

# How to exercise people with chronic fatigue syndrome: evidence-based practice guidelines

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## ABSTRACT

**Background** Despite the large number of studies emphasizing the effectiveness of graded exercise therapy (GET) and cognitive behavioural therapy (CBT) for people with chronic fatigue syndrome (CFS), clinicians are left wondering how exactly to apply exercise therapy to their patients with CFS. The aim of this literature review is to identify the appropriate exercise modalities (i.e. exercise duration, mode, number of treatment sessions, session length, duration of treatment, exercise intensity and whether or not to apply home exercise program) for people with CFS.

**Materials and methods** All studies that were identified through electronic databases (PubMed and PEDro) were assessed for methodological quality by using selection criteria (Delphi score).

**Results** In this literature review, 12 studies fulfilled all study requirements. One study had a low methodological quality. The parameters used in the GET and CBT interventions were divided into subgroups: (i) time or symptom contingent, (ii) exercise frequency and (iii) exercise modality.

**Conclusion** The lack of uniformity in outcome measures and CFS diagnostic criteria make it difficult to compare the findings across studies. Based on the available evidence, exercise therapy for people with CFS should be aerobic and must comprise of 10–11 sessions spread over a period of 4–5 months. A time-contingent approach is preferred over a symptom-contingent way of exercising. In addition, people with CFS can perform home exercises five times a week with an initial duration of 5–15 min per exercise session. The exercise duration can be gradually increased up to 30 min.

**Keywords** Chronic fatigue syndrome, chronic fatigue syndrome treatment, exercise therapy, physical therapy modalities, physiotherapy rehabilitation, training modalities.

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## Introduction

Chronic fatigue syndrome (CFS) is a condition characterized by extreme fatigue not resolving with (bed) rest [1,2]. According to the Center for Disease Control and Prevention (CDC), CFS is defined as clinically evaluated, unexplained, persistent or relapsing chronic fatigue that is of new or definite onset, should result in a substantial reduction in previous levels of occupational, educational, social or personal activities. Furthermore, at least four of the following symptoms must have persisted or recurred during six or more consecutive months and must not have predated the fatigue: impairment in short-term memory or concentration, sore throat, tender cervical or axillary lymph nodes, muscle or multi-joint pain, headache,

unrefreshing sleep and postexertional malaise, which remain for a period of more than 24 h [3]. Recently, a new set of diagnostic criteria has been proposed, emphasizing the importance of postexertional malaise (i.e. the severe exacerbations following vigorous exercise) for the diagnosis of CFS [4]. The severity of the symptoms may vary strongly in function of the patient as well as the time [5]. CFS may present itself not only with adults but also with children. Like every chronic illness, CFS impacts upon physical, psychological and social well-being.

Chronic fatigue syndrome is a common disorder, which is increasingly recognized by the medical community as a major

healthcare problem. Reported prevalence of CFS varies between 0.075% and 2.54%, depending on definitions and methods applied for obtaining data [6]. Peak incidence is in the 20–40 years age range, with a preponderance of women [6].

The aetiology of the illness remains unclear, although various hypotheses exist implicating immunological, virological, psychological and neuro-endocrinological mechanisms. There is a lack of overwhelming evidence for any one of these hypotheses [7], but cumulating data suggest that central sensitization (i.e. hyper-responsiveness of the central nervous system) dominates the clinical picture of CFS [8]. Importantly, central sensitization is in line with our current understanding of CFS: it corroborates with the presence of several psychological influences on the illness, the presence of infectious agents and immune dysfunctions, and the dysfunctional hypothalamus–pituitary–adrenal axis as seen in these severely debilitated patients [8]. Hence, an adequate patient approach should be preferably based on the biopsychosocial model.

Many patients with CFS do not seek treatment either because of a lack of treatment opportunities in their vicinity or because of their inability to attend treatment. Most patients with CFS are unable to work full time [9], leading to financial problems. CFS may also have a negative influence on the school performance. Patients with CFS are often in need of a comprehensive rehabilitation programme that includes medical treatment, psychological support and occupational therapy to accommodate a successful return to work or to school. Patients who suffer from CFS have a tendency to limit their level of physical activity to minimize their symptoms [10]. The Surgeon General has suggested that moderate aerobic training (e.g. brisk walking), for a period of 30 min three times a week, can result in significant health improvements and subsequently improve the quality of life of persons without a functional impairment [11]. Patients with CFS are capable of performing mild to moderate efforts (40%  $\text{VO}_2$  max) without the symptoms manifesting themselves [12].

Graded exercise therapy (GET) and cognitive behavioural therapy (CBT) are two partly overlapping treatments that have proven to be beneficial for patients with CFS [13]. The rationale for applying GET and CBT comes from chronic pain research. Vlaeyen *et al.* [14] developed the cognitive behavioural model for fear of pain/movement/injury. This model is based on the assumption that for some patients, a pain experience will lead to kinesiophobia and consequently to avoidance behaviour. In this chain of events, the fact whether or not a patient exaggerates his pain experience level plays a key role. In the long term, extreme avoidance of movement results in invalidating and psychological changes that contribute to the complaint pattern of chronic pain patients. Most protocols developed for this kind of treatment are based on three important factors: programmed body movement, the control of and handling of (illness associated) stress and cognitive restructuring [15]. Evidence in sup-

port for a similar cognitive behavioural model in people with CFS has been provided [16–18].

In general, people with CFS need to be encouraged to perform physical and intellectual tasks, starting from a tolerable level that does not result in postexertional malaise. If exercise tolerance improves, the length and the frequency of the exercise sessions may be increased.

A systematic review of randomized controlled trials of treatments for CFS concluded that GET and CBT are effective for patients with CFS [5]. An updated Cochrane review on CBT in adults with CFS concluded that this approach is effective in decreasing fatigue [19]. A Cochrane review on GET in patients with CFS found that, on average, patients benefit from this therapy, but some patients find this approach unacceptable [20].

Despite the large number of studies emphasizing the effectiveness of GET for people with CFS [5,20], clinicians are left wondering how exactly applying exercise therapy to their patients with CFS. Indeed, treatment modalities for GET in patients with CFS vary considerably across studies, and published systematic literature reviews on GET in CFS focus on the effectiveness of the intervention rather than the treatment modalities. This is a shortcoming as evidence-based practice guidelines require clear suggestions of treatment modalities like exercise duration, mode, frequency and intensity. Clinicians working with people with CFS know that GET is an effective treatment, but they do not know how to apply GET to their patients. For these reasons, the aim of this literature review is to identify the appropriate exercise modalities (i.e. exercise duration, mode, number of treatment sessions, session length, duration of treatment, exercise intensity and whether or not applying a home exercise programme) for people with CFS.

## Material and methods

### Literature search

The following databases were used: PubMed (National Library of Medicine) and PEDro (Physiotherapy Evidence Database). First, an inventory of keywords was compiled, so we could come to a shortlist later. The terms used in the search strategy refer to the condition and/or intervention that this review is about. MeSH terms have been used to be as complete as possible in the search for scientific literature.

The following keywords were entered: chronic fatigue syndrome, chronic fatigue syndrome treatment, exercise therapy, physical therapy modalities, training modalities, training characteristics, exercise prescription. If one of these keywords or MeSH terms (only for PubMed) were entered in a database, many unusable references were obtained. Therefore, Boolean operators (AND, OR and NOT) were used during the search strategy. We applied these Boolean operators in using combinations of keywords to search more exactly. The most successful

search formula was as follows: 'Fatigue Syndrome, Chronic [Mesh] AND 'Exercise Therapy [Majr]' OR 'Physical Therapy Modalities [Mesh].

### Inclusion and exclusion criteria

Articles were included when they contained the following characteristics:

*Intervention:* any intervention or combination of interventions used in the treatment, management or rehabilitation of people with CFS.

*Population:* adults and/or children with a diagnosis of CFS based on any official criteria (i.e. CDC criteria, Oxford criteria, Canadian criteria).

*Outcomes:* the fatigue and physical function reported in included studies were considered.

*Study design:* only randomized or controlled clinical trials were eligible for inclusion.

*Language articles:* Dutch or English.

Articles were excluded when they contained the following characteristics:

- Studies where the treatment consists of medication, electrotherapy, acupuncture or any other intervention. One of the examined intervention methods had to contain some type of exercise therapy.
- Studies where the patients had dementia, psychiatric disorder or fibromyalgia without being diagnosed as a CFS case.
- Articles without information about the author(s).

After entering the keywords, the titles and abstracts were read. If the articles met the selection criteria, then the reference was added to the bibliography and screened on quality.

### Data extraction

From each selected article, the treatment parameters were used. These treatment parameters (time or symptom contingent, the exercise frequency and exercise modality) were used in the intervention and the effect of these treatment parameters on the fatigue and the physical function of people with CFS. These data were included in the text of the literature and organized by category. In this systematic literature study, the results were considered significant when the *P*-value was < 0.05.

### Quality assessment

Each study can be assessed for quality according to the type of research that was conducted. The methodological quality of a randomized controlled trial was assessed by using the Delphi score [21]. The Delphi score includes information about data presentation, internal and external validity. Internal validity refers to the extent to which the results of an empirical research

can be adequately interpreted and the extent to which people can have confidence in these interpretations. External validity refers to the degree to which the results of an empirical study are generalizable to a wider population and/or other circumstances. There was no minimum score achieved on the score lists. This was a conscious decision to get a comprehensive view on the results. The selected articles were reviewed by the first author. When it came to RCTs, the evaluation was compared with the score provided by PEDro.

## Results

### The methodological quality of the selected articles

All studies on the content of the treatment and outcome measures were assessed for quality. As there was no minimum score, both high quality and poor methodological studies were included in this study. This has been done purposefully to obtain a comprehensive result. The level of evidence for the efficacy of interventions depends on the number of studies with good methodological quality and consistency of their reported results. The general quality of the selected articles was moderate to good.

The most common shortcomings in the RCT's were a lack of adequate randomization, failure to apply intention-to-treat analysis, inadequate or missing information about the blinding of patients: assessors and impact assessors, and inadequate or missing information on the degree of compliance: side effects and co-interventions. A comprehensive view of the methodological quality of each RCT is shown in Table 1. One [22] of the 12 RCT's received a Delphi score below 50/100.

### Exercise therapy treatment modalities

Because numerous studies showed the positive effect on GET in people with CFS (see Introduction), we searched for the parameters that were applied during this type of intervention. This is to come to a general directive about how to offer the best exercise in people with CFS.

In this literature review, 12 studies were included based on the inclusion and exclusion criteria. In eight studies [15,23–29], adults were treated, in one study [30], children were treated, and in three studies [12,22,31], both children and adults were treated. In each study, the majority of study participants were women.

These 12 studies also confirm the positive effect ( $P < 0.05$ ) of CBT and GET on fatigue and physical functioning of people with CFS. The parameters used in the GET and CBT interventions were divided into subgroups: (i) time or symptom contingent, (ii) the exercise frequency and (iii) exercise modality.

**Table 1** A comprehensive view of the methodological quality of each trial included in the literature review

	A (4)	B (6)	C (15)	D (10)	E (7)	F (7)	G (G <sub>1</sub> : 6) (G <sub>2</sub> : 6)	H (5)	I (1)	J (1)	K (4)	L (10)	M (6)	N (2)	O (10)	Total (100)	Pedro
Deale <i>et al.</i> (1997)	4	6	5	8	6	3.5	1: 5 2: 5	2.5	0	0	4	8	5	1	10	73/100	8/10
Deale <i>et al.</i> (2001)	3	3	5	6	5	4.5	1: 3 2: 3	0	0	0	0	6	5	0	10	53.5/100	5/10
Fulcher <i>et al.</i> (1997)	4	6	5	7	5	3.5	1: 4 2: 4	2.5	0	0	0	6	5	0	10	62/100	7/10
O'Dowd <i>et al.</i> (2006)	4	6	10	8	5	5.5	1: 2 2: 6	2.5	0	0	4	8	5	0	10	76/100	8/10
Powell <i>et al.</i> (2001)	3	6	5	7	7	4	1: 2 2: 4	0	0	0	0	7	5	0	10	60/100	7/10
Powell <i>et al.</i> (2004)	3	3	5	4	5	2	1: 1 2: 3	0	0	0	0	5	5	0	10	46/100	5/10
Prins <i>et al.</i> (2001)	4	4	15	6	5	2	1: 3 2: 3	0	0	0	0	6	5	0	5	58/100	6/10
Sharpe <i>et al.</i> (1996)	4	6	5	8	7	7	1: 3 2: 4	2.5	0	0	4	8	5	0	10	73.5/100	8/10
Stulemeijer <i>et al.</i> (2005)	3	5	5	7	3.5	4.5	1: 2 2: 4	0	0	0	0	7	5	0	10	56/100	7/10
Wallman <i>et al.</i> (2004)	3	3	5	5	4	3.5	1: 3 2: 4	2.5	0	0	0	5	5	0	10	53/100	5/10
Wearden <i>et al.</i> (2010)	4	6	15	7	5	5	1: 2 2: 4	0	0	0	0	7	5	0	10	75/100	7/10
White <i>et al.</i> (2011)	4	6	15	7	4	7	1: 5 2: 5	2.5	0	0	0	7	5	0	10	77.5/100	/

A, study population; B, randomization; C, group size; D, prognostic comparability of groups; E, dropouts; F, loss to follow-up; G<sub>1</sub>, description control group; G<sub>2</sub>, description intervention group; H, co-interventions; I, assessor blinding; J, patient blinding; K, provider blinding; L, relevant effect sizes; M, adequate follow-up; N, side effects; O, adequate data presentation and adequate analyse.

**Time or symptom contingent.** Only one study [29], the PACE study, compared a time-contingent with a symptom-contingent approach. In this study, White *et al.* compared standard medical care alone with other treatments, adaptive pacing therapy (APT) with CBT and APT with GET.

In this study, the APT used a symptom-contingent approach, CBT and GET on the contrary used a time-contingent approach. The CBT and GET were associated with significantly less fatigue (CBT,  $P = 0.0027$ ; GET,  $P < 0.0059$ ) and improved physical function (CBT,  $P = 0.0002$ ; GET,  $P < 0.0001$ ) as compared to the APT. Fatigue was measured using the 'Chalder Fatigue Questionnaire' and physical function using the 'shortened SF-36', subscale physical function.

Furthermore, seven studies [15,24–28,30] used a time-contingent approach. One study [26] used GET as a treatment,

and six studies [15,24,25,27,28,30] applied CBT as a treatment in people with CFS. All these studies showed a significant decrease in fatigue (measured by the subscale fatigue severity of the 'Checklist individual strength' and 'Chalder Fatigue Questionnaire') and physical functioning (measured by 'The medical outcomes study short form general health survey', 'Shorted SF-36' and 'Karnofsky scale'), comparing with a control intervention (flexibility or relaxation therapy).

Four studies [12,22,23,31] used a symptom-contingent approach. These studies used GET as a treatment for people with CFS, and all of them reported a significant improvement ( $P < 0.05$ ) in fatigue (measured by 'self-rated visual analogue scale' and 'Chalder Fatigue scale') and physical functioning (measured by 'SF-36': subscale physical functioning)

compared with a control intervention (flexibility or relaxation therapy).

**Number of sessions, session length and duration of treatment.** Only two studies [22,31] compared three different doses (number of sessions and time with the therapist) of GET treatments (symptom-focused approach) to each other (and also to a control group). The three groups consisted of: the minimum intervention group, the telephone intervention group and the maximum intervention group. The minimum intervention group received two individual sessions (total: 3 h), the maximum intervention group received two individual sessions (total: 3 h) and seven individual sessions (each session lasted 1 h, and sessions were spread over 3 months), and the telephone intervention group received two individual sessions (total: 3 h) and seven phone calls (each call lasted about 30 min, spread over 3 months). They found no significant difference between the three intervention groups in fatigue or physical functioning. They found a similar improvement ( $P < 0.001$ ) in all three intervention groups in fatigue and physical functioning, as compared to the control group (receiving standard medical care and a short information booklet that encouraged increased activity and positive thinking without explanation of symptoms).

Two studies [24,28] required 16 individual sessions of CBT treatments (time-contingent approach). In both studies, the individual session lasted 1 h. In the study of Prins *et al.* [24], 16 sessions were spread over 8 months. The study by Sharpe *et al.* [28] required 16 sessions that were spread over 4 months. Both studies showed a significant improvement ( $P < 0.05$ ) in fatigue and physical functioning in people with CFS.

The two studies by Deale *et al.* [15,25] applied 13 individual sessions of CBT treatments (time-contingent approach) spread over 4–6 months. The sessions were given every week or every 2 weeks so that each patient had spent an average of 15 h with the therapist.

Two studies [26,30] required 10 individual sessions of CBT or GET treatments (time-contingent approach). In the study by Stulemeijer *et al.* [30], 10 individual sessions were spread over 5 months. The study by Wearden *et al.* [26] applied 10 home visits spread over 18 weeks. The home visit took 90 min in week 1, 1 h in weeks 2, 4, 10 and 18, and was replaced by a 30-min telephone call in weeks 3, 6, 8, 12 and 15. Both studies showed significant improvement ( $P < 0.05$ ) in fatigue and physical functioning compared with the control group in people with CFS.

Wallman *et al.* [12] applied six individual sessions of GET (symptom contingent) spread over 12 weeks (once every 2 weeks). The study by O'Dowd *et al.* [27] required eight sessions of CBT (time contingent) spread over 16 weeks. The patients attended the treatments in groups of 8–12 individuals. These sessions were given every 2 weeks.

Fulcher *et al.* [23] used 12 sessions of GET (symptom contingent) spread over 12 weeks (once every week). The study by White *et al.* [29] applied 14 treatment sessions (CBT, GET, APT) during the first 23 weeks. The first four sessions were given every week; the next sessions were given once every 2 weeks.

**Home exercises.** Three studies [12,23,29] gave information about home exercises as part of CBT or GET for people with CFS. In two studies [23,29], the home exercises comprised of five exercise bouts a week with a maximum of 30 min. In the study by Fulcher *et al.* [23], home exercises had to be performed five times a week. In the beginning, these exercises were performed at an intensity of 40% of  $\text{VO}_2$  max, with a duration of 5–15 min. The intensity was gradually increased to 60%  $\text{VO}_2$  max, with a duration of 30 min per exercise session. The study by White *et al.* [29] described home exercises for the patients in the GET group as follows: heart rate was used to determine the exercise intensity, and target heartbeats were used to avoid overactivity, which eventually led to five times a week 30 min of light home exercises. The intensity of the aerobic exercises was gradually increased.

The home exercises used in the study of Wallman *et al.* [12] were described as follows: the initial exercise duration was between 5 and 15 min, and the intensity was based on the average heart rate obtained from a submaximal exercise test. Participants were advised to practice 2 days, unless they had a flare. When this occurred, or when the symptoms got worse, the next exercise session was reduced or omitted.

**Exercise modality.** Five studies [12,15,23,25,29] used aerobic exercise for people with CFS. Four [12,15,23,25] of these five studies mainly used aerobic activity like walking, swimming or cycling. O'Dowd *et al.* [27] used aerobic (especially cycling), strength, balance and stretching exercises for people with CFS. The pragmatic rehabilitation programme in the study by Wearden *et al.* [26] also applied relaxation exercises.

Five studies [12,15,23,25,27] compared a CBT or GET with a flexibility or relaxation therapy for people with CFS. These five studies showed that flexibility or relaxation therapy, as a stand-alone treatment for people with CFS, did not significantly improve ( $P > 0.05$ ) fatigue levels or physical functioning. Compared with a flexibility or relaxation therapy, GET or CBT always showed a significant improvement ( $P < 0.05$ ) in fatigue and physical functioning in people with CFS.

## Discussion

This literature review aimed at answering the following question: 'What are the evidence-based treatment modalities of an exercise programme for people with CFS?' Clinicians working

with patients with CFS know that GET is an effective treatment, but they do not know how to apply GET to their patients. This keeps physiotherapists and rehabilitation specialists in the dark about the application of exercise for people with CFS. Based on the available studies, the appropriate exercise modalities were identified.

### Symptom- or time-contingent approach

In practice, both a symptom-contingent and a time-contingent approach are used for the treatment of people with CFS. Only one study, the PACE study [29], compared a time-contingent with a symptom-contingent approach. In this study standard, medical care alone was compared with other treatments (i.e. APT vs. CBT, and GET vs. APT). In this study, APT used a symptom-contingent approach, CBT and GET on the contrary used a time-contingent approach. The CBT and GET were associated with significantly less fatigue (CBT,  $P = 0.0027$ ; GET,  $P < 0.0059$ ) and improved physical function (CBT,  $P = 0.0002$ ; GET,  $P < 0.0001$ ) as compared to APT. This study obtained a very high Delphi score (77.5/100).

Furthermore, seven studies [15,24–28,30] applied the time-contingent approach, while four [12,22,23,31] used a symptom-contingent approach. The studies applying a time-contingent approach had a higher methodological quality score (mean Delphi score = 66.4/100 and the mean score on PEDro = 7/10) than the studies applying a symptom-contingent approach (mean Delphi score = 55.25 and mean score on PEDro = 6/10). From the above information, we can conclude that the time-contingent approach to exercise therapy for patients with CFS is superior over the symptom-contingent approach.

It is clinically not so straightforward to provide very strict time-contingent exercise therapy; we should also take into account post exertional malaise associated with CFS. When combining the available evidence with our current understanding of postexertional malaise in CFS, we advocate applying pacing and exercise therapy in a time-contingent manner. In other words: time-contingent does not mean that we do not practice in function of the tolerance levels of the patient. On the contrary, a time-contingent approach to pacing and exercise interventions implies that exercise and activity levels are tailored in line with the load tolerance of the individual patients and that exercises/activities are followed by rest periods to account for the delayed recovery following physical activity, etc.

### Number of sessions, session length and duration of treatment

Despite the many studies, there is still no consensus on the most appropriate parameters for exercise therapy in the treatment of patients with CFS. Only two studies [22,31] compared the effects of three different doses (number of sessions and time with the therapist) of GET treatments (symptom-contingent approach).

However, when analysing the effects on fatigue and physical functioning, no significant differences between the three intervention groups were found. For many of the studied patients, providing the therapy using between 2 and 4 telephone calls was sufficient to demonstrate the clinical benefits.

Because of the wide variety of treatment modalities identified in this literature study, it is difficult to identify the most appropriate ones. Still, the available studies point towards a treatment of 10–11 sessions, spread over a time period of 4–5 months. This is based on the outcome of two studies [26,30] that have used this exercise modality with positive effects on fatigue and physical functioning in people with CFS. These studies obtained a high score for methodological quality (Stulemeijer *et al.* [30]: 56/100 and Wearden *et al.* [26]: 75/100 on the Delphi scoring list). In addition, the number of treatment sessions and the duration of the treatment used in other studies ranged around these values (mean number of sessions: 11.8 sessions and mean total treatment period = 4.42 months).

### Home exercises

Because home exercises have no disadvantages, they provide an added value to the treatment. Three studies [12,23,29] gave information about home exercises as part of CBT or GET for people with CFS. These three studies obtained a good methodological quality (53–77.5/100) on the Delphi score. In two studies [23,29], the home exercises comprised of five exercise bouts a week, with a maximum of 30 min of home exercises. Two [12,29] of these three studies used the heart rate to determine the intensity. To avoid a flare or overactivity, heart rate monitors can be a useful guide for determining individually tailored exercise intensity. In the three studies, it was advised to initiate the exercises with an exercise duration between 5 and 15 min and to gradually increase the exercise duration to 30 min.

### Exercise modality

Five studies [12,15,23,25,29] have used aerobic exercise for people with CFS. These studies obtained a good methodological quality (53–77.5/100) on the Delphi scoring list. Four [12,15,23,25] of these five studies mainly used aerobic activity like walking, swimming or cycling. The study by O'Dowd *et al.* [27] used aerobic (especially cycling), strength, balance and stretching exercises for people with CFS. The pragmatic rehabilitation programme in the study by Wearden *et al.* [26] also applied relaxation exercises.

Five studies [12,15,23,25,27] compared CBT or GET with flexibility training or relaxation therapy for people with CFS. These five studies showed that flexibility or relaxation therapy, as a stand-alone treatment for people with CFS, did not significantly improve ( $P > 0.05$ ) fatigue levels or physical functioning. Compared with flexibility training or relaxation therapy, GET or

CBT always showed superior results (i.e. improvements ( $P < 0.05$ ) in fatigue and physical functioning).

From the above information, it can be concluded that aerobic activity is the most appropriate exercise modality for people with CFS. Walking is especially recommended, but swimming or cycling should also be encouraged. Furthermore, strength, balance, stretching and relaxation exercises can be added to the aerobic exercise protocol, but as a stand-alone treatment, these interventions are not effective for people with CFS.

### Clinical messages

It is advocated that clinicians applying exercise therapy to people with CFS comply with these guidelines (summarized in Fig. 1). If not, the effectiveness of exercise therapy for CFS is not backed-up by evidence from scientific studies. This accounts for centres applying exercise therapy *in house*, where patients are obliged to return to the centre twice a week for performing their exercise programme. Instead, treatment sessions at the centre/practice should be limited in number and should be used to discuss and adopt the exercise programme with the patient. The exercise therapy itself should be done at home. This approach is in line with the evidence and is likely to be cost-effective as well.

Importantly, the available evidence supporting exercise therapy for CFS comes from monodisciplinary studies. Although an interdisciplinary approach seems warranted for a complex disorder like CFS, monodisciplinary interventions like GET and CBT are effective in improving functioning of people with CFS. This implies that the evidence-based practice guidelines for exercise therapy in CFS, as presented here, are applicable to monodisciplinary settings, including primary care. This is an

important finding, because people with CFS are frequently seen in primary care in many Western countries.

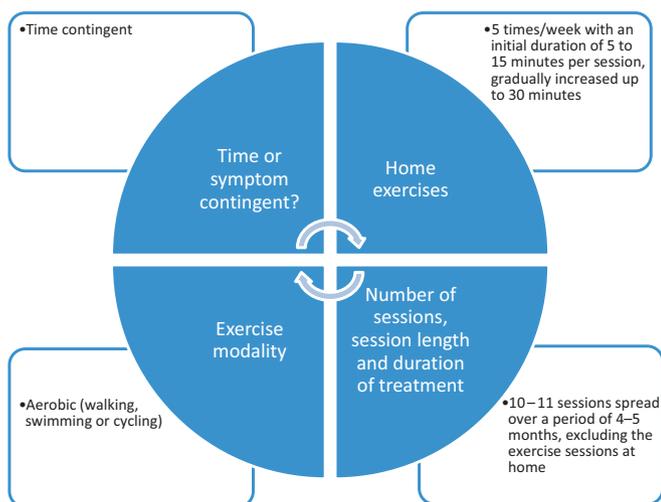
Another important message for clinicians reading this study is that exercise therapy is not a cure for CFS. Despite the consistent positive outcomes of exercise therapy studies for CFS, full recovery from CFS is rare. In addition, exercise therapy is not a sole treatment for people with CFS. A comprehensive treatment for CFS comprises of education of the aetiology and pathophysiology of the illness, stress management, cognitive restructuring, sleep hygiene and GET together with graded activity. But even such a comprehensive rehabilitation programme only rarely results in full recovery. At current, evidence in support of drug treatments for CFS is very limited, with inconclusive or negative findings in randomized controlled trials. Hence, drug treatment for CFS remains experimental.

Previous work showed that patients with CFS perform less physical activity during daily life and have less peak isometric muscle strength as compared to healthy sedentary control subjects [32]. Addressing physiological exercise capacity, the literature points towards variability in the CFS population, but the weighted evidence indicates a reduced physiological exercise capacity in CFS [32]. Still, increasing activity levels or improving physiological exercise capacity should not be the primary treatment goal. Moreover, previous work showed that clinically important improvements in quality of life during rehabilitation for people with CFS occur independent from alterations in physiological exercise capacity [33]. This underscores the importance of goal setting, a strategy allowing patients to pick their own short- and long-term functional treatment goals.

### Study limitations

The findings from this systematic literature review, although methodologically scored, should interpret with some caution, given the following study limitations.

**Outcomes.** The studies used various types of instruments to measure the fatigue. This makes it difficult to compare the results across studies. Eight studies [15,22,25–29,31] used the ‘Chalder Fatigue Questionnaire’; two studies [12,23], the ‘self-rated visual analogue scale’; and two studies [24,30], the ‘Checklist Individual Strength (subscale: fatigue severity)’. Some studies have used specific questionnaires for measuring fatigue in people with CFS and other made use of general questionnaires. Likewise, different questionnaires were used for the measurement of physical function. Seven studies [22,23,26,27,29–31] used the ‘short form SF-36 (subscale physical functioning)’; two studies [15,25] made use of the ‘Sickness Impact Profile’; and one study [28] used the ‘Karnofsky performance scale’. There is a need for standard outcome measures used in the studies to assess the interventions for CFS, so that the results can be compared in a meaningful way.



**Figure 1** Chart summarizing the clinical messages: exercise therapy for people with chronic fatigue syndrome.

**Blinding.** In most studies, there was no blinding of patients, assessors and outcome assessors, which may have influenced the results. Three studies [15,27,28] made use of blinding of the outcome assessor.

**Patient population.** Nine studies [15,23–29,34] were performed in adults, one study [30] in children and three studies [12,22,31] both in children and adults. Among the participants in each study, there was a higher percentage of women than men, what suits the unequal gender distribution of the CFS population. The treatment is not adapted for children. There is a need for more research addressing exercise modalities for children with CFS. A disadvantage of this literature review is that most studies admitted people with CFS who could come independently to the hospital, what implies a certain degree of physical activity. Those who were not able to walk or get out of bed were automatically excluded, and therefore, it was not possible to examine whether exercise therapy was effective, ineffective or even harmful for a more seriously disabled group of people with CFS.

**Methodological quality.** Given the low methodological quality of one study [22], caution is required when interpreting these findings. The results of the intervention in the study by Wallman *et al.* [12] and Deale *et al.* [25] should be interpreted in light of the fact that no intention-to-treat analysis was conducted. Both studies had an average methodological quality (53/100 on the Delphi score). Most studies gave no information addressing the treatment compliance.

The quality of this systematic review would have been superior if the articles were assessed by an independent jury. In this study, the quality of the articles was assessed by a researcher with a master of science degree in rehabilitation sciences. At the time of data analysis and quality assessment, the assessor was new in the area of CFS research and inexperienced as a clinician with CFS patients, implying that she could not have been biased by her personal view or ties with any of the authors of the published exercise therapy studies. Therefore, the assessor can also be regarded as independent.

## Conclusion

This literature study shows that, compared with a symptom-contingent approach, a time-contingent approach in the treatment of people with CFS offers more advantages with respect to improvements in fatigue and physical functioning. Still, four studies applying a symptom-contingent approach gave a positive effect on fatigue and physical functioning as well, suggesting that this approach is effective as well for patients with CFS. Exercise therapy for people with CFS

should comprise of 10–11 sessions spread over a time period of 4–5 months. In addition, people with CFS can perform home exercises five times a week with an initial duration of 5–15 min. The exercise duration can be gradually increased up to 30 min. The exercise intensity can be determined by using the individually derived target heart rate [(220 minus age) · 0.75]. Target heart rates can be used to avoid overexertion. Aerobic activity is the preferred exercise modality in the treatment of people with CFS. Walking is especially recommended, but swimming or cycling should also be encouraged. Furthermore, strength, balance, stretching and relaxation exercises can be added to the aerobic protocol, but as a stand-alone treatment, these interventions are not effective for people with CFS.

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