Guided graded exercise self-help as a treatment of fatigue in chronic fatigue syndrome

In *The Lancet*, Lucy Clark and colleagues show that, in the GETSET trial (n=211), patients with chronic fatigue syndrome who were treated with a 12 week guided graded exercise self-help programme in addition to ongoing specialist medical care had significantly lower mean fatigue score (reduction by 4·2 points [95% CI 2·3–6·1], p<0·0001; effect size 0·53) and higher self-reported physical function score (increase by 6·3 points [1·8–10·8], p=0·006; effect size 0·20) than did patients managed with specialist medical care alone. This pragmatic randomised controlled trial was done at two secondary-care centres in the UK, and its findings support the results of the previously reported PACE trial—ie, that graded exercise therapy is an effective treatment for chronic fatigue syndrome—although the GETSET trial involved much less intensive use of physiotherapists. In the GETSET trial, physiotherapists guided the patients through graded exercise using a self-help booklet, and face-to-face contact was minimal (maximum of one episode of face-to-face contact, and then up to three other appointments via telephone or Skype not lasting more than 90 min in total). The finding that graded exercise therapy is effective even when exercise is not being witnessed and directly guided by a physiotherapist is a substantial advance, since many patients with chronic fatigue syndrome and other functional impairment have difficulty getting to physiotherapy or do not have access to appropriately trained physiotherapists.

Following results of the PACE trial, advocacy groups questioned whether the same results would have been noted in patients defined by chronic fatigue syndrome criteria other than those used for the trial. In both the PACE trial and the GETSET trial, the investigators assessed each participant with three different diagnostic criteria and did sensitivity analyses showing that no differences were seen in the effect of graded exercise regardless of the definition of chronic fatigue syndrome used. Other sensitivity analyses in the GETSET trial showed that individuals with worse physical function scores at baseline, further supporting the finding that graded exercise is effective even in individuals with severe symptoms. However, some individuals with the most severe forms of chronic fatigue syndrome might have been unable to attend secondary-care clinics, which made them ineligible for participation in this trial, and the same could be said about participation in the PACE trial.

Partly because of these concerns raised after the initial publication of the PACE trial, the investigators of the GETSET trial also looked carefully for adverse effects of graded exercise treatment, since many patients were concerned that any type of exercise would lead to an exacerbation of their symptoms. In both the PACE trial and the GETSET trial, relatively few serious adverse events or reactions were reported. In the GETSET trial, non-serious adverse events were reported by 27 (28%) of 97 participants who received guided graded exercise self-help and by 23 (23%) of 102 patients who received specialist medical care only, with no significant differences between the two groups (χ²=0·67; p=0·41). No serious adverse reactions were reported. Only two participants actively withdrew from graded exercise treatment, suggesting that this treatment was well tolerated in most individuals.

Fatigue (measured by the updated Chalder fatigue questionnaire) is the symptom that improved the most in the GETSET trial, and similar findings have been noted in many previous studies that assessed this outcome in chronic fatigue syndrome or related conditions such as fibromyalgia, making graded exercise a cornerstone of treatment recommendations in these conditions. In fact, although one might argue that some alternative pharmacological and non-pharmacological therapies might yield similarly small improvements in physical function or mood to those noted in the GETSET trial, far fewer available alternative therapies have this magnitude of effect on fatigue. The results of the GETSET trial are consistent with other work on exercise as a treatment of fatigue in chronic fatigue syndrome and other related conditions such as fibromyalgia, in which exercise has also been used as a non-specific treatment since the cause of these conditions is not known.
entirely clear. Results from these studies also typically show that the effect size for fatigue is often similar or greater than the effect size seen for other domains such as function, pain, and mood. Thus, results of the GETSET trial add to the accumulating evidence that graded exercise (with or without cognitive behavioural therapy) should probably be considered the gold standard for treatment of fatigue in chronic fatigue syndrome and related conditions.²

Another concern of patient advocates regarding the PACE trial is that the overall results of the intervention were fairly modest, and thus it would be inappropriate to consider graded exercise as an effective treatment for chronic fatigue syndrome. This concern is valid, and the same can be said about the overall effects of the intervention in the GETSET trial. Only 17 (18%) of 97 participants who received graded exercise noted improvements (“much” or “very much better”) in overall health, compared with five (5%) in the control group, and only 14 (15%) patients who received graded exercise reported improvements in symptoms of chronic fatigue syndrome, compared with six (6%) in the control group.³ In the PACE trial,² 37 (25%) of 160 patients reported improvement in overall health after therapist-delivered graded exercise therapy at 12 week follow-up.²

In summary, findings from this pragmatic randomised controlled trial add to the evidence that straightforward, non-pharmacological therapies can be helpful in the management of symptoms such as fatigue in individuals with chronic fatigue syndrome. Many of these cognitive and behavioural therapies (of which guided graded exercise self-help is an example) can be very helpful to patients and will be used more frequently in routine clinical practice only when we abandon the notion that these therapies need to be administered through face-to-face contact with highly trained therapists.

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I declare no competing interests.

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5. Kindlon T. People want to learn as much as possible from the PACE trial for chronic fatigue syndrome. BMJ 2013; 347: f5731.


