these findings. The majority of respondents had tried other therapies, medications and approaches over time to aid their symptoms. One participant felt an

approach based on meditation in combination with the CFS service had been of most assistance to her, another discussed feeling that attending a neuro-linguistic programming based residential course had aided her recovery. These additional interventions may lead to bias study results, but also seem key in individualizing the treatment offered. The service could act to signpost to other approaches that participants have felt were useful. Although these findings do not provide the overarching evidence that there is one treatment that can be standardized and offered to CFS patients, that a diverse range of interventions, and in some studies comparator groups were found to be as efficacious, provide hope that there are a lot of options for CFS patients, some of which may assist their condition if they were appropriately individualized.

Critique of study

Due to the longitudinal nature of the study design, time intervals between pre, post and follow up assessments varied for all participants. This limited the choice of analysis available, and meant that the statistics chosen were complex. It also meant the study had no comparator group, and therefore was a lower quality design than controlled trials. It was not possible to compare the outcomes from sub samples of group and individual interventions. However, the findings of the analysis of the interview data, was that the combination of approaches was viewed as ideal for some participants. Interventions varied for each participant and are likely to have been individualised, with the number of sessions and period the intervention

lasted fluctuating by participant. However, this intervention is more realistic, more acceptable to patients, and potentially more generalisable than research trials attempting to offer all participants the same intervention.

Outcome measures were determined by the service at its inception, and the research battery of questionnaires was lengthy, providing a large amount of data, some of which showed to be not useful as outcomes for this client group. On some of the questionnaire responses, participants commented that they found it hard to classify themselves, or they put ticks between two responses. In this situation, the response was rounded down to the more negative category. The other comments section of the questionnaire provided a lot of information that was reviewed and incorporated where appropriate into the study, but a full analysis of this information was not carried out due to time limitations within the current study.

A multi-method design was used as it best fit the aims of the current research, however the statistical analysis was given most prominence, resulting in the thematic analysis of telephone interviews contributing a smaller amount to the overall study. It may have been helpful if possible to carry out more in-depth, longer, telephone interviews, and conduct a more in depth analysis of the data gathered. The thematic analysis approach lent itself well to the semi structured interview data gathered, but was less detailed due to the interview design. It may have been helpful to hold a service user focus group to assist with theme development. A further source

of bias may have been introduced with the researcher also being the interviewer.

The response rate to the postal questionnaire was 33%, which fulfilled the power requirements of the study. Due to financial constraints, no monetary incentive was offered as part of the research process, however this may have increased the response rate.

As with any self-selecting research sample, people who chose to take part may have been those doing particularly well, or particularly poorly. A small sample of data of non-respondents suggested that the participants were not significantly different to non-responders, however a larger selection of non-respondent information would be ideal to confirm this further.

Future Research

Although the results of the current study were positive in favour of gains being made for patients with CFS, and mostly being maintained over time, this is not representative of much of the research literature into CFS. Most findings suggest that a CBT approach can be useful, but not necessarily more efficacious than comparator groups, particularly Graded Exercise Therapy, and gains made often diminish over time. Further research, in particular, incorporating long term outcomes is essential in order to best direct service provision. Research into alternative interventions to CBT

would be highly clinically relevant, as UK clinical guidance is based on research findings and this may allow further interventions to be offered as standard, providing a higher level of choice, and individualization of treatment to patients.

Research with CFS patients should use as few, and as relevant outcome measures as possible in order to reduce participant burden and prevent irrelevant information being collected. More appropriate, condition specific measures could be developed with patients who have the condition.

The current study collected information provided in the 'other comments' section on the questionnaire, and future research could analyse these in more detail. The telephone interviews used in the research were short and based on a semi-structured schedule. The high number of participants who consented to be contacted for interview suggests future qualitative research to gather more in depth information about service users' experiences may be beneficial to assist in future service development. In particular, in a condition with such a wide range of symptoms and treatment uncertainty, the more detailed information provided by qualitative analysis is essential to inform results found in quantitative analysis.

Conclusion

The results of the current study refuted predictions, finding outcomes for patients with CFS using a multi disciplinary service continued to be maintained or improve over time. These results suggest that the target service was offering an approach which was effective and was found to be highly acceptable to participants. The interviews highlighted that participants found the approach offered by the service provided validation, education and a flexible structure. The interviews showed the service could improve access, offer both group and individual approaches, where applicable in combination, and offer a more holistic approach. Increasing telephone-based appointments would assist the service in offering help to patients unable to attend due to the severity of their condition. The service offered some GP training, and they could broaden this to other health service professionals. The theme of validation of the condition was key to participants as so many had faced a battle to gain a diagnosis and be believed about their condition, it is unfortunate that service contact prior to a specialist CFS service did not provide such validation, and training and understanding may be a key factor in this. For the patients who were not assisted by the approach taken by the service, further interventions could be incorporated and researched to make clinical interventions for CFS as useful as possible, and bridge the gap between research, which often lacks real life application, and clinical practice.

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Critical Appraisal

This section will identify the reasons I was interested in this area of research, and my experience of the research process.

The birth of the project

Coming up with an idea for a thesis level project was a difficult task for me. I feel this was partly because I lacked confidence that I could complete something so huge and seemingly important, and partly because I did not have a specific area of interest that I was passionate enough to know it would keep me going through the whole project. I was aware from hearing staff research presentations that I wanted to do something that I had developed, as opposed to an "off-the shelf" idea. I wonder if this was partly pride and partly feeling, particularly at the start of the training process, that I had to prove myself. As the project, and training, progressed, I was better able to see the benefits of doing a pre-existing project, however I am still grateful that a project I devised myself was achievable.

My interest in CFS/ME stems from having a close relative with the condition. Over the years I have watched him receive several different 'treatments' and his understanding and knowledge of the condition develop. From a clinician's perspective, he is a nightmare patient. CFS leaves him struggling to think clearly and impacts on his memory, so the idea of planning or keeping diaries (both key aspects to a CBT based intervention for CFS) are implausible to him. He saw a trainee psychologist over a few sessions, who

tried a few different approaches, then left to get married, in his eyes, not having helped at all. Partly I feel his personality affects his attitude, as well as his desperate need for a cure, but I also feel his condition adds to this. In some ways, I believe that personality factors are inextricable with the condition, some would say precipitating, others perpetuating, symptoms. My motivation for the current research was perhaps partly, because of my personal experience; I would love to find a way to effectively treat this condition. Partly, the motivation may also stem from the fear of a lack of competence of working with patients suffering with CFS.

These motivations led me to decide that a project evaluating a service for CFS would be something by which I was inspired enough to possibly use as a thesis. I researched local service provision, and was lucky enough that the first service I contacted were keen to be involved in research. They had been part of previous research projects, and were able to give useful information on what type of research might be achievable, and what type of data they had available. My findings from the first year literature review, was that there were very few long-term outcome studies for CFS. Discussing this with the service, it was decided this was a plausible research idea which would be beneficial to them.

I was inspired by meeting the clinicians at the service and brimming with passion about the difference this research could make. I enjoyed writing my proposal and feel like perhaps it was one of the only pieces of work I had done that I was putting my full self into. I was adamant that a mixed

methods approach would be most suitable to meet the needs of the research question and the service itself. I felt able to fully defend this in the review of my proposal, being aware of the challenges this would pose. Reviewing this decision, I still feel it was the right choice. This was supported in comments made in the interviews that interviewees struggled to fit themselves into questionnaire boxes. I was concerned at times that the interview schedule was perhaps too repetitive of the questionnaire questions, but was really surprised at how much material the interviews generated.

Ethics

I would describe the ethics process as painful, and perhaps the area where most luck is involved as to whether it drastically changes the research timescale or not. As having previously worked as a Clinical Studies Officer, and been on the receiving end of NHS NRES forms, I perhaps had an unrealistic expectation as to how easy the process may be. A key issue was that the NHS ethics forms are not suitably tailored to fit the requirements of psychological studies, with a lot of emphasis on medical research. There was a real lack of clarity about the process for local Research and Development Board applications, and perhaps the most frustrating point, listening to cohort experiences as a whole, was the wide range of responses from local ethics committees. My experience was that the officer dealing with my case changed part way through the ethics process, and in the meantime, lost all of the paperwork that I sent to them. This led to a lot of

chasing up, resending of information, and frustration at my end, and probably theirs too. The massive gap between LREC approval and local Trust R & D approval was most difficult, as the longer it went on, the less time I had to receive the questionnaire returns and enter the data. Final ethics and R & D approval felt more like a frustrating ending as opposed to an exciting beginning.

Finance

One of the difficulties of doing a postal survey was the cost. I underestimated the cost of printing and postage and, although the DClinPsy course budget partly funded it, there was quite a lot of personal financing required. In particular I felt it was important to let participants have a summary of the findings if they wished, and this was something I was aware I would have to pay for totally myself. Financing was a key decider in whether a payment incentive could be offered in order to improve response rate. Initially I was hoping to offer a £5.00 shop voucher, but had to abandon that idea. The final response rate of 33% was about what had been anticipated, but I feel an incentive may have improved this. The issue of finance led to difficulties when the service claimed not to have a budget to pay for research-related postage. This meant the postage went through the University, and was franked with their post-mark. One participant contacted the service complaining that they had not consented for the NHS to pass their details on to a university for the research. This complaint would have

been avoided if, firstly the letters were sent from the service, or, as originally planned, an initial letter had gone out from the service prior to the research pack being sent. The local R & D Board had decided this was not essential on the grounds that it would be less intrusive for people to receive just one letter. Following the complaint, the service were much more cooperative in sending the reminder mail out from their postal system.

Interviews

I found the interview process really positive; I was nervous when I started carrying out the telephone interviews, but my confidence grew as they went on. I was surprised at how keen people were to take time out of their day to discuss their condition and their experiences. I became very aware of the differences in being a therapist and being a researcher. At times, I found it very hard to separate these, and not offer suggestions or advice to the interviewees. The interviews were not expected to last longer than 15 minutes, yet one call lasted 40 minutes. I checked with the interviewee if they wanted to continue, and they were keen to discuss their experiences more fully. I am still unsure as to whether I should have ended the interview earlier or let them carry on, bearing in mind principles of pacing for CFS sufferers. One participant was doing a university research project and was interested in how the thesis was going, and I found this difficult as I was unsure how much to share with her. This also made me feel a need to be a "good" researcher, perhaps feeling I was being judged by someone about my research skills.

Data entry and analysis

Data entry was probably something I felt would be emotionally benign and a part of the work I would be able to do without too much thinking involved. Interestingly, I feel this was more difficult that I anticipated: most respondents had written long comments in the ‘extra information’ section of the questionnaire, and these were often humbling and incredibly sad to read. It brought home what a tragic impact this condition has on peoples’ quality of life, the stigma still suffered by many, and the sometimes life saving benefit of accessing the right services. I also felt angry and sad for my own relative, that services like this are rare and still fail to cover much of the UK, and that he has inevitably experienced many of these difficulties and rarely shared them with me.

The analysis of the data was the area I was least confident in. We had incredibly helpful input from a statistician linked to the University, which assisted my analysis choice. When in one meeting he told me that the test I needed was very complicated, I realised how naively I went into the project, thinking that statistics would not be too much of an issue

Learning experience

I feel that doing a large research project has helped me to develop both academically and clinically. I have a much better understanding of research about CFS (and its downfalls) as well as a fuller understanding about why the research with this client group is so difficult to undertake. There has been some media coverage about the tension between research foci for CFS, and whether it takes a more psychological or medical approach. Some researchers have left the field due to the negative attitudes they encountered from some CFS sufferers who felt that a psychological orientation was demeaning to their real physical suffering. Interestingly, I also experienced such a negative attitude when I had an email from a participant who was angry that a psychologist was undertaking the research. They assumed that I viewed CFS to have a psychological not medical cause, and did not see that psychology had a place in its management. I was able to respond to this, highlighting I did not have a view on the causation of the condition, and was aware this was still an area being investigated. I can fully understand why there is such a volatile reaction to a condition that many people have had to battle with medics for years to get recognised and treated.

I found the overall positive response to the research overwhelming. The majority of respondents not only completed a fairly long battery of questionnaires, but also wrote a lot of additional information at the end of the questionnaire pack. The fact that over half of respondents consented to take part in the telephone interviews was also a surprise to me. Several participants thanked me for carrying out research, which made me feel optimistic, and pressured to make sure my work justified this gratitude.

Clinically, the research has helped inform my client work. I have started working with a client suffering CFS and have been able to apply some of the ideas suggested by the current respondents, as well as feeling a lot more confident in working with clients with this condition. As the symptoms of CFS are so varied, ways to manage them are often applicable to people suffering several different conditions, which I feel will be beneficial for me in future working.

The research process is difficult and stressful to navigate, and any future research I undertake will be with several other people prepared to share some of that burden. I used to believe it was unethical for clinical psychologists to work without doing research; perhaps I still feel that, but I can also understand why people would shy away from being involved in research. I was lucky enough to have the structure of the training course and allocated time in which to do the research, and still found it incredibly difficult to manage the multiplicity of tasks. At one point, I went through a few weeks of suffering high levels of anxiety continually, which looking back,

was probably a combination of workload and the knowledge that in a short period I had to write a thesis, go to job interviews and start thinking about relocating when the course ended. I wonder if knowing that high stress levels can be a real contributing factor to developing CFS, made me very aware of the potential consequences of overworking and focusing on what my priorities should be.

Appendix A: National Institute for Clinical Excellence Diagnostic Guidance. (Turnbull et al., 2007)

Box 1 Symptoms that may indicate CFS/ME

Consider the possibility of CFS/ME if a person has:

- fatigue with all of the following features:
  - new or had a specific onset (that is, it is not life long)
  - persistent and/or recurrent
  - unexplained by other conditions
  - has resulted in a substantial reduction in **activity** level characterised by post-exertional malaise and/or fatigue (typically delayed, for example by at least 24 hours, with slow recovery over several days)

and

- one or more of the following symptoms:
  - difficulty with sleeping, such as insomnia, hypersomnia, unrefreshing sleep, a disturbed sleep–wake cycle
  - muscle and/or joint pain that is multi-site and without evidence of inflammation
  - headaches
  - painful lymph nodes without pathological enlargement
  - sore throat
  - cognitive dysfunction, such as difficulty thinking, inability to concentrate, impairment of short-term memory, and difficulties with word-finding, planning/organising thoughts and information processing
  - physical or mental exertion makes symptoms worse
  - general malaise or 'flu-like' symptoms
  - dizziness and/or nausea
  - palpitations in the absence of identified cardiac pathology.

The symptoms of CFS/ME fluctuate in severity and may change in nature over time.

Box 2 Consider other diagnoses or comorbidities before attributing clinical features to CFS/ME

In particular, investigate these 'red flag' features:

- localising/focal neurological signs
- signs and symptoms of inflammatory arthritis or connective tissue disease
- signs and symptoms of cardiorespiratory disease
- significant weight loss
- sleep apnoea
- clinically significant lymphadenopathy.

Follow 'Referral guidelines for suspected cancer' (NICE clinical guideline 27) or other NICE guidelines as the symptoms indicate. See www.nice.org.uk for details.

● Be prepared to reassess the diagnosis ● Investigate significant symptoms

Appendix B
Downs and Black (1998) Measure

Appendix

Checklist for measuring study quality

Reporting

1. *Is the hypothesis/aim/objective of the study clearly described?*

yes	1
no	0

2. *Are the main outcomes to be measured clearly described in the Introduction or Methods section?*
If the main outcomes are first mentioned in the Results section, the question should be answered no.

yes	1
no	0

3. *Are the characteristics of the patients included in the study clearly described ?*
In cohort studies and trials, inclusion and/or exclusion criteria should be given. In case-control studies, a case-definition and the source for controls should be given.

yes	1
no	0

4. *Are the interventions of interest clearly described?*
Treatments and placebo (where relevant) that are to be compared should be clearly described.

yes	1
no	0

5. *Are the distributions of principal confounders in each group of subjects to be compared clearly described?*
A list of principal confounders is provided.

yes	2
partially	1
no	0

6. *Are the main findings of the study clearly described?*
Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (This question does not cover statistical tests which are considered below).

yes	1
no	0

7. *Does the study provide estimates of the random variability in the data for the main outcomes?*
In non normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered yes.

yes	1
no	0

8. *Have all important adverse events that may be a consequence of the intervention been reported?*
This should be answered yes if the study demonstrates that there was a comprehensive attempt to measure adverse events. (A list of possible adverse events is provided).

yes	1
no	0

9. *Have the characteristics of patients lost to follow-up been described?*
This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small that findings would be unaffected by their inclusion. This should be answered no where a study does not report the number of patients lost to follow-up.

yes	1
no	0

10. *Have actual probability values been reported(e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?*

yes	1
no	0

External validity

All the following criteria attempt to address the representativeness of the findings of the study and whether they may be generalised to the population from which the study subjects were derived.

11. *Were the subjects asked to participate in the study representative of the entire population from which they were recruited?*
The study must identify the source population for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant

population exists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as unable to determine.

yes	1
no	0
unable to determine	0

12. *Were those subjects who were prepared to participate representative of the entire population from which they were recruited?*
The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the main confounding factors was the same in the study sample and the source population.

yes	1
no	0
unable to determine	0

13. *Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?*
For the question to be answered yes the study should demonstrate that the intervention was representative of that in use in the source population. The question should be answered no if, for example, the intervention was undertaken in a specialist centre unrepresentative of the hospitals most of the source population would attend.

yes	1
no	0
unable to determine	0

Internal validity - bias

14. *Was an attempt made to blind study subjects to the intervention they have received ?*
For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.

yes	1
no	0
unable to determine	0

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

yes	1
no	0
unable to determine	0

16. *If any of the results of the study were based on "data dredging", was this made clear?*
Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.

yes	1
no	0
unable to determine	0

17. *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls ?*
Where follow-up was the same for all study patients the answer should yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.

yes	1
no	0
unable to determine	0

18. *Were the statistical tests used to assess the main outcomes appropriate?*
The statistical techniques used must be appropriate to the data. For example non-parametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.

yes	1
no	0
unable to determine	0

19. *Was compliance with the intervention/s reliable?*
Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.

yes	1
no	0
unable to determine	0

20. *Were the main outcome measures used accurate (valid and reliable)?*

For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.

yes	1
no	0
unable to determine	0

Internal validity - confounding (selection bias)

21. *Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?*
For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.

yes	1
no	0
unable to determine	0

22. *Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?*
For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.

yes	1
no	0
unable to determine	0

23. *Were study subjects randomised to intervention groups?*
Studies which state that subjects wererandomised should be answered yes except where method of randomisation would not ensure random allocation. For example alternate allocation would score no because it is predictable.

yes	1
no	0
unable to determine	0

24. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*
All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.

yes	1
no	0
unable to determine	0

25. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*
This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.

yes	1
no	0
unable to determine	0

26. *Were losses of patients to follow-up taken into account?*
If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes.

yes	1
no	0
unable to determine	0

Power

27. *Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?*
Sample sizes have been calculated to detect a difference of x% and y%.

	Size of *smallest* intervention group	
A	$<n_1$	0
B	n_1–n_2	1
C	n_3–n_4	2
D	n_5–n_6	3
E	n_7–n_8	4
F	n_8+	5

Appendix C
Table 1. Studies Used in critical Review

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Akagi et al. (2001) **UK** **Cognitive behavioral therapy for chronic fatigue syndrome in a general hospital—feasible and effective**	Retrospective questionnaire follow up	**Number and attrition:** 94, 51 of returned questionnaires had completed treatment. 38% dropout (36), 2 unanswered questionnaires **Demographics:** Average age 39, 37% male, 63% female, unclear if these are just questionnaire respondents or entire sample **Diagnostic Criteria:** ICD CFS/neurasthenia (F.48) **Average length of fatigue:** 96% had more than 6 months fatigue **Exclusion Criteria:** Unstated	**Intervention:** Individual CBT. **Length and duration:** Average 6 sessions over 6 months, length of session not stated. **Comparators:** Control group-naturalistic outcome study of patients presenting at the hospital before CBT was available **Therapists:** Liaison psychiatrist, clinical psychologist and clinical nurse specialist all trained in CBT for CFS Patients referred to department of psychological medicine	Individual self report Questionnaire mailed out to patients. Participants asked to answer for when illness was at its worst, and compare it to the month before follow up. **Assessment Points:** therapist rating at end of treatment, and follow up 3-66 month, average of 20 months	9 (18%) of treatment group described self as recovered "back to normal", 38 (75%) described self as functionally impaired. 51% felt moderately or very much improved, 22% unchanged and 10% worse.	41 (81%) of treatment group had fatigue at follow up

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Bazelmans et al. (2005) **Netherlands** **Cognitive Behaviour Group Therapy for Chronic Fatigue Syndrome: A Non-Randomised Waiting List Controlled Study**	Non randomised waiting list control	**Number and attrition:** 67, dropout 2 (3%) **Demographics:** Average age 36.6, 18 male (27%), 4449 female (73%) **Diagnostic Criteria:** CDC **Average length of fatigue:** 5.8 years **Exclusion Criteria** Had to stop any other intervention	**Intervention:** Group CBT (n=31), 7-10 per group **Length and duration:** 12 x 2 hour sessions over 6 months **Comparators:** Waiting list control (n=36) **Therapists:** 6 therapists in total, 2 per group. Discipline not stated. Supervised weekly by CBT for CFS specialists	**Physical Functioning:** Sickness Impact profile **Fatigue:** Checklist of Individual Strengths **Assessment Points**: Baseline and post intervention (6 months)	Functional Impairment improved significantly in waiting list, but not in CBT group	Moderate effect on fatigue and non significant trend in favour of CBT group

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Friedberg and Sohl (2009) **USA** **Cognitive-Behavior Therapy in Chronic Fatigue Syndrome: Is Improvement Related to Increased Physical Activity?**	Before and After design	**Number and attrition:** 30, 63% dropout (19) **Demographics:** Average age of completers 45.8, 100% (11) female **Diagnostic Criteria:** CDC **Average length of fatigue:** 8.4 years **Exclusion Criteria** Stated used CDC exclusion, most exclusions due to melancholic depression	**Intervention:** Individual graded activity orientated CBT **Length and duration:** Between 6 and 32 (average 12). Initially 1 hour sessions reduced to 45 minutes then 30 minutes, weekly or bi-weekly, 7-35 weeks. Some telephone based Based on Friedberg (2004) manualized CBT **Comparators:** None **Therapists:** Author, qualified psychologist	**Physical Functioning:** MOS SF36 **Fatigue**: Fatigue Severity Scale **Assessment Points**: Baseline and post intervention	3/11 clinically significantly improved, Small effect size (0.35)	6/11 Clinically significantly improved. Moderate effect size. (-0.78)

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Jason et al. (2007) **USA** **Non-pharmacologic Interventions for CFS: A Randomized Trial**	Randomized Controlled Trial	**Number and attrition:** 114, 24 excluded (25%) **Demographics:** Average age 44, 19 male (17%), 95 female (83%) **Diagnostic Criteria:** CDC **Average length of fatigue:** Not stated **Exclusion Criteria** -under 18 -wheelchair users -bedridden -pregnant	**Intervention:** Group CBT (n=29, not stated if split) **Length and duration:** 13 x 45 minute sessions fortnightly **Comparators:** Anaerobic Therapy Group (n=29) Cognitive Therapy Group (n =28) Relaxation Group control (n=28) **Therapists:** 2 x nurse therapists involved in all groups	**Physical Functioning:** MOS SF36 **Fatigue**: Fatigue Severity Scale **Assessment Points**: Baseline, post intervention, 6 month and 12 month	Physical functioning significantly higher in cognitive and CBT groups compared to anaerobic therapy and relaxation groups.	Trend for fatigue improvement over time in all groups. CBT and cognitive groups best improvements at 12 months..

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Nunez et al. (2011) **Spain** **Health-related quality of life in patients with chronic fatigue syndrome: group cognitive behavioural therapy and graded exercise versus usual treatment. A randomised controlled trial with 1 year of follow-up**	Prospective Randomized Controlled Trial	**Number and attrition**: 115, dropout 5 (4%) **Demographics:** Average age 43, 12 male (1%), 101 female (89%) **Diagnostic Criteria**: CDC **Average length of fatigue**: 2.8 years **Exclusion Criteria** -Past or current major depressive disorder -inability to attend sessions	**Intervention:** Multi disciplinary Group CBT with Graded Exercise Therapy and Pharmacological input (n 16) **Length and duration:** 9 x 90 minute sessions twice a week **Comparators**: Exercise counselling and pharmacological input **Therapists:** Clinical Psychologist for CBT group, Physiotherapist for exercise counselling group.	**Physical Functioning**: MOS SF36 **Fatigue**: Not assessed **Assessment Points**: Baseline, and 12 month	Physical functioning significantly worse in treatment group	Not assessed

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
O'Dowd et al. (2006*)* **UK** **Cognitive behavioural therapy in chronic fatigue syndrome: a randomised controlled trial of an outpatient group programme**	Double Blind Randomized Controlled Trial	**Number and attrition: 153,** 31 did not complete 6 and 12 month follow up (20%) **Demographics:** Average age 41, 51 male (33%), 102 female (67%) **Diagnostic Criteria:** CDC **Average length of fatigue:** Over 50% sample 5 years or more **Exclusion Criteria** -concurrent severe mental illness -planned or concurrent rehabilitation -inability to attend sessions	**Intervention:** Group CBT (n=52, 8-12 per group) **Length and duration:** 8 x 2 hour fortnightly sessions **Comparators:** Education and Support Group (n 50) 8 x 2 hour fortnightly sessions Standard medical Care (n=51**)** **Therapists:** Clinical Psychologist, Physiotherapist, Occupational Therapist. Same therapists for each group, at same time and same duration	**Physical Functioning:** MOS SF36 **Fatigue:** Chalder Fatigue Scale **Assessment Points**: Baseline, 6 month and 12 month	Little Change from baseline, and no differences between groups at 6 and 12 months	Mean score significantly lower for CBT group than other groups when pooled across time points

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Prins et al. (2001) **Netherlands** **Cognitive behaviour therapy for chronic fatigue syndrome: a multicentre randomised controlled trial**	Multi-Centre Randomized Controlled Trial	**Number and attrition:** 186 completed (25% dropout) **Demographics:** Average age 37, 58 male (21%), 212 female (79%) **Diagnostic Criteria:** CDC **Average length of fatigue:** 5.6 years ***Exclusion Criteria*** -under 18/over 60 -live within 1.5 hr travel time of clinic -pregnant or trying -not in other CFS research	**Intervention:** Group CBT **Length and duration:** 16 x 1 hour sessions over 8 months Comparators: Guided Support, x 1.5 hours over 8 months Natural Course **Therapists:** 13 x behaviour therapists (psychologists, psychiatrists, health scientists). Social worker with support group. Supervised by specialist in CBT for CFS	**Physical Functioning:** Sickness Impact profile Fatigue: **Checklist of Individual Strengths** **Assessment Points**: Baseline, post intervention and at 6 months post intervention (14 months)	CBT group significantly improved physical functioning compared to comparators at 8 and 14 months	CBT significantly better at CIS fatigue than comparator groups at 8 and 14 months .Support groups equivalent to natural course

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Ridsdale et al. (2001) **UK** **Chronic fatigue in general practice: is counselling as good as cognitive behaviour therapy? A UK randomised trial**	Randomized Controlled Trial	**Number and attrition:** 160, dropout 54 (24%), 31 lost to follow up. 48 classed as having CFS diagnosis **Demographics:** Average age 39.4 43 (27% male), 117 (73% female) **Diagnostic Criteria:** 3 months or more fatigue + CDC criteria-not all study had CFS **Average length of fatigue** 4.7 years **Exclusion Criteria:** -Psychotic -Inability to read/speak English -Current psychiatry, psychology or counselling treatment, -ability to attend -Learning disability which would affect measure completion	**Intervention:** Individual CBT **Length and duration:** 6 sessions lasting up to 1 hour. Duration not stated **Comparators:** Individual Psychodynamic Counselling **Therapists:** 3x CBT therapists or 3 x Counsellors Participants recruited to study by GP's	**Physical Functioning:** Not assessed **Fatigue:** Chalder Fatigue Scale **Assessment Points:** Pre treatment, post treatment (approx 3 months) , and follow up at 6 months	Not assessed	Scores reduced for all CFS participants, non significant trend in favour of counselling..

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Saxty & Hansen, (2005) **UK** **Group Cognitive Behavioural Therapy for Chronic Fatigue Syndrome: A Pilot Study**	Before and after study	**Number and attrition:** 6 **Demographics:** Average age 42, 2, male (33%), 4 female (67%) **Diagnostic Criteria:** CDC **Average length of fatigue:** 4.6 years **Exclusion Criteria** Not stated	**Intervention:** **CBT Group** **Length and duration:** 10 x 1 hour sessions weekly then fortnightly **Comparators:** Exercise counselling and pharmacological input **Therapists:** Liaison Nurse therapist, CBT trainee	**Physical Functioning:** Not assessed **Fatigue:** Chalder Fatigue Scale **Assessment Points**: Baseline, post intervention, and 3 months	Not assessed	Significant improvement in fatigue post intervention and 4/6 maintained at 3 month follow up,

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Scheeres et al (2008) **Netherlands** **Implementing Cognitive Behavioral Therapy for Chronic Fatigue Syndrome in a Mental Health Center: A Benchmarking Evaluation**	Clinical evaluation and Benchmarking against Randomized Controlled Trials	**Number and attrition:** 112, 28 non starters and 12 dropped out (11%) **Demographics:** Average age 39, 38 (34%) male, 74 (66%) female **Diagnostic Criteria:** CDC **Average length of fatigue:** 5.5 years **Exclusion Criteria:** -under 18 -involved in claim for disability benefit	**Intervention:** Individual CBT **Length and duration:** **16 x 1 hour sessions over 6-8 months.** **Comparators:** Benchmarking against RC's **Therapists:** 9 x behaviour therapists trained by two CBT specialists	**Physical Functioning**: MOS SF36 **Fatigue:** Fatigue Severity on Checklist of Individual Strengths,	Physical functioning increased from 53.5 to 69.1 (effect size 0.64) Not as efficacious as some of the benchmarked RCT's	Fatigue reduced from average 48.7 to 35.4 (effect size1.12)

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Schreurs et al. (2011) **Netherlands** **Cognitive behavioural treatment for chronic fatigue syndrome in a rehabilitation setting: Effectiveness and predictors of outcome**	Before and after study	**Number and attrition:** 149 completed (7% dropout) **Demographics:** Average age 34, 19 male (12%), 141 female (88%) **Diagnostic Criteria:** CDC **Average length of fatigue:** 6.8 years **Exclusion Criteria** -over 18 -severe psychopathology Ability for therapy 5 hours a day -extensive cognitive deficits -those involved in a legal procedure were scrutinized	**Intervention:** **CBT Group (n=6)** **Length and duration:** 75 sessions over 25 weeks. Length not stated. **Comparators:** None **Therapists:** Psychologist, Rehabilitation physician, Physiotherapist, Occupational Therapist, Sports instructor, Social worker	**Physical Functioning:** MOS SF36 **Fatigue:** Checklist of Individual Strengths **Assessment Points**: Baseline, post intervention, and 6 months	Physical functioning significantly improved from baseline to post treatment, and improvement maintained at follow up	Fatigue significantly improved from baseline to post treatment-improvements maintained at follow up. At post treatment 33.8% significant clinical improvement, 30.6% at 6 month

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Stubhaug et al. (2008) **Norway** **Cognitive–behavioural therapy v. mirtazapine for chronic fatigue and neurasthenia: randomised placebo-controlled trial**	Randomized Controlled Trial and Combined Treatment Crossover	**Number and attrition:** 72 completed, dropout 9 (13%) **Demographics:** Average age 46, 13 male (18%), 59 female (82%) **Diagnostic Criteria:** CDC **Average length of fatigue:** not stated **Exclusion Criteria:** -Somatic or psychological disorders	**Intervention: Comprehensive CBT Group (n12-25)** **Length and duration:** 2 x 1.5 hours a week, duration not stated **Comparators:** Mirtazapine (anti depressant)/Placebo CBT then Mirtazapine/Placebo Mirtazapine/Placebo+CBT **Therapists:** Psychiatrist, Psychiatric Nurse, Physiotherapist	**Physical Functioning:** MOS SF36 **Fatigue:** Chalder Fatigue Scale **Assessment Points**: Baseline, 12 week, 24 week	Physical functioning no significant differences between groups	At 12 week assessment, CCBT group significantly better than comparators. At 24 weeks CCBT +Mirtazapine significantly better than comparators (including Mirtazapine+CBT)

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Tummers et al. (2010) **Netherlands** **Effectiveness of Stepped Care for Chronic Fatigue Syndrome: A Randomized Noninferiority Trial**	Randomized non-inferiority study	**Number and attrition:** 171, 2 excluded due to medical explanation- then group size changed depending on whether they opted for further CBT 12% dropout **Demographics:** Average age 37.4, 35 (21%) male, 133 (79%) female **Diagnostic Criteria:** CDC **Average length of fatigue:** 7 years **Exclusion Criteria:** -Under 18 -ability to speak/read Dutch, -exclusion of other causes of fatigue -involvement in legal procedure about sickness benefit	**Intervention:** Individual CBT using participants involved in previous trial of guided self instruction (Knoop et al. 2008). Minimal guided self instruction followed by CBT (Stepped care). **Length and duration:** Minimal intervention of at least 16 weeks guided self instruction involving email contact with a therapist and a final face to face session. 14 x one hour sessions over 6 months **Comparators:** Care as Usual (waiting list followed by CBT if requested) **Therapists:** 5 x Cognitive Behavioural Therapists involved in both interventions	**Physical Functioning:** Disability scale of Sickness outcome Inventory, MOS SF36 **Fatigue**: Fatigue Severity on Checklist of Individual Strengths, **Assessment Points**: Baseline, after either waiting list or guided self instruction, then again after CBT	No significant differences between the groups. Effect sizes Physical Functioning: Stepped Care: 0.88 Care as Usual: 0.70 Patients who had Guided Self Instruction followed by CBT required less sessions than those on waiting list followed by CBT. Stepped Care approach had more participants with clinically significant improvement than Care as Usual	No significant differences between the groups. Effect Sizes Fatigue: Stepped care: 1.37 Care as Usual: 1.42 Stepped Care approach had more participants with clinically significant improvement than Care as Usual

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
White et al. (2011) *UK* **Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial**	Parallel Group Randomized Trial	**Number and attrition:** 640, 2% dropout **Demographics:** Average age 38, 145 male (23%), 495 females (77%) **Diagnostic Criteria:** Oxford and CDC **Average length of fatigue:** 2.7 years **Exclusion Criteria:** -Under 18 -Risk of self harm, -Ability to read/ speak English, -Ability to attend appointments -Received a trial treatment at a Pace clinic before	**Intervention:** Individual Standard Medical Care (SMC) +CBT (n=161) **Length and duration:** Initial 90 minute sessions reduced to 50 minutes. Average of 14 sessions over 24 weeks. **Comparators:** *SMC +Adaptive Pacing* (APT) (n= 160) - planning and pacing activity- 10 sessions of therapy *SMC+ Graded Exercise* Therapy (n= 160)- incremental increases in exercise from an individualised baseline *Control: SMC (n=160),* 3 sessions **Therapists:** trained by expert therapists in CFS. CBT was by clinical psychologist and nurse therapists, GET was by physiotherapist and APT by Occupational Therapist	**Physical Functioning:** Medical Outcomes Study Short Form36 **Fatigue:** Chalder Fatigue Scale **Assessment points:** Baseline, 12 week (mid), 24 week(post), one year after randomising	Both GET and CBT significantly more improved than SMC and APT. Improvement from baseline 71% CBT, 70% GET, 58% SMC, 49% APT. Change continued increasing at 52 weeks	Both GET and CBT significantly more improved than SMC and APT. The number most improved from baseline was higher in the GET group than CBT group (80% vs 76%) No difference in improvement from baseline between APT and SMC change continued increasing at 52 weeks

Authors, location and Title	Design	Participants	Intervention	Outcome measure and Assessment Points	Results physical Functioning	Results fatigue
Wittowski et al. (2004) **UK** **A cognitive behaviour therapy group for patients with chronic fatigue syndrome: a preliminary investigation**	Before-and-after	**Number and attrition:** 5 completed, 1 dropout (17%) **Demographics:** Average age 43, 6 females (100%) **Diagnostic Criteria:** CDC **Average length of fatigue:** two to seven years *Exclusion Criteria:* -No primary Psychiatric diagnosis	**Intervention:** **CBT group (n=6)** **Length and duration:** 8 x 1.5 hours a week **Comparators:** None **Therapists:** **2 x Trainee Clinical Psychologists, supervised by senior psychologist**	**Physical Functioning:** Not assessed **Fatigue:** Chalder Fatigue Scale, Profile of Fatigue Related Symptoms **Assessment Points**: Baseline, Mid group, Post group, 3 months.	Not assessed	Reduction in fatigue

Table 2. Downs and Black Methodological Scoring Measure results for Group Studies

Group Studies	Design	Total	Reporting (max 11)	External Validity (max 3)	Internal Validity Bias (max 7)	Internal validity confounding (max 6)	Power (max 5)
Bazelmans et al (2005)	non randomized controlled study	22	8	**3**	4	2	5
Jason et al (2007)	RCT	22	7	**2**	5	3	5
Nunez et al (2011)	RCT	25	8	**3**	4	5	5
O'Dowd et al (2006)	RCT double blind	27	8	**3**	6	5	5
Prins et al (2001)	RCT	27	8	**3**	6	5	5
Saxty and Hansen (2005)	Before-and-after	18	7	**3**	4	1	3
Schreurs et al (2011)	Before-and-after	24	7	**3**	5	4	5
Stubhaug et al (2008)	RCT and combined treatment crossover	28	9	**3**	6	5	5
Wittkowski et al (2004)	Before-and-after	18	6	**3**	4	2	3

Table 3. CBT elements of Group Studies

Author	Manualized	Graded Exercise Increase	Graded activity	Activity management and pacing	Goal Setting	Sleep Management	Relaxation Techniques
Bazelmans et al (2005)			yes	yes			
Jason et al (2007)		yes	yes	yes	yes	yes	
Nunez et al (2011)		yes				yes	yes
O'Dowd et al (2006)		yes	yes	yes	yes	yes	yes
Prins et al (2001)		yes	yes	yes	yes		
Saxty and Hansen (2005)		yes	yes	yes		yes	
Schreurs et al (2011)		yes		yes	yes		
Stubhaug et al (2008)		yes			yes		
Wittkowski et al (2004)			yes	yes		yes	yes

Author	Stress Management	cognitive challenging	Psychoeducation	Problem solving	Relapse prevention	Homework	Given literature	Individualised
Bazelmans et al (2005)		yes				yes	yes	
Jason et al (2007)		yes			yes	yes		yes
Nunez et al (2011)		yes	yes		yes			
O'Dowd et al (2006)	yes	yes	yes		yes		yes	
Prins et al (2001)		yes	yes		yes			
Saxty and Hansen (2005)		yes	yes	yes	yes		yes	
Schreurs et al (2011)		yes		yes				
Stubhaug et al (2008)		not stated						
Wittkowski et al (2004)	yes	yes	yes		yes	yes	yes	

Table 4. Downs and Black methodological scoring measure results for individual studies

Study	Design	Total	Reporting (max 11)	External Validity (max 3)	Internal Validity Bias (max 7)	Internal validity confounding (max 6)	Power (max 5)
Akagi et al (2001)	case series	21	7	**2**	5	2	5
Friedberg and Sohl (2009)	Before-and-after	20	7	**2**	4	2	5
Ridsdale et al (2001)	RCT	27	8	**3**	5	6	5
Scheeres et al (2008)	Before-and-after	23	7	**3**	5	3	5
Tummers et al (2010)	Randomised noninferiority study	26	8	**3**	5	5	5
White et al (2011)	RCT	28	9	**3**	6	5	5

Table 5. CBT characteristics for Individual intervention

Author	Manualized	Graded Exercise Increase	Graded activity	Activity management and pacing	Goal Setting	Sleep Management	Relaxation Techniques
Akagi et al (2001)		yes					
Friedberg and Sohl (2009)	yes	yes	yes			yes	yes
Ridsdale et al (2001)				yes		yes	
Scheeres et al (2008)		yes	yes	yes	yes		
Tummers et al (2010)			yes	yes	yes		
White et al (2011)	yes		yes	yes	yes	yes	

Author	Stress Management	cognitive challenging	Psychoeducation	Problem solving	Relapse prevention	Homework	Given literature	Individualised
Akagi et al (2001)		yes	yes	yes			yes	
Friedberg and Sohl (2009)		yes						yes
Ridsdale et al (2001)		yes	yes		yes	yes		
Scheeres et al (2008)		yes						yes
Tummers et al (2010)		yes	yes		yes			
White et al (2011)		yes		yes	yes			

Appendix D
Search Results

Search Term	Cognitive behavioural therapy	CBT	Cognitive Therapy	Behaviour Therapy	Graded Exercise Therapy	Activity Management	Pacing
Chronic Fatigue Syndrome OR CFS, AND							
Psychinfo (8/8/11)	117 (CFS AND) 56	75 (CFS AND 61)	179 (CFS AND 113)	132 (CFS AND 87)	29 (CFS AND 19)	4 (CFS AND 3)	6 (CFS AND 4)
Pubmed (1/10/11)	367	67	367	315	67	59	15
Scopus (1/1/12)	66	84	494	86	44	3	15

Myalgic Encephalopathy AND	Cognitive behavioural therapy	CBT	Cognitive therapy	Behaviour therapy	Graded Exercise Therapy	Activity Management	Pacing
Psychinfo (8/8/11)	4	5	8	3	4	1	1
Pubmed (1/10/11)	3	1	3	3	1	1	1
Scopus (1/1/12)	1	1	5	1	2	0	1

Table 6. Search Terms and Results

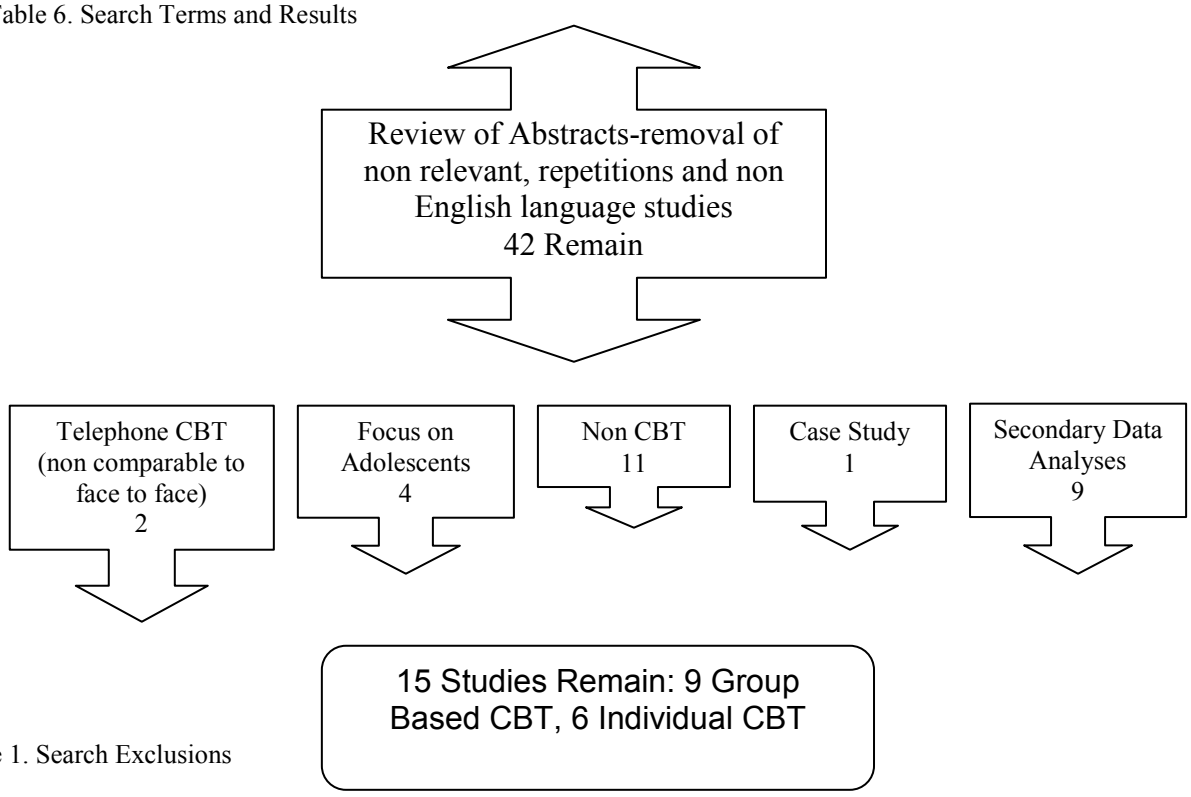

Figure 1. Search Exclusions

Appendix E

Data extraction form

Author	Design	No. of participants completed	Dropout	Dropout %	Completed all measures and follow up	Country	Ind or group	size of group	No of sessions	length	Time
Intervention 1	**Intervention 2**	Intervention 3	**Intervention 4**	**Control**	**Assessment times**	**Follow UP**	**Average Age**	**described baseline with controls**	**Male**	**Female**	**Length of duration**
Setting	**Outcome Measure**	**Therapist**	**supervision**	**experienced**	**results physical health**	**results fatigue**					

Appendix F
Treatment Approach of Research Service

Treatment approach of Research service

Treatments offered are based on the NICE guidelines for CFS/ME (2007). They are based on a cognitive behavioural model, addressing identified perpetuating factors and include graded activity and exercise.

- Psycho-education of CFS/ME
- Activity management
- Effective Rest
- Sleep hygiene
- Diet
- Stress Management
- Relaxation Training
- Thoughts, feelings and behaviour links
- Dealing with memory and concentration problems
- Graded exercise
- Goal setting
- Advice regarding workplace adjustments and returning to work
- Dealing with setbacks incorporating wellness recovery action plans (WRAP)

Appendix G
Research Questionnaire

Questionnaire Pack

- Each questionnaire has instructions, which you should read before answering the questions. There are no right or wrong answers.
- Please try and answer every question
- Please do not spend too long on each question. The total pack should take no more than 25 minutes to complete.
- Some of the questionnaires are double sided, please ensure you have completed both sides.

1.While using the CFS/ME service, did you receive (please tick):
Individual input? ☐ Group input? ☐ Both? ☐

2.What other help have you used for managing your Chronic Fatigue Syndrome/ME? E.g. *medication*, *other therapy, support group*

……

……

3.After using the service how confident do you feel in managing your condition (please tick)?

I feel less confident than before ☐ same as before ☐ more confident than before ☐

4.Approximately how many years ago do you feel you became ill with CFS?

…..Years ……Months

5.Approximately how long ago were you diagnosed as having CFS?

……Years …….Months

6.Please give details of how you spend your time.

Paid work ☐ Unpaid work ☐ Childcare ☐
Other activities (please specify)
……

7. During the time you saw the CFS service you should have been given handouts of information discussed. How often do you refer back to these (please tick)?
Often ☐ Never ☐ Sometimes ☐

8.Did you use the service again after the first time you used it? Yes ☐ No ☐

9.If so how helpful did you find it the second time?
……..

Appendix H

SF-36 Physical Functioning Scale

These questions are about activities you might do during a typical day.

Does your health limit you in these activities?

Please circle one answer for each question.

1.Vigorous activities such as running, lifting heavy objects, participating in strenuous sports

Yes-limited a lot Yes-limited a little No-not limited at all

2. Moderate activities such as moving a table, pushing a vacuum cleaner, bowling or playing golf.

Yes-limited a lot Yes-limited a little No-not limited at all

3. Lifting or carrying groceries

Yes-limited a lot Yes-limited a little No-not limited at all

4. Climbing several flights of stairs

Yes-limited a lot Yes-limited a little No-not limited at all

5. Climbing one flight of stairs

Yes-limited a lot Yes-limited a little No-not limited at all

6. Bending, kneeling or stooping

Yes-limited a lot Yes-limited a little No-not limited at all

7. Walking more than a mile

Yes-limited a lot Yes-limited a little No-not limited at all

8. Walking several blocks (about half a mile)

Yes-limited a lot Yes-limited a little No-not limited at all

9. Walking one block (about 100 yards)

Yes-limited a lot Yes-limited a little No-not limited at all

10. Bathing or dressing yourself

Yes-limited a lot Yes-limited a little No-not limited at all

Appendix I

Chalder Fatigue Questionnaire

We would like to know about any problems you have had with feeling tired, weak or lacking in energy in the last month. Please answer all the questions by circling the answer which applies most closely to you. If you have been feeling this way for a long while then compare yourself to how you felt when you were last well.

1. Do you have problems with tiredness?

Less than usual No more than usual More than usual Much more than usual

2. Do you need to rest more?

Less than usual No more than usual More than usual Much more than usual

3. Do you feel sleepy or drowsy?

Less than usual No more than usual More than usual Much more than usual

4. Do you have problems starting things?

Less than usual No more than usual More than usual Much more than usual

5. Do you lack energy?

Less than usual No more than usual More than usual Much more than usual

6. Do you have less strength in your muscles?

Less than usual No more than usual More than usual Much more than usual

7. Do you feel weak?

Less than usual No more than usual More than usual Much more than usual

8. Do you have difficulty concentrating?

Less than usual No more than usual More than usual Much more than usual

9. Do you make slips of the tongue when speaking?

Less than usual No more than usual More than usual Much more than usual

10. Do you find it more difficult to find the correct word?

Less than usual No more than usual More than usual Much more than usual

11. How is your memory?

Better than usual No worse than usual Worse than usual Much worse than Usual

Appendix J
Symptom Checklist

Please answer each question by circling yes or no even if the question does not seem to apply to your situation-the questionnaire is designed to cover a variety of medical conditions.

In the last few weeks: (please circle)

1. Tremors or involuntary movements have Inconvenienced me	Yes	No
2. I have usually managed to get enough sleep	Yes	No
3. I have been getting abnormally tired	Yes	No
4. I have been comfortable in the chair I usually sit in	Yes	No
5. I have been able to control the position of my head easily	Yes	No
6. I have had a good appetite	Yes	No
7. I have had difficulty swallowing	Yes	No
8. I have had too much saliva, causing drooling	Yes	No
9. My breathing has been comfortable and easy	Yes	No
10. Pain has been a problem for me?	Yes	No
11. My bowels have been working normally	Yes	No
12, I have had a leakage of faeces from the bowels	Yes	No
13. I have had urinary (water) problems	Yes	No
14. I have been having painful muscle spasms	Yes	No
15. I have been troubled by tingling, itching or numbness	Yes	No
16. I have sometimes felt very weak	Yes	No
17. My memory and concentration are as good as people of the same age as me	Yes	No
18. I have seen or heard things which are really not there	Yes	No

19. My vision has been normal	Yes	No
20. Stiffness has been a problem	Yes	No
21. My balance has been good	Yes	No
22. I have been able to do things at normal speed	Yes	No
23. Clumsiness has been a problem	Yes	No
24. I have often felt sad or depressed	Yes	No
25. My hearing has caused problems	Yes	No
26. My weight has been steady	Yes	No

In the last few months:

27. I have had blackouts or 'funny turns'	Yes	No
28. I have had sexual problems	Yes	No
29. My periods have been trouble free (pre menopausal women only)	Yes	No

In the last few weeks I have been troubled by other symptoms: (please specify)

……

……
……

Appendix K
Hospital Anxiety and Depression Scale (HADS)

Please read every sentence and **circle one answer for each question** which best describes how you have been feeling over the last few weeks. You do not have to think too much to answer. In this questionnaire spontaneous answers are more important.

I feel tense or wound up:
Most of the time
A lot of the time
From time to time, occasionally
Not at all

I still enjoy the things I used to enjoy
Definitely as much
Not quite so much
Only a little
Hardly at all

I get a sort of frightened feeling as if Something awful is about to happen
Very definitely and quite badly
Yes but not too badly
A little but it doesn't worry me
Not at all

I can laugh and see the funny side of things
As much as I always could
Not quite so much now
Definitely not so much now
Not at all

Worrying thoughts go through My mind
A great deal of the time
A lot of the time
Not too often
Very little

I feel cheerful
Never
Not often
Sometimes
Most of the time

I can sit at ease and feel relaxed
Definitely
Usually
Not often
Not at all

I feel as if I am slowed down
Nearly all the time
Very often
Sometimes
Not at all

I get a sort of frightened feeling like 'butterflies' in the stomach'
Not at all
Occasionally
Quite often
Very often

I have lost interest in my appearance
Definitely
I don't take as much care as I should
I may not take quite as much care
I take just as much care as ever

I feel restless as if I have to be on the move
Very much indeed
Quite a lot
Not very much
Not at all

I look forward with enjoyment to things
As much as I ever did
Rather less than I used to
Definitely less than I used to
Hardly at all

I get a sudden feeling of panic
Very often indeed
Quite often
Not very often
Not at all

I can enjoy a good book or radio or TV programme
Often
Sometimes
Not often
Very seldom

Appendix L
Self Efficacy Questionnaire

Please circle the appropriate response for the 10 questions below.

1. I can always manage to solve difficult problems if I try hard enough

Not true at all *Hardly true* *Moderately true* *Exactly true*

2. If someone opposes me, I can find the means and ways to get what I want

Not true at all *Hardly true* *Moderately true* *Exactly true*

3. It is easy for me to stick to my aims and accomplish my goals.

Not true at all *Hardly true* *Moderately true* *Exactly true*

4. I am confident that I could deal efficiently with unexpected events.

Not true at all *Hardly true* *Moderately true* *Exactly true*

5. Thanks to my resourcefulness, I know how to handle unforeseen situations.

Not true at all *Hardly true* *Moderately true* *Exactly true*

6. I can solve most problems if I invest the necessary effort.

Not true at all *Hardly true* *Moderately true* *Exactly true*

7. I can remain calm when facing difficulties because I can rely on my coping abilities

Not true at all *Hardly true* *Moderately true* *Exactly true*

8. When I am confronted with a problem, I can usually find several solutions.

Not true at all *Hardly true* *Moderately true* *Exactly true*

9. If I am in trouble, I can usually think of a solution.

Not true at all *Hardly true* *Moderately true* *Exactly true*

10. I can usually handle whatever comes my way.

Not true at all *Hardly true* *Moderately true* *Exactly true*

Appendix M

Clinical Global Improvement Scale

Overall how much do you feel your illness has changed since you were first assessed by the CFS service (please circle one)?

Very much better

Much better

A little better

No change

A little worse

Much worse

Very much worse

Please mark the line to describe the severity of your pain (if you do not experience pain please mark at the 'no pain' end of the line)

No Pain _____ **Pain as bad As possible**

Please mark the line to describe the quality of your sleep.(good quality sleep would be for example if you feel you sleep well and feel refreshed after sleeping)

Very good _____ Very Poor

Appendix N

Epworth Sleepiness Scale

Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations?
Answer considering how you have felt over the past week or so.

0 = Would never doze
1 = Slight chance of dozing
2 = Moderate chance of dozing
3 = High chance of dozing

1. Sitting and reading	
2. Watching TV	
3. Sitting inactive in a public place (e.g., theater or meeting)	
4. As a passenger in a car for an hour without a break	
5. Lying down to rest in the afternoon when able	
6. Sitting and talking to someone	
7. Sitting quietly after a lunch without alcohol	
8. In a car while stopped for a few minutes in traffic	

Appendix O
Further Comments

Thank you very much for taking the time to complete this questionnaire pack. Please use this sheet to write any other comments you have about your experience of using the xxxxx CFS service.

Appendix P

Fatigue Severity Scale (Krupp et al., 1989)

The FSS questionnaire contains nine statements that rate the severity of your fatigue symptoms. Read each statement and circle a number from 1 to 7, based on how accurately it reflects your condition during the past week and the extent to which you agree or disagree that the statement applies to you.

- A low value (e.g., 1); indicates strong disagreement with the statement, whereas a high value (e.g., 7); indicates strong agreement.
- It is important that you circle a number (1 to 7); for every question.

FSS Questionnaire							
During the past week, I have found that:	**Disagree <----------> Agree**						
My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
Exercise brings on my fatigue.	1	2	3	4	5	6	7
I am easily fatigued.	1	2	3	4	5	6	7
Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7
Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
My fatigue prevents sustained physical functioning.	1	2	3	4	5	6	7
Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
Fatigue is among my three most disabling symptoms.	1	2	3	4	5	6	7
Fatigue interferes with my work, family, or social life.	1	2	3	4	5	6	7

Appendix Q
Semi-Structured Interview Schedule

Semi Structured Interview Schedule

When the telephone is answered the interviewer will ask to speak to the participant. If they are not the person answering the phone the information that the interviewer will provide about the telephone call is as follows:
I work for the university of Leicester and I am contacting X as they agreed to take part in a study. If prompted for more information: *the study is an evaluation of a service that X has used.*

Interview Questions
What aspects of the service were most helpful?

What aspects were least helpful?
-is there anything you would change

What was your experience of the group approach?

What was your experience of the one to one approach?

Did you use access the service again?
If so did you feel that was beneficial?

How helpful did you find the information leaflets provided by the service?
Did you refer back to these after discharge from the service?

Have you used any other interventions apart from the xxxxx service?

Is there any thing else you would like to say about the service?

Appendix R
Ethics Approval

23 March 2011

Miss Amalia Houlton
Trainee Clinical Psychologist
Leicestershire Partnership Trust
Department of Clinical Psychology
104 Regent Road
Leicester
LE1 7LT

Dear Miss Houlton

Study title: **A long term follow up of a multi-disciplinary approach to Chronic Fatigue Syndrome**

REC reference: **11/EM/0038**

Thank you for your letter of 17 March 2011, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice-Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Please see the attached Consent Form, with tracked changes made by Helen Sammons (Vice Chair). Please note that Helen has commented that the Consent Form is not in the standard format, but that the format will be acceptable as long as the changes she has demonstrated are made. Please could you send a copy of the amended Consent Form, in order that we have confirmation that the conditions of Ethical Approval have been met.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Confirmation should also be provided to host organisations together with relevant documentation.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Protocol	3	03 December 2010
Response to Request for Further Information		
REC application		07 February 2011
CV for Marilyn Christie		
Letter with Questionnaire Pack	2	17 March 2011
Participant Information Sheet	4	17 March 2011
Investigator CV		25 January 2011
Participant Consent Form	1	17 March 2011
Questionnaire: Questionnaire Pack	2	20 January 2011
Referees or other scientific critique report		25 November 2010
Covering Letter		
Letter from service to patients	2	20 November 2011
Reminder letter with questionnaire pack	2	20 January 2011

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

11/EM/0038	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely

pp JRlea

Mr Peter Korczak
Chair

Appendix S
Participant Information pack

Name
Add1
Add 2
Add 3
Post

Date Random Code

Dear xxxxx,

We are contacting you as you have previously used the xxxxx Chronic Fatigue Syndrome/ME Service. A researcher from the University of Leicester is interested in carrying out a long term follow up study of patients who used the service in the past and we have enclosed information about the study. We would encourage you to participate, as we would like to know how patients who have used our service are doing after being treated.

If you feel you do not want to participate in the research please complete the opt-out slip below and return in the stamped addressed envelope enclosed. Not participating in this study will not have any impact on use of the service in future.

Yours sincerely,

xxxxxx

xxxxxx CFS/ME Service Co-ordinator

I do not wish to take part in the research study.

Print Name:…….

Sign …….

Dear xxxxx,

Please find enclosed an information sheet, questionnaire pack, consent form and a stamped addressed envelope. The questionnaires should take no more than 25 minutes to complete and you do not need to complete it all in one go.

If you wish to take part in the interview element of the study, please complete the enclosed consent form and information about which days and times are best for you to be contacted. This will involve a telephone interview by myself about your experiences of using the service. It is expected the call will last no more than 20 minutes.

If you are interested in receiving a report of the results of the study, please complete the information below and return with your questionnaire. All consent information is separated from the questionnaire answers to maintain anonymity.

If participating in the questionnaire raises any concerns for you about your illness, I recommend you contact your GP. If you wish to raise any issues about the service with the hospital you can contact the hospital patient advice and liaison service on xxxxxxxx

Many thanks,

Amalia Houlton
University of Leicester

Results
I would like to be sent a summary of the results:

Print Name……

Consent Form

For this research I will compare your answers on the questionnaire pack with the answers given on the same questionnaires while you were using the xxxxx service. To do this I will need to access the notes held by the service to see the original questionnaire responses only. This will be done for all participants to enable me to see what differences there are for people while they were using the service and now, a few years after they have finished using the service. In order for me to do this, I will need your consent.

I consent for access to the medical notes held by the xxxxx Chronic Fatigue Syndrome/ME service for this research.

Print Name……

Signed…… Date……

Telephone Interview: (optional)

If you wish to take part in the telephone interview, please complete the information below and sign to consent to being contacted by the researcher. If you do not wish to take part in the interview, please leave this blank.

I wish to take part in the telephone interview and consent to the researcher contacting me for a telephone interview.

Print Name……

Signed……
Date…….

The best days and times for me to be contacted are:

…….

Please enclose this form with your questionnaire in the stamped addressed envelope provided.

Information Sheet

Study Title: A long term follow up of a multi-disciplinary approach to Chronic Fatigue Syndrome/ME

I am a postgraduate student from the University of Leicester and I would like to invite you to take part in my research study. Before you decide, I would like you to understand why the research is being done and what it would involve for you. Part 1. Tells you about the purpose of this study and Part 2. provides more information about how it will be conducted.

Part 1.

1.1 What is the purpose of the study?

I am conducting research for the xxxxx Chronic Fatigue Syndrome/ME Service. The purpose of the research is to gain feedback from individuals like yourself who have used the service to evaluate your experiences. The research is looking at outcome measures used by the service as part of a long term follow up.

1.2 Why have I been invited?

You have been invited to take part in this research as you have previously used the xxxxx Chronic Fatigue Syndrome/ME Service.

1.3 Do I have to take part?

Taking part in this research is voluntary and is your choice. This information sheet will describe what will happen if you choose to take part in the study. You are free to withdraw at any time without giving a reason. Any future care you receive from the service will not be affected by whether you choose to take part in this study or not.

If you do not wish to take part in the research, please complete the opt-out slip attached to the letter from the xxxx Chronic Fatigue Syndrome/ME service and return in the stamped addressed envelope provided.

Part 2.

2.1 What will happen if I take part?

If you would like to take part in the research, please complete the enclosed questionnaire and return in the stamped addressed envelope provided. These are the same questionnaires the service uses to evaluate how patients are doing, so it is likely you will have completed some or all of the questionnaires before. The questionnaire pack includes instructions on filling in the questionnaires, it is expected the questionnaires will take no longer than 25 minutes in total to complete. If I do not receive an opt out slip from you, and I do not receive a questionnaire within three weeks of it being sent out, I will send a reminder letter with a questionnaire attached in case you have misplaced it.

A second stage of the study, which you can take part in if you wish, is a telephone interview to ask about your experiences of using the service. There is a consent form with your questionnaire pack asking if you would like to be involved in the interview stage, and if so which are the best days and times to contact you. The telephone interview will be conducted by myself and is expected to last no longer than 20 minutes. I hope to carry out 10-12 telephone interviews and depending on response rate you may or may not be contacted.

2.2 Advantages and disadvantages of taking part in the research.

It is anticipated that the results of this research will be used to inform the way the xxxxx service, and other services for Chronic Fatigue Syndrome/ME are run. Therefore participation will help to develop these services to be as useful to people with Chronic Fatigue Syndrome/ME as possible.
It is not expected there will be any risk in taking part in the research. It is possible that taking part in this research may raise some questions or concerns for you about your illness. If this occurs it is recommended you contact your GP.

2.3 What happens after I have taken part in the study?

Once completed, the questionnaire pack is returned to myself at the University of Leicester and the xxxxx service do not see the responses. This is to maintain anonymity and confidentiality. I will compare your answers on the questionnaire pack with the answers given on the questionnaires while you were using the service. To do this I will need to access the notes held by the service to see the original questionnaire responses. This will be done for all participants to enable me to see what differences there are for people while they were using the service, and now, a few years after they have finished using the service. In order for me to do this, I will need your consent. There is a consent form attached to the questionnaire pack for this purpose which you will need to sign and date and return with the questionnaire. If you wish to take part in the telephone interview stage, your consent will also be needed. There is a section to complete on the enclosed consent form for this purpose which will need to be returned with the questionnaire in the stamped addressed envelope provided. If you take part in the telephone interviews, the answers given by everybody interviewed will be compared to look at themes that come out of the interviews.
I will also be creating a summary of results of the research and there is a space on the questionnaire pack to write your name if you would like to be sent a copy of the results.

2.4 Will my taking part in the study be confidential?

As I am a student at the University of Leicester, I am not linked to the xxxxx service. All questionnaires will have a random code assigned to them which will mean I can link information from the questionnaires completed by a patient when using the service, and their responses now. The xxxxx service will not have access to this information and will not know who has participated in the research. The consent forms will be separated from the questionnaires so your answers remain anonymous. I am the only person who will see your responses on the questionnaires.
All information will be kept on an encrypted, password protected memory stick and hard drive. All data collected from the study will be kept in locked drawers and destroyed when the research is complete.

2.5 Capacity

I need to ensure that you have full capacity to understand the study when you participate. If you complete and return the questionnaire it is assumed you have capacity to do this. If you participate in the telephone interviews, I will check that you understand the study and are happy to proceed with the telephone interview before it begins.

2.6 Further support

If you feel you would like further support with your condition, it is advised that you contact your GP, who will be responsible for referring you back to the xxxxx CFS/ME service if it is appropriate. If you are involved in the telephone interview and I felt you may benefit from further support, I would discuss this with you and suggest you contact your GP.

2.7 What will happen if I don't want to carry on with the study?

If you decide part way through you do not wish to carry on with the study, you can contact myself and let me know. Any previous information you have provided will be taken out of the study if you wish and destroyed.

2.8 What if there is a problem?

If you have a concern about the study, I recommend in the first instance you contact the researcher xxxxx The person at the university supervising the research is xxxxxx

Further Information

If you would like any more information about the study or have any questions please feel free to contact me using the details provided below.

xxxxx

DATE XXXX

Dear Sir/Madam,

A few weeks ago you should have received some information about a long term follow up study I am conducting with patients who have used the Xxxxx Chronic Fatigue/ME service. In case you did not receive this or have misplaced it and would like to participate in the study, I have enclosed some information, the questionnaire pack and a stamped addressed envelope.

It is expected the questionnaires will take no longer than 25 minutes to complete, and you do not have to complete them all at once.

If you wish to take part in the interview element of the study, please complete the information on the consent form attached to the questionnaire about which days and times are best for you to be contacted. This will involve a telephone interview by myself about your experiences of using the service. It is expected the call will last no more than 20 minutes.

If you have already contacted the service, opted out of the research or returned your research pack, please ignore this letter.

Many thanks,

Amalia Houlton

Trainee Clinical Psychologist
University of Leicester

Appendix T
Example of Coding

Question	Codes (number of times they occurred)	Themes
What aspects of the service were most helpful?	• Making Up illness (2) • Never felt stupid (1) • Naming (1) • Learning personal reactions to stress (1) • Advice (7) • Education on CFS (3) • Feeling listened to (7) • Individualised (2) • Open appointment (1) • Confirm and challenge (1) • Flexible appointment (1) • Different ways of seeing things (1) • Frequency of support (1)	Education-advice/changing perceptions/learning about the condition Validation-Listened to//named/believed Flexibility-individualised/open appointment
What aspects were not so helpful	• None (6) (3 then did not state more) • Don't want to criticise (1) • GP lack of awareness (1) • GP not wanting to send (1) • Parking and distance (2) • A[pijntment too short (1) • More holistic approach 1) • Over confidence by consultant (1) • Hard to commit to group (1) • Service update about new information (1) • CD more useful at start	Gatekeeping Not Holistic Practical Unhelpful optimism
Did you use any other interventions apart from the service?	• None (1) • Private CBT (2) • Massage (1) • Reflexology (1) • Swimming (1) • Money concerns (1) • Complimentary medication (3) • Offered antidepressants but did not take (1) • Took HRT to prove not hormones (1) • Own research (2) • Trained as hypotherapist (1) • Took part in other research (2) • Counselling (2) • Took antidepressants (1) • Acupuncture (1) • Job centre life skills "dreadful" (1) • Support group (negative) (1) • Medication from abroad (1)	Complimentary Therapies-medication/training/cost Medication Talking therapies Other approach

Appendix U
Epistemological Position

The research philosophy for the current report is based on principles of Critical Realism. The researcher felt to best answer the research aims, a quantitative approach allowing for data analyses would provide important information about outcomes for patients using the service. However, this was unlikely to tell the whole story of the data, and an in-depth thematic analysis of telephone interviews was conducted in order to explore the more subjective elements of the results.

Appendix V
Research Timeline

Task	***Date***
Proposal development	*Up to September 2010*
Submit to peer review	*November 2010*
Ethics Submission	*January 2011*
Ethical Approval	*March 2011*
Research and Development Approval	*September 2011*
Research pack sent to participants	*September 2011*
Reminder Research Pack	*October 2011*
Interviews conducted	*December 2011-January 2012*
Data input	*November 2011-Januray 2012*
Data cleaning	*February 2012*
Data analysis	*February 2012*

Appendix W
Author guidelines
British Medical Journal

Article requirements

Please ensure that anything you submit to the **BMJ** conforms to the uniform requirements for manuscripts submitted to biomedical journals, drawn up by the International Committee of Medical Journal Editors (ICMJE).

The ICMJE requirements are long and comprehensive, and the **BMJ** also has specific requirements for different types of articles and particularly detailed ones for research articles. We urge you to look carefully at all of these.

Here, however, is an overview of the requirements for all BMJ manuscripts:

- Title - all manuscripts - Title page
- Names, addresses, and positions of all authors plus email address for corresponding author, ensuring that all people listed as authors fulfil the criteria for authorship - all manuscripts
- Copyright/licence for publication - all manuscripts
- A competing interest declaration - all manuscripts
- Details of contributors and the name of the guarantor - all original research articles
- Signed patient consent forms - all manuscripts with personal information about a patient
- Statements regarding ethics approval; informed consent from participants; funding; the role of the study sponsor in study design and the collection, analysis, and interpretation of data and the writing of the article and the decision to submit it for publication; the independence of researchers from funders and sponsors; and the access of researchers to all the data - all original research articles
- All the information recommended in the relevant reporting statement, for example CONSORT. We do not use reporting guidelines as critical appraisal tools to evaluate study quality or filter out articles. We're simply aiming to make research articles so clear that peer reviewers, editors, clinicians, educators, ethicists, policy makers, systematic reviewers, guideline writers, journalists, patients, and the general public can tell what really happened during a study. -all original research articles
- If you are submitting a report of a randomised controlled trial please send with your manuscript a completed checklist and flowchart in accordance with the appropriate CONSORT guidelines, the trial protocol, and the registration details of the trial. In accordance with ICMJE uniform requirements, trials commenced after July 2005 must have been registered prospectively before patient recruitment; for older trials retrospective registration will be acceptable but only if done before submission of the manuscript to the journal.
- If you are submitting a report of:

- a systematic review or meta-analysis of randomised trials and other evaluation studies please follow the PRISMA guidelines (these have superceded the QUOROM guidelines) and submit as a supplemental file the study protocol, if there is one
- a meta-analysis of observational studies please follow the MOOSE guidelines and submit as a supplemental file the study protocol, if there is one
- a study of diagnostic accuracy please follow the STARD guidelines
- an observational study please follow the STROBE guidelines and submit as a supplemental file the study protocol, if there is one
- a health economics paper please follow our health economics checklist ([node:105536])
- a clinical guidelines paper we would encourage you to follow the GRADE guidance for grading evidence, but will not insist on this

Because we aim to improve **BMJ** papers' reporting and increase reviewers' understanding we ask our research authors to follow such reporting guidelines and to complete the appropriate reporting checklist before submission (or before external peer review if not done sooner). We do not, however, use reporting guidelines as critical appraisal tools to evaluate study quality or filter out articles.

These and other reporting guidelines are collected together in one place: the website of the EQUATOR Network. This network seeks to improve the quality of scientific publications by promoting transparent and accurate reporting of health research.

Another resource, the Authors' Submission Toolkit: A practical guide to getting your research published, summarises general tips and best practices to increase awareness of journals' editorial requirements, how to choose the right journal, submission processes, publication ethics, peer review, and effective communication with editors - much of which has traditionally been seen as mysterious to authors.