

Commentary

Graded exercise therapy and cognitive behavior therapy do not improve employment outcomes in ME/CFS

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1. Introduction

In a 1989 article, Wessely et al. [1] proposed a model of the onset and perpetuation of chronic fatigue syndrome, the illness often called myalgic encephalomyelitis and now frequently referred to as ME/CFS. In this model, patients' symptoms were attributed to the effects of deconditioning following an acute illness. The symptoms were said to be perpetuated by patients' persistent but purportedly unwarranted conviction that they continued to suffer from a medical disease that was exacerbated by exertion. The proposed treatment strategy combined gradual increases in activity to reverse the presumed deconditioning with efforts to alter patients' supposedly misguided perceptions about their ailment.

ME/CFS has long been associated with marked disability and long-term sickness absences [2], with estimated rates of unemployment among patients ranging from 35% to 69% [3]. From the start, the promotion of behavioral and psychological rehabilitation has been intertwined with questions about whether ME/CFS patients with limited capacity to work should be able to receive some form of income or dis-

ability support. In a section on “sickness benefits” in the 1989 paper [1], the authors argued that decisions about social welfare payments should be linked to patients' willingness to undergo behavioral and psychological interventions. “It is reasonable to expect a patient to cooperate with treatment before being labelled as chronically disabled,” noted the authors, notwithstanding the theoretical and unproven status of their model.

This rehabilitative approach achieved dominance over the next couple of decades, not only in the UK but in the US and many other countries. Graded exercise therapy (GET) and an illness-specific form of cognitive behavior therapy (CBT) became the predominant and most heavily researched ME/CFS interventions and were enshrined in multiple clinical guidelines. A 2005 review of the natural history of the illness [4], which found that only 5% of patients fully recovered spontaneously, noted “increasing evidence” for GET and CBT and therefore advised that “medical retirement should be postponed until a trial of such treatment has been given.”

While many studies have included employment status as a demographic data point [2, 3], fewer have specifically examined the relationship between GET and CBT and employment-related outcomes. Nonetheless, the results from the latter group are consistent and clear: The interventions do not

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lead to improved outcomes in employment status [5–13].

This question has taken on renewed urgency given the overlaps between ME/CFS and the phenomenon known as long Covid, or more formally as post-acute sequelae of SARS CoV-2 (PASC). A significant proportion of patients with prolonged symptoms after a coronavirus infection appear to suffer from the same cluster of symptoms that characterize ME/CFS, including pronounced exhaustion, relapses after minimal exertion known as post-exertional malaise (PEM), cognitive impairments, and orthostatic intolerance, among others. Like ME/CFS patients, many of this new PASC cohort have found that they are unable to sustain their previous level of employment. While the similarities between the two conditions have been widely noted by clinicians and medical investigators, they have also led to efforts to promote the traditional ME/CFS rehabilitation paradigm for this large wave of post-viral patients.

2. Employment outcomes in the PACE trial

After gaining momentum during the 1990s and 2000s, the GET/CBT approach was significantly reinforced with the 2011 publication in the *Lancet* of the first results of the PACE trial, the largest study of the two interventions for ME/CFS [5]. Additional PACE results were published in 2012 and 2013 [6, 7]. The study was partially funded by the UK's Department for Work and Pensions (DWP). Officials at the agency presumably believed or hoped that the trial would provide robust data to support the use of these two strategies.

The PACE investigators presumably hoped for that as well; key members of the team maintained strong links with disability insurance companies, advising them that GET and CBT were effective in helping this group of challenging patients recover. In a 2002 essay for a UNUM Provident report on trends in disability [14], Michael Sharpe, a lead PACE investigator, wrote that “symptoms and disability” in patients with unexplained conditions “are shaped by psychological factors,” and in particular by “patients’ beliefs and fears.” He suggested that the promotion of biological disease models by ME/CFS patient advocates could impact health outcomes among insurance claimants.

Commenting on how public messaging and related “social factors” influenced the course of illness for these patients, Sharpe wrote: “*Relevant factors include the information patients receive about*

the symptoms and how to cope with them. This information may be helpful or may stress the chronicity of the illness and promote helplessness. Such unhelpful information is found in “self-help” (!) books and increasingly on the Internet (see for example: www.meassociation.org.uk)...Other social factors that perpetuate illness are anger with the person or organisation the illness is attributed to, or toward the insurer for not believing them.” In the article, Sharpe further argued that receiving financial benefits ultimately discouraged such claimants from getting better.

However, the data from PACE did not provide evidence that GET and CBT were effective in helping ME/CFS patients in the employment domain [6]. With 641 participants, PACE was the largest treatment trial for ME/CFS [5]. The investigators themselves referred to it as the “definitive” test of the two interventions [15]. In touting it as a success, they reported that around 60% had improved and 22% had recovered after treatment with GET and CBT, much more than in the other groups [5, 7]. However, these positive findings were all from subjective, self-reported measures. When such measures are paired with unblinded treatments, as in the PACE trial, they are subject to an unknown amount of bias.

PACE also included an employment measure as one of four objective outcomes, along with whether or not the participant was receiving social welfare or disability benefits, a step-test to assess fitness, and a six-minute-walking test. The results were uniformly poor. The first three measures produced null findings across the board, with no advantages conferred by the interventions [6, 7]; in the six-minute walking test, the GET group showed a statistically significant but clinically insignificant improvement [5]. In terms of employment, the percentage of participants in the GET group reporting lost days of work increased from 83% at baseline to 86% at 12 months after randomization; in the CBT group, the percentage was 84% both before and after treatment. In all study arms, the percentage of participants receiving unemployment or disability benefits was higher after treatment [6].

In promoting GET and CBT as effective, the PACE authors downplayed the findings on employment, receipt of disability or unemployment support, and other objective results, suggesting these should be ignored when determining whether patients had improved and recovered. In correspondence, they challenged the reliability and even the objectivity of the measures they themselves had pre-designated

as objective. As they wrote: “*Recovery from illness is a health status, not an economic one, and plenty of working people are unwell, while well people do not necessarily work. Some of our participants were either past the age of retirement or were not in paid employment when they fell ill. In addition, follow-up at 6 months after the end of therapy may be too short a period to affect either benefits or employment*” [16].

It is indisputable that other factors besides health status play a role in employment outcomes. Nonetheless, if the PACE trial’s reported results of significant improvement and recovery were accurate, then a measurable benefit from GET and CBT in employment and in the receipt of financial support would have been expected. As has been well-documented, the investigators weakened key subjective outcome measures in ways that dramatically improved their reported results; published re-analyses of trial data have found that no one achieved “recovery” from either of the therapies, and rates of improvement were so marginal that they were likely due to bias and expectation effects [17, 18]. Given these findings, the similarly disappointing results for employment outcomes in PACE should not be surprising.

3. Other studies on CBT/GET and employment outcomes

In a review of treatment studies that included employment outcomes, Vink and Vink-Niese [8] found that the standard interventions did not have an overall positive effect on work status. Besides PACE, among the studies reviewed were two other randomized trials and five observational studies based on data from clinical services. The two other trials, one in the Netherlands with 278 participants and one in England with 153, both investigated CBT and reported no statistically significant differences in employment outcomes between the intervention and control groups [9, 10]. The largest observational study included 952 patients seeking care at specialty clinics in England, although a great many did not provide post-treatment outcomes; among a subgroup of 394, 18% reported having returned to work or increased work hours, while 30% reported having stopped work or reduced work hours [11]. According to a Belgian report, a review of 655 patients attending domestic clinics found that “employment status decreased” when assessed after treatment while the percentage of those “living from a sickness allowance” rose from 54% to 57% [12].

Other observational research had similarly unpromising findings. In the most recent study, Stevelink et al. [13], of 508 patients who attended clinical services between 2007 and 2014, only 316 provided information about post-treatment employment status, among other measures. Of those, 9% had returned to work after not having worked at baseline. On the other hand, 6% had stopped working after having been working at baseline, leaving a net return-to-work after treatment of just 3%—a handful of people. Moreover, that figure is likely to be overstated, given the high loss-to-follow-up from the initial sample of 508. The drop-outs were more seriously ill at baseline, so they might be expected to have worse employment outcomes than those who ended up providing data at the final time point.

According to the authors, “unhelpful beliefs such as fear of activity and exercise and concerns about causing damage, combined with all or nothing behaviour and behavioural avoidance, were associated with not working” [13]. This statement is problematic because “fear of activity,” “concerns about causing damage” and related indications of caution should be considered reasonable and prudent perspectives, not “unhelpful beliefs,” among patients with the core ME/CFS symptom of PEM. Beyond that, the study itself documented little or no change after treatment in the domains of “fear-avoidance,” “catastrophizing,” “embarrassment avoidance,” “symptom focusing,” “all-or-nothing behaviour,” and “avoidance/resting behaviour,” even though such factors were “specifically targeted in CBT and, to some extent, GET.”

Moreover, the authors reported no change in subjective fatigue scores, and only a marginal increase in subjective physical function scores, with participants remaining seriously disabled even after treatment. Thus, although the authors noted correctly that “meaningful occupation is important for well-being and psychosocial needs,” their study documented that their approach failed to impact factors presumed to be essential to helping participants achieve that important goal. (Since Stevelink et al.’s senior author was one of the lead PACE investigators, it is unclear why the paper did not mention the null employment results from that “definitive” study.)

The theoretical illness model underlying all of these studies is essentially the one outlined by Wesely et al. more than three decades ago [1]. That illness model is at odds with the extensive physiological abnormalities that have been found in ME/CFS [17, 19]. Research findings have also undermined two core

assumptions of the model—specifically, that ME/CFS patients are deconditioned and have an unwarranted fear of activity or exercise [20–22]. In 2017, the US Centers for Disease Control and Prevention dropped its recommendations for GET and CBT as ME/CFS treatments. In 2021, the UK National Institute for Health and Care Excellence (NICE) reversed its earlier support for the interventions in new ME/CFS guidelines; in its analysis, NICE assessed the quality of the evidence supporting GET and CBT as either “very low” or merely “low” [23]. These developments are consistent with the failure of GET and CBT to lead to improved employment outcomes in PACE and other studies.

4. Conclusion

In a recent study of employment status among clinic attendees, Stevelink et al. [13] wrote that “work-related outcomes should be targeted” in treatment for ME/CFS. It is certain that people with ME/CFS experience disrupted occupational lives and that it would be desirable to identify treatments that could restore their full capacity for employment. However, the most common behavioral and psychological interventions—that is, GET and CBT—have already been tested sufficiently to reach a conclusive assessment that they do not lead overall to meaningful improvements in work status. These poor results are consistent across randomized trials, including the high-profile and “definitive” PACE study, as well as observational studies of patients seeking clinical services for their illness.

Some investigators and medical experts continue to promote GET and CBT as treatments for ME/CFS patients based on subjective findings from flawed studies. They also seek to extend these recommendations to patients with long Covid, or PASC, many of whom are receiving ME/CFS diagnoses and facing employment challenges. It is time to state the obvious: The objective data on work outcomes indicate that GET and CBT do not lead to readily apparent benefits in this domain. In consequence, they should no longer be recommended to ME/CFS patients as a strategy for achieving occupational rehabilitation and related benefits.

Ethical approval

Not applicable.

Informed consent

Not applicable.

Conflict of interest

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Not applicable.

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